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Acta Cryst. (1995). C**51**, 1919–1921

2,6,6-Trimethyl-2-oxo-1,3-dioxa-6-azonia-2-phosphocyclooctane Iodide

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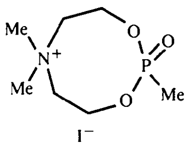
Abstract

The eight-membered ring in the title compound, $C_7H_{17}NO_3P^+.I^-$, has a boat-chair conformation, with the local mirror plane passing through the cyclic O atom and methylene C atom adjacent to the N atom. The P═O bond is pseudo-axial and the P—CH$_3$ bond is pseudo-equatorial. The P—N distance is 3.821 (2) Å.

Comment

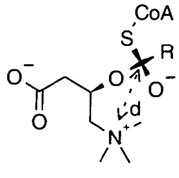
We are interested in the design and synthesis of conformationally restricted reaction-intermediate-analogue inhibitors of carnitine acyltransferases (Gandour *et al.*, 1992). Our inhibitor design suggests that an eight-membered ring would be an excellent match for the putative tetrahedral intermediate in the reactions catalyzed by carnitine acyltransferases. We have produced the title compound, (I), in order to perform the conformational analysis of the eight-membered phosphorus-containing ring.



(I)

Eight-membered phosphorus heterocycles with heteroatoms located in positions 1, 2, 3 and 6 provide interesting models for studying transannular interactions. For example, 2-methyl-2-oxo-6-phenyl-1,3-dioxa-6-aza-2-phosphacynan (Kalinin, Andrianov & Struchkov, 1975) exists in the solid state in the chair-chair or crown conformation and a close contact between the P and N atoms [3.22 Å] indicates a transannular P···N interaction. Another compound, 2-thio-2,6-dimethyl-1,3-dioxa-6-aza-2-phosphacynan (Dutasta, 1980), also exists in the solid state in the crown conformation (Dutasta, Robert & Wiesenfeld, 1980) with a transannular P···N distance shorter than the sum of the van der Waals radii (Piccinni-Leonardi *et al.*, 1986).

Unlike the neutral phosphorus compounds mentioned above, the title compound exists in the solid state in a boat-chair conformation, with the local mirror plane passing through the cyclic O atom and methylene C atom adjacent to the N atom. The P═O bond is pseudo-axial and the P—CH$_3$ bond is pseudo-equatorial.



(II)

In this conformation, the P···N distance [3.821 (2) Å] mimics the distance (d = 3.84 Å) between the tetrahedral C atom and the quaternary N atom of the proposed (Gandour *et al.*, 1992) intermediate, (II), which was calculated by *PCMODEL* (Gajewski & Gilbert, 1992), in the acyl transfer to carnitine. In addition, the N—

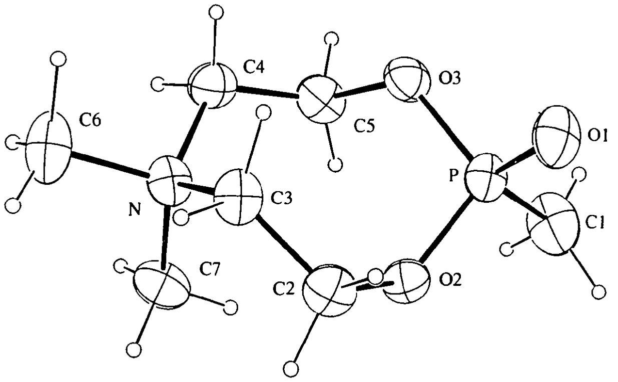


Fig. 1. Plot (*ORTEP*; Johnson, 1965) of the heterocyclic cation. Displacement ellipsoids are drawn at the 40% probability level, with H atoms shown as spheres of arbitrary radii.

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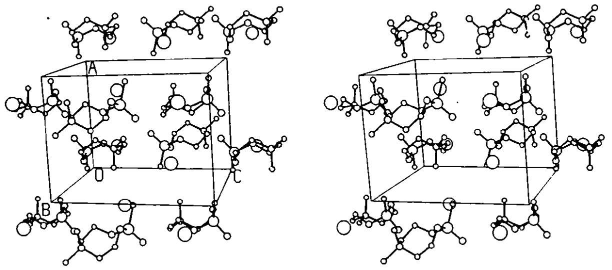

Fig. 2. Stereoview of the unit cell, illustrating the packing of the ions.

C4—C5—O3 torsion angle of −75.9 (3)° in the ring of the title compound is similar to the N⁺—C—C—O torsion angle of −86.2° in (II).

In conclusion, a substituted analogue of this eight-membered phosphorus ring is an appropriate target for the synthesis of new reaction-intermediate-analogue inhibitors of carnitine acyltransferases.

Experimental

The title compound was prepared by the reaction of *N*-methyldiethanolamine with $POCH_3Cl$ in ether in the presence of triethylamine, followed by treatment with CH_3I. Crystals were obtained from methylene chloride and methanol by solvent evaporation (Godovikov, Vikhreva & Kabachnik, 1975).

Crystal data

$C_7H_{17}NO_3P^+.I^-$
$M_r = 321.1$
Monoclinic
$P2_1/c$
$a = 9.0653\ (5)$ Å
$b = 11.1733\ (6)$ Å
$c = 11.8981\ (7)$ Å
$\beta = 91.253\ (5)°$
$V = 1204.9\ (2)$ Å^3
$Z = 4$
$D_x = 1.770$ Mg m^{-3}

Mo $K\alpha$ radiation
$\lambda = 0.71073$ Å
Cell parameters from 25 reflections
$\theta = 10–12°$
$\mu = 2.74$ mm^{-1}
$T = 296$ K
Prism
0.65 × 0.38 × 0.20 mm
Colorless

Data collection

Enraf–Nonius CAD-4 diffractometer
ω–2θ scans
Absorption correction: ψ scan (North, Phillips & Mathews, 1968)
$T_{\min} = 0.707$, $T_{\max} = 0.999$
5775 measured reflections
5292 independent reflections

3475 observed reflections $[I > 3\sigma(I)]$
$R_{\rm int} = 0.017$
$\theta_{\max} = 35°$
$h = 0 \rightarrow 14$
$k = 0 \rightarrow 18$
$l = -19 \rightarrow 19$
3 standard reflections
frequency: 166.67 min
intensity decay: 6.8% (linear correction)

Refinement

Refinement on F
$R = 0.033$
$wR = 0.040$
$S = 2.074$

$\Delta\rho_{\max} = 0.99$ e Å^{-3}
$\Delta\rho_{\min} = -0.13$ e Å^{-3}
Extinction correction: $(1 + gI_c)^{-1}$ applied to F_c

3475 reflections
187 parameters
All H-atom parameters refined
$w = 4F_o^2/[\sigma^2(I) + (0.02F_o^2)^2]$
$(\Delta/\sigma)_{\max} = 0.01$

Extinction coefficient: $g = 2.8\ (3) \times 10^{-7}$
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters* (Å^2)

$$B_{\rm eq} = (8\pi^2/3)\Sigma_i\Sigma_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	$B_{\rm eq}$
I	0.20062 (2)	0.55435 (2)	0.67483 (2)	4.369 (4)
P	0.25017 (6)	0.13586 (6)	0.56056 (5)	2.85 (1)
O1	0.3622 (2)	0.1581 (2)	0.4765 (1)	3.94 (4)
O2	0.2003 (2)	0.0019 (2)	0.5784 (1)	3.12 (3)
O3	0.3150 (2)	0.1761 (2)	0.6790 (1)	3.30 (3)
N	0.3335 (2)	−0.0722 (2)	0.8088 (2)	2.95 (3)
C1	0.0775 (3)	0.2060 (3)	0.5371 (3)	4.87 (6)
C2	0.3048 (3)	−0.0945 (2)	0.5921 (2)	3.44 (4)
C3	0.4052 (2)	−0.0872 (2)	0.6945 (2)	3.14 (4)
C4	0.3347 (3)	0.0568 (2)	0.8487 (2)	3.39 (4)
C5	0.2439 (3)	0.1450 (2)	0.7824 (2)	3.39 (4)
C6	0.4288 (3)	−0.1408 (3)	0.8926 (2)	4.61 (6)
C7	0.1812 (3)	−0.1231 (2)	0.8124 (2)	3.75 (5)

Table 2. *Selected geometric parameters* (Å, °)

P—O1	1.462 (2)	N—C3	1.529 (3)
P—O2	1.579 (2)	N—C4	1.518 (3)
P—O3	1.580 (2)	N—C6	1.513 (3)
P—C1	1.767 (3)	N—C7	1.494 (3)
O2—C2	1.442 (3)	C2—C3	1.507 (3)
O3—C5	1.444 (3)	C4—C5	1.497 (3)
O1—P—O2	117.3 (1)	C3—N—C6	106.4 (2)
O1—P—O3	108.1 (1)	C3—N—C7	113.2 (2)
O1—P—C1	116.3 (1)	C4—N—C6	106.0 (2)
O2—P—O3	104.56 (9)	C4—N—C7	110.7 (2)
O2—P—C1	100.7 (1)	C6—N—C7	107.7 (2)
O3—P—C1	109.0 (1)	O2—C2—C3	115.7 (2)
P—O2—C2	122.3 (1)	N—C3—C2	117.7 (2)
P—O3—C5	121.9 (1)	N—C4—C5	117.4 (2)
C3—N—C4	112.5 (2)	O3—C5—C4	110.9 (2)
O3—P—O2—C2	−72.0 (2)	C4—N—C3—C2	−98.9 (3)
O2—P—O3—C5	−42.1 (2)	C3—N—C4—C5	66.1 (3)
P—O2—C2—C3	63.2 (3)	O2—C2—C3—N	53.5 (3)
P—O3—C5—C4	111.0 (2)	N—C4—C5—O3	−75.9 (3)

The crystal was sealed in a capillary for data collection. It was colorless at the beginning of the experiment and had turned yellow by the end. Calculations were carried out using the Enraf–Nonius *SDP* programs (Frenz & Okaya, 1980). Molecular graphics were obtained using *ORTEP* (Johnson, 1965).

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: BK1019). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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3,4-Di-*O*-acetyl-2,5-anhydro-1,6-di-*O*-(*p*-tolylsulfonyl)-D-mannitol

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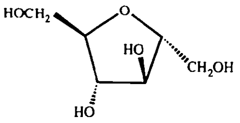
Abstract

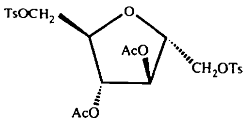
The title compound, 2,5-bis(4-methylphenylsulfonyloxymethyl)oxolane-3,4-diyl diacetate, $C_{24}H_{28}O_{11}S_2$, lies on a crystallographic twofold axis. It adopts a perfect twist ^3_4T conformation in the solid state. The puckering parameters of the tetrahydrofuran ring are $q = 0.32\,(8)$ Å and $\varphi = 92.3\,(5)°$. The acetyl groups are planar, with the non-H atoms deviating less than 0.002 (3) Å from their mean plane. They have an (*S*)-*cis* conformation with the C—O and C=O bonds eclipsed, and each acetyl group is orientated with the C=O group syndiaxial to the C—H bond at the ring C atom to which the group is attached.

Comment

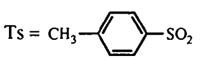
We have utilized structurally locked fructofuranose analogs to establish the anomeric specificity of the active and regulatory sites of phosphofructokinase and certain other enzymes (Younathan, Voll & Koerner, 1981). We have also reported that 2,5-anhydro-D-mannitol, (1), lowers blood sugar in both normal and experimentally diabetic rats (Hanson, Ho, Wiseberg, Simpson, Younathan & Blair, 1984). As part of our study on the biological effects of analogs of 2,5-anhydro-D-mannitol, we have synthesized a variety of 2,5-anhydro-D-mannitol derivatives. Interestingly, we have discovered that some of these derivatives may adopt different conformations in the solid state from those adopted in solution (Shalaby, Fronczek, Lee & Younathan, 1995).

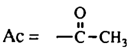


(1)



(2)





$$\mathrm{Ac} = -\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}-\mathrm{CH_3}$$

The title compound, 3,4-di-*O*-acetyl-2,5-anhydro-1,6-di-*O*-(*p*-tolylsulfonyl)-D-mannitol, (2), was found to adopt similar conformations both in the solid state and in solution. The ^{13}C NMR spectrum of (2) in solution shows resonances consistent with C_2 symmetry. The ^{1}H NMR spectrum also shows a high degree of symmetry in solution. Similarly, the X-ray data reveal that the molecule lies on a twofold axis of symmetry; its furanose ring adopts a perfect twist ^3_4T conformation (Cremer & Pople, 1975), with a phase angle (P) of 180° and a pseudorotation amplitude (τ_m) of −28.41° (Altona & Sundaralingam, 1972). The corresponding puckering parameters (Cremer & Pople, 1975) are $q = 0.32\,(8)$ Å and $\varphi = 92.3\,(5)°$.

The C—C bond lengths in the furanose ring, 1.518 (3) and 1.523 (3) Å, are normal, while the ring C—O distance is 1.421 (3) Å. These are in good agreement with the values reported for other carbohydrates (Allen, Kennard, Watson, Brammer, Orpen & Taylor, 1987). Also, the O-atom ring valence angle [111.6 (2)°] is normal and similar to that of 109.7 (2)° found in 2,5-anhydro-D-mannitol (Watkins, Abboud, Voll, Koerner & Younathan, 1983).

The C11—O5 bond length of 1.348 (3) Å agrees well with those found in several peracetylated pentofuranoses (Luger & Paulsen, 1978). The C=O bond length of 1.199 (3) Å is within the range of expected values for the carbonyl group. The acetyl groups have an (*S*)-*cis* conformation with the C—O and C=O bonds eclipsed. This is the conformation most commonly observed in simple esters (Leung & Marchessault, 1974; Shalaby, Fronczek & Younathan, 1994). The acetyl groups are planar, with the non-H atoms deviating by less than 0.002 Å from their mean plane. The acetyl group is oriented with the C=O group syndiaxial to the C—H bond at the ring C atom to which the group is attached (John & Radom, 1977; Oliver & Strickland, 1984). Comparison of the data for the tosyl grouping shows no notable differences from those values observed in the unsymmetrical ditosylated compound, methyl 3,4-anhydro-1,6-di-1,6-*O*-(*p*-tolylsulfonyl)-*β*-D-tagatofuranoside (Guthrie, Jenkins, Yamasaki, Skelton & White, 1981).