



Short communication

Facile synthesis of novel blue light and large Stoke shift emitting tetradentate polyazines based on imidazo[1,5-a]pyridine

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ABSTRACT

A facile double condensation procedure, through both standard and microwave heating, provides a versatile one step approach for the synthesis of multidentate nitrogen heterocyclic ligands containing the imidazo[1,5-a]pyridine moiety. The obtained compounds show interesting optical properties: blue fluorescent emissions, moderate quantum yields and large Stokes shifts, enabling their technological application.

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1. Introduction

In the last years the polyazine moieties, especially the poly-pyridine skeletons, have attracted a great attention because of the unique photophysical properties of their metal complexes [1–7]. In fact, they have found application in several fields like organic light-emitting diodes (OLED) [8–11], non linear optics (NLO) [12–14] and molecular-based photovoltaic (PV) [15] devices as dye-sensitized solar cells (DSCs) [7,16]. Nevertheless, synthetic approaches toward ligands containing three or four conjugated azine rings have been poorly reported [17–21], if compared to the vast investigation on diazines, e.g. bipyridine-based complexes [22]. This is mainly because the compounds are synthetically difficult to access. Typically, in order to prepare symmetric as well as non symmetric functionalized multi azine systems, methods involving multi step cross-coupling of halo intermediates with organometallic ones have so far been developed; e.g., halopyridines are coupled with pyridylstannates (Stille) [17–21], pyridylborates (Suzuki) [7], or pyridylzinc reagents (Negishi) [1,23,24]. These approaches display overall yields rarely exceeding 30% and always involve many steps, requiring harsh and expensive reaction conditions, because of the use of highly sensitive and perhaps toxic reagents.

Among the various types of azine ligands, we focused our attention on the pyridylimidazo[1,5-a]pyridine based ligands that possess photophysical and coordinating properties similar or superior to the polypyridine skeleton. In fact their peculiar structure allows large Stokes shift characteristics both in the free ligands and the related complexes [25]. Moreover, due to their biological properties [26], such molecules have been used for pharmaceutical applications [27,28] such as HIV-protease inhibitors [29], cardio-tonic agents [30], aromatase inhibitors in oestrogen dependent diseases [31] and thromboxane A2 synthetase inhibitors [32]. Different synthetic methodologies have been used in the past years to prepare the imidazo[1,5-a]pyridine derivatives, involving the use of Pd-catalysts [33,34], sensitive Lewis acids [35,36], elemental sulphur (S8) [37,38] or the oxidization of Schiff bases [39]. However, also an interesting three component condensation reaction has been reported to provide imidazo[1,5-a]pyridine with high yields, using pyridin-2-yl-methanones, aldehydes and ammonium acetate [40–43].

Our goal is, starting from this simple methodology, to develop a convenient one step preparation of a tetradentate polyazine skeleton, under mild conditions and with minimal waste production. Here we report the synthesis and characterization of six bis-substituted bis(1-imidazo[1,5-a]pyridine-3-yl)benzene derivatives (Fig. 1) showing interesting optical and chelating properties, with good fluorescent emissions, moderate quantum yields and remarkable Stokes shifts.

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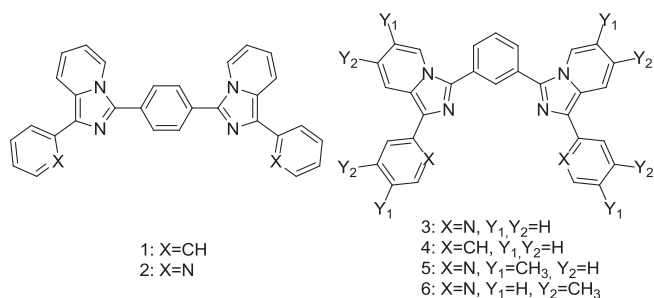


Fig. 1. General structures of synthesized compounds.

2. Results and discussion

2.1. Synthesis

The synthetic pathway proceeded through the direct double cyclization of differently substituted methanones with isophthalaldehyde or terephthalaldehyde in presence of ammonium acetate (Scheme 1, Table 1). Notably, this double condensation provides reaction yields on average much higher respect to the single condensation previously reported [40–43].

The reaction is straightforward: it consists of a single reaction step and does not require the use of any highly sensitive Lewis acids or catalysts. Moreover, the reaction can give a variety of bis(1-imidazo[1,5-a]pyridin-3-yl)benzene in quantitative yields with only water as a byproduct.

As previously reported in the case of monocyclization [44] this reaction is tolerant to various aldehyde substrates [40–43] and also to differently substituted methanones. A first cyclization reaction was carried out between phenyl(pyridin-2-yl)methanone and terephthalaldehyde in acetic acid and ammonium acetate. The product **1** was recovered quantitatively as a yellow powder. The same procedure, using isophthalaldehyde, gave the position isomer **4**.

The synthetic versatility of this double cyclization met the challenge to prepare a variety of compounds in a single step. Then, using the di(pyridin-2-yl)methanone we got products (**2** and **3**) containing the imidazo[1,5-a]pyridine nucleus and two pendant pyridine. Finally, with the same approach but using the two methyl-substituted di(pyridin-2-yl)methanones, we obtained compounds **5** and **6** which have the typical structural motif of tetrapyridine ligands.

It is noteworthy that using two different aldehydes, namely isophthalaldehyde and terephthalaldehyde, it is possible to obtain two similar tetradentate ligands (**2** and **3**). Unfortunately, attempting the same reaction using the *o*-phthalaldehyde was unsuccessful. Indeed, the product of the cyclization is represented by the isoindole core instead of a tetradentate ligand [44]. All the

Table 1
General synthetic conditions for the synthesis of compounds 1–6.

Entry (compound)	X	Y ₁	Y ₂	Dialdehyde	Method	Yields (%)
1 (1)	C	H	H	para	A	98
2 (1)	C	H	H	para	B	96
3 (2)	N	H	H	para	A	96
4 (2)	N	H	H	para	B	96
5 (3)	N	H	H	meta	A	98
6 (3)	N	H	H	meta	B	96
7 (4)	C	H	H	meta	A	96
8 (4)	C	H	H	meta	B	95
9 (5)	N	CH ₃	H	meta	A	98
10 (5)	N	CH ₃	H	meta	B	96
11 (6)	N	H	CH ₃	meta	A	97
12 (6)	N	H	CH ₃	meta	B	96

Method A: methanone (3.36 mmol), aldehyde (1.46 mmol), ammonium acetate (21.85 mmol), 25 mL acetic acid, 118 °C, 12 h; Method B: in sealed MW tube, methanone (3.36 mmol), aldehyde (1.46 mmol), ammonium acetate (21.85 mmol), 15 mL acetic acid, 180 °C, 50 min.

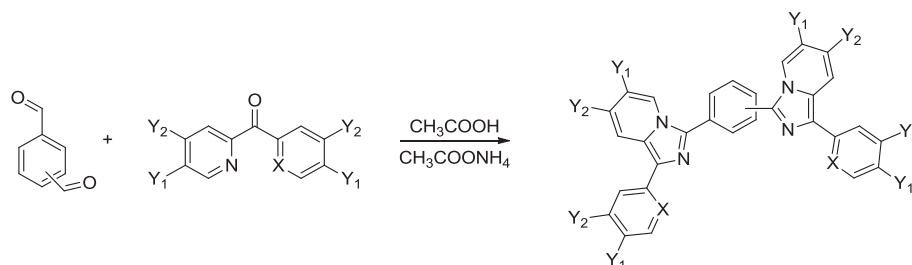
reported reactions were carried out both with standard heating and in a sealed microwave tube reactor. In all the cases the microwave irradiation allowed to reduce significantly solvent amount and reaction times, maintaining quantitative yields (see ESI for details).

The molecules reported in this work can be also considered as potential tetradentate ligands. In fact compound **2** was already employed (even if its synthesis is not described) as bidentate ligand for the synthesis of Os and Ru bimetallic complexes [45]. Similarly, the core imidazo[1,5-a]pyridine substituted in **1** with a pendant pyridine was used to coordinate transition metal ions, as in the case of 3-substituted-1-(pyridin-2-yl)imidazo[1,5-a]pyridine [46–48]. Furthermore, the phenylimidazole unit has been reported to act as a cyclometalating ligand [49–54], like the more widespread 2-phenylpyridine.

2.2. Optical properties

The imidazo[1,5-a]pyridine nucleus is known in literature also for its photophysical properties [25,37,38,46–48]. It is reasonable to think that the introduction of additional π -system into imidazo[1,5-a]pyridine nucleus influences their photophysical properties [33,34]. Electronic absorption and emission properties of compound **1–6** have been investigated in solution (CH₃CN). The main photophysical parameters are reported in Table 2 while the electronic absorption and emission spectra of all the compounds in acetonitrile solution are depicted in Fig. S1 in the ESI.

For all the compounds, the absorption maximum does not extend beyond 380 nm and ϵ values are comprised between 11,000 and 46,000 m² mol⁻¹. The solvent effects on the absorption behaviour of all the compounds were evaluated (see Figure S2–S7 of the Supporting Information). Solvent polarity little influences the absorption spectra of **1–6** heterocycles suggesting low charge



Scheme 1. General synthesis of compounds 1–6.

Table 2
Absorption and Emission Properties of compounds **1–6** (CH₃CN).

	λ_{abs} (nm)	ϵ (M ⁻¹ cm ⁻¹)	λ_{em} (nm)	Stokes shift (nm)	ϕ^a
1	305	28,571	480	101	9
	379	31,797			
2	233	30,111	465	86	22
	289	23,580			
	333	25,364			
	379	35,567			
3	331	43,794	460	102	17
	358	38,113			
	349	26,717			
4	282	11,055	480	131	11
	349	26,717			
5	236	45,526	470	109	16
	252	43,688			
	288	40,900			
	334	35,550			
	361	36,504			
	361	36,504			
6	332	33,578	475	107	10
	358	28,473			
	358	28,473			

^a determined using as reference quinine sulphate in 0.1 M aqueous sulphuric acid.

transfer character of the electronic transitions. Under UV–vis excitation, all the synthesized compounds present an emission band at about 460–480 nm, with quantum yields ranging from 9 to 22%, comparable to the best reported result for imidazo[1,5-a]pyridine based compounds [40–43]. All the compounds show a wide Stokes shift of about 100 nm, with **4**, **5** and **6** displaying the greatest bathochromic shift. Comparison of **1** with **2** and of **4** with **3** shows that the substitution of a benzene ring with a pyridine one greatly increases the quantum yield and causes a blue shift in the emission spectra.

2.3. Computational modelling

To gain an insight into the structural, electronic, and optical properties of **1–6**, we performed DFT/TDDFT calculations at the B3LYP/6-31G**/PCM level of theory (See the computational section of the ESI for details), using acetonitrile as solvent. The six compounds are characterized by a structural arrangement that slightly deviates from planarity. The isodensity plots of the frontier molecular orbitals (see Table S7 in the ESI) show that the HOMO and HOMO–1 are delocalized over the whole molecule while the five virtual orbitals are localized on the 1-substituted-imidazo[1,5-a]pyridine moiety of **3–6** and on the bis(1-imidazo[1,5-a]pyridine-3-yl)benzene in the case of **1** and **2**. A full summary of the computational results is reported in the ESI.

The comparison of experimental and calculated absorption spectra (Fig. 2 and Fig. S8 in the ESI) shows an excellent agreement along the series, allowing to characterize the absorption of the investigated compounds as essentially originating from π – π^* electronic transitions even if a limited intramolecular charge-transfer character is also observable for the transitions at higher energy.

2.4. Crystallographic characterization

Crystals of compound **3**, suitable for single crystal X-ray analysis, were obtained by slow evaporation of a saturated ethanol solution. The compound has twofold crystallographic symmetry in the solid state (Fig. 3) and the structure was solved by ab-initio methods in non-centrosymmetric group P21212. The molecule shows helical chirality arising from the hindered rotation along the C3–C5 axis. The C4–C3–C5–N1 torsional angle of 34.52° found in the crystallized molecule confirms the theoretical calculations. The absolute

configuration could not be determined due to the lacking of strong anomalous scatterers. In the crystal, the moieties are linked by a network of intermolecular C–H...N interactions and they form a zig-zag pattern along the a axis (for details see Fig. S9, S10 and S11 in the ESI). π – π interactions are present between the C12–C13–C14–C15–C16–N3 ring of one molecule and the C7–C8–C9–C10–C11–N2 ring of another molecule at a distance of 3.9 Å.

3. Conclusions

In conclusion, we have presented a convenient methodology to perform an efficient one-step double cyclization providing new large Stoke shift poliazine compounds. These compounds represent an unexplored class of fluorescent polidentate ligands easily tuneable with potential interest in the fields of DSCs, OLED, NLO and for pharmaceutical applications. Moreover, quantitative yields, absence of catalysts, high accessibility and stability, ease of handling and preparation, no toxicity of reagents and derivatives make this microwave based synthetic approach useful for a systematic screening and up-scaling of a large number of these compounds.

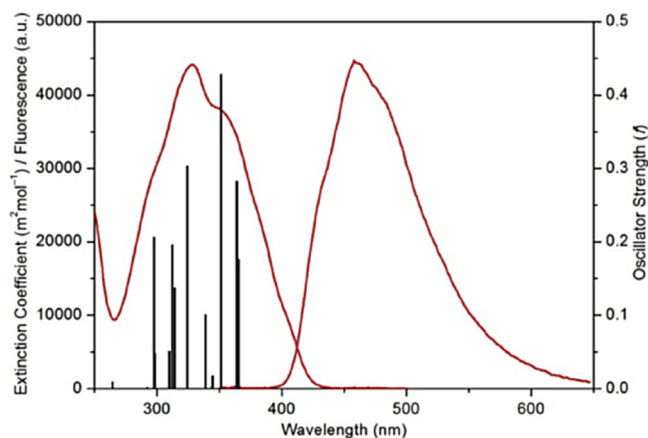


Fig. 2. Experimental electronic absorption (left) and emission (right) spectra of **1** in CH₃CN solution together with calculated singlet excited state transitions (vertical bars with height equal to the oscillator strength (*f*) values).

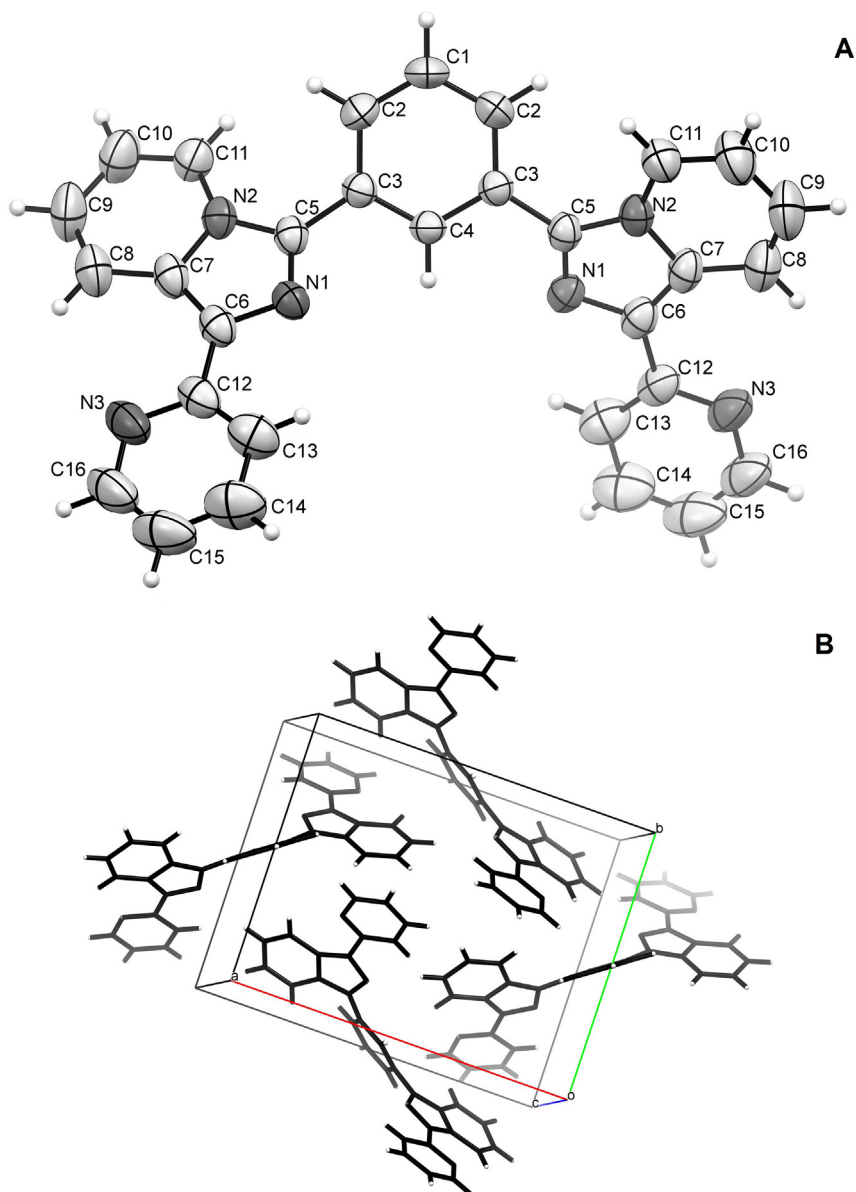


Fig. 3. Crystal structure[†] (A) and packing (B) of **3**.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.dyepig.2015.12.005>.

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