C(5)–C(6) is larger than C(10)–C(5)–C(4). Similar differences of about 4° are consistently observed throughout the series (*cf.* Fig. 3*a*).

Third, the fragment C(2)=C(3)–O(11)–C(11) has a nearly ideal synperiplanar conformation and agrees with the *syn* conformation observed by Durig & Compton (1978) in gaseous methyl vinyl ether. Again throughout the series, the valence angles Cl(2)–C(2)=C(3) and C(2)=C(3)–O(11) are extremely large, *viz.* 130 and 135° respectively. Although the parts C(1)–C(2)=C(3)–C(4) and Cl(2)–C(2)=C(3)–O(11) are individually planar, the total arrangement around C(2)=C(3) is slightly bent. The plane Cl(2)C(2)=C(3)O(11) is turned away from C(7) and is at an angle of 7° to the C(1)C(2)=C(3)C(4) plane (Fig. 3*b*).

Again it seems that 1–4 interactions, now between the Cl atoms on the bridge C atoms and the opposed substituent on the C(sp^2) ring C atoms, cause this deviation from planarity. Indeed the torsion angles Cl–C(bridge)–C(sp^2)–substituent are about 20–27° in all three norbornenes of the series which is 4–10° more than they would be in an analogous planar configuration around C(2)=C(3).

All these effects together show that the interaction between substituent and ring system affects the substituent geometry and destroys any local symmetry that intuitively might be expected at the junction.

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The Absolute Configuration of Active and Inactive Fosfomycin

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Abstract. $C_3H_6O_3P^-.C_8H_{12}N^+.H_2O$ (inactive), $P2_1$, a = 11·530 (1), b = 6·1490 (3), c = 10·199 (1) Å, β = 102·76 (1)°, $Z = 2$, D_x = 1·305 Mg m^{-3}. The structure was refined with 1306 observed Friedel pairs to R_{obs} = 0·040 with Cu $K\alpha$ radiation. The X-ray intensities were used to determine the absolute stereochemistry of both enantiomers of fosfomycin. The active form is 1*R*,2*S*, the inactive form being 1*S*,2*R*.

Introduction. Fosfomycin, (–)-(1*R*,2*S*)-(1,2-epoxypropyl)phosphonic acid (Christensen, Leanza, Beattle, Patchett, Arison, Ormond, Kuehl, Albers-Schonberg & Jardetzky, 1969), is now one of the most frequently used antibiotics, because of its effectiveness in inhibiting the growth of various microorganisms (Mastroeni, Nistico, Carbone & Rotiroti, 1980). Experiments have shown that the action of fosfomycin has been identified with the first phase of the bacterial cell-wall synthesis at the stage when the wall component *N*-acetylmuramylpeptide is forming. The enzyme involved is uridinediphospho-*N*-acetylglucosamine-3-*O*-enolpyruvyltransferase, otherwise known as pyruvyltransferase (Kahan, Kahan, Cassidy & Kropp, 1974).

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Table 1. *Atomic parameters for inactive fosfomycin*

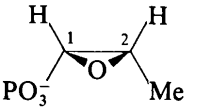
$$U_{eq} = \tfrac{1}{3}\sum_i \sum_j U_{ij} a_i^* a_j^* a_i a_j \cos(a_i a_j).$$

	x	y	z	U_{eq} ($Å^2 \times 10^4$)	Δ (Å)
P	0·88051 (3)	0·74672	0·72612 (4)	284 (1)	0·019 (1)
O(1)	0·9346 (1)	0·8672 (3)	0·8525 (1)	406 (4)	0·015 (3)
O(2)	0·8998 (1)	0·8427 (3)	0·5974 (1)	369 (4)	0·008 (3)
O(3)	0·9256 (1)	0·5052 (2)	0·7341 (1)	431 (4)	0·011 (3)
O(4)	0·6412 (1)	0·6741 (3)	0·6014 (2)	515 (5)	0·017 (4)
O(*W*1)	0·8960 (1)	0·2765 (3)	0·9289 (1)	484 (4)	0·116 (3)
N	0·9300 (1)	0·6723 (3)	0·3591 (1)	330 (4)	0·023 (4)
C(1)	0·7245 (2)	0·7210 (4)	0·7260 (2)	381 (5)	0·069 (6)
C(2)	0·6321 (2)	0·8771 (5)	0·6682 (2)	498 (7)	0·022 (6)
C(3)	0·6518 (2)	1·0801 (5)	0·5981 (3)	655 (9)	0·022 (6)
C(4)	0·8257 (2)	0·5666 (4)	0·2681 (2)	389 (6)	0·011 (4)
C(5)	0·7838 (2)	0·3836 (4)	0·3494 (3)	605 (8)	0·022 (6)
C(6)	0·7324 (1)	0·7344 (4)	0·2109 (2)	373 (5)	0·022 (5)
C(7)	0·6352 (2)	0·7751 (5)	0·2658 (2)	473 (7)	0·015 (5)
C(8)	0·5520 (2)	0·9282 (5)	0·2106 (3)	559 (8)	0·025 (6)
C(9)	0·5644 (2)	1·0428 (5)	0·0986 (3)	598 (8)	0·023 (5)
C(10)	0·6605 (2)	1·0085 (6)	0·0434 (2)	597 (8)	0·023 (6)
C(11)	0·7440 (2)	0·8536 (5)	0·0988 (2)	511 (7)	0·020 (6)

The crystal structure of the inactive enantiomer, fosfomycin(+), as mono-(−)-α-phenethylammonium (+)-*cis*-(1*S*,2*R*)-(1,2-epoxypropyl)phosphonate, has been determined by X-ray diffraction. We have obtained this salt by chemical synthesis, modifying the method of Glamkowski, Gal, Purick, Davidson & Sletzinger (1970). The melting point is 398–399 K (MeOH:AcOH) and the rotatory power is $[\alpha]_D^{25°C} = -19·4°$ (*N*,*N*-dimethylformamide). 1327 Friedel pairs were collected using graphite-monochromated Cu $K\alpha$ radiation up to $\theta = 65°$. 1306 pairs had $I > 2\sigma(I)$ and were used for the refinement of the crystal structure. The unit-cell dimensions, which should be identical to those found for the same salt of active fosfomycin reported by Perales & García-Blanco (1978), differ by less than 0·01 Å and 0·3° from the active form. The starting atomic parameters for the refinement were those of active fosfomycin and convergence was achieved with $R = 0·040$ using a convenient weighting scheme.* Table 1 shows the final parameters of the inactive enantiomer. Although it is accepted that these two sets of parameters should be identical, the atomic displacements between this enantiomer and the active one are also shown in Table 1.

* Lists of structure factors, anisotropic thermal parameters and the H atom parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 36932 (24 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Discussion. The absolute configuration of fosfomycin(+) has been determined by X-ray Cu $K\alpha$ anomalous dispersion using the 147 Bijvoet pairs with $\Delta F_{calc} > 0·5$. Among them, the averaged Bijvoet difference was 0·212 for the 1*S*,2*R* enantiomer against 1·439 for the 1*R*,2*S*, the corresponding averaged Bijvoet ratio being 0·054 compared with 0·378.



Active fosfomycin (−)

On the other hand, the supposed absolute configuration of the active fosfomycin(−) has been confirmed using Cu $K\alpha$ X-ray radiation. For that, the intensities of the 15 Bijvoet pairs with the greatest ΔF_{calc} were measured in all possible equivalent directions. A deposited table shows that the observed ΔF_{obs} were unequivocally consistent with the 1*R*,2*S* enantiomer.

The calculations were carried out with the XRAY 70 system (Stewart, Kundell & Baldwin, 1970).

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