Short Communication

Crystal Structure of Methyl (2S,3S)-3-Triphenylmethylaminooxolan-2-ylacetate

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We have recently investigated the syntheses of some chiral γ-aminobutyric acid (GABA) analogues.[1] The key step in these syntheses is the cyclisation (Fig. 1) of (S),(E)-6-hydroxy-4-(triphenylmethylamino)hex-2-enoic acid methyl ester (1). Treatment of 1 with tetrabutylammonium fluoride trihydrate (TBAF) yields the diastereomeric esters 2 and 3 in the proportion 1:3. While elemental analysis and mass spectrometry showed the molecular formula to be $C_{26}H_{27}NO_3$ and the gross structure was readily confirmed by chemical and spectroscopic methods, assignment of the stereochemistry at C(2) could only be tentatively inferred on the basis of the ^1H NMR data.[1] The present X-ray structure determination proves the cis relationship of the C(2)-methoxycarbonyl and C(3)-amino groups, and since the absolute stereochemistry at C(3) is known the assignment of the crystalline ester 2 as methyl (2S,3S)-3-triphenylmethylaminooxolan-2-ylacetate.

In general, the molecular structure (Fig. 2) of 2 has no unusual features and the magnitude of bond distances, bond angles and torsional angles do not deviate significantly from expected values. The oxolane ring in 2 accommodates the bulky substituents at C(1) and C(2) by adopting a half-chair conformation and the observed torsional angle C(5)−C(2)−C(1)−N of 48° corresponds with the calculated maximum value for a 1,2-cis-substituted cyclo-
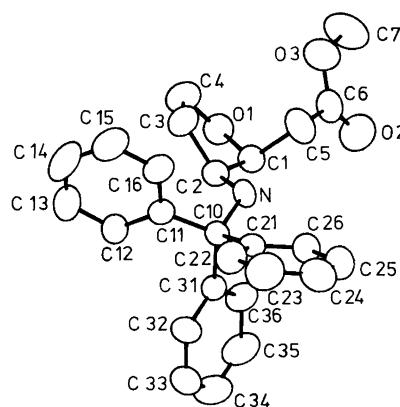

Fig. 2. Structure of methyl (2S,3S)-3-triphenylmethylaminooxolan-2-ylacetate (2).

pentane half-chair.[2] Bond distances may be compared with those for tetrahydrofuranyluracil[3] and while the bonds C(1)−C(2) and C(2)−C(3) were longer than in that case, the observed values were not unusual. The trityl moiety adopts the expected propeller-like conformation which is the established way of reducing steric interaction between the phenyl rings in this group.[4]
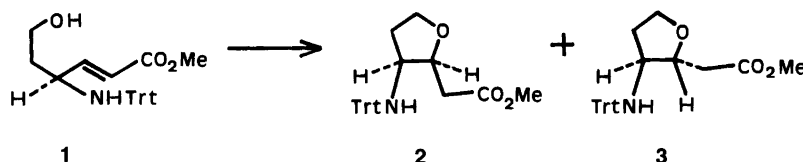

Fig. 1. Tetrabutylammonium fluoride catalysed cyclisation of (S),(E)-6-hydroxy-4-(triphenylmethylamino)hex-2-enoic acid methyl ester (1).

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Experimental

Methyl (2S,3S)-3-triphenylmethylaminooxolan-2-ylacetate (**2**). (*S*),(*E*)-6-hydroxy-4-(triphenylmethylamino)hex-2-enoic acid methyl ester (2.25 g, 5.6 mmol) was dissolved in tetrahydrofuran (40 ml). TBAF (1.83 g, 5.8 mmol) was added to the stirred solution at room temperature. Reaction was seen to be complete by TLC after 15 min and the resulting solution was diluted with a 5 % aqueous solution of citric acid (100 ml) and then extracted with diethyl ether (2×100 ml). The combined ethereal layers were washed with water, dried with Na_2SO_4, and evaporated under reduced pressure to leave an unalloyed mixture of the diastereomeric esters **2** and **3** (2.18 g). Preparative HPLC was undertaken on a Jobin-Yvon Miniprep LC, using silica gel 60H (15 μm [Merck]) as the stationary phase and ethyl acetate/ petroleum ether b.p. 60–80°C/ toluene (1:8:1) as the mobile phase. This provided **2** (0.45 g) and **3** (1.22 g). Compound **2** was recrystallised from diethyl ether/petroleum ether b.p. 60–80°C to give colourless prisms, m.p. 150°C, $[\alpha]_D^{25}$ −111.5° (*c* 1, $CHCl_3$). Anal. $C_{26}H_{27}NO_3$: C,H,N. Full spectroscopic details will be given elsewhere.[1]

Structure analysis. All computer programs used in the structure analysis were part of the Enraf-Nonius Structure Determination Package (1987). The determination of unit-cell parameters and data collection were carried out at room temperature on an Enraf-Nonius CAD4 diffractometer using monochromated Mo K_α radiation (λ = 0.71073 Å). The crystal was cut to an approximately orthogonal shape, 0.15×0.20×0.35 mm³. Cell parameters are based on a least-squares fit to diffractometer settings for 25 general reflections with 2θ ≥ 29°. Unit-cell dimensions were determined to be as follows: orthorhombic; *a* = 10.165(1) Å; *b* = 12.929(1) Å; *c* = 16.417(2) Å; *V* = 2157.6(7) Å³; *M* = 401.51 amu; *Z* = 4; D_x = 1.236 g cm⁻³; μ = 0.749 cm; *F*(000) = 856. The space group was $P2_12_12_1$ (No. 19).

Intensity data were collected using the ω-scan technique (scan speed 4 to 1° min⁻¹) over the range 0° < 2θ < 56°. The minimum scan width was 1.5°, including 2×0.25 for background counts. Three standard reflections were measured every 2 h and the data corrected accordingly. Minimum and maximum corrections were 0.97 and 1.06, respectively. Crystal orientation was checked every 300 reflections. 2930 reflections were recorded and 1594 of these with *I* > 2σ(*I*) were included in the structure analysis. MULTAN[5] gave all non-H positions and H-atoms were placed geometrically. Least-squares refinement (379 parameters), using isotropic temperature factors, preceded empirical absorption correction,[5-7] minimum and maximum corrections 0.96 and 1.07, respectively, with an average value of 0.97. Least-squares refinement, including anisotropic thermal parameters for non-H atoms, minimising $w(F_o-F_c)^2$, where $w = 4 \cdot Lp \cdot I/ [\sigma^2(I) + (0.02 \cdot I)^2]$ and $I = I_{count}$, converged with $R = (\Sigma\ F_o-F_c)/\Sigma F_o = 4.3\%$, $R_w = [\Sigma w(F_o-F_c)^2/\Sigma wF_o^2]^{1/2} = 3.7\%$ and $S = [\Sigma w(F_o-F_c)^2/(1594-379)]^{1/2} = 1.420$. The

Table 1. Table of positional parameters and their estimated standard deviations.

Atom	x	y	z	B/Å² [a]
O(1)	0.1062(2)	0.3015(2)	−0.0691(1)	4.21(5)
O(2)	0.2051(3)	0.5493(2)	−0.0041(2)	6.86(8)
O(3)	0.3024(3)	0.4859(2)	−0.1125(2)	5.78(7)
N	0.2865(2)	0.1963(2)	0.1042(1)	3.18(5)
C(1)	0.1686(3)	0.3131(3)	0.0078(2)	3.47(7)
C(2)	0.1983(3)	0.2014(2)	0.0344(2)	3.32(7)
C(3)	0.2406(4)	0.1535(3)	−0.0470(2)	4.61(9)
C(4)	0.1675(4)	0.2169(3)	−0.1102(2)	5.6(1)
C(5)	0.2924(4)	0.3790(3)	0.0008(2)	4.96(9)
C(6)	0.2610(4)	0.4805(3)	−0.0370(2)	4.42(8)
C(7)	0.2708(5)	0.5778(3)	−0.1579(3)	7.8(1)
C(10)	0.2678(3)	0.1089(2)	0.1604(2)	2.89(6)
C(11)	0.2629(4)	0.0077(2)	0.1111(2)	3.59(7)
C(12)	0.1462(4)	−0.0432(3)	0.0929(2)	4.66(9)
C(13)	0.1466(5)	−0.1253(3)	0.0387(2)	6.2(1)
C(14)	0.2596(6)	−0.1592(3)	0.0040(2)	7.3(1)
C(15)	0.3771(5)	−0.1106(3)	0.0215(2)	6.2(1)
C(16)	0.3791(4)	−0.0273(3)	0.0742(2)	4.35(8)
C(21)	0.3814(3)	0.1115(3)	0.2225(2)	3.25(7)
C(22)	0.4331(4)	0.0227(3)	0.2555(2)	4.96(9)
C(23)	0.5277(4)	0.0304(3)	0.3168(2)	6.3(1)
C(24)	0.5676(4)	0.1226(4)	0.3465(2)	5.9(1)
C(25)	0.5171(4)	0.2100(3)	0.3133(2)	5.4(1)
C(26)	0.4235(3)	0.2054(3)	0.2520(2)	4.15(8)
C(31)	0.1431(3)	0.1255(3)	0.2120(2)	3.49(7)
C(32)	0.1035(4)	0.0489(3)	0.2659(2)	4.98(9)
C(33)	−0.0033(4)	0.0650(3)	0.3175(3)	6.4(1)
C(34)	−0.0688(4)	0.1552(4)	0.3175(3)	7.0(1)
C(35)	−0.0312(4)	0.2308(4)	0.2653(2)	6.1(1)
C(36)	0.0763(3)	0.2178(3)	0.2123(2)	4.57(9)

[a] $B = 4/3[a^2B(1,1) + b^2B(2,2) + c^2B(3,3) + ab(\cos\gamma)B(1,2) + ac(\cos\beta)B(1,3) + bc(\cos\alpha)B(2,3)]$.

final difference electron density map showed maximum and minimum values of +0.13 and −0.12 e Å⁻³. Secondary extinction coefficients were found to be negligible.

The structure factor list may be obtained from the authors upon request. Atomic parameters are given in Table 1 and an ORTEP[8] drawing may be found in Fig. 2.

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