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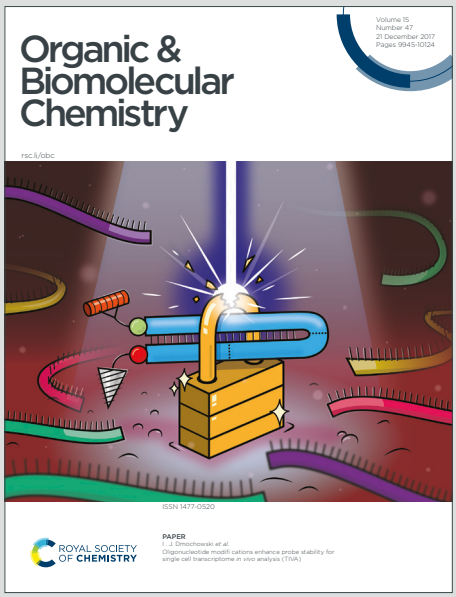

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Synthesis and Photophysical Evaluation of Polarity Sensitive Push-pull Isoquinolines and their alkynyl precursors

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ABSTRACT: Two sets of unprecedented push-pull isoquinolines, characterized by an opposite "dipolar moment" with respect to the longitudinal axis of the molecule, have been prepared. The key step of the approach is the microwave-promoted domino imination/cycloisomerization of 2-alkynyl benzaldehydes in the presence of methanolic ammonia. Absorption spectra, and emission spectra of the D-π-A isoquinolines and their alkynyl precursors in nine different solvents have been recorded. The absolute QYs of all compounds have been recorded in three solvent with different polarity properties, i.e. toluene, DMSO and ethanol. Among the D-π-A isoquinolines prepared – nicknamed QuinaChroms – two compounds characterized by opposite dipolar moments, i.e. 3-(4-Methoxyphenyl)-7-nitroisoquinoline **1a** and *N,N*-diethyl-3-(4-(methylsulfonyl)phenyl)isoquinolin-7-amine **2b** displayed the more interesting photophysical profiles, whereas 5-(diethylamino)-2-(A)arylethynylbenzaldehydes precursors **8a-c** – having a free aldehyde group suitable for possible conjugation − exhibited strong fluorescence and wide Stokes shifts. These products are interesting for a potential use as polarity-sensitive fluorescent probes or advanced functional materials.

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INTRODUCTION

In the last ten years, the study of (hetero)polycyclic aromatic molecules end-capped with conjugated electron-donating and electron-withdrawing groups (D-π-A or push-pull systems) has witnessed an increasing growth, due to the particular properties of these compounds.[1] The peculiar electronic features of these conjugated systems are useful in different applications such as environment-sensitive probes to monitor local properties of cell districts and biological structures[2] as well as in the development of advanced functional materials.[3] Environment-sensitive molecules can modify their spectroscopic properties (in particular their fluorescence emission), in reply to a change of the chemical or physical properties of their surroundings. In this context, polarity-sensitive dyes[4] are a subclass of molecules that change their emission band as a function of the polarity of the medium (*i.e.,* solvent or environment). The optimal spectroscopic requirements of a polarity-sensitive dye are strong solvatochromism, absorption near to the visible range, wide Stokes shifts, and high extinction coefficient (ε), quantum yield (QY), and photostability.

For some years, our group has been fascinated by the development of synthetic approaches for the preparation of original push-pull heterocyclic systems. Five years ago, we synthesized a small library of polarity-sensitive fluorescent dyes - nicknamed MediaChroms[5] - characterized by a pyrimidoindolone backbone, which displayed promising photophysical profiles. One of them has been tested as a probe for biological investigations. More recently, we developed ten unprecedented D-π-A isocoumarin-based derivatives - nicknamed CumaChroms[6]- with interesting spectroscopic properties.

At the same time, we have been also very active in the development of new domino and multicomponent (MCR) strategies for the synthesis of functionalized heterocycles starting from alkynes bearing a proximate nucleophile. From a methodological point of view, the use of alternative energy sources (such as microwaves) and the catalysis promoted by coinage metals (i.e. silver and gold), are effective tools to reach the goals. In particular, in the last years, we developed some approaches to isoquinolines - and closely related *N*-heterocycles - through a domino imination/cycloisomerization of γ- and δ-ketoalkynes in the presence of an ammonia source,[7] also as MCR.[8]

The fluorescence properties of isoquinolines, in particular, those characterized by the presence of a nitrogen[9] or an oxygen[10] on the C-3, have been well documented. Conversely, the environment-sensitive properties of properly functionalized isoquinoline nuclei have been only rarely explored. Ihmels and co-workers reported very recently the preparation of nine 3-hydroxy-4-pyridyl-3-isoquinolines and one of them (the parent compound) displayed interesting solvatochromic and halochromic properties (**Figure 1**, A).[11] In another recent example, the 1-isoquinolinyl fragment was employed to chelate the boron atom

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in a series of five boron compounds characterized by a dual emission, where the charge transfer emission is related to the solvent polarity (**Figure 1**, B).[12] In 2020 the research group of Rodríguez-López studied the synthesis and the photophysical properties of some new push-pull isoquinoline chromophores in which the isoquinoline was the pulling unit (**Figure 1**, C).[13]

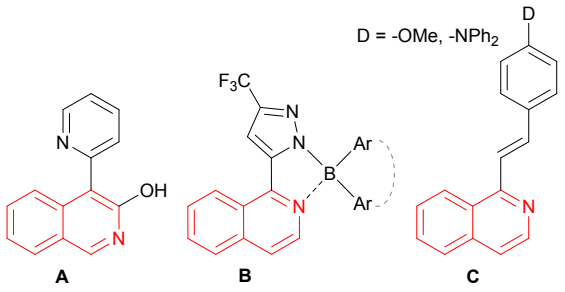

Figure 1: Polarity-sensitive isoquinoline-containing compounds

We were surprised to discover that, to the best of our knowledge, the synthesis and the evaluation of photophysical features of push-pull isoquinolines where the isoquinoline is the π-unit is practically unexplored. For this reason, we were intrigued to prepare and evaluate the spectroscopic properties of some original D-π-A isoquinolines, - nicknamed QuinaChroms - as potential polarity-sensitive fluorophores and/or organic structures for optoelectronic applications (**Figure 2**). In this work, we describe our findings.

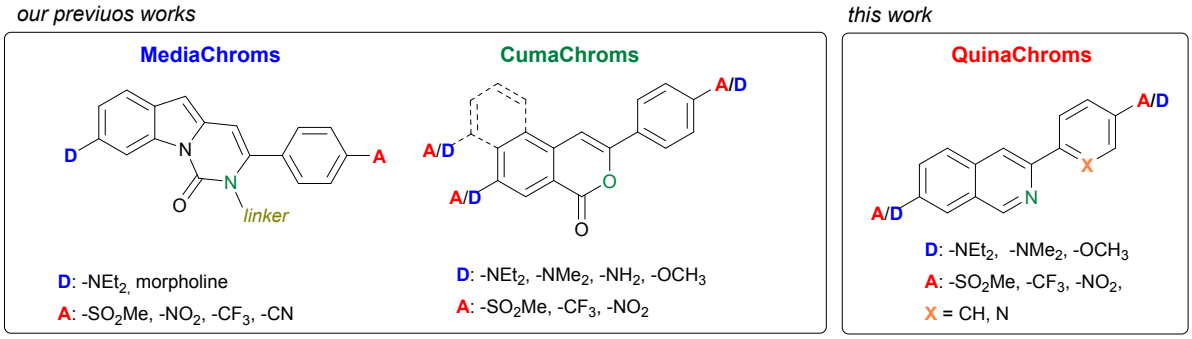

Figure 2: The D-π-A systems developed in our group.

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RESULTS and DISCUSSION

Synthesis of the isoquinoline-based library

To create an effective push-pull system, the electron-donating (D) and electron-withdrawing (A) groups to connect to the isoquinoline backbone have been selected taking into account the suggestions reported in the review of Bures,[1] and the recent experience of our group.[5,6] So, dialkylamino groups and the methoxy group have been chosen as EDGs. Regarding the selection of the EW groups, the choice fell on those groups that displayed more interesting features in our previous works, and in particular: i) the methylsulfonyl group, that gave remarkable results in the CumaChrom series,[6] ii) the nitro group, for its availability and versatility in subsequent transformations, iii) the trifluoromethyl group, a substituent hardly investigated in this context[14] that provided unexpected outcomes in the MediaChrom series,[5] and iv) the pyridine whose ability to impart solvatochromic and halochromic properties to isoquinoline nucleus has been recently disclosed.[11]

Therefore, we planned to prepare five original push-pull isoquinolines (**Scheme 1**). The new QuinaChroms can be divided into two series, **1a,b**, and **2a-c** respectively, according to a reversed "dipolar moment" with respect to the longitudinal axis of the molecule. This choice arises from the interesting result obtained in the CumaChrom series,[6] in which a reversed position of the functional groups resulted in a switch from positive to negative solvatochromic behavior.

We reasoned that isoquinolines **1a** and **1b** could be obtained by a standard Sonogashira coupling between 5-nitro-2-bromobenzaldehyde and suitable electron-rich acetylenes, (i.e., 4-methoxyphenylacetylene and 4-dimethylaminophenylacetylene, respectively), followed by an imination/cyclization sequence (**Scheme 1**). For the synthesis to compounds **2a-c**, after the coupling with the appropriate electron-poor arylacetylene (i.e., 4-trifluorophenylacetylene, 4-methylsulfonyl-phenylacetylene, and 2-ethynylpyridine, respectively) and the subsequent imination/cyclization domino reaction to give the A-π-A isoquinolines **1c-e**, the approach had to foresee the reduction of nitro to an amino group, followed by *N*-alkylation (**Scheme 1**).

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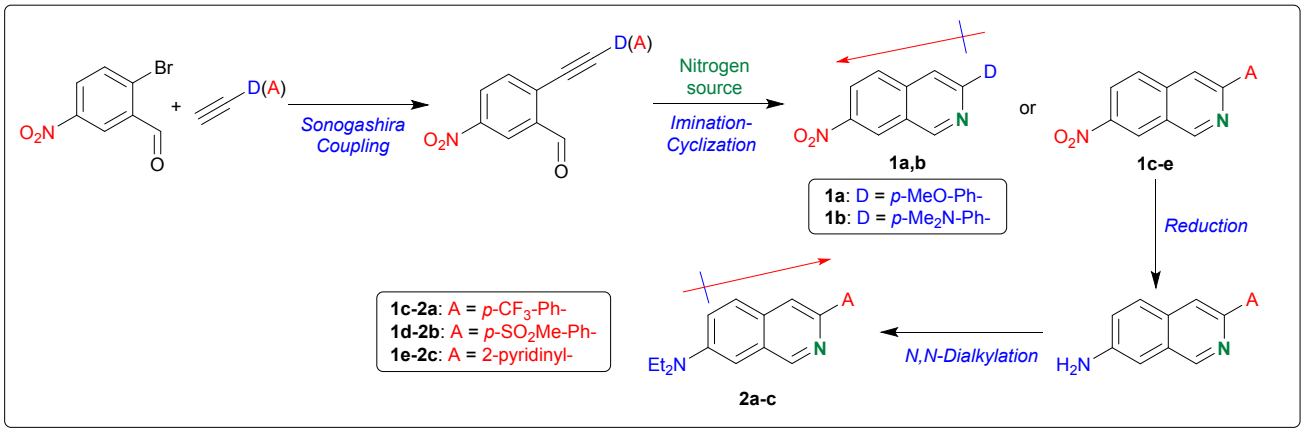
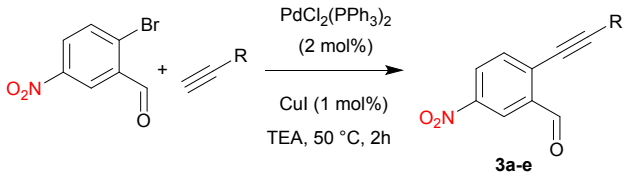


Scheme 1: Planned synthetic approaches

Therefore, 2-alkynyl-5-nitrobenzaldehydes **3**, were prepared by a Sonogashira cross-coupling reaction,[15] under the reaction conditions already optimized in our laboratory, starting from cheap and commercially available 2-bromo-5-nitrobenzaldehyde and the proper aryl alkynes. The reactions, performed in freshly distilled trimethylamine (TEA) at 50 °C under a nitrogen atmosphere and in the presence of *bis*(triphenylphosphine)palladium(II) chloride and copper iodide as catalysts, gave the desired 2-alkynyl-5-nitrobenzaldehydes **5** in very good yields (**Table 1**).

Table 1: Synthesis of starting materials



Entry	3	R	Yield[a] (%)
1	**a**	*p*-MeO-Ph-	95
2	**b**	*p*-Me_2N-Ph-	92
3	**c**	*p*-CF_3-Ph-	88
4	**d**	*p*-$MeSO_2$-Ph-	95
5	**e**	2-pyridyl-	76

[a] referred to the pure isolated product.

To define the optimal reaction conditions for the cyclization of 2-alkynyl-5-nitrobenzaldehydes **3a-e** to give the corresponding isoquinolines, we selected the 2-((4-methoxyphenyl)ethynyl)-5-nitrobenzaldehyde **3a** as a model substrate. Despite our experience in this kind of reaction,[7] the presence of a strong EWG such as the nitro group on the benzaldehyde moiety suggested a possible adverse effect that could make the reaction trickier. Therefore, we tried the reaction in the presence of different nitrogen

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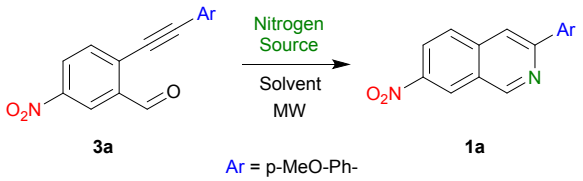
sources, solvents, and temperatures. As an energy source, we selected microwaves due to their well-established efficiency.[7b-d] Results are summarized in **Table 2**.

Table 2. Screening of optimal imination/cyclization conditions



Entry	Nitrogen Source	Solvent	Time	MW (T)	Yield[a]
1	$AcONH_4$ 20 equiv.	DMSO	30 min	80 °C	15 %
2	$AcONH_4$ 20 equiv.	DMF	30 min	80 °C	20 %
3	$AcONH_4$ 20 equiv.	CH_3CN	30 min	80 °C	14 %
4	$AcONH_4$ 20 equiv.	Toluene	30 min	80 °C	31 %
5	$AcONH_4$ 20 equiv.	MeOH	30 min	80 °C	29 %
6	NH_3 2M	MeOH	30 min	80 °C	39 %
7	NH_3 2M	MeOH	1 h	80 °C	40 %
8	NH_3 2M	MeOH	2 h	80 °C	52 %
9	NH_3 2M	MeOH	4 h	70 °C	44 %
10	NH_3 2M	MeOH	2 h	100 °C	56 %
11	NH_3 2M	MeOH	4 h	100 °C	53 %
12	NH_3 2M	MeOH	2 h	120 °C	18 %

[a] referred to the pure isolated product.

Based on our recent results concerning the imination/cyclization of 2-propargyl benzaldehydes,[7b] we tried the reaction in DMSO with ammonium acetate as nitrogen source and 80 °C by microwave heating for 30 mins, but we observed the formation of **1a** in poor yields (**Table 1**, entry 1). We explored the solvent effect under these conditions (**Table 1**, entries 2-5) finding that toluene and methanol gave the best results, although still unsatisfactory (**Table 1**, entries 4 and 5 respectively). Being methanol a suitable solvent, according to our previous studies[7d] we switched to 2M ammonia in methanol as a nitrogen source (**Table 1**, entries 6-12). After some tries at different temperatures (ranging from 70 to 120 °C) and times (ranging from 0.5 to 4 h), we identified as best reaction conditions the microwaves heating at 100 °C for 2 hours (**Table 1**, entry 10). It is worth noting that also under the optimized reaction conditions the reaction yields do not exceed 56 %. This is probably due to the already mentioned unfavorable-effect due to the presence of the nitro group on the alkynyl benzaldehyde able to decrease the reactivity both at carbonyl terminus as well as at the triple bond level.

Next, we extend the cyclization approach to the other 2-alkynyl-5-nitrobenzaldehydes **3b-e**. The results are depicted in the following **Scheme 2**.

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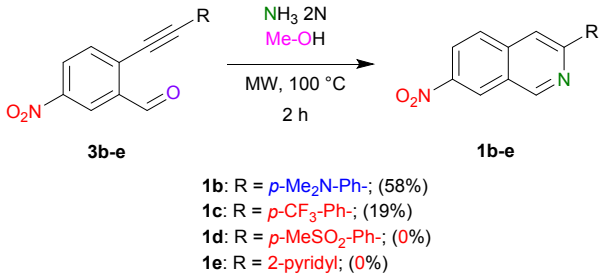

Scheme 2: Scope and limitation of the approach

As observed for **3a**, in the presence of an EDG on the alkyne terminus the cyclization of the alkynylbenzaldehyde **3b** works well to give the desired isoquinoline **1b** in 58% yield. Conversely, the presence of EWG seems to hamper strongly the reaction. Starting from aldehyde **3c**, characterized by the presence of a trifluoromethyl group, the corresponding isoquinoline **1c** was obtained in very poor yield (19%). Moreover, the reactions of aldehydes **3d** and **3e** failed to give the desired isoquinolines, and mixtures of unidentified by-products were obtained.[16] Perhaps, the presence of two conjugated strong EWGs at the opposite sides of the diarylalkyne, strongly perturbs the electronic properties of C≡C π system, quenching its reactivity toward the intramolecular nucleophilic addition of the imine intermediate to the triple bond.

We tried to overcome this problem by carrying out some additional experiment on **2c** by a further fine-tuning of the reaction conditions, also in the presence of a silver salt as the catalyst,[7c] but unfortunately, we were not able to improve the yields over the 15%.

Then, we planned a different route to obtain isoquinolines **2a-c**. We thought to transform the nitro group into an amino group in an earlier stage (**Scheme 3**). We assumed that the reduction of the nitro group on 2-alkynyl-5-nitrobenzaldehydes could be troublesome due to the number of reducible π-system in the molecule, i.e., the nitro, the aldehyde, the alkyne. Therefore, we decide to reduce directly the nitro group of 5-nitro-2-bromobenzaldehyde, after proper protection of the aldehyde as acetal that occurred under standard conditions to give the 2-(2-bromo-5-nitrophenyl)-1,3-dioxolane **4** in 94% yield. Among some different reduction methods tested, the chemical reduction in the presence of iron and ammonium chloride gave the best result: the desired 4-bromo-3-(1,3-dioxolan-2-yl)aniline **5** was obtained in a satisfactory 96% yield. The corresponding 4-bromo-3-(1,3-dioxolan-2-yl)-*N,N*-diethylaniline **6** was obtained by treatment with an excess of iodoethane under basic conditions in good yield (77%). The following deprotection ran in quantitative yield to give the key starting material, the 2-bromo-5-(diethylamino)benzaldehyde **7**, sufficiently pure that no further purification was needed (see ESI for experimental details).

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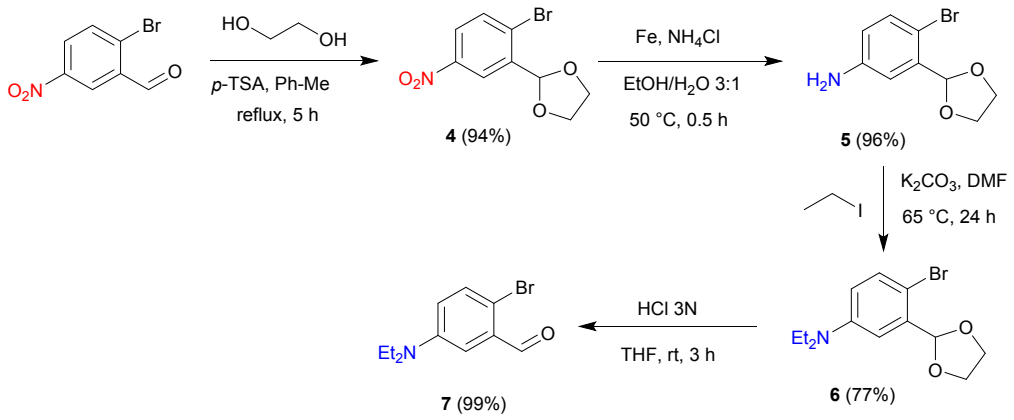
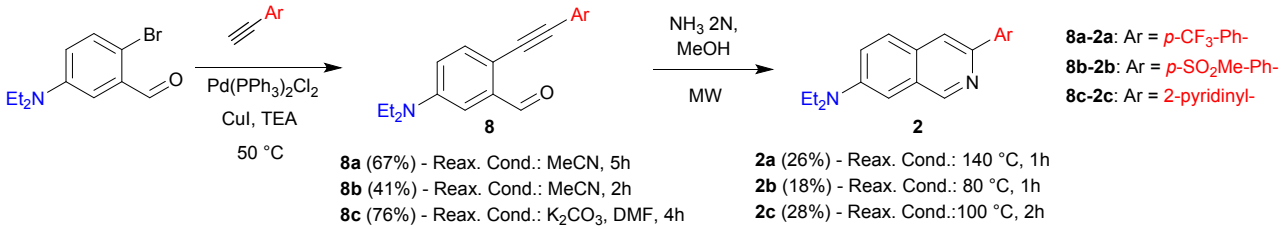


Scheme 3: Synthesis of key-intermediate **7**.

The Sonogashira reaction between aldehyde **7** and the selected alkynes gave the desired push-pull 2-alkynyl-5-dietylaminobenzaldehydes **8a-c**. Some modifications to the standard Sonogashira reaction condition were necessary to obtain good yields. This is probably due to the presence of the amino group on the aldehyde moiety and the electron-poor nature of the alkynes involved. The cyclization step too required some modification with respect to the standard conditions, and despite our efforts, the desired D-π-A isoquinolines **2a-c** were obtained only in modest yields, but in high purities, (**Scheme 4**) beside unidentified by-products, probably arising from polymerization processes. All QuinaChroms are isoquinolines unknown in the literature and have been fully characterized through mono and/or bidimensional NMR spectroscopy, mass spectrometry, and elemental analysis.



Scheme 4: Synthesis of QuinaChroms **2a-c**.

The photophysical properties of QuinaChroms **1a-b** and **2a-c** were then evaluated. We collected the UV/Vis absorption spectra in nine different solvents with different polarities (toluene, dichloromethane, tetrahydrofuran, ethyl acetate, acetone, ethanol, *N,N*-dimethylformamide, dimethylsulfoxide, and water). Most of the molecules synthesized are well soluble in the explored solvents. A mother solution of 0.5 mg/mL in DMSO was prepared for all compounds. From the absorbance values in DMSO, we obtained the ε using the linear regression method. The UV absorption and emission spectra in the different solvents have been recorded by dissolving 28 μL of the stock DMSO solution (1 mg/mL) in the suitable media,

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to obtain a final concentration of 0.014 mg/mL (**Table 3**). Additionally, we measured the absolute QYs in three solvents with different polarities (**Table 4**).

		1a		**1b**		**2a**		**2b**^		**2c**	
Solvent	**$E_T(30)$**[4a]	λ_{abs} (nm)	λ_{em}[$] (nm)	λ_{abs} (nm)	λ_{em}[$] (nm)	λ_{abs} (nm)	λ_{em}[$] (nm)	λ_{abs} (nm)	λ_{em}[$] (nm)	λ_{abs} (nm)	λ_{em}[$] (nm)
Toluene	33.9	371	476[§]	431	601[+]	347	431	357	429	347	427[+]
THF	37.4	366	506[+]	428	648[+]	348	439	359	445	347	434
Ethyl Acetate	38.1	365	509[+]	423	650[+]	346	437	355	444	345	434
DCM	40.7	368	548	433	700[§]	348	439	364	449	350	437
Acetone	42.2	365	549	425	513[§]	349	445	303	464[§]	348	443
DMF	43.2	371	568	432	554[§]	352	454	362	477	351	448
DMSO	45.1	**375** (18643)[#]	585[+]	**438** (23985)[#]	438[§]	**356** (30885)[#]	457	**367** (25412)[#]	487	**354** (23436)[#]	454
Ethanol	51.9	361	561[§]	419	575[§]	346	451	359	468	348	449
Water	63.1	387	551[+]	412	570[§]	340	431[+]	367	523[+]	344	473[+]
Solvatochromic shift		**14**	**109**	**19**	**n.d.**	**10**	**26**	**11**	**58**	**7**	**27**
Stokes shift (Toluene)		**105**		**170**		**84**		**72**		**80**	

^ c em = 0.007 mg/mL
[$] the excitation has been carried out at the λ corresponding to the absorption maxima
[#] ε expressed as $M^{-1}\cdot cm^{-1}$
[+] moderately fluorescent
[§] extremely little fluorescent

Table 3. Absorption peak wavelength (λ_{abs}) and fluorescent emission peak wavelength (λ_{em}) of QuinaChroms **1a,b,** and **2a-c** in different solvents (c = 0.014 mg/mL).

	Solvent		
	Toluene	**DMSO**	**EtOH**
Compound	QY (%)	QY (%)	QY (%)
1a	45,8	15,7	2,4
1b	77,8	not determinable	not determinable
2a	14,2	28,1	13,8
2b	24,2	62,6	35,7
2c	17,6	27,2	13,5

Table 4. Absolute QYs of QuinaChroms **1a,b,** and **2a-c** in three solvents with different polarities (c = 0.014 mg/mL).

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All isoquinolines **1a,b**, and **2a-c** showed a high ε in DMSO, comparable to other well-established fluorescent molecular probes, such as 1,8-ANS (8-Anilinonaphthalene-1-sulfonic acid, ε = 18000). All compounds displayed strong absorbance in all tested solvents except for water where solubility problems have been experienced, less pronounced only in the case of **2c**. As expected, the range of absorption maxima in the different solvents is quite tight, ranging from 7 nm for **2c** to 19 nm for **1b**. All isoquinolines displayed their more red-shifted absorption maxima in DMSO, but whereas **1a** and **2a-c** have their maximum absorption peaks in the UV-A region (from 354 to 375 nm), **1b** display the more pronounced red-shifted maxima in the visible region (438 nm). This behavior suggest that the isoquinoline scaffold allows a more efficient ICT from position 3 to 7 rather than to opposite arrangement. When the isoquinolines were irradiated at their maximum absorption wavelength for the specific solvent, fluorescent emission peaks were recorded with moderate to good intensities except for **1b** whose fluorescence is moderate for toluene, THF, and ethyl acetate and extremely poor for all the other seven solvents. This scarce fluorescence makes the emission data of **1b** unreliable and problematic to translate. The fluorescence in water is moderate or poor for all compounds, but again this might be due to the extremely poor solubility observed in this medium.

A bathochromic effect of the emission maxima according to the increasing of the polarity of the medium was observed for compounds **1a** and **2a-c**, while **1b** seems to display a particular reversed hypsochromic shift. However, as pointed above, the fluorescence of **1b** is very low in almost all solvents strongly undermining the reliability of these data. Despite Stokes and solvatochromism shift of **1b** are wide, and the QY of this compound in toluene is notable, the poor emissive properties in all other solvents, as stated above, represent a strong drawback for whatever possible application as environment-sensitive probe or advanced materials.

Isoquinoline **1a** displays the widest solvatochromic shift (Δλ = 109 nm) but the intensity of fluorescence is moderate and very different among the solvents (in particular in toluene and ethanol is very low). Compounds **2a-c** display a consistent intense fluorescence in almost all solvents. Among these three isoquinolines, **2b** has the widest solvatochromic shift (Δλ = 58 nm) and the highest QY in all the solvent tested. Considering the important characteristics that distinguish an optimal polarity sensitive probe (i.e. solubility, fluorescence intensity, wide solvatochromic shift, absorption close to the visible range, large Stokes shift, high QY), compounds **1a** and **2b** are the more interesting solvatochromic isoquinolines prepared in this study (see ESI for absorption and emission spectra of all isoquinolines in the different solvents). While the solvatochromic features of **2b** are somewhat predictable in agreement with the

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behavior of the corresponding Cumachrom,[6] on the contrary, the pronounced solvatochromism of **1a,** characterized by the presence of a weaker EDG such as methoxy group,[1] is rather surprising and unexpected, in particular when related to the equally unexpected poor performances of **1b**. To verify that the lack of fluorescence of **1b** was not related to fast degradation of the molecule in solution, we recorded two ^{1}H NMR spectra of **1a** in DMSO five days apart from each other, and we verified that any degradation occurred (see ^{1}H NMR spectra in ESI). Taking in mind the recent work of Rodríguez-López,[13] we briefly evaluated, as comparison, the photophysical properties of the 3-(4-methoxyphenyl)isoquinoline in which the isoquinoline represent the pulling unit, whose synthesis was reported by us in 2010.[8] As expected, the lacking of a conjugated π-system strongly affected the photophysical properties. The UV-Vis absorption maxima in many cases overlap the absorption of the solvents and the molecule does not display neither fluorescence nor solvatochromic properties when pulled under a UV lamp at 254 nm (see ESI for details).

Then, we decide to evaluate also the photophysical properties of the starting alkynyl aldehydes **3a,b**, and **8a-c**, to make a comparison between the characteristics of the push-pull isoquinolines (**1a,b**, and **2a-c**) and those of the corresponding starting alkynyl aldehydes (**3a,b**, and **8a-c**). Moreover, this evaluation allowed us to verify if the presence of the dimethylamino and the nitro groups at the extremities of an extended π-conjugated system could be the reason for the quenching of fluorescence observed for **1b**. We recorded the UV/Vis absorption and emission spectra in nine different solvents as done for isoquinolines, and ε were calculated from the absorbance values in DMSO (**Table 5**). Furthermore, we measured the absolute QYs in three solvent with different polarities (**Table 6**).

		3a		**3b**		**8a**^		**8b**^		**8c**^	
Solvent	**E_T(30)** [4a]	λ_{abs} (nm)	λ_{em}[$] (nm)	λ_{abs} (nm)	λ_{em}[$] (nm)	λ_{abs} (nm)	λ_{em}[$] (nm)	λ_{abs} (nm)	λ_{em}[$] (nm)	λ_{abs} (nm)	λ_{em}[$] (nm)
Toluene	33.9	440	507[+]	374	570[+]	347	472	355	475	342	473
THF	37.4	440	505	369	619[+]	345	481	352	480	340	477
Ethyl Acetate	38.1	434	501[+]	367	613[+]	343	482	350	482	338	480
DCM	40.7	447	534	371	554[§]	347	503	357	504	344	503
Acetone	42.2	437	534	367	542[§]	343	498	351	501	339	497
DMF	43.2	447	548[+]	373	554[§]	347	508	354	508	342	507
DMSO	45.1	**454** (16483)[#]	565[+]	**376** (18824)[#]	579[§]	**348** (24943)[#]	521	**356** (26319)[#]	521	**345** (29000)[#]	517
Ethanol	51.9	437	415[§]	362	554[§]	343	546[§]	352	557[§]	343	562[§]
Water	63.1	416	538	403	546[§]	345	547[§]	360	531[§]	344	612[§]

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Solvatochromic shift		**20**	**64**	**14**	**n.d.**	**5**	**49**	**5**	**46**	**7**	**44**
Stokes shift (Toluene)		**67**		**196**		**125**		**120**		**131**	

^ c em = 0.007 mg/mL
$ the excitation has been carried out at the λ corresponding to the absorption maxima
# ε expressed as $M^{-1}\cdot cm^{-1}$
+ moderately fluorescent
§ extremely little fluorescent

Table 5. Absorption peak wavelength (λ_{abs}) and fluorescent emission peak wavelength (λ_{em}) of alkynylbenzaldehydes **3a,b,** and **8a-c** in different solvents (c = 0.014 mg/mL).

	Solvent		
	Toluene	**DMSO**	**EtOH**
Compound	QY (%)	QY (%)	QY (%)
3a	67	not determinable	not determinable
3b	not determinable	25,1	not determinable
8a	65,5	71	3,4
8b	71,4	88,5	4,4
8c	73,6	84,6	3,6

Table 6. Absolute QYs of alkynylbenzaldehydes **3a,b,** and **8a-c** in different (c = 0.014 mg/mL).

As observed for the isoquinoline **1b**, the corresponding alkynylbenzaldehyde **3b** displayed a very poor fluorescence too in almost all solvents, and the QY is undeterminable in toluene and ethanol. This seemed to confirm a sort of "fluorogenic incompatibility" among nitro and dimethylamino groups at the extremities of a highly conjugated system. This is in agreement with the limited fluorescence solvatochromism generally observed in 4-amino-7-nitro-2,1,3-benzoxadiazole (NBD) analogues.[2,17] In this series too, compounds with the EDGs on the benzaldehyde moiety (**8a-c**) displayed brighter fluorescence and high QY in toluene and DMSO. The poor water solubility of the alkynylbenzaldehydes makes the results for this solvent unreliable. While the performances of **3a** are worse with respect to the corresponding isoquinoline **1a** (also testified by the indeterminability of QY in polar solvents), aldehydes **8a-c** displayed broader Stokes shifts compared with the corresponding isoquinolines **2a-c**, but while **8a** and **8c** displayed also larger solvatochromic shifts, for **8b** this value is comparable to that of **2b**.

View Article Online
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CONCLUSIONS

We prepared five unprecedented isoquinolines – nicknamed QuinaChroms – endowed with a conjugated D-π-A system. The key step of the syntheses involves a microwave promoted highly regioselective imination/cyclization domino sequence of properly substituted 2-alkynylbenzaldehydes in the presence of methanolic ammonia. The preparation was challenging because the presence of conjugated strong ED and EW groups on the extremities of the starting alkynyl benzaldehydes affect the electronic asset of the molecules and such perturbation on the triple bond make the cyclization steps trickier. The polarity-sensitive properties of the D-π-A isoquinolines and their alkynyl precursors have been investigated in nine solvents with different polarity. Among the QuinaChroms, compounds **1a** and **2b** displayed the more interesting spectroscopic profiles, whereas alkynylbenzaldehydes **8a-c** – which have the benefit of owning a free aldehyde group suitable for possible conjugation − showed strong fluorescence and wide Stokes shifts. Both heterocyclic and linear compounds could be useful for possible applications as polarity-sensitive probes for the study of biological interactions or for the development of new nonlinear optical materials.

EXPERIMENTAL SECTION

General. Anhydrous solvents are commercially available. All the reactions that involve the use of reagents sensitive to oxygen or water, were carried out under nitrogen. The chromatographic column separations were performed by a flash technique, using silica gel (pore size 60 Å, particle size 230−400 mesh). TLC Alu foils with a fluorescent indicator (254 nm) were used for TLC analysis, and the detection was performed by irradiation with UV light (λ = 254 nm and/or 366 nm). ^{1}H NMR analyses were performed with a 300 MHz spectrometer at rt. Spectra were referenced to residual solvent. The coupling constants (*J*) are expressed in Hertz (Hz), the chemical shifts (δ) in ppm. ^{13}C NMR analyses were performed with the same instruments at 75 MHz. Attached Proton Test (APT) sequence was used to distinguish the methine and methyl carbon signals from those arising from methylene and quaternary carbon atoms. All ^{13}C NMR spectra were recorded with complete proton decoupling. Low-resolution MS spectra were recorded with electron impact source and electrospray/ion trap equipped instrument, using a syringe pump device to directly inject sample solutions. The values are reported as mass-charge ratio and the relative intensities of the most significant peaks are shown in brackets. UV-visible and fluorescence spectra were collected at 20 °C. Absolute photoluminescence QYs were measured using an absolute PL quantum yield spectrometer at rt.

View Article Online
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General procedure for the synthesis of 5-nitro-2-alkynylbenzaldehydes 3a-e: In a round-bottom flask, $PdCl_2(PPh_3)_2$ (2 mol%) was added to a well-stirred N_2-flushed solution of commercially available 2-bromo-5-nitro-benzaldehyde (1.0 equiv) and the suitable terminal arylalkyne (1.2 equiv) in anhydrous triethylamine. The reaction mixture was stirred for 15 minutes at rt, then CuI (1 mol%) was added. The reaction mixture was warmed at 50°C and stirred for 2h. The reaction mixture was filtered on a thin diatomite pad and the triethylamine was removed under reduced pressure. The crude was purified by flash column chromatography over silica gel affording 2-alkynyl-5-nitrobenzadehydes **3a-e**.

2-((4-Methoxyphenyl)ethynyl)-5-nitrobenzaldehyde **3a**: General procedure was followed by using: 2-bromo-5-nitrobenzaldehyde (400 mg, 1.73 mmol) , $PdCl_2(PPh_3)_2$ (38 mg, 0.03 mmol), 2-ethynyl-4-methoxybenzene (274 mg, 2.08 mmol) and CuI (5 mg, 0.02 mmol). Eluent for chromatography: Hexane/EtOAc (9:1). Yellow solid. Yield 95% (464 mg). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 10.64 (s, 1H), 8.75 (d, J = 2.4 Hz, 1H), 8.39 (dd, J = 8.6, 2.4 Hz, 1H), 7.77 (d, J = 8.6 Hz, 1H), 7.54 (d, J = 8.9 Hz, 2H), 6.94 (d, J = 8.9 Hz, 2H), 3.86 (s, 3H). NMR data are in agreement with those reported in the literature.[18]

2-((4(Dimethylamino)phenyl)ethynyl)-5-nitrobenzaldehyde **3b**: General procedure was followed by using: 2-bromo-5-nitrobenzaldehyde (400 mg, 1.73 mmol), $PdCl_2(PPh_3)_2$ (38 mg, 0.03 mmol), 4-ethynyl-*N,N*-dimethylaniline (301 mg, 2.08 mmol) and CuI (5 mg, 0.02 mmol). Eluent for chromatography: hexane/EtOAc (from 9:1 to 3:1). Yellow solid. Yield 92% (467 mg). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 10.64 (s, 1H), 8.71 (d, J = 2.5 Hz, 1H), 8.34 (dd, J = 8.6, 2.5 Hz, 1H), 7.71 (d, J = 8.6 Hz, 1H), 7.44 (d, J = 9.1 Hz, 2H), 6.67 (d, J = 9.1 Hz, 2H), 3.04 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 189.7 (CH), 151.3 (C), 146.4 (C), 135.6 (C), 133.7 (C), 133.6 (CH), 133.5 (2 × CH), 127.5 (CH), 122.7 (CH), 111.7 (2 × CH), 107.3 (C), 104.9 (C), 83.1 (C), 40.0 (2 × CH_3). **ESI(+)-MS**: m/z (%) = 295.25 (100) $[MH]^+$; 296.30 (20). Calcd for $C_{17}H_{14}N_2O_3$ (294.31): C, 69.38; H, 4.79; N, 9.52; found: C, 69.21; H, 4.70; N, 9.61.

5-Nitro-2-((4-(trifluoromethyl)phenyl)ethynyl)benzaldehyde **3c**: General procedure was followed by using: 2-bromo-5-nitrobenzaldehyde 3 (400 mg, 1.73 mmol), $PdCl_2(PPh_3)_2$ (38 mg, 0,03 mmol), 1-ethynyl-4-(trifluoromethyl)benzene (353 mg, 2.08 mmol) and CuI (5 mg, 0.02 mmol). Eluent for chromatography: hexane/EtOAc (9:1). Yellow solid. Yield 88% (487 mg). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 10.63 (s, 1H), 8.79 (dd, J = 2.4, 0.5 Hz, 1H), 8.45 (dd, J = 8.5, 2.4 Hz, 1H), 7.86 (dd, J = 8.5, 0.5 Hz, 1H), 7.79 – 7.62 (m, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 188.8 (CH), 147.7 (C), 136.8 (C), 134.6 (CH), 132.3 (2 × CH), 131.7 (q, $^2J(C,F)$ = 32.9 Hz, C), 131.3 (C), 129.0, (C) 127.7 (CH), 125.7 (q, $^3J(C,F)$ = 3.8 Hz, 2 × CH), 125.4 (C), 125.0 (C), 123.6 (q, $^1J(C,F)$ = 272.5 Hz, C), 122.9 (CH), 99.4 (C), 85.5 (C). **ESI(-)-MS**: m/z (%) = 319.63 (45) $[M]^-$; 336.71 (100) $[M + OH]^-$; 351.63 (100) $[M + MeOH]^-$. Calcd for $C_{16}H_8F_3NO_3$ (319.04): C, 60.20; H, 2.53; N, 4.39; found: C, 60.36; H, 2.48; N, 4.35.

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2-((4-(Methylsulfonyl)ethynyl)-5-nitrobenzaldehyde **3d**: General procedure was followed by using: 2-bromo-5-nitrobenzaldehyde **3** (300 mg, 1.30 mmol), $PdCl_2(PPh_3)_2$ (18 mg , 0.026 mmol) , 1-ethynyl-4-methylsulfonylbenzene (282 mg, 1.56 mmol) and CuI (2 mg, 0.01 mmol). Eluent for chromatography: hexane/EtOAc (from 9:1 to 8:2). Yellow solid. Yield 95% (408 mg). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 10.61 (s, 1H), 8.79 (d, *J* = 2.4 Hz, 1H), 8.46 (dd, *J* = 8.5, 2.4 Hz, 1H), 8.02 (d, *J* = 8.6 Hz, 2H), 7.87 (d, *J* = 8.5 Hz, 1H), 7.80 (d, *J* = 8.6 Hz, 2H), 3.10 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 188.5 (CH), 141.6 (C), 137.0 (C), 134.7 (CH), 132.7 (2 × CH), 130.7 (C), 127.74 (2 × CH), 127.71 (CH), 126.9 (C), 123.1 (CH), 120.5 (C), 98.6 (C), 86.8 (C), 44.4 (CH_3). **ESI(-)-MS**: m/z (%) = 329.63 (35) $[M]^-$; 346.61 (100) $[M + OH]^-$; 361.58 (100) $[M + MeOH]^-$. Calcd for $C_{16}H_{11}NO_5S$ (329.33): C, 58.35; H, 3.37; N, 4.25; found: C, 58.22; H, 3.34; N, 4.25.

5-Nitro-2-(pyridin-2-ylethynyl)benzaldehyde **3e**: General procedure was followed by using: 2-bromo-5-nitrobenzaldehyde **3** (400 mg, 1.73 mmol), $PdCl_2(PPh_3)_2$ (38 mg, 0.03 mmol), 2-ethynylpyridine (214 mg, 2.08 mmol) and CuI (5 mg, 0.02 mmol). Eluent for chromatography: hexane/EtOAc (2:1). Violet solid. Yield 76% (331 mg). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 10.67 (s, 1H), 8.78 (dd, *J* = 2.4, 0.4 Hz, 1H), 8.70 (ddd, *J* = 4.9, 1.7, 1.2 Hz, 1H), 8.44 (dd, *J* = 8.5, 2.4 Hz, 1H), 7.90 (dd, *J* = 8.5, 0.4 Hz, 1H), 7.78 (td, *J* = 7.7, 1.7 Hz, 1H), 7.63 (dt, *J* = 7.7, 1.2 Hz, 1H), 7.37 (ddd, *J* = 7.7, 4.9, 1.2 Hz, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 188.8 (CH), 150.6 (CH), 147.9 (C), 141.7 (C), 137.2 (C), 136.5 (CH), 134.8 (CH), 131.1 (C), 127.8 (CH), 127.6 (CH), 124.2 (CH), 122.7 (CH), 99.6 (C), 82.5 (C). **ESI(+)-MS**: m/z (%) = 253.25 (9) $[MH]^+$; 275.25 (6) $[M + Na]^+$; 307.13 (100) $[M + Na + MeOH]^+$. Calcd for $C_{14}H_8N_2O_3$ (252.22): C, 66.67; H, 3.20; N, 11.11; found: C, 66.51; H, 3.17; N, 11.03.

General procedure for the microwave-assisted synthesis of isoquinolines 1a-c: A stirred solution of the appropriate 2-alkynyl-5-nitrobenzaldehyde (0.28 mmol) in ammonia in methanol (2M, 3 mL) was heated at 100 °C in a microwave test tube with a screw cap under microwave irradiation for 2 h. The solvent was removed under reduced pressure. The crude product was purified by flash chromatography over silica gel affording the corresponding isoquinolines **1a-c**.

3-(4-Methoxyphenyl)-7-nitroisoquinoline **1a**: Eluent for chromatography: hexane/DCM (1:2 to 1:4). Yellow solid. Yield 56% (47 mg). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 9.48 (s, 1H), 8.93 (d, *J* = 2.1 Hz, 1H), 8.43 (dd, *J* = 9.1, 2.2 Hz, 1H), 8.14 (d, *J* = 8.9 Hz, 2H), 8.08 (s, 1H), 7.97 (d, *J* = 9.1 Hz, 1H), 7.06 (d, *J* = 8.9 Hz, 2H), 3.90 (s, 3H). **^{13}C NMR** (75 MHz, DMSO): δ 161.1 (C), 155.0 (CH), 153.5 (C), 145.7 (C), 139.4 (C), 130.8 (C), 129.4 (CH), 128.9 (2 × CH), 125.9 (C), 125.3 (CH), 124.3 (CH), 114.88 (CH), 114.85 (2 × CH), 55.8 (CH_3). **ESI(+)-MS**: m/z (%) = 170.00 (50); 178.56 (33) $[M – Ph\text{-}NMe_2]^+$ 281.14

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(100) $[MH]^+$; 282.12 (20). Calcd for $C_{16}H_{12}N_2O_3$ (280.28): C, 68.56; H, 4.32; N, 9.99; found: C, 68.69; H, 4.38; N, 10.10.

N,N-Dimethyl-4-(7-nitroisoquinolin-3-yl)anilina **1b**: Eluent for chromatography: hexane/DCM (1:2 to 1:4). Violet solid. Yield 58% (47 mg). **^{1}H NMR** (300 MHz, CD_2Cl_2) δ 9.43 (s, 1H), 8.89 (d, *J* = 2.3 Hz, 1H), 8.37 (dd, *J* = 9.1, 2.3 Hz, 1H), 8.13 (d, *J* = 9.1 Hz, 2H), 8.06 (s, 1H), 7.94 (d, *J* = 9.1 Hz, 1H), 6.84 (d, *J* = 9.1 Hz, 2H), 3.07 (s, 7H). **^{13}C NMR** (75 MHz, CD_2Cl_2): δ 155.0 (C), 154.9 (C), 153.9 (CH), 151.6 (C), 139.4 (C), 128,2 (CH), 128.1 (2 × CH), 125.6 (C), 125.3 (C), 124.6 (CH), 123.5 (CH), 112.9 (CH), 112.0 (2 × CH), 40.0 (2 × CH_3). **ESI(+)-MS**: m/z (%) = 248.21 (100) $[MH – NO_2]^+$; 294.23 (80) $[MH]^+$; 295.24 (20). Calcd for $C_{17}H_{15}N_3O_2$ (293.33): C, 69.61; H, 5.15; N, 14.33; found: C, 69.39; H, 5.06; N, 14.28.

7-Nitro-3-(4-(trifluoromethyl)phenyl)isoquinoline **1c**: Eluent for chromatography: hexane/DCM (1:2 to 1:4). Violet solid. Yield 19% (15 mg). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 9.55 (s, 1H), 8.98 (d, J = 2.2 Hz, 1H), 8.50 (dd, J = 9.0, 2.2 Hz, 1H), 8.30 (d, J = 8.1 Hz, 2H), 8.22 (s, 1H), 8.06 (d, J = 9.0 Hz, 1H), 7.79 (d, J = 8.1 Hz, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 154.3 (CH), 153.1 (C), 146.4 (C), 141.7 (C), 139.0 (C), 131.4 (q, $^2J(C,F)$ = 32.6 Hz, C), 128.9 (CH), 127.6 (2 × CH), 126.6 (C), 125.9 (q, $^3J(C,F)$ = 3.8 Hz, 2 × CH), 124.4 (CH), 124.2 (CH), 124.1 (q, $^1J(C,F)$ = 272.4 Hz, C), 116.6 (CH). **ESI(+)-MS**: m/z(%) = 319.32 (100) $[MH]^+$; 320.33 (20). Calcd for $C_{16}H_9F_3N_2O_2$ (318.26): C, 60.38; H, 2.85; N, 8.80; found: C, 60.15; H, 2.77; N, 8.75.

5-(Diethylamino)-2-((4-(trifluoromethyl)phenyl)ethynyl)benzaldehyde **8a**: In a round-bottom flask, $PdCl_2(PPh_3)_2$ (41 mg, 0.059 mmol, 5 mol%) was added to a well-stirred N_2-flushed solution of 2-bromo-5-(diethylamino)benzaldehyde **7** (300 mg, 1.71 mmol), 1-ethynyl-4-(trifluoromethyl)benzene (219 mg, 1.29 mmol) and trimethylamine (178 mg, 0.245 mL, 1.76 mmol) in anhydrous acetonitrile (1.3 mL). The reaction mixture was stirred for 15 minutes at rt, then CuI (2.0 mg, 0.012 mmol, 1 mol%) was added. The reaction mixture was warmed at 50 °C and stirred for 5h. The reaction mixture was filtered on a thin diatomite pad and the solvent was removed under reduced pressure. The crude was purified by flash column chromatography over silica gel (eluent: hexane/EtOAc (2:1)) affording **8a** in 67% yield (278 mg). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 10.60 (s, 1H), 7.63 (m, 4H), 7.52 (d, *J* = 8.7 Hz, 1H), 7.24 (bs, 1H), 6.96 (bs, 1H), 3.46 (q, *J* = 7.1 Hz, 1H), 1.23 (t, *J* = 7.1 Hz, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 192.1 (CH), 147.6 (C), 137.0 (C), 134.7 (CH), 131.4 (2 × CH), 129.6 (q, $^2J(C,F)$ = 31.2 Hz, C), 128.7 (C), 127.2 (C), 125.3 (q, $^3J(C,F)$ = 3.9 Hz, 2 × CH), 124.0 (q, $^1J(C,F)$ = 272.8 Hz, C), 117.3 (CH), 109.2 (CH), 92.3 (C), 88.7 (C), 44.8 (2 × CH_2), 12.4 (2 × CH_3). **ESI(+)-MS**: m/z(%) = 346.14 (55) $[MH]^+$;

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378.23 (100) [MH + MeOH]$^+$. Calcd for $C_{20}H_{18}F_3NO$ (345.37): C, 69.56; H, 5.25; N, 4.06; found: C, 69.42; H, 5.32; N, 3.99.

5-(Diethylamino)-2-((4-(methylsulfonyl)phenyl)ethynyl)benzaldehyde **8b**: In a round-bottom flask, $PdCl_2(PPh_3)_2$ (32 mg, 0.045 mmol, 5 mol%) was added to a well-stirred N_2-flushed solution of 2-bromo-5-(diethylamino)benzaldehyde **7** (236 mg, 0.92 mmol), 1-ethynyl-4-(methylsulfonyl)benzene (183 mg, 1.01 mmol) and trimethylamine (137 mg, 0.188 mL, 1.35 mmol) in anhydrous acetonitrile (1.0 mL). The reaction mixture was stirred for 15 minutes at rt, then CuI (1.7 mg, 0.00 mmol, 1 mol%) was added. The reaction mixture was warmed at 50 °C and stirred for 2h. The reaction mixture was filtered on a thin diatomite pad and the solvent was removed under reduced pressure. The crude was purified by flash column chromatography over silica gel (eluent: hexane/EtOAc (7:3)) affording **8b** in 41% yield (134 mg). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 10.54 (s, 1H), 7.91 (d, *J* = 8.7 Hz, 2H), 7.66 (d, *J* = 8.7 Hz, 2H), 7.48 (d, *J* = 8.7 Hz, 1H), 6.85 (dd, *J* = 8.8, 2.9 Hz, 1H), 3.43 (q, *J* = 7.1 Hz, 4H), 3.06 (s, 3H), 1.20 (t, *J* = 7.1 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 191.9 (CH), 148.2 (C), 139.3 (C), 137.2 (C), 134.8 (CH), 131.8 (2 × CH), 129.4 (C), 127.4 (2 × CH), 116.5 (CH), 111.1 (C), 109.1 (CH), 91.7 (C), 90.9 (C), 44.48 (CH_3), 44.5 (2 × CH_2), 12.4 (2 × CH_3). **ESI(+)-MS**: m/z(%) = 356.21 (18) [MH]$^+$; 378.02 (100) [M + Na]$^+$. Calcd for $C_{20}H_{21}NO_3S$ (355.45): C, 67.58; H, 5.96; N, 3.94; found: C, 67.75; H, 5.91; N, 4.02.

5-(Diethylamino)-2-(pyridin-2-ylethynyl)benzaldehyde **8c**: In a round-bottom flask, $PdCl_2(PPh_3)_2$ (41 mg, 0.059 mmol, 5 mol%) was added to a well-stirred N_2-flushed solution of 2-bromo-5-(diethylamino)benzaldehyde **7** (300 mg, 1.71 mmol), 2-ethynylpyridine (145 mg, 1.41 mmol), K_2CO_3 (810 mg, 5.86 mmol) and trimethylamine (178 mg, 0.245 mL, 1.76 mmol) in anhydrous DMF (5 mL). The reaction mixture was stirred for 15 minutes at rt, then CuI (2.0 mg, 0.012 mmol, 1 mol%) was added. The reaction mixture was warmed at 50 °C and stirred for 4h. The reaction mixture was poured in water (70 mL) end extracted with EtOAc (3 × 20 mL). The solvent was removed under reduced pressure. The crude was purified by flash column chromatography over silica gel (eluent: hexane/EtOAc/isopropanol (80:20:1)) affording **8c** in 76% yield (248 mg). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 10.60 (s, 1H), 8.60 (d, *J* = 4.8 Hz, 1H), 7.66 (td, *J* = 7.7, 1.8 Hz, 1H), 7.54 (d, *J* = 8.7 Hz, 1H), 7.49 (d, *J* = 7.8 Hz, 1H), 7.21 (ddd, *J* = 7.5, 4.9, 1.1 Hz, 1H), 7.16 (d, *J* = 2.9 Hz, 1H), 6.84 (dd, *J* = 8.8, 2.9 Hz, 1H), 3.41 (q, *J* = 7.1 Hz, 4H), 1.18 (t, *J* = 7.1 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 192.1 (CH), 150.1 (CH), 148.1 (C), 143.7 (C), 137.3 (C), 136.1 (CH), 135.0 (CH), 126.9 (CH), 122.4 (CH), 116.5 (CH), 111.4 (C), 108.7 (CH), 92.8 (C), 86.5 (C), 44.4 (2 × CH_2), 12.4 (2 × CH_3). **ESI(+)-MS**: m/z(%) = 279.27 (100) [MH]$^+$; 280.27 (22). Calcd for $C_{18}H_{18}N_2O$ (278.36): C, 77.67; H, 6.52; N, 10.06; found: C, 77.62; H, 6.50; N, 10.02.

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N,N-Diethyl-3-(4-(trifluoromethyl)phenyl)isoquinolin-7-amine **2a**: A stirred solution of **8a** (69 mg, 0.20 mmol) in ammonia in methanol (2M, 3 mL) was heated at 140 °C in a microwave test tube with screw cap under microwave irradiation for 1 h. The solvent was removed under reduced pressure. The crude product was purified by flash chromatography over silica gel (eluent: heptane/EtOAc (9:1)) affording **2a** in 26% yield (18 mg). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 9.10 (s, 1H), 8.26 (d, J = 8.1 Hz, 2H), 8.00 (s, 1H), 7.75 (m, 3H), 7.33 (dd, J = 9.1, 2.6 Hz, 1H), 6.97 (d, J = 2.5 Hz, 1H), 3.52 (q, J = 7.1 Hz, 4H), 1.26 (t, J = 7.1 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 150.4 (CH), 147.2 (C), 144.9 (C), 143.7 (C), 130.5 (C), 128.9 (q, $^2J(C,F)$ = 31.2 Hz, C), 128.4 (C), 128.0 (CH), 126.2 (2 × CH), 125.4 (q, $^3J(C,F)$ = 4.3 Hz, 2 × CH), 124.6 (q, $^1J(C,F)$ = 271.4 Hz, C), 120,0 (CH), 116.6 (CH), 103.5 (CH), 44.5 (2 × CH_2), 12.3 (2 × CH_3). **ESI(+)-MS**: m/z(%) = 345.23 (100) $[MH]^+$; 346.25 (17). Calcd for $C_{20}H_{19}F_3N_2$ (344.38): C, 69.75; H, 5.56; N, 8.13; found: C, 69.68; H, 5.52; N, 8.18.

N,N-Diethyl-3-(4-(methylsulfonyl)phenyl)isoquinolin-7-amine **2b**: A stirred solution of **8b** (71 mg, 0.20 mmol) in ammonia in methanol (2M, 2 mL) was heated at 80 °C in a microwave test tube with screw cap under microwave irradiation for 1 h. The solvent was removed under reduced pressure. The crude product was purified by flash chromatography over silica gel (eluent: hexane/EtOAc (6:4)) affording **2b** in 18% yield (13 mg). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 9.16 (s, 1H), 8.31 (d, J = 8.6 Hz, 1H), 8.15 – 8.00 (m, 3H), 7.79 (d, J = 9.1 Hz, 1H), 7.37 (dd, J = 9.2, 2.4 Hz, 1H), 7.00 (bs, 1H), 3.54 (q, J = 7.1 Hz, 2H), 3.12 (s, 1H), 1.29 (t, J = 7.0 Hz, 4H).**^{13}C NMR** (75 MHz, $CDCl_3$) δ 149.6 (CH), 147.5 (C), 143.8 (C), 142.9 (C), 139.4 (C), 130.3 (C), 128.9 (C), 128.5 (CH), 127.9 (2 × CH), 127.2 (2 × CH), 121.1 (CH) 118.5 (CH), 103.7 (CH), 44.8 (2 × CH_2), 44.7 (CH_3), 12.5 (2 × CH_3). **ESI(+)-MS**: m/z(%) = 355.24 (100) $[MH]^+$; 356.27 (25). Calcd for $C_{20}H_{22}N_2O_2S$ (354.47): C, 67.77; H, 6.26; N, 7.90; found: C, 67.65; H, 6.21; N, 7.94.

N,N-Diethyl-3-(pyridin-2-yl)isoquinolin-7-amine **2c**: A stirred solution of **8c** (56 mg, 0.20 mmol) in ammonia in methanol (2M, 2 mL) was heated at 100 °C in a microwave test tube with screw cap under microwave irradiation for 2 h. The solvent was removed under reduced pressure. The crude product was purified by flash chromatography over silica gel (eluent: heptane/EtOAc/TEA (70:30:1)) affording **2c** in 18% yield (13 mg). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 9.08 (s, 1H), 8.68 (ddd, J = 4.8, 1.8, 0.9 Hz, 1H), 8.59 (s, 1H), 8.43 (d, J = 8.0 Hz, 1H), 7.85 – 7.74 (m, 2H), 7.33 – 7.18 (m, 2H), 6.94 (d, J = 2.4 Hz, 1H), 3.50 (q, J = 7.1 Hz, 4H), 1.25 (t, J = 7.1 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 157.2 (C), 149.9 (CH), 149.1 (CH), 147.1 (C), 145.9 (C), 136.7 (CH), 131.0 (C), 128.8 (CH), 122.3 (CH), 120.5 (CH), 119.9 (CH), 117.5 (CH), 103.7 (CH) 44.6 (2 × CH_2), 12.6 (2 × CH_3). **ESI(+)-MS**: m/z(%) = 278.22 (100) $[MH]^+$;

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279.21 (27). Calcd for $C_{18}H_{19}N_3$ (277.37): C, 77.95; H, 6.90; N, 15.15; found: C, 78.09; H, 6.82; N, 15.14.

Absorption spectroscopy: Stock solutions of isoquinolines (1 mg/mL) were prepared by dissolving the powders in DMSO and stored protected from light. For each absorption spectrum, 28 μL of stock solutions were dissolved in the suitable media, to obtain a final concentration of 0.014 mg/mL. Absorption spectra were recorded at 300 nm/min at 20 °C with a 1 cm path length quartz cuvette on a spectrophotometer equipped with a thermostated cell-holder.

Fluorescent spectroscopy: Fluorescence spectra were collected recording the emission signal upon excitation at the maximum absorbance wavelength, with slits set at 2 nm and an integration time of 0.1 seconds. The concentration of compounds was 0.014 mg/mL for **1a**, **1b**, **2a**, **2c**, **3a**, and **3b**, and 0.007mg/L for **2b**, **8a**, **8b**, and **8c**.

Absolute QY determination: A description of the experimental setup and measurement method can be found in the paper of K. Suzuki and co-workers.[19] For any fixed excitation wavelength, the fluorescence quantum yield Φ is given by:

$$\Phi = \frac{\mathrm{PN(Em)}}{\mathrm{PN(Abs)}} = \frac{\int \frac{\lambda}{hc}\left[\mathrm{I}_{em}^{sample}(\lambda) - \mathrm{I}_{em}^{reference}(\lambda)\right] d\lambda}{\int \frac{\lambda}{hc}\left[\mathrm{I}_{ex}^{reference}(\lambda) - \mathrm{I}_{ex}^{sample}(\lambda)\right] d\lambda}$$

where PN(Em) is the number of photons emitted from a sample and PN(Abs) is the number of photons absorbed by a sample, λ is the wavelength, h is Planck's constant, c is the velocity of light, $\mathrm{I}_{em}^{sample}(\lambda)$ and $\mathrm{I}_{em}^{reference}(\lambda)$ are the photoluminescence intensities with and without a sample, respectively, $\mathrm{I}_{ex}^{sample}(\lambda)$ and $\mathrm{I}_{ex}^{reference}(\lambda)$ are the integrated intensities of the excitation light with and without a sample, respectively. PN(Em) is calculated in the wavelength interval $[\lambda_i, \lambda_f]$, where λ_i is taken 10 nm below the excitation wavelength, while λ_f is the upper end wavelength in the emission spectrum.

Conflict of interest: There are no conflicts to declare.

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