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Synthesis and solid state structural analysis *exo*-bisbidentate ligands based on [1.1.1.1]metacyclophane in 1,3-alternate conformation bearing 2,2′-bipyridine or bisquinoline chelates

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Abstract

The synthesis and structural analysis of two new exoligands **1** and **2** based on a [1.1.1.1]-metacyclophane backbone bearing either 2,2′-bipyridine or bisquinoline chelating units have been achieved.

For a decade the design and preparation of coordination networks, hybrid metalloorganic architectures based on the self-assembly of organic exoligands in which the coordination sites are oriented in divergent manner and metal cations, has been under active investigation. The majority of networks reported to date are based on combinations of bis-monodentate exoligands and transition metal cations.[1] However, examples of coordination polymers based on either bis-bidentate[2,3] or tetradentate exoligands[4,5] in which the coordination sites are located by two sets of two interaction sites, have also been reported. Finally, only a few examples of structurally characterised coordination networks based on bis-tridentate ligands have been published.[6,7] We have previously reported the synthesis of exoligands of mercaptocalix[4]arene[8] and mercaptocyclophane[9] types as well as macrocyclic ligands based on bipyridine units[10] and calix[4]arene derivatives bearing four catechol[11] or pyridine[12] moieties. In continuation of our efforts[13] to design new coordination networks, we report here the synthesis and structural analysis of two new exoligands **1** and **2** based on a [1.1.1.1]cyclophane backbone bearing either a 2,2′-bipyridine or bisquinoline chelating units.

The design of both ligands **1** and **2** is based on the use of a backbone allowing two chelating sites to be positioned below and above a plane and with a 90° angle between them (Scheme 1). For such a design the cyclophane **3**, for which a synthetic procedure has been reported,[14] appeared as an interesting candidate since **3** has been shown to adopt the 1,3-alternate

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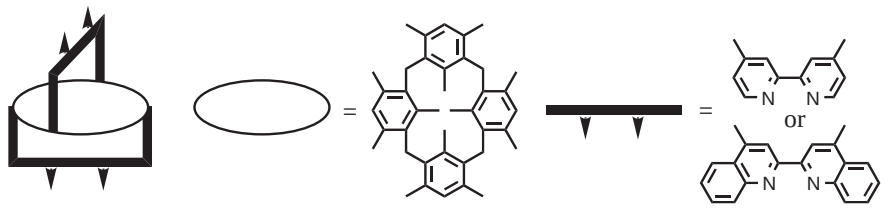
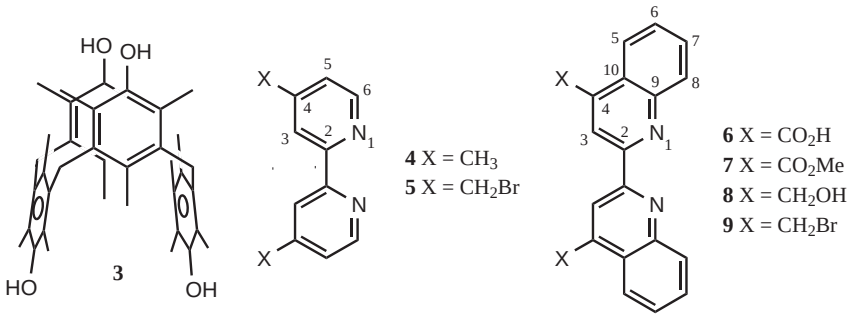


Scheme 1.

conformation thus leading to divergent orientation of the four OH groups below and above the main plane of the cyclophane; and on the other hand, the presence of the hydroxy groups may be exploited to connect the chelating units (Scheme 2). An example of compound **3** bearing a single bipyridine unit connected at the 6 and 6′ positions has been previously reported.[14] For the ligand **1**, as the chelating moiety, the 2,2′-bipyridine, the most used chelating unit,[15] was considered because of its ability to bind metal cations, whereas for the ligand **2**, 2,2′-bisquinoline was chosen because, in contrast to the 2,2′-bipyridine which would not select any coordination geometry, it should lead to tetrahedral coordination around the metal cations. Dealing with the connection of the chelating units to the cyclophane **3**, the 4,4′ positions on bipyridine and on bisquinoline have been chosen since such linkages should orient the chelating units in a divergent fashion.

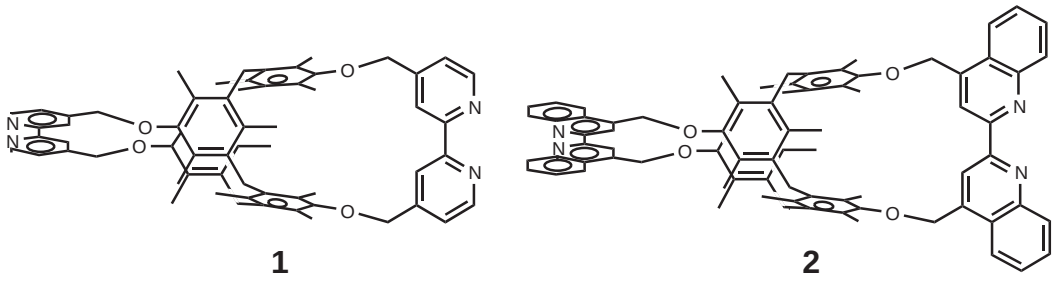


Scheme 2.

The synthesis of ligand **1**[16] (Scheme 3) was based on the coupling of cyclophane **3**, prepared in two steps according to reported procedures,[14] with dibromo 2,2′-bipyridine derivative **5** in dry DMF and in the presence of Cs_2CO_3 as the base. Compound **5** was prepared by first coupling γ-picoline to generate compound **4** and then by bromination of the latter again according to published procedures (Scheme 2).[17]

It is worth noting that the yield of compound **1** depends strongly on the addition rate of reagents and a 9% yield could be obtained for a dropwise addition time of 74 hours.

The synthesis of **2**[18] (Scheme 3) was again based on a coupling reaction between the cyclophane **3** and the dibromo derivative of bisquinoline **9** (Scheme 2). The latter was prepared in three steps starting with the commercially available acid derivative **6**, which was first esterified (MeOH, H_2SO_4) yielding the diester **7** in 89% yield as a white powder. The latter was reduced to the diol **8** in 86% yield using $NaBH_4$ in EtOH. Finally, treatment of **8** by 33% HBr/AcOH



Scheme 3.

afforded the dibromo compound **9** in 69% yield. As in the case of ligand **1** mentioned above, the condensation of compounds **3** and **9** in dry DMF in the presence of Cs_2CO_3 (addition time 120 h) afforded the desired ligand **2** in 19% yield.

Whereas for compound **1** no suitable single crystals could be obtained so far, for ligand **2** its solid state structure was investigated by X-ray crystallography on single crystals (Fig. 1).[19] Although the obtained crystals show suitable quality, they diffract poorly and therefore an *R* factor of only 0.11 was reached during the refinement. The study revealed the following relevant features. As expected, the cyclophane backbone is indeed in 1,3-alternate conformation. Probably due to the rigidity of the cyclophane and the ether junction (dCO = 1.405 Å, with an average COC angle of ca. 114.6°) between the bisquinoline units and the macrocycle, the two quinoline moieties are in *syn* conformation (average NCCN dihedral angle of ca. −1.1°). As it can be seen in Fig. 1, due to the presence of the CH_2 group between chelating units and oxygen atoms of the cyclophane, the two bisquinoline units are tilted with CCOC dihedral angles of 86.4 and −82.9°.

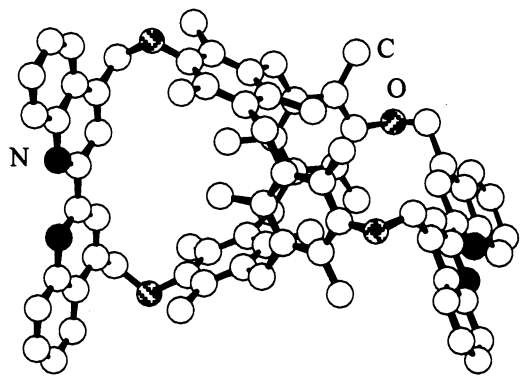


Figure 1. Solid state structure of ligand **2**. H atoms and solvent molecules are not represented for sake of clarity. For bond distances and angles see text

In conclusion, using cyclophane **3** in 1,3-alternate conformation, two new exoligands **1** and **2** based either on 2,2′-bipyridine or on bisquinoline units have been prepared. Ligand **2** was characterised in the solid state using the X-ray diffraction method. The use of both ligands in the design of coordination networks, in particular of the helical type, is currently under investigation.

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16. Compound **1**: a dry DMF solution (100 ml) containing both compound **3**[14] (216 mg, 0.365 mmol) and **5**[17] (250 mg, 0.731 mmol) was added dropwise (74 h) to a dry DMF suspension (100 ml) of Cs_2CO_3 (2.85 g, 8.76 mmol) at 55°C. The reaction mixture was further stirred at rt overnight before it was filtered and the solvent removed under vacuum. The brownish residue thus obtained was washed with MeOH and the brown solid was dissolved in CH_2Cl_2 (200 ml) and filtered. The filtrate was evaporated to dryness and the residue was purified by column chromatography (Al_2O_3; CH_2Cl_2/MeOH: 97/3 then 95/5) affording the pure compound **1** (30 mg, 9% yield) as a white powder. ^{1}H NMR ($CDCl_3$, 300 MHz, 25°C) δ (ppm): 0.80 (s, 12H, *CH*$_3$), 2.03 (s, 24H, *CH*$_3$), 3.71 (s, 8H, Ar–*CH*$_2$–Ar), 4.90 (s, 8H, –*CH*$_2$–O–), 7.17 (s, 4H, *CH*), 7.59 (d, J=4.9 Hz, 4H, *CH*), 8.77 (d, J=4.9 Hz, 4H, *CH*); ^{13}C NMR ($CDCl_3$, 75 MHz, 25°C) δ (ppm): 14.96, 17.13, 33.78, 74.90, 121.54, 125.88, 126.47, 131.14, 138.05, 145.80, 150.32, 152.27, 154.66; % calcd for $C_{64}H_{64}N_4O_4.5H_2O$: C, 73.68; H, 7.14; found: C, 73.57; H, 7.04.
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18. Compound **7**: a solution of the commercially available compound **6** (500 mg, 1.4 mmol) in abs. MeOH (50 ml) was refluxed in the presence of conc. H_2SO_4 (1 ml) for four days. The reaction mixture was then poured into H_2O (50 ml) and basified to pH 8–9 by addition of a solution of NaOH before it was extracted with CH_2Cl_2 (3×50 ml). The organic layer was isolated and dried ($MgSO_4$) before the solvent was removed affording the compound **7** (478 mg, 89% yield) as a white powder. ^{1}H NMR ($CDCl_3$, 500 MHz, 25°C) δ (ppm): 4.13 (s, 6H, *CH*$_3$), 7.70 (dt, J=1.5 and 8.4 Hz, 2H, *CH*–Ar), 7.82 (dt, J=1.5 and 8.4 Hz, 2H, *CH*–Ar), 8.32 (d, J=8.4 Hz, 2H, *CH*–Ar), 8.81 (d, J=8.4 Hz, 2H, *CH*–Ar), 9.32 (s, 2H, *CH*); ^{13}C NMR ($CDCl_3$, 125 MHz, 25°C) δ (ppm): 52.77, 120.45, 125.31, 125.62, 128.73, 129.97, 130.52, 135.87, 148.83, 154.93, 166.88. Compound **8**: to a suspension of compound **7** (1.01 g, 2.73 mmol) in dry EtOH (65 ml), $NaBH_4$ (2.45 g, 64.8 mmol) was added and the mixture refluxed for 5 h. After allowing the mixture to reach rt, the excess $NaBH_4$ was neutralised with a saturated NH_4Cl solution (50 ml) before the solvents were removed under vacuum. The residue was further dried before the desired compound **8** was extracted (soxhlet) into ethyl acetate, which was dried ($MgSO_4$) and evaporated leaving the pure

compound **8** (0.74 g, 86% yield) as a white powder. ^{1}H NMR (CD_3OD, 300 MHz, 25°C) δ (ppm): 5.31 (s, 4H, *CH*$_2$OH), 7.70 (dt, $J=1.5$ and 8.4 Hz, 2H, *CH*–Ar), 7.86 (dt, $J=1.5$ and 8.4 Hz, 2H, *CH*–Ar), 8.16 (d, $J=8.4$ Hz, 2H, *CH*–Ar), 8.26 (d, $J=8.4$ Hz, 2H, *CH*–Ar), 8.89 (s, 2H, *CH*); ^{13}C NMR (d^6-DMSO, 75 MHz, 25°C) δ (ppm): 60.09, 115.68, 123.36, 125.72, 126.88, 129.40, 129.85, 147.08, 148.58, 155.43; % calcd for $C_{22}H_{16}N_2O_4$: C, 75.93; H, 5.10; N, 8.85; found: C, 75.88; H, 5.21; N, 8.39. Compound **9**: a suspension of compound **8** (739 mg, 2.33 mmol) in 33% HBr in acetic acid (75 ml) was heated to 60°C for 20 h. After the mixture was allowed to cool to rt, the suspension was filtered, washed with acetic acid and ether affording a yellow solid which was suspended in H_2O (150 ml) and then CH_2Cl_2 (200 ml) was added and the mixture basified to pH 11–12 using a K_2CO_3 solution. The organic layer was isolated and evaporated to dryness affording the compound **9** (709 mg, 69% yield) as a slightly yellowish powder. ^{1}H NMR ($CDCl_3$, 300 MHz, 25°C) δ (ppm): 5.01 (s, 4H, *CH*$_2$Br), 7.2 (dt, $J=1.5$ and 8.4 Hz, 2H, *CH*–Ar), 7.3 (dt, $J=1.5$ and 8.4 Hz, 2H, *CH*–Ar), 8.2 (d, $J=8.4$ Hz, 2H, *CH*–Ar), 8.3 (d, $J=8.4$ Hz, 2H, *CH*–Ar), 8.9 (s, 2H, *CH*); ^{13}C NMR (d^6-DMSO, 50 MHz, 25°C) δ (ppm); 29.67, 119.19, 124.20, 125.81, 127.77, 129.91, 130.44, 144.46, 147.55, 154.62. Compound **2**: a dry DMF solution (100 ml) containing both compound **3** (135 mg, 0.228 mmol) and **9** (200 mg, 0.456 mmol) was added dropwise (120 h) to a dry DMF suspension (100 ml) of Cs_2CO_3 (1.7 g, 5.22 mmol) at 55°C. The reaction mixture was further stirred at rt for three days before it was filtered and the solvent removed under vacuum. The brownish residue thus obtained was washed with MeOH and the brown solid was suspended in CH_2Cl_2 (200 ml) and filtered. The filtrate was evaporated to dryness and the pure compound **2** (50 mg, 19% yield) was obtained as a white solid after crystallisation from a CH_2Cl_2/MeOH mixture. ^{1}H NMR ($CDCl_3$, 300 MHz, 25°C) δ (ppm); 0.97 (s, 12H, *CH*$_3$), 1.60 (s, 24H, *CH*$_3$), 3.49 (s, 8H, Ar–*CH*$_2$–Ar), 5.29 (s, 8H, *CH*$_2$–O–), 7.50 (s, 4H, *CH*), 7.74 (dt, $J=1.5$ and 8.4 Hz, 4H, *CH*), 7.83 (dt, $J=1.5$ and 8.4 Hz, 4H, *CH*), 8.48 (d, $J=8.4$ Hz, 4H, *CH*), 8.52 (d, $J=8.4$ Hz, 4H, *CH*); ^{13}C NMR ($CDCl_3$, 75 MHz, 25°C) δ (ppm): 14.34, 17.16, 33.47, 74.73, 119.18, 124.32, 127.82, 127.95, 129.93, 131.00, 131.70, 131.86, 138.12, 143.39, 148.89, 152.66, 153.66; % calcd for $C_{80}H_{72}N_4O_4\cdot5.5H_20$: C, 76.71; H, 6.68; found: C, 76.43; H, 6.55.

19. X-Ray data for **2**: $C_{80}H_{36}N_4O_4\cdot H_2O\cdot2CH_2Cl_2\cdot4CH_3OH$ (colourless), $M=1433.25$, monoclinic, $a=31.118(1)$, $b=22.199(1)$, $c=11.7830(5)$ Å, $\beta=99.349(5)°$, $U=8031(1)$ Å^3, space group $C12/c1$, $Z=4$, $D_c=1.19$ g cm^{-3}, μ(Mo Kα) $=0.205$ mm^{-1}. Crystal dimensions 0.18×0.07×0.06 mm. Data were measured at 173 K on a kappa CCD diffractometer and the structure was solved by direct methods using OpenMoleN 2.2 and refined anisotropically using absorption corrected data. $R=0.11$, $Rw=0.14$ for 2765. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.