Deep Eutectic Solvents as sustainable media for organic transformations

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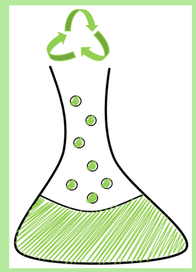
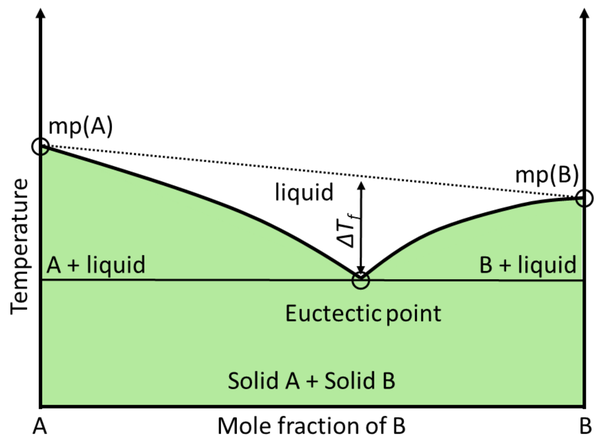
General purpose:

Development of new synthetic approaches in mild, safe & sustainable reaction conditions



Deep Eutectic Solvents (DES)

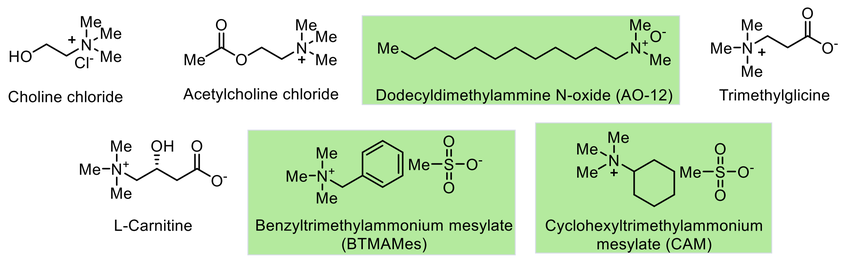
- DES are modern green solvents composed of a **mixture of two reagents** that are generally solid at room temperature, but when combined at a particular molar ratio, become liquid, generating a **eutectic mixture;**
- The binary mixture A + B is easily obtained by mixing a **hydrogen bond acceptor** (HBA) and a **hydrogen bonds donor** (HBD);



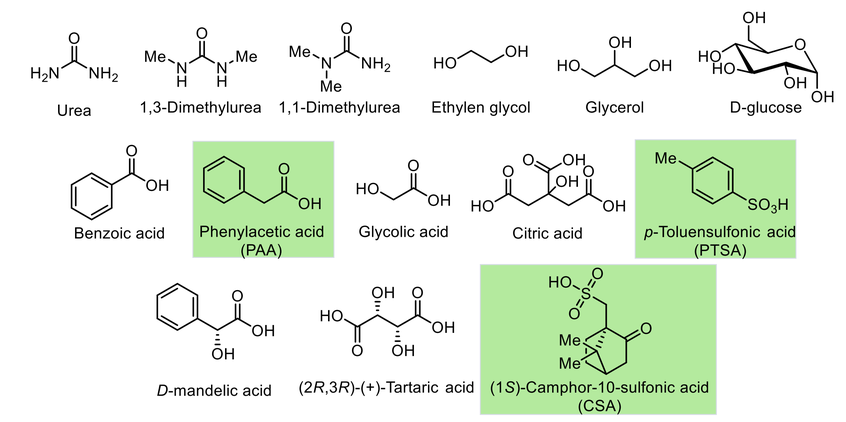
Features:

- Natural and **renewable** sources
- Great number of possible combinations between HBA and HBD
- Low **vapor pressure**
- Low Toxicity
- **Biodegradable**
- **Recyclable**
- Easy **dissolution** of a plethora of organic and inorganic compounds
- **Chiral** version available
- Simple solvent or **active** DES

Hydrogen bond acceptor

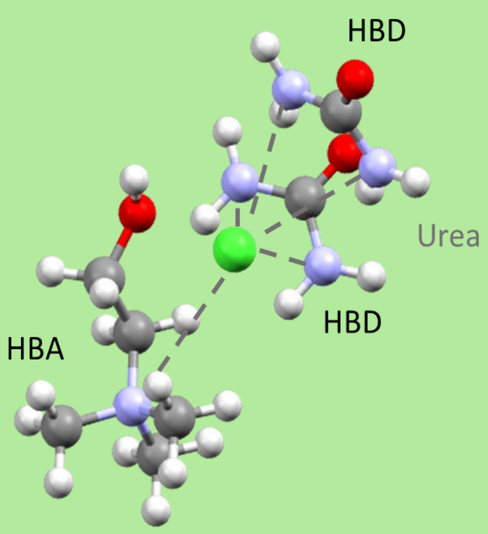


Hydrogen bond donor



Reviews: Chem. Rev. **2014**, *114*, 11060; *Eur. J. Org. Chem.* **2016**, 612; *Chem. Rev.* **2021**, *121*, 1232.

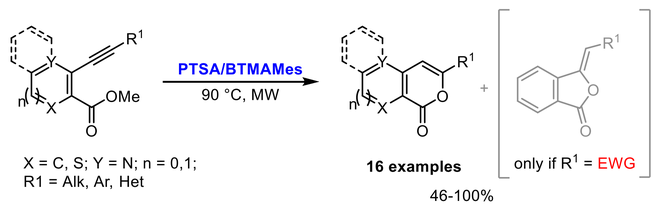
DES



PAA/AO-12

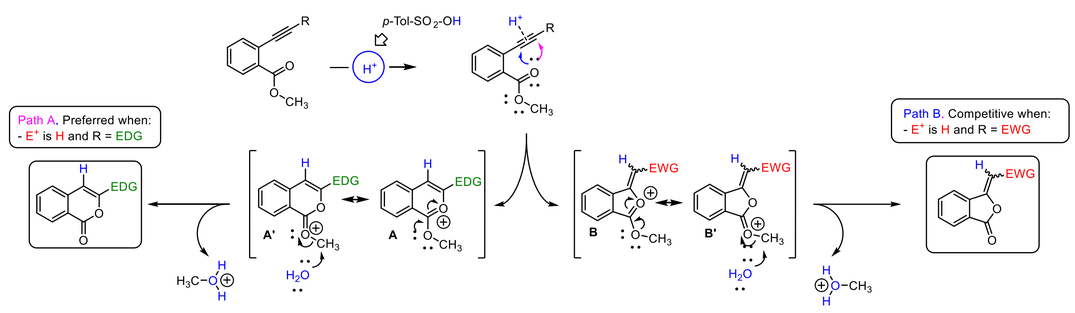
PTSA/BTMAMes +CSA/CAM

Cyclization of 2-alkynyl-(hetero)-arylcarboxylates in DES as active solvent



- Broad reaction scope
- Broad functional group tolerance
- If R^1 is an EWG: mixture of products in variable ratio

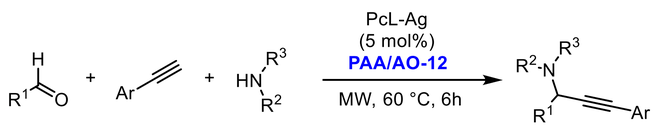
Proposed mechanism

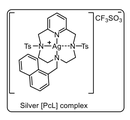


Partecipation of DES as electrophile (H^+) donor

F. Curti, M. Tiecco, V. Pirovano, R. Germani, A. Caselli, E. Rossi, G. Abbiati, *Eur. J. Org. Chem.* **2019**, 1904.

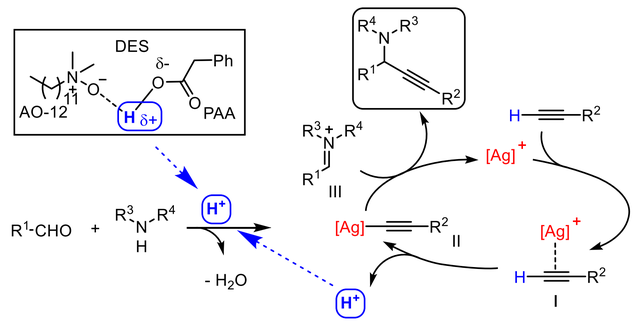
A3-coupling promoted by DES





- Aromatic and aliphatic aldehydes
- Aromatic alkynes
- Secondary aliphatic amines

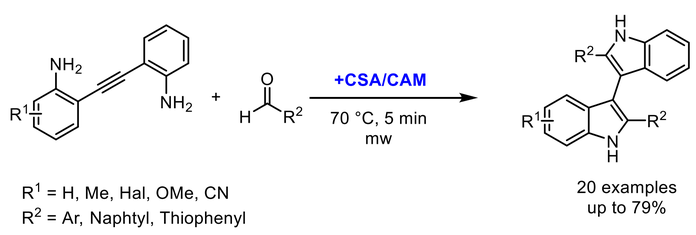
Proposed mechanism



Partecipation of DES in the formation of the imine intermediate (III)

E. Brambilla, A. Bortolla, V. Pirovano, A. Caselli, M. Tiecco, G. Abbiati, *Appl. Organomet. Chem.* **2022**, , *36*, e6669.

Synthesis of bis-indole mediated by active DES



- Rapid and efficient transformation
- Selective 5-*exo-dig* cyclization
- Broad scope

Partecipation of DES in the promotion of double cyclization

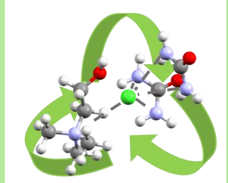
Reached goals:

- ✓ *Development of cyclization and multicomponent reactions in **Deep Eutectic Solvents***
- ✓ ***DES** employed as "active" solvent*
- ✓ *Mild reaction conditions*
- ✓ ***Recycle DES** trials*

Future perspective:

*Development of **enantioselective** transformations employing **chiral DESs***

DES



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