Synthesis and photophysical properties of a series of pyrazine-based push-pull chromophores.

Kellyn Hoffert,[a] Raphaël J. Durand,[a] Sébastien Gauthier,[a] Françoise Robin-le Guen,[a] Sylvain Achelle*[a]

[a]Institut des Sciences Chimiques de Rennes, UMR CNRS 6226, IUT de Lannion, rue Edouard Branly, BP 30219, F22302 Lannion Cedex, France.

Corresponding author: *E-mail: sylvain.achelle@univ-rennes1.fr

Abstract

A series of push-pull pyrazine fluorophores was described. Methoxy, dimethylamino and diphenylamino groups were used as electron-donating groups, and six π-conjugated systems consisting of multiple bonds and 1,4-phenylene moieties were used for the connection to the pyrazine core. The chromophores were obtained by Knoevenagel condensations and palladium catalyzed cross couplings starting from commercially available 2-methyl or 2-chloropyrazine. The optical absorption and emission properties of these chromophores were studied in different solvents. Some of them revealed to be highly emissive and exhibit a strong emission solvatochromism that suggests a highly polar emitting state, characteristic of compounds that undergo intramolecular charge transfer (ICT). The influences of the nature of the electron donating group and the π-conjugated system on the emission and ICT were carefully studied.

Keywords: Pyrazine, Donor-acceptor systems, Conjugation, Fluorescence, Intramolecular Charge Transfer.

Introduction

Accepted Manuscript

Push–pull structures composed of a π-conjugated core substituted by electron-donating (D) and electron-attracting (A) groups have attracted significant interest due to the potential applications related to strong emission behavior and nonlinear optical properties.[1] In such D-π-A structure, intramolecular charge transfer (ICT) leads to polarization of the chromophore and generation of a molecular dipole.[2] Photophysical properties of push-pull molecules can be easily tuned by varying various parameters such as the nature of the electron donating and withdrawing couple and the length of the conjugation pathway.[3]

Pyrazine is a six-membered heterocycle with two nitrogen atoms (1,4-diazine). Due to its electron-deficient character, this heterocycle can be used as the electron-withdrawing part in push-pull structures. The incorporation of pyrazine units in luminescent materials has been recently reviewed.[4] The luminescence of push-pull pyrazine chromophores can be easily tuned by external stimuli.[5] The ability of protonation, hydrogen bond formation, and chelation of the nitrogen atom can be efficiently used for sensing applications. Pyrazine push-pull derivatives are known for their strong positive solvatochromism and their halochromic properties.[6] Some pyrazine fluorophores have been designed as fluorescent protein sensors.[7] Some pyrazine derivatives have been also described as emitting layer in organic light emitting diodes[8] or used as chromophores for dye-sensitized solar cells.[9] Pyrazine fragments have also been incorporated in the structure of second order[10] (frequency doubling) and third order[8,11] (two photon absorption) nonlinear optical (NLO) chromophores. Even if the NLO responses of pyrazine derivatives are generally lower than their pyrimidine (1,3-diazine) analogues,[12] these compounds are generally significantly more emissive.[12a,13]

The main purpose of the present article is to design, synthesize and study the photophysical properties of push-pull pyrazine derivatives with six different π-conjugated cores. Our study was focused on π-conjugated systems consisting of multiple bonds and 1,4-phenylene

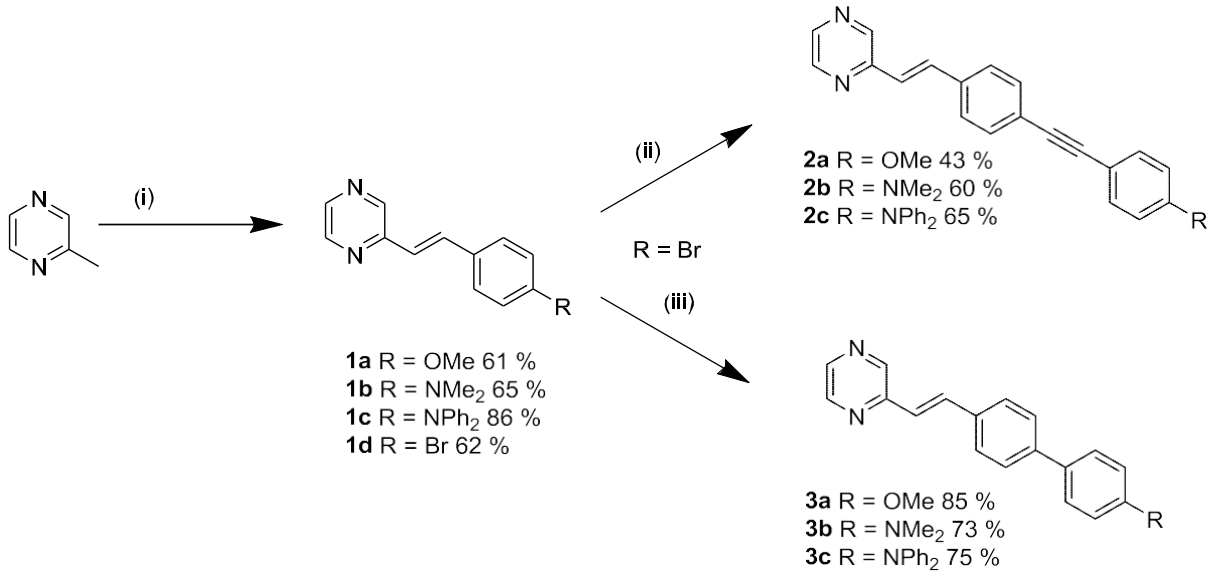
Accepted Manuscript

moieties. Influence of the length and composition of the π-linker as well as the nature of the electron-donating group on the photophysical properties will be thoroughly studied.

Result and Discussion

Synthesis

Styryl derivatives **1** were obtained by Knoevenagel condensation of the corresponding aldehyde with commercially available 2-methylpyrazine (Scheme 1). Potassium hydroxide in DMSO (dimsyl potassium), according to the conditions initially described by Pan *et al.*,[14] afforded the condensation products **1** in moderate to good yields, generally without the need of chromatography purification (except for **1c**). Bromine derivative **1d** was used as a coupling partner in Sonogashira and Suzuki cross-coupling conditions to obtain tricyclic linear oligomers **2** and **3** respectively (Scheme 1). Good yields (73-85 %) were obtained for Suzuki cross coupling reaction. The yields of Sonogashira coupling were more limited (43-65 %).

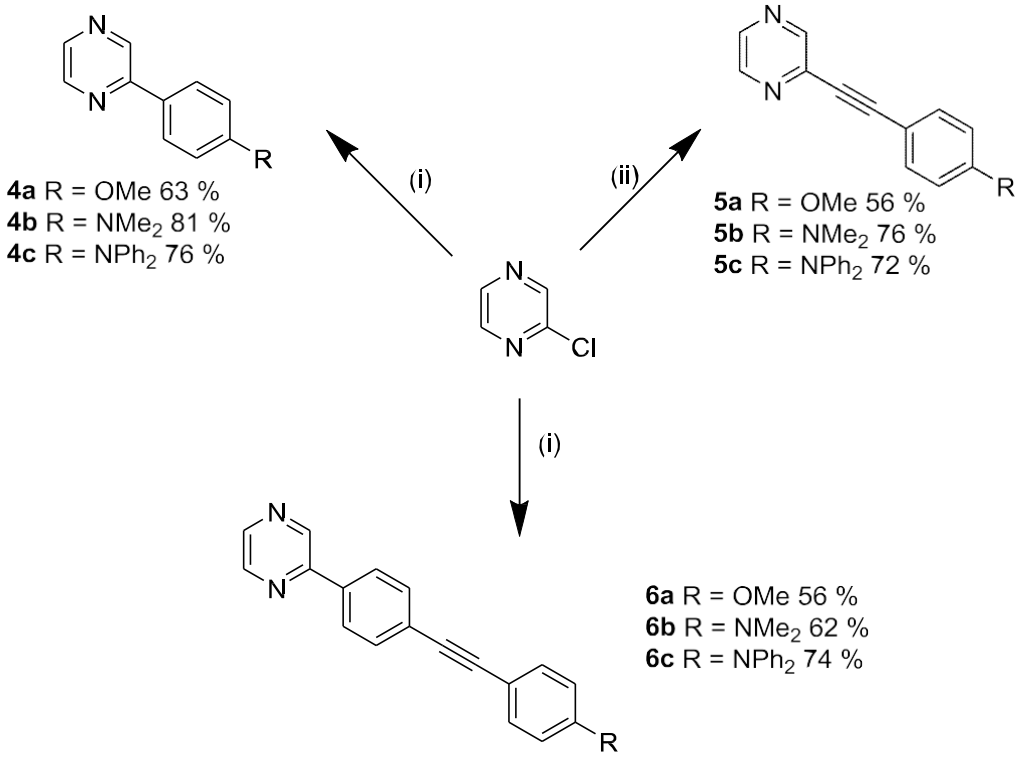


Scheme 1: Synthesis of compounds **1-3**. (i) *p*R-C_6H_4-CHO, KOH, DMSO, rt, 15 h. (ii) *p*R-C_6H_4-C≡CH, $Pd(PPh_3)_2Cl_2$, CuI, $HN(iPr)_2$, Δ, 15 h. (iii) *p*R-C_6H_4-$B(OH)_2$, $Pd(PPh_3)_4$, K_2CO_3aq, Toluene/EtOH, Δ, 15 h.

Due to the electron-withdrawing character of the pyrazine ring, palladium-catalyzed cross-coupling reactions can be performed from commercially available 2-chloropyrazine without

Accepted Manuscript

the use of specialized and expensive ligands.[15] Indeed the electron-withdrawing character of this heterocycle makes possible the oxidative addition of palladium in the chlorine-carbon bond.[16] Using $Pd(PPh_3)_4$ as a catalyst, Suzuki cross-coupling reactions afforded compounds **4** and **6** in good yields (Scheme 2). Ethynylpyrazines **5** were obtained by Sonogashira coupling using $Pd(PPh_3)_2Cl_2$ and CuI as a catalytic mixture (Scheme 2). In all cases, performing the reaction in a pressurized tube permits a reduction in reaction time and increases the yields.



Scheme 2: Synthesis of compounds **4-7**. (i) corresponding boronic acid, $Pd(PPh_3)_4$, K_2CO_3aq, Toluene/EtOH, Δ, 15 h. (ii) corresponding terminal alkyne, $Pd(PPh_3)_2Cl_2$, CuI, $HN(i\text{Pr})_2$, Δ, 15 h.

All the compounds were thoroughly characterized by ^1H, ^{13}C NMR and high resolution mass spectra. The stereochemistry of the double bonds in compounds **1-3** was unequivocally established on the basis of the coupling constant for the vinylic protons in the ^1H spectra ($J \approx$ 16Hz).

Optical properties

Accepted Manuscript

The UV/Vis and photoluminescence (PL) spectroscopic data of compounds **1**-**6** measured in CH_2Cl_2 at room temperature are presented in Table 1. The analyses were carried out using low concentrated solutions ($1.0\text{-}3.0 \times 10^{-5}$ M). The absorption spectra showed a π-π^* transition in the UV region at λ_{max} = 318-397 nm accompanied by one or two extra bands at higher energies. All compounds are luminescent with high quantum yield (up to 0.81) in some cases. It should be noted that the quantum yields of compounds **1b** and **1c** that we measured were significantly higher than previously reported.[12b] Except for the phenylene coupounds **4**, the methoxy derivatives exhibit emission maxima in the purple-blue region, whereas the amino derivatives emit in the green-yellow region upon irradiating the solution. As an example, spectra for derivatives **1b**, **2a** and **3c** in dichloromethane are shown on Fig.1. The Stokes shifts are rather large, and significantly higher for amino derivatives than for their methoxy analogues. Both the absorption and emission maxima were found to be red-shifted when going from a phenylene (**4**) to a phenylenethynylene (**5**) and a phenylenvinylene (**1**) linker. As previously observed on the pyrimidine series,[17] extension of the π-conjugated linker by a second phenylene fragment (**1** *vs* **2** or **3**, **4** *vs* **6**) resulted in a moderate modification of the absorption maxima. However, a more important red shift of the emission is observed leading to an increase of the Stokes shift. In the case of methoxy derivatives, this is also associated with a dramatic enhancement of the fluorescence quantum yield, this tendency is less obvious for amino derivatives. When comparing compounds **2** with compounds **3**, it appears that the ethynylene linker between the two phenyl rings had a limited influence on the position of absorption and emission maxima. On the contrary, addition of a vinylene linker between the pyrazine core and the first phenyl ring (**2** *versus* **6**) leads to a significant red-shift of both absorption and emission maxima.

Table 1: UV/Vis and PL data in CH_2Cl_2.

	UV/vis λ_{max}, nm	PL	Stokes shift

Accepted Manuscript

Compd[a]	(ε, $mM^{-1}\cdot cm^{-1}$)	λ_{max}, nm	Φ_{Fb}	cm^{-1}
1a	293 (18.8), 346 (30.8)	431	0.03	5700
1b	271 (8.7), 329 (10.3), 391 (28.5)	522	0.40	6418
1c	297 (19.5), 397 (25.5)	528	0.78	6250
2a	300 (18.4), 357 (41.1)	449	0.79	5739
2b	292 (28.0), 383 (31.9)	579	0.62	8838
2c	309 (0.69), 383 (0.81)	563	0.79	8348
3a	300sh (13.8), 351 (29.3)	451	0.46	6317
3b	294 (18.1), 380 (32.3)	570	0.69	8771
3c	303 (35.0), 379 (39.1)	557	0.72	8431
4a	266 (23.5), 291 (27.4), 318sh (18.8)	386	0.14	5539
4b	325 (13.4), 354 (13.7)	489	0.59	7799
4c	210 (19.4), 304 (26.1), 366 (41.2)	496	0.68	7161
5a	288sh (17.6), 313sh (23.9), 328 (25.2)	403	0.28	5674
5b	277 (13.2), 324 (13.6), 370 (28.2)	523	0.17	7907
5c	288 (20.1), 378 (29.5)	517	0.52	7113
6a	270sh (15.1), 331 (38.0)	416	0.81	6173
6b	288 (20.1), 367 (27.8)	530	0.60	8380
6c	297 (33.7), 374 (42.3)	516	0.79	7358

[a] All spectra were recorded at room temperature at $c = 1.0 \times 10^{-5}$ M to 3.0×10^{-5}. [b] Fluorescence quantum yield (±10%) determined relative to 9,10-Bis-phenylethynyl-anthracene in cyclohexane ($\Phi_F = 1.00$).[18]

Accepted Manuscript

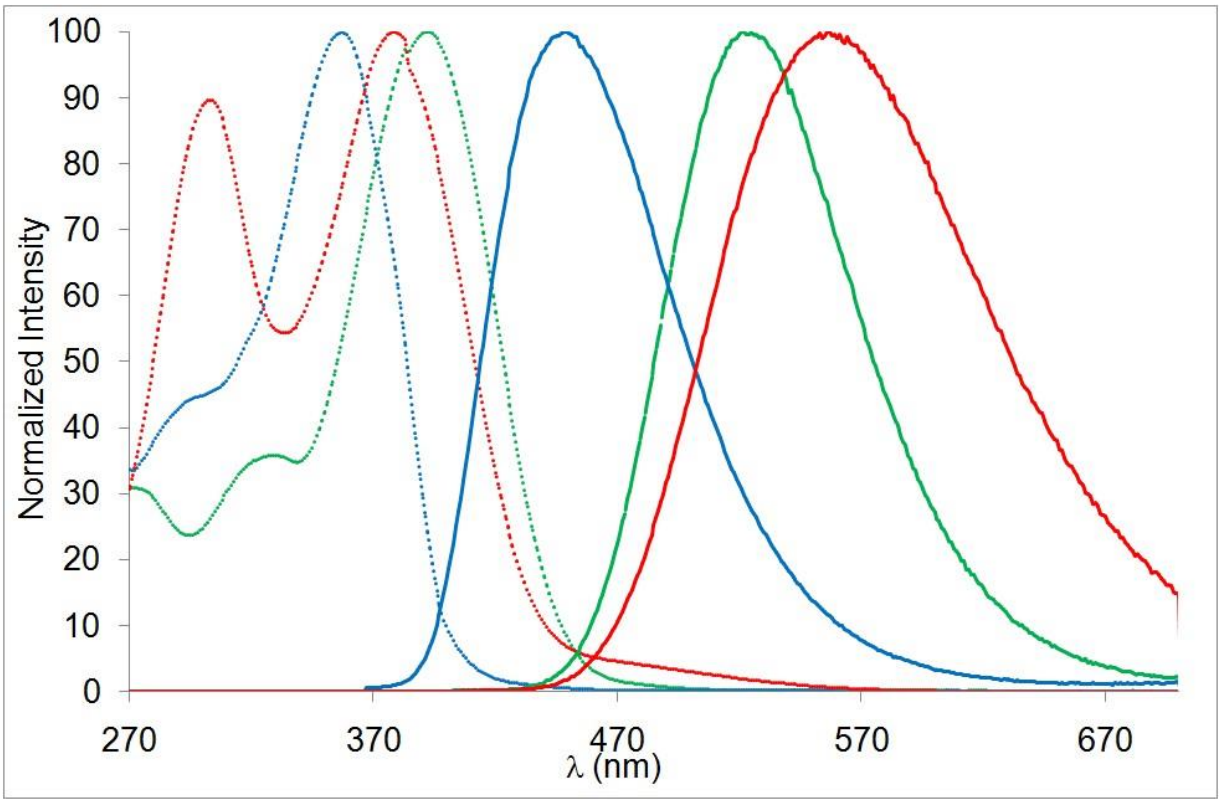


Figure 1: Normalized UV/Vis (dashed line) and emission spectra (solid lines) of compounds **1b** (green), **2a** (blue) and **3c** (red).

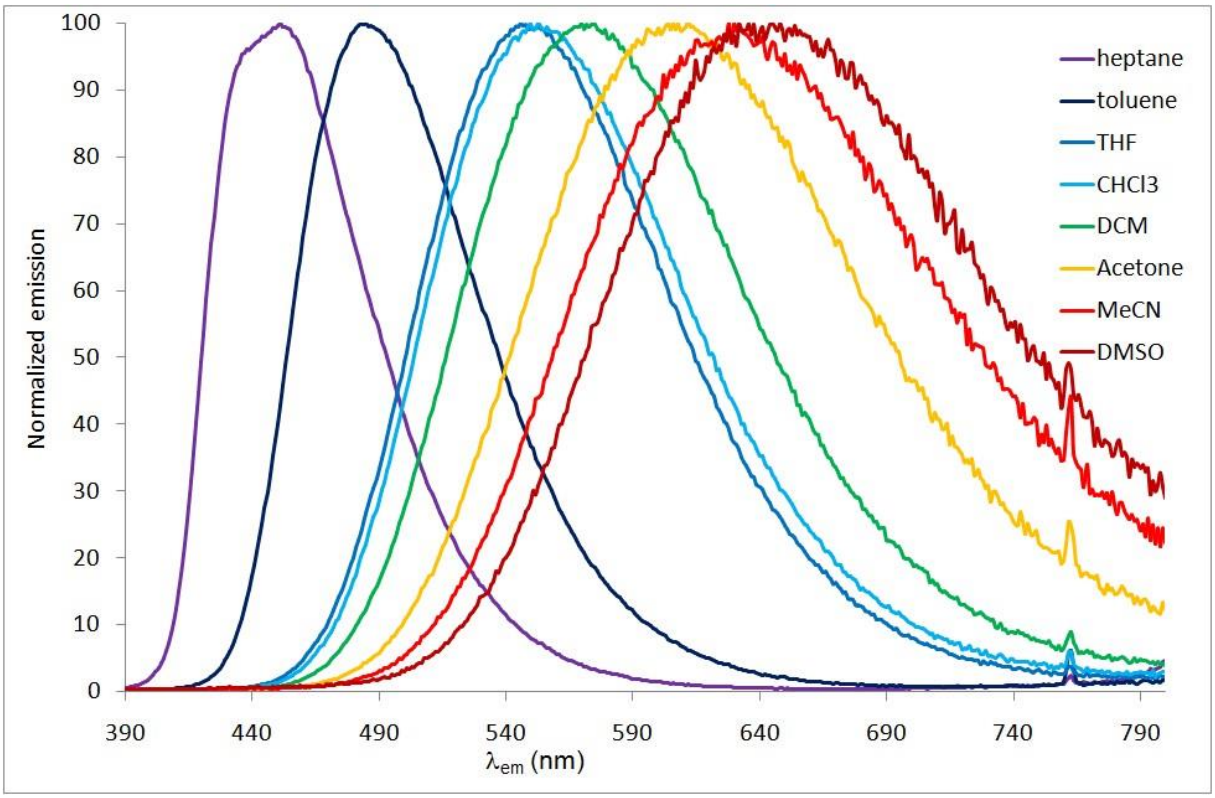
In push-pull compounds, the effect of the polarity on the position of the absorption band can be moderate.[19] In contrast, significant emission solvatochromism can be observed in such fluorescent dyes.[6,17,20] This solvatochromic behavior results from the stabilization of the highly polar emitting state by polar solvents.[21] The emission properties of compounds **1-6** were measured in seven aprotic solvents of various polarity. The results of these investigations are summarized in Table 2. It should be noted that, in some cases, in low polar solvents (heptane, toluene) two well-developed emission bands are observed due to increase of the vibronic structure. All compounds show a marked positive emission solvatochromism: increasing solvent polarity as predicted by the Dimroth-Reichardt polarity parameter ($E_T(30)$)[22] leads to a pronounced bathochromic shift of the emission band. As examples, the PL spectra for compound **3b**, and color change under UV irradiation for compound **3c** in various solvents are shown in Fig. 2 and 3.

Accepted Manuscript

Table 2: Emission solvatochromism of pyrazine derivatives **1-6** in various aprotic solvents.

Compd	Heptane $E_T(30)^a$ = 30.9 λ_{max}, nm	Toluene $E_T(30)^a$ = 33.9 λ_{max}, nm	THF $E_T(30)^a$ = 37.4 λ_{max}, nm	CH_2Cl_2 $E_T(30)^a$ = 40.7 λ_{max}, nm	Acetone $E_T(30)^a$ = 42.2 λ_{max}, nm	MeCN $E_T(30)^a$ = 45.6 λ_{max}, nm	DMSO $E_T(30)^a$ = 45.1 λ_{max}, nm
1a	398	412	418	431	429	442	450
1b	443	470	497	522	532	549	560
1c	428	461	493	528	532	549	552
2a	390/412	405/422	431	449	451	464	471
2b	431/449	478	560	579	629	-[b]	-[b]
2c	425/449	457	522	563	597	622	635
3a	396/408	420	432	451	455	461	469
3b	461	483	546	570	604	632	645
3c	450	474	524	557	571	602	608
4a	358	365	372	386	386	387	396
4b	400	433	459	480	501	517	526
4c	420	437	458	496	494	519	514
5a	365	376	386	402	413	421	431
5b	409	442	493	523	564	594	601
5c	414	437	476	517	531	558	561
6a	364/378	382	400	416	422	432	439
6b	399/417	450	512	530	579	601	623
6c	410	432	484	516	538	571	577

[a] Dimroth–Reichardt polarity parameter, $kJ \cdot mol^{-1}$. [b] no signal detected



Accepted Manuscript

Figure 2: Normalized emission spectra of **3b** in different aprotic solvents.

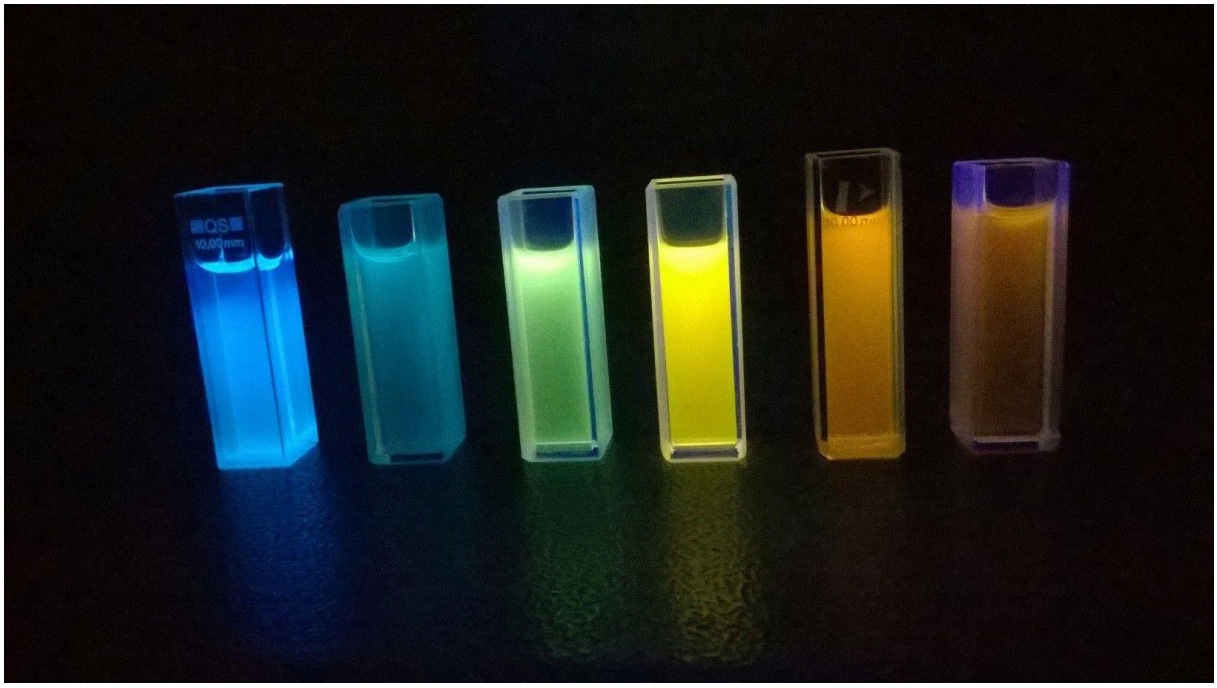


Figure 3: Fluorescence colour changes of **3c** in various solvents (from left to right: heptane, toluene, THF, CH_2Cl_2, MeCN, DMSO. Picture was taken in the dark upon irradiation with a hand-held UV lamp (λ_{exc} = 366 nm)

Studying emission solvatochromism is a way to evaluate ICT in push pull-structures. For all compounds, the emission maxima were plotted versus $E_T(30)$ (Figures 4, S26 and S27). For all the chromophores, a good linearity was obtained. When comparing the three electron-donating groups for all the π-conjugated linkers, the solvatochromic range increases in the following order: -OMe < $-NPh_2$ < $-NMe_2$, in accordance with the electron-donating ability of these groups, as estimated by Hamett constant.[23] When comparing compounds **2** with their 4-substituted pyrimidine analogues, it appears that the pyrazine derivatives exhibits slightly lower solvatochromic range.[24] In the dimethylamino series, the slopes of the corresponding regression lines indicate that the solvatochromic range increases in the following order: **1b** ≈ **4b** < **3b** ≈ **5b** ≈ **6b** < **2b** (Figure 4) and seems to indicate that a vinylene phenylenethynylenphenylene linker between the pyrazine and the dimethylamino group is the

Accepted Manuscript

most efficient in terms of ICT. The same tendency is observed in diphenylamino series, but surprisingly not with methoxy derivatives.

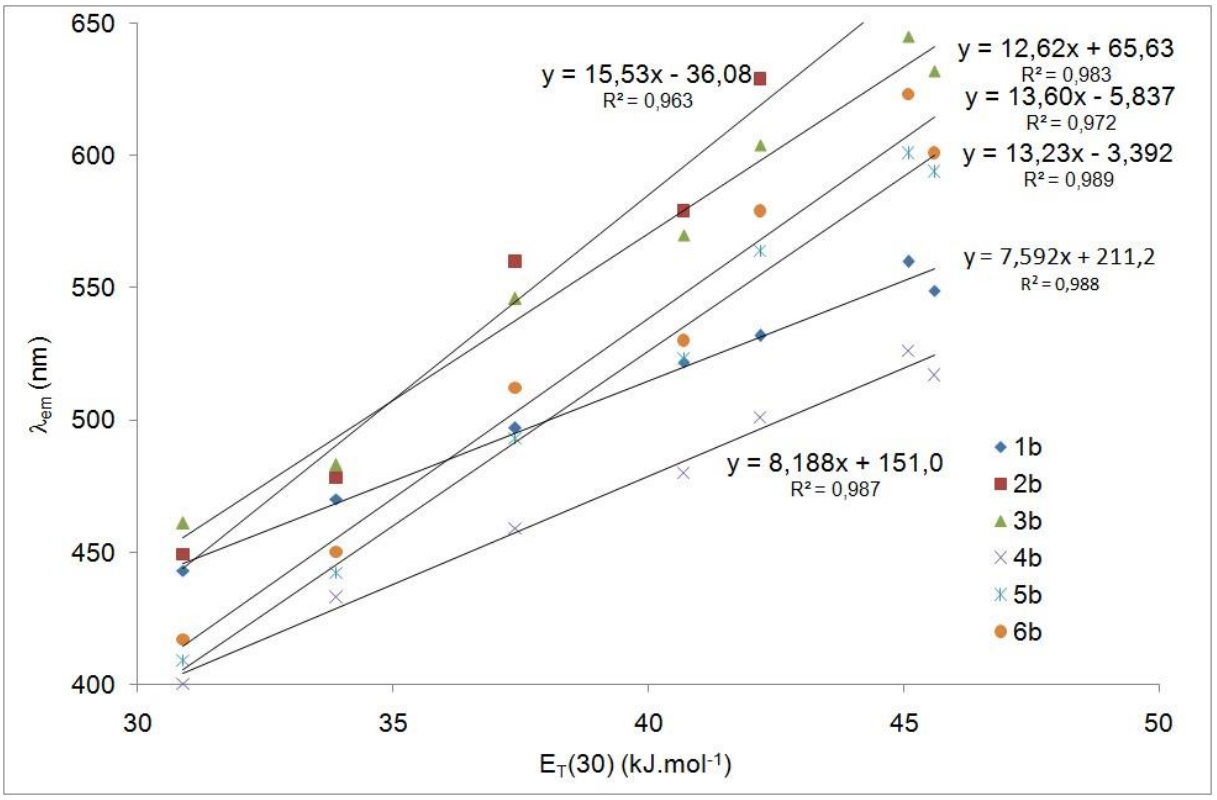


Figure 4: Emission maxima (λ_{em}) as a function of Dimroth-Reichardt polarity parameter for dimethylamino derivatives **1b**, **2b**, **3b**, **4b**, **5b**, and **6b.**

Conclusion

In summary, a series of eighteen pyrazine push-pull chromophores as synthesized by Knoevenagel condensation as well as Suzuki and Sonogashira cross coupling reactions. Their absorption and emission properties were measured and some of the compounds were found to be highly fluorescent in dichloromethane solution (Φ_F up to 0.8). Extension of the π-conjugated linker revealed to be a mean to dramatically increase the fluorescence intensity of methoxy derivatives. These chromophores, more particularly the dimethylamino derivatives, exhibit strong emission solvatochromism, indicating the formation of very polar excited ICT states. Therefore, these compounds appear as promising fluorescent polarity sensors and potential NLO chromophores.

Accepted Manuscript

Experimental Section

General. All chemicals were purchased from commercial sources and were used without further purification. Boronic acids used for the synthesis of compounds **6** were obtained according to reported procedures.[25] Compound **1d** was obtained as described previously.[12a] Analytical thin layer chromatography was performed with silica gel plates (Merk® TCL silica gel 60 F_{254}) and compounds were detected by irradiation with UV light (365 nm). The chromatographic purification of compounds was achieved with silica gel (Acros, 60-80 mesh). All air- and moisture-sensitive reactions were carried out in flame-dried glassware that was subsequently cooled under nitrogen. NMR spectra were acquired at room temperature on a Bruker AC-300 spectrometer. Chemical shifts are given in parts per million relative to TMS (^{1}H, 0.0 ppm) and $CDCl_3$ (^{13}C, 77.0 ppm). Acidic impurities in $CDCl_3$ were removed by treatment with anhydrous K_2CO_3. High resolution MALDI MS spectra were measured using method "dried droplet" on a MALDI mass spectrometer *LTQ Orbitrap XL* (Thermo Fisher Scientific, Bremen, Germany) equipped with nitrogen UV laser (337 nm, 60 Hz). The LTQ Orbitrap instrument was operated in positive-ion mode over a normal mass range (m/z 50–2000) with the resolution 100,000 at m/z = 400. The used matrix was 2,5-dihydroxybenzoic acid (DHB). UV/vis spectra were recorded with a UVIKON xm SECOMAM spectrometer using standard 1 cm quartz cells. Fluorescence spectra were recorded using Spex FluoroMax-3 Jobin-Yvon Horiba apparatus. Compounds were excited at their absorption maxima (longest-wavelength absorption band) to record the emission spectra. The Φ_F values were calculated using a well-known procedure using 9,10-diphenylethynylanthracene in cyclohexane as standard.[18] Stokes shifts were calculated by considering the lowest energetic absorption band.

General procedure for Knoevenagel condensation: The corresponding aldehyde (10 mmol) and 2-methylpyrazine (936 mg, 10 mmol) were dissolved in DMSO (6 mL). Powdered KOH

Accepted Manuscript

(2.2 g, 40 mmol) was added and the reaction mixture was stirred at room temperature for 15 h and then poured into 200 mL of water. The resulting precipitate was filtered and washed with water (2 x 150 mL) The crude product was used without further purification (except in case of **1c**).

General procedure for Sonogashira cross-coupling reactions for compounds 2 and 5 : A suspension of the corresponding halogeno derivative (1.0 mmol), $Pd(PPh_3)_2Cl_2$ (75 mg, 0.10 mmol), and CuI (10mg, 0.05 mmol) in diisopropylamine (10 mL) was degassed three times in a pressure tube. The acetylene derivative (1.2 mmol) was then added. The mixture was heated at 80°C overnight. The suspension was then diluted with a mixture of water and dichloromethane (1:1, 30 mL) and the organic layer was extracted with dichloromethane (2 × 30 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and evaporated.

General Procedure for Suzuki cross-coupling reactions for the synthesis of compounds 3, 4, and 6: A stirred mixture of halogeno derivative (1 mmol), arylboronic acid (1.2 mmol), $Pd(PPh_3)_4$ (0.05 mmol), aqueous 1 M sodium carbonate (2.2 mmol, 2.2 mL) and ethanol (1.5 mL) in degassed toluene (10mL) was heated at reflux under nitrogen for 15 h in Schlenk tube. The reaction mixture was cooled, filtered, and dissolved with a mixture of AcOEt and water 1:1 (50mL) and the organic layer was separated. The aqueous layer was extracted with AcOEt (2 x 25 mL). The combined organic extracts were dried with $MgSO_4$ and the solvents evaporated.

(E)-2-(4-methoxystyryl)pyrazine (1a): Cream solid. Yield: 61% (1.29 g) Mp: 109-110°C (lit.[26] 104-105°C). ^{1}H NMR (300MHz, $CDCl_3$): δ 3.85 (s, 3H), 6.93 (d, 2H, *J* = 8.7 Hz), 7.03 (d, 1H, *J* = 15.9 Hz), 7.54 (d, 2H, *J* = 8.7 Hz), 7.70 (d, 1H, *J* = 15.9 Hz), 8.37 (d, 1H, *J* = 2.7

Accepted Manuscript

Hz), 8.51 (dd, 1H, J_1 = 2.7 Hz, J_2 = 1.5 Hz), 8.61 (d, 1H, J = 1.5 Hz). Data similar to the literature.[26]

(E)-2-(4-dimethylaminostyryl)pyrazine (1b): Yellow solid. Yield: 65% (1.46 g) Mp: 125-126°C (lit:[12b] 117-118°C). ^{1}H NMR (300MHz, $CDCl_3$) : δ 3.03 (s, 6H), 6.72 (d, 2H, J = 8.7 Hz), 6.94 (d, 1H, J = 15.9 Hz), 7.49 (d, 2H, J = 8.7 Hz), 7.67 (d, 1H, J = 15.9 Hz), 8.31 (d, 1H, J = 2.7 Hz), 8.48 (dd, 1H, J_1= 2.7 Hz, J_2 = 1.5 Hz), 8.58 (d, 1H, J = 1.5 Hz) Data similar to the literature.[12b]

(E)-2-(4-diphenylaminostyryl)pyrazine (1c): Purified by column chromatography (petroleum ether/EtAcO, 7/3), yellow solid. Yield: 86% (3.00 g) Mp: 140-141°C (lit:[12b] 135-136°C). ^{1}H NMR (300MHz, $CDCl_3$) : δ 7.03 (d, 1H, J = 15.9 Hz), 7.09-7.05 (m, 4H) , 7.14 (dd, 4H, J_1 = 8.7 Hz, J_2 = 1Hz), 7.30-7.27 (m, 4H), 7.45 (d, 2H, J = 8.7 Hz), 7.68 (d, 1H, J = 15.9 Hz), 8.36 (d, 1H, J = 2.7 Hz), 8.51 (d, 1H, J= 2.7 Hz), 8.61 (broad s, 1H). Data similar to the literature.[12b]

(*E*)-2-(4-((4-methoxyphenyl)ethynyl)styryl)pyrazine (2a): Purified by column chromatography (petroleum ether/EtAcO, 7/3), pale yellow solid. Yield: 43% (134 mg) Mp: 184-186°C. ^{1}H NMR (300MHz, $CDCl_3$) : δ 3.84 (s, 3H), 6.89 (d, 2H, J = 8.7 Hz), 7.17 (d, 1H, J = 15.9 Hz), 7.48 (d, 2H, J = 8.7 Hz), 7.52 (d, 2H, J = 8.7 Hz), 7.57 (d, 2H, J = 8.7 Hz), 7.74 (d, 1H, J = 15.9 Hz), 8.41-8.42 (m, 1H), 8.55-8.54 (m, 1H), 8.65-8.64 (m, 1H). ^{13}C NMR and JMOD (75MHz, $CDCl_3$): δ 55,3 (CH_3), 88.1 (C), 91.1 (C), 114.1 (CH), 115.2 (C), 124.2 (C), 124.5 (CH), 127.2 (CH), 131.8 (CH), 133.1 (CH), 134.5 (CH), 135.5 (C), 142.9 (CH), 143.9 (CH), 144.4 (CH), 151.1 (C), 159.8 (C). HRMS (MALDI), *m/z* calculated for $C_{21}H_{16}N_2O$ $[M]^{\bullet+}$ 312.1257 found 312.1267

(*E*)-2-(4-((4- dimethylaminophenyl)ethynyl)styryl)pyrazine (2b): Purified by column chromatography (petroleum ether/EtAcO, 1/1), orange solid. Yield: 60% (195 mg) Mp: 177-179°C. ^{1}H NMR (300MHz, $CDCl_3$) : δ 3.00 (s, 6H), 6.67 (d, 2H, J = 8.7 Hz), 7.14 (d, 1H, J =

Accepted Manuscript

15.9 Hz), 7.43 (d, 2H, *J* = 8.7 Hz), 7.52 (d, 2H, *J* = 8.7 Hz), 7.56 (d, 2H, *J* = 8.7 Hz), 7.74 (d, 1H, *J* = 15.9 Hz), 8.41-8.42 (m, 1H), 8.55-8.54 (m, 1H), 8.64-8.63 (m, 1H). ^{13}C NMR and JMOD (75MHz, $CDCl_3$): δ 40.1 (CH_3), 87.5 (C), 92.6 (C), 109.8 (C), 111.8 (CH), 124.2 (CH), 124.8 (C), 127.2 (CH), 131.6 (CH), 132.8 (CH), 134.6 (CH), 135.0 (C), 142.7 (CH), 143.8 (CH), 144.4 (CH), 150.2 (C), 151.2 (C). HRMS (MALDI), *m/z* calculated for $C_{22}H_{19}N_3$ $[M]^{\bullet+}$ 325.1573 found 325.1581

(*E*)-2-(4-((4- diphenylaminophenyl)ethynyl)styryl)pyrazine (2c): Purified by column chromatography (petroleum ether/EtAcO, 7/3 to 1/1), orange solid. Yield: 65% (292 mg) Mp: 152-154°C. ^{1}H NMR (300MHz, $CDCl_3$) : δ 7.07-7.20 (m, 9H), 7.33-7.38 (m, 4H), 7.46 (d, 2H, *J* = 8.4 Hz), 7.59 (d, 2H, *J* = 8.5 Hz), 7.64 (d, 2H, *J* = 8.5 Hz), 7.81 (d, 1H, *J* = 15.9 Hz), 8.48 (d, 1H, *J* = 2.7 Hz), 8.91(broad s, 1H), 8.71 (broad s, 1H). ^{13}C NMR and JMOD (75MHz, $CDCl_3$): δ 88.6 (C), 91.5 (C), 115.8 (C), 122.2 (CH), 123.6 (CH), 124.2 (C), 124.5 (CH), 125.0 (CH), 127.3 (CH), 129.4 (CH), 131.9 (CH), 132.6 (CH), 134.5 (CH), 135.5 (C), 142.8 (CH), 143.9 (CH), 144.4 (CH), 147.2 (C), 148.1 (C), 151.1 (C). HRMS (MALDI), *m/z* calculated for $C_{32}H_{23}N_3$ $[M]^{\bullet+}$ 449.1886 found 449.1879

(*E*)-2-(2-(4'-methoxy-[1,1'-biphenyl]-4-yl)vinyl)pyrazine (3a): Purified by column chromatography (petroleum ether/EtAcO, 7/3), pale yellow solid. Yield: 85% (231 mg) Mp: 207-208°C. ^{1}H NMR (300MHz, $CDCl_3$) : δ 3.86 (s, 3H), 6.98 (d, 2H, *J* = 8.7 Hz), 7.17 (d, 1H, *J* = 16.2 Hz), 7.57 (d, 2H, *J* = 8.7 Hz), 7.58 (d, 2H, *J* = 8.7 Hz), 7.65 (d, 2H, *J* = 8.7 Hz), 7.76 (d, 1H, *J* = 16.2 Hz), 8.41 (broad s, 1H), 8.55 (broad s, 1H), 8.66 (broad s, 1H). ^{13}C NMR and JMOD (75MHz, $CDCl_3$): δ 55,4 (CH_3), 114.3 (CH), 123.6 (CH), 127.0 (CH), 127.8 (CH), 128.0 (CH), 132.9 (C), 134.4 (C), 134.8 (CH), 141.4 (C), 142.6 (CH), 143.8 (CH), 144.4 (CH), 151.4 (C), 159.5 (C). HRMS (MALDI), *m/z* calculated for $C_{19}H_{18}N_2O$ $[M + 2H]^+$ 290.1414 found 290.1421

Accepted Manuscript

(*E*)-2-(2-(4'-dimethylamino-[1,1'-biphenyl]-4-yl)vinyl)pyrazine (3b): Purified by column chromatography (petroleum ether/EtAcO, 7/3 to 1/1), yellow solid. Yield: 73% (220 mg) Mp: 237-238°C. ^{1}H NMR (300MHz, $CDCl_3$) : δ 3.01 (s, 6H), 6.80 (d, 2H, *J* = 8.7 Hz), 7.15 (d, 1H, *J* = 15.9 Hz), 7.55 (d, 2H, *J* = 8.7 Hz), 7.60 (d, 2H, *J* = 8.7 Hz), 7.62 (d, 2H, *J* = 8.7 Hz), 7.77 (d, 1H, *J* = 15.9 Hz), 8.39-8.40 (m, 1H), 8.54-8.53 (m, 1H), 8.65-8.64 (m, 1H). ^{13}C NMR and JMOD (75MHz, $CDCl_3$): δ 40.5 (CH_3), 112.7 (CH), 123.1 (CH), 126.4 (CH), 127.6 (CH), 127.8 (CH), 128.2 (C), 133.7 (C), 135.0 (CH), 141.8 (C), 142.5 (CH), 143.7 (CH), 144.3 (CH), 150.2 (C), 151.5 (C). HRMS (MALDI), *m/z* calculated for $C_{20}H_{19}N_3$ $[M]^{\bullet+}$ 301.1573 found 301.1580

(*E*)-2-(2-(4'-diphenylamino-[1,1'-biphenyl]-4-yl)vinyl)pyrazine (3c): Purified by column chromatography (petroleum ether/EtAcO, 7/3), yellow solid. Yield: 75% (320 mg) Mp: 194-195°C. ^{1}H NMR (300MHz, $CDCl_3$) : δ 7.04 (t, 2H, *J* = 7.5 Hz), 7.12-7.14 (m, 6H), 7.22 (d, 1H, *J* = 15.9 Hz), 7.24-7.29 (m, 4H), 7.50 (d, 2H, *J* = 8.7 Hz), 7.59 (d, 2H, *J* = 8.7 Hz), 7.64 (d, 2H, *J* = 8.7 Hz), 7.77 (d, 1H, *J* = 15.9 Hz), 8.39-8.40 (m, 1H), 8.53 (broad s, 1H), 8.64 (broad s, 1H). ^{13}C NMR and JMOD (75MHz, $CDCl_3$): δ 113.1 (CH), 127.7 (CH), 124.6 (CH), 126.9 (CH), 127.6 (CH), 127.8 (CH), 129.3 (CH), 134.0 (C), 134.5 (C), 134.8 (CH), 141.2 (C), 142.6 (CH), 143.8 (CH), 144.4 (CH), 147.5 (C), 151.4 (C). HRMS (MALDI), *m/z* calculated for $C_{30}H_{23}N_3$ $[M]^{\bullet+}$ 425.1886 found 425.1884

2-(4-methoxyphenyl)pyrazine (4a): Purified by column chromatography (petroleum ether/EtAcO, 7/3), cream solid. Yield: 63% (117 mg) Mp: 93-95°C (lit:[27] 55-56°C). ^{1}H NMR (300MHz, $CDCl_3$) : δ 3.89 (s, 3H), 7.04 (d, 2H, *J* = 8.7 Hz), 8.00 (d, 2H, *J* = 8.7 Hz), 8.45 (d, 1H, *J* = 2.7 Hz), 8.59 (broad s, 1H), 8.99 (broad s, 1H). Data similar to the literature.[27]

2-(4-dimethylaminophenyl)pyrazine (4b): Purified by column chromatography (petroleum ether/EtAcO, 7/3 to 1/1), yellow solid. Yield: 81% (161 mg) Mp: 107-108°C. ^{1}H NMR (300MHz, $CDCl_3$) : δ 3.04 (s, 6H), 6.80 (d, 2H, *J* = 8.7 Hz), 7.94 (d, 2H, *J* = 8.7 Hz), 8.33 (d,

Accepted Manuscript

1H, *J* = 2.7 Hz), 8.52 (dd, 1H, J_1 = 2.7 Hz, J_2 = 1.5 Hz), 8.94 (d, 1H, *J* = 1.5 Hz). ^{13}C NMR and JMOD (75MHz, $CDCl_3$): δ 40.2 (CH_3), 112.2 (CH), 128.8 (C), 127.8 (CH), 141.0 (CH), 141.2 (CH), 143.9 (CH), 151.6 (C), 153.1 (C). HRMS (MALDI), *m/z* calculated for $C_{12}H_{13}N_3$ $[M]^{\bullet+}$ 199.1104 found 199.1107

2-(4-diphenylaminophenyl)pyrazine (4c): Purified by column chromatography (petroleum ether/EtAcO, 7/3), yellow solid. Yield: 76% (245 mg). Mp: 85-86°C (lit:[28] 81-82°C). ^{1}H NMR (300MHz, $CDCl_3$) : δ 7.10 (t, 2H, J = 7.2 Hz), 7.20-7.16 (m, 6H), 7.34-7.29 (m, 4H), 7.90 (d, 1H, *J* = 8.7 Hz), 8.44 (d, 1H, *J* = 2.7 Hz), 8.59 (dd, 1H, J_1 = 2.7 Hz, J_2 = 1.5 Hz), 8.99 (d, 1H, *J* = 1.5 Hz). Data similar to the literature.[28]

2-((4-methoxyphenyl)ethynyl)pyrazine (5a): Purified by column chromatography (petroleum ether/EtAcO, 7/3 to 1/1), yellow solid. Yield: 56% (118 mg) Mp: 60-61°C (lit.[29]: 55-56°C). ^{1}H NMR (300MHz, $CDCl_3$) : δ 3.84 (s, 3H), 6.91 (d, 2H, *J* = 8.7 Hz), 7.56 (d, 2H, *J* = 8.7 Hz), 8.45 (d, 1H, *J* = 2.7 Hz), 8.55 (dd, 1H, J_1 = 2.7 Hz, J_2 = 1.5 Hz), 8.73 (d, 1H, *J* = 1.5 Hz). ^{13}C NMR and JMOD (75MHz, $CDCl_3$): δ 55.4 (CH_3), 84.9 (C), 93.8 (C), 113.5 (C), 114.2 (CH), 133.8 (CH), 140.7 (C), 142.4 (CH), 144.4 (CH), 147.6 (CH), 160.7 (C). HRMS (MALDI), *m/z* calculated for $C_{13}H_{11}N_2O$ $[M + H]^+$ 211.0866 found 211.0872

2-((4-dimethylaminophenyl)ethynyl)pyrazine (5b): Purified by column chromatography (petroleum ether/EtAcO, 7/3), yellow solid. Yield: 76% (170 mg) Mp: 95-97°C. ^{1}H NMR (300MHz, $CDCl_3$) : δ 3.02 (s, 6H), 6.66 (d, 2H, *J* = 8.7 Hz), 7.49 (d, 2H, *J* = 8.7 Hz), 8.40 (d, 1H, *J* = 2.7 Hz), 8.52 (dd, 1H, J_1 = 2.7 Hz, J_2 = 1.5 Hz), 8.70 (d, 1H, *J* = 1.5 Hz). ^{13}C NMR and JMOD (75MHz, $CDCl_3$): δ 40,1 (CH_3), 84.7 (C), 95.7 (C), 107.8 (C), 111.7 (CH), 133.5 (CH), 141.3 (C), 141.7 (CH), 144.2 (CH), 147.4 (CH), 150.9 (C). HRMS (MALDI), *m/z* calculated for $C_{14}H_{13}N_3$ $[M]^{\bullet+}$ 223.1104 found 223.1110

2-((4-diphenylaminophenyl)ethynyl)pyrazine (5c): Purified by column chromatography (petroleum ether/EtAcO, 7/3), yellow solid. Yield: 72% (250 mg) Mp: 107-108°C. ^{1}H NMR

Accepted Manuscript

(300MHz, $CDCl_3$) : δ 7.02-6.98 (m, 2H), 7.14-7.07 (m, 6H), 7.32-7.27 (m, 4H), 7.44 (d, 2H, *J* = 8.7 Hz), 8.44 (d, 1H, *J* = 2.7 Hz), 8.54 (dd, 1H, J_1 = 2.7 Hz, J_2 = 1.5 Hz), 8.72 (d, 1H, *J* = 1.5 Hz). ^{13}C NMR and JMOD (75MHz, $CDCl_3$): δ 85.3 (C), 94.3 (C), 113.5 (C), 121.3 (CH), 124.1 (CH), 125.5 (CH), 129.5 (CH), 133.2 (CH), 140.8 (C), 142.3 (CH), 144.4 (CH), 146.8 (C), 147.6 (CH), 149.1 (C). HRMS (MALDI), *m/z* calculated for $C_{24}H_{17}N_3$ $[M]^{\bullet+}$ 347.1417 found 347.1426

2-(4-((4-methoxyphenyl)ethynyl)phenyl)pyrazine (6a): Purified by column chromatography (petroleum ether/EtAcO, 5/5), white solid. Yield: 56% (118 mg) Mp: 162-163°C. ^{1}H NMR (300MHz, $CDCl_3$) : δ 3.82 (s, 3H), 6.88 (d, 2H, *J* = 8.3 Hz), 7.50 (d, 2H, *J* = 8.3 Hz), 7.64 (d, 2H, *J* = 8.7 Hz), 8.01(d, 2H, *J* = 8.7 Hz), 8.50 (broad s, 1H), 8.62 (broad s, 1H), 9.04 (broad s, 1H). ^{13}C NMR and JMOD (75MHz, $CDCl_3$): δ 55.4 (CH_3), 87.9 (C), 91.6 (C), 114.2 (CH), 115.2 (C), 125.5 (C), 126.8 (CH), 132.1 (CH), 133.3 (CH), 135.6 (C), 142.2 (CH), 143.1 (CH), 144.3 (CH), 152.1 (C), 160.0 (C). HRMS (MALDI), *m/z* calculated for $C_{19}H_{15}N_2O$ $[M + H]^+$ 288.1179 found 288.1186

2-(4-((4-dimethylaminophenyl)ethynyl)phenyl)pyrazine (6b): Purified by column chromatography (petroleum ether/EtAcO, 7/3), yellow solid. Yield: 62% (185 mg) Mp: 204-205°C. ^{1}H NMR (300MHz, $CDCl_3$) : δ 3.00 (s, 3H), 6.67 (d, 2H, *J* = 9.0 Hz), 7.44 (d, 2H, *J* = 9.0 Hz), 7.63 (d, 2H, *J* = 9.0 Hz), 8.00 (d, 2H, *J* = 9.0 Hz), 8.50 (d, 1H, *J* = 2.7 Hz), 8.63 (broad s, 1H), 9.04 (d, 1H, *J* = 1.5 Hz). ^{13}C NMR and JMOD (75MHz, $CDCl_3$): δ 40.2 (CH_3), 87.1 (C), 93.0 (C), 109.7 (C), 111.8 (CH), 126.0 (C), 126.7 (CH), 131.9 (CH), 132.9 (CH), 135.0 (C), 142.1 (CH), 142.9 (CH), 144.2 (CH), 150.3 (C), 152.2 (C). HRMS (MALDI), *m/z* calculated for $C_{20}H_{17}N_3$ $[M]^{\bullet+}$ 299.1417 found 299.1423

2-(4-((4-diphenylaminophenyl)ethynyl)phenyl)pyrazine (6b): Purified by column chromatography (petroleum ether/EtAcO, 7/3), yellow solid. Yield: 74% (313 mg) Mp: 154-156°C. ^{1}H NMR (300MHz, $CDCl_3$) : δ 7.16-7.03 (m, 8H), 7.34-7.28 (m, 4H), 7.42 (d, 2H, *J* =

Accepted Manuscript

8.7 Hz), 7.67 (d, 2H, *J* = 8.4 Hz), 8.04 (d, 2H, *J* = 8.4 Hz), 8.53 (d, 1H, *J* = 2.7 Hz), 8.66 (broad s, 1H), 9.07 (broad s, 1H). ^{13}C NMR and JMOD (75MHz, $CDCl_3$): δ 88.3 (C), 91.9 (C), 115.6 (C), 122.1 (CH), 123.7 (CH), 125.1 (CH), 125.4 (C), 126.7 (CH), 129.4 (CH), 132.1 (CH), 132.6 (CH), 135.5 (C), 142.1 (CH), 143.0 (CH), 144.2 (CH), 147.1 (C), 148.2 (C), 152.1 (C). HRMS (MALDI), *m/z* calculated for $C_{30}H_{21}N_3$ $[M]^{\bullet+}$ 423.1730 found 423.1728

Acknowledgments

KH thanks the Northern Kentucky University College of Arts & Sciences and Center for Global Engagement and International Affairs for their financial support to international mobility.

[1] (a) H. N. Kim, Z. Guo, W. Zhu, J. Yoon, H. Tian, *Chem. Soc. Rev.* **2011**, *40*, 79-93. (b) G. S. He, L.-S. Tan, Q. Zheng, P. N. Prasad. *Chem. Rev.* **2008**, *108*, 1245-1330.

[2] (*a*) M. Kivala, F. Diederich, *Acc. Chem. Res.* **2009**, *42*, 235-248. (*b*) S.-i. Kato, F. Diederich, *Chem. Commun.* **2010**, *46*, 1994-2006. (*c*) H. Meier, *Angew. Chem. Int. Ed.* 2005, **44**, 2482-2506.

[3] F. Bureš, *RSC Adv.* **2014**, *4*, 58826-58851.

[4] S. Achelle; C. Baudequin, N. Plé, *Dyes Pigm.* **2013**, *98*, 575-600.

[5] Z. Qin, Y. Wang, X. Lu, Y. Chen, J. Peng, G. Zhou, *Chem. Asian J.* **2016**, *11*, 285-293.

[6] (a) V. Schmitt, S. Moschel, H. Detert, *Eur. J. Org. Chem.* **2013**, 5655-5669. (b) C. Wink, H. Detert, *J. Phys. Org. Chem.* **2013**, *26*, 144-150. (c) V. Schmitt, J. Fisher, H. Detert, *ISRN Org. Chem.* **2011**, 5890012. (d) A. M. Asirir, K. A. Alamry, M. Pannipara, A. G. Al-sehemi, S. A. El-Daly, *Spectrochimica Acta A* **2015**, *149*, 722-730.

[7] (a) S. Yan, R. Huang, Y. Zhou, M. Zhang, M. Deng, X. Wang, X. Weng, X. Zhou, *Chem. Commun.* **2011**, *47*, 1273-1275. (b) R. Rajagopalan, W. L. Neumann, A. R. Poreddy, R. M. Fitch, J. N. Freskos, B. Asmelash, K. R. Gaston, K. P. Galen, J.-J. Shieh, R. B. Dorshow, *J. Med. Chem.* **2011**, *54*, 5048-5058. (c) A. Boländer, D. Kieser, C. Voss, S. Bauer, C. Schön, S.

Accepted Manuscript

Burgold, T. Bittner, J. Hölzer, R. Heyny-von Haußen, G. Mall, V. Goetchy, C. Czech, H. Knust, R. Berger, J. Herms, I. Hilger, B. Schmidt, *J. Med. Chem.* **2012**, *55*, 9170-9180.

[8] M. Chem, H. Nie, B. Song, L. Li, J. Z. Sun, A. Qin, B. Z. Tang, *J. Mater. Chem. C* **2016**, *4*, 2901-2908.

[9] Y. Ooyama, K. Uenaka, Y. Harima, J. Ohshita, *RSC Adv.* **2014**, *4*, 30225-30228.

[10] (a) N. Hebbar, Y. Ramondenc, G. Plé, G. Dupas, N. Plé, *Tetrahedron*, **2009**, *65*, 4190-4200. (b) F. Bureš, H. Čermáková, J. Kulhánek, M. Ludwig, W. Kuznik, I. V. Kityk, T. Mikysek, A. Růžička, *Eur. J. Org. Chem.* **2012**, 529-538. (c) S. Gauthier, N. Vologdin, S. Achelle, A. Barsella, B. Caro, F. Robin-le Guen, *Tetrahedron*, **2013**, *69*, 8392-8399.

[11] (a) M. Rumi, S. J. K. Pond, T. Meyer-Friedrichen, Q. Zhang, M. Bshop, Y. Zhang, S. Barlow, S. R. Marder, J. W. Perry, *J. Phys. Chem. C* **2008**, *112*, 8061-8071. (b) Y. Sun. X.-T. Liu, J.-F. Guo, A.-M. Ren, D. Wang, *J. Phys. Org. Chem.* **2013**, *26*, 822-833.

[12] (a) D. Cvejn, S. Achelle, O. Pytela, J.-P. Malval, A. Spangenberg, N. Cabon, F. Bureš, F. Robin-le Guen, *Dyes Pigm*. **2016**, *124*, 100-109. (b) S. Achelle, A. Barsella, C. Baudequin, B. Caro, F. Robin-le Guen, *J. Org. Chem.* **2012**, *77*, 4087-4096. (c) S. Achelle, S. Kahlal, J.-Y. Saillard, N. Cabon, B. Caro, F. Robin-le Guen, *Tetrahedron*, **2014**, *70*, 2804-2815. (d) F. Castet, A. Pic, B. Champagne, *Dyes Pigm.* **2014**, *110*, 256-260.

[13] S. Achelle, J. Rodríguez-López, F. Bureš, F. Robin-le Guen, *Dyes Pigm.* **2015**, *121*, 305-311.

[14] H. Pan, X. Gao, Y. Zhang, P. N. Prasad, B. Reinhardt, R. Kanna, *Chem. Mater.* **1995**, *7*, 816-821.

[15] (a) A. Petrosyan, P. Ehlers, S. Reimann, T. V. Ghochikyan, A. S. Saghyan, A. Spannenberg, S. Lochbrunner, P. Langer, *Tetrahedron*, **2015**, *71*, 6803-6812. (b) H. Ali, J. E. van Lier, *Tetrahedron Lett.* **2012**, *53*, 4824-4827. (c) M. Darabantu, L. Boully, A. Turck, N. Plé, *Tetrahedron*, **2005**, *61*, 2897-2905.

Accepted Manuscript

[16] A. F. Littke, G. C. Fu, *Angew. Chem. Int. Ed.* **2002**, *41*, 4176-4211.

[17] C. Denneval, S. Achelle, C. Baudequin, F. Robin-le Guen, *Dyes Pigm.* **2014**, *110*, 49-55.

[18] D. F. Eaton, *Pure Appl. Chem.* **1988**, *60*, 1107–1114.

[19] P. D. Zoon, A. M. Brouwer, *Photochem. Photobiol. Sci.* **2009**, *8*, 345-353.

[20] (a) Y. Niko, S. Kawauchi, G.-i. Konishi, *Chem. Eur. J.* **2013**, *19*, 9760-9765. (b) L. Giordano, V. Shvadchak, J. A. Fauerbach, E. A. Jares-Erjman, T. M. Jovin, *J. Phys. Chem. Lett.* **2012**, *3*, 1011-1016. (c) U. Balijapilli, S. Manickam, M. D. Thiyagarajan, S. K. Iyer, *RSC Adv.* **2016**, *6*, 58549-58560. (d) N. Friebe, K. Schreiter, J. Kubel, B. Dietzek, N. Moszner, P. Burtscher, A. Oehlke, S. Spange, *New J. Chem.* **2015**, *39*, 5171-4179. (e) F. Mahuteau-Betzer, S. Piguel, *Tetrahedron Lett.* **2013**, *54*, 3188-3193.

[21] (a) C. Katan, F. Terenziani, O. Mongin, M. H. V. Wertz, L. Porrès, T. Pons, J. Mertz, S. Tretiak, M. Blanchard-Desce, *J. Phys. Chem. A* **2005**, *109*, 3024-3037. (b) R. Lartia, C. Allain, B. Bordeau, F. Schmidt, C. Fiorini-Debuischert, F. Charra and M.-P. Teulade-Fichou, *J. Org. Chem.* **2008**, *73*, 1732-1744.

[22] (a) C. Reichardt, *Chem. Rev.* **1994**, *94*, 2319-2358. (b) J. P. Cerón-Carrasco, D. Jacquemin, C. Laurence, A. Planchay, C. Reichardt, K. Sraïdi, K. *J. Phys. Org. Chem.* **2014**, *27*, 512-518.

[23] C. Hansch, A. Leo, R. W. Taft, *Chem. Rev.* **1991**, *91*, 165-195.

[24] S. Achelle, A. Barsella, B. Caro, F. Robin-le Guen, *RSC Adv.* **2015**, *5*, 39218-39227.

[25] S. Achelle, F. Mathevet, D. Kreher, A.-J. Attias, A. Turck, N. Plé, *Heterocycles*, **2008**, *75*, 357-374.

[26] S. A. Haroutounian, J. A. Katzenellenbogen, *Tetrahedron*, **1995**, *51*, 1585-1598.

[27] L. Boully, M. Darabantu, A. Turck, N. Plé, *J. Heterocycl. Chem.* **2005**, *42*, 1423-1428.

[28] C. Li, Q. Ni, J. Qiu, *Eur. J. Org. Chem.* **2011**, 3009-3015.

[29] H. Peng, Y-Q Chen, S.-L. Mao, Y.-X. Pi, Y. Chen, Z.-Y. Lian, S.-H. Liu, G.-A. Yu, *Org. Biomol. Chem.* **2014**, *12*, 6944-6952.

Accepted Manuscript