Synthesis and characterization of four novel 1,3-azole based push-pull heterocyclic systems

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Abstract

Benz[X]azole derivatives are interesting compounds due to their diverse biological activities and interesting optical properties. The benzothiazole, benzimidazole and benzoxazole heterocycles are heteroaromatic electron deficient moieties that act as both acceptor groups and π-conjugated spacers with auxiliary electron withdrawing ability. Moreover, benzimidazole derivatives offers the possibility of substitution on the nitrogen atom for further tuning of their optical and electronic properties.

Recently we have reported the synthesis and evaluation of the electronic, thermal and optical properties of a large number of series of benz[X]azole derivatives functionalized with different π-spacers having in mind their application as optical chemosensors, nonlinear optical and photochromic materials, and emissive organic components for OLEDs.

In continuation of the work developed in our research group, we report in this work the synthesis, the characterization and the evaluation of the optical properties of four novel 1-(4-thiophene-2-yl)phenyl)-*1H*-pyrrole derivatives functionalized with different benz[X]azole moieties (benzothiazole, benzimidazole and benzoxazole). The results showed that the optical properties could be readily tuned by changing the electronic nature of the azole ring, or even by introduction of a strong acceptor group.

Keywords

benz[X]azole, thiophene and pyrrole π-spacers, push-pull heterocyclic systems,

1. Introduction

Push-pull π-conjugated systems are molecules end-capped with an electron donor group (D) and an electron acceptor group (A) interacting through a π-system. This molecular arrangement allows for intramolecular charge-transfer (ICT), which favors a new low energy molecular orbital, with electrons easily excited by visible light. Therefore, push-pull molecules are generally colored and referred to as charge-transfer chromophores. Organic CT chromophores are usually of easy synthesis, have well-defined and easily modified structures, and readily tunable properties, like HOMO and LUMO levels, position of the longest-wavelength absorption maxima, and dipole moment, by modification of the electron donor or acceptor moieties, alteration of the spacer, and by varying the overall chromophore arrangement. [1]

The heteroaromatic thiazole, imidazole, and oxazole moieties are electron deficient groups that act as both acceptor and π-conjugated spacers with auxiliary electron withdrawing ability. These moieties when fused with a phenyl ring (benzothiazole, benzimidazole, and benzoxazole) represent a way of extending the π-conjugation of the system.[2,3] Moreover, the imidazole moiety offers the possibility of substitution on the nitrogen atom for further tuning of their optical and electronic properties.

Benz[X]azole derivatives are interesting compounds due to their diverse biological activities[4] and interesting optical properties.[2]

Our research group has reported the synthesis and evaluation of the electronic, thermal and optical properties of several series of benz[X]azole derivatives functionalized with different π-spacers having in mind their application as optical chemosensors, nonlinear optical and photochromic materials, and emissive organic components for OLEDs.[2]

In this communication, and as an extension of the work developed by this research group, we report the synthesis, the characterization and the evaluation of the optical properties of four novel 1-(4-thiophene-2-yl)phenyl)-*1H*-pyrrole derivatives functionalized with different benz[X]azole moieties (benzothiazole, benzimidazole and benzoxazole).

2. Experimental

2.1. Methods and Materials

NMR spectra were obtained on a Brucker Avance III 400 at an operating frequency of 400 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. 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 (Φ_F = 0.95)[5] 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 5-(4-(*1H*-pyrrol-1-yl)phenyl)thiophene-2-carbaldehyde **1** was reported elsewhere.[6]

2.2. Synthesis

Procedure for the synthesis of benzothiazole derivative **2a**:

5-(4-(*1H*-Pyrrol-1-yl)phenyl)thiophene-2-carbaldehyde **1**[6] (1 equiv.) and *o*-aminobenzenethiol (1 equiv.) were heated in DMSO (1 mL/mmol) at 120ºC with stirring for 7 h. The reaction was followed by TLC. When the reaction was complete, the reaction mixture was allowed to cool, poured into water and extracted with ethyl acetate (3 x 50 mL). The organic layer was dried with magnesium sulphate and evaporated under reduced pressure. The crude residue was submitted to silica gel column chromatography using mixtures of diethyl ether and light petroleum of increasing polarity. The fractions containing the purified product were collected and evaporated under vacuum.

2-(5’-(4’’-(*1H*-Pyrrol-1’’’-yl)phenyl)thiophen-2’-yl)benzo[*d*]thiazole **2a**. Light brown solid (14 %). Mp: 205-207ºC. UV (ethanol): λ_{max} nm (ε, $M^{-1}cm^{-1}$) 373 (27,941). IR (liquid film) ν 3411, 3141, 1605, 1547, 1523, 1483, 1444, 1433, 1331, 1312, 1282, 1255, 1232, 1077, 1012, 962, 940, 917, 903, 820, 812, 759 cm^{-1}. ^{1}H NMR (DMSO-d_6, 400 MHz) δ 6.29 (t, 2H, H-3’’’, H-4’’’, *J* = 2.0 Hz), 7.45 (m, 3H, H-2’’’, H-5’’’, H-6), 7.51 (m, 1H, H-5), 7.67 (m, 3H, H-4’, H-2’’, H-6’’), 7.68 (m, 3H, H-3’, H-3’’, H-5’’), 7.99 (d, 1H, H-7, *J* = 8.0 Hz), 8.10 (d, 1H, H-4, *J* = 8.0 Hz) ppm.

General procedure for the synthesis of benzimidazole derivatives **2b-c**:

5-(4-(*1H*-Pyrrol-1-yl)phenyl)thiophene-2-carbaldehyde **1** (1 equiv.) and sodium bissulphite (1.3 equiv.) were stirred in ethanol (5mL) for 4 h at room temperature. *o*-Phenylenediamine or 4-nitro-*o*-phenylenediamine (1 equiv.) dissolved in DMF (5 mL) was added to the mixture and heated to 80 ºC for another 4 h. When the reaction was complete, the reaction mixture was allowed to cool, poured into water and extracted with ethyl acetate (3 x 50 mL). The organic layer was dried with magnesium sulphate and evaporated under reduced pressure. The crude residue was submitted to silica gel column chromatography using mixtures of diethyl ether and light petroleum of increasing polarity. The fractions containing the purified product were collected and evaporated under vacuum.

2-(5’-(4’’-(*1H*-Pyrrol-1’’’-yl)phenyl)thiophen-2’-yl)-1H-benzo[*d*]imidazole **2b**. Light brown solid (21 %). Mp: 224-226 ºC. UV (ethanol): λ_{max} nm (ε, $M^{-1}cm^{-1}$) 361 (29,757). IR (liquid film) ν 3362, 2358, 1889, 1646, 1603, 1571, 1533, 1501, 1480, 1455, 1407, 1333, 1244, 1212, 1085, 930, 827, 801, 763 cm^{-1}. ^{1}H NMR (DMSO-d_6, 400 MHz) δ 6.28 (t, 2H, H-3’’’, H-4’’’), 7.42 (t, 2H, H-2’’’, H-5’’’, *J* = 2.0 Hz), 7.64 (m, 4H, H-2’’, H-3’’, H-5’’, H-6’’), 7.79 (d, 2H, H-5, H-6, *J* = 9.6 Hz), 7.81 (d, 1H, H-4’, *J* = 5.6 Hz), 7.85 (d, 1H, H-3’, *J* = 5.6 Hz), 7.92 (d, 2H, H-4, H-7, *J* = 8.8 Hz), 13.0 (br s, 1H, NH) ppm.

2-(5’-(4’’-(*1H*-Pyrrol-1’’’-yl)phenyl)thiophen-2’-yl)-6-nitro-1*H*-benzo[*d*]imidazole **2c**. Light brown solid (23%). Mp: 173-175 ºC. UV (ethanol): λ_{max} nm (ε, $M^{-1}cm^{-1}$) 380 (22,675). IR (liquid film) ν 3438, 2358, 1889, 1646, 1603, 1571, 1533, 1501, 1480, 1455, 1407, 1333, 1244, 1212, 1085, 930, 827, 801, 763 cm^{-1}. ^{1}H NMR (DMSO-d_6, 400 MHz) δ 6.28 (t, 2H, H-3’’’, H-4’’’), 7.42 (t, 2H, H-2’’’, H-5’’’, *J* = 2.0 Hz), 7.65 (m, 4H, H-4, H-4’, H-3’’, H-5’’), 7.80 (d,

2H, H-2'', H-6'', *J* = 8.8 Hz), 7.90 (d, 1H, H-3', *J* = 4.0 Hz), 8.05 (dd, 1H, H-5, *J* = 8.0 Hz, *J* = 2.0 Hz), 8.40 (d, 1H, H-7, *J* = 2.4 Hz) ppm.

General procedure for the synthesis of benzoxazole derivative **2d**:

5-(4-(*1H*-Pyrrol-1-yl)phenyl)thiophene-2-carbaldehyde **1** (1 equiv.) and 2-amino-5-methylphenol (1.2 equiv) were refluxed in ethanol (5 mL) for 7 h. After evaporating the solvent, lead tetracetate (3 equiv) in DMSO (5mL) was added, and the mixture left stirring at room temperature. The reaction was followed by TLC. When the reaction was complete, the reaction mixture was allowed to cool, poured into water and extracted with ethyl acetate (3 x 50 mL). The organic layer was dried with magnesium sulphate and evaporated under reduced pressure. The crude residue was submitted to silica gel column chromatography using mixtures of diethyl ether and light petroleum of increasing polarity. The fractions containing the purified product were collected and evaporated under vacuum.

2-(5'-(4''-(*1H*-Pyrrol-1'''-yl)phenyl)thiophen-2'-yl)-6-methylbenzo[*d*]oxazole **2d**. Light brown solid (15 %). Mp: 205-207ºC. UV (ethanol): λ_{max} nm (ε, $M^{-1}cm^{-1}$) 360 (38,916). IR (liquid film) ν 3403, 3141, 2366, 1885, 1787, 1612, 1573, 1533, 1533, 1502, 1445, 1332, 1263, 1132, 1075, 997, 956, 937, 866, 807, 719 cm^{-1}. ^{1}H NMR (DMSO-d_6, 400 MHz) δ 2.48 (s, 3H, CH_3), 6.29 (t, 2H, H-3''', H-4'''), 7.20 (dd, 1H, H-5, *J* = 8.0 Hz, *J* = 0.8 Hz), 7.38 (t, 2H, H-2''', H-5''', *J* = 2.0 Hz), 7.52 (s, 1H, H-7), 7.59 (d, 1H, H-4, *J* = 8.0 Hz), 7.64 (m, 3H, H-4', H-3'', H-5''), 7.80 (d, 2H, H-2'', H6'', *J* = 8.4 Hz), 8.89 (d, 1H, H-3', *J* = 4.0 Hz) ppm.

3. Results and Discussion

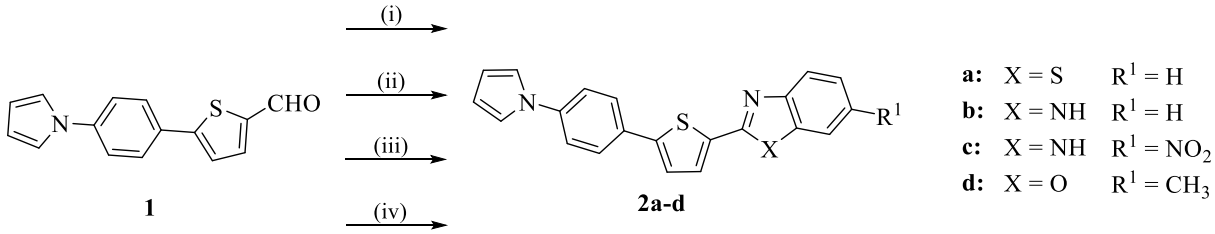
3.1. Synthesis

A series of heterocyclic chromophores were designed and synthesized in order to study the effect of different benz[X]azole acceptor moieties in their optical properties. All designed π-conjugated systems are based on a 1-(4-thiophene-2-yl)phenyl)-*1H*-pyrrole system which acts simultaneously as electron donor group and π-spacer.

The preparation of the aldehyde precursor **1** has been previously reports by our research group

elsewhere.[6] The final push-pull chromophores were achieved by cyclization between aldehyde **1** and the appropriate functionalized phenyl derivatives (Scheme 1) in fair yields (14-23 %).

The heterocyclic compounds **2** were characterized by standard spectroscopic techniques. The disappearance of the IV band and ^{1}H NMR signal corresponding to the -CHO group was observed, as well as the presence of new ^{1}H NMR signals attributed to the phenyl ring fused to the 1,3-azole heterocycle.



Scheme 1. Synthesis of 1-(4-thiophene-2-yl)phenyl)-*1H*-pyrrole derivatives **2**: (i) o-aminobenzenethiol, DMSO, 120 ºC; (ii) $NaHSO_3$, EtOH, r.t., *o*-phenylenediamine, DMF, 80 ºC; (iii) $NaHSO_3$, EtOH, r.t., 4-nitro-*o*-phenylenediamine, DMF, 80 ºC; (iv) 2-amino-5-methylphenol, EtOH, reflux, $Pb(CH_3COO)_4$, DMSO, r.t.

3.2. Optical Study

The electronic absorption spectra of benz[X]azoles **2** in ethanol solutions (10^{-4} M) show intense lowest energy charge-transfer absorption bands in the UV-visible region between 360-380 nm. The results showed that the position of these bands depends on the electronic nature of the heteroaromatic 1,3-azole linked to the thiophene heterocycle (Table 1, Figure 1).

The benzimidazole derivative **2c** exhibit the longer wavelength of maxima absorption (λ = 380 nm), indicating the stronger ICT, due to the additional electron withdrawing effect of the $–NO_2$ substituent, that is responsible for the bathochromic shift of 19 nm relative to the analogous benzimidazole **2b**. In this series of compounds the second longer wavelength of maxima absorption was found at λ = 373 nm for the benzothiazole derivative **2a**, that can be attributed to the bathochromic effect of the sulphur. The benzimidazole **2b** and the benzoxazole with a methyl substituent **2d**, show very similar ICT, exhibited by the maxima of the absorption bands at 361 and 360 nm, respectively.

Benz[X]azoles **2** 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 solution of 9,10-diphenylanthracene in ethanol as fluorescence standard (Φ_F = 0.95).[5] In general, the synthesized chromophores show strong emissive properties, with relative quantum fluorescence yields ranging from 0.68 to 0.92. Benzimidazole **2c** exhibited the lowest relative quantum fluorescence yield, at 0.21, that can be attributed to the existence of low-lying n→π* transitions due to the –NO_2 group.[7]

Table 1. UV-visible absorption and emission data for benz[X]azoles **2**, in ethanol.

Cpds	UV-vis		Fluorescence		
	λ_{max} (nm)	ε ($M^{-1}cm^{-1}$)	λ_{em} (nm)	Φ_F	Stokes' shift (nm)
2a	373	27,941	456	0.92	83
2b	361	29,757	430	0.86	69
2c	380	22,675	499	0.21	119
2d	360	38,916	443	0.68	83

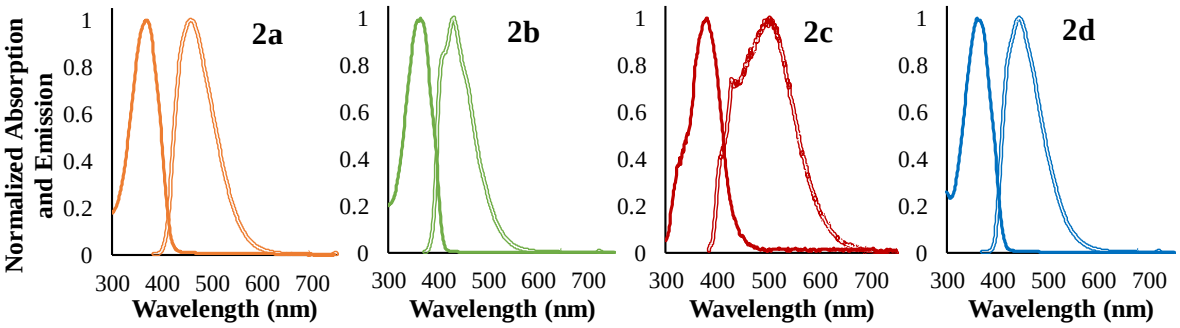


Figure 1. Normalized UV-visible absorption (full line) and emission (double line) data for benz[X]azoles **2a-d**, in ethanol.

4. Conclusions

Four novel 1-(4-thiophene-2-yl)phenyl-*1H*-pyrrole derivatives functionalized with different benz[X]azole moieties (benzothiazole, benzimidazole and benzoxazole) have been synthesized by cyclization between an aldehyde precursor and appropriate substituted phenyl derivatives, in fair yields.

A study of the optical properties of the prepared chromophores showed that the UV-vis absorption and emission properties could be readily tuned by changing the electronic nature of

the azole ring. It is noticeable bathochromic shifts in the benzothiazole derivative **2a** due to the presence of sulphur, and in benzimidazole **2c** when compared to chromophore **2b** due to the introduction of a strong acceptor group like $–NO_2$. The emission spectra followed the same trend as absorption. The prepared chromophores showed high relative quantum fluorescence yields (Φ_F = 0.68-0.92), the exception being chromophore **2c** (Φ_F = 0.21) due to functionalization of the benzimidazole ring with the $–NO_2$ group, which is a well-known quencher of fluorescence.

Due to their optical properties and push-pull character, π-conjugated heterocyclic systems **2** can have potential application as nonlinear optical second harmonic generators (SHG), two-photon absorption (TPA) fluorophores or luminescent organic components for OLEDs.

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