Structural characterisation of the first mononuclear bismuth porphyrin

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A single carboxylate picket bismuth porphyrin has been characterised in the solid state as the first instance of a nondimeric structure; the carboxylate picket, bent over the macrocycle, is coordinated to the bismuth, inducing a significant distortion of the porphyrin core.

The coordination chemistry of bismuth with different types of ligands has recently regained interest both at the fundamental and application levels.¹ In the latter case, this can be explained by the 212 and 213 isotope of bismuth that could be applied in α radio-immunotherapy.² Of particular interest among these ligands is the porphyrin core. Indeed, until the early nineties, only two reports of bismuth porphyrins were known in the literature.³ More recently, several studies of new bismuth porphyrins⁴ have been published including the X-ray structure of the metal complexes.⁵ Owing to these solid state structures, the out-of-plane coordination of the bismuth cation was confirmed. Additionally, all the complexes crystallise as dimers with either bridging halide or nitrate ions, or solvents molecules.

In 2000, we reported the synthesis and the characterisation of a bismuth porphyrin bearing four ester pendant arms.⁶ We had designed this new ligand with potentially oxygen-atom donors around the metallic cation. We had chosen an aliphatic and flexible group such as the ethyl succinyl residue to allow an eventual folding of the pickets over the coordination site. Actually, the X-ray structure revealed that the coordination of the ester carbonyl group occurs through the formation of a centrosymmetric dimer and for only one picket. Indeed, the bismuth atom was found to be eight-coordinate with a bidentate nitrato ligand and a water molecule. Thus, it appeared that the three other pickets were not in direct interaction with the bismuth itself.

These observations prompted us to synthesise a related porphyrinoid ligand with only one picket of the same length and flexibility than the previously used motif. On the other hand, we decided to investigate the possible coordination of a carboxylate group in lieu of the ester function. Indeed, this group could eventually represent the counter-anion of the bismuth cation in the porphyrin core and therefore, satisfy its coordination sphere.

The preparation of the succinic acid (SA) picket porphyrin **1Bi** is outlined in Scheme 1. The first step of the synthesis requires the protection of three amino groups of the *meso*(tetra *o*-aminophenyl)porphyrin (atropisomer $\alpha\alpha\alpha\alpha$, TAPP) with acetyl chloride in dry THF. The optimisation of the yield (55%) towards the three-protected porphyrin **2** requires the use of 3 eq. of the acylation reagent and the separation of undesired compounds such as the tetra- and di-acylated porphyrins was performed on a silica-gel chromatography. The remaining amino group was functionalised with 1.1 eq. of ethyl succinyl chloride to obtain **3** (89%) whose ester group was hydrolysed with KOH, leading to **1**.[†] The metal insertion was achieved by heating at 50 °C the free-base porphyrin in pyridine with bismuth nitrate. It is worth noting that the bismuth complex **1Bi** is as stable as its four pickets counterpart 4ESBi(NO₃) previously described.⁶ No demetallation was observed either during the purification process or over long periods of time. We were able to obtain crystals[‡] suitable for X-ray study by diffusion of water onto a solution of **1Bi** in pyridine.

Obviously, as depicted in Fig. 1, the main difference with all bismuth porphyrins reported to date, for which X-ray data were obtained, is the mononuclear structure with the counter-anion delivered by the unique arm of the ligand. Indeed, the two oxygen atoms of the carboxylate group (O4 and O5) bound to the metal centre are stabilised by two hydrogen bonds with the neighbouring nitrogen from the amide linkage, N7 and N8 respectively. The two other coordination sites are occupied by two water molecules (O7 and O8), the bismuth being eight-coordinate and lying 1.145 Å above the N₄ plane. The mean Bi–N bond length is 2.343(2) Å, the same value as 2.340(2) Å in 4ESBi(NO₃).⁶ The two coordinated water molecules are also included in a hydrogen bonding net. The first one, O7 is hydrogen bonded to O5 from the carboxylate group and to N5



Scheme 1 Reagents and conditions: i, CH₃COCl (3 eq.), NEt₃, THF; ii, ClCO(CH₂)₂CO₂Et (1.1 eq.), NEt₃, THF; iii, KOH, EtOH, 55 °C; iv, Bi(NO₃)₃·5H₂O (3 eq.), 50 °C, pyridine.



Fig. 1 ORTEP diagram (30% thermal ellipsoids) of 3Ac1SABi 1Bi.

from an acetamide residue. The second one, O8 is hydrogen bonded to N10 of a solvated pyridine molecule and to another water molecule (O9) itself hydrogen bonded to N6, also from an acetamide residue.

The bismuth atom is coordinated in a distorted antiprismatic geometry as shown in Fig. 2. This distortion is particularly appreciable with the O7-Bi-O8 and O4-Bi-O8 angles which are 76.87 ° and 76.31° respectively, where the O4-Bi-O5 and O5–Bi–O7 are 46.97 $^{\circ}$ and 58.30 $^{\circ}$. It is reasonable to correlate this distortion to the deformation of the porphyrin plane which adopt a "saddle-shaped" and ruffled conformation (Fig. 3).7 To the best of our knowledge, this type of deformation of the macrocycle has never been reported for bismuth porphyrins. Indeed, the carbon atoms in the opposite meso positions (5,15 and 10, 20) are not located in the 24-atom least-squares plane but above or below. More precisely, the deviations (Cm) from the mean porphyrin plane of the four meso carbons are 0.297 Å, -0.150 Å, 0.243 Å and -0.164 Å, leading to an average value of 0.213 Å, smaller than that observed for highly distorted nickel porphyrins.8 Furthermore, the dihedral angles between the two opposite pyrrole planes -e.g. C7–C8 and C17–C18 or C2–C3 and C12–C13 – are 15.5 ° and 12.8 ° respectively. These two major distortions seem to be the result of a too short length of the coordinating arm as the latter has to pull the meso carbon on which it is tethered to be able to coordinate the metal. However, this hypothesis could be simply probed by the substitution of the succinate by the glutarate motif which possesses one more carbon.

In conclusion, this is the second example of a picket porphyrin able to stabilise a metal such as bismuth. We have been able to demonstrate that a suitable group located around the metal can dramatically change the structure – and presumably the properties – of the complex. Thus, in the case of a carboxylate residue, the bismuth does not require an 'external' counter-anion and the complex exhibits a mononuclear structure. On the other hand, the present study reminds us of the importance of the steric factor as revealed by the significant distortion of the porphyrinic core.



Fig. 2 Coordination geometry of bismuth in 1Bi.



Fig. 3 Side view of 1Bi looking along the N2–Bi–N4 axis. For the sake of clarity, the hydrogen bonding net has been omitted.

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Notes and references

[†] Selected data for 3Ac1ES 3: HR-MS (FAB): m/z 929.3763 [(M + H)⁺, 100%]. $\delta_{\rm H}(300 \text{ MHz}, \text{CDCl}_3, 300 \text{ K})$: 8.87 (s, 8H, β -pyr), 8.71 (br s, 4H, aro), 7.8 (br s, 8H, aro), 7.55 (br s, 4H, aro), 6.97 (s, 4H, -NHCO), 3.55 (q, J = 6.4 Hz, 2H, $-CH_2CH_3$), 2.19 (br s, 2H, $-CH_2CH_2$ -), 1.60 (br s, 2H, $-CH_2CH_2-$), 1.30 (br s, 9H, $-CH_3$), 0.87 (t, J = 6.4 Hz, 3H, $-CH_2CH_3$), -2.71 (s, 2H, -NH pyr). For 3Ac1SA 1: HR-MS (ESI): m/z 939.3017 [(M + K)⁺, 100%]. $\delta_{H}(500$ MHz, DMSO-d₆, 298 K): 11.85 (s, 1H, –COOH), 8.81 (br s, 2H, –NHCO), 8.78 (br s, 2H, –NHCO), 8.70 (s, 8H, β-pyr), 8.14 (d, J = 7.5 Hz, 4H, aro), 8.10 (d, J = 7.5 Hz, 2H, aro), 7.94 (d, J = 7.0 Hz, 3.10 Hz, 3.104H, aro), 7.83 (t, J = 8 Hz, 4H, aro), 7.57 (t, J = 6.5 Hz, 4H, aro), 1.99 (t, J = 5 Hz, 2H, -CH₂CH₂-), 1.64 (br s, 2H, -CH₂CH₂-), 1.24 (s, 3H, -CH₃), 1.22 (s, 6H, -CH₃), -2.72 (s, 2H, -NH pyr). For 3Ac1SABi 1Bi: HR-MS (ESI): m/z 1129.2863 [(M + Na)+, 100%].UV-VIS (CH₂Cl₂): λ_{max}/nm (log ε/dm² mol⁻¹cm⁻¹): 350 (4.8), 472 (13.5), 598 (1.7), 646 (1.5). FTIR (of crystals, KBr, cm⁻¹): 1670 (CO); 990 ρ(Bi–Np). δ_H(500 MHz, DMSO-d₆, 300 K): 9.03 (d, J = 4.5 Hz, 2H, β -pyr), 9.03 (d, J = 4.5 Hz, 2H, β -pyr), 8.99 (d, J = 8 Hz, 6H, Pyr), 8.97 (d, J = 5 Hz, 2H, β -pyr), 8.89 (d, J = 5Hz, 2H, β-pyr), 8.72 (br s, 4H, aro), 8.55 (t, J = 7 Hz, 3H, Pyr), 8.33 (br s, 1H, aro), 8.33–8.26 (m, 2H, aro), 8.07 (t, J = 6.6, 1H, aro), 7.99 (t, J = 7.8Hz, 6H, Pyr), 7.90 (m, 3H, aro), 7.73 (br s, 1H, aro), 7.45 (br s, 4H, -NHCO), 7.36 (t, J = 7 Hz, 2H, aro), 7.16 (m, 2H, aro), 1.87 (br s, 2H, -CH₂-), 1.63 (br s, 2H, -CH₂-), 1.49 (s, 9H, -CH₃).

 $Crystal data: C_{54}H_{41}BiN_8O_6 \cdot 3H_2O \cdot 1.5(C_5H_5N): M = 2664.31$, triclinic, space group $P\overline{1}$, a = 12.7605(1), $\overline{b} = 13.8671(2)$, c = 15.7654(2) Å, $\alpha = 15.7654(2)$ Å, $\alpha = 15.7654(2)$ 78.693(1), $\beta = 89.696(1)$, $\gamma = 77.096(1)^{\circ}$, V = 2664.31(6) Å³, Z = 2, $D_x = 1.595$ Mg m⁻³, λ (MoK α) = 0.71073 Å, $\mu = 33.79$ cm⁻¹, F(000) = 1290, T = 120 K. The sample (0.32*0.32*0.12 mm) is studied on a NONIUS Kappa CCD with graphite monochromatized MoKa radiation. The cell parameters are obtained with Denzo and Scalepack9 with 10 frames (psi rotation : 1° per frame). The data collection (Nonius, 1999) ($2\theta_{max}$ = 60°, 310 frames via 2.0° omega rotation and 30 s per frame, range HKL : H 0,16 K -18,18 L -20,20) gives 71226 reflections. The data reduction with Denzo and Scalepack9 leads to 12259 independent reflections from which 11368 with $I > 2.0\sigma(I)$. The structure was solved with SIR-2002¹⁰ which reveals the non hydrogen atoms of structure. After anisotropic refinement, many hydrogen atoms may be found with a Fourier Difference. The whole structure was refined with SHELXH¹¹ by the full-matrix least-square techniques (use of F square magnitude; x, y, z, β_{ij} for Bi, O, N and C atoms, x, y, z in riding mode for H atoms; 707 variables and 11368 observations with $I > 2.0\sigma(I)$; calc w = $1/[\sigma^2 (Fo^2) + (0.036P)^2 + 6.55P]$ where P = (Fo²) $+ 2Fc^{2}$ /3 with the resulting R = 0.033, $R_{w} = 0.082$ and $S_{w} = 1.077$, $\Delta \rho < 0.082$ 2.17 eÅ-3. Atomic scattering factors from International Tables for X-ray Crystallography.¹² Ortep views created with POV-Ray. CCDC 215678. See http://www.rsc.org/suppdata/cc/b3/b309615g/ for crystallographic data in .cif or other electronic format

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