Synthesis and photophysical characterization of novel tri-(hetero)arylimidazoles

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Abstract: A series of new tri-(hetero)arylimidazoles **2a-d** were synthesized in moderate to excellent yields by condensation of diphenylethanedione with heterocyclic aldehydes **1a-d** in the presence of ammonium acetate in glacial acetic acid. The photophysical properties were evaluated by UV-vis absorption and fluorescence spectroscopy and revealed that the novel tri-(hetero)arylimidazoles **2** are highly emissive with Stokes' shifts in the range 66-90 nm.

Keywords*:* Imidazole; Furan; Thiophene; Five-membered heterocycles; Fluorescence.

1. Introduction

The imidazole nucleus is of great importance in medicinal chemistry because it plays an important role in biochemical processes as structural component of several biomolecules (for example, histidine, vitamin B_{12}, nucleotides, histamine and biotin), and also has various pharmacological activities (anti-HIV, anti-convulsing, calcium antagonist, inhibitors of thromboxane A_2 synthase, antihistaminic, anti-parkinsonism and MAO inhibitor).[1]

Besides their application in medicinal chemistry, 2,4,5-tri(hetero)aryl-imidazoles are also a versatile class of compounds in materials chemistry due to their optoelectronic properties. They have been recognized as suitable chromophores for two-photon absorption applications, including photonic and optoelectronic areas such as fluorescence probes for imaging, two-photon fluorescence microscopy, high density storage and 3D microfabrication.[2] Earlier studies reported by us showed that the optical and thermal properties of these derivatives could be tuned by substitution of aryl groups at positions 2, 4 and 5 by five-membered heterocycles giving rise to innovative applications of these π-conjugated systems in nonlinear optics (*e.g.* second harmonic generators (SHG)), chemosensors, OLEDs and DNA intercalators.[3]

In this communication, we describe the synthesis of new 2,4,5-tri-(hetero)arylimidazoles, functionalized with different heterocycles, namely furan and thiophene, to evaluate the photophysical properties of the resulting compounds. These heterocycles were chosen due to their interesting photophysical properties which were reported earlier by us.[3]

2. Experimental

2.1. General procedure for the synthesis of compounds 2a-d

The heterocyclic aldehyde **1** (1 mmol), diphenylethanedione (1mmol) and NH_4OAc (20 mmol) were dissolved in glacial acetic acid (5 mL), followed by stirring and heating at reflux for 8 h. The mixture was then cooled to room temperature, ethyl acetate was added (15 mL) and washed with water (3 x 10 mL). After drying with anhydrous $MgSO_4$, the solution was filtered and the solvent was evaporated to dryness. The resulting solid was dissolved in acetone and precipitation with petroleum ether afforded the pure compound.

4,5-Diphenyl-2-(4-(thiophen-2’-yl)phenyl)-1*H*-imidazole 2a was obtained as a white solid (55 mg, 74%). Mp 234.3-235.8 ºC. UV-vis (ethanol): λ_{max} nm (log ε) 342 (4.50). ^{1}H NMR (DMSO-d_6, 300 MHz): δ = 7.15-7.6 (m, 13H), 7.77 (d, J = 8.7 Hz, 2H), 8.1 (d, J = 8.1 Hz, 2H), 12.7 (s, 1H) ppm. IR (KBr): ν = 3411, 3062, 2868, 2791, 1806, 1603, 1488, 1436, 1385, 1261, 1205, 1128, 1071, 969, 695 cm^{-1}.

4,5-Diphenyl-2-(4-(furan-2’-yl)phenyl)-1*H*-imidazole 2b was obtained as a white solid (116 mg, 79%). Mp 270.8-271.6 ºC. UV-vis (ethanol): λ_{max} nm (log ε) 334 (4.90). ^{1}H NMR (DMSO-d_6, 300 MHz): δ = 6.62 (dd, J = 3.2 and 1.6 Hz, 1H), 7.02 (d, J = 3.6 Hz, 1H), 7.52-7.54 (m, 10H), 7.77 – 7.81 (m, 3H), 8.13 (d, J = 8.8 Hz, 2H), 12.73 (s, 1H) ppm. IR (KBr): ν = 3419, 2097, 1641, 1449, 969, 840, 742, 697 cm^{-1}.

4,5-Diphenyl-2-(5-(furan-2’-yl)thiophen-2-yl)-1*H*-imidazole 2c was obtained as a dark brown solid (61 mg, 49%). Mp 267.2-268.1 ºC. UV-vis (ethanol): λ_{max} nm (log ε) 354 (4.40). ^{1}H NMR (DMSO-d_6, 400 MHz): δ = 6.90 (d, J = 3.6 Hz, 1H), 7.04 (d, J = 3.6 Hz, 1H), 7.14-7.16 (m, 1H), 7.20-7.53 (m, 11H), 7.57 (dd, J = 4.8 and 1.2 Hz, 1H), 12.80 (s, 1H) ppm. IR (KBr): ν = 3025, 2771, 1602, 1584, 1499, 1486, 1450, 1423, 1400, 1363, 1199, 1152, 1073, 998, 765, 696 cm^{-1}.

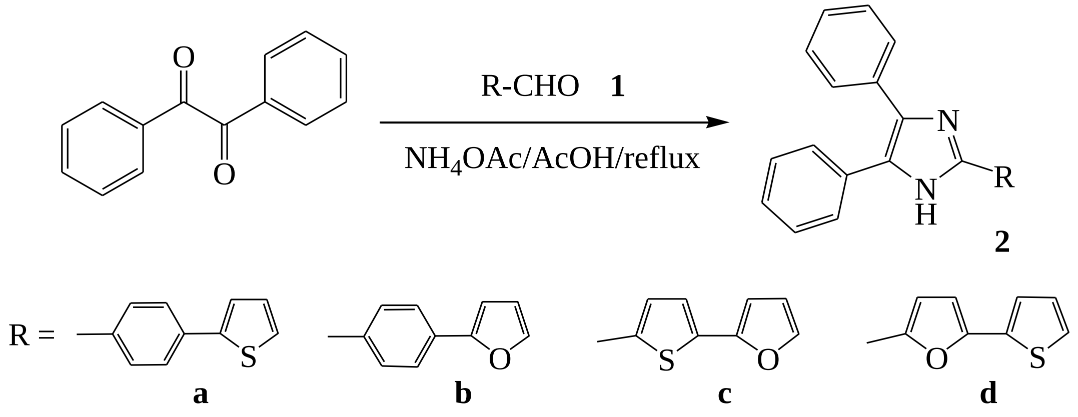
4,5-Diphenyl-2-(5-(thiophen-2’-yl)furan-2-yl)-1*H*-imidazole 2d was obtained as a brown solid (105 mg, 84%). Mp 284.2-284.8 ºC. UV-vis (ethanol): λ_{max} nm (log ε) 365 (4.45). ^{1}H NMR (DMSO-d_6, 400 MHz): δ = 6.60-6.62 (m, 1H), 6.82 (d, J = 3.2 Hz, 1H), 7.22-7.52 (m, 11H), 7.63 (d, J = 4.0 Hz, 1H), 7.74 (dd, J = 1.6 and 0.4 Hz, 1H), 12.85 (s, 1H, NH) ppm. IR (KBr): ν = 3429, 3057, 2968, 2860, 2744, 1951, 1899, 1756, 1592, 1592, 1486, 1447, 1414, 1250, 1197, 1107, 1072, 1014, 766, 696 cm^{-1}.

3. Results and discussion

3.1. Synthesis and characterization

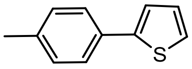
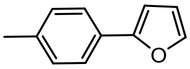
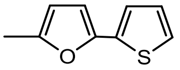
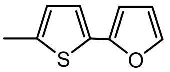
The new imidazoles **2a-d** were synthesized in moderate to good yields (49-84%), by condensation of heterocyclic aldehydes **1** with diphenylethanedione in glacial acetic acid, heated at reflux (Scheme). The new compounds were completely characterized by the usual spectroscopic techniques (Table 1).

The precursor aldehydes **1a-d** were previously synthesized by us through Suzuki cross-coupling reactions.[3f,h]



Scheme. Synthesis of imidazole derivatives **2a-d**.

Table 1. Yields, IR absorption and ^{1}H NMR data of imidazole derivatives **2a-d**.

Cpd	R	Yield (%)	IR ν (cm^{-1})[a]	δ_H (ppm)[b]
2a		74	3411	12.70
2b		79	3419	12.73
2c		49	3424	12.80
2d		84	3429	12.85

[a] For the NH stretching band (recorded in KBr)

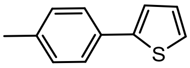
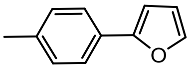
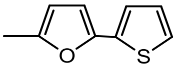
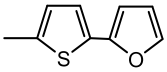
[b] For the NH proton of the imidazole ring for compounds **2** (DMSO-d_6)

The absorption and emission spectra of imidazoles **2a-d** were measured in ethanol solutions (Table 2). The imidazole derivatives **2a-d**, differing in the substituent at position 2 of the imidazole ring, displayed bathochromic shifts according the electronic character of the substituent: replacement of the phenyl ring by a five membered ring resulted in a red shift of the wavelength of maximum absorption and emission.

The relative fluorescence quantum yields were determined by using 10^{-6} M solutions of DPA in ethanol as standard ($\Phi_F = 0.95$).[4] For the Φ_F determination, the fluorescence standard was excited at the wavelengths of maximum absorption found for each of the compounds to be tested and in all fluorimetric measurements the absorbance of the solution did not exceed 0.1.

Imidazole derivatives **2** exhibited excellent fluorescence quantum yields in ethanol (Φ_F = 0.44 and 0.91), the highest being for **2b** (Table 2).

Table 2. UV-visible absorption and fluorescence data for imidazoles **2a-d** in ethanol solution.

Cpd	R	UV/Vis λ_{max} (nm)	log ε	Fluorescence λ_{em} (nm)	Φ_F	Stokes' shift (nm)
2a		342	4.50	412	0.70	70
2b		334	3.90	400	0.91	66
2c		354	4.40	444	0.44	90
2d		365	4.45	434	0.50	69

4. Conclusions

The synthesis of new imidazole derivatives **2a-d** was achieved by a simple procedure in moderate to excellent yields. The photophysical properties were evaluated by fluorescence spectroscopy and revealed that the imidazole derivatives are highly emissive, especially the imidazole bearing the arylfuran moiety **2b**, with a fluorescence quantum yield of 0.91. Due to their high fluorescence quantum yields and large Stokes' shifts, these novel heterocyclic fluorophores could have potential application as two-photon absorbers.

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01-0124-FEDER-009457)], and a PhD grant to R.C.M. Ferreira (SFRH/BD/86408/2012). The NMR spectrometer Bruker Avance III 400 is part of the National NMR Network and was purchased with funds from FCT and FEDER.

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