Acta Cryst. (1993). C**49**, 40–42

Structure of 1,2,4-Trideoxy-1,4-imino-3,5;6,7-di-*O*-isopropylidene-L-*glycero*-D-*gluco*-octitol: a Key Intermediate in the Enantioselective Synthesis of 8-Epicastanospermine

BY T. GALLAGHER, M. E. GILES, M. F. MAHON AND K. C. MOLLOY

School of Chemistry, University of Bath, Claverton Down, Bath BA2 7AY, England

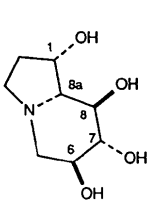
M. S. HADLEY

SmithKline Beecham Pharmaceuticals, Coldharbour Road, The Pinnacles, Harlow CM19 5AD, England

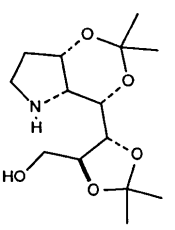
(*Received* 28 *January* 1992; *accepted* 22 *April* 1992)

Abstract. 5-(2,2-Dimethyl-4a,6,7,7a-tetrahydro-2*H*,-4*H*-[1,3]dioxino[5,4-*b*]pyrrol-4-yl)-2,2-dimethyl-4,5-dihydro-2*H*-1,3-dioxole-4-methanol, $C_{14}H_{25}NO_5$, M_r = 287.4, trigonal, $P3_221$, a = 11.831 (2), c = 19.948 (7) Å, V = 2418.1 Å^3, Z = 6, D_x = 1.18 g cm^{-3}, λ(Mo $K\alpha$) = 0.71069 Å, μ = 0.54 cm^{-1}, $F(000)$ = 936, room temperature, R = 0.0707, wR = 0.0780 for 1628 unique reflections. The structure of the title compound shows it to contain *S*, *R*, *S* stereochemistry at C1, C8a and C8 (castanospermine numbering), respectively. Molecules dimerize in a head-to-tail manner in the solid state through O—H···N hydrogen bonds.

Introduction. The aldol reactivity of enolates based on *N*-substituted pyrrolidin-3-ones provides an efficient and synthetically flexible entry to the biologically important polyhydroxyindolizidines related to castanospermine (1). The outcome of subsequent synthetic manipulations depends on a knowledge of the stereochemical course of this key aldol reaction, and in this paper we describe the structure of pyrrolidine (2) which is a key intermediate in the synthesis of this class of aza sugars. The initial aldol reaction served to set the stereocentres at C8 and C8a (castanospermine numbering) of (2), and stereoselective reduction of a ketone function introduced the stereocentre at C1. Removal of protecting groups from nitrogen (—CO_2Et) and the primary hydroxyl (—CH_2Ph) gave crystalline (2).



(1)



(2)

Experimental. The synthesis of the compound has been reported previously (Gallagher, Giles, Subramanian & Hadley, 1992). Crystals were obtained by recrystallization from ethyl acetate–hexane.

A crystal of approximate dimensions 0.25 × 0.25 × 0.30 mm was used for data collection. Data were measured at room temperature on a Hilger & Watts Y290 four-circle diffractometer using ω–2θ scans for $2 \le \theta \le 22°$, covering the ranges h −11→11, k −11→0, l 0→20. Cell dimensions were determined from the positions of 12 accurately centred reflections in the range $12 < \theta < 17°$. 2180 reflections were collected (R_{int} = 0.0431) of which 1628 were unique with $I \ge 3\sigma(I)$. A standard reflection measured every 50 reflections showed no systematic crystal decay. Data were corrected for Lorentz and polarization effects but not for absorption. The structure was solved by conventional direct methods and refined using least-squares methods based on F within the *SHELX* suite of programs (Sheldrick, 1976, 1986). The only systematic absence observed in the data was 00l, l = 3n, which corresponds to $P3_1$ (No. 144), $P3_2$ (No. 145), $P3_112$ (No. 151), $P3_121$ (No. 152), $P3_212$ (No. 153), $P3_221$ (No. 154), $P6_2$ (No. 171), $P6_4$ (No. 172) (all with Z = 6), and $P6_222$ (No. 180), $P6_422$ (No. 181) (both Z = 12) as possible space groups. Attempts to solve the structure in each of these alternatives only gave solutions in the case of $P3_121$ and $P3_221$. Of the four possible coordinate sets (two enantiomers for each of the two space groups), two gave divergent refinements. Equally satisfactory refinements were obtained for the coordinate set reported herein in space group $P3_221$ and the inverted coordinate set in $P3_121$. Based on knowledge of the fixed (*S*,*S*) stereochemistry at C6 and C7 of (2), space group $P3_221$ {origin on 2[110], at 3_2(1,1,2)1} was adopted. In the final least-squares cycles all non-H atoms were allowed to vibrate anisotropically. The H atoms associated with N1 and

0108-2701/93/010040-03$06.00

© 1993 International Union of Crystallography

Table 1. *Fractional atomic coordinates and equivalent isotropic temperature factors* ($Å^2$) *for* (2)

	x	y	z	U_{eq}
N1	−0.6729 (5)	−0.6626 (5)	−0.1123 (2)	0.057 (3)
O1	−0.7818 (4)	−0.9419 (4)	−0.1039 (2)	0.062 (3)
O2	−0.6090 (4)	−0.8338 (4)	−0.0288 (2)	0.055 (2)
O3	−0.3387 (4)	−0.5348 (4)	−0.0919 (2)	0.065 (3)
O4	−0.2177 (4)	−0.5234 (5)	−0.0014 (2)	0.073 (3)
O5	−0.3964 (4)	−0.5548 (5)	0.1034 (2)	0.071 (3)
C1	−0.7099 (6)	−0.8625 (6)	−0.1601 (3)	0.056 (4)
C2	−0.7999 (7)	−0.8283 (7)	−0.1965 (3)	0.075 (5)
C3	−0.7776 (7)	−0.7012 (8)	−0.1624 (4)	0.085 (5)
C5	−0.3790 (6)	−0.6553 (7)	0.0787 (3)	0.063 (4)
C6	−0.3393 (6)	−0.6404 (6)	0.0059 (3)	0.055 (4)
C7	−0.4275 (6)	−0.6227 (6)	−0.0426 (3)	0.049 (3)
C8a	−0.6019 (5)	−0.7299 (6)	−0.1340 (3)	0.047 (3)
C8	−0.5235 (5)	−0.7468 (5)	−0.0792 (3)	0.047 (3)
C9	−0.7039 (7)	−0.9571 (6)	−0.0555 (3)	0.063 (5)
C10	−0.6419 (9)	−1.0349 (8)	−0.0802 (4)	0.095 (6)
C11	−0.7925 (8)	−1.0233 (8)	0.0041 (4)	0.089 (6)
C12	−0.2133 (8)	−0.4733 (9)	−0.0640 (4)	0.079 (6)
C13	−0.1601 (15)	−0.3406 (12)	−0.0626 (8)	0.235 (17)
C14	−0.1272 (9)	−0.5030 (16)	−0.1069 (5)	0.188 (13)

Table 2. *Intramolecular bond distances* (Å) *and angles* (°) *for* (2)

N1—C3	1.476 (8)	N1—C8a	1.481 (7)
O1—C1	1.438 (7)	O1—C9	1.406 (8)
O2—C8	1.433 (7)	O2—C9	1.426 (8)
O3—C7	1.435 (7)	O3—C12	1.400 (8)
O4—C6	1.420 (7)	O4—C12	1.371 (8)
O5—C5	1.394 (8)	C1—C2	1.502 (10)
C1—C8a	1.536 (8)	C2—C3	1.548 (10)
C5—C6	1.510 (8)	C6—C7	1.513 (8)
C7—C8	1.521 (8)	C8a—C8	1.511 (7)
C9—C10	1.518 (11)	C9—C11	1.518 (10)
C12—C13	1.368 (14)	C12—C14	1.502 (15)
C8a—N1—C3	104.5 (5)	C9—O1—C1	114.1 (5)
C9—O2—C8	112.7 (4)	C12—O3—C7	107.7 (5)
C12—O4—C6	108.4 (5)	C2—C1—O1	106.6 (5)
C8a—C1—O1	108.7 (4)	C8a—C1—C2	103.2 (5)
C3—C2—C1	104.5 (5)	C2—C3—N1	107.8 (6)
C6—C5—O5	114.2 (6)	C5—C6—O4	108.5 (5)
C7—C6—O4	103.4 (5)	C7—C6—C5	115.8 (5)
C6—C7—O3	103.5 (4)	C8—C7—O3	107.1 (4)
C8—C7—C6	114.0 (5)	C8—C8a—C1	111.3 (5)
C1—C8a—N1	104.1 (4)	C8a—C8—O2	110.1 (5)
C8—C8a—N1	114.2 (4)	C8a—C8—C7	115.6 (5)
C7—C8—O2	106.0 (4)	C11—C9—C10	111.1 (7)
O2—C9—O1	110.9 (5)	C10—C9—O1	113.6 (6)
C10—C9—O2	111.7 (6)	C11—C9—O2	102.9 (6)
C11—C9—O1	106.0 (6)	C14—C12—C13	108.0 (10)
O4—C12—O3	109.7 (6)	C13—C12—O3	111.4 (9)
C13—C12—O4	112.0 (9)	C14—C12—O3	108.5 (7)
C14—C12—O4	107.5 (9)		

O5 were located in the penultimate difference Fourier map and refined at a fixed distance of 0.98 Å from the parent atoms with $U = 0.05$ $Å^2$, while the remaining H atoms were included at calculated positions (C—H 1.08 Å), also with fixed isotropic temperature factors ($U = 0.05$ $Å^2$).

Final residuals after eight cycles of full-matrix least-squares refinement were $R = 0.0707$ and $wR = 0.0780$, for a weighting scheme of $w = 2.8906/[\sigma^2(F) + 0.0005(F)^2]$ and a GOF value of 3.25. Scattering factors were taken from the usual sources (*International Tables for X-ray Crystallography*, 1974, Vol. IV). The total number of parameters varied was 187. Maximum final shift/e.s.d. was 0.009, the average being 0.006. The maximum and minimum residual densities were 0.20 and -0.15 e $Å^{-3}$ respectively. Final fractional atomic coordinates and equivalent isotropic thermal parameters are given in Table 1;* bond distances and angles are given in Table 2. The asymmetric unit of (2) is shown in Fig. 1 along with the labelling scheme used.

Discussion. The stereocentres at C6 and C7 of (2) (*S,S*) were originally derived from (*R,R*)-diethyl tartrate, and served as a convenient reference to assign the stereochemistry at C1, C8a and C8 as *S*, *R* and *S*, respectively. Pyrrolidine (2) has been efficiently converted (two steps, 60% yield) to the

* Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 55413 (11 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: AL1005]

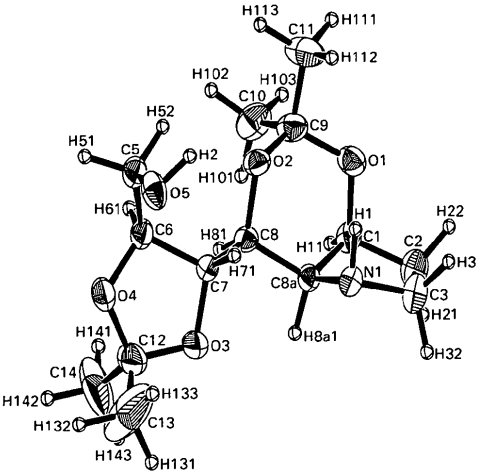


Fig. 1. The asymmetric unit of (2) showing the atomic labelling used in Tables 1 and 2.

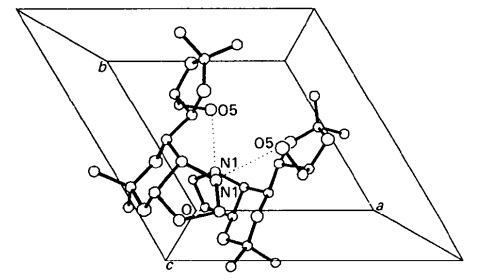


Fig. 2. A section of the unit cell of (2) showing the 'head-to-tail' dimerization of molecules through O—H···N hydrogen bonds.

bicyclic aza sugar, 8-epicastanospermine, without loss of stereochemical integrity. In the solid state, molecules dimerize in a 'head-to-tail' manner through O—H···N hydrogen bonds (O5—N1 2.74 Å), as shown in the section of the unit cell depicted in Fig. 2.

References

GALLAGHER, T., GILES, M. E., SUBRAMANIAN, R. S. & HADLEY, M. S. (1992). *J. Chem. Soc. Chem. Commun.* pp. 166–168.

SHELDRICK, G. M. (1976). *SHELX*76. Program for crystal structure determination. Univ. of Cambridge, England.

SHELDRICK, G. M. (1986). *SHELXS*86. Program for the solution of crystal structures. Univ. of Göttingen, Germany.

Acta Cryst. (1993). C**49**, 42–44

Structure of (3β,7α)-3,7-Dihydroxykaur-16-en-18-yl Acetate (Linearol)

BY ÖMER ERGIN

UU Necatibey Education Faculty, Department of Physics, Balıkesir, Turkey

REIJO SILLANPÄÄ

Department of Chemistry, University of Turku, SF-20500 Turku 50, Finland

AND NURTEN EZER

HU Pharmacy Faculty, Department of Pharmacognosy, Ankara, Turkey

(*Received* 17 *July* 1991; *accepted* 26 *March* 1992)

Abstract. $C_{22}H_{34}O_4$, $M_r = 362.51$, monoclinic, $P2_1$, $a = 7.785$ (9), $b = 11.688$ (6), $c = 11.792$ (7) Å, $\beta = 107.18$ (6)°, $V = 1025$ (1) Å^3, $Z = 2$, $D_m = 1.145$ (4) (by flotation), $D_x = 1.174$ g cm^{-3}, λ(Mo $K\alpha$) = 0.71069 Å, $\mu = 0.74$ cm^{-1}, $F(000) = 396$, $T = 296$ K, $R = 0.042$ for 1240 observed independent reflections. The skeleton of the molecule consists of contacting bicyclo[3.2.1]octane and bicyclo[4.4.0]decane (*trans*-decalin) systems. All of the cyclohexanes have an approximate chair conformation while the cyclopentane presents an envelope conformation. The CH_3 groups occupy axial positions. The $COCOCH_3$ group and its neighbouring OH group are in equatorial positions. The other OH group is in an axial position.

Introduction. *Sideritis* species (Lamiaceae) are used in traditional medicine for their anti-inflammatory (Villar, Jimenez & Alcaraz, 1986; Yeşilada & Ezer, 1989), antimicrobial and cytostatic activity (Diaz, Garcia-Granados, Moreno, Parra, Quevedo-Sarmiento & Saenz de Buruaga, 1987; Darias, Bravo, Rabanal, Sanchez-Mateo & Martin-Herrera, 1990). *Sideritis congesta* Davis et Huber-Morath, which is endemic to Turkey, is the most widely used species of the genus in Turkish folk medicine as herbal tea (Sezik & Ezer, 1983). From the aerial parts of this plant, we isolated flavonoids and a major diterpenoid, linearol, which was determined on the basis of spectroscopic data (IR, MS, NMR) (Ezer, 1980). In this study, the crystal and molecular structure of linearol has been determined by X-ray diffraction.

Experimental. A prismatic colourless crystal, 0.20 × 0.25 × 0.30 mm, was used for data collection on a Rigaku AFC-5 diffractometer with graphite-monochromated Mo $K\alpha$ radiation. Lattice parameters were determined from a least-squares fit of 25 centred reflections in the 2θ range 20.2–32.2°. Intensity data were measured by ω–2θ-scan technique with a scan rate of 4° min^{-1} in 2θ, and for $6.0 \le 2\theta \le 50.0°$ and hkl ranges 0, 0, −14 to 9, 13, 12. Of a total of 2053 reflections measured, 1907 were independent ($R_{int} = 0.024$), of which 1240 reflections with $I > 2.00\sigma(I)$ were used for structure solution and refinement. Three standard reflections ($\bar{1}3\bar{1}$, $\bar{1}1\bar{3}$, 032) monitored at intervals of 150 showed no significant variation. No absorption correction, but Lorentz, polarization and secondary-extinction (coefficient = 0.31645×10^{-5}) corrections were applied. The structure was solved by direct methods (Gilmore, 1984; Beurskens, 1984), and refinement, based on $|F|$ values, was carried out by full-matrix least squares, with non-H atoms refined anisotropically. 337 parameters were refined. Final $R = 0.042$, $wR = 0.042$ with the weighting scheme $w = 4F_o^2/\sigma^2(F_o^2)$; $S = 1.40$. Maximum final shift to e.s.d. ratio was 0.09, and maximum and minimum peak heights in the final difference Fourier map were 0.13 and −0.13 e Å^{-3}. All calculations were performed with

0108-2701/93/010042-03$06.00 © 1993 International Union of Crystallography