Acta Cryst. (1986). C**42**, 758–760

Methyl 2,6-Anhydro-3-azido-4-*O*-benzoyl-3-deoxy-α-D-idopyranoside, a New 2,5-Dioxabicyclo[2.2.2]octane Derivative

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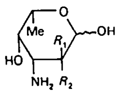
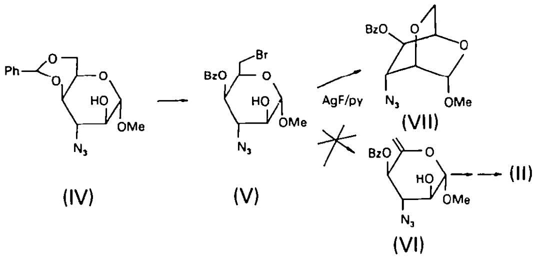
(*Received* 23 *October* 1985; *accepted* 21 *January* 1986)

Abstract. $C_{14}H_{15}N_3O_5$, $M_r = 305{\cdot}3$, monoclinic, $P2_1$, $a = 5{\cdot}796$ (2), $b = 7{\cdot}392$ (2), $c = 16{\cdot}406$ (6) Å, $\beta = 91{\cdot}20$ (3)°, $V = 702{\cdot}7$ Å^3, $D_m = 1{\cdot}43$, $D_x = 1{\cdot}44$ Mg m^{-3}, $Z = 2$, $\lambda(\text{Mo } K\alpha) = 0{\cdot}71073$ Å, $\mu = 0{\cdot}072$ mm^{-1}, $F(000) = 320$, $R = 0{\cdot}072$ for 1100 reflections with $I > 2\sigma(I)$. X-ray analysis of the title compound confirmed the structure of a new 2,5-dioxabicyclo[2.2.2]octane derivative, which was unexpectedly obtained when treating methyl 3-azido-4-*O*-benzoyl-6-bromo-3,6-dideoxy-α-D-idopyranoside with AgF/pyridine. There are no unusual bond distances or angles.

Introduction. The biological properties of the α,β-fluoroamino saccharides (Molloy, Fuller & Hauser, 1973) prompted us to undertake the synthesis of (I) and (II) (Baptistella, Marsaioli, Imamura, Castillon, Olesker & Lukacs, 1985; Baptistella, Marsaioli, Souza Filho *et al.*, 1985) which are fluoro analogues of daunosamine (III) (Horton & Weckerle, 1975), the sugar moiety of the antibiotics daunorubicin and doxorubicin. In the synthesis of (II) we proposed that compound (VI), a key intermediate, could be obtained by treating (IV) (Hanessian & Haskell, 1965) with *N*-bromosuccinimide followed by AgF/pyridine.



(I) $R_1 = F, R_2 = H$
(II) $R_1 = H, R_2 = F$
(III) $R_1 = R_2 = H$



However this reaction yielded a crystalline compound (71% yield) showing spectroscopic data which were incompatible with structure (VI). The lack of an OH stretching in the IR spectrum together with the presence of a triplet ($\delta\,^{13}C = 62{\cdot}4$) in the ^{13}C NMR spectrum, attributable to a $-CH_2O$, led us to suggest the structure of a new 2,5-dioxabicyclo[2.2.2]octane derivative, (VII), for this reaction product.

To obtain conclusive proof of this hypothesis and the conformation of the compound, a three-dimensional crystal structure determination was undertaken.

Experimental. Transparent crystal at 277 K; Nonius CAD-4 diffractometer, graphite-monochromated Mo $K\alpha$; cell parameters by least squares on setting angles for 25 reflections; $16 \le 2\theta < 32°$; ω–2θ scans, scan width $(0{\cdot}80 + 0{\cdot}25\,\text{tg}\theta)°$, scan speed 6·7° min^{-1} max.; range of hkl: $-6 < h < 6$, $0 < k < 8$, $0 < l < 19$; standard reflection 007 varied ±2% of mean intensity over data collection; 3246 reflections measured, 2197 unique, $R_{\text{int}} = 0{\cdot}019$, 1100 observed above $2\sigma(I)$; Lp corrections. The structure was solved by direct methods; H atoms located on geometrical grounds; least-squares refinement minimizing $\sum w(|F_o| - |F_c|)^2$ with $w = 1/[\sigma^2(F_o) + 0{\cdot}0005|F_o|^2]$; 196 parameters refined: coordinates and anisotropic thermal parameters for non-H atoms, phenyl ring as rigid body (C—C 1·395, C—H 1·09 Å all angles 120°), all H atoms with common $B = 3{\cdot}95$ Å^2; unobserved reflections and reflection 001 excluded; $R = 0{\cdot}072$; $wR = 0{\cdot}059$; inspection of F_c and F_o values indicated secondary-extinction correction required: $F_{\text{corr}} = F_c/(1 - 10^{-4}xF_c^2/\sin\theta)$, where x refined to 0·0306 in the final run; $(\Delta/\sigma)_{\max} = 0{\cdot}03$, $\Delta\rho$ excursions within 0·3 and $-0{\cdot}2$ e Å^{-3}. Scattering factors for non-H atoms from Cromer & Mann (1968) with corrections for anomalous dispersion from Cromer & Liberman (1970) and for H from Stewart, Davidson & Simpson (1965);

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programs used: *SHELX*76 (Sheldrick, 1976), *MULTAN*80 (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980) and *ORTEP* (Johnson, 1965).

Discussion. The main result of this paper is the unambiguous characterization of the new compound named in the title.

A perspective view of the molecule, down the direction defined by the mid-points of the bonds C(1)–C(2) and C(4)–C(5), is shown in Fig. 1. Positional parameters and equivalent isotropic temperature factors are given in Table 1.* Bond lengths and angles are given in Table 2; all values are within the expected range, although the estimated standard deviations associated with them are somewhat high because of the low value for the ratio of number of independent reflections to parameters resulting from the poor diffracting quality of the crystal (hence high *R* value also).

The six-membered ring C(1)–O(5)–C(5)–C(4)–C(3)–C(2) is in a very approximate twist-boat conformation, with the Cremer & Pople (1975) ring parameters: $q_2 = 0{\cdot}821$ (6), $q_3 = -0{\cdot}041$ (5), $Q = 0{\cdot}822$ (6) Å, $\psi_2 = -43{\cdot}2$ (4) and $\theta_2 = 92{\cdot}9$ (4)°.

The other two rings, C(1)–C(2)–O(2)–C(6)–C(5)–O(5) and C(2)–O(2)–C(6)–C(5)–C(4)–C(3), have a conformation between boat and twist-boat with Cremer & Pople parameters: $q_2 = 0{\cdot}820$ (5), $q_3 = 0{\cdot}019$ (6), $Q = 0{\cdot}820$ (5) Å, $\psi_2 = 69{\cdot}6$ (3), $\theta_2 = 88{\cdot}7$ (4)° and $q_2 = 0{\cdot}857$ (5), $q_3 = 0{\cdot}022$ (5), $Q = 0{\cdot}858$ (5) Å, $\psi_2 = -17{\cdot}22$ (3), $\theta_2 = 88{\cdot}5$ (3)°, respectively.

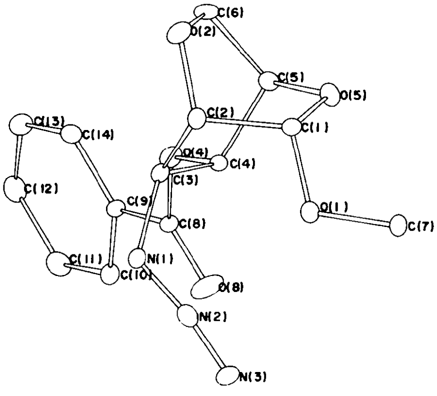

Fig. 1. A perspective view of the molecule.

Table 1. *Fractional coordinates and equivalent isotropic temperature factors* (Å^2) *with e.s.d.'s in parentheses*

$B_{eq} = \frac{4}{3}\sum_i\sum_j B_{ij}(\mathbf{a}_i.\mathbf{a}_j)$ (Hamilton, 1959).

	x	y	z	B_{eq}
C(1)	0·0187 (8)	−0·3627 (9)	−0·0753 (3)	3·5 (2)
C(2)	0·1826 (9)	−0·2690 (9)	−0·1330 (3)	3·6 (2)
C(3)	0·0573 (8)	−0·1982 (8)	−0·2090 (3)	3·1 (2)
C(4)	−0·1135 (8)	−0·3417 (8)	−0·2362 (3)	2·9 (2)
C(5)	−0·0309 (9)	−0·5201 (9)	−0·1990 (3)	3·6 (2)
C(6)	0·2309 (9)	−0·5373 (9)	−0·2087 (3)	4·2 (2)
C(7)	−0·2981 (9)	−0·3011 (9)	0·0069 (3)	4·0 (2)
C(8)	−0·2976 (8)	−0·2944 (8)	−0·3669 (3)	3·5 (2)
C(9)	−0·2724 (5)	−0·3143 (6)	−0·4542 (1)	3·0 (2)
C(10)	−0·4525 (5)	−0·2509 (6)	−0·5042 (1)	3·9 (2)
C(11)	−0·4388 (5)	−0·2661 (6)	−0·5887 (1)	4·8 (2)
C(12)	−0·2450 (5)	−0·3447 (6)	−0·6232 (1)	4·8 (2)
C(13)	−0·0649 (5)	−0·4081 (6)	−0·5732 (1)	4·5 (2)
C(14)	−0·0786 (5)	−0·3929 (6)	−0·4887 (1)	3·8 (2)
O(1)	−0·1518 (6)	−0·2376 (6)	−0·0560 (2)	3·8 (1)
O(2)	0·3437 (6)	−0·4042 (7)	−0·1580 (2)	4·4 (1)
O(4)	−0·1160 (5)	−0·3599 (6)	−0·3233 (2)	3·8 (1)
O(5)	−0·0760 (6)	−0·5188 (5)	−0·1144 (2)	3·8 (1)
O(8)	−0·4583 (7)	−0·2256 (9)	−0·3340 (2)	7·3 (2)
N(1)	−0·0284 (8)	−0·0108 (7)	−0·2013 (3)	4·2 (2)
N(2)	−0·228 (1)	0·0119 (7)	−0·1801 (3)	4·4 (2)
N(3)	−0·4083 (9)	0·0543 (9)	−0·1622 (4)	6·9 (3)

Table 2. *Bond distances* (Å) *and angles* (°) *with e.s.d.'s in parentheses*

C(1)–C(2)	1·522 (8)	C(7)–O(1)	1·429 (6)
C(1)–O(1)	1·395 (7)	C(8)–C(9)	1·450 (5)
C(1)–O(5)	1·425 (7)	C(8)–O(4)	1·350 (6)
C(2)–C(3)	1·523 (7)	C(8)–O(8)	1·199 (7)
C(2)–O(2)	1·434 (7)	C(9)–C(10)	1·395 (4)
C(3)–C(4)	1·512 (7)	C(9)–C(14)	1·395 (5)
C(3)–N(1)	1·478 (7)	C(10)–C(11)	1·395 (3)
C(4)–C(5)	1·526 (8)	C(11)–C(12)	1·395 (5)
C(4)–O(4)	1·435 (6)	C(12)–C(13)	1·395 (4)
C(5)–C(6)	1·534 (8)	C(13)–C(14)	1·395 (3)
C(5)–O(5)	1·418 (6)	N(1)–N(2)	1·227 (7)
C(6)–O(2)	1·437 (7)	N(2)–N(3)	1·136 (8)

C(2)–C(1)–O(1)	107·1 (4)	C(9)–C(8)–O(8)	125·6 (5)
C(2)–C(1)–O(5)	109·2 (4)	O(4)–C(8)–O(8)	121·2 (5)
O(1)–C(1)–O(5)	111·8 (4)	C(8)–C(9)–C(10)	117·2 (3)
C(1)–C(2)–C(3)	111·9 (5)	C(8)–C(9)–C(14)	122·8 (3)
C(1)–C(2)–O(2)	106·2 (4)	C(10)–C(9)–C(14)	120·0 (3)
C(3)–C(2)–O(2)	107·9 (4)	C(9)–C(10)–C(11)	120·0 (3)
C(2)–C(3)–C(4)	107·4 (4)	C(10)–C(11)–C(12)	120·0 (3)
C(2)–C(3)–N(1)	114·1 (4)	C(11)–C(12)–C(13)	120·0 (3)
C(4)–C(3)–N(1)	117·6 (4)	C(12)–C(13)–C(14)	120·0 (3)
C(3)–C(4)–C(5)	106·9 (4)	C(9)–C(14)–C(13)	120·0 (3)
C(3)–C(4)–O(4)	110·6 (4)	C(1)–O(1)–C(7)	112·3 (4)
C(5)–C(4)–O(4)	108·3 (4)	C(2)–O(2)–C(6)	110·6 (4)
C(4)–C(5)–C(6)	109·4 (4)	C(4)–O(4)–C(8)	119·0 (4)
C(4)–C(5)–O(5)	108·8 (4)	C(1)–O(5)–C(5)	111·7 (4)
C(6)–C(5)–O(5)	107·8 (4)	C(3)–N(1)–N(2)	118·2 (5)
C(5)–C(6)–O(2)	108·8 (4)	N(1)–N(2)–N(3)	171·8 (6)
C(9)–C(8)–O(4)	113·2 (4)		

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* Lists of H-atom positions, anisotropical thermal parameters and structure factors have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 42776 (11 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Acta Cryst. (1986). C**42**, 760–762

Calcium-Selective Ligands. 1. Structure of 3,12-Bis(carboxymethyl)-6,9-dioxa-3,12-diazatetradecanedioic Acid (H_4egta)

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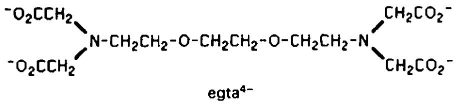
(*Received* 2 *September* 1985; *accepted* 13 *February* 1986)

Abstract. $C_{14}H_{24}N_2O_{10}$, $M_r = 380·35$, triclinic, $P\bar{1}$, $a = 6·702$ (2), $b = 6·792$ (2), $c = 10·048$ (3) Å, $\alpha = 82·23$ (2), $\beta = 78·82$ (2), $\gamma = 71·33$ (2)°, $V = 424·1$ (1) Å^3, $Z = 1$, $D_x = 1·49$ g cm^{-3}, λ(Mo $K\alpha$) = 0·71073 Å, $\mu = 1·19$ cm^{-1}, $F(000) = 202$, room temperature. $R = 0·055$ for 1269 observed reflections. H_4egta exists in the solid state as an infinite network of hydrogen-bonded zwitterions. Each $R_2R'NH^+$ group is involved in two intramolecular and one intermolecular hydrogen bond to carboxylate O atoms. Additional intermolecular linkages occur *via* short hydrogen bonds [O···O = 2·444 (3), 2·450 (3) Å] between anionic carboxylate groups across the crystallographic inversion center; these hydrogen bonds may be symmetric. The infrared spectrum contains features characteristic of strong O—H—O hydrogen bonding [ν_{as}(O—H—O) ≈ 750 cm^{-1}, $\Delta\nu \approx 1000$ cm^{-1}].

Introduction. The potentially octadentate ligand egta^{4-} (see below) exhibits a binding constant for calcium which is five orders of magnitude larger than that for magnesium (Sillén & Martell, 1971). For comparison, the calcium-binding preference exhibited by the familiar ligand edta^{4-} is less than two orders of magnitude. This high degree of calcium selectivity is similar to that exhibited by calcium-binding proteins (Potter & Gergely, 1975). To initiate a study of the bases for this selectivity, the structure of the tetraprotonated neutral H_4egta ligand has been determined.



$$({}^{-}O_2CCH_2)_2N\text{-}CH_2CH_2\text{-}O\text{-}CH_2CH_2\text{-}O\text{-}CH_2CH_2\text{-}N(CH_2CO_2^{-})_2$$

egta^{4-}

Experimental. H_4egta purchased from J. T. Baker Chemical Company. Crystal [0·35 (100 → $\bar{1}$00) × 0·12 (001 → 00$\bar{1}$) × 0·07 mm (010 → 0$\bar{1}$0)] obtained by slow cooling of hot aqueous solution (0·26 *M* in H_4egta). Nicolet *R*3*m* diffractometer, cell constants from least-squares fitting of setting angles for 24 reflections ($2\theta_{av.} = 13·30°$). Data collected for $3·5 \le 2\theta \le 50·0°$, $-7 \le h \le 7$, $-7 \le k \le 7$, $0 \le l \le 10$, $\theta/2\theta$ scans. Three control reflections (020, $\bar{4}$00, 0$\bar{1}\bar{4}$), monitored every 97 reflections, showed no significant variation. Lorentz and polarization corrections applied, but no absorption correction; of 1495 unique reflections, 1269 observed [$I \ge 2\sigma(I)$] and used in further calculations. Structure solved by direct methods using *RANT* (Sheldrick, 1983); all non-H atoms refined anisotropically; C-bound H atoms included in calculated positions, carboxylate H atoms fixed on inversion center, positional parameters refined for N—H H atom. Block, weighted $\{w = [\sigma^2(F) + gF^2]^{-1}, g = 3·5 \times 10^{-3}\}$ least-squares refinement on F yielded $R = 0·055$, $wR = 0·076$, and $S = 1·15$ at convergence (mean shift/e.s.d. < 0·01, max. shift/e.s.d. < 0·04, over last four cycles) with largest peak in final Fourier synthesis of +0·33 e Å^{-3} and a minimum of −0·37 e Å^{-3}. Neutral-atom scattering factors used (*International Tables for X-ray Crystallography*, 1974); software for diffractometer provided with Nicolet *R*3*m*; *SHELXTL*

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