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(−)-(1*R*,2*S*,2′*R*,5*R*)-2-(1-Hydroxyprop-2-yl)-5-methylcyclohexanol

Ferdinand Körner, Markus Schürmann, Hans Preut* and Wolfgang Kreiser

Fachbereich Chemie, Universität Dortmund, Otto-Hahn-Straße 6, 44221 Dortmund, Germany
Correspondence e-mail: uch002@uxp1.hrz.uni-dortmund.de

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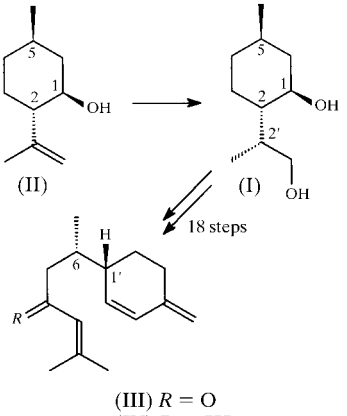
Stereoselective hydroboration of (−)-isopulegol and subsequent fractional crystallization furnishes the title compound, $C_{10}H_{20}O_2$. The relative configuration of the stereogenic centres has been assigned by means of X-ray diffraction analysis since the monoterpenediol is employed as a versatile chiral building block in stereospecific natural product synthesis.

Comment

The preparation of the title compound, (−)-(I), by hydroboration of (−)-isopulegol, (II), was first reported by Schulte-Elte & Ohloff (1967). In the meantime, (−)-(I) has found broad application as an optically active starting material in the synthesis of natural products, especially of the antimalarial drug artemisinin and a number of its analogues (Imakura *et al.*, 1988; Constantino *et al.*, 1996; Avery *et al.*, 1990, 1994; Hui *et al.*, 1997). Although the stereochemistry of (−)-(I) appears to



(III) R = O
(IV) R = CH_2

be well established in the literature by NMR data and by the configuration of derivatives synthesized from it, the crystal structure of the important relay compound itself is still lacking. During our 18-step stereospecific preparation of the bis-abolane sesquiterpenes β-turmerone, (III), and β-sesquiphellandrene, (IV) (Kreiser & Körner, 1999), we succeeded in determining the relative configuration of the vicinal asymmetric C atoms by X-ray diffraction analysis of their synthetic intermediate (−)-(I), since during further transformation, C2 and C2′ of (−)-(I) become C1′ and C6 in the corresponding sesquiterpenes. (−)-(I) was prepared from technical grade (−)-isopulegol, (II), of moderate enantiomeric and diastereomeric purity, but after repeated crystallization from Et_2O, the material was identical in melting point and optical rotation with the data reported for (−)-(I) derived from highly pure (II). Therefore, the configuration given in Fig. 1 is most likely to be the absolute one.

In the crystalline state, the cyclohexane part of (−)-(I) displays an almost perfect undistorted chair conformation since all the six torsion angles involving the three substituents (O1—C1—C2—C3, O1—C1—C6—C5, C2′—C2—C3—C4, C6—C1—C2—C2′, C3—C4—C5—C5*A* and C5*A*—C5—C6—C1) are in the range 176.8 (3)–179.5 (3)°. Accordingly, the hydroxy, isopropyl and methyl substituents (O1, C2′ and C5*A*, respectively) are found in ideal all-equatorial positions. Consequently, the relative arrangement of the hydroxy and isopropyl groups is *anti*, and of the hydroxy and the methyl groups is *syn*, in accordance with the predicted 1*R*,2*S*,5*R* stereochemistry. Considering that the stereogenic centres at C1 and C5 are going to be extinguished during the course of further synthetic manipulation, the most important aspect is the relative stereochemistry between C2 and C2′, which can be deduced from Fig. 1. Provided that the configuration at C2 is *S*, that at C2′ has to be *R*.

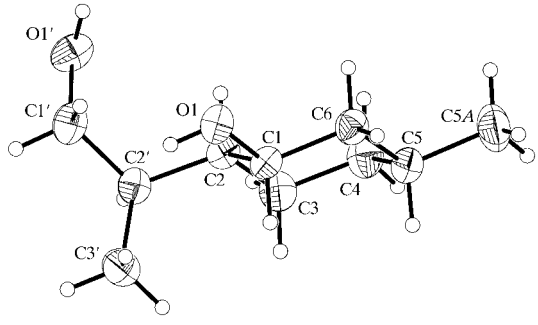


Figure 1
A view of the title compound showing the labelling of all non-H atoms. Displacement ellipsoids are shown at 50% probability levels and H atoms are drawn as circles of an arbitrary radius.

Experimental

The preparation of (−)-(I) from (II) is described by Kreiser & Körner (1999). For the X-ray diffraction analysis, pure (I) (1.00 g, 5.80 mmol) was dissolved completely in the required amount of dry Et_2O at reflux temperature. Thereafter, further Et_2O (10 ml) was added and crystals [m.p. 377.5–378 K, $[\alpha]_D^{295} = -19.6°$ (c = 2.67, $CHCl_3$)] were grown slowly at 273 K.

Crystal data

$C_{10}H_{20}O_2$
$M_r = 172.26$
Monoclinic, $P2_1$
$a = 8.5710$ (7) Å
$b = 6.4665$ (3) Å
$c = 9.8502$ (8) Å
$\beta = 106.783$ (3)°
$V = 522.69$ (7) Å^3
$Z = 2$
$D_x = 1.094$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 6694 reflections
$\theta = 3.73$–$25.76°$
$\mu = 0.074$ mm^{-1}
$T = 291$ (1) K
Needle, colourless
0.30 × 0.08 × 0.05 mm

Data collection

Nonius KappaCCD diffractometer
360 frames *via* ω rotation ($\Delta\omega = 1°$) and 2 × 60 s per frame scans
Absorption correction: none
6694 measured reflections
1935 independent reflections
1299 reflections with $I > 2\sigma(I)$
$R_{int} = 0.027$
$\theta_{max} = 25.76°$
$h = -10 \rightarrow 10$
$k = -7 \rightarrow 7$
$l = -11 \rightarrow 11$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.050$
$wR(F^2) = 0.187$
$S = 0.721$
1935 reflections
112 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.1903P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.21$ e Å^{-3}
$\Delta\rho_{min} = -0.28$ e Å^{-3}

The weighting scheme proposed by the refinement resulted in the low goodness-of-fit value.

Data collection: *KappaCCD Software* (Nonius, 1997); cell refinement: *DENZO* and *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO* and *SCALEPACK*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *SHELXTL-Plus* (Sheldrick, 1991); software used to prepare material for publication: *SHELXL*97 (Sheldrick, 1997) and *PARST*95 (Nardelli, 1995).

Table 1
Selected torsion angles (°).

C6—C1—C2—C2′	−178.5 (2)	C3—C4—C5—C5*A*	−177.8 (3)
O1—C1—C2—C3	177.7 (2)	O1—C1—C6—C5	−179.3 (3)
C2′—C2—C3—C4	176.8 (3)	C5*A*—C5—C6—C1	179.5 (3)

Table 2
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O1′—H1′···O1^{i}	0.82	1.89	2.702 (3)	170

Symmetry code: (i) $1-x, y-\frac{1}{2}, 1-z$.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: NA1422). Services for accessing these data are described at the back of the journal.

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