Synthesis and characterization of novel thienyl-phthalazine based heterocyclic systems functionalized with (bi)thiophene moieties

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Abstract

The phthalazine moiety has a highly π-deficient aromatic character that makes it a good candidate to be incorporated as electron acceptor group, or even as spacer with auxiliary electron withdrawing abilities, into push-pull systems. Additionally, offers the possibility of protonation, hydrogen bond formation, and chelation through the nitrogen atoms.

Phthalazine derivatives have applications as therapeutic agents, chemiluminescent materials, ligands in transition metal catalysis, and as optical materials.

Some time ago, our research group developed a methodology for the preparation of phthalazine derivatives in three steps, affording halo-thienyl-phthalazine derivatives that play an important role in diazine chemistry since they offer great potential for further functionalization by nucleophilic displacement of the halogen, making numerous otherwise inaccessible diazines become available.

In continuation of the work developed before by our research group, we report in this communication the synthesis and the evaluation of the optical properties of two novel thienyl-phthalazine derivatives, having in mind further functionalization to prepare push-pull heterocyclic systems for several optical and photovoltaic applications. These studies showed that the optical properties could be readily tuned by varying the π-conjugation path length through the introduction of a second thiophene unit.

1. Introduction

For the last decades, research targeting dipolar chromophores has been considerably growing due to its interesting and tuneable properties and numerous applications as therapeutic agents,[1] chemiluminescent materials,[2] ligands in transition metal catalysis,[3] and as optical materials.[4]

The electronic arrangement of push-pull compounds is based on an electron donor group (D) and an electron acceptor group (A) interacting through a π-conjugated spacer, allowing for intramolecular charge-transfer (ICT). The tuning of the molecular properties of these systems for the desired applications can be achieved through modification of the electron donor or acceptor end-cap groups, or modification of the π-bridge. Recently, the incorporation of heterocycles with different electronic natures (electron-rich or electron deficient) into the π-conjugated systems has proven to induce higher photochemical and thermal stabilities and will modulate the optoelectronic properties.[5] The phthalazine moiety is a good candidate to be incorporated into dipolar systems as electron acceptor group, or as a spacer with auxiliary electron withdrawing abilities due to its highly π-deficient aromatic character. It also allows for further functionalization though protonation, hydrogen bond formation, and chelation through the nitrogen atoms.[6]

Some time ago, this research group reported the preparation of halo-thienyl-phthalazine derivatives, that can play an important role in diazine chemistry due to their great potential for further functionalization by nucleophilic displacement of the halogen.[7] In continuation of the work developed by this research group in the preparation of push-pull heterocyclic systems for several optical and photovoltaic applications,[3b-c, 7-8] we report the synthesis and the evaluation of the optical properties of two novel thienyl-phthalazine derivatives as precursors in the preparation of a large variety of donor-acceptor π-conjugated chromophores.

2. Experimental

2.1. Methods and Materials

NMR spectra were obtained on a Varian Unity Plus Spectrometer at an operating frequency of 300 MHz for ^{1}H 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. 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 ($\Phi_F = 0.95$)[9] as standard. All melting points were measured on a Gallenkamp melting point apparatus and are uncorrected.

All reagents were purchased from Aldrich or Acros Organics 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). The synthesis of precursor 3-bromo-6-(thiophen-2-yl)phthalazine **1** was reported elsewhere.[7]

2.2. Synthesis

General procedure for the synthesis of 3-(thiophen-2-yl)phthalazine derivatives **3a-b** from 3-bromo-6-(thiophen-2-yl)phthalazine **1** by Suzuki-Miyaura cross-coupling:

3-Bromo-6-(thiophen-2-yl)phthalazine **1**[7] (0.5 mmol) was coupled with the appropriate heterocyclic boronic acid **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 °C, under nitrogen. The reaction was monitored by TLC, which determined the reaction time (48 h). After cooling, the mixture was extracted with chloroform (3×20 ml) and a saturated solution of NaCl (20 mL). The organic phase was washed with water (3×10 mL) and with 10 mL of a solution of NaOH (10%). 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 dichloromethane and light petroleum of increasing polarity to afford the coupled products **3**. Recrystallization from *n*-hexane / dichloromethane gave the pure compounds.

1-(5'-Hexylthiophen-2'-yl)-4-(thiophen-2''-yl)phthalazine **3a**. Yellow solid (26%). UV (ethanol): λ_{max} nm (ε, $M^{-1}cm^{-1}$) 360 (17,538). ^{1}H NMR (C*D*Cl_3, 300 MHz) δ 0.90 (t, 3H, CH_3, *J* = 7.0 Hz), 1.33 (m, 4H, $C\underline{H}_2C\underline{H}_2CH_2CH_3$), 1.40 (m, 2H, $C\underline{H}_2CH_3$), 1.76 (quint, 2H, thioph-$CH_2C\underline{H}_2$), 2.90 (t, 2H, thioph-$C\underline{H}_2$, *J* = 7.6 Hz), 6.91 (d, 1H, H-4', *J* = 3.6 Hz), 7.22 (dd, 1H, H-4’’, *J* = 4.8 Hz, *J* = 3.6 Hz), 7.55 (d, 1H, H-3’, *J* = 3.6 Hz), 7.57 (dd, 1H, H-5’’, *J* = 5.2 Hz, *J* = 1.2 Hz), 7.68 (dd, 1H, H-3’’, *J* = 3.6 Hz, *J* = 1.2 Hz), 7.87 (m, 2H, H-6, H-7), 8.47-8.50 (m, 1H, H-8), 8.52-8.56 (m, 1H, H-5) ppm. HRMS: m/z (EI) for $C_{22}H_{22}N_2S_2$; calcd 378.1224; found: 378.1222.

1-(5’’-Hexyl-(2’,2’’-bithiophen)-5’-yl)-4-(thiophene-2’’’-yl)phthalazine **3b**. Yellow solid (19%). UV (ethanol): λ_{max} nm (ε, $M^{-1}cm^{-1}$) 398, (20,045). ^1H NMR ($CDCl_3$, 300 MHz) δ 0.90 (t, 3H, CH_3, *J* = 6.8 Hz), 1.26-1.43 (m, 6H, $C\underline{H}_2C\underline{H}_2C\underline{H}_2CH_3$), 1.69 (m, 2H, thioph-$CH_2C\underline{H}_2$), 2.79 (t, 2H, thioph-$C\underline{H}_2$, *J* = 7.4 Hz), 6.71 (d, 1H, H-4’’, *J* = 3.6 Hz), 7.10 (d, 1H, H-3’’, *J* = 3.6 Hz), 7.17 (d, 1H, H-4’, *J* = 3.6 Hz), 7.22 (dd, 1H, H-4’’’, *J* = 5.2 Hz, *J* = 3.6 Hz), 7.57 (dd, 1H, H-5’’’, *J* = 5.2 Hz, *J* = 1.2 Hz), 7.60 (d, 1H, H-3’, *J* = 3.6 Hz), 7.68 (dd, 1H, H-3’’’, *J* = 3.6 Hz, *J* = 0.8 Hz), 7.87-7.92 (m, 2H, H-6, H-7), 8.46-8.52 (m, 2H, H-5, H-8) ppm. HRMS: m/z (EI) for $C_{26}H_{24}N_2S_3$; calcd 460.1102; found: 460.1103.

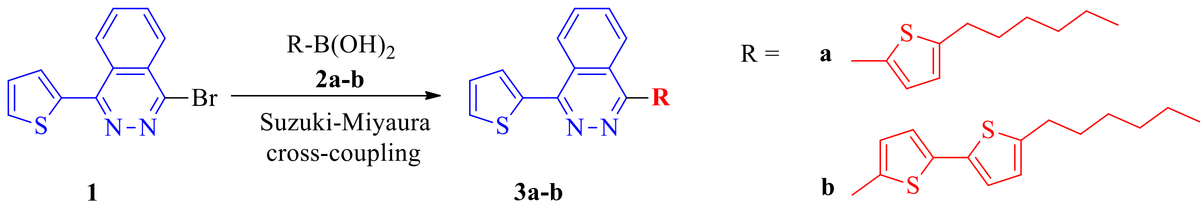
3. Results and Discussion

3.1. Synthesis

Two heterocyclic chromophores were designed and synthesized, having in mind further functionalization to prepare push-pull heterocyclic systems for several optical and photovoltaic applications. Both π-conjugated systems are based on an electron deficient phthalazine moiety as spacer, substituted with hexyl-(bi)thienyl groups.

The preparation of precursor 3-bromo-6-(thiophen-2-yl)phthalazine **1** has been previously reported by this research group elsewhere.[7] The final chromophores **3a-b** where obtained by Suzuki-Miyaura cross-coupling between precursor **1** and selected boronic acids **2** in fair yieds (19-26 %).

Heterocyclic chromophores **3** were characterized by standard spectroscopic techniques. The presence of two (**3a**) or four (**3b**) new aromatic protons in the ^1H NMR analysis is observed, due to the protons of the thiophene(s) ring(s) as well as a set of signals that are attributed to the aliphatic protons of the hexyl chain.



Scheme 1. Synthesis of 3-(thiophen-2-yl)phthalazine derivatives **3**: DME, $Pd(PPh_3)_4$, 5-hexyl-2-thiopheneboronic acid **2a** or 5’-hexyl-2,2’-bithiophene-5-boronic acid **2b**, EtOH, Na_2CO_3 (aq), N_2.

3.2. Optical Study

The optical absorption spectra of 3-(thiophen-2-yl)phthalazine derivatives **3** in ethanol solutions (10^{-4} M) show intense absorption bands at 360 and 398 nm for chromophores **3a** and **3b**, respectively. The results showed that the introduction of a second thiophene unit into the system induced a bathochromic shift of 38 nm that can be attributed to the increase of extension of the π-conjugated path length (Table 1, Figure 1).

Phthalazines **3** were excited at the wavelength of maxima absorption, at room temperature, in order to study their fluorescence properties (Table 1, Figure 1). The relative fluorescence quantum yields were determined using a solution of 9,10-diphenylanthracene in ethanol as fluorescence standard ($\Phi_F = 0.95$).[9] Chromophore **3a** exhibits weak emissive properties ($\Phi_F = 0.02$), while chromophore **3b** shows a higher relative quantum fluorescence yield (0.22). The bathochromic shift of 91 nm in the fluorescence spectra and the increase of the relative quantum fluorescence yield of chromophore **3b** compared to **3a** can be explain having in mind the functionalization of the heterocyclic system by an additional thiophene ring.[10]

Table 1. UV-visible absorption and emission data for thienyl-phthalazines **3**, in ethanol.

Cpds	UV-vis		Fluorescence		
	λ_{max} (nm)	ε ($M^{-1}cm^{-1}$)	λ_{em} (nm)	Φ_F	Stokes’ shift (nm)
3a	360	17,538	429	0.02	69
3b	398	20,045	520	0.22	122

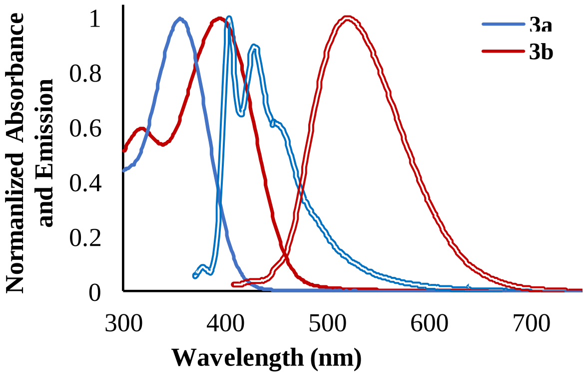


Figure 1. Normalized UV-visible absorption (full line) and emission (double line) data for thienyl-phthalazines **3a-b**, in ethanol.

4. Conclusions

Two novel thienyl-phthalazine derivatives functionalized with hexyl-(bi)thienyl moieties have been synthesized by Suzuki-Miyaura cross-coupling in fair yields.

The study of the optical properties of the prepared chromophores showed the effect caused by the introduction of a second thiophene into the conjugated system in the UV-vis absorption and emission properties: bathochromic shifts in the absorption and emission spectra, as well as increased relative quantum fluorescence yield.

Due to their optical properties, π-conjugated heterocyclic systems **3** are versatile precursors that could be used for the preparation of nonlinear optical (SHG, TPA), OLEDs and DSSCs materials.

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