Design, synthesis and structural studies on polynucleating ligands based on atropoisomerism of catechol bearing porphyrins

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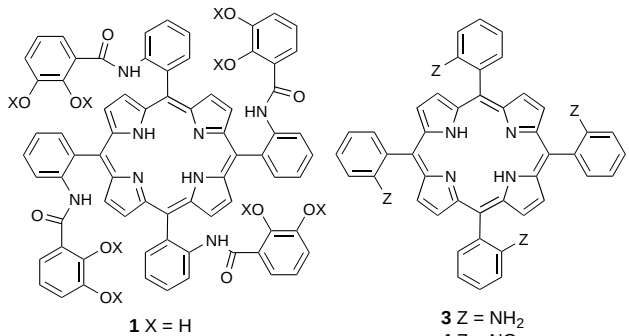
High yield syntheses of all four atropoisomers of the *meso*-tetrakis(*o*-catecholamidophenyl)porphyrin has been achieved; all four atropoisomers were isolated and characterised by NMR spectroscopy; for the methyl protected $2_{\alpha\beta\alpha\beta}$ and $2_{\alpha 4}$ atropoisomers obtained as water and chloroform solvates respectively, X-ray analysis was used to assign their structure.

Porphyrins, used in chemistry, biology, medicine and material science, are among the most fascinating organic molecules. These tetradentate macrocycles bind a large variety of metal cations and exhibit interesting redox as well as photochemical properties. Furthermore their functionalisation either at the β-pyrrolic or *meso* positions has been well established. The porphyrin backbone may be used as a preorganised complexing core for the elaboration of di- and poly-nucleating ligands. Examples of porphyrins bearing neutral bidentate ligands such as bipyridine and phenanthroline have been reported.[1] So far, two examples of porphyrins bearing dianionic bidentate catecholate units have been published.[2,3] Whereas in the first case, two catechols were directly incorporated at the meso positions,[2] in the second example, the porphyrin was functionalised by one to four *m*-catecholamidophenyl units at the *meso* positions.[3] On the other hand, diaza-,[4] triaza- and tetraaza-macrocycles[5] as well as a calix[4]arene derivative[6] bearing pendant catechol units have been also reported.

In our search for polynuclear complexes, we thought that one could take advantage of atropoisomerism,[7] previously elegantly used for the preparation of picket fence porphyrins,[8] for the design of new polynucleating ligands. Thus, the *meso*-tetrakis(*o*-catecholamidophenyl)porphyrin atropoisomers appeared to be interesting targets. Indeed, owing to high rotational barriers, one would expect four atropoisomers designated as



1 X = H
2 X = Me

3 Z = NH_2
4 Z = NO_2

$\mathbf{1}_{\alpha 4}$, $\mathbf{1}_{\alpha 3\beta}$, $\mathbf{1}_{\alpha 2\beta 2}$ and $\mathbf{1}_{\alpha\beta\alpha\beta}$ for the *meso*-tetraphenylporphyrin bearing bulky catecholamido groups at the *ortho* position on the phenyl groups (Fig. 1).

Whereas the $\mathbf{1}_{\alpha 4}$ atropoisomer may lead to heterodinuclear complexes by simultaneous binding of transition and lanthanide cations, the $\mathbf{1}_{\alpha 2\beta 2}$ and $\mathbf{1}_{\alpha\beta\alpha\beta}$ isomers may form homo- or heterotrinuclear species with transition metals. Furthermore, for the $\mathbf{1}_{\alpha\beta\alpha\beta}$ atropoisomer, the formation of infinite coordination polymers with metals adopting octa-coordination around cubic arrangements may also be envisaged. Here, we report the synthesis and structural analysis of the above mentioned ligands.

The synthesis of all four protected atropoisomers $\mathbf{2}_{\alpha 4}$, $\mathbf{2}_{\alpha 3\beta}$, $\mathbf{2}_{\alpha 2\beta 2}$ and $\mathbf{2}_{\alpha\beta\alpha\beta}$ was first achieved by condensation of a statistical mixture of the *meso*-tetrakis(*o*-aminophenyl)-porphyrin **3** isomers with the acyl chloride derivative of the methyl protected catechol[9] in THF in the presence of NEt_3. **3** was obtained as a statistical mixture by reduction of the nitro compound **4** prepared from *ortho*-nitrobenzaldehyde and pyrrole.[8] Although the condensation reaction proceeded quantitatively, the separation of the mixture appeared to be extremely tedious. Indeed, whereas based on TLC analysis [SiO_2, CCl_4–ethyl acetate (1/1)], the separation of atropoisomers could have been straightforward, because of their low solubility, the purification on a preparative silica column yielded, after at least three passages, only small quantities of the pure isomers. The separation of the zinc complexes, obtained by treatment of the mixture by zinc acetate, was as difficult as for the free prophyrin derivatives. Attempts to reach better results using chromatotron or preparative HPLC also failed. An alternative strategy, consisting of the separation of all four atropoisomers of **3**[8] and then condensation with the acyl chloride derivative of the methyl protected catechol, was followed to avoid the purification difficulties mentioned above. In order to minimise the atropoisomerisation, the reactions were carried out at −15 °C in THF and in the presence of NEt_3. Again, the condensation reaction proceeded with almost quantitative yields. After chromatography on silica and crystallisation from $CHCl_3$–ethyl acetate mixtures, the protected atropoisomers $\mathbf{2}_{\alpha\beta\alpha\beta}$ [CH_2Cl_2; CH_2Cl_2–AcOEt (96 : 4); $CHCl_3$], $\mathbf{2}_{\alpha 2\beta 2}$ [CH_2Cl_2; CH_2Cl_2–AcOEt (96 : 4); $CHCl_3$], $\mathbf{2}_{\alpha 3\beta}$ [toluene–$CHCl_3$–MeOH (25 : 5 : 5)] and $\mathbf{2}_{\alpha 4}$ [toluene–$CHCl_3$–AcOEt (25 : 5 : 5)–

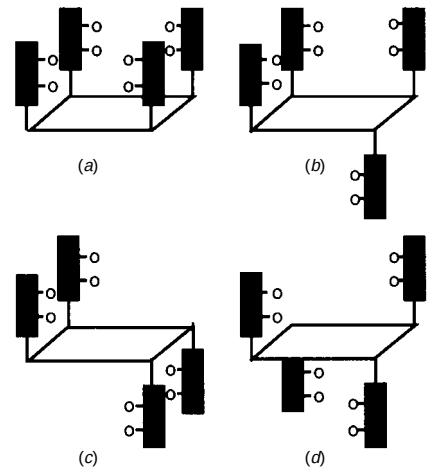


Fig. 1 Schematic representations of α_4 (a), $\alpha_3\beta$ (b), $\alpha_2\beta_2$ (c) and $\alpha\beta\alpha\beta$ (d) atropoisomers of the porphyrins **1**–**4**

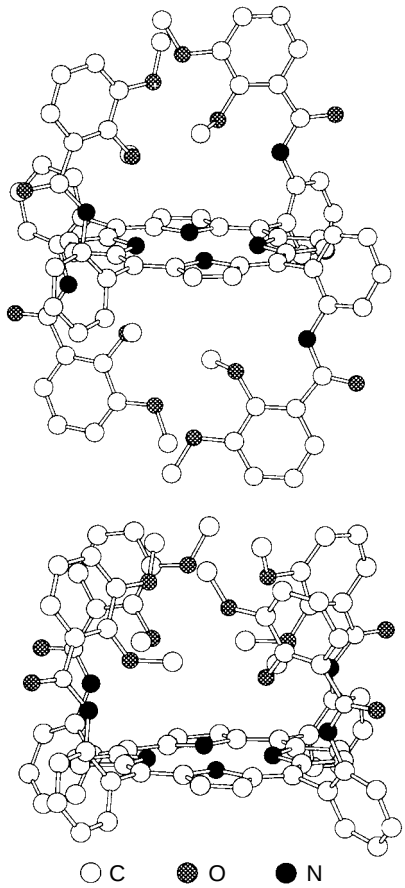


Fig. 2 X-Ray crystal structures of $\mathbf{2}_{\alpha4}$ (top) and $\mathbf{2}_{\alpha\beta\alpha\beta}$ (bottom); solvent molecules as well as H atoms are not shown for clarity. In both cases, the core of the porphyrin was almost planar, the amide groups were in *trans* configuration and the catechol units were found to be oriented in a convergent manner.

(25 : 10 : 5)] could be obtained in 57, 63, 70 and 60% isolated yields, respectively.

Based on symmetry, the ^{1}H NMR signals for $\mathbf{2}_{\alpha3\beta}$ (C_s) could be unambiguously assigned. For the other three $\mathbf{2}_{\alpha4}$ (C_{4v}), $\mathbf{2}_{\alpha\beta\alpha\beta}$ (D_{2d}) and $\mathbf{2}_{\alpha2\beta2}$ (C_{2h}) atropoisomers, only the latter could be identified by the observation of two singlets for the β-pyrrolic protons, whereas for the remaining atropoisomers the assignments could not be achieved without taking into account their polarity. In order to confirm the structural assignment, both $\mathbf{2}_{\alpha4}$ and $\mathbf{2}_{\alpha\beta\alpha\beta}$ atropoisomers were studied by X-ray diffraction (Fig. 2).‡ In both cases, suitable monocrystals were obtained as water and chloroform solvates respectively upon slow liquid–liquid diffusion of MeOH into a chloroform solution of either $\mathbf{2}_{\alpha4}$ or $\mathbf{2}_{\alpha\beta\alpha\beta}$. The X-ray analysis revealed the following common features: (*i*) the core of the porphyrin was almost planar, however, owing to steric reasons, the deformation was slightly greater for $\mathbf{2}_{\alpha4}$; (*ii*) the amide groups were in *trans* configuration with NH hydrogen atoms inwardly oriented towards oxygen atoms belonging to the catechol units and the CO groups oriented in divergent fashion towards the periphery of the porphyrin backbone; (*iii*) both in the case of $\mathbf{2}_{\alpha4}$ for which all four protected catechol units were localised on the same face of the molecule [Fig. 2(top)] and of $\mathbf{2}_{\alpha\beta\alpha\beta}$ for which the two sets of two protected catechols were localised below and above the mean plane of the porphyrin [Fig. 2(bottom)], the catechol units were found to be oriented in a convergent manner. Dealing with the $\mathbf{2}_{\alpha3\beta}$ isomer, although its structure was also established by X-ray analysis which revealed the same common features as for the above two isomers, the data are not reported because of rather low resolution.

The deprotection of $\mathbf{2}_{\alpha4}$, $\mathbf{2}_{\alpha3\beta}$, $\mathbf{2}_{\alpha2\beta2}$ and $\mathbf{2}_{\alpha\beta\alpha\beta}$ atropoisomers at −78 °C using the classical BBr_3–CH_2Cl_2 method[10] afforded the desired compounds $\mathbf{1}_{\alpha4}$, $\mathbf{1}_{\alpha3\beta}$, $\mathbf{1}_{\alpha2\beta2}$ and $\mathbf{1}_{\alpha\beta\alpha\beta}$ as the hydrobromide salts after several precipitations from MeOH–ethyl–ether mixtures. Whereas in the solid state all four atropoisomers were stable, in solution the protonated $\mathbf{1}_{\alpha4}$, $\mathbf{1}_{\alpha3\beta}$ and $\mathbf{1}_{\alpha2\beta2}$ isomers were found to undergo atropoisomerisation. Interestingly, probably due to steric reasons, all three isomers were converted into the lowest energy atropoisomer $\mathbf{1}_{\alpha\beta\alpha\beta}$ under heating at 50 °C for 48 h. This observation is not unprecedented since it has been previously reported for another porphyrin derivative[11] that the protonation of the porphyrin core induces considerable deformation[12] leading to thermal atropoisomerisation.

In summary, high yield syntheses of all four atropoisomers $\mathbf{1}_{\alpha4}$, $\mathbf{1}_{\alpha3\beta}$, $\mathbf{1}_{\alpha2\beta2}$ and $\mathbf{1}_{\alpha\beta\alpha\beta}$ of *meso*-tetrakis(*o*-catecholamidophenyl)porphyrin was achieved and their structures assigned based on X-ray and NMR analysis. Furthermore, it has been established that all three protonated $\mathbf{1}_{\alpha4}$, $\mathbf{1}_{\alpha3\beta}$, $\mathbf{1}_{\alpha2\beta2}$ atropoisomers may be converted into the most stable $\mathbf{1}_{\alpha\beta\alpha\beta}$ isomer upon heating. The formation of the bi- and tri-nuclear complexes using different atropoisomers of **1** with a variety of transition metal cations as well as the formation of coordination polymers are under current investigation.

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Notes and References

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‡ *Crystallographic data*: for $\mathbf{2}_{\alpha4}$ (dark red crystals, 294 K): $C_{80}H_{66}N_8O_{12}\cdot2H_2O$, M = 1367.5, monolcinic, space group $C2/c$, a = 29.447(2), b = 10.672(1) c = 27.067(3) Å, β = 123.449(6), U = 7096(2) Å^3, Z = 4, D_c = 1.28 g cm^{-3}, T = 294 K, μ = 0.083 mm^{-1}, Mo-Kα graphite monochromated radiation, 3111 data with $I > 3\sigma(I)$, R = 0.087, R_w = 0.129. For $\mathbf{2}_{\alpha\beta\alpha\beta}$ (red crystals, 173 K): $C_{80}H_{66}N_8O_{12}\cdot2CHCl_3$, M = 1570.2, triclinic, space group $P\bar{1}$, a = 16.305(5), b = 17.578(5), c = 13.881(4) Å, α = 105.29(2), β = 100.09(2), γ = 98.28(2), U = 3701.7 Å^3, Z = 2, D_c = 1.409 g cm^{-3}, T = 173 K, μ = 2.72 mm^{-1}, Cu-Kα, graphite monochromated radiation, 6342 data with $I > 3\sigma(I)$, R = 0.063, R_w = 0.099. Both structures were solved using OpenMoleN 2.2. CCDC 182/775.

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