Table 4. *Hydrogen-bonding geometry (Å, °) for (II)*

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C2—H2···O1^{ii}	0.92 (2)	2.60 (2)	3.358 (2)	139 (1)
C3—H3···O3^{iii}	0.96 (2)	2.44 (2)	3.337 (2)	155 (1)

Symmetry codes: (ii) $-x, y-\frac{1}{2}, \frac{1}{2}-z$; (iii) $2-x, 2-y, 1-z$.

In compound (I), scan widths were (1.50 + 0.35tanθ)° in ω, with a background/scan time ratio of 0.5. The data were corrected for Lorentz and polarization effects. The Laue group assignment and intensity statistics were consistent with centrosymmetry and indicated space group $P\bar{1}$ (No. 2); since refinement proceeded well it was adopted. Fourier difference methods were used to locate the initial H-atom positions. In later stages of refinement, all H atoms except the carboxylic H atoms (H4 and H5) were made canonical with C—H = 0.98 Å and U_{iso} = 1.2U_{eq} of the attached C atom. The carboxylic H atoms were refined isotropically. H atoms of the (disordered) methyl groups of the disordered DMSO molecule were assigned fixed occupancies of 0.5 consistent with the refined S-atom populations of the two disorder components; canonical methyl-group geometries were generated using not less than two experimentally determined H-atom locations per methyl group. The maximum effect of extinction was 5.7% of F_o for $02\bar{2}$. The maximum positive residual peak was located near the midpoint of the S2*A*—C18 bond; the maximum negative peak was located ~0.6 Å from S1. In compound (II), scan widths were (1.35 + 0.35tanθ)° in ω, with a background/scan time ratio of 0.5. The data were corrected for Lorentz and polarization effects. The Laue group assignment, systematic absences and intensity statistics were consistent with centrosymmetry and indicated space group $P2_1/c$ (No. 14); since refinement proceeded well it was adopted. Fourier difference methods were used to locate the initial H-atom positions; both H atoms were refined isotropically. The maximum effect of extinction was 14.9% of F_o for $11\bar{3}$. The maximum positive residual peak was located very near the center of symmetry between C5 and C5^i [symmetry code: (i) $1-x, 1-y, 1-z$]; the maximum negative peak was located near the center of the benzenoid ring.

For both compounds, data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1988); cell refinement: *MSC/AFC Diffractometer Control Software*; data reduction: *TEXSAN* (Molecular Structure Corporation, 1989); program(s) used to solve structures: *SHELXS86* (Sheldrick, 1985); program(s) used to refine structures: *TEXSAN*; molecular graphics: *ORTEP*II (Johnson, 1976); software used to prepare material for publication: *TEXSAN*.

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(5a*S*,7*S*)-7-Isopropenyl-3-methyl-5a,6,8,9-tetrahydro-1*H*,7*H*-pyrano[4,3-*b*][1]benzopyran-1-one

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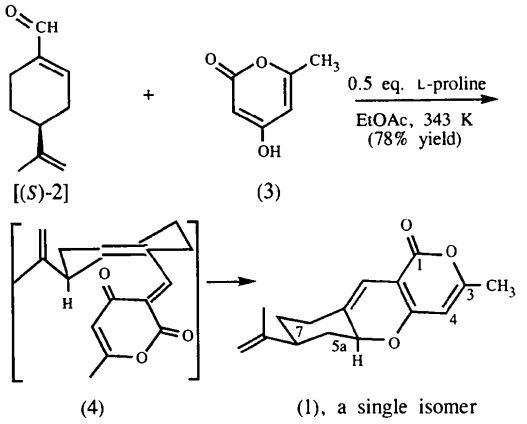
Abstract

A remarkable asymmetric induction was observed in the one-pot condensation reaction of (*S*)-(−)-perillaldehyde with 4-hydroxy-6-methyl-2-pyrone in the presence of L-proline which provided the title compound, $C_{16}H_{18}O_3$, a tricyclic pyrone, as a single diastereomer in 78% yield. As the configuration of the cyclohexane C atom holding the isopropenyl group is the same as that in the (*S*)-aldehyde substrate, the total absolute stereochemistry

could be elucidated from its X-ray structure. The cyclohexane ring has a chair conformation in which the juncture H atom (H5a) is axially oriented and the isopropenyl substituent is equatorial.

Comment

We recently discovered a one-pot condensation of 6-substituted 4-hydroxypyrones with 1-cyclohexenecarboxaldehydes which provides various tricyclic pyrones. When the aldehyde was an enantiomer, a remarkable asymmetric induction was observed. Thus, an ethyl acetate solution of (*S*)-(−)-perillaldehyde, (2), treated with 4-hydroxy-6-methyl-2-pyrone, (3), and 0.5 equivalent of L-proline at 343 K, produced a single diastereomer, isolated in 78% yield. No other regio- or stereoisomer was detected. The general structure and relative stereochemistry at the asymmetric centers are not readily solved by spectroscopy. The configuration of the C atom holding the isopropenyl group being the same as that of the (*S*)-aldehyde substrate (2), it was reasonable to turn to X-ray analysis to determine the total absolute structure of (1) unambiguously.



The X-ray structure determination (Fig. 1) shows the product to be the tricyclic pyrone (1), the title compound. The cyclohexane ring has a chair conformation with the C5a-H atom axially oriented and the C7-isopropenyl group equatorial. The pyran and pyrone rings are essentially coplanar, the angle between their least-squares planes being 2.1 (2)°. The bond lengths and angles of (1) are mostly within the expected range. However, C1—C10a [1.423 (4) Å] and C4a—C10a [1.365 (3) Å] are shorter than the corresponding bonds C2—C3 [1.438 (9) Å] and C3—C4 [1.398 (8) Å] in 4-hydroxy-3-(3-hydroxy-1-oxo-3-phenyl-2-propenyl)-6-methyl-2-pyrone (Thailambal, Pattabhi & Gabe, 1986), and C4a—O5 [1.348 (3) Å] is longer than the corresponding bond C4—O17 [1.316 (8) Å] in this 2-pyrone. The angle C1—O2—C3 [121.8 (2)°] is smaller than the corresponding angle C2—O1—C6 [123.6 (4)°] in the above mentioned 2-pyrone (Thailambal, Pattabhi & Gabe, 1986), and the angle O2—C1—C10a [117.4 (2)°] is slightly larger than the corresponding angle O1—C2—C3 [116.5 (5)°] of the same 2-pyrone. Some additional bond distances and angles of interest are given in Table 1.

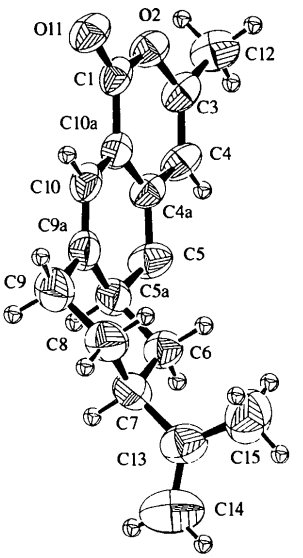


Fig. 1. The molecular structure and atom-numbering scheme for (1), with displacement ellipsoids at the 50% probablility level.

The mechanism leading to the formation of (1), as illustrated above, presumably involves nucleophilic addition of the C atom α to the carbonyl in (3) (enolic C atom) to the carbonyl C atom of (2), followed by dehydration to produce the dienone (4). Subsequent electrocyclic ring closure of (4) affords (1) in a process apparently occurring on the equatorial face of the cyclohexene ring. The isopropenyl group on the (*S*)-C7 atom assumes the equatorial orientation in this process, concurrently inducing an *S* configuration to C5a and an axial orientation to its appended H atom. The stereochemistry of this type of electrocyclic ring closure has not been reported previously.

This class of tricyclic pyrone possesses various types of important biological activity, including the inhibition of DNA synthesis and tumor cell growth *in vitro* (Perchellet *et al.*, 1997).

Experimental

A solution of 1.19 g (7.93 mmol) of (*S*)-4-isopropenyl-1-cyclohexenecarboxaldehyde, (2) (perillaldehyde; Aldrich), 1.00 g (7.93 mmol) of 4-hydroxy-6-methyl-2-pyrone, (3) (Aldrich), and 0.46 g (3.97 mmol) of L-proline in 45 ml of ethyl acetate was heated at 343 K under an argon atmosphere for 24 h. The mixture was cooled to room temperature, diluted with 300 ml of methylene chloride, washed twice with 70 ml portions of saturated aqueous $NaHCO_3$ solution, with 100 ml

of water, and then with 60 ml of brine, dried ($MgSO_4$), filtered, and concentrated to give 1.95 g of crude product. Column chromatography of the crude product on silica gel using a gradient mixture of hexane–ether as eluant gave 1.596 g (78% yield) of (1); yellow solid, m.p. 413–414 K. $[\alpha]_D^{22}$ = +31.9° (*c* 0.75, $CHCl_3$). Recrystallization of (1) from diethyl ether–hexane provided the crystal used for the X-ray study. The tricyclic pyrone (1) displayed satisfactory ^1H NMR (400 Mhz), ^{13}C NMR (100 MHz), IR, and low-resolution mass spectra, and elemental analysis.

Crystal data

$C_{16}H_{18}O_3$	Mo $K\alpha$ radiation
M_r = 258.32	λ = 0.71069 Å
Monoclinic	Cell parameters from 25 reflections
$P2_1$	θ = 12.62–15.00°
a = 7.3743 (9) Å	μ = 0.084 mm^{-1}
b = 6.6684 (7) Å	T = 296 K
c = 14.1803 (11) Å	Plate
β = 95.074 (9)°	0.49 × 0.43 × 0.11 mm
V = 694.58 (12) $Å^3$	Colorless
Z = 2	
D_x = 1.235 Mg m^{-3}	
D_m not measured	

Data collection

Rigaku AFC-5*S* diffractometer	θ_{max} = 27.55°
ω scans (rate 3° min^{-1} in ω)	$h = 0 \rightarrow 9$
Absorption correction: none	$k = 0 \rightarrow 8$
1870 measured reflections	$l = -18 \rightarrow 18$
1740 independent reflections	3 standard reflections
945 reflections with $I > 2\sigma(I)$	every 100 reflections
R_{int} = 0.013	intensity decay: −0.1%

Refinement

Refinement on F^2	$\Delta\rho_{max}$ = 0.135 e $Å^{-3}$
$R(F)$ = 0.0378	$\Delta\rho_{min}$ = −0.141 e $Å^{-3}$
$wR(F^2)$ = 0.0891	Extinction correction: none
S = 1.128	Scattering factors from *International Tables for Crystallography* (Vol. C)
1740 reflections	Absolute configuration: from the known configuration of the (*S*)-aldehyde substrate [Flack (1983) parameter = −1 (2)]
174 parameters	
H-atom parameters constrained	
$w = 1/[\sigma^2(F_o^2) + (0.0385P)^2 + 0.1438P]$ where $P = (F_o^2 + 2F_c^2)/3$	
$(\Delta/\sigma)_{max} < 0.001$	

Table 1. *Selected geometric parameters (Å, °)*

O5—C4a	1.348 (3)	C5a—C9a	1.513 (4)
O5—C5a	1.451 (3)	C9a—C9	1.492 (4)
C1—C10a	1.423 (4)	C10a—C10	1.447 (4)
C4—C4a	1.414 (4)		
O5—C4a—C4	116.3 (2)	C9—C9a—C5a	113.7 (3)
O5—C5a—C9a	114.8 (2)	C1—C10a—C10	121.3 (2)

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1996). Cell refinement: *MSC/AFC Diffractometer Control Software*. Data reduction: *TEXSAN PROCESS* (Molecular Structure Corporation, 1995). Program(s) used to solve structure: *SHELXS86* (Sheldrick, 1985) and *TRACOR* (Beurskens *et al.*, 1987) in *TEXSAN*. Program(s) used to refine structure: *TEXSAN LS* and *SHELXL93* (Sheldrick, 1993). Molecular graphics: *ORTEP* (Johnson, 1965). Software used to prepare material for publication: *TEXSAN*, *SHELXL93* and *PLATON* (Spek, 1990).

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