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1:1 Molecular Complex Between Water and a Macrocyclic Crown Phosphonamide

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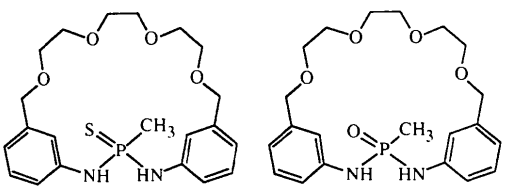
Abstract

The 21-membered macrocycle 3-methyl-11,14,17,20-tetraoxa-2,4-diaza-3-phosphatricyclo[20.3.1.1^{5,9}]heptacosa-1(26),5,7,9(27),22,24-hexaene 3-sulfide and water form a 1:1 inclusion compound, $C_{21}H_{29}N_2O_4PS.H_2O$. The structure reveals host–guest hydrogen bonding with N and O binding sites. One NH$\cdots$OH$_2$ hydrogen bond and close contacts with three consecutive O atoms of the polyether chain maintain the water molecule inside the macrocyclic cavity. The thiophosphoryl group is directed outward and the $-OCH_2CH_2O-$ units adopt the ($ag^{\pm}a$) conformation. The crystal is composed of centrosymmetrically related dimeric units of the complex.

Comment

Water has been proved to interact strongly with crowns in solution and to play an essential role in the solvation processes (Vögtle, Sieger & Müller, 1981; Goldberg, 1984; Grootenhuis *et al.*, 1986; Weber, 1987). Coordination of H_2O molecules to cyclic polyethers involving uncharged NH– or OH– moieties has been observed to form crystalline complexes (Goldberg, 1978; Newkome, Fronczek & Kohli, 1981; Newkome, Taylor *et al.*, 1981; Fuller, Stoddart & Williams, 1982; Bradshaw *et al.*, 1985, 1986; Goldberg & Doxsee, 1986; Weber, Newkome, Fronczek & Franken, 1988; Simonov, Fonari, Ganin, Bocelli & Cantoni, 1996). However, analogous complexes involving phosphoramidic units are rare in the literature (Dutasta, Declercq, Esteban-Calderon & Tinant, 1989; Declercq *et al.*, 1996). The phosphonamide group was introduced in a crown structure in order to increase binding power and selectivity towards various guests. Compound (1) and some of its derivatives are precursors of preorganized ligands that exhibit good binding properties toward metal and ammonium cations (Delangle, Dutasta, Van Oostenryck, Tinant & Declercq, 1996). We have reported the X-ray structures of the phosphorylated (P=O) macrocyclic molecule (2) and its potassium complex (2).KSCN (Van Oostenryck, Tinant, Declercq, Dutasta & Simon, 1993). The crystal structure of the free host (2) did not show inclusion of water molecules. In the complex, the K^+ cation was located inside the macrocyclic cavity and additionally coordinated by P=O of a symmetry-related molecule.



(1) (2)

We report here the X-ray crystal structure of the 1:1 molecular complex formed between thiophosphorylated crown (1) and water (Fig. 1). The macrocyclic phosphonamide (1) was prepared as previously described (Van Oostenryck *et al.*, 1993) and was shown by satisfactory elemental analysis to exist as a monohydrate. This was further supported by the ^{1}H NMR spectrum of (1) in chloroform solution, where the downfield shift of the signal of the water molecule (δ = 2.90 p.p.m.) relative to that of the free guest (δ = 1.56 p.p.m.) indicates the formation of a hydrogen-bonded complex. Interestingly, (2) gave an elemental analysis corresponding to the anhydrous compound in agreement with the crystal analysis (Van Oostenryck *et al.*, 1993). Thus, it was of interest to investigate the solid-state structure of the thiophosphorylated compound (1), the complexing properties of which were expected to be different from those of (2).

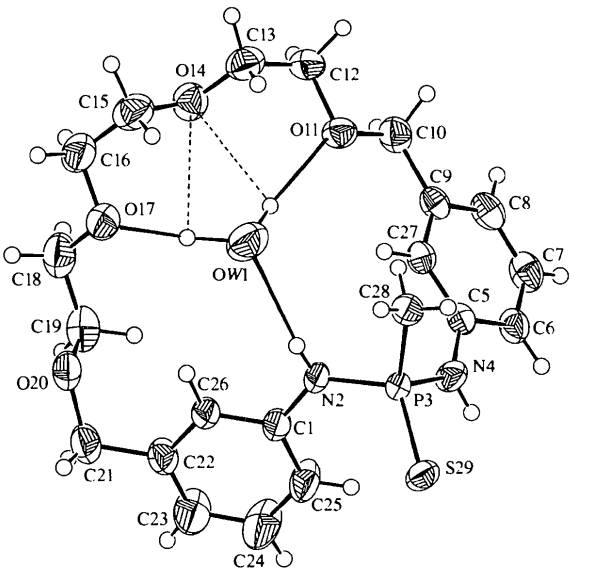


Fig. 1. View of (1).H_2O with the atom labelling. Displacement ellipsoids are shown at the 50% probability level.

The macrocycle has a non-symmetric structure with a well defined cavity occupied by a water molecule (Fig. 1). The heteroatoms of the macrocyclic cavity deviate from the plane defined by all of them as follows: N2 −0.69, N4 0.34, O11 0.32, O14 −0.32, O17 0.01 and O20 0.36 Å. The water molecule is located in the centre of the cavity in a perching position 0.45 Å away from the plane defined by the heteroatoms O11, O14, O17 and N2, which lie in this plane to within 0.38 Å. The guest molecule forms three hydrogen bonds with the O11, O17 and N2 atoms (Table 2). The water O atom interacts with the central ether O14 atom with weaker hydrogen bonds. The remaining heteroatoms are beyond bonding distances (OW···O20 4.38 and OW···N4 4.69 Å).

The polyether fragment adopts the energetically favourable conformation (ag^+a, ag^-a, ag^-a). Comparison of the X-ray crystal structure of (1).H_2O with the recently reported structure of the anhydrous phosphorylated compound (2) shows similarity in the conformation of the polyether chain with the same set of torsion angles. The main difference arises from the phosphorus moiety where the (g^+a) conformation of the N—P—N group in (2) forces the two N—H bonds to be on the same side of the macrocycle, whereas in (1), the (g^-g^-) conformation directs the two N—H bonds in opposite directions. Consequently, in (1), the P=S bond points away from the macrocyclic cavity.

Bond lengths and angles are similar to those determined in other parent compounds. The N atoms are close to planarity. The differences observed between the two N—P=S and C—P—N angles are a consequence of the different conformations around the P—N bonds. Smaller N—P=S or C—P—N bond angles correspond to an *anti* conformation of the S=P—N—C or C—P—N—C dihedral angles. Larger bond angles correspond to *gauche* conformations. The N4 atom is engaged in a weak N—H···S=P intermolecular hydrogen bond between the molecules connected by the symmetry operation ($1-x$, $1-y$, $1-z$), forming a centrosymmetrically related dimeric assembly.

The ability of the thiophosphonamide macrocyclic compound to encircle a water molecule is strongly related to the combination of the NH—P(S)—NH group with a polyether chain and to the inherent structural spacing produced by the aromatic moieties in the macrocycle. This arrangement provides a potential cavity in the macrocyclic structure that allows the water molecule to hydrogen bond perfectly without extensive strong conformational rearrangement. In conclusion, we may state that the thiophosphorylated (1) (P=S) and phosphorylated (2) (P=O) macrocyclic phosphonamides adopt similar conformations with a cavity able to complex cationic or neutral guests. Furthermore, the combination of a phosphonamide group and a polyether chain in a suitable macrocyclic structure provides powerful and complementary hydrogen-bond acceptor and donor binding sites.

Experimental

The preparation and characterization of the macrocyclic phosphonamide (1) has been reported (Van Oostenryck *et al.*, 1993).

Crystal data

$C_{21}H_{29}N_2O_4PS.H_2O$
M_r = 454.52
Triclinic
$P\bar{1}$
a = 10.766 (2) Å
b = 10.825 (2) Å
c = 11.857 (3) Å
α = 71.88 (2)°
β = 63.47 (2)°
γ = 73.18 (2)°
V = 1156.5 (4) Å^3
Z = 2
D_x = 1.305 Mg m^{-3}
D_m not measured
Mo $K\alpha$ radiation
λ = 0.71069 Å
Cell parameters from 17 reflections
θ = 5–15°
μ = 0.243 mm^{-1}
T = 293 (2) K
Parallelepiped
0.28 × 0.20 × 0.16 mm
Colourless

Data collection

Huber four-circle diffractometer
ω scan
Absorption correction: none
5307 measured reflections
5307 independent reflections
3952 reflections with $F > 4\sigma(F)$
θ_{max} = 27.5°
$h = 0 \rightarrow 12$
$k = -13 \rightarrow 14$
$l = -13 \rightarrow 15$
1 standard reflection every 50 reflections
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.050
$wR(F^2)$ = 0.140
S = 1.022
5307 reflections
365 parameters
All H atoms refined
$w = 1/[\sigma^2(F_o^2) + (0.0893P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = −0.006
$\Delta\rho_{max}$ = 0.387 e Å^{-3}
$\Delta\rho_{min}$ = −0.240 e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for Crystallography* (Vol. C)

Table 1. *Selected geometric parameters (Å, °)*

C1—N2	1.407 (3)	P3—C28	1.790 (2)
N2—P3	1.651 (2)	P3—S29	1.9503 (9)
P3—N4	1.659 (2)	N4—C5	1.411 (3)
C1—N2—P3	128.78 (14)	N2—P3—S29	116.25 (8)
N2—P3—N4	110.44 (10)	N4—P3—S29	107.09 (7)
N2—P3—C28	100.99 (11)	C28—P3—S29	114.01 (9)
N4—P3—C28	107.77 (11)	C5—N4—P3	131.51 (15)

Table 2. *Hydrogen-bonding geometry (Å, °)*

D—H···A	D—H	H···A	D···A	D—H···A
N4—H4···S29^i	0.82 (3)	2.83 (3)	3.565 (3)	150 (2)
OW1—HW1···O11	1.07 (3)	2.00 (3)	2.969 (3)	149 (2)
OW1—HW1···O14	1.07 (3)	2.50 (3)	3.008 (3)	107 (2)
OW1—HW2···O14	1.02 (3)	2.58 (3)	3.008 (3)	105 (2)
OW1—HW2···O17	1.02 (3)	2.01 (3)	2.998 (3)	163 (2)
N2—H2···OW1	0.75 (2)	2.29 (3)	2.933 (4)	145 (2)

Symmetry code: (i) $1-x$, $1-y$, $1-z$.

All the H atoms were refined with a common isotropic displacement parameter (U_{iso} = 0.071 Å^2).

Data collection: local program. Cell refinement: local program. Data reduction: local program. Program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993). Molecular graphics: *PLATON* (Spek, 1995). Software used to prepare material for publication: *SHELXL*93.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: JZ1208). Services for accessing these data are described at the back of the journal.

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Out-of-Plane Orientation of the Carbamoyl Group in an NAD Model Compound: Preferred 1,3-Diaxial Methyl Configuration

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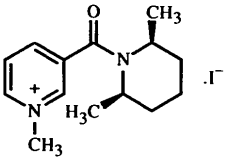
Abstract

The carbamoyl group in 3-(*cis*-2,6-dimethylpiperidinylcarbonyl)-1-methylpyridinium iodide, $C_{14}H_{21}N_2O^+.I^-$, has an out-of-plane orientation in the crystalline state. The planarity of the amide moiety is conserved and the two methyl groups in the piperidine ring are both in axial configurations.

Comment

There has been much argument by chemists and biologists over how the NAD-dependent enzymes discriminate the face of the coenzyme (Fisher, Conn, Vennesland & Westheimer, 1953; Nambiar, Stauffer, Kolodziej & Benner, 1983; You, 1985). There is a fascinating view on understanding this event based on the orientation of the carbamoyl dipole (Donkersloot & Buck, 1981; Okamura, Mikata, Yamazaki, Tsutsumi & Ohno, 1993; Ohno *et al.*, 1994). According to this argument, the carbonyl oxygen plays an important role in determining the reactive face of the coenzyme. A novel NAD model compound, (I), was synthesized having bulky substituents at the amide nitrogen in order to investigate the effect on the carbonyl group. Judging from the HPLC analysis (Daicel Chiralcel OD), the carbamoyl rotation of (I) occurred freely in solution at room temperature, however, the most stable conformation in the crystalline state is an out-of-plane conformation with respect to the carbonyl oxygen orientation, as depicted in Fig. 1. The two methyl groups in the piperidine ring are in the diaxial direction in order to avoid steric repulsion between the pyridine ring and the equatorial methyl group. The planarity of the amide group in the NAD model compound is conserved in spite of the disadvantage of the



(I)