Società Chimica Italiana
Divisione di Chimica Organica

Atti

del

XXXVIII Convegno Nazionale della Divisione di Chimica Organica

della

Società Chimica Italiana

CDCO

Milano, 9-13 Settembre 2018

UNIVERSITÀ DEGLI STUDI DI MILANO

UNIVERSITÀ DEGLI STUDI DI MILANO BICOCCA

FEDERCHIMICA CONFINDUSTRIA

ASSOLOMBARDA

www.cdco2018.it – cdco2018 – facebook.com/cdco2018 – segreteria.cdco2018@unimi.it

Indice

Comitato Scientifico

Gianluca Farinola (chairman)
Università di Bari
gianlucamaria.farinola@uniba.it

Roberto Ballini
Università di Camerino
roberto.ballini@unicam.it

Anna Bernardi
Università degli Studi di Milano
anna.bernardi@unimi.it

Maria Valeria D'Auria
Università di Napoli Federico II
mariavaleria.dauria@unina.it

Marco Lucarini
Università di Bologna
marco.lucarini@unibo.it

Alessandro Mordini
ICCOM - CNR Firenze
alessandro.mordini@iccom.cnr.it

Gabriele Razzetti
DiPharma Francis S.r.l. – Milano
gabriele.razzetti@dipharma.com

Andrea Pace
Università degli Studi di Palermo
andrea.pace@unipa.it

Claudio Villani
Università di Roma Sapienza
claudio.villani@uniroma1.it

In aggiunta, per la sessione di lunedi mattina presso la sede Assolombarda di via Pantano:

Aaron Tagliabue
Vice Presidente del Gruppo Chimici, Assolombarda
aaron.tagliabue@roadmaster.it

Giovanni Floridi
Group Research Director, Lamberti S.p.A. - Chemical Specialties, Federchimica
giovanni.floridi@lamberti.com

Comitato Organizzatore

Cesare Gennari
Università degli Studi di Milano
cesare.gennari@unimi.it

Francesco Nicotra
Università degli Studi di Milano-Bicocca
francesco.nicotra@unimib.it

Emanuela Licandro
Università degli Studi di Milano
emanuela.licandro@unimi.it

Alessandro Abbotto
Università degli Studi di Milano-Bicocca
alessandro.abbotto@unimib.it

Maurizio Benaglia
Università degli Studi di Milano
maurizio.benaglia@unimi.it

Francesco Peri
Università degli Studi di Milano-Bicocca
francesco.peri@unimib.it

Giorgio Abbiati
Università degli Studi di Milano
giorgio.abbiati@unimi.it

Laura Cipolla
Università degli Studi di Milano-Bicocca
laura.cipolla@unimib.it

Luca Beverina
Università degli Studi di Milano-Bicocca
luca.beverina@unimib.it

Barbara La Ferla
Università degli Studi di Milano-Bicocca
barbara.laferla@unimib.it

Sara Pellegrino
Università degli Studi di Milano
sara.pellegrino@unimi.it

Sergio Rossi
Università degli Studi di Milano
sergio.rossi@unimi.it

Silvia Cauteruccio
Università degli Studi di Milano
silvia.cauteruccio@unimi.it

Luca Zoia
Università degli Studi di Milano-Bicocca
luca.zoia@unimib.it

Benvenuto

Benvenuti al XXXVIII Convegno Nazionale della Divisione di Chimica Organica. Ad ospitare il nostro evento annuale per il 2018 è la città di Milano, e lo farà secondo la sua rinomata dinamicità accogliendoci in entrambe le Università che, con le loro molteplici attività scientifiche e didattiche, tanto contribuiscono alla vita della Chimica Organica italiana: l'Università degli Studi di Milano presso la sua sede storica, la rinascimentale Ca' Granda, nel cuore del centro cittadino, e le moderne strutture dell'Università di Milano-Bicocca.

La novità della cornice logistica riflette lo spirito che anima l'organizzazione di questa edizione del Convegno, all'insegna della **pluralità** e della **vivacità** della Chimica Organica Italiana.

Il Consiglio Direttivo della nostra Divisione insieme al Comitato Organizzatore locale composto da Soci dei due Atenei milanesi offrirà un programma intenso ed interessante nel quale troveranno spazio, accanto alle voci della **ricerca accademica** italiana nella nostra disciplina, quelle dei chimici organici che operano negli **enti di ricerca**, nelle **industrie**, particolarmente floride in questo territorio, nell'**imprenditoria**, nelle **professioni** e nell'**insegnamento**. Anche quest'anno celebreremo le eccellenze con le **medaglie** ed i **premi** della Divisione di Chimica Organica, ed inviteremo prestigiosi speakers sulle tematiche d'avanguardia.

Soprattutto, stimoleremo i contributi dei nostri Soci più giovani, dei quali la Divisione supporterà la partecipazione con numerose **borse di studio**. Il Convegno sarà anche un momento importante di **confronto** e di **discussione**, a cui in questa edizione dedicheremo uno spazio particolarmente ampio nella Assemblea dei Soci.

Non mancheranno, infine, gli eventi sociali che ci permetteranno di stare insieme in alcuni sorprendenti luoghi di questa bellissima città.

Il Convegno CDCO Milano 2018, è un'occasione importante per gli scambi scientifici e professionali ed un momento privilegiato per rafforzare i legami della nostra Comunità e contribuire alla sua crescita ed al suo rinnovamento.

Un caro saluto a tutti, e benvenuti a Milano.

Presidente della Divisione
di Chimica Organica

MEDAGLIE e PREMI

MEDAGLIE

Medaglia d'oro *Angelo Mangini:*

Paolo Scrimin - *Università di Padova*

Per le sue ricerche di frontiera sulla progettazione e realizzazione di architetture supramolecolari auto-organizzate in grado di svolgere processi cooperativi di riconoscimento e catalisi. i suoi studi pionieristici hanno contribuito in modo determinante ad estendere gli strumenti concettuali propri della chimica fisica organica alla costruzione e controllo di un'ampia varietà di sistemi funzionali alla nanoscala.

Medaglia d'oro *Adolfo Quilico:*

Graziano Guella - *Università di Trento*

Per l'originalità e la varietà dei suoi contributi alla chimica dei composti organici naturali marini e terrestri di rilevanza biologica, ecologica e chemotassonomica, e per lo sviluppo di approcci metodologici rigorosi e innovativi con interessanti applicazioni alle scienze "omiche" e allo studio di processi biologici complessi.

Medaglia d'argento *Giacomo Ciamician:*

Fabio Parmeggiani - *University of Manchester*

Per i suoi contributi originali alla produzione e utilizzo di nuovi catalizzatori biologici per la sintesi stereoselettiva di molecole organiche chirali, con l'ottimizzazione di procedure multi-enzimatiche e chemo-enzimatiche a cascata ad alta produttività e ridotto impatto ambientale.

PREMI ALLA RICERCA

Premio alla ricerca Chimica Organica per l'Ambiente, l'Energia e le Nanoscienze (Senior):
Giancarlo Cravotto - *Università di Torino*
Per l'innovatività e l'ampiezza delle sue ricerche volte allo sviluppo di processi sintetici non convenzionali a ridotto impatto ambientale di grande interesse industriale, a partire da materie prime naturali ed a basso costo.

Premio alla ricerca Chimica Organica per l'Ambiente, l'Energia e le Nanoscienze (Junior):
Francesca Arcudi - *Università di Trieste*
Per i suoi studi innovativi sulla progettazione razionale, la sintesi e la caratterizzazione di nanodots di carbonio con peculiari proprietà fotofisiche ed elettrochimiche.

Premio alla ricerca Chimica Organica nei suoi Aspetti Metodologici (Senior):
Maurizio Fagnoni - *Università di Pavia*
Per l'alto interesse dei suoi studi sulla generazione indotta da luce di intermedi reattivi ed il loro utilizzo in processi sintetici eco-sostenibili.

Premio alla ricerca Chimica Organica nei suoi Aspetti Metodologici (Junior):
Gianpiero Cera - *Università di Parma*
Per i suoi importanti contributi allo sviluppo e all'applicazione di catalizzatori metallici innovativi e versatili per la sintesi e derivatizzazione di sistemi eteroaromatici.

Premio alla ricerca Chimica Organica per le Scienze della Vita (Senior):
Antonio Molinaro - *Università di Napoli Federico II*
Per l'originalità e l'ampio impatto scientifico dei suoi studi relativi alla decodificazione chimica e biologica di glicoconiugati di origine batterica.

Premio alla ricerca Chimica Organica per le Scienze della Vita (Junior):
Alex Manicardi - *University of Ghent*
Per i suoi importanti contributi alla realizzazione di sistemi polifunzionali basati su acidi peptidonucleici in grado di condurre reazioni mirate su specifiche sequenze di DNA e RNA di grande rilevanza biologica.

Premio alla ricerca Chimica Organica per lo Sviluppo di Processi e Prodotti nell'Industria (Senior):
Pietro Allegrini – *Indena*
Per la varietà e l'importanza dei suoi contributi alla progettazione e sviluppo di processi chimici industriali rivolti alla sintesi di prodotti farmaceutici e per la valorizzazione industriale di prodotti naturali di origine vegetale.

Premio alla ricerca Chimica Organica per lo Sviluppo di Processi e Prodotti nell'Industria (Junior):

Giuseppe Marzano - *Dipharma*

Per i suoi originali contributi allo sviluppo di strategie di sintesi aventi potenziali ricadute nella definizione di processi industriali innovativi.

PREMI DI DOTTORATO

Premio Tesi di Dottorato Chimica Organica per l'Ambiente, l'Energia e le Nanoscienze:
Ilaria Monaco - *Università di Bologna*
Per i suoi originali studi sulla funzionalizzazione di nanostrutture metalliche.

Premio Tesi di Dottorato Chimica Organica per le Scienze della Vita:
Michela Zuffo - *Università di Pavia*
Per i suoi interessanti risultati sullo sviluppo di sistemi in grado di riconoscere specifiche strutture G-quadruplex.

Premio Tesi di Dottorato Chimica Organica nei suoi Aspetti Metodologici:
Davide Brenna - *Università di Milano*
Per i suoi interessanti studi su metodologie ecosostenibili per la preparazione di molecole chirali altamente funzionalizzate.

PROGRAMMA SCIENTIFICO

Domenica 9 Settembre
(Presso Aula Magna, Università degli Studi di Milano, via Festa del Perdono, 7)

14.30-15.00 Opening Saluti e Premiazioni

Chairman: Prof. Maurizio Taddei

15.00-15.30 **M1** Medaglia MANGINI
Scrimin P. *Cooperativity between molecules: a life journey*

Chairman: Prof. Raffaele Riccio

15.30-16.00 **M2** Medaglia QUILICO
Guella G. *Learning Chemistry from Nature*

16.00-16.30 **PS1** Premio Chimica Organica per l'Ambiente, l'Energia e le Nanoscienze:
Cravotto G. *Organic Chemistry: a true ally of Energy, the Environment and Nanosciences*

16.30-17.00 Coffee Break

Chairman: Prof.ssa Valeria Conte

17.00-17.30 **PS2** Premio Chimica Organica nei suoi aspetti Metodologici:
Fagnoni M. *Eco-friendly (solar) light induced generation and application of reactive intermediates in synthesis*

17.30-18.00 **KN1 Brimble M.** *Nature's Medicine Chest: Opportunities for Synthesis and Drug Discovery*

18.00-18.30 **KN2 Hayashi Y.** *Diphenylprolinol Silyl Ether in the Pot Synthesis of Biologically Active Molecules*

Lunedì 10 Settembre – Mattino

(Presso Assolombarda auditorium - Via Pantano, 9)

9.00-9.15	Apertura dei lavori **Bonomi C.** Presidente Assolombarda **Agostiano A.** Presidente Società Chimica italiana
9.15-9.45	**Squinzi M.** Direttore Ricerca e Sviluppo Mapei, Consiglio di Presidenza Federchimica *Fare impresa nella chimica*
9.45-10.00	**Bellato R.** Presidente Gruppo Chimici e Green Economy Network Assolombarda *L'industria chimica e farmaceutica nel Paese: dimensione economica, sociale e ambientale*
10.00-11.00	**Donati D.** Direttore del Dipartimento di Chimica Medicinale, Nerviano Medical Sciences Srl **Negrisoli G P.** Presidente e Amministratore Delegato, Flamma Spa **Valentini T D.** Manager Waste Planning & Logistics, Syndial Spa *Modelli e pratiche di collaborazione università-impresa su ricerca e didattica*
11.00-11.15	Coffee Break
11.15-12.15	**Ventura A.** Direttore Risorse Umane, Indena Spa *La ricerca e l'innovazione che passa dai giovani* *Testimonianze di start-up*
12.15-12.30	**Farinola G.** Presidente Divisione Chimica Organica – Società Chimica Italiana Chiusura dei lavori

Lunedì 10 Settembre – Pomeriggio

(Presso Università degli Studi di Milano, via Festa del Perdono, 7)

12.30-14.00 Pranzo Buffet - Catering Porticato San Nazzaro

13.00-15.00 **Sessione POSTER A** - Porticato Largo Richini

Sessione parallela #1 (aula 208)

Chairman: Prof. Giuseppe Musumarra

15.00-15.20 **OC1 Paolino M.** *Imidazole-Reactive Molecules for the Functionalization of Poly-Histidine Leading to Fishbone-Like Architectures*

15.20-15.40 **OC2 Casertano M.** *The thiazinoquinone scaffold as chemical starting point for the design and synthesis of antiparasitic drugs*

15.40-16.00 **OC3 De Marco R.** *c[RGDfK] and MPUPA-LDV-diamine for the functionalization the 3th generation of devices for diagnosis of several disease*

16.00-16.20 **OC4 Goracci L.** *A structure-activity relationship study on the α-Chymotrypsin superactivation by quaternary ammonium salts*

16.20-16.40 **OC5 Terracciano S.** *Identification of the first selective BAG3 modulators: a turning point toward the development of new anticancer drugs*

Sessione parallela #2 (aula 302)

Chairman: Prof.ssa Olga Bortolini

15.00-15.20 **OC6 Pezzella A.** *Eumelanins exploitation in bioelectronics: perspectives and challenges*

15.20-15.40 **OC7 Manini P.** *Synthetic Allomelanins from 1,8-Dihydroxynaphthalene: Toward Innovative Biocompatible Functional Materials*

15.40-16.00 **OC8 Della Sala P.** *Chemically modified cycloparaphenylenes with novel optoelectronic and supramolecular properties*

16.00-16.20 **OC9 Gatti T**. *Decorating carbon nanostructures with organics for advanced energy materials*

16.20-16.40 **OC10 Barbera V.** *Tailor made functionalizations of graphene layers and their application as carbocatalyst for organic reaction*

16.40-17.10 Coffee Break

Sessione parallela #3 (aula 208)

Chairman: Prof. Fabrizio Mancin

17.10-17.30 **OC11 Ciceri S.** *Biocatalytic Approach to the Synthesis of Pharmacologically Active Compounds*

17.30-17.50 **OC12 Palumbo Piccionello A**. *Novel Curcumin-like derivatives can modulate toxic Tau Oligomers*

17.50-18.10 **OC13 Fiammengo R.** *Selective targeting of αVβ3 integrins with gold nanoparticles carrying RGD-semipeptides*

18.10-18.30 **OC14 Di Mauro G.** *Design of new selective VEGFR-2 Tyrosine kinase and COX-1 inhibitors for the inhibition of angiogenesis*

18.30-18.50 **OC15 Pina A.** *Synthesis and biological evaluation of new RGD-drug conjugates for tumor targeting via αvβ3 integrin*

18.50-19.10 **OC16 Massa A.** *Synthesis of 2-acylbenzonitriles and their reactivity in tandem reactions: easy access to isoindolinones with a tetrasubstituted stereocenter*

Sessione parallela #4 (aula 302)

Chairman: Prof. Marco D'Ischia

17.10-17.30 **OC17 Riva S.** *Blue enzymes for green chemistry: Laccases-catalyzed dimerization of substituted phenols*

17.30-17.50 **OC18 Gardossi L.** *Targeted surface functionalization of poly(lactic acid) and lignocellulosic materials using laccases and cutinases: taking inspiration from nature*

17.50-18.10 **OC19 Carlone A.** *Organocatalysis and Molecular Machines: the Development of an Autonomous Chemically Fuelled Small Molecule Motor*

18.10-18.30 **OC20 Sabuzi F.** *Understanding KuQuinones Equilibria in Solution*

18.30-18.50 **OC21 Fin A.** *From fluorescent nucleosides to emissive cofactors*

18.50-19.10 **OC22 Rizzo F.** *Novel highly fluorescent water soluble spirobifluorene-based dye and its bio-applications*

Martedì 11 Settembre

(Presso Università di Milano-Bicocca, Piazza della Scienza, edifici U3 e U4)

Sessione parallela #5 (aula U4-08, piano -1)

Chairman: Prof.ssa Dörthe Mellmann

9.00-9.30 **KN3 (CPSE Lecture) Destri S.** *Semiconducting polymers; from free standing insoluble materials to water processed nanoparticles.*

9.30-9.50 **OC23 Boldrini C. L.** *Organic sensitizers for dye-sensitized water splitting*

9.50-10.10 **OC24 Calamante M.** *New D-π-A conjugates compounds for H2 production by photoreforming of sacrificial electron donors (SEDs)*

10.10-10.30 **OC25 Grisorio R.** *Efficient Hole Transport Materials with Sulphur-Functional Groups Facilitating Hole Transfer in Perovskite Solar Cells*

Sessione parallela #6 (aula U3-02, piano -1)

Chairman: Prof. Bartolo Gabriele

9.00-9.30 **PJ2** Premio Chimica Organica per lo sviluppo di processi e prodotti nell'industria (junior):
Marzano G. *Moving From Lab to Fab: the Role of Synthetic Organic Chemists*

9.30-9.50 **OC26 Caruana L.** *Process Development of Enclomiphene Citrate: process chemistry remarks, solid state characterization and IP aspects*

9.50-10.10 **OC27 Mantegazza S.** *Old fashioned Mathews' reaction for a new synthesis of Apremilast*

10.10-10.30 **OC28 Roletto J.** *Pirfenidone: process development and industrial scale up*

10.30-11.00 Coffee Break Galleria della Scienza (piano -1)

11.00-13.00 **Assemblea Soci** (Aula U4-08)

13.00-14.00 Pranzo Libero (seguire suggerimenti su mappe sito web)

14.00-15.00 **Sessione POSTER B** Galleria della Scienza (piano -1)

Sessione parallela #7 (aula U4-08, piano -1)

Chairman: Prof. Stefano Maiorana

15.00-15.30 **PJ3** Premio Chimica Organica per le Scienze della Vita (junior) **Manicardi A.** *Peptide Nucleic Acids (PNAs): a simple tunable scaffold with limitless potentialities*

15.30-15.50 **C29 Sansone F.** *Ammonium containing calixarenes as vectors for peptide nucleic acid (PNA) delivery*

15.50-16.10 **OC30 Lupidi G.** *New Sustainable Strategies for the Synthesis of Biologically Active Polyfunctionalized Heterocycles*

16.10-16.30 **OC31 Pace V.** *Building-up molecular complexity with carbenoids: new vistas in homologation chemistry*

Sessione parallela #8 (aula U3-02, piano -1)

Chairman: Prof.ssa Cinzia Chiappe

15.00-15.30 **PJ4** Premio Chimica Organica nei suoi aspetti metodologici (junior):
Cera G. *Late and Base-Transition Metals-Catalyzed C–H Functionalization with Alkynes*

15.30-15.50 **OC32 Senaldi L.** *An improved process for the preparation of Lenvatinib mesylate*

15.50-16.10 **OC33 Lanzalunga O.** *Hydrogen Atom Transfer Processes Promoted by Short-Lived N-oxyl Radicals: Structural and Medium Effect on the Reactivity and Selectivity*

16.10-16.30 **OC34 Valgimigli L.** *Explaining the chemopreventive antioxidant activity of nitroxides: the unexplored reductive catalytic cycle with superoxide in aprotic media*

16.30-17.00 Coffee Break Galleria della Scienza (piano -1)

Sessione parallela #9 (aula U4-08, piano -1)

Chairman: Prof. Enrico Marcantoni

17.00-17.20 **OC35 Zappimbulso N.** *Solvent-Free Pd-Catalyzed Heteroaryl-Aryl Coupling Reactions via C−H Bond Activation*

17.20-17.40 **OC36 Calabrese C.** *Supported Imidazolium Functionalized POSS Hybrids as Palladium Platform for C-C Cross-Couplings*

17.40-18.00 **OC37 Mancuso R**. *Regio- and Stereoselective Synthesis of (Z)-2-(2-Oxopyrrolidin-3-ylidene)acetates by Pd-Catalyzed Carbonylation of N-substituted-3-yn-1-amines*

18.00-18.20 **OC38 Perna F.** *Metal-catalyzed and Metal-mediated Organic Reactions in Deep Eutectic Solvents and in Water*

18.20-18.40 **OC39 Lessi M.** *Cross-Dehydrogenative-Couplings of Azoles*

Sessione parallela #10 (aula U3-02, piano -1)

Chairman: Prof. Alberto Brandi

17.00-17.20 **OC40 Bietti M**. *Site-selective and product chemoselective hydrogen atom transfer based aliphatic C–H bond functionalization*

17.20-17.40 **OC41 Olivo G.** *Selective, Remote C-H Oxidation guided by Supramolecular Recognition*

17.40-18.00 **OC42 Baschieri A.** *Reducing ability of hydroperoxyl radical (HOO•)*

18.00-18.20 **OC43 Salamone M.** *Hydrogen Atom Transfer from Amino Acid C–H Bonds. Structural and Medium Effects on Reactivity and Site-Selectivity*

18.20-18.40 **OC44 Martin T.** *Hydrogen Atom Transfer based aliphatic C–H bond functionalization. A kinetic evaluation of the role of electronic and torsional effects*

Dalle 19.00

Tour guidati visita piazza Gae Aulenti (partenze presso Libreria Feltrinelli, p.zza Gae Aulenti, ogni 30 minuti tra le 19.00 e le 20.30).

Mercoledì 12 Settembre

(Presso Università di Milano-Bicocca, Piazza della Scienza, edifici U3 e U4)

Sessione parallela #11 (aula U4-08, piano -1)

Chairman: Prof. Guido Viscardi

9.00-9.30 **KN4 Po R.** *Organic solar cells: the path to the industrialization*

9.30-9.50 **OC45 Parenti F.** *Thiophene based A-D-A small molecules with a dithienosilole core: synthesis, theoretical calculations and optoelectronic properties*

9.50-10.10 **OC46 Pomarico G.** *Electronic communication in Ni-tetraferrocenylporphyrin*

10.10-10.30 **OC47 Nitti A.** *Direct Arylation – Cross Aldol Condensation Cascade Reactions as Tools for the Sustainable and Scalable Synthesis of Organic Electronic Materials*

Sessione parallela #12 (aula U3-02, piano -1)

Chairman: Dott. Samuele Staderini

9.00-9.30 **KN5 (gruppo Giovani) Leonori D.** *Photoinduced Formation of C–N Bonds*

9.30-9.50 **OC48 Martinelli J.** *New phenolate-containing AAZTA-ligands for MRI and PET applications*

9.50-10.10 **OC49 Rosa-Gastaldo D.** *Monolayer-Coated Gold Nanoparticles as a Multimodal Probe for 19F-NMR Detection and Imaging*

10.10-10.30 **OC50 D'Andrea L. D.** *Chemical Synthesis of a mirror image protein by native chemical ligatio*

Sessione parallela #13 (aula U3-10, piano terra)

Chairman: Prof. Francesco De Angelis

9.00-9.30 **KN6 Novara F. R.** *Dealing with Scientific Misconduct - A Part of an Editor's Day-to-Day*

9.30-9.50 **OC51 Albano G.** *Outstanding chiroptical features in thin films of new chiral π-conjugated oligomers*

9.50-10.10 **OC52 Mancinelli M.** *Xanthines having chiral axes: Conformational Analysis and Absolute Configuration*

10.10-10.30 **OC53 Tiecco M.** *Novel Chiral Deep Eutectic Solvents as chiral reaction media*

10.30-11.00 Coffee Break Galleria della Scienza (piano -1)

Sessione parallela #14 (aula U4-08, piano -1)

Chairman: Prof. Fabio Bellina

11.00-11.20 **OC54 Fiorani G.** *Dialkyl Carbonates for the Upgrade of Renewable Alcohols*

11.20-11.40 **OC55 Porcheddu A.** *Mech@nochemistry: a Disruptive Innovation*

11.40-12.00 **OC56 Orlandi M.** *Mechanistic Investigations of the Pd(0)-Catalyzed Enantioselective 1,1-Diarylation of Benzyl Acrylates*

12.00-12.20 **OC57 Algieri V.** *Metal Catalysts in Non-Conventional Solvents as Efficient Recyclable Systems for 1,3-Dipolar Cycloaddition Reactions of Azides*

12.20-12.40 **OC58 Calcio Gaudino E.** *Highly Efficient Microwave-Assisted Synthetic Protocols in the Presence of Recyclable Pd/β-Cyclodextrin Cross-Linked Catalyst*

12.40-13.00 **OC59 Basso A.** *Photoinduced and Photocatalyzed Multicomponent Reactions*

Sessione parallela #15 (aula U3-02, piano -1)

Chairman: Prof. Luciano Mayol

11.00-11.20 **OC60 Cacioppo M.** *Tailoring Carbon Nanodots*

11.20-11.40 **OC61 Blangetti M.** *Carborane-BODIPY Dyads: New Photoluminescent Materials Through an Efficient Heck Coupling approach*

11.40-12.00 **OC62 Rossi B.** *Synthesis and anti-bacterial activity of a library of 1,2-benzisothiazol-3(2H)-one (BIT) derivatives amenable of crosslinking to Polysaccharides*

12.00-12.20 **OC63 Locatelli E.** *One-step esterification of nanocellulose in Brønsted acid Ionic Liquid for drug delivery application*

12.20-12.40 **OC64 Alfei S.** *Not PAMAM Dendrimer Nanodispersions and Pectine Microdispersion: two biocompatible approaches to increase Ellagic Acid water solubility and allow its more ways therapeutic administration*

12.40-13.00 **OC65 Guaragna A.** *Synthesis of N-Alkylated l-Iminosugars and their Therapeutic Application in Cystic Fibrosis Lung Disease*

Sessione parallela #16 (aula U3-10, piano terra)

Chairman: Prof.ssa Cristina Nativi

11.00-11.20 **OC66 Piemontese L.** *Deep Eutectic Solvents as effective media for the synthesis of Donepezil structure-based hybrids with metal-chelating properties*

11.20-11.40 **OC67 Guazzelli L.** *Synthesis of new bio-based ionic liquids and their use in the dissolution and modification of cellulose*

11.40-12.00 **OC68 Lange H.** *Carbenes and nascent hydrogen for reductive derivatisation of technical lignins*

12.00-12.20 **OC69 Puglisi A.** *Supported chiral organocatalysts for stereoselective reductions in batch and in flow*

12.20-12.40 **OC70 Dell'Amico L.** *Microfluidic Photoreactor Enables 2-Methyl-benzophenone Light-Driven Reactions with Superior Performance*

12.40-13.00 **OC71 Di Stefano S.** *Controlling the Motions of Acid-base Operated Molecular Machines*

13.00-14.30 Pranzo Libero (seguire suggerimenti su mappe sito web)

Sessione parallela #17 (aula U4-08, piano -1)

Chairman: Prof. Lucio Pellacani

14.30-14.50 **PD1** Premio Tesi di Dottorato per l'Ambiente, l'Energia e le Nanoscienze **Monaco I.** *Design, synthesis and characterizations of hybrid nanosystems: nanomedicine applications in theranostics*

14.50-15.10 **OC72 Christodolou M. S.** *Intramolecular transition-metals catalyzed hydroarylation processes for the synthesis of pyranoquinolines*

15.10-15.30 **OC73 Fini F.** *Oxidative Alkoxycarbonylation of Alkynes and Olefins Catalyzed by Aryl α-Diimine Palladium(II) Complexes*

15.30-15.50 **OC74 Lenci E.** *Accessing new areas of the chemical space by using acetal chemistry*

15.50-16.10 **OC75 Pirovano V.** *[Copper(I)(Pyridine-Containing Ligand)] Catalyzed Regio- and Steroselective Synthesis of 2-Vinylcyclopropa[b]indolines from 2-Vinylindoles*

16.10-16.30 **Premio Poster ChemPubSoc Europe**

Sessione parallela #18 (aula U3-02, piano -1)

Chairman: Prof.ssa Cristina Prandi

14.30-14.50 **PD2** Premio Tesi di Dottorato per le Scienze della vita: **Zuffo M.** *Targeting of specific G-quadruplex structures: small molecule based strategies*

14.50-15.10 **OC76 Metrangolo P.** *Halogenation controls structures and functions of supramolecular peptide assemblies*

15.10-15.30 **OC77 Esposito G.** *Combined LC-MS/MS and Molecular Networking approach for an early detection of cyanotoxins*

15.30-15.50 **OC78 Nocera P.** *Phytotoxins produced by two species of pathogenic Ascochyta, fungi responsible for legume diseases*

15.50-16.10 **OC79 Tedeschi T.** *Major Allergens in Cow Milk's whey: Study of the Effects of the Technological Treatments through the Identification and Synthesis of the Lactosylated Epitopes*

16.10-16.30 **Premio Poster Gruppo Interdivisionale DCC**

Sessione parallela #19 (aula U3-10, piano terra)

Chairman: Prof.ssa Egle Beccalli

14.30-14.50 **PD3** Premio Tesi di Dottorato per la Chimica Organica nei suoi aspetti metodologici:
Brenna D. *Sustainable preparation of Active Pharmaceutical Ingredients (API) in batch & flow mode, and Iron catalyzed transformations*

14.50-15.10 **OC80 Floresta G.** *Cucurbit[7]uril as a supramolecular macrocycle for microwave assisted synthesis of 2-methyl-3,5-diarylisoxazolidines in water*

15.10-15.30 **OC81 Massolo E.** *NO_2 reduction and amide bond formation in a one pot-two step procedure*

15.30-15.50 **OC82 D'Errico S.** *cADPR Analagues as Probes for the Cellular Ca2+ Ions Signaling*

15.50-16.10 **OC83 Salerno T. M. G.** *Curcumin from nature to laboratory: new ways to improve its properties*

16.10-16.30 **OC84 Bencivenni G**. *Enantioselective Synthesis of Alkylidene Cyclohexanes Displaying Axial Chirality via Knoevenagel Condensation*

16.30-16.40. Foto di gruppo

16.40-17.10 Coffee Break Galleria della Scienza (piano -1)

Dalle 18.30

Visita guidata riservata al Museo Nazionale della Scienza e della Tecnologia "Leonardo da Vinci" (MUST), via San Vittore 21, Milano (M2 Verde fermata *S. Ambrogio*; vedi mappe dettagliate su sito web); durata della visita 1 ora; partenze ogni 10-15 minuti a partire dalle 18.30, al completamento del gruppo; ***ultima partenza alle 19.30***

Al termine della visita in coincidenza dell'arrivo dei gruppi:
Aperitivo Buffet, punto di arrivo della visita, sala adiacente alla cena sociale.

20.30

Cena Sociale

Museo Nazionale della Scienza e della Tecnologia "Leonardo da Vinci" *(MUST).*
Ingresso diretto (se non si proviene dalla visita guidata) da Via Olona 6 bis, aperto dalle 19.30. L'ingresso di Via san Vittore, 21 viene chiuso alle 19.30.
Padiglione Aeronavale, Livello 0, Spazio Polene

Giovedì 13 Settembre

(Presso Aula Magna, Edificio U6, Università di Milano-Bicocca, Piazza dell'Ateneo Nuovo,1)

(ACCESSO TRAMITE INGRESSO RISERVATO AL CONGRESSO CONSENTITO SOLO CON BADGE; SEGUIRE LE INDICAZIONI SUL LUOGO E SULLE MAPPE DEL SITO WEB; NON UTILIZZARE L'INGRESSO PRINCIPALE)

Chairman: Prof. Domenico Misiti

9.00-9.30 **M3** Medaglia CIAMICIAN
Parmeggiani F. *Biocatalysis hand in hand with organic synthesis: developing new tools for the synthetic chemist*

Chairman: Dott. Sergio Riva

9.30-10.00 **PS3** Premio Chimica Organica per le Scienze della Vita (senior):
Molinaro A. *Chemical structure of microbial glycoconjugates and their role in the elicitation/suppression of eukaryotic innate immunity*

Chairman: Prof. Luigi Campanella

10.00-10.30 **KN7 Knauf R.** (Reach) (Gruppo Senior lecture) *10 anni di Regolamento REACH - uno stimolo o un ostacolo per l'innovazione?*

10.30-11.00 Coffee Break (Adiacente Aula Magna)

11.00-13.00 (aula U6-24, piano 1) ***Assemblea Generale Gruppo Senior***

Chairman: Prof. Francesco Sannicolò

11.00-11.30 **PS4** Premio Chimica Organica per lo sviluppo dei Processi e Prodotti nell'Industria (senior): **Allegrini P.** *Tecnica e Rito (Technology and Rite): the industrial research carrier as an attempt to clarify this ambiguous dualism*

Chairman: Prof.ssa Elena Lenci

11.30-12.00 **KN8** (Divulgazione) **Mautino B.** *È lo scientifichese, bellezza*

Chairman: Dott.ssa Sara Tortorella

12.00-12.30 **KN9** (Divulgazione) **Cecchi Paone A.** *L'equivoco del biologico*

12.30-13.00 Conclusione lavori

Lectures MEDAGLIE

M01

Cooperativity between molecules: a life journey

P. Scrimin

University of Padova, Department of Chemical Sciences, via Marzolo, 1 – 35131 Padova
e-mail*: paolo.scrimin@unipd.it*

Conventional chemistry studies the interactions between molecules as single, isolated entities. However, if we have a look at what happens in the biological world (where chemistry was first developed) we discover that this is rarely the case: molecules interact in a concerted fashion and often as multiple entities. In a word: they operate cooperatively. Think for instance to a cell. Starting from its membrane, composed by clusters of lipids with embedded proteins, going through the cellular enzymes with clusters of functional groups in their catalytic sites, and ending with the nucleus with the genetic information, cooperativity is the norm.

During my talk, I will share with the audience what I have learned during almost 40 years of research studying molecules that operate cooperatively: from micelles and vesicles, to supramolecular complexes, and nanoparticles. As often happens also between human beings, in many cases 1+1 makes much more than 2. The stages of this journey are highlighted in the review articles reported below.[1-6]

References:

[1] P. Scrimin, P. Tecilla, *Curr. Opin. Chem. Biol*. **1999**, *3*, 730-736.
[2] L. J. Prins, P. Scrimin, *Angew. Chem. Int. Ed*. **2009**, *48*, 2288-2306.
[3] F. Mancin, P. Scrimin, P. Tecilla, U. Tonellato, *Coord. Chem. Rev*. **2009**, *253*, 2150-2165.
[4] L. J. Prins, F. Mancin, P. Scrimin, *Curr. Org. Chem*. **2009**, *13*, 1050-1064.
[5] F. Mancin, L. J. Prins, P. Scrimin, *Curr. Opin. Colloid Interface Science* **2013**, *18*, 61–69.
[6] F. Mancin, L. J. Prins, P. Pengo, L. Pasquato, P. Tecilla, P. Scrimin, *Molecules* **2016**, *21*, 1014-1032.

M02

Learning Chemistry from Nature

G. Guella [a]

[a] *University of Trento, Department of Physics, Bioorganic Chemistry Lab, Via Sommarive 4 Povo, Trento, Italy*
e-mail*: graziano.guella@unitn.it*

The enormous biodiversity developed by Nature during several billion years of evolution has offered a wealth of chemically diverse compounds that have been preselected to modulate biochemical pathways, thus representing a rich source of lead molecules in drug discovery. As metabolites represent the final downstream products of gene transcription, changes in the metabolome are amplified relative to changes in transcriptome and proteome systems. In particular, accurate investigations of stereochemical relationships in a biosynthetic cascade may relate the metabolite distribution to lineages; this is a task that genetics cannot yet perform. The modern development of new analytical methodologies allows the natural product chemists to cope, with better perspectives than before, with severe challenges presented by the high chemo-diversity and the wide dynamic range of Natural Products. Results taken from our investigations of terpenoids produced by algae and ciliates[1] will be presented, outlining the main aspects (structure elucidation, total synthesis, *ab initio* computations) which currently represent the main bottlenecks in natural products chemistry. Last results from our recent adventures in the metabolomics/lipidomics[2] world will be also discussed.

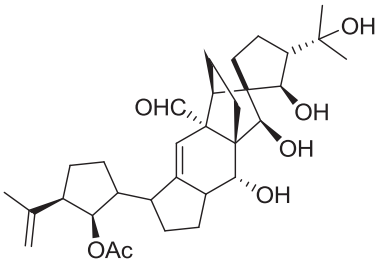


Figure 1 : vannusal B

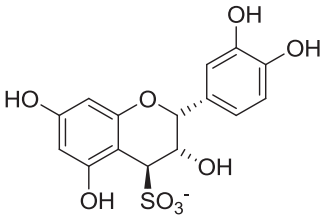


Figure 2 : epicatechin-sulfonate

References:

[1] a) G. Guella, F. Dini, F. Pietra. *Angew. Chem. Int. Ed.* **1999**, *38*, 1134-1136; b) K.C. Nicolaou; A.Ortiz; H.J. Zhang; G. Guella, *J. Am. Chem. Soc.* **2010**, *132*, 7153-7176; c) G. Guella, D. Skropeta;G. Di Giuseppe; F. Dini *Marine Drugs* **2010**, *8*, 2080 -2116.

[2]a) F. Mattivi, U.Vrhovsek, G.Malacarne, D.Masuero, L.Zulini, M.Stefanini, C. Moser, R.Velasco, G.Guella, *J. Agric. Food Chem*. **2011**, *59*, 5364 -5375; b) P. Arapitsas, G. Guella, F. Mattivi *Sci. Rep.* **2018**, *8*(1):858.

M03

Biocatalysis hand in hand with organic synthesis: developing new tools for the synthetic chemist

F. Parmeggiani[a,b]

[a] *The University of Manchester, 131 Princess Street, M1 7DN, Manchester (UK)*
[b]*Dip. CMIC "G. Natta", Politecnico di Milano, Via Mancinelli 7, 20131, Milano (Italy)*
e-mail*: fabio.parmeggiani@manchester.ac.uk ; fabio.parmeggiani@polimi.it*

Biocatalysis is defined as the use of biological catalysts (enzymes or microorganisms) to perform useful chemical reactions. In the last few decades, a very wide range of biocatalytic processes have been developed to support and complement the toolbox available to organic chemists, in particular for the synthesis of small chiral molecules in enantiomerically pure form. In this talk, several different approaches will be discussed, along with specific examples, to showcase the great synergy between biocatalysis and traditional organic synthesis (Figure 1).

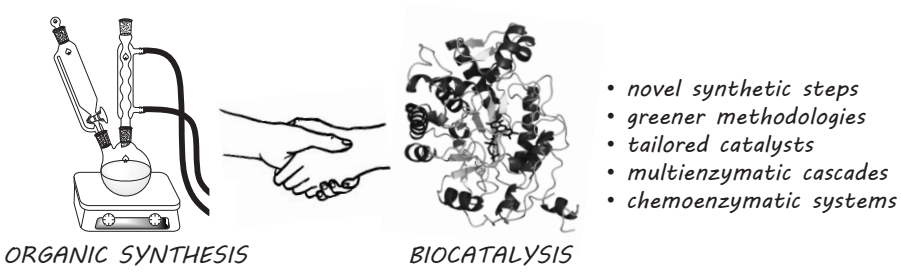


Figure 1: useful concepts in biocatalysis that can complement organic synthesis.

The implementation of biocatalytic steps enables the development of completely new synthetic routes, especially in the light of green chemistry principles, since bioprocesses can often replace key transformations that require toxic, expensive or otherwise dangerous reagents/solvents/catalysts. Just a few examples are C=C bond reductions, hydroaminations, amide synthesis in water, deracemisations and oligosaccharide synthesis. Nonetheless, rather frequently, enzymes that match all the requirements of activity, selectivity or stability of the intended process are not already available. In those cases, either better candidates can be identified in the ever-growing genomic databases (the "enzyme discovery" approach) or the available ones can be rapidly evolved in the laboratory to suit the requirements of the chemistry to be performed (the "enzyme engineering" approach). Specific examples will be provided for both these strategies.

One of the most advantageous aspects of biocatalysis for organic synthesis is that most enzymes have evolved to be able to work together in the same environment, and therefore they are intrinsically compatible. The one-pot combination of multiple biocatalytic steps allows completely different reactions to proceed in a cascade fashion, even if they would be chemically incompatible. Examples are oxidation/reduction, reduction/amination, double oxidations, etc. Similarly, one-pot combinations of enzymatic and traditional chemical steps without isolation of the intermediates can be very advantageous to improve the productivity and reduce the overall complexity of the process. Multiple examples of such systems will be discussed, highlighting the potential advantages of biocatalytic steps in the planning of countless synthetic routes.

Lectures PREMI SENIOR

PS01

Organic Chemistry: a true ally of Energy, the Environment and Nanosciences

G. Cravotto

Dipartimento di Scienza e Tecnologia del Farmaco, University of Turin, Via P. Giuria 9, 10125- Turin

e-mail*: giancarlo.cravotto@unito.it*

The new generation of organic chemists has grown up fully aware of how significant their contribution, in terms of smarter and greener synthetic processes with lower carbon footprints, will be for the preservation of the environment. By contrast to previous generations of chemists who were involved in reducing pollutant amounts, but were reluctant to design new protocols, the last two decades have seen new enabling technologies pave the way for environmentally friendly processes that have a benign impact on human life and the planet. There are a great many relevant instances to illustrate the Italian approach to invention and innovation: the pioneering work of Mario Biazzi, who designed the first flow-reactor production process for nitroglycerin,[1] and the ultrasound-assisted hydrogenation of unsaturated esters conceived by Saracco and Arzano,[2] just to name a couple. Despite convincing scientific evidence to support it, the scale-up and further industrialization of new processes is generally troublesome, while industrial set-up requires long periods of study and optimization, even in the most promising of cases. The fact that research laboratories and industrial plants are still separated by such a divide is the main reason for this. In order to help bridge the gap between academia and large-scale production, we have established a "Green Technologies Development Platform", which is made up of a series of multifunctional laboratories that are equipped with non-conventional pilot reactors. The platform has been developed in direct collaboration with partner companies and has brought together research, R&D and production expertise. The reproduction of lab, gram-scale data in pilot, kilogram-scale reactors was a challenging project. This strategy has enabled the principle heat and mass transfer data to be obtained and a potential industrial plant to be designed. In collaboration with industrial partners, we have pursued a number of multifaceted strategies that include: *i*) new advanced oxidation processes under non-conventional energy sources;[3] *ii*) selective adsorption/desorption from industrial waste water by means of chemically modified active charcoals[4] and efficient photodegradation;[5] *iii*) the green process intensification of critical synthetic processes with kinetic bottlenecks[6,7] and the preparation of greener catalysts;[8] *iv*) the design of efficient procedures for the conversion of industrial by-products into platform chemicals;[9] *v*) biofuel production in flow reactors,[10] and finally, *vi*) new technologies for the preparation of green and highly efficient nano-catalysts.[11] A challenging, but promising, future lies in wait for innovation in organic chemistry.

References:

[1] http://www.dipharma.com/index.aspx?IDDOC=174515. [2] G. Saracco, F. Arzano, *La Chimica e l'Industria* **1968**, *50*, 314-318. [3] G. Cravotto, W. Tumiatti, C.M. Roggero, PCT Int. Appl. (2006), WO 2006040648. [4] Z. Wu, G. Cravotto, X. Wei, X. Ge, X. He, Z. Wu, *J. Molecular Liq.* **2018**, *255*, 160-167. [5] F. Tian, Z. Wu, Y. Tong, Z. Wu, G. Cravotto, *Nanoscale Res. Lett.* **2015**, *10*, 1-12. [6] A. Barge, F. Baricco, G. Cravotto, R. Fretta, L. Lattuada, L. Patent Appl. (2016): EP16202152.1. [7] E. Calcio Gaudino, M. Manzoli, D. Carnaroglio, *et al. RCS Advances* **2018**, *8*, 7029-7039. [8] G. Cravotto, W. Bonrath, J. Medlock, E. *et al.* PCT Int. (2015), WO 2015044411 and WO 2015044410. [9] D. Carnaroglio, S. Tabasso, B. Kwasek, E. Calcio Gaudino *et al. ChemSusChem* **2015**, *8*, 1342-1349. [10] Choedkiatsakula, I.; Ngaosuwan, K.; Mantegna, S.; Cravotto G.; *Renew. Energy* **2015**, *83*, 25-29. [11] K. Martina, F. Baricco, M. Caporaso, G. Berlier, G. Cravotto, *ChemCatChem* **2016**, *8*, 1176-1184.

PS02

Eco-friendly (solar) light induced generation and application of reactive intermediates in synthesis

M. Fagnoni, C. Raviola, S. Crespi, L. Capaldo, S. Protti, D. Ravelli

PhotoGreen Lab, Department of Chemistry, University of Pavia
V. Le Taramelli 12, 27100 Pavia, Italy
e-mail*: fagnoni@unipv.it*

Photochemistry offers a way for the mild generation of highly reactive intermediates since light is successfully used to promote many organic transformations.[1] The use of solar/visible light offers a clean path towards sustainable synthesis. In the last years we were involved in two different eco-sustainable approaches for the construction of C-C bonds. The first one involves the direct activation of aliphatic C-H bonds in extremely unreactive substrates (R-H, e.g. aldehydes, ethers, amides, alcohols and even alkanes) upon exposure to UV-A (or solar) light in the presence of a photocatalyst ($(n\text{Bu}_4\text{N})_4[\text{W}_{10}\text{O}_{32}]$, TBADT, Figure 1a).[2] Accordingly, useful reactions (mainly alkylation and acylation of olefins or azodicarboxylates) can take place by simply placing the reaction vessel under the sun. TBADT is also well suited for applications in dual catalytic processes,[3] as well as for the smooth conversion of a $-CH_2-$ group into a carbonyl.[4]

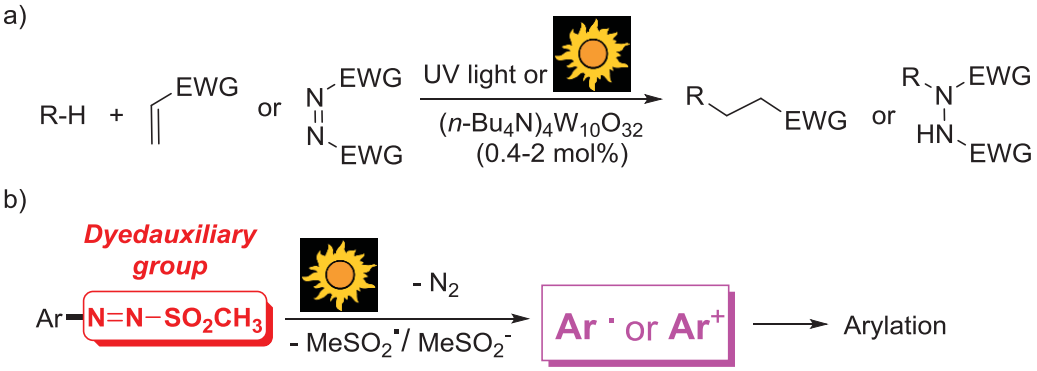


Figure 1: Eco-friendly photocatalyzed (a) and photoinduced (b) formation of C-C (C-N) bonds.

A different green photochemical approach for the exploitation of visible (solar) light is making use of colored organic compounds. Thus, a photolabile, colored moiety was incorporated in a colorless organic compound with the aim of generating highly reactive intermediates upon exposure to light. The amino group in anilines was converted to a colored, thermally stable, yet photolabile moiety ($-N_2SO_2R$) via the intermediacy of unstable arene diazonium salts. We proposed that such structural motif that imparts both color and photoreactivity is dubbed as *dyedauxiliary group* (Figure 1b).[5] A wavelength selective generation of aryl radicals and aryl cations can be attained at will from the resulting arylazo sulfones for valuable arylation reactions.

References:

[1] D. Ravelli, S. Protti, M. Fagnoni, *Chem. Rev.* **2016**, *116*, 9850–9913.
[2] D. Ravelli, S. Protti, M. Fagnoni, *Acc. Chem. Res.* **2016**, *49*, 2232–2242.
[3] J. J. Murphy, D. Bastida, S. Paria, M. Fagnoni, P. Melchiorre, *Nature* **2016**, *532*, 218–222.
[4] G. Laudadio, S. Govaerts, Y. Wang, D. Ravelli, H. F. Koolman, M. Fagnoni, S. W. Djuric, T. Noël, *Angew. Chem. Int. Ed.* **2018,** *57*, 4078–4082.
[5] S. Crespi, S. Protti, M. Fagnoni, *J. Org. Chem.* **2016**, *81*, 9612–9621.

PS03

Chemical structure of microbial glycoconjugates and their role in the elicitation/suppression of eukaryotic innate immunity

A. Molinaro[a, b]

[a] *Department of Chemical Sciences, University of Napoli Federico II, Via Cintia 4, I-80126 Napoli, ITALY*

[b] *Department of Chemistry, School of Science, Osaka University, 1-1 Machikaneyama, Toyonaka, Osaka, 560-0043, JAPAN*

e-mail*: molinaro@unina.it.*

Innate immunity is the first line of defence against invading microorganisms in vertebrates and the only line of defence in invertebrates and plants and therefore plays a crucial role in the early recognition and subsequent triggering of a pro-inflammatory response to invading pathogens.
This mechanism relies on recognition of evolutionarily conserved structures on microbes, termed microbe-associated molecular patterns (MAMPs), through a limited number of germ line-encoded pattern recognition receptors. MAMPs are characterized by being invariant among entire classes of microbes, essential for their survival, and distinguishable from "self"; interestingly, many of them are glycosylated.

Microbial cell surface molecules, such as lipopolysaccharide and peptidoglycan, are very important cell wall glycoconjugates and act as MAMPs in eukaryotic/bacteria interactions. Besides their general architectural principle, a number of subtle chemical variations are at the basis of the dynamic host-guest recognition that in case of pathogens is followed by the innate response and in case of symbiosis is followed by its suppression. Therefore, the chemical study of such glycoconjugates involved as virulence or beneficial factors in animal or plant interactions is a pivotal pre-requisite for the comprehension at molecular level of the innate immunity mechanisms. [for example, references 1-4]

In this communication, I will show some examples of isolation, structure determination and elicitation and/or suppression of plant and animal innate immunity by cell wall glycoconjugates from pathogen and symbiotic microbes.

References:

[1] C. De Castro I. Speciale, G. Duncan, D. D. Dunigan, I. Agarkova, R. Lanzetta, L.Sturiale, A. Palmigiano, D. Garozzo, A. Molinaro, M. Tonetti, J. L. Van Etten *Angew. Chem. Int. Ed.* **2016**, 55, 654-658.

[2] W. Li, A. Silipo, L.B. Andersen Gersby, M.-A.Newman, A. Molinaro, B. Yu *Angew. Chem. Int. Ed.* **2017**, 129, 2124-2128.

[3] B. Lagrange, S. Benaoudia, P. Wallet, F. Magnotti, A. Provost, F. Michal, A. Martin, F. Di Lorenzo, B.F. Py, A. Molinaro, T. Henry *Nat. Comm.*,**2018**, 9, 242.

[4] B. J. Belin, N. Busset, E. Giraud, A. Molinaro, A. Silipo, D. K. Newman *Nat. Rev Microbiol.*, **2018**, 16, 304-315.

PS04

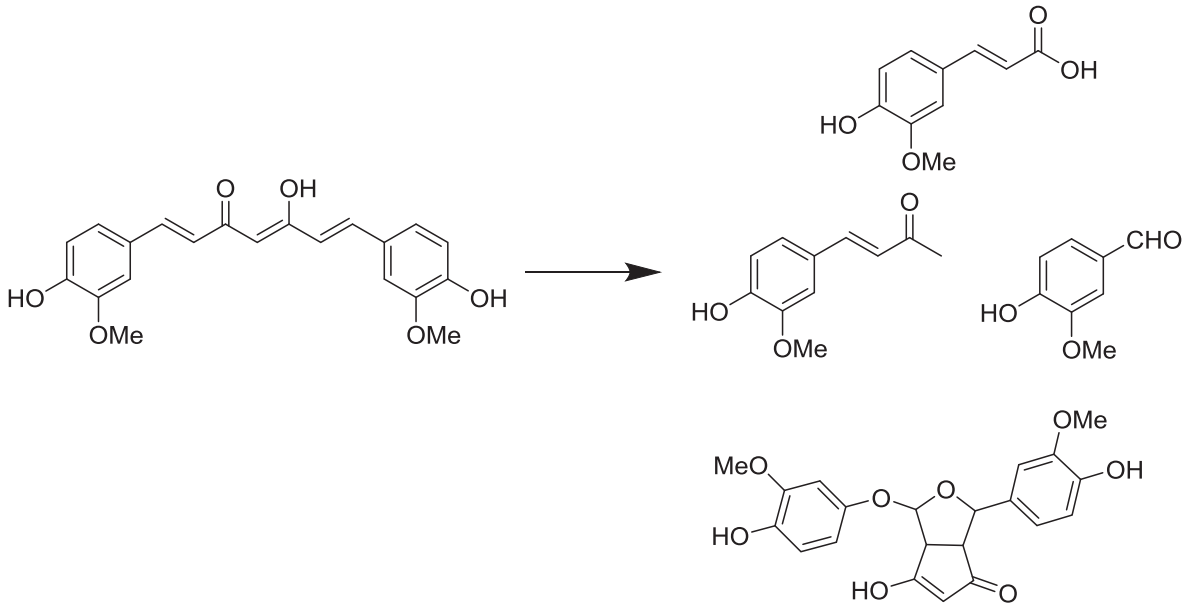
Tecnica e Rito (Technology and Rite): the industrial research carrier as an attempt to clarify this ambiguous dualism

P. Allegrini

Indena SpA, Viale Ortles 12, 20139 Milan Italy
e-mail*: pietro.allegrini@indena.com*

The synthesis and performance characterization of organic photochromic dyes belonging to spiro naphthoxazine and chromenes seems weakly related to the other challenges of my professional career, i.e. the chemistry of high energy compounds, the process research related to the synthesis of active pharmaceutical ingredients and, namely of botanical dietary supplements. The major target of the presentation is to show that a common thread links the industrial research in these very different sectors, hence – as per the lecture title - the ambiguous dualism between technology and rite.

A good example of this dualism is the use of turmeric derivatives as dietary supplement, that in western countries is booming and becoming a modern "rite", even though the official science is still very skeptical[1] on its efficacy. The long-standing issue of curcuminoids' stability[2] in the gastrointestinal tract, one of the main arguments of the curcumin mistrustful party, will be discussed in details.



References:

[1] K.N. Nelson, J.L. Dahlin, J. Bisson, J. Graham, G.F. Pauli, M.A. Walters, *J. Med. Chem.* **2017**, 60, 1620-1637.

[2] T. Tsuda, *Food Funct.* **2018**. *9*, 705-714.

Lectures PREMI JUNIOR

PJ02

Moving From Lab to Fab: the Role of Synthetic Organic Chemists

G. Marzano,[a,b]

[a] *Dipharma Francis Srl, via Bissone 5, 20021 Baranzate (MI) - Italy*
[b]*Sasol Italy S.p.A, Stabilimento di Augusta, C.da Marcellino s.n. C.P. 119, 96011 Augusta (SR) - Italy*
e-mail*: giuseppe.marzano@it.sasol.com*

Organic synthesis plays a central role in the chemical industry covering a huge number of products and applications, from polymers to active pharmaceutical ingredients (APIs). However, to successfully transfer results obtained in a research laboratory up to the industrial level, some key aspects have to be carefully considered. Not only the freedom to operate a commercial process, the atom economy of the whole synthetic cascade, but also the choice of inexpensive starting materials, the use of non-toxic safe and easy-handling reagents, an easy isolation of pure products and the disposal of wastes contribute to make a synthetic process viable from the industrial perspective.
In this context, the present communication will aim to emphasize both the research criteria adopted in an industrial feasibility study and the common issues encountered by organic chemists working in industry during the definition of a new synthetic process. All these aspects will be also discussed in the light of some pertinent case studies.

PJ03

Peptide Nucleic Acids (PNAs): a simple tunable scaffold with limitless potentialities

A. Manicardi[a]

[a] *Organic and Biomimetic Chemistry Research group (OBCR), Department of Organic and Macromolecular Chemistry, Faculty of Sciences - Ghent University - Krijgslaan 281 S4, 9000 Gent (Belgium)*
E-mail: alex.manicardi@ugent.be

Peptide nucleic acids (PNAs) are artificial nucleic acid mimics that combine the sequence selective recognition of nucleic acid targets with the chemical flexibility and a unique stability towards chemical and enzymatic degradation. Moreover, the neutral backbone enables them to bind their target with higher stability and selectivity, with stabilities that are less affected by variations in experimental conditions (i.e. ionic strength, presence of organic solvents or chaotropic agents).[1] Properly designed PNA molecules can perform strand invasion of the dsDNA with single base mismatch recognition.[2] Chemical engineering the modification of the PNA original structure has emerged as a good strategy for overcoming innate drawbacks or for introducing additional groups with specific functions, allowing for the development of increasingly efficient tools.[3]

In this communication will be presented some applications developed in the last years where the rational design of backbone and nucleobase modifications introduced new properties and functionalities into the PNA strand. Application of these modified strands in the realization of tools for gene therapy and diagnostic devices will be also shown. Finally, some preliminary results in the building of supramolecular architectures will be presented.

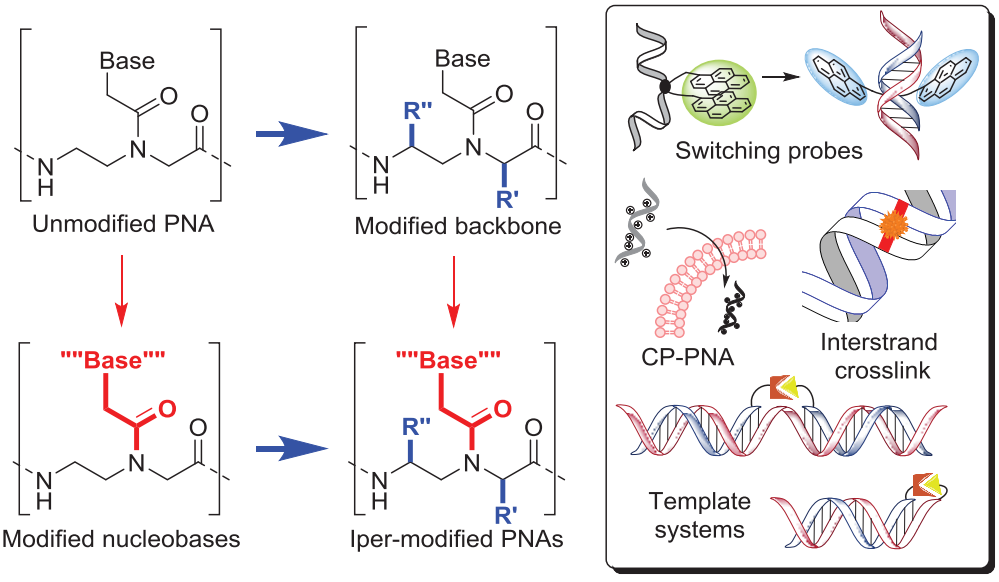


Figure 1: possible modifications of PNA structure and examples of their application (insert).

References:

[1] P. E. Nielsen *Mol. Biotechnol.* **2004**, *26*, 233–248.
[2] G. He, S. Rapireddy, R. Bahal, B. Sahu, D. Ly *J. Am. Chem. Soc.* **2009**, *131*, 12088–12090.
[3] A. Manicardi, A. Rozzi, S. Korom, R. Corradini, *Supramol. Chem.* **2017**, *29*, 1–12.

PJ04

Late and Base-Transition Metals-Catalyzed C–H Functionalization with Alkynes

G. Cera[a]

[a] *Università di Parma – Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale, Parco Area delle Scienze, 11/A, 431234, Parma*
e-mail*: gianpiero.cera@unipr.it*

Recently, C─H functionalization methodologies have emerged as a powerful tool to develop new C─C bond forming reactions, overcoming the limitations often linked to the use of traditional metal-catalyzed cross-couplings.[1] Among all the strategies which have been developed in this field,[2] the use of alkynes as coupling partners, allows different viable approaches to synthesize highly functionalized polycyclic molecules in a high atom- and step-economical fashion.[3] Within this presentation, catalytic functionalizations of C(sp^2) as well as thermodynamically inert C(sp^3)─H bonds with alkynes will be discussed in details, exploiting the properties of late- and base transition metals.[4]

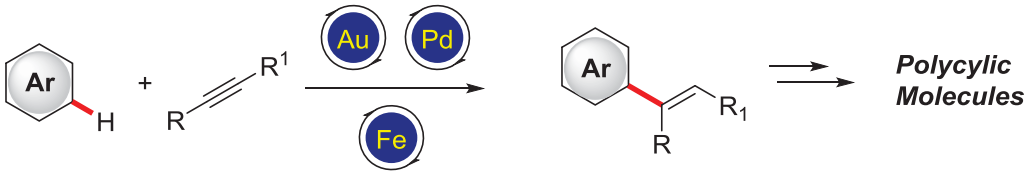


Figure 1: Late and Base-TM-catalyzed C─H Functionalizations with Alkynes

References:

[1] L. Ackermann*, Chem. Rev.* **2011***, 111,* 1315-1345.

[2] T. Gensch, M. Hopkinson, F. Glorius, J. Wencel-Delord, *Chem. Soc. Rev.* **2016**, *45*, 2900-2936.

[3] Y. Yamamoto, *Chem. Soc. Rev.* **2014**, *43*, 1575-1600.

[4] a) G. Cera, M. Lanzi, D. Balestri, N. Della Ca', R. Maggi, F. Bigi, M. Malacria, G. Maestri, *Org. Lett.* **2018**, *20*, 3220-3224; b) G. Cera, T. Haven, L. Ackermann, *Chem. Commun.* **2017**, *53*, 6460-6463. c*)* G. Cera, T. Haven, L. Ackermann, *Chem. Eur. J.* **2017**, *23*, 3577-3582. d*)* G. Cera, M. Chiarucci, F. Dosi, M. Bandini, *Adv. Synt. Cat*. **2013**, *355,* 2227–2231.

KEYNOTES

KN01

Nature's Medicine Chest: Opportunities for Synthesis and Drug Discovery

M. Brimble[a]

[a]*School of chemical Sciences and the Maurice Wilkins Centre for Molecular Biodiscovery, University of Auckland, New Zealand*
e-mail*: m.brimble@auckland.ac.nz*

Professor Brimble's research focuses on the synthesis of bioactive natural products and the synthesis of peptides, lipopeptides and glycopeptides as potential therapeutic agents. Prof Brimble's lecture will showcase the intricate science of natural products synthesis and will also describe her lab's research on the synthesis of peptides, lipopeptides and glycopeptides as a platform for the discovery and development of peptide therapeutics as agents to treat neurogenetic disorders, infectious disease, cancer and diabetes. Professor Brimble discovered the peptide drug candidate trofinetide (NNZ2566) that has been granted orphan drug status and fast track designation by the US FDA and is currently being evaluated in a final phase III clinical trial undertaken by Neuren Pharmaceuticals (see: http://www.neurenpharma.com/IRM/content/default.aspx) to treat Rett Syndrome. Professor Brimble recently co-founded the spin-out company SapVax with US$5.5 million investment from BioMotiv in Cleveland, Ohio to develop a suite of "first-in-class cancer vaccines" based on a novel self-adjuvanting peptide chemistry platform for immuno-oncology applications (see: https://sapvaxllc.com). She also established a Medsafe NZ-approved laboratory that has manufactured clinical grade peptide antigens for use as vaccines in human clinical trials to treat melanoma.

KN02

Diphenylprolinol Silyl Ether in the Pot Synthesis of Biologically Active Molecules

Y. Hayashi

Department of Chemistry, Graduate School of Science, Tohoku University Aobaku, Sendai, Japan
e-mail*: yhayashi@m.tohoku.ac.jp*

Diphenylprolinol silyl ether was developed by our group[1] and Jørgensen's group,[2] independently, which is an effective organocatalyst for both reactions involving an enamine and a iminium ion as reactive intermediates. We have successfully applied this catalyst to several asymmetric reactions such as Diels-Alder reaction, Michael reaction, oxidation, carbo [3+3] cycloaddition reaction, aza [3+3] cycloaddition reaction and so on, which afford the corresponding products with excellent enantioselectivity.

On the other hand, one-pot operations are an effective method for both carrying out several transformations and forming several bonds in a single-pot, while at the same time cutting out several purifications, minimizing chemical waste generation, and saving time.[3] Thus, a one-pot reaction can be not only efficient, but also green and environmentally friendly. We have been investigating the application of diphenylprolinol silyl ether to the one-pot synthesis of biologically active molecules.

In this talk, we will describe our recent development of the synthesis of (-)-Oseltamivir[4, 5] and estradiol methyl ether[6] using pot reactions and organocatalyst.

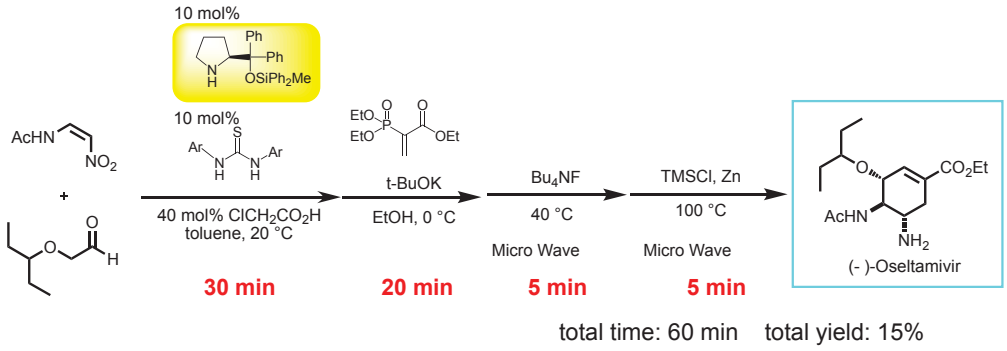


Figure 1.

References:

[1] Y. Hayashi, H. Gotoh, T. Hayashi, M. Shoji, *Angew. Chem. Int. Ed*. **2005**, *44*, 4212.
[2] M. Marigo, T. C. Wabnitz, D. Fielenbach, K. A. Jørgensen, *Angew. Chem. Int. Ed*. **2005**, *44*, 794.
[3] Y. Hayashi, *Chem. Sci.* **2016**, *7*, 866.
[4] Y. Hayashi, S. Ogasawara, *Org. Lett.* **2016**, *18*, 3426.
[5] S. Ogasawara, Y. Hayashi, *Synthesis* **2017**, *49*, 424.
[6] Y. Hayashi, S. Koshino, K. Ojima, E. Kwon, *Angew. Chem. Int. Ed*. **2017**, *56*, 11812.

KN03

Semiconducting polymers; from free standing insoluble materials to water processed nanoparticles

S. Destri,[a] S. Zappia[a]

[a]*Istituto per lo Studio delle Macromolecole-CNR, via A. Corti, 12 20133-Milan, Italy.*

In the early eighties a free standing shiny film hit the scientific headlines. It was polyacetylene insoluble and infusible, to get film it was necessary to coat the wall vessel by the catalytic system before introducing the gas. Other materials as polythiophene and polyphenylene were black powders hard to handle. The introduction of alkyl chains at suitable positions of thienylene or phenylene rings allowed for developing a huge am ount of materials which could be processed from solution of chlorinated or aromatic or mixture of both solvents. Many type of devices optoelectronic, electronic, electrochemical could be fabricated OLED, polymer solar cells (OPV), Field effect transistors (FET), sensors, dye Synthesized Solar Cells (DSSC). Thanks to chemistry supply the polymer backbone has been modified and always more tricky structures have been designed even in two directions to increase conjugation and planarity hence optoelectronic and electronic properties. The solubility needs became more important and branched long chains were used to impart solubility and processability to get homogenous thin large area films for devices fabricated by continuous processes, as roll to roll for example. The use of chlorinated solvents, mostly the aromatic ones, became compulsory to process these materials very frequently associated to high temperature or solvent annealing and to additive use for obtaining the suitable morphology for the charge transport in the different devices. The amount of environment dangerous solvents which must be disposed correctly (e.g. 16 milion liters of chlorobenzene for the production of 1 GWp of polymer solar) make the Energy PayBack Time (EPBT) risen. To dispose the before cited waste chlorinated solvents, 880 TJ of cumulative thermal energy production that means 10 days more to EPBT; versus 17 TJ only 4 days if water were used.[1] Employing side chains able to dissolve photoactive polymers in aqueous medium reveiled useful only for polyalkythiophenes (PAT) and LBG oligomers. Since ten years many research groups are working on the use of aqueous colloidal solution of these semiconducting polymers, mostly PAT as benchmark. Besides the technical advantages in using non-toxyx solvents, the preparation of water-processable nanoparticles (NPs) containing a blend of a semiconducting polymer and a fullerene derivative recently emerged as a smart strategy to control the nanoscale morphology, that is necessari rito achieve high efficiency in the devices. Different strategies have been employed to produce these colloidal solutions: miniemulsion by using surfactats[2], nanoprecipitation[3] giving normally unstable NPs, chemical modification[4] of the polymer backbone Amphiphilic block copolymers can be use for these porpose too. Designing well defined block copolymers we were able to prepare active layers for organic solar cells showing an efficiency equal to 75% of that obtained using the established procedure with chlorinated solvent (oDCB).[5] By determining the right length of the flexible hydrophilic segment with respect to the nature and size of the rigid hydrophobic block it is possible to develop a new tool for producing aqueous inks for active layers of many devices, as OLEDs, OFETs, and OPVs.

References:

[1] a) K. Landfester, R. Montenegro, U. Scherf, R. Güntner, U. Asawapirom, S. Patil, D. Neher, T. Kietzke, *Adv. Mater.* **2002**, *14*, 651–655; b) D. Darwis, N. Holmes, D. Elkington, A. L. D. Kilcoyne, G. Bryant, X. Zhou, P. Dastoor, W. Belcher, *Sol. Energy Mater. Sol. Cells* **2014**, *121*, 99–107.

[2] S. Gärtner, M. Christmann, S. Sankaran, H. Röhm, E.-M. Prinz, F. Penth, A. Pütz, A. E. Tureli, B. Penth, B. Baumstümmler, A. Colsmann, *Adv. Mater.* **2014**, *26*, 6653–6657.

[3] F. Di Maria, A. Zanelli, A. Liscio, A. Kovtun, E. Salatelli, R. Mazzaro, V. Morandi, G. Bergamini, A. Shaffer, S. Rozen, *ACS Nano* **2017**, *11*, 1991−1999.

[4] S. Zappia, G. Scavia, A. M. Ferretti, U. Giovanella, V. Vohra, S. Destri, *Adv. Sustainable Syst.* **2018**, *2*, 1700155.

KN04

Organic solar cells: the path to the industrialization

R. Po, A. Bernardi, G. Bianchi, C. Carbonera, G. Corso

Research Center for Renewable Energies and Environment
Eni S.p.A., Via Fauser 4, 2800 Novara (Italia)
e-mail*: riccardo.po@eni.com*

While organic photovoltaic (OPV) technology has recently reached on the laboratory scale very promising results in term of efficiency (η=14.6% [1]) and durability (up to 15 years), a significant gap still remains when large area modules, capable to enter the market, are considered.[2,3] As a matter of fact, very few companies are currently selling OPV panels (with not terrific performances, η<5%). There are several reasons accounting for this gap. One of them is related to the synthetic complexity of the active materials,[4] which impacts on the costs and, in the end, on the possibility to transfer the results obtained on lab-scale devices to large area commercial modules.

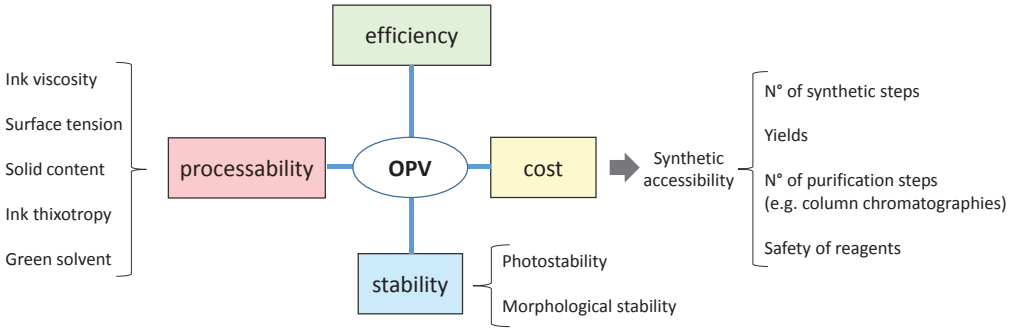


Figure 1.

In this communication, a brief overview of OPV technology will be presented, showing the main achievements and the critical issues. The problem of the synthetic accessibility of the materials will be discussed and some guidelines to simplify the synthesis of the electron-donor polymers will be given.[5-8]

References:

[1] H. Li, Z. Xiao, L. Ding, J. Wang, *Sci. Bull.* **2018**, doi: 10.1016/j.scib.2018.02.015.
[2] J.E. Carlè, M. Helgesen, O. Hagemann, M. Hösel, I.M. Heckler, E. Bundgaard, S.A. Gevorgyan, R.R. Søndergaard, M. Jørgensen, R. Garcìa-Valverde, S. Chaouki-Almagro, J.A. Villarejo, F.C. Krebs, *Joule* **2017**, *1*, 274-289.
[3] R. Po, A. Bernardi, A. Calabrese, C. Carbonera, G. Corso, A. Pellegrino, *Energy Environ. Sci.* **2014**, *7*, 925-943.
[4] R. Po, G. Bianchi, C. Carbonera, A. Pellegrino, *Macromolecules* **2015**, *48*, 453-461.
[5] D. Kotowski, S. Luzzati, G. Bianchi, A. Calabrese, A. Pellegrino, R. Po, G. Schimperna, A. Tacca, *J. Mater. Chem. A* **2013**, *1*, 10736-10744.
[6] G. Bianchi, R. Po, M. Sassi, L. Beverina, S. Chiaberge, S. Spera, A. Cominetti, *ACS Omega* **2017**, *2*, 4347-4355.
[7] G. Marzano, D. Kotowski, F. Babudri, R. Musio, A. Pellegrino, S. Luzzati, R. Po, G.M. Farinola, *Macromolecules* **2015**, *48*, 7039-7048.
[8] G. Marzano, F. Carulli, F. Babudri, A. Pellegrino, R. Po, S. Luzzati, G.M. Farinola, *J. Mater. Chem. A*, **2016**, *4*, 17163-17170.

KN05

Photoinduced Formation of C–N Bonds

D. Leonori[a]

[a]*School of Chemistry, University of Manchester, Oxford Road, M13 9PL Manchester, UK*
e-mail*: daniele.leonori@manchester.ac.uk*

Nitrogen-containing compounds are a privileged class of molecules, which have applications in medicines, agrochemicals, dyes and materials. As a result, the construction of C–N bonds is an extremely active area of research. Nitrogen-centered radicals are a versatile class of intermediates however, the difficulties associated with their generation have significantly thwarted their use in synthetic chemistry.[1] Photoredox catalysis has emerged as a powerful technique through which single electron transfer reactions can be performed under mild conditions.[2]

We have accomplished the formation and use of iminyl,[3] amidyl[4] and aminyl[5] radicals in novel aminofunctionalization reactions through the design of a new class of reactive O-aryl oximes, hydroxyamides and hydroxylamines. Owing to their low reduction potentials, the inexpensive organic dye eosin Y could be used as the photoredox catalyst.

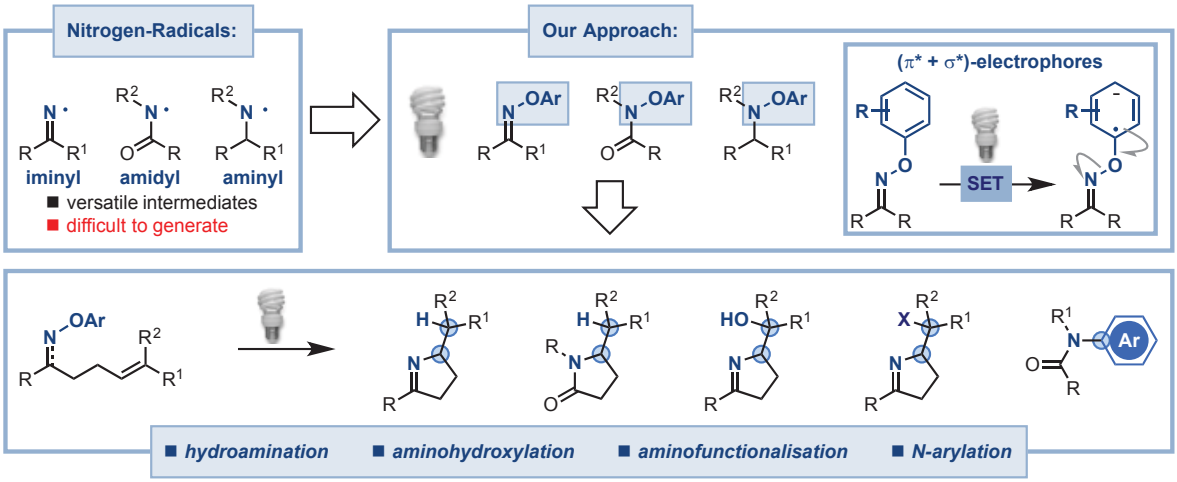


Figure 1: Nitrogen Radicals.

References:

[1] (a) S. Z. Zard, *Chem. Soc. Rev.* **2008**, *37*, 1603; (b) J.-R. Chen, X.-Q. Hu, L.-Q. Lu, W.-J. Xiao, *Chem. Soc. Rev.* **2016**, *45*, 2044.

[2] C. K. Prier, D. A. Rankic, D. W. MacMillan**,** *Chem. Rev.* **2013**, *113*, 5322.

[3] (a) J. Davies, S. Booth, S. Essafi, R. Dryfe, D. Leonori, *Angew. Chem. Int. Ed.* **2015**, *54*, 14017; (b) J. Davies, N. S. Sheikh, D. Leonori, *Angew. Chem. Int. Ed.* **2017**, *56*, 13361.

[4] J. Davies, T. D. Svejstrup, D. Fernandez Reina, N. S. Sheikh, D. Leonori, *J. Am. Chem. Soc.* **2016**, *138*, 8092.

[5] T. D. Svejstrup, A. Ruffoni, F. Julia, V. M. Aubert and D. Leonori *Angew. Chem. Int. Ed.* **2017**, *56*, 14948.

KN06

Dealing with Scientific Misconduct - A Part of an Editor's Day-to-Day Work

F. R. Novara[a]

[a]*Chemistry - A European Journal - Wiley-VCH*
e-mail*: frnovara@wiley.com*

Ethical publishing is integral to the reliability of the scientific record. Therefore, in the peer review process, the journal editors and the scientists who act as authors and referees share the responsibility for publishing according to ethical guidelines. Wiley-VCH journals, including *Chemistry - A European Journal*, adhere to the ethical guidelines of the European Association for Chemical and Molecular Sciences (EuCheMS), in which the responsibilities of authors, editors, and reviewers are outlined. While editors should ensure that manuscripts are handled and decided upon in an efficient and fair manner, authors have to report their findings with integrity and objectivity. In this lecture it will be shown how important ethical decisions are involved in almost every stage of the process of publishing scientific literature. An overview of the different types of ethical infractions including some real-life examples will be given together with a description of the measures taken in our Editorial Office and the tools available to us (such as the software IThenticate). Unethical or fraudulent publication practices not only undermine the trust in the scientific record, but they also represent a waste of time and resources.

KN07

10 years of REACH Regulation – an incentive or an obstacle for innovation?

R. Knauf
Centro Reach Srl
e-mail: R.Knauf@centroreach.it

The Reach Regulation which came into force over 10 years ago was presented by the European Commission as an important incentive to boost innovation.

Up to about 1 year ago, the EU Commission and ECHA, the EU Chemicals Agency, did foresee a total of approx. 30,000 registrations of phase-in substances for the period 2010 - May 2018.

This prediction turned out to be incorrect and the actual number of registrations was rather low with a share of the participation of SMEs that at 31 May 2018 was less than 20%.

How did the companies behave, especially SMEs which are of fundamental importance for the functioning of the Supply Chain in Italy? Did they look at first to protect the existing substance-product portfolio or did they dedicate to finding and developing new solutions from early beginning?

10 anni di Regolamento REACH - uno stimolo oppure un ostacolo per l'innovazione?

R. Knauf
Centro Reach Srl
e-mail: R.Knauf@centroreach.it

Il Regolamento Reach entrato in vigore oltre 10 anni fa è stato presentato dalla Commissione Europea come un importante spinta all'innovazione.

La Commissione EU e l'ECHA, l'Agenzia Europea per la Chimica di Helsinki, fino a ca 1 anno fa prevedevano la registrazione complessiva di ca. 30.000 sostanze phase-in per il periodo 2010 – maggio 2018.

Questa previsione si è rivelata errata ed il numero effettivo delle registrazioni è stato piuttosto basso con una quota di partecipazione delle PMI che al 31 maggio 2018 era inferiore al 20 %. Come si sono comportate le imprese, in particolare le PMI che sono di fondamentale importanza per il funzionamento della Supply Chain in Italia? Hanno cercato di proteggere con priorità il portafoglio sostanze -prodotti esistente oppure si sono orientate a trovare e sviluppare da subito nuove soluzioni?

KN08

È lo scientifichese, bellezza

B. Mautino

Siamo sommersi da ogni tipo di informazione sui cosmetici. La televisione ci bombarda di pubblicità, le riviste reclamizzano le ultime novità in fatto di mascara e di miracolosi shampoo riparatori e, in particolar modo su internet, ci imbattiamo di continuo in articoli che ci mettono in allarme su prodotti e ingredienti che ci possono causare disturbi e malattie.

La chimica affascina e allo stesso tempo fa paura. Là dove ci aspettiamo che un cosmetico «faccia qualcosa», di scienza ne vogliamo tanta. Non la vogliamo altrove, dove invece preferiamo il naturale, il green, il «senza», come nei deodoranti o negli shampoo.

Il marketing cosmetico accoglie e soddisfa questi bisogni apparentemente contrastanti e contribuisce a creare l'immaginario pubblico della chimica e, necessariamente, dei chimici.

KN09

L'equivoco del biologico

A. Cecchi Paone

Negli ultimi anni, dal logo di expo alle pubblicità ai contenuti dei talk show televisivi più seguiti, è stata diffusa purtroppo con successo una mentalità popolare avversa a tutto ciò che è "Sintetico" a favore di tutto ciò che è "naturale".

Con l'utilizzo degli strumenti della scienza e della sociologia della comunicazione di massa, che insegno da 15 anni in diverse università italiane, delinero' interessi sottesi, archetipi inconsci ed elementi di antropologia culturale che sorreggono tale dannosissima operazione.

Passerò infine a segnalare punti di resistenza e di controffensiva utilizzabili dal mondo scientifico e dagli approcci più moderni e razionali per invertire la tendenza a vantaggio di un paese più avanzato, affidandomi all'epistemologia più aggiornata ma anche alla filosofia umanistica del Leopardi del "Dialogo fra la Natura e un esquimese".

Lectures PREMI DOTTORATO

PD01

Design, synthesis and characterizations of hybrid nanosystems: nanomedicine applications in theranostics

I. Monaco,[a] M. Comes Franchini [a]

[a] *Department of Industrial Chemistry "Toso Montanari", Viale Risorgimento 4, 40136, Bologna*

e-mail*: ilaria.monaco3@unibo.it*

In the last decades, the progress in nanotechnologies allows the developments of nanoagents with a significant potential in medicine applications.

Based on the unique properties of nanomaterials, the possibility to reformulate traditional therapies by introducing the use of drug delivery nanosystems and/or by developing technologies able to take advance of the intrinsic chemical-physic nature of these materials, led to the development of the nanomedicine. In this PhD thesis different nanosystems have been developed and synthetized in order to investigate their potential as theranostic and diagnostic tools in nanomedicine applications.
At first, polymeric nanoparticles have been exploited as drug delivery systems for the treatment of Glioblastoma Multiforme, the most aggressive form of brain tumour. For this purpose, a bio-molecule able to target the platelet-derived growth factor receptors (PDGFRs) overexpressed in human glial tumors (the antiPDGFRs-aptamer, GINT.4), has been conjugated on the polymeric nanoparticles surface in order to enhance their accumulation in the brain tumour cells. The *in vivo* studies showed that the distribution of aptamer-conjugated polymeric nanoparticles in the tumor was significantly higher compare to not targeted systems.[1]

After that, metallic nanoparticles able to absorb near infrared light and convert it into heat, have been exploited as photothermal nanoagents for hyperthermia therapy applications. In particular, gold nanorods (GNRs) have been synthetized, modified on the surface and entrapped in polymeric nanoparticles, in combination with curcumin, used for its anticancer properties. The developed system has been tested in biological experiments in order to investigate the synergism of photothermal behavior of GNRs and the anticancer activity of curcumin for the treatment of Barrett's esophageal and esophageal adenocarcinoma (EAC).[2] Lastly, a multifunctional nanosystem made of iron/silica/gold core−shell nanoparticles (Fe_3O_4@SiO_2@Au NPs) characterized by magnetic and optical properties have been synthesized to obtain a promising MRI−PAI dual imaging agents. To improve their biocompatibility, the obtained multilayer nanoparticles have been entrapped in polymeric micelles, decorated with folic acid moieties, and tested *in vivo* for photoacoustic and magnetic resonance imaging detection of ovarian cancer.[3]

References:

[1] I. Monaco, S. Camorani, D. Colecchia, E. Locatelli, P. Calandro, A. Oudin, S. Niclou, C. Arra, M.Chiariello, L. Cerchia, M. Comes Franchini; J. Med. Chem. 2017, 60, 4510 - 4518.

[2] R. C. Martin, E, Locatelli, Y. Li, P. Matteini, I. Monaco, G. Cui, S. Li, M. Banchelli, R Pini, M. Comes Franchini; J.Mater. Chem. B,2016, 4, 207-213.

[3] I.Monaco, F. Arena, S. Biffi, E. Locatelli, B. Bortot, F. La Cava, G. M. Marini, G. M. Severini, E. Terreno, M. Comes Franchini. Bioconjugate Chem. 2017, 28, 1382.

PD02

Targeting of specific G-quadruplex structures: small molecule based strategies

M. Zuffo[a,§]

[a] *Department of Chemistry, University of Pavia, V.le Taramelli 10, 27100, Pavia, Italy*
[§] *Present address: CNRS UMR9187, INSERM U1196, Institut Curie – Centre de Recherche, Rue Henri Becquerel, 91400, Orsay, France*
e-mail*: michela.zuffo@curie.fr*

G-quadruplexes (G4s) have received considerable attention in recent years, due to evidences of their occurrence in live cells.[1] Formed by stacks of guanine quartets, they belong to the wide class of non-canonical nucleic acid structures.[2] Interestingly, putative G4 forming sequences are distributed in genomic regions relevant for a number of pathologies, spanning from cancer to viral infections,[3] where they can act as regulators of genetic information transfer.[4] In this context, G4s stabilization is regarded as a novel therapeutic approach for the associated diseases.[5] In order to put in place a viable strategy, though, it is mandatory to restrict the targeting to the specific G4s of interest. Unfortunately, no known ligand displays such a refined selectivity. To address this lack, we examined two opposite approaches. The first is a bottom-up strategy. Starting from a scaffolds library, the most suitable structures are implemented step-by-step, to attain a suitable level of selectivity and understand how to control it.[6,7] Instead of focussing on a G4 chosen *a priori*, the goal is to establish widely applicable guidelines for G4 ligands design. The top-down approach is instead centred on the specific G4, through its fingerprint recognition by a tailored construct. A critical overview of the two strategies will be provided, with examples involving naphthalene diimides implementation for the scopes.

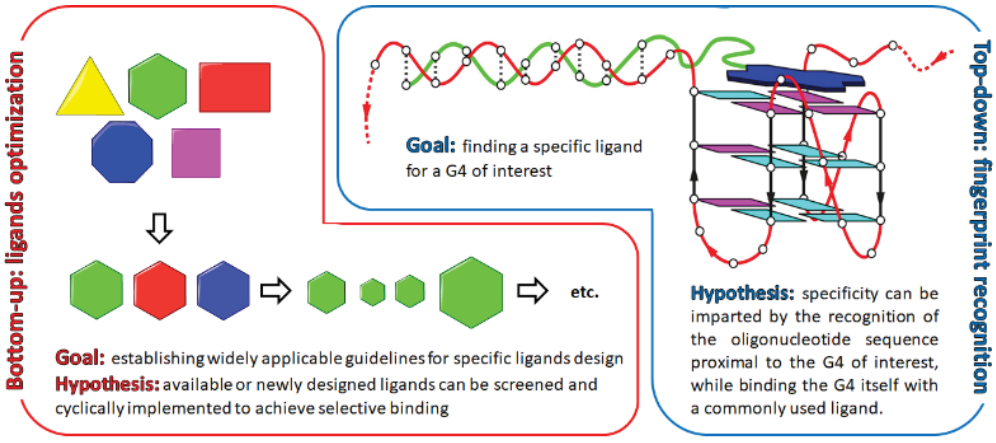


Figure 1: Top-down and bottom-up approaches outline for the targeting of specific G4 structures.

References:

[1] G. Biffi, D. Tannahill, J. McCafferty, S. Balasubramanian, Nat Chem 2013, 5, 182.
[2] R. Hänsel-Hertsch, M. Di Antonio, S. Balasubramanian, Nat Rev Mol Cell Biol 2017, 18, 279.
[3] A. K. Todd, M. Johnston, S. Neidle, Nucleic Acids Res 2005, 33, 2901.
[4] D. Rhodes, H. J. Lipps, Nucleic Acids Res 2015, 43, 8627.
[5] S. Balasubramanian, L. H. Hurley, S. Neidle, Nat rev Drug Discov 2011, 10, 261.
[6] M. Zuffo, F. Doria, S. Botti, G. Bergamaschi, M. Freccero, BBA - Gen Sub 2017, 1861, 1303.
[7] M. Zuffo, S. Ladame, F. Doria, M. Freccero, Sensors Actuat B Chem 2017, 245, 780.

PD03

"Sustainable preparation of Active Pharmaceutical Ingredients (API) in batch & flow mode, and Iron catalyzed transformations"

D. Brenna,[a,b] M. Benaglia[a]

[a]*Università degli Studi di Milano,Dipartimento di Chimica, Via Golgi 19, Milano*
[b]*Dipharma Francis srl, R&D, via Bissone 5, Baranzate*
e-mail*: davide.brenna@dipharma.com*

During my PhD, we focused our attention on the application of the green chemistry principle[1] for the preparation of active pharmaceutical ingredients (API) and, more in general, of highly functionalized chiral molecules, as fine chemicals or building blocks of high value for further synthetic manipulations. Mainly the topics of our interest were: (Figure 1)

1- The use of $HSiCl_3$, a byproduct from silicon industry, for imines reduction either in batch[2] and flow mode[3].
2- The use of iron complexes, the Knölker type, for the hydrogenations of chiral imines[4]. The use of cheap and readily available Iron complex, $Fe(hmds)_2$, for the trimerization of acetylenes[5], using for the first time a reducing agent free protocol.
3- The use of 3D-printed reactors for the preparation of APIs[6], engineering new reactors in order to perform continuous multi-step synthesis.
4- The use of Deep eutectic solvents (DES) as reaction media for Proline catalyzed aldol reaction.

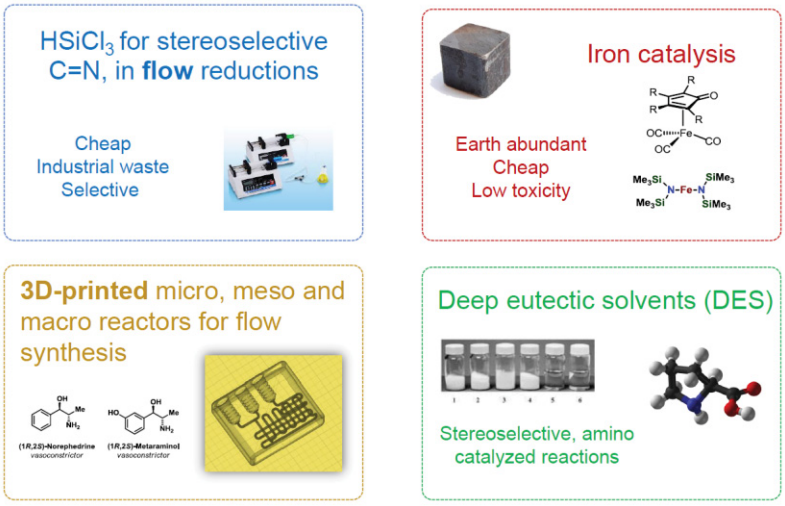


Figure 1: main researched topics during PhD.

References:

[1]https://www.acs.org/content/acs/en/greenchemistry/what-is-green-chemistry/principles/12-principles-of-green-chemistry.html

[2] D. Brenna, R. Porta, E. Massolo, L. Raimondi , M. Benaglia. *Chem. Cat. Chem.* **2017**, *9*, 941 - 945.

[3] a) D. Brenna, M. Benaglia, R. Porta, S. Fernandes, A. Burke *Eur. J. Org. Chem*, **2017**, 39 - 44; b) D. Brenna, M. Pirola, L. Raimondi and Maurizio Benaglia *Bioorg. & Med. Chem.,* **2017**, DOI: 10.1016/j.bmc.2017.01.023.

[4] D. Brenna, S. Rossi, F. Cozzi, M. Benaglia *Org. Biomol. Chem*, **2017**, *15*, 5685 - 5688.

[5] D. Brenna, M. Villa, T. N. Gieshoff, F. Fischer, M. Hapke, A. Jacobi von Wangelin, *Angew. Chem. Int. Ed.* ,**2017**, *56*, 8451 - 8455.

[6] S. Rossi, R. Porta, D. Brenna, A. Puglisi , M. Benaglia, *Angew. Chem. Int. Ed.*, **2017**, *56*, 4290 - 4294.

[7] D. Brenna, E. Massolo, A. Puglisi, S. Rossi, G. Celentano, M. Benaglia and V. Capriati *Beilstein J. Org. Chem*, **2016**, *12*, 2620 – 2626.

Comunicazioni ORALI

OC01

Imidazole-Reactive Molecules for the Functionalization of Poly-Histidine Leading to Fishbone-Like Architectures

M. Paolino,[a] V. Razzano,[a] A. Reale,[a] G. Giorgi,[a] G. Caselli,[b] F. Samperi,[c] C. Botta,[c] A. Cappelli.[a]

[a]*Dipartimento di Biotecnologie, Chimica e Farmacia and European Research Centre for Drug Discovery and Development, Università di Siena, Via A. Moro 2, 53100 Siena, Italy*
[b]*Rottapharm Biotech S.p.A., Via Valosa di Sopra 9, 20900 Monza, Italy*
[c]*IPCB di Catania (CNR), Via Gaifami 18, 95126 Catania, Italy,*
[c]*Istituto per lo Studio delle Macromolecole (CNR), Via A. Corti 12, 20133 Milano, Italy*
e-mail*: paomar@oneonline.it*

Histidine (His) is of crucial importance in many life processes. In fact, It plays a role as a buffer within the cellular environment,[1] is capable of complex metal ions and is involved in many catalytic sites.[2] Moreover, His is used in the synthesis of aminoacidic polymers for gene delivery while poly-HIS was introduced as tags in recombinant proteins. Alkylation of imidazole residues in poly-HIS is a difficult task owing to its low reactivity in conventional alkylation reactions.

Here, we report a series of Morita-Baylis–Hillman adduct (MBHA) derivatives as alkylating agents of imidazole,[3] N-acetylhistidine, and N-acetylhexahistidine as models of poly-histidine derivatives.[4] Intriguingly, the reaction of MBHA derivatives with imidazole in acetonitrile-phosphate buffered saline (PBS) gave the imidazolium salt biadducts as the main reaction products. These results were confirmed by experiments performed with N-acetylhistidine and suggested the possible occurrence of these structures in the reaction products of poly-His with MBHA derivatives. By insertion of oligo(ethylene glycol) chains we prepare the corresponding water-soluble MBHA derivatives and their reactivity was evaluated in experiments with N-acetylhexahistidine (Ac-His-6) in PBS. The structure of obtained polymeric materials was investigated by mass spectrometry, NMR spectroscopy, and photophysical studies, which suggested the predominant presence of biadduct residues also in the polymeric materials giving an unusual fishbone like structure.[3]

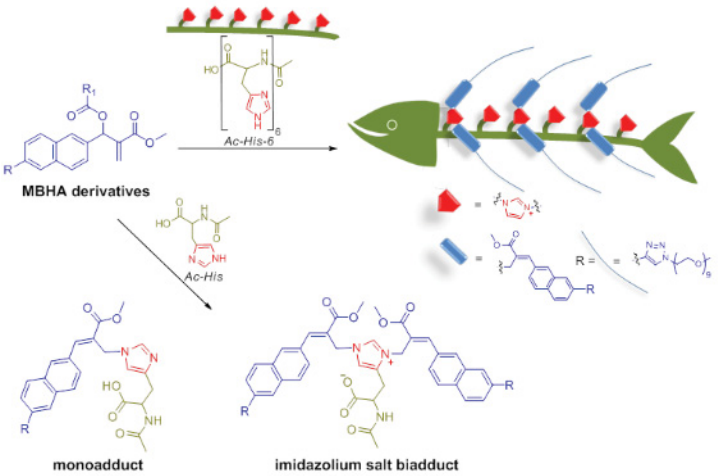


Figure 1: Application of Imidazole-Reactive Molecules with Ac-His and Ac-His-6

References:

[1] E. S. Lee, K. Na, Y. H. Bae, *Nano Lett.*, **2005**, *5*, 325–329.
[2] R. J. Sundberd, R. B. Martin, *Chem. Rev.*, **1974**, *74*, 471–517.
[3] V. Razzano, M. Paolino, A. Reale, G. Giuliani, R. Artusi, G.Caselli, M. Visintin, F. Makovec, A. Donati, F. Villafiorita-Monteleone, C. Botta and A. Cappelli, *ACS Omega* **2017**, *2*, 5453–5459.
[4] V. Razzano, M. Paolino, A. Reale, G. Giuliani, R. Artusi, G.Caselli, M. Visintin, F. Makovec, A. Donati, F. Villafiorita-Monteleone, C. Botta and A. Cappelli, *RSC Adv.*, **2018**, *8*, 8638-8656.

OC02

The thiazinoquinone scaffold as chemical starting point for the design and synthesis of antiparasitic drugs.

M. Casertano,[a] C. Imperatore,[a] M. Menna,[a] A. Aiello,[a] C. Fattorusso,[a] P. Luciano,[a] M. Persico,[a] R. Gimmelli,[b] F. Saccoccia,[b] A. Guidi,[b] G. Ruberti,[b] N. Basilico,[c] S. Parapini,[d] D. Taramelli[d]

[a]*Department of Pharmacy, University of Naples "Federico II", via D. Montesano 49, 80131 Naples, Italy.*
[b]*Institute of Cell Biology and Neurobiology, National Research Council, Via E. Ramarini 32,00015 Monterotondo Scalo (Rome), Italy.*
[c]*Department of Biomedical, Surgical and Dental Sciences, University of Milan, Via Pascal 36, 20133 Milan, Italy.*
[d]*Department of Pharmacological and Biomolecular Sciences, University of Milan, Via Pascal 36, 20133 Milan, Italy.*
e-mail*: marcello.casertano@unina.it*

Neglected parasitic diseases (NTDs) are still considered one of the most prevalent public health problems in 149 tropical and subtropical countries affecting more than 1 billion people annually. The available chemical entities to treat neglected diseases such as malaria and schistosomiasis are associated with various limitations, in particular, the widespread drug resistance, severe adverse effects and the absence of financial attractive. Currently, the pharmaceutical treatment is still based on few chemical scaffolds.[1] Thus, the development of new drugs active against *Plasmodium falciparum* and *Schistosoma mansoni*, obtained through an efficient and inexpensive synthesis, represents today a compelling priority.

It is well known that some similar redox processes characterize the digestion of hemoglobin of the protozoon *Plasmodium* and the blood fluke *Schistosoma* and, on this basis, two effective antimalarials, artemisinin and mefloquine, have shown antischistosomal properties.[2] Similarly, several natural and synthetic quinone derivatives have previously highlighted to be effective against both human parasistics.[3,4] In this perspective, a number of compounds with dioxothiazine ring fused to the quinone moiety has been synthesized and a possible antimalarial and schistosomicidal activity has been investigated.

Interestingly, the pharmacological results allowed to observe that the antiparasitic activity is most likely related to some structural requirements, in particular, the regiochemistry of dioxothiazine ring and the type of the substituents on the quinone play a crucial role on the antiparasitic effects. Overall these data clearly point out the thiazinoquinone scaffold as potential new lead structure for neglected disease drugs discovery.

References:

[1] R. Pink, A. Hudson, M.A. Mouriès, M. Bendig, *Nat. Rev. Drug Discov.* **2005**, *4*, 727–740.
[2] J. Keiser, J. Utzinger, *Curr. Pharm. Des.* **2012**, *18*, 3531-3538.
[3] F.P.D. Viegas, A.T. de Castro, A.P. Castro, Í. Siqueira, W. Rosa, P.F. Espuri, L.F.L. Coelho, M.J. Marques, G. Soares, *S. Afr. J. Bot.,* **2017**, *111*, 365-370.
[4] D. A. Lanfranchi, E. Cesar-Rodo, B. Bertrand, H.H. Huang, L. Day, L. Johann, M. Elhabiri, K. Becker, D. L. Williams, E. Davioud-Charvet, *Org. Biomol. Chem.,* **2012**, *10*, 6375-6387.

OC03

c[RGDfK] and MPUPA-LDV-diamine for the functionalization the 3th generation of devices for diagnosis of several disease

R. De Marco,[a] S.D.Deianira,[b] S. Spampinato,[b] N. Calonghi[b], A. Motealleh[c], N.S. Kehr[c], L. De Cola[d], L. Gentilucci[a]

[a]*Department of Chemistry "G. Ciamician", via Selmi 2 Bologna, Italy*
[b]*Department of Pharmacy and Biotechnology, via Irnerio 48, Bologna, Italy*
[c]*Center for Nanotechnology CeNTech, Heisenbergstrasse 11, Muenster,Germany*
[d] *Institut de science et d'ingénierie supramoléculaires (ISIS), Université de Strasbourg, 8 Allée Gaspard Monge, Strasbourg, France*
e-mail*: rossella.demarco2@unibo.it*

Integrins are heterodimeric glycoprotein receptors that mediate cellular attachment to the extracellular matrix (ECM) and to other cells. They interact with specific ligands (i.e., fibrinogen, fibronectin, plasminogen) and they are involved in various cellular functions, such as adhesion, migration, invasion, proliferation, and survival/anoikis. In this context we have focused on two different integrins, αvβ3 and α4β1 as potential biomarkers for development simple, non-invasive and accessible tests for the diagnosis of tumor and inflammatory diseases, to be carried out in biological samples easily obtainable from patients. The integrin αvβ3 is involved in the development of invasive tumors and the recognition motif in FN is the RGD sequence. The α4β1 integrin, or very late antigen-4 (VLA-4), or CD49d/CD29, is involved in inflammatory diseases and the recognition motif in FN is LDV sequence. Hence, we coated self-assembled monolayer (SAM) of nanoparticles with the integrin ligands for the development of three generations of diagnostic devices. In the first generation, we used the c[RGDfK] ligand for the capture of HeLa, Glioma C6, and control T-293 cells. After rapid incubation we observed a high adhesion and selectivity for cancer cells.[1] In the second generation of devices, we used the diphenylurea-LDV selective ligand of α4β1 integrin. The sequence MPUPA-LDV-diamine showed high adhesion of the α4β1 integrin-expressing Jurkat cells, and excellent selectivity over HEK-293 cells, utilized as a negative reference[2]. Finally, we proposed a third generation of devices, consisting in SAMs coated with both integrins ligand c[RGDfK] and MPUPA-LDV-diamine for αvβ3 and α4β1, respectively. Each peptide is linked onto the surfaces in gradient concentration, opposite to each other, hence the SAMs show at each side maximal concentration of one peptide, and varying compositions in between. The aim of this last generation is the separation of different integrin expressing cells from complex matrices such as blood or other biological fluids.

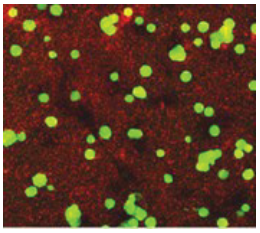


Figure 1: Confocal microscopy image of integrin ligand-SAM. The cells are visualized in green.

References:

[1] R. De Marco, et al. *Bioconjugate Chem*. **2015**, *26*, 1873-1878.
[2] R. De Marco, et al. *Biopolymers.* **2017**, e23081-e2309.

OC04

A structure-activity relationship study on the α-Chymotrypsin superactivation by quaternary ammonium salts

L. Goracci,[a] F. Gabriele,[b] M. Tiecco,[c] R. Germani[c] and N. Spreti[b]

[a] *Department of Chemistry, Biology and Biotechnology, University of Perugia, Via Elce di Sotto 8, I-06123 Perugia, Italy*

[b] *Department of Physical and Chemical Sciences, University of L'Aquila, Via Vetoio, I-67100 Coppito, Italy*

[c] *CEMIN, Centre of Excellence on Nanostructured Innovative Materials, Department of Chemistry, Biology and Biotechnology, University of Perugia, Via Elce di Sotto 8, I-06123 Perugia, Italy*

e-mail*: laura.goracci@unipg.it*

A number of quaternary ammonium salts with bulky hydrophobic portions are known to provoke a superactivation of α-chymotrypsin (α-CT) in aqueous solution.[1,2] In order to achieve a broader knowledge of the enzyme–additive interactions, the activity and stability of α-CT were tested in the presence of additives with slightly modified bulky ammonium groups, specifically selected or synthesized to evaluate the effect of hydrophobicity, flexibility and potential specific interactions with the enzyme. Thus, a chemioinformatic approach was developed to model the α-CT/additive interaction aiming at rationalizing the experimental observations.[3] Finally, the model was validated by designing and the synthesizing novel quaternary ammonium salts predicted to be either superactivators or not. The proposed in silico model suggests that the interaction with the residue Trp215 in the α-CT's cavity acts as an anchor point for the quaternary ammonium salts with superactivation effect; in addition two different hydrophobic regions in the cavity play a role in the biological effect of the additives.

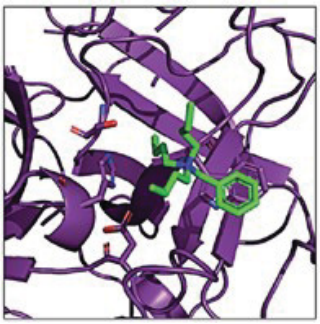


Figure 1: Example of the proposed binding pose for benzyltributylammonium bromide

References:

[1] N. Spreti, F. Alfani, M. Cantarella, F. D'Amico, R. Germani and G. Savelli, *J. Mol. Catal. B: Enzym.,* **1999**, 6, 99-110.

[2] N. Spreti, P. Di Profio, L. Marte, S. Bufali, L. Brinchi and G. Savelli, *Eur. J. Biochem*., **2001**, 268, 6491-6497.

[3] L. De Matteis, F. Di Renzo, R. Germani, L. Goracci, N. Spreti, M. Tiecco *RSC Adv.,* **2016,** *6*, 46202-46211.

OC05

Identification of the first selective BAG3 modulators: a turning point toward the development of new anticancer drugs

S. Terracciano,[a] G. Lauro,[a] A. Russo,[a] M.C. Vaccaro,[a] R. Riccio, [a] G. Bifulco, [a] I. Bruno [a]

[a]*Department of Pharmacy, University of Salerno, Via Giovanni Paolo II 132, 84084, Fisciano (Sa)*
e-mail*: sterracciano@unisa.it*

Bcl2-associated athanogene 3 (BAG3), a co-chaperone of the heat shock protein (Hsp) 70, is a multidomain protein able to regulate key biological processes, such as cell survival, apoptosis, cytoskeleton organization and autophagy.[1,2] Its over-expression in different tumor cell lines, including the adenocarcinoma pancreatic cancer, quite irresponsive to the classic chemotherapy, has been reported.[3] In addition, in different tumor types, BAG3 protein was found to sustain cell survival, resistance to therapy, and metastatization.[4,5]

In light of these evidences, BAG3 protein has emerged as a novel and attractive biological target for new anticancer drugs.

However, despite its central role in human malignancies, no selective BAG3 modulator has been yet discovered. Taking advantage of a multi disciplinary approach, involving computer aided-based drug discovery strategy and biophysical analysis, we succeed to disclose new chemical entities able to interact with this protein, featuring a 2,4-thiazolidindione core.

In order to expand the chemical diversity around the scaffold, a small collection of differently decorated thiazolidindione derivatives were designed, synthesized and afterwards subjected to a deeply biological investigation. The results obtained provided the identification of a new very interesting hit that can open the way for the development of potential BAG domain modulators of BAG3 protein, as promising candidates for a new class of chemotherapeutics.

References:

[1] A. Rosati, M. Ammirante, A. Gentilella, A. Basile, M. Festa, M. Pascale, *et al*. *Int. J. Biochem. Cell. Biol*. **2007**, *39*, 1337–1342.

[2] A. Rosati, V. Graziano, V. De Laurenzi, M. Pascale, M.C. Turco, *Cell Death and Disease* **2011**, *2*, e141.

[3] A. Rosati, A. Basile, R. D'Auria, M. d'Avenia, M. De Marco, A. Falco, M. Festa, et al. *Nat Commun.* **2015**, *6*, *8695.*

[4] P. Liu, B. Xu, J. Li, H. Lu, *FEBS Lett* **2009**, *583*, 401-406.

[5] H. Shi, H. Xu, Z. Li, et al. *Tumor Biol.* **2016**, *37*, 5591-5597.

OC06

Eumelanins exploitation in bioelectronics: perspectives and challenges

A. Pezzella[a,b,c]

[a]*Department of Chemical Sciences, University of Naples "Federico II", Naples, Italy*
[b]*National Interuniversity Consortium of Materials Science and Technology (INSTM), Florence, Italy*
[c]*Institute for Polymers, Composites and Biomaterials (IPCB), CNR, Pozzuoli (Na), Italy*
e-mail*: alessandro.pezzella@unina.it*

Eumelanins are the black insoluble pigments of human skin, eyes and substantia nigra (neuromelanin), featuring unique assortment of chemical physical properties, i.e. broadband absorption in the UV-visible range, intrinsic free radical character, water-dependent hybrid ionic–electronic conductor behaviour.[1]

These pigments, arising biogenetically from the aminoacid tyrosine via the oxidative polymerization of 5,6-dihydroxyindole (DHI) and/or 5,6-dihydroxyindole-2-carboxylic acid (DHICA),[1] stand, today, as a unique source of inspiration for the design and implementation of soft biocompatible multifunctional materials for bio-optoelectronic devices. Interest in eumelanins stems from bioavailability, biocompatibility and their peculiar set of physicochemical properties, chiefly the electrical conductivity, which support optimistic feelings about a possible rise of eumelanin-mimics as innovative bioinspired solutions for organic bioelectronics.

To date, a number of conceptual and technological gaps still hinder rapid progress of melanin-based organic electronics and bioelectronics, including in particular the limited contribution of electronic conductivity and current decay with time under biasing. Herein, we provide a concise overview of the structural and optoelectronic properties of melanins with a view to bringing to focus main issues and challenges en route to bioelectronic applications.[2]

Basic structure-property function relationships, fundamental tailoring strategies, processing and the balance of ionic-electronic processes will be addressed along with representative examples of eumelanin-based hybrids to orient ongoing efforts toward efficient and competitive eumelanin-based technology.

References:

[1] M. d'Ischia, K. Wakamatsu, A. Napolitano, S. Briganti, J.C. Garcia-Borron et al. *Pigment cell & melanoma research* **2013**, *26*, 616-633.
[2] M. Berggren, and A. Richter-Dahlfors *Adv Mater*, **2007**, *19*, 3201-3213.

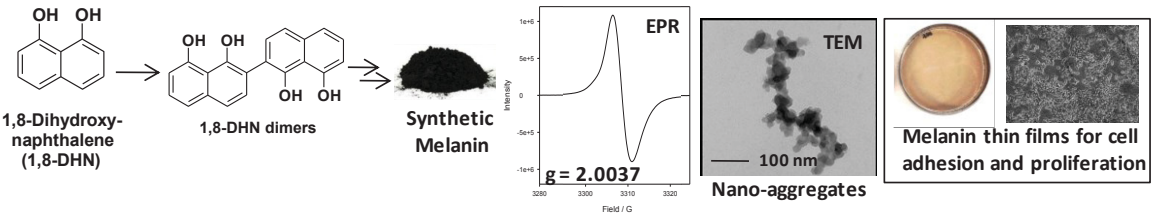
OC07

Synthetic Allomelanins from 1,8-Dihydroxynaphthalene: Toward Innovative Biocompatible Functional Materials

P. Manini,[a] G. D'Errico,[a] G. Falco,[b] M. Bietti,[c] O. Lanzalunga,[d] O. Crescenzi,[a] F. De Angelis,[e] C. Chiappe,[f] A. Napolitano,[a] M. d'Ischia[a]

[a]Dip. Scienze Chimiche, Univ. Napoli Federico II, via Cintia 4, Napoli; [b]Dip. Biologia, Univ. Napoli Federico II, via Cintia 4, Napoli; [c]Dip. Scienze e Tecnologie Chimiche, Univ. Tor Vergata, Via della Ricerca Scientifica, Roma; [d]Dip. Chimica e Istituto CNR di Metodologie Chimiche, Univ. Roma La Sapienza, P.le A. Moro 5, Roma; [e]Dip. Scienze Fisiche e Chimiche, Univ. dell'Aquila, Via Vetoio, Coppito, L'Aquila; [f]Dip. Farmacia, Univ. Pisa, via Bonanno Pisano 6, Pisa
e-mail*: paola.manini@unina.it*

Allomelanins comprise a group of black insoluble and non-nitrogenous melanin pigments found in plants, bacteria and fungi, which arise biogenetically from the oxidative polymerization of phenolic derivatives.[1] Particular interest in this context has been focused on the allomelanin from the fungus *Aspergillus fumigatus,* which derives from the oxidative polymerization of 1,8-dihydroxynaphthalene (1,8-DHN). Recent studies have suggested that this pigment enhances the capacity of the fungi to inhabit extreme environments such as Arcticand Antarctic regions,[2] and to resist to very high background radiation levels like those occurring in the destroyed reactor in Chernobyl[3] and on orbiting spacecrafts.[4] Moreover allomelanins are believed to play a role in the virulence of pathogenic fungi. Inspired by the intriguing biological roles of *Aspergillus* allomelanin and the potential applications of synthetic allomelanins in materials science for e.g. surface functionalization, bioelectronics, nanotechnology and biomedicine, we have recently undertaken a detailed investigation of the structure and properties of the synthetic allomelanin produced by the biomimetic oxidation of 1,8-DHN with the peroxidase/hydrogen peroxide system.[5,6] Herein we report: a) the first isolation and structural characterization of the main oligomer intermediates in the oxidative polymerization of 1,8-DHN to melanin; b) a DFT approach to the mechanism of polymerization; c) an integrated characterization of 1,8-DHN allomelanin by mass spectrometry, solid state NMR, EPR and UV-visible spectroscopy; d) the preparation, morphological characterization and cell compatibility of thin films obtained by solid state polymerization of 1,8-DHN. The potential biomedical and technological applications of the new films will be briefly addressed.



References:

[1] Nicolaus, R.A., *In* Melanins. **1968**, Hermann, Paris. [2] Robinson, C.H. *New Phytol.* **2001**, *151*, 341–353. [3] Mironenko, N.V., Alekhina, I.A., Zhdanova, N.N., and Bulat, S.A. *Ecotoxicol. Environ. Saf.* **2000**, *45*, 177–187. [4] Novikova N, De Boever P, Poddubko S, Deshevaya E, Polikarpov N, Rakova N, Coninx I, Mergeay, M. *Res. Microbiol.* **2006**, *157*, 5–12. [5] Cecchini, M. M.; Reale, S.; Manini, P.; d'Ischia, M.; De Angelis, F. *Chemistry - A European Journal*, **2017**, *23*, 8092-8098. [6] Manini, P.; Bietti, M.; Galeotti, M.; Salamone, M.; Lanzalunga, O.; Cecchini, M. M.; Reale, S.; Crescenzi, O.; Napolitano, A.; De Angelis, F.; Barone, V.; d'Ischia, M. *ACS Omega*, **2018**, *3*, 3918–3927.

OC08

Chemically modified cycloparaphenylenes with novel optoelectronic and supramolecular properties.

P. Della Sala,[a] T. Caruso,[a] C. Talotta,[a] A. Capobianco, [a] M. De Rosa,[a] A. Soriente, [a] A. Peluso, [a] P. Neri [a] e C. Gaeta [a]

[a] *Dipartimento di Chimica e Biologia "A. Zambelli", Università degli Studi di Salerno, Via Giovanni Paolo II 132, I-84084 Fisciano (Salerno), Italy*
e-mail*: pdellasala@unisa.it*

Cyclo**P**ara**P**henylenes ([*n*]CPPs)[1] are fully conjugated macrocycles consisting of *n* para-linked benzene units (Figure 1) which have originally raised much interest as potential seeds for growing uniform single-walled carbon nanotubes.[2] CPPs possess intriguing size dependent optical and electronic properties,[1] arising from a delicate interplay between the macrocycle strain energy and the π-electron conjugation: the key feature is the narrowing of the HOMO-LUMO gap as the number of aromatic units decrease and consequently, the emission spectra of CPP derivatives are blue-shifted and quantum efficiency increases as the macrocycle become larger.[1] The introduction of new chemical susbstituents into the CPP skeleton affects the optoelectronic properties of those compounds, widening their field of potential applications. On these basis we have recently showed[3] that the anthracene-incorporated [8]CPP **1** undergoes visibile light up conversion in the presence of octaethylporphyrin Pd complex as sensitizer.[3] In addition, we have synthesized a [8]CPP derivative **2**[4] bearing an electron-rich 1,4-dimethoxybenzene ring and its optoelectronic properties have been studied by UV-vis spectroscopy, cyclic voltammetry, and DFT calculations. Finally the recognition abilities of CPP **2** towards pyridinium guests were investigated.[4]

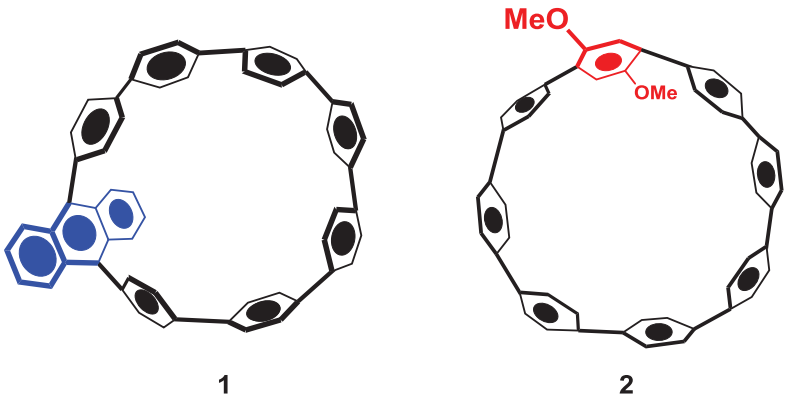


Figure 1: Chemical drawing of CPP derivatives **1** and **2** investigated in the present work.

References:

[1] E. R. Darzi, R. Jasti, *Chem. Soc. Rev*. **2015**, *44*, 6401–6410.
[2] H. Omachi, T. Nakayama, E. Takahashi, Y. Segawa, K. Itami, *Nat. Chem.* **2013**, *5*, 572–576.
[3] P. Della Sala, A. Capobianco, T. Caruso, C. Talotta, M. De Rosa, P. Neri, A. Peluso, C. Gaeta, *J. Org. Chem*. **2018**, *83*, 220–227.
[4] P. Della Sala, C. Talotta, T. Caruso, M. De Rosa, A. Soriente, P. Neri, C. Gaeta, *J. Org. Chem*. **2017**, *82*, 9885–9889.

OC09

Decorating carbon nanostructures with organics for advanced energy materials

T. Gatti,[a] E. Menna[a]

[a]*Dipartimento di scienze chimiche, Università di Padova, via Marzolo 1, Padova, Italy*
e-mail*: teresa.gatti@unipd.it*

We exploit organic functionalization of carbon nanostructures (CNSs), such as fullerenes, single and multi-walled carbon nanotubes (SWCNTs, MWCNTs) and graphene-based materials (GBMs) to achieve improvements in their dispersion in organic media, i.e. solvents and polymer phases. This last aspect is particularly appealing for the production of polymeric nanocomposites with potential uses as stimuli-responsive smart materials in several applications, ranging from optoelectronics to sensing and biomedicine.[1]

We recently mainly focused on the diazotization process, commonly referred to as Tour reaction,[2] to produce functionalized CNS derivatives, which can be employed as nano-fillers for polymer phases, improving the homogeneity of the dispersion and the physical properties of the final nanocomposite. The 1,3 dipolar cycloaddition of azomethine ylides to double bonds in CNSs (also called Prato-reaction) is another functionalization process of which we often make use.[3]

Specifically, we targeted photovoltaic (PV) applications, by combining functionalized CNSs with semiconducting polymers, small molecules and surfaces.

In the field of non-conventional PV, we focus on perovskite solar cells (PSCs), contributing to the development of new materials for both hole[4] and electron transporting layers[5] and on dye sensitized solar cells (DSSCs), proposing novel organic dye-graphene hybrids as photosensitizers.[6]

During this talk, we will report on these findings, highlighting the advantages of our approach for future commercial applications and providing perspectives.

References:

[1] T. Gatti, N. Vicentini, M. Mba, E. Menna, *Eur. J. Org. Chem.* **2016**, 1071-1090. Microreview

[2] J. Bahr, J. Tour, *Chem. Mater.* **2001**, *13*, 3823.

[3] M. Maggini, G. Scorrano, M. Prato, *J. Am. Chem. Soc.* **1993**, *115*, 9798.

[4] a) T. Gatti, S. Casaluci, M. Prato, M. Salerno, F. Di Stasio, A. Ansaldo, E. Menna, A. Di Carlo, F. Bonaccorso, *Adv. Funct. Mater.* **2016**, *26*, 7443–7453. b) T. Gatti, F. Lamberti, P. Topolovsek, M. Abdu-Aguye, R. Sorrentino, L. Perino, M. Salerno, L. Girardi, C. Marega, G. A. Rizzi, M. A. Loi, A. Petrozza, E. Menna, *Solar RRL*, **2018**, DOI: 10.1002/solr.201800013.

[5] a) P. Topolovsek, F. Lamberti, T. Gatti, A. Cito, J. M. Ball, E. Menna, C. Gadermaier, A. Petrozza, *J. Mater. Chem. A*, **2017**, *5*, 11882-11893. b) T. Gatti, E. Menna, M. Meneghetti, M. Maggini, A. Petrozza, F. Lamberti; *Nano Energy*, **2017**, *41*, 84-100.

[6] a) T. Gatti, N. Manfredi, C. Boldrini, F. Lamberti, A. Abbotto, E. Menna, *Carbon*, **2017**, *115*, 746-753. b) P. Guarracino, T. Gatti, N. Canever, M. Abdu-Aguye, M. A. Loi, E. Menna, L. *Franco Phys. Chem. Chem. Phys.*, **2017**, *19*, 27716-27724.

OC10

Tailor made functionalizations of graphene layers and their application as carbocatalyst for organic reaction

V. Barbera,[a] M. Galimberti,[a] L. Brambilla,[a] R. Bongiovanni,[b] A. Vitale[b], A. Porta,[a] G. Torrisi[a]

[a] *Politecnico di Milano, Department of Chemistry, Materials and Chemical Engineering "G. Natta", Via Mancinelli 7, 20131 Milano, Italy*

[b] *Politecnico di Torino, Department of Applied Science and Technology, Corso Duca degli Abruzzi 24, 10129 Torino, Italy*

e-mail: vincenzina.barbera@polimi.it

Over the last decades, huge interest and research activity have been focused on sp^2 carbon allotropes with nanosize and high aspect ratio, hence with high surface area. It is widely acknowledged that carbon nanotubes, graphene and graphene related materials have outstanding mechanical, electrical and thermal properties.[1] Such properties are essentially due to their six atoms aromatic ring core. In this field, graphene functionalization has great importance. Functional groups affect electronic and solubility properties, self-assembly and phase forming behaviour and can promote further reactions.

In this work functionalizations of sp^2 carbon allotropes were performed, modifying their solubility parameter without appreciably altering their chemical and bulk structure, and to use them as catalyst for organic reaction and as building blocks for innovative polymer nanocomposites. Functionalization methods used were inspired to the basic principle of green chemistry, using easily available chemicals.[2-4] Graphene layers (G) were then decorated with hydroxyl (G-OH), aldehydic (G-CHO) and carboxy groups (G-COOH). Tuning of reaction conditions led to obtain selective edge functionalization of graphene layers (Figure 1).[4]

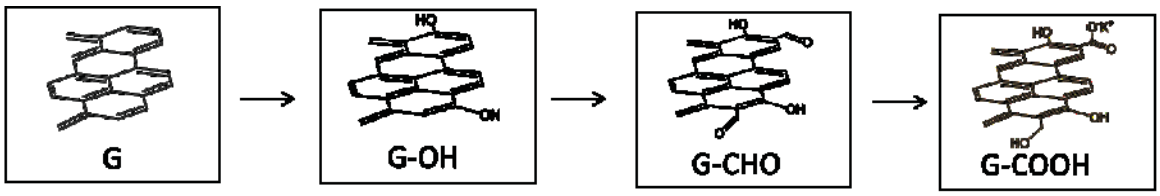


Figure 1: Block diagram describing the synthetic route adopted in this work.

References:

[1] K. Novoselov, D. Jiang, *F.* Schedin, T.J. Booth, V.V. Khotkevich, S.V. Morozov, & A.K. Geim, *Science* **2004**, *306*, 666 – 669.

[2] V. Barbera, A. Porta, L. Brambilla, S. Guerra, A. Serafini, A.M. Valerio, & M. Galimberti, *RSC Advances* **2016**, *6*, 87767 – 87777.

[3] V. Barbera, A. Bernardi, A. Palazzolo, A. Rosengart, L. Brambilla, M. Galimberti, *Pure Appl. Chem.* **2018,** 90, 253–270.

[4] V. Barbera, L. Brambilla, A. Porta, R. Bongiovanni, A. Vitale, G. Torrisi, M. Galimberti, *J. Mater. Chem. A,* **2018**, Accepted Manuscript. The article was first published on 03 Apr 2018. http://dx.doi.org/10.1039/C8TA01606BV.

OC11

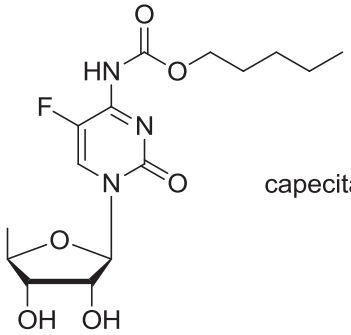
Biocatalytic Approach to the Synthesis of Pharmacologically Active Compounds

P. Ferraboschi,[a] S. Ciceri,[a] B. Guidi,[a] S. Reza Elahi,[a] P. Grisenti[b]

[a]*Dipartimento di Biotecnologie Mediche e Medicina Traslazionale, Università degli Studi di Milano, Via Saldini 50, 20133 Milano, Italy*
[b]*Serichim Srl, Piazzale Marinotti 1, 33050 Torviscosa (UD), Italy*
e-mail*: samuele.ciceri@guest.unimi.it*

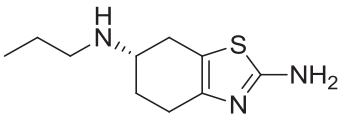
Several pharmacologically active compounds present in their structure different functional groups and stereocenters so, for their synthesis, chemo-, regio-, stereoselective transformations are required. This selectivity can be achieved using biocatalysis (enzymes and microorganisms).
The aim of our work is the preparation of some pharmacologically active compounds using biocatalytic methodologies which can lead to important improvements compared to traditional approaches, such as better yields and shorter synthetic pathways. Moreover, the use of biocatalysts in synthesis is a green approach.

For example, in our laboratory through a regioselective transformation catalysed by an enzyme, Alcalase CLEA, we have achieved the synthesis of capecitabine (Xeloda), an antitumor with a nucleosidic scaffold.

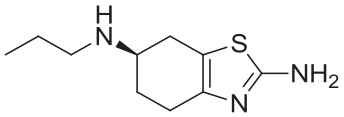


capecitabine (Xeloda)

After the investigation of the activity of different enzymes and microorganisms we have obtained both the enantiomerically pure synthons for the preparation of (S)-pramipexole, a synthetic dopaminergic agonist utilized as anti-Parkinson agent, and (R)-pramipexole, which has been studied for the treatment of amyotrophic lateral sclerosis (ALS).



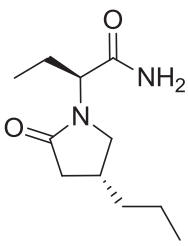
(S)-pramipexole



(R)-pramipexole

With a similar biocatalytic approach is under development the synthesis of brivaracetam, a novel anticonvulsant drug. The crucial step of the synthesis of this molecule is the obtainment of the stereocenter bearing the propyl moiety with the proper configuration.

The preliminary results are very encouraging and this biocatalytic method could be very interesting in a future application on large scale.



brivaracetam

OC12

Novel Curcumin-like derivatives can modulate toxic Tau Oligomers

A. Palumbo Piccionello,[a] F. Lo Cascio,[b] P. Marzullo,[a] S. Buscemi,[a] A. Pace,[a] R. Kayed[b]

[a]*Università degli Studi di Palermo, Dip. STEBICEF, V.le delle Scienze Ed.17, Palermo*
[b] *University of Texas Medical Branch-UTMB, Galveston, TX, USA*
e-mail*: antonio.palumbopiccionello@unipa.it*

Alzheimer's Disease (AD) is a devastating age-related neurodegenerative disorder characterized by the pathological aggregation and accumulation of Beta-Amyloid Peptide (Aβ) and the microtubule-associated protein tau.[1] Their subsequent deposition in different aggregated form includes Senile Plaques and neurofibrillary tangles (NFTs). Recent research suggest that these forms are less toxic form of such aggregates. However, the smaller, dynamic and soluble oligomers have been shown to be more toxic and efficient seeds for the propagation of pathology.[2] Thus, depleting the disease-relevant structures by using small molecules could be a powerful therapeutic strategy that targets toxicity regardless of other factors involved in the formation of toxic oligomeric strains.[3]

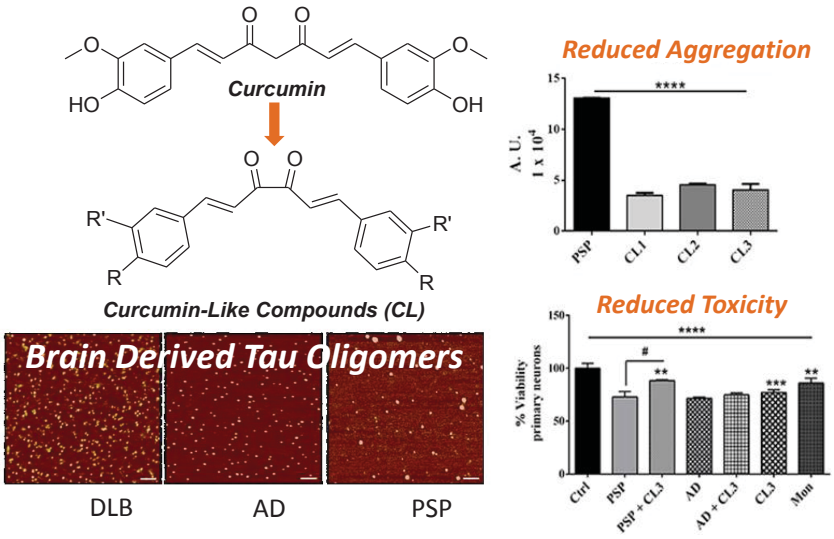


Figure 1.

Herein we synthetized and screened new curcumin-like compounds to target and modulate tau oligomeric strains toxicity. Modulating their conformations through the use of novel curcumin derivatives, could be useful for the prevention of tau oligomers formation and toxicity. We used in vitro techniques as well as biophysical assays to characterize oligomeric aggregates and their reactivity in the presence and absence of curcumin derivatives. Interestingly, novel curcumin derivatives bind and are able to alter aggregation pathways of tau protein, resulting in the formation of structures with decreased toxicity (Figure 1).

References:

[1] I. W. Hamley, *Chem. Rev.* **2012**, *112*, 5147– 5192.
[2] J. Gerson, R. Kayed, *Curr. Pharm. Des.* **2016**, *22*, 4028 – 4039.
[3] A. Martorana, V. Giacalone, R. Bonsignore, A. Pace, C. Gentile, I. Pibiri, S. Buscemi, A. Lauria, A. Palumbo Piccionello, *Curr. Pharm. Des.* **2016**, *22*, 3971 – 3995.

OC13

Selective targeting of $\alpha_V\beta_3$ integrins with gold nanoparticles carrying RGD-semipeptides

R. Fiammengo,[a] V. Maggi,[a,e] F. Bianchini,[b] E. Portioli,[c] S. Peppicelli,[b] M. Lulli,[b] D. Bani,[d] R. Del Sole,[e] F. Zanardi,[c] A. Sartori,[c]

[a]Center for Biomolecular Nanotechnologies@UniLe, Istituto Italiano di Tecnologia (IIT), Via Barsanti, 73010 Arnesano, Lecce; [b]Department of Experimental and Clinical Biomedical Sciences "Mario Serio", University of Florence, Viale Morgagni 50, 50134, Florence; [c]Food and Drug Department, University of Parma, Parco Area delle Scienze 27a, 43124 Parma; [d]Department of Experimental and Clinical Medicine, University of Florence, Viale Pieraccini 6, 50139 Florence; [e]Department of Engineering for Innovation, University of Salento, Via per Monteroni Km 1, 73100, Lecce.
e-mail*: Roberto.fiammengo@iit.it*

Effective and selective targeting of the $\alpha_V\beta_3$ integrin subtype is of high relevance in cancer research for the development of therapeutic systems and of diagnostic imaging probes.[1] In this contribution, we will discuss the molecular design, the preparation and characterization of a new class of highly selective, $\alpha_V\beta_3$-targeted gold nanoparticles (AuNPs), which carry cyclic 4-aminoproline-RGD semipeptides (cAmpRGD)[2] as the targeting moiety immobilized at low surface density on the poly(ethylene glycol) (PEG)-based nanoparticle coating.[3] We will show that these nanoparticles are potent inhibitors of integrin-mediated cell adhesion to vitronectin and that they are selectively internalized via receptor-mediated endocytosis by melanoma tumour cells M21. Furthermore, we have developed bifunctional cAmpRGD-functionalized AuNPs by conjugation of a fluorophore (FAM or TAMRA) to a separate set of reactive groups on the PEG-based coating. These bifunctional AuNPs not only recapitulate the binding properties of cAmpRGD-AuNPs but also can be visualized via confocal laser microscopy, allowing direct observation of nanoparticle internalization. The precisely defined architecture at the molecular level of these nanoparticles accounts for their selective integrin binding with very low nonspecific background.[4]

References:

[1] a) U. K. Marelli, F. Rechenmacher, T. R. A. Sobahi, C. Mas-Moruno, H. Kessler, *Front. Oncol.* **2013**, *3*; b) Z. Bakhtiary, A. A. Saei, M. J. Hajipour, M. Raoufi, O. Vermesh, M. Mahmoudi, *Nanomedicine (N. Y., NY, U. S.)* **2016**, *12*, 287-307; c) S. Liu, *Bioconjugate Chem.* **2015**, *26*, 1413-1438.

[2] F. Zanardi, P. Burreddu, G. Rassu, L. Auzzas, L. Battistini, C. Curti, A. Sartori, G. Nicastro, G. Menchi, N. Cini, A. Bottoncetti, S. Raspanti, G. Casiraghi, *J. Med. Chem.* **2008**, *51*, 1771-1782.

[3] L. Maus, O. Dick, H. Bading, J. P. Spatz, R. Fiammengo, *ACS Nano* **2010**, *4*, 6617-6628.

[4] V. Maggi, F. Bianchini, E. Portioli, S. Peppicelli, M. Lulli, D. Bani, R. Del Sole, F. Zanardi, A. Sartori, R. Fiammengo, *Submitted* **2018**.

OC14

Design of new selective VEGFR-2 Tyrosine kinase and COX-1 inhibitors for the inhibition of angiogenesis

G. Di Mauro,[a] A. Scilimati,[b] M.G. Perrone,[b] C.G. Fortuna,[a] C. Bonaccorso[a], F. Mugheddu[a]

[a] *Università degli Studi di Catania - Viale Andrea Doria, 6, 95125 Catania CT*
[b] *Università degli Studi di Bari Aldo Moro, Piazza Umberto I, 1, 70121 Bari BA*
e-mail*: dimauro.g@studium.unict.it*

The Vascular Endothelial Growth Factor (VEGFR) is the key regulator of physiological angiogenesis during the embryogenesis, skeletal growth and reproductive functions. There are 5 different structures: VEGFA, VEGFB, VEGFC, VEGFD and PIGF.

VEGFs are also involved in neoplasms, neovascular intraocular disorders and other diseases. The biological effects are leaded by two tyrosine kinase receptors (RTKs), VEGFR-A and VEGFR-2.[1]

Recently a correlation between the VEGFR-2 and COX-1 (Cyclooxygenase) has been observed.[2] COX-1 is involved in several diseases such as inflammation processes, arteriosclerosis and neoplasms.[3,4]

The activity is focused on the design of new selective VEGFR-2 and COX-1 inhibitors in order to induce an inhibition of angiogenesis.

Starting by natural compounds[5] and using chemoinformatics tools such as FLAP[6,7] (fingerprints for ligands and proteins), VolSurf+[8] and Metasite will be discovered new lead compounds. These tool allow to provide the ADME[9] results. Lead compounds will be modified in order to improve their activities and tested in vivo.

References:

[1] N. Ferrara, H.P. Gerber, *Nature Medicine* ***(2003)*** doi:10.1038/nm0603-669 , 9, 669 – 676.
[2] J. F. Murphy 2, D. J. Fitzgerald, *FASEB J.* ***2001*** *Jul*;15(9):1667-9.
[3] O. A. Belton, A. Duffy, S. Toomey, D. J. Fitzgerald, *Circulation* ***2003***, 108, 3017−2303.
[4] M. G. Perrone, A. Scilimati, L. Simone, P. Vitale *Curr. Med. Chem.* ***2010***, 17, 3769−3805.
[5] M. Feher, J. M. Schmidt, *Chem. Inf. Comput. Sci*., **2003**, 43 (1), pp 218–227.
[6] L. Siragusa; *Studio di Antagonisti del Recettore A2A tramite la Procedura Computazionale FLAP, tesi di master in Drug Design and Sythesis* ***(a.a. 2008/2009)***.
[7] M. Baroni, G. Cruciani; *J. Chem. Inf. Model.,* ***(2007)*** 47 (2), 279-294.
[8] G. Cruciani; *Corso di Modellistica Molecolare - Chimica Organica IV, Perugia* ***(a.a. 2007/2008)***.
[9] C.G. Fortuna, V. Barresi, G. Berellini, G. Musumarra; *Bioo. And Med. Chem.* ***(2008)*** 16, 41-50-4159.

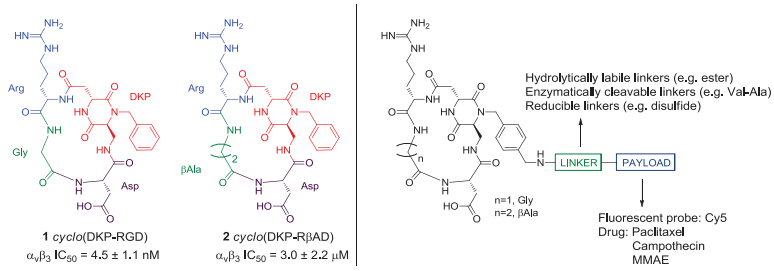
OC15

Synthesis and biological evaluation of new RGD-drug conjugates for tumor targeting via $\alpha_v\beta_3$ integrin

A. Pina,[a] A. Dean,[a] M. Caruso,[b] Laura Belvisi,[a,c] D. Arosio,[c] L. Pignataro,[a] A. Dal Corso,[a] C. Gennari[a,c]

[a] *Dipartimento di Chimica, Università degli Studi di Milano, Milano*
[b] *Nerviano Medical Sciences, Nerviano*
[c] *CNR, Istituto di Scienze e Tecnologie Molecolari (ISTM), Milano*
e-mail*: arianna.pina@unimi.it*

The conjugation of cytotoxic agents to targeting carriers (e.g. antibodies or small molecules) capable of selectively binding to tumor-specific antigens, is a successful strategy to enhance the efficacy of traditional chemotherapy.[1] Being over-expressed by several human tumors, $\alpha_v\beta_3$ integrin can be considered as a suitable target for cancer therapy. This transmembrane heterodimeric protein is efficiently recognized by the Arg-Gly-Asp (RGD) peptide and for this reason several RGD-bearing ligands have been conjugated to anticancer agents to improve their accumulation at the site of disease. There, the drug release is made possible by a "clever" linker, which should ideally be cleaved under the specific conditions of the tumor micro-environment (e.g. acidic pH, reductive conditions, enzyme over-expression).[2] Our research group has developed a potent peptidomimetic ligand of $\alpha_v\beta_3$ integrin, based on the RGD sequence and a diketopiperazine (DKP) scaffold: *cyclo*[DKP-RGD] (**1**).[3] The latter has been conjugated to a number of cytotoxic payloads through different linkers.[4] To evaluate the ability of these compounds to selectively target $\alpha_v\beta_3$+ tumor cells *in vitro,* we prepared an analogous conjugate, showing almost identical physical-chemical properties and the same linker-payload module, while exhibiting negligible affinity for the integrin receptor. This "negative control" conjugate was synthesized by mutating the Gly residue of the RGD sequence into a β-alanine (**2**). In this communication, we describe the design and synthesis of new *cyclo*[DKP-RGD]-drug conjugates and their biological evaluation in comparison to the corresponding RβAD-bearing analogues. As expected, the resulting compounds with the *cyclo*[DKP-RβAD] peptidomimetic exhibited a 1000-fold lower integrin affinity than the parent RGD-bearing conjugates. The direct comparison between the RGD- and RβAD-drug conjugates in cell-viability assays (using tumor cells overexpressing integrin $\alpha_v\beta_3$) attests the potential of RGD peptidomimetics as tools for selective delivery of cytotoxic agents.



References:

[1] T. Lammers, G. Storm *et al*., *J. Control. Release* **2012**, *161*, 175-187. [2] A. Dal Corso, C. Gennari *et al*., *Curr. Top. Med. Chem.* **2016**, *16*, 314-329. [3] M. Marchini, C. Gennari *et al*., *Chem. Eur. J.* **2012**, *18*, 6195-6207. [4] a) R. Colombo, C. Gennari *et al.*, *J. Med. Chem*. **2012**, *55*, 10460-10474; b) A. Dal Corso, C. Gennari *et al*., *Chem. Eur. J*. **2015**, *21*, 6921-6929; c) A. Pina, C. Gennari *et al.*, *ChemistrySelect* **2017**, *2*, 4759-4766; d) P. López Rivas, C. Gennari, U. Piarulli *et al.*, *Beilstein J. Org. Chem*. **2018**, *14*, 407-415.

Acknowledgements: We gratefully acknowledge MIUR (PRIN project 20157WW5EH) for funding. A. Dean thanks the Erasmus+ Programme for a fellowship.

OC16

Synthesis of 2-acylbenzonitriles and their reactivity in tandem reactions: easy access to isoindolinones with a tetrasubstituted stereocenter.

A. Massa, F. Romano, A. Di Mola

Dipartimento di Chimica e Biologia "A. Zambelli", Università di Salerno,
Via Giovanni Paolo II, 132, 84084 Fisciano, (SA), Italy.
e-mail*: amassa@unisa.it*

The interest of the chemical community towards "one-pot" reactions increased rapidly over the past two decades. These processes, which also include tandem reactions, are characterized by a high level of atom and step economy.[1] Tandem reactions are often used to prepare heterocycles of high biopharmacological value.[2] To facilitate the reaction design, the utilization of bifunctional building blocks in tandem reactions has emerged as an important research area of organic chemistry. However, most of the bifunctional compounds are not easy to synthesize due to the difficulty of installing two or more reactive sites into one molecule. Many 2-substituted benzaldehydes belong to this class and have been widely used in tandem reactions for the synthesis of heterocyclic compounds. Particularly in recent years, one-pot cross aldol-initiated tandem reactions of 2-formylbenzonitriles (2-cyanobenzaldehydes) have become a powerful tool for the synthesis of several heterocyclic compounds of great value.[3] In this context, even though ketones are less electrophilic than aldehydes, the investigation of the reactivity of 2-acylbenzonitriles and related ketones appears to be of high interest because of the possibility to obtaining derivatives with tetrasubstituted stereocenters in a single pot process. Thus, in the present communication, the scope and the great synthetic utility of bifunctional aromatic ketones as *eletrophiles* in tandem reactions will be discussed (Figure 1).[4] In addition, a convenient synthesis of 2-acylbenzonitriles starting from readily available materials is proposed (Figure 1).[4]

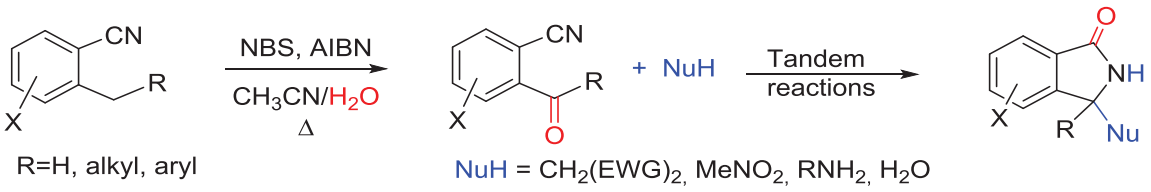


Figure 1: Oxidation of 2-alkylbenzonitriles and tandem reactions of the obtained ketones

References:

[1] a) T. Chanda, J.C.-G. Zhao, *Adv. Synth. Catal*. **2018**, *360*, 2. b) A. Grossmann, D. Enders, *Angew. Chem. Int. Ed.* **2012**, *51*, 314. c) D. E. Fogg, E. N. dos Santos, *Coord. Chem. Rev*. **2004**, 2365. d) L. F. Tietze, U. Beifuss, *Angew. Chem. Int. Ed. Engl*. **1993**, 131.

[2] P. Ravichandiran, B. Lai, Y. Gu, *Chem. Rec*. **2017**, *17*, 142.

[3] c) A. Massa, A. Roscigno, P. De Caprariis, R. Filosa, A. Di Mola, *Adv. Synth. Catal*. **2010**, 3348. d) C. Petronzi, S. Collarile, G. Croce, R. Filosa, P. De Caprariis, A. Peduto, L. Palombi, V. Intintoli, A. Di Mola, A. Massa, *Eur. J. Org. Chem*. **2012**, 5357

[4] a) V. Capaccio, A. Capobianco, A. Stanzione, G. Pierri, C. Tedesco, A. Di Mola, A. Massa, L. Palombi, *Adv. Synth. Cat.* **2017**, *359,* 2874. b) A. Di Mola, M. Di Martino, V. Capaccio, G. Pierri, L. Palombi, C. Tedesco, A. Massa *Eur. J. Org. Chem*. **2018** 10.1002/ejoc.201800240.

OC17

Blue enzymes for green chemistry: Laccases-catalyzed dimerization of substituted phenols

S. Riva,[a] I. Bassanini,[a] P. Gavezzotti,[a] D. Monti.[a]

[a]*Istituto di Chimica del Riconoscimento Molecolare, C.N.R.*
via Mario bianco 9, 20131 Milano
e-mail*: sergio.riva@icrm.cnr.it*

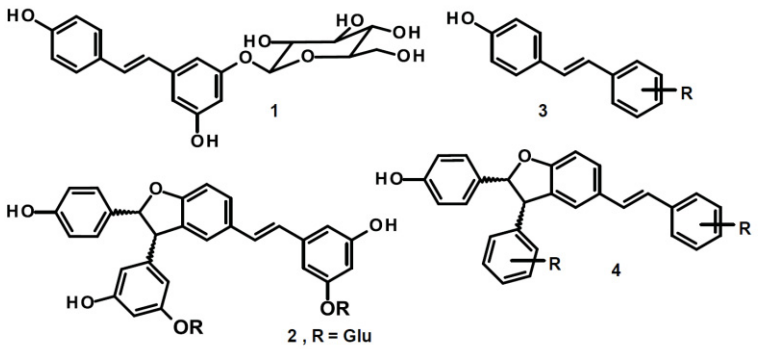
Laccases are oxidoreductases belonging to the multinuclear copper-containing oxidases. The overall outcome of their catalytic cycle is the reduction of one molecule of oxygen to two molecules of water and the concomitant oxidation of four substrate molecules to give four radicals.[1]

Typical substrates of laccases are phenols and aliphatic or aromatic amines, the reaction products being usually mixtures of dimers or oligomers derived by the coupling of the reactive radical intermediates. However, this is not always the case, and in the past years we exploited this biocatalyzed oxidative reaction to isolate new dimeric derivatives of natural phenols, i.e., resveratrol and its analogues, β-estradiol, totarol, sylibin and its analogues. In these studies, quite often a significant influence of the solvent on the reaction outcomes was also been observed.[2]

In this presentation two recent examples will be discussed.

The laccase-catalyzed oxidation of piceid, the 3-β-glucopyranoside of resveratrol (**1**) gave the corresponding trans-dehydrodimer **2**. In a further enzymatic elaboration, compound **2** was submitted to the action of a small library of commercially available hydrolases. While the cellulase from Trichoderma viride was able to fully hydrolyze the diglycosylated dimer, the β-glucosidase from almonds allowed the isolation of a monoglycosylated intermediate. The isomeric products could be isolated as pure diastereoisomers or enantiomers on a preparative scale using a semipreparative chiral column.[3]

In another investigation, the (homo)-coupling of (E)-4-styrylphenols (3) allowed the facile, versatile and selective synthesis of a library of substituted (E)-2,3-diaryl-5-styryl-trans-2,3-dihydrobenzofurans (**4**), potential allosteric modulators of the Heat shock protein 90 (Hsp90).[4]



References:

[1] a) D. Monti, G. Ottolina, G. Carrea, S. Riva *Chem. Rev.* **2011***, 111*, 4111-4140, b) S. Riva, *Trends Biotechnol.* **2006**, *24*, 219-226.

[2] S. Ncanana, L. Baratto, L. Roncaglia, S. Riva, S.G. Burton *Adv. Synth. Catal*. **2007**, *349*, 1507-1513.

[3] P. Gavezzotti, F. Bertacchi, G. Fronza, V. Křen, D. Monti, S. Riva *Adv.Synth.Catal*. **2015**, *357*, 1831-9.

[4] I. Bassanini, I. D'Annessa, M. Costa, D. Monti, G. Colombo, S. Riva, *Org. Biomol. Chem.,* **2018**, DOI: 10.1039/C8OB00644J.

OC18

Targeted surface functionalization of poly(lactic acid) and lignocellulosic materials using laccases and cutinases: taking inspiration from nature

L. Gardossi,[a] A. Pellis,[b] G.M. Guebitz,[b] N. Cefarin,[c] L. Vaccari,[c] C. Ebert,[a] M. Cespugli.[a]

[a]*Università degli Studi di Trieste, Dipartimento di Scienze Chimiche e Farmaceutiche, Trieste, Italy*

[b] *University of Natural Resources and Life Sciences, Institute for Environmental Biotechnology, Konrad Lorenz Strasse 20, 3430 Tulln an der Donau, Austria.*

[c] *Elettra - Sincrotrone Trieste, Synchrotron Infrared Source for Spectroscopy and Imaging – SISSI, 34149, Basovizza, Trieste, Italy.*

e-mail*: gardossi@units.it*

Biocatalysts have the potential of adding higher value to biopolymers and bio-based polymers by catalyzing targeted modifications and degradations that are not possible with conventional chemical strategies.[1,2] Here we present the application of laccases and cutinases for surface modification of lignocellulosic composite materials and poly(lactic acid) (PLLA) respectively. These enzymes are very different for their mechanisms but they are both biosynthesized in nature by fungi that have evolved the ability to attack and degrade superficial layers on plants, either the bark or the cutin of leaves. Their high efficiency under mild conditions was exploited in the present study for introducing carboxylic , hydroxyl and aldehyde groups, which are prone for further functionalization and the anchoring of biomolecules. Most importantly, this enzymatic approach introduced surface functionalization while leaving the bulk properties of the materials unchanged. In all cases, the experimental work was combined with computational studies in order to elucidate the molecular basis of enzyme efficiency and stability.

Poly(lactic acid) (PLLA), as a biodegradable thermoplastic polyester, has received increasing attention for a wide range of applications such as food packaging, textiles and biomedical devices. Enzymatic hydrolysis of the PLLA film was achieved using *Humicola insolens* cutinase, which increased the number of hydroxyl and carboxylic groups on the outer polymer chains. The negative charges generated on the PLA films was exploited for loading with the positively charged doxorubicin.

Laccases are some of the few oxidoreductases commercialized as industrial catalysts, with applications in biobleaching, dye decolorization, diagnostic, and synthetic uses. These enzymes exhibit broad substrate specificity towards monophenols, diphenols, aminophenols, polyphenols, aryl amines, and this can be enhanced by the addition of redox mediators.[4] We have employed laccases for the oxidation of the cellulosic component of rice husk in the presence of TEMPO mediator. The functionalized rice husk was characterized morphologically to confirm the integrity of the bulk structure of rice husk. The obtained aldehyde groups were then conjugated to a different enzymes that were experimentally tested for their activity.[5] The modification of rice husk surface opens new perspectives for the exploitation of this widely available lignocellulosic biomass as carriers for biomolecules but also as inexpensive adsorbent material for environmental applications.

References:

[1] A. Pellis, et al. *Process Biochem*., **2017**, 59, 77-83. [2] A. Pellis , et al., *Green Chem*., **2017**, 2017,19, 490-502 [3] V. Ferrario, et al., *Catalysts* **2016**, 6, 205; https://doi.org/10.3390/catal6120205 [4] V. Ferrario et al., *ChemBioChem*, **2015**, 16, 2365-2372. [5] L. Corici, et al., *RSC Adv*., **2016**, 6, 63256-63270.

OC19

Organocatalysis and Molecular Machines: the Development of an Autonomous Chemically Fuelled Small Molecule Motor

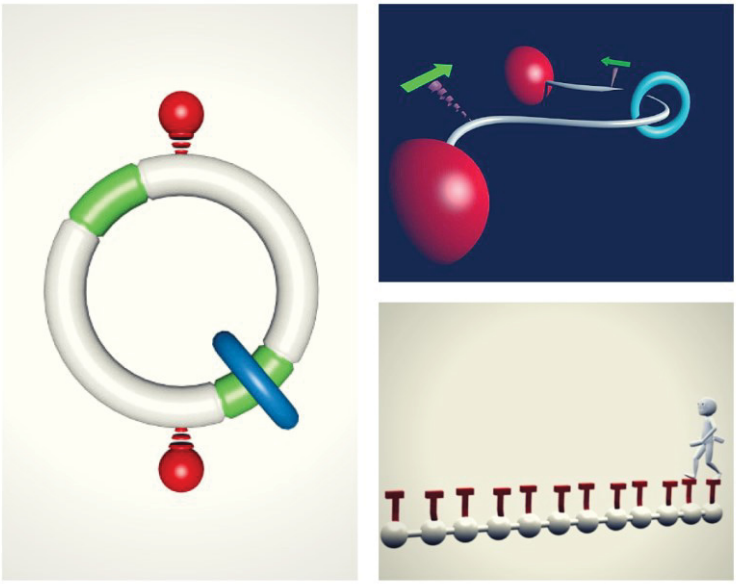
A. Carlone[a]

[a]*Università degli Studi dell'Aquila, Department of Physical and Chemical Sciences, via Vetoio, 67100 L'Aquila*
e-mail*: armando.carlone@univaq.it*

Over the last two decades, organocatalysis[1] has become an established and powerful synthetic tool for the chemo- and enantioselective functionalisation of organic compounds, and has already had significant impact in the synthesis of natural products, intermediates for pharmaceuticals and other structurally complex biologically active compounds.

In parallel, another exciting field has attracted a lot of interest; a number of synthetic molecular machines have been developed which enable controlled movement, including Brownian ratchets, molecular synthesisers, and walking molecules. Biological processes commonly use molecular motors to drive chemical systems away from equilibrium thus enabling work to be done. This has inspired efforts to create synthetic rotary motors which mimic the key properties of their biological counterparts, namely autonomy and directionality with the use of a chemical fuel.

The combination of organocatalysis and molecular motors enabled, for the first time, the incorporation of autonomy, directionality and the use of a chemical fuel in a synthetic rotary motor.[2] The design, synthesis and operation of an autonomous, chemically-fuelled, directional rotary motor will be discussed.



References:

[1] P. Melchiorre; M. Marigo; A. Carlone; G. Bartoli *Angew. Chem., Int. Ed.* **2008**, *47*, 6138−6171.

[2] a) A. Carlone, S. M. Goldup, N. Lebrasseur, D. A. Leigh, A. Wilson, *J. Am. Chem. Soc.*, **2012**, *134*, 8321-8323; b) A. G. Campaña, A. Carlone, K. Chen, D. T. F. Dryden, D. A. Leigh, U. Lewandowska, K. M. Mullen, *Angew. Chem. Int. Ed.*, **2012**, *51*, 5480-5483; c) M. R. Wilson, J. Solà, A. Carlone, S. M. Goldup, N. Lebrasseur, D. A. Leigh, *Nature,* **2016**, *534*, 235-240.

OC20

Understanding KuQuinones Equilibria in Solution

F. Sabuzi[a], O. Bortolini[b], B. Floris[a], V. Conte[a], P. Galloni[a]

[a] *Università degli Studi di Roma Tor Vergata, Via della Ricerca Scientifica, 00133 Roma*
[b] *Università di Ferrara, via Luigi Borsari 46, 44121 Ferrara*
e-mail*: federica.sabuzi@uniroma2.it*

In 2012, we described a one-pot reaction for the synthesis of a new class of quinoid compounds, called KuQuinones (KuQs).[1] The pentacyclic and fully conjugated structure of KuQs is a crucial feature for their application as dye sensitizers in photoelectrochemical devices,[2] being responsible for their intense and broad absorption in the visible region of the spectrum. However, changing solvent properties significant variations affecting molar extinction coefficients and spectrum shape were observed.[1,3] Considering the structural features of KuQuinones, the intramolecular hydrogen bond between enol oxygen and the vicinal carbonyl oxygen has a fundamental role: since KuQuinones contain two naphthoquinone units, keto−enol tautomerization (that leads to the generation of four different species, i.e., the *enol*, the *enolate*, the *external enol* and the *diquinoid* species) could be the cause of such spectral variations. Keto−enol tautomerization of diketones has been previously investigated and it is established that keto/enol ratio is generally dependent on the solvent polarity.[4]

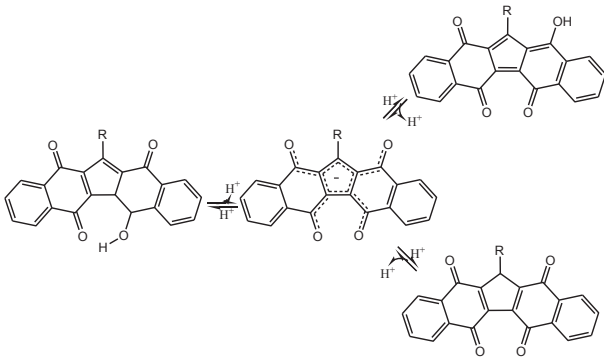


Figure 1. Possible keto-enol tautomerism in KuQuinones.

The comprehension of tautomeric equilibria of KuQuinones is strongly required in order to explain their behavior in solution and in biological environment. In this communication, a detailed study of KuQuinones in solution will be presented, using UV-vis and ^{1}H NMR spectroscopies and experimental data will be compared with theoretical ones obtained using DFT calculations.

References:

[1] A. Coletti, S. Lentini, V. Conte, B. Floris, O. Bortolini, F. Sforza, F. Grepioni, P. Galloni, *J. Org. Chem.* **2012**, *77*, 6873−6879.

[2] F. Sabuzi, V. Armuzza, V. Conte, B. Floris, M. Venanzi, P. Galloni, E. Gatto, *J. Mater. Chem. C* **2016**, *4*, 622-629; M. Bonomo, F. Sabuzi, A. Di Carlo, V. Conte, D. Dini, P. Galloni, *New J. Chem*. **2017**, *41*, 2769-2779.

[3] F. Sabuzi, S. Lentini, F. Sforza, S. Pezzola, S. Fratelli, O. Bortolini, B. Floris, V. Conte, P. Galloni, *J. Org. Chem*. **2017**, *82*, 10129-10138.

[4] J. Emsley, *Struct. Bonding. (Berlin)* **1984**, *57*, 147−191.

OC21

From fluorescent nucleosides to emissive cofactors

A. Fin,[a,b] A. R Rovira,[a] F. Hallé,[a] Y. Tor,[a] G. Viscardi[b]

[a] *Department of Chemistry and Biochemistry, University of California San Diego 9500 Gilman Drive, La Jolla, CA 92093-0358*

[b]*Dipartimento di Chimica, Università degli Studi di Torino, Via Pietro Giuria 7 10125 Torino*

e-mail*: afin@ucsd.edu ; andrea.fin@unito.it*

Fluorescent nucleoside analogs have been developed to overcome the non-emissive nature of the natural occurring DNA and RNA building blocks. Isomorphic structure to the native counterpart along with remarkable photophysical features are key parameters in the implementation of artificial nucleosides and their derivatives for the investigation of biological relevant structures and processes.[1,2] Here we present the synthetic preparation of two families of emissive and isomorphic nucleosides and their chemo-enzymatic conversion into biological relevant cofactors, analogs of S-Adenosyl methionine (SAM) and Nicotinamide adenine dinucleotide (NAD).[3-5] Enzyme-mediated reactions with the thiophene and/or the isothiazole-based cofactors have shown results comparable to the natural analogs. The unique photophysical properties of these probes allowed monitoring relevant enzymatic processes in vitro by real-time fluorescence spectroscopy, suggesting potential utility in the design of biophysical assays in living system.

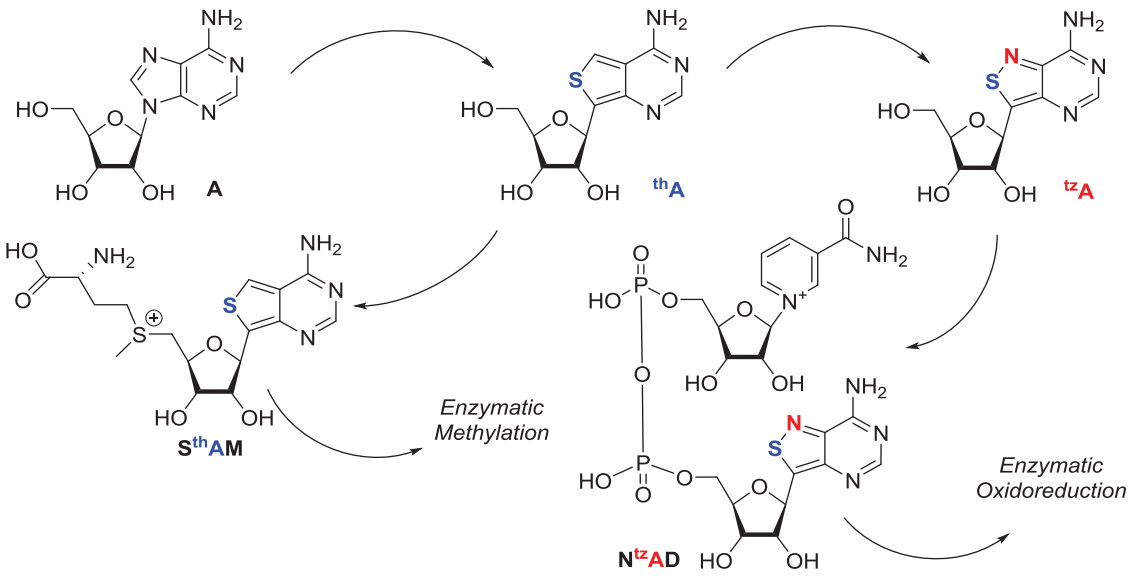


Figure 1: Thiophene and isothiazole-based emissive nucleosides and cofactors.

References:

[1] D.Shin, R. W. Sinkeldam, Y. Tor, *J. Am. Chem. Soc.* **2011**, *133*, 14912 – 14915.

[2] A. R. Rovira,, A. Fin, Y. Tor, *J. Am. Chem. Soc.* **2015**, *137*, 14602 – 14605.

[3] C. Vranken, A. Fin, P. Tufar, J. Hofkens, M. Burkart, Y. Tor, *Org. Biomol. Chem.* **2016**, *14*, 6189 – 6192.

[4] A. R. Rovira,, A. Fin, Y. Tor, *J. Am. Chem. Soc.* **2017**, *139*, 15556 – 15559.

[5] F. Hallé, A. Fin, A. R. Rovira, Y. Tor, *Angew. Chem. Int. Ed.* **2017**, *57*, 1087 – 1090.

OC22

Novel highly fluorescent water soluble spirobifluorene-based dye and its bio-applications

F. Rizzo,[a,b] F. Schlüter,[b] K. Riehemann,[c] N. S. Kehr,[c] S. Quici,[a] C. G. Daniliuc[b]

[a] *Istituto di Scienze e Tecnologie Molecolari (ISTM), Consiglio Nazionale delle Ricerche (CNR), via Golgi, 19, 20133 Milano, Italy*

[b] *Organic Chemistry Institute, Westfälische Wilhelms-Universität Münster, Corrensstrasse 40, 48149 Münster, Germany*

[c] *Physics Institute, Westfälische Wilhelms-Universität Münster and CeNTech, Heisenbergstrasse 11, 48149 Münster, Germany*

e-mail: *fabio.rizzo@cnr.it*

Despite the large variety of dyes reported so far, the combination of large Stokes shift, high molar extinction coefficient and high quantum yield (QY) to give high brightness values in aqueous solution,[1] as well as low cytotoxicity in the same molecule is still challenging. Among polyaromatic compounds, spirobifluorene-based emitters attract growing interest due to chemical stability and versatility allowing their use in several technological applications.[2] Nonetheless, the lack of water solubility precluded the application of spirobifluorene compounds in biological field to date.

Here, we disclose the synthetic approach to obtain the first water soluble spirobifluorene-based fluorescent dye and its interaction with proteins as model system for biological purposes.[3] The dye is characterized by high blue-greenish photoluminescence QY (50-70%) and very large Stokes shift (> 6000 cm^{-1}) in both organic and aqueous solution. Noteworthy, in presence of bovine serum albumin (BSA) the emission peak shows a hypsochromic shift with an impressive increased QY in water from 50% to 95%. The outstanding detection limit of BSA and the effect of BSA:dye interactions and local microenvironment on the emission will be also presented. Investigations on cellular uptake and cytotoxicity revealed that this chromophore is biocompatible and taken up by living cells, indicating the potential application for live cell imaging. To conclude, we show the earliest example of a new class of spirobifluorene-based emitters with outstanding fluorescent properties in water, opening novel scenario for bio-applications.

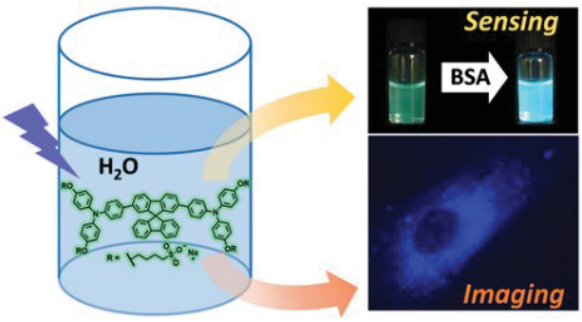


Figure 1: Chemical structure and bio-applications of the water soluble spirobifluorene dye.

References:

[1] H. Kobayashi, M. Ogawa, R. Alford, P.L. Choyke, Y. Urano, *Chem. Rev.* **2010**, *110*, 2620-2640.

[2] F. Rizzo, F. Polo, G. Bottaro, S. Fantacci, S. Antonello, L. Armelao, S. Quici, F. Maran, *J. Am. Chem. Soc.* **2017**, *139*, 2060-2069.

[3] F. Schlüter, K. Riehemann, N.S. Kehr, S. Quici, C.G. Daniliuc, F. Rizzo, *Chem. Commun*. **2018**, *54*, 642-645.

OC23

Organic sensitizers for dye-sensitized water splitting

C. L. Boldrini, N. Manfredi, A. Abbotto

Department of Materials Science and Solar Energy Research Center MIB-SOLAR, University of Milano-Bicocca, and INSTM Milano-Bicocca Research Unit, Via Cozzi 55, 20125 Milano, Italy
e-mail*: c.boldrini@campus.unimib.it*

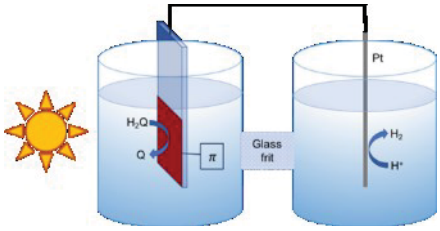


Figure 2: Scheme of a device for dye-sensitized generation of H_2 (π = organic sensitizer).

Among the new approaches to solar energy conversion, photoelectrochemical cells (PEC) represent an interesting solution to obtain hydrogen and oxygen from solar driven water splitting. Hydrogen is a clean fuel, with zero carbon footprint, and is very versatile since it can be used to produce electricity but also as an automotive fuel that ensures a far bigger range than batteries for electric cars.

Dye-sensitized PEC (DS-PEC) is an emerging technology, where the organic design is strategic in order to get improved performances. in the last years we have pioneered a multi-branched multi-anchoring D(-π-A)$_2$ geometry, now widely used in the field of dye-sensitized solar cells.[1]

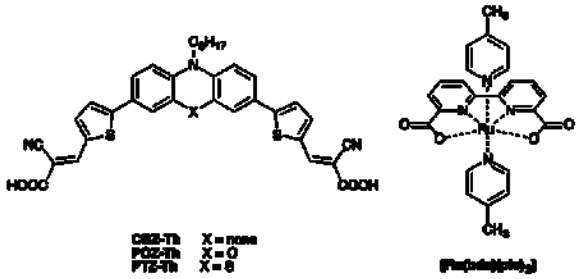


Figure 3: Sensitizers and Ru-catalyst investigated in this work.

In this work we present the first systematic study on specifically engineered di-branched dyes for water splitting in DS-PEC (Fig. 1). Namely, we tested D-(π-A)$_2$ dyes where D is a substituted phenothiazine, phenoxazine or carbazole donor core, A is the acceptor-anchoring cyano-acrylic group, and π is a thiophene spacer (Fig. 2), previously used in photocatalytic hydrogen production.[2, 3] The dyes were studied both in presence of a sacrificial electron donor (hydroquinone, H_2Q) and of a common Ru-based water oxidation catalyst (Ru(bda)pic$_2$). The reference dye (phenothiazine-based dye)[4] gave the best results thanks to its optical properties, IPCE and enhanced photocurrent in photoelectrochemical experiments.

References:

[1] N. Manfredi, B. Cecconi, A. Abbotto, *Eur. J. Org. Chem.* **2014**, 7069 (review).
[2] N. Manfredi, M. Monai, T. Montini, M. M. Salamone, R. Ruffo, P. Fornasiero, A. Abbotto, *Sustainable Energy Fuels*, **2017**, 1, 694-698.
[3] (A). N. Manfredi, M. Monai, T. Montini, F. Peri, F. De Angelis, P. Fornasiero, A. Abbotto, *ACS Energy Letters*, **2017**, DOI: 10.1021/acsenergylett.7b00896, 85-91. (B). N. Manfredi, B. Cecconi, V. Calabrese, A. Minotti, F. Peri, R. Ruffo, M. Monai, I. Romero-Ocana, T. Montini, P. Fornasiero, A. Abbotto, *ChemComm* **2016**, *52*, 6977.
[4] B. Cecconi, N. Manfredi, R. Ruffo, T. Montini, I. Romero-Ocaña, P. Fornasiero, A. Abbotto, *ChemSusChem* **2015**, *8*, 4216.

OC24

New D-π-A conjugates compounds for H_2 production by photoreforming of sacrificial electron donors (SEDs)

M. Calamante,[a,b] M. Bartolini,[a,b,c] M. Bessi,[a,c,d] O. Bettucci,[a,b,c] A. Dessì,[a] A. Mordini,[a,b] G. Reginato,[a] L. Zani[a]

[a] *Institute of Chemistry of Organometallic Compounds (CNR-ICCOM), via Madonna del Piano 10, 50019 Sesto Fiorentino, Italy.*

[b] *Department of Chemistry «U. Schiff», University of Florence, via della Lastruccia 13, 50019 Sesto Fiorentino, Italy.*

[c] *Department of Biotechnology, Chemistry and Pharmacy, University of Siena, via A. Moro 1, 53100 Siena, Italy.*

[d] *Université de Strasbourg, 1 rue Blaise Pascal, 67008 Strasbourg Cedex, France.*

e-mail*: mcalamante@iccom.cnr.it*

Organic dyes with D-π-A structure are commonly used as sensitizer in dye sensitizer solar cells (DSSC). Recently the use of this class of molecules are involved in the photocatalytic H_2 production.[1] The photocatalytic reforming is a valid approach to produce H_2 under ambient conditions and using sunlight, the cheapest energy source available on earth.

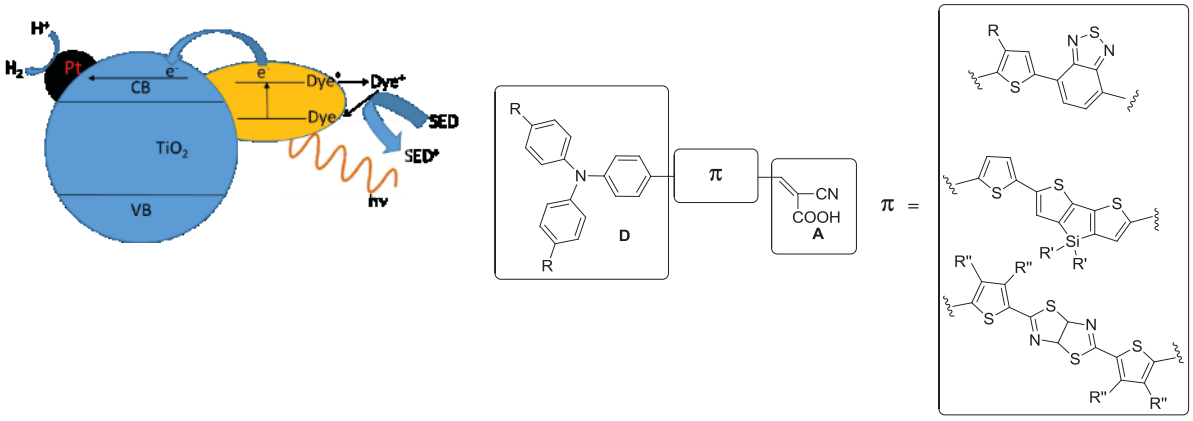


Figure 1: Mechanism of photocatalytic hydrogen production and dyes' structure.

This method of hydrogen production is also particularly advantageous if the sacrificial electron donor (SED) used comes from renewable sources (ethanol, methanol, glycerol, etc.). In this communication new D-π-A molecules for photocatalytic reforming will be presented. They are characterized by structural differences both as regards heterocyclic systems used and as regards the presence or absence of hydrophobic and hydrophilic side chains. Their synthesis, characterization and the efficiency in the production of hydrogen will be presented, highlighting how the structural differences can influence the choice of triethanolamine or ethanol as SED.[2]

References:

[1] B. Cecconi, N. Manfredi, T. Montini, P. Fornasiero,A. Abbotto *Eur. J. Org. Chem*., **2016**, 5194-5215.

[2] A. Dessì, M. Monai, M. Bessi, T. Montini, M. Calamante, A. Mordini, G. Reginato, C.Trono, P. Fornasiero, L. Zani, *ChemSusChem*, **2018**, *11*, 793-805.

OC25

Efficient Hole Transport Materials with Sulphur-Functional Groups Facilitating Hole Transfer in Perovskite Solar Cells

R. Grisorio,[a,b] Qiong Wang,[c] Christian Wolff,[d] Junming Li,[c] Dieter Neher,[d] G. P. Suranna,[a,b] Antonio Abate[c]

[a]*DICATECh—Politecnico di Bari, Via Orabona, 4 I-70125 Bari, Italy*
[b]*CNR-NANOTEC, c/o Campus Ecotekne, Via Monteroni, 73100 Lecce, Italy*
[c]*Helmholtz-Z. Berlin für Materialien und Energie, Kekuléstraße 5, 12489 Berlin, Germany*
[d]*Institute for Physics and Astronomy, University of Potsdam, Karl-Liebknecht-Straße 24−25, 14476 Potsdam-Golm, Germany*
e-mail*: roberto.grisorio@poliba.it*

Organic-inorganic lead halide perovskites have been firmly recognised as truly promising candidates to produce highly efficient photovoltaics.[1] In devices, the free photo-generated holes within the perovskite material need to be extracted and transported by suitable hole-transporting materials (HTMs).[2] To date, the highest reported efficiency values have been reached by using the expensive Spiro-OMeTAD. Several new HTMs have been conceived with the main effort to reduce the production costs of Spiro-OMeTAD.[3] Aiming at improving device performances, researchers are also focusing on optimization of the perovskite/HTM interface, where there are more possibilities to play manipulating the organic component. This communication deals with the synthesis and characterization of two new HTMs bearing sulphur functional groups, denoted as **FS** and **DFS** (Figure 1). Their properties as HTMs in perovskite solar cells are investigated with and without dopants. The time-resolved photoluminescence decay measurement together with the impedance spectra show a more efficient charge extraction for these new HTMs. As these two materials share similar highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) positions with respect to Spiro-OMeTAD, we attribute the enhanced hole extraction of **FS** and **DFS** to the difference in molecular structure. More specifically, we suspect that the sulphur functionality in these two HTMs bind with the superficial lead atoms of perovskite, promoting an alternative path for the hole extraction process. Moreover, while holding a similar photovoltaic performance (>18% at 1.0 Sun AM1.5G illumination), **FS** and **DFS** are synthesized at a much lower cost than that of Spiro-OMeTAD, paving the way to their future commercialization.

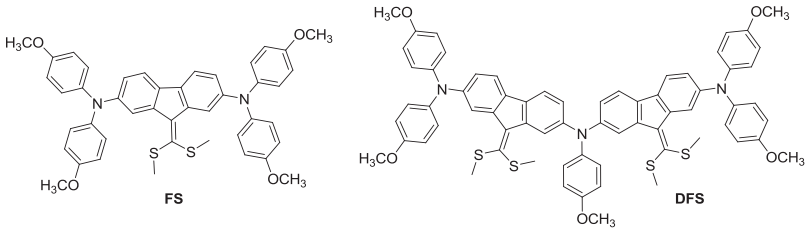


Figure 1: Molecular structure of the two HTMs **FS** and **DFS**.

References:

[1] A. Kojima, K. Teshima, Y. Shirai, T. Miyasaka, *J. Am. Chem. Soc.*, **2009**, *131*, 6050 – 6051.
[2] N. J. Jeon, J. H. Noh, W. S. Yang, Y. C. Kim, S. Ryu, J. Seo, S. I. Seok, *Nature*, **2015**, *517*, 476 – 480.
[3] M. Saliba, S. Orlandi, T. Matsui, S. Aghazada, M. Cavazzini, J. P. Correa-Baena, P. Gao, R. Scopelliti, E. Mosconi, K.-H. Dahmen, F. De Angelis, A. Abate, A. Hagfeldt, G. Pozzi, M. Graetzel, M. K. Nazeeruddin, *Nat. Energy*, **2016**, *1*, 15017-23.

OC26

Process Development of Enclomiphene Citrate: process chemistry remarks, solid state characterization and IP aspects

L. Caruana,[a] P.Padovan,[a] F.Fontana,[a] A. Paio[a], A. Leganza[a]

[a] *F.I.S. – Fabbrica Italiana Sintetici, Viale Milano 26, 36075 Montecchio Maggiore (VI)*

Clomiphene is a mixture of two geometric isomers, **Enclomiphene** (*E*-isomer) and **Zuclomiphene** (*Z*-isomer). **Enclomiphene** (trade name Androxal), is a non-steroidal estrogen receptor antagonist that promotes gonadotropin-dependent testosterone secretion by the testes. In clinical trials conducted to date, Enclomiphene demonstrated significant efficacy in the physiological restoration of testosterone levels in males with secondary hypogonadism. However, Enclomiphene also demonstrates promise in the management of secondary hypogonadism associated with obesity, metabolic syndrome and, possibly, infertility.

The obtainment of Enclomiphene by isomers separation from Clomiphene appeared to be known in the literature[1]. Thus, the aim of the project was the development and optimization of a route of synthesis for this API, which would have been sustainable from a cost point of view. Clomiphene citrate has been manufactured in FIS since several years and its synthesis had been subjected to several improvements over the time. For this reason, the most promising route in terms of raw material costs to obtain Enclomiphene citrate appeared to be the isomers separation from Clomiphene citrate. Since Clomiphene possesses a basic moiety, isomers separation was obtained by using as acidic resolving agent the commercially available racemic mixture of Binaphthyl Phosphoric Acid (BPA), giving two diastereroisomeric derivatives salts that were finally separated through selective crystallization. Given the great impact of BPA on the overall process costs, a procedure for its recovery was developed. Finally, a thoroughly investigation on polymorph forms of Enclomiphene Citrate was achieved, resulting in the identification of stable and non-hygroscopic needle morphology suitable for API formulation.

Despite the presence of some apparent prior art [1,2], it has been possible to get the valid patent protection for the Enclomiphene citrate having needle crystals in many jurisdictions such as EP, USA, Canada.[3]

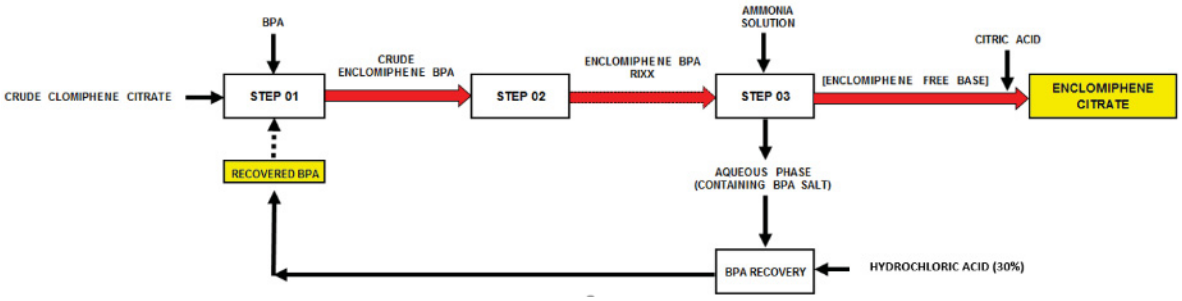


Figure 1: Process Flow Diagram.

References:

[1] US Patent number US3848030, N. R. Viterbo, J. Jacques, 12 November 1974.

[2] PCT Application WO2014031177, N. J. Podolski, K. HSU, 27 February 2014.

[3] European Patent number EP3083552B1, US patent number US9822063 (B2), Canadian patent number CA2943891 (C); P. Padovan *et al*.

OC27

Old fashioned Mathews' reaction for a new synthesis of Apremilast

S. Mantegazza,[a] E. Attolino,[a] G. Razzetti,[a]

[a]*Dipharma Francis S.r.l, Via Bissone 5, Baranzate*
e-mail*: simone.mantegazza@dipharma.com*

The Mathews' reaction[1,2] is a one pot preparation of a carboxylic acid and a phtalimide starting from the corresponding amide and phtalic anhydride (Figure1).

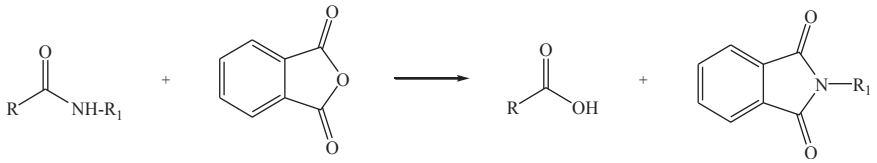


Figure 1: Mathews' reaction.

Even if this reaction has been known since the end of the 19th century, it is scarcely described in the scientific literature, not having been often applied in organic synthesis. In this communication a new synthetic route to Apremilast[3] will be presented, which makes use of a Mathews' reaction as key step. Apremilast is an active pharmaceutical ingredient used for the treatment of psoriasis and psoriatic arthritis. The process presented herein is novel and allows for a cheap preparation of Apremilast also suitable for scaling-up[4] in the pharmaceutical industry (Figure 2). The optical purity of the product is achieved by a traditional resolution via diastereomeric salt formation and the material with undesired configuration may be recycled in the process.

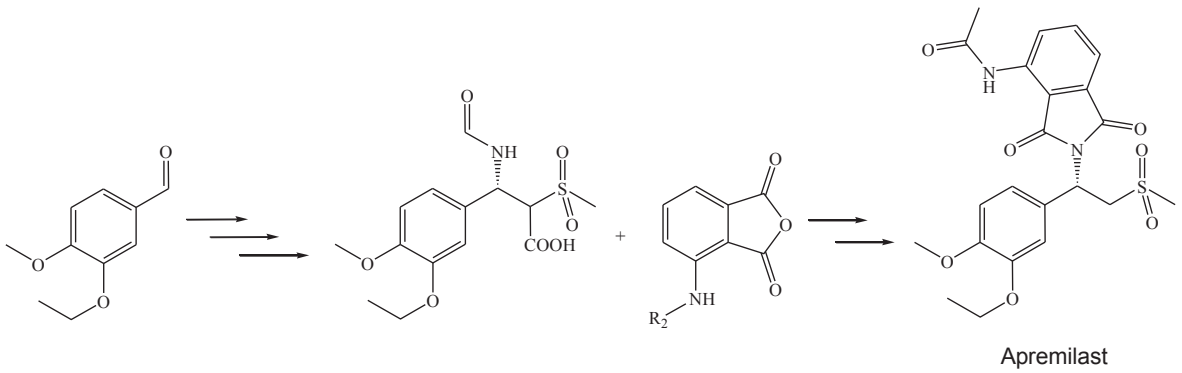


Figure 2: Apremilast synthetic route.

References:

[1] J. A. Mathews, *J. Am. Chem. Soc.* **1896**, *18*, 679 – 682.
[2] J. A. Mathews, *J. Am. Chem. Soc.* **1898**, *20*, 648 – 668.
[3] S. Mantegazza, E. Attolino, G. Razzetti, IT 102016-83132.
[4] S. Mantegazza, E. Attolino, G. Razzetti, IT 102017-20784.

OC28

Pirfenidone: process development and industrial scale up

J. Roletto,[1] P. Paissoni[1], M. Mossotti[1], A. Barozza[1]

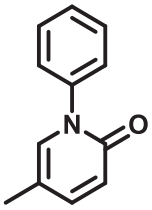
[1]*Procos S.p.A., via Matteotti 249, Cameri (NO)*

e-mail: roletto@procos.it

The development of a synthetic process for a generic API suitable for the commercial scale has to take into consideration several different factors: patents, safety, quality, regulatory, efficiency and costs. The final process is the optimized combination of all these elements.

On ground of several process patents, filed in the most recent years as demonstration of great economical interest, an innovative synthetic strategy for Pirfenidone is described.

The study of inherently safe and economically competitive process suitable for the industrial scale up (some hundreds of Kg/batch) is reported. The discussion includes the process optimization for the diazotisation reaction and for the copper (I) catalyzed *N*-arylation of amides (Goldberg-Ullman's reaction) with particular focus on the scalability of each process step.



OC29

Ammonium containing calixarenes as vectors for peptide nucleic acid (PNA) delivery

F. Sansone,[a] A. Finotti,[b] J. Gasparello,[b] A. Manicardi,[a] A. Casnati,[a] R. Corradini,[a] R. Gambari[b]

[a] *Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale, Università di Parma, Parco Area delle Scienze 17/a, 43124 Parma, Italy*

[b] *Dipartimento di Scienze della vita e biotecnologie, Università di Ferrara, Via Fossato di Mortara 74, 44121 Ferrara, Italy*

e-mail*: francesco.sansone@unipr.it*

Peptide nucleic acids (PNAs), DNA analogues in which the sugar-phosphate backbone is replaced by N-(2-aminoethyl)glycine units, efficiently hybridize with complementary DNA and RNA, forming dipex and triplex structures.[1] Due to these interesting properties, they have been proposed for antisense, anti-gene, anti-miR therapy in a number of studies,[1-3] and , more recently, they have been used for precise gene editing.[4] For these applications, however, one of the most important unresolved issues is the uptake by target cells. In fact, the major limit in the use of PNA for alteration of gene expression is the low uptake by eukaryotic cells. In order to solve this drawback, several approaches have been considered. A possible strategy already validated by some of us is to covalently link PNAs to polyarginine tails, based on the observation that these cell-membrane penetrating oligopeptides are able to facilitate uptake of conjugated molecules.[5]

As alternative to the chemical modification, for PNA delivery it results particularly interesting the use of carriers able to interact with the cargo in a non-covalent and reversible way.[6,7] This approach would allow in principle to make available a system effective with all native PNA sequences that are intended to transport into cells. Currently no particularly efficient systems of this type are available. To this end, we recently explored the use of ammonium containing calix[4]arenes[8] as PNA vectors.[9] Some of them evidenced high efficiency in delivery and negligible toxicity and the biological activity of the delivered PNA resulted maintained. These findings indicate these calixarene derivatives as potential universal vectors for the transport into cells of unmodified PNAs, drastically simplifying the study and application of these nucleic acid mimics as antisense or anti-gene molecules.

References:

[1] P.E. Nielsen *Chem Biodivers* **2010**, *7*, 786-804.

[2] C.J. Cheng, R. Bahal, I.A. Babar, Z. Pincus, F. Barrera, C. Liu, A. Svoronos, D.T. Braddock, P.E. Glazer, D.M. Engelman, W.M Salzman, F.J. Slack *Nature* **2014**, *518*,107-110

[3] Gambari R, Fabbri E, Borgatti M, Lampronti I, Finotti A, Brognara E, Bianchi N, Manicardi A, Marchelli R, Corradini R. *Biochem Pharmacol*. **2011**, *82*, 1416-1429.

[4] A.S. Ricciardi, E. Quijano, R. Putman, W.M. Salzman, P.E. Glazer, *Molecules* **2018**, *23*, 632

[5] E. Brognara, E. Fabbri, F. Aimi, A. Manicardi, N. Bianchi, A. Finotti, G. Breveglieri, M. Borgatti, R. Corradini, R. Marchelli, R. Gambari. *Int J Oncol*. **2012**;*41*, 2119-2127.

[6] C. Avitabile, A. Accardo, P. Ringhieri, G. Morelli, M. Saviano, G. Montagner, E. Fabbri, E. Gallerani, R. Gambari, A. Romanelli, *Bioconjug Chem.* **2015**, *26*, 1533-1541.

[7] A. Bertucci, E.A. Prasetyanto, D. Septiadi, A. Manicardi, E. Brognara, R. Gambari, R. Corradini, L. De Cola, *Small* **2015**, *11* , 5687-5695.

[8] V. Bagnacani, V. Franceschi, M. Bassi, M. Lomazzi, G. Donofrio, F. Sansone, A. Casnati, R. Ungaro, *Nat Commun.* **2013**, *4*:1721.

[9] Patent pending.

OC30

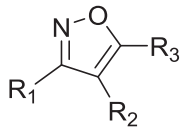
New Sustainable Strategies for the Synthesis of Biologically Active Polyfunctionalized Heterocycles

G. Lupidi,[a] C. Cimarelli,[a] E. Marcantoni,[a] P. Piermattei,[a] F. V. Rossi,[a] A. Aramini,[b] G. Bianchini,[b] S. Lillini,[c] M. Tomassetti[c]

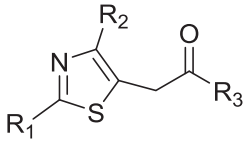
[a]*University of Camerino, School of Science and Technology, Chemistry Division, Via S. Agostino 1, 62032, Camerino (Italy)*
[b]*Dompé farmaceutici s.p.a.; Via Campo di Pile, 67100, L'Aquila (Italy)*
[c]*Dompé farmaceutici s.p.a.; Via Pietro Castellino 111, 80131, Napoli (Italy)*
e-mail*: gabriele.lupidi@unicam.it*

The polysubstituted heterocycles have a wide range of biological activities, and the introduction of appropriate functionalizations in a heterocyclic core is always an exciting area of research for organic and medicinal chemists. Even if the incorporation of functional groups in a pre-existing heterocycle is well studied, increasing the complexity of the system, regio- and chemoselectivity remain a big problem to overcome, especially in the presence of different heteroatoms. Only through the appropriate choices of the reaction conditions we were recently able to obtain the monofunctionalization of a primary hydroxyl group of the b-cyclodextrin without the use of protecting groups.

In the course of our program aimed at studying general methods for the selective synthesis of polysubstituted heterocycles,[1,2] we were able to develop cyclization of acyclic precursors that contain linearly encoded functional groups for giving targets with high regio- and stereochemical control.[3] Through the appropriate choice of the catalytic system or even better catalyst-free conditions, during this study we also were able to synthesize important building blocks in medicinal chemistry such as polysubstituted isoxazoles (**1**) and acylaminothiazoles (**2**).



1



2

References:

[1] R. Properzi, E. Marcantoni, *Chem. Soc. Rev.* **2014**, *43*, 779-791.
[2] M. Tomassetti, M. Fani, G. Bianchini, S. Giuli, A. Aramini, S. Colagioia, G. Nano, S. Lillini, *Tetrahedron Lett.* **2013**, *54*, 6247-6250.
[3] C. Cimarelli, S. Bordi, P. Piermattei, M. Pellei, F. Del Bello, E. Marcantoni, *Synthesis* **2017**, *49*, 5387-5395.

OC31

Building-up molecular complexity with carbenoids: New vistas in homologation chemistry

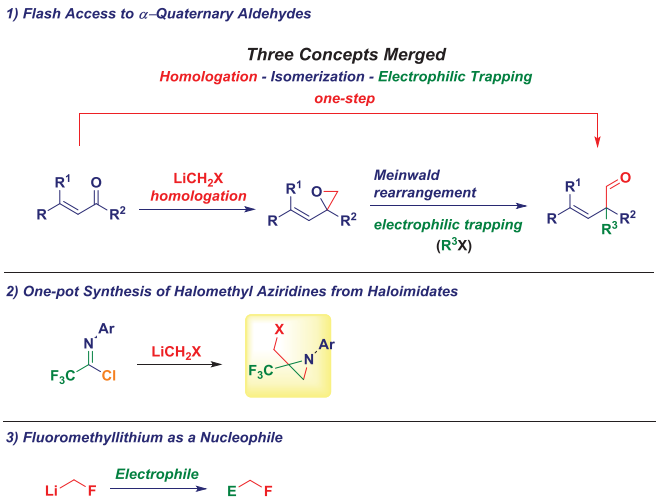
V. Pace*

Department of Pharmaceutical Chemistry, University of Vienna, Althanstrasse 14, 1090 Vienna (Austria)

**e-mail:* vittorio.pace@univie.ac.at - http://drugsynthesis.univie.ac.at/

Homologation chemistry with carbenoid reagents represents nowadays an established tool for synthetic chemists with focus on medicinal applications.[1] As documented in recent work by our group, these reagents enable the construction of a new functionalized C-CH_2X bond through a single synthetic operation thus, making rapid the installation of a reactive fragment.[2]

New reactivity concepts for the straightforward construction of complex building blocks through a single synthetic operation will be presented. 1) A flash access to α-quaternary aldehydes;[3] 2) The one-pot synthesis of halomethyl aziridines from haloimidates;[4] 3) The employment of fluoromethyllithium as nucleophile for homologation reactions.[5]



References:

[1] (a) Pace, V.; Holzer, W.; De Kimpe, N. *Chem. Rec.* **2016**, *16*, 2061-2076. (b) Pace, V.; Castoldi, L.; Monticelli, S.; Rui, M.; Collina, S. *Synlett* **2017**, *28*, 879-888; (c) Castoldi, L.; Monticelli, S.; Senatore, R.; Ielo, L.; Pace, V. *Chem. Commun.* **2018**, *in press*, ID: CC-FEA-03-2018-002499

[2] (a) Pace, V.; Pelosi, A.; Antermite, D.; Rosati, O.; Curini, M.; Holzer, W. *Chem. Commun.* **2016**, *52*, 2639-2642. (b) Pace, V.; Murgia, I.; Westermayer, S.; Langer, T.; Holzer, W. *Chem. Commun.* **2016**, *52*, 7584-7587. (c) Pace, V.; de la Vega-Hernández, K.; Urban, E.; Langer, T. *Org. Lett.* **2016**, *18*, 2750-2753. (d) Pace, V.; Castoldi, L.; Mamuye, A. D.; Langer, T.; Holzer, W. *Adv. Synth. Catal.* **2016**, *358*, 172-177. (e) Pace, V.; Castoldi, L.; Holzer, W. *Adv. Synth. Catal.* **2014**, *356*, 1761-1766. (f) Pace, V.; Holzer, W.; Verniest, G.; Alcántara, A. R.; De Kimpe, N. *Adv. Synth. Catal.* **2013**, *355*, 919-926. (g) Pace, V.; Castoldi, L.; Holzer, W. *Chem. Commun.* **2013**, *49*, 8383-8385. (h) Pace, V.; Castoldi, L.; Holzer, W. *J. Org. Chem.* **2013**, *78*, 7764-7770. (h) Senatore, R.; Castoldi, L.; Ielo, L.; Holzer, W.; Pace, V. *Org. Lett.* **2018**, *20*, 2685-2688. (i) Castoldi, L.; Holzer, W.; Langer, T.; Pace, V. *Chem. Commun.* **2017**, *53*, 9498-9501.

[3] Pace, V.; Castoldi, L.; Mazzeo, E.; Rui, M.; Langer, T.; Holzer, W. *Angew. Chem. Int. Ed.* **2017**, *56*, 12677-12682.

[4] Ielo, L.; Touqeer, S.; Holzer, W.; Pace, V. *manuscript in preparation* **2018**.

[5] Parisi, G.; Colella, M.; Monticelli, S.; Romanazzi, G.; Holzer, W.; Langer, T.; Degennaro, L.; Pace, V.; Luisi, R. *J. Am. Chem. Soc.* **2017**, *139*, 13648-13651.

OC32

An improved process for the preparation of Lenvatinib mesylate

L. Senaldi,[a,b] D. Ciceri,[a] A. Bernardi,[b] P. Allegrini[a]

[a]*Indena, Via Don Minzoni 6, Settala (MI)*
[b]*Dipartimento di Chimica, Università degli Studi di Milano, Via Golgi 19, Milano*
e-mail*: luca.senaldi@indena.com*

Lenvatinib mesylate is an-anticancer drug used in the treatment of advanced renal carcinoma and differentiated thyroid carcinoma (DTC) refractory to radioactive iodine. Lenvatinib **4** can be synthesized by coupling 4-chloro-7-methoxyquinoline-6-carboxamide **3** and 1-(2-chloro-4-hydroxyphenyl)-3-cyclopropylurea **2**, which can be obtained from 4-amino-3-chloro-phenol **1** (Figure 1a). The reaction conditions described in the state of the art[1] yield a product contaminated by several impurities. Their high amounts would require an impractical number of crystallizations with a detrimental effect on the process yield. Therefore, the process, especially the coupling step, was optimized in order to minimize the formation of impurities. The new conditions allowed to obtain Lenvatinib **4** with HPLC purity ≥ 99.4 % after a single recrystallization.

Finally, the mesylate salt **4·Ms** was formed with methanesulfonic acid and crystallized in 3:1 Acetic acid: ethyl acetate to afford a new polymorph (XRPD diffractogram is shown in Figure 1b).[2]

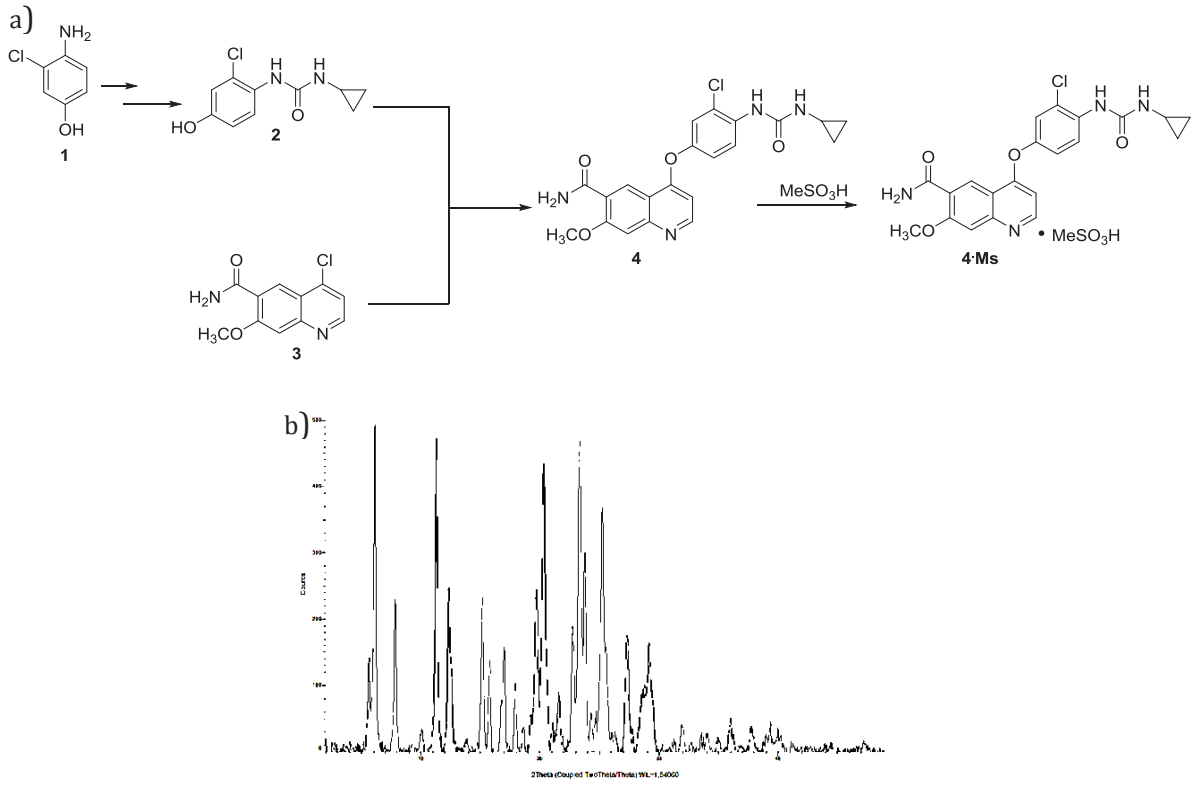


Figure 1: a) synthetic route for the preparation of Lenvatinib mesylate; b) XRPD diffractogram of the new polymorph of Lenvatinib mesylate

References:

[1] T. Naito, K. Yoshizawa, patent US7683172.
[2] N. Sardone, S. Giaffreda, A. Gambini, A. Petrolati, P. Allegrini, E. Modena, patent WO2018054792.

OC33

Hydrogen Atom Transfer Processes Promoted by Short-Lived *N*-oxyl Radicals: Structural and Medium Effect on the Reactivity and Selectivity

O. Lanzalunga,[a] A. Barbieri,[a] A. Lapi,[a] B. Ticconi[a]

[a]*Dipartimento di Chimica, Università di Roma "La Sapienza" and Istituto CNR di Metodologie Chimiche (IMC-CNR), Sezione Meccanismi di Reazione, P.le A. Moro, 5 I-00185 Rome, Italy*

e-mail*: osvaldo.lanzalunga@uniroma1.it*

Hydrogen atom transfer (HAT) processes promoted by short-lived *N*-oxyl radicals such as the phthalimide-*N*-oxyl radical (PINO), have received a special attention for the key role played in the aerobic oxidation of organic substrates catalyzed by *N*-hydroxyimides. Recent studies have shown that reactivity and selectivity of HAT processes promoted by PINO are strongly influenced by structural and medium effects.[1] In order to provide a detailed analysis of these effects which can be helpful in the optimization of the experimental conditions for a selective and efficient oxidation process, we have investigated, by kinetic and product studies, the HAT reactions from several hydrogen donors to a series of *N*-oxyl radicals in different solvents in the presence or absence of acid additives. Addition of Lewis acids had almost no effect on the HAT reactivity of aliphatic substrates. On the contrary a significant increase of the HAT rate constants was observed in the reaction of aromatic substrates with PINO due to the stabilizing effect of the Lewis acid on the charge separation which develops in the π-stacked transition state of the HAT process (Figure 1).

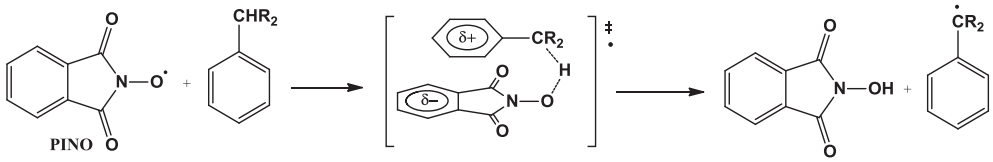


Figure 1

Addition of Brønsted or Lewis acids determines a significant deactivation of C-H bonds α to the nitrogen in amides.[2] On the same line in the HAT from 4-alkyl-*N,N*-dimethylbenzylamines to PINO a change in regioselectivity has been observed by effect of protonation.[3] An increase of the HAT reactivity by addition of Brønsted or Lewis acids was instead observed with the quinolinimide-*N*-oxyl radical (QINO) by effect of the protonation or complexation with the Lewis acid of the pyridine nitrogen that leads to a significant decrease of the electron density in the *N*-oxyl radical.[4]

Thus, by changing the structure of the *N*-oxyl radical or the reaction medium it is possible to control the reactivity and selectivity in the HAT processes promoted by these species and consequently in the aerobic oxidations catalyzed by *N*-hydroxyimides.

References:

[1] E. Gaster, S. Kozuch, D. Pappo, *Angew. Chem. Int. Ed.* **2017***, 56,* 5912-5915. P. A. Gunchenko, J. Li, B. Liu, H. Chen, A. E. Pashenko,V. V. Bakhonsky, T. S. Zhuk, A. A. Fokin, *Mol. Catal.* **2018**, *447*, 72-79.

[2] M. Bietti, V. Forcina, O. Lanzalunga, A. Lapi, T. Martin, M. Mazzonna, M. Salamone *J. Org. Chem*. **2016**, *81*, 1194-11931.

[3] M. Bietti, O. Lanzalunga, A. Lapi, T. Martin, M. Mazzonna, M. Polin, M. Salamone *J. Org. Chem*. **2017**, *82*, 5761-5768.

[4] G. A. DiLabio, P. Franchi, O. Lanzalunga, A. Lapi, F. Lucarini, M. Lucarini, M. Mazzonna, V. Kumar Prasad, B. Ticconi *J. Org. Chem*. **2017**, *82*, 6133-6141.

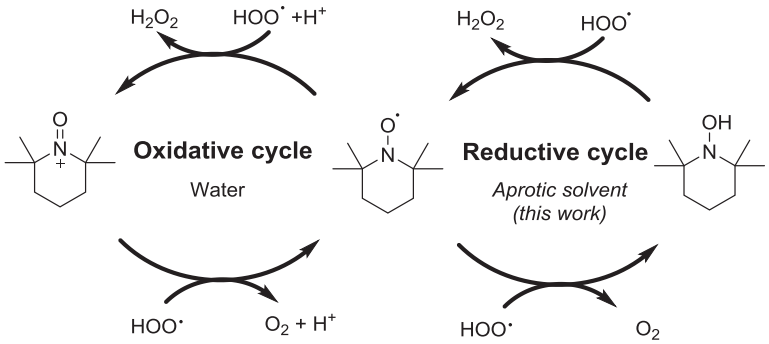
OC34

Explaining the chemopreventive antioxidant activity of nitroxides: the unexplored reductive catalytic cycle with superoxide in aprotic media

L. Valgimigli, A. Baschieri, R. Amorati

Department of Chemistry "G. Ciamician", Via S. Giacomo 11, 40126 Bologna, Italy
e-mail*: luca.valgimigli@unibo.it*

Nitroxides like TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl) are reported to act as chemopreventive agents in a variety of oxidative-stress related conditions.[1] Their reaction with alkylperoxyl radicals ROO• requires an acid as the proton source.[2,3] Hence, this mechanism cannot be invoked in the many cases in which nitroxides reduce the extent of autoxidation in lipophilic environments such as the interior of membranes. Superoxide (HOO•/O_2) is arguably the most abundant oxygen-centred radical in biological systems, being formed during mitochondrial respiratory chain, or by ROO• to HOO• chain-transfer during lipid peroxidation, in the presence of biologically relevant compounds like cyclohexadienes (e.g. γ-terpinene) or 1,4-hydroquinones (e.g. ubiquinol).[4] Kinetic and spectroscopic experiments in aprotic solvents along with DFT calculations demonstrate the occurrence of extremely fast reductive reaction TEMPO + HOO• →TEMPOH + O_2, and reoxidation TEMPOH + HOO• →TEMPO + H_2O_2, The two reactions compose a very efficient novel catalytic cycle that does not involve the formation of oxoammonium ions, being alternative to the cycle established in protic media (Scheme 1).[5] We demonstrate that the novel cycle can provide dramatic protection from lipid peroxidation, outperforming Nature's best lipid soluble antioxidants like α-tocopherol.[5] The relevance and applications of this chemistry are discussed.



Scheme 1. Catalytic quenching of HOO• by TEMPO.

References:

[1] Zilka, O.; Shah, R.; Li, B.; Friedmann Angeli, J. P.; Griesser, M.; Conrad, M.; Pratt, D. A. *ACS Cent. Sci.* **2017**, 3 (3), 232−243; Lahiani, A.; Hidmi, A.; Katzhendler, J.; Yavin, E.; Lazarovici, P. *ACS Chem. Neurosci*. **2016**, 7, 1452−1462.
[2] Amorati, R.; Pedulli, G. F.; Pratt, D. A.; Valgimigli, L. *Chem. Commun.* **2010**, *46*, 5139–5141.
[3] Haidasz, E. A.; Meng, D.; Amorati, R.; Baschieri, A.; Ingold, K. U.; Valgimigli, L.; Pratt, D. A. *J. Am. Chem. Soc*. **2016**, *138* (16), 5290−5298.
[4] Valgimigli, L.; Amorati, R.; Fumo, M. G.; DiLabio, G. A.; Pedulli, G. F.; Ingold, K. U.; Pratt, D. A. *J. Org. Chem*. **2008**, *73*, 1830-1841
[5] Baschieri, A.; Valgimigli, L.; Gabbanini, S.; DiLabio, G.; Romero-Montalvo, E.; Amorati, R. *J. Am. Chem. Soc.* **2018**, submitted.

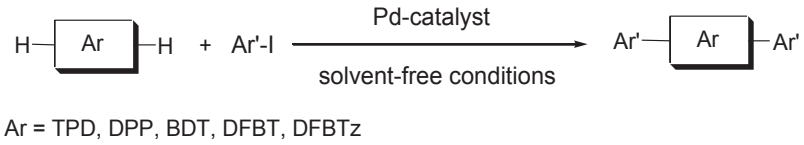
OC35

Solvent-Free Pd-Catalyzed Heteroaryl-Aryl Coupling Reactions via C−H Bond Activation

N. Zappimbulso,[a] A. Punzi,[a] G. M. Farinola[a]

[a]*Department of Chemistry, University of Bari, Via Orabona 4, 70010 Bari, Italy*
e-mail*: nicola.zappimbulso@uniba.it*

Palladium-catalyzed direct arylation *via* aromatic C-H bond activation[1][2] is one of the most attractive ways for synthesizing complex organic molecules. In particular C-H arylation represents a versatile approach for step-economical synthesis of diverse biaryl motifs with respect to traditional cross-coupling reactions avoiding the use of preformed organometallic reagents, which are sensitivite to air and moisture, expensive and, often, toxic. In this context, we have reported a thiophene-aryl direct coupling reaction in a green, convenient, and inexpensive deep eutectic solvent, a choline chloride/urea mixture.[3] As an alternative approach, solvent-free palladium-catalyzed direct arylation reactions would provide an environmentally attractive procedure for the preparation of biaryls. In fact, solvent-free conditions not only avoid the hazards and toxicity associated with the use of solvents, but also reduce energy costs due to shorter reaction times, and simplify reaction procedures and workup.



Scheme 1: Pd-catalyzed direct coupling reactions via C−H bond activation in solvent-free conditions.

The reaction is performed in non-anhydrous conditions and without exclusion of air and tolerates a number of functional groups on both coupling partners. Thieno-pyrrole-4,6-dione (TPD), diketopyrrolopyrrole (DPP), benzodithiophene (BDT), 5,6-difluorobenzo[1,2,5]thiadiazole (DFBT) and 5,6-difluoro-2-heptadecyl-2H-benzo[d][1,2,3]triazole (DFBTZ)-based cores as the C−H activated substrate have been used (scheme 1), in consideration of their interest in the construction of donor - acceptor molecular and polymeric semiconductors for optoelectronics applications [4][5].

References:

[1] G. Marzano, C. V. Ciasca, F. Babudri, G. Bianchi, A. Pellegrino, R. Po, G. M. Farinola, *Eur. J. Org. Chem.* **2014**, 6583–6614.

[2] S. Santoro, S. I. Kozhushkov, L. Ackermann, L. Vaccaro, *Green Chem.* **2016**, *18*, 3471-3493.

[3] A. Punzi, D. I. Coppi, S. Matera, M. A. M. Capozzi, A. Operamolla, R. Ragni, F. Babudri, G. M. Farinola, *Org. Lett.* **2017**, *19*, 4754-4757

[4] G. Marzano, D. Kotowski, F. Babudri, R. Musio, A. Pellegrino, S. Luzzati, R. Po, G.M. Farinola, *Macromolecules* **2015**, *48*, 7039-7048

[5] G. Marzano, F. Carulli, F. Babudri, A. Pellegrino, R. Po, S. Luzzati, G. M. Farinola, *J. Mater. Chem. A* **2016**, *4*, 17163-17170.

OC36

Supported Imidazolium Functionalized POSS Hybrids as Palladium Platform for C-C Cross-Couplings

C. Calabrese,[a,b] L. F. Liotta,[c] F. Giacalone,[a] C. Aprile,[b] M. Gruttadauria[a]

[a]*Dipartimento di Scienze e Tecnologie Biologiche Chimiche e Farmaceutiche, Università di Palermo, Viale delle Scienze Ed. 17, 90128, Palermo (Italy)*
[b]*Département de Chimie, Université de Namur, Rue de Bruxelles, 5000, Namur (Belgium)*
[c]*Istituto per lo Studio dei Materiali Nanostruttuarati (ISMN-CNR), Via Ugo La Malfa 153, 90146, Palermo (Italy)*
e-mail*: carla.calabrese@unipa.it*

The increasing demand of highly active and recyclable catalytic materials for C-C cross coupling reactions pushed the scientific research toward the design of performing heterogeneous hybrids. It is well known that palladium catalysed C-C cross couplings represent one of the most versatile tools in this field.[1] Herein, supported imidazolium modified polyhedral oligomeric silsesquioxanes (POSS) have been used as platform for Pd^{II} species. Such material was successfully used as pre-catalyst for Suzuki-Miyaura and Heck couplings. In both cases, the solid proved to be highly efficient and easily recoverable from the reaction mixture. The recyclability was tested for up to seven cycles without showing any activity decrease. Therefore, the versatility of our material was investigated with a set of various aryl halides endowed with electron-donating or electron-withdrawing groups. Moreover, palladium supported hybrid was able to promote both Suzuki and Heck reactions down to 0.0007 mol% showing outstanding turnover number (TON) values of 113,515 and 96,487, respectively.

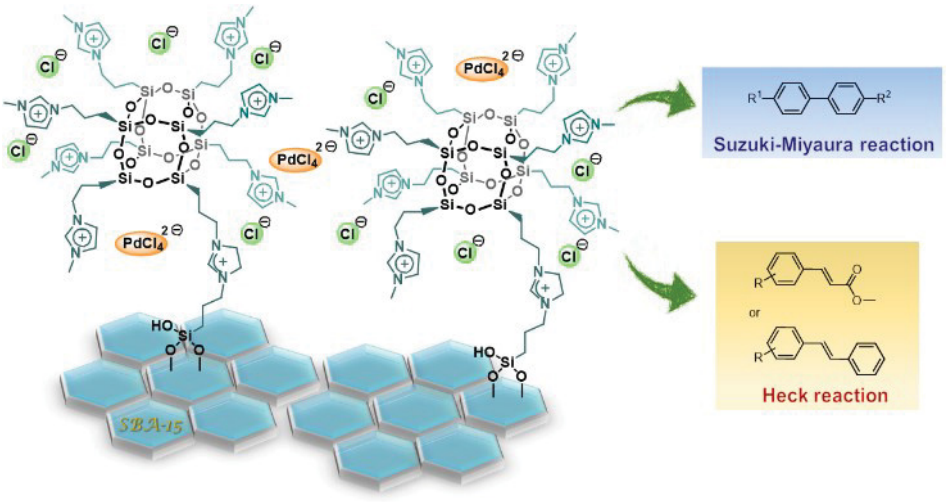


Figure 1: Palladium supported POSS-imidazolium hybrids for C-C couplings.

References:

[1] C. C. C. Johansson Seechurn, M. O. Kitching, T. J. Colacot, V. Snieckus, *Angew. Chem. Int. Ed.* **2012**, *51*, 5062 – 5085.

OC37

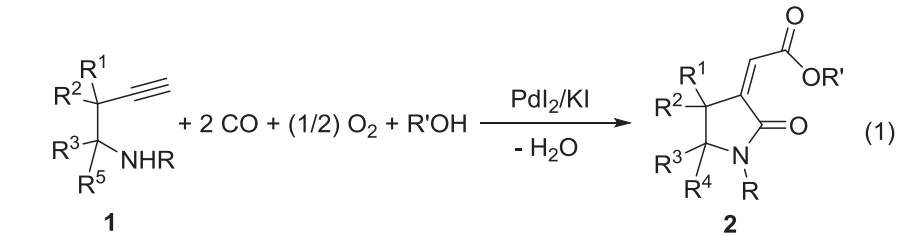
Regio- and Stereoselective Synthesis of (*Z*)-2-(2-Oxopyrrolidin-3-ylidene)acetates by Pd-Catalyzed Carbonylation of *N*-substituted-3-yn-1-amines

R. Mancuso, I. Ziccarelli, B. Gabriele

Laboratory of Industrial and Synthetic Organic Chemistry (LISOC),
Department of Chemistry and Chemical Technology, University of Calabria,
Via Pietro Bucci, 12/C, 87036 Arcavacata di Rende (CS), Italy.
e-mail: *raffaella.mancuso@unical.it*

γ-Lactam is an important structural motif in a large number of biologically active natural products and synthetic small pharmaceutical molecules[1] for the potential treatment of cancer, cardiac arrhythmia, hypertension and disorders of the central nervous system. Carbonylative heterocyclization of alkynylamines may provide an efficient entry to this important class of compounds, as it is known that carbonylation reactions are particularly efficient and convenient processes for the direct synthesis of carbonylated heterocycles.[2]

In this contribution, we report a new synthesis of functionalized (*Z*)-2-(2-oxopyrrolidin-3-ylidene)acetates **2** by regioselective and stereoselective PdI_2-catalyzed oxidative heterocyclocarbonylation-alkoxycarbonylation of *N*-substituted-3-yn-1-amines **1**, according to Eqaution 1. The structure of representative product (R^1-R^4=H, R^5=Ph, R'=Me) has been confirmed by XRD analysis.



1 **2**

R= alkyl, aryl
R^1, R^2, R^3, R^4= H, alkyl, aryl

Reactions are carried out in alcoholic solvents (R'=Me, Et, *i*-Pr, *t*-Bu), under relatively mild conditions (100°C under 40 atm of a 4:1 mixture of CO-air for 2 h) using 2 mol% of PdI_2, in conjunction with 20 mol% of KI, to give **2** in satisfactory isolated yields (50-85%)

References:

[1] (a) G. F. Vafina , R. V. Kuz'mich, F. Z. Galin, M. S. Yunusov, *Chemistry of Natural Compounds* **2013**, 49, 4; (b) S. Rachid, L. Huo, J. Herrmann, M. Stadler, B. Köpcke, J. Bitzer, R. Müller, *ChemBioChem* **2011**, 12, 922 – 931; (c) R. R. Manam, S. Teisan, D. J. White, B. Nicholson, J. Grodberg, *J. Nat. Prod*. **2005**, 68, 240−243.
[2] B. Gabriele, R. Mancuso, G. Salerno, *Eur. J. Org. Chem*. **2012**, 6825-6839.

OC38

Metal-catalyzed and Metal-mediated Organic Reactions in Deep Eutectic Solvents and in Water

F. M. Perna,[a] G. Dilauro,[a] L. Cicco,[a] M. Dell'Aera,[a] S. Mata,[b] P. Vitale,[a] V. Capriati[a]

[a]*Dipartimento di Farmacia-Scienze del Farmaco, Università di Bari "Aldo Moro", Consorzio C.I.N.M.P.I.S., Via Orabona 4, I-70125, Bari, Italy*

[b]*Departamento de Química Orgánica e Inorgánica, Universidad de Oviedo, c/ J. Clavería 8, 33006, Oviedo, Spain*

e-mail*: filippo.perna@uniba.it*

Deep Eutectic Solvents (DESs) are generally referred to as combination of two or three safe and inexpensive components able to engage in reciprocal hydrogen bond interactions to form an eutectic mixture. DESs display attractive advantages, such as low price, non-flammability, recyclability, low vapour pressure, and are believed to be more biodegradable compared to traditional ionic liquids because of their environmentally friendly components.[1] The application of DESs and other unconventional solvents in the fields of metal-catalyzed and metal-mediated organic reactions,[2a] organocatalysis,[2b] biocatalysis,[2c] solar technology,[2d] and photosynthesis[2e] have been experiencing an exponential growth and development, particularly in the last years. In this communication, we discuss recent findings from our research group on the nucleophilic addition of highly polar organometallic reagents to carbonyl derivatives and imines in water and in DESs, at room temperature and under air.[3] Moreover, ligand-free, bio-inspired Suzuki-Miyaura couplings, using organotrifluoroborates as competent partners in DESs, with a catalyst loading as low as 1 mol%, and an efficient catalyst/DES recycling to up to 6 times (E factor = 9.3) will be discussed as well.

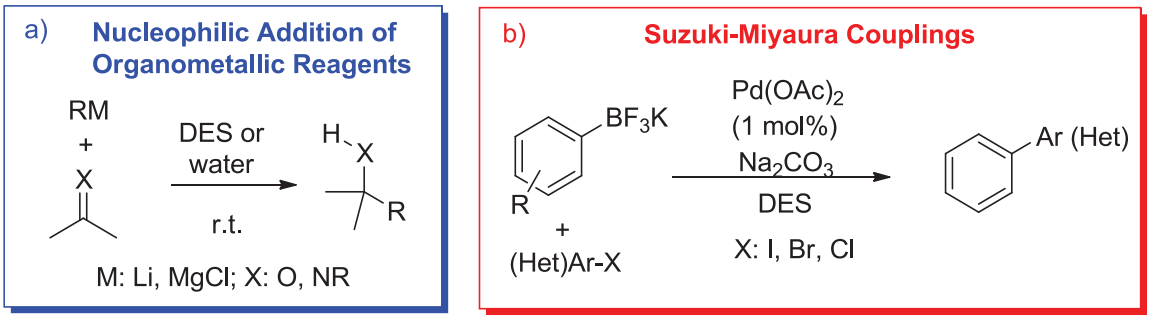


Figure 1: a) Nucleophilic additions and b) Suzuki-Miyaura couplings in unconventional solvents.

References:

[1] D.A. Alonso, A. Baeza, R. Chinchilla, G. Guillena, I.M. Pastor, D.J. Ramón, *Eur. J. Org. Chem.*, **2016**, 612.

[2] (a) J. García-Álvarez, E. Hevia, V. Capriati, *Eur. J. Org. Chem.* **2015**, 6779; (b) E. Massolo, S. Palmieri, M. Benaglia, V. Capriati, F.M. Perna, *Green Chem.* **2016**, *18*, 792; (c) P. Vitale, V.M. Abbinante, F.M. Perna, A. Salomone, C. Cardellicchio, V. Capriati, *Adv. Synth. Catal.* **2017**, *359*, 1049; (d) C.L. Boldrini, N. Manfredi, F.M. Perna, V. Trifiletti, V. Capriati, A. Abbotto, *Energy Technol.* **2017**, *5*, 345; (e) F. Milano, L. Giotta, M. R. Guascito, A. Agostiano, S. Sblendorio, L. Valli, F.M. Perna, L. Cicco, M. Trotta, V. Capriati, *ACS Sustainable Chem. Eng.* **2017**, *5*, 7768.

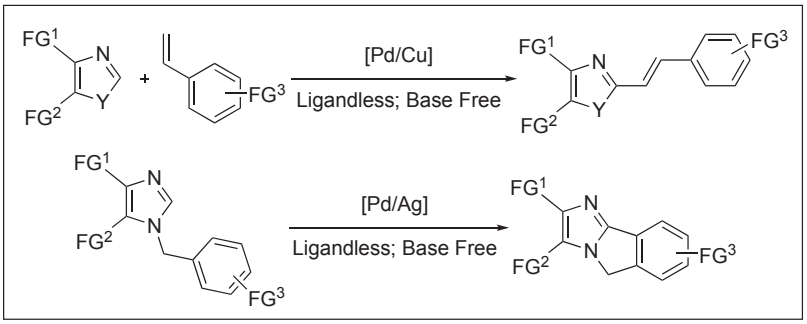
[3] (a) L. Cicco, S. Sblendorio, R. Mansueto, F.M. Perna, A. Salomone, S. Florio, V. Capriati, *Chem. Sci.* **2016**, *7*, 1192; (b) G. Dilauro, M. Dell'Aera, P. Vitale, V. Capriati, F.M. Perna, *Angew Chem. Int. Ed.* **2017**, *56*, 10200.

OC39

Cross-Dehydrogenative-Couplings of Azoles

M. Lessi,[a] L. Lodone,[a] A. Lucci,[a] F. Bellina[a]

[a]*Department of Chemistry and Industrial Chemistry, University of Pisa, Via Moruzzi 13, 56124 Pisa, Italy*
e-mail*: marco.lessi@unipi.it*



The current need of environmental friendly processes to produce organic materials has driven the chemists to develop new synthetic protocols able to give complex materials and low waste amount.

Among these synthetic protocols a lot of attention has been devoted to the C-C bond formation, the so called cross-coupling reactions. These reactions, in their traditional form, provide the coupling of pre-functionalized compounds, in general represented by an organometallic compound and a (pseudo)halide, in the presence of a catalytic system with the formation, along with the desired product, of at least equimolar amount of inorganic waste.[1] To overcome the pre-functionalization steps and the production of inorganic wastes ideally two C-H bonds should be directly coupled. Nowadays, this approach is known as cross-dehydrogenative-coupling (CDC).[2]

Due to the high importance of (hetero)aryl compounds, from a pharmaceutical and organic functional materials point of view, many efforts were done by the organic chemistry community to develop selective and efficient CDC protocols for the functionalization of (hetero)aromatic cores.[3]

In this contest we present our last results about CDC involving 1,3-azoles, which are structural cores of many natural compounds and organic dyes.[4] In particular, we optimized a protocol for the C-2 regioselective dehydrogenative alkenylation of 5-aryl-1-methylimidazoles and benzoazoles with styrenes, in the presence of $Pd(OAc)_2$ as the transition metal precatalyst, $Cu(OAc)_2$ as the oxidant and using propionic acid as the solvent.

Further, we developed a new intramolecular dehydrogenative C-2 arylation method involving 1-benzyl-(benzo)imidazoles bearing differed substituents on the benzyl and azole cores. Here again the coupling was carried out using a catalytic amount of $Pd(OAc)_2$, but $Ag(TFA)_2$ as the oxidant and pivalic acid as the solvent were found to give the best results.

References:

[1] A. Biffis, P. Centomo, A. Del Zotto, M. Zecca, *Chem Rev.*, **2018**, *18*, 2249-2295.

[2] Chao-Jun Li, *From C-H to C-C Bonds: Cross-Dehydrogenative-Coupling*, RSC Green Chemistry, **2015**, 1-316.

[3] a) L. Ackermann, R. Vicente, A.R. Kapdi, *Angew. Chem. Int. Ed.* **2009**, *48*, 9792-9826; b) X. Bugaut, F. Glorius, *Angew, Chem. Int. Ed.* **2011**, *50*, 7479-7481.

[4] a) G. Fontana, *Curr. Bioact. Comp.*, **2010**, *6*, 284-308; b) E.D. Faulkner, R.J. Schwartz, *High performance pigments,* WILEY-VCH, **2009**, 1-516.

OC40

Site-selective and product chemoselective hydrogen atom transfer based aliphatic C–H bond functionalization

M. Milan,[a] M. Salamone,[b] M. Costas,[a] M.Bietti,[b]

[a]*QBIS Research Group, Institut de Química Computacional i Catàlisi, Departament de Química, Universitat de Girona, Campus Montilivi, Girona E-17071, Catalonia, Spain.*
[b]*Dipartimento di Scienze e Tecnologie Chimiche, Università "Tor Vergata", Via della Ricerca Scientifica, 1 I-00133 Rome, Italy.*
e-mail*: bietti@uniroma2.it*

Site-selective aliphatic C−H bond functionalization represents an important goal of modern synthetic organic chemistry. By avoiding the prefunctionalization of substrates associated to traditional functional group manipulations and interconversions, the direct functionalization of these bonds represents a transformation of high synthetic potential that can offer advantages both in terms of decreased waste generation and reaction step economy.

Among the available methodologies, those based on hydrogen atom transfer (HAT) to radical and radical-like species have attracted considerable interest and accordingly, the factors that govern reactivity and site-selectivity in these processes have been discussed in detail. These include bond strengths, electronic, steric and stereoelectronic effects, conjugation and hyperconjugation, and, with cyclohexane derivatives, torsional effects.[1-3] Medium effects have also emerged as a powerful tool that has been successfully employed to dramatically alter both reactivity and site-selectivity in HAT based C−H functionalization procedures.[4]

Within this framework, we have been interested in the study of HAT reactions from aliphatic C−H bonds, with the main objective of obtaining quantitative kinetic information on the role of structural and medium effects on the reactivity and selectivity patterns, to be then exploited in synthetically useful aliphatic C−H bond oxidation reactions. This goal has been achieved through time-resolved kinetic studies on the reactions of the cumyloxyl radical ($PhC(CH_3)_2O$, $CumO^{\bullet}$) with a wide variety of substrates, accompanied by product studies on C−H bond oxidation of selected substrates with hydrogen peroxide catalyzed by iron and manganese complexes. The results of this combined approach will be discussed.

References:

[1] T. Newhouse, P. S. Baran, *Angew. Chem. Int. Ed.* **2011**, *50*, 3362-3374.
[2] M. C. White, *Science* **2012**, *335*, 807-809.
[3] M. Salamone, M. Bietti, *Acc. Chem. Res.* **2015**, *48*, 2895-2903.
[4] (a) J. Twilton, M. Christensen, D. A. DiRocco, R. T. Ruck, I. W. Davies, D. W. C. MacMillan, *Angew. Chem. Int. Ed.* **2018**, *57*, 5369-5373. (b) V. Dantignana, M. Milan, O. Cussó, A. Company, M. Bietti, M. Costas, *ACS Cent. Sci.* **2017**, 3, 1350-1358. (c) D. M. Schultz, F. Lévesque, D. A. DiRocco, M. Reibarkh, Y. Ji, L. A. Joyce, J. F. Dropinski, H. Sheng, B. D. Sherry, I. W. Davies, *Angew. Chem. Int. Ed.* **2017**, *56*, 15274-15278. (d) J. B. C. Mack, J. D. Gipson, J. Du Bois, M. S. Sigman, *J. Am. Chem. Soc.* **2017**, *139*, 9503-9506. (e) M. Lee, M. S. Sanford, *Org. Lett.* **2017**, *19*, 572-575. (f) J. M. Howell, K. B. Feng, J. R. Clark, L. J. Trzepkowski, M. C. White, *J. Am. Chem. Soc.* **2015**, *137*, 14590-14593.

OC41

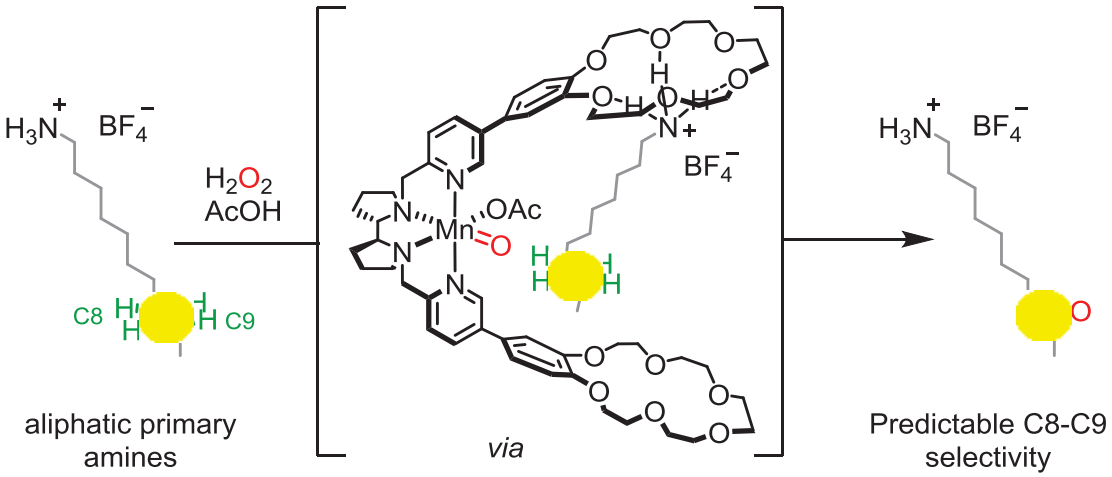
Selective, Remote C-H Oxidation guided by Supramolecular Recognition

G. Olivo,[a] G. Farinelli,[b] A. Barbieri, [b] O. Lanzalunga, [b] S. Di Stefano, [b] and M. Costas [a]

[a] *QBIS-Cat, IQCC, Universidad de Girona, Girona, Spain*
[b] *Università di Roma La Sapienza, Rome, Italy*
e-mail*: giorgio.olivo@udg.edu*

The search for predictable, site-selective oxidation protocol of aliphatic C-H bonds stands a longstanding goal in organic synthesis. In the last decade, iron and manganese coordination complexes emerged as promising candidates to carry out such reactions. The hydroxylation selectivity, essentially dictated by the electronic and steric properties of the substrate, can be tuned to some extent by careful modification of the catalyst structure.[1] However, when multiple C-H bonds display a comparable reactivity, such as in linear alkyl chains or elaborated structures, a selective oxidation could become rather challenging, affording (statistical) mixtures of products. With the aim of overcoming this limitation, we explored a supramolecular strategy to geometrically control the hydroxylation selectivity (Scheme 1).

The binding of a protonated primary amine to a receptor (18-crown-6 ether) anchored to the Mn catalyst orientates remote C8 and C9 C-H bonds in the range of the oxidizing unit, and allows selective, remote oxidation of amines.[2] Remarkably, this geometric selectivity is retained even in the presence of structural modifications of the substrate.



Scheme 1

References

[1] P. E. Gorminsky, M. C. White, *J. Am. Chem. Soc.* **2013**, *135*, 14052–14055; G. Olivo, O. Cussó, M. Costas, *Chem. - An Asian J.* **2016**, *11*, 3148–3158.

[2] G. Olivo, G. Farinelli, A. Barbieri, O. Lanzalunga, S. Di Stefano, M. Costas, *Angew. Chem. Int. Ed.* **2017**, *129*, 16565-16569.

OC42

Reducing ability of hydroperoxyl radical (HOO•)

A. Baschieri,[a] L. Sambri,[b] L. Valgimigli,[a] R. Amorati[a]

[a]*Department of Chemistry "G. Ciamician", Via S. Giacomo 11, 40126 Bologna, Italy*
[b]*Department of Industrial Chemistry "T. Montanari", Viale Risorgimento 4, 40136 Bologna, Italy*
e-mail*: andrea.baschieri2@unibo.it*

Hydroperoxyl radical (HOO•) is formed in (bio)chemical systems by redox reactions involving O_2 and, usually, it is a mediator of many oxidative processes of wide current interest.[1] It is generally believed that HOO• acts similarly to the well know alkylperoxyl (ROO•) radicals, but knowledge on its reducing properties is still very limited. The "double face" behaviour of HOO• was discovered during the investigation of reaction of HOO• with an analogue of the physiologic antioxidant α-tocopherol (α-TOH). We found that HOO• was able to reduce and regenerate a large fraction of α-TO• radicals back to α-TOH, extending its antioxidant activity (Figure 1A).[2] Another example is the reaction of HOO• radicals with nitroxides in apolar organic solvents. On studying the autoxidation of 1,4-cyclohexadiene which occurs through the release of HOO•, it was found that nitroxides (such as TEMPO) act as catalytic inhibitors via their reduction (by HOO•) to the corresponding hydroxylamine which are then oxidized back by a second HOO• radical forming a catalytic cycle with good efficiency (Figure 1B).[3] Finally, we report our recent studies on the reduction of *para* or *orto* quinones (**1** or **3**) to the corresponding hydroquinones (**2**) or catechol (**4**) using 1,4-cyclohexadiene as H-atom source. The key mechanism of this reaction is the formation of HOO• that acts as reducing agent. The reactions are performed under air, in mild conditions and without use metal catalysts (Figure 1C).

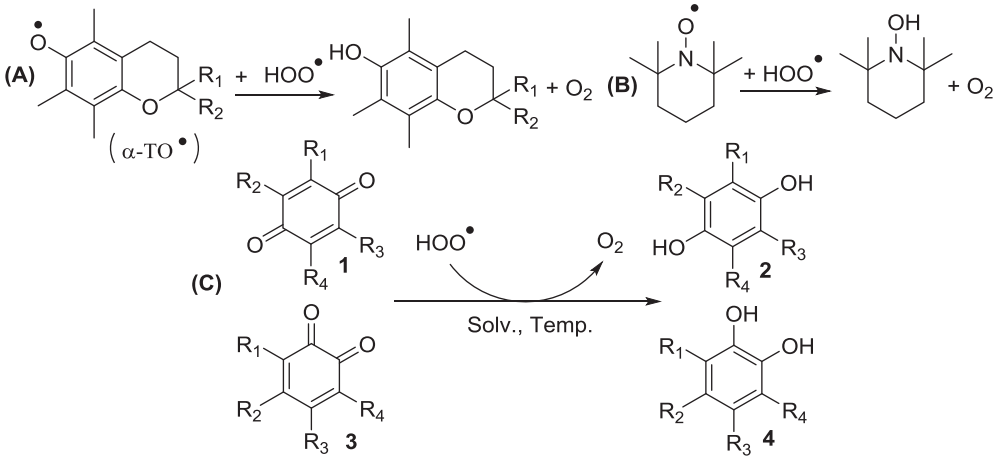


Figure 1: different uses of hydroperoxyl radical as reducing agent.

References:

[1] M. Kumar, J. S. Francisco, *Angew. Chem. Int. Ed.* **2015**, *54*, 15711 – 15714, J.C. Colmenares, R. Luque, *Chem. Soc. Rev.* **2014**, *43*, 765 – 778, J. A. Howard, K. U. Ingold, *Can. J. Chem.* **1967**, *45*, 785 – 792.

[2] J. Cedrowski, G. Litwinienko, A. Baschieri, R. Amorati, *Chem. Eur. J.* **2016**, *22*, 16441 – 16445.

[3] A. Baschieri, L. Valgimigli, S. Gabbanini, G. DiLabio, E. Romero-Montalvo, R. Amorati, Unexpected reaction between nitroxides and HOO• radicals: extremely fast reductive hydrogen atom transfer and implication in co-antioxidant systems, *Submitted* **2018**.

OC43

Hydrogen Atom Transfer from Amino Acid C–H Bonds. Structural and Medium Effects on Reactivity and Site-Selectivity

M. Salamone,[a] M. Bietti[a]

[a]*Dipartimento di Scienze e Tecnologie Chimiche, Università "Tor Vergata", Via della Ricerca Scientifica, 1 I-00133 Rome, Italy*
e-mail*: michela.salamone@uniroma2.it*

The selective functionalization of aliphatic C–H bonds is currently a mainstream topic of organic chemistry and one of the most investigated approaches to develop new synthetic metodology.[1] Among the available procedures, those based on hydrogen atom transfer (HAT) to radical or radical like species have attracted considerable interest, and the factors that govern reactivity and site selectivity have been discussed in detail.[2,3]

Within this framework, medium effects have emerged as a powerful tool that can alter both reactivity and selectivity. Hydrogen bonding and Brønsted and Lewis acid-base interactions have been employed to promote deactivation/activation toward electrophilic HAT reagents of C–H bonds that are α- to basic/acidic centers.[4-6] In this context, α-amino acids can represent preferential substrates for a detailed understanding of the role of medium effects, since the protonation state of both the NH_2 and the CO_2H groups as well as the introduction of protecting groups can strongly influence the electron density at the α-C–H, eventually allowing discrimination between this site and more remote positions (Fig. 1).

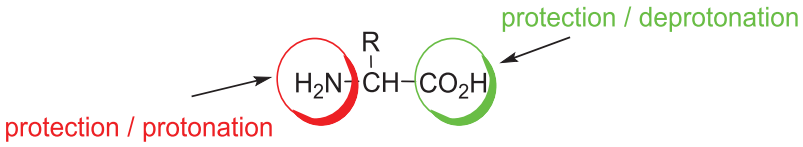


Fig 1: Possible modifications for α-C–H activation and deactivation

In order to obtain quantitative information on the reactivity and selectivity patterns of these reactions, the effect of CO_2H deprotonation on HAT from the C–H bonds of a series of *N*-Boc-protected amino acids bearing aliphatic side chains to the electrophilic cumyloxyl radical CumO$^\bullet$ has been carried out by means of a time-resolved kinetic study. The results obtained will be discussed in comparison to those obtained previously for the corresponding reactions with the neutral forms.[7]

References:

[1] J. F. Harwig, M. A. Larsen, *ACS Cent. Sci.* **2016**, *2*, 281-292.
[2] M. C. White, *Science* **2012**, *335*, 807-809.
[3] D. Ravelli, M. Fagnoni, T. Fukuyama, T. Nishikawa, I. Ryu, *ACS Catal.* **2018**, *8*, 701-713.
[4] M. Salamone, M. Bietti, *Acc. Chem. Res*. **2015**, *48*, 2895-2903.
[5] J. B. C. Mack, J. D. Gipson, J. Du Bois, M. S. Sigman, *J. Am. Chem. Soc.* **2017**, *139*, 9503-9506.
[6] J. Twilon, M. Christensen, D. A. DiRocco, R. T. Ruck, I. W. Davies, D. W. C. MacMillan, *Angew. Chem. Int. Ed.* **2018**, *57*, DOI 10.1002/anie.201800749.
[7] M. Salamone, F. Basili, M. Bietti, *J. Org. Chem.* **2015**, *80*, 3643-3650.

OC44

Hydrogen Atom Transfer based aliphatic C–H bond functionalization. A kinetic evaluation of the role of electronic and torsional effects

T. Martin, M. Salamone, M. Bietti

Dipartimento di Scienze e Tecnologie Chimiche, Università di Roma "Tor Vergata"
Via della Ricerca Scientifica, 1 00133 Roma
e-mail*: teo.martin@uniroma2.it*

Selective functionalization of aliphatic C–H bonds represents a topic of increasing interest in modern synthetic organic chemistry, because these reactions can offer advantages both in terms of decreased waste generation and reaction step economy.[1] Methodologies based on Hydrogen Atom Transfer (HAT) to radical and radical-like species have proven to be successful in pursuing this challenging goal.[2]

Due to the electrophilic nature of most of the commonly employed HAT reagents, electronic effects are central in these reactions, and it can be reasonably predicted that, in a molecule containing different reactive sites, HAT will preferentially occur from an electron-rich and thus activated C−H bond rather than from an electron-poor and deactivated one. With cyclohexane derivatives, torsional effects have also been shown to play an important role.[3]

In order to obtain a deeper understanding of the role of electronic and torsional effects on these processes, we have carried out a detailed time-resolved kinetic study on the reactions of an extended series of 1-*Z*-pentyl, 1-*Z*-propyl, and *Z*-cyclohexyl derivatives (*Z* = H, Ph, OH, OAc, NH_2, NHAc, NPhth, CO_2Me, Cl, Br, CN), and of a series of acyclic and cyclic alkanols and alkanediols with a representative alkoxyl radical such as cumyloxyl ($PhC(CH_3)_2O^{\bullet}$, CumO$^{\bullet}$).[4] The results of these studies will be discussed.

References:

[1] (a) T. Newhouse, P. S. Baran, *Angew. Chem. Int. Ed.* **2011**, *50*, 3362– 3374. (b) M. C. White, *Science* **2012**, *335*, 807– 809.

[2] (a) R. K. Quinn, Z. A. Könst, S. E. D. Michalak, Y. Schmidt, A. R. Szklarski, A. R. Flores, S. Nam, D. A. Home, C. D. Vanderwal, E. J. Alexanian, *J. Am. Chem. Soc.* **2016**, *138*, 696-702. (b) C. Le, Y. Liang, R. W. Evans, X. Li, D. W. C. MacMillan, *Nature* **2017**, *547*, 79-83. (c) Y. Kawamata, M. Yan, Z. Liu, D-H. Bao, J. Chen, J. T. Starr, P. S. Baran, *J. Am. Chem. Soc.* **2017**, *139*, 7448-7451. (d) D. Ravelli, M. Fagnoni, T. Fukuyama, T. Nishikawa, I. Ryu, *ACS Catal.* **2018**, *8*, 701-713.

[3] (a) L. Zou, R. S. Paton, A. Eschenmoser, T. Newhouse, P. S. Baran, K. N. Houk, *J. Org. Chem.* **2013**, *78*, 4037–4048. (b) M. Salamone, V. B. Ortega, M. Bietti, *J. Org. Chem.* **2015**, *80*, 4710-4715.

[4] M. Salamone, T. Martin, M. Milan, M. Costas, M. Bietti, *J. Org. Chem.* **2017**, *82*, 13542–13549.

OC45

Thiophene based A-D-A small molecules with a dithienosilole core: synthesis, theoretical calculations and optoelectronic properties

F. Parenti,[a] M. Buffagni,[a] M. Caselli,[a] A. Mucci,[a] L. Pigani,[a] D. Vanossi,[a] A. Zambon[a]

[a]*Dipartimento di Scienze Chimiche e Geologiche, Via Campi 103, 41125 Modena, Italy*
e-mail*: francesca.parenti@unimore.it*

Polythiophenes are conjugated materials finding application in many optoelectronic devices.[1] Recently, much attention has been devoted to oligothiophenes, the shorter analogous compounds of these polymers. These semiconductor materials are structurally well-defined, monodisperse, free of defects and often possess higher polarizability and charge mobility with respect to the corresponding polymers.[2] Thiophene-based small molecules[3] are well studied as photoactive materials in organic solar cells. In particular, molecules with A-π-D-π-A architecture, formed by a central electron donating building block (D) and two terminal electron accepting groups (A) linked by π-conjugated bridges, show a low energy absorption band making them suitable as active layers in organic solar cells.[4,5] Little modifications of the backbone, i.e. by changing the length of the alkyl substituents or the type of the functional groups, will often result in remarkable modification of the band gap and other optical properties.

Here, we present the theoretical calculations, the synthesis and the characterization of two A-π-D-π-A small molecules **E1** and **E2**, where the central unit is a dithienosilole, the terminal units are methyldicyanovinyl functionalized thiophene rings and the π-bridges are alkyl or alkylsulfanyl functionalized thiophene rings, respectively. The aim of this research is to study the structural, electronic and optical properties of these molecules to better understand the role of the sulfur atom of the alkylsulfanyl chains and to gain insight on the properties of these materials in view of their application in optoelectronic and photovoltaic devices.

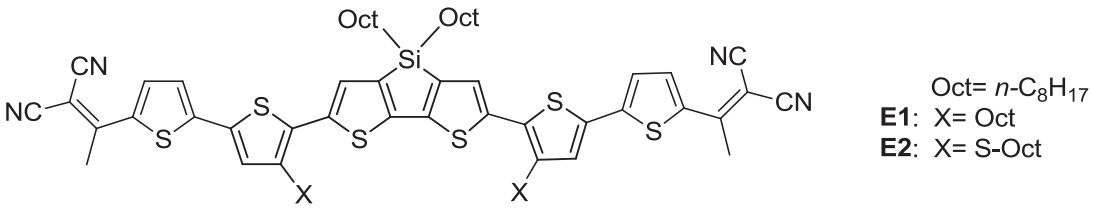


Figure 1: target thiophene-based small molecules.

References:

[1] I. F. Perepichka, D. F. Perepichka*, Handbook of Thiophene-based materials* **2009***, Vol.1*, Ed Wiley VCH.
[2] A. Mishra, C. Q. Ma, P. Bäuerle, *Chem. Rev.* **2009**, *109*, 1141-1276.
[3] A. Mishra, P. Bäuerle, *Angew. Chem. Int. Ed.* **2012**, *51*, 2020-2067.
[4] J. Min, Y. N. Luponosov, N. Gasparini, L. Xue, F.V. Drozdov, S. M. Peregudova, P. V. Dmitryakov, K. L. Gerasimov, D. V. Anokhin, Z. G. Zhang, T. Ameri, S. N. Chvalun, D. A. Ivanov, Y. Li, S. A. Ponomarenko, C. J. Brabecaj, *J. Mater. Chem. A* **2015**, *3*, 22695-22707.
[5] L. G. Mercier, A. Mishra, Y. Ishigaki, F. Henne, G. Schulz, P. Bäuerle, *Org. Lett.* **2014**, *16*, 2642-2645.

OC46

Electronic communication in Ni-tetraferrocenylporphyrin

G. Pomarico,[a] P. Galloni,[a] B. Floris,[a] V. Nemikin,[b] V. Conte[a]

[a]*University of Rome "Tor Vergata", Department of Chemical Science and Technologies, Via della Ricerca Scientifica snc, 00133, Rome*

[b]*University of Manitoba, Department of Chemistry, Winnipeg, MB R3T 2N2, Canada*

e-mail*: pomarico@scienze.uniroma2.it*

Porphyrins free base or metal complexes functionalized with ferrocenyl (Fc) units represent an interesting organic material due to their electrochemical properties.[1] The aromatic system of the macrocycle permits the electronic communication among the Fc groups. It means that after the formation of the oxidized species, the positive charge is not fixed on one site but it is exchanged among the molecule components, a phenomenon called mixed valence state. The behaviour of porphyrin free base, or metal complexes (Zn and Ni) when the oxidation is carried out by means of chemical methods was investigated, leading to the identification of different pathway (oxidation, protonation or oxidation/HAT) for the achievement of oxidized species. UV-vis, IR, ^{1}H NMR and DFT techniques were used to understand the nature of the products.

The presence of electronically communicating Fe(II) and Fe(III) centres, confirmed by experimental and theoretical data, allows to consider this class of molecules as intermediate class II-III in the Robin and Day classification of mixed-valence species.

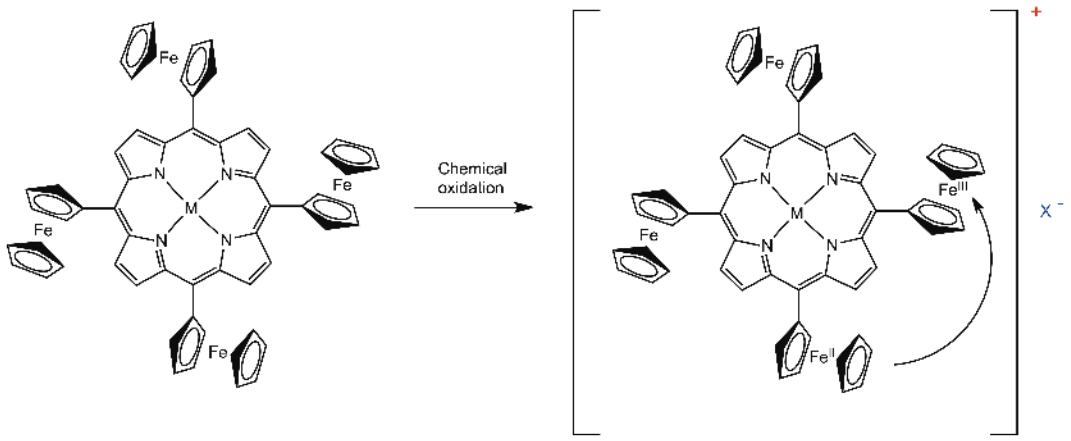


Figure 1: oxidation of tetraferrocenylporphyrin metal complexes; the product is a mixed valence species.

References:

[1] A. Vecchi, P. Galloni, B. Floris, S. V. Dudkin, V. N. Nemykin, *Coord. Chem. Rev.* **2015**, *291*, 95-171.

OC47

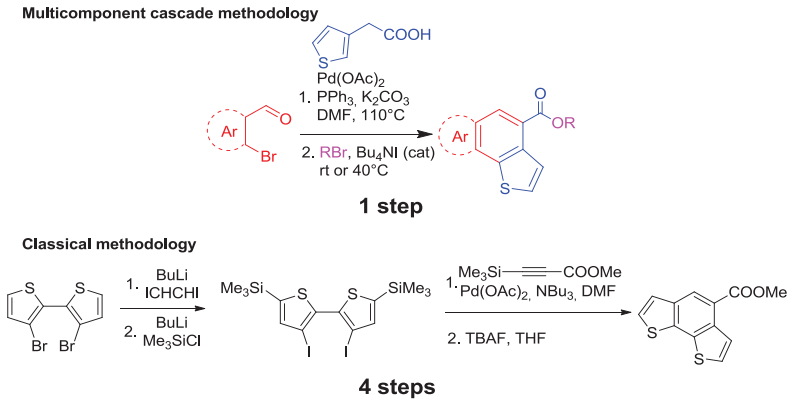
Direct Arylation – Cross Aldol Condensation Cascade Reactions as Tools for the Sustainable and Scalable Synthesis of Organic Electronic Materials

A. Nitti,[a] D. Pasini[a]

[a] *Department of Chemistry, University of Pavia, Viale Taramelli 10, 27100, Pavia, Italy.*
email:andrea.nitti01@universitadipavia.it

Successful technologies based on organic electronic materials have created a demand for the development of sustainable and efficient methodologies for the synthesis of π-extended organic compounds and polymers. In fact, the state of art materials are the result of complex syntheses that in the great majority of the cases are not scalable at industrial level.[1] Sustainability and scalability of the synthetic process plays a fundamental role for definitive consecration of the organic electronic technologies, and generally it depends from: (a) the number of synthetic steps; (b) the cost of the materials; (c) yields; (d) the number of steps of purification that require column chromatography. The main parameter used to define a sustainable process on industrial scale is the *E*-factor. In pharmaceuticals industry, where commercial product requires a number of synthetic steps comparable with those of electronic materials, acceptable *E*-factor values are included in 10^2-10^3 range. This threshold value in the case of electronic materials is respected only in very few cases. A synthetic strategy that use domino/cascade reaction for the rapid construction of π-scaffold of monomers, widely used for the synthesis of fine chemicals, can lead to cost reduction, scalability and sustainability of the synthesis processes for the synthesis of performing organic electronics materials.[2]

We will report our continuing efforts for the development of one pot protocols combining direct arylation reactions (DAr) with an intramolecular cross aldol condensation for the rapid synthesis of electronic materials.[3] The application of the DAr-cross aldol condensation protocol was used with success for the synthesis with low *E*-factor of several classes of thiophene-based compounds such as naphtothiophene, benzodithiophene and anthradithiophene and related furan-based scaffolds. This classes of compounds was used for the synthesis of oligomeric polymeric and materials and its properties have been preliminarly explored in devices.



References:

[1] Nitti, A.; Po, R.; Bianchi, G.; Pasini, D. *Molecules* **2017**, *22*, 21-31.

[2] Lu, L.-Q.; Chen, J.-R.; Xiao, W.-J. *Acc. Chem. Res.* **2012**, *45*, 1278–1293.

[3] Nitti, A.; Bianchi, G.; Po, R.; Swager, T. M.; Pasini, D. *J. Am. Chem. Soc.* **2017**, *139*, 8788–8791.

OC48

New phenolate-containing AAZTA-ligands for MRI and PET applications

J. Martinelli, L. Tei

Dipartimento di Scienze e Innovazione Tecnologica, Università del Piemonte Orientale "Amedeo Avogadro", Viale T. Michel 11, 15121 – Alessandria, Italy.
e-mail*: jonathan.martinelli@uniupo.it*

Magnetic resonance imaging (MRI) and positron emission tomography (PET) are leading techniques in modern clinical diagnostics. Contrast-enhanced MRI requires the use of suitable paramagnetic metals (*e.g.* Gd^{3+}) that increase the water-protons relaxation rate (R_1). Proper chelators are also necessary to bind the β^+-emitter radionuclides (*e.g.* $^{68}Ga^{III}$ and $^{44}Sc^{III}$) exploited in PET applications. We have designed new ligands based on the AAZTA platform (*Figure*),[1] since it has proved to chelate lanthanide and *p*-block ions with excellent thermodynamic stability and kinetic inertness, which is crucial to ensure *in vivo* safety. GdAAZTA possesses optimal parameters to attain a high MRI performance, particularly two water molecules coordinated to the metal center (q = 2), affording a R_1-enhancement per millimolar Gd-concentration (*relaxivity,* r_{1p}) of 7.1 mM^{-1} s^{-1} at 20 MHz and 25 °C. Moreover, the fast and efficient labelling of AAZTA with ^{44}Sc and ^{68}Ga has recently shown the great versatility of such a chelating platform.[2] Our novel ligands (*Figure*) contain one (**L1** and **L2**) or two (**L3**) phenolic moieties in addition to traditional acetate arms. Phenolate anions can be strong donor groups, and macrocyclic and acyclic chelates functionalized with hydroxyphenyl units are widely reported in the literature as ligands for transition-metal ions. However, their applications as lanthanide chelators is very limited, particularly for use in aqueous environments. Only a few cases are reported for Gd^{III} and Ga^{III}.[3] The synthesis of **L1**-**L3** (*Figure*) involves a nitro-Mannich cyclization with a suitable disubstituted ethylenediamine to obtain a 6-nitroperhydro-1,4-diazepine, followed by reduction of the nitro-group and mono- or dialkylation of the resulting primary amine with *t*-butyl bromoacetate. The protected phenolic moieties are introduced by reacting the primary or secondary amine(s) with 2-(bromomethyl)phenyl acetate. The ligands are obtained upon deprotection of the acetate and hydroxybenzyl arms. Gd^{3+}-complexations and a preliminary relaxometric characterization (20 MHz, 25 °C) allowed to determine r_{1p} values of 7.2, 7.5 and 4.9 mM^{-1} s^{-1} for Gd**L1**, Gd**L2** and Gd**L3** respectively, with the first two confirming a q = 2 as for GdAAZTA. Further investigations are in progress on these promising chelators and their potential MRI and PET applications (^{68}Ga labelling).

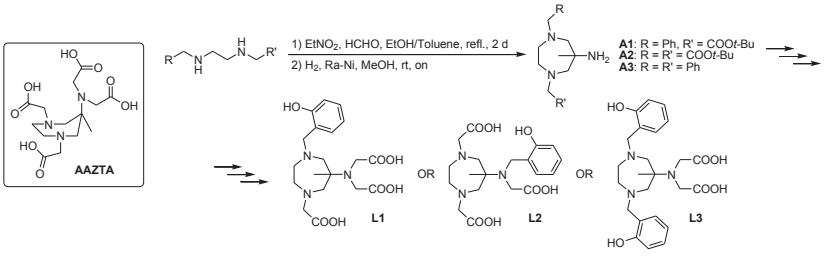


Figure: AAZTA-ligand and synthetic pathway for ligands **L1**-**L3**.

References:

[1] Aime, S. *et al.*; *Inorg. Chem.* **2004**, *43*, 7588. [2] Nagy, G. *et al.*; *Angew. Chem. Int. Ed.* **2017**, *56*, 2118; Pfister J. *et al.*; *EJNMMI Research* **2015**, *5*, 74. [3] Woods M. *et al.*; *J. Am. Chem. Soc.*, **2004**, *126*, 9248; Tsionou M. I. *et al.*; *RSC Adv.*, **2017**, *7*, 49586.

OC49

Monolayer-Coated Gold Nanoparticles as a Multimodal Probe for ^{19}F-NMR Detection and Imaging

D. Rosa-Gastaldo,[a] F. Mancin[a]

Dipartimento di Scienze Chimiche, Università di Padova, via Marzolo 1, 35121, Padova
e-mail*: daniele.rosagastaldo@studenti.unipd.it*

The ^{19}F nucleus has 100% natural isotopic abundance, spin value of ½ and its gyromagnetic ratio is close to the one of ^{1}H nucleus. These three properties, together with the absence of background signals in aqueous and biological systems, make the ^{19}F nucleus really promising for NMR sensing and MRI.[1] In this work we explore the possibility to realize innovative sensing systems by combining the properties of ^{19}F with those of gold nanoparticles in solution. Monolayer protected gold nanoparticles offer an interesting route to the development of supramolecular receptors by self-organization. They provide the possibility to form bidimensional arrays of organic molecules grafted to the gold surface. In principle, a large diversity of nanoparticles with different coatings could be generated by simply assembling different molecules.[2] It's also well known that the signals of any species bound to a nanoparticle experience a fast T_2 relaxation and a broadening of the NMR signals: they are conformationally hindered and they acquire the slowly tumbling motions of the nanoparticle. However, with a careful design it is possible to modulate the T_2 of the ligands by modulating the stiffness of the monolayer.

In this work we explore the possibility of tuning the ^{19}F nanoparticle signal by exploiting the interaction of a fluorinated ethylenediamine derivative introduced in the monolayer with metal cations. Interacting with more than one ethylenediamine ligand, the metal ion grafts together different coating molecules sensibly increasing their rigidity and consequently decreasing both T_2 and the intensity of the fluorine signals as shown in *Figure 1*

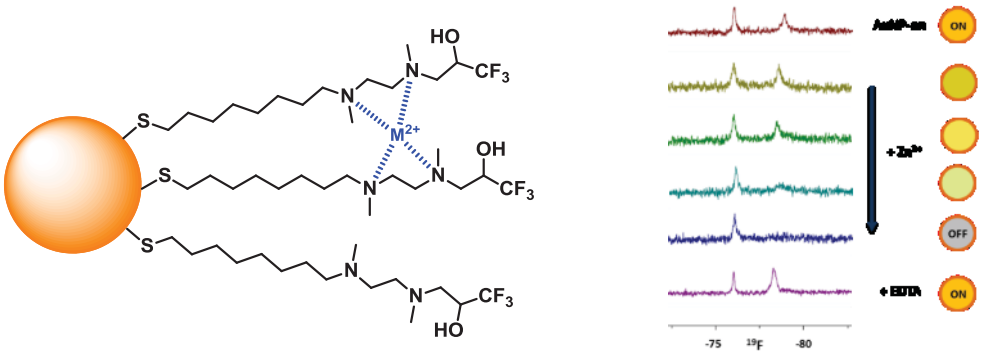


Figure 1. a) schematic representation of the interaction between the gold nanoparticle coated with the modified ethylenediamine (AuNP-en) and a metal cation. b) top to bottom: spectrum of a solution of the gold nanoparticle in water (ON) and subsequent zinc addition (fading of the signal until OFF state). Addition of EDTA restores the ON state.

This approach can be extended to other substrates amenable of multipoint intraction, enabling both NMR and MRI detection.

References:

[1] I. Tirotta, V. Dichiarante, C. Pigliacelli, G Cavallo, G. Terraneo, F. Baldelli Bombelli, P. Metrangolo, G. Resnati, *Chem. Rev.* **2015**, *115*, 1106-1129.
[2] M.V. Salvia, G. Salassa, L. Gabrielli, S. Springhetti, D. Rosa-Gastaldo, L. Trevisan, F. Rastrelli, F. Mancin, Patent application WO2017017245A1 (30/7/2015).

OC50

Chemical Synthesis of a mirror image protein by native chemical ligation

L. De Rosa,[a] R. Di Stasi,[a] L. D. D'Andrea,[a,b]

[a]*Istituto di Biostrutture e Bioimagini, CNR, Via Mezzocannone 16, Napoli*
[b]*Istituto di Biostrutture e Bioimagini, CNR, Via Nizza 52, Torino*
e-mail*: luca.dandrea@cnr.it*

Axl is a tyrosine kinases receptor belonging to the TAM family, which also includes Tyro-3 and Mer members. Axl signaling plays important role in several cellular responses, as the receptor activation promotes cellular proliferation, survival, adhesion, migration, autophagy, invasion, angiogenesis, platelet aggregation and natural killer cells differentiation.[1] Besides, Axl is potent negative regulator of innate immune responses, thus protecting against an overzealous inflammatory response. Structurally, Axl is characterized by an extracellular domain containing two N-terminal immunoglobulin (Ig)-like domains and two fibronectin type III (FNIII) repeats, a transmembrane domain and a cytoplasmic tyrosine kinase domain.[2] Axl can be activated through a number of different mechanisms, mainly upon ligand-induced dimerization. The vitamin K-dependent growth arrest-specific 6 (Gas6) protein is the principal natural ligand of Axl receptor. Upon binding of Gas6 to Axl Ig-like domains, the receptor dimerizes and its tyrosine kinase domain becomes activated.

We intend develop peptides targeting Axl extracellular domains for pharmaceutical applications using the approach called "mirror phage display library".[3] To get this aim we need to prepare a mirror image form, i.e. composed of all D-amino acids, of Axl extracellular domains. The D-protein will be immobilized on a solid support and used as bait to find binders through phage display library screening. The selected L-peptide binds to the all-D protein, this implies that the D-peptide will bind the natural L-protein. In this way a metabolically stable D-peptide binder will be developed.

Here, we report the total chemical synthesis of the mirror image form of the second Ig domain of Axl (D-Ig2^{Axl}) by native chemical ligation (NCL).[4] NCL is based on the chemoselective reaction between peptide thioester and a peptide ending with a N-terminal cysteine. The amino acid sequence of D-Ig2^{Axl} protein (88 residues) was dissected in four peptide fragments which were synthesized and purified. A biotin was introduced at the N-terminal position. The four fragments were successful ligated in solution performing three consecutive ligation reactions. Finally, the full-length D-Ig2^{Axl} was purified, characterized and refolded.

References:

[1] G. Lembe, *Cold Spring Harb Perspect Biol* **2013**, *5*, a009076.
[2] T. Sasaki, P.G. Knyazev, N.J. Clout, Y. Cheburkin, W. Gohring, A. Ullrich, R. Timpl, E. Hohenester, *EMBO J.* **2006**, *25*, 80 – 87.
[3] T.N.M Schumacher, L.M. Mayr, D.L. Minor, M.A. Milhollen, M.W. Burgess, P.S. Kim, *Science* **1996**, *271*, 1854 – 1857.
[4] P.E. Dawson, T.W. Muir, I. Clark-Lewis, S.B.H. Kent, *Science* **1994**, *266*, 776 – 779.

OC51

Outstanding chiroptical features in thin films of new chiral π-conjugated oligomers

G. Albano, L. Portus, L. A. Aronica, L. Di Bari

Dipartimento di Chimica e Chimica Industriale, Università di Pisa, via G. Moruzzi 13, 56124 Pisa, Italy

e-mail*: gianluigi.albano@dcci.unipi.it*

Chirality in organic optoelectronics is a topic which is rapidly gaining interest:[1] in fact, it is a means to drive and control the supramolecular order of π-conjugated molecules constituting the active layers of the devices,[2] and secondly it opens the way to highly specialized applications, such as producing (CP-OLED),[3] or detecting (CP-OFET)[4] circularly polarized (CP) light or specifically responding to enantiomers in analytical sensors.[5] A current research goal is to obtain thin films of organic semiconductors displaying high discrimination of CP-light in absorption (electronic circular dichroism, ECD) or in emission (circularly polarized luminescence, CPL). Chiral supramolecular architectures of π-conjugated oligomers could be the key to achieve this goal.

Starting from this consideration, we synthesized a set of new oligothiophenes functionalized with inexpensive alkyl chiral groups from natural sources (**Figure 1a**), studying their (chiro)optical features in thin films. Surprisingly, for some of them we found the uncommon property of ECD signal inversion by sample flipping (**Figure 1b**)[6]. This is due to the interference between linear dichroism and linear birefringence, called LDLB effect, which is theoretically well understood, but to date only rarely reported in the literature. In particular, we investigated the impact of LDLB in thin films depending on the deposition technique (drop casting vs. spin coating) and the chemical structure (by changing the alkyl chiral chains or the π-conjugated backbone).

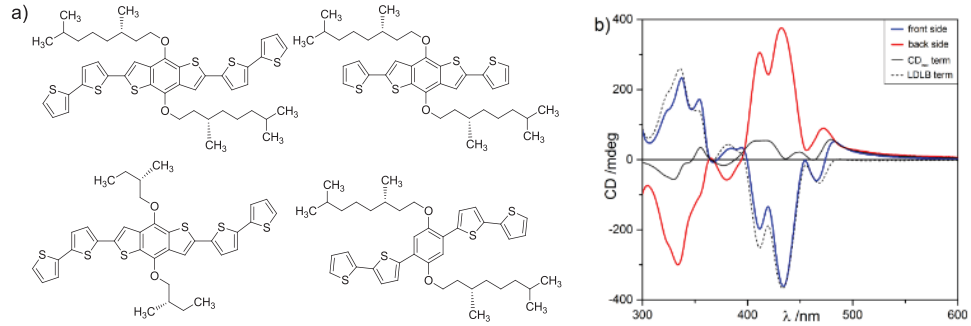


Figure 1: a) Chemical structure of new chiral oligothiophenes recently investigated by our group. b) ECD spectrum inversion by sample flipping due to LDLB effect in thin films of our compounds.

References:

[1] J. R. Brandt, F. Salerno, M. J. Fuchter, *Nat. Rev. Chem.* **2017**, *1*, 0045. [2] a) Y. Yang, Y. Zhang, Z. Wei, *Adv. Mater.* **2013**, *25*, 6039-6049; b) M. Liu, L. Zhang, T. Wang, *Chem. Rev.* **2015**, *115*, 7304-7397. [3] a) J. R. Brandt, X. Wang, Y. Yang, A. J. Campbell, M. J. Fuchter, *J. Am. Chem. Soc.* **2016**, *138*, 9743-9746; b) D.-M. Lee, J.-W. Song, Y.-J. Lee, C.-J. Yu, J.-H. Kim, *Adv. Mater.* **2017**, *29*, 1700907. [4] a) Y. Yang, R. C. da Costa, M. J. Fuchter, A. J. Campbell, *Nat. Photon.* **2013**, *7*, 634-638; b) X. Shang, I. Song, H. Ohtsu, Y. H. Lee, T. Zhao, T. Kojima, J. H. Jung, M. Kawano, J. H. Oh, *Adv. Mater.* 2017, **29**, 1605828. [5] L. Torsi, G. M. Farinola, F. Marinelli, M. C. Tanese, O. H. Omar, L. Valli, F. Babudri, F. Palmisano, P. G. Zambonin, F. Naso, *Nat. Mater.* **2008**, *7*, 412-417. [6] a) G. Albano, M. Lissia, G. Pescitelli, L. A. Aronica, L. Di Bari, *Mater. Chem. Front.* **2017**, *1*, 2047-2056; b) G. Albano, F. Salerno, L. Portus, W. Porzio, L.A. Aronica, L. Di Bari, *J. Mater. Chem. C* **2018**, *Submitted*.

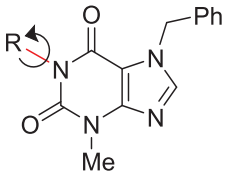
OC52

Xanthines having chiral axes: Conformational Analysis and Absolute Configuration [1]

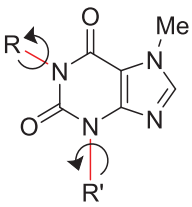
M. Mancinelli[a], S. Perticarari[a], L. Prati[a], A. Mazzanti[a]

[a] *Department of Industrial Chemistry "Toso Montanari" University of Bologna; Viale del Risorgimento 4, 40136, Bologna, Italy.*
e-mail: michele.mancinelli@unibo.it

Modified purine bases play an important role in biology, and they are interesting system under biochemical, pharmacological, and chemical points of view. Although is not possible to install an ordinary stereogenic center without modify any of its essential functional groups, it is possible to install chiral axes on xanthines. The 1-aryl and 1,3-bis aryl-xanthines prepared for this study are shown in Figure 1.



R= *o*-tolyl, **4**
R= *o*-nitrophenyl, **5**
R= 1-naphthyl, **6**



R = R' = *o*-tolyl, **7a** (*syn*), **7b** (*anti*)
R = *o*-tolyl, R' = *p*-methoxy-phenyl, **8a**
R = *p*-methoxy-phenyl, R' = *o*-tolyl, **8b**
R = 1-naphthyl, R' = *p*-methoxy-phenyl, **9a**
R = *p*-methoxy-phenyl, R' = 1-naphthyl, **9b**

Figure 1. 1-aryl and 1,3 bis aryl-xanthines prepared.

The xanthine backbone is a planar framework in which an aryl substituent linked in the 1 or 3 position is driven out of the xanthine plane because of the steric hindrance, caused by the two carbonyls. Depending on the hindrance of the *ortho*-substituents, the resulting conformational enantiomers were found to be either stereo labile or configurationally stable. In the case of compounds **6**, **9a** and **9b** the atropisomeric pair has been resolved (Figure 2), and the absolute configuration determined by chiro-optical methods supported by TD-DFT calculations.

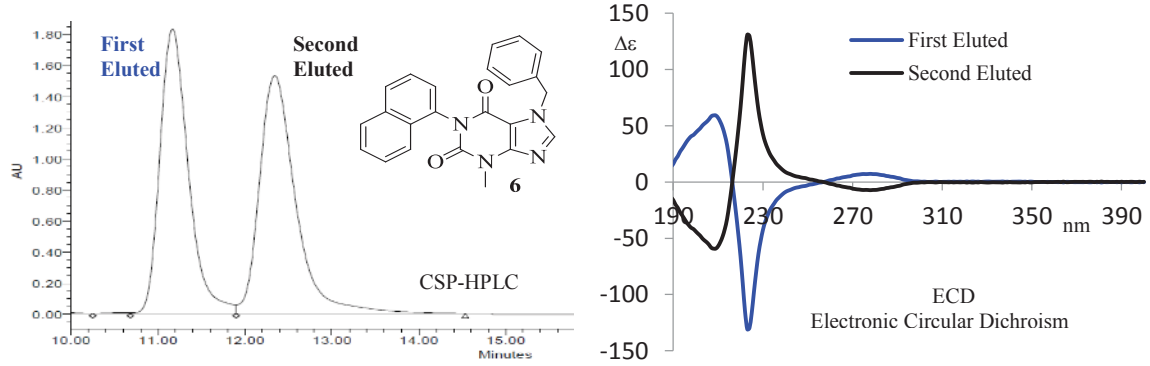


Figure 2. Compund **6**. Left: CSP-HPLC; Right: Electronic Circular Dichroism

References:

[1] . M. Mancinelli, S. Perticarari, L. Prati, A. Mazzanti *J. Org. Chem.* **2017**, *82*, 6874-6885.

OC53

Novel Chiral Deep Eutectic Solvents as chiral reaction media

M. Tiecco,[a] G. Ciancaleoni,[b] T. Palomba,[a] F. Ianni,[c] T. Del Giacco,[a] R. Germani.[a]

[a]*Dep. of Chemistry, Biology and Biotechnology, Università degli Studi di Perugia, via Elce di Sotto 8 - 06124, Perugia.*
[b]*Dep. of Chemistry and Industrial Chemistry, University of Pisa, via G. Moruzzi 13 - 56124 Pisa.*
[c]*Dep. of Pharmaceutical Sciences, University of Perugia, Via del Liceo 1 - 06123, Perugia.*
e-mail*: matteotiecco@gmail.com*

Deep Eutectic Solvents (DESs) are rapidly emerging in the field of novel organic solvents thanks to their unique properties.[1] These systems are formed by simply mixing and heating two high-melting points solids at the proper molar ratio. The two solids are a HBD compound (urea, carboxylic acids, polyols, etc.) and a HBA one (ammonium salts, betaine, zwitterionic compounds). The hydrogen bond interactions occurring between them lead to a liquid formation even at room temperature, generally thanks to a decrease of electrostatic interactions in the salts. In addition to the green properties and to the environmental benefits of these liquids,[2] there are many advantages in the use of DESs in synthetic organic chemistry as it is emerging from the recent literature.[3] They were used as solvents in reactions that normally require anhydrous conditions without need of water removal in the DES or without any air-contact prevention; they can be used in "out of the hood" procedures if the products are water insoluble by simply adding water at the end of the reaction and precipitating them; they can act as "active DESs" as acid catalysts; they can provoke a super-activation of chiral auxiliaries with H-bond interactions with them increasing the enantiomeric excess of a reaction.[3]

We present the realization and the structural properties of novel chiral Deep Eutectic Solvents.[4] These liquids are formed by mixtures of chiral HBD and HBA molecules that are common, relatively cheap and commercially available (the two enantiomers of camphorsulfonic acid as HBD) or easily one-step synthesized molecules from commercially available compounds (functionalized chiral amines as HBA). Their structural features were analyzed via ^{1}H Pulsed Field gradient Spin Echo (PGSE) NMR, NMR titration, ^{1}H NMR analyses of formation and differences in the chemical shifts of the peaks of the liquids. Density Functional Theory (DFT) optimization helped to define the structures of these liquids. Finally, these liquids were used as reaction media / chiral organocatalysts / acid catalysts in a probe reaction. These liquids proved to be highly-structured as showed by different yields and enantiomeric excesses observed, suggesting these liquids to form diastereoisomerically different liquids by changing one of the two enantiomers. These chiral Deep Eutectic Solvents revealed to be promising novel high-structured media for enantioselective reactions.

References:

[1] D. A. Alonso, A. Baeza, R. Chinchilla, G. Guillena, I. M. Pastor, D. J. Ramón, *Eur. J. Org. Chem.*, **2016**, *4*, 612-632.

[2] A. Paiva, R. Craveiro, I. Aroso, M. Martins, R.L. Reis, A.R.C. Duarte, *ACS Sustain. Chem. Eng.* **2014**, *2*, 1063–1071.

[3] a. M. Tiecco, R. Germani, F. Cardellini, *RSC Adv.* **2016**, *6(49)*, 43740-43747. b. R. Martínez, L. Berbegal, G. Guillena, D. J. Ramón, *Green Chem.* **2016**, *18(6)*, 1724-1730. c. C. Vidal, J. García-Álvarez, A. Hernán-Gómez, A. R. Kennedy, E. Hevia, *Angew. Chem. Int. Edit.* **2014**, *53(23)*, 5969-5973.

[4] T. Palomba, G. Ciancaleoni, T. Del Giacco, R. Germani, F. Ianni, M. Tiecco, *J. Mol. Liq.* **2018**, in press.

OC54

Dialkyl Carbonates for the Upgrade of Renewable Alcohols

L. Cattelan,[a] M. Selva,[b] A. Perosa,[b] G. Fiorani[b]

[a]*Laboratory of Advanced Catalysis for Sustainability, School of Chemistry, The University of Sydney, NSW 2006 (Australia)*
[b]*Università Ca' Foscari Venezia Dipartimento di Scienze Molecolari e Nanosistemi Via Torino, 155 - 30172 Venezia Mestre (VE)*
e-*mail*: giulia.fiorani@unive.it

In recent years, linear and cyclic organic carbonates have found an increasing number of applications, including synthetic ones as chlorine-free alkylating and acylating reagents, solvents for lithium batteries and, more recently, as sustainable reagents for the upgrade of renewable based molecules and for the preparation of phosgene-free polycarbonates and polyurethanes.[1]

Organic carbonates can be synthesized in a sustainable fashion starting from CO_2 and MeOH to give dimethyl carbonate (DMC), which, in presence of higher MW alcohols, can then be further employed as a) a carboxymethylation reagent to prepare the corresponding symmetrical and asymmetrical organic carbonates, or b) as a methylating agent to give the corresponding methyl ether(s).

We will discuss the recent developments by our group in synthesis and utilization of alkyl carbonates towards the upgrade of bio-based derivatives. We will focus in particular on valorisation of glycerol and its acetal derivatives (*e. g.* solketal and glycerol formal) by selective batch and continuous flow (CF) processes in the presence of basic heterogeneous catalysts easily obtainable by calcination of commercially available hydrotalcites (HTs). The key sustainable features of these processes will be highlighted and discussed, ultimately aiming at the development of green scalable processes.

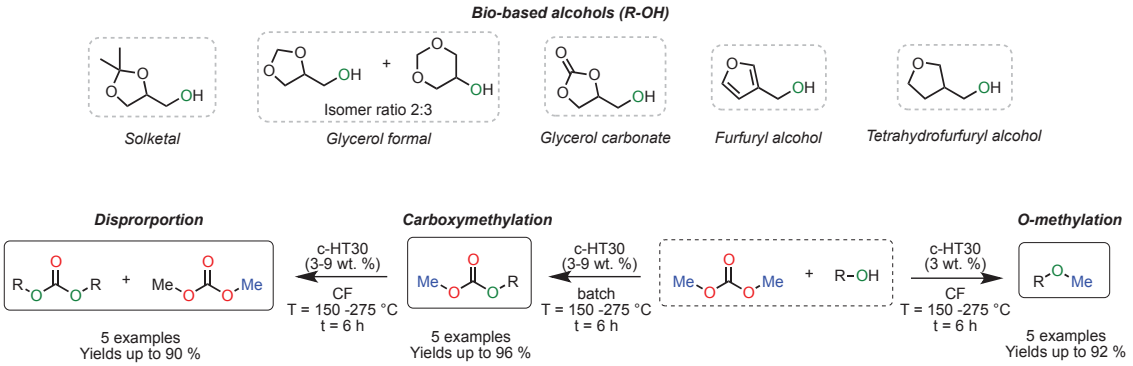


Figure 1: DMC based carboxymethylation/disproportion (bottom left) and *O*-methylation (bottom right) for renewable based alcohols valorisation.

References:

[1] G. Fiorani, A. Perosa, M. Selva, *Green. Chem.* **2018**, *20*, 288 - 322.

[2] a) L. Cattelan, A. Perosa, P. Riello, T. Maschmeyer, M. Selva, *ChemSusChem* **2017**, *10*, 1571 – 1583; b) L. Cattelan, G. Fiorani, A. Perosa, T. Maschmeyer, M. Selva, *ACS Sustainable Chem. Eng.* **2018**, under revision.

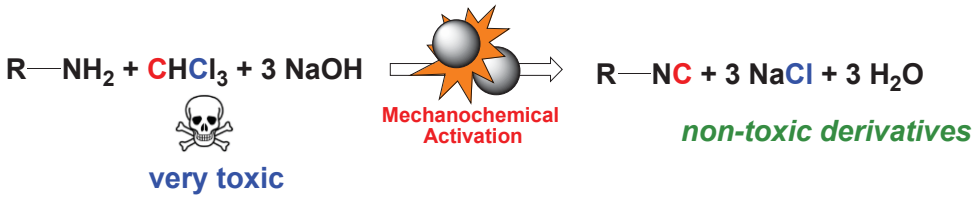
OC55

Mech@nochemistry: a Disruptive Innovation

A. Porcheddu,[a] E. Colacino,[b] F. Delogu,[a] R. Mocci[a]

[a]*Università degli Studi di Cagliari, Dipartimento di Scienze Chimiche e Geologiche, Cittadella Universitaria, SS 554 bivio per Sestu, 09042-Monserrato (CA), Italy.*
[b]*Institut des Biomolécules Max Mousseron (IBMM) UMR5247 CNRS-UM-ENSCM, cc1703, Place Eugène Bataillon, 34095 Montpellier Cedex 05, France*
e-mail*: porcheddu@unica.it*

In public perception, organic chemistry is often considered negative and dangerous, therefore there is a strong effort to rethink the way by which chemists conduct organic reactions. Fortunately, the organic chemistry is changing its wasteful ways embracing the green chemistry philosophy, i.e. the idea that we can cut the hazardous chemicals given off as waste without giving up all of the benefits of chemical products. From a green chemistry point of view, solvent-free syntheses are unquestionably more desirable than reactions in any kind of solvents becoming a very popular research topic. Mechanochemical reactions, conducted by milling, grinding, or shearing are rapidly emerging as an attractive, clean, energy- and materials-efficient alternative to conventional solution-based synthesis and are considered to be promising candidates in solvent-free synthesis. In this scenario, "*mechanical energy*" represents an alternative mean to activate chemical processes, which have not been widely explored yet. Moreover, the *mechanochemical activation* of organic synthesis allows overcoming some of the issues of classical synthesis in solution, enables the design of unexplored synthetic strategies, thus expanding the scope of chemical reactions to insoluble starting materials (Scheme 1). In this communication, the potential of "*Mechanochemistry*" applied to some significant reactions recently developed in our laboratories, and some of the related challenges, will be discussed in detail.[1-4]



Scheme 1

References:

[1] A. Porcheddu, E. Colacino, G. Cravotto, F. Delogu, L. De Luca, *Beilstein J Org. Chem.* **2017**, *13*, 2049–2055.
[2] S. Gaspa, A. Porcheddu, A. Valentoni, S. Garroni, S. Enzo, L. De Luca, *Eur. J. Org. Chem.* **2017**, 5519-5526.
[3] R. Mocci, S. Murgia, L. De Luca, E. Colacino, F. Delogu, A. Porcheddu, *Org. Chem. Front.* **2018**, *5*, 531-538.
[4] K. Martina, L. Rotolo, A. Porcheddu, F. Delogu, S. R. Bisouth, G. Cravotto, E. Colacino, *Chem. Comm.* **2018**, 54, 551-554.

OC56

Mechanistic Investigations of the Pd(0)-Catalyzed Enantioselective 1,1-Diarylation of Benzyl Acrylates

M. Orlandi,[a] M. J. Hilton,[a] E. Yamamoto,[a] F. D. Toste,[b] M. S. Sigman[a]

[a] *Department of Chemistry, University of Utah, 315 South 1400 East, Salt Lake City, USA.*
[b] *Department of Chemistry, University of California, Berkeley, California 94720, USA.*
e-mail: *manuel.orlandi@unimi.it*

As asymmetric catalysis has evolved as a significant resource in stereoselective synthesis, so has the mechanistic underpinnings of such catalytic processes, on the basis of which this field continues to mature. In this context, stereoselective, multicomponent catalytic reactions have also been developed, accessing complex products from the union of simple starting materials. However, multicomponent reactions are intrinsically prone to the formation of undesired byproducts and are challenging to render enantioselective. Thus, the selective combination of multiple building blocks into a single chiral product remains an emerging technology for synthetic chemists.

A mechanistic study of the Pd-catalyzed enantioselective 1,1-diarylation of benzyl acrylates that is facilitated by a Chiral Anion Phase Transfer (CAPT) process is presented (Figure 1).[1] Kinetic analysis, D-labeling, crossover and non-linear effect experiments confirm the hypothesized general mechanism and reveal the role of the phosphate counterion in the CAPT catalysis. The phosphate was found to be involved in the phase transfer step and in the stereoinduction process as expected, but also in the unproductive reaction that provides the traditional Heck byproduct. A combination of multivariate correlations and DFT transition state analyses[2-3] revealed the weak interactions responsible for enantioselectivity. Such putative interactions include π-stacking and a CH···O electrostatic attraction between the substrate benzyl moiety and the phosphate.

The presented work provides the first comprehensive study of the combined use of CAPT and transition metal catalysis setting the foundation for future applications.

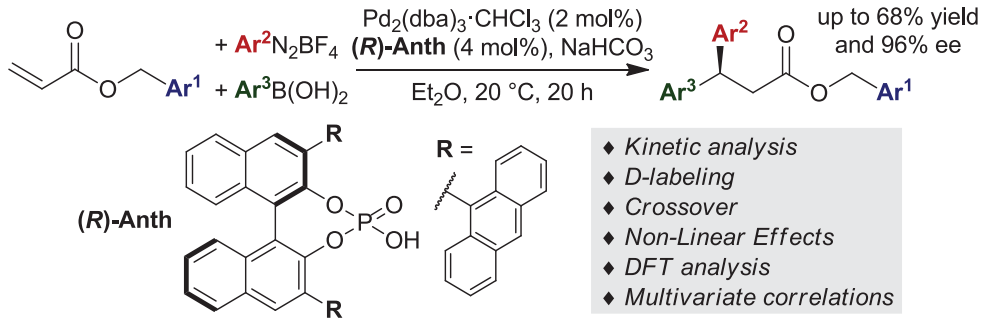


Figure 1: Palladium-catalyzed enantioselective 1,1-diarylation of benzyl acrylates.

References:

[1] M. Orlandi, M. J. Hilton, E. Yamamoto, F. D. Toste, M. S. Sigman, *J. Am. Chem. Soc.* **2017***, 139,* 12688-12695.

[2] (a) M. S. Sigman, K. C. Harper, E. N. Bess, A. Milo, *Acc. Chem. Res.* **2016**, *49*, 1292-1301. (b) C. B. Santiago, J.-Y. Guo, M. S. Sigman, *Chem. Sci.* **2018**, *9*, 2398-2412.

[3] M. Orlandi, J. A. S. Coelho, M. J. Hilton, F. D. Toste, M. S. Sigman, *J. Am. Chem. Soc.* **2017**, *139*, 6803-6806.

OC57

Metal Catalysts in Non-Conventional Solvents as Efficient Recyclable Systems for 1,3-Dipolar Cycloaddition Reactions of Azides

V. Algieri,[a] A. De Nino,[a] L. Maiuolo,[a] P. Merino,[b] B. Russo,[a] I. Delso[b,c]

[a] *Dipartimento di Chimica e Tecnologie Chimiche, Università della Calabria, Ponte Bucci cubo 12/C, 87036, Arcavacata di Rende (CS), Italy;* [b] *Department of Organic Chemistry, Faculty of Sciences. Institute of Biocomputation and Physics of Complex Systems (BIFI), University of Zaragoza, Campus San Francisco, 50009 Zaragoza, Aragon, Spain;* [c] *Servicio de Resonancia Magnetica Nuclear, CEQMA, Universidad de Zaragoza-CSIC, 50009 Zaragoza, Aragon, Spain.*

e-mail*: vincenzo.algieri@unical.it*

In recent years, extensive studies have been focused on ionic and eutectic liquids for their efficient characteristics as eco-friendly solvents. In fact they are used for different organic reactions, especially in biologically active heterocyclic ring synthesis. The 1,2,3-triazole and tetrazole rings represent a significant class of pharmacologically active nitrogen compounds that exhibit a number of important biological properties, such as antibacterial, antifungal, anticancer, antiviral, antitubercular, analgesic, anti-inflammatory, anticonvulsant, antidepressant and anti-arrhythmic activities.[1] Moreover, these compounds have found industrial applications as dyes, agrochemicals, corrosion inhibitors, and photostabilizers.[1]

On the basis of our experience in cycloaddition reactions (1,3-Dipolar Cycloadditions, Diels-Alder etc.) with recoverable catalytic systems,[2,3] we report the synthesis of 1,2,3-triazoles and tetrazoles carried out by using different azides, dipolarophile (ω-nitrostyrene derivatives or nitriles) and a catalytic system such as Metal catalyst Lewis Acid/IL/H_2O (**Figure 1**). In fact, the ionic liquid/catalyst system can be readily separated and recovered in excellent purity for direct reuse.

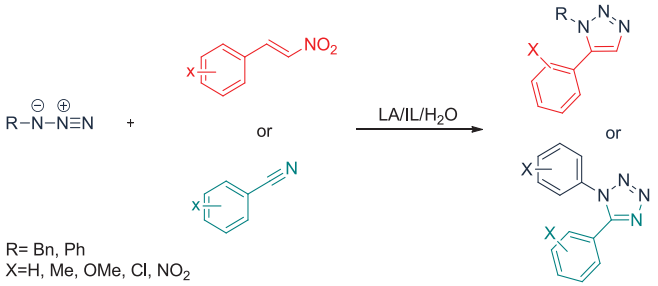


Figure 1: General reaction scheme.

Moreover, we will illustrate the use of ionic liquids and deep eutectic solvents as a green, efficient and recoverable reaction medium for the cycloaddition reaction of azides with different dipolarophiles to afford the corresponding 1,2,3-triazoles and tetrazoles.

References:

[1] Wei C.-X., Bian M., Gong G.-H. *Molecules*, **2015**, 20, 5528-5553.

[2] De Nino A., Garofalo A., Maiuolo L., Procopio A., Russo B., Bortolini O. *Appl. Catal. A*, **2010**, 372, 124–129.

[3] De Nino A., Maiuolo L., Merino P., Nardi M., Procopio A., Roca-López D., Russo B., Algieri V., *ChemCatChem*, **2015**, 7, 830-835.

OC58

Highly Efficient Microwave-Assisted Synthetic Protocols in the Presence of Recyclable Pd/β-Cyclodextrin Cross-Linked Catalyst

E. Calcio Gaudino, K. Martina, S. Tagliapietra, A. Barge, A. Binello, G. Cravotto

Dip.to di Scienza e Tecnologia del Farmaco, University of Turin, Via P. Giuria 9, 10125 Turin (Italy)
e-mail*: emanuela.calcio@unito.it*

Chemical process sustainability is one of the main challenges currently facing environmental science. At this regards, the use of *ad hoc* tailored heterogeneous catalysts under microwave (MW) dielectric heating [1] strongly promotes a number of sustainable synthetic protocols.

In this context, we recently described the preparation and the application of a series of recyclable β-cyclodextrin-cross linked Pd catalysts (Pd/CβCAT) well suited for MW-assisted reactions. These Pd catalysts have been successfully used to perform efficient C-C couplings (mainly Heck and Suzuki) [2] and aminocarbonylations [3]. The bimetallic Pd-Cu/CβCAT catalyst was successfully applied in Sonogashira alkynylations [4]. Our synthetic protocol includes alternative green solvents such as the bio-derived γ-valerolactone (GVL) [5], applied in aminocarbonylative couplings for the clean synthesis of several 4(*3H*)-quinazolinones under MW irradiation [6]. The Pd-catalyzed, four-component carbonylative coupling reactions of *o*-iodoanilines, trimethyl orthoformate and a variety of amines have been carried out under CO pressure (2.5 bar) (Figure 1). This protocol was found to be highly efficient and selective for 4(*3H*)-quinazolinones, which were isolated in good yields with the recyclable catalyst (Pd/CβCAT). The synthetic procedure can easily be scaled up to gram scale and carried out in flow mode using a modern MW flow reactor that enables heterogeneous catalysis under gas pressure, thus paving the way for safer, energy saving and more environmentally benign synthetic protocols.

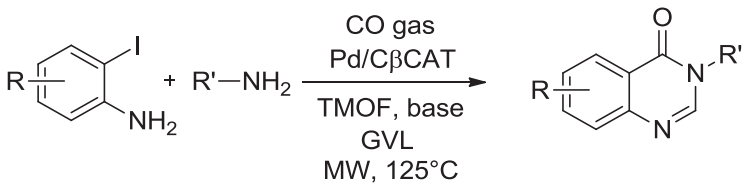


Figure 1: MW–assisted 4(*3H*)-quinazolinones synthesis in green solvent (GVL)

References:

[1] G. Cravotto and D. Carnaroglio *eds.* "*Microwave Chemistry*", De Gruyter Graduate, Berlin, **2017**.
[2] G. Cravotto, E. Calcio Gaudino , S. Tagliapietra *et al*. *Green Process. Synth.* **2012**, *1*, 269–273.
[3] E. Calcio Gaudino, D. Carnaroglio, K. Martina *et al. Org. Process Res. Dev.* **2015**, *19*, 499–505.
[4] P. Cintas, G. Cravotto, E. Calcio Gaudino, L. Orio, L. Boffa, *Catal. Sci. Technol*. **2012**, *2*, 85–87.
[5] I. T. Horváth, *Green Chem.* **2008**, *10*, 1024–1028.
[6] E. Calcio Gaudino, S. Tagliapietra, G. Palmisano *et al. ACS Sust. Chem. Eng.* **2017**, *5*, 9233–9243.

OC59

Photoinduced and Photocatalyzed Multicomponent Reactions

A. Basso, M. Anselmo, P. Capurro, L. Moni, L. Banfi, R. Riva

Università degli Studi di Genova.
Dipartimento di Chimica e Chimica Industriale, Via Dodecaneso 31, Genova
e-mail*: andrea.basso@unige.it*

Multicomponent reactions have emerged as a very powerful tool to generate structural complexity in a straightforward and efficient manner. According to the principles of green chemistry, issues such atom and step economy, ease of purification or reduced use of solvents are fulfilled.

Photochemistry is of immense importance in nature, but also synthetic organic chemistry largely benefit of the possibility to perform complex reactions under mild conditions, thus fulfilling another requirement of green chemistry, that is energy saving.

The combination of multicomponent and photochemical approaches (Figure 1) is indeed a very promising and fruitful field of research.[1] In principle two distinct approaches can be followed: A) photochemistry is used to directly generate a reactive intermediate, which becomes one reagent of a multicomponent reaction, B) photochemistry is used to activate a catalyst, which in turn catalyzes the formation of a reactive species, able to trigger a multicomponent process.

In this communication both approaches will be illustrated, with examples taken from our laboratories.

Regarding photoinduced multicomponent reactions, the latest results on the ketene three-component reaction will be illustrated. The use of silanols as surrogated of carboxylic acids and the applications of the resulting silyl enol ethers have been the subject of a recent publication.[2]

Regarding photocatalyzed multicomponent reactions, the synthesis of benzo-fused heterocycles starting from diazonium salts will be shown, with emphasis on different approaches and possible developments.[3]

It will be also shown how enabling technologies, such as flow systems, can be implemented into the synthetic approaches and how these can be improved in terms of selectivity.

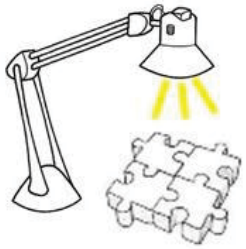


Figure 1

References:

[1] S. Garbarino, D. Ravelli, S. Protti, A. Basso *Angew. Chem. Int. Ed.* **2016**, *55*, 15476-15484.
[2] F. Ibba, P. Capurro, S. Garbarino, M. Anselmo, L. Moni, A. Basso *Org. Lett.* **2018**, *20*, 1098-1101.
[3] M. Anselmo, L. Moni, H. Ismail, D. Comoretto, R. Riva, A. Basso *Beilstein J. Org. Chem.* **2017**, *13*, 1456-1462.

OC60

Tailoring Carbon Nanodots

M. Cacioppo,[a] F. Arcudi,[a] L. Đorđevic,[a] M. Prato [a,b,c]

[a] *Department of Chemical and Pharmaceutical Sciences, INSTM UdR Trieste, Via Licio Giorgieri 1, University of Trieste, 34127 Trieste, Italy*

[b] *Carbon Nanobiotechnology Laboratory, CIC biomaGUNE, Paseo de Miramón 182, 20014 Donostia-San Sebastián, Spain*

[c] *Basque Foundation for Science, Ikerbasque, 48013 Bilbao, Spain*

e-mail*: michele.cacioppo@phd.units.it*

Carbon Nanodots (CNDs) are an emergent class of carbon nanomaterials that include quasi-spherical nanoparticles with size below 10 nm.[1] They possess many unique and attractive characteristics including the possible use of easily available and cheap precursors, facile and low cost production, low toxicity, biocompatibility, tunable emission, low photobleaching and good solubility in a variety of solvents.[2] These features have prompted their application in a wide range of technologies, eventually outperforming heavy metal based quantum dots, which still reserve toxicity concerns even possessing excellent optical properties. Over the past few years a variety of synthetic methods for CNDs have been explored. They can be generally classified into two main categories, namely, top-down and bottom-up synthetic approaches.[2] The latter provide more accessible and cost-effective processes by applying external energy as heating and microwave or template-assisted synthesis, through the possible use of facile experimental set-up and inexpensive starting materials. Apart from appropriate synthetic conditions, a proficient choice of the starting precursors is of pivotal importance. Regrettably, besides element doping, there are no rational synthetic approaches for preparing materials with predictable properties, this field being driven mainly by empirical evidence. Our laboratory tackles a rather simple strategy, based on the rational choice of small molecular building blocks as CND precursors, which are able to induce the desired physicochemical properties from the molecular level to the nanoscale, in a controlled fashion.[3] Recently we reported a straightforward approach to tailor their emission or customizing their energy levels.[4,5] Current efforts are focused on the design principles for the preparation of chiral CNDs to convey chirality from molecular to nanoscale level.

References:

[1] X. Xu, R. Ray, Y. Gu, et al., *J. Am. Chem. Soc.* **2004**, *126*, 12736 - 12737.

[2] V. Georgakilas, J.A. Perman, J. Tucek, R. Zboril, *Chem. Rev.* **2015**, *115*, 4744 - 4822.

[3] F. Arcudi, L. Đorđevic, M. Prato, *Angew. Chemie - Int. Ed.* **2016**, *55*, 2107 - 2112.

[4] F. Arcudi, L. Đorđevic, M. Prato, *Angew. Chemie - Int. Ed.* **2017**, *56*, 4170 - 4173.

[5] F. Rigodanza, L. Đorđevic, F. Arcudi, M. Prato, *Angew. Chemie - Int. Ed.* **2018**, *57*, 5062 – 5067.

OC61

Carborane-BODIPY Dyads: New Photoluminescent Materials Through an Efficient Heck Coupling approach

M. Blangetti,[a] C. Bellomo,[a] J. Cabrera-González,[b] M. Chaari,[b] N. Gaztelumendi,[c] C. Nogués,[c] R. Nuñez[b] and C. Prandi[a]

[a]*Department of Chemistry, University of Turin, Via P. Giuria 7, I-10125 Torino (ITALY)*
[b]*ICMAB-CSIC, Campus de la UAB, E-08193, Bellatera, Barcelona (SPAIN)*
[c]*BCFI, Universitat Autònoma de Barcelona, E-08193, Bellatera, Barcelona (SPAIN)*
e-mail*: marco.blangetti@unito.it*

Carboranes are well-known interesting chemical species part of the boron cluster chemistry with unique physico-chemical features.[1] Many new synthetic procedures have been developed to functionalize these compounds, and the interest in studying their photoluminescent (PL) analogues in view of new applications in several fields has noticeably increased recently.[2] In fact, the carboranyl cage directly influences the PL properties of the final material and gives an additional thermal stability, which is crucial in tuning the final properties of a certain material.

Owing to their unique spectroscopic properties and their easiness of functionalization, BODIPY (4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene) dyes have emerged as an interesting new class of fluorophores for boron clusters functionalization.[3] As part of our studies aimed at tagging a class of biological relevant compounds using fluorescent probes for live-cell imaging applications,[4a] we recently reported the optimization of a Heck coupling reaction on an asymmetric aza-BODIPY core.[4b] Starting from these grounds, we envisaged that styrene-containing carborane derivatives might represent a very suitable coupling partner for Heck reaction with halogenated BODIPY fluorophores and their aza-analogues. We herein report the synthesis of a small library of carborane-BODIPY/aza-BODIPY dyads by means of a novel convergent synthetic approach where the key step is a Pd-catalyzed Heck coupling reaction (Figure 1). The spectroscopic and photochemical properties of these new compounds, together with their internalization in HeLa cancer cells, are also discussed.

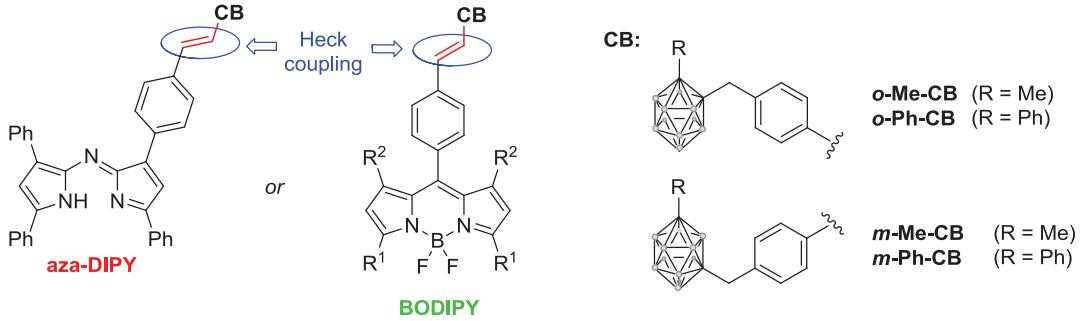


Figure 1: novel carborane-fluorophore dyads by means of Heck coupling reaction.

References:

[1] M. Scholz, E. Hey-Hawkins, *Chem. Rev.* **2011**, *111*, 7035-7062.
[2] R. Núñez, M. Tarrés, A. Ferrer-Ugalde, F. F. de Biani, F. Teixidor, *Chem. Rev.* **2016**, *116*, 14307-14378.
[3] S. Xuan, N. Zhao, Z. Zhou, F. R. Fronczek, M. G. H. Vicente, *J. Med. Chem.* **2016**, *59*, 2109-2117
[4] a) C. Prandi, H. Rosso, B. Lace, E. G. Occhiato, A. Oppedisano, S. Tabasso, G. Alberto, M. Blangetti, *Mol. Plant* **2013**, *6*, 113-127. b) S. Parisotto, B. Lace, E. Artuso, C. Lombardi, A. Deagostino, R. Scudu, C. Garino, C. Medana, C. Prandi, *Org. Biomol. Chem.* **2017**, *15*, 884-893.

OC62

Synthesis and anti-bacterial activity of a library of 1,2-benzisothiazol-3(2H)-one (BIT) derivatives amenable of crosslinking to Polysaccharides

B. Rossi[a,b] F. Viani,[b] L.Merlini,[c] Y.M. Galanter[c]

[a]*Dipartimento CMIC "Giulio Natta" Politecnico di Milano, P.zza Leonardo da Vinci, 20133, Milano, Italy*
[b]*Istituto di Chimica del Riconoscimento Molecolare, C.N.R., Via Mancinelli 7, 20131 Milano, Italy*
[c]*Istituto di Chimica del Riconoscimento Molecolare, C.N.R., Via M. Bianco 9, 20131 Milano, Italy*
e-mail*: bianca.rossi@polimi.it*

Polymers from natural sources, particularly plant polysaccharides, are employed in a growing number of industrial applications, in their native or in chemically and/or biochemically modified forms. In particular, galactomannans (GM) are high molecular weight polysaccharides found in the seed endosperms of some Leguminosa. These biodegradable compounds are used mostly as: emulsion stabilizers, rheology modifiers; agents for coating etc.[1] However, GM are susceptible to degradation by microbial contamination from the environment.[2] Therefore, to prevent damages due to microbial contaminations, it is common practice to add various amounts of chemical biocides to protect them. These are small molecular weight molecules, with different degrees of toxicity and sensitization to humans. 1,2-Benzisothiazol-3(2H)-one (BIT) is one of the most common chemical biocides in industrial products, with a heterocyclic structure and a wide range of antimicrobial activity. Current regulations impose strict limitations on its concentration due to its (relative) human toxicity. [3] The goal of this work is to covalently link synthetic biocide (BIT) molecules to leguminous GM in order to substantially increase their "biostability", their efficacy, efficiency and halflife thus eliminating, or at least decreasing, the use of free biocides.

Here we report a library of 18 BIT derivatives.[4] Four sites on the BIT core were targeted: the nitrogen and the oxygen atoms on the heterocyclic ring, the C5 and the C6 positions on the aromatic ring, where functional groups are introduced. The ultimate aim of this work is to establish whether by covalently linking a biocide to GM polymers, their "biostability" can be improved.

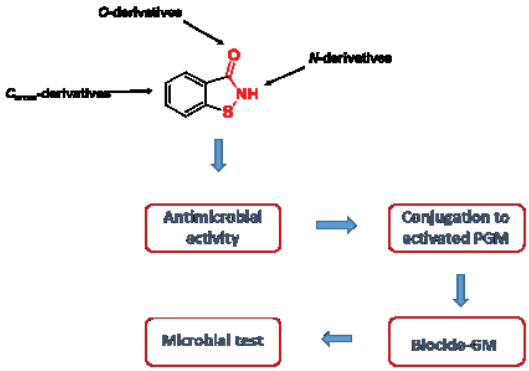


Figure: Synthesis of BIT-derivatives and conjugation to GM**.**

References:

[1] Y. Cheng, R.K. Prud'homme, J. Chick, D.C. Rau. Macromol. **2002**,*35*, 10155-10161. [2] Cheroni S, Formantici C, Galante YM. Enzyme Microb Technol. **2010**; *47*, 348-354. [3] H. Reddy, S.M. Cooper. Contact Dermat**. 2009**, *61*(3), 184-185. [4] F. Viani, B.Rossi , W. Panzeri, L. Merlini, A. M. Martorana, A. Polissic, Y.M. Galante. Tetrahedron, **2017**, *73*, 1745-1761.

OC63

One-step esterification of nanocellulose in Brønsted acid Ionic Liquid for drug delivery application.

E. Locatelli,[a] L. Cellante,[a] R. Costa,[b] I. Monaco,[a] G. Cenacchi.[b]

[a] *Department of Industrial Chemistry "TosoMontanari", Bologna, Italy*
[b] *Department of Biomedical and Neuromotor Sciences – DIBINEM, Bologna, Italy.*
e-mail*: erica.locatelli2@unibo.it*

There is worldwide an increasing demand of products made from renewable resources that are biodegradable and have low safety risks on human health. In this light nanocellulose presents both biodegradability and biocompatibility deriving from the most aboundant natural bulk material (cellulose) with the addition of peculiar properties arising from the nanometric dimensions. Attracted by these advantages, nanomedicine has recently addressed its attention on nanocellulose. Several reactions for the surface modification of nanocellulose and for linkage of biologically active molecules have been successfully attempted, but these reactions often require the use of organic solvents and of several reactants, which clearly limit the biocompatibility of the process and potential industrial scalability. Fischer esterification may represent a brilliant strategy for introduction of proteins (that often present free carboxyl groups) onto nanocellulose, which is naturally abundant in hydroxyl groups.

With these premises, we proposed for the first time the easy, one-step, esterification of nanocellulose in a Brønsted acid ionic liquid, which acts as both solvent and catalyst, thus avoiding the employment of any organic solvents or reactants in the process. The protein Chlorotoxin (Cltx) has been bonded onto the nanocellulose surface through the esterification reaction. The obtained nanocellulose showed excellent properties in terms of biocompatibility and internalization in the U87MG glioblastoma cell line, thus demonstrating the possible use of this material as novel drug delivery carrier.[1]

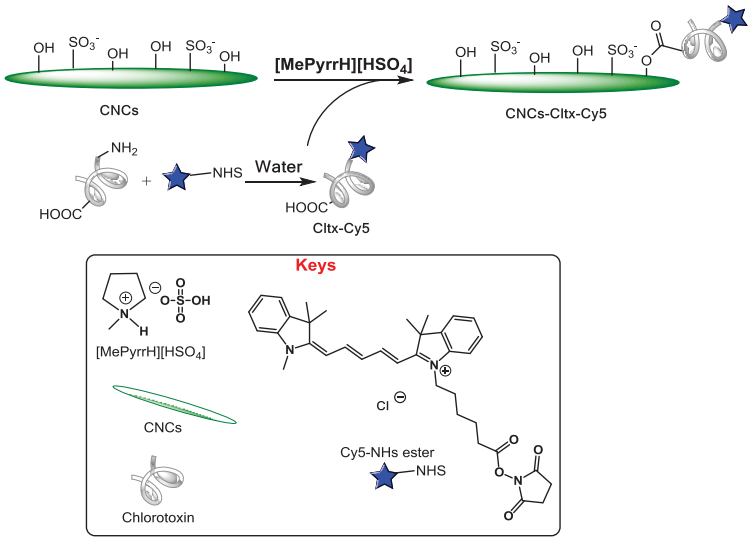


Figure 1: schematic procedure of the reaction.

References:

[1] L. Cellante, R. Costa, I. Monaco, G. Cenacchi, E. Locatelli. *New Journal of Chemistry*, **2018**, 42, 5237-5242.

OC64

Not PAMAM Dendrimer Nanodispersions and Pectine Microdispersion: two biocompatible approaches to increase Ellagic Acid water solubility and allow its more ways therapeutic administration

F. Turrini, S. Alfei, C. Silvia, P. Zunin, B. Parodi, G. Zuccari, A.M. Pittaluga, R. Boggia

Dipartimento di Farmacia, Università di Genova, Viale Cembrano 4
I-16148 Genova, Italy
e-mail: alfei@difar.unige.it

Ellagic acid (EA) **1** (Figure 1), a polyphenol present in some fruits, nuts and seeds has antioxidant and other several healthy properties. EA daily dietary intake is irrelevant for therapeutic purposes, but the administration of its effective doses could be a solution. This idea is hardly realizable due to EA water insolubility and low oral bioavailability. Toxic excipients and harmful solubilizing agents were extensively used for the obtainment of administrable drug formulations and for realizing the delivery of not water soluble drugs with unpleasant side effects. Nanoparticles represent a better alternative and even if highly cytotoxic, polycationic PAMAM dendrimers were among the most investigated materials. Today, neutral dendrimer scaffolds decorated with biocompatible protonable amino acids are preferred. Then, EA was incorporated inside not charged amino acid-modified hydrophilic (**2**)[1] and amphiphilic (**3**)[2] dendrimers by a synthetic procedure (Figure 1).

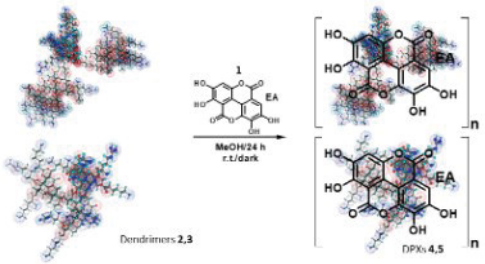


Figure 1: Encapsulation reactions of **1** into dendrimers **2-3**.

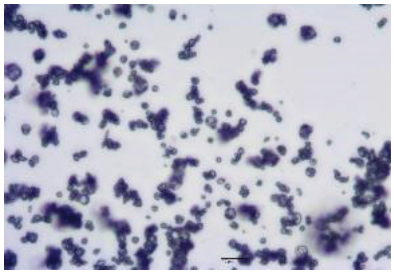


Figure 2: EA microsphere image from Optical Microscopy Analysis.

Two nanosized (150-160 nm) EA formulations (DPXs) were obtained. Thanks to their surprisingly increased water solubility (300-1000 times), 46-53% DL, good antioxidant activity, very good buffer capacity, DPXs could be suitable for safe and effective parenteral administration of EA. Another total natural EA formulation was than prepared by EA entrapment in a tasteless food compatible pectin matrix. A solid microdispersion (EAMS, 10-20 μm, Figure 2) was obtained by spray drying technique and the commonly used organic co-solvent PEG-400 was avoided. EAMS shown 22% DL, 30 times improved water solubility and very good antioxidant power. As a research in progress has already proved, food compatible EAMS are suitable for oral administration of EA therapeutic doses and as additive in EA enriched functional foods preparation.

References:

[1] S. Alfei, S. Catena, **2018**, submitted to *Polym. Advan. Technol.* on April 13th and under review.
[2] S. Alfei, S. Catena, **2018**, submitted to *Polym. Int.* on April 9th and under review.

OC65

Synthesis of *N*-Alkylated L-Iminosugars and their Therapeutic Application in Cystic Fibrosis Lung Disease

D. D'Alonzo,[a] M. De Fenza,[a] A. Esposito,[a] S. Munari,[b] N. Loberto,[c] A. Santangelo,[b] I. Lampronti,[d] A. Tamanini,[b] A. Rossi,[e] S. Ranucci,[e] I. De Fino,[e] A. Bragonzi,[e] M. Aureli,[c] A. Sonnino,[c] G. Lippi,[b] R. Gambari,[d] G. Cabrini,[b] M.C. Dechecchi,[b] A. Guaragna[a]

[a] *Department of Chemical Sciences, University of Napoli Federico II, Napoli*
[b] *Department of Pathology and Diagnostics. University Hospital of Verona, Verona*
[c] *Department of Med. Biotech. and Translational Medicine, University of Milano, Milano*
[d] *Department of Life Sciences and Biotechnology, University of Ferrara, Ferrara*
[e] *CFaCore, Infection and CF Unit, San Raffaele Scientific Institute, Milano*
e-mail*: annalisa.guaragna@unina.it*

Iminosugars represent the most promising class of therapeutically useful glycomimetics. Because of their ability to mimic structure and properties of natural monosaccharides, iminosugars are able to interfere with disease-related carbohydrate-processing enzymes.[1] Despite their great therapeutic potential, iminosugars suffer of poor selectivity, thereby leading to the onset of undesired side effects after prolonged administration. In this area, a valid alternative is offered by L-iminosugars. The last ones are non-superimposable mirror images of natural iminosugars; studies have demonstrated that they act as either inhibitors or chaperones of various glycosidases, although working in a more markedly selective manner.[2] Herein, the study on L-iminosugars has been widened to *N*-alkyl-L-iminosugars. The corresponding D-enantiomers have recently exhibited an anti-inflammatory effect in Cystic Fibrosis (CF) bronchial cells, by targeting β-glucosidase 2 (GBA2).[3] Based on this observation, we were interested to evaluate the effect that *N*-alkyl-L-iminosugars alone or as racemic mixtures could have in reducing the inflammatory response to *P. aeruginosa* infection in CF bronchial cells.

Herein, the synthesis of L-DNJ by a *de novo* approach will be described, along with an environmental friendly and scalable procedure for the synthesis of the alkyl chains and subsequent iminosugar *N*-alkylation.

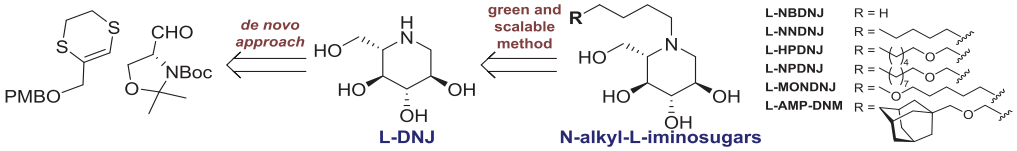


Figure 1: Retrosynthetic path to *N*-alkyl-L-iminosugars.

Furthermore, the effects as anti-inflammatory agents in CF bronchial cells and murine models of lung infection will be shown.

References:

[1]. D. D'Alonzo, A. Guaragna, G. Palumbo *Curr. Med. Chem.* **2009**, *16*, 473−505.
[2] D. D'Alonzo, M. De Fenza, C. Porto, R. Iacono, M. Huebecker, B. Cobucci-Ponzano, D.A. Priestman, F. Platt, G. Parenti, M. Moracci, G. Palumbo, A. Guaragna *J. Med. Chem.* **2017**, *60*, 9462−9469.
[3] N. Loberto, M. Tebon, I. Lampronti, N. Marchetti, M. Aureli, R. Bassi, M.G. Giri, V. Bezzerri, V. Lovato, C. Cantù, S. Munari, S.H. Cheng, A. Cavazzini, R. Gambari, S. Sonnino, G. Cabrini, M.C. Dechecchi, *PLoS ONE* **2014**, *9*, e104763.
This research was supported by the Italian Cystic Fibrosis Research Foundation grant FFC #22/2015 to MCD and MA.

OC66

Deep Eutectic Solvents as effective media for the synthesis of Donepezil structure-based hybrids with metal-chelating properties

L. Piemontese,[a,b] F. Rinaldo,[a,b] G. Dilauro,[a] D. Tomás,[b] S. Chaves,[b] M. A. Santos,[b] V. Capriati[a]

[a] *Dipartimento di Farmacia–Scienze del Farmaco, Università degli Studi di Bari "Aldo Moro", Consortium C.I.N.M.P.I.S., Via E. Orabona 4, I-70125 Bari, Italy.*

[b] *Centro de Química Estrutural, Instituto Superior Técnico, Universidade de Lisboa, Av. Rovisco Pais 1, 1049-001 Lisboa, Portugal.*

e-mail*: luca.piemontese@uniba.it*

Starting from a series of hybrids based on the framework of the acetylcholinesterase (AChE) inhibitor Donepezil,[1] the synthesis of new multi-functional ligands with chelating abilities towards Cu^{2+}, potentially useful in Alzheimer's disease (AD) treatment, has been designed (**Figure 1**). A crucial synthetic step has been optimized by using the so-called Deep Eutectic Solvents (DESs) as alternative and bio-renewable reaction media in place of harsh and volatile organic compounds (VOCs). DESs are fluids that are usually composed of two or three safe and inexpensive components that are able to interact mainly through hydrogen-bonding interactions to form a eutectic mixture with a melting point much lower than that of either of the individual components. Thanks to their shallow ecological footprint, they are progressively replacing conventional VOCs in many fields of modern chemistry.[2] Building on our recent successes in the synthesis of heterocycles in DESs,[3] in this Communication we discuss in particular the optimization of the conditions of preparation of a series of benzimidazole-based derivatives, to be included in new potential multi-target ligands. The functionalization of the phenolic ring could have effect on some important biological properties for the treatment of AD (e.g. metal chelating capacity, inhibition of AChE and Aβ aggregation) compared to the non-substituted analogue.[1]

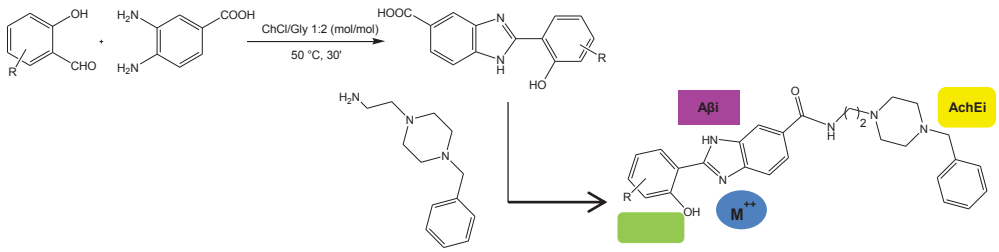


Figure 1. Representative structure of a benzimidazole-based hybrid and its synthetic pathway

Intervento cofinanziato dal Fondo di Sviluppo e Coesione 2007-2013 –APQ Ricerca Regione Puglia "Programma regionale a sostegno della specializzazione intelligente e della sostenibilità sociale ed ambientale - Future In Research". Project ID: I2PCTF6.

References:

[1] a) L. Piemontese, D. Tomás, S. Chaves, M. A. Santos et al., submitted. b) S. Chaves, D. Tomás, L. Piemontese, M. A. Santos et al., submitted.

[2] D. A. Alonso, D. J. Ramon et al., *Eur. J. Org. Chem.*, **2016**, *4*, 612.

[3] (a) M. Capua, V. Capriati et al., *Molecules*, **2016**, *21*, 924; (b) L. Cicco, V. Capriati et al. *Chem. Sci*,. **2016**, 7, 1192; (c) E. Massolo, M. Benaglia, V. Capriati et. al. *Green Chem.*, **2016**, 18, 792; (d) G. Dilauro, V. Capriati et al. *C. R. Chimie*, **2017**, 20, 617.

OC67

Synthesis of new bio-based ionic liquids and their use in the dissolution and modification of cellulose

L. Guazzelli,[a] M. Mezzetta,[a] S. Becherini,[a] C. Chiappe[a]

[a]*Dipartimento di Farmacia, Università di Pisa, Via Bonanno 6, 56126, Pisa*
e-mail*: lorenzo.guazzelli@unipi.it*

Ionic liquids (ILs) are salts composed of an organic cation and an organic or an inorganic anion which are liquid at or near room temperature. ILs have attracted a great deal of interest in the last 20 years due to some unique physicochemical properties such as the large electrochemical window, the chemical and thermal stability, the negligible volatility, and the no flammability, to mention a few. At the beginning, ILs have been mainly studied as alternative to the traditional volatile organic solvents, while nowadays they are used in a plethora of different applications. Recent trends in the IL field encompass the investigation of environmentally friendlier synthetic pathways to access them as well as the substitution of at least one of the common petroleum derived ions with natural or bio-based components.[1]

Polysaccharides such as cellulose, chitosan and chitin are highly abundant renewable feedstocks and represent a potential solution (and challenge at the same time) for the replacement of traditional fuel and plastic material. Cellulose is composed of glucose moieties β1→4 linked to each other (Figure 1), with several intra- and intermolecular hydrogen bonds. This native hydrogen bonding, which renders these polysaccharides recalcitrant toward their dissolution in almost all common solvents, hampers the development of new biomaterials.

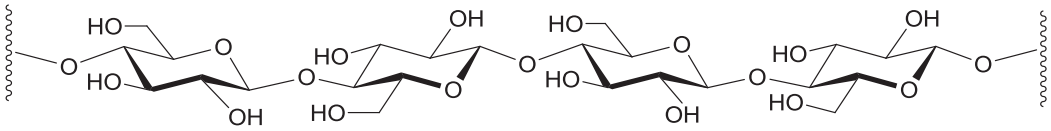


Figure 1. Structure of cellulose.

ILs are one of the few solvents able to disrupt the native hydrogen bonds present within the biopolymers,[2] thus allowing to dissolve them in good quantity and permit their further modifications.[3,4]

Herein, we report the development of new bio-based ionic liquids in a single step through an easy clean procedure, which has the potential to be scaled-up. The proposed three different classes of ILs showed remarkable ability of dissolving cellulose. The role played by the bio-based anion in the dissolution mechanism was also studied. The ILs-cellulose solutions allowed for the modification of the polysaccharide structure in homogenous conditions.

References:

[1] J. Hulsbosch, D. E. De Vos, K. Binnemans, R. Ameloot, *ACS Sustainable Chem. Eng.*, **2016**, *4*, 2917 – 2931.

[2] R.P. Swatloski, S.K. Spear, J.D. Holbrey, R.D. Rogers, *J. Am. Chem. Soc*, **2002**, *124*, 4974 – 4975.

[3] A. Takada and J.-I. Kadokawa, *Biomolecules*, **2015**, *5*, 244 – 266.

[4] A. Mezzetta, L. Guazzelli, C. Chiappe, *Green Chemistry,* **2017**, *19*, 1235 – 1239.

OC68

Carbenes and nascent hydrogen for reductive derivatisation of technical lignins

H. Lange,[a,*] F. Zikeli,[b] C. Crestini[a]

[a] *University of Rome 'Tor Vergata', Department of Chemical Sciences and Technologies Via della Ricerca Scientifica, 00133 Rome, Italy*

[b] *University of Tuscia, Department of Ecological and Biological Sciences, Via S. Camillo de Lellis, 44, 01100 Viterbo, Italy*

e-mail*: heiko.lange@uniroma2.it*

Motivation: Traditional pulp and paper processes as well as emerging biorefineries generating cellulosic ethanol from lignocellulosic agricultural waste material lead to large amounts of kraft lignin and side-stream straw lignin.[1] Both types of technical lignins, *i.e.*, organosolv lignins and kraft lignins, offer various amounts of different functional groups, mainly aliphatic and phenolic hydroxyl groups and double bonds.[2,3] Whereas the hydroxyl groups are normally used for lignin functionalisation, a more versatile type of functionalisation is obtained when leaving the hydroxyl groups intact and creating carbon-carbon bonds.

Design of experiment: Lignin modification was thus performed using nascent hydrogen, as well as carbenes of varying reactivity. Exploiting the possibilities for *in situ* production of the reactive species, various technical lignins were subjected to standardised reactions conditions. Re-isolated modified lignin samples were subjected to GPC analysis,[4] FTIR analysis, quantitative ^{31}P NMR after phosphitylation,[5] as well as quantitative {^{13}C-^{1}H}-HSQC analyses.[6,7]

Results: Molar mass distribution effects were noted in the modified lignins. In case of carbenes, detection of new, unexpected cross-peaks in the HSQC spectra area specific for newly emerging C=C bonds were observed, while other 'typical' lignin signals in the aromatic region underwent drastic changes. Together with unexpectedly decreased amounts of the respective free phenolic OH groups in the modified lignins, quinone-formation involving G- and H-type aromatic rings of lignins through a Reimer-Tiemann mechanism[8] is postulated, among other reactions and rearrangements. In case of treatment of lignins with nascent hydrogen, structural changes lead to yet different, 'atypical' lignins.

References:

[1] M. Aresta, A. Dibenedetto, F. Dumeignil, *Biorefineries, An Introduction*, De Gruyter, Berlin, Boston, **2015**.
[2] H. Lange, P. Schiffels, M. Sette, O. Sevastyanova, C. Crestini, *ACS Sustain. Chem. Eng.* **2016**, *4*, 5136–5151.
[3] C. Crestini, H. Lange, M. Sette, D. S. Argyropoulos, *Green Chem.* **2017**, *19*, 4104–4121.
[4] H. Lange, F. Rulli, C. Crestini, *ACS Sustain. Chem. Eng.* **2016**, *4*, 5167–5180.
[5] A. Granata, D. S. Argyropoulos, *J. Agric. Food Chem.* **1995**, *43*, 1538–1544.
[6] D. J. Peterson, N. M. Loening, *Magn. Reson. Chem.* **2007**, *45*, 937–941.
[7] M. Sette, H. Lange, C. Crestini, *Comput. Struct. Biotechnol. J.* **2013**, *6*, 1–7.
[8] Reimer K., Tiemann Ferd., *Berichte Dtsch. Chem. Ges.* **1876**, *9*, 1268–1278.

OC69

Supported chiral organocatalysts for stereoselective reductions in batch and in flow

A. Puglisi,[a] R. Porta,[a] M. Benaglia[a]

[a]*Dipartimento di Chimica, Università degli Studi di Milano, via Golgi, 19 -20133 Milano*
e-mail*: Alessandra.puglisi@unimi.it*

Chiral amines are very important pharmacophores that can be found in several biologically active molecules and agrochemical compounds. The reduction of ketimines is a very convenient strategy to access to this class of molecules. Among the available catalytic methods, the stereoselective reduction of imines with trichlorosilane ($HSiCl_3$) promoted by chiral Lewis bases has been investigated by several research groups and has proved to be very efficient. Our research group has recently reported a new class of highly active chiral Lewis bases, able to promote the reduction of a variety of imines with low catalyst loading, occurring in quantitative yields and with enantioselectivities usually higher than 90%.[1] Here we report the immobilization of this new class of imidazolidinone-based picolinamides onto different solid supports and their use in the enantioselective C=N bond reduction.[2]

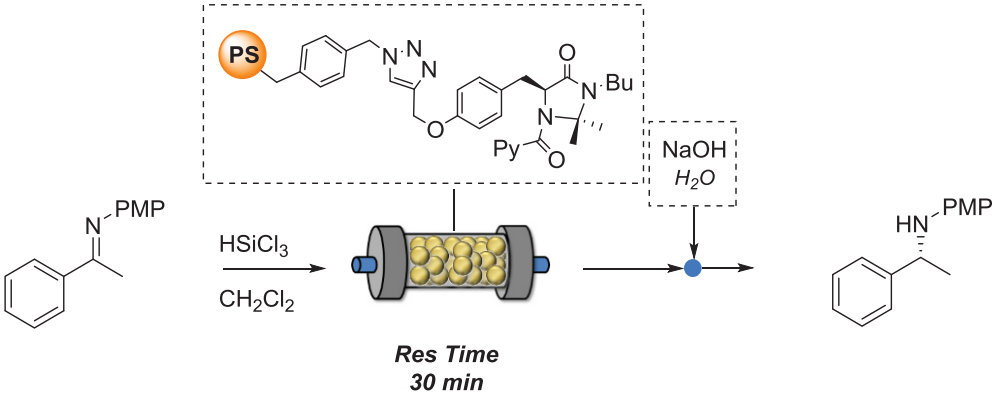


Figure 1: polystyrene-supported chiral picolinamide for stereoselective reductions in a flow reactor

The heterogenized catalysts showed great catalytic efficiency in batch promoting the reaction in high yields and stereoselectivities up to 98% ee, even at 1 mol% loading. The recyclability was demonstrated under batch conditions; for the first time, a chiral organocatalytic reactor for the enantioselective, trichlorosilane mediated imine reduction under continuous flow conditions[3] was successfully prepared and employed for the in-flow synthesis of chiral amines, including advanced intermediates of pharmaceutically relevant compounds such as rivastigmine.

References:

[1] D. Brenna, R. Porta, E. Massolo, L.Raimondi, M. Benaglia, *ChemCatChem* **2017**, *9*, 941-945.
[2] R. Porta, M. Benaglia, R. Annunziata, A. Puglisi, G. Celentano, *Adv. Synth. Catal*. **2017**, *359*, 2375-2382.
[3] S. D. Fernandes, R. Porta, P. C. Barrulas, A. Puglisi, A. J. Burke, M. Benaglia, *Molecules* **2016**, *21*,1182-1190.

OC70

Microfluidic Photoreactor Enables 2-Methylbenzophenone Light-Driven Reactions with Superior Performance

J. Mateos, A. Cherubini, T. Carofiglio, M. Bonchio, X. Companyo, L. Dell'Amico*

Department of Chemical Sciences, University of Padova, Via Marzolo 1, Padova
e-mail*: luca.dellamico@unipd.it*

Recently, 2-methylbenzophenones (2-MBPs) have increasingly attracted the interests of the photochemical community. Different research groups developed independently innovative photoreactions based on the ability of such molecule to generate highly reactive hydroxy-*o*-quinodimethane (photoenol) intermediate upon light irradiation.[1] This fleeting intermediate can react with many different partners, generating highly diversified molecular architectures.[2]

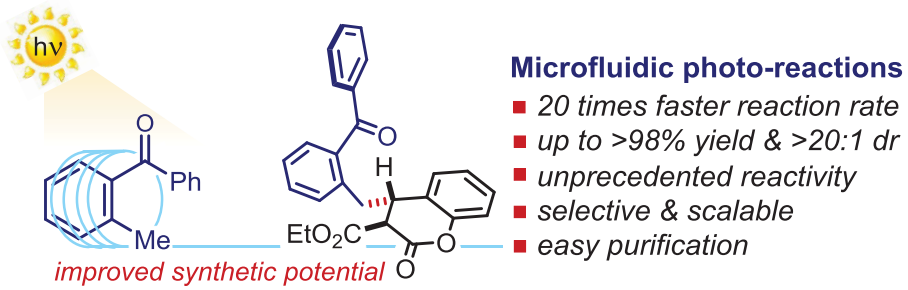


Figure 1: Development of a novel microfluidic synthetic platform for 2-methylbenzophenones light-driven reactions

Here is reported how an easy microfluidic photoreactor was used as a general setup for a number of light-driven transformations based on the photochemical reactivity of 2-MBPs.[3]

The developed platform was pivotal to access the direct photo-benzylation of coumarins, that represent a new class of reaction partners for 2-MBPs (see figure 1). In this regard, coumarin dimerisation was successfully circumvented under microfluidic conditions, selectively yielding a broad range of 4-benzylated-2-chromanones with high yield and diastereocontrol.[4]

References:

[1] L. Dell'Amico, A. Vega, S. Cuadros, P. Melchiorre, *Angew. Chem. Int. Ed.* **2016**, *55*, 3313-3317.
[2] L. Dell'Amico, V. Fernández, F. Maseras, P. Melchiorre, *Angew. Chem. Int. Ed.* **2017**, *56*, 3304-3307.
[3] J. Mateos, A. Cherubini-Celli, T. Carofiglio, M. Bonchio, N. Marino, X. Companyó, L. Dell'Amico *Chem. Comm.* **2018**, DOI: 10.1039/C8CC01373J
[4] J. Mateos, F. Rigodanza, L. Dell'Amico *Unpublished results*.

OC71

Controlling the Motions of Acid-base Operated Molecular Machines

S. Di Stefano, S. Albano, O. Lanzalunga, L. Mandolini ,C. Biagini

Dipartimento di Chimica, Università di Roma La Sapienza and Istituto CNR di Metodologie Chimiche (IMC-CNR), Sezione Meccanismi di Reazione P.le A. Moro 5, I-00185 Roma

The great interest for the development of molecular machines (switches or motors)[1] is mainly due to future applications in the different fields of (nano)technologies, which are hardly imaginable at the moment. The assignment of the Nobel Prize for Chemistry for 2016 to Feringa, Sauvage and Stoddart witnesses an extraordinary interest of the scientific community to this topic.

Our contribution to the field concerns the use of the decarboxylation reaction of activated carboxylic acids as a source of energy for the motions of acid –base operated molecular machines.[2] Back and forth motions of this kind of machines have been shown to occur on addition of our fuels (or other fuels based on the same principle) with no need of subsequent addition of any antifuel.[2,3,4] In other words, the energy supplied by the degradation of one only chemical fuel is exploited for the operation of a molecular machine that alternatively switches between the two states **A** and **B** (Figure 1).

In this communication it will be shown how it is possible to control the efficiency of our fuels in terms of activation from pre-fuels[5] and of motion rate[6] of the fuelled molecular machine by modification of the fuel molecular structure.

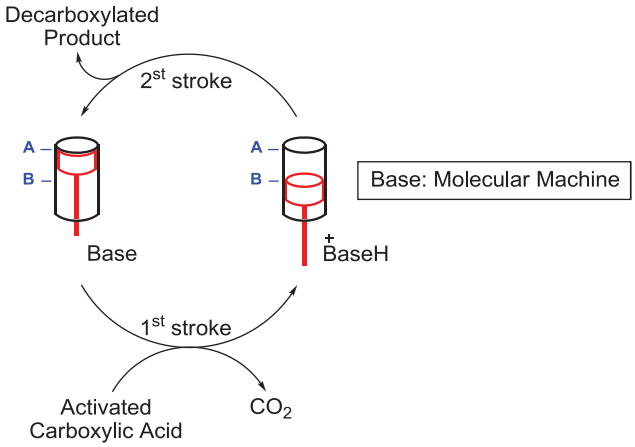


Figure 1: Schematic representation of a molecular machine moving from state **A** to state **B** and back again to state **A** under the influence of an activated carboxylic acid used as a chemical fuel.

References:

[1] S. Erbaş-Çakmak, D. A. Leigh, C. T. McTernan, A. L. Nussbaumer, *Chem. Rev.*, **2015**, *115*, 10081-10206.

[2] J. A. Berrocal, C. Biagini, L. Mandolini, S. Di Stefano, *Angew. Chem, Int. Ed.*, **2016**, *55*, 6997-7001.

[3] S. Erbas-Cakmak, S. D. P. Fielden, U. Karaca, D. A. Leigh, C. T. McTernan, D. J. Tetlow, M. R. Wilson, *Science*, **2017**, *358*, 340–343.

[4] A. Ghosh, I. Paul, M. Adlung, C. Wickleder, M. Schmittel. *Org. Lett.* **2018**, *20*, 1046−1049.

[5] C. Biagini, F. Di Pietri, L. Mandolini, O. Lanzalunga, S. Di Stefano *Chem. Eur. J.* **2018**, DOI: 10.1002/chem.201800474.

[6] C. Biagini, S. Albano, L. Mandolini, J. A. Berrocal, S. Di Stefano *Chem. Sci.* **2018**, *9*, 181–188.

OC72

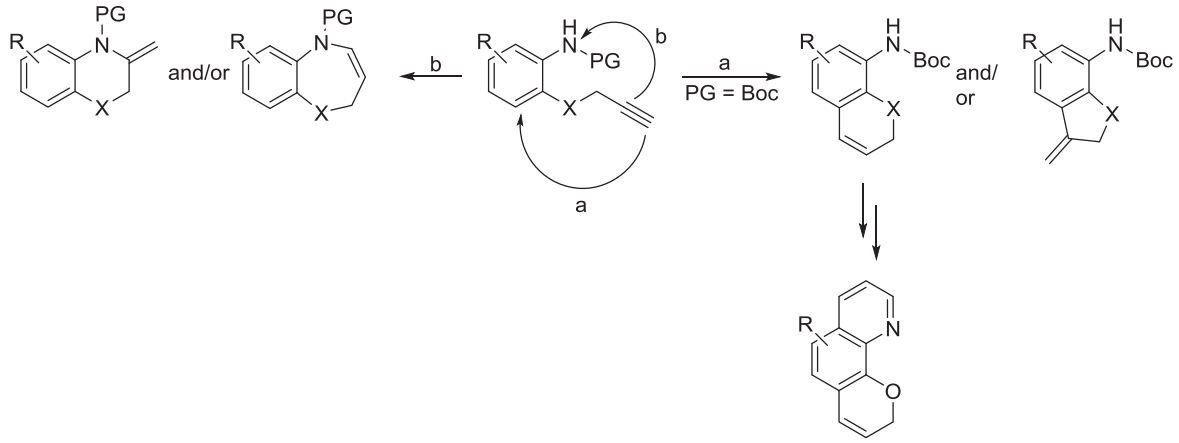
Intramolecular transition-metals catalyzed hydroarylation processes for the synthesis of pyranoquinolines

M. S. Christodoulou,[a] S. Giofrè,[a] E. M. Beccalli,[a]

[a]*DISFARM, Sezione di Chimica Generale e Organica "A. Marchesini" Università degli Studi di Milano Via Venezian 21, 20133 Milano, Italy*
e-mail: michail.christodoulou@unimi.it

The transition-metals catalyzed reactions of unsaturated systems tethered to arene represent a useful method to obtain heterocyclic systems, with the advantage of using the non-activated substrates, thus avoiding the requirement for a halogen substituent.[1,2] Moreover, the activation of a multiple bond offers the possibility of obtaining different regioisomeric products.

Starting from substituted arenes bearing a carbamate group and a C-C triple bond, the use of palladium catalysis resulted in an intramolecular hydroamination reaction providing benzofused heterocycle systems, the ring-size of which depends on the carbon atom of the triple bond involved in the nucleophilic attack. The use of a different transition-metal catalyst, such as platinum salts, gave a different reactivity preferring an hydroarylation process.[3] When the substrate consists of phenol derivatives, the formation of substituted benzopyranes was observed. In this case, the reaction involves the terminal carbon of the triple bond through a selective 6-*endo-dig* cyclization.



In the case of o-amino phenols bearing a double bond, different cyclization products were reported, through hydroamination or domino aminohalogenation processes depending on the different transition metals used.

References:

[1] V. P. Boyarskiy, D. S. Ryabukhin, N. A. Bokach, A. V. Vasilyev, *Chem. Rev.* **2016**, *116*, 5894 – 5986.
[2] T. Kitamura, *Eur. J. Org. Chem.* **2009**, 1111–1125.
[3] S. J. Pastine, S. W. Youn, D. Sames, *Tetrahedron* **2003**, *59*, 8859–8868.

OC73

Oxidative Alkoxycarbonylation of Alkynes and Olefins Catalyzed by Aryl α-Diimine Palladium(II) Complexes

D. Olivieri,[a] C. Carfagna,[a] B. Gabriele,[b] R. Mancuso,[b] F. Fini[c]

[a] *Department of Industrial Chemistry "T. Montanari", University of Bologna, Viale Risorgimento 4, 40136 Bologna (BO), Italy*
[b] *Department of Chemistry and Chemical Technologies, University of Calabria, Via P. Bucci 12/C, 87036 Arcavacata di Rende (CS), Italy*
c *Department of Life Sciences, University of Modena and Reggio Emilia, Via G. Campi 103, 41125 Modena (MO), Italy*
e-mail*: francesco.fini@unimore.it*

Oxidative carbonylations are useful reactions in organic and medicinal chemistry for their ability to convert inexpensive feedstock in highly valuable compounds.[1] On the basis of the bis-alkoxycarbonylation of terminal olefins,[2] we have further developed this reaction with alkynes[3] and 1,2-disubstituted alkenes.[4] The mono-alkoxycarbonylation reaction of variously substituted phenylacetylenes **1** was selectively achieved by using Pd(II) catalyst bearing the sterically demanding aryl α-diimine ligand **3**, in combination with AgOTf (figure 1, top).[3]

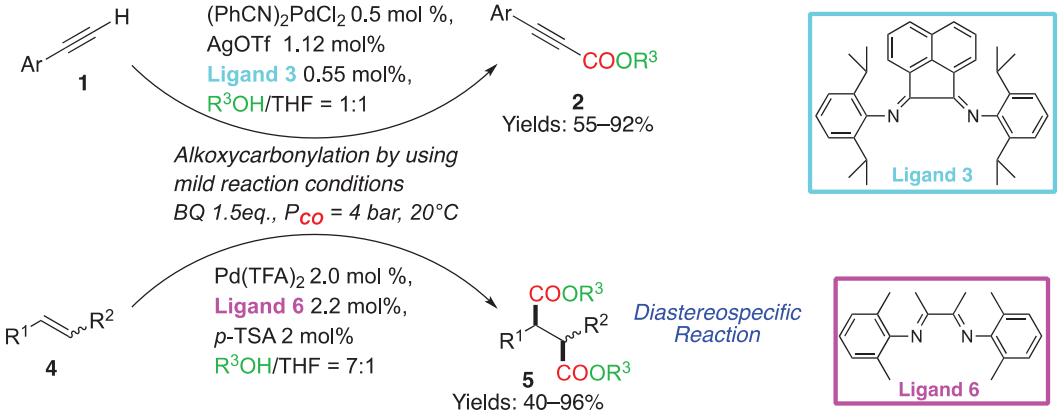


Figure 1: Alkoxycarbonylation reactions of alkynes **1** and 1,2-disubstituted olefins **3**.

The *diastereospecific* bis-alkoxycarbonylation of 1,2-disubstituted alkenes **4**, by using $Pd(TFA)_2$ and the easy to synthesize nitrogen ligand **6**, was attained from a *syn* overall addition of the carboxyl moieties to the olefins **4** (figure 1, bottom).[4]

Propiolic esters **2** and 3,4-disubstituted succinic esters **5** were obtained with moderate to excellent yields by using methanol, isopropanol and benzyl alcohol as nucleophiles (Figure 1).

References:

[1] X.-F. Wu, H. Neumann, M. Beller, *Chem. Sus. Chem.* **2013**, *6*, 229–241.
[2] F. Fini, M. Beltrani, R. Mancuso, B. Gabriele, C. Carfagna, *Adv. Synth. Catal.* **2015**, *357*, 177– 84.
[3] M. Beltrani, C. Carfagna, B. Milani, R. Mancuso, B. Gabriele, F. Fini, *Adv. Synth. Catal.* **2016**, *358*, 3244–3253.
[4] D. Olivieri, F. Fini, R. Mazzoni, S. Zacchini, N. Della Ca', G. Spadoni, B. Gabriele, R. Mancuso, V. Zanotti, C. Carfagna *Adv. Synth. Catal.* **2018**, DOI:*10.1002/adsc.201701597* (in press).

OC74

Accessing new areas of the chemical space by using acetal chemistry

E. Lenci,[a] R. Innocenti,[a] G. Menchi,[a,b] A. Trabocchi[a,b]

[a]*Dipartimento di Chimica "Ugo Schiff", Università degli Studi di Firenze, Via della Lastruccia 13, 50019, Sesto Fiorentino (FI), Italia*
[b]*Interdepartmental Center for Preclinical Development of Molecular Imaging (CISPIM), Università degli Studi di Firenze, Viale Morgagni 85, 50134 Firenze, Italia*
e-mail*: elena.lenci@unifi.it*

Bicyclic acetals represent a powerful class of natural product-derived skeletons for the development of small molecule libraries, due to their intrinsic biological value and their unique structural features.[1] In particular, the skeletal diversity that comes from the conformational and configurational flexibility of these moieties highlights the potential of their use in Diversity-Oriented Synthesis.[2]

Our contribution in this field involves the development of sugar and amino-acid derived molecular scaffolds around the morpholine nucleus, through short build/couple/pair strategies that exploit *trans*-acetalization reaction and acetal rearrengement processes.[3] Chemioinformatic analysis revelead the relevance of the use of this chemistry to access new areas of the chemical space, as the structures obtained possess an higher Fsp^3 ratio and a more tridimensional complexity, as compared to top-selling drugs (Figure 1). Moreover, the screening of some libraries, developed around selected molecular scaffolds, has opened the way to several biological applications in the field of cell growth modulators for a breast carcinoma cell line and for the development of peptidomimetic inhibitors against different aspartyl proteases.

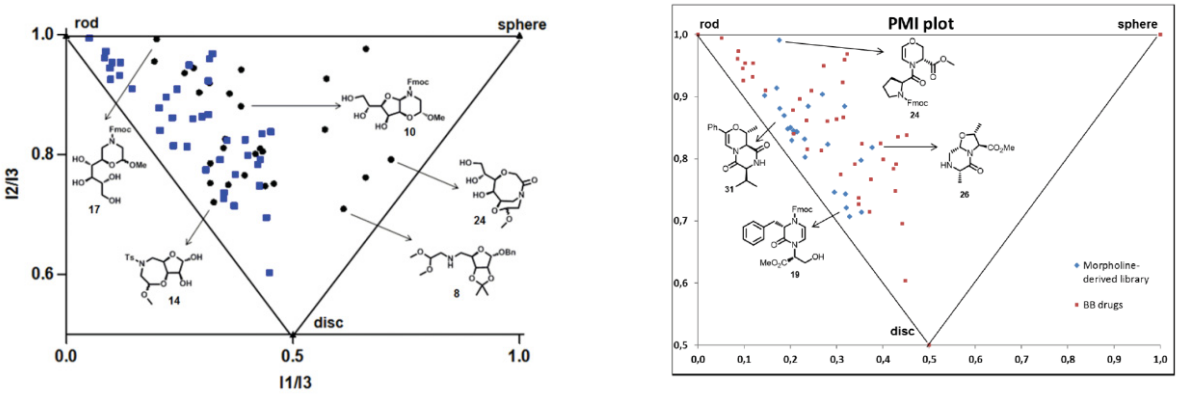


Figure 1: Principal moment of inertia (PMI) plots showing the skeletal diversity of mannose-derived (left) and morpholine-derived compounds (right) with respect to top-selling drugs.

References:

[1] F.-M. Zhang, S.-Y. Zhang, Y.-Q. Tu, *Nat. Prod. Rep.* **2018**, *35,* 75-104.

[2] "Diversity-Oriented Synthesis: Basics and Applications in Organic Synthesis, Drug Discovery, and Chemical Biology", Trabocchi, A., Ed.; Wiley and Sons, **2013**.

[3] (a) E. Lenci, G. Menchi, A. Guarna, A. Trabocchi, *J. Org. Chem.* **2015**, *80*, 2182-2191; (b) E. Lenci, R. Innocenti, G. Menchi, C. Faggi, A. Trabocchi, *Org. Biomol. Chem.* **2015**, *13*, 7013-7019; (c) E. Lenci, A. Rossi, G. Menchi, A. Trabocchi, *Org. Biomol. Chem*. **2017**, *13*, 9710-9717.

OC75

[Copper(I)(Pyridine-Containing Ligand)] Catalyzed Regio- and Steroselective Synthesis of 2-Vinylcyclopropa[b]indolines from 2-Vinylindoles

V. Pirovano,[a] E. Brambilla,[a] G. Abbiati,[a] E. Rossi[a]

[a]*Dipartimento di Scienze Farmaceutiche - Sez. di Chimica Generale e Organica "A. Marchesini", Via Venezian 21, 20133, Milano*
e-mail*: valentina.pirovano@unimi.it*

The functionalization of indole core is an interesting research field because the indole moiety is present in a huge number of bioactive natural products and pharmaceutical compounds.[1] For this reason, the proposal of new methodologies for indole synthesis and functionalization is still of great interest in synthetic organic chemistry. In the context of our studies on metal-catalyzed cycloaddition reactions of vinylindoles[2] and on functionalization of indole core,[3] we decided to investigate the reactivity of 2-vinylindoles with diazo compounds. We envisioned in this way to functionalize these indole derivatives by means of a new reaction pattern. Thus, the reaction between 2-vinylindole and ethyl diazoacetate was conducted in the presence of copper(I) complexes having a pyridine-containing macrocycle as ligand and led to a series of cyclopropyl vinylindolines with satisfactory yields and with complete regio- and diasteroselectivity (Figure 1). Optimization of conditions, scope and proposed mechanism of the reaction will be illustrated, with preliminary results on an enantioselective version.[4]

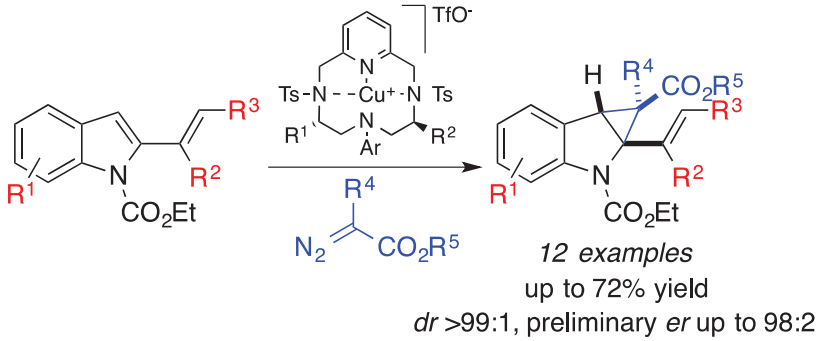


Figure 1

References:

[1] a) A. W. Schmidt, K. R. Reddy, H.-J. Knölker, *Chem. Rev.* **2012**, *112*, 3193-3328; b) A. Głuszyńska, *Eur. J. Med. Chem.* **2015**, *94*, 405-426; c) L. S. Tsutsumi, D. Gundisch, D. Sun, *Curr. Top. Med. Chem.* **2016**, *16* 1290-1313.

[2] E. Rossi, V. Pirovano, G. Abbiati, *Eur. J. Org. Chem.* **2017**, 4512-4529.

[3] V. Pirovano, D. Facoetti, M. Dell'Acqua, E. Della Fontana, G. Abbiati, E. Rossi, *Org. Lett.* **2013**, *15*, 3812-3815; b) V. Pirovano, M. Negrato, G. Abbiati, M. Dell'Acqua, E. Rossi, *Org. Lett.* **2016**, *18*, 4798-4801.

[4] V. Pirovano, E. Brambilla, G. Tseberlidis, *Org. Lett.* **2018**, *20*, 405-408.

OC76

Halogenation controls structures and functions of supramolecular peptide assemblies

P. Metrangolo,[a,b] F. Baldelli Bombelli,[a] G. Bergamaschi,[c] G. Cavallo,[a] A. Gori,[c] C. Pigliacelli,[a] A. Pizzi,[a] G. Terraneo[a]

[a]*Laboratory of Supramolecular and Bio-Nanomaterials (SBNLab), Department of Chemistry, Materials, and Chemical Engineering "Giulio Natta", Politecnico di Milano, Via L. Mancinelli 7, 20131 Milan, Italy*

[b]*Istituto di Chimica del Riconoscimento Molecolare, CNR, Via Mario Bianco 9, 20131 Milan, Italy*

[c]*HYBER Centre of Excellence, Department of Applied Physics, Aalto University, P.O. Box 15100, FI-02150, Espoo, Finland*

e-mail: pierangelo.metrangolo@polimi.it

A halogen bond occurs when there is evidence of a net attractive interaction between an electrophilic region associated with a halogen atom in a molecular entity and a nucleophilic region in another, or the same, molecular entity.[1] Although many modifications of amyloidogenic sequences have been utilized to tune their self-assembly behavior, halogenation has rarely been pursued. The advantage of a strategy based on the introduction of halogen atoms on peptide motifs lies in the fact that halogenation is a minimal structural modification, which, on the other hand, may induce a large difference in the peptide supramolecular behavior as a consequence of the rich variety of noncovalent interactions given by halogen atoms.

In this presentation, I will show how the halogen bond can be used to promote the molecular self-assembly of peptides. We have applied this new supramolecular concept to the augmented fibrillation of amyloidogenic peptides[2,3] and the control of their nanostructures[4] (Figure 1). The obtainment of a novel unnatural amino acid functioning as strong halogen-bond donor has allowed to engineer the hydrophobic cavity of an amyloid fibril. Examples of halogenated peptides showing biomimetic elastomeric behaviour will also be presented.

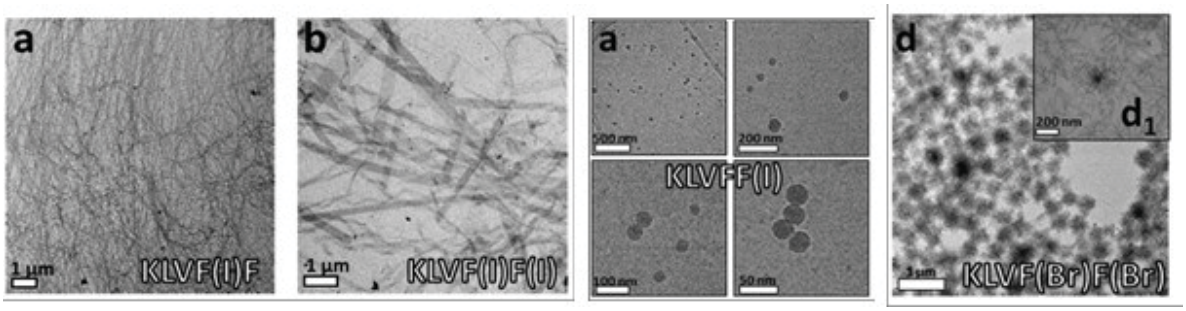


Figure 1: Halogenated derivatives of KLVFF showing various nanoarchitectures.

References:

[1] G. Cavallo, *et al.*, *Chem. Rev.* **2016**, *116*, 2478-2601 (Hot Paper).

[2] A. Bertolani, *et al.*, *Chem. Eur. J.* **2017**, *22*, 2051-2058 (Hot Paper and Front Cover).

[3] A. Bertolani, *et al.*, *Nat. Commun.* **2015**, *6:7574*, DOI: 10.1038/ncomms8574.

[4] A. Pizzi, A. *et al.*, *CrystEngComm* **2017**, *19*, 1870-1874 (Front Cover).

[5] A. Pizzi, *et al.*, *Nanoscale* **2017**, *9*, 9805-9810.

OC77

Combined LC-MS/MS and Molecular Networking approach for an early detection of cyanotoxins

G. Esposito,[a] R. Teta,[a] R. Marrone,[b] A. Anastasio,[b] M. Lega,[c] V. Costantino[a]

[a]*NeaNat group, TheBlueChemistryLab, Dipartimento di Farmacia, Università degli Studi di Napoli "Federico II", Napoli, Italy;*
[b]*Dipartimento di Medicina Veterinaria e Produzioni Animali, Università degli Studi di Napoli "Federico II", Napoli, Italy;*
[c]*Dipartimento di Ingegneria, Università di Napoli "Parthenope", Napoli, Italy*
e-mail: germana.esposito@unina.it

Cyanobacteria are one of the most important group of bacteria present in surface waters. They are ubiquitous and cosmopolitan organisms, which present considerable tolerance to extreme conditions of temperature, light intensity, drought and nutrients, but above all they have a great ability to adapt to various conditions. They are photosynthetic microorganisms characterized by a great morphological variability, with unicellular and colonial forms, the latter global or filamentous. They are able to produce a great number of secondary metabolites that can be used as lead compound in drug discovery.

However, cyanobacteria are also well known as producers of a number of cyanotoxins, dangerous for humans and animals. Eutrophic conditions allow cyanobacteria to blooms, producing large green mats covering water surfaces. In this condition, the production of cyanotoxins dramatically increases giving rise to a serious problems to municipalities and local governments for the negative impact on population and related activities.

Our studies[1] allowed setting up a multidisciplinary strategy for an early detection and constant monitoring of cyanobacteria blooms using remote/proximal sensing data coupled with analytical/biotech analyses. Different from other approaches commonly used to monitor toxic cyanobacteria blooms, our system works in a "pre-bloom phase" and allows making reliable prediction when the green mat is not yet appeared on the water surface.

The monitoring study has been done during summer 2017 and analytical data for the presence of cyanobacteria and related cyanotoxins in different matrix, such as water samples and bivalves were analyzed using a potent bioformatic tool.

In this communication, it will be described data obtained that allowed to recognize the presence of lyngbyatoxin, thanks to the analysis of LC-MS/MS data and submission of these data in Molecular Networking.

References:

[1] R. Teta, V. Romano, G. Della Sala, S. Picchio, C. De Sterlich, A. Mangoni, G. Di Tullio, V. Costantino, M. Lega, *Environ. Res. Lett.* **2017**,12.

OC78

Phytotoxins produced by two species of pathogenic Ascochyta, fungi responsible for legume diseases.

P. Nocera[a], M. C. Zonno[b], M. Masi[a], A. Boari[b], A. Cimmino[a], A. Infantino[c], M. Vurro[b], A. Evidente[a]

[a]*Department of Chemical Sciences, University of Naples "Federico II", Complesso Universitario Montesant'Angelo, via Cinthia 4, 80126, Naples, Italy.*
[b]*Intitute of Sciences of Food Production, National Research Council, via Amendola 122/O, 70126 Bari, Italy.*
[c]*Council for Research in Agriculture and the Analysis of Agricultural Economics, Research Center for Plant Pathology, Via C.G. Bertero 22, 00156 Rome, Italy.*
e-mail*: paola.nocera@unina.it*

Ascochyta blights are the most important diseases of legumes worldwide[1]. They are caused by different pathogens, e.g. *Ascochyta rabiei* (Pass.) Labr. in chickpea (*Cicer arietinum* L.), *Ascochyta fabae* Speg. in faba bean (*Vicia faba* L.) and *A. lentis* in lentil (*Lens culinaris* Medik.)[2].

Ascochyta lentis var. *lathyri* is a fungal species that causes necrotic lesions on leaves and stems of grasspea (*Lathyrus sativus* L.) plants, recently described for the first time in Italy.

Several species of this genus proved to produce phytotoxic metabolites partially involved in the appearance of disease symptoms[3,4].

Recently, one strain of *A. lentis* var. *lathyri* and one of *A. lentis* were grown *in vitro* on liquid and solid substrates, both for ascertain their capability to produce phytotoxic metabolites, and for a metabolomic comparison. Both strains proved to produce several bioactive metabolites, interestingly showing different metabolomic profiles.

This communication will illustrate the isolation, and the chemical and biological characterization of the secondary metabolites produced by the two strains of *A. lentis* var. *lathyri* and *A. lentis*, discussing their possible role in the development of disease symptoms.

References:

[1] D. Rubiales, S. Fondevilla, *Frontiers in plant science* **2012**, 3: 27.
[2] B. Tivoli et al. *Euphytica* **2006**, 147.1-2, 223-253.
[3] M. Vurro et al., *Mycotoxin research* **1992**, 8.1, 17-20.
[4] A. Andolfi et al., *J. Agric. Food Chem* **2013**, 61, 7301-7308.

OC79

Major Allergens in Cow Milk's whey: Study of the Effects of the Technological Treatments through the Identification and Synthesis of the Lactosylated Epitopes

Tullia Tedeschi, Alessandra Gasparini and Stefano Sforza

University of Parma, Food and Drug Department,
Parco Area Scienze 27/A 43124Parma, Italy
e-mail*: tullia.tedeschi@unipr.it*

Milk undergoes several technological treatments to guarantee its safety and stability for human consumption, such as pasteurization and the Ultra High Temperature (UHT) treatment. The application of high temperatures might affect milk proteins inducing structural and chemical modifications.[1] The major common modification is the Maillard reaction that occurs between lactose, the main sugar present in milk, and the amino group of lysine residues in proteins.

This modification can affect milk allergens, such as whey proteins α-lactalbumin (α-LA) and β-lactoglobulin (β-LG). The aim of this work is to investigate the effect of lysine lactosylation at a molecular level on proteins allergenicity. With this purpose an initial screening on different UHT and pasteurized milk samples was performed in order to identify the lactosylation sites. α-LA and β-LG were isolated from milk samples, purified with semi-preparative HPLC and digested with trypsin and chymotrypsin. Through LTQ-Orbitrap and UPLC-MS analysis lactosylated residues were identified in the mixtures of peptides produced and compared with the known epitopes reported in literature confirming the presence of some modified lysines in these epitopes. Four epitopes were selected and synthesised using the standard Fmoc protocol on a rink amide resin. In order to assess at a molecular level the impact of lactose on allergenicity response the synthesis of the sugar modified form of one of the selected epitopes was also initially approached.[2] Experimental conditions were optimized.

Finally, further studies were performed to investigate if this modification is resistant to the human gastro-intestinal digestion. Adopting the Minekus standard protocol suitable for food,[3] kinetics studies were performed on whey proteins concentrates in order to obtain a digestion profile for the whey proteins in their lactosylated form.

References:

[1] J. Meltretter, J. Wüst, and M. Pischetsrieder, *Journal of Agricultural and Food Chemistry*, **2014**, *62*, 10903-10915.

[2] S.Carganico, P. Rovero, J. A. Halperin, A. M. Papini, M. Chorev, *Journal of Peptide Science,* **2009**, *15 (2)*, 67-71.

[3] M. Minekus, M Alminger, P Alvito, S. Balance, T Bohn, C. Bourlieu, et al., A. Brodkorb, *Food and Function*, **2014,** *5*, 1113-1124.

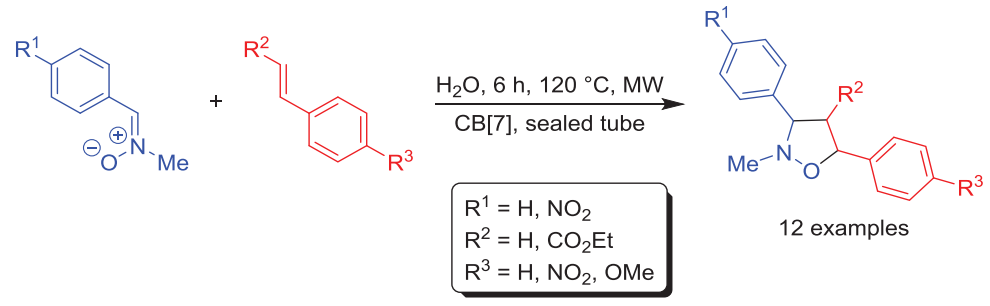
OC80

Cucurbit[7]uril as a supramolecular macrocycle for microwave assisted synthesis of 2-methyl-3,5-diarylisoxazolidines in water

D. Gentile,[a,b] G. Floresta,[a,b] V. Patamia,[a] A. Rescifina[a]

[a]*Dipartimento di Scienze del Farmaco, Università di Catania, Viale Andrea Doria 6, 95125 - Catania, Italy*
[b]*Dipartimento di Scienze Chimiche, Università di Catania, Viale Andrea Doria 6, 95125 - Catania, Italy*
e-mail*: giuseppe.floresta@unict.it*

The microwave assisted 1,3-dipolar cycloaddition with a catalytic amount of cucurbit[7]uril in water was investigated. This class of macrocycle can shield organic molecules from aqueous environments while encapsulating them in a hydrophobic cavity and promote cycloaddition reactions. Cucurbit[n]uril macrocycles, CB[7] in particular, for its high water solubility, are ideal candidates to foster 1,3-dipolar cycloaddition in an aqueous environment.[1,2] Substituted isoxazolidines were obtained from the cycloaddition of nitrones with different styrenes and cinnamates in water at 120 °C in 6 h, under microwave irradiation, with a catalytic equivalent of CB [7] (0.2 eq.), obtaining moderate diastereosimeric inversion with respect to the reaction carried out in toluene. The mechanism of reaction and the inclusion of reagents and products in CB[7] have been studied and rationalized by NMR spectroscopy experiments and molecular modeling calculations. The credit to this protocol include high yields and catalyst reusability, and preclude use of organic solvents. The present method is very much milder but more advanced than those previously reported.



References
[1] B. Chen, S.-F. Cheng, G.-H. Liao, X.-W. Li, L.-P. Zhang, C.-H.Tung, L.-Z. Wu, Photochem. *Photobiol. Sci.* **2011**, *10*, 1441–1444.
[2] W. L. Mock, T. A. Irra, J. P. Wepsiec and T. L. Manimaran. *J. Org. Chem*., **1983**, *48*, 3619–3620.

OC81

NO_2 reduction and amide bond formation in a one pot-two step procedure

E. Massolo,[a] S. Rossi,[a] J. Ortiz,[a] M. Orlandi,[a] M. Benaglia[a]

[a]*Università degli Studi di Milano, Via Golgi 19, Milano*
e-mail*: elisabetta.massolo@unimi.it*

A one-pot two-step reaction has been developed for the formation of amide bond from aromatic nitro compounds and carboxylic acids derivatives. This approach allows bypassing the synthesis and manipulation of toxic anilines giving straight access to valuable final products.

The present method relies on the *in situ* reduction of NO_2 by the $HSiCl_3$-Et_3N system[2] to afford the amine intermediate directly undergoing acyl substitution. In order to establish the scope of the reaction, functional group tolerance has been tested and electrophiles of different nature have been screened. Extensive optimization of the reaction conditions aimed to mold an effective and robust strategy with potential for large scale application.

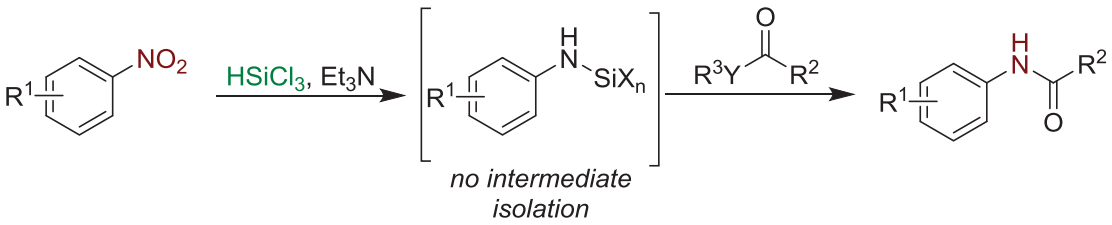


Figure 1: General scheme of the developed strategy.

The reduction step is performed under the mild and metal free conditions previously developed in our group,[3] relying on the use of a green and cheap reactant – trichlorosilane. The amine formation mechanism having been already elucidated, further investigation focused on the coupling step are currently underway.

References:

[1] V. R. Pattabiraman, J. W. Bode *Nature,* **2011**, *480*, 471-479.
[2] M. Orlandi, F. Tosi, M. Bonsignore, M. Benaglia *Org. Lett.* **2015**, *17*, 3941−3943.
[3] M. Orlandi, M. Benaglia, F. Tosi, R. Annunziata, F. Cozzi *J. Org. Chem.* **2016**, *81*, 3037−3041.

OC82

cADPR Analagues as Probes for the Cellular Ca^{2+} Ions Signaling

S. D'Errico,[a] G. Oliviero,[b] N. Borbone,[a] B. Catalanotti,[b] V. Costantino,[a] G. Piccialli,[a]

[a]*Dipartimento di Farmacia, Università degli Studi di Napoli 'Federico II', via D. Montesano, 49 – 80131 Napoli*
[b]*Dipartimento di Medicina Molecolare e Biotecnologie Mediche, Università degli Studi di Napoli 'Federico II', via S. Pansini, 5 – 80131 Napoli*
e-mail*: stefano.derrico@unina.it*

Cyclic ADP-ribose (cADPR) is a natural occurring metabolite of NAD^+ capable of mobilizing Ca^{2+} ions from intracellular stores. It was firstly isolated from sea urchin eggs extract, but it was later established that it is also produced in many other mammalian cells, including pancreatic β-cells, T-lymphocytes, smooth and cardiac muscle cells and cerebellar neurons, acting as a Ca^{2+}-mobilizing agent. For this activity, cADPR has been classified as a second messenger that, activating the ryanodine receptors of the sarcoplasmatic reticulum, is able to mobilize the calcium ions from intracellular stores. cADPR is involved in many physiological processes related to the variation of the Ca^{2+} concentration, such as the synaptic homeostasis in neurons, as well as fertilization and cellular proliferation. The chemical instability of cADPR N1 glycosidic bond at physiological pH together with its low ability to cross membranes for the presence of the strong negative charge at the pyrophosphate moiety pushed chemists to develop semi-synthetic and/or synthetic methodologies to obtain novel non-hydrolysable and cell permeant cADPR analogues. In the last years, we reported on the syntheses of several cIDPR analogues, focusing our attention on derivatives containing alkyl chains in place of the "northern" or "southern" riboses. We found promising Ca^{2+} releasing activities in neuronal PC12 cells for the cpIDP derivative with the "northern" ribose replaced by a pentyl chain.[1] With cpIDP in hand, we asked if it would be possible to obtain more potent analogues by tuning its molecular polarity. Herein, we report on the preliminary Ca^{2+} mobilizing activities of the novel cpIPP,[2] containing the pentyl chain and the unprecedented phosphono-phospate moiety in the place of the "northern" ribose and pyrophosphate respectively.

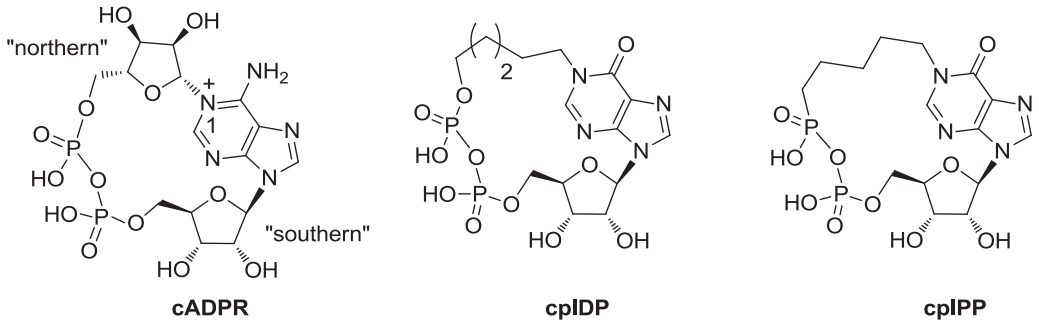


Figure 1: cADPR analogues

References:

[1] A. Mahal, S. D'Errico et al., *Beilstein J. Org. Chem.* **2015**, *11*, 2689 – 2695.
[2] S. D'Errico, G. Oliviero et al., *Mar. Drugs* **2018**, *16*, 89 – 102.

OC83

Curcumin from nature to laboratory: new ways to improve its properties

T. M.G. Salerno, A. Barattucci, A. Mancuso, F. Puntoriero, S. Campagna, P. Bonaccorsi

University of Messina, Department of Scienze Chimiche, Biologiche, Farmaceutiche ed Ambientali, Viale F. Stagno d'Alcontres 31, 98166, Messina, Italy

e-mail*: tsalerno@unime.it*

Curcumin, a natural pigment extracted from *Curcuma longa*, has gained, in recent years, much attention due to its significant biological activity, but its use is limited by its chemical instability and poor bioavailability, due to the low water solubility. Despite it has been intensively studied as an anti-inflammatory, antiproliferative, antimetastatic agent,[1] and as a drug in modern medical applications, with hundreds of papers and patents published in the last ten years, no clinical trial has proved specific therapeutic effect, so Curcumin is now considered both as a PAINS (pan assay interference compounds) and IMPS (invalid metabolic panacea).[2]

Nevertheless, Curcumin is a natural dye, with a low cost, good solubility in organic solvent and with a structure that allows different chemical modifications involving the β-diketo group, the methylene carbon atom and the phenolic position. Curcumin shows an absorption band around 410−430 nm and a fluorescence band within 460−560 nm; these photochemical properties depend on the polarity of its environment, solvent and pH.[3] However, this natural dye does not emitt in the biological window (700-900 nm) needed for *in vivo* biological application.

Recent studies, proved also that encapsulation of Curcumin into mesophorous silica nanoparticles, a biocompatible and stable material, leads to drug nanocarriers system, with improved stability and biovalability.[4] On the basis of this study and our experience on bi-chromophoric artificial antenna systems,[5] we have synthesized and studied Curcumin-based bi-chromophoric systems, using Bodipy (borodipyrromethene) and Anthracene derivatives as other chromophores. The incapsulation into silica nanoparticles COK-12, and the spectroscopic and biological evaluation of this new nanomaterial will be also discussed in this communication.

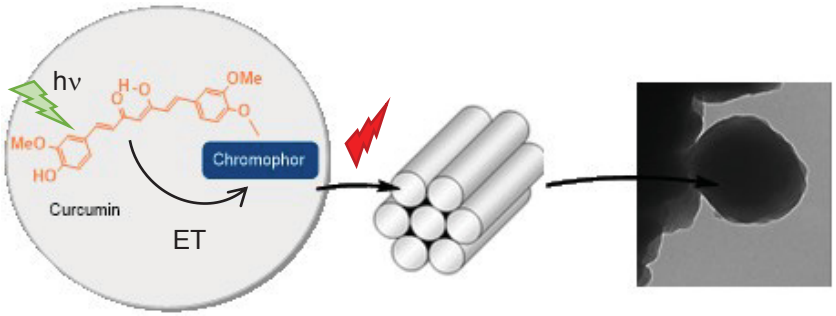


Figure 1: Schematic representation of the study.

References:

[1] T. Esatbeyoglu, P. Huebbe, I.M.A. Ernst, D. Chin, A. E. Wagner, G. Rimbach, *Angew. Chem. Int. Ed*. **2012**, *51*, 5308 – 5332.

[2] K. M. Nelson, J. L. Dahlin, J. Bisson, J. Graham, G. F. Pauli, M. A. Walters, *J. Med. Chem*. **2017**, *60,* 1620−1637; M. Baker, *Nature,* **2017**, *541*, 144-145.

[3] D. Patra, C. Barakat., *Spectrochimica Acta Part A* **2011**, *79*, 1034–1041.

[4] X. Xu, S. Lü, C. Gao, C. Feng, C. Wu, X. Bai, N. Gao, Z. Wang, M. Liu, *Chem. Eng. J.* **2016**, *300*, 185-192.

[5] S. Campagna, F. Puntoriero, P. Bonaccorsi, A. Barattucci, T. M. G. Salerno, T. Papalia, C. Rosano, P. Castagnola, M. Viale, M. Monticone, *Dalton Trans* **2018**. DOI: 10.1039/C7DT04850E.

OC84

Enantioselective Synthesis of Alkylidene Cyclohexanes Displaying Axial Chirality via Knoevenagel Condensation

G. Bencivenni,[a] S. Crotti,[a] N. Di Iorio,[a] C. Artusi,[a] A. Mazzanti,[a] P. Righi[a]

[a]*Dept. of Industrial Chemistry "Toso Montanari", University of Bologna, viale del Risorgimento 4, 40136-Bologna*
e-mail*: giorgio.bencivenni2@unibo.it*

Atropisomers are stereoisomers characterized by axial chirality along a rotable single bond. The stereogenic axis is a structural feature of many natural compounds as well as catalysts or ligands for asymmetric synthesis.[1] Biaryls, represent the most diffuse class of atropisomers, but nowadays also non-biaryl atropisomers such as, amides, anilides and imides are emerging as new type of atropisomeric compounds.[2] Axial chirality is also characteristic of rigid systems such as alkylidene-cycloalkanes, an important class of compounds less studied in enantioselective transformations.[3] Historically, their asymmetric synthesis have been realized using a stoichiometric amount of chiral Horner-Wadsworth-Emmons or Wittig-type reagents. Recently, the group of Bernardi synthesized axially chiral trisubstituted alkylidenes with poor ee and yields, through bis-thiourea-cyclohexanediamine or TADDOL catalyzed Wittig reaction.[4] In this context, the absence of an efficient enantioselective catalytic olefination reactions, prompted us to explore the unprecedented asymmetric Knoevenagel condensation for the preparation of novel alkylidene-cyclohexanes displaying axial chirality. Preliminary results showed the ability of a chiral primary amine to promote the Knoevenagel reaction of 4-substituted cyclohexanones with methylenic nucleophiles through an iminium ion activation strategy (Figure 1). The reaction proceeds with high yield and very good enantioselectivity. Mechanistic investigation and scope of the reaction will be discussed.

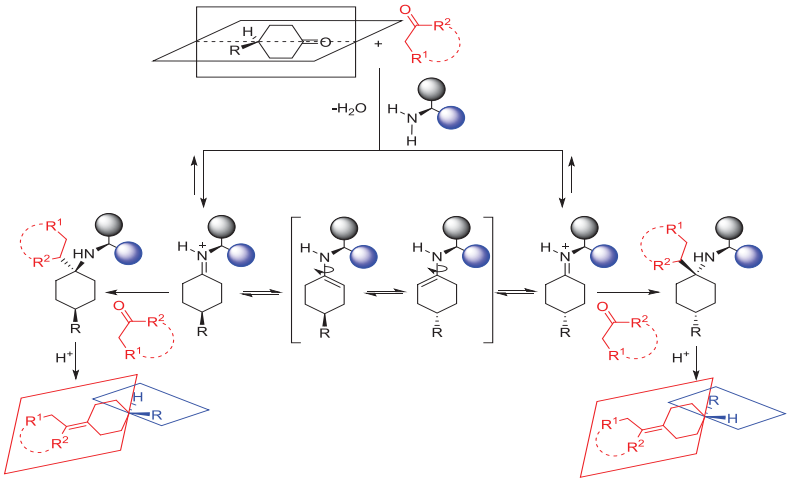


Figure 1: Synthesis of alkylidene cyclohexanes displaying axial chirality via Knoevenagel condensation.

References:

[1] a) P. Kočovskỳ, S. Vyskočil, M. Smrčina, M. *Chem. Rev.* **2003**, *103*, 3213. b) J. E. Smyth, N. M. Butler, P. A. Keller, *Nat. Prod. Rep*., **2015**, *32*, 1562.

[2] E. Kumarasamy, R. Raghunathan, M. P. Sibi, J. Sivaguru, *Chem. Rev.* **2015**, 11239.

[3] B. Testa, *Helvetica Chemica Acta*, **2013**, *96*, 351.

[4] L. Gramigna, S. Duce, G. Filippini, M. F. Fochi, M. Comes Franchini, L. Bernardi, *Synlett*, **2011**, 2745.

Comunicazioni POSTER

Sessione
Università Statale di Milano

P01

Synthesis of 3-alkylideneisoindolin-1-ones through cyclocarbonylative Sonogashira reactions

G. Albano, S. Giuntini, L. A. Aronica

Dipartimento di Chimica e Chimica Industriale, Università di Pisa, via G. Moruzzi 13, 56124 Pisa, Italy
e-mail*: gianluigi.albano@dcci.unipi.it*

The isoindolin-1-one moiety has been found in a growing number of naturally occurring compounds, such as fumaridine and fumaramine from *Fumaria parviflora* and *Fumaria vaillantii*.[1] Many isoindolin-1-ones -based compounds revealed biological and pharmacological activities,[2] while others have found application as moisture- and temperature-resistant pigments. Furthermore, 3-alkylideneisoindolin-1-ones are building blocks for the synthesis of more complex heterocycles: benzodiazepines, piperidines, subporphyrins and spiro-compounds.[3] Due to their versatility, several cyclization protocol have been developed for their preparation.[4]

Recently, we reported that 1-alkylidenephthalans and 1-alkylideneisochromans can be easily obtained, respectively, from suitable *o*-alkynylbenzyl and *o*-alkynylhomobenzyl alcohols by means of palladium-catalysed cyclocarbonylative Sonogashira reactions with functionalized aryl iodides.[5] The same protocol was then extended to *N*-Boc and *N*-tosyl *o*-ethynylbenzylamine as substrates, giving 1-alkylideneisoindolines as main products.[6] Starting from these results, here we describe the application of Pd-catalyzed cyclocarbonylative Sonogashira coupling to the synthesis of 3-alkylideneisoindolin-1-ones. The reactions were performed using 2-ethynylbenzamide and functionalized iodoarenes under CO pressure (20 atm) with an excess of Et_3N, catalytic $PdCl_2(PPh_3)_2$ (0.4 mol%), at 100 °C for 4 h (optimized conditions), yielding the corresponding (*Z*)-3-alkylideneisoindolin-1-ones as main products (**Figure 1**). Unexpectedly, depending on the solvent used, different interesting by-products were obtained (3-amino-1*H*-inden-1-ones with CH_2Cl_2, benzonitrile derivatives with THF), and their formation will be tentatively explained.

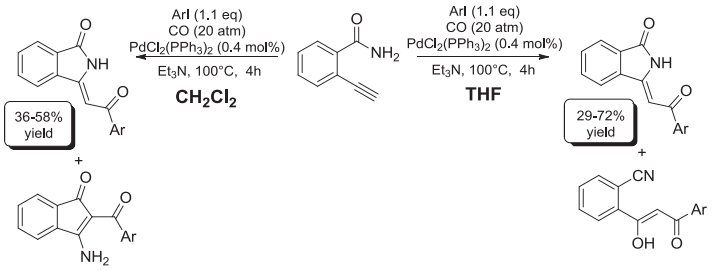


Figure 1: Synthesis of (*Z*)-3-alkylideneisoindolin-1-ones by cyclocarbonylative Sonogashira reaction of 2-ethynylbenzamide with aryl iodides.

References:

[1] S. F. Hussain, R. D. Minard, A. J. Freyer, M. Shamma, *J. Nat. Prod.* **1981**, *44*, 169-178. [2] J. R. Wetterau, R. E. Gregg, T. W. Harrity, C. Arbeeny, M. Cap et al., *Science* **1998**, *282*, 751-754. [3] S. Gowrisankar, S. J. Kim, J. Lee, J. N. Kim, *Tetrahedron Lett.* **2007**, 48, 4419-4422. [4] a) R. K. Howe, *J. Heterocyclic Chem.* **1985**, *22*, 71-72; b) N. G. Kundu, M. W. Khan, *Tetrahedron Lett.* **1997**, *38*, 6937-6940; c) M. Wu, L. Chang, L. Wei, C. Lin, *Tetrahedron* **1999**, *55*, 13193-13200; d) C. Petronzi, S. Collarile, G. Croce, R. Filosa, P. De Capriis et al., *Eur. J. Org. Chem.* **2012**, *2012*, 5357-5365. [5] a) L. A. Aronica, L. Giannotti, G. Tuci, F. Zinna, *Eur. J. Org. Chem.* **2015**, *2015*, 4944-4949.; b) L. A. Aronica, L. Giannotti, S. Giuntini, A. M. Caporusso, *Eur. J. Org. Chem.* **2014**, *2014*, 6858-6862. [6] L. A. Aronica, G. Albano, L. Giannotti, E. Meucci, *Eur. J. Org. Chem.* **2017**, *2017*, 955-963.

P02

Pd/C-Catalyzed Aerobic Oxidative *ortho*-C-H olefination of anilides in biomass derived γ-valerolactone

I. Anastasiou,[a] S. Santoro,[a] L. Vaccaro,[a]

[a]*Laboratory of Green Synthetic Organic Chemistry, Dipartimento di Chimica, Biologia e Biotecnologie, di Perugia, Via Elce di Sotto 8, 06123 Perugia, Italy. E-mail: luigi.vaccaro@unipg.it*

The heterogeneous palladium-catalyzed cross-dehydrogenative-coupling of anilides with alkenes is under investigation. The approach is characterized by using molecular oxygen as the terminal oxidant, and provides a straightforward and environmentally benign route to functionalized anilides (figure 1).

In an attempt to develop increasingly sustainable protocols we have recently reported the C-H alkenylation of acetanilides with various electron-poor alkenes.[1] In this process, but also in earlier works published by our group,[2] it has been successfully used a heterogeneous catalytic system, consisting of commercially available catalysts such as Pd/C and Pd/Al_2O_3 in a biomass derived reaction medium such as GVL. In the aforementioned work, as in the most Pd-catalyzed C-H activation coupling reactions, the use of stoichiomentric organic and inorganic oxidants such as benzoquinone, $PhI(OAc)_2$, AgOAc, Ag_2CO_3 and $Cu(OAc)_2$ can lead to waste production, reducing the sustainability of the process. Alternatively, the use of oxygen turns out to be advantageous both from the point of view of the "greenness" of the process, as water is the only by-product that is formed, and from the viewpoint of economical efficiency.

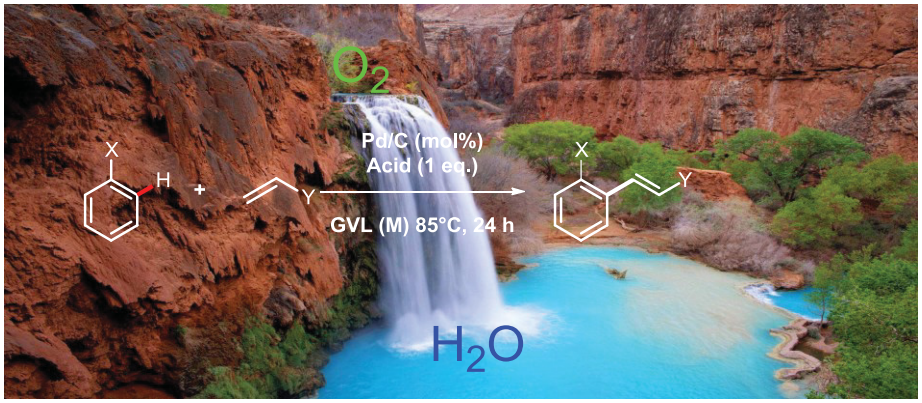


Figure 1: Aerobic Oxidative *ortho*-C-H olefination of anilides in GVL

References:

[1] F. Ferlin, S. Santoro, L. Ackermann, L. Vaccaro, *Green Chem* **2017**,*19,* 2510-2514

[2] (a)D. Rasina, A. Kahler-Quesada, S. Ziarelli, S. Warratz, H. Cao, S. Santoro, L. Ackermann and L. Vaccaro, *Green Chem.* **2016**, *18,* 5025. (b) X. Tian, F. Yang, D. Rasina, M. Bauer, S. Warratz, F. Ferlin, L. Vaccaro and L. Ackermann, *Chem. Commun.* **2016**, *52*, 9777.(c) G. Strappaveccia, E. Ismalaj, C. Petrucci, D. Lanari, A. Marrocchi, M. Drees, A. Facchetti and L. Vaccaro, *Green Chem.* **2015**, *17*, 365. (d) G. Strappaveccia, L. Luciani, E. Bartollini, A. Marrocchi, F. Pizzo and L. Vaccaro, *Green Chem.* **2015**, *17*, 1071. (e) E. Ismalaj, G. Strappaveccia, E. Ballerini, F. Elisei, O. Piermatti, D. Gelman and L. Vaccaro, *ACS Sustainable Chem. Eng.* **2014**, *2*, 2461.

P03

Energy transfer studies on a bodipy dyad

L. Baldini,[a] I. Tosi,[a] F. Sansone,[a] B. Bardi,[a] F. Terenziani,[a] M. Di Donato[b]

[a]*Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale, Università di Parma, Parco Area delle Scienze 17A, 43124 Parma, Italy*
[b]*LENS, European Laboratory for Non-linear Spectroscopy, Via N. Carrara 1, I-50019 Sesto Fiorentino, Firenze, Italy*
e-mail*: laura.baldini@unipr.it*

With the aim of developing artificial 'photosynthetic devices', research has been directed towards the synthesis of multichromophoric systems, able to absorb solar light and promote energy and charge transfer among the different dyes.[1] To achieve good performances of these systems, a key step is the optimization of the spectral properties of the chromophores and of the factors affecting the efficiency of energy and charge transfer. A combination of different parameters, among which the type of linker between the chromophores, their mutual orientation and the external medium, however, may contribute to the last aspect, thus rendering this task particularly difficult for complex systems. For this reason, the synthesis and spectroscopic analysis of simple bi-chromophoric systems may play an important role, since the contribution of the different factors can be more easily dissected.[2]

In this communication, we report the synthesis and characterization of a bichromophoric system, based on two different bodipy dyes connected through a calixarene scaffold (Figure 1). The chromophores have been chosen because of their high fluorescence quantum yield, high chemical stability and the possibility to tune their spectral properties by modifying the chemical substituents linked to the central bodipy core. The calixarene scaffold ensures a good control over the mutual distance and orientation of the chromophores. We have investigated the dynamics of photo-induced energy transfer through static and time-resolved absorption spectroscopy and rationalized the role of the solvent on the rates and efficiency of energy transfer.

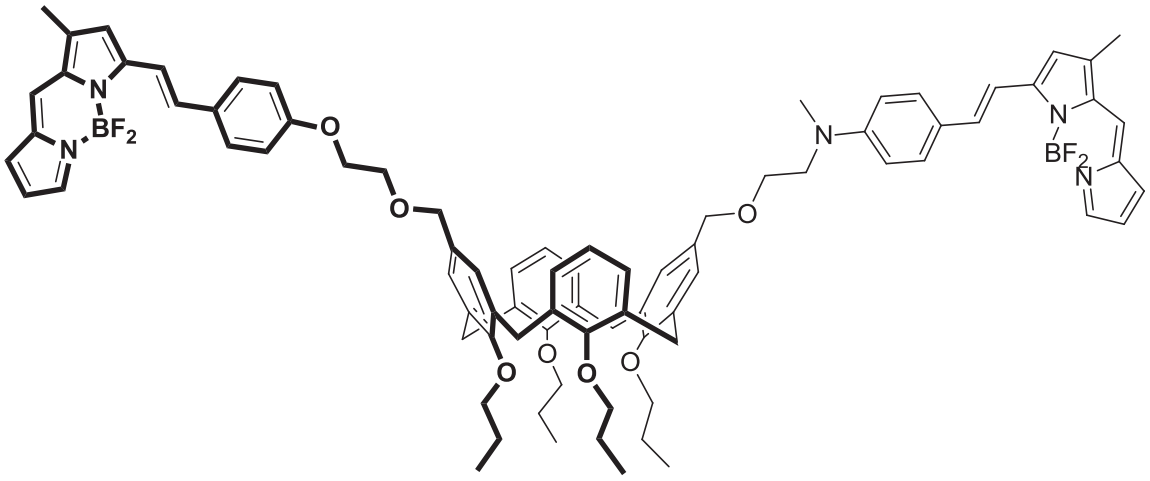


Figure 1: the bodipy dyad.

References:

[1] S.A. Denisov, et al., *ChemPhysChem* **2016**, *17*, 1794-1804.
[2] I. Tosi et al., *ChemPhysChem* **2016**, *17*, 1686 – 1706.

P04

Phytochemical analysis of the ethanolic extract of *Agathis robusta* (C. Moore ex F. Muell.) F.M. Bailey

A. Bianco,[a] M. Serafini,[b] S. Foddai,[b] C. Campanelli[c], A. Venditti[a], C. Frezza[b]

[a]Dipartimento di Chimica, [b]Dipartimento di Biologia Ambientale, [c]Dipartimento di Chimica e Tecnologie del Farmaco: Università di Roma 'La Sapienza', Piazzale Aldo Moro 5 - 00185 Rome (Italy)
e-mail*: armandodoriano.bianco@uniroma1.it*

Agathis robusta (C. Moore ex F. Muell.) F. M. Bailey (syn. *Dammara robusta* C. Moore ex F. Muell.) is a coniferous tree belonging to the Araucariaceae family[1]. It is principally known with the common names of Kauri pine and represents one of the most ancient trees that still inhabit this world[2] even if its presence is now limited to only a few nations of the Southern Hemisphere[1,2].
This work reports the phytochemical analysis of the ethanolic extract obtained from the leaves of this species collected in early June 2015 from a living tree growing in the Botanical Garden of the University of Rome "La Sapienza". The analysis was carried out by means of Column Chromatography, NMR and MS evidencing the presence of six compounds such as agathisflavone (**1**), 7″-*O*-methyl-agathisflavone (**2**), cupressuflavone (**3**), rutin (**4**), shikimic acid (**5**) and (2*S*)-1,2-di-*O*-[(9*Z*,12*Z*,15*Z*)-octadeca-9,12,15-trienoyl]-3-*O*-β-D-galactopyranosyl-glycerol (**6**)[3].
To the best of our knowledge, compounds (**3-6**) were identified for the first time in this study as constituents of *A. robusta.*

Anyway the presence of the majority of the identified components is fully in accordance with the current botanical classification of the species since chemotaxonomic parallelisms with other species of the genus were clearly detected as well as intra-family chemosystematic relations[3].
In addition, all the evidenced compounds present several medicinal properties among which the antibacterial, anti-inflammatory, antineoplastic, hepatoprotective, antimicrobial, antiallergic and antifungal ones are the most important and may explain why this species has been widely used in the ethnopharmacological field.

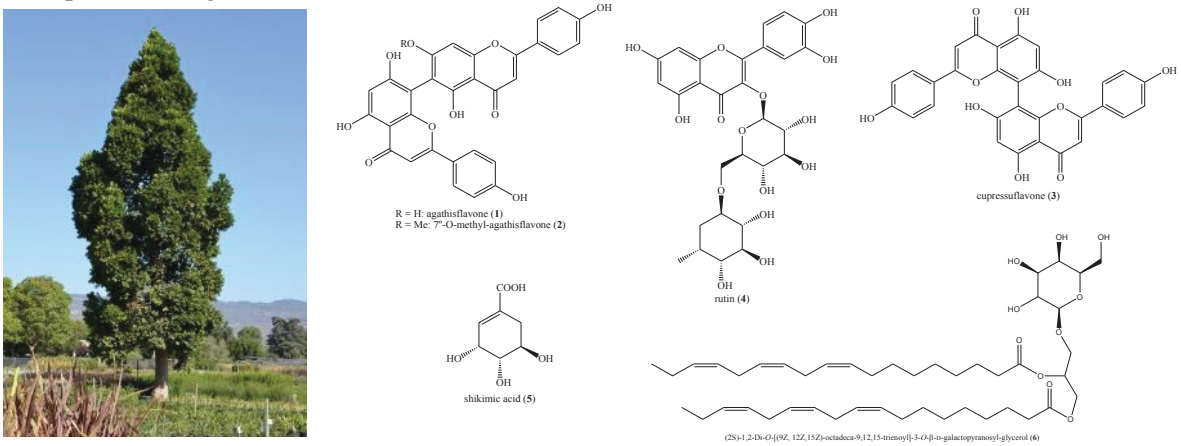


Figure 1: *A. robusta* (left) and Chemical structures of the evidenced compounds (right)

References:

[1] D.J. Boland, M.I.H. Brooker, G.M. Chippendale, N. Hall, B.P.M. Hyland, R.D. Johnston, D.A. Kleinig, J.D. Jurner, *Forest trees of Australia*, **1985**, Melbourne: Nelson, CSIRO.
[2] R.S. Verma, R.C. Padalia, P. Goswami, S,.K. Verma, A. Chauhan, M.P. Darokar, *Journal of Wood Chemistry and Techn*ology, **2016**, *36*, 270-277.
[3] A. Venditti, C. Frezza, C. Campanelli, S. Foddai, A. Bianco, M. Serafini, *Natural Product Research*, **2017**, *31(14)*, 1604-1611.

P05

New developments in the synthesis of EMICORON, a promising inhibitor of telomerase

A. Bianco,[a] M. Franceschin[a], C. Frezza[b], M. Pitorri[a]

[a]*Dipartimento di Chimica,* [b]*Dipartimento di Biologia Ambientale, Università di Roma 'La Sapienza', Piazzale Aldo Moro 5 - 00185 Rome (Italy)*
e-mail*: armandodoriano.bianco@uniroma1.it*

EMICORON is a compoud which was synthesized for the first time in our own laboratory in 2012[1,2]. From the chemical point of view, it is a benzo[*ghi*]perylen-diimmide presenting a piperidin group on the minor axis of the molecule directly linked to the bay area of the perylen core and three ethyl-piperidin chains, one linked to the aromatic area of the core and the other two linked to the major axis by a diimmidic bond.
This compound has proved to be able to inhibit the growth of tumor cells through a double mechanism i.e. the inhibition of telomerase at high doses and, at minor concentrations, the induction of apopotosis of the tumor cells by rapidly triggering extensive DNA damage of telomeres, associated with the delocalization of telomeric protein protection of telomeres 1 (POT1)[1]. EMICORON has also showed to be effective in inhibiting the colon-rectal tumors in rats[3] both as single compound both in a synergic effect with other conventional antitumor drugs[3,4].
In this work, we report the modification of two synthetic steps in respect with the usual ones in order to obtain a final higher yield for this compound. In particular, for what concerns the first one, we modified the times and the work up of the reaction whereas, for what concerns the second one, we completely modified the reaction conditions. We eliminated dioxane and hydroquinone and the new reaction occurred in shorter times, at lower temperatures and piperidine was used as reagent and solvent contemporaneously (Figure). With the modifications made to these two reaction steps, the global yield of the process has increased passing from 28% (original procedure)[1] to 40%.
Thus, this new procedure may be more suitable in order to get larger amounts of EMICORON to carry out further preclinical studies.

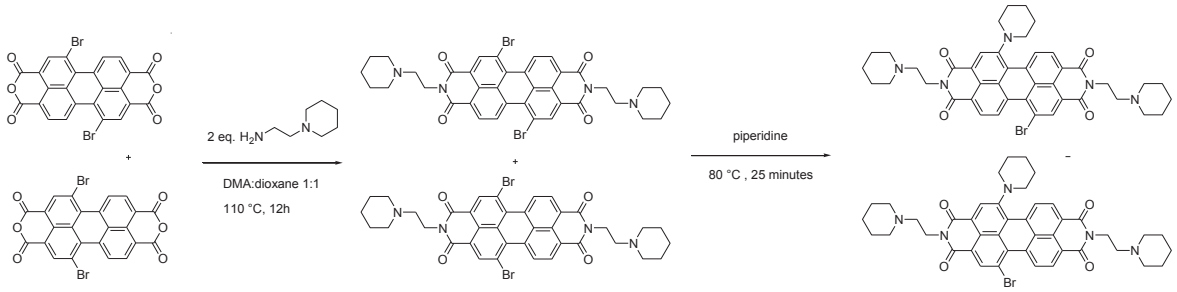


Figure: Scheme of the two modified synthetic steps within the usual procedure

References:

[1] M. Franceschin, A. Rizzo, V. Casagrande, E. Salvati, A. Alvino, A. Altieri, A. Ciammaichella, S. Iachettini, C. Leonetti, G. Ortaggi, M. Porru, A. Bianco, A. Biroccio, *Chemistry and Medicinal Chemistry*, **2012**, *7*, 2144 -2154.

[2] G. Ortaggi, A. Bianco, M. Franceschin, A. Biroccio, V. Casagrande (2012) Patent numbers: RM2012A000486, WO 2014/057511.

[3] M. Porru, S. Artuso, E. Salvati, A. Bianco, M. Franceschin, M.G. Diodoro, D. Passeri, A. Orlandi, F. Savorani, M. D'Incalci, A. Biroccio, C. Leonetti, *Molecular Cancer Therapy*, **2015**, *14(11)*, 2541-2551.

[4] M. Porru, P. Zizza, M. Franceschin, C. Leonetti, A. Biroccio, *Biochimica and Biophysica Acta*, **2017**, *1861*, 1362-1370.

P06

Synthesis of smenamide A functional-analogues in the 16-*epi*-series and evaluation of their antiproliferative activity

A. Caso,[a] I. Laurenzana,[c] D. Lamorte,[c] S. Trino,[c] G. Esposito,[a] V. Piccialli,[b] V. Costantino.[a]

[a] *Department of Pharmacy, University of Naples Federico II, 80131 Napoli, Italy*
[b] *Department of Chemical Sciences, University of Naples Federico II, via Cintia 4, 80126 Naples, Italy*
[c] *Laboratory of Pre-Clinical and Translational Research, IRCCS – Referral Cancer Center of Basilicata, Rionero in Vulture (PZ), Italy*
e-mail: alessia.caso@unina.it

Smenamides are an intriguing class of peptide/polyketide molecules of marine origin showing antiproliferative activity against lung cancer Calu-1 cells at nanomolar concentrations through a clear pro-apoptotic mechanism [1]. In order to investigate the role of the activity-determining structural features of smenamides family, a series of smenamide A analogues (Figure 1) have been designed and prepared using a flexible synthetic route [2,3].

In this communication, the evaluation of the antiproliferative activity of 16-*epi*-smenamide A and *ent*-smenamide A, together with the preparation of eight functional-analogues in the 16-*epi*-series will be discussed.

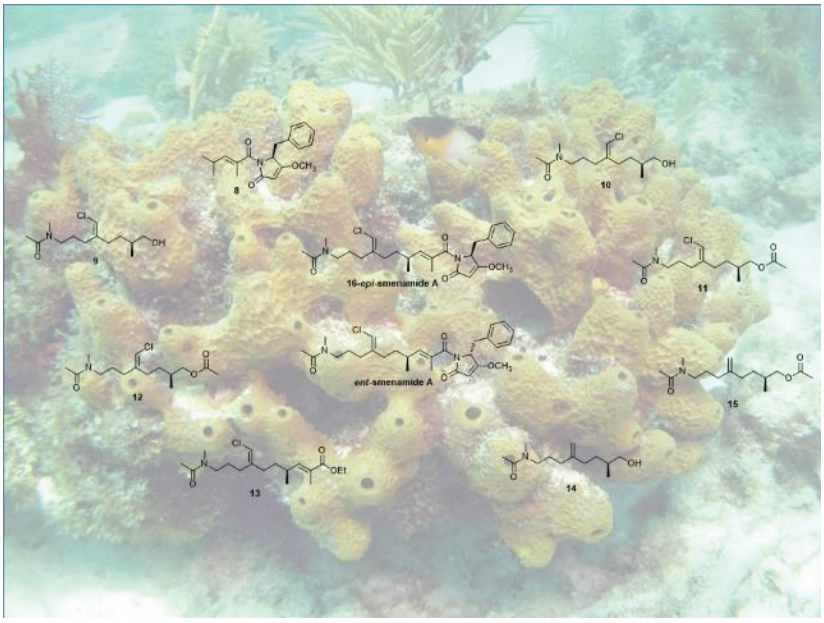


Figure 1: *ent*-smenamide A, 16-*epi*-smenamide A, and eight functional-analogues in the 16-epi-series.

References:

[1] Teta R., Irollo E., Della Sala G., Pirozzi G., Mangoni A., Costantino V., *Mar. Drugs*, **2013**, 11, 4451-4463.
[2] A. Caso, A. Mangoni, G. Piccialli, V. Costantino, and V. Piccialli, *ACS Omega*, **2017**, *2*(4), 1477–1488.
[3] A. Caso, I. Laurenzana, D. Lamorte, S. Trino, G. Esposito, V. Piccialli, and V. Costantino, *Mar. Drugs*, **2018**, accepted.

P07

Amphiphilic Aminoglycosides-based vectors for cell transfection: synthesis and biological validation.

C. Pennetta,[a] N. Bono,[b] F. Viani,[c] G. Candiani,[a,b] A. Volonterio.[a]

[a]Department of Chemistry, Materials and Chemical Engineering "Giulio Natta", Politecnico di Milano, Via Mancinelli 7 - 20131 Milan (Italy) [b]Politecnico di Milano Research Unit, National Interuniversity Consortium of Materials Science and Technology – INSTM, Via Mancinelli 7 - 20131 Milan (Italy) [c]Istituto di Chimica del Riconoscimento Molecolare, C.N.R., Via Mario Bianco 9, 20131 Milano, Italy
e-mail*: chiara.pennetta@polimi.it*

Designing effective and non-cytotoxic non-viral vectors is still a challenging issue in gene delivery. Aminoglycosides (AGs), a class of naturally occurring antibiotics particularly effective against gram-negative bacteria, have already been used to design cationic lipids[1] and polymeric[2] vectors because able to interact electrostatically with nucleic acids.

Our group is currently dedicated to the synthesis of novel AGs-based gene delivery carriers by linking different aminoglycosides (such as Neomycin, Paromomycin) with a variety of scaffolds, in order to build cationic lipid or dendrimeric carriers[3].

Herein we report the synthesis and characterization of a library of lipidic gene carriers based on AGs linked on a melamine scaffold. The synthetic strategy exploits the different reactivity of the three chlorine atoms 2,4,6-tricholoro-1,3,5-triazine, which are subsequently displaced by one (or two) long chain lipophilic amines and by an aminoglycoside that constitutes the polar head of the amphiphilic vectors (Fig.1). DNA/triazine-AG nanoassemblies, everyone tested at their optimal CR (ratio between the positive charges of the gene delivery vector and negative charges of the DNA cargo), displayed good transfection efficiency in HeLa cells, along with low-to-negligible cytotoxicity. Such amphiphilic triazine-AGs vectors represent a novel class of efficient multifunctional carriers for the delivery of nucleic acids.

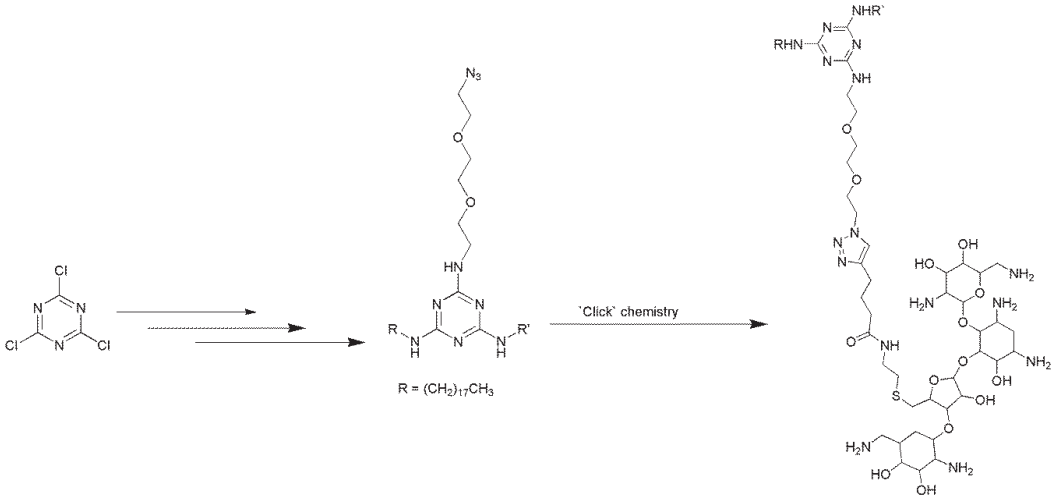


Figure 1: Scheme of the synthetic strategy

References:

[1] T. Colombani et al, *J Control Realease* **2017**, *249*, 131.
[2] B. Miryala et al, *Int J Pharm* **2015**, *489*, 18.
[3] A. Ghilardi et al, *Bioconj Chem* **2013**, *24*, 1928.

P08

NMR-based screening of green and roasted coffee extracts to identify anti-amyloidogenic compounds

C. Ciaramelli,[a] A. Palmioli,[a] A. De Luigi,[b] L. Colombo,[b] G. Sala,[c,d] C. Riva,[c,d] C. P. Zoia,[c,d] M. Salmona,[b] C. Airoldi[a,d]

[a] *Department of Biotechnologies and Biosciences, University of Milano-Bicocca, P.zza della Scienza 2, 20126 Milano, Italy.* [b] *Department of Molecular Biochemistry and Pharmacology, IRCCS- Istituto di Ricerche Farmacologiche "Mario Negri", Via G. La Masa 19, 20156 Milano, Italy.* [c] *School of Medicine and Surgery, University of Milano-Bicocca, Via Cadore 48, 20900 Monza, Italy.* [d] *Milan Center of Neuroscience (NeuroMI), 20126 Milano Italy.*
e-mail*: carlotta.ciaramelli@unimib.it*

In recent years, the research of foods and natural products to be employed as nutraceuticals has largely increased, becoming of great importance in the field of prevention against diseases lacking of effective therapies. An experimental protocol that combines NMR spectroscopy and atomic force microscopy, *in vitro* biochemical and *ex vivo* cell assays was developed to detect anti-Aβ molecules in natural edible matrices, in order to identify food and beverages able to provide the regular intake of natural compounds capable of interfering with toxic amyloidogenic aggregates. In particular, this approach was used to investigate the potential anti-amyloidogenic properties of green and roasted coffee extracts and their molecular constituents.[1]

Our data showed that green and roasted coffee extracts and their main components, the 5-O-caffeoylquinic acid and melanoidins, can hinder Aβ aggregation and toxicity in a human neuroblastoma SH-SY5Y cell line. In particular, the molecular interaction with a neurodegenerative amyloid oligomers model (Aβ1-42 oligomers) was demonstrated by means of STD-NMR and trNOESY-NMR spectroscopy.[2] Their antioxidant and anti-amyloidogenic activities were evaluated by cellular and biochemical assays, validating the existence of a correlation among the recognition of the molecular targets and the biological responses. Moreover, coffee extracts and melanoidins also counteract hydrogen peroxide- and rotenone-induced cytotoxicity and modulate some autophagic pathways in the same neuroblastoma cell line.

Notably, chlorogenic acids (CGAs), the most abundant family of polyphenols contained in green coffee, but also in other foods from plant origin, show other beneficial biological activities, including anti-oxidant, anti-carcinogenic,[3] anti-aging activity,[4] accounting for their potential employment as nutraceuticals.

Acknowledgements. *Coffee samples were kindly provided by Beyers Koffie, Belgium. We thank Fondazione Cariplo - Regione Lombardia for grant # 2015-0763.*

References:

[1] C. Ciaramelli, A. Palmioli, A. De Luigi, L. Colombo, G. Sala, C. Riva, C. P. Zoia, M. Salmona, C. Airoldi, *Food Chemistry* **2018**, *252*, 171–180.

[2] E. Sironi, L. Colombo, A. Lompo, M. Messa, M. Bonanomi, M. E. Regonesi, M. Salmona, C. Airoldi, *Chem. Eur. J.* **2014**, *20*, 13793–13800.

[3] A. Palmioli, C. Ciaramelli, R. Tisi, M. Spinelli, G. De Sanctis, E. Sacco, C. Airoldi, *Chem. Asian J.* **2017**, *12*, 2457 – 2466.

[4] L. Amigoni, M. Stuknytė, C. Ciaramelli, C. Magoni, I. Bruni, I. De Noni, C. Airoldi, M. E. Regonesi, A. Palmioli, *J. Funct. Foods* **2017**, *33*, 297-306.

P09

9-amino-9-deoxy-9-epi-quinine and acid catalyst co-supported on silica for stereoselective batch heterogeneous reactions.

F. Ferri[a], S. Crotti[b], N. Di Iorio[b], G. Bencivenni[b], M. Pierini[a], C. Villani[a], A. Ciogli[a].

[a]*Dip. di Chimica e tecnologie del farmaco, Sapienza Università di Roma, piazzale A. Moro, 5, 00185, Roma, Italy*

[b] *Dip. di Chimica Industriale "Toso Montanari", Alma Mater Studiorum-Università di Bologna, Viale del Risorgimento 4, 40136 Bologna.*

e-mail*: alessia.ciogli@uniroma1.it*

Heterogeneous organocatalysis is one of the hot research topics in advanced organic chemistry due to its potential in catalyst reuse and easy transfer to continuous flow systems [1,2]. Recently, in the field of asymmetric aminocatalysis, 9-amino-9-deoxy-epi-quinine has been supported on solid media, like silica or organic polymers as well, to investigate its catalytic ability in several transformations by either enamine or iminium ion formations [3,4]. In all tested reactions an additional co-catalyst (frequently benzoic acid) has been added to the reaction mixture. Here, we report the preparation and use of a ***Cat-co-Cat*** silica matrix with both catalyst and co-catalyst anchored to the solid surface.

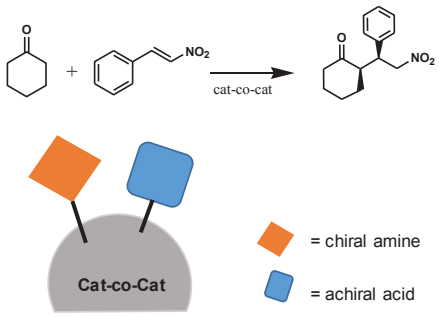


Figure 1: A simplified draw of ***Cat-co-Cat*** and an example of investigated reaction.

The solid material has been in depth characterized by elemental analysis, FT-IR and solid-state NMR. The heterogenized catalyst efficiently promoted the reaction of aldehyde or ketones with β-nitrostyrene, with diastereomeric ratio and enantioselectivity comparable to the homogeneous counterpart (up to d.r. = 90/10 and 90% ee). In addition, the catalyst retained a constant activity for at least four cycles. The synergistic (chiral amine/achiral acid) solid supported system, making an even easier work-out, increases safety, represents a valuable tool for green chemistry and is attractive for large scale applications.

References:

[1] I. R. Shaikh, *Journal of Catalysis*, **2014**, *vol. 2014*, 1-35.

[2] A. E. Allen, D. W. C. MacMillan, *Chem. Sci*., **2012**, *3*, 633-658.

[3] R. Porta, F. Coccia, R. Annunziata, A. Puglisi, *ChemCatChem*, **2015**, *7*, 1490 – 1499.

[4] R. Porta, M. Benaglia, F. Coccia, F. Cozzi, A. Puglisi, *Adv. Synth. Catal*., **2015**, *357*, 377 – 383.

P10

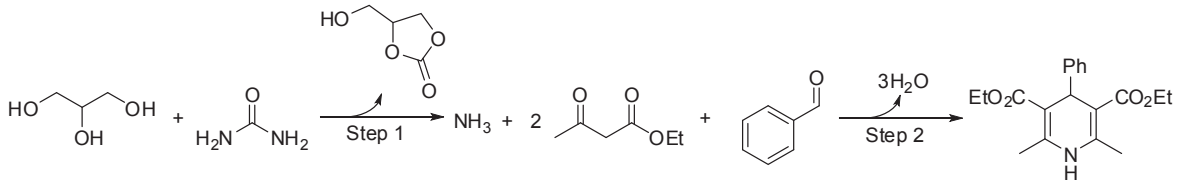
First Multicomponent Reaction Exploiting Glycerol Carbonate Synthesis

P. Costanzo,[a] C. Calandruccio,[a] M. L. Di Gioia,[b] M. Nardi,[c] M. Oliverio,[a] A. Procopio[a]

[a] *Dipartimento di Scienze della Salute, Università Magna Graecia, Viale Europa, 88100-Germaneto (CZ)*
[b] *Dipartimento di Farmacia e Scienze della Salute e della Nutrizione, Università della Calabria, Edificio Polifunzionale, 87036-Arcavacata di Rende (CS)*
[c] *Dipartimento di Agraria Università Telematica San Raffaele Via di Val Cannuta, 247, 00166-Roma, Italy*
e-mail*: pcostanzo@unicz.it*

Glycerol carbonate (GC) is one of the most interesting products derived from Glycerol (GLY), the main byproduct coming from biofuel industrial production. Urea glycerolysis is an attractive alternative method to produce GC from GLY, because urea is a bio-based reactant containing a CO_2 activated form.[1] However, the hard reaction conditions needed and the production of gaseous Ammonia as byproduct, limit the industrial application. Ammonia removal is than crucial both for the urea glycerolysis equilibrium[2] and for the process safety.

In this study, we propose a radical change of approach to urea glycerolysis consisting both in the alternative assistance of a slight pressure equipment like Q-Tube and the contemporary ammonia removal by two subsequent irreversible reactions. In particular, downstream of urea glycerolysis, we realized the "in cascade" multicomponent Hantzsch synthesis of 1,4-dihydropyridines (1,4-DHPs) as depicted in Scheme 1.



Scheme 1: Urea glycerolysis as ammonia source for Hantzsch reaction.

Then, the first example of the use of ammonia, the waste material of the bulk glycerol carbonate (GC) production, for the formation of another valuable organic molecule, a 1,4-dihydropyridine (1,4-DHP), by in line two reactor system was presented. Two Q-tube reactors, one is for the urea glycerolysis and the other for the Hantzsch reaction, connected through a PTFE tube, were used. Urea glycerolysis using La_2O_3 as heterogeneous catalyst, under N_2 pressure or vacuum conditions, was optimized. Catalyst and organic solvent free conditions were selected to realize a Hantzsch reaction in ecofriendly way. As best result, glycerol carbonate was obtained at 36% with 47% as selectivity, and at the same time the Hantzsch product was synthesized with a 75% of yield.[3]

References:

[1] M. O. Sonnati, S. Amigoni, E. P. Taffin De Givenchy, T. Darmanin, O. Choulet, F. Guittard, *Green Chem.* **2013**, *15*, 283–306.
[2] L. Wang, Y. Ma, Y. Wang, S. Liu, Y. Deng, *Catal. Comm.* **2011**, *12*, 1458–1462.
[3] P. Costanzo, C. Calandruccio, M. L. Di Gioia, M. Nardi, M Oliverio, A. Procopio, *J. Clean. Prod.* 2018**,** submitted.

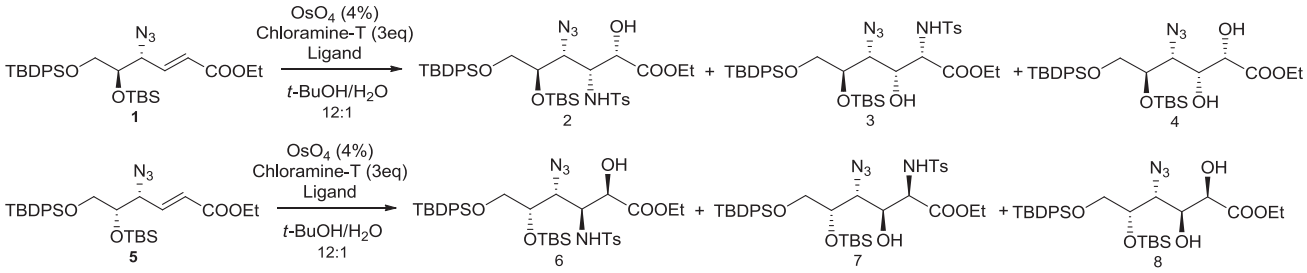
P11

Regio- and stereocontrol in asymmetric aminohydroxylation reaction on unsaturated azido alcohols

M. De Angelis[a], I. Ben Romdan[a], G. Forte[a], A. Petti[a], G. Righi[b]

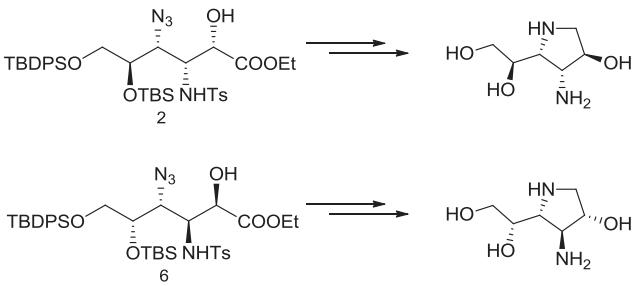
[a]Dipartimento di Chimica, Sapienza Università di Roma, P.le A. Moro 5, 00185 Roma; CNR-IBPM, [b]Dipartimento di Chimica, Sapienza Università di Roma, P.le A. Moro 5, 00185 Roma; m.deangelis@uniroma1.it

Recently, the amino derivatives of the iminosugars have stimulated significant interest for their higher efficiency and selectivity in the inibition of some enzymes compared to their analogous iminosugars.[1,2] In this work we propose a synthetic strategy for the stereocontrolled preparation of pyrrolidine amino iminosugars, using asymmetric aminohydroxylation reaction (AA) as the key step.[3] From this perspective a systematic study about AA reaction, in terms of regio- and chemoselectivity, is being undertaken using *Cinchona* alkaloids derivatives as chiral ligands (*Scheme 1*)



Scheme 1

The substrates chosen for this study are two stereoisomers of the usaturated azido alcohol (**1** and **5**) identified in our precedent studies as ideal precursor of pyrrolidine ring.[4] From this study it was found that the ligands to choose for the achievement of aminoalcoholic products are different depending on the substrate stereochemistry. Once we obtain the aminoalcoholic products is possible to continue the synthesis towards their respective amino iminosugars.



Scheme 2

References:

[1]. K.L. Curtis, J. Fawcett, S. Handa, *Tet. Lett* **2005,** *46*, 5297–5300.
[2]. L. Czollner, J. Kuzsmann, A. Vasella, *Helv. Chim. Acta* **1990**, *73*, 1338-1358.
[3] T.T. Upadhya.and A. Sudalai, *Tetrahedron: Asymmetry* **1997**, *8*, 3685-3689.
[4] G. Righi, E. Mandic',C. Sappino, E. Dema, P. Bovicelli, *Carbohyd. Res.* **2016**, *435*, 100-105.

P12

Amine Protection by *In Situ* Formation of Deep Eutectic Solvents

M. L. Di Gioia,[a] A. De Nino,[c] M. Nardi,[b,c] M. Oliverio,[d] A. Procopio,[d] G. Sindona[c]

[a]Dip.to di Farmacia e Scienze della Salute e della Nutrizione, Università della Calabria, Arcavacata di Rende, CS, Italy. [b]Dip.to di Agraria, Università Telematica San Raffaele, Roma, Italy[c]Dip.to di Chimica e Tecnologie Chimiche, Università della Calabria, Arcavacata di Rende, CS, Italy[d]Dip.to di Scienze della Salute, Università Magna Græcia di Catanzaro, Italy
e-mail*: ml.digioia@unical.it*

In recent years, there have been many governmental and industrial efforts to replace, eliminate or reduce the use of solvents in pharmaceutical and chemical industries. This effort has been driven by the need to reduce any possible human health impact, process safety risks, and negative effects to the environment.[1] The use of ‘‘green’’ solvents is the aim to minimize the environmental impact resulting from their use in chemical production.[2]

Since amines are noteworthy functionality present in a wide range of biologically active compounds, their protection is an important and a frequently required exercise in synthetic organic and medicinal chemistry owing to their high nucleophilicity and basicity.[3] Various methods for the protection of amine groups have been reported in which hazardous, toxic, and volatile organic solvents have been replaced by the use of green solvents such as water,[4] or ionic liquids. [5]

Recently, deep eutectic solvents (DESs) have begun to be evaluated as superior green, biorenewable, and biodegradable reaction media to perform chemical transformations.

DESs are generally obtained by the complexation of a quaternary ammonium salt such as choline chloride with a metal salt or hydrogen bond donor like urea, carboxylic acid, sugar and amide.[6]

Herein we report a novel procedure for the amino group protection in which a DES is formed consisting of choline chloride and the amine. As a consequence, the amine is not only a reactant, but simultaneously part of the solvent (Figure 1).

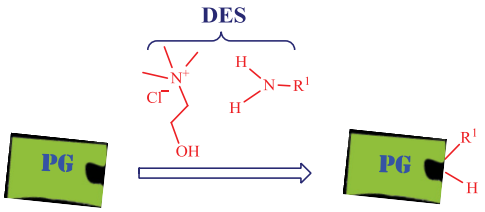


Figure 1: Amine protection by *in situ* formed DES.

The method is quite general for all the relevant amino protecting groups such as Fmoc, Boc, Cbz, Tosyl and acetyl groups. Various aromatic, aryl and alkyl amines were converted to their *N*-protected derivatives in excellent yields. Selective protection of amines in the presence of other functional groups was also achieved by this method.

References:

[1] P. Pollet, E.A. Davey, E.E. Ureña-Benavides, C.A. Eckert, C.L. Liotta, *Green Chem.*,**2014,** *16*, 1034-1055.
[2] C. Capello, U. Fischer, K. Hungerbühler *Green Chem,* **2007**, *9*, 927-934.
[3] G. Sartori, R. Ballini, F. Bigi, G. Bosica, R. Maggi, P. Righi, *Chem. Rev.* **2004**, *104*, 199-250.
[4] M. Nardi, N. Herrera Cano, P. Costanzo, M. Oliverio, G. Sindona, A. Procopio *RSC Adv.*, **2015**, *5*,18751-18760
[5] M. L. Di Gioia, A. Gagliardi, A. Leggio, V. Leotta, E. Romio, A. Liguori *RSC Adv.*, **2015**,*5*, 63407-63420
[6] A. P. Abbott, G. Capper, D. L. Davies, R. K. Rasheed, V. Tambyrajah *Chem. Commun.*, **2003**, 70-71.

P13

New procedure and linkers for liposomes glycorandomization

R. Edwards,[a] B. Formicola, R. Dal Magro, F. Re,[b]
F. Nicotra,[a] L. Russo[a]

[a]*Dip. di Biotecnologie e Bioscienze, Università degli Studi di Milano-Bicocca, Piazza della Scienza 2, Milano;*
[b]*Dip. di Medicina e Chirurgia, Università degli Studi di Milano-Bicocca, Via Alfred Nobel, Vedano al Lambro MB*

The role of carbohydrates in cellular communication and biological targeting has been a major topic of study in recent years. Different pathologies including cancer tend to overexpress lectin receptors that bind specifically to selected sugar moieties. Based on this fact, simple and complex carbohydrates have become interesting candidates for specific cellular targeting.
The study conducted aimed to create small thiol linkers that can attach to nanomaterials such as liposomes, PLGA, collagen, etc. via maleimide-thiol coupling from one end, and have the ability to load on synthetically unmodified simple and complex sugars from the other end using glycorandomization methods. This approach allows for the creation of a library of diverse sets of nanoparticles decorated with different carbohydrates in order to evaluate the efficacy of the decorated nanocarriers in selective targeting. Accordingly, liposomes functionalized with two different linkers: aminooxy- and phenylhydrazine-, each distinctively coupled with two sugars: Glucose and Mannose to assemble four different types of glycoliposomes were fully characterized and tested in vitro.
Novel characterization methods were utilized to detect and quantify the presence of the carbohydrates on the outer surface of the liposomes. Furthermore, cytotoxicity and cell-uptake experiments were conducted on macrophage cell line to analyze the safety of the linkers synthesized and the function of the assembled liposomes. This study highlights new methods for the glyco-functionalization of liposomes and nanomaterials along with characterization techniques specific to carbohydrates, thus creating a glyco-model with a wide range of potential translational applications.

Acknowledgments: this research is funded by H2020-MSCA-ITN-2014-GA-642028 NABBA project “Design and development of advanced NAnomedicines to overcome Biological BArriers and to treat severe diseases”.

P14

Synthesis of a new class of isoxazole derivatives with a dual FXR agonistic and COX-2 inhibitory activity

C. Finamore,[c,a] V. Sepe,[a] D. Masullo,[a] S. Fiorucci,[b] A. Zampella[a]

[a]University of Naples Federico II, Department of Pharmacy, Via Domenico Montesano 49, 80131, Naples, Italy. [b]Departmentof Experimental and Clinical Medicine, Piazza L. Severi, 1, 06132, S. Andrea delle Fratte, Perugia, Italy. [c]University of Molise, Department of Bioscience and Territory, Contrada Fonte Lappone, Pesche (Isernia), Italy.
e-mail: claudia.finamore@unina.it

The farnesoid-X-receptor (FXR, NR1H4) belongs to the nuclear receptors (NRs) super-family, and is highly expressed in enterohepatic tissues, kidney, adrenalgland, pancreas, reproductive tissues and in lower levels in adipose tissue.[1] Since its activation is linked to the control of different metabolic and enterohepatic functions, it could be considered an efficient target in the treatment of several human diseases, such as cholestasis, primitive biliary cirrhosis and others. The most potent FXR endogenous activator is the chenodeoxycholic acid (CDCA) and for these reasons, for many years, bile acids have been investigated as potential therapy in the treatment of hepatic and metabolic disorders. However, recently, a non-steroidal derivative,GW4064 (Fig. 1) has been identified as FXR agonist, endowed with a potency of 70 nM and an efficacy of 140% respect the CDCA. Since its disclosure, serial modifications have been performed around this scaffold, with the aim to improve its limited intestinal absorption (<10%) and to reduce its intrinsic photo-instability due to the presence of the widely delocalized π-electron system in the stilbene moiety, that is associated with a potential cell toxicity. Thus, several research groups, ranging from academy to industry, have harnessed the chemical space around the stilbene moiety, the position of the carboxyl group on the terminal aryl unit, the nature of classical linker, while the central isoxazole core, the isopropyl group at C-5 and the 2,6-dihalogen substituted phenyl at C-3, have been conserved.[2] In this work, maintaining the trisubstituted isoxazole unit, a novel family of GW4064 derivatives has been prepared, with modifications on the length and functionalization of the aromatic portion on C-4. Of interest, in a preliminary pharmacological analysis some of them resulted potent FXR agonists. Moreover, their structural similarity with the most notorious FANS (non-steroidal anti-inflammatory drugs), pointed us to evaluate their activity on cyclooxygenase enzymes, and in particular two derivatives showed 20% inhibition of COX-2 activity. To the best of our knowledge, this result represents the first report of small molecules with dual FXR/COX-2 activity.

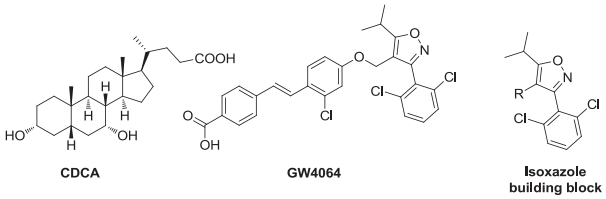


Figure 1: Structures of CDCA,GW4064 and of Isoxazole building block

References:

[1] S. Fiorucci, G. Rizzo, et al. *Trends Mol. Med.* **2007**, *13*, 298-309.
[2] C. Gege, O. Kinzel, et al. *Curr. Top. Med. Chem.* **2014**, *14*, 2143-58.

P15

Bioinspired supramolecular organocatalysis mediated by macrocyclic scaffolds

S. Gambaro, M. De Rosa, P. La Manna, A. Soriente, C. Gaeta, C. Talotta, P. Neri

Dipartimento di Chimica e Biologia "A. Zambelli", Università di Salerno, Via Giovanni Paolo II, 132, 84084, Fisciano (SA)

e-mail*: sgambaro@unisa.it*

Enzymes are the fascinating promoters of biosynthetic processes and are responsible for their high efficiency and selectivity. During the last years, the development of new bioinspired artificial catalytic systems taking natural enzymes as a blueprint has become an exciting area of research.[1,2] Many kinds of artificial enzymes have been prepared based on different supramolecular scaffolds ranging from macrocycles to molecular containers trying to mimic the confined environment and the molecular recognition abilities of the enzyme pocket.[3]

As a part of our ongoing investigations on the design and use supramolecular enzyme mimics,[4,6] we report here our recent results based on the use of calixarene derivatives as supramolecular organocatalysts in the synthesis of heterocyclic rings, building blocks in various biologically and pharmacologically active compounds. These macrocycles, thanks to their hydrophobic cavities, are able to recognize and to host selectively the substrates isolating them from the reaction environment. Their ease of functionalization permits to introduce useful functional groups in close proximity of the hydrophobic binding sites.

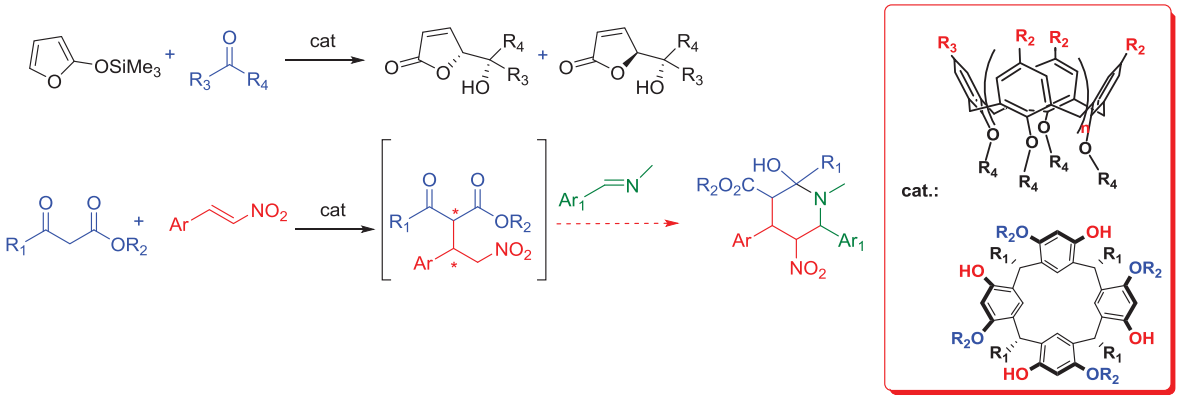


Figure 1: Calixarene derivatives as supramolecular organocatalysts in C-C bond-forming reactions.

References:

[1] M. Raynal, P. Ballester, A. Vidal-Ferran, P. W. N. M. van Leeuwen, *Chem. Soc. Rev.*, **2014**, *43*, 1737-1787.

[2] Z. Dong, Q. Luo, J. Liu, *Chem. Soc. Rev.*, **2012**, *41*, 7890-7908 .

[3] E. Kuah, S. Toh, J. Yee, Q. Ma, Z. Gao, *Chem. Eur. J.* **2016**, *22*, 8404-8430.

[4] M. De Rosa, P. La Manna, A. Soriente, C. Gaeta, C. Talotta, N. Hickey, S. Geremia, P. Neri, *Chem. Eur. J.*, **2017**, *23*, 7142-7152.

[5] M. De Rosa, P. La Manna, A. Soriente, C. Gaeta, C. Talotta, P. Neri, *RSC Adv,*. **2016**, *6*, 91846-91851.

[6] P. La Manna, M. De Rosa, C. Talotta, C. Gaeta,; A. Soriente, G. Floresta, A. Rescifina, P. Neri, *Org. Chem. Front.,* **2018**, *5*, 827-837.

P16

Synthesis of bifunctional calixarene hosts

V. Iuliano, C. Talotta, C. Gaeta, M. De Rosa, A. Soriente, P. Neri

Department of Chemistry and Biology "A. Zambelli", University of Salerno, via Giovanni Paolo II 132, 84084 Fisciano, Italy;
e-mail: viuliano@unisa.it

Calix[*n*]arenes constitute an interesting class of macrocyclic compounds due to their peculiar capability to form host-guest complexes with different kinds of ions and neutral compounds[1,2].
New binding sites can be introduced on the native macrocycles by simple chemical modification at the lower and/or upper rim. Typical binding sites contain H-bond-donating, H-bond-accepting, electron-withdrawing, or electron-donating groups[1,2]. In this communication, we report the synthesis of bifunctional calix[*n*]arenes containing both electron-poor sites and H-bond-acceptor groups (Figure 1). Anion and cation recognition abilities, optoelectronic properties, and applications in organocatalysis will be studied. In addition, their applications for the synthesis of interpenetrated[3-7] and interlocked supramolecular systems[8] will be also considered.

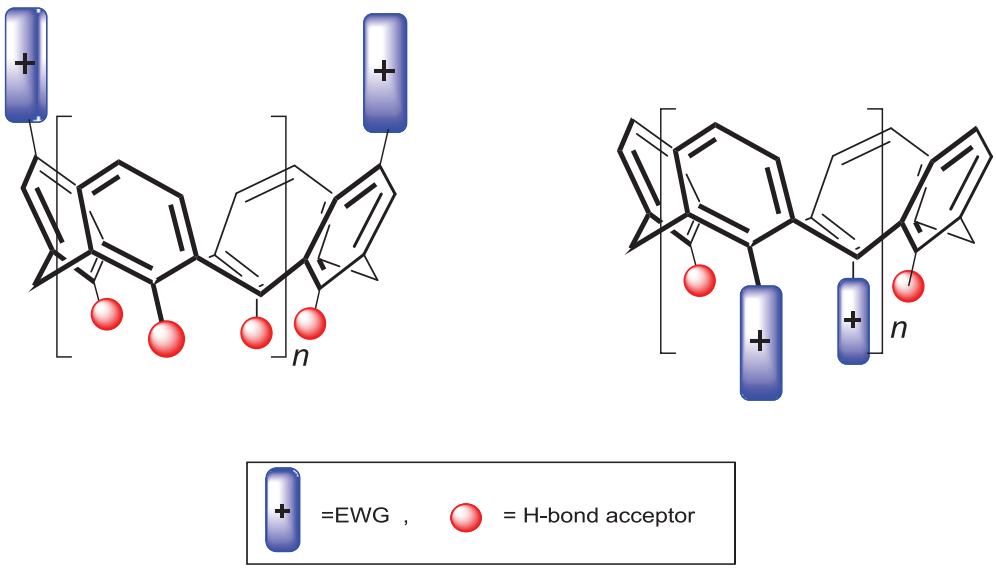


Figure 1: Bifunctional calixarenes

References:

[1] C. D. Gutsche, Calixarenes, An Introduction, Royal Society of Chemistry, Cambridge, UK, **2008**.
[2] P. Neri, J. L. Sessler, M. –X. Wang (Eds), Calixarenes and Beyond, Springer, Dordrecht, **2016**.
[3] Chuyang Cheng, P. R. McGonigal, S. T. Schneebeli, H. Li, N. A. Vermeulen, C. Ke, J. F. Stoddart, *Nat. Nanotechnol.* **2015**, *10*, 547–553.
[4] G. De Bo, M. A. Y. Gall, M. O. Kitching, S. Kuschel, D. A. Leigh, D. J. Tetlow, J. W. Ward, *J. Am. Chem. Soc.* **2017**, *139*, 10875−10879.
[5] T. Pierro, C. Gaeta, C. Talotta, A. Casapullo, P. Neri, *Org. Lett.* **2011**, *13*, 2650-2653.
[6] C.Talotta, C. Gaeta, P. Neri, *Org. Lett.* **2012**, *14*, 3104.
[7] C. Gaeta, C. Talotta, S. Mirra, L. Margarucci, A. Casapullo, P. Neri, *Org. Lett.* **2013**, 15, 116-119.
[8] C. Talotta, C. Gaeta, Z. Qi, C. A. Schalley, P. Neri, *Angew. Chem. Int. Ed.* **2013**, *52*, 7437 –7441.

P17

Functionalized Cellulose Nanocrystals as Drug-Delivery for Bone Diseases

B. La Ferla,[a] L. Zoia,[b] P. Bigini,[c] A. Morelli[a]

[a]Department of Biotechnology and Biosciences, University of Milano-Bicocca, Piazza della Scienza 2, 20126 Milano, Italy. [b]Department of Earth and Environmental Science, University of Milano-Bicocca, Piazza della Scienza 1, 20126 Milan, Italy. [c]IRCCS-Istituto di Ricerche Farmacologiche "Mario Negri", via La Masa 19, 20156 Milan, Italy
e-mail*: barbara.laferla@unimib.it*

Cellulose-Nano-Crystals (CNCs), thanks to their physico-chemical properties, low production cost and abundance, are a potential candidate material for the development of new emerging nano-tools in the biomedical field. These NPs present a rod-shape morphology that has been reported to possess higher specificity versus endothelial targets compared to their spherical counterparts, thus suggesting a potential use of elongated NPs for theranostic purposes, with particular application towards bone-disorders, the cure of which is extremely challenging due to the very low tropism of drugs towards this target[1]. In our labs we carried out a careful evaluation of the biodistribution, accumulation and clearance in filter organs of CNCs in mice, using fluorescent labelled CNCs detectable by in vivo Optical Imaging[2], and demonstrated the localization of the CNCs at the hind limbs most probably due to the favorable interaction of the sulphated CNCs with the bone matrix and in particular with the positively charged calcium ion. In the present work we aimed at improving the already present bone tropism through the surface chemical modification of native CNCs. In particular, we modified the surface by substituting the sulphates with other anionic groups: carboxylates, introduced through TEMPO oxydation, and the better calcium chelating pyrophosphonates, obtained through EDC coupling of the carboxylates with a primary amine compound bearing a pyrophosphonate (known as Alendronate). Biodistribution studies on these modified CNCs revealed increased bone tropism, therefore suggesting development of potential new therapeutic approaches in bone diseases.

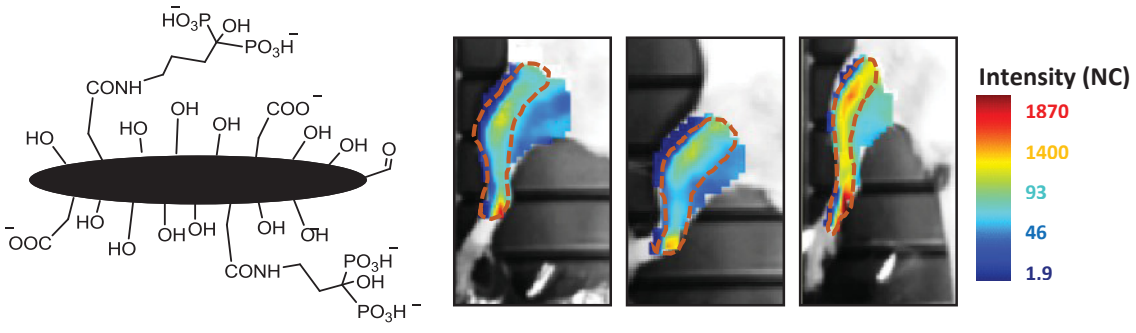


Figure 1: CNC-Alendronate modified (left); b) CNCs specific signal in bone matrix.

References:

[1] P. Decuzzi, R. Pasqualini, W. Arap, M. Ferrari, *Pharma Res*., **2009**, *26*, 235-43.
[2] L. Colombo, L. Zoia, M. B. Violatto, S. Previdi, L. Talamini, L. Sitia, F. Nicotra, M. Orlandi, M. Salmona, P. Bigini, B. La Ferla. *Biomacromolecules*, **2015**, *16*, 2862-2871.

P18

Friedel-Crafts Reaction Promoted by Hexameric Resorcinarene Capsule

P. La Manna,[a], C. Talotta,[a], G. Floresta,[b], M. De Rosa[a], A. Soriente[a], A. Rescifina[b], C. Gaeta[a], P. Neri[a]

[a]*Dipartimento di Chimica e Biologia, Università di Salerno, Via Giovanni Paolo II 132, Fisciano (SA), Italy.* [b]*Dipartimento di Scienze del Farmaco, Università di Catania, Viale Andrea Doria 6, 95125, Catania (CT), Italy*

e-mail*: plamanna@unisa.it*

In the last years, hydrogen-bonded hexameric capsules of resorcinarenes[1] have been intensively investigated as nanoreactors in catalysis[2]. In particular, their ability to stabilize cationic reactive intermediates[3] and to create an unique nanoenvironment[4] has been exploited for a series of chemical reactions ranging from terpene cyclization[5] to carbonyl-olefin metathesis[6]. In this communication, we will show that the bridged water molecules of the resorcinarene capsule are able to activate the C-Cl bond of benzyl chloride by H-bonding interaction (**Figure 1**), in order to promote a mild Friedel-Crafts benzylation of several arenes and heteroarenes. Moreover, we will show that the self-assembled capsule is able to exert a supramolecular control on the reaction outcome, as evidenced by the unusual benzylation at the β-position of *N*-methylpyrrole and by the altered nucleophile reactivity, which is determined by their affinity for the inner cavity of the capsule rather than by their nucleophilicity[7].

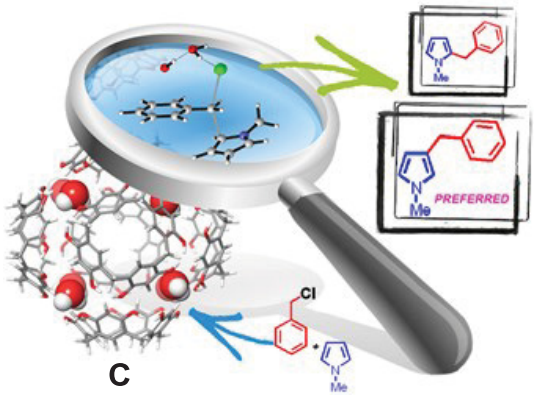


Figure 1: Water molecules of the resorcinarene capsule (**C**) are able to activate C-Cl bond and to promote benzylation of *N*-methylpyrrole at the *β*-position.

References:

[1] (a) L. R. MacGillivray, J. L. Atwood, *Nature* **1997**, *389*, 469-472; (b) L. Avram, Y. Cohen, *J. Am. Chem. Soc*. **2002**, *124*, 15148-15149.

[2] (a) G. La Sorella, L. Sperni, G. Strukul, A. Scarso, *Adv. Synth. Catal*. **2016**, *358*, 3443-3449; (b) P. La Manna, M. De Rosa, C. Talotta, C. Gaeta, A. Soriente, G. Floresta, A. Rescifina, P. Neri, *Org. Chem. Front*. **2018**, *5*, 827-837.

[3] Q. Zhang, K. Tiefenbacher, *J. Am. Chem. Soc.* **2013**, *135*, 16213-16219.

[4] A. Cavarzan, A. Scarso, P. Sgarbossa, G. Strukul, J. N. H. Reek, *J. Am. Chem. Soc.* **2011**, *133*, 2848-2851.

[5] Q. Zhang, K. Tiefenbacher, *Nat. Chem.* **2015**, *7*, 197-202.

[6] L. Catti, K. Tiefenbacher, *Angew. Chem. Int. Ed*. **2018**, *57*, 1-5.

[7] P. La Manna, C. Talotta, G. Floresta, M. De Rosa, A. Soriente, A. Rescifina, C. Gaeta, P. Neri, *Angew. Chem. Int. Ed*. **2018**, *Accepted*. DOI: 10.1002/anie.201801642.

P19

Studies for amino acid catalyzed enantioselective aldol reactions

G. Lucarelli[a], F. Leonelli[b], A. La Bella[a], L. M. Migneco[a], R. Marini Bettolo[a].

[a]*Department of Chemistry,* [b]*Department of Environmental Biology, "La Sapienza" University of Rome, P.le Aldo Moro, 5, I-00185 Roma, Italy*
e-mail*: giulio.lucarelli@uniroma1.it*

Diterpenes compounds are well known for their interesting biological activities[1] and many strategies have been developed for their synthesis. The object of this work is the obtaining of unknown 4-((1-methyl-2,6-dioxo-cyclohexyl)methyl)-pent-4-enal **1**, that could be envisioned as a key intermediate of many diterpenes syntheses, due to its adaptable functional groups.

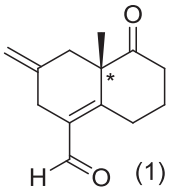
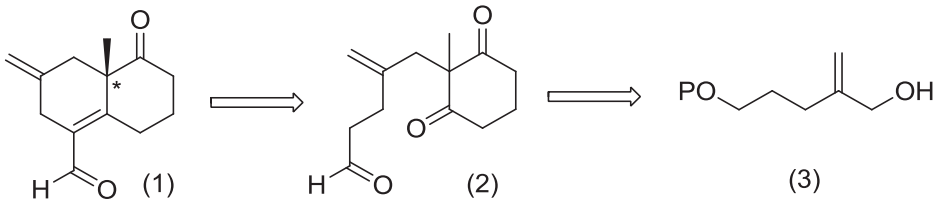


Figure 1: 4-((1-methyl-2,6-dioxo-cyclohexyl)methyl)-pent-4-enal.

We wish here to describe the enantioselective preparation of carbaldehyde **1** from compound **3**, as shown in scheme 1. The first step of retrosynthetic analysis is an enantioselective intramolecular aldol reaction of compound **2**; as this compound **1** resembles Wieland Miescher ketone, whose enantioselective synthesis was accomplished using proline as organocanocatalyst[2], different proline derivate catalysts[3] and other catalysts from chiral pool, were tested and used with good results.



Scheme 1: retrosynthesis for obtaining **1**.

References:

[1] Pablo Anselmo García, Alaíde Braga de Oliveira and Ronan Batista, *Molecules* **2007**, *12*, 455 – 483.

[2] Zoltan G. Hajos and David R. Parrish, *Journal of Organic Chemistry* **1974**, *39,* 1615 – 1621.

[3] Yujiro Hayashi, Hiromi Sekizawa, Junichiro Yamaguchi, and Hiroaki Gotoh, *Journal of Organic Chemistry* **2007**, *72*, 6493 – 6499.

P20

Calix[4]arene-based sensitizer for host-guest supramolecular dyad for solar energy conversion

N. Manfredi,[*,a] C. L. Boldrini,[a] F. Faroldi,[b] C. Quarti,[c] L. Baldini,[*,b] A. Abbotto[*,a]

[a]*Department of Materials Science and Milano-Bicocca Solar Energy Research Center – MIB-Solar, University of Milano-Bicocca, Via Cozzi 55, I-20125 Milano, Italy*
[b]*Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale, Università di Parma, Parco Area delle Scienze 17A, 43124 Parma, Italy*
[c]*Université de Mons, Place du Parc 20, 7000, Mons, Belgium*
e-mail*: norberto.manfredi@unimib.it*

The need for an oil free energy policy is one of the most important goals of the next decades. Moreover, the need of hydrocarbons for more significant applications claims a reduction of consumption of these precious resources in energy production to keep their price acceptable. In this scenario, the organic design is strategic in order to get improved technological performances in dye-sensitized solar technologies (dye-sensitized solar cells, DSSCs, and dye-sensitized photoelectrochemical cells, DS-PECs). In the frame of our investigation on dye-sensitized solar cells in the last years we have pioneered a multi-branched multi-anchoring D(-π-A)$_2$ geometry, now widely used in the field,[1-2] and recently we have introduced the importance of supramolecular aproach.[3] Moreover, the use of supramolecular assembly in DS-PEC has been successfully exploited by Sun and coworkers.[4] Here, we present the application of specifically engineered supramolecular assembly of di-branched dyes to the dye-sensitized photo(electro)chemical solar fuels production. (Figure 1) The exploitation of the superior host-guest properties of calix[4]arene fragment have been combined with an easy to synthesize D(-π-A)$_2$ organic dyes to boost photoelectrochemical water oxidation in presence of a properly designed water oxidation catalyst (WOC) as guest in the calix[4]arene cavity, showing enhanced light harvesting and photoelectrochemical properties.

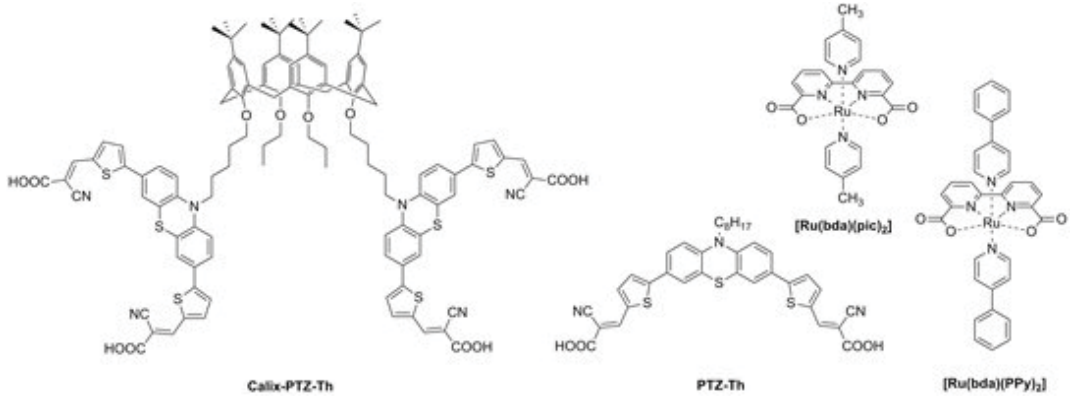


Figure 1: Calix-based host sensitizer (**Calix-PTZ-Th**) and his guest WOC **[Ru(bda)(PPy)$_2$]**, and corresponding reference sensitizer and catalyst.

References:

[1] B. Cecconi, N. Manfredi, T. Montini, P. Fornasiero, A. Abbotto, *Eur. J. Org. Chem.* **2016,** 5194-5215.
[2] N. Manfredi, B. Cecconi, A. Abbotto, *Eur. J. Org. Chem.* **2014**, 7069-7086.
[3] N. Manfredi, M. Monai, T. Montini, F. Peri, F. De Angelis, P. Fornasiero, A. Abbotto, *ACS Energy Lett.* **2018**, 85-91.
[4] H. Li, F. Li, Y. Wang, L. Bai, F. Yu, L. Sun, *ChemPlusChem* **2016**, *81*, 1056-1059.

P21

Multimodal functionalized nanoparticles as diagnostic tools in diabetes therapy

F. Mazzieri,[a] L. Rabbachin,[a] M. Pozzi,[a] F. Nicotra,[a] E. Prépost,[b] K. Kerekes,[b] Z. Csikos,[b] L. Russo[a]

[a]Università degli Studi di Milano-Bicocca, Dipartimento di Biotecnologie e Bioscienze, Piazza della Scienza 2, Milano, Italy
[b]BBS Nanotechnology, Böszörményi út 212, Debrecen 4032, Hungary
laura.russo@unimib.it

In the context of a H2020 project aimed to apply nanotechnologies to monitor the viability of porcine pancreatic islet producing insulin in a medical device, we plan to generate nanoparticles functionalized with a ligand of living beta-cells and two detectable agents, suitable for diagnostic protocols applicable on patients.

The nanoparticles will be obtained, exploiting a protocol of BBS, by self-assembling of Chitosan and Polyglutamic acid (PGA). The two components have been functionalised in different ways in order to conjugate: i) Exendin-4, a peptide that acts as ligand of GLP1 receptor overexpressed by living beta-cells, ii) a linker containing a chelator of metals utilised for PET and SPECT diagnosis, iii) a NIR dye to develop a new optoacoustic diagnostic protocol (MSOT).

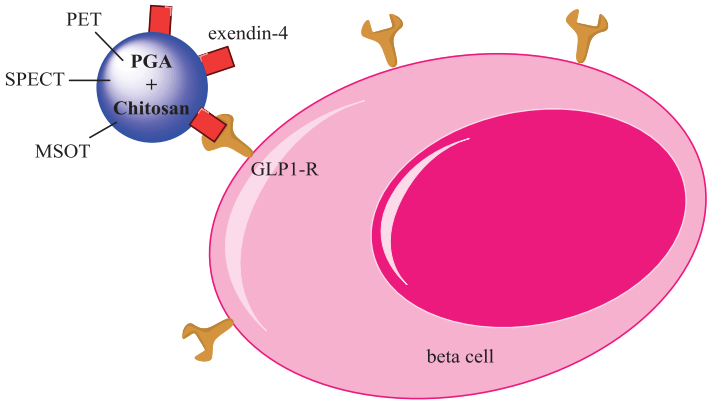


Figure 1: Nanoparticle and its identification on the beta-cell

Both Chitosan and PGA have been functionalised with azido and thiol groups to allow a "click" coupling with Exendin-4 and chelator, whiches in turn have been functionalised with the complementary chemoselective functional groups. The intensity of functionalization has been tuned in order to maintain their capacity to auto-assemble generating the nanoparticles.

Acknowledgments: this project is funded by **H2020-NMBP-15-2017- GA-760986 — iNanoBIT** (1.10.2017-30.9.2022) Integration of Nano- and Biotechnology for beta-cell and islet Transplantation. http://inanobit.eu/about-inanobit/

P22

Chemoselective Palladium-Catalysed Cross-couplings in Deep Eutectic Solvents

F. Messa,[a] M. Capua,[a] S. Perrone,[a] F. Tolomeo,[a] L. Troisi,[a] V. Capriati,[b] A. Salomone[a]

[a] Dipartimento di Scienze e Tecnologie Biologiche e Ambientali, Università del Salento Prov.le Lecce-Monteroni, Lecce, I-73100, Italy. [b] Dipartimento di Farmacia-Scienze del Farmaco, Università degli Studi di Bari "Aldo Moro", Consorzio C.I.N.M.P.I.S., Via E. Orabona 4, Bari, I-70125, Italy

e-mail: *francesco.messa@unisalento.it*

In a modern vision of synthetic chemistry, the design of new chemical processes should be as respectful as possible of the guiding framework outlined by the famous Twelve Principles of Green Chemistry.[1] Metal-catalysed reactions are a cornerstone of modern organic synthesis in the preparation of useful product for our daily life. Palladium-catalysed carbonylation, in particular, are known to convert olefins and halides into precious compounds such as ketones, esters or amides, whereas Sonogashira coupling of terminal acetylenes with aryl halides is an important method of C–C bond formations with several applications in different areas including organic light-emitting diodes (OLEDs), polymer LEDs, and carbohydrate sensing.[2] Deep Eutectic Solvents (DESs) are a promising class of biorenewable solvents, potential substitute of conventional and hazardous volatile organic solvents (VOCs), easily formed by mixing and gently heating naturally occurring hydrogen-bond donors (e.g., urea, renewable polyols, carbohydrates, carboxylic acids, amines, amides) and hydrogen-bond acceptors (e.g., choline chloride (ChCl), phosphonium salts).[4] Building on our recent studies on the development of new sustainable methodologies in unconventional solvents for the obtainment of valuable products,[3] in the present communication we report the first chemoselective palladium-catalysed aminocarbonylation and Sonogashira couplings of aryl iodides in DESs. Notable features of these Pd-catalysed transformations are (a) phosphine-free and mild conditions (60–80 °C) with respect to those usually applied in molecular solvents,[5] (b) absence of VOCs, (c) efficient recycling of both DES and catalyst, and (d) broad substrate scope.

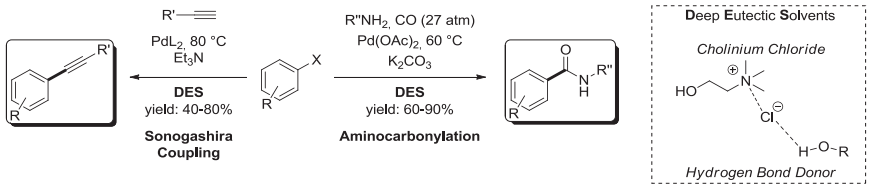


Figure 1.

References:

[1] P. Anastas, N. Eghbali, *Chem. Soc. Rev.* **2010**, *39*, 301. [2] (a) C. H. Lee, T. Yamamoto, *Tetrahedron Lett.* **2001**, *42*, 3993; (b) N. Matsumi, K. Naka, Y. Chujo, *J. Am. Chem. Soc.*, **1998**, *120*, 5112; (c) R. E. Martin, F. Diederich, *Angew. Chem. Int. Ed.* **1999**, *38*, 1350. [3] (a) M. Capua, S. Perrone, F. M. Perna, P. Vitale, L. Troisi, A. Salomone, V. Capriati, *Molecules* **2016**, *21*, 924; (b) S. Perrone, M. Capua, F. Messa, A. Salomone, L. Troisi, *Tetrahedron* **2017**, *73,* 6193; (c) L. Cicco, M. J. Rodríguez-Àlvarez, F. M. Perna, J. García-Àlvarez, V. Capriati, *Green Chem*. **2017**, 19, 306; (d) G. Dilauro, M. Dell'Aera, P. Vitale, V. Capriati, F. M. Perna, *Angew. Chem. Int. Ed.* **2017**, *56*, 10200. [4] (a) E. L. Smith, A. P. Abbott, K. S. Ryder, *Chem. Rev.*, **2014**, *114*, 11060; (b) J. García-Àlvarez, E. Hevia, V. Capriati, *Eur. J. Org. Chem*. **2015**, 6779. [5] (a) C. Yi, R. Hua, *J. Org. Chem.*, **2006**, *71*, 2535–2537; (b) S. T. Gadge, B. M. Bhanage, *RSC Adv*. **2014**, *4*, 10367.

P23

Gold-catalysed intramolecular hydroarylation of heterocyclic 1,3-enynes

S. Nejrotti,[a] S. Ghinato,[a] E. C. Gini,[a] E. G. Occhiato,[b] C. Prandi[a]

[a]*Dipartimento di Chimica, Università degli Studi di Torino, via Pietro Giuria 7, 10125 Torino, Italy*

[b]*Dipartimento di Chimica "Ugo Schiff", Università degli Studi di Firenze, via della Lastruccia 13, 50019 Sesto Fiorentino (FI), Italy*

e-mail*: stefano.nejrotti@unito.it*

Gold catalysis is nowadays a powerful tool for the construction of molecular complexity, due to the ability of gold complexes to activate triple bonds toward the attack of various nucleophilic species, in mild conditions and generally with no need to exclude air and moisture.[1] Within the framework of our interest in the chemistry of lactam- and lactone-derived substituted heterocycles, we recently studied the reactivity of heterocyclic 1,3-enynes in the presence of gold catalysts.[2] Aiming to extend the methodology, we synthesized a class of heterocyclic 1,3-enyne substrates bearing an aryl moiety on the nitrogen ring (Figure 1), and investigated their intramolecular hydroarylation catalysed by gold complexes. The aryl group can act as a nucleophile and attack the triple bond, activated by coordination of the gold catalyst; subsequent aromatization of the intermediate[3] leads to polyaromatic nitrogen heterocycles, with different substituents on the aromatic ring (Figure 1).

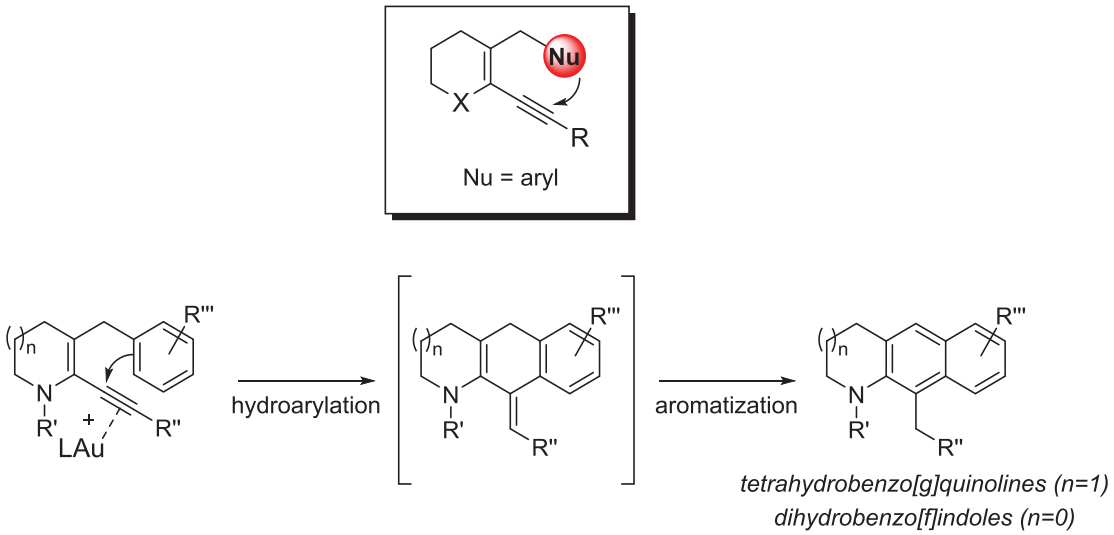


Figure 1: Gold-catalysed hydroarylation of substituted heterocyclic 1,3-enynes.

References:

[1] a) D. Pflästerer, A. S. K. Hashmi, *Chem. Soc. Rev.* **2016**, *45*, 1331-1367; b) R. Dorel, A. M. Echavarren, *Chem. Rev.* **2015**, *115*, 9028-9072.

[2] a) A. Oppedisano, C. Prandi, P. Venturello, A. Deagostino, G. Goti, D. Scarpi, E. G. Occhiato, *J. Org. Chem.* **2013**, *78*, 11007-11016; b) D. Scarpi, S. Begliomini, C. Prandi, A. Oppedisano, A. Deagostino, E. Gómez-Bengoa, B. Fiser, E. G. Occhiato, *Eur. J. Org. Chem.* **2015**, 3251-3265; c) S. Nejrotti, G. Prina Cerai, A. Oppedisano, A. Maranzana, E. G. Occhiato, D. Scarpi, A. Deagostino, C. Prandi, *Eur. J. Org. Chem.* **2017**, 6228-6238.

[3] C. Shu, C.-B. Chen, W.-X. Chen, L.-W. Ye, *Org. Lett.* **2013**, *15*, 5542-5545.

P24

Green synthetic approaches to benzimidazole derivatives.

F. Olivito,[a] M. L. Di Gioia,[b] M. Nardi,[c,d] M. Oliverio,[a] A. Procopio,[a] G. Sindona[c]

[a]*Dip.to di Scienze della Salute, Università Magna Græcia di Catanzaro, Italy*
[b]*Dip.to di Farmacia e Scienze della Salute e della Nutrizione, Università della Calabria, Arcavacata di Rende, CS, Italy.*
[c]*Dip.to di Agraria, Università Telematica San Raffaele, Roma, Italy*
[d]*Dip.to di Chimica e Tecnologie Chimiche, Università della Calabria, Arcavacata di Rende, CS, Italy*
e-mail*: fabrizioolivito@gmail.com*

The procedures for the synthesis of benzimidazoles have become a focus in synthetic organic chemistry, as they are building blocks of strong interest for the development of compounds with pharmacological activity. Various benzimidazole derivatives exhibit important activities such as antimicrobial, antiviral, anticancer, anti-inflammatory and analgesic.[1] Some of the already synthesized compounds from the above mentioned field have found very strong application in medicine praxis.[2]

Most of the procedures for the synthesis of benzimidazole derivatives involve the condensation of *o*-phenylenediamine with aldehydes.[3,4] However, the reaction is not always selective, affording both 2-substituted (a) and 1,2-di- substituted benzimidazoles (b).

We report a simple and sustainable method for the synthesis in green medium of 1,2-di-substituted or 2-substituted benzimidazoles, starting from *o*-phenylenediamine in the presence of different aldehydes. The use of an ionic liquid (IL) or a deep eutectic solvent (DES) enables to prepare selectively 1,2-disubstituted benzimidazoles or 2-substituted benzimidazoles in high yields and short reaction times (Figure 1).

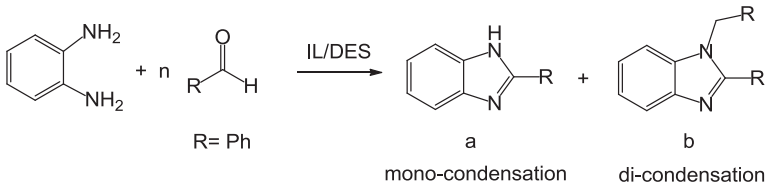


Figure 1: Synthesis of benzimidazole derivatives in green media

References:

[1] M. Amari, M. Fodili, B. Nedjar-kolli, *J. Heterocycl. Chem.* **2002**, *39*, 811-814.

[2] A. T. Mavrova, K. K. Anichina, D. I. Vuchev, J. A. Tsenov, P. S. Denkova, S. K. Magdalena, M. K. Micheva, *Eur. J. Med. Chem.* **2006**, *41*, 1412-1420.

[3] M. Nardi, A. Cozza, L. Maiuolo, M. Oliverio, A. Procopio, *Tetrahedron Lett*. **2011**, *52*, 4827–4834.

[4] N. Herrera Cano, J. G. Uranga, M. Nardi, A. Procopio, D. A. Wunderlin, A. N. Santiago *Beilstein J. Org. Chem.* **2016,** *12,* 2410–2419.

P25

NMR characterization of Bombesin binding to GRP Receptor and synthesis of potential mimetics: a combined approach to target GRP-R expressing tumors

A. Palmioli,[a] C. Ceresa,[b] M. Rocchetti,[a] B. La Ferla,[b] C. Airoldi,[a]

[a]*Dept of Biotechnology and Biosciences, Unimib, P.zza della Scienza 2, Milano, Italy.*
[b]*Dept of Medicine and Surgery, Unimib, Via Cadore, 48, Monza, Italy*
e-mail*: alessandro.palmioli@unimib.it*

Bombesin (BN) is a 14-residue peptide originally isolated from the amphibian Bombina bombina[1]. It belongs to a family of peptides showing a variety of biological activities in numerous tissues and cell types,[2] exerted through their interaction with the Gastrin-Releasing Peptide Receptors (GRPR), transmembrane G-proteins coupled receptors triggering different signaling transduction pathways, resulting, among which, in the stimulation of cell proliferation. GRPRs are significantly involved in the pathogenesis of different human cancers[3], and are recently emerged as tumoral markers in early prostate and breast cancers diagnosis[4]. For these reasons, the research of new GRPR ligands as antagonists or carriers for cytotoxic and imaging molecular tools might be a promising strategy for the treatment and diagnosis of human tumoral malignancies[5]. In this scenario, structural data about BN binding to GRPR are required for the design and synthesis of high affinity receptor ligands, but, unfortunately, they are not yet available. BN conformation has been studied in various solvents demonstrating that it adopts an unordered structure in aqueous media and in dimethyl sulfoxide[6], while a partial helical structure has been observed in aqueous solutions containing TFE[7]. According to proposed models, this is the conformation that, probably, BN presents when anchored to biological membranes.

With the aim to verify this hypothesis, we studied the effect of d_{25}-SDS (a biological membrane mimetic) on BN by CD and NMR spectroscopy. As for BN-GPCR interaction, the heptapeptide BN(8–14) has been shown to be the minimal carboxyl fragment interacting with the receptor, the same experiment were performed also on the BN C-terminal heptapeptide. Moreover, to discover the structural determinants of BN interaction with GRPR, the binding of both BN and BN(8-14) to human prostate carcinoma cell line (PC-3) over-expressing the receptor has been studied thought on-cell STD-NMR experiments.

In addition, we synthesized a library of ligands based on a rigid and spatially defined selected glycidic scaffold, differing for the nature of the potential pharmacophoric moieties. The biological activity of these compounds was preliminary screened by evaluating their ability to modulate the level of cytosolic Ca^{2+} (agonist or antagonist activity) in PC-3 cell.

Authors acknowledge AIRC for funding project 17030 - Targeting of Gastrin-Releasing Peptide receptor expressing tumors: NMR characterization of Bombesin/GRP-R interaction.

References:

[1] A. Anastasi, V. Erspamer and M. Bucci, *Experientia* **1971**, *27*, 166-167.
[2] R. Bruzzone, *European Journal of Biochemistry* **1989**, *179*, 323-331.
[3] I. Ramos-Álvarez, P. Moreno, S. A. Mantey, T. Nakamura, B. Nuche-Berenguer, T. W. Moody, D. H. Coy and R. T. Jensen, *Peptides* **2015**, *72*, 128-144.
[4] R. Mansi, A. Fleischmann, H. R. Macke and J. C. Reubi, *Nat Rev Urol* **2013**, *10*, 235-244.
[5] F. Hohla and A. V. Schally, *Cell Cycle* **2010**, *9*, 1738-1741.
[6] J. A. Carver, *European Journal of Biochemistry* **1987**, *168*, 193-199.
[7] a) J. A. Carver and J. G. Collins, *European Journal of Biochemistry* **1990**, *187*, 645-650; b) M. D. Díaz, M. Fioroni, K. Burger and S. Berger, *Chemistry-A European Journal* **2002**, *8*, 1663-1669.

P26

Glycofunctionalization of Poly(lactic-co-glycolic acid) Polymers: Building Blocks for the Generation of Defined Sugar-Coated Nanoparticles

A. Palmioli,[a] B. La Ferla[a]

[a]*Dept of Biotechnology and Biosciences, Unimib, P.zza della Scienza 2, Milano, Italy.*

Nowadays, surface-functionalized nanoparticles (NPs) are gaining great importance in the biomedical field due to the emerging role of nanomedicine. The presence of a specific molecular entity (ligand) on the NPs' surface can target the nanodevice to specific tissue such as a tumor, overexpressing a specific receptor for the introduced ligand[1]. In this context, sugars have already been extensively used for the functionalization of NPs due to their key role in the molecular interaction process[2]. Among the sugar-decorated NPs, poly(lactic-co-glycolic acid) (PLGA) NPs have already been reported in the literature as tissue-targeting drug-carrier nanodevices.[3] Despite the significant biological outcomes reported with the sugar decorated NPs, the methods described for the sugar linkage to the polymer are varied and not always chemically well-defined and/or characterized. Aiming at the establishment of a possible general, versatile functionalization protocol for sugar functionalized PLGA polymers, we here report the synthesis and characterization of PLGA derivatized with sugars modified at the anomeric position with a 2-(2-aminoethoxy)ethanol linker. We have also conjugated the polymer to a multivalent sugar dendrimer, thus allowing the sugar units to be introduced in a clustered form, which better mimics the multivalent presentation found in Nature. In addition, exploiting an hetero bifunctional amino-methyl aminooxy linker[4], we report a chemoselective method that can be extended to the conjugation of any sugar/oligosaccharide moiety bearing a reducing end[5]. The modified polymers have allowed the preparation of sugar-decorated NPs, important sought tools for nanodevices development. The described method could easily be translated to polymers other than PLGA, rendering the procedure of extended general interest.

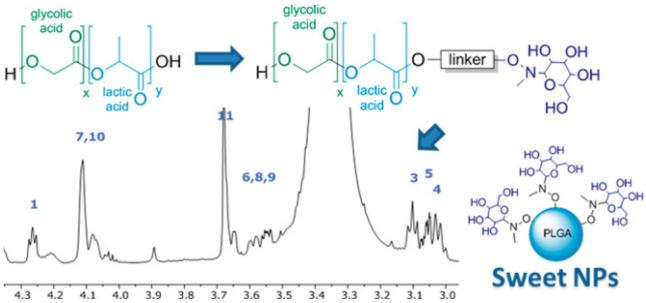


Figure 1.

References

[1] D. Peer, J. M. Karp, S. Hong, O. C. Farokhzad, R. Margalit and R. Langer, *Nature Nanotechnology* **2007**, *2*, 751.

[2] K. Jain, P. Kesharwani, U. Gupta and N. K. Jain, *Biomaterials* **2012**, *33*, 4166-4186.

[3] a) H. Azita, H. Samar, G. Zahra, S. John and L. Afsaneh, *Nanotechnology* **2014**, *25*, 355101; b) Y.-I. Chung, J. C. Kim, Y. H. Kim, G. Tae, S.-Y. Lee, K. Kim and I. C. Kwon, *Journal of Controlled Release* **2010**, *143*, 374-382; c) S. Gupta, A. Agarwal, N. K. Gupta, G. Saraogi, H. Agrawal and G. P. Agrawal, *Drug Development and Industrial Pharmacy* **2013**, *39*, 1866-1873.

[4] A. Palmioli, A. Aliprandi, D. Septiadi, M. Mauro, M. Panigati, A. Bernardi and L. De Cola, *Organic & Biomolecular Chemistry* **2017**, *15*, 1686-1699.

[5] A. Palmioli and B. La Ferla, *Organic Letters* **2018**.

P27

A synthetic approach to the preparation of nitroalkyl vinyl esters

E. Chiurchiù, S. Gabrielli, N. Mariotti, M. Petrini, A. Palmieri

School of Science and Technology, Chemistry Division, Università di Camerino, Italy
e-mail*: marino.petrini@unicam.it*

Vinyl esters are pivotal intermediates in a notable number of synthetic processes involving the utilization of unsaturated systems. The nucleophilic properties of the enolate group can be exploited in aldol-type reactions as well as in cycloaddition reactions. The introduction of a nitro group in allylic position to the vinyl ester greatly expands the synthetic opportunities offered by the utilization of these derivatives. As a matter of fact, the juxtaposition of these two important moieties may open new scenarios in the preparation of densely functionalized molecules combining the chemistry of enolates with that of allylnitro compounds (Figure 1).[1]

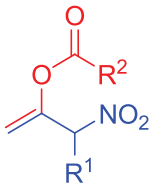


Figure 1: Nitroalkyl vinyl esters as doubly functionalized compounds

Currently, these derivatives are practically unknown and therefore an original procedure for their preparation has been devised.[2] The synthetic approach is based on the preliminary nitroaldol reaction of phenylselenyl acetaldehyde with nitroalkanes followed by a proper esterification of the hydroxy group.[3] The subsequent oxidation of the selenium atom has been revealed particularly troublesome but can be efficiently carried out under flow conditions.[4] The final step entails an elimination reaction which allows the generation of the enol moiety in the nitroalkyl vinyl esters.

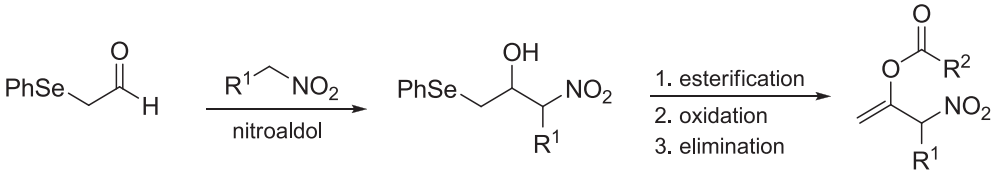


Figure 2: Synthetic strategy for their preparation of nitroalkyl vinyl esters

Application of the prepared nitroalkyl vinyl esters to C-C bond forming processes will be reported.

References:

[1] N. Ono, *The Nitro Group in Organic Synthesis*, Wiley-VCH, New York, **2001**.
[2] R. O. Duthaler, *Helv. Chim. Acta* **1983**, *66*, 1475–1492.
[3] F. A. Luzzio, *Tetrahedron* **2001**, *57*, 915–945.
[4] J. C. Pastre, D. L. Brownw, S. V. Ley, *Chem. Soc. Rev.* **2013**, *42*, 8849–8869.

P28

Direct Enantioselective Vinylogous Mannich-type Reactions of Enals: New Experimental Insights into the *E/Z*-Dilemma

A. Menichetti,[a] F. Berti,[a] M. Vargiu,[a,b] V. Di Bussolo,[b] L. Favero,[a] M. Pineschi[a]*

[a]*Dipartimento di Farmacia, Sede di Chimica Bioorganica e Biofarmacia, Università di Pisa, Via Bonanno 33, 56126 Pisa, Italy*
[b]*Dipartimento di Chimica e Chimica Industriale, Università di Pisa, via G. Moruzzi 3, 56124, Pisa, Italy*
e-mail*: mauro.pineschi@unipi.it*

Remote-stereocontrol is a very challenging goal in asymmetric catalysis. Despite the consolidated use of preformed vinylogous nucleophiles with classical electrophiles such as carbonyl groups and Michael acceptors,[1] there was a considerably less attention in the exploitation of selective γ-reactivity using unmodified carbonyl compounds in combination with alternative electrophiles.[2] Herein we report the development of a direct γ-regioselective heterofunctionalization of α,β-unsaturated aldehydes with N,O-acetals (Figure 1). The use of synergistic cooperative dual catalysis provides the contemporary in situ generation of the reactive species (i.e. cyclic N-acyl quinolinium/dihydroisoquinolinium and chiral dienamine) to give δ-amino-α,β-unsaturated aldehydes.

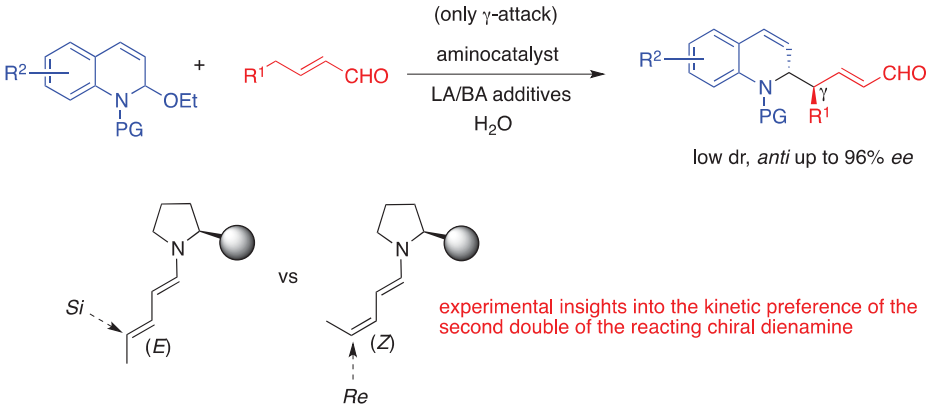


Figure 1: Regio- and stereoselective nucleophilic reactivity of enals with N,O-acetals.

The presence of water was shown to be crucial for having S_N-reactivity of dienamine species with an efficient catalyst turnover. The stereoselective outcomes obtained by us shed some light on the reactive configuration of the second double bond in dienamine catalysis ("*Z/E*-dilemma"),[3] as experimental insights useful for the comprehension of this problem are still very limited.[4]

References:

[1] Casiraghi, G.; Battistini, L.; Curti, C.; Rassu, G.; Zanardi, F. *Chem. Rev.* **2011**, *111*, 3076.
[2] (a) Bergonzini, G.; Vera, S.; Melchiorre, P. *Angew. Chem. Int. Ed*. **2010**, *49*, 9685. (b) Stiller, J.; Marqués-López, E.; Herrera, R. P.; Fröhlich, R.; Strohmann, C.; Christmann, M. *Org. Lett.* **2011**, *13*, 70.
[3] For NMR and computational data about remote stereocontrol in dienamine catalysis, see: Seegerer, A.; Hioe, J.; Hammer, M. M.; Morana, F.; Fuchs, P. J. W.; Gschwind, R. M. *J. Am. Chem. Soc.* **2016**, *138*, 9864.
[4] Manuscript in preparation.

P29

Synthesis and characterization of a paramagnetic [2]-rotaxane based on a crown ether-like wheel incorporating a nitroxide motif

V. Bleve,[a] C. Poderi,[a] P. Franchi,[a] E. Konstanteli,[a,b] L. Gualandi,[a] S. M. Goldup,[c] E. Mezzina,[*a] M. Lucarini[*a]

[a]Department of Chemistry "Giacomo Ciamician", University of Bologna, Via S. Giacomo 11, 40126 Bologna, Italy. [b]National and Kapodistrian University of Athens, Athens, 157 72, Greece .[c]Department of Chemistry, University of Southampton, Southampton, SO17 1BJ-UK
e-mail: *cecilia.poderi2@unibo.it*

In the last decade, different works involving the synthesis of supramolecular systems (rotaxanes) containing persistent nitroxide radicals have been reported.[1] However, in most of these works the interaction between the radical motifs was only used to probe the shuttling process of the macrocycle and it was not employed in the recognition process. Starting from this, we decided to investigate the synthesis of a new crown ether macrocycle containing a dialkyl nitroxide radical and to use it as spin-probe and as recognition site in a [2]-rotaxane system incorporating 4,4'-bipyridinium (BPY^{2+}) and dialkylammonium (NH_2^+) stations (**Figure 1**).[2] The synthesis of the macrocycle was afforded by adapting the original procedure proposed in 1983 by Keana *et al.*[3] to yield the preferred *cis*-stereoisomer of the desired nitroxide crown ether. The paramagnetic rotaxane was then prepared by following the conventional threading-stoppering synthetic pathway and its formation was verified by ESI-MS, UV-visible and EPR spectroscopy. We were able to probe the displacement of the macrocycle between the two recognition sites of the [2]-rotaxane by measuring the nitrogen hyperfine splitting in the EPR spectrum, before and after treatment with a base. In addition, we performed the study of the reduction kinetics comparing the [2]-rotaxane and the macrocycle behaviour by means of EPR spectroscopy. In conclusion, this work represented the first example of a rotaxane system in which the paramagnetic unit on the wheel acts as recognition site during the threading process.[4] The future work will be focused on the design of new mechanically interlocked molecules containing paramagnetic groups, in view of interesting applications in the field of radical molecular machines.

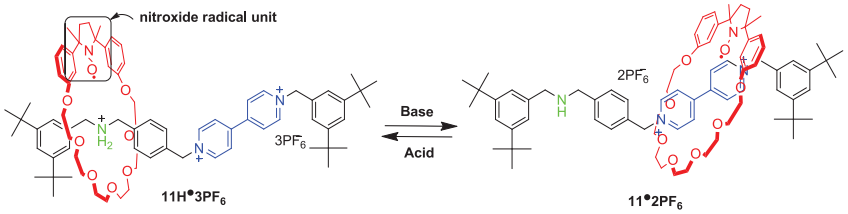


Figure 1: Ring displacement upon treatment with acid/base in the [2]-rotaxane system.

References:

[1] M. Lucarini, E. Mezzina in *Electron Paramagnetic Resonance: (Specialist Periodical Reports)*, *22* (Eds. B. C. Gilbert, V. Chechick, D. M. Murphy), RSC Publishing, Cambridge, **2010**.

[2] P. R. Ashton, R. Ballardini, V. Balzani, I. Baxter, A. Credi, M. Fyfe, M. Gandolfi, M. Gûmez-Lûpez, M. Martinez, A. Piersanti, N. Spencer, J. F. Stoddart, M. Venturi, A. J. P. White, D. J. Williams, *J. Am. Chem. Soc.* **1998**, *120*, 11932-11942.

[3] J. F. W. Keana, J. Cuomo, L. Lex, S. E. Seyedrezai, *J. Org. Chem*. **1983**, *48*, 2647-2654.

[4] V. Bleve, P. Franchi, E. Konstanteli, L. Gualandi, S. M. Goldup, E. Mezzina, M. Lucarini, *Chem. Eur. J.* **2018,** *24,* 1198-1203.

P30

From SnAP-reagents to substituted saturated heterocycles as new potential mPGES-1 inhibitors

M. Potenza, M. G. Chini, G. Lauro, J.W. Bode*, G. Bifulco*

Department of Pharmacy, University of Salerno, Fisciano, Italy
Department of Chemistry and Applied Biosciences, ETH, Zurich, Switzerland
e-mail: mpotenza@unisa.it

Microsomal prostaglandin E_2 synthase-1 (mPGES-1) enzyme has emerged as an attractive target for the discovery and development of new efficient anti-inflammatory and anticancer drugs.[1] This enzyme is responsible of the conversion of COX-derived unstable peroxide prostaglandin H_2 (PGH_2) in prostaglandin E_2 (PGE_2), and it is over expressed in several inflammatory disorders as well as in many human tumors. Thanks to the resolution of human mPGES-1 X-ray structure,[1] and starting from our previous results, we report the structure based drug design of new potential mPGES-1 inhibitors using the SnAP (Tin Amine Protocol) reagents.[2]

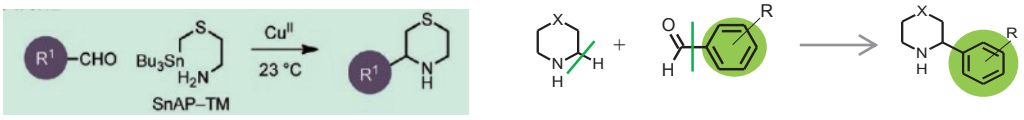


Figure 1: Synthetic strategy and generation of libraries

Starting from the synthons related to the synthetic strategy (Fig. 1), we combined SnAP-reagents with a commercially available library of aldehydes following a multi-step computational protocol: a) generation of libraries using *Combiglide* and *LigPrep*[3-4] b) application of qualitative filters using *QikProp* and *Ligfilter*[4-5] c) *Virtual Screening Workflow* for the docking studies (*Glide software)*.[6-7] The key interactions with the target were accounted for the selection of the most promising substituted saturated heterocycles. The synthesis of the 21 compounds selected from the large libraries is in progress (Fig. 2), with the aim of testing them in a cell-free assay for evaluating their mPGES-1 inhibitory activity.

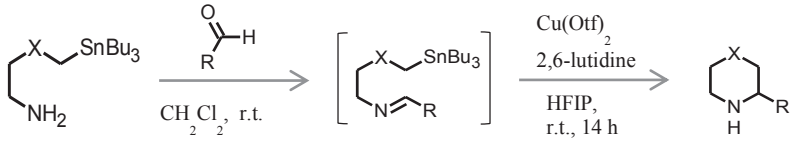


Figure 2: Synthetic conditions

References:

[1] J. G. Luz, S. Antonysamy, S. L. Kuklish, B. Condon, M. R. Lee, D. Allison, X.-P. Yu, S. Chandrasekhar, R. Backer, A. Zhang, M. Russel, S.S. Chang, A. Harvey; A. V. Sloan; M. J. Fisher, *J Med Chem* **2015**, *58*, 4727. [2] C.-V. Vo, G. Mikutis, J. W. Bode; *Angew. Chem. Int. Ed*. **2013**, *52*, 1705. [3] CombiGlide, version 3.8, Schrödinger, LLC, New York, NY, **2015**. [4] Maestro, version 9.6, Schrödinger, LLC, New York, NY, **2015**. [5] QikProp, version 4.6, Schrödinger, LLC, New York, NY, **2015**. [6] Glide, version 6.8, Schrödinger, LLC, New York, NY, **2015**. [7] R. A. Friesner, R. B. Murphy, M. P. Repasky, L. L. Frye, J. R. Greenwood, T. A. Halgren, P. C. Sanschagrin, D. T. Mainz, *J Med Chem* **2006**, *49*, 6177.

P31

Exploration of the aryl bromide scaffold for the development of new potential anti-inflammatory and anti-cancer agents blocking mPGES-1 enzyme

D. Ruggiero,[a] S. Terracciano,[a] A. Russo,[a] S. Di Micco,[a] R. Riccio,[a] G. Bifulco,[a] I. Bruno[a]

[a]*Department of Pharmacy, University of Salerno, Via Giovanni Paolo II 132, 84084 Fisciano, Italy*

e-mail*: druggiero@unisa.it*

Arachidonic acid (AA) is the substrate of numerous enzymes involved in inflammatory processes. Among these enzymes we have to mention the cyclooxygenases, the constitutively expressed form COX-1, and the inducible form COX-2, which transform AA into prostaglandin PGH2. PGH2 appears to be a key intermediate in the inflammatory process since it is subsequently converted into a series of mediators, such as PGE2 which possesses pleiotropic functions. PGE2 showed to be upregulated in inflammation and overexpressed in tumors. Three synthases govern the biosynthesis of PGE2: cPGES, a cytosolic synthase isoform, and mPGES-1 and 2, two membrane-associated enzymes. cPGES and mPGES-2 are constitutively expressed whereas mPGES-1 is an inducible isoform [1]. Our attention has been focused on microsomal prostaglandin E synthase-1 (mPGES-1) since it is able to selectively control PGE2 levels induced by inflammatory stimuli, without affecting the constitutively produced PGE2 levels. Its modulation, therefore, may represent a better strategy to control the disorders related to PGE2, compared to the use of classic anti-inflammatory drugs characterized by several side effects. The mPGES-1 inhibitors represent promising candidates for the development of new drugs; however, despite the efforts made in this research area, none of the disclosed molecules, with the exception of LY3023705 which has recently entered clinical trials, is available for clinical use. As a consequence, the discovery of new mPGES-1 inhibitors with better pharmacological properties represents an urgent need [2]. Starting from an aryl bromide scaffold, we decided to create a new collection of potential mPGES-1 modulators guided by a computer aided approach. These inhibitors are characterized by the presence of some recurrent chemical features found in several known potent mPGES-1 inhibitors and can be realized through rapid and versatile chemical reactions. The synthesis was achieved via a Pd-catalyzed Suzuki-Miyaura cross-coupling reaction between the aryl bromide and the appropriately substituted and commercially available arylboronic acids. The Suzuki Miyaura reaction was chosen because it represents an efficient and versatile method for highly functionalized biaryls synthesis, in good yields under mild conditions [3].

References:

[1] M. Nakanishi, V. Gokhale, E. J. Meuillet, and D.W. Rosenberg, *Biochimie*, **2010,** *92*, 660–664.

[2] S. Di Micco, S. Terracciano, V. Cantone, K. Fischer, A. Koeberle, A. Foglia, R. Riccio, O. Werz, I. Bruno, G. Bifulco, *Eur. J. Med. Chem.*, **2018**, *143*, 1419-1427.

[3] G. Lauro, M. Strocchia, S. Terracciano, I. Bruno, K. Fischer, C. Pergola, O. Werz, R. Riccio, G. Bifulco, *Eur. J. Med. Chem*., **2014**, *80*, 407-415.

P32

Synthesis of 3D-printable Extracellular Matrix Mimetics

V. Bellotti,[a] M. Collarile,[a] J. Andrieu,[a] F. Nicotra,[a] L. Russo[a]

[a]*Università degli Studi di Milano-Bicocca, Dipartimento di Biotecnologie e Bioscienze, Piazza della Scienza 2, Milano, Italy*
e-mail*: laura.russo@unimib.it*

The native Extracellular Matrix (ECM) is a dynamic and hierarchically organized microenvironment secreted by cells in the space between them, with a crucial role in both normal and disease processes. This intricate network is characterized by a wide variety of polysaccharides, proteins and glycidic-based motifs that goes from glycosaminoglycans (GAGs) and proteoglycans (PGs) to glycoproteins and glycolipids. This milieu is dynamically degraded and remodelled by cells during their biological functions. The ECM has multiple roles: it provides the physical support holding cells and tissues together and coordinates their functions by activating intramolecular signalling pathway that control differentiation, cells growth and gene expression.

In the last decades, the development of regenerative medicine was in charge of the design of biomaterials because of their capability to mimic the complex ECM microenvironment and their utility in different field, such as drug screening, cell biology studies and tissue engineering. Herein the attention is focused on tissue engineering and for this aim the hydrogels, cross-linked 3D networks containing hydrophilic polymer chains able to adsorb a significant amount of water, have been employed. High versatility of chemical, mechanical and physical properties makes hydrogels suitable to mimics several roles of natural ECM.

The abilities of hydrogels to regulate essential cellular functions (i.e. adhesion, proliferation, differentiation) have been obtained and controlled by a spatial functionalization of these biomaterials that allow to induce desired stimuli. Different biomolecules have been functionalized through chemoselective reactions that enable the formation of cross-linked 3D network, obtaining different kind of hydrogels.

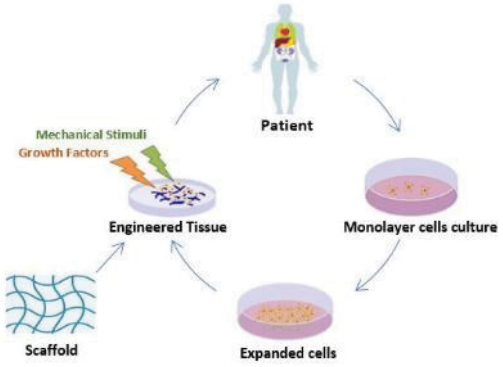


Figure 1.

Acknowledgments: This research is funded by the EC, H2020-MSCA-ITN-2014-GA-642028, Design and development of advanced NAnomedicines to overcome Biological BArriers and to treat severe diseases (NABBA).

P33

Liposome functionalisation with phage displayed brain targeting peptides

J. Andrieu,[a] F. Barbugian,[a] F. Nicotra,[a] M. Masserini,[b] F. Re,[b] L. Russo[a]

[a]*University of Milano-Bicocca, Department of Biotechnology and Biosciences, Piazza della Scienza 2, 20126, Milan*

[b]*University of Milano-Bicocca, Department of Medicine and Surgery, Via Alfred Nobel, Vedano al Lambro MB*

e-mail*: laura.russo@unimib.it*

Phage display is a powerful approach to identify targeting peptides that can be used to functionalise nanoparticles in order to improve the efficiency of drug delivery by targeting specific tissues, biological barriers, cells or molecules. In this work, two novel peptides with probable brain targeting capabilities, that favour crossing the blood-brain barrier, were identified by in-vivo phage display. Four rounds were carried out in three parallel experiments in female CD-1 mice, using a commercial M13 12-mer library. Phage recovered from the last round was amplified, random individual clones were sequenced and peptides DYHDPSLPTLRK (P1) and QVNGLGERSQQM (P2) were identified as adequate targeting candidates. The phage pool bearing P1 was amplified further and panned in-vitro against hCMEC/D3 human brain endothelial cells, as well as HUVEC (human umbilical endothelial cells) and A549 (human lung cancer cells) as negative controls. Interestingly, P1 and P2 were recovered exclusively from hCMEC/D3 lysates, even though the collagen coating required to culture this cell line did not allow an accurate quantification of phage binding, due to non-specific interactions with the phage. These peptides, never identified before as targeting agents, were used to functionalise PEGylated liposomes by a thiol-maleimide coupling reaction. To that end, a cysteine was added to the N-terminus in both cases. Besides, the C-terminal lysine in P1 and an additional lysine in P2 were used to attach a green fluorophore (FITC), to be able to carry out in-vitro imaging experiments.

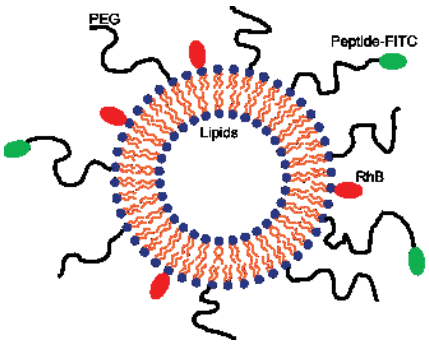


Figure 1: Liposomes functionalized with phage displayed targeted peptide.

Acknowledgments: This research is funded by the EC, H2020-MSCA-ITN-2014-GA-642028, Design and development of advanced NAnomedicines to overcome Biological BArriers and to treat severe diseases (NABBA).

P34

Calixarene-based inhibitors for carbonic anhydrases

F. Sansone,[a] D. Sbravati,[a] S. Bua,[b] M. Bianchi,[a] F. Carta,[b] A. Casnati,[a] C. T. Supuran[b]

[a] *Department of Chemistry, Life Sciences and Environmental Sustainability, Università di Parma, Parco Area delle Scienze 17/a, 43124, Parma, Italy*
[b] *Neurofarba Department, Università di Firenze, Via Ugo Schiff 6, Polo Scientifico, 50019 Sesto Fiorentino (Firenze) Italy*
e-mail*: francesco.sansone@unipr.it*

Calixarenes are synthetic macrocyclic compounds very popular in supramolecular chemistry as receptors. In the last two decades, they have been widely employed in the targeting of bio-macromolecules such as nucleic acids, enzymes, proteins.[1] Calixarenes can be functionalized in several ways to expose active units, for instance pharmacophores, in multiple copies and different orientations in space. This feature allows to exploit the so called "multivalency effect" that can result in a complexation activity towards the biological target significantly more efficient with respect to analogous monomeric ligands. Usually, multivalent ligands as those based on calixarene scaffolds show the beneficial effects of multivalency in the binding to macromolecules presenting multiple copies of equivalent recognition sites.[2] However, recently some attempts have been done to verify this effect in the inhibition of enzymes and interesting results have been obtained.[3]

In this context, we have prepared a small library of potential inhibitors for Carbonic Anhydrases (CAs) based on calixarenes exposing multiple copies of benzenesulfonamide (Figure 1) or ammonium ion. CAs are considered an important target for the treatment of some tumours and infections. Efficiency and selectivity are addressed in the development of potential inhibitors of these enzymes. The compounds we synthesized have been tested towards six different CA isoforms[4] (hCAI, hCAII, hCAIX, VchCAβ, Can2, MgCA) and compared with two monomeric analogues and acetazolamide, a commercial drug used in therapy against glaucoma. Some derivatives have shown Ki values in the μM-nM range. Synthesis of the ligands and results of the inhibition studies will be reported.

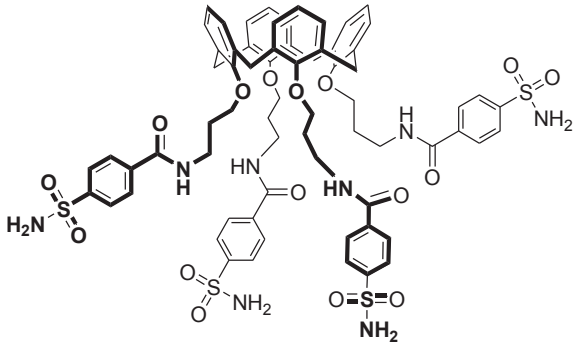


Figure 1: an example of calixarene functionalized with sulphonamide units.

References:

[1] M. Giuliani, I. Morbioli, F. Sansone, A. Casnati, *Chem. Commun.* **2015**, *51*, 14140-14159.
[2] F. Sansone, A. Casnati, *Chem. Soc. Rev.* **2013**, *42*, 4623-4639.
[3] N. Kanfar, E. Bartolami, R. Zelli, A. Marra, J.-Y. Winum, S. Ulrich, P. Dumy, *Org. Biomol. Chem*. **2015**, *13*, 9894–9906.
[4] V. Alterio, A. Di Fiore, K. D'Ambrosio, C. T. Supuran, G. De Simone, *Chem. Rev.* **2012**, *112*, 4421-4468.

P35

Synthesis of a novel TetraPyrazinoPorphirazine

L. Scapinello,[a*] A. Penoni,[a] L. Vaghi,[b] G. Palmisano[a]

[a]*Dipartimento di Scienza e Alta Tecnologia, Università degli Studi dell'Insubria, via Valleggio 9, 22100, Como – Italy*
[b]*Dipartimento di Scienza dei Materiali, Università degli Studi di Milano-Bicocca, Via Cozzi 55, 20125, Milano – Italy*
e-mail*: l.scapinello@uninsubria.it*

In the family of highly conjugated macrocyclic compounds, TetraPyrazinoPorphyrazines (TPyzPzs) are molecules particularly studied[1]: many examples of TPyzPzs and their metal complexes were illustrated as electronic devices, organic transitors, pigments, liquid-crystaline films and singlet oxygen photoactivators[2].

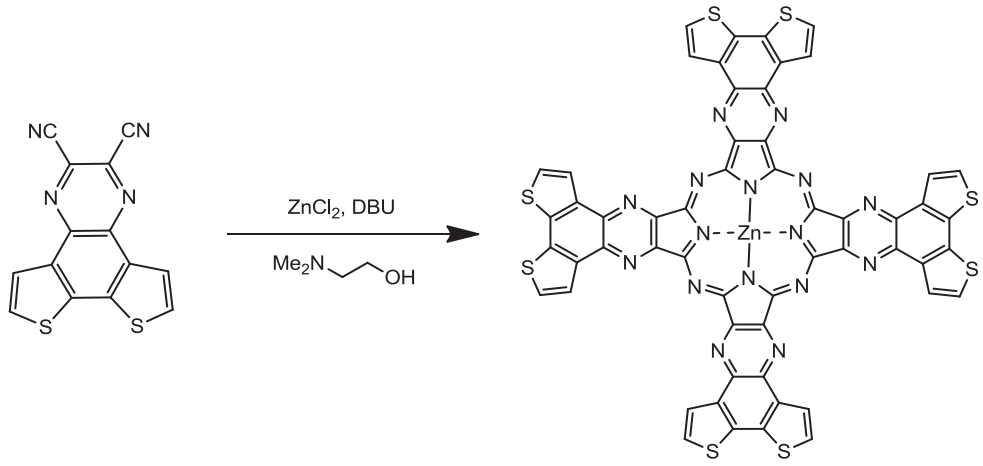


Figure 1: macrocyclization reaction.

Usually metal-complexes can be directly synthesized by the reaction of dinitrile precursors at high temperature in the presence of metal salts. We started with this research following our previous interest in TPyzPzs[3], putting our efforts to synthetize a new compound with a benzoditiophene moiety in order to test soon its possible applications in material science field.

References:

[1] M. P. Donzello, C. Ercolani, V. Novakova, P. Zimcik, P. A. Stuzhin, *Coord. Chem. Rev.* **2016**, *309*, 107-179.

[2] A. A. Trabanco, A. G. Montalban, G. Rumbles, A. G. M. Barrett, B. M. Hoffman, *Synlett*, **2000**, *7*, 1010-1012.

[3] M. Parravicini, L. Vaghi, G. Cravotto, N. Masciocchi, A. Maspero, G. Palmisano, A. Penoni, *ARKIVOC* **2014**, *vi*, 72-85.

P36

Highly diastereoselective Michael addition of non-activated phthalides under phase transfer catalysis conditions

M. Sicignano,[a] F. De Riccardis,[a] I. Izzo,[a] G. Della Sala[a]

[a] *Dipartimento di Chimica e Biologia "A. Zambelli", Università degli Studi di Salerno, Via Giovanni Paolo II 132, 84084 Fisciano (SA) Italy*
e-mail*: msicignano@unisa.it*

Functionalized phthalides are structural motifs widely distributed in natural and therapeutically useful agents. They exhibit a broad range of biological activities and also act as versatile building blocks in organic synthesis.[1] Due to their intriguing chemical properties, 3-substituted phthalides are very attractive scaffolds, and a number of catalytic methods have been developed for their synthesis. Most of the stereoselective approaches to 3-substituted phthalides involve the stereocontrolled construction of the lactone ring, while methods based on stereoselective insertion of alkyl groups at C-3 of an unsubstituted phthalide are much less investigated.[2] The arylogous Michael reaction (AMR) with electron-poor alkenes represents an expedient way to insert alkyl group at the weakly acid C-3 position. Methods described to date use strong bases (LDA or metal alkoxides), yielding Michael adduct with no stereoselectivity.[3,4]

In this communication we report the first highly diastereoselective Michael addition of unactivated phthalides with both aliphatic and aromatic α,β-unsaturated ketones under phase transfer catalysis conditions. Achiral and inexpensive crown ethers efficiently promoted the AMR in the presence of BSA (*N*,*O*-bis(trimethylsilyl)-acetamide) as silylating agent. In most cases, s*yn*-diastereoselectivity higher than 20:1 has been achieved.

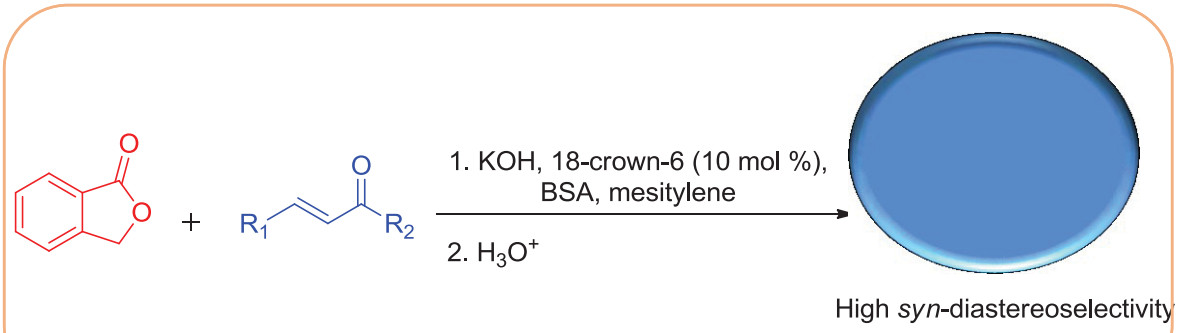


Figure 1

References:

[1] G. Lin, S. S.-K. Chan, H.-S. Chung, S. L. Li, *Stud. Nat. Prod. Chem.* **2005**, *32*, 611 – 669.
[2] R. Karmakar, P. Pahari, D. Mal, *Chem. Rev.* **2014**, *114,* 6213 - 6284.
[3] W. K. Janowski, R. H. Prager, *Aust. J. Chem.* **1985**, *38*, 921 - 929.
[4] N. J. P. Broom, P. G. Sammes, *Chem. Soc., Perkin Trans. 1*, **1981**, 465 – 670.

P37

Synthesis of graphene oxide quantum dots as drug delivery sistems

A. Ventrella,[a] A. Di Crescenzo,[a] A. Fontana[a]
[a]*Department of Pharmacy, "G. D'Annunzio" University, Chieti, Italy.*
e-mail*: alessia.ventrella@unich.it*

Quantum dots are tiny particles or nanocrystals of a semiconducting material with diameters in the range of 2-10 nanometers (10-50 atoms). They were first discovered in 1980[1]. Quantum dots display unique electronic properties, intermediate between those of bulk semiconductors and discrete molecules, that are partly the result of the unusually high surface-to-volume ratios for these particles.[2-3]In this work the graphene oxide (GO) was used as starting material to produce graphene quantum dots (GQDs). The chemical synthesis consists in an acidic oxidation of GO, to obtain these nanoparticles, that were purified from secondary products using a dialysis membrane.[4]

These nanoparticles were characterized through dimensional analysis, and fluorescence measurements. The samples were also analyzed with Atomic Force Microscope (AFM), that outlines the three-dimensional profile of their surface. The objective of the work is the use of these nanoparticles in theranostic applications as drug delivery systems. Indeed we exploit their photoluminescence emissions,[5]the functionalities present on GOD and the consequent possibility to bind them with proper targetting agent as well as the possibility to load the obtained carrier with doxorubicin via π- π stacking interactions.

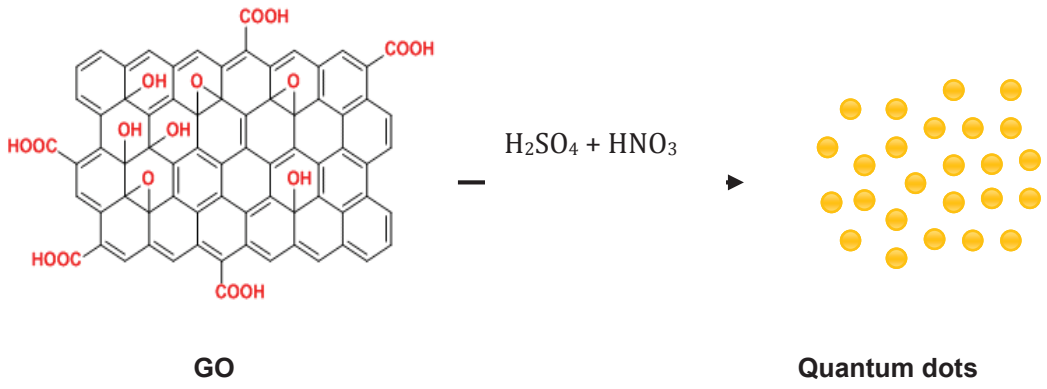


Figure 1: Schematic representation of graphene oxide quantum dots synthesis.

References:

[1] A. I. Ekimov, A. A.Onushchenko, *JETP Lett.* **1981**, *34*, 345–349.
[2] M. A. Kastner, *Phys. Today* **1993**, *46*, 24.
[3] R. C. Ashoori, *Nature* **1996**, *379*, 413-419.
[4] D. Tang, J. Liu, X.Yan, L. Kang, *RSC Adv.* **2016**, *6*, 50609-50617.
[5] D. Wang, J.-F. Chen, L. Dai, Part. Part. *Syst. Charact.* **2015**, *32*, 515–523.

P38

Stereoselective Organocatalytic Approach to 1,5-Benzothiazepines

C. Volpe, I. Quaratesi, S. Meninno, A. Lattanzi

Dipartimento di Chimica e Biologia, Università di Salerno, Via Giovanni Paolo II, Fisciano, Italy
e-mail: *cvolpe@unisa.it*

Organocatalytic domino reactions are appealing synthetic tools both in academia and in industry.[1] Chiral organic molecules, the organocatalysts, are able to catalyse two or more successive chemical transformations in one reactor with high stereocontrol. The importance of these methodologies is evident when applied to the synthesis of relevant bioactive heterocyclic compounds and pharmaceuticals.[2] In this contribution, we illustrate convenient and effective catalytic methodologies, to produce highly enantioenriched popular drugs, i.e. *N*-unprotected 1,5-benzothiazepines, bearing one, or two stereogenic centers, by using only 1-5 mol% loading of chiral squaramides or thioureas, readily obtained from the chiral pool. The products are obtained in good to high yield and enantioselectivity. Both *cis*- and *trans*-diastereoisomers of *N*-unprotected 1,5-benzothiazepines can also be obtained with very good level of asymmetric induction.[3b]

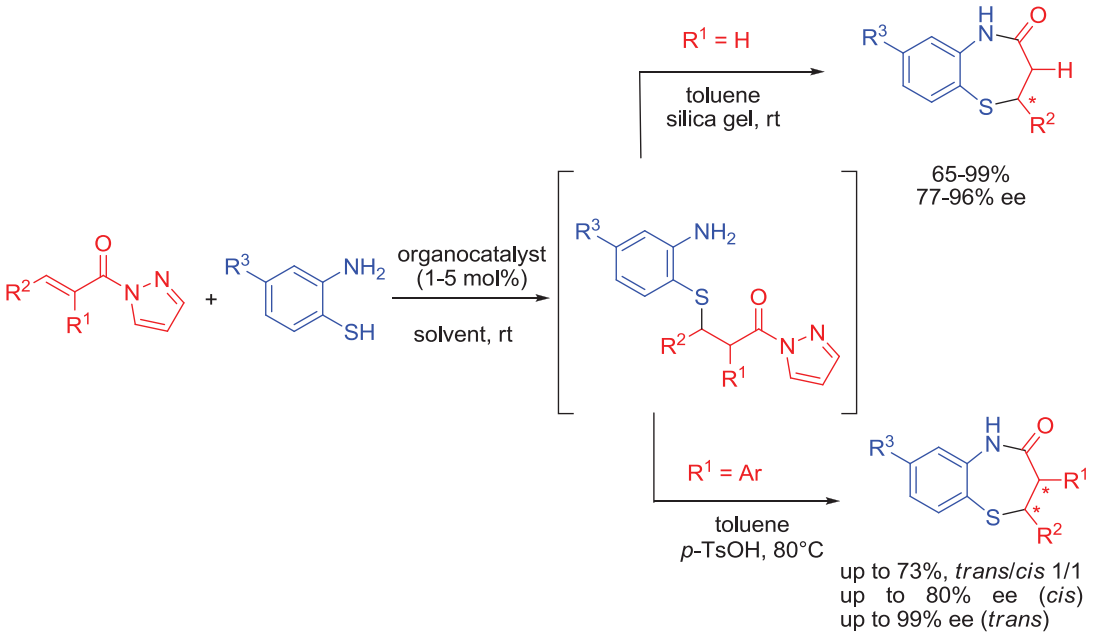


Figure 1: Stereoselective synthesis of *N*-unprotected 1,5-benzothiazepines

References:

[1] a) C. Grondal, M. Jeanty, D. Enders, *Nat. Chem*. **2010**, *2*, 167 - 178. b) C. M. R. Volla, I. Atodiresei, M. Rueping, *Chem. Rev.* **2014**, *114*, 2390 - 2431. c) L. F. Tietze, *Domino Reactions: Concepts for Efficient Organic Synthesis*, Wiley-VCH, **2014**.

[2] a) C. Vaxelaire, P. Winter, M. Christmann, *Angew. Chem. Int. Ed.* **2011**, *50*, 3605 - 3607. b) A. Moyano, R. Rios, *Chem. Rev.* **2011**, *111*, 4703 - 4832.

[3] a) S. Meninno, C. Volpe, A. Lattanzi, *Chem. Eur. J.* **2017**, *23*, 4547 - 4550; b) Unpublished results.

P39

Stereoselective Synthesis of Bicyclic Pyrazolidinones

C. Volpe, S. Meninno, A. Lattanzi

Dipartimento di Chimica e Biologia, Università di Salerno, Via Giovanni Paolo II, Fisciano, Italy
e-mail*: cvolpe@unisa.it*

The pyrazolidinone structural motif is a skeleton present in molecules with a wide range of biological and farmaceutical properties[1] and only recently a few stereoselective metodologies were reported for their synthesis.[2] Here, we illustrate a convenient methodology to obtain bicyclic pyrazolidinones via an organocatalytic [3+2]-cycloaddition reaction working under mild conditions and using readily available reagents. The bicyclic pyrazolidinones, bearing two stereogenic centers, are obtained in good yield and high *trans*-diastereoselectivity. Efforts are also devoted to develop a diastereo- and enantioselective approach to this class of important heterocycles employing bifunctional organocatalysts.

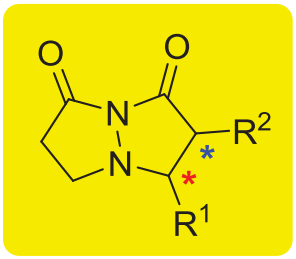


Figure 1: Bicyclic pyrazolidinones

References:

[1] a) S. Hanessian, G. McNaughton-Smith, H.-G. Lombart, W. D. Lubell, *Tetrahedron* **1997**, *53*, 12789−12854. b) E. M. Kosower, A. E. Radkowsky, A. H. Fairlamb, S. L. Croft, R. A. Neal, *Eur. J. Med. Chem*. **1995**, *30*, 659−671. c) E. M. Kosower, E. Hershkowitz, *Isr. Patent*, ISXXAQ IL 94658 [Chem. Abstr. 1994, 122, 214077].

[2] a) S. E. Winterton, J. M. Ready, *Org. Lett.* **2016**, *18*, 2608-2611. (b) M. Mondal, K. A. Wheeler, N. J. Kerrigan *Org. Lett.* **2016**, *18*, 4108-411.

P40

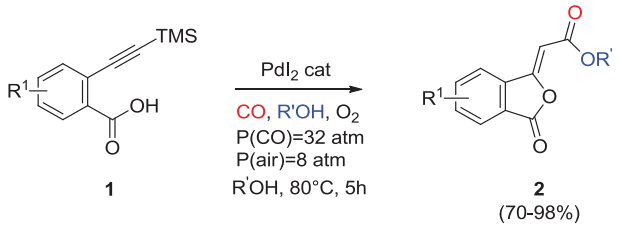
Synthesis of (*Z*)-3-[(Alkoxycarbonyl)methylene]isobenzofuranone Derivatives by Palladium-Catalyzed Carbonylation of 2-Alkynylbenzoic Acids

I. Ziccarelli,[a] R. Mancuso,[a] B. Gabriele[a]

Laboratory of Industrial and Synthetic Organic Chemistry (LISOC)
Department of Chemistry and Chemical Technology, University of Calabria
Via Pietro Bucci, 12/C, 87036 Arcavacata di Rende (CS), Italy
e-mail*: idaziccarelli@gmail.com*

PdI_2-catalyzed oxidative carbonylation of acetylenic substrates bearing a suitably placed nucleophilic group is a powerful methodology for the direct synthesis of carbonylated heterocycles.[1]

We report here a novel method for the synthesis of functionalized (*Z*)-3-[(alkoxycarbonyl)methylene]isobenzofuranone derivatives **2** based on PdI_2-catalyzed oxidative heterocyclization-carbonylation of 2-alkynylbenzoic acids **1** (*Scheme 1*).



Scheme 1

In the presence of catalytic amount of PdI_2 (2 mol%) in conjuction with KI (20 mol%) and under relatively mild reaction conditions (80 °C under 40 atm of a 4:1 mixture of CO-air) different 2-[(trimethylsilyl)ethynyl]benzoic acids **1** were converted into the corresponding (*Z*)-3-[(alkoxycarbonyl)methylene]isobenzofuranones **2** through and ordered sequence of steps, involving in situ deprotection followed by *syn* 5-*exo*-dig cyclization, carbon monoxide insertion, and nucleophilic displacement by an alcohol.

The reaction is regio- and stereoselective and leads to the desired products in high to excellent yields (70-98%); the structure of some representative products were confirmed by XRD analysis.

The heterocyclic derivatives synthesized in this work belong to particularly important classes of heterocycles, known to possess a wide range of biological activities.

References:

[1] (a) X.-F. Wu, H. Neumann, M. Beller, *Chem Rev.* **2013**, *113*, 13–5. (b) B. Gabriele, R. Mancuso, G. Salerno, *Eur. J. Org. Chem.* **2012**, 6825–6839.

Comunicazioni POSTER

Sessione
Università di Milano Bicocca

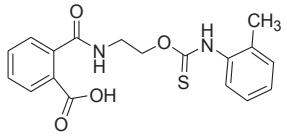
P41

Characterization of water soluble dendrimer formulations of an insoluble thiocarbamate derivative with moderate anti HIV-1 activity: an overview

S. Alfei,[a] A. Spallarossa,[a] S. Catena

Dipartimento di Farmacia, Università di Genova, Viale Cembrano 4, I-16148 Genova, Italy
e-mail: alfei@difar.unige.it

Drug delivery is an engineered technology focused on the development of Drug Delivery Systems (DDSs) able to transport, release and maintain for long time the useful load of therapeutics in the body as needed for safe playing out the desired therapeutic effects. Nanosized dendritic polycationic polymers such as commercially available PAMAMs, are the most exploited materials for preparing smart DDSs, but unfortunately, the excessive cationic feature of the inner framework results in a high level of cytotoxicity. Nowadays, not charged amino acid-modified dendrimer scaffolds are considered as better solutions. These dendrimers have a more controlled number of nitrogen atoms and can be protonated at physiological pH. In order to improve the water solubility of the thiocarbamate non-nucleoside HIV-1 reverse transcriptase inhibitor **1** (Figure 1)[1] five prodrugs were prepared by its entrapment inside not PAMAM amino acids-modified *core-shell* hydrophilic[2] (Figure 2) and amphiphilic[3] (Figure 3) dendrimers. As detailed in this communication an overview, organized in tables, graphs and NMR spectra of the physicochemical properties which identified obtained dendriplexes (DPXs) was provided.



***N*-(2-*o*-Tolylthiocarbamoyloxy-ethyl)-phthalamic acid (1)**

Figure 1: O-TC derivative **1**.

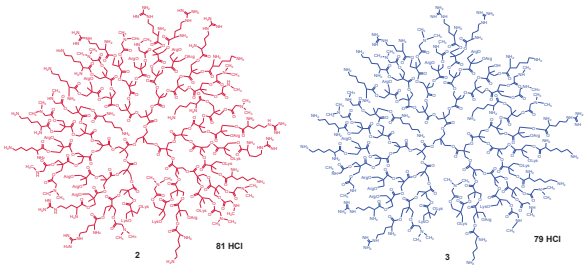


Figure 2: Hydrophilic dendrimers **2**,**3**.

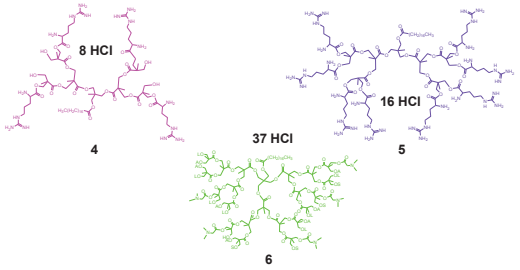


Figure 3: Amphiphilic dendrimers **4-6**.

As estimated by NMR analysis, DPXs showed good load capacity. Mean size of their particles is suitable for avoiding rapid renal clearance while the release profile of the drug is favourable to a low spreading of drug in blood and to a massive release only within the cell. DPXs are soluble in water, EtOH and MeOH, have proper but not excessive cationic character and an optimal buffer capacity for enhanced cellular up take and pH-responsive endosomal escape once inside the cell.

References:

[1] A. Spallarossa, A. Ranise, et al., *Eur. J. Med. Chem.* **2009**, *44*, 1650-1663.
[2] S. Alfei, S. Catena, **2018**, submitted to *Polym. Advan. Technol.* on April 13th and under review.
[3] S. Alfei, S. Catena, **2018**, submitted to *Polym. Int.* on April 9th and under review.

P42

Hydrophilic and amphiphilic water-soluble dendrimer formulations of a not-soluble thiocarbamate derivative with moderate anti HIV activity for biomedical applications

S. Alfei,[a] A. Spallarossa,[a] S. Catena[a]

Dipartimento di Farmacia, Università di Genova, Viale Cembrano 4, I-16148 Genova, Italy
e-mail: alfei@difar.unige.it

The engineered technology known as *Drug delivery* concerns the approaches, formulations, technologies and systems for transporting therapeutics in the body and delivering them as needed. Advanced controlled Drug Delivery Systems (DDSs) able to release an effective load of drug and to maintain its concentration for long time in a limited area around the target site have been developed. These "smart" DDSs allowed to reduce dosages, administrations frequency and drugs toxicity and to improve therapeutic efficacy. Nanosized and dendritic polycationic polymers such as PAMAMs are the most exploited materials for getting advanced smart DDSs and can covalently bind or encapsulate drugs. However, the high number of protonable nitrogen atoms widespread on the whole matrix involves high cytotoxicity. The modern research is increasingly oriented towards the use of not charged dendrimer scaffolds decorated with biocompatible amino acids protonable at physiological pH. Thiocarbamate **1** (Figure 1) is a non-nucleoside HIV-1 reverse transcriptase inhibitor (EC_{50} = 27 μM) characterized by a free carboxylic group and endowed with poor water solubility.[1] With the aim at improving both its solubility and activity, derivative **1** was physically incorporated inside not-toxic amino acid-modified *core-shell* hydrophilic (**2**,**3**)[2] and amphiphilic (**4-6**)[3] dendrimers. The encapsulation procedure is a straightforward protocol that involves stirring derivative **1** and the starting dendrimer at r.t. in methanol (Figure 1).

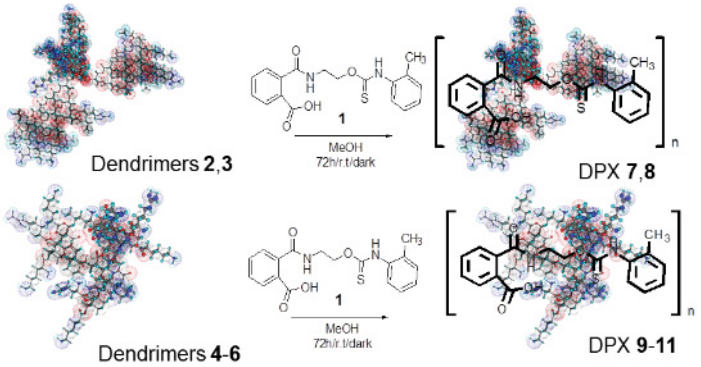


Figure 1: Encapsulation reactions of **1** into dendrimers **2-6**.

The obtained dendriplexes (DPXs **7-11**) showed a very good DL%, a proper particle size, an adequate buffer capacity and above all were well soluble in water. Therefore, they represent an appealing and promising crew of new smart DDSs for safe *in vivo* clinical administrations of **1**.

References:

[1] A. Spallarossa, A. Ranise, et al., *Eur. J. Med. Chem.* **2009**, *44*, 1650-1663.
[2] S. Alfei, S. Catena, **2018**, submitted to *Polym. Advan. Technol.* on April 13th and under review.
[3] S. Alfei, S. Catena, **2018**, submitted to *Polym. Int.* on April 9th and under review.

P43

Structural properties and mechanism of formation of mussel-inspired polydopamine thin films

M.L. Alfieri,[a] L. Panzella,[a] O. Crescenzi,[a] S.L. Oscurato,[b] P. Maddalena,[b] A. Napolitano,[a] M. d'Ischia[a]

[a]*Department of Chemical Sciences, University of Naples Federico II, I-80126, Naples*
[b]*Department of Physics "Ettore Pancini", University of Naples Federico II, I-80126, Naples*
e-mail*: marialaura.alfieri@unina.it*

Inspired by the robust adhesion properties of catechol- and amine-rich mussel adhesive proteins, polydopamine (PDA), a black insoluble and structurally disordered eumelanin-like material produced by the oxidative polymerization of dopamine under alkaline conditions, stands todate as the state-of-the-art for surface functionalization and coating and for various nanotechnological and biomedical applications.[1] PDA thin films can be deposited by simple dipping of substrates of different materials, including metals, oxides, inorganic semiconductors, ceramics, and polymers in an aqueous solution of dopamine, buffered to an alkaline pH (Figure), can bind cells, biomolecules, metal ions, and can be used to control or modify the hydrophobicity of a variety of interfaces. Because of its robustness, universal adhesion properties and biocompatibility, definition of PDA structure−property−function relationships is a major goal for optimizing its performances for tailored applications. Until 2012 two different speculative structural models were commonly assumed: the "open-chain polycatechol/quinone" model, based on linear sequences of catecholamine units linked through biphenyl-type bonds, and the "eumelanin" model, which envisaged a 5,6-dihydroxyindole (DHI) polymer arising by cyclization of dopaminequinone (Figure).[2] In the light of previous literature reports in this work the structural features accounting for the polydopamine film forming properties were investigated in comparison with model polymers from 5,6-dihydroxyindole and its 2,7'-dimer to assess the role of the units derived from DHI in the adhesion properties of PDA. MALDI-MS data showed that PDA is structurally different from DHI melanin and does not contain species compatible with DHI-based oligomers as primary building blocks. It is concluded that PDA film deposition involves structural components unrelated to DHI-based oligomers, which, on mechanism-based analysis, may arise by quinone−amine conjugation leading to polycyclic systems with extensive chain breakdown.[3] Other information on the structural features of PDA and the film forming mechanisms were obtained by EPR, solid state ^{13}C NMR analysis and model studies.

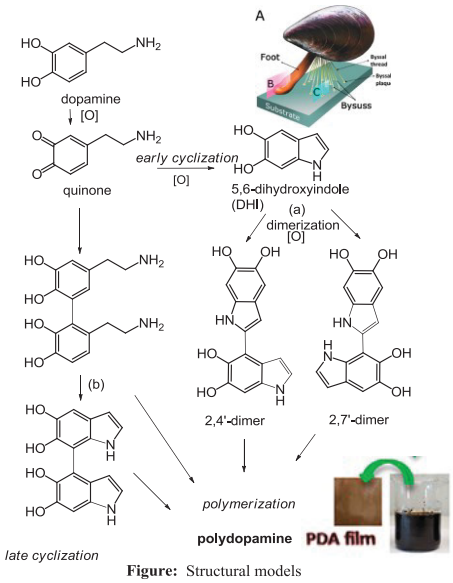


Figure: Structural models

References:

[1] J.H. Ryu, P.B. Messersmith, H. Lee, *ACS Appl. Mater.Interfaces* **2018**, *10*, 7523-7540.[2] N.F. Della Vecchia, R. Avolio, M. Alfè, M.E. Errico, A. Napolitano, M. d'Ischia, *Adv. Funct. Mater.* **2013**, *23*, 1331−1340. [3] M. L. Alfieri, R. Micillo, L. Panzella, O. Crescenzi, S.L. Oscurato, P. Maddalena, A. Napolitano, V. Ball, M. d'Ischia, *ACS Appl. Mater.Interfaces,* **2018**, *10*, 7670-7680.

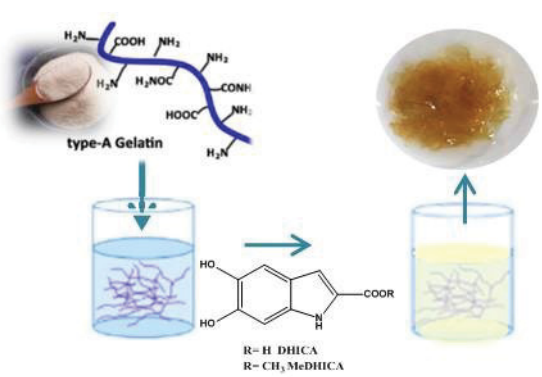
P44

An assessment of the potential of gelatin for the controlled release of melanin-related metabolites with antioxidant and anti-inflammatory activity

M. L. Alfieri,[a] R. Guizzardi,[b] L. Panzella,[a] L. Cipolla,[b] A. Napolitano[a]

[a]*Dept. of Chemical Sciences, University of Naples Federico II, I-80126, Naples*
[b]*Dept. of Biotechnology and Biosciences,University of Milano-Bicocca, I-20126, Milan*
e-mail:*marialaura.alfieri@unina.it*

Gelatin, the product of collagen hydrolysis, has been extensively investigated as system for controlled drug release, since its chemical nature offers many advantages, including historical safe use in a wide range of medical applications. Gelatin versatility allows the design of different carrier systems, spanning from micro or nanoparticles, to fibers and hydrogels. Gelatin hydrogels are able to trap bioactive molecules and/or drugs into the polymer network, thus allowing their controlled release, e.g. for pain treatment and wound healing applications.[1,2] Within this framework we have investigated the ability of gelatin-based hydrogels of incorporating and releasing under controlled conditions 5,6-dihydroxyindole-2-carboxylic acid (DHICA), a key intermediate in the biosynthesis of melanins, the main epidermal human pigments. The rationale guiding this choice stemmed from recent evidence indicating that this compound, that circulates at nM levels in blood and body fluids, may exert an antioxidant and protective function *per se* unrelated to pigment synthesis. The antioxidant profile characterized in *in vitro* assays suggested that it may act as a diffusible protective mediator under oxidative stress conditions.[3] In addition studies on primary cultures of human keratinocytes disclosed its remarkable protective and differentiating effects.[4]



In preliminary experiments,swelled type A gelatin from porcine skin was treated with 10 mM DHICA, or its methyl ester, MeDHICA, over 24 h. After repeated washings in methanol the extent of incorporation of the indole compound (λ_{max}320 nm) was evaluated by UV-vis spectrophotometric analysis as 50% and 30% in the case of MeDHICA and DHICA, respectively. The kinetics of release of the incorporated compound from gelatin under different conditions e.g. organic solvents or physiological media like PBS were also defined. These and other results including evaluation of the incorporation in gelatin of other DHICA-related products,e.g.oligomers, will be reported. The possibility of preparing gelatins having DHICA derivatives covalently linked at reactive sites, typically lysine residues, was also actively explored. The results obtained prompted to a preliminary assessment of the toxicity of all materials on keratinocyte cell lines in the perspective of their exploitation in wound healing applications.

References:

[1] M. Foox, M. Zilberman, *Expert Opin. Drug Deliv.* **2015,** *12,* 1547-1563. [2] A. Sgambato, L. Cipolla, L. Russo*Gels*, **2016,** *2*, 28. [3] L. Panzella, A. Napolitano, M. d'Ischia*, Pigment Cell Melanoma Res.***2010,***24*, 248-249. [4]D. Kovacs, E. Flori, V. Maresca, M. Ottaviani, N. Aspite, M.L. Dell'Anna, L. Panzella, A. Napolitano,M. Picardo, M. d'Ischia, *J. Invest. Dermatol.***2012**, *132*, 1196-1205.

P45

Synthesis of indole and pyrrole carboxamides and their application in domino processes

L. Bagnoli,[a] M. Palomba,[a] F. Marini,[a] C. Santi[a]

[a] *Department of Pharmaceutical Sciences, Via del Liceo 1, University of Perugia, Italy*
e-mail*: luana.bagnoli@unipg.it*

The synthesis of carboxamides, obtained by coupling reactions between 2-indole or 2-pyrrole carboxylic acids with ammines or amino acids, is particularly interesting for their potential biological activities[1] and application in domino processes. Using differently functionalized carboxamides and easily accessible vinyl selenones[2] pyrazine-indoles and pyrroles as well as N-vinyl azoles were obtained through addition/cyclization or addition/elimination cascade reactions, respectively. These new strategies that give access to compounds with two or three points of diversity appear highly useful for the synthesis of *drug-like* molecules. In fact pyrazino derivatives are basic structural units of several natural products and drug candidates.[3]

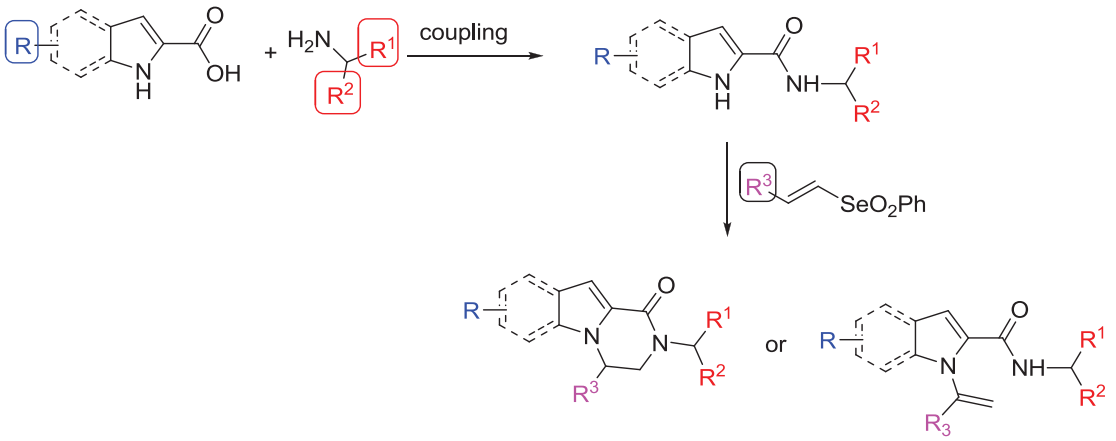


Figure 1: Synthesis of indole and pyrrole carboxamides and their reactivity with vinyl selenones.

References:

[1] (a) G. La Regina, R. Silvestri, V. Gatti, A. Lavecchia, E. Novellino, O. Befani, P. Turini, E. Agostinelli, *Bioorg. Med. Chem.* **2008**, *16*, 9729-9740; (b) K. L. Milkiewicz, T.H. Marsilje, R. P. Woodworth, N. Bifulco, M .J. Hangauer, D. G. Hangauer, *Bioorg. Med. Chem. Lett.* **2000**, *10*, 483-486.

[2] (a) L. Bagnoli, C. Scarponi, M. G. Rossi, L. Testaferri, M. Tiecco, *Chem. Eur. J.,* **2011**, *17*, 993-999; (b) L. Bagnoli, S. Casini, F. Marini, C. Santi, L. Testaferri, *Tetrahedron* **2013**, *69*, 481-486; (c) M. Palomba, E. Vinti, F. Marini, C. Santi, L. Bagnoli, *Tetrahedron* **2016**, *72*, 7059-7064.

[3] (a) B. M. Trost, M. Osipov, G. Dong, *J. Am. Chem. Soc.* **2010**, *132*, 15800-15807; (b) M. Bandini, A. Eichholzer, M. Monari, F. Piccinelli, A. Umani-Ronchi, *Eur. J. Org. Chem.* **2007**, 2917-2920.

P46

New synthesis of benzo[1,2-b:4,5-b′]dithiophene (BDT)

C. Baldoli,[a] S. Cauteruccio,[b] E. Licandro[b]

[a]*CNR- Istituto di Scienze e Tecnologie Molecolari (ISTM). Via C. Golgi 19, 20133 Milano*
[b]*Dipartimento di Chimica, Università degli Studi di Milano. Via C. Golgi 19, 20133 Milano*
e-mail*: clara.baldoli@istm.cnr.it*

Thiophene-containing polycondensed aromatic compounds are important source of functional organic materials for different applications. Within this class of molecules, benzo[1,2-b:4,5-b′]dithiophene (**BDT**, figure 1) is recognized as one of the most successful building blocks in the synthesis of highly efficient photovoltaic and semiconducting materials.[1] In fact the rigid and planar conjugated structure of **BDT** makes it attractive for achieving highly tunable molecular energy levels and optical band gaps as well as high hole mobilities. In recent years, benzannulation and thieannulation approaches, involving several steps, have been applied to the synthesis of **BDT** and of π-extended thienoacenes,[2] but the search of alternative easy access to this class of heterocycles is always a valuable synthetic target.
We present here a new two-step synthesis of **BDT**, starting from 3-thiophene carbaldehyde as unique thiophene precursor.

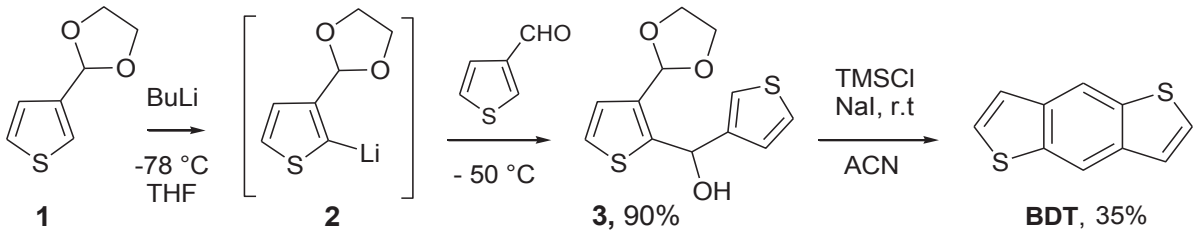


Figure 1

Although the second step of the synthesis needs to be optimized, this new methodology is certainly competitive to the classical approach[3] which involves four steps, more expensive reagents and gives a comparable overall yield.
In addition, the use of different hetero/aromatic aldehydes in the reaction with intermediate **2** gives access to a series of thiophene benzocondensed heterocycles.

References:

[1] J. Hou, H. Yao *et al., Chem. Rev.* **2016***, 116,* 7397−7457.
[2] K. Takimiya, I. Osaka *et al*., *Eur. J. Org. Chem.* **2013**, 217-227.
[3] G. Kossmehl, P. Beimling, *Chem. Ber.* **1986,** *119*, 3198-3203.

P47

Axially chiral benzo[1,2-*b*:4,3-*b*']dithiophene derivatives as key intermediates for enantiopure tetrathia[7]helicenes

V. Pelliccioli,[a] S. Cauteruccio,[a] C. Baldoli,[b] R. Franzini,[c] C. Villani,[c] E. Licandro[a]

[a]*Dipartimento di Chimica, Università degli Studi di Milano, Via Golgi 19, 20133 Milano*
[b]*CNR-Istituto di Scienze e Tecnologie Molecolari, Via Golgi 19, 20133 Milano*
[c]*Dipartimento di Chimica e Tecnologie del Farmaco, Sapienza Università di Roma, Piazzale Aldo Moro 5, 00185 Roma*
valentina.pelliccioli@unimi.it

Thiophene-containing fused aromatic compounds are an interesting class of π-conjugated systems with applications in functional organic materials.[1] Among them, benzo[1,2-*b*:4,3-*b*']dithiophene (**BDT**) and its derivatives are widely studied, for instance as units in mono and polydisperse oligomers in the field of materials science,[2] and as π-spacers in push-pull organic chromophores for photovoltaic applications.[3] Furthermore, **BDT** is a key intermediate for the synthesis of inherently chiral helical systems such as tetrathia[7]helicenes.[4] Thus, **BDT** can be identified as a key starting molecule, which can allow access to more complex and interesting systems through a judicious functionalization of the α-position of the thiophene rings. In our ongoing studies on the synthesis and functionalization of **BDT**s,[5] we have developed a novel synthesis to prepare systems **2**, starting from bromides **1** (Figure 1).

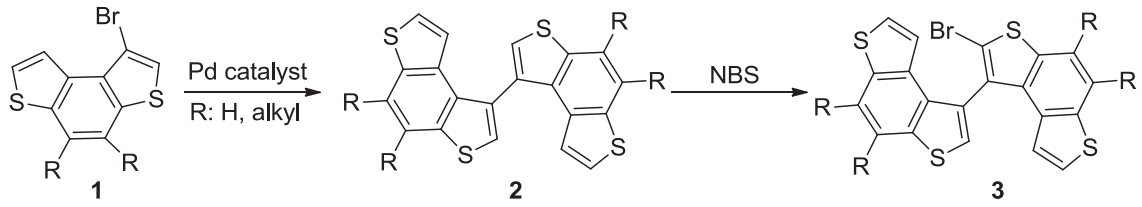


Figure 1: scheme of synthesis.

Compounds **2** are an interesting class of chiral atropisomeric heterobiaryl derivatives with C_2-symmetry, which can be selectively functionalized into bromides **3**, starting reagents for an innovative non-photochemical synthesis of tetrathiahelicenes through Pd-catalysed annulation with internal alkynes as key step. Asymmetric versions of this synthesis is under study thanks to the chiroptical properties of **3**, which represent useful intermediates for the enantioselective synthesis of the corresponding tetrathiahelicene derivatives.

References:

[1] J. Roncali, *Acc. Chem. Res*. **2009**, *42*, 1719−1730.
[2] Y. Nishide, H. Osuga, M. Saito, T. Aiba, Y. Inagaki, Y. Doge, K. Tanaka, *J. Org. Chem.* **2007**, *72*, 9141−9151.
[3] E. Longhi, A. Bossi, G. Di Carlo, S. Maiorana, F. De Angelis, P. Salvatori, A. Petrozza, M. Binda, V. Roiati, P. R. Mussini, C. Baldoli, E. Licandro, *Eur. J. Org. Chem.* **2013**, 8494.
[4] E. Licandro, C. Rigamonti, M. T. Ticozzelli, M. Monteforte, C. Baldoli, C. Giannini, S. Maiorana, *Synthesis* **2006**, 3670−3678.
[5] a) S. Cauteruccio, D. Dova, C. Graiff, C. Carrara, J. Doulcet, G. R. Stephenson, E. Licandro, *New J. Chem.* **2014**, *38*, 22412244. b) G. R. Stephenson, S. Cauteruccio, J. Doulcet, *Synlett* **2014**, *25*, 701707.

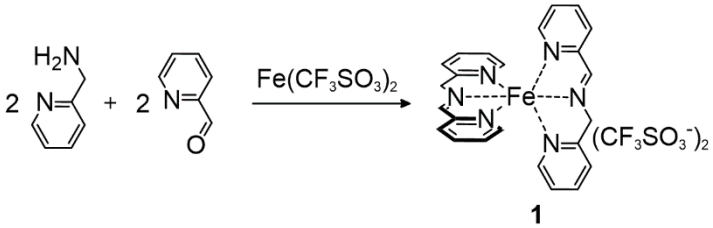
P48

Oxidation of organic compounds with H_2O_2 catalyzed by a nonheme imine-based iron complex

A. Barbieri,[a] G. Capocasa,[a] A. Cerrato, O. Lanzalunga,[a] S. Di Stefano,[a] G. Olivo,[b] B. Ticconi[a]

[a]Dipartimento di Chimica, Università "La Sapienza" and Istituto CNR di Metodologie Chimiche (IMC-CNR), Sezione Meccanismi di Reazione, Roma.
[b]Departament de Quimica, Universitat de Girona, Campus de Montolivi, Spain.
Author:alessia.barbieri@uniroma1.it

Selective oxidations of organic compounds with H_2O_2 catalyzed by nonheme iron complexes have attracted a special attention in recent years. Expensive synthetic procedures and complex ligand architectures are often required to achieve good catalyst's activity and selectivity. In order to overcome these problems, we have synthetized and employed a simple nonheme imine-based iron complex (**1**) assembled *in situ* from cheap and commercially available reagents (2-picolylamine and 2-picolylaldehyde and Fe(II) triflate, Figure 1).[1,2]



1

Figure 1

This complex exhibited high turnover numbers in aliphatic C-H hydroxylation using H_2O_2 as terminal oxidant. The **1**/H_2O_2 catalytic system is also efficient in the oxidation of aliphatic alcohols and in the oxidation of aromatic compounds.[3,4] We have now extended the application of this catalyst to the oxidation of aliphatic and aromatic amino acids and alkylaromatic substrates. In the latter compounds the competition between aromatic hydroxylation and side-chain oxidation has been investigated.

References:

[1] Olivo, G.; Arancio, G.; Mandolini, L.; Lanzalunga, O.; Di Stefano, S. *Catal. Sci. Technol.* **2014**, *4,* 2900.
[2] Olivo, G.; Nardi, M.; Vidal, D.; Barbieri, A.; Lapi, A.; Gomez, L.; Lanzalunga, O.; Costas, M.; Di Stefano, S. *Inorg. Chem.*. **2015**, *54,* 10141
[3] G. Olivo, S. Giosia, A. Barbieri, O. Lanzalunga, S. Di Stefano, *Org & Biomol. Chem.* **2016**, *14*, 10630.
[4] G. Capocasa, G. Olivo, A. Barbieri, O. Lanzalunga, S. Di Stefano, *Catal. Sci. Technol.* **2017**, *7,* 5677.

P49

Chemoselective aerobic esterification of glycerol promoted by supported N-heterocyclic carbenes under batch and flow conditions

O. Bortolini,[a] A. Massi,[a] D. Ragno,[a] A. Brandolese,[a] D. Urbani[a]

[a]*Dipartimento di Scienze Chimiche e Farmaceutiche, Università di Ferrara, Via Luigi Borsari, 46, I-44121 Ferrara, Italy.*
e-mail*: olga.bortolini@unife.it*

Glycerol esterification is one of the mostly studied route for glycerol valorization affording mono-, di- and tri-acyl esters. In particular, monoacylglycerols (MAGs) find wide applications in food, pharmaceutical, cosmetic, and nutraceutical fields. Accordingly, the design of novel protocols for the chemoselective esterification of glycerol represents an important goal in this area of research.[1] The chemoselective aerobic esterification of glycerol promoted by N-heterocyclic carbenes (NHCs) is herein presented as a novel route towards valuable MAG derivatives. Aerobic oxidation conditions were made possible using a biomimetic strategy relying on the use of electron transport mediators (ETMs).[2] Preliminary batch conditions were investigated in homogeneous phase, followed by catalyst immobilization onto silica and polystyrene supports and final reaction optimization under heterogeneous batch conditions. Fabrication of fixed-bed microreactors functionalized with the NHC precursor allowed for the study of the continuous-flow process.

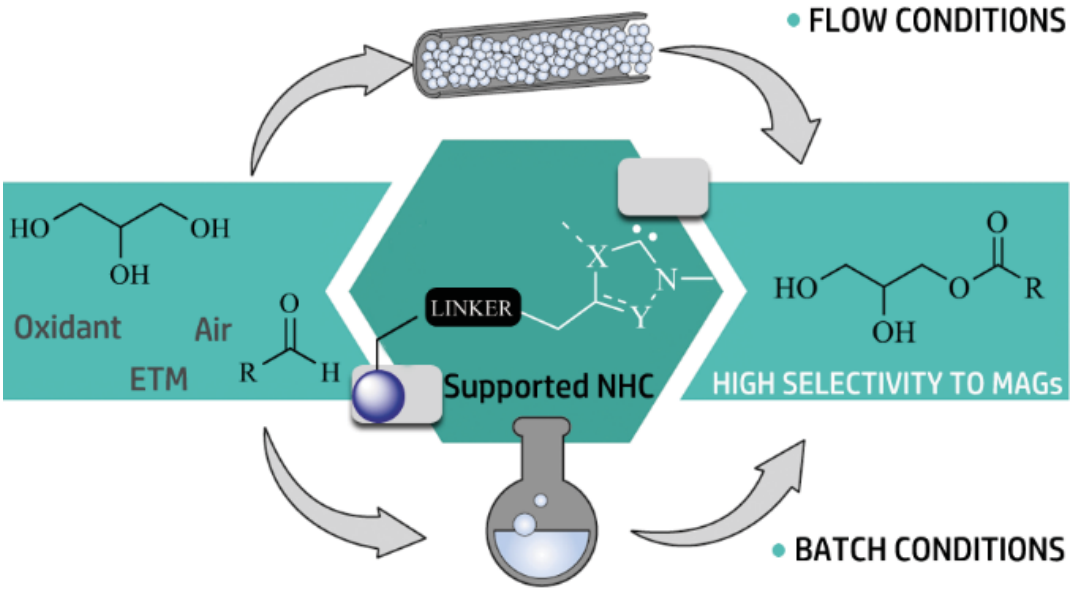


Figure 1: Production of MAGs by NHC oxidative esterification.

References:
[1] P. U. Okoye, B.H. Hameed, *Renewable Sustainable Energy Rev.* **2016**, *53*, 558-574; C. Zhou, J. N. Beltramini, Y. Fan, G. Q. Lu, *Chem. Soc. Rev.* **2008**, *37*, 527-549.
[2] J. E. Bäckvall, A. K. Awasthi, Z. D. Renko, *J. Am. Chem. Soc.* **1987**, *109*, 4750-4752; J. Piera, K. Närhi, J. E. Bäckvall, *Angew. Chem., Int. Ed.*, **2006**, *45*, 6914-6917.

P50

Synthesis of bicyclic Δ^2 isoxazoline derivative as parallel turn mimics

R. Bucci, S. Giofrè, R. Frigerio, S. Pellegrino, M. L. Gelmi

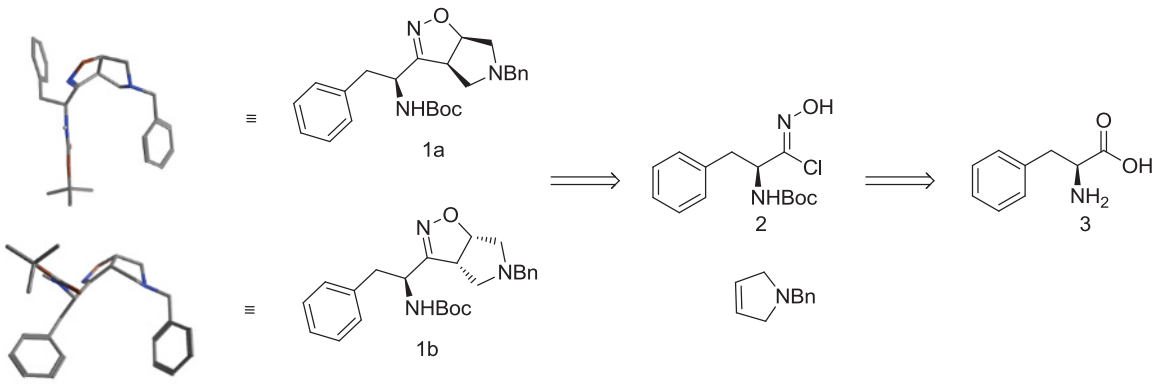
[a]*DISFARM, Università degli Studi di Milano, Milan, Italy*
e-mail*: raffaella.bucci@unimi.it*

Hybrid peptides containing natural amino acids and non-natural molecular architecture mimicking secondary structure elements (such as turn mimics) are widely used in different applications, from catalysis to electrochemistry, biology and nanomedicine[1]. In this content, bicyclic compounds are extensively exploited as turn secondary structure inducers.

The aim of this work is the preparation of diastereoisomeric Δ^2-isoxazoline compounds fused with a pyrrolidine ring (Scheme 1). The presence of two amino groups makes indeed this bicyclic scaffold a good candidate as a parallel turn inducer. In addition, the isoxazole ring is present in a large number of pharmaceutically active compounds[2].

Compounds **1a** and **1b** were prepared through a [1,3]-dipolar cycloaddition reaction between chloroxime **2** and 1-benzyl-3-pyrroline. A good control of the diastereoselection (3:1 ratio) was obtained in polar solvents and organic bases that favor the obtainment of the 3a*R*, 6a*S* isomer (**1b**, Scheme 1) through π–π stabilization of the transition state.

When inserted in model peptides, the major isomer induced the formation of a stable turn conformation, suggesting the possibility of its use for the preparation of parallel β-hairpin.



Scheme 1: Retrosynthetic pathway of compounds **1a** and **1b**

References:

[1] (a) W. Yao, Y. Yan, L. Xue, C. Zhang, G. Li, Q. Zheng, Y.S. Zhao, H. Jiang, J. Yao, *Angewante Chemie*, **2013**, *125*, 8875−8879; (b) S.F. Torabi, Y. Lu, *Current Opinion in Biotechnology*, **2014**, *28*, 88−95.

[2] Norman, B. H., Gruber, J. M., Hollinshead, S. P., Wilson, J. W., Starling, J. J., Law, K. L., Dantzig, A. H., *Bioorganic and Medicinal Chemistry Letters,* **2002**, *12*, 883–886.

P51

Alternative Strategies for the Preparation of Biodiesel: Homogeneous and Heterogeneous Catalysis

C. Carlucci [a], L. Degennaro [a], R. Luisi [a]

[a] *Flow Chemistry and Microreactor Technology FLAME-Lab; Dipartimento di Farmacia - Scienze del Farmaco, Università degli Studi di Bari, Via Orabona 4, 70125 Bari, Italy.*
e-mail: claudia.carlucci@uniba.it

The World Energy Forum has estimated that fossil fuels will run out in less than ten decades if they are not replaced by an alternative energy source. [1]

The depletion of these resources is due to the rapid rise of the population and to the growth of industrialization. The discovery of alternative fuels that can replace conventional fuels has therefore become the goal of many scientific researches. [2]

Biodiesel can be produced from vegetable oils through a transesterification reaction that converts triglycerides into fatty acid methyl esters (FAME) with the use of a low molecular weight alcohol such as methanol or ethanol.

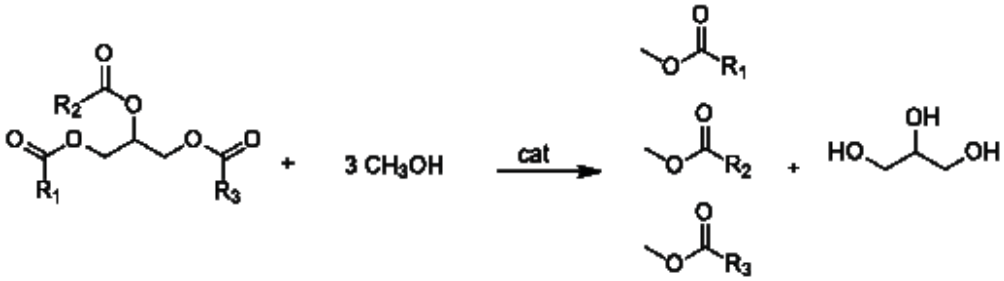


Figure 1: biodiesel production.

In recent years, the trend has shifted to use waste materials as a primary source for biodiesel production, thus turning a waste into a resource. [3]

A sustainable process for the production of biodiesel from waste oils, and the re-use of existing waste products in the production of biodiesel has been developed. Furthermore, the use of micro-technologies and the development of micro reactors, able to make possible chemical transformations not feasible with traditional techniques, could enable a reduction of costs and a greater environmental protection in the field of biodiesel production. [4]

References:

[1] M. K. Lam, K. T. Lee, A. R. Mohamed, *Biotechnology Advances* **2010**, *28*, 500-518.
[2] L.T. Thanh, K. Okitsu, L. Van Boi, Y. Maeda, *Catalysts* **2012**, *2*, 191-222.
[3] M. Canakci, *Bioresour Tech* **2007**, *98*, 183-190.
[4] A. Tiwari, V. M. Rajesh, S. Yadav, *Energy for Sustainable Development* **2018**, 43, 143-161.

P52

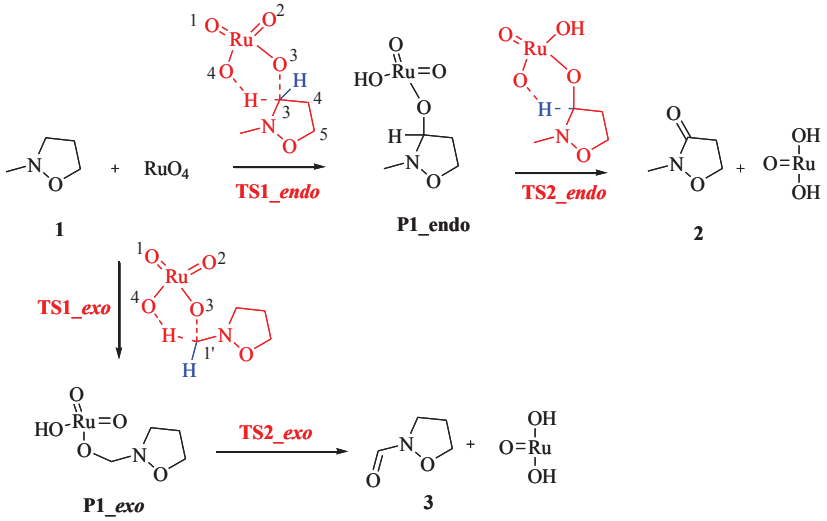
Computational Mechanistic Study of Ruthenium Tetroxide Oxidation of 2-methylisoxazolidine

M. A. Chiacchio,[a,c] S. V. Giofrè,[b] R. Romeo,[b] S. Piacentini,[c] L. Legnani[a,c]

[a]*Dipartimento di Scienze del Farmaco, Università di Catania, V.le Doria 6, 95125 Catania, Italy.*
[b]*Dipartimento di Scienze Chimiche, Biologiche, Farmaceutiche e Ambientali, University of Messina, Via S.S. Annunziata, 98168 Messina, Italy.*
[c]*Dipartimento di Chimica, Università di Pavia, Via Taramelli 12, 27100 Pavia, Italy.*
e-mail*: ma.chiacchio@unict.it*

The first example of an oxidation of organic substrates with ruthenium tetroxide (RuO_4) dates back to 1953. Only in the 90s, the first successful applications of this metal oxide, as an oxidant in a reaction, appeared in literature and several research groups used RuO_4 for the oxyfunctionalization of saturated hydrocarbons.

More recently, some of us reported the first example of a direct oxidation of the isoxazolidine nucleus to the 3-isoxazolidone [1].



Scheme 1.

In order to rationalize the selective oxidation of the C3 of 2-methylisoxazolidine and clarify the reaction mechanism [2], after a careful investigation to select the better level of calculation, a complete computational mechanistic study of the reaction of 2-methylisoxazolidine with ruthenium tetroxide was carried out. All calculations were performed using the Gaussian09 program package, through optimizations with the Truhlar's functional M062X and 6-31G(d) basis set for all atoms, while the Stuttgart/Dresden ECP was used for Ru. Optimizations were repeated in solvent (methylpropanoate), at the same level, in the classical polarizable continuum model (PCM).

References:

[1] Piperno, A.; Chiacchio, U.; Iannazzo, D.; Giofre`, S. V.; Romeo, G.; Romeo R. *J. Org. Chem.* **2007**, *72*, 3958-3960.
[2] Plietker, B. *Synthesis* **2005**, *15*, 2453.

P53

β-Nitroacrylates: useful precursor of *N*-containing heterocyclic systems

E. Chiurchiù, S. Gabrielli, R. Ballini, A. Palmieri

University of Camerino, Via S. Agostino 1, 62032 Camerino
e-mail*: elena.chiurchiu@unicam.it*

β-Nitroacrylates are a class of electron-poor alkenes having two electron-withdrawing group in α- and β-positions. This peculiarity makes their chemical behaviour more interesting with respect to the classical conjugated nitroalkanes and, for this reason, in the last few years there has been a growing interest in their chemistry. In particular, they have proved to be precious precursor of *N*-containing heterocyclic systems (Figure 1), which in turn are the core of a wide number of biological active molecules and are present in the 59% of small-molecules drugs (U.S. FDA).[1] Among the *N*-containing heterocyclic systems, pyrroles and indoles derivatives surely play a predominant role. In fact, indoles are considered a "privileged structures"[2] due to its ability to bind many receptors with high affinity and pyrroles have application in several fields of chemistry such as medicinal, pharmaceutical and material science.[3]

Some synthetic applications of β-nitroacrylates as precursor of pyrroles and indoles, under mild conditions, will be presented in the poster.

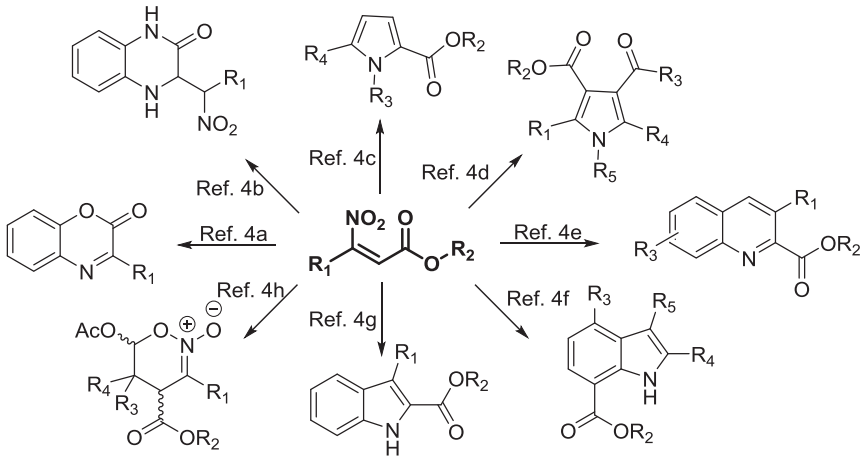


Figure 1: Synthetic examples of *N*-containing heterocycles.

References:

[1] E. Vitaku, D. T. Smith, J.T. Njardson, *J. Med. Chem.* **2014**, *57*, 10257 – 10274.
[2] F. R. de Sà Alves, E. J. Barreiro, C. A. Manssour Fraga, *Mini-Rev. in Med. Chem.* **2009**, *9*, 782 – 793.
[3] V. Bhardwaj, D. Gumber, V. Abbot, S. Dhiman, P. Sharma, *RSC Adv.* **2015**, *5*, 15233 – 15266.
[4] (a) R. Ballini, A. Palmieri, M. A. Talaq, S. Gabrielli, *Adv. Synth. Catal.* **2009**, *351*, 2611 – 2614. (b) R. Ballini, S. Gabrielli, A. Palmieri, *Synlett* **2009**, *6*, 965 – 967. (c) A. Palmieri, S. Gabrielli, M. Parlapiano, R. Ballini, *RSC Adv.* **2015**, *5*, 4210 – 4213. (d) A. Palmieri, S. Gabrielli, C. Cimarelli, R. Ballini, *Green Chem.*, **2011**, *13*, 3333 – 3336. (e) S. Gabrielli, A. Giardinieri, S. Sampaolesi, R. Ballini, A. Palmieri, *Molecules*, **2016**, *21*, 776. (f) A. Palmieri, S. Gabrielli, D. Lanari, L. Vaccaro, R. Ballini, *Adv. Synth. Catal.* **2011**, *353*, 1425 – 1428. (g) A. Palmieri, S. Gabrielli, R. Maggi, R. Ballini. *Synlett* **2014**, *25*, 128 – 132. (h) R. Ballini, G. Bosica, S. Gabrielli, A. Palmieri, *Tetrahedron* **2009**, *65*, 2916 – 2920.

P54

The A^3 Coupling Reactions Catalyzed by Efficient Lewis Acid Systems

C. Cimarelli,[a] F. Navazio,[a] F. V. Rossi,[a] G. Lupidi,[a] E. Marcantoni[a]

[a]*School of Science and Technology - Chemistry Division, University of Camerino, Via S. Agostino 1, 62032 Camerino*
e-mail*: cristina.cimarelli@unicam.it*

Propargylamines belong to a widely studied[1] class of building blocks because of their particular molecular skeleton that contains an amine group, suitable for nucleophilic reactions, located in β-position to an alkyne moiety, that can act both as an electrophile and as a source of electrons in nucleophilic reactions.[2]

Our goal was the development of green and simple Lewis acid catalyzed methodologies to the A^3 reaction for the synthesis of primary propargylamines from aldehydes, primary amines and alkynes. In particular, we applied two different Lewis acid catalysts to this reaction: the $CuSO_4$/NaI system in one pot fashion and the $CeCl_3$/CuI system in one pot/two steps way.

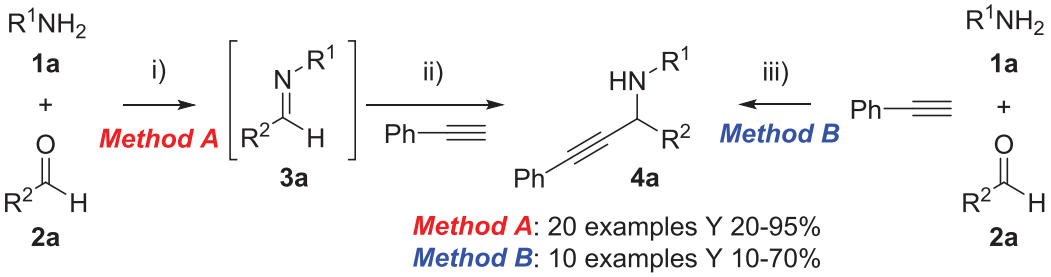


Figure 1 – $CeCl_3 \cdot 7H_2O$/CuI and $CuSO_4$/NaI catalyzed A^3 reaction. Reaction conditions:
i) $MgSO_4$, $CeCl_3 \cdot 7H_2O$ 30% mol, solventless, N_2, r.t., 0.25h.
ii) CuI 30% mol, solventless, N_2, 40°C
iii) $CuSO_4$ 30% mol/NaI 60% mol, PhCOOH 5% mol, solventless, N_2, 80°C

Heptahydrated $CeCl_3$ is a very good catalyst for the formation of imines, widely used also in the synthesis of several classes of organic compounds.[3] Its efficacy is enhanced in the presence of inorganic iodides[4] and being copper the transition metal of choice for A^3 reactions, CuI was used.

Also the $CuSO_4$/NaI couple has revealed to be an interesting Lewis acid system, alternative to $CeCl_3$/CuI system. The reaction has been applied also to chiral starting materials and, in general, the amine has no effect on the reaction outcome. Typically $CuSO_4$/NaI catalysed reactions are faster, but suffer of some disadvantages, such as lower yields, and a narrower applicability. The relevant Glaser coupling drawback observed in these conditions has been suppressed by adding some benzoic acid, and has not been observed with the $CeCl_3$/CuI system.

References:

[1] K. Lauder, A. Toscani, N. Scalacci, D. Castagnolo *Chem. Rev.* **2017**, *117*, 14091 – 1420.
[2] V. A. Peshkov, O. P. Pereshivko, E. V. Van der Eycken *Chem. Soc. Rev.* **2012**, *41*, 3790 – 3807.
[3] R. Properzi, E. Marcantoni *Chem. Soc. Rev.*, **2014**, ***43***, 779 - 791.
[4] G. Bartoli, E. Marcantoni, M. Marcolini, L. Sambri *Chem. Rev.* **2010**, *110*, 6104 – 6143.

P55

Anti-miR Peptide Nucleic Acids for CFTR activity modulation in cystic fibrosis

T. Jakova,[a] M. Neri,[a] A. Rozzi,[a] A.Tamanini,[b] E. Fabbri,[c], J. Gasparello,[c] A. Manicardi,[a] A. Finotti,[c] M. Borgatti,[b] I. Lampronti,[b] S. Munari,[b] M. C. Dechecchi,[b] G. Cabrini,[b] R. Gambari,[c] R. Corradini[a]

[a] *Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale, Università di Parma, Parco Area delle Scienze 17/a, 43124 Parma, Italy.* [b] *Laboratory of Molecular Pathology, University-Hospital, Piazzale Stefani 1, I-37126 Verona, Italy.* [c]*Dipartimento di Scienze della vita e Biotecnologie, Università di Ferrara, Via Fossato di Mortara 74, 44121 Ferrara, Italy*

e-mail*: roberto.corradini@unipr.it*

Cystic fibrosis (CF) is a genetic disease which leads to severe illness arising from mutations in the Cystic Fibrosis Transmembrane conductance Regulator (CFTR), preventing correct transport of chloride ions in the epithelial cells. Epigenetic regulation of expression of CFTR can be a very important tool in the study of the CF disease and for proposing new and unprecedented treatments. In this field, the regulation of microRNA, short dsRNA which inhibit translation of target mRNA into proteins, is one of the most rational and effective approaches.

This poster communication reports the results obtained in a pilot study in which we explored the possibility of using peptide nucleic acids (PNAs), oligonucleotide mimics with a polyamide backbone, for the regulation of the expression of CFTR by acting on the microRNA that target either the mRNA of CFTR or CFTR regulators, i.e. proteins known to interact with the CFTR protein and regulate its folding (Figure 1).

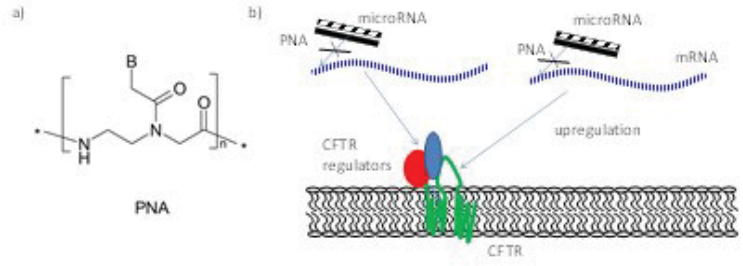


Figure 1: a) Peptide Nucleic Acid structure. b) Mechanism of regulation of CFTR activity by PNA.

For this purpose, the design and synthesis of PNAs targeting microRNA known to control expression of CFTR (for instance miR-145-5p) and its up-regulators were performed and several PNAs were synthesised, conjugated to a polyarginine tail using solid-phase synthesis and characterized with respect to the ability to induce increase of CFTR.[1]

Results obtained using this approach for the regulation of CFTR in Calu-3 cells will be summarised, and perspectives of this approach for future studies will be discussed.

This study was funded by the Fondazione Fibrosi Cistica (MICRORNA-CF, FFC#3/2016)

References:

[1] E. Fabbri, A. Tamanini, T. Jakova, J. Gasparello, A. Manicardi, R.O Corradini, G. Sabbioni, A. Finotti, M. Borgatti, I. Lampronti, S. Munari, M. C. Dechecchi, G. Cabrini, R. Gambari *Molecules*, **2018,** *23*, 71.

P56

Viruses autonomous glycosylation: the case of Mimivirus

C. De Castro,[a] A. Notaro,[b,d] A. Molinaro,[b] M. Tonetti,[c] C. Abergel[d]

[a]*Department of Agricultural Sciences, University of Naples. Naples. Italy.* [b]*Department of Chemical Sciences, University of Naples. Naples. Italy*
[c]*Department of Experimental Medicine and Center of Excellence for Biomedical Research, University of Genova. Genova. Italy*
[d]*Information Génomique et Structurale, Centre National de la Recherche Scientifique-UPR 2589, Aix-Marseille University, IMM, Parc Scientifique de Luminy. Marseille. France.*
e-mail*: decastro@unina.it*

Mimivirus is the prototype of the growing Mimiviridae family and infects some species of the amoebozoan genus Acanthamoeba. This virus is approximately 700 nm diameter and it contains a dsDNA genome of 1,18 Mb encoding more than 1000 genes, blurring the boundary between viruses and bacteria.[1] Of interest is the evidence Mimivirus genome has many glyco-related genes, indeed it encodes a functional pathway for UDP-N-acetyl-D-glucosamine production and enzymes for the biosynthesis of viosamine (4-ammino-4,6-dideoxy-D-glucopyranose).[2,3] This information, along with the presence of many other genes apparently encoding proteins involved in glycan formation, supports the notion that *Mimivirus* has an autonomous glycosylation machinery. The concept of autonomous viral glycosylation system emerged for the first for *Paramecium bursaria* chlorella virus (PBCV-1) which has the capsid decorated with an unusual glycan,[4] presenting a conserved core structure different from any other form of life and shared only from viruses belonging to the same family.[5]
For *Mimivirus*, the first evidence of the presence of glycosylated fibrils came from the Gram-positive staining of the viral particles, and the chemical and spectroscopical strategies that have succeeded in the determination of the structure of the two polysaccharides that compose the fibers (Figure 1) is here discussed along with the information available for the role that these glycans have in the viral infectivity.

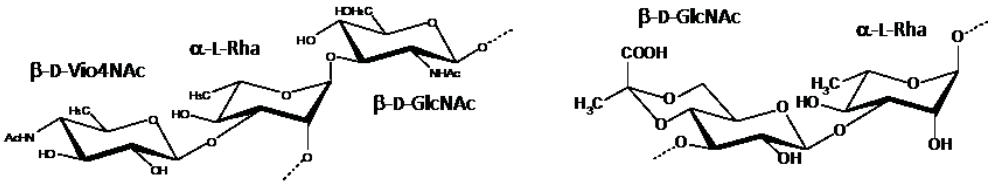


Figure 1. Structure of the repeating units of the two polysaccharides present in the fibers of Mimivirus.

References:

[1] M. Legendre, S. Santini, C. Abergel, J.M. Claviere, *Virology J*. **2011**, 8 – 2.
[2] F. Piacente, M. Marin, A. Molinaro, C. De Castro, V. Seltzer, A. Salis, G. Damonte, C. Bernardini, J.M. Claviere, C. Abergel, M. Tonetti, *J. Biol. Chem*. **2012**, *278*, 21559 – 21565.
[3] F. Piacente, C. De Castro, S. Jeudy, A. Molinaro, A. Salis, G. Damonte, C. Bernardi, C. Abergel, M. Tonetti, *J. Biol. Chem*. **2014**, *289*, 24428 – 24439
[4] C. De Castro, A. Molinaro, F. Piacente, J.R. Gurnon, L. Sturiale, A. Palmigiano, R. Lanzetta, M. Parrilli, D. Garozzo, M. Tonetti, J. Van Etten, *Proc. Nat. Acad. Sc*. **2013**, *110*, 13956 – 13960.
[5] C. De Castro, I. Speciale, G. Duncan, D.D. Dunigan, I. Agarkova, R. Lanzetta, L. Sturiale, A. Palmigiano, D. Garozzo, A. Molinaro, M. Tonetti, J.L. Van Etten. *Angew. Chem. Int. Ed*. **2016**, *55*, 654 – 658.

P57

Metal and solvent-free synthesis of α-H-chlorinated alkylaromatic hydrocarbons from toluenes by sunlight

L. De Luca,[a] S. Gaspa[a]

[a]*Dipartimento di Chimica e Farmacia, Università degli Studi di Sassari, Via Vienna 2, Sassari*

e-mail*: ldeluca@uniss.it*

Benzyl chloride and substituted benzyl chloride are significant intermediates in the industrial preparation of amphetamine-class drugs, artificial resins, dyes, gum petrol inhibitor and photographic developer[1]. The major drawbacks related to the major industrial processes are the use of hazardous reagents, hard reaction conditions, low selectivity, conversions and yields. In addition, the use of gaseous components (HCl) and other aggressive reagents requires the design and construction of custom expensive reactors.

In relation to our interest in the development of green and solvent-free procedure[3] and in the use of trichloroisocyanuric acid[2] as an oxidizing and chlorinating reagent, we have carried out a new procedure for the α-H chlorination of toluene and alkylaromatic hydrocarbons by the use of sunlight.

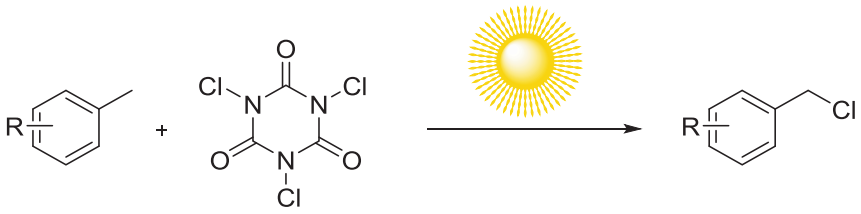


Figure 1: Visible light induced strategy to benzyl chlorides

The reported process is configured as solvent, metal and additive free, with very high yields and conversions. Moreover the product isolation procedure (easy filtration on a short-column chromatography) is very simple. The proposed methodology can be carried out by the use of sunlight or visible light. It is to underline that this methodology makes use of inexpensive and easily available organic reagents, unlike photochemistry and photocatalysis which are normally based on cromophores and metal-based photocatalyst.

References:

[1] Ullmann's Encyclopedia of Industrial Chemistry, Weinheim: Wiley-VCH, **2005**, doi.org/10.1002%2F14356007.a06_233.pub2.

[2] S. Gaspa, A. Porcheddu, A. Valentoni, S. Garroni, S. Enzo and L. De Luca, *Eur. J. Org. Chem.* **2017**, 5519-5526.

[3] a) S. Gaspa, I. Amura, A. Porcheddu and L. De Luca, *New J. Chem.* **2017**, *41*, 931-939; b) S. Gaspa, A. Porcheddu and L. De Luca, *Tetrahedron Lett.* **2017**, *58*, 2533-2536; c) S. Gaspa, A. Porcheddu and L. De Luca, *Adv. Synth. Catal.* **2016**, *358*, 154-158; d) S. Gaspa, A. Porcheddu and L. De Luca, *Org. Lett.* **2015**, *17*, 3666-3669;

P58

Drug Delivery Systems for Combination Therapy: Preliminary Biodistribution of Functionalized Carbon Nanotubes via PET/CT and Efficacy

F. Pisaneschi,[a] G. Biagiotti,[a,b] S. Gammon,[a] P. Paoli,[c] D. Piwnica-Worms,[a] A. Brandi,[b] G. Giambastiani,[d] G. Tuci,[d] F. Machetti,[d] S. Cicchi [b]

[a] *Cancer Systems Imaging, UT MD Anderson Cancer Center, Houston, Texas, USA*
[b]*Dep. of Chemistry "Ugo Schiff", Univ. di Firenze, Firenze, Italy*
[c]*Dep. of Exp. and Clin. Biomed. Sciences "Mario Serio", Univ. di Firenze, Firenze, Italy*
[d] *Inst. of Chemistry of OrganoMetallic Compounds ICCOM-CNR, Sesto Fiorentino, Italy*

e-mail*: stefano.cicchi@unifi.it*

The ability of carbon nanotubes (CNT) to translocate into cells, together with the flexibility of their functionalization chemistry, has promoted their use as Drug Delivery Systems (DDS).[1] CNT have been investigated in oncology as mono-agents, while the potential for use as DDS for combination therapy is emerging and showing promise.[2] Despite growing interest, few studies have reported on the biodistribution of CNT in vivo, especially in tumour-bearing mouse models.[3] Our goal was to synthesize a short oxidized multi-walled CNT bearing a combination of drugs and a chelation moiety for radiolabeling to investigate the in vivo biodistribution by PET/CT imaging and pilot therapeutic efficacy. Herein, we conjugated MWCNT with doxorubicin, a first-line chemotherapeutic agent for breast cancer, and metformin, a metabolically active compound that reduces serum glucose and shows anti-tumour activity for the treatment of chemo-resistant tumors mediated, in part, by inhibition of mitochondrial oxidative phosphorylation. The nanotube was further conjugated with biotin for tumour targeting, and bifunctional chelators bearing DOTA or NOTA, enabling radiolabeling with copper-64 or gallium-68. For analysis in vivo, 4T1 tumour-bearing mice, a reliable syngeneic model of triple-negative breast cancer, also known to overexpress biotin receptors, was used. Biodistribution was assessed by PET/CT imaging. A pilot study of efficacy was also performed on a cohort of 4T1 tumour-bearing mice, where the group treated with targeted-MWCNT (n=5) showed a survival profile prolonged by 12 days when compared to group treated with vehicle alone (n=5) and 5 days compared to the group treated with the unconjugated combination of the two drugs (n=5).

References:

[1] C. Fabbro, H. Ali-Boucetta, T. Da Ros, K. Kostarelos, A. Bianco, M. Prato, *Chem. Commun*. **2012**,*48*, 3911 – 3926

[2] G. Biagiotti, S. Fedeli, G. Tuci, L. Luconi, G. Giambastiani, A. Brandi, F. Pisaneschi, S. Cicchi, P. Paoli, *J. Mater. Chem. B* **2018**, *6*, 2022 – 2035.

[3] N. R. Jacobsen, P. Møller, P. A. Clausen,. A. T. Saber,; C. Micheletti,; K. A. Jensen,.; H. Wallin, U. Vogel, *Basic Clin. Pharmacol. Toxicol*. **2017**, *121*, 30 – 43.

P59

Design and synthesis of simplified analogs of the anticancer peptaibol Culicinin D

M. De Zotti,[a] C. Piccolo,[a] R. Tavano,[b] E. Papini,[b] F. Formaggio[a]

[a]*Department of Chemistry, University of Padova, via Marzolo 1, Padova*
[b]*Department of Biomedical Sciences, University of Padova, via G. Colombo 3, Padova*
e-mail*: fernando.formaggio@unipd.it*

The peptaibol Culicinin D, synthesized by the fungus *Culicinomyce clavisporus*, displays interesting anticancer activity. It exhibits selective toxicity towards MDA468 breast tumor cells with an IC_{50} value of less than 6 nM.[1,2] Its sequence is characterized by the presence of the non-coded residue Aib (α-aminoisobutyric acid), a C-terminal 1,2-aminoalcohol and an acylated N-terminus. The primary structure of Culicinin D is as follows: But-Pro-**(*R*)-AHMOD**-Aib-Aib-**AMD**-Leu-Aib-Leu-βAla-**APAE**, where **(*R*)-AHMOD** is 2-amino-6-hydroxy-4-methyl-8-oxo-decanoic acid, **AMD** is 2-amino-4-methyldecanoic acid, and **APAE** is 2-(2-aminopropylamino)ethanol (Figure 1).

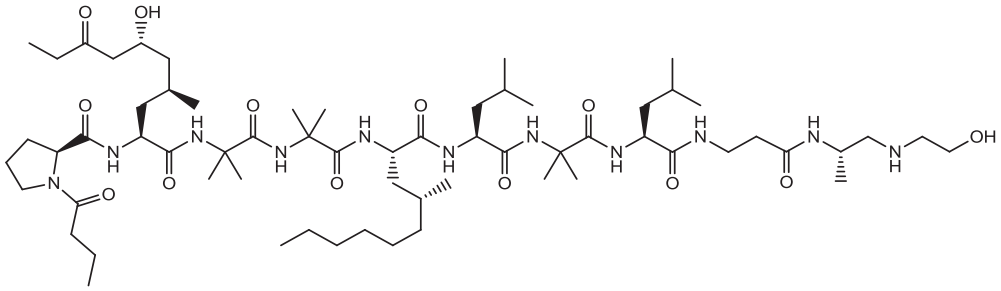


Figure 1: Sequence of the naturally-occurring anticancer peptaibol Culicinin D

Because of its anticancer activity in the low nanomolar range, Culicinin D is a promising lead compound for the development of peptide-based drugs. In addition, the presence of as many as seven non-coded residues out of ten impart the peptide with a high proteolytic stability. However, its difficult total synthesis[2,3] prevents it from being attractive to pharmaceutical companies

To overcome this drawback, we planned the preparation of a few analogs endowed with simplified structures, but preserving the side-chain main features, such as polar moieties and steric hindrance. The design, synthetic strategy, and characterization of three *simplified* analogs are reported in this communication, together with preliminary results on their antitumor activity.

References:

[1] H. He, J. E. Janso, H. Y. Yang, V. S. Bernan, S. L. Lin, K. Yu, *J. Nat. Prod.* **2006**, *69*, 736–741.
[2] K. Y. Hung, P. W. R. Harris, M. A. Brimble, *Org. Lett*. **2012**, *14*, 5784-5787.
[3] M. Stach, A. J. Weidkamp, S.H. Yang, K. Y. Hung, D. P. Furkert, P. W. R. Harris, J. B. Smaill, A. V. Patterson, M. A. Brimble, *Eur. J. Org. Chem*. **2015**, 6341-6350.

P60

A bioconjugated system for drug delivery through a peptide carrier

F. Formaggio,[a] E. Papini,[b] R. Tavano,[b] A. Moretto,[a] M. De Zotti[a]

[a]*Department of Chemistry, University of Padova, via Marzolo 1, Padova*
[b]*Department of Biomedical Sciences, University of Padova, via G. Colombo 3, Padova*
e-mail*: fernando.formaggio@unipd.it*

The exploitation of cargo delivery to selectively target tumor cell lines has been extensively investigated in the last decade[1]. One of the most promising strategies consists in the conjugation of a cytotoxic agent to a tumor-targeting carrier, such as a protein, by means of an acid-labile linker, stable at physiological pH. Once the conjugated system is internalized into the tumor cell, the acidic environment would cleave the linker causing the cytotoxin release and subsequent death of the tumor cell. Attaching a cytotoxin to a tumor targeting protein through a selectively cleavable linker not only reduces its general toxicity to healthy tissues, but can also significantly improve the pharmacological properties of the cytotoxic agents[2].

In this presentation, we describe a novel bioconjugated system based on a drug-carrier short peptide, that is effectively internalized into tumor cells[3]. Its sequence mimics that of trichogin, a natural peptide produced by the fungus *Trichoderma Longibrachiatum* as part of its defence system against other microorganisms. To load the cargo onto the peptide carrier we exploited the well known, acid-labile benzoic-imine linker[4]. Finally, the commercially-available cytotoxic agent proflavine was used as cargo (Figure 1). A detailed conformational analysis by means of several spectroscopic techniques is presented, along with the synthetic strategy followed to obtain the conjugated system and the results of our preliminary cytotoxicity assays.

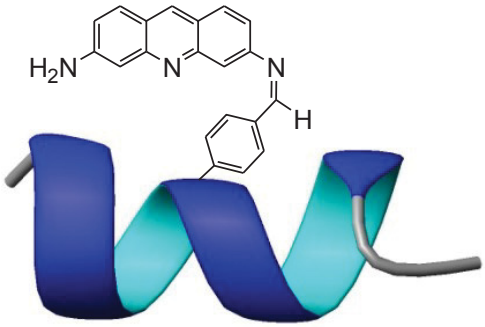


Figure 1: A schematic representation of the presented bioconjugated system for drug delivery.

References:

[1] R. V. J. Chari, *Acc. Chem. Res.* **2008**, *41*, 98–107.

[2] V. Indira Chandran, L. Matesic, J. M. Locke, D. Skropeta, M. Ranson, K. L. Vine, *Cancer Letters* **2012**, *316*, 151–156.

[3] R. Tavano, G. Malachin, M. De Zotti, C. Peggion, B. Biondi, F. Formaggio, E. Papini, *Biochim. Biophys. Acta (Biomembranes)* **2015**, *1848*, 134-144.

[4] C. Ding, J. Gu, X. Qu, Z. Yang, *Bioconjugate Chem.* **2009**, *20*, 1163–1170.

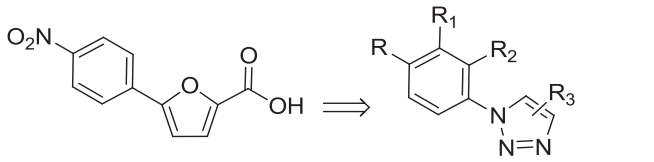
P61

A click chemistry approach to explore a new scaffold for potential antitubercular agents

Arianna Gelain[a], Matteo Mori[a], Stefania Villa[a], Laurent R. Chiarelli[b], Fiorella Meneghetti[a]

[a] *Dipartimento di Scienze Farmaceutiche, via L. Mangiagalli 25, 20133 Milano*
[b] *Dipartimento di Biologia e Biotecnologie "Lazzaro Spallanzani", via Ferrata 9, 27100 Pavia*
e-mail*: arianna.gelain@unimi.it*

Our ongoing researches are aimed to discover novel potential antitubercular agents targeting siderophore biosynthesis[1]. Previously, we identified compound **I** (Figure 1) as an MbtI (*Mycobacterium turbeculosis* Salicylate Synthase) inhibitor (% residual enzymatic activity = 18.2)[2] and we decided to gain an insight into the biological relevance of the heterocycle. Therefore, we initially substituted the furan with the triazole ring, privileging the brevity and the versatility of the synthetic pathway. Considering the activity of **I** and the related compounds, we designed and synthesized some new triazole derivatives (**1a-d** and **2a-d**, Figure 1), bearing opportune substituents. The two regioisomers obtained from each cycloaddition reaction were isolated and tested as MbtI inhibitors. The results will be presented and discussed.



I **1a-d** and **2a-d**

R = NO_2, CF_3
R_1 = CF_3
R_2 = Cl
R_3 = 4-COOH, 5-COOH

Figure 1: Structures of compound **I** and triazole derivatives

References:

[1] F. Meneghetti, S. Villa, A. Gelain, D. Barlocco, L. R. Chiarelli, M. R. Pasca, L. Costantino, *Curr. Med. Chem.*, **2016**, *23*, 4009-4026.

[2] L. R. Chiarelli, M. Mori, D. Barlocco, G. Beretta, A. Gelain, E. Pini, M. Porcino, G. Mori, G. Stelitano, L. Costantino, M. Lapillo, D. Bonanni, G. Poli, T. Tuccinardi, S. Villa, F. Meneghetti, *Discovery and development of novel salycilate synthase (MbtI) furanic inhibitors as antitubercolar agents*, submitted.

P62

Synthesis and the effect of telomeric PNA oligomers on cancer cells

C. Giannini,[a] D. Malpicci,[a] A. Previtali,[a] A. Kotlyar,[b] S. Deyev,[c] G. Proshkina[c]

[a]*Chemistry Department, University of Milan, 20133 Milan, ITALY*
[b]*Department of Biochemistry and Molecular Biology, George S. Wise Faculty of Life Sciences, Tel Aviv University, Ramat Aviv, Tel Aviv 69978, ISRAEL*
[c]*Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry, Russian Academy of Sciences, Miklukho-Maklaya St, 16/10, Moscow 117997, RUSSIA*
e-mail*: clelia.giannini@unimi.it*

Peptide nucleic acids (PNA) are oligonucleotide analogues which can recognize complementary sequences of DNA and RNA with high affinity and specificity.[1] This property of makes PNA useful in molecular biology, diagnostics and therapy.[2,3] The use of PNA in bioresearch is limited by low solubility of the compound under physiological conditions. Due to their low solubility at neutral (physiological pH) high quantities of PNA cannot be delivered to cells.[4] One way to address this challenge is to use liposomes as cargo carriers. We have recently showed that liposomes containing large quantities of colorful or toxic proteins and functionalized with the designed ankyrin repeat protein (DARPin), which targets human epidermal growth factor receptor 2 (HER2) can specifically stain and kill in sub-nanomolar concentrations cancer cells, overexpressing HER2. In the present communication we show that as many as thousands telomere PNA oligonucleotide (CCCTAACCCTAA or CCCTAACCCTAACCCTAACCCT) molecules can be encapsulated into a liposome (80-90 nm in diameter). The liposomes were functionalized with DARPin_9−29 that specifically binds to HER2 receptors overexpressed in SKBR-3 cells. These PNA-containing DARPin-functionalized are liposomes are shown to specifically eradicate in sub-nanomolar concentrations cancer cells overexpressing HER2. Specific eradication of the receptor-positive cells makes the DARPin-functionalized liposomes carrying large quantities of PNA a promising candidate for tumor detection and therapy.

References:

[1] P. E. Nielsen, M. Egholm, R. H. Berg, O. Buchardt, *Science* **1991**, *254*, 1497-1500.
[2] N. Winssinger, J. L. Harris, *Chem. Eur. J.* **2005**, *11*, 6792-6801.
[3] K. E. Lundin, L. Good, R. Strömberg, A. Gräslund, C. I. Smith, *Adv. Genet.* **2006**, *56*, 1-51.
[4] A. Gupta, R. Bahal, M. Gupta, P.M. Glazer, W.M. Saltzman, *J. Control. Release* **2016**, *240*, 302-311.

P63

Influence of the Dicationic Ionic Liquids (DILs) structure on the synthesis of cyclic carbonates

L. Guglielmero,[a] A. Mezzetta,[a] L. Guazzelli,[a] C.S. Pomelli,[a] C. Chiappe[a]

[a]*Dipartimento di Farmacia, Università di Pisa, Via Bonanno 33, 56126, Pisa, Italy*
e-mail: *luca.guglielmero@gmail.com*

In recent years carbon capture and storage (CCS), as well as CO_2 utilization, have become highly important challenges which the scientific community has demanded to address. CO_2 can be seen as a safe, abundant, renewable, and inexpensive C1 source for the formation of valuable chemicals.[1,2]

From the viewpoint of "green chemistry" and "atom economy", the development of efficient approaches which use CO_2 as raw material and convert it into high value chemicals such as organic carbonates (both in their cyclic and acyclic forms) is extremely desirable.[3] Organic carbonates are generally proposed as environmentally friendly solvents, gasoline additives, and starting material for the synthesis of polycarbonates.

Ionic liquids (ILs) have been proven as efficient homogeneous catalysts for the synthesis of cyclic carbonates. Many task-specific ILs, combined with Lewis acids [4], have been used in the formation of cyclic carbonates.

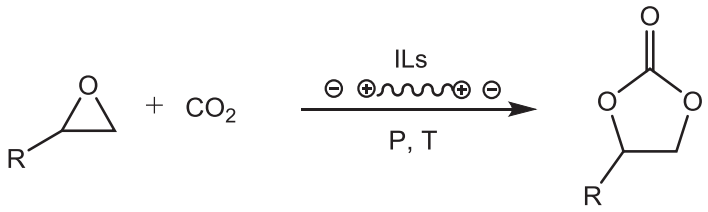


Figure 1: Schematic synthesis of cyclic carbonates.

In this context, we prepared and fully characterized (^{1}H-, ^{13}C-NMR, FT-IR) a series of different dicationic ionic liquids (DILs) and also studied their thermal behavior (thermogravimetric analysis and differential scanning calorimetry). The correlation between DILs structures (linker chain type, lateral alkyl chain length) and their catalytic activity in the cycloaddition reaction of CO_2 to different epoxides was investigated. The results obtained were then compared to the parent monocationic and dianionic compounds. Finally, a computational study was performed in order to rationalize the obtained results.

References:

[1] A. A. Lacis, G. A. Schmidt, D. Rind, R. A. Ruedy, *Science* **2010**, *330*, 356-359.
[2] W. H. Wang, Y. Himeda, J. T. Muckerman, G. F. Manbeck, E. Fujita, *Chem. Rev.* **2015**, *115*, 12936-12937.
[3] S. Klaus, M. W. Lehenmeier, C.-E. Anderson, B. Rieger, *Coordin. Chem. Rev.* **2011**, *255*, 1460-1479.
[4] D. Kim, Y.Moon, D. Ji, H. Kim, D.H. Cho, *ACS Sustain. Chem. Eng.* **2016**, *4*, 4591–4600.

P64

Graphene Quantum Dots based systems as HIV Inhibitors

D. Iannazzo,[a] A. Pistone,[a] C. Celesti,[a] S. Ferro,[b] L. De Luca,[b] R. Romeo,[b] S.V. Giofré,[b] A. M. Monforte, M. R. Buemi,[b] C. Pannecouque[c]

[a]*Department of Engineering, University of Messina, Contrada Di Dio, I-98166, Messina*
[b]*Department of Chemical, Biological, Pharmaceutical and Environmental Sciences, University of Messina, Viale Annunziata, I-98168 Messina*
[c]*Rega Institute for Medical Research, Katholieke Universiteit Leuven, Minderbroedersstraat 10, B-3000 Leuven*
e-mail*: diannazzo@unime.it*

Graphene quantum dots (GQD) are the next generation of carbon-based nanomaterials with great potential in drug delivery and target-specific HIV inhibition.[1] These nanomaterials have shown to be less toxic and more hydrophobic with respect to graphene and are endowed of stable strong fluorescence, thus allowing the efficient tracking of human cells in vitro.[2]
We investigated the antiviral activity of graphene-based nanomaterials, by using water soluble GQD synthesized by acidic oxidation and exfoliation of MWCNT and compared their anti-HIV activity with that exerted by reverse transcriptase inhibitors (RTI) conjugated with the same nanomaterial (Fig. 1). The antiretroviral agents chosen in this study CHI499 and CDF119 belong to a series of active non-nucleoside reverse transcriptase inhibitors (NNRTI).[3] From this study emerged the RTI-conjugated compounds as good candidate for HIV treatment. The target of action in the replicative cycle of HIV of the drug-conjugated samples GQD-CHI499 and GQD-CDF119 was also investigated by a time of addiction (TOA) method, showing for both conjugated samples a similar mechanism of action to that exerted by RTI drugs.

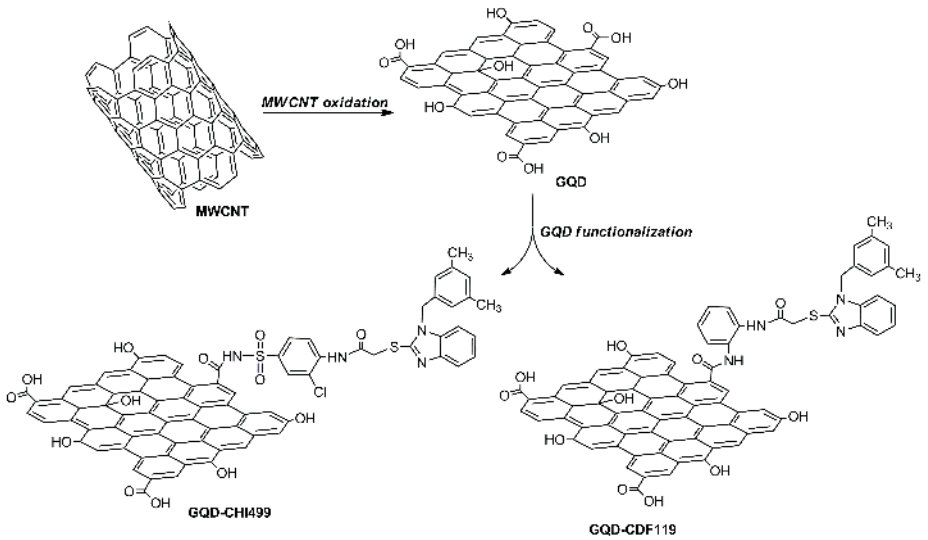


Figure 1: GQD and GQD-RTI conjugates.

References:

[1] D. Iannazzo, I. Ziccarelli, A. Pistone, *J. Mat. Chem. B,* **2017***,* 5, 6471–6489.
[2] D. Iannazzo, A. Pistone, M. Salamò, et al., *Int. J. Pharm.,* **2017,** *518*, 185–192
[3] A. M. Monforte, P. Logoteta, L. De Luca, et al., *Bioorg. Med. Chem.*, **2010**, *18*, 1702–1710.

P65

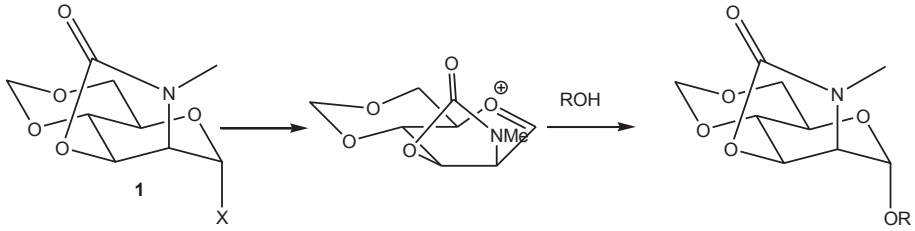
A Computational Study of the β-Mannosylation Reaction

L. Legnani,[a,b] L. Toma,[b] F. Compostella,[c] L. Morelli,[c] S. Ronchi,[c] M. A. Chiacchio[a]

[a] *Dipartimento di Scienze del Farmaco, Università di Catania, V.le Doria 6, 95125 Catania, Italy.*
[b] *Dipartimento di Chimica, Università di Pavia, Via Taramelli 12, 27100 Pavia, Italy.*
[c] *Dipartimento di Biotecnologie Mediche e Medicina Traslazionale, Università di Milano, Via Saldini* 50, *20133 Milano, Italy.*
e-mail*: laura.legnani@unipv.it*

Capsular polysaccharides (CPS) are found in pathogenic bacteria and are important antigens. Indeed, they can induce an immune response and the generation of specific antibodies [1]. An encapsulated human pathogen, that has caught our attention in the last years, is *Streptococcus pneumoniae* type 19F, a Gram-positive bacterium that can cause pneumonia, otitis media, and meningitis. Its CPS consists of a trisaccharide repeating unit, (→4)-β-D-ManpNAc-(1→4)-α-D-Glcp-(1→2)-α-L-Rhap-(1-PO_4^-→), with a phosphodiester bridge which connects the reducing end of one unit to the non-reducing end of the following one. In order to find a hydrolytically stable analogue of the natural repeating unit, we planned the synthesis of the corresponding phosphono derivative, linking the different monomeric units through glycosylation reaction.

The glycosylation reaction is a condensation between a glycosyl donor like **1** and a glycosyl acceptor (ROH) to form a glycosidic linkage, passing through an intermediate oxocarbenium ion (Scheme 1) [2].



Scheme 1.

In particular, in our synthetic route, we aim to directly link a β-mannosamine moiety to a disaccharide acceptor. However, when the reaction was experimentally performed, the undesidered α-derivative was predominantly obtained.

In order to clarify the reasons of the stereochemical outcome of the reaction, a complete mechanistic study of the β-mannosylation reaction of compound **1** was performed by locating all the intermediates and the transition states, using the Gaussian09 program package at the B3LYP/6-31G(d) level of calculation.

References:

[1] S. Segal, A. J. Pollard, *J. Br. Med. Bull.* **2005**, *72*, 65 – 81.
[2] D. Crich, *J. Org. Chem.* **2011**, *76*, 9193 – 9209.

P66

Nanoassemblies formed by ultrashort peptides for the vehiculation of hydrophobic molecules

S. Locarno,[a] S. Argentiere,[b] C. Lenardi,[b] F. Clerici[a]

[a]*Università degli Studi di Milano, via Venezian 21, Milan*
[b]*Università degli Studi di Milano, via Celoria 16, Milan*
e-mail*: silvia.locarno@unimi.it*

Over the last several decades, many papers report on spontaneous supramolecular assembly into ordered nanostructures with a variety of morphologies and this number is still expanding[1]. Among self-assembled supramolecules, peptides have attracted a great attention for biological applications due to their versatility and interesting chemical properties. In particular, our group is focused on the study of self-assembly of ultrashort peptides containing Cα-tetrasubstituted amino acids that are able to form soluble supramolecular structures in water, despite their hydrophobic nature[2].

Here we present a short alanine (Ala), α-aminoisobutyric acid (Aib) based pentapeptide (Figure 1) that self-assemble into nanostructure having a spherical shape and a diameter around 300-400 nm (DLS results). These nanoassemblies could be exploited to vehiculate in an aqueous environment hydrophobic molecules, using encapsulation approach. As a proof of concept, we selected Curcumin, a polyphenol isolated from the rhizome of Curcuma longa. Curcumin is a fluorescent polyphenol with antioxidant, anti-inflammatory and anti-tumorigenic properties. On the other hand, it shows a very poor bioavailability in vivo, due to its low aqueous solubility and instability, rapid metabolism, and clearance, that definitely limits its use both as a nutraceutical and as a drug.

Fluorescence studies on curcumin loaded nanoaggregates show that the molecular interactions between Curcumin and the pentapeptide induce a blue shift and a change in the shape of the emission and absorption peaks of the fluorophore. The nature of these interactions is further being investigated with different techniques in order to demonstrate and explain the encapsulation process of hydrophobic molecules.

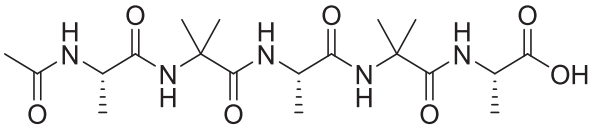


Figure 1: Ultra short Ala-Aib peptide.

References:

[1] C. Aleman, A. Bianco, M. Venanzi*, Peptide materials. From nanostructures to applications* **2013**, ISBN: 978-1-119-95373-9.

[2] A. Ruffoni, M. V. Cavanna, S. Argentiere, S. Locarno, S. Pellegrino, M.L. Gelmi, F. Clerici, *RSC Advances* **2016**, *6*, 90754 – 90759.

P67

Glicoamino OPEs: from *bioimaging* to nanotechnology

A. Mancuso, P. Bonaccorsi, T. M. G. Salerno, A. Barattucci

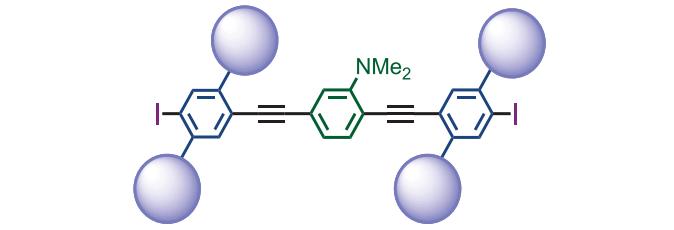
Dipartimento di Scienze Chimiche, Biologiche, Farmaceutiche ed Ambientali (ChiBioFarAm), Università di Messina, Viale F. Stagno d'Alcontres 31, 98166, vill. S. Agata - Messina

e-mail*: mancusoaurora@gmail.com*

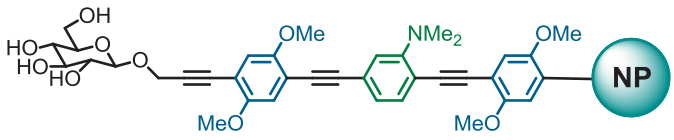
Oligo(phenylene-ethynylene)s (OPEs) are conjugated molecules that have found a wide range of applications in electrically conducting materials, bio-chemical sensors, and supramolecular assemblies.[1]

Recently, we reported the synthesis of end-only glucose functionalized OPEs where the synergy of the amino substituent at the central core, the chain length and the carbohydrate decoration, is the keystone for their use in the biological field. In fact, the balanced contribution of the hydrophilic (sugar) and hydrophobic (aryl conjugated system) moieties gives rise to the permeation of some of these OPEs to the cellular membrane, showing their potential uses as dyes in fluorescent imaging microscopy. Furthermore, the presence of the dimethylamino group is responsible of the generation of singlet oxygen, opening the way in their use as Photosensitizers in Photodynamic Therapy (PDT).[2]

Going on with our research, and in order to explore the possibility to improve their use in this kind of medical procedure, we have synthesized new OPEs, some by changing the chain substituents, *e.g.* by introducing heavy atoms that can improve the singlet oxygen production (Heavy Atom Effect) (**A** in Figure 1), and some others by desymmetrizing the chain. One of the aim of this last modification is to anchor our biocompatible systems to upconverting lanthanide nanoparticles (**B** in Figure 1).



A



B

Figure 1.

References:

[1] Kaliginedi, V.; Moreno-García, P.; Valkenier, H.; Hong, W.; García-Suárez, V. M.;.Buiter, P.; Otten, J. L. H.; Hummelen, J. C.; Lambert, C. J.; Wandlowski, T. *J. Am. Chem. Soc.,* **2012**, 134, 5262.

[2] Deni, E.; Zamarrón, A.;Bonaccorsi, P.; Carreño, M. C.; Juarranz, Á.; Puntoriero, F.; Sciortino, M.T.; Ribagorda, M.; Barattucci, A. *Eur. J. Med .Chem*. **2016**, 111, 58. Barattucci, A.; Deni, E.; Bonaccorsi, P.; Ceraolo, M. G.; Papalia, T.; Santoro, A.; Sciortino, M. T.; Puntoriero, F. *J. Org. Chem*. **2014**, 79, 5113.

P68

In vitro antiproliferative and proapoptotic activities of 2-oxazolidinone derivatives

R. Mancuso,[a] B. Armentano,[b] L. Frattaruolo, [b] M. Brindisi,[b] R. Curcio,[b] V. Rago,[b] R. Lappano,[b] M. Fiorillo,[b] V. Dolce,[b] M. Maggiolini,[b] B. Gabriele,[a] A.R. Cappello[b]

[a] *Laboratory of Industrial and Synthetic Organic Chemistry (LISOC), Department of Chemistry and Chemical Technologies, University of Calabria, Via Pietro Bucci 12/C, 87036 Arcavacata di Rende (CS), Italy.* [b] *Department of Pharmacy, Health and Nutritional Sciences, University of Calabria, Via Pietro Bucci, 87036 Arcavacata di Rende (CS), Italy*
e-mail*: raffaella.mancuso@unical.it*

Oxazolidinones are synthetic heterocyclic compounds endowed with antibacterial, antifungal, antidiabetic, anticonvulsant and anticancer activity[1].

In this communication, we evaluated the anticancer properties of 2-oxazolidinone derivatives **3**, synthesized through an auto-tandem catalysis process (Figure 1),[2] on estrogen receptor-positive breast cancer (MCF-7) and uterin cervix adenocarcinoma (HeLa) human cells.

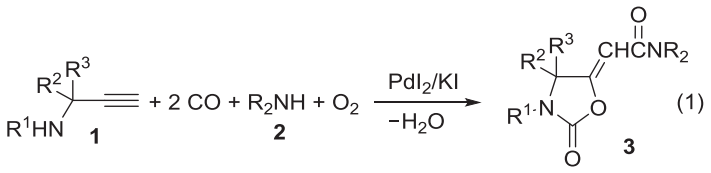


Figure 1.

2-Oxazolidinones **3** were prepared in good yields by reacting disubstituted 2-ynylamines **1**, secondary amines **2**, and oxugen at 100 °C and under 20 atm of a 4:1 mixture of CO-air, in the presence of PdI_2 (1%), KI (10%), and H_2O (5 equiv).

Oxazolidinone derivatives **3** displayed an interesting anti-proliferative activity. Treatment with oxazolidinones **3** elicited the highest effect by reducing both MCF-7 and HeLa cells viability, in a dose-dependent manner, with half-maximal inhibitory concentration values of 17.66 μM and 31.10 μM, respectively. Oxazolidinones **3** treatment induced cell cycle arrest in G1/S phase and apoptosis by activating caspase-9 and generating reactive oxygen species (ROS). Furthermore, they induced mitochondrial membrane damage followed by cytochrome c release into the cytosol, suggesting that apoptosis occurs in a mitochondrial-dependent pathway.

The cytotoxic effect promoted by oxazolidinone drivatives **3** was prevented by pretreating both cell lines with vitamin E, suggesting that oxidative stress has a pivotal role in 2-oxazolidinones-mediated cell death. Differently from doxorubicin, a widely used anti-cancer drug, employed as a control in our experiments, 2-oxazolidinones **3** treatment did not induce any antiproliferative effects on non-tumorigenic breast epithelial (MCF-10A) cells. Hence, 2-oxazolidinone derivatives **3** can selectively promote cancer cell death.

References:

[1] J. Furtado Campos, M. C. Pereira, *Pharmacological Reports* **2017**, *69*, 633–641.

[2] (a) B. Gabriele, P. Plastina, G. Salerno, R. Mancuso, M. Costa, *Org. Lett,* **2007**, *9*, 3319-3322, (b) R. Mancuso, A. Maner, I. Ziccarelli, C. Pomelli, C. Chiappe, N. Della Ca, L. Veltri, B. Gabriele, *Molecules* **2016**, *21*, 897.

P69

Deoxycholic acid-functionalized dimeric and hexameric GdAAZTA-agents for DCE-MRI applications

J. Martinelli,[a] L.Tei,[a] G. Gambino,[a] M. Botta,[a] D. Longo,[b] L. Consolino[b]

[a]*Dipartimento di Scienze e Innovazione Tecnologica, Università del Piemonte Orientale, Viale T. Michel 11, 15121 Alessandria, Italy.*

[b]*Department of Molecular Biotechnology and Health Sciences, Molecular Imaging Center University of Torino, Via Nizza 52, 10126, Torino, Italy*

e-mail*: jonathan.martinelli@uniupo.it*

Multimeric Gd-chelates with medium molecular weight (3-5 kDa) can show MRI contrast enhancement over a wide range of magnetic fields (1-3 T).[1] With an appropriate targeting vector, they can carry several Gd units to the target. Our study aimed at synthesizing a bifunctional hexameric chelate conjugated to a deoxycholic acid for binding to HSA.[2] **AAZTA$_6$-MADEC** was prepared by attaching three dimeric AAZTA-units bearing an isothiocyanate group (**AAZTA$_2$-NCS**)[3] to 1,4,7,10-tetraazacyclododecane (cyclen), followed by conjugation to methyl 3-aminodeoxycholate (MADEC) on the remaining amine of cyclen (*Figure*). Deprotection of all carboxylic groups yielded the hexameric ligand, whose complex **(GdAAZTA)$_6$-MADEC** was obtained by reaction with $GdCl_3$. Also the **(GdAAZTA)$_2$-MADEC** dimer was synthesized aiming at evaluating an intermediate system between the larger hexameric probe and the smaller monomeric one.

The magnetic field-dependence of relaxivity r_1 for the hexamer and its HSA-adduct, and the binding affinity to HSA were investigated. r_1 (298 K, 1 T) is 26.5 $mM^{-1}\,s^{-1}$ (per Gd), compared to 13.9 $mM^{-1}\,s^{-1}$ for the monomer,[2] but the binding affinity to HSA resulted lower than that of **GdAAZTA-MADEC** ($K_A = 2.7\times10^3$ *vs*. $8.9\times10^5\ M^{-1}$) due to the hindering of the targeting vector by the complexes at short distance. *In vivo* angiographic images and tumour contrast enhanced images were acquired on tumour-bearing mice on benchtop 1T-MRI scanner, showing that the injection of the same dose of Gd results in similar contrast enhancement with respect to the monomeric system.[2]

The **(GdAAZTA)$_2$-MADEC** dimer is expected to show a MRI contrast enhancement higher than the monomer thanks to the two Gd-complexes per system and to the stronger interaction with HSA. Such a ditopic Gd-chelate with an appropriately short and hydrophilic spacer would retain a short reorientational time and the other relaxometric parameters optimized, thus showing a significant relaxivity gain even above 1.5 T. This is particularly important when considering the high magnetic field strengths of the MRI scanners exploited at present for clinical diagnosis (1.5-3 T, up to 7 T) that allow higher signal-to-noise ratio and better resolution.

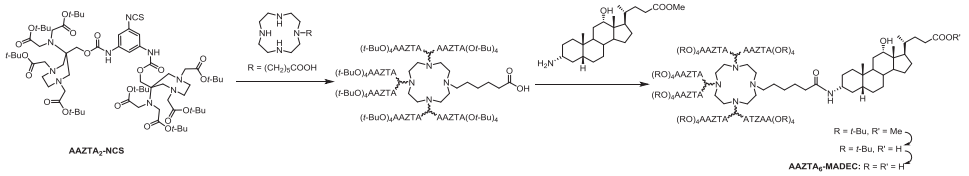


Figure 1: synthesis of ligand **AAZTA$_6$-MADEC.**

References

[1] P. Caravan *et al.*, *Contrast Media Mol. Imaging* **2009**, *4*, 89-100.

[2] D. L. Longo *et al.*, *Biomaterials* **2016**, *75*, 47-57.

[3] G. Gugliotta *et al.*, *Org. Biomol. Chem*. **2010**, *8*, 4569-4574.

P70

Microfluidic Photoreactor Enables 2-Methylbenzophenone Light-Driven Reactions with Superior Performance

J. Mateos, A. Cherubini-Celli, T. Carofiglio, M. Bonchio, N.Marino, X. Companyó, and L. Dell'Amico

Università degli Studi di Padova, Via Marzolo 1, 35131 Padova
e-mail*: javier.mateoslopez@unipd.it*

Synthetic photochemistry is emerging as a key enabling technology for the construction of molecular architectures. Recently, the implementation of continuous flow microfluidic photoreactors (MFP) in organic chemistry transformations enabled the optimisation and development of new light-driven reactions.[1]

The use of 2-methylbenzophenones (2-MBPs) as competent reaction partners for diverse electron-poor species has been widely reported. The chemistry is based on the ability of such molecule to generate highly reactive hydroxy-*o*-quinodimethane (photoenol) intermediate upon light irradiation (Figure 1a).

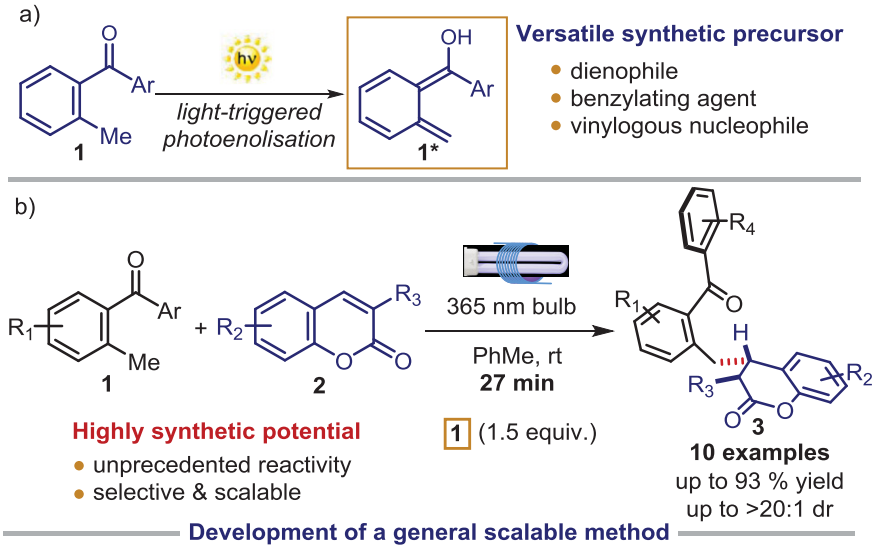


Figure 1: a) The photochemical reactivity of 2-methylbenzophenones **1** and b) unprecedented reactivity of **1** with coumarins **2** under the developed MFP setup.

Here is reported how an easy microfluidic photoreactor setup was pivotal to access the direct photo-benzylation of coumarin derivatives (figure 1b), that represent a new class of reaction partners for 2-MBPs.[2] By using this methodology, coumarin dimerisation was successfully circumvented, selectively yielding a broad range of 4-benzylated-2-chromanones with high diastereocontrol and up to 93% isolated yield. In addition, the protocol was robust for large-scale synthesis.

References:

[1] D. Cambié, C. Bottecchia, N. J. W. Straathof, V. Hessel, T. Noël, N. *Chem. Rev* **2016**, *116*, 10276-10341
[2] J. Mateos, A. Cherubini-Celli, T. Carofiglio, M. Bonchio, N. Marino, X. Companyó, L. Dell'Amico, *Chem. Commun.* **2018**, DOI: 10.1039/c8cc01373j.

P71

Cannabis through the looking glass: ‘‘Inverted Chirality Columns Approach’’ for chiral recognition and determination of extreme enantiomeric excess of naturally occurring cannabinoids

G. Mazzoccanti,[a] O. H. Ismail[a]
[a]*Dipartimento di Chimica e Tecnologie del Farmaco, Sapienza Universita` di Roma, p.le A. Moro 5, 00185 Roma, Italy.*
e-mail*: giulia.mazzoccanti@uniroma1.it*

Cannabinoids (or phytocannabinoids) are one of the constituents of marijuana, the crude drug derived from the plant *Cannabis sativa* L. A fascinating feature of phytocannabinoids is that most of them are chiral. In nature, chiral natural products are usually produced in optically pure form; however, occasionally both enantiomers are formed. It becomes evident, therefore, the importance of determination of the enantiomeric purity (namely, enantiomeric excess, *ee*) in naturally occurring samples, in both single and in more complex mixtures, as well as, the importance of the evaluation of stereochemical efficiency of synthetic pathways to unnatural chiral cannabinoid analogues. The first problem we faced in stereoselective analysis of Cannabis plant extracts was that vegetable extracts are highly enriched complex mixtures and often the minor enantiomers or the racemates, are not available as reference samples. To overcome this limitation, our group has previously developed a method for the identification of enantiomeric couples and accurate quantification of the minor enantiomer in trace analysis of natural products, named the ‘‘Inverted Chirality Columns Approach’’ (ICCA) [1,2] . We propose to the scientific community, for the first time, an efficient protocol of general applicability for the control of stereochemistry in highly enriched chiral natural products by using cutting-edge techniques such as the enantioselective “*e*” Ultra High Performance Supercritical Fluid Chromatography (*e*UHPSFC), based on the use of the new sub-2-µm Whelk-O1 chromatographic columns, developed in our laboratories. This method is capable of predicting the chromatographic behavior for those compounds not available as the racemate (see, for example, (–)-cannabidiol and (–)-cannabidivarin) and to determine the enantiomeric excess (ee) of (–)-Δ^9-THC in medicinal marijuana (Bedrocans). The *ee* was high (99.73%), but the concentration of the (+)-enantiomer (0.13_5%) was not negligible, and it is worth a systematic evaluation of bioactivity[3]. Therefore, it can be considered as an useful tool for anyone who faces the item of the evaluation of the optical purity of chiral natural products or those coming from asymmetric synthesis, where the classical analytical methods are seriously hampered.

References:

[1] E. Badaloni, et Al. *Anal. Chem*., **2007**, *79*, 6013 – 6019.
[2] E. Badaloni, et Al. *J. Chromatogr. A*, **2010**, *1217*, 1024 – 1032 .
[3] G. Mazzoccanti et Al. *Chem. Commun.* **2017**, *53*, 12262 – 12265.

P72

Two-dimensional Silver ion adsorption Thin Layer Chromatography in the study of the composition of Paulownia tomentosa wood fatty acids and triglycerides

M. Mecca,[a] T. Rosenau,[b] S. Böhmdorfer,[b] M. D'Auria[a]

[a]*Department of Science, University of Basilicata, Viale dell'Ateneo Lucano 10, 85100 Potenza*

[b]*Division of Chemistry of Renewable Resources, University of Natural Resources and Life Sciences, Konrad Lorenz-Straße 24, 3430 Tulln*

e-mail*: marisabelmecca@libero.it*

Wood raw material undergoes appropriate working processes that transform them into semi-finished products for industry. All of these processes can modify the property and performance of wood products influencing, as in case of thermo-treatment, some structural compounds and also the secondary metabolites, such as extractives. Despite the numerous investigations of the effect of thermo-treatment on different wooden plant characteristics, the composition and the relative variation of extractives of *Paulownia tomentosa* wood under thermal effect is an underexplored area. Wood material was previously thermo-treated at 180 °C, 200 °C and 210 °C for 3 hours using a press vacuum technology. Extractives of untreated and thermo-treated wood material achieved with Accelerated solvent extraction (ASE) techniques[1] with ethanol/toluene mixture were obtained. Then the extracts were chromatographed by using thin layer chromatography[2].

The TLC technique on silica gel with silver nitrate ($AgNO_3$-TLC) separates fat TGs according to the degree of unsaturation because of weak interactions between the π electrons of the double bonds and the silver ions[3]. Other factors, such as geometric configuration and chain length, are also involved in TG separation on silica gel. In this research using two-dimensional TLC, we have developed a system which allows the complete separation of all known fatty acids and triglycerides components of wood extractives, and thus also allows an estimate of changes due to heat treatment: two-dimensional TLC through the use of esterification with $NaOCH_3$ and $AgNO_3$-TLC.[4]

By initial separation on the TLC, spray with sodium methoxide, impregnation with silver nitrate and development in the second direction, a fingerprinting of the triglycerides of the extractives could be obtained, and a semi-quantitative estimation of individual triglycerides made.

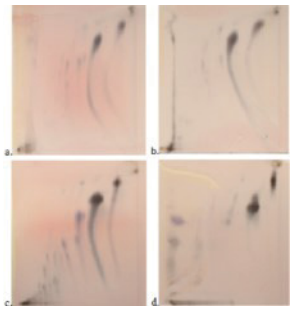


Figure 1: 2-D TLC of extractives of untreated (a) and thermo-treated (b,c,d) *Paulownia tomentosa*

References:

[1] K. B. Thurbide, D. M. Hughes, *Industrial & engineering chemistry research* **2000**, *39*, 3112-3115.
[2] D. Abramson, M. Blecher, *Journal of Lipid Research* **1964**, *5*, 628-631.
[3] J. Myher, A. Kuksis, L. Marai, *Journal of Chromatography* **1988**, *452*, 93-118.
[4] M. J. Fraga, J. Fontecha, L. Lozada, *Journal of Agricultural and Food Chemistry* **1998**, *46,* 1836-1843.

P73

Enzymatic synthesis of ©-glutamyl derivatives catalyzed by a new mutant ©-glutamyltransferase with improved transpeptidase activity

M. Massone,[a] C. Calvio,[b] G. Speranza,[a] C. F. Morelli[a]

[a]*Università degli Studi di Milano, Dipartimento di Chimica via Golgi, 19 -20133 Milano*
[b]*Università degli Studi di Pavia Dipartimento di Biologia e Biotecnologie "Lazzaro Spallanzani" via Ferrata, 9 – 27100 Pavia*
e-mail*: carlo.morelli@unimi.it*

Despite their potential applicative interest as biologically active compounds and as flavor enhancers, ©-glutamyl derivatives are commercially underexploited compounds. This is mainly due to the difficulties connected with their supply at a reasonable cost. As a consequence, enzymatic approaches to their preparation, based on the use of ©-glutamyltransferases (GGTs), have been proposed[1] to circumvent both the low-yielding extractive procedures from natural sources and the troublesome chemical synthesis, rendered uneconomical by the need of protection and deprotection steps.

GGTs catalyze the transfer of a ©-glutamyl moiety from a donor substrate (e.g. glutathione) to the primary amino group of an acceptor compound in a so-called transpeptidation reaction, through the formation of a ©-glutamyl-enzyme intermediate. However, also the use of GGTs as biocatalysts is not free from drawbacks. In addition to the transpeptidase activity, GGTs show a non-negligible hydrolase activity towards both the donor substrate and the newly formed transpeptidation product, affording irreversibly glutamic acid.[2]

In our ongoing studies on bacterial GGTs, we found that the presence of the lid loop – a short amino acids sequence covering the active site in most of the known GGTs – not only affects substrate selection, but also modulates hydrolase/transpeptidase activities.[3] Within the TailGluTran Project,[4] aimed at the development of mutant GGTs with improved transpeptidase activity, is currently under investigation a mutant enzyme obtained by inserting the sequence of the lid loop on the structure of a GGT naturally lacking it. The mutant enzyme shows promising high transpeptidase activity with respect to wild type counterparts and represents a starting point for further modifications in the search of a suitable biocatalyst intended for preparative purposes.

References:

[1] G. Speranza, C. F. Morelli, *J. Mol. Catal. B: enzymatic*. **2012**, *84*, 65-71..
[2] C. F. Morelli, C. Calvio; M. Biagiotti, G. Speranza, *FEBS J*. **2014**, *281*-232-245.
[3] C. Calvio, F. Romagnuolo, F. Vulcano, G. Speranza, C. F. Morelli, *Enz. Micr. Technol*. **2018**, *114*, 55-62.
[4] The TailGluTran Project is founded by Fondazione Cariplo, Bando 2016 sulle Bietecnologie Industriali e la Bioeconomia, n. 2016-0741.

P74

Extraction of Phenolic Compounds from Olive Oil Industrial By-Products using Deep Eutectic Solvents

M. Nardi,[a,b] P. Costanzo,[c] M. L. Di Gioia,[d] L. Maiuolo,[b] A. Procopio,[c] G. Sindona[b]

[a]*Dip.to di Agraria, Università Telematica San Raffaele, Roma, Italy*
[b]*Dip.to di Chimica e Tecnologie Chimiche, Università della Calabria, Arcavacata di Rende, CS, Italy*
[c]*Dip.to di Scienze della Salute, Università Magna Græcia di Catanzaro, Italy*
[d]*Dip.to di Farmacia e Scienze della Salute e della Nutrizione, Università della Calabria, Arcavacata di Rende, CS, Italy*
e-mail*: monica.nardi@unical.it*

The idea of turning ‘‘waste to wealth” by means of industrial food residues can considerably contribute to sustainable development. The by-products of olive oil industry are an extraordinary source of bioactive phenolic compounds that are receiving great interest due to their antimicrobial and antioxidant activity, strongly related to cancer prevention, inflammatory disorders and cardiovascular diseases.[1]

One of the key principle in Green Chemistry is to substitute or minimize the use of hazardous solvents. In the last decade, a new generation of green solvents to be used both in synthetic transformations and in extraction processes has been developed. Deep eutectic solvents (DESs) are solvents with excellent properties such as negligible volatility at room temperature, that are water miscible, non-flammable, and highly viscous. They have attracted increasing attention in chemistry for the extraction and separation of target bioactive compounds from various natural samples.

In continuation of our interest towards development of useful green methodologies,[2-4] in this study we report a novel and sustainable approach for the extraction and derivatization of phenolic compounds from olive oil industry by-products (Figure 1) using deep eutectic solvents under microwave assistance.

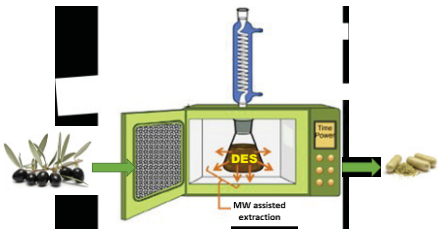


Figure 1: MW-assisted extraction of phenolic compounds in DESs.

This procedure offers an efficient, safe, sustainable, and cost effective alternative to conventional methods for extraction and derivatization of bioactive compounds from olive oil industry by-products.

References:

[1] M. I. Alarcón Flores, R. Romero-González, A. Garrido Frenich, J. L. Martínez Vidal, *Food Chem*, **2012**, 134(4), 2465–2472.

[2] P. Costanzo, S. Bonacci, L. Cariati, M. Nardi, M. Oliverio, A. Procopio, *Food Chem*, **2018**, *245*, 410-414.

[3] M. Nardi, S. Bonacci, L. Cariati, M. Oliverio, G. Sindona, A. Procopio, *Food & Function,* **2017**, *8*, 4684-4692.

[4] A. Procopio, S. Alcaro, M. Nardi, M. Oliverio, F. Ortuso, P. Sacchetta, D. Pieragostino, G. Sindona, *J Agr Food Chem*, **2009**, *57(23),* 11161-11167.

P75

Development of Thermomechanical Selective Scissions for Recycling of Rubber Waste

G. Pastore,[a] S. Gabrielli,[a] E. Marcantoni,[a] A. Menchi,[a] F. V. Rossi,[a] E. Ladikos[b]

[a]*University of Camerino, School of Science and Technology, Chemistry Division, Via S. Agostino 1, 62032, Camerino (Italy)*

[b]*Producta Sas di Ladikos Eleftherios & C., Via F. Giulietti 4, 62010 Montelupone (MC)*

e-mail*: genny.pastore@unicam.it*

The rubber elastomers are used in our daily lives. Huge amounts of them are continually manufactured causing a big problem in the whole world regarding the discarded end-of-life. Jumping from linear economy, in which 'take-make-dispose' model is followed, to a circular one, where products are designeted to be recycled, recycling has become a very important issue in terms of limiting the use of finite resource and the need to manage waste disposal.[1] Usually recycling process for rubber waste is complex, and introduction of new solutions could be achieved by an appropriate process.

In the last years, the problem of recycled rubber was attempted to be solved by several methods leading to products ready to be used in determined conditions, in most economic and ecological way.[2] Often, the necessary devulcanization process, used for recycling rubber waste, leads to a totally or partially cleavage of mono-, di-, and polysulfide crosslink.[3] During this process the crosslink density is reduced, but also carbon-carbon bonds undergo cleavage, and free radicals are produced that can cause the formation of main chain radicals. In order to be able to add the recycled rubber to the vergin polymer in specific amounts and subjected to the vulcanization process for obtaining new rubber profiles, selective cleavage of C-S and S-S bond devulcanization must be achieved (Figure 1).[4]

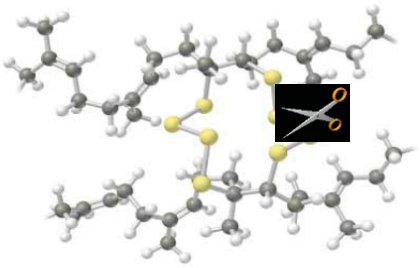


Figure 1: – Selective scission devulcanization process

We have determined the percentage of devulcanization the crosslink density (CLD) before and after the process,[5] therefore the chemical agent necessary to have a selective cleavage was identified. The addition of a chemical agent in the thermomechanical process leads to a better devulcanization and the recycled product could be vulcanized again.

References:

[1] Y. L. Jiun, C. T. Tze, U. Moosa, A. T. Mou'ad, *Polym. Polym. Compos.* **2016**, *24*, 735-741.

[2] M. Myhre, D. A. MacKillop, *Rubber Chem. Techn.* **2002**, *75*, 429-474.

[3] M. Meysami, C. Tzoganakis, P. Mytyala, S. H. Zhu, M. Bulsari, *Int. Polym. Proc.* **2017**, *32*, 183-193.

[4] M. J. Anu, G. Benny, K. N. Madhusoodanan, A. Rosamma *Rubber Sci.* **2016**, *29*, 62–100.

[5] S. O. Movahed, A. Ansarifar, G. Zohuri, N. Ghaneie, Y. Kermany1 *J. Elastomers Plast.* **2016**, 48, 122-144.

P76

Evaluation of the stereochemical lability of some benzocycloheptene-based drugs endowed with potentially modulable planar chirality

F. Buonsenso,[a] R. Cirilli,[b] M. Colombo,[c] A. Marchesi,[c] C. Panella,[b] M. Pierini[a]

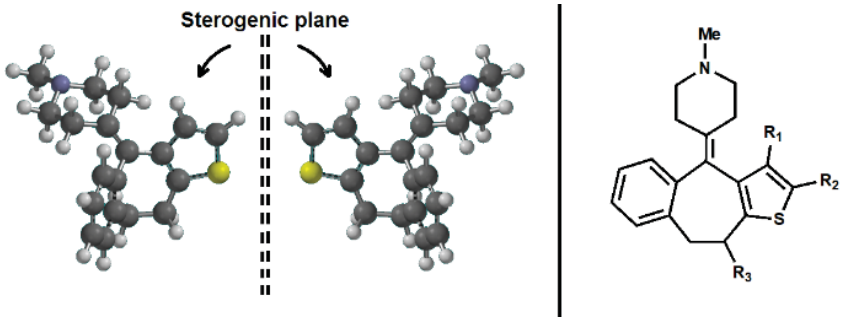
[a]*Dip. di Chimica e Tecnologie del Farmaco, "Sapienza, Università di Roma", Piazzale Aldo Moro 5, 00185, Rome, Italy*

[b]*Istituto Superiore di Sanità, Centro Nazionale per il Controllo e la Valutazione dei Farmaci, Viale Regina Elena 299, 00161, Rome, Italy*

[c]*Laboratori Alchemia S. r. L., via San Faustino 68, 20134, Milano, Italy*

e-mail*: marco.pierini@uniroma1.it*

It is well known that stereoisomerism may play exceptional effects in the case of drugs with regard to the expression of pharmacodynamic and/or pharmacokinetic properties [1]. As an example, drugs containing a stereocenter or a stereogenic axis or plane exist in two enantiomeric forms, and it is strongly probable that one of them would manifest pharmacologic and/or toxic effects significantly different with respect to the other one [2]. This is the reason why, in recent years, drug stereochemistry has become a significant issue for both pharmaceutical industry and regulatory authorities [1]. Relevant to such a subject is also the unfavourable effect that the possible lability of a stereogenic element possessed by drugs administrated as single enantiomers can have on the pharmaceutical activity, since, in the biological environment, the manifestation of stereochemical fragility could give rise to racemization. With attention focused on this matter, here we present a both experimental and theoretical study addressed to analyse the configurational lability possessed by the enantiomers of some popular second-generation antihistaminic drugs, endowed with a central seven-membered benzo-cycloheptadiene non-planar ring, which gives rise to chirality (Figure 1). The energy barrier that opposes the inversion of the tricyclic scaffold in the presence of some different R_1, R_2 and R_3 substituents has been investigated by resorting to Dynamic–HPLC, Dynamic–HNMR and off-column racemization (monitored by decay of the CD signal) techniques, as well as through assessments based on molecular modelling approaches. Interesting indications have been obtained about the possibility to design structural modifications suitable to allow an accurate control of the stereolability characterizing the tricyclic framework.



$R_1 = R_2 = R_3 = H$

Figure 1: Essential structure of the investigated benzocycloheptene-based drugs.

[1] G. B. Baker, T. I. Prior, *Ann. Med.* **2002**, *34*, 537 – 543.

[2] R. T. Coutts, G. B. Baker, *Chirality* **1989**, *1*, 99 – 120.

P77

Synthesis of a decahydroquinoxaline-based new Chiral Brønsted Acid

V. M. Abbinante[a], T. Benincori[a], M. Benaglia[b], S. Rossi[b] , M. Orlandi[b]

[a] *Università degli Studi dell'Insubria, Dipartimento di Scienza e Alta Tecnologia, via Valleggio, 11 - 22100, Como, Italy*
[b] *Università degli Studi di Milano, Dipartimento di Chimica, via Golgi, 19 - 20133, Milano, Italy*
e-mail*: vmabbinante@studenti.uninsubria.it*

Chiral Brønsted Acids (CBA) emerged as efficient catalysts for a wide range of stereoselective transformations involving the formation of C-O, C-N and C-C bonds.[1] Despite numerous chiral CBAs have been reported, almost all of them rely on the scaffolds of BINOL and SPINOL. So the development of new cheaper and easy-to-synthetize alternative scaffolds is therefore highly desirable.

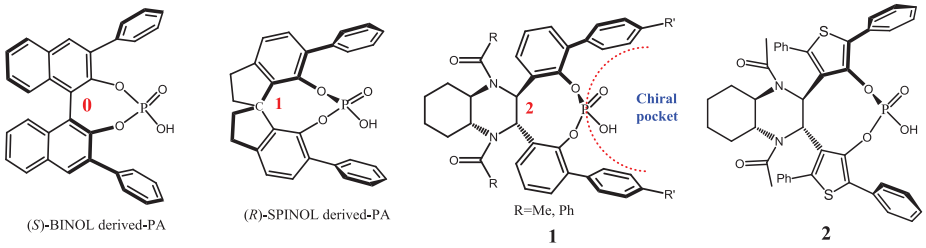


Figure 1: Most used CBAs compared with new decahydroquinoxaline-based ones.

Recently, our group investigated a new family of CBAs **1,** based on the structure of the decahydroquinoxaline, which represents a scaffold characterized by a two-carbon spacer. These compounds were employed as organocatalysts in some preliminary stereoselective reactions, affording the products with moderate to good levels of enantioselectivity.[2] In order to investigate the role in the catalytic processes of the chiral pocket's size, we designed the CBA **2** in which the phenyl groups in the positions 2 and 3 of the decahydroquinoxalinic ring are substituted with two thiophene units. Here we reported the different strategies followed for its synthesis and some preliminary stereoselective catalytic results.

References:
[1] T. Akiyama, K. Mori, *Chem. Rev.* **2015**, *115*, 9277.
[2] M. Orlandi, M. Benaglia, F. Cozzi, Unpublished results.

P78

Trichlorosilane: a versatile reagent for nitroalkanes transformations

M. Pirola,[a] M. Orlandi,[a] M. Benaglia[a]

[a]*Università degli Studi di Milano, Via Golgi 19, 20133 Milano*
e-mail*: margherita.pirola@unimi.it*

Nitroalkanes have proven to be a valuable and versatile class of compounds in organic synthesis. Transformations that permit the interconversion of nitro groups into other functionalities are therefore of primary importance as they potentially broaden the utility of nitroalkanes as intermediates in synthesis.[1]

Our group has recently reported an unprecedented metal-free protocol for the reduction of nitro derivatives into amines based on the use of trichlorosilane ($HSiCl_3$)[2] an inexpensive and readily commercially available compound produced as a waste by the silicon industry. Specifically, it was observed that nitro compounds could be reduced to the corresponding amines when reacted in the presence of $HSiCl_3$ and a tertiary amine under mild reaction conditions. A systematic screening of substrates revealed that this reduction protocol is applicable to both aryl and aliphatic nitro compounds, and was successfully employed in the total synthesis of complex molecules.[3] However, depending on the nature of the aliphatic substrate, the corresponding cyano derivative could be observed as a substantial reaction byproduct.

Herein we report our efforts for the optimization of this protocol that resulted in the chemoselective, divergent transformation of aliphatic nitro compounds into the corresponding amine or cyano derivative by fine tuning of the reaction conditions. Specifically, by using 8 equiv. of triethylamine (TEA) or diisopropylethylamine (DIPEA) at –20 °C, it is possible to obtain phenylacetonitrile starting from phenylnitroethane, with up to 80% conversion. On the other hand, using 3.5 equivalents of a sterically hindered base, such as pentamethylpiperidine (PMP), leads to the formation of phenylethylamine in up to 98% conversion (unpublished results).

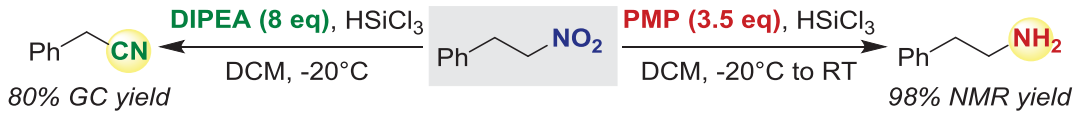


Figure 1: divergent transformation of aliphatic nitro compounds into amine or cyano derivatives.

The reduction protocol relies on the use of inexpensive and readily available chemicals, features a simple experimental procedure, and is performed under mild conditions. Additionally, the use of transition metals typically used for the reduction of nitro compounds is avoided, which provides an environmentally friendly reaction that excludes the contamination of the products by potentially toxic metal impurities.

References:

[1] Review: M. Orlandi, D. Brenna, R. Harms, S. Jost, M. Benaglia, *Org. Process Res. Dev.* **2018**, *22*, 430– 445.
[2] M. Orlandi, F. Tosi, M. Bonsignore, M. Benaglia, *Org. Lett.* **2015**, *17*, 3941 – 3943; M. Orlandi, M. Benaglia, F. Tosi, R. Annunziata, F. Cozzi, *J. Org. Chem.* **2016**, *81*, 3037 – 3041.
[3] S. Rossi, M. Benaglia, R. Porta, L. Cotarca, P. Maragni, M. Verzini, *Eur. J. Org. Chem.* **2015**, *11*, 2531 – 2537.

P79

Organocatalytic α-trifluoromethylthiolation of carbonyl compounds

S. Rossi,[a] M. Benaglia[a]

[a]*Dipartimento di Chimica – Università degli Studi di Milano, via Golgi 19, 20133 Milano*
e-mail*: sergio.rossi@unimi.it*

The incorporation of a SCF_3 group into organic molecules is a topic of great interest, especially for the pharmaceutical and agrochemical industries.[1] Due to its high lipophilicity and high electron-withdrawing character (Hansch lipophilicity parameter πR =1.44 vs πR= 0.88 for CF_3),[2] the SCF_3 moiety represents a powerful opportunity to influence the pharmacokinetics properties of a drug molecule increasing the transmembrane permeation.

In the last few decades, numerous methods for the introduction of a trifluoromethylthio group into organic compounds have been reported;[3] however, only few examples of efficient methods to introduce catalytically and directly the SCF_3 group in alpha- position of a carbonyl function were reported.

In this contest, we have developed a novel approach for the organocatalytic α-trifluoromethylthiolation of unactivated ketones, starting from the corresponding silylenol ethers using N-(trifluoromethylthio)saccharin as trifluoromethylthiolating reagent that is activated by the presence of catalytic amounts of a Lewis base (Figure 1).[4] Tetrahydrothiophene was identified as the best organocatalyst and it was successfully employed to promote the synthesis of different α-trifluoromethylketones; the reaction has been performed under a traditional batch methodology and under continuous flow conditions. In general, yields obtained using the traditional batch process were higher than those observed when the reaction was performed in micro(meso)reactors.

However, short reaction times, higher productivity and higher space time yields were observed when a flow system process was employed. Preliminary DFT calculations were also performed in order to elucidate the mechanism of the reaction; recent experimental results and a proposed catalytic cycle of the reaction will be presented and discussed.

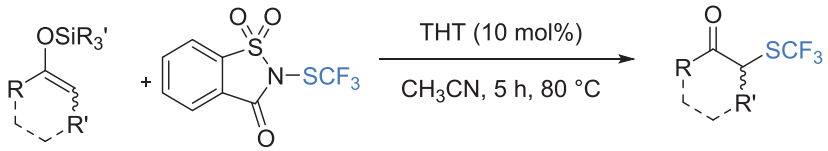


Figure 1: Organocatalytic α-trifluoromethylthiolation of carbonyl compounds

References:

[1] W. K. Hagmann, *J. Med. Chem*. **2008**, *51*, 4359-4369.

[2] C. Hansch, A. Leo, R.W. Taft, *Chem. Rev*. **1991**, *91*, 165-195.

[3] S. Rossi, A. Puglisi, L. Raimondi, M. Benaglia, *ChemCatChem* **2018**, *doi: 10.1002/cctc.201800170.*

[4] S. S. Abubakar, M. Benaglia, S. Rossi, R. Annunziata, *Catalysis Today* **2018**, *308*, 94-101.

P80

Arylazo sulfones in visible-light driven allylation and vinylation reactions

A. Dossena,[a] L. Onuigbo,[a] H. I. M. Amin,[b] A. Ahmed,[b] S. Sampaolesi,[c]

S. Protti,[a] M. Fagnoni[a]

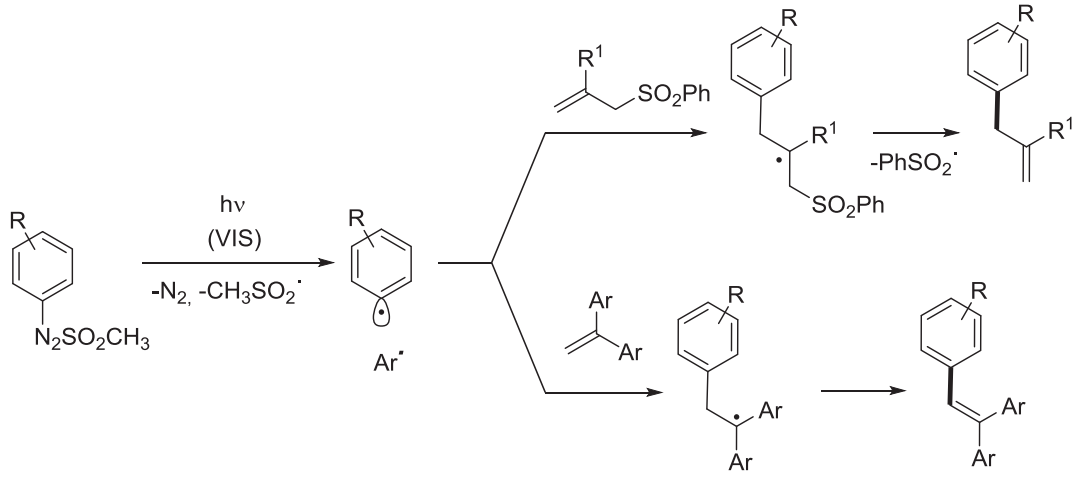
[a]*PhotoGreen Lab, Department of Chemistry University of Pavia, Viale Taramelli 10, 27100 Pavia, Italy*

[b]*Department of Chemistry, Salahaddin University-Erbil, Kurdistan /* Iraq

[c]*Green Chemistry Group, School of Science and Technology Chemistry Division, University of Camerino Via S. Agostino 1, 62032 Camerino (MC), Italy*

e-mail*: stefano.protti@unipv.it*

The formation of Ar-C_{sp2} and Ar-C_{sp3} bond under (transition) metal-free conditions is a significant goal in synthesis. We recently focused our attention on a class of photoactive compounds, namely arylazo sulfones, able to generate aryl radicals (Ar$^{\bullet}$, Scheme 1), upon visible light exposure[1]. These intermediates can be smoothly trapped by different olefins. Such reactivity has been exploited by our research group for allylations and vinylations of aromatics under (photo)catalyst- free conditions. In particular, the reaction of aryl radicals with an allyl sulfone resulted in the formation of a radical adduct which, upon loss of a sulfonyl radical, forms the corresponding allylarene[2]. On the other hand, trapping of the photogenerated Ar$^{\bullet}$ by a 1,1-diarylethylene afforded the corresponding triarylethylene[3].



Scheme 1: Visible-light mediated synthesis of allyl arenes and triarylethylenes.

The optimization of the same reaction under flow conditions, by having recourse to a "sunflow" reactor[4] is currently under study.

References:

[1] S. Crespi, S. Protti, M. Fagnoni, *J. Org. Chem*. **2016**, *81*, 9612-9619.

[2] A. Dossena, S. Sampaolesi, A. Palmieri, S. Protti, M. Fagnoni, *J. Org. Chem.* **2017**, *82*, 10687−10692.

[3] L. Onuigbo, C. Raviola, S. Protti, M. Fagnoni, *submitted*.

[4] A. M. Nauth, A. Lipp, B. Lipp, T. Opatz, *Eur. J. Org. Chem.* **2017**, 2099–2103.

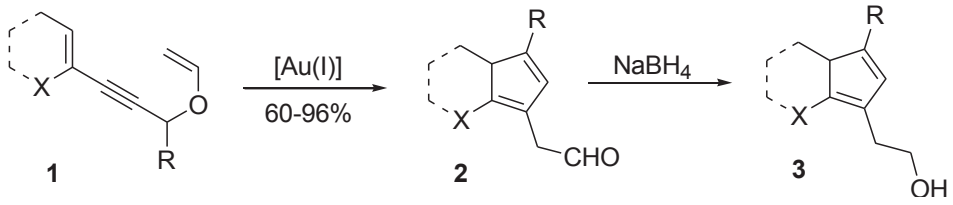
P81

Pentannulation Reaction by the Tandem Gold(I)-Catalyzed Propargyl Claisen Rearrangement/Nazarov Cyclization

A. Rinaldi,[a] D. Scarpi,[a] S. Magnolfi,[a] E. G. Occhiato[a]

[a]*Department of Chemistry "U. Schiff", University of Florence, Via della Lastruccia 13, 50019, Sesto Fiorentino (Italy)*
e-mail*: antonia.rinaldi@unifi.it*

The Nazarov reaction ranks as one of the most important and versatile tool for the construction of pentannulated compounds,[1] as in the last two decades a number of innovative approaches have been developed for the generation of the requisite pentadienyl cation undergoing the cyclization process,[2] including gold-catalyzed transformations. According to the previous works of our research group,[3] we present the tandem gold(I)-catalyzed rearrangement/Nazarov reaction of vinyl propargyl ethers which efficiently provides cyclopentadienes.[4] Readily available enol triflates and phospates are converted into propargyl alcohols under Sonogashira conditions. After *O*-vinylation, the gold-catalyzed rearrangement of the vinyl propargyl ethers **1** occurs under mild conditions (Scheme 1). The rearrangement generates a pentadienyl cation which undergoes a 4π electrocyclization leading to the target compound **2**. This bears, on the side chain, an aldehyde group which could be subjected to further elaboration. The obtained pentannulated *N*-heterocycles and carbacycles (Figure 1) are useful intermediates in organic synthesis as their skeleton is comprised in several naturally occurring compounds.



Scheme 1: The tandem Gold(I)-catalyzed propargyl Claisen rearrangement/Nazarov reaction.

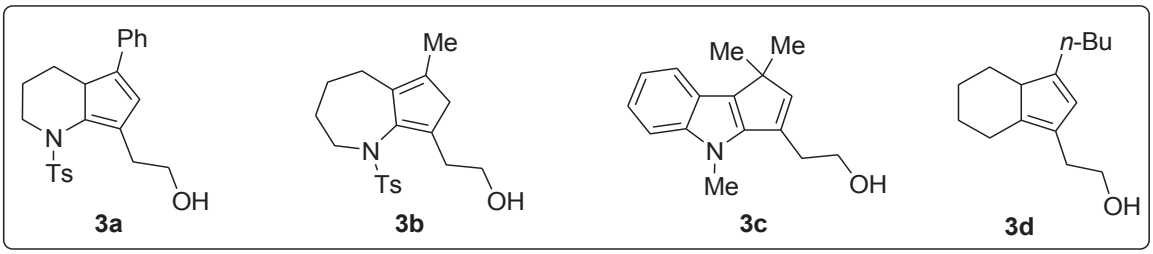


Figure 1: Selected examples.

References:

[1] Most recent reviews on the Nazarov reaction: (a) M. G. Vinogradov, O. V. Turova, S. G. Zlotin, *Org. Biomol. Chem.* **2017**, *15*, 8245-8269; (b) Sheikh, N. S. *Org. Biomol. Chem.* **2015**, *13*, 10774-10796

[2] W. T. Spencer III, T. Vaidya, A. J. Frontier, *Eur. J. Org. Chem.* **2013**, *18*, 3621 - 3633.

[3] (a) D. Scarpi, M. Petrović, B. Fiser, E. Gómez-Bengoa, E. G. Occhiato, *Org. Lett.* **2016**, *18*, 3922−3925. (b) M. Petrović, D. Scarpi, B. Fiser, E. Gómez-Bengoa, E. G. Occhiato, *Eur. J. Org. Chem.* **2015**, *18*, 3943-3956.

[4] A. Rinaldi, M. Petrovic, S. Magnolfi, D. Scarpi, E. G. Occhiato, manuscript submitted.

P82

Structural characterization of regenerated Silk Fibroin through different solubilization protocols

G. Rizzo,[a] M. Lo Presti,[a] G. M. Farinola[a]

[a]*Department of Chemistry, University of Bari, Via Orabona 4, 70126 Bari, Italy*
e-mail*: giorgio.rizzo@uniba.it*

Silk is a fibrous protein polymer spun into fibers by different animals, characterized by extraordinary mechanical properties, such as high tensile strength and extensibility, as well as biological compatibility. Its toughness is higher than Kevlar polymer. This mechanical superiority is thought to be dependent on the molecular assembly of silk fibrins[1,2]. Among them, *Bombyx mori* silk fibroin represent the most easily available and interesting silk[3,4,5].

Herzog and Jancke collected silk X-ray Diffraction Pattern in 1920[6], but it remained unsolved until Linus Pauling, in 1955, was able to rationalize the typical fibrous pattern observed[7]. The diffraction pattern showed a micrometric crystallite domain made of antiparallel β-sheet polypeptides, further arranged in a nanometric symmetry along the fibre axis.

Due to the extremely stable structure, silk is a difficult material to process. Indeed, the mere solubilization requires harsh conditions and tedious purification steps. First of all, silk is boiled in Na_2CO_3 0.02 M in order to remove sericine coatings, then it's heated at 60°C for 4 hours in a highly concentrated LiBr solution (about 10 M). Finally, it requires long dialysis procedure to remove the excess salt used[8]. This procedure is actually the standard process widely used. An older protocol consists in a similar decoating process, followed by heating the material in a 3.8 M $CaCl_2$ hydroalcoholic solution[9]. Despite the enormous number of papers involving treatment of silk, there is not yet a satisfactory rationalization of the dissolution process, neither a valid explanation of the lithium and calcium interactions with the polypeptide.

Our study aims mainly to rationalize the evidence that only lithium and calcium seem to be able to dissolve silk. To address this observation we have used different techniques, such as WAXS, SAXS, NMR and DLS. Starting from the hypothesis that the ion charges and the ionic radii must play a key role in the whole process, we also investigated lanthanide ions such as cerium (III) and gadolinium (III) due to the identical ionic radii of calcium (II) but exhibiting a bigger ion charge, in order to address the ionic charge contribution to the dissolution process. In a completely unexpected way, we obtained a new fibrous material from the dialysis of lanthanide treated silk. The new fibre formation can not be achieved with lithium and calcium treatment, because the samples gelify, completely losing a long-range hierarchical ordered structure.

References:

[1] J. M. Gosline, P. A. Guerette, C. S Ortlepp, K. N. Savage, *J. Exp. Biol.* ***1999****, 23, 3295-3303.* [2] B. B. Mandal, S. C. Kundu*, Biotechnology and Bioengineering,* ***2008****, 6, 1237-1250.* [3] M. Mondal, K. Trivedy, S. N. Kumar*, Caspian J. Env. Sci.,* ***2007****, 2, 63-76.* [4] A. Borgohain*, JAIR,* ***2015,*** *3, 626-628.* [5] O. Hakimi, D. P. Knight, F. Vollrath, P. Vadgama*, Composites, Part B,* ***2008,*** *38, 324-337.* [6] R. O. Herzog, W. Jancke, *Berlin,* ***1920****, 53, 2162-2164.* [7] R. E. Marsh, R. B. Corey, L. Pauling*, Biochimica et Biophysica Acta,* ***1955****, 16, 1-34.* [8] D. N. Rockwood, R. C. Preda, T. Yucel, X. Wang, M. L. Lovett, D. Kaplan*, Nature Protocols,* ***2011****, 6, 1612-1631.* [9] A. Ajisawa, *The Journal of Sericultural Science of Japan,* ***1998****, 67, 91-94.*

P83

Triterpenoids hydroxamates as HIF Prolyl Hydrolase inhibitor

F. Rogati,[a] A. Minassi,[a] E. Munoz,[b] G. Appendino[a]

[a]*Dipartimento di Scienze del Farmaco, Università del Piemonte Orientale A. Avogadro, L.go Donegani 2, Novara*

[b]*University of Cordoba, Avda. Menéndez Pidal, s/n, 14004 Cordoba, Spain*

e-mail*: federica.rogati@uniupo.it*

The carboxylate-to-hydroxamate transformation had a remarkable effect on the biological profile of pentacyclic triterpenoid acids (PCTTA). Affinity for the transcription factors targeted by the natural compounds (NF-□B, STAT3, Nrf2, TGR5) was de-emphasized, while inhibitory activity on HIF prolyl hydrolases was selectively induced. Activity was reversible, isoform-selective, dependent on the hydroxamate location on the triterpenoid scaffold, and unremarkable when this element was replaced by other chelating groups. The hydroxamate of betulinic acid (**Figure 1**) was selected for further studies, evaluating its effect on HIF-1α expression under normal and hypoxic conditions, its pattern of induction of HIF-dependent gene-expression and angiogenesis, and its neuroprotective activity in vitro. The positive results obtained provided a rationale to evaluate the hydroxamate of betulinic acid in a murine model of neuronal striatal degeneration, qualifying it as a promising agent for further development.

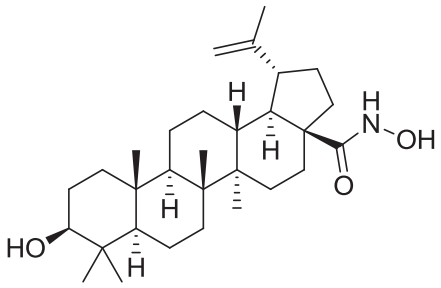


Figure 1: Hydroxamate of betulinic acid.

P84

Identification of new GPBAR1 selective agonists containing an epoxide group on cholane side chains

V. Sepe,[a] S. De Marino,[a] C. Festa,[a] C. Finamore,[a] M. V. D'Auria,[a] S. Fiorucci,[b] A. Zampella[a]

[a]*Department of Pharmacy, University of Naples "Federico II", Naples, Italy*
[b]*Department of Surgery and Biomedical Sciences, Nuova Facoltà di Medicina, Perugia, Italy*
e-mail*: valentina.sepe@unina.it*

GPBAR1 was the first reported example of transmembrane G protein–coupled receptor, activated by bile acids.[1] It is expressed in numerous tissues, like liver, gallbladder, ileum, colon, muscle, brown adipose tissue, macrophages, etc. and its activation may include gallbladder relaxation, increased energy expenditure, improved intestinal motility, glucose metabolism and insulin sensitivity.

It was demonstrated that GPBAR1 activation reduces liver steatosis,[2] regulates bile homeostasis,[3] intestinal motility and it has been reported to have beneficial effects on inflammatory diseases, such as atherosclerosis and colitis.

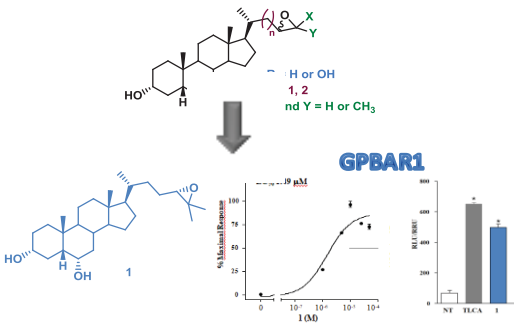


Figure 1: HDCA derivatives and pharmacological activity of **1**

Consequently, modulation of GPBAR1 by small molecules represents an attractive strategy to treat severe enterohepatic and metabolic disorders such as nonalcoholic steatohepatitis[4] (NASH), hypercholesterolaemia, hypertriglyceridaemia, and type 2 diabetes mellitus (T2DM).

In this communication, we report the design, synthesis and *in vitro* pharmacological evaluation of a new family of bile acids derivatives with an epoxide ring on their side chains.[5] Pharmacological results showed that these compounds are endowed with a good activity on GPBAR1, with compound **1** the most potent of the series (figure 1). The binding mode of compound **1** in the GPBAR1-LBD was also elucidated by computational studies. As a result, from this study, we have identified a new class of GPBAR1 selective agonists, useful for the treatment of enterohepatic and metabolic disorders.

References:

[1] T. Maruyama, Y. Miyamoto, T. Nakamura, Y. Tamai, H. Okada, E. Sugiyama, T. Nakamura, H. Itadani, K. Tanaka, *Biochem. Biophys. Res. Commun*., **2002**, *298*, 714-719.

[2] G. Vassileva, W. Hu, L. Hoos, G. Tetzloff, S. Yang, L. Liu, L. Kang, H. R. Davis, J. A. Hedrick, H. Lan, T. Kowalski, E. L. Gustafson, *J. Endocrinol*., **2010**, *205*, 225-232.

[3] N. Pean, I. Doignon, I. Garcin, A. Besnard, B. Julien, B. Liu, S. Branchereau, A. Spraul, C. Guettier, L. Humbert, K. Schoonjans, D. Rainteau, T. Tordjmann, *Hepatology*, **2013**, *58*, 1451-1460.

[4] V.Z. Rocha, P. Libby *Nat. Rev. Cardiol*., **2009**, 6, 399-409.

[5] S. De Marino, A. Carino, D. Masullo, C. Finamore, V. Sepe, S. Marchianò, F. S. Di Leva, V. Limongelli, S. Fiorucci, A. Zampella *RSC Adv*., **2017**, *7*, 32877-32885.

P85

Effect of the inclusion of calix[4]resorcinarenes in liposomes used as membrane model

G. Siani,[a] R. Zappacosta,[a] A. Fontana,[a] A. Ammazzalorso,[a] P. Di Profio,[a] M. Aschi[b]

[a]*Dipartimento di Farmacia, Università "G. D'Annunzio", Via dei Vestini, 31, 66013 Chieti*
[b]*Dipartimento di Scienze Fisiche e Chimiche, Università degli Studi de L'Aquila, Via Vetoio (Coppito 1), 67100 Coppito (AQ)*
e-mail*: siani@unich.it*

Resorcinarenes, and the related calixarenes, are macrocyclic molecules with a basket shaped structure and they are considered a fascinating class of macrocycles as they can form complexes with both cations and anions and with neutral molecules.[1] Moreover, they can be inserted into a lipid bilayer as they contain both polar and apolar molecular regions. While the ability of calixarene scaffolds to promote trans-membrane transport as ion channel or mobile carriers is well documented,[2] less is known about resorcinarenes.

In this work, unilamellar liposomes have been prepared from 1-palmitoyl-2-oleoyl-*sn*-glycerol-3-phosphocholine to mimic the cell membrane. Beside the application as membrane model, liposomes are particularly useful in diagnostic and therapeutic as drug delivery systems because of their ability to entrap both hydrophilic and hydrophobic compounds and their low inherent toxicity. Two types of calix[4]resorcinarenes, which differ in the length of the alkyl chain on the methylene bridge between the aromatic rings, have been embedded in the liposomes in three host/guest ratios, following two different procedures. Moreover, a calix[4]resorcinarene cavitand has been synthetized by bridging the neighbouring hydroxyl groups to obtain a molecule with an extremely rigid conformation compared to the parent resorcinarene.

First, the effect of the insertion of the guests on the liposome structure has been evaluated through the measurements of the viscosity, the polarity and the kinetic stability of the liposomal systems by means of fluorescent probes like pyrene and 5(6)-carboxy-fluorescein. The presence of the guests reduces the viscosity of the POPC liposomes, suggesting a modification of the bilayer structure. However, this does not affect the liposome stability. The free energy of the insertion of the substrates in the lipid bilayer were evaluated by means of the Umbrella Sampling procedure.[3]

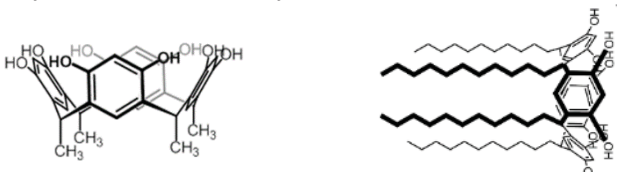


Figure 1: Structures of the calix[4]resorcinarenes used in this study

Finally, the binding ability of the so-obtained embedded resorcinarenes has been tested.

References:

[1] B. Mokhtari, K. Pourabdollah, *Asian J. Chem.* **2011**, *23*, 4717 – 4734.

[2] V. Sidorov, F. W. Kotcg, G. Abdrakhnanova, R. Mizani, J. C. Fettinger, J. T. Davis, *J. Am. Chem. Soc.* **2002**, *124*, 2267 – 2278; R. Zappacosta, A. Fontana, A. Credi, A. Arduini, A. Secchi, *Asian J. Chem.* **2015**, *4*, 262 – 270.

[3] S. Kumar, J. M. Rosenberg, D. Bouzida, R. H. Swendsen, P. A. Kollman, *J. Comp. Chem.* **1992**, *13*, 1011–1021.

P86

DSSC: a synthetic approach for FRET increasing LHE dyes

S. Staderini,[a] A. Dessì,[a] D. Franchi,[a,b] G. Forti,[a] L. Zani,[a] M. Calamante,[a,b] A. Mordini,[a,b] G. Reginato,[a]

[a]*ICCOM-CNR, Via Madonna del Piano 10, 50019 Sesto Fiorentino (FI)*
[b]*Dipartimento di Chimica "Ugo Schiff", Università degli Studi di Firenze, Via della Lastruccia 3-13, 50019-Sesto Fiorentino, Italy*
e-mail*: sstaderini@iccom.cnr.it*

Since the early nineties, dyes have been extensively studied for application in photovoltaic technologies such as dye-sensitized solar cells (DSSC). Large libraries of different kinds of dyes have been synthesized in order to increase solar cell efficiency: natural pigments, ruthenium complexes and metal-free organic compounds are the main categories[1].

Within the last of these families, our group has focused its attention on D-π-A organic molecules. This kind of compounds is characterized by a common motif: an electron rich donor (D) linked to an electron poor acceptor (A) through a highly conjugated spacer. Upon light absorption, this particular structure allows intramolecular charge transfer (ICT) process from donor to acceptor. To have an efficient ICT process molecules must have the HOMO localized over the donor region and the LUMO over the acceptor one[2].

Light Harvesting Efficiency (LHE) is one of the critical points for dyes aimed at solar cells application.; on the other hand the design and the synthesis of these compounds, with high molar extinction coefficient in a large range of wavelength, can result challenging.

The aim of this work has been to design a photosensitizer able to exploit Forster Resonance Energy Transfer (FRET)[3] to increase the LHE. This can be realized linking a series of fluorescent donors (antennas) to the dye. These donors must have fluorescence spectra overlapping (<30%) with absorption spectra of dyes and must be spatially adjacent to the chromophore (max 100 Å).

To verify this concept we decided to prepare a model dye to be coupled to a series of fluorescents antennas, using the Cu(I) azido-alkyne coupling (CuAAC) click reaction as a simple and versatile synthetic tool. The methodology is very promising as it might allow the preparation of libraries of dyes to measure the LHE values due to FRET effect.

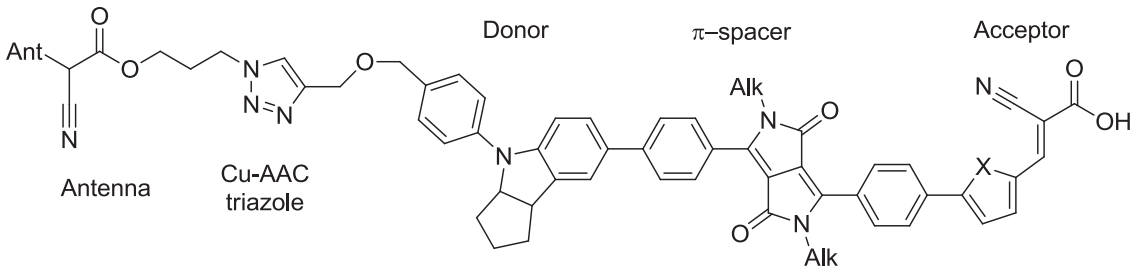


Figure 1: Model of dye-antenna coupled molecule.

References:

[1] M. R. Narayan, *Renew. Sust. Energ. Rev.*, **2012**, *12*, 208–215.
[2] Y. Ooyama, Y. Harima, *ChemPhysChem,* **2012**, *13*, 4032–4080.
[3] F. Odobel, Y. Pellegrin, J. Warnan, *Energy Environ. Sci.*, **2013**, *6*, 2041–2052.

P87

Antioxidants Macromolecular Additives

L. Tofani,[a] S. Al-Malaika,[b] S. Losio,[c] G. Luciano,[d] P. Stagnaro,[d] C. Viglianisi,[a] S. Menichetti[a]

[a]*Department of Chemistry "Ugo Schiff", University of Florence, Via Della Lastruccia 3-13, 50019, Sesto Fiorentino, FI, Italy*
[b]*School of Engineering & Applied Science, Aston University, Birmingham B4 7ET, England, UK*
[c]*ISMAC-CNR, Via E. Bassini 15, 20133 Milano, Italy,* [d]*ISMAC-CNR, Via De Marini 6, 16149 Genova, Italy*
e-mail*: lorenzo.tofani@unifi.it*

Commodity plastics like polyolefins undergo inevitable thermo- and/or photo-oxidative degradation processes both during processing and service use, resulting in the loss of their native mechanic properties and the consequent shortening of their lifespan.[1] Traditional chain-breaking antioxidants like BHT and BHA (Figure 1) are generally added into the polymer matrix in order to delay these oxidation processes, but their tendency to physical loss by volatilization or migration limits their stabilizing performance and represent a potential toxicological risk in plastics used for direct human-contact applications.

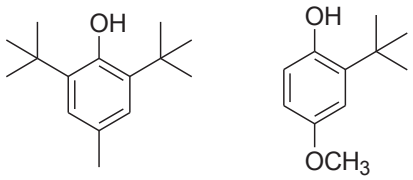
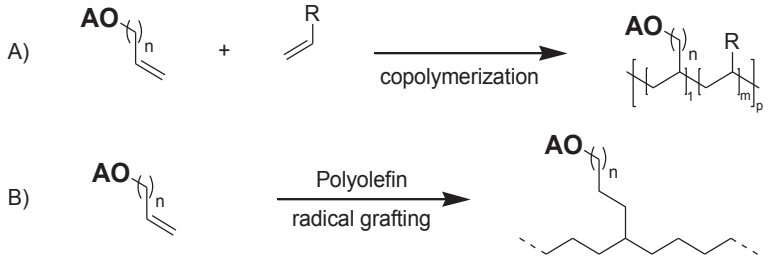


Figure 4

The increase of the physical persistence of stabilizers in the polymer is then mandatory for the enhancement of both protective performance and health safety. In our work, this goal was pursued by using properly modified traditional antioxidants for the preparation of macromolecular additives through a copolymerization reaction (Scheme 1, A) or a radical grafting reaction on a virgin polymer (Scheme 1, B).



Scheme 1: AO = antioxidant unit

The preparation and characterization of these innovative macromolecular antioxidant systems, as well as the study of their stabilizing performance will be discussed in this communication.

References:

[1] N. C. Billingham, *Mater. Sci. Technol.* **2013**, 469 – 507.

P88

Design of novel heterogeneous Pd-based catalysts

F. Valentini,[a] L. A. Bivona,[b] C. Aprile,[b] L.Vaccaro[a]

[a]*Laboratory of Green Synthetic Organic Chemistry, Dipartimento di Chimica, Biologia e Biotecnologie, Università degli Studi di Perugia I-06123 Perugia*
http://www.dcbb.unipg.it/greensoc
[b]*Laboratory of Applied Material Chemistry (CMA), University of Namur, 61 rue de Bruxelles, 5000 Namur, Belgium*
e-mail*: federicavalentinimail@gmail.com*

Nowadays, the ever increasing environmental concerns are focusing the efforts of organic synthesis towards the development of more sustainable and economic processes in both academic and industrial areas.

In last few years many alternative metal has been used in both C−C coupling or C−H functionalization,[1] palladium remains an extremely versatile metal useful for realizing many efficient chemical syntheses.

Palladium residues in the final products must be anyway kept at very low levels and immobilization technologies should be adopted in order to recover and minimize the waste of previous metal catalysts. An alternative way to separate and reuse metal is the use of biphasic reaction medium (ionic liquid-organic solvent).[2] Indeed ionic liquids (ILs) are known in that they can be used in reactions to dissolve metal ions which are insoluble in organic solvents. Organic Ionic tags possess the advantage of stabilizing metal nanoparticles.[3] Therefore we have decided to combine this feature with the high mechanical stability of our newly designed gel-type polystyrene based resin.[4]

Herein we present the develop and characterization of novel heterogeneous palladium-based catalysts based on the use of supported bis-imidazolium and bis-triazolium moieties that are able to stabilize anionic Pd(II) and Pd(0). Both palladium species are effective in the catalysis of Mizoroki-Heck reaction used as representative cross-coupling process to evaluate the mechanism of action of the newly prepared solid catalyst, their recovery and reuse and their stability in different reaction media.

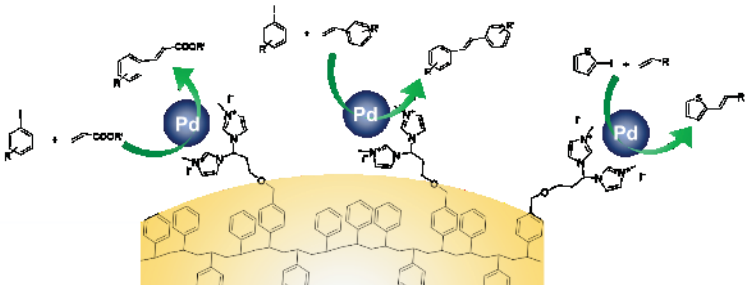


Figure 1

References:

[1] (a) H.-Q. Do and O. Daugulis, *J. Am. Chem. Soc.*, **2008**, *130*, 1128–1129; (b) W.Song, S. Lackner, L. Ackermann *Angew. Chem. Int. Ed.* **2014**, *53*, 2477 –2480.

[2] A. J. Carmichael, M. J. Earle, J. D. Holbrey, P. B. McCormac and K. R. Seddon, *Org. Lett.*, **1999**, *1*, 997–1000.

[3] P. Migowski and J. Dupont, *Chem.–Eur. J.,* **2007**, *13*, 32–39.

[4] A. Marrocchi, P. Adriaensens , E. Bartollini, B. Barkakati, R. Carleer, J. Chen, D. K. Hensley, C. Petrucci, M.Tassi, L. Vaccaro *Eur. Pol. J.* **2015**, 73, 391–401.

P89

KuQuinones: from water to hydrogen peroxide. A new organic photocatalyst

F. Valentini, F. Sabuzi, V. Conte, P. Galloni
University of Rome "Tor Vergata", Department of Chemical Science and Technologies, viale della Ricerca Scientifica snc, 00133, Rome, Italy.
e-mail*: f.valentini@scienze.uniroma2.it*

Hydrogen peroxide uses are numerous, just to cite a few it is a green strong oxidant, a bleach and an antiseptic. As of today, it is synthetized industrially by the "anthraquinone process", which is costly as well as energy consuming. Moreover, its production is about 2,2 megatons annually. So it should be very interesting to find new processes for its production and possibly *in situ*. Few years ago we developed a new one-pot synthesis for the preparation of a novel quinoid compounds, called KuQuinones (KuQs)[1]. They are pentacyclic molecules characterized by fully conjugated skeleton. The peculiar features of such molecules are favourable reduction potential and large absorption spectrum in the visible region. Starting from a general synthetic protocol, various KuQs, differing for length and functional groups of side chain, were prepared. Recently the amphiphilic derivate 1-(9-hydroxynonil)KuQuinone (KuQ9OH) was used for deposition on ITO surface through Langmuir-Blodgett technique and tested as photosensitizer in photoelectrochemical cells, with good results in terms of IPCE[2]. Moreover, a recent study showed[3] that these compounds are able to oxidize water both to oxygen and hydrogen peroxide. For these reasons we suppose that, KuQ9OH may act both as sensitizer and catalyst in hydrogen peroxide production.

In this contribution, the preliminary results of KuQuinone as photoactive species in catalytic water oxidation to hydrogen peroxide will be presented.

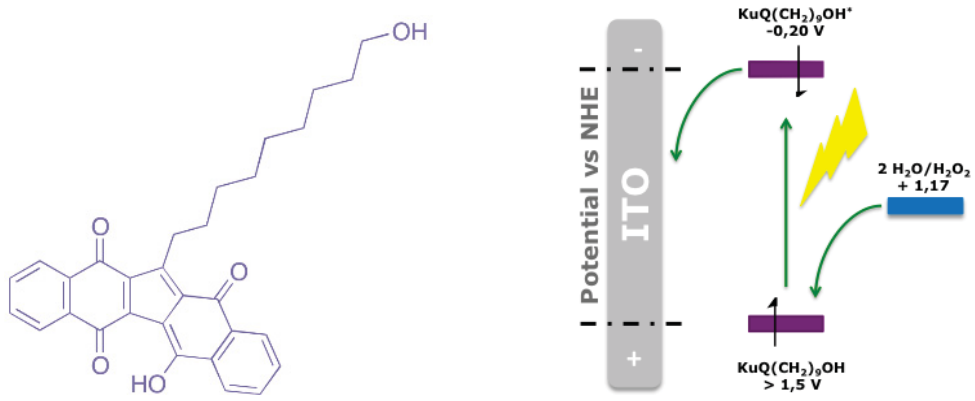


Figure 1: **(left)** Structure of KuQ derivate **(right)** Energy diagram for photocatalytic water oxidation perform by KuQ in ITO surface.

References:

[1] A. Coletti, S. Lentini, V. Conte, B. Floris, O. Bortolini, F. Sforza, F. Grepioni, P. Galloni, *J. Org. Chem.* **2012**, *77*, 6873-6879.

[2] F. Sabuzi, V. Armuzza, V. Conte, B. Floris, M. Venanzi, P. Galloni, E. Gatto, *J. Mater. Chem. C*, **2016**, *4*, 622-629.

[3] M. Bonomo, F. Sabuzi, A. Di Carlo, V. Conte, D. Dini, P. Galloni, *New J. Chem.* **2017**, *41*, 2769-2779.

P90

Organic and Hybrid Photosensitizers: synthesis, characterization and application in PDT

G. Viscardi,[a] N. Barbero,[a] B. Ciubini,[a] G. Chinigo,[a] P. Quagliotto,[a] A. Fin,[a] C. Barolo,[a] A. Fiorio Pla,[b] S. Visentin[c]

[a]*Department of Chemistry, NIS Interdepartmental and INSTM Reference Centre, University of Torino, Via Pietro Giuria 7, 10125 Torino, Italy*
[b]*Dipartimento di Scienze della Vita e Biologia dei Sistemi, University of Torino, Via Accademia Albertina 13, 10123 Torino, Italy*
[c]*Department of Molecular Biotechnology and Health Sciences, University of Torino, via Quarello 15A, 10135 Torino, Italy*
e-mail*: guido.viscardi@unito.it*

Near-infrared (NIR) dyes are extensively studied in the development of biological applications, especially for photodynamic therapy (PDT) and imaging.[1,2] Between them, polymethine dyes deserve to be counted among innovative potential photosensitizers (PSs) for their strong absorption in the NIR region, perfectly matching the biological tissues' transparency window (600-900 nm).[3] Moreover, squaraines and cyanines possess high absorption coefficients, bright fluorescence and photostability in organic media.[4] However, in physiological conditions, their chemical instability and self-aggregation properties limit their widely applications. In this context, the incorporation of these dyes in nanoparticles (NPs) is extremely important to prevent the formation of dye aggregates in aqueous environment and protect the photophysical characteristics from nucleophilic attacks.

The present contribution deals with the design and synthesis of a new series of NIR absorbing polymethine dyes with different substitution groups to implement a structure-activity study and to determine the substitutions influence on the reactive oxygen species (ROS) production, cellular uptake and photodynamic activity.[5] These dyes were then encapsulated in solid lipid nanoparticles (SLN) to promote their use in physiological conditions. SLN-dye complexes exhibit excellent optical properties, remarkable photostability, biocompatibility and efficient cellular internalization.

References:

[1] H. Abrahamse, M. R. Hamblin. *Biochem J.* **2016**, *47,* 347–364.
[2] S. Luo, E. Zhang, Y. Su, T. Cheng, C. Shi *Biomaterials* **2011**, *32,* 7127–38.
[3] R.R. Avirah, D.T. Jayaram, N. Adarsh, D. Ramaiah *Org. Biomol. Chem.* **2012**, *10*, 911–920.
[4] N. Barbero, C. Magistris, J. Park, D. Saccone, P. Quagliotto, R. Buscaino, C. Medana, C. Barolo, G. Viscardi, *Org. Lett.* **2015**, *17,* 3306–3309.
[5] L. Serpe, S. Ellena, N. Barbero, F. Foglietta, F. Prandini, M.P. Gallo, R. Levi, C. Barolo, R. Canaparo, S. Visentin, *Eur. J. Med. Chem.* **2016**, *113,* 187-197.

P91

Lactic Acid Bacteria as New Whole-Cells Biocatalysts for the Stereoselective Synthesis of Chiral Enantiopure Building Blocks

P. Vitale,[a] F. M. Perna,[a] F. Valerio,[b] P. Lavermicocca,[b] V. Capriati[a]

[a]*Dipartimento di Farmacia–Scienze del Farmaco, University of Bari "A. Moro", Consorzio C.I.N.M.P.I.S., Via E. Orabona 4, Bari, Italy.*

[b]*CNR Institute of Sciences of Food Production (ISPA), via Amendola 122/O, Bari, Italy.*

e-mail*: paola.vitale@uniba.it*

Biocatalytic processes represent one of the most heavily used green methodologies in preparative chemistry to perform highly chemo-, regio-, and stereoselective organic transformations, which are typically run under very mild reaction conditions (*e.g.*, almost neutral pH buffer solutions, ambient temperature or mild heating, atmospheric pressure).[1] Whole-cell microorganisms offer several positive features as biocatalysts with respect to isolated enzymes as they are more accessible, stable and easier to handle. Moreover, the presence of efficient internal cofactors regeneration systems (*e.g.*, NADH or NADPH in reduction reactions) allows for cheap biocatalytic processes to be carried out often using glucose as the sole carbon source.[2]

In this Communication, we discuss the asymmetric bioreduction of aromatic ketones to enantiopure secondary alcohols using lactic acid bacteria (LAB) as new whole-cells biocatalysts. Several strains among LAB and spore-forming bacteria (*Bacillus* spp.) from the culture collection of the Institute of Sciences of Food Production (CNR-ISPA, Bari) have been screened. Interestingly, among LAB, *Weissella* strains were found to be the most effective ones for the stereoselective reduction of acetophenones to the corresponding *S*-alcohols, with high yields and enantiomeric excesses (ees), despite to the known *R*-stereopreference exhibited by other LAB species as Lactobacilli (Figure).[2a,3] Overall, this methodology holds potential to become a promising cheap and environment-friendly approach for the preparation of chiral nonracemic secondary alcohols and Active Pharmaceutical Ingredients (APIs).[3]

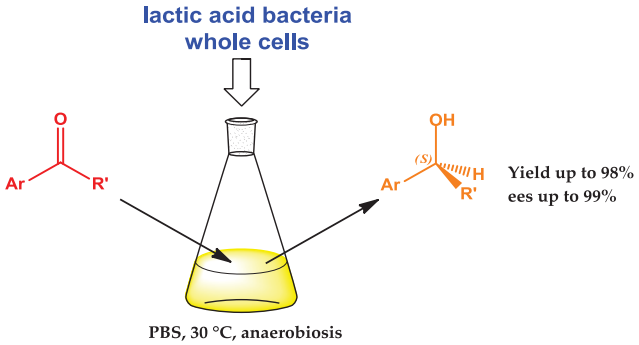


Figure 1: Stereoselective synthesis of chiral secondary alcohols by lactic acid bacteria.

References:

[1] *(a)* K. Faber, Biotransformations In Organic Chemistry: A Textbook, 6ed., Springer-Verlag: Berlin/Heidelberg, Germany, 2011; *(b)* R. C. Simon, F. G. Mutti, W. Kroutil, *Drug Discov. Today Technol.* **2013**, *10*, e37–e44.

[2] *(a)* P. Vitale, F. M. Perna, G. Agrimi, A. Scilimati, A. Salomone, C. Cardellicchio, V. Capriati, V. *Org. Biomol. Chem.* **2016**, *14*, 11438; *(b)* P. Vitale, V. M. Abbinante, F. M. Perna, A. Salomone, C. Cardellicchio, V. Capriati, *Adv. Synth. Catal.* **2017**, *359*, 1049.

[3] P. Vitale, F. M. Perna, G. Agrimi, I. Pisano, F. Mirizzi, R. Capobianco, V. Capriati, *Catalysts* **2018**, *8*, 55.

P92

En route to sustainability: blend nanoparticles for water-processable active layer of organic solar cells

S. Zappia,[a] S. Destri,[a] A. M. Ferretti,[b] U. Giovanella,[a] G. Scavia,[a] V. Vohra[c]

[a] *Istituto per lo Studio delle Macromolecole (ISMAC), CNR, via A. Corti 12, 20133, Milano, Italy*
[b] *Istituto di Scienze e tecnologie molecolari (ISTM), CNR, Lab. Nanotecnologie, via G. Fantoli 16/15, 20138 Milano, Italy*
[c] *Department of Engineering Science, University of Electro-Communications 1-5-1 Chofugaoka, Chofu, Tokyo 182-8585, Japan*
e-mail*: s.zappia@ismac.cnr.it*

Water-processable nanoparticles (WPNPs) of semiconducting polymers received considerable attention for optoelectronic and biological applications due to their simple preparation method, and their tunable optical properties.[1] WPNPs are appealing for optoelectronic devices such as organic photovoltaics (OPVs), organic light-emitting diodes, and organic field-effect transistors to address the morphology of the active layer, that is strictly related to device performances.[2] Through the miniemulsion approach, WPNPs dispersion can be obtained using great amount of surfactants to ensure their stability. This approach allows for lowering the chlorinated solvent amount used in active layer fabrication reducing the environmental payback of devices, but the excess of surfactant has to be removed at the end of the process.[3]

Amphiphilic block copolymers (ABCPs) are a powerful tool to produce nanostructured or supramolecular objects with enhanced properties for electronics, optoelectronics, sensors and biotechnological applications because of their capability to self-assembly, influenced by the physico-chemical differences between the blocks, including the relative block length, block polarity, volume fraction, chain flexibility, etc.[4]

Here we reported about a series of ABCP, PCPDTBT-*b*-P4VP, recently investigated in our group. These polymers are constituted by a low band-gap copolymer, PCPDTBT as the rigid segment, and tailored segments of poly-4-vinylpyridine (P4VP). The rod block was studied as donor material in hybrid and organic devices, whilst P4VP is able to interact with acceptor materials, as fullerene derivatives.[5] Taking advantage of hydrophilic behaviour of the coil, we studied the capability of PCPDTBT-*b*-P4VP to prepare WPNPs dispersion in aqueous medium through miniemulsion method, neat or in blend with fullerene derivatives, without use of surfactants avoiding purification steps. The so-obtained WPNPs were optically, morphologically (DLS, AFM, TEM) and electrically characterized, showing suitable properties for the preparation of active layers and they were tested in sustainable WPNP-based OPVs with good efficiencies.

References:

[1] F. Cicoira, C. Santato, *Organic Electronics: Emerging Concepts and Technologies* **2013**, Wiley-VCH Verlag GmbH & Co. KGaA.
[2] X. Zhou, W. Belcher, P. Dastoor, *Polymers* **2014**, *6*, 2832.
[3] S. Zhang, L. Ye, H. Zhang, J. Hou, *Materials Today* **2016**, *19*, 533.
[4] B.D. Olsen, R.A. Segalman, *Mater Sci Eng R* **2008**, *62*, 37.
[5] S. Zappia, R. Mendichi, S. Battiato, G. Scavia, R. Mastria, F. Samperi, S. Destri, *Polymer*, **2015**, *80*, 245.
[6] S. Zappia, G. Scavia, A.M. Ferretti, U. Giovanella, V. Vohra, S. Destri, *Adv sustainabl Syst* **2018**, *2*, 1700155.

Elenco dei Partecipanti

ABBIATI GIORGIO
Università degli Studi di Milano
giorgio.abbiati@unimi.it

ABBINANTE VINCENZO MIRCO
Università degli Studi dell'Insubria
vmabbinante@studenti.uninsubria.it

ABBOTTO ALESSANDRO
Università degli Studi di Milano - Bicocca
alessandro.abbotto@unimib.it

AIROLDI CRISTINA
Università degli Studi di Milano - Bicocca
cristina.airoldi@unimib.it

ALBANO GIANLUIGI
Università di Pisa
gianluigi.albano@dcci.unipi.it

ALFEI SILVANA
Università di Genova
alfei@difar.unige.it

ALFIERI MARIA LAURA
Università degli Studi di Napoli Federico II
marialaura.alfieri@unina.it

ALGIERI VINCENZO
Università della Calabria
vincenzo.algieri@unical.it

ALHAIQUE FRANCO
Università di Roma "La Sapienza"
franco.alhaique@uniroma1.it

ALLEGRINI PIETRO
INDENA Spa
pietro.allegrini@indena.com

ANASTASIOU IOANNIS
Università degli Studi di Perugia
ioannis.anastasiou@studenti.unipg.it

ASSFALG MICHAEL
Università degli Studi di Verona
michael.assfalg@univr.it

BAGNOLI LUANA
Università degli Studi di Perugia
luana.bagnoli@unipg.it

BALDINI LAURA
Università di Parma
laura.baldini@unipr.it

BALDOLI CLARA
Consiglio Nazionale delle Ricerche (CNR)
clara.baldoli@istm.cnr.it

BALLINI ROBERTO
Università di Camerino
roberto.ballini@unicam.it

BARBERA VINCENZINA
Politecnico di Milano
vincenzina.barbera@polimi.it

BARBIERI ALESSIA
Università di Roma "La Sapienza"
alessia.barbieri@uniroma1.it

BARTOLO GABRIELE
Università della Calabria
bartolo.gabriele@unical.it

BASCHIERI ANDREA
Università di Bologna
andrea.baschieri2@unibo.it

BASSO ANDREA
Università degli Studi di Genova
andrea.basso@unige.it

BECCALLI EGLE
Università degli Studi di Milano
egle.beccalli@unimi.it

BELLINA FABIO
Università di Pisa
fabio.bellina@unipi.it

BENAGLIA MAURIZIO
Università degli Studi di Milano
maurizio.benaglia@unimi.it

BENCIVENNI GIORGIO
Università degli Studi di Bologna
giorgio.bencivenni2@unibo.it

BENINCORI TIZIANA
Università degli Studi dell'Insubria
tiziana.benincori@uninsubria.it

BERNARDI ANNA
Università degli Studi di Milano
anna.bernardi@unimi.it

BEVERINA LUCA
Università degli Studi di Milano - Bicocca
luca.beverina@unimib.it

BIAGGI CINZIA
Olon s.p.a.
cbiaggi@olonspa.it

BIANCO ARMANDODORIANO
Università di Roma "La Sapienza"
armandodoriano.bianco@uniroma1.it

BIETTI MASSIMO
Università di Roma "Tor Vergata"
bietti@uniroma2.it

BINETTI SIMONA OLGA
Università degli Studi di Milano - Bicocca
simona.binetti@unimib.it

BLANGETTI MARCO
Università degli Studi di Torino
marco.blangetti@unito.it

BOLDRINI CHIARA LILIANA
Università degli Studi di Milano - Bicocca
c.boldrini@campus.unimib.it

BORBONE NICOLA
Università degli Studi di Napoli Federico II
nicola.borbone@unina.it

BORTOLINI OLGA
Università di Ferrara
olga.bortolini@unife.it

BRAMBILLA ELISA
Università degli studi di Milano
elisa.brambilla@unimi.it

BRANDI ALBERTO
Università di Firenze
alberto.brandi@unifi.it

BRENNA DAVIDE
Dipharma Francis srl
davide.brenna1990@gmail.com

BRIMBLE MARGARET
University of Auckland
m.brimble@auckland.ac.nz

BRUNO INES
Università degli Studi Salerno
brunoin@unisa.it

BUCCI RAFFAELLA
Università degli Studi di Milano
raff.bucci@gmail.com

CACIOPPO MICHELE
Università degli Studi di Trieste
michelecacioppo@gmail.com

CALABRESE CARLA
Università degli Studi di Palermo
carla.calabrese@unipa.it

CALAMANTE MASSIMO
Consiglio Nazionale delle Ricerche (CNR)
mcalamante@iccom.cnr.it

CALCIO GAUDINO EMANUELA
Università degli Studi di Torino
emanuela.calcio@unito.it

CAMPANELLA LUIGI
Università di Roma "La Sapienza"
luigi.campanella@uniroma1.it

CAPPARELLA ELISA
ENDURA S.P.A.
ecapparella@endura.it

CAPRIATI VITO
Università degli Studi di Bari
vito.capriati@uniba.it

CARLONE ARMANDO
Università dell'Aquila
armando.carlone@univaq.it

CARLUCCI CLAUDIA
Università degli Studi di Bari
claudia.carlucci@uniba.it

CARUANA LORENZO
F.I.S - FABBRICA ITALIANA SINTETICI
sabrina.camerra@fisvi.com

CASERTANO MARCELLO
Università degli Studi di Napoli Federico II
marcello.casertano@unina.it

CASO ALESSIA
Università degli Studi di Napoli Federico II
alessia.caso@unina.it

CAUTERUCCIO SILVIA
Università degli Studi di Milano
silvia.cauteruccio@unimi.it

CECCHI PAONE ALESSANDRO
alexpaone@hotmail.com

CERA GIANPIERO
Università di Parma
gianpiero.cera@unipr.it

CHIACCHIO MARIA ASSUNTA
Università di Catania
ma.chiacchio@unict.it

CHIAPPE CINZIA
Università di Pisa
cinzia.chiappe@unipi.it

CHIURCHIU' ELENA
Università di Camerino
elena.chiurchiu@unicam.it

CHRISTODOULOU MICHAIL
Università degli Studi di Milano
michail.christodoulou@unimi.it

CIARAMELLI CARLOTTA
Università degli Studi di Milano - Bicocca
carlotta.ciaramelli@unimib.it

CICCHI STEFANO
Università di Firenze
stefano.cicchi@unifi.it

CICERI SAMUELE
Università degli Studi di Milano
samuele.ciceri@gmail.com

CIMARELLI CRISTINA
Università di Camerino
cristina.cimarelli@unicam.it

CIOGLI ALESSIA
Università di Roma "La Sapienza"
alessia.ciogli@uniroma1.it

CIPOLLA LAURA
Università degli Studi di Milano - Bicocca
laura.cipolla@unimib.it

CIRILLI ROBERTO
Istituto Superiore di Sanità
roberto.cirilli@iss.it

CLERICI FRANCESCA
Università degli Studi di Milano
francesca.clerici@unimi.it

COCHET FLORENT
Università degli Studi di Milano - Bicocca
f.cochet@campus.unimib.it

CONTE VALERIA
Università di Roma "Tor Vergata"
valeria.conte@uniroma2.it

CORRADINI ROBERTO
Università di Parma
roberto.corradin@unipr.it

COSTANTINO VALERIA
Università di Napoli "Federico II"
valeria.costantino@unina.it

COSTANZO PAOLA
Università degli Studi "Magna Graecia" di Catanzaro
pcostanzo@unicz.it

CRAVOTTO GIANCARLO
Università degli Studi di Torino
editor.cravotto@unito.it

CURTI CLAUDIO
Università di Parma
claudio.curti@unipr.it

DAL CORSO ALBERTO
Università Degli Studi Di Milano
alberto.dalcorso@unimi.it

DALLA CORT ANTONELLA
Università di Roma "La Sapienza"
antonella.dallacort@uniroma1.it

D'ANDREA LUCA DOMENICO
Consiglio Nazionale delle Ricerche (CNR)
luca.dandrea@cnr.it

D'AURIA VALERIA
Università degli Studi di Napoli Federico II
madauria@unina.it

DE ANGELIS MARTINA
Università di Roma "La Sapienza"
m.deangelis@uniroma1.it

DE ANGELIS FRANCESCO
Univesrità dell'Aquila
francesco.deangelis@univaq.it

DE CASTRO CRISTINA
Università degli Studi di Napoli Federico II
decastro@unina.it

DE FIORE STELLA
Olon s.p.a.
sdefiore@olonspa.it

DE GENNARO SALVATORE
Olon s.p.a.
sdegennaro@olonspa.it

DE LUCA LIDIA
Università degli Studi di Sassari
ldeluca@uniss.it

DE MARCO ROSSELLA
Università di Bologna
rossella.demarco2@unibo.it

DE MARINO SIMONA
Università degli Studi di Napoli Federico II
sidemari@unina.it

DE NAPOLI LORENZO
Università degli studi di Napoli Federico II
denapoli@unina.it

DELLA SALA PAOLO
Università degli Studi di Salerno
pdellasala@unisa.it

DELL'AMICO LUCA
Università di Padova
luca.dellamico@nemo.unipr.it

D'ERRICO STEFANO
Università di Napoli "Federico II"
stefano.derrico@unina.it

DESTRI SILVIA
Istituto per lo Studio delle Macromolecole-CNR
s.destri@ismac.cnr.it

DI GIOIA MARIA LUISA
Università della Calabria
ml.digioia@unical.it

DI MAURO GIUSEPPE
Università degli Studi di Catania
giuseppe.dimairo@gmail.com

DI STEFANO STEFANO
Università di Roma "La Sapienza"
stefano.distefano@uniroma1.it

D'ISCHIA MARCO
Università degli Studi di Napoli Federico II
dischia@unina.it

DOMENICI VALENTINA
Università di Pisa
valentina.domenici@unipi.it

D'ONOFRIO MARIAPINA
Università di Verona
mariapina.donofrio@univr.it

DOSSENA ARNALDO
Università di Parma
arnaldo.dossena@unipr.it

ESPOSITO GERMANA
Università degli studi di Napoli Federico II
germana.esposito@unina.it

FAGNONI MAURIZIO
Università di Pavia
fagnoni@unipv.it

FARINOLA GIANLUCA MARIA
Università degli Studi di Bari
gianlucamaria.farinola@uniba.it

FERRABOSCHI PATRIZIA
Università degli Studi di Milano
patrizia.ferraboschi@unimi.it

FERRARI STEFANO
INDENA Spa
stefano.ferrari@indena.com

FIAMMENGO ROBERTO
FOND. ISTITUTO ITALIANO DI TECNOLOGIA
roberto.fiammengo@iit.it

FIN ANDREA
Università di Torino
andrea.fin.phd@gmail.com

FINAMORE CLAUDIA
Università degli Studi di Napoli "Federico II"
claudiafinamore@gmail.com

FINI FRANCESCO
Università di Modena e Reggio Emilia
francesco.fini@unimore.it

FIORANI GIULIA
Università "Ca' Foscari" Venezia
giulia.fiorani@unive.it

FLORESTA GIUSEPPE
Università di Catania
floresta.giuseppe@studium.unict.it

FONTANA ANTONELLA
Università degli Studi "G. d'Annunzio" Chieti
fontana@unich.it

FORMAGGIO FERNANDO
Università di Padova
fernando.formaggio@unipd.it

FORTUNA COSIMO G.
Università di Catania
cg.fortuna@unict.it

FRANZINI ROBERTA
Università di Roma "La Sapienza"
roberta.franzini@uniroma1.it

FUNICELLO MARIA
Università degli Studi della Basilicata
maria.funicello@unibas.it

GAMBARO STEFANIA
Università degli Studi Salerno
sgambaro@unisa.it

GARDOSSI LUCIA
Università degli Studi di Trieste
gardossi@univ.trieste.it

GATTI TERESA
Università di Padova
teresa.gatti@unipd.it

GELAIN ARIANNA
Università degli Studi di Milano
arianna.gelain@unimi.it

GELMI MARIA LUISA
Università degli Studi di Milano
marialuisa.gelmi@unimi.it

GENNARI CESARE
Università degli Studi di Milano
cesare.gennari@unimi.it

GIACOBONI JESSICA
Università degli Studi di Milano
jessica.giacoboni@unimi.it

GIANNINI CLELIA
Università degli Studi di Milano
clelia.giannini@unimi.it

GIARMANA' STEFANO
Olon s.p.a.
sgiarmana@olonspa.it

GIOFRE' SALVATORE VINCENZO
Università degli Studi di Messina
sgiofre@unime.it

GORACCI LAURA
Università degli Studi di Perugia
laura@chemiome.chm.unipg.it

GRISENTI PARIDE
SERICHIM
grisenti.paride60@gmail.com

GRISORIO ROBERTO
Politecnico di Bari
roberto.grisorio@poliba.it

GUARAGNA ANNALISA
Università di Napoli "Federico II"
annalisa.guaragna@unina.it

GUAZZELLI LORENZO
Università di Pisa
lorenzo.guazzelli@unipi.it

GUELLA GRAZIANO
Università di Trento
graziano.guella@unitn.it

GUGLIELMERO LUCA
Università di Pisa
luca.guglielmero@gmail.com

GUISO MARCELLA
Università di Roma "La Sapienza"
marcella.guiso@uniroma1.it

HAYASHI YUJIRO
Tohoku University
yhayashi@m.tohoku.ac.jp

IULIANO VERONICA
Università degli Studi Salerno
viuliano@unisa.it

KNAUF RALF
Centro Reach Srl
r.knauf@centroreach.it

LA FERLA BARBARA
Università degli Studi di Milano - Bicocca
barbara.laferla@unimib.it

LA MANNA PELLEGRINO
Università degli Studi Di Salerno
plamanna@unisa.it

LANGE HEIKO
Università di Roma "Tor Vergata"
heiko.lange@uniroma2.it

LANZALUNGA OSVALDO
Università di Roma "La Sapienza"
osvaldo.lanzalunga@uniroma1.it

LATTUADA LUCIANO
Bracco Spa
luciano.lattuada@bracco.com

LEGNANI LAURA
Universita' di Pavia
laura.legnani@unipv.it

LENCI ELENA
Università degli Studi di Firenze
elena.lenci@unifi.it

LEONI LUCA
Università di Roma "La Sapienza"
luca.leoni@uniroma1.it

LEONORI DANIELE
University of Manchester
daniele.leonori@manchester.ac.uk

LESSI MARCO
Università di Pisa
mlessi79@virgilio.it

LICANDRO EMANUELA
Università degli Studi di Milano
emanuela.licandro@unimi.it

LOCARNO SILVIA ALICE
Università degli Studi di Milano
silvia.locarno@unimi.it

LOCATELLI ERICA
Università di Bologna
erica.locatelli2@unibo.it

LUCARELLI GIULIO
Università di Roma "La Sapienza"
giulio.lucarelli@uniroma1.it

LUCARINI MARCO
Università di Bologna
marco.lucarini@unibo.it

LUPIDI GABRIELE
Università di Camerino
gabriele.lupidi@unicam.it

LURAGHI ANDREA
Università degli Studi di Milano - Bicocca
a.luraghi2@campus.unimib.it

MAIORANA STEFANO
Università degli Studi di Milano
stefano.maiorana@unimi.it

MANCIN FABRIZIO
Università di Padova
fabrizio.mancin@unipd.it

MANCINELLI MICHELE
Università di Bologna
michele.mancinelli@unibo.it

MANCUSO AURORA
Università degli Studi di Messina
mancusoaurora@gmail.com

MANCUSO RAFFAELLA
Università della Calabria
raffaella.mancuso@unical.it

MANFREDI NORBERTO
Università degli Studi di Milano - Bicocca
norberto.manfredi@unimib.it

MANGONI ALFONSO
Università degli Studi di Napoli "Federico II"
alfonso.mangoni@unina.it

MANICARDI ALEX
GENT UNIVERSITY
alex.manicardi@ugent.be

MANINI PAOLA
Università degli Studi di Napoli "Federico II"
pmanini@unina.it

MANTEGAZZA SIMONA
Dipharma Francis Srl
simone.mantegazza@dipharma.com

MARCANTONI ENRICO
Università degli Studi di Camerino
enrico.marcantoni@unicam.it

MARINI FRANCESCA
Università degli Studi di Perugia
francesca.marini@unipg.it

MARINONI STEVEN
stevenmarinoni99@gmail.com

MARTIN TEO
Università di Roma "Tor Vergata"
teo.martin@uniroma2.it

MARTINELLI JONATHAN
Università del Piemonte Orientale
jonathan.martinelli@uniupo.it

MARZANO GIUSEPPE
Università degli studi di Bari "Aldo Moro"
giuseppe.marzano1@uniba.it

MASSA ANTONIO
Università degli Studi Salerno
amassa@unisa.it

MASSI ALESSANDRO
Università di Ferrara
alessandro.massi@unife.it

MASSOLO ELISABETTA
Università degli Studi di Milano
elisabetta.massolo@gmail.com

MATEOS JAVIER
Università di Padova
javier.mateoslopez@unipd.it

MATTIELLO SARA
Università degli Studi di Milano - Bicocca
sara.mattiello@unimib.it

MAUTINO BEATRICE
beatrice.mautino@gmail.com

MAYOL LUCIANO
Università degli Studi di Napoli "Federico II"
mayoll@unina.it

MAZZANTI ANDREA
Università di Bologna
andrea.mazzanti@unibo.it

MAZZIERI FEDERICA
Università degli Studi di Milano - Bicocca
f.mazzieri1@campus.unimib.it

MAZZOCCANTI GIULIA
Università di Roma "La Sapienza"
giulia.mazzoccanti@uniroma1.it

MECCA MARISABEL
Università degli Studi della Basilicata
marisabelmecca@libero.it

MELLERIO GIORGIO
Università di Pavia
giorgiogiacomo.mellerio@unipv.it

MELLMANN DÖRTHE
Wiley-VCH
dmellmann@wiley.com

MENNA ENZO
Università di Padova
enzo.menna@unipd.it

MESSA FRANCESCO
Università del Salento
fmessa92@gmail.com

METRANGOLO PIERANGELO
Politecnico di Milano
pierangelo.metrangolo@polimi.it

MEZZINA ELISABETTA
Università di Bologna
elisabetta.mezzina@unibo.it

MINASSI ALBERTO
Università del Piemonte Orientale
alberto.minassi@uniupo.it

MISITI DOMENICO
Università di Roma "La Sapienza"
domenico.misiti@uniroma1.it

MOLINARO ANTONIO
Università degli Studi di Napoli "Federico II"
molinaro@unina.it

MONACO ILARIA
Università di Bologna
ilaria.monaco3@unibo.it

MORDINI ALESSANDRO
ICCOM - CNR
alessandro.mordini@unifi.it

MORELLI CARLO F.
Università di Milano
carlo.morelli@unimi.it

MUSUMARRA GIUSEPPE
Università di Catania
gmusumarra@unict.it

NAPOLITANO ALESSANDRA
Università degli Studi di Napoli "Federico II"
alesnapo@unina.it

NATIVI CRISTINA
Università di Firenze
cristina.nativi@unifi.it

NEJROTTI STEFANO
Università degli Studi di Torino
stefano.nejrotti@unito.it

NICOTRA FRANCESCO
Università degli Studi di Milano - Bicocca
francesco.nicotra@unimib.it

NITTI ANDREA
Università di Pavia
andrea.nitti01@universitadipavia.it

NOCERA PAOLA
Università degli Studi di Napoli "Federico II"
paola.nocera@unina.it

NOVARA FRANCESCA
Wiley-VCH
frnovara@wiley.com

OLIVIERO GIORGIA
Università degli Studi di Napoli "Federico II"
golivier@unina.it

OLIVITO FABRIZIO
Università Magna Graecia di Catanzaro
fabrizioolivito@gmail.com

OLIVO GIORGIO
Universitat de Girona
giorgio.olivo@udg.edu

ORLANDI MANUEL
Università degli Studi di Milano
manuel.orlandi87@gmail.com

PACE ANDREA
Università degli Studi di Palermo
andrea.pace@unipa.it

PACE VITTORIO
UNIVERSITY OF VIENNA
vittorio.pace@univie.ac.at

PALMIOLI ALESSANDRO
Università degli Studi di Milano - Bicocca
alessandro.palmioli@unimib.it

PALUMBO PICCIONELLO ANTONIO
Università di Palermo
antonio.palumbopiccionello@unipa.it

PAOLINO MARCO
Università degli Studi di Siena
paomar@oneonline.it

PAPAGNI ANTONIO
Università degli Studi di Milano - Bicocca
antonio.papagni@unimib.it

PARENTI FRANCESCA
Università di Modena e Reggio Emilia
francesca.parenti@unimore.it

PARMEGGIANI FABIO
University of Manchester
hegelrast@gmail.com

PASQUATO LUCIA
Università di Trieste
lpasquato@units.it

PASSARELLA DANIELE
Università degli Studi di Milano
daniele.passarella@unimi.it

PASTORE GENNY
Università di Camerino
genny.pastore@unicam.it

PELLACANI LUCIO
Università di Roma "La Sapienza"
lucio.pellacani@uniroma1.it

PELLEGRINO SARA
Università degli Studi di Milano
sara.pellegrino@unimi.it

PELLICCIOLI VALENTINA
Università degli Studi di Milano
valentina.pelliccioli@unimi.it

PENGO PAOLO
Università di Trieste
ppengo@units.it

PENNETTA CHIARA
Politecnico di Milano
pennetta90@gmail.com

PERI FRANCESCO
Università degli Studi di Milano - Bicocca
francesco.peri@unimib.it

PERNA FILIPPO MARIA
Università degli Studi di Bari
filippo.perna@uniba.it

PETRINI MARINO
Università di Camerino
marino.petrini@unicam.it

PEZZELLA ALESSANDRO
Università degli Studi di Napoli "Federico II"
alessandro.pezzella@unina.it

PIARULLI UMBERTO
Università degli Studi dell'Insubria
umberto.piarulli@uninsubria.it

PICCIALLI GENNARO
Università degli Studi di Napoli "Federico II"
picciall@unina.it

PIEMONTESE LUCA
Università degli Studi di Bari
luca.piemontese@uniba.it

PIERINI MARCO
Università di Roma "La Sapienza"
marco.pierini@uniroma1.it

PIERSANTI GIOVANNI
Università di Urbino Carlo Bo
giovanni.piersanti@uniurb.it

PINA ARIANNA
Università degli studi di Milano
arianna.pina@unimi.it

PINESCHI MAURO
Università di Pisa
pineschi@farm.unipi.it

PIROLA MARGHERITA
Università degli Studi di Milano
margherita.pirola@unimi.it

PIROVANO VALENTINA
Universita degli Studi di Milano
valentina.pirovano@unimi.it

PO RICCARDO
Eni S.p.A.
riccardo.po@eni.com

POCAR DONATO
Universita degli Studi di Milano
donato.pocar@unimi.it

PODERI CECILIA
Università di Bologna
cecilia.poderi2@unibo.it

POMARICO GIUSEPPE
Università di Roma "Tor Vergata"
pomarico@scienze.uniroma2.it

PORCHEDDU ANDREA
Università degli Studi di Cagliari
porcheddu@unica.it

POTENZA MARIANNA
Università degli Studi Salerno
mpotenza@unisa.it

PRANDI CRISTINA
Università degli Studi di Torino
cristina.prandi@unito.it

PRINS LEONARD
Università di Padova
leonard.prins@unipd.it

PROTTI STEFANO
Università di Pavia
prottistefano@gmail.com

PUGLISI ALESSANDRA
Università degli Studi di Milano
alessandra.puglisi@unimi.it

RABBACHIN LINDA
Università degli Studi di Milano - Bicocca
l.rabbachin@campus.unimib.it

RASTRELLI FEDERICO
Università di Padova
federico.rastrelli@unipd.it

RAZZETTI GABRIELE
Dipharma Francis Srl
gabriele.razzetti@dipharma.com

REGINATO GIANNA
Consiglio Nazionale delle Ricerche (CNR)
gianna.reginato@iccom.cnr.it

RESCIFINA ANTONIO
Università di Catania
arescifina@unict.it

RICCARDI CLAUDIA
Università degli Studi di Napoli "Federico II"
claudia.riccardi@unina.it

RICCIO RAFFAELE
Università di Salerno
raffaele.riccio@soc.chim.it

RICHICHI BARBARA
Università degli Studi di Firenze
barbara.richichi@unifi.it

RINALDI ANTONIA
Università degli Studi di Firenze
antonia.rinaldi@unifi.it

RIVA SERGIO
Consiglio Nazionale delle Ricerche (CNR)
sergio.riva@icrm.cnr.it

RIZZO FABIO
Consiglio Nazionale delle Ricerche (CNR)
fabio.rizzo@cnr.it

RIZZO SIMONA
ISTM-CNR
simona.rizzo@istm.cnr.it

RIZZO GIORGIO
Università degli Studi di Bari
giorgio.rizzo.1000@gmail.com

ROGATI FEDERICA
Università del Piemonte Orientale A. Avogadro
federica.rogati@uniupo.it

ROLETTO JACOPO
CBC Procos s.p.a.
roletto@procos.it

ROSA-GASTALDO DANIELE
Università di Padova
daniele.rosag@gmail.com

ROSSI BIANCA
Politecnico di Milano
bianca984@libero.it

ROSSI ELISABETTA
Università degli Studi di Milano
elisabetta.rossi@unimi.it

ROSSI SERGIO
Università degli Studi di Milano
sergio.rossi@unimi.it

RUGGIERO DAFNE
Università degli Studi di Salerno
druggiero@unisa.it

RUSSO LAURA
Università degli Studi di Milano - Bicocca
laura.russo@unimib.it

SABUZI FEDERICA
Università di Roma "Tor Vergata"
federica.sabuzi@uniroma2.it

SALAMONE MICHELA
Università di Roma "Tor Vergata"
michela.salamone@uniroma2.it

SALERNO GIANLUCA
Università degli Studi di Firenze
gianluca.salerno@unifi.it

SALERNO TANIA MARIA GRAZIA
Università di Messina
tsalerno@unime.it

SAMPAOLESI SUSANNA
Università degli Studi di Milano Bicocca
susanna.sampaolesi@gmail.com

SANNICOLO' FRANCESCO
LABORATORI ALCHEMIA SRL
francesco.sannicolo@unimi.it

SANSONE FRANCESCO
Università di Parma
francesco.sansone@unipr.it

SASSI MAURO
Università degli Studi di Milano - Bicocca
mauro.sassi@unimib.it

SATTIN SARA
Università degli Studi di Milano
sara.sattin@unimi.it

SCAPINELLO LUCA
Università degli studi dell'Insubria
l.scapinello@uninsubria.it

SCRIMIN PAOLO
Università di Padova
paolo.scrimin@unipd.it

SENALDI LUCA
INDENA Spa
luca.senaldi@indena.com

SEPE VALENTINA
Università degli Studi di Napoli "Federico II"
valentina.sepe@unina.it

SFORZA STEFANO
Università di Parma
stefano.sforza@unipr.it

SIANI GABRIELLA
Università "G. D'Annunzio" Chieti-Pescara
siani@unich.it

SICIGNANO MARINA
Università degli Studi Salerno
msicignano@unisa.it

SILIPO ALBA
Università degli Studi di Napoli "Federico II"
silipo@unina.it

SORARU' ANTONIO
Università degli Studi di Milano
Antonio.soraru@unimi.it

SPERANZA GIOVANNA
Università degli Studi di Milano
giovanna.speranza@unimi.it

SPINI NICOLE
nicolespini99@gmail.com

STADERINI SAMUELE
Consiglio Nazionale delle Ricerche (CNR)
stade84@gmail.com

SURANNA GIAN PAOLO
Politecnico di Bari
surannag@poliba.it

TADDEI MAURIZIO
Università di Siena
maurizio.taddei@unisi.it

TECILLA PAOLO
Università di Trieste
ptecilla@units.it

TEDESCHI TULLIA
Università di Parma
tullia.tedeschi@unipr.it

TERRACCIANO STEFANIA
Università degli Studi Salerno
sterracciano@unisa.it

TIECCO MATTEO
Università degli Studi di Perugia
matteotiecco@gmail.com

TOFANI LORENZO
Università degli Studi di Firenze
lorenzo.tofani.ita@gmail.com

TROISI LUIGINO
Università del Salento
luigino.troisi@unisalento.it

VALENTINI FEDERICA
Università degli Studi di Perugia
federicavalentinimail@gmail.com

VALENTINI FRANCESCA
Università di Roma "Tor Vergata"
f.valentini@scienze.uniroma2.it

VALGIMIGLI LUCA
Università di Bologna
luca.valgimigli@unibo.it

VENTRELLA ALESSIA
Università degli Studi "G. d'Annunzio" Chieti
alessia.ventrella@unich.it

VENTURI SILVIA
Politecnico di Milano
silvia.venturi@polimi.it

VILLANI CLAUDIO
Università di Roma "La Sapienza"
claudio.villani@uniroma1.it

VISCARDI ENRICO
Olon s.p.a.
eviscardi@olonspa.it

VISCARDI GUIDO
Università degli Studi di Torino
guido.viscardi@unito.it

VITA FINZI PAOLA
Università degli Studi di Pavia
vitafinz@unipv.it

VOLPE CHIARA
Università degli Studi Salerno
cvolpe@unisa.it

ZAMPELLA ANGELA
Università degli Studi di Napoli "Federico II"
azampell@unina.it

ZAPPIA STEFANIA
ISMAC-CNR
stefania.zappia@ismac.cnr.it

ZAPPIMBULSO NICOLA
Università degli Studi di Bari
nicola.zappimbulso@uniba.it

ZICCARELLI IDA
Università della Calabria
idaziccarelli@gmail.com

ZOIA LUCA
Università degli Studi di Milano - Bicocca
luca.zoia@unimib.it

ZUFFO MICHELA
Institute Curie
michela.zuffo@curie.fr

SPONSOR ISTITUZIONALI

UNIVERSITÀ DEGLI STUDI DI MILANO

ChemPubSoc Europe

UNIVERSITÀ DEGLI STUDI DI MILANO BICOCCA

SILVER SPONSOR

DASITGROUP | CARLO ERBA REAGENTS

MERCK

Flamma S.p.A.

BIANCHETTI • BRACCO • MINOJA
STUDIO CONSULENZA BREVETTUALE

JACOBACCI & PARTNERS

BRONZE SPONSOR

BRUKER

Biotage

Since 1949 Dipharma

CBC GROUP procos SPA

BRACCO LIFE FROM INSIDE

olon s.p.a.

EdiSES

Waters THE SCIENCE OF WHAT'S POSSIBLE.™

TCI EUROPE N.V. Division of TOKYO CHEMICAL INDUSTRY

indena®

deltek

SepaChrom

VICI DBS™

seneco SCIENCE

OTHER SPONSOR

JEOL

pharmaceuticals an Open Access Journal by MDPI

ISBN 978-88-3319-015-0