Design, Synthesis and Structural Analysis of Exoditopic Macrocyclic Ligands Based on Bipyridine Units

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Abstract: The synthesis of new unsymmetrical and symmetrical macrocycles based on 2,2'-bipyridine units bearing two or four phenyl groups at the 6 and 6' positions was achieved by an oxidative coupling reaction using 1,2-dibromoethane and organolithium derivatives of bipyridine. Among all new compounds prepared, two of them were structurally analysed in the solid state by X-ray diffraction.
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Coordination polymers are metalloorganic entities composed of metal centres bridged by organic connectors. In marked contrast with coordinating polymers, *i.e.* polymers bearing ligating sites allowing the coordination of metals, for coordination polymers, metal centres are incorporated within the structure of the polymer, behaving thus as structural knots. Because metals offer a vast variety of coordination geometry as well as different oxidation states, the design and preparation of coordination polymers with controlled structures and thus, properties, are currently under active investigation.[1] The strategy for the formation of coordination polymers may be based on iterative assembling processes between metals and organic ligands. In this context, the design of the organic part is of special importance. In order to allow the interconnection between metallic centres, ligands in which the coordination sites are oriented outwardly (exo-ligands) are needed. Divergent bis-tridentate ligands were shown to form molecular wires in the solid state in the presence of transition metal cations.[2] Recently, we have embarked upon a program dealing with the design and the synthesis of exo-ligands. In this vein, we have prepared exo-ligands based on mercaptocalix[4]arenes[3], calix[4]arene bearing bidentate catechol units[4] and macrocyclic frameworks containing bipyridine units.[5] In the latter case, the ligand **9** was previously prepared and its ability to form discrete binuclear complexes with transition metals was demonstrated.[5b] Other exo-ligands based on bipyridine units have also been reported.[6]

In our early design, the divergent orientation of the coordination sites in the ligand **9** was imposed by the interconnection of the two chelating 2,2'-bipyridine units by ethylene chains at the 4 and 4' positions in a macrocyclic framework.[5b] The coordination ability of the 2,2'-bipyridine towards transition metals is well established.[7] However, the unsubstituted 2,2'-bipyridine was shown to form complexes with square planar, tetrahedral and octahedral coordination geometries. In order to control the coordination geometry around the metal centre, we designed the symmetrical exo-ligand **5** and the unsymmetrical compound **8** both based on compound **9**. Indeed, it has been demonstrated that by introducing substituants, in particular phenyl groups at 6

and 6' positions of the 2,2'-bipyridine skeleton, one may exclusively impose a tetrahedral coordination geometry. Thus, whereas the exo-ligand **5** should only form tetrahedral complexes, the compound **8** may accommodate metals with tetrahedral geometry at the bipyridine unit bearing phenyl groups and square planar or octahedral geometries at the unsubstituted bipyridine site.

In the present paper, we describe the synthesis and the structural analysis of both compounds **5** and **8**.

Our strategy for the synthesis of macrocyclic compounds **5** and **8** was based on an oxidative coupling reaction previously observed by us.[5b] Indeed, we have noticed that the reaction of the bis lithium derivative **2** with 1,2-dibromoethane, in addition to linear bipyridine containing oligomers, also affords macrocyclic bipyridine based ligands such as compound **9**.[5b] This oxidative coupling reaction has been previously reported for the synthesis of linear bis bipyridine and bis phenanthroline derivatives.[8]

| 1 X = H | 3 X = H |
| 2 X = Li | 4 X = Li |

5　　　　　　　6　　　　　　　7

Scheme 1
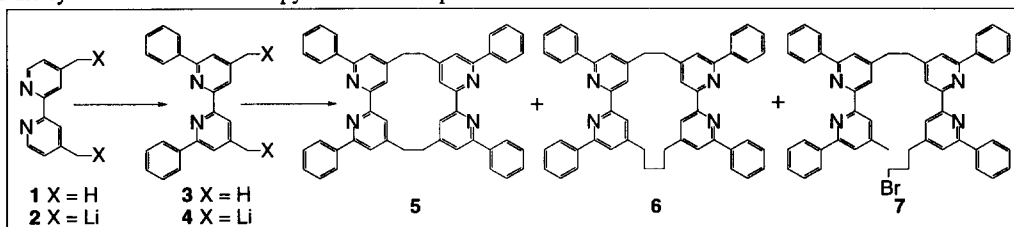
The common starting material for the synthesis of macrocycles **5** and **8** was the 4,4'-dimethyl-2,2'-bipyridine **1** which was prepared by Raney Ni coupling of 4-picoline.[9] The synthesis of **3** was based on the reported procedure for unsubstituted bipyridine derivatives.[10] Treatment of compound **1** by 5 eq. of PhLi in toluene followed by reoxidation with MnO_2 afforded the desired compound **3** in 20 % yield.[11] The oxidative coupling reaction of the dilithium derivative **4**, generated under argon by treatment of **3** with LDA in dry THF, with 1,2-dibromoethane in dry THF at r.t. and under high dilution conditions gave, after chromatography (SiO_2, CH_2Cl_2/hexane), in addition to the desired macrocycle **5**[11] (27 %) two other compounds **6**[11] (3 %) and **7** (2 %). The formation of the last two compounds is due to the competition between the oxidative coupling and the nucleophilic displacement of bromide at 1,2-dibromoethane by the organolithium derivative (scheme 1).
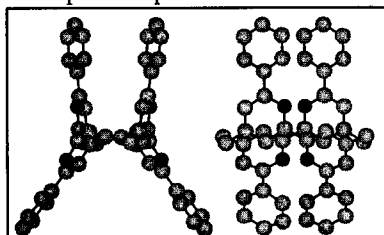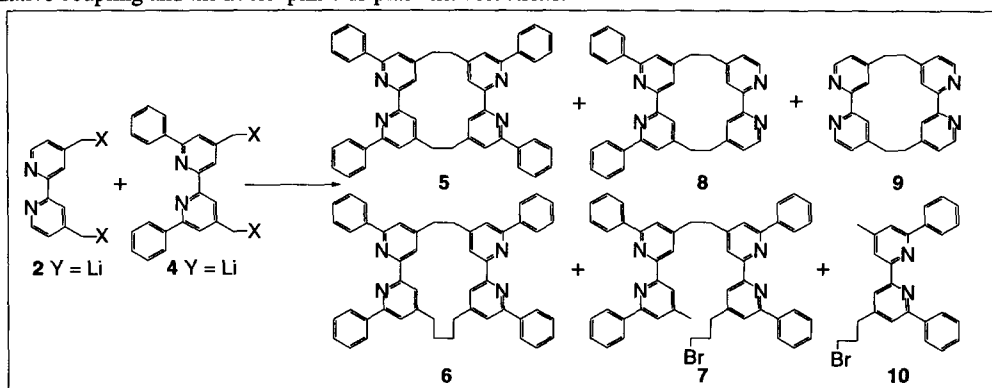
Figure 1: X-ray structure of the ligand 5 (carbon atoms grey, nitrogen atoms black).View parallel (left) and perpendicular (right) to bipyridine units . For the sake of clarity, hydrogen atoms are not presented.

The structure of **5** was established by an X-ray analysis[15] performed on suitable crystals obtained from a toluene/hexane mixture (Figure 1). The two 2,2'-bipyridine units adopt, as often observed, a transoid conformation with NCCN dihedral angles of 136.4° and 141.9°. The phenyl groups are tilted with respect to the adjacent pyridine rings by 25.8°, 28.6°, 29.2° and 30.8°.

The synthesis of the unsymmetrical compound **8** was first attempted using a statistical procedure (Scheme 2). The addition at r.t., under high dilution, of 1,2-dibromoethane to a 2:1 mixture of **2** and **4**, both obtained by treatment of **1** and of **3** with LDA in THF,

gave a mixture of several products. After a rather tedious separation by chromatography (SiO_2, CH_2Cl_2/hexane), six different new compounds could be isolated. As expected, in addition to the centrosymmetric **5**[11] (10 %) and **9**[5b] (4 %) resulting from the oxidative homo coupling of **2** or **4**, the desired unsymmetrical compound **8**[11] (13 %), resulting from the oxidative coupling of **2** with **4**, were obtained. The

other three isolated compounds **6** (1 %), **7** (1 %) and **10** (0.5 %) resulted from the competition between the oxidative coupling and the nucleophilic displacement reactions.

Scheme 2

Figure 2: X-ray structure of the ligand **8** (carbon atoms grey, nitrogen atoms black).View parallel (left) and perpendicular (right) to bipyridine units . For the sake of clarity, hydrogen atoms are not presented.

The structure of **8** was also established in the solid state by an X-ray analysis[15] performed on suitable crystals obtained from a CHCl₃/hexane mixture (Figure 2). The two 2,2'-bipyridine units adopt a transoid conformation with NCCN dihedral angles of -141.4 ° and -153.0 °. The phenyl groups are tilted with respect to the adjacent pyridine rings by -28 °.

Finally, although **8** could be prepared using the above mentioned statistical approach, in order to avoid the rather tedious chromatographic isolation, its synthesis was also achieved using nucleophilic displacement of bromides on **11** by **4** (scheme 3).
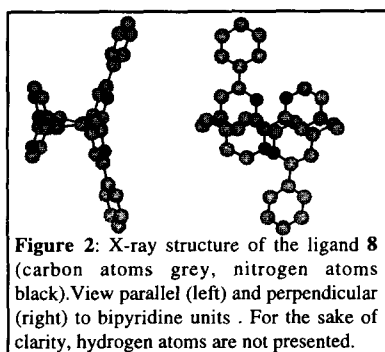
The formation of **11** by bromination of **1** using NBS has been reported with a 30 % yield[12]. Since, in our hands, the yield for this reaction, repeated several times, never exceeded 5 %, we followed a sequential strategy for its synthesis. The oxidation of **1** affording the diacid **12** was achieved either by treatment with KMnO₄ in dilute H₂SO₄[13] or by CrO₃ in conc. H₂SO₄[14]. The later reaction appeared to give higher yields. The esterification of the diacid gave the diester **13**[13] which was reduced by NaBH₄/EtOH to the diol **14**.[13] The dibromo **11** was obtained by treatment of **14** with 48 % HBr in the presence of few drops of conc. H₂SO₄. The condensation in dry THF at r.t. and under high dilution conditions of the dibromo **11** with the bis lithium derivative **4**, in addition to **8** (6 %), afforded the large tetrabipyridine-containing macrocycle **15** with the poor yield of ca 1 %.
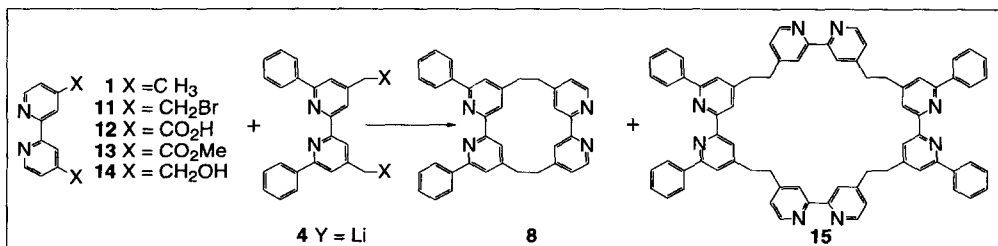
Scheme 3

In summary, the synthesis of new macrocyclic exo-ligands based on 2,2'-bipyridine units bearing phenyl groups at 6 and 6' positions and interconnected at 4 and 4' positions by alkyle bridges was achieved. Two of the prepared compounds were structurally analysed in the solid state by X-ray diffraction. The coordination ability of the new ligands towards transition metals was established and will be reported elsewhere.

References and notes

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11. Selected NMR (δ(ppm)) data: **3**: ^{1}H (CDCl$_3$, 300 MHz, 25 °C): 2.54 (s, 6H, CH$_3$); 7.43 (m, 2H, CH$_{ph}$(δ)); 7.51 (m, 4H, CH$_{ph}$(χ)); 7.60 (s, 2H, CH$_{pyr}$(5,5')); 8.15 (m, 4H, CH$_{ph}$(β)); 8.42 (s, 2H, CH$_{pyr}$(3,3')); ^{13}C (CDCl$_3$, 75 MHz, 25 °C): 21.50 (CH$_3$); 120.55, 121.32 (C$_{pyr}$(3,3'), C$_{pyr}$(5,5')); 127.01, 128.64, 128.77 (C$_{ph}$(β), C$_{ph}$(χ), C$_{ph}$(δ)); 139.63 (C$_{ph}$(α)); 148.52 (C$_{pyr}$(4,4')); 155.91, 156.35 (C$_{pyr}$(2,2'), C$_{pyr}$(6,6')); **5**: ^{1}H (CDCl$_3$, 300 MHz, 25 °C): 3.04 (s, 8H, CH$_2$); 6.56 (d, 1.43 Hz, 4H, CH$_{pyr}$(3,3')); 7.31 (m, 12H, CH$_{ph}$(χ), CH$_{ph}$(δ)); 7.61 (d, 1.44 Hz, 4H, CH$_{pyr}$(5,5')); 7.86 (m, 8H, CH$_{ph}$(β)); ^{13}C (CDCl$_3$, 75 MHz, 25 °C): 37.70 (CH$_2$); 120.47, 123.49 (C$_{pyr}$(3,3'), C$_{pyr}$(5,5')); 127.19, 128.56, 128.67 (C$_{ph}$(β), C$_{ph}$(χ), C$_{ph}$(δ)); 139.62 (C$_{ph}$(α)); 149.76 (C$_{pyr}$(4,4')); 156.09 (C$_{pyr}$(2,2')); 157.59 (C$_{pyr}$(6,6')); **6**: ^{1}H (CDCl$_3$, 300 MHz, 25 °C): 1.61 (bs, 4H, CH$_2$(b)); 2.69 (bs, 4H, CH$_2$(a)); 3.12 (s, 4H, CH$_2$(a')); 7.00 (d, 1.2 Hz, 2H, CH$_{pyr}$(3)); 7.20-7.45 (m, 16H, CH$_{ph}$(χ), CH$_{ph}$(δ), CH$_{pyr}$(3'), CH$_{pyr}$(5'), CH$_{ph}$(χ'), CH$_{ph}$(δ')); 7.72 (d, 1.2Hz, CH$_{pyr}$(5)); 7.75-7.78 (m, 4H, CH$_{ph}$(β')); 8.00 (m, 4H, CH$_{ph}$(β)); ^{13}C (CDCl$_3$, 75 MHz, 25 °C): 27.23 (CH$_2$(b)); 34.55 (CH$_2$(a)); 37.42 (CH$_2$(a')); 119.11, 120.35, 122.21, 122.63 (C$_{pyr}$(3), C$_{pyr}$(3'), C$_{pyr}$(5), C$_{pyr}$(5')); 127.11, 127.20, 128.50, 128.62, 128.70 (C$_{ph}$(β'), C$_{ph}$(β), C$_{ph}$(χ), C$_{ph}$(χ'), C$_{ph}$(δ,δ')); 139.56, 140.95 (C$_{ph}$(α)); 149.84, 152.18 (C$_{pyr}$(4), C$_{pyr}$(4')); 155.33, 156.49, 157.03 (C$_{pyr}$(2,2'), C$_{pyr}$(6), C$_{pyr}$(6')); **8**: ^{1}H (C$_2$D$_2$Cl$_4$, 300 MHz, 25 °C): 2.95 (m, 8H, CH$_2$); 6.33, 6.39 (2d, 1.2 Hz, 4H, CH$_{pyr}$(3), CH$_{pyr}$(3')); 7.21 (dd, 5.0 Hz, 1.6 Hz, 2H, CH$_{pyr}$(5)); 7.51 (m, 6H, CH$_{ph}$(χ), CH$_{ph}$(δ)); 7.60 (d, 1.2 Hz, 2H, CH$_{pyr}$(5')); 7.98 (dd, 8.2 Hz, 1.4 Hz, 4H, CH$_{ph}$(β)); 8.44 (d, 5.0 Hz, 2H, CH$_{pyr}$(6)); ^{13}C (C$_2$D$_2$Cl$_4$, 75 MHz, 25 °C): 37.25, 37.48 (CH$_2$); 120.22 (C$_{pyr}$(5')); 123.30, 123.39 (C$_{pyr}$(3), C$_{pyr}$(3')); 125.04 (C$_{pyr}$(5)); 127.06, 128.71, 128.99 (C$_{ph}$(β), C$_{ph}$(χ), C$_{ph}$(δ)); 139.38 (C$_{ph}$(α)); 148.98, 149.44, 149.70 (C$_{pyr}$(4), C$_{pyr}$(4'), C$_{pyr}$(6)); 155.86 (C$_{pyr}$(2,2')); 157.10 (C$_{pyr}$(6')).

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15. *X-ray data for* **5**: C$_{48}$H$_{36}$N$_4$.C$_6$H$_{14}$, M = 755.0, triclinic, a = 12.104(3), b = 12.957(3), c = 14.441(4) Å, α = 84.88(2) °, β = 71.95(2) °, γ = 88.21(2) °, U = 2144(8) Å^3, space group P-1, Z = 2, Dc = 1.169 gcm^{-3}, μ(Mo-$K\alpha$) = 0.635 cm^{-1}. Crystal dimensions 0.40x0.35x0.25 mm. Data were measured at 293K on a MACH3 diffractometer with graphite monochromated Mo-Kα radiation. The structure was solved by direct methods and refined anisotropically using absorption corrected data to give R = 0.062, Rw = 0.085 for 3402 independent observed reflections [$|F_0| > 3\sigma(|F_0|)$]; *Data for 8*: C$_{35}$H$_{28}$N$_4$, M = 516.65, tetragonal, a = 9.579(3), b = 9.579(3), c = 29.724(9) Å, U = 2727(2) Å^3, space group P 41 21 2, Z = 2, Dc = 1.26 gcm^{-3}, μ(Cu-$K\alpha$) = 0.544 cm^{-1}. Crystal dimensions 0.40x0.40x0.40 mm. Data were measured at 173K on a Philips PW1100 diffractometer with graphite monochromated Cu-Kα radiation. The structure was solved by direct methods and refined anisotropically using absorption corrected data to give R = 0.031, Rw = 0.041 for 1288 independent observed reflections [$|F_0| > 3\sigma(|F_0|)$]. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.