Synthesis of new fluorescent 2-(2', 2''-bithienyl)-1,3-benzothiazoles

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Abstract - Bithienyl-1,3-benzothiazole derivatives were synthesised by reacting various 5-formyl-5'-alkoxy- or 5-formyl-5'-*N,N*-dialkylamino-2,2'-bithiophenes with *ortho*-aminobenzenethiol in good to excellent yields. Evaluation of the fluorescence properties of these compounds was carried out. They show strong fluorescence in the 450-600 nm region, as well as high quantum yields and large Stokes' shifts.

Keywords: fluorescence, solvatochromism, 5-formyl-5'-alkoxy-2,2'-bithiophenes, 5-formyl-5'-*N,N*-dialkylamino-2,2'-bithiophenes, 1,3-benzothiazoles, 2-(2',2''-bithienyl)-1,3-benzothiazoles

Fluorescent compounds have found widespread use in scientific and industrial areas, for example as fluorescent brightening agents for textiles, plastics, inks and paints, tuneable dye lasers and biological stains. Other applications include electroluminescent and liquid crystals displays, solar collectors, materials science and optoelectronics. The benzothiazole nucleus appears in many fluorescent compounds that have useful applications as a result of the ease of synthesis of this heterocycle and the high fluorescence quantum yields obtained when this small, rigid moiety is present in compounds.[1]

Thiophenes and oligothiophenes substituted by donor/acceptor groups have been extensively investigated. These compounds are often used as energy transfer and light-harvesting systems and for optical and electronic devices.[2-4] Thiophene and

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oligothiophene derivatives are also characterised by important electroluminescent properties. Due to their strong fluorescence, these compounds have also found application as fluorescent markers.[5-11] In this communication we wish to report the synthesis of the new fluorescent bithienyl-1,3-benzothiazole derivatives **1** from 5-formyl-5'-alkoxy- or 5-formyl-5'-*N,N*-dialkylamino-2,2'-bithiophenes **2** with *o*-aminobenzenethiol. As far as we know, this is the first time that the synthesis and evaluation of the fluorescence properties of 2-(2', 2''-bithienyl)-1,3-benzothiazole derivatives has been reported.

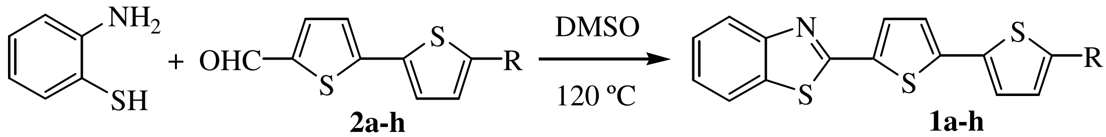
In recent years we have been interested in the synthesis and study of the fluorescence properties of a series of heterocyclic compounds of the benzothiazole type, substituted with several groups such as indolyl, carbazolyl, coumaryl and thienyl.[12-14] The most promising results were obtained for the 2-(2'-thienyl)-1,3-benzothiazoles,[12] substituted at position 5' with electron donating groups, and these findings prompted us to evaluate the bithiophene moiety, with various groups such as alkoxy- or *N,N*-dialkylamino.

Our recently reported synthesis of 5-formyl-5'-alkoxy- and 5-formyl-5'-*N,N*-dialkylamino-2,2'-bithiophenes **2** made these compounds available in reasonable amounts, ready for further applications.[15] Indeed, we were able to use these compounds with success as substrates for the synthesis of 1,3-benzothiazole derivatives **1a-h**. Therefore the synthesis, UV/Vis and fluorescence properties of a series of heterocyclic fluorophores of the benzothiazole type containing a bithienyl moiety have been investigated.

The benzothiazole moiety was obtained by the simple reaction of *o*-aminobenzenethiol with 5-formyl-substituted bithiophenes **2a-h**, in DMSO at 120 ºC for 30-60 min (Scheme 1). Purification of the crude products by column chromatography gave the pure benzothiazoles **1a-h** in good to excellent yields (56-96%), (Table 1).

The reaction is initiated by the formation of the corresponding imine that cyclises spontaneously, yielding the benzothiazoline, which is oxidised to the benzothiazole, aided by the oxidising character of DMSO.

Scheme 1



a R= H
b R= OMe,
c R= OEt
d R= NMe_2
e R= NEt_2
f R= N(Pr-*i*)$_2$
g R= piperidino
h R= morpholino

The UV/Vis absorption and fluorescence spectra of 3 x 10^{-6} M solutions of compounds **1a-h** were measured, excitation and emission maxima and fluorescence quantum yields are also reported (Table 1).

Table 1. Yields, UV/Vis and fluorescence data for compounds **1a-h**.

Compound	**R**	**Yield (%)**	**UV/Vis*** λ_{max} **[nm]**	**log ε**	**Fluorescence*** λ_{em} **[nm]**	ϕ	**Stokes'shift [nm]**
1a	H	92	378	4.55	454	0.25	76
1b	OMe	96	390	4.43	498	0.58	108
1c	OEt	94	391	4.50	500	0.56	109
1d	NMe_2	65	440	4.19	587	0.48	147
1e	NEt_2	56	455	4.20	587	0.46	132
1f	N(Pr-*i*)$_2$	59	452	4.12	588	0.41	136
1g	piperidino	81	432	4.31	593	0.52	161
1h	morpholino	65	420	4.29	582	0.48	162

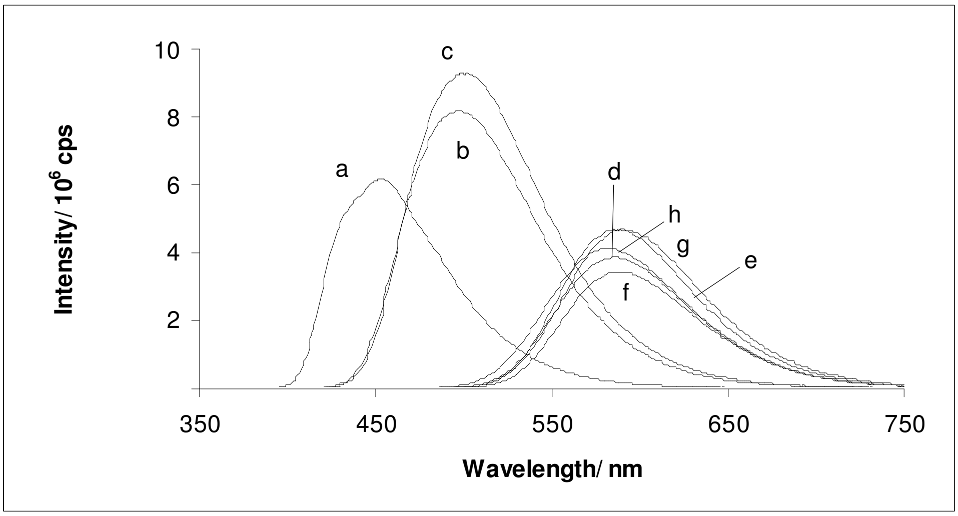
* Spectra were run in degassed absolute ethanol.

Absorption spectra were run in 13 different solvents, in order to perform a solvatochromic study (Table 2), and emission spectra of compounds **1a-h** were run in degassed absolute ethanol, using 9,10-diphenylanthracene as standard (ϕ = 0.95 in ethanol). The higher electron-donating character of *N,N*-dialkylamino groups leads to a bathochromic shift in both the absorption and emission maxima, as the longest wavelength transition is shifted from 378 nm for **1a** to 455 nm for **1e** (absorption) and from 454 nm for **1a** to 593 nm for **1g** (emission).

All the compounds exhibit high levels of fluorescence, especially **1b** and **1c** (ϕ = 0.58 and 0.56, respectively) and show large Stokes' shift (the lowest being 76 nm for **1a** and the highest 162 nm for **1h**). This shift to longer wavelength (lower energy) of the emission relative to the absorption is caused by energy losses due to dissipation of vibrational energy during the decay and is influenced by interactions between the fluorophore and the solvent molecules, such as the altered dipole moment of the fluorophore in the excited state, the reorientation of solvent molecules around the excited state dipole, hydrogen bonding and formation of charge complexes. With regard to compounds **1a-h**, there seems to be a relationship between the substituent group, its electron-donating character and the magnitude of the Stokes' shift, as *N,N*- dialkylamino groups show larger Stokes' shift (132-162 nm) in comparison with alkoxy groups (108-109 nm) and the unsubstituted bitiophene moiety (76 nm).

In Fig. 1, the various emission spectra for **1a-h** are compared, showing that the nature of the substituent group on the bithienyl moiety influences the fluorescence quantum yield, as well as the wavelength of maximum emission. Due to their strong fluorescence, the new 2-(2', 2''-bithienyl)-1,3-benzothiazoles **1** described above could find application as fluorescent markers.

Figure 1. Emission spectra for compounds **1a-h**.



Solvatochromism is easily quantified by UV/Vis spectroscopy and is particularly suitable for the empirical determination of the polarity of a solvent on a molecular-microscopic level. To evaluate the intermolecular forces between the solvents and the solute molecules we measured the absorption spectra of compounds **1a-h** in 13 solvents of different solvatation character. The wavelength maxima λ_{max} and wavenumber maxima ν_{max} of compounds **1a-h** are listed in Table 2 and compared with the π^* values for each solvent determined by Kamlet and Taft.[16]

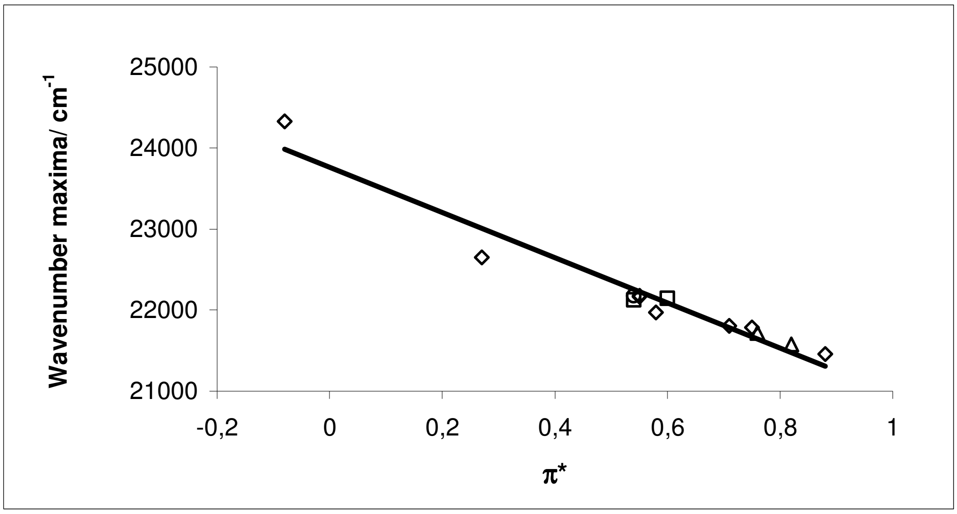
Table 2. UV/Vis absorption maxima of compounds **1a-h** in various solvents in comparison with π^* values by Kamlet and Taft.[16]

Solvent	π*	1a		1b		1c		1d		1e		1f		1g		1h	
		λ_{max} [nm]	υ_{max} [cm^{-1}]	λ_{max} [nm]	υ_{max} [cm^{-1}]	λ_{max} [nm]	υ_{max} [cm^{-1}]	λ_{max} [nm]	υ_{max} [cm^{-1}]	λ_{max} [nm]	υ_{max} [cm^{-1}]	λ_{max} [nm]	υ_{max} [cm^{-1}]	λ_{max} [nm]	υ_{max} [cm^{-1}]	λ_{max} [nm]	υ_{max} [cm^{-1}]
n-hexane	-0.08	370.8	26969	386.4	25880	388.0	25773	425.0	23529	437.8	22841	411.0	24331	420.2	23798	391.4	25549
diethyl ether	0.27	373.0	26810	389.2	25694	388.4	25747	433.0	23095	445.4	22452	441.5	22650	425.4	23507	407.4	24546
ethanol	0.54	378.0	26455	390.0	25641	391.0	25641	440.0	22727	455.0	21978	452.0	22124	432.0	23148	420.0	23810
toluene	0.54	378.6	26413	394.8	25329	395.4	25291	443.0	22573	452.5	22099	451.0	22173	435.5	22962	415.0	24096
dioxane	0.55	376.2	26582	393.8	25394	393.6	25407	439.0	22779	451.5	22148	451.0	22173	433.5	23068	411.0	24331
ethyl acetate	0.55	375.6	26624	390.6	25602	390.8	25589	439.8	22738	451.2	22163	451.2	22163	433.2	23084	410.0	24390
tetrahydrofuran	0.58	377.6	26483	393.6	25407	394.0	25381	443.6	22543	456.8	21891	455.2	21968	437.4	22862	414.8	24108
methanol	0.60	374.2	26724	391.0	25575	393.0	25445	436.4	22915	460.4	21720	451.6	22143	431.4	23180	408.4	24486
acetone	0.71	375.8	26610	391.4	25549	392.8	25458	443.4	22553	456.8	21891	458.6	21805	435.8	22946	413.4	24190
acetonitrile	0.75	373.5	26774	389.0	25707	391.6	25366	441.5	22650	456.5	21906	459.0	21786	437.5	22857	412.5	24242
chloroform	0.76	377.5	26490	393.5	25413	398.0	25126	444.0	22523	459.0	21786	460.5	21716	438.5	22805	416.0	24038
dichloromethane	0.82	377.5	26490	392.0	25510	395.5	25284	446.5	22396	461.0	21692	463.5	21575	440.0	22727	417.5	23952
DMF	0.88	378.8	26399	398.2	25113	396.4	25227	451.0	22173	464.0	21552	466.0	21459	442.2	22614	418.2	23912

For all compounds the highest energy transitions are found with *n*-hexane, a nonpolar solvent, and more polar solvents such as DMF result in lower energy transitions, thus indicating a positive solvatochromic response (between $\Delta\nu_{max}$= 570 cm^{-1} for **1a** and $\Delta\nu_{max}$= 2872 cm^{-1} for **1f**) that is related to a greater stabilization of the excited state relative to the ground state with increasing polarity of the solvent.

All compounds show good correlation between wavenumber maxima and π^* values for the 13 solvents tested. Due to the evident solvatochromism and the good correlation with π^* values (r = 0.9704), compound **1f** could be used as a solvent polarity indicator dye (Figure 2).

Figure 2. Correlation between absorption wavenumbers ν_{max} and the π^* scale according to Kamlet and Taft for compound **1f**. Solvents: apolar and polar aprotic (◊), protic (□), chlorinated (Δ) and aromatic (○).



All the compounds synthesized show good stability in the solid state and in solution.

The new compounds **1a-h** were characterised by elemental analysis or high resolution mass spectrometry, ^{1}H and ^{13}C NMR spectroscopy and UV/Vis spectroscopy. The synthesis of formyl bithiophenes **2a-g** has been described elsewhere.[15]

Method for the syntheses of 1a-h (described for 1b)

5-Formyl-5'-methoxy-2,2'-bithiophene **2b** (30 mg, 0.13 mmol) and *o*-aminobenzenethiol (0.014 ml, 0.13 mmol) were heated in DMSO (2 ml) at 120 ºC with stirring for 30-60 min. The reaction was followed by TLC using chloroform/hexane 1:1 as eluent. When the reaction was complete, the reaction mixture was allowed to cool and poured into water and extracted with ethyl acetate. The organic layer was dried with magnesium sulphate and evaporated under vacuum. The crude residue was submitted to silica gel column chromatography using mixtures of hexane and chloroform of increasing polarity. The fractions containing the purified product were collected and evaporated.

2-(5''-Methoxy-2',2''-bithienyl)-1,3-benzothiazole **1b**. Greenish-yellow solid (96%). Mp. 135-137 ºC. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.94 (s, 3H, OCH_3), 6.18 (d, 1H, *J*=4 Hz, 4''-H), 6.96 (d, 1H, *J*=4 Hz, 3''-H), 7.01 (d, 1H, *J*=4 Hz, 3'-H), 7.36 (dt, 1H, *J*=7 and 1.2 Hz, 5-H), 7.47 (dt, 1H, *J*=7 and 1.2 Hz, 6-H), 7.51 (d, 1H, *J*=4 Hz, 4'-H), 7.84 (dd, 1H, *J*=7 and 1.2 Hz, 7-H), 8.00 (dd, 1H, *J*=7 and 1.2 Hz, 4-H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 60.31 (OCH_3), 104.75 (4''-C), 121.39 (7-C), 122.53 (3'-C), 122.74 (4-C), 122.85 (2''-C and 3''-C), 125.06 (5-C), 126.42 (6-C), 129.28 (4'-C), 134.06 (2-C), 134.54 (4a-C), 142.09 (2'-C), 153.67 (7a-C), 161.05 (5'-C), 166.68 (5''-C). HRMS: *m/z* (EI) for: $C_{16}H_{11}NOS_3$; calcd: 329.0003; found: 329.0008.

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