Acta Cryst. (1984). C**40**, 357–359

Sodium Salt of the Monomethyl Ester of Fosfomycin, $Na^+.C_4H_8O_4P^-$

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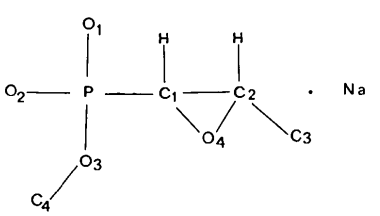
(*Received* 26 *May* 1983; *accepted* 10 *October* 1983)

Abstract. $M_r = 174{\cdot}1$, monoclinic, $P2_1$, $a = 11{\cdot}098$ (4), $b = 10{\cdot}301$ (3), $c = 6{\cdot}448$ (3) Å, $\beta = 96{\cdot}67$ (3)°, $V = 736{\cdot}56$ (1) Å^3, $Z = 4$, $D_x = 1{\cdot}57$ g cm^{-3}, λ(Cu $K\alpha$) = 1·54178 Å, $\mu = 36{\cdot}1$ cm^{-1}, $F(000) = 360$, $T = 295$ K, $R = 0{\cdot}042$ for 1238 Friedel pairs. In the structure of this synthetic monosodium salt of biologically inactive fosfomycin the two crystallographically independent molecules of fosfomycin, having identical configurations, differ drastically in their conformations around the bond between the phosphate and epoxy groups. Both independent Na^+ ions are five-coordinated. In both cases four short Na—O bonds are formed with the O atoms of the phosphate groups, and a longer Na—O bond involves the epoxy O atom of one of the fosfomycin molecules. The structure contains parallel infinite hybrid chains of type $(NaO_2—NaO_3)_n$.

Introduction. Fosfomycin [(1,2-epoxypropyl)phosphonic acid] (Perales & García-Blanco, 1977), a bacterial antibiotic isolated from strains of *Streptomyces* has been shown to be a potent and irreversible inhibitor of pyruvyltransferase (uridinephospho-*N*-acetylglucosamine-3-*O*-enolpyruvyltransferase), in the early steps of the bacterial cell-wall synthesis. The antibiotic is highly polar, optically active and has a low molecular weight. This paper is a part of studies (Perales, Martínez-Ripoll, Fayos, von Carstenn & Fernandez, 1982) to clarify the mechanism of action of fosfomycin. The structure reported here corresponds to a sodium salt of an inactive form of a fosfomycin derivative. Its atomic labelling is shown below.



Experimental. Powder specimen of the compound kindly supplied by Drs Von Carstenn and Fernandez (von Carstenn, Fernandez, Galvez-Ruano & Bellanato, 1982). Single crystals from propanol. Unit-cell dimensions by least-squares fit of 24 θ angles in the range 10–30°. Intensity collection: $\omega/2\theta$ scan, four-circle diffractometer, sample of size 0·10 × 0·15 × 0·30 mm, graphite-monochromated Cu $K\alpha$ radiation. Two reference reflexions monitored every 90 min showed no crystal decomposition or instrumental instability. $R_{int} = 0{\cdot}03$ for 120 merged reflexions. Total of 1324 Friedel pairs alternately collected ($2\theta \leq 130°$), 1238 considered as observed [$I > 2\sigma(I)$] and used in remaining calculations. Absorption effects neglected. Scattering factors for neutral atoms and anomalous-dispersion coefficients from *International Tables for X-ray Crystallography* (1974). Structure partially solved using *MULTAN* (Main *et al.*, 1980). Subsequent Fourier maps revealed the rest of the structure. Positional and anisotropic thermal parameters refined by full-matrix least squares on F, unit weights; $R = 0{\cdot}062$. All H atoms appeared as the most prominent peaks of a difference map and were included in the refinement as fixed isotropic contributors. A convenient weighting scheme (Martínez-Ripoll & Cano, 1975) was used to prevent bias in $\langle w\Delta^2F\rangle$ *vs* $\langle F_o\rangle$ and *vs* $\langle \sin\theta/\lambda\rangle$. The last cycle of refinement, including both hkl and $\bar{h}\bar{k}\bar{l}$ reflexions, gave $R = 0{\cdot}042$, $wR = 0{\cdot}052$ and $S = 3{\cdot}18$ for 180 refined parameters with $(\Delta/\sigma)_{max} = 0{\cdot}22$; final $\Delta\rho$ peaks $\leq |0{\cdot}85|$ e Å^{-3}. The absolute configuration was determined by comparing the 115 more relevant Bijvoet pairs with $\Delta F_c > 0{\cdot}50$. The average Bijvoet difference, $\langle|(|F_o^+|-|F_o^-|)-(|F_c^+|-|F_c^-|)|\rangle$, for the correct enantiomer is 0·535 *vs* 1·469 for the wrong model. Most calculations performed with the XRAY70 system (Stewart, Kundell & Baldwin, 1970).

Discussion. Table 1 shows the final atomic parameters, Table 2 the bond distances and angles.*

A partial perspective drawing of the crystal structure is shown in Fig. 1. The crystallographically independent fosfomycin molecules (labelled *A* and *B*) have identical configurations but differ in their conformations. A comparison of both molecular conformations with that presented by active fosfomycin

* Lists of structure factors, anisotropic thermal parameters and H-atom coordinates have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 38952 (21 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

0108-2701/84/030357-03$01.50

Table 1. *Atomic coordinates* ($\times 10^4$) *and equivalent isotropic thermal parameters* ($Å^2 \times 10^4$)

$U_{eq} = \frac{1}{3}\sum_i\sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j.$

	x	y	z	U_{eq}
P(*A*)	1585 (1)	4289 (3)	4750 (1)	274 (3)
Na(*A*)	292 (2)	1352 (3)	2841 (2)	357 (5)
O(1*A*)	1030 (3)	5600	4913 (5)	352 (9)
O(2*A*)	855 (3)	3111 (4)	5085 (5)	378 (10)
O(3*A*)	2789 (2)	4178 (4)	6354 (4)	400 (9)
O(4*A*)	3271 (3)	4656 (4)	1872 (5)	481 (10)
C(1*A*)	2075 (3)	4190 (5)	2170 (5)	325 (11)
C(2*A*)	2987 (5)	3298 (6)	1483 (8)	443 (15)
C(3*A*)	3675 (7)	2340 (8)	2866 (10)	716 (21)
C(4*A*)	3592 (5)	5274 (7)	6761 (8)	578 (17)
P(*B*)	−1431 (1)	3960 (3)	322 (1)	299 (3)
Na(*B*)	242 (1)	1776 (3)	−2395 (2)	332 (5)
O(1*B*)	−902 (3)	5238 (4)	−114 (4)	381 (9)
O(2*B*)	−692 (3)	2752 (3)	199 (5)	418 (10)
O(3*B*)	−2651 (3)	3857 (4)	−1250 (5)	434 (10)
O(4*B*)	−1714 (3)	5228 (4)	4076 (4)	440 (9)
C(1*B*)	−1904 (3)	4009 (5)	2945 (6)	337 (11)
C(2*B*)	−2934 (4)	4772 (6)	3543 (7)	383 (13)
C(3*B*)	−3742 (5)	5572 (7)	2066 (9)	631 (20)
C(4*B*)	−3320 (7)	2673 (8)	−1429 (12)	840 (27)

Table 2. *Bond distances* (Å) *and angles* (°) *for molecules A and B*

C atoms are denoted by their numbers alone.

	Molecule *A*	Molecule *B*
1–2	1·465 (6)	1·479 (5)
2–3	1·489 (7)	1·490 (6)
1–O(4)	1·444 (5)	1·457 (5)
2–O(4)	1·441 (5)	1·437 (5)
P–1	1·823 (4)	1·841 (4)
P–O(1)	1·494 (3)	1·482 (3)
P–O(2)	1·488 (3)	1·497 (3)
P–O(3)	1·597 (3)	1·601 (3)
O(3)–4	1·440 (6)	1·428 (7)
2–1–O(4)	59·4 (3)	58·6 (2)
1–2–O(4)	59·6 (3)	59·9 (2)
1–O(4)–2	61·1 (3)	61·5 (2)
1–2–3	124·4 (4)	123·5 (4)
O(4)–2–3	117·5 (4)	117·1 (4)
P–1–2	126·7 (3)	125·0 (3)
P–1–O(4)	118·7 (2)	116·7 (3)
1–P–O(1)	106·6 (2)	108·4 (2)
1–P–O(2)	108·2 (2)	106·8 (2)
1–P–O(3)	106·1 (2)	106·2 (2)
O(1)–P–O(2)	119·3 (2)	119·7 (2)
O(1)–P–O(3)	109·8 (2)	105·1 (2)
O(2)–P–O(3)	106·1 (2)	109·9 (2)
P–O(3)–4	121·5 (3)	120·6 (3)

Table 3. *Some significant torsional angles* (°), *for molecules A, B and active fosfomycin* (–)

	Molecule *A*	Molecule *B*	(–)
P–1–2–3	−0·5 (7)	2·0 (6)	1·9 (7)
2–1–P–O(1)	159·4 (3)	70·0 (4)	−91·6 (4)
2–1–P–O(2)	−71·1 (4)	−159·8 (3)	35·6 (5)
2–1–P–O(3)	42·3 (4)	−42·5 (4)	152·1 (4)
1–P–O(3)–[4,H(3)]	77·2 (4)	−73·3 (4)	61 (1)
H(1)–1–2–H(2)	−8 (1)	−10 (1)	0 (1)

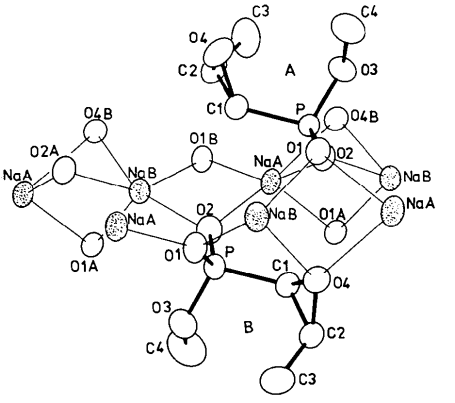


Fig. 1. Packing diagram of the title compound.

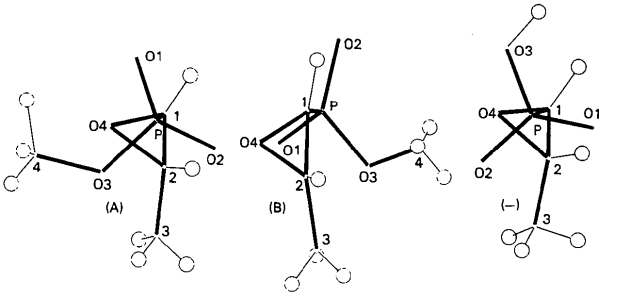


Fig. 2. Comparative view of the conformations of molecules *A*, *B* and active fosfomycin (–).

(Perales & García-Blanco, 1977) is shown in Table 3. Molecules *A* and *B* differ only in the torsional angle around the P–C(1) bond. Fig. 2 shows the different conformations of molecules *A*, *B* and that present in active fosfomycin. The conformations around P–C(1) of molecules *A* and *B* are related by mirror symmetry, with the mirror face defined by the atoms P, C(1) and C(2).

Using CNDO approximations (Quantum Chemistry Program Exchange) the molecular energy of molecule *A* is 9·46 kJ mol^{-1} lower than for molecule *B*. The low-energy molecule *A* has approximately the same conformation as that of active fosfomycin. The dipole moments of molecules *A* and *B* and active fosfomycin have also been calculated with reference to an orthogonal system defined as follows: *xz* on the plane formed by atoms C(1), C(2) and C(3), *z* axis in the sense C(1)–C(2) and *x* axis towards C(3) with the origin on C(1). The components of the dipole moments ($\times 10^{-30}$ Cm) are (−41·4, 0·7, 24·0) for *A*, (−43·0, 14·0, 23·7) for *B* and (−51·7, 10·0, 13·3) for the active molecule.

The Na^+ ions form a somewhat distorted layer perpendicular to the *a* axis (Fig. 1) and connect

Table 4. *Geometrical features around* Na^+ *ions* (Å)

Na(*A*)–O(1*B*)	2·275 (3)	Na(*B*)–O(1*B*)	2·330 (3)
–O(2*B*)	2·403 (3)	–O(2*B*)	2·306 (3)
–O(1*A*)	2·318 (3)	–O(1*A*)	2·362 (3)
–O(2*A*)	2·362 (3)	–O(2*A*)	2·301 (3)
–O(4*B*)	2·666 (3)	–O(4*B*)	2·612 (3)

molecules *A* and *B*. Both independent Na^+ ions are five-coordinated. Four short Na—O bonds are formed (Table 4) with the O atoms of the phosphate groups and build distorted tetrahedral $(NaO_2)_n$ chains. The fifth Na—O bond is ~13% elongated with respect to the other bonds and involves the O(4) atom of the epoxy group of molecule *B* (Fig. 1). Thus, the oxygen polyhedra around the Na^+ ions are actually forming infinite hybrid chains of the type $(NaO_2–NaO_3)_n$ along the *c* axis. This type of infinite chain has not been reported up to now and only a dimer of the type $O_3NaO_2NaO_3$ has been described (Bright, Milburn & Truter, 1971).

Disregarding O(4), the structure has a pseudocentre at $(0,0{\cdot}4,\frac{1}{4})$. This makes the space-group symmetry pseudo $P2_1/c$.

We thank the staff of the CPD of MEC (Spain) for allowing us the use of a Univac 1108 computer. We also thank Professor García-Blanco for his sponsorship.

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Acta Cryst. (1984). C**40**, 359–362

[2,9-Bis(*N*-methylhydrazino)-1,10-phenanthroline]dichlororhodium(III) Tetrafluoroborate Sesquihydrate, $[RhCl_2(C_{14}H_{16}N_6)]BF_4.1{\cdot}5H_2O$

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(*Received* 28 *July* 1983; *accepted* 19 *October* 1983)

Abstract. $M_r = 555{\cdot}98$, triclinic, $P\bar{1}$, $a = 12{\cdot}200$ (2), $b = 13{\cdot}171$ (3), $c = 14{\cdot}259$ (3) Å, $\alpha = 110{\cdot}31$ (2), $\beta = 93{\cdot}90$ (1), $\gamma = 102{\cdot}60$ (2)°, $U = 2071{\cdot}0$ (7) Å^3, $Z = 4$, $D_x = 1{\cdot}783$ Mg m^{-3}, λ(Mo $K\alpha$) = 0·71069 Å, μ(Mo $K\alpha$) = 1·08 mm^{-1}, $F(000) = 1112$, $T = 288$ K, final $R = 0{\cdot}058$ for 4925 unique observed reflections. The asymmetric unit contains two structurally similar mononuclear Rh^{3+} cations and the associated BF_4^- anions; three water molecules are involved in hydrogen bonding with both the cations and the anions. In each cation the Rh atom adopts a distorted octahedral geometry with the two Cl atoms in *trans* axial positions while the four equatorial positions are occupied by four N atoms of the planar hydrazino-phenanthroline ligand.

Introduction. Complexes of the 2,9-bis(*N*-methylhydrazino)-1,10-phenanthroline ligand have been reported previously for the first-row transition metals and for Zn^{II}, Cd^{II} and Hg^{II} (Lewis & O'Donoghue, 1980). In every case the ligand is assumed to be tetradentate *via* the phenanthroline N donors and the terminal $-NH_2$ groups, although there are no crystallographic data available. In an extension of this work a study of the complexes of this ligand with second- and third-row transition metals has been undertaken. The Rh^{III} complex has been obtained in a highly crystalline form, and it was decided to carry out a single-crystal X-ray analysis in order to confirm the molecular geometry and because, to our knowledge, there have been no

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0108-2701/84/030359-04$01.50