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Structure of an Epimeric Aldol Intermediate* Toward the Synthesis of Erythronolide A

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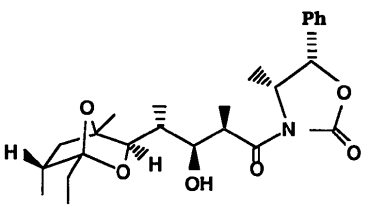
Abstract. $C_{25}H_{35}NO_6$, $M_r = 445{\cdot}56$, monoclinic, $P2_1$, $a = 11{\cdot}969$ (5), $b = 8{\cdot}732$ (3), $c = 12{\cdot}265$ (3) Å, $\beta = 110{\cdot}80$ (2)°, $V = 1198{\cdot}3$ (7) Å^3, $Z = 2$, $D_x = 1{\cdot}23$ g cm^{-3}, Mo $K\alpha$, $\lambda = 0{\cdot}71069$ Å, $\mu = 0{\cdot}818$ cm^{-1}, $F(000) = 480$, $T = 163$ K, $R = 0{\cdot}0574$ for 2292 reflections [$F_o \geq 4\sigma(F_o)$]. The absolute configuration is assigned on the basis of internal comparison to the oxazolidinone moiety. There is an intramolecular H bond involving the hydroxyl group and one of the O atoms of the bicyclic ring with an O···O distance of 2·832 (4) Å, an O···H distance of 2·01 (5) Å and an O—H···O angle of 134 (4)°. However, no such intermolecular contacts are observed.

Experimental. Synthesis of (1) will be described elsewhere (Martin & Mulhern, 1987). The chiral auxiliary upon which the assignment of absolute configuration was made, (4*R*,5*S*)-(+)-4-methyl-5-phenyl-2-oxazolidinone, was purchased from the Aldrich Chemical Company. Colorless plate, cut from a larger crystal, 0·27 × 0·41 × 0·47 mm from diethyl ether. Syntex $P2_1$ diffractometer, graphite monochromator, Syntex LT-1 low-temperature delivery system (163 K). Lattice parameters from least-squares refinement of 41 reflections with $20{\cdot}4 < 2\theta < 30{\cdot}8°$. ω-scan technique (5698 reflections, 2937 unique, $R_{int} = 0{\cdot}0365$; no averaging of hkl and $h\bar{k}l$ reflections), 2θ range 4·0–55·0°, 1° ω scan at a constant 10·0° min^{-1} ($h = -15 \rightarrow 14$, $k = -11 \rightarrow 11$, $l = -15 \rightarrow 14$). Four reflections (113; 30$\bar{3}$; 203; 0$\bar{2}$0) remeasured every 196 reflections to monitor instrument and crystal stability [maximum correction on I was 2·1%; Henslee & Davis (1975)]. Data also corrected for Lp effects and absorption (based on crystal shape; transmission-factor range 0·932–0·987). Data reduction described in Riley & Davis (1976). Reflections having $F_o < 4\sigma(F_o)$ considered unobserved (645 reflections). Structure solved by direct methods (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978) and refined by full-matrix least squares (Sheldrick, 1976) in blocks of 243 and 187 parameters with scale factor refined in both blocks for 429 parameters refined. Origin defined by fixing of atom positions in block not being refined. Non-H atoms refined with anisotropic thermal parameters. H atoms from a ΔF map and refined with isotropic thermal parameters. $\sum w(|F_o| - |F_c|)^2$ minimized, where $w = 1/[\sigma(F_o)]^2$ and $\sigma(F_o) = (0{\cdot}5kI^{-1/2}\{[\sigma(I)]^2 + (0{\cdot}02I)^2\}^{1/2})$.



(1)

Table 1. *Fractional coordinates and equivalent isotropic thermal parameters* (Å^2) *for non-H atoms of* $C_{25}H_{35}NO_6$

	x	*y*	*z*	*U**
N1	0·1179 (2)	0·3704 (4)	0·3667 (2)	0·0282 (11)
C2	0·1990 (3)	0·4192 (5)	0·3161 (3)	0·0293 (14)
O3	0·1654 (2)	0·5580 (4)	0·2691 (2)	0·0346 (10)
C4	0·0645 (3)	0·6153 (5)	0·2989 (3)	0·0316 (15)
C5	0·0122 (3)	0·4695 (5)	0·3320 (3)	0·0318 (15)
O6	0·2858 (2)	0·3563 (4)	0·3104 (2)	0·0366 (10)
C7	−0·0931 (4)	0·3974 (6)	0·2316 (4)	0·037 (2)
C8	−0·0149 (3)	0·7103 (5)	0·1996 (3)	0·035 (2)
C9	−0·0935 (5)	0·8121 (6)	0·2192 (5)	0·059 (2)
C10	−0·1704 (5)	0·8979 (8)	0·1272 (5)	0·078 (3)
C11	−0·1709 (4)	0·8803 (7)	0·0144 (4)	0·057 (2)
C12	−0·0922 (4)	0·7793 (6)	−0·0038 (4)	0·046 (2)
C13	−0·0148 (3)	0·6930 (5)	0·0869 (3)	0·035 (2)
C14	0·1228 (3)	0·2341 (5)	0·4336 (3)	0·0341 (15)
O15	0·0359 (2)	0·2047 (4)	0·4586 (2)	0·0424 (11)
C16	0·2372 (3)	0·1432 (5)	0·4717 (3)	0·033 (2)
C17	0·2128 (5)	−0·0193 (6)	0·5028 (5)	0·046 (2)
C18	0·3323 (3)	0·2284 (5)	0·5731 (3)	0·0340 (15)
O19	0·2812 (2)	0·2432 (4)	0·6621 (2)	0·0448 (12)
C20	0·4536 (3)	0·1497 (5)	0·6161 (3)	0·0337 (15)
C21	0·5030 (4)	0·1381 (7)	0·5163 (3)	0·043 (2)
C22	0·5471 (3)	0·2313 (5)	0·7191 (3)	0·0320 (15)
O23	0·5407 (2)	0·3923 (3)	0·6984 (2)	0·0331 (10)
C24	0·5487 (4)	0·4630 (5)	0·8065 (3)	0·036 (2)
C25	0·6777 (4)	0·4360 (5)	0·8938 (4)	0·042 (2)
C26	0·6707 (4)	0·2679 (6)	0·9275 (4)	0·047 (2)
C27	0·5443 (4)	0·2225 (5)	0·8448 (3)	0·037 (2)
O28	0·4784 (2)	0·3610 (4)	0·8483 (2)	0·0398 (11)
C29	0·4919 (5)	0·0797 (6)	0·8775 (4)	0·045 (2)
C30	0·7728 (4)	0·4687 (6)	0·8414 (4)	0·050 (2)
C31	0·5048 (5)	0·6247 (6)	0·7897 (4)	0·046 (2)
C32	0·3740 (5)	0·6428 (8)	0·7143 (5)	0·055 (2)

* For anisotropic atoms, the U value is U_{eq}, calculated as $U_{eq} = \frac{1}{3}\sum_i\sum_j U_{ij}a_i^*a_j^*A_{ij}$, where A_{ij} is the dot product of the ith and jth direct-space unit-cell vectors.

* (4*R*,5*S*)-3-((2′*R*,3′*S*,4′*R*)-4′-{(1″*S*,3″*R*,4″*R*,6″*R*)-1″-ethyl-4″,6″-dimethyl-2″,7″-dioxabicyclo[2.2.1]heptan-3″-yl}-3′-hydroxy-2′-methylvaleryl)-4-methyl-5-phenyl-1,3-oxazolidin-2-one.

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Table 2. *Bond lengths* (Å) *and angles* (°) *for the non*-H *atoms of* $C_{25}H_{35}NO_6$

1	2	3	1–2	1–2–3	1	2	3	1–2	1–2–3
C2	N1	C5	1·391 (5)	110·9 (3)	C25	C24	O28	1·553 (6)	103·0 (3)
C5	N1	C14	1·466 (5)	120·8 (3)	C25	C24	C31		117·0 (3)
C14	N1	C2	1·435 (5)	128·0 (3)	C25	C24	O23		107·2 (4)
O3	C2	O6	1·341 (5)	121·5 (4)	O28	C24	C31	1·439 (6)	114·3 (4)
O3	C2	N1		108·6 (3)	O28	C24	O23		101·9 (3)
O6	C2	N1	1·199 (5)	129·9 (4)	C31	C24	O23	1·495 (6)	112·0 (3)
C4	O3	C2	1·469 (5)	110·4 (3)	C26	C25	C30	1·535 (7)	114·5 (4)
C5	C4	C8	1·535 (6)	118·2 (3)	C26	C25	C24		101·2 (4)
C5	C4	O3		103·4 (3)	C30	C25	C24	1·520 (8)	113·0 (4)
C8	C4	O3	1·501 (5)	109·0 (3)	C27	C26	C25	1·544 (6)	101·7 (3)
C7	C5	N1	1·549 (5)	111·4 (4)	O28	C27	C29	1·453 (6)	113·4 (4)
C7	C5	C4		114·8 (3)	O28	C27	C22		101·0 (3)
N1	C5	C4		100·1 (3)	O28	C27	C26		100·5 (3)
C9	C8	C13	1·376 (7)	119·0 (4)	C29	C27	C22	1·513 (7)	117·4 (4)
C9	C8	C4		119·4 (4)	C29	C27	C26		116·0 (3)
C13	C8	C4	1·391 (6)	121·5 (4)	C22	C27	C26		106·1 (4)
C10	C9	C8	1·394 (7)	120·1 (5)	C24	O28	C27		96·4 (3)
C11	C10	C9	1·389 (9)	121·0 (6)	C32	C31	C24	1·518 (7)	114·7 (4)
C12	C11	C10	1·366 (8)	118·4 (5)	O19	C18	C16		105·3 (3)
C13	C12	C11	1·390 (6)	121·4 (5)	C20	C18	C16	1·521 (6)	113·6 (4)
C8	C13	C12		120·1 (4)	C21	C20	C22	1·541 (7)	108·1 (3)
O15	C14	C16	1·213 (5)	125·3 (4)	C21	C20	C18		110·0 (3)
O15	C14	N1		117·1 (3)	C22	C20	C18	1·534 (5)	113·8 (4)
C16	C14	N1	1·506 (6)	117·5 (4)	O23	C22	C27	1·425 (5)	101·9 (3)
C17	C16	C18	1·524 (7)	113·5 (3)	O23	C22	C20		109·5 (3)
C17	C16	C14		109·5 (4)	C27	C22	C20	1·555 (6)	121·8 (4)
C18	C16	C14	1·546 (5)	109·0 (3)	C24	O23	C22	1·435 (5)	106·1 (3)
O19	C18	C20	1·435 (5)	112·9 (3)					

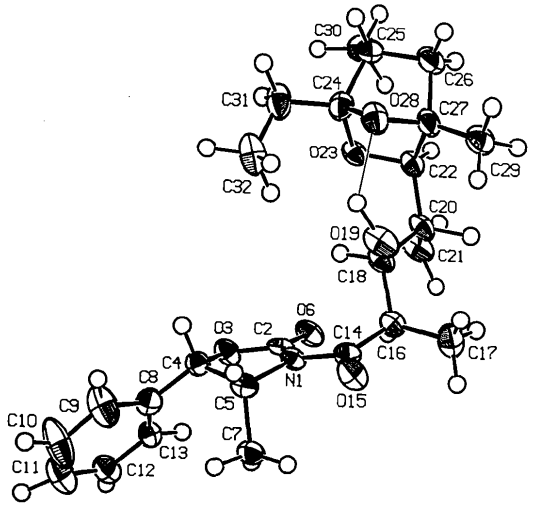

Fig. 1. View showing atom-labeling scheme. Thermal ellipsoids are scaled to the 50% probability level.

Intensity, I, given by $(I_{peak} - I_{background}) \times$ (scan rate); 0·02 is a factor to downweight intense reflections and to account for instrument instability and k is the correction due to Lp effects, absorption and decay. $\sigma(I)$ estimated from counting satistics; $\sigma(I) = [(I_{peak} + I_{background})^{1/2} \times$ (scan rate)]. Final $R = 0{\cdot}0574$ for 2292 reflections, $wR = 0{\cdot}0407$ ($R_{all} = 0{\cdot}0798$, $wR_{all} = 0{\cdot}0421$) and goodness of fit = 2·009. Maximum $|\Delta/\sigma| < 0{\cdot}1$ in the final refinement cycle and the minimum and maximum peaks in the final ΔF map were −0·24 and 0·26 e Å^{-3}, respectively. The stereochemistry of the substituents on the oxazolidinone ring, which was reported by Evans, Bartroli & Shih (1981), was used to differentiate between enantiomorphs. Differentiation could not be made on the basis of the X-ray results ($wR = 0{\cdot}0407$ for the enantiomorph). Scattering factors for the non-H atoms from Cromer & Mann (1968), with anomalous-dispersion corrections from Cromer & Liberman (1970), while scattering factors for the H atoms from Stewart, Davidson & Simpson (1965); linear absorption coefficient from *International Tables for X-ray Crystallography* (1974).* Positional and thermal parameters for non-H atoms are listed in Table 1, while the bond lengths and angles for the non-H atoms are listed in Table 2. The atom-labeling scheme is shown in Fig. 1. The least-squares-planes program was supplied by Cordes (1983); other computer programs from reference 11 of Gadol & Davis (1982).

Related literature. The syntheses of some erythronolides have been described by Kinoshita, Arai, Ohsawa & Nakata (1986) and in references cited therein.

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* Tables of anisotropic thermal parameters, H-atom positional parameters, bond distances and angles involving the H atoms, torsion angles, least-squares planes, structure-factor amplitudes and a unit-cell packing diagram have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 44171 (28 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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