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Tripod molecules based on the *N*,*C*-pyrazolyl-pyridine motif

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Abstract—The synthesis of four new podands with three arms containing the *N*,*C*-pyrazolyl-pyridine chromophore is described with the aim of using the resulting tripods as ligands to sensitize lanthanide luminescence.

Podands in which three polydentate co-ordinating arms are attached to a central linking group are common tripods which may confer high stability to metal complexes.[1] Tris-chelate podands have been synthesized containing a wide variety of side-arms based on chelating groups such as pyrazole,[2] 2,2′-bipyridine and many other heteroaromatic structures.[3] Lanthanide ions in co-ordination complexes rely on weak crystal-field effects induced by the precise arrangement of the donor atoms in the first co-ordination sphere.[4] The large co-ordination numbers of these metals (8–10) makes it essential to have multiple chelating points in the limbs of the tripod structure and enough flexibility to comply with the steric-demanding metal co-ordination. Polyheteroaryl ligands as 2,6-bis(*N*-pyrazolyl)pyridine and the related *N*,*C*-pyrazolyl-pyridine[5] may play the necessary role to this effect. Besides, the pyrazolyl-pyridine motifs have been shown to be extremely effective in lanthanide sensitization (antenna effect) when incorporated in chelates,[6] macrocycles[7] or cryptates,[8] leading to compounds with outstanding luminescent properties.

We hereby describe the synthesis of a new family of tris-chelating podand ligands **L1**–**L3** (Scheme 1)[9] based on the *N*,*C*-pyrazolyl-pyridine chromophore. Attachment of chelating substituents to the 3-position of the pyrazole or pyridine rings is a strategy for preparing complexes in which the metal centre might be efficiently shielded against deleterious solvent OH vibronic deactivation. A glimpse of the molecular models of Figure 1 (Hyperchem AM1/MM+ calculations) suggest that the podands of Scheme 1 may in fact be a tight enclosure for transition or lanthanide metals.

The synthesis of the podands is outlined in Scheme 1 as a four-legged process starting from the potassium salt of 3-methylpyrazole, obtained in situ. The reaction of this pyrazolate with 2-chloropicoline afforded the dimethyl pyrazole-pyridine derivative **1** which was transformed either into monobromide **2** with one equivalent of NBS or into carboxylic acid **3** by oxidation.

The predominant regioselectivity of these reactions is in accordance with the predicted (AM1 semiempirical calculations) higher relative stability of the radical beside the pyrazole ring (ca. 2.4 kcal/mol). Monobromide **2** was treated with anhydrous ammonia affording podand **L1** in good yield.[10] Esterification of the carboxylic acid **3** and bromination yielded the bromoester derivative **4** which was transformed into podand **L2**.[11] On the other hand, treatment of the potassium salt of 3-methylpyrazole with ethyl 6-bromopyridine-2-carboxylate afforded pyridyl ester **5**[12] from which the synthesis of podand **L3** was straightforward in three steps.[13]

Podands **L1**–**L3** absorbed light at the λ_{max} value expected for the *N*,*C*-pyrazolyl-pyridine chromophore (288 nm, acetonitrile or methanol) with reasonable molar absorptivity. However we found the fly in the ointment because, to our utter dismay, preliminary

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Keywords: Luminescence; Lanthanide chelates; Podands; Tripods.

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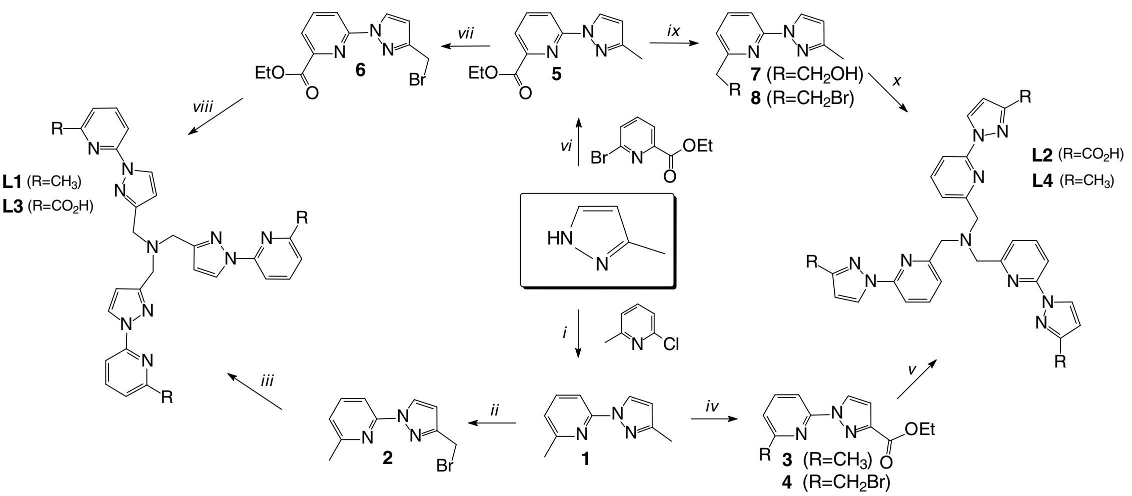

Scheme 1. Reagents and conditions: (i) K/dyglime, 140 °C autoclave 96 h (76%); (ii) NBS/CCl_4/BzOOBz (cat.) (85%); (iii) NH_3 (0.4 equiv), Na_2CO_3/CH_3CN 100 °C autoclave 18 h (56%); (iv) (a) $KMnO_4$/H_2O–Py (3:1), reflux 14 h (55%); (b) $SOCl_2$/EtOH reflux 18 h (85%); (c) NBS/CCl_4/BzOOBz (cat.) (34%); (v) (a) NH_3 (0.4 equiv), Na_2CO_3/CH_3CN 100 °C autoclave 18 h (46%); (b) NaOH/H_2O–THF (1:1) 60 °C 16 h (88%); (vi) K/dyglime, 60 °C autoclave 65 h (46%); (vii) NBS/CCl_4/BzOOBz (cat.) (47%); (viii) NH_3 (0.4 equiv), Na_2CO_3/CH_3CN 100 °C autoclave 12 h (75%); (ix, x) proposed steps: (a) LAH/THF; (b) PBr_3/THF; (c) NH_3 (0.4 equiv), Na_2CO_3/CH_3CN 100 °C autoclave (see Ref. 9).

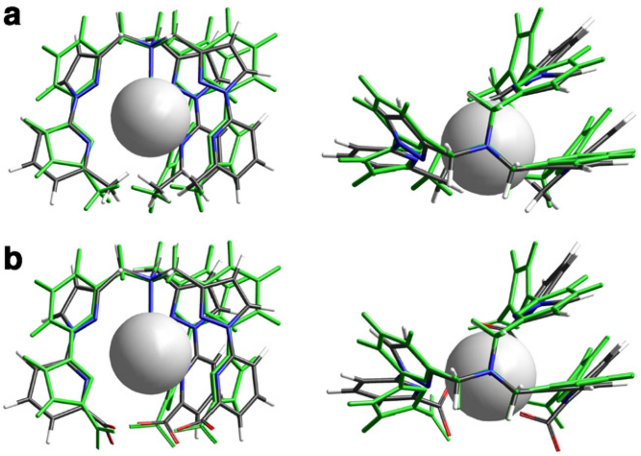

Figure 1. AM1/MM+ Hyperchem calculations of the podands studied in this work [a: superimposed **L1**–**L4** (green); b: superimposed **L2** (green)–**L3**] in lateral and upper views.

luminescence studies did not show the expected strong lanthanide emission. In fact, **L1** did not emit at all even after its reflux in nonaqueous solvents with $LnCl_3$. The same happened for **L2** and **L3** when refluxed in aqueous borate buffer. Yet, we were able to measure a feeble emission ($q < 0.1\%$, $\tau = 0.9 \pm 0.1$ ms) in MeOH after refluxing **L2** and **L3** overnight with $TbCl_3$ in that solvent. It thus appears to be essential the metal charge compensation offered by the carboxylate groups, which nevertheless seemed unable to protect the Ln ion against the strong deactivation induced by water, provided the complexes of **L2** and **L3** were ever formed in that solvent. Experiments and theoretical calculations are under way to understand the reasons causing the observed lack of luminescence intensity in order to design a second generation of podands to efficiently promote the pursued lanthanide emission.

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9. Podand **L4** was not finally prepared in this work in view of the inability of **L1**–**L3** to display the sought strong luminescence when complexed with lanthanides. A plausible synthetic path for its preparation is nevertheless outlined in Scheme 1.
10. Podand **L1**: ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.53 [3H, d, $J = 2.5$ Hz, Pz(5)*H*]; 7.75 [3H, t, $J = 8.1$ Hz, Py(5)*H*];

7.65 [3H, dd, $J_1 = 8.1$, $J_2 = 7.3$ Hz, Py(4)*H*]; 6.99 [3H, d, $J = 7.3$ Hz, Py(3)*H*]; 6.57 [3H, d, $J = 2.5$ Hz, Pz(4)*H*]; 3.86 [6H, s, PzCH_2N]; 2.54 [9H, s, CH_3Py]. MS (FAB+): 531.3 (M+H$^+$); Elemental analysis calcd for $C_{30}H_{30}N_{10}$: C, 67.9; H, 5.7; N, 26.4. Found: C, 67.3; H, 5.9; N, 25.8.

11. Podand **L2**: ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.42 [3H, d, $J = 2.7$ Hz, Pz(5)*H*]; 8.04 [3H, dd, $J_1 = 8.2$, $J_2 = 7.5$ Hz, Py(4)*H*]; 7.83 [3H, d, $J = 8.2$ Hz, Py(5)*H*]; 7.96 [3H, d, $J = 7.5$ Hz, Py(3)*H*]; 6.93 [3H, d, $J = 2.7$ Hz, Pz(4)*H*]; 4.03 [6H, s, PzCH_2N]. MS (ester precursor; FAB+): 727.1 (M+Na$^+$). Elemental analysis calcd for $C_{36}H_{36}N_{10}O_6$ (ester precursor): C, 61.3; H, 5.2; N, 19.9. Found: C, 61.0; H, 5.9; N, 25.8.
12. Compound **5**: ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.65 [1H, dc, $J_1 = 2.7$, $J_2 = 0.4$ Hz, Pz(5)*H*]; 8.21 [1H, dd, $J_1 = 5.7$, $J = 3.5$ Hz, Py(5)*H*]; 8.02–7.95 [2H, m, Py(3,4)*H*]; 6.36 [1H, d, $J_1 = 2.7$, $J_2 = 0.4$ Hz, Pz(4)*H*]; 4.47 [2H, c, $J = 7.1$ Hz, CH_2OCO]; 2.47 [3H, t, $J = 0.4$ Hz PzCH_3]; 1.45 [3H, t, $J = 7.1$ Hz, CH_3CH$_2$OCO].
13. Podand **L3:** ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.62 [3H, d, $J = 2.6$ Hz, Pz(5)*H*]; 8.13 [3H, dd, $J_1 = 7.3$, $J_2 = 1.9$ Hz, Py(5)*H*]; 7.96 [3H, dd, $J_1 = 7.3$, $J_2 = 1.9$ Hz, Py(3)*H*]; 7.91 [3H, t, $J = 7.3$ Hz, Py(4)*H*]; 6.57 [3H, d, $J = 2.6$ Hz, Pz(4)*H*]; 3.84 [6H, s, PzCH_2N]. MS (ester precursor; EI+): 705.1 (M$^+$, I = 59); 230.0 ([CH$_2$PzPy CO$_2$Et]$^+$, I = 100).