The folded, tetrameric phosph(III)azane macrocycle $[\{P(\mu\text{-}N^tBu)\}_2\{1,4\text{-}(NH)_2C_6H_4\}]_4$

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The tetrameric macrocycle $[\{P(\mu\text{-}N^tBu)\}_2\{1,4\text{-}(NH)_2C_6H_4\}]_4$, obtained from the reaction of the phosphazane dimer $[ClP(\mu\text{-}N^tBu)]_2$ with *p*-phenylenediamine, has an unusual folded conformation in the solid state and contains a roughly tetrahedral arrangement of *endo* N–H groups for the potential coordination of anions.

One of the major challenges in inorganic synthesis is the development of selective and predictable synthetic strategies to broad classes of compounds. For main group elements beyond the second period, this goal is complicated by several factors such as the thermodynamic instability and extreme polarity of bonds, and the possibility of variable oxidation states, geometries and orbital use. In spite of these features, the stability of $P^{III/V}$–N bonds[1] results in extremely diverse families of compounds, many of which are isoelectronic with and closely related to carbon-based relatives.[2] Our interest in this area has concerned the development of synthetic strategies to unusual macrocycles based on P^{III}-N bonded cyclophosph(III)azane arrangements of the type shown in Fig. 1a.[3–5] The formation of macrocycles of this type (as opposed to chain oligomers or polymers) is preorganised by the thermodynamic preference for the *cis* conformation of the P_2N_2 ring units.[3] So far, the vast majority of macrocyclic anion-hosts have been based on carbon.[6] Far less is known about the anion-coordination characteristics of related inorganic macrocycles, having frameworks based on non-carbon atoms.[7] We have shown recently that the incorporation of N–H functionality into cyclophosphazane macrocycles (*e.g.*, the trimer in Fig. 1b) allows these species to behave as novel ('inorganic') anion receptors.[3c]

Earlier reports had suggested that the reactions of cyclophosphazane dimers $[ClP(\mu\text{-}NR)]_2$ with bifunctional organic acids produce mainly monomers ($n = 1$, Fig. 1a).[4] More recent studies, however, showed that larger macrocycles ($n > 1$) can be readily obtained from such reactions, depending on the orientation of the heteroatoms (E) within the organic spacer and the reaction conditions.[5,7,8] The suggestion of a link between these macrocycles and classical organic counterparts was provided by the trimer $[\{P(\mu\text{-}N^tBu)\}_2\{2,5\text{-}(NH)_2C_{10}H_6\}]_3$ (Fig. 1b), whose cone-shaped core and solvent-inclusion properties resemble the behaviour of calixarenes.[8] We report here the synthesis and characterisation of the tetramer $[\{P(\mu\text{-}N^tBu)\}_2\{1,4\text{-}(NH)_2C_6H_4\}]_4$ (**1**), which not only is the largest macrocycle of this type reported but has a unique folded conformation in the solid state, providing the potential for tetrahedral capsulation of anionic guests.

The *in situ* $^{31}P\{^1H\}$ NMR spectrum of the 1 : 1 stoichiometric reaction of $1,4\text{-}(NH_2)_2\text{-}C_6H_4$ with $[ClP(\mu\text{-}N^tBu)]_2$ in thf–toluene in the presence of Et_3N (using a d_6-acetone capillary to obtain a lock) shows the formation of two macrocyclic oligomers. The major product is the tetramer **1** (*ca.* 90%) which is characterised by two singlets at δ 101.2 and 100.3, while the minor oligomer **2** (*ca.* 10%) exhibits two singlets at δ 105.0 and 98.1. In the ^1H-coupled ^{31}P NMR spectrum the resonances at lower chemical shift for each oligomer (*i.e.*, δ 100.3 and 98.1) split into 1 : 1 doublets, with coupling constants which are typical of those for $^2J_{P\text{-}H}$ (37.2 and 36.8Hz). Similar behaviour has been observed for the macrocyclic

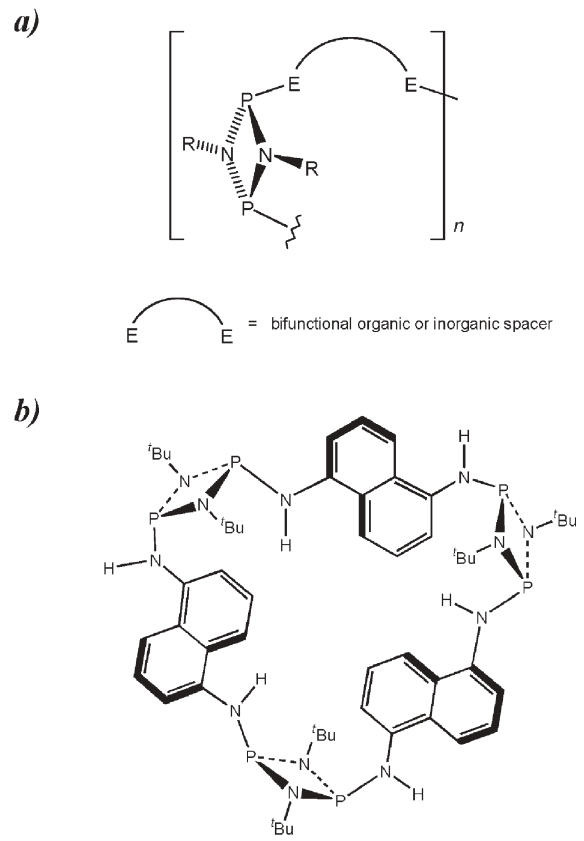

Fig. 1 (a) Connectivity in cyclophosph(III)azane macrocyles. (b) The trimer $[\{P(\mu\text{-}N^tBu)\}_2\{2,5\text{-}(NH)_2C_{10}H_6\}]_3$.

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dimer [{P(μ-N^{t}Bu)}$_2${2,6-(NH)$_2$-C$_5$H$_3$N}]$_2$ [δ 112.3 and 103.3 ($^2J_{P\text{-}H}$ = 34.3Hz)][5b] and for the trimer [{P(μ-N^{t}Bu)}$_2${2,5-(NH)$_2$C$_{10}$H$_6$}]$_3$ [δ 100.2 and 98.7 $^2J_{P\text{-}H}$ = 38.3Hz)],[8] the two ^{31}P resonances arising from the presence of *exo*- and *endo*-N–H groups within the backbones of macrocycles of this type (resulting in the chemical inequivalence of the P atoms of the P_2N_2 ring units). Further evidence of the presence of *exo*- and *endo*-N–H protons is seen in the IR spectrum of solid **1**, which shows two sharp N–H stretching bands at 3365 and 3324 cm^{-1}. Significantly, the highest molecular ion observed in the positive ion electrospray mass spectrum of the crude mixture of **1** and **2** is that for [tetramerH]$^+$ (m/z = 1241.0). Although no high-abundance peaks for the [dimerH]$^+$ or [trimerH$^+$] are found in the spectrum, we conclude from a comparison of the ^{31}P NMR chemical shifts for **2** with those for previously reported oligomers that this species is a lower oligomer (*i.e.*, a dimer or trimer).

Pure **1** can be obtained by extraction of the crude mixture of **1** and **2** with *n*-pentane (in 45% yield).† Crystals of the solvate **1**·{1.5(*n*-pentane)} suitable for X-ray analysis were obtained from a solution of *n*-pentane–toluene. Unfortunately, it has not been possible to obtain pure samples of **2** so far. The ^{1}H NMR spectrum of pure **1** in toluene shows the presence of two distinct *exo*- and *endo*-N–H resonances [at δ 4.42 ($^2J_{P\text{-}H}$ = 5.1Hz) and 4.21 ($^2J_{P\text{-}H}$ = 37.5Hz), respectively]. Warming to 63 °C results in coalescence of the separate N–H and P environments in the ^{1}H and ^{31}P NMR spectra, confirming that the fluxional process involved is that of *exo*-/*endo*-N–H inversion (Fig. 2). The Activation Gibb's Free Energy Change[9] for this process ($\Delta G^{\ddagger}$ = 83 kJ mol^{-1}) is considerably greater than that observed previously in the dimer [{P(μ-N^{t}Bu)}$_2$(OCH$_2$C(Me)$_2$CH$_2$O)]$_2$ ($\Delta G^{\ddagger}$ = 31 kJ mol^{-1}), containing a far more flexible OCH$_2$C(Me)$_2$CH$_2$O linker.[5b] This *exo*-/*endo*-inversion at the N–H centres in **1** should result in large changes in the overall conformation of the tetrameric backbone. Evidence of this is seen from the fact that below the coalescence temperature two major ^{t}Bu environments are found in the ^{1}H NMR in 1 : 1 ratio (δ 1.51 and 1.31), suggesting that the solid-state structure found later for **1** predominates in solution, in which there is a 1 : 1 ratio of *exo*- and *endo*-^{t}Bu groups. Above the coalescence temperature, these resonances merge into a single peak.

Tetrameric macrocyles of **1** have an unusual folded arrangement in the solid state (Fig. 3a).‡ Each of the –NH–C$_6$H$_4$–NH– linkers has one *exo*- and one *endo*-N–H group of the macrocycle with respect to the internal cavity of the molecule, with the N–H groups alternating *exo*,*endo*/*exo*,*endo* (*etc*.) around the ring. This bonding pattern results in the magnetic inequivalence of the two P centres within the *cis*-P_2N_2 ring units of **1**, which are attached to one *exo*- and one *endo*-N–H group respectively, and to the inequivalence of the ^{t}Bu groups, which are aligned *exo*- and *endo*- to the core. Thus,

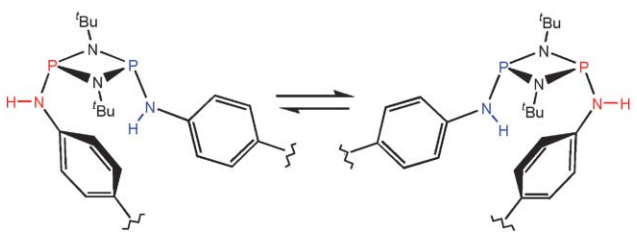

Fig. 2 *Exo*-/*endo*-inversion of the N–H groups of **1** (blue-*endo*, red-*exo*).

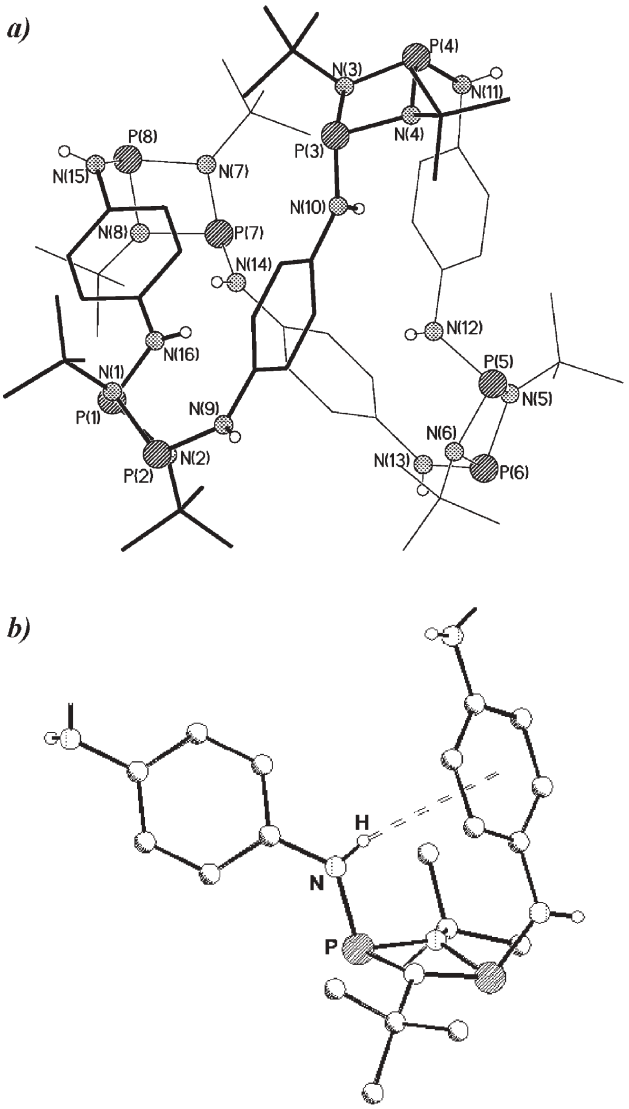

Fig. 3 (a) Folded molecular structure of the macrocyclic tetramer **1**. Selected bond lengths (Å) and angles (°); P-μ-N(-H) range 1.669(3)–1.707(3), P-μ-N^{t}Bu range 1.709(3)–1.727(3), C–N(-H) range 1.399(4)–1.440(4), P-N(H)-C range 122.5(2)–128.6(3), N(^{t}Bu)-P-N(^{t}Bu) range 80.4(1)–81.4(1), P-N(^{t}Bu)-P range 97.8(2)–98.8(1), mean dihedral angle of P_2N_2 folding about N···N mean 12.3; (b) N–H···arene contacts within the units of **1**, H···arene (centroid) 2.53–3.07 (N–H···arene 161.7–169.2) (range H···C 2.68–3.90).

the solid-state structure of **1** is entirely consistent with its solution structure below *ca*. 60 °C. A likely reason for the adoption of this folded structural arrangement and its apparent persistence in solution over a broad temperature range is the presence of relatively short intramolecular N–H$_{endo}$···arene contacts which span the cavity of **1**. The axes of each of the four *endo*-N–H bonds are aligned toward the centre of an adjacent phenyl ring (Fig. 3b). The distances involved [H···arene$_{(centroid)}$ range 2.53–3.07 Å (N–H···arene$_{(centroid)}$ 161.7–169.2°)] are within or significantly lower than the range of values expected for a van der Waal's interaction (2.85–3.15 Å).[10] Indeed, the majority of the H···C(arene) contacts in **1** (overall range 2.68–3.90 Å) are similar to authenticated N–H···arene interactions found in indoles and

porphyrins (range *ca.* 2.21–3.43 Å).[11] Interestingly, it has been proposed that this type of non-classical N–H···arene bonding is the principal factor determining the conformation and potentially the activity of the plant-growth promoter indole-3-acetic acid ('auxin') and its derivatives.[11] In addition, the common occurrence of N–H···arene and related interactions has also been noted in proteins.[12] The structure of **1** provides a unique example, to our knowledge, of a macrocylic species in which intramolecular N–H···arene interactions are implicated as a structure-directing influence. Previous gas-phase, semi-empirical calculations reveal that these interactions can be as strong as *ca.* 12 kJ mol^{-1} each (*i.e.*, up to *ca.* 48 kJ mol^{-1} in **1**).[11]

Overall, the structure of **1** appears to be relatively unstrained, with the angles at the N and P centres within the P_2N_2 ring units being typical of those found in phosph(III)azane dimers. Significantly, unlike the trimer $[\{P(\mu\text{-}N^tBu)\}_2(2,5\text{-}NC_{10}H_6)]_3$ in which the geometries at the *endo*-N(-H) centres exhibit a marked deviation from sp^2 hybridisation [C–N_{endo}(-H)-P mean 133.0°; *cf.* 127.7° for C–N_{exo}(H)-P angle], the angles at the *exo*- and *endo*-N–H centres in **1** are less distorted and are all relatively uniform [range 122.5(2)–128.6(3)°]. These structural features serve to emphasise further the flexible nature of the backbone of the macrocycle, as witnessed in the NMR spectroscopic studies. Bearing in mind the observed flexibility of **1**, there would appear to be a good prospect of coordinating various anions (X) within the cavity *via* N–H···X H-bonding. The four *endo*-N–H centres within its structure form a roughly tetrahedral 'pocket' within the cavity of the molecule, measuring *ca.* 3.44 Å in radius [with respect to the centroid of N(10), N(12), N(14) and N(16)]. Studies of the coordination anion coordination properties of **1** are underway.

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Notes and references

† Synthesis of **1**: To a solution of *p*-phenylenediamine (0.216 g, 2.0 mmol) in thf (30 ml) and Et_3N (1.2 ml, 8.0 mmol, excess) at −78 °C was added dropwise a solution of $[ClP(\mu\text{-}N^tBu)]_2$ (0.550 g, 2.0 mmol) in toluene (40 ml). The mixture was allowed to warm to room temperature and then brought to reflux (16 h). The solvent was removed under vacuum and the residue extracted with *n*-pentane (60 ml) and filtered through Celite (P4). The solvent was removed under vacuum to give an amorphous powder of **1**. Yield 0.28 g, 45%. IR (Nujol, NaCl windows), ν/cm^{-1} = 3365 (m) (N–H str.), 3324(m) (N–H str.), *ca.* 3030(w) (aryl C–H str.), 1097(vs), 1917 (vs), 865 (s), 800(vs). ^{1}H NMR (500.20 MHz, +25 °C, D_8-toluene), δ = 6.96 (mult., 4H, aryl C–H), 4.42 (d, 1 H, $^2J_{P\text{-}H}$ = 5.1 Hz, N–H), 4.21 (d, 1 H, $^2J_{P\text{-}H}$ = 37.5 Hz, N–H), 1.51 (s, major), 1.37 (s, trace) and 1.31 (s, major) (18 H, ^{t}Bu) [coalescence of the NH and ^{t}Bu resonances occurs at *ca.* 330 K]. ^{31}P{^{1}H} NMR (202.48 MHz, +25 °C, D_8-toluene), δ = 102.4 (s), 101.4 (s) [^{1}H-coupled, the resonance splits into a doublet with $^2J_{P\text{-}H}$ = 37.5 Hz] (coalescence occurs at 336 K) ($\Delta G^{\ddagger}$ = 83 kJ mol^{-1}). Electrospray MS (positive ion), m/z = 1241.0 [tetramerH]. Crystals of **1**·{1.5(*n*-C_5H_{12})} were grown from an *n*-pentane–toluene solution at room temperature.

‡ Crystal data for **1**·{1.5(*n*-C_5H_{12})}: $C_{63.50}H_{114}N_{16}P_8$, M = 1349.47, Monoclinic, space group $C2/c$, Z = 8, a = 36.887(7), b = 22.223(4), c = 25.007(5)Å, β = 129.86(3)°, V = 15734(5)Å^3, μ(Mo–Kα) = 0.223 mm^{-1}, ρ_{calc} = 1.139 Mg m^{-3}, T = 180(2) K. Data were collected on a Nonius KappaCCD diffractometer. Of a total of 63538 reflections collected, 13817 were unique (R_{int} = 0.056). The *n*-pentane molecules in the lattice are not well resolved, being located between the molecules of **1** and not impinging on the cavity of the macrocylic units. The structure was solved by direct methods and refined by full-matrix least squares on F^2 (G. M. Sheldrick, *SHELX-97*, Göttingen, Germany, 1997). Final $R1$ = 0.060 [$I>2\sigma(I)$] and $wR2$ = 0.147 (all data). CCDC 279778. See http://dx.doi.org/10.1039/b510636b for crystallographic data in CIF or other electronic format.

1 H. Goldwhite, *Introduction to Phosphorus Chemistry*, Cambridge University Press, 1981, p. 31.
2 N. R. Allcock, *Phosphorus-Nitrogen Compounds*, Academic Press Inc., New York, 1972.
3 For examples of macrocycles based entirely on P–N bonding, see: (*a*) A. Bashall, E. L. Doyle, C. Tubb, S. J. Kidd, M. McPartlin, A. D. Woods and D. S. Wright, *Chem. Commun.*, 2001, 2542; (*b*) A. Bashall, A. D. Bond, E. L. Doyle, F. García, S. Kidd, G. T. Lawson, M. McPartlin, M. C. Parry, A. D. Woods and D. S. Wright, *Chem. Eur. J.*, 2002, **8**, 3377; (*c*) F. García, J. M. Goodman, R. A. Kowenicki, I. Kuzu, M. McPartlin, M. A. Silva, L. Riera, A. D. Woods and D. S. Wright, *Chem. Eur. J.*, 2004, **10**, 6066 (Cl^-, Br^- and I^- coordinated).
4 For simple monomers containing organic linkers, n = 1, see: (*a*) S. S. Kumaravel, S. S. Krishnamurthy, T. S. Cameron and A. Linden, *Inorg. Chem.*, 1988, **27**, 4546; (*b*) M. Vijjulatha, S. Kumaraswamy, K. C. K. Swamy and U. Engelhardt, *Polyhedron*, 1999, **18**, 2557; (*c*) P. Kommana and K. C. K. Swamy, *Inorg. Chem.*, 2000, **39**, 4384.
5 For dimers, n = 2, containing organic linkers, see: (*a*) P. Kommana, K. V. P. P. Kumar and K. C. K. Swamy, *Indian J. Chem.*, 2003, **42A**, 2371; (*b*) F. Garcia, R. A. Kowenicki, I. Kuzu, L. Riera, M. McPartlin and D. S. Wright, *Dalton Trans.*, 2004, 2904.
6 B. Dietrich and M. W. Hosseini, Historical View on the Development of Anion Coordination Chemistry, in *Supramolecular Chemistry of Anions*, ed. A. Bianchi, K. Bowman-James, E. García-España, Wiley-VCH, New York, 1997, ch. 2, p. 45; F. P. Schmidtchen, Artificial Anion Hosts. Concepts for Structure and Guest Binding, in *Supramolecular Chemistry of Anions*, ed. A. Bianchi, K. Bowman-James, E. García-España, Wiley-VCH, New York, 1997, ch. 4, p. 79.
7 For examples, see: M. F. Hawthorne and Z. Zheng, *Acc. Chem. Res.*, 1997, **30**, 267; R. E. Mulvey, *Chem. Commun.*, 2001, 1049.
8 F. Dodds, F. García, R. A. Kowenicki, M. McPartlin, A. Steiner and D. S. Wright, *Chem. Commun.*, 2005, 3733.
9 D. H. Williams and I. Flemming, *Spectoscopic Methods in Organic Chemistry*, McGraw-Hill, London, 1989, p. 103.
10 J. Huheey, E. A. Keiter and R. L. Keiter, *Inorganic Chemistry; Principles of Structure and Reactivity*, 4th edn., Harper-Collins, 1997, p. 292 and references therein.
11 C. S. Page and H. S. Rzepa, N–H···π-Facial Hydrogen Bonding Interactions: A Structural and Theoretical Investigation, *Electronic Conference on Trends in Organic Chemistry (ECTOC-1)*, ed. H. S. Rzepa, J. M. Goodman and C. Leach, Royal Society of Chemistry, Cambridge, UK, 1996, ISBN 0 85404 899 5 (CD-ROM) and references therein.
12 M. Levitt and M. F. Perutz, *J. Mol. Biol.*, 1988, **201**, 751; S. K. Burley and G. A. Petsko, *Science*, 1985, **229**, 23; M. F. Perutz, G. Fermi, D. J. Abraham, C. Poyart and E. Bursaux, *J. Am. Chem. Soc.*, 1986, **108**, 1064; E. Tüchsen and C. Woodward, *Biochemistry*, 1987, **26**, 1918.