Synthesis and characterization of formyl-thienylpyridazines as versatile precursors for several optical applications

Sara S. M. Fernandes, M. Manuela M. Raposo

Centre of Chemistry, University of Minho, Campus de Gualtar, 4710-057, Braga, Portugal

email: mfox@quimica.uminho.pt

Abstract: Novel thienylpyridazines **3**-**4** functionalized with the formyl group on the aryl or heteroaryl moieties were synthesized through Suzuki coupling of bromo-thienylpyridazine **2** with commercially available (hetero)aryl-boronic acids. On the other hand precursor **2** was prepared by reaction of thienylpyridazinone **1** with $POBr_3$. The new heterocyclic systems **3**-**4** were characterised by the usual spectroscopic techniques. In the future, these versatile formyl precursors will be further functionalized and characterized in order to evaluate their potential application as novel NLO-chromophores or as dyes sensitizers for DSSCs.

Keywords: Suzuki coupling, Heterocyclic aldehydes, Pyridazine, π-conjugated systems, Nonlinear optical (NLO) precursors, Dye-sensitized solar cells (DSSC)

1. Introduction

Formyl heterocyclic compounds are versatile “crossroads” intermediates. Not surprisingly, a large number of methods have been developed in order to obtain these functionalized heterocycles. Vilsmeier formylation, Vilsmeier-Haack-Arnold reaction, metalation followed by quenching with DMF as well as palladium catalyzed cross coupling reactions (Stille, Suzuki) constitute the most important routes for the preparation of formyl-substituted thiophenes, pyrroles and furans [1].

Dipolar chromophores are currently of great interest because of their applicability to optical and photovoltaic devices such as nonlinear optics (NLO) and dye-sensitized solar cells (DSSCs), and their potential for improving has only been partially realized. The electronic arrangement in this type of molecules (electron donor and electron acceptor groups linked through a π-conjugated bridge) assures efficient intramolecular charge transfer and generates a dipolar push-pull system featuring low energy and intense charge transfer absorption. The push-pull system can be improved by modification of the electron donor, electron acceptor, or/and the π-bridge of the molecule. However, despite intensive theoretical and experimental activity it remains at present unclear what the right strategy will be to optimize their properties because there is very little information concerning the relation between molecular structure and effective material properties. Recent approaches to the design of these compounds are based on the presence of a five-membered heterocyclic ring in a push-pull donor-acceptor chromophore. Another approach currently explored in modulating the π-bridge is to use an electron rich and/or electron poor aromatic ring that can act as an auxiliary electron donor/acceptor group [2].

Electron-rich thiophene and furan heterocycles linked to the electron-deficient pyridazine ring substituted with appropriate acceptor groups are promising candidates among such push-pull systems. Having in mind these facts and also our recent work, in which we have used formyl heterocyclic systems (oligothiophenes, arylthiophenes, thienylpyrroles, arylfurans and thienylfurans) [1] as precursors for the synthesis of more complex molecules (dicyanovinyl- and thiobarbituric derivatives, benzothiazoles, (benz)imidazoles, benzoxazoles, BODIPYs, Schiff-bases, imidazo-crown ethers, thiosemicarbazones etc. for several optoelectronic (OLEDs, SHG, TPA) and sensors applications [3], we decided to synthesize the new formyl-thienylpyridazines **3**-**4** in order to study the influence of the electronic nature of the (hetero)aryl group linked to the diazine moiety on the optical properties (UV-visible) of compounds **3-4**. Moreover, compounds **3-4** will be used in the future as versatile synthons in the preparation of a large

variety of heterocyclic donor-acceptor π-conjugated systems for several applications such as nonlinear optics and DSSCs.

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 shifts, 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. All melting points were measured on a Gallenkamp melting point apparatus and are uncorrected.

2.2. Materials

Phosphorous (V) oxybromide and boronic acids were purchased from Aldrich, Acros Organics and Fluka and used as received. TLC analyses were carried out on 0.25 mm thick precoated silica plates (Merck Fertigplatten Kieselgel 60F_{254}) and spots were visualized under UV light. Chromatography on silica gel was carried out on Merck Kieselgel (200-300 mesh).

2.3. Synthesis

Procedure for the synthesis of 3-bromo-6-(thiophen-2-yl)pyridazine **2**: A mixture of 6-(thiophen-2-yl)pyridazin-3(2H)-one **1** (2.8 mmol, 0.5 g) and $POBr_3$ (5.5 mmol, 1.6g) was heated for 6 h at 110-120 ºC. This mixture was cooled till room temperature and then poured onto ice-water, basified with a solution of ammonia (2 M) and stirred for 30 min. to give a brown solid which was filtered and washed with water and light petroleum to give the pure thienylpyridazine **2** as brown solid (76%). ^{1}H NMR (Acetone-d_6, 400MHz) δ 7.26 (dd, 1H, H-4', J=5.2 Hz, J= 3.6 Hz), 7.76 (dd, 1H, H-5', J= 5.2Hz, J= 1.2Hz), 7.94 (dd, 1H, H-3', J= 3.6Hz, J= 1.2Hz), 7.96 (d, 2H, H-5, J= 9.2 Hz), 8.14 (d, 1H, H-4, J= 9.2 Hz) ppm.

General procedure for the synthesis of aldehydes **3**-**4** through Suzuki coupling: 3-Bromo-6-(thiophen-2-yl)pyridazine **2** (0.5 mmol) was coupled to boronic acids (0.6 mmol) in a mixture of DME (6 mL), aqueous 2 M Na_2CO_3 (1 mL) and $Pd(PPh_3)_4$ (5%) at 80°C under nitrogen. The reactions were monitored by TLC which determined the different reaction times (24-48 h). The mixture was cooled to room temperature, and neutralized with a saturated solution of sodium acetate. The organic layer was extracted with chloroform, dried with anhydrous $MgSO_4$ and the solvent was evaporated under reduced pressure. The product was purified by column chromatography on silica gel with increasing amounts of dichloromethane in light petroleum as solvent. The solvent was evaporated to give the coupled products as solids. Recrystallization from dichloromethane/hexane gave the pure compounds **3**-**4**.

4-(6'-(Thiophen-2''-yl)pyridazin-3'-yl)benzaldehyde **3**. Yellow solid (15%). Mp: 214-216ºC. UV (chloroform): λ_{max} nm (ε, $M^{-1}cm^{-1}$) 332 (25990). IR ν 1639 (CO) cm^{-1}. ^{1}H NMR (Acetone-d_6, 400MHz) δ 7.29 (dd, 1H, H-4'', J=5.2 Hz, J=3.6 Hz), 7.77 (dd, 1H, H-5'', J=4.8 Hz, J=1.2 Hz), 7.99 (dd, 1H, H-3'', J=3.6 Hz, J=1.2 Hz), 8.14 (d, 2H, H-2 and H-6, J=8.4 Hz), 8.30 (d, 1H, H-4', J=9.2 Hz), 8.35 (d, 1H, H-5', J=8.8 Hz), 8.48 (d, 2H, H-3 and H-5, J=8.4 Hz), 10.19 (s, 1H, CHO) ppm. ^{13}C NMR (Acetone-d_6, 400MHz) δ 123.63, 125.78, 128.06, 128.19, 129.20, 130.62, 130.80, 138.32 141.56, 142.56, 155.14, 157.20, 192.65 ppm.

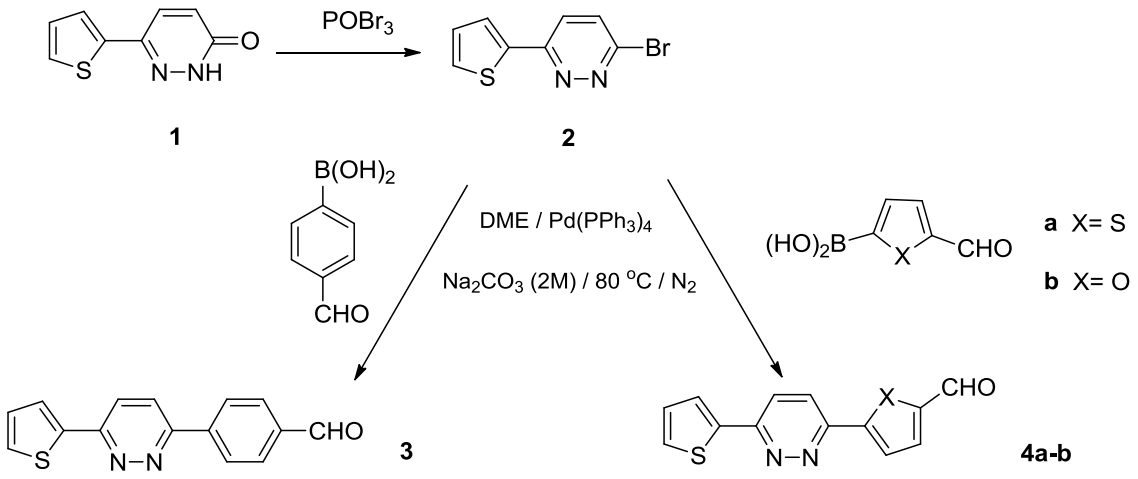
5-(6'-Thiophen-2''-yl)pyridazin-3'-yl)thiophene-2-carbaldehyde **4a**. Light brown solid (28%). Mp: 247-250ºC. UV (chloroform): λ_{max} nm (ε, $M^{-1}cm^{-1}$) 357, (29790). IR ν 1657 (CO) cm^{-1}. ^{1}H NMR (Acetone-d_6, 400 MHz) δ 7.28 (dd, 1H, H-4'', J=5.2 Hz, J=3.6 Hz), 7.77 (dd, 1H, H-5'', J=5.2Hz, J=1.2 Hz), 7.98 (dd, 1H, H-3'', J=3.6 Hz, J=1.2Hz), 8.08 (d, 2H, H-3 and H-4, J=0.8 Hz), 8.27 (d, 1H, H-5', J=9.2Hz), 8.33 (d, 1H, H-4', J=9.2 Hz), 10.06 (s, 1H, CHO) ppm. ^{13}C NMR (Acetone-d_6, 400MHz) δ 123.61, 124.54, 128.06, 128.24, 129.24, 130.86, 138.29, 141.43, 146.25, 150.04, 153.59, 155.49, 184.50 ppm.

5-(6'-(Thiophen-2''-yl)pyridazin-3'-yl)furan-2-carbaldehyde **4b.** Yellow solid (14%). Mp: 207-210ºC. UV (chloroform): λ_{max} nm (ε, $M^{-1}cm^{-1}$) 354 (27790). IR ν 1664 (CO) cm^{-1}. ^{1}H NMR (Acetone-d_6, 400 MHz) δ 7.29 (dd, 1H, H-4'', J=4.9 Hz, J=3.6 Hz), 7.58 (d, 1H, H-4, J=3.9 Hz), 7.68 (d, 1H, H-3, J=3.9 Hz), 7.78 (dd, 1H, H-5'', J=4.9 Hz, J=0.9 Hz), 8.00 (dd, 1H, H-3'', J=3.6 Hz, J=1.2Hz), 8.18 (d, 1H, H-4', J=8.7 Hz), 8.31 (d, 1H, H-5', J=9.3 Hz), 9.81 (s, 1H, CHO) ppm. ^{13}C NMR (Acetone-d_6, 400MHz) δ 112.41, 123.49, 124.21, 128.31, 129.30, 130.93, 141.42, 150.56, 154.47, 155.23, 156.27, 178.57 ppm.

3. Results and Discussion

3.1. Synthesis

The precursor pyridazinone **1** was synthesized by condensation of methyl 4-oxo-4-(thiophen-2yl)butanoate with hydrazine hydrate in ethanol. On the other hand the bromo-thienylpyridazine **2** was prepared by reaction of thienylpyridazinone **1** with $POBr_3$. Formyl derivatives **3**-**4** were synthesized by Suzuki cross-coupling reaction of 3-bromo-6-(thiophen-2-yl)pyridazine **2** with commercially available (hetero)aryl-boronic acids in fair yields (14-28%) (Table 1, Scheme 1). The new heterocyclic systems **3**-**4** were characterised by the usual spectroscopic techniques.



Scheme 1. Synthesis of bromo-thienylpyridazine **2** and formyl-thienylpyridazines **3**-**4**.

Table 1. Yields, UV-visible, IR and ^{1}H NMR data of formyl-thienylpyridazines **3**-**4**.

Compound	Yield (%)	Reaction time (h)	λ_{max} (nm) [(a)]	ε ($M^{-1}cm^{-1}$) [(a)]	IR υ_{CHO} (cm^{-1})	δ_{CHO} (ppm) [(b)]
3	15	24	332	25,990	1639	10.19
4a	28	48	357	29,790	1657	10.06
4b	14	45	354	27,790	1664	9.81

(a) All the UV-visible spectra were run in chloroform.

(b) For the CHO proton of formyl-thienylpyridazines **3**-**4** (Acetone-d_6, 400 MHz).

3.2. UV-Visible study

The electronic spectra of formyl-thienylpyridazine **3-4**, recorded in chloroform solutions (10^{-4} M) showed an intense lowest energy charge-transfer absorption band in the UV-visible region. The position of this band depended on the electronic nature of the of the aryl or (hetero)aryl group linked at position 3 of the pyridazine moiety (Table, Figure 1). A bathochromic shift (22-25 nm) is observed upon substitution of the aryl group (**3**) with five-membered heterocycles (**4**). This observation confirms previously obtained results [1b, 1e, 1g, 2g] showing that the incorporation of thiophene or furan heterocycles in push-pull compounds enhances their charge-transfer properties, which can be explained considering the bathochromic effect of sulphur (**4a**), and the partial decrease of aromatic character (**4a-b**).

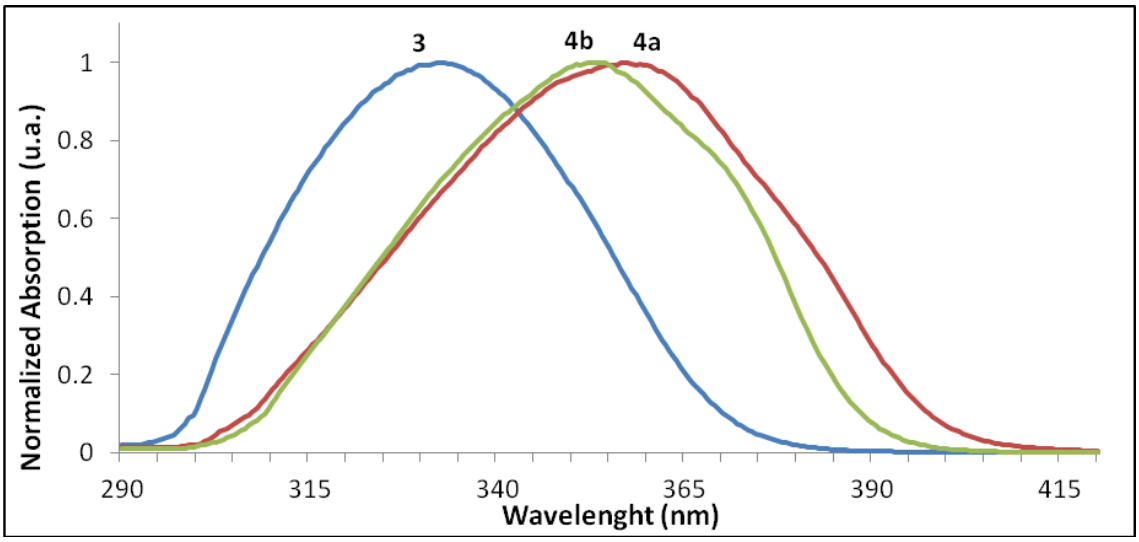


Figure 1. UV-visible spectra of thienylphthalazines **3** and **4a**-**b** recorded in chloroform.

4. Conclusions

Three novel formyl-thienylpyridazines **3**-**4** were synthesized in moderate yields through Suzuki coupling. Compounds **3-4** exhibit an absorption band in the UV-visible range influenced by electronic nature of the aryl or heteroaryl group substituted on the thienyl-pyridazine conjugated bridge. Due to their structure and optical properties the synthesized thienylpyridazines **3-4** will be used in the future, as precursors in the preparation of push-pull systems which should exhibit interesting NLO properties and/or DSSCs applications.

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