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Structure of Dimethyl 4-*O*-Methyltrioxanoate

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Abstract. (2*R*,3a*S*,4*R*,9b*S*)-Dimethyl 2-dimethoxymethyl-4-methoxy-9-methyl-3a,9b-dihydrospiro(2,4-methano-4*H*-benzo[*b*][1,3]dioxolo[4,5-*d*]pyran-10,2′-oxiran)-6,7-dicarboxylate, $C_{21}H_{24}O_{11}$, $M_r = 452{\cdot}4$, orthorhombic, $P2_12_12_1$, $a = 10{\cdot}333$ (1), $b = 23{\cdot}310$ (3), $c = 9{\cdot}029$ (2) Å, $Z = 4$, $D_x = 1{\cdot}382$ g cm^{-3}, Cu $K\alpha$, $\lambda = 1{\cdot}54184$ Å, $\mu = 9{\cdot}219$ cm^{-1}, $F(000) = 952$, $T = 293$ K, $wR = 0{\cdot}048$ for 2216 observed reflections. The molecule contains a unique tricyclo skeleton. The dioxabicycloheptane ring adopts a structure similar to that of norbornane. The dihydropyran adopts a twist conformation. The absolute configuration was determined by the Bijvoet method.

Introduction. Antibiotic trioxacarcin A which is isolated from the culture broth of *Streptomyces ochraceus* shows anticancer activity against mouse Sarcoma 180 and Leukemia P-388 and also antibacterial activity against both Gram-positive and Gram-negative bacteria (Tomita, Tamaoki, Morimoto & Fujimoto, 1981). The structural characteristics of the anticancer antibiotic have been studied by chemical and spectroscopic methods to show that it contains a relatively complex aglycone moiety the structure of which was difficult to determine unequivocally by these methods. To disclose its structure, we have undertaken the degradation of trioxacarcin A (Shirahata, Iida & Hirayama, 1981). After oxidation followed by methanolysis of trioxacarcin A, the title compound, which maintains the most complex moiety, was obtained. The present X-ray analysis was undertaken to establish the structure.

Experimental. Colourless crystals from a mixture of acetone and cyclohexane (2:1), dimensions $0{\cdot}40 \times 0{\cdot}37 \times 0{\cdot}20$ mm. Enraf–Nonius CAD-4 diffractometer, graphite-monochromated Cu $K\alpha$ radiation. Cell dimensions from setting angles of 21 independent reflections with $24{\cdot}0 \leq \theta \leq 34{\cdot}0°$. 2574 reflections surveyed in the range $4 \leq 2\theta \leq 150°$; $0 \leq h \leq 12$, $0 \leq k \leq 29$, $0 \leq l \leq 11$; 2233 independent reflections with $I > 3{\cdot}0\sigma(I)$. Three reference reflections monitored periodically showed no significant variation in intensity. Empirical absorption correction (North, Phillips & Mathews, 1968) was applied (transmission 0·873–0·999). A secondary-extinction correction (Zachariasen, 1963) was applied (refined coefficient $3{\cdot}8 \times 10^{-6}$). Structure solved using *MULTAN*11/82 (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1982) and Fourier-map recycling. Refinement using the *SDP* package (Frenz, 1985), full-matrix least-squares refinement on *F*, with non-H atoms having anisotropic temperature factors and H atoms (located from a difference Fourier synthesis) having isotropic temperature factors. Weight $w = 4F_o^2/[\sigma(I_o)^2 + (0{\cdot}04I_o)^2]^{1/2}/\text{Lp}$, final $R = 0{\cdot}036$, $wR = 0{\cdot}048$, $S = 2{\cdot}04$, maximum shift/e.s.d. in the final least-squares cycle 0·14, maximum and minimum peaks in the final difference map 0·37(8) and −0·34(9) e Å^{-3}, respectively. The absolute configuration was determined with Bijvoet differences (Bijvoet, Peerdeman & van Bommel, 1951) using the anomalous dispersion of O and N to Cu $K\alpha$ radiation. After structure refinement a set of reflections was chosen which were those the most sensitive to the anomalous-dispersion effects, based on the largest values for $||F^+| - |F^-||$calc./

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Table 1. *Positional parameters and equivalent isotropic temperature factors of non-*H *atoms with e.s.d.'s in parentheses*

$$B_{eq} = \tfrac{4}{3}\textstyle\sum_i \sum_j \beta_{ij}\mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	B_{eq}(Å^2)
O(1)	0·8509 (1)	0·16685 (6)	0·2517 (2)	4·51 (3)
O(2)	1·0760 (2)	0·15614 (7)	0·4016 (2)	4·91 (3)
O(3)	0·9393 (1)	0·10812 (5)	0·0816 (2)	4·05 (3)
O(4)	1·1994 (1)	0·20825 (6)	0·0481 (2)	3·85 (2)
O(5)	1·0304 (1)	0·25420 (5)	0·1502 (2)	4·25 (3)
O(6)	0·9278 (2)	−0·02485 (7)	0·0866 (2)	6·51 (4)
O(7)	0·7979 (2)	0·00292 (7)	−0·0986 (2)	5·25 (3)
O(8)	1·0973 (2)	−0·03362 (8)	−0·4281 (2)	7·31 (4)
O(9)	1·0115 (2)	−0·07075 (7)	−0·2231 (3)	7·74 (5)
O(10)	1·3395 (2)	0·22048 (8)	0·3097 (2)	5·48 (3)
O(11)	1·2687 (2)	0·30604 (7)	0·2162 (2)	5·59 (3)
C(1)	1·1635 (2)	0·12358 (9)	−0·2342 (2)	4·27 (4)
C(2)	1·1542 (2)	0·0684 (1)	−0·2899 (2)	4·68 (4)
C(3)	1·0722 (2)	0·02792 (9)	−0·2250 (2)	4·41 (4)
C(4)	1·0023 (2)	0·04177 (8)	−0·0980 (2)	3·98 (4)
C(5)	1·0125 (2)	0·09750 (8)	−0·0421 (2)	3·66 (3)
C(6)	1·0893 (2)	0·13882 (8)	−0·1097 (2)	3·80 (3)
C(7)	1·2557 (2)	0·1655 (1)	−0·3035 (3)	5·10 (5)
C(8)	1·0569 (2)	−0·0310 (1)	−0·2881 (3)	5·43 (5)
C(9)	1·0776 (4)	−0·0889 (1)	−0·4996 (4)	9·65 (8)
C(10)	0·9077 (2)	0·00205 (8)	−0·0243 (2)	4·39 (4)
C(11)	0·6943 (3)	−0·0325 (1)	−0·0444 (4)	7·30 (7)
C(12)	1·0888 (2)	0·19898 (8)	−0·0506 (2)	3·95 (3)
C(13)	0·9745 (2)	0·21277 (8)	0·0511 (2)	3·99 (4)
C(14)	0·9546 (2)	0·16175 (8)	0·1564 (2)	3·68 (3)
C(15)	1·1418 (2)	0·22110 (8)	0·1877 (2)	3·64 (3)
C(16)	1·0809 (2)	0·16576 (8)	0·2470 (2)	3·59 (3)
C(17)	1·1490 (2)	0·1174 (1)	0·3095 (3)	4·88 (4)
C(18)	0·7256 (2)	0·1600 (1)	0·1839 (4)	5·82 (6)
C(19)	1·2320 (2)	0·25506 (9)	0·2860 (2)	4·42 (4)
C(20)	1·4276 (3)	0·2439 (1)	0·4166 (3)	7·27 (7)
C(21)	1·2183 (5)	0·3567 (1)	0·2764 (4)	11·1 (1)

Table 2. *Bond lengths* (Å) *and angles* (°); *numbers in parentheses are e.s.d.'s in the least significant digits*

O(1)	C(14)	1·379 (2)	O(7)	C(11)	1·438 (3)	C(3)	C(4)	1·392 (2)
O(1)	C(18)	1·441 (2)	O(8)	C(8)	1·331 (3)	C(3)	C(8)	1·495 (3)
O(2)	C(16)	1·413 (2)	O(8)	C(9)	1·456 (3)	C(4)	C(5)	1·397 (2)
O(2)	C(17)	1·440 (2)	O(9)	C(8)	1·192 (3)	C(4)	C(10)	1·502 (2)
O(3)	C(5)	1·371 (2)	O(10)	C(19)	1·388 (2)	C(5)	C(6)	1·389 (2)
O(3)	C(14)	1·429 (2)	O(10)	C(20)	1·434 (2)	C(6)	C(12)	1·500 (2)
O(4)	C(12)	1·464 (2)	O(11)	C(19)	1·397 (2)	C(12)	C(13)	1·530 (3)
O(4)	C(15)	1·425 (2)	O(11)	C(21)	1·401 (4)	C(13)	C(14)	1·536 (2)
O(5)	C(13)	1·437 (2)	C(1)	C(2)	1·383 (3)	C(14)	C(16)	1·543 (2)
O(5)	C(15)	1·425 (2)	C(1)	C(6)	1·405 (2)	C(15)	C(16)	1·531 (2)
O(6)	C(10)	1·199 (2)	C(1)	C(7)	1·500 (2)	C(15)	C(19)	1·511 (2)
O(7)	C(10)	1·318 (2)	C(2)	C(3)	1·396 (3)	C(16)	C(17)	1·442 (2)

C(14)	O(1)	C(18)	115·1 (1)	O(7)	C(10)	C(4)	109·0 (1)
C(16)	O(2)	C(17)	60·7 (1)	O(4)	C(12)	C(6)	110·6 (1)
C(5)	O(3)	C(14)	118·8 (1)	O(4)	C(12)	C(13)	101·9 (1)
C(12)	O(4)	C(15)	104·1 (1)	C(6)	C(12)	C(13)	114·3 (1)
C(13)	O(5)	C(15)	96·2 (1)	O(5)	C(13)	C(12)	101·7 (1)
C(10)	O(7)	C(11)	117·3 (2)	O(5)	C(13)	C(14)	100·9 (1)
C(8)	O(8)	C(9)	114·6 (2)	C(12)	C(13)	C(14)	108·2 (1)
C(19)	O(10)	C(20)	113·0 (2)	O(1)	C(14)	O(3)	106·5 (1)
C(19)	O(11)	C(21)	116·2 (2)	O(1)	C(14)	C(13)	115·0 (1)
C(2)	C(1)	C(6)	119·2 (2)	O(1)	C(14)	C(16)	108·8 (1)
C(2)	C(1)	C(7)	119·8 (2)	O(3)	C(14)	C(13)	113·5 (1)
C(6)	C(1)	C(7)	121·0 (2)	O(3)	C(14)	C(16)	113·4 (1)
C(1)	C(2)	C(3)	121·2 (2)	C(13)	C(14)	C(16)	99·7 (1)
C(2)	C(3)	C(4)	120·2 (2)	O(4)	C(15)	O(5)	104·0 (1)
C(2)	C(3)	C(8)	121·7 (2)	O(4)	C(15)	C(16)	107·7 (1)
C(4)	C(3)	C(8)	118·1 (2)	O(4)	C(15)	C(19)	111·8 (1)
C(3)	C(4)	C(5)	118·3 (1)	O(5)	C(15)	C(16)	102·0 (1)
C(3)	C(4)	C(10)	124·0 (1)	O(5)	C(15)	C(19)	110·7 (1)
C(5)	C(4)	C(10)	117·5 (1)	C(16)	C(15)	C(19)	119·3 (1)
O(3)	C(5)	C(4)	114·9 (1)	O(2)	C(16)	C(14)	118·9 (1)
O(3)	C(5)	C(6)	123·2 (1)	O(2)	C(16)	C(15)	119·6 (1)
C(4)	C(5)	C(6)	121·9 (2)	O(2)	C(16)	C(17)	60·5 (1)
C(1)	C(6)	C(5)	119·2 (1)	C(14)	C(16)	C(15)	102·3 (1)
C(1)	C(6)	C(12)	121·5 (1)	C(14)	C(16)	C(17)	124·9 (1)
C(5)	C(6)	C(12)	119·3 (1)	C(15)	C(16)	C(17)	126·4 (2)
O(8)	C(8)	O(9)	123·7 (2)	O(2)	C(17)	C(16)	58·7 (1)
O(8)	C(8)	C(3)	111·7 (2)	O(10)	C(19)	O(11)	110·2 (1)
O(9)	C(8)	C(3)	124·6 (2)	O(10)	C(19)	C(15)	106·3 (1)
O(6)	C(10)	O(7)	125·6 (2)	O(11)	C(19)	C(15)	110·4 (1)
O(6)	C(10)	C(4)	125·4 (2)				

$\sigma(F)$obs. The selected set of reflections were measured repeatedly in all octants. 16 of 17 reflections indicated the absolute configuration shown in the figures. Scattering factors from *International Tables for X-ray Crystallography* (1974).

Final fractional coordinates and equivalent B values are listed in Table 1.*

Discussion. Fig. 1 shows the atom-labelling scheme. An *ORTEP*II drawing (Johnson, 1976) of the molecule is shown in Fig. 2. Bond lengths and angles are listed in Table 2. Dihydropyran takes a twist conformation and C(13) and C(14) deviate by −0·449 (2) and 0·234 (2) Å from the least-squares plane defined by C(12), C(6), C(5) and O(3). The dioxabicycloheptane ring takes a similar structure to that of norbornane

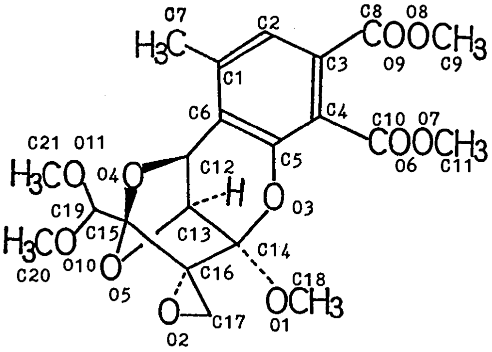

Fig. 1. Chemical structure and atomic notation of the molecule.

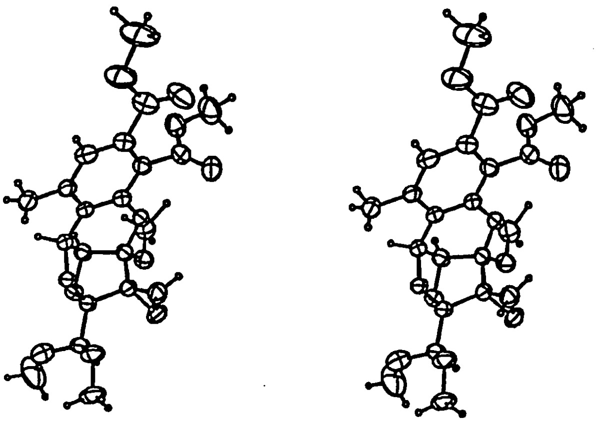

Fig. 2. View of the molecule with thermal ellipsoids at 30% probability.

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* Lists of structure factors, anisotropic thermal parameters, H-atom parameters and selected torsion angles have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51559 (15 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

(Hamor & Hamor, 1978). The sums of bond angles in the dioxolane and tetrahydrofuran rings are 507·9 and 501·3°, respectively. The dioxolane and tetrahydrofuran rings adopt an envelope conformation with O(5) deviating 0·76 (1) and 0·815 (1) Å, respectively, from the planes containing the other four atoms in the rings. The dihedral angle between the two least-squares planes is 111·4 (1)°.

The dihedral angle between the plane defined by C(13), C(14), C(15) and C(16) and the epoxide plane is 90·5 (1)°. The rather short distance between C(13) and C(15) [2·132 (2) Å] and the small angle C(13)—O(5)—C(15) are also seen in norbornane skeletons. Two pairs of C—O bonds in the dioxolane ring reveal the asymmetry in the bond lengths. C(15)—O(5) and C(15)—O(4) are significantly shorter than C(13)—O(5) and C(12)—O(4), respectively. The two methyl ester groups linked to the phenyl ring take different conformations with respect to the phenyl ring. One is almost perpendicular and the other nearly parallel to the ring.

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Structure of the Linear Oligopeptide *tert*-Butyl 1-[1-(Benzyloxycarbonyl)amino-1-cyclohexanecarboxamido]-1-cyclohexanecarboxylate*

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Abstract. $C_{26}H_{38}N_2O_5$, $M_r = 458{\cdot}60$, triclinic, $P\bar{1}$, $a = 5{\cdot}971\ (5)$, $b = 14{\cdot}033\ (5)$, $c = 16{\cdot}011\ (11)$ Å, $\alpha = 103{\cdot}30\ (39)$, $\beta = 92{\cdot}97\ (65)$, $\gamma = 93{\cdot}25\ (44)$°, $V = 1301\ (3)$ Å^3, $Z = 2$, $D_x = 1{\cdot}171$ g cm^{-3}, $D_m = 1{\cdot}16$ g cm^{-3}, $\lambda(\mathrm{Cu}\ K\alpha) = 1{\cdot}5418$ Å, $\mu = 6{\cdot}166$ cm^{-1}, $F(000) = 496$, $T = 295$ K. The final R value for 2298 observed $[I \geq 3\sigma(I)]$ reflections is 0·068. The conformations of the urethane and peptide —CONH— groups is *trans*. The two Ac$_6$c residues show φ, ψ sets of torsion angles both falling in the region of the conformational energy map where α- and 3_{10}-helices are found, but their handedness is opposite. The two cyclohexyl rings adopt a slightly distorted chair conformation with the —NH group in the axial position.

Introduction. Our conformational energy computations on Ac-Ac$_6$c-NHMe (Ac acetyl, Ac$_6$c 1-aminocyclohexane-1-carboxylic acid and NHMe methylamino) (Paul, Sukumar, Bardi, Piazzesi, Valle, Toniolo & Balaram, 1986; Pavone, Benedetti, Barone, Di Blasio, Lelj, Pedone, Santini, Crisma, Bonora & Toniolo, 1988) indicated that this $C^{\alpha,\alpha}$-dialkylated, cyclic α-amino acid residue is conformationally restricted and that its minimum energy conformation falls in the $\alpha/3_{10}$-helical region, irrespective of the position (either axial or equatorial) of the α-amino group. The results of the theoretical analysis were corroborated by crystal-state investigations (Bardi, Piazzesi, Toniolo, Sukumar, Raj & Balaram, 1985; Paul, Sukumar, Bardi, Piazzesi, Valle, Toniolo & Balaram, 1986; Pavone, Benedetti, Barone, Di Blasio, Lelj, Pedone, Santini, Crisma, Bonora & Toniolo, 1988) of Ac$_6$c-rich tri- and

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* Linear Oligopeptides. 197. Part 196: Moretto, Crisma, Bonora, Toniolo & Balaram (1988).

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