First structural characterization of a covalently bonded porphyrin–carborane system

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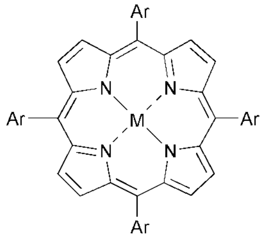
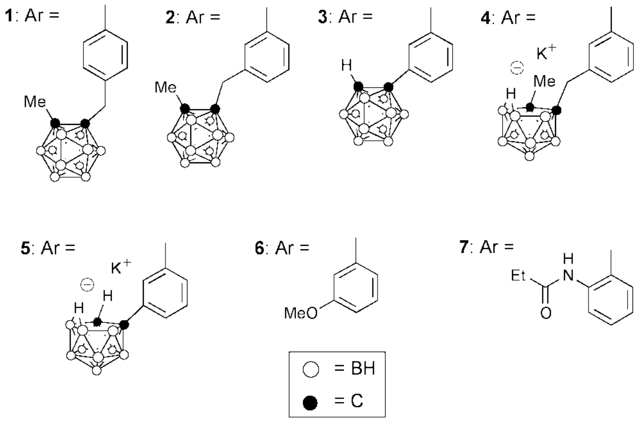
The first definitive crystal structure of a covalently bonded carborane–porphyrin system is reported; unusual inter- and intra-molecular carborane–porphyrin interactions are observed in the molecular structure and in variable temperature ^{1}H NMR experiments.

In the past few decades, porphyrins have assumed broad importance in applications as diverse as medicine,[1,2] catalysis,[3] and molecular electronics.[4,5] Many of these novel applications have employed 5,10,15,20-tetraarylporphyrins as the substrate because this type of porphyrin platform can be readily synthesized.[6] Recently, carboranyl-substituted tetraarylporphyrins have been identified as useful agents in boron neutron capture therapy (BNCT) of cancer because of their ability to localize in tumors, and their high boron content.[7,8] However, to date, carboranyl-substituted tetraarylporphyrins have not been well-characterized and it is not known if the large carborane substituent confers any novel structural or spectroscopic properties on these porphyrins. Herein, we present the first crystal structure of a carboranylporphyrin [**1** (M = Zn)] and detailed proton NMR studies of several carboranyl-substituted tetraphenylporphyrins (**2**–**5**) which demonstrate unusual interactions between the carborane group and the porphyrin macrocycle.



M = 2H, Zn, Ni



Several *m*- and *p*-carboranylarylporphyrins were synthesized in order to investigate structure–activity relationships in BNCT.[9] Insertion of zinc and nickel using normal procedures ($ZnCl_2$ in THF–CH_2Cl_2 1:10 or Ni(II) acetylacetonate in toluene) produced the corresponding metallo-carboranylporphyrins. Repeated attempts to grow X-ray quality crystals of these compounds were unsuccessful until the *para*-substituted porphyrin **1** (M = Zn) was crystallized and the structure determined.† The molecular structure of **1** (M = Zn), the first definitive crystallographic investigation for a covalently bonded porphyrin–carborane molecule, is shown in Figs. 1 and 2.‡[10]

The porphyrin macrocycle exhibits a non-planar waved conformation[11] (Fig. 2) with a mean deviation of the 24 macrocycle atoms from their least-squares plane of 0.062 Å. The Zn–N bond lengths of 2.062(2) Å are within the range typically seen for zinc porphyrins.[12] An unusual feature of the structure is the close intermolecular contacts between the BH hydrogens of one porphyrin and the zinc atom of another; this produces a *pseudo-hexacoordinate* zinc complex (Fig. 2). Zinc

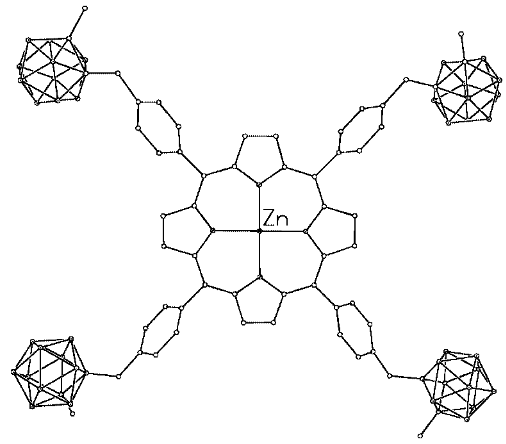


Fig. 1 The molecular structure of **1** (M = Zn). Hydrogen atoms have been omitted for clarity.

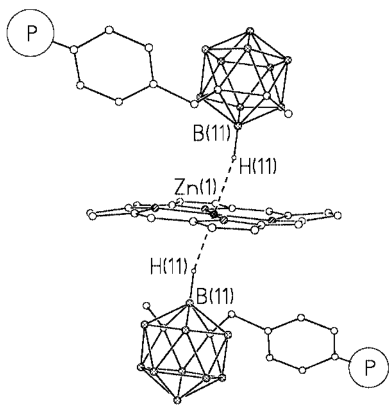


Fig. 2 View of the crystal structure of **1** (M = Zn) showing the waved porphyrin macrocycle and *pseudo-hexacoordinate* zinc(II) ion. Hydrogen atoms, except for the two involved in the B(11)–H(11)···Zn1···H(11)–B(11) bridge, and methylcarboranylphenyl substituents attached to the illustrated porphyrin macrocycle have been omitted (P = porphyrinyl).

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Table 1 Activation energies ($\Delta G^{\ddagger}$; kJ mol^{-1}) for aryl–porphyrin rotation in porphyrins **2**–**7**^{a}

Porphyrin	M = 2H	M = Zn	M = Ni
2	72 (313 K)^{b}	80 (368 K)	
3	72 (323 K)	79 (348 K)	55 (243 K)
4	73 (323 K)	79 (353 K)	
5	71 (323 K)	76 (338 K)	54 (258 K)
6	45[16]		
7	122[15]	131[15]	108[15]
Δ (**7**–**3**)^{c}	50	52	53

^{a} Proton NMR spectra were measured at 400 MHz using $CDCl_3$ [**2** (M = 2H) and **3** (M = 2H, Ni)], $C_6D_5CD_3$ [**2** and **3** (M = Zn)], CD_3COCD_3 [**4** (M = 2H) and **5** (M = 2H, Ni)] or CD_3SOCD_3 [**4** and **5** (M = Zn)] as solvent. ^{b} Activation energies for aryl–porphyrin rotation in porphyrins **2**–**5** were calculated at the coalescence temperatures which are given in parentheses. ^{c} Difference in activation energies for aryl–porphyrin rotation in porphyrins **7** and **3**.

porphyrin structures are generally either four-coordinate or contain one or two axial ligands bound *via* a lone pair from nitrogen or oxygen.[12] The hydrogen atom positions were treated with a riding model which afforded Zn(1)···H(11)–B(11) distances of 2.09 and 1.12 Å [when H(11) was freely refined the bond distances 2.16 and 1.06 Å were obtained]. An examination of the more than 250 zinc porphyrin crystal structures in the Cambridge Structural Database did not reveal any examples of axial ligands coordinating *via* a hydrogen atom, so this appears to be the first example of this type of bonding. There were however, two reported crystal structures that are similar enough to be mentioned; firstly, the structure of [Fe(III)TPP]·[$(CB_{11}H_{12})^-$][13] shows the $(CB_{11}H_{12})^-$ anion co-ordinated to the Fe(III) ion *via* one of its hydrogen atoms, with Fe···H–B distances of 1.82 and 1.25 Å. Secondly, the structure of $[(C_6H_5)_3P]_3Rh(CB_{10}H_{10}C–C_6H_5)$[14] exhibits a Rh···H–B bridge with a Rh–H distance of 2.06 Å. We believe that the unusual interaction between the carborane and the zinc ion in **1** (M = Zn) is probably a result of the electronic properties of the carborane cages combined with an efficient cell packing of this structural motif.

The ^{1}H NMR spectrum of the *para*-substituted carboranylporphyrin **1** (M = 2H) showed a singlet (8.85 ppm) for the pyrrole protons and two doublets (7.59 and 8.20 ppm, J = 8.0 Hz) for the *ortho* and *meta* phenyl protons, consistent with the fourfold symmetry expected for this molecule. In contrast, the ^{1}H NMR spectra of the *meta*-substituted carboranylporphyrins **2** and **3** (M = 2H) and the open cage species **4** and **5** (M = 2H) showed multiple signals for the pyrrole protons consistent with the presence of atropisomers (due to restricted rotation about the aryl–porphyrin bond).[15] *meta*-Substituted tetraarylporphyrins [*e.g.* **6** (M = 2H)][16] normally show fast exchange between atropisomers at rt. The presence of multiple β-pyrrolic signals for porphyrins **2**–**5** (M = 2H) at rt thus suggests that the barriers for aryl rotation in these compounds are markedly increased by the carborane substituents. This suggestion was confirmed by variable temperature ^{1}H NMR studies, which showed that the activation energies for aryl rotation in porphyrins **2**–**5** (M = 2H) were intermediate between those of porphyrins with *meta*-substituents [*e.g.* **6** (M = 2H)] and porphyrins with *ortho*-substituents [*e.g.* **7** (M = 2H)] (Table 1).

Proof that aryl–porphyrin rotation was the dynamic process being observed was obtained by varying the core substituent M, which is known to modulate the rotational barriers in *ortho*-substituted porphyrins such as **7**.[15] The activation energies determined for the dynamic processes in porphyrins **2**–**5** showed a similar response to the incorporation of zinc or nickel into the porphyrin core (Table 1). Interestingly, no significant difference in the aryl–porphyrin rotational barriers was seen for the *o*-carboranes (**2** and **3**) *vs.* the anionic *nido*-carboranes (**4** and **5**) nor for the porphyrins with methylene bridges between the carborane and aryl groups (**2** and **4**) and those without bridges (**3** and **5**). No attempt was made to physically separate the atropisomers given the short lifetimes calculated from the activation energies in Table 1.

In summary, the present work provides evidence of novel carborane–porphyrin inter- and intra-molecular interactions that can be related to the unusual size and electronic properties of the carborane group.

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Notes and references

† Crystals were grown by slow diffusion of MeOH into a chlorobenzene solution of **1** (M = Zn) [$C_{60}H_{84.8}B_{40}N_4Zn_{0.6}\cdot(C_6H_5Cl)$, FW = 1447.21]. The crystals were found to consist of **1** (M = Zn) and **1** (M = 2H) due to acid catalyzed demetalation. The selected crystal (0.30 × 0.10 × 0.10 mm) had a monoclinic unit cell, space group $P2(1)/c$, with cell dimensions a = 13.3139(5), b = 18.6428(8), c = 15.7642(6) Å, β = 93.9630(10)°, V = 3903.5(3) Å^3, and Z = 2. Data were collected on a Bruker SMART 1000 diffractometer with a sealed tube source [λ(Mo-Kα) = 0.71073 Å] at 90(2) K. A 2θ cutoff of 55° was applied to the data to afford 33815 total reflections of which 8971 were unique and of those 5897 were observed ($I > 2\sigma$) [R_{int} = 0.071, T_{min} = 0.92, T_{max} = 0.97, ρ_{calc} = 1.226 g cm^{-3}, μ = 0.274 mm^{-1}]. The structure was solved by direct methods and refined (based on F^2 using all data) by full matrix least-squares methods with 515 parameters (Bruker SHELXS-97, SHELXL-97). All hydrogen atom positions were refined with a riding model. The occupancy of the zinc atom was determined to be 60% from free variable refinement with fixed isotropic parameter of 0.020 Å. Final R factors were $R1$ = 0.069 (observed data) and w$R2$ = 0.191 (all data). Atomic coordinates, bond lengths and angles, and thermal parameters for **1** (M = Zn) have been deposited at the Cambridge Crystallographic Data Center (CCDC). Any request to the CCDC for this material should quote the full literature citation and reference number 155418. See http://www.rsc.org/suppdata/cc/b1/b100231g/ for crystallographic files in .cif format.

‡ A search of the Cambridge Structural Database did not reveal any structures of carborane-substituted porphyrins. However, a semiquantitative structure (R = 0.25) has been reported.[10]

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