Design, synthesis and characterization of novel thienylpyridazine derivatives for optical applications

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Abstract: We report in this work the synthesis and the photophysical characterization of novel pyridazine derivatives, functionalized in position 3, with different (hetero)aromatic groups (indole, cyanophenyl, nitrophenyl). The diazines were synthesized by Suzuki coupling of 3-bromo-6-(thiophen-2-*yl*)pyridazine with commercially available (hetero)aryl-boronic acids. Due to their optical properties these push-pull π-conjugated systems can have application as versatile building blocks for the preparation of DSSCs, OLEDs, and nonlinear optical (SHG) materials.

Keywords: push-pull π–conjugated systems, thiophene, indole, pyridazine, Suzuki coupling, optical applications

1. Introduction

In recent years, push-pull π-conjugated systems bearing electron rich (thiophene, pyrrole, furan) and electron deficient heterocycles ((benz)imidazole, (benzo)thiazole, pyridine, piridazine, phthalazine, etc.) have been widely used as NLO and photochromic materials, metal free organic sensitizers for DSSCs, OLEDs, etc. due to their easy synthesis and electronic arrangement that assures and efficient tuning of the photophysical properties through small structural modifications. The tuning of the optoelectronic properties of these push-pull systems can be achieved by modification of the electron donor, electron acceptor, and/or by modification of the electronic nature of the π-bridge. Concerning the π-spacer, several studies published in the past three decades have confirmed that substitution of the benzene ring of a chromophore bridge with easily delocalizable electro-rich and/or electron-poor heterocycles results in improved molecular optical (linear and nonlinear) properties of the corresponding push-pull systems. Due to their electronic nature and low aromaticity, they can act efficiently as π-bridges as well as auxiliary donors (electron-rich heterocycles) or as auxiliary acceptors (electron-poor heterocycles). Additionally, these heterocyclic systems are also thermally and photochemically stable. [1-13]

During the last decade our research group has published experimental and theoretical results concerning the auxiliary donor/acceptor effect of electron rich and electron deficient heterocycles on π–conjugated systems for several optical applications. [5-13]

Based on our earlier work we were motivated to extend these studies in order to explore the potential application of a new series of donor-acceptor substituted thienylpyridazines in which the pyridazine heterocycle plays the dual role of π-bridge and acceptor/auxiliary acceptor moiety. Therefore, the pyridazine ring was functionalized in position 3 with different (hetero)aryl-based groups (indole, benzonitrile and nitrophenyl) in order to study the effect of their electronic nature on the optical properties of the push-pull systems.

We report in this work the synthesis and the photophysical characterization of novel thienylpyridazine derivatives which were synthesized through Suzuki coupling of 3-bromo-6-(thiophen-2-*yl*)pyridazine [14] with commercially available (hetero)aryl-boronic acids.

2. Experimental

2.1. Instruments

NMR spectra were obtained on a Varian Unity Plus Spectrometer at an operating frequency of 300 MHz for ^{1}H NMR and 75.4 MHz for ^{13}C NMR, or a Brucker Avance III 400 at an operating frequency of 400 MHz for ^{1}H NMR and 100.6 MHz for ^{13}C NMR using the solvent peak as internal reference at 25 ºC (δ relative to TMS). All chemical shifts are given in Hz. Assignments were made by comparison of chemical shift, peak multiplicities and *J* values, and were supported by spin decoupling-double resonance and bidimensional heteronuclear HMBC and HMQC correlation techniques. IR spectra were determined on a BOMEM MB 104 spectrophotometer. UV-Visible absorption spectra (200-800 nm) were obtained using a Shimadzu UV/2501PC spectrophotometer. Fluorescence spectra were collected using a FluoroMax-4 spectrofluorometer. Luminescence quantum yields were measured in comparison with ethanol solution of

9,10-diphenylanthracene ($\Phi_F = 0.95$) [15] as standard. All melting points were measured on a Gallenkamp melting point apparatus and are uncorrected. Mass spectrometry analysis were performed at the C.A.C.T.I. – Unidad de Espectrometria de Masas of University of Vigo, Spain.

2.2. Materials

Boronic acids were purchased from Aldrich and used as received. TLC analysis were carried out on 0.25 mm thick precoated silica plates (Merck Fertigplatten Kieselgel $60F_{254}$) and the spots were visualized under UV light. Chromatography on silica gel was carried out on Merck Kieselgel (200-300 mesh).

2.3. Synthesis

General procedure for the synthesis of thienyl-pyridazine derivatives **3** through Suzuki coupling: 3-bromo-6-(thiophen-2-yl)pyridazine **1** (0.5 mmol, 120 mg) was coupled with (hetero)arylboronic acids **2** (0.6 mmol) in a mixture of DME (8 mL), ethanol (2 mL), aqueous 2 M Na_2CO_3 (1 mL) and $Pd(PPh_3)_4$ (5 mol %) at 80 ºC under nitrogen. The reaction was monitored by TLC, which determined the reaction time (24-36 h). After cooling, the mixture was extracted with chloroform (3x20 mL), a saturated solution of NaCl was added (20 mL) and the phases were separated. The organic phase was washed with water (3x10 mL) and with aqueous solution NaOH 10% (10 mL). The organic phase obtained was dried (over $MgSO_4$), filtered, and the solvent removed to give a crude mixture. The crude product was purified through a silica gel chromatography column using mixtures of chloroform and light petroleum of increasing polarity to afford the coupled products **3**. Recrystallization from *n*-hexane / dichloromethane gave the pure compounds.

1-Methyl-5-(6’-(thiophen-2’’-yl)pyridazin-3’-yl)-1*H*-indole **3a**. Beige solid (16%). Mp: 224-228 ºC (recrystallized from dichloromethane / *n*-hexane). UV (ethanol): λ_{max} nm (ε, $M^{-1}cm^{-1}$) 326, (25,282). IR (liquid film) ν 3426, 2085, 1640, 1545, 1432, 1406, 1296, 1241, 1151, 807 cm^{-1}. ^{1}H NMR (Acetone-*d*$_6$, 400 MHz) δ 3.94 (s, 3H, CH_3), 6.61 (dd, 1H, H-3, *J* = 3.2 and 1.2 Hz), 7.26 (dd, 1H, H-4’’, *J* = 4.8 and 4.0 Hz), 7.35 (d, 1H, H-2, *J* = 3.2 Hz), 7.59 (d, 1H, H-7, *J* = 8.4 Hz), 7.69 (dd, 1H, H-5’’, *J* = 5.2 and 1.2 Hz), 7.90 (dd, 1H, H-3’’, *J* = 3.6 and 1.2 Hz), 8.15 (dd, 1H, H-6, *J* = 8.4 and 1.6 Hz), 8.16 (d, 1H, H-5’, *J* = 9.2 Hz), 8.22 (d, 1H, H-4’, *J* = 9.2 Hz), 8.46 (d, 1H, H-4, *J* = 1.2 Hz) ppm. ^{13}C NMR (Acetone-*d*$_6$, 400 MHz) δ 33.0 (CH_3), 102.5 (C-3), 110.8 (C-7), 120.3 (C-4), 121.1 (C-6), 123.4 (C-5’), 124.5 (C-4’), 126.9 (C-3’’), 128.4

(C-5), 129.0 (C-4''), 129.5 (C-5''), 129.9 (C-7a), 131.3 (C-2), 138.8 (C-3a), 142.3 (C-2''), 153.8 (C-6'), 159.5 (C-3') ppm. MS (EI) m/z (%) = 292 ([M]+, 6), 291 (33), 155 (100), 154 (26). HRMS: m/z (EI) for $C_{17}H_{13}N_3S$; calcd 291.0830; found 291.0831.

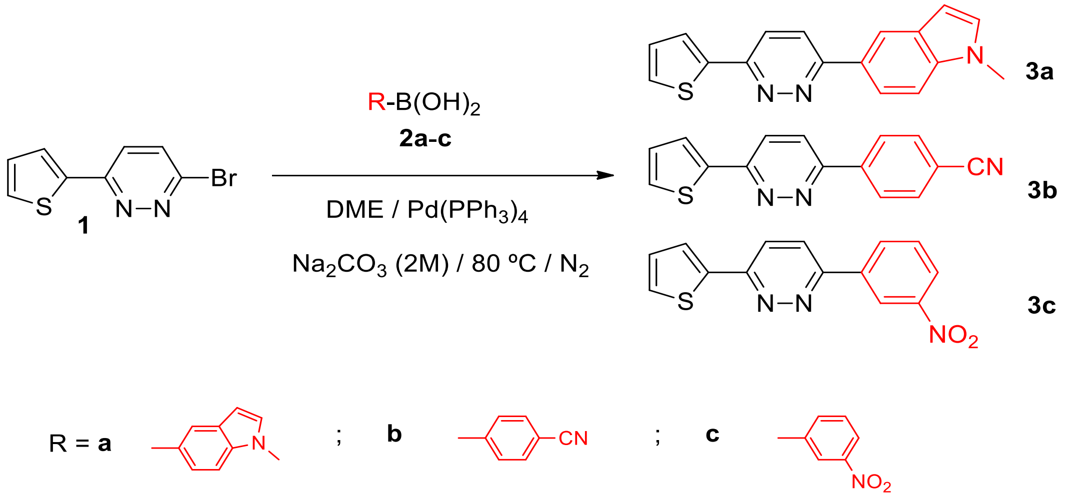
4-(6'-(Thiophen-2''-yl)pyridazin-3'-yl)benzonitrile **3b**. Yellow solid (28%). Mp: 249-252 ºC (recrystallized from dichloromethane / *n*-hexane). UV (ethanol): λ_{max} nm (ε, $M^{-1}cm^{-1}$) 323, (26,086). IR (liquid film) ν 3094, 2233, 1577, 1433, 1401, 1297, 1134, 852, 827, 720 cm^{-1}. ^{1}H NMR (Acetone-d_6, 400 MHz) δ 7.29 (dd, 1H, H-4'', *J* = 5.2 and 3.6 Hz), 7.76 (dd, 1H, H-5'', *J* = 5.0 and 1.2 Hz), 7.98 (dd, 1H, H-3'', *J* = 3.8 and 1.2 Hz), 8.00 (d, 2H, H-2 and H-6, *J* = 8.8 Hz), 8.29 (d, 1H, H-5', *J* = 9.2 Hz), 8.34 (d, 1H, H-4', *J* = 9.2 Hz), 8.46 (d, 2H, H-3 and H-5, *J* = 8.8 Hz) ppm. ^{13}C NMR (Acetone-d_6, 400 MHz) δ 114.1 (C-4), 119.1 (C-1), 123.7 (C-4' or C-5'), 125.7 (C-4' or C-5'), 128.2 (C-3''), 128.3 (C-2 and C-6), 129.2 (C-4''), 130.7 (C-5''), 133.6 (C-3 and C-5), 141.5 (C-2''), 155.3 (C-6'), 156.7 (C-3'), 206.1 (CN) ppm. MS (EI) m/z (%) = 264 ([M]+, 5), 263 (31), 127 (6), 109 (6), 108 (100). HRMS: m/z (EI) for $C_{15}H_9N_3S$; calcd 263.0517; found 263.0516.

3-(3'-Nitrophenyl)-6-(thiophen-2''-yl)pyridazine **3c**. Yellow solid (25%). Mp: 249-252 ºC (recrystallized from dichloromethane / *n*-hexane). UV (ethanol): λ_{max} nm (ε, $M^{-1}cm^{-1}$) 314, (24,105). IR (liquid film) ν 3409, 2094, 1639, 1524, 1444, 1402, 1351, 1311, 1276, 1111, 1081, 1056, 838, 812, 727 cm^{-1}. ^{1}H NMR (Acetone-d_6, 300 MHz) δ 7.29 (dd, 1H, H-4'', *J* = 5.2 and 3.6 Hz), 7.78 (dd, 1H, H-5'', *J* = 5.2 and 0.8 Hz), 7.92 (t, 1H, H-5', *J* = 8.2), 8.00 (dd, 1H, H-3'', *J* = 3.2 and 1.2 Hz), 8.33 (d, 1H, H-5, *J* = 9.2 Hz), 8.42 (dd, 1H, H-6', *J* = 8.0 and 1.2 Hz), 8.43 (d, 1H, H-4, *J* = 9.2 Hz), 8.70 (dd, 1H, H-4', *J* = 7.8 and 0.8 Hz), 9.10 (t, 1H, H-2', *J* = 1.8 Hz) ppm. ^{13}C NMR (Acetone-d_6, 300 MHz) δ 122.1 (C-2'), 123.8 (C-5), 125.1 (C-4), 125.6 (C-6'), 128.2 (C-3''), 129.2 (C-4''), 130.7 (C-5''), 131.3 (C-5'), 133.5 (C-4'), 139.0 (C-1'), 141.4 (C-2''), 149.8 (C-3'), 155.4 (C-6), 156.2 (C-3) ppm. MS (EI) m/z (%) = 284 ([M]+, 4), 283 (47), 253 (27), 117 (70), 108 (100). HRMS: m/z (EI) for $C_{14}H_9N_3O_2S$; calcd 283.0415; found 283.0414.

3. Results and Discussion

3.1. Synthesis

The precursor bromo-thienylpyridazine **1** was synthesized by reaction of thienyl-pyridazinone with $POBr_3$, which in turn, was previously prepared by condensation of methyl-4-oxo-4-(thiophen-2-*yl*)butanoate with hydrazine hydrate in ethanol.[14] Compounds **3a-c** were prepared by Suzuki cross-coupling reaction of 3-bromo-6-(thiophen-2-yl)pyridazine **1** with commercially available (hetero)aryl-boronic acids **2a-c** in fair yields (16-25 %) (Table 1, Scheme 1). The new thienyl-pyridazine derivatives **3** were characterized by the usual spectroscopic techniques.



Scheme 1. Synthesis of thienyl-pyridazine derivatives **3**.

Table 1. Yields, UV-Visible absorption and emission data for thienyl-pyridazines **3**.

Cp	**Yield** (%)	λ_{max} (nm)	ε ($M^{-1}cm^{-1}$)	λ_{em} (nm)	Φ_F	**Stokes Shift** (nm)
3a	16	326	25,282	427	0.007	101
3b	28	323	26,086	404	0.006	81
3c	25	314	24,105	408	0.008	94

3.2. Optical properties

Electronic absorption spectra of pyridazines **3** in ethanol solutions (10^{-4} M) show intense lowest energy charge-transfer absorption bands in the UV-visible region between 314-326 nm. The position of these bands depends on the electronic nature of the (hetero)aromatic substituent linked in position 3 of the pyridazine heterocycle as well as the degree of the electronic delocalization (Table 1, Figure 1).

Therefore, the indole derivative **3a** with the highest delocalizated π-conjugate system exhibit the highest λ_{max} value (326 nm). On the other hand, compound **3b** bearing the strong acceptor cyano group in position 4 of the phenyl ring (withdrawing mesomeric effect) exhibit a bathochromic shift of 9 nm when compared to compound **3c** which is functionalized with a nitro group (inductive withdrawing effect) in position 3 of the phenyl ring. These results are in agreement with the higher electron-withdrawing ability of the acceptor groups, in the order 3-nitrophenyl < 4-cyanophenyl (Figure 1).

Thienylpyridazines **3** were excited at the wavelength of maximum absorption, at room temperature, in order to study their fluorescence properties (Figure 1). The relative fluorescence quantum yields were determined using a 10^{-6} M solution of 9,10-diphenylanthracene in ethanol as fluorescence standard ($\Phi_F = 0.95$).[15] Compound **3a** showed the longer wavelength of emission maxima (λ_{em} = 427 nm), compared to derivatives **3b-c** (λ_{em} = 404-408 nm). All compounds showed weak emissive properties, with relative fluorescence quantum yields ranging from 0.006 to 0.008 and large Stokes' shifts (the lowest being 81 nm and the highest 101 nm).

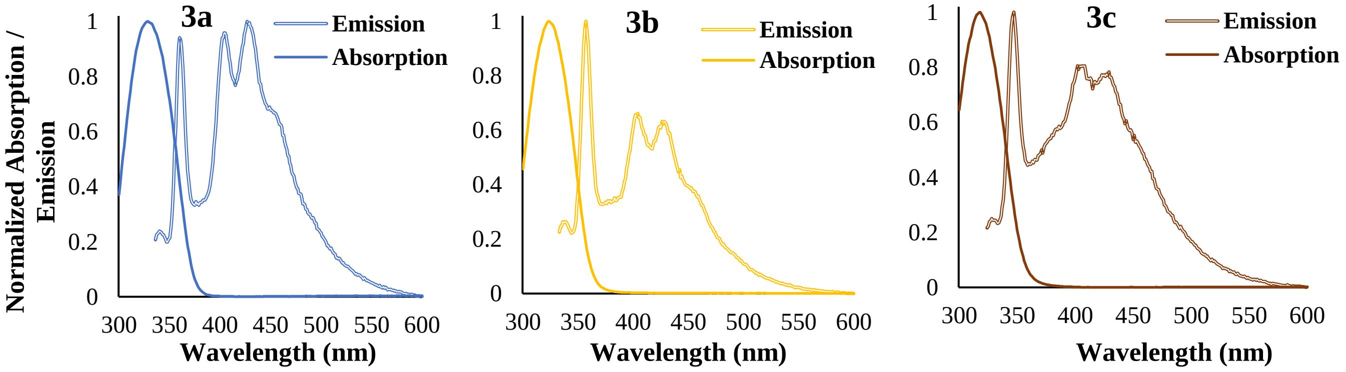


Figure 1. UV-Visible absorption and emission spectra of the novel thienyl-pyridazines **3** in ethanol solution.

4. Conclusions

Three novel thienyl-pyridazines **3a-c** were synthesized in fair yields through Suzuki coupling. The compounds exhibit absorption and emission bands in the UV-visible range which are influenced by the electronic nature of the (hetero)aromatic group linked in position 3 of the pyridazine heterocycle as well as the degree of the electronic delocalization of the π-conjugated system.

Due to their optical properties push-pull π-conjugated systems **3** can have application as versatile building blocks for the preparation of DSSCs, OLEDs, and nonlinear optical (SHG) materials.

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