X-ray Investigation of Bicyclic α -Methylene- δ -valerolactones. VI. (4a*S*,7*S*,8a*S*)-7-Isopropenyl-4a-methyl-3-methyleneperhydro-chromen-2-one

Jakub WOJCIECHOWSKI,* Henryk KRAWCZYK,** Marcin ŚLIWIŃSKI,** and Wojciech M. WOLF*†

*Institute of General and Ecological Chemistry, Technical University of Łódź, ul. Żeromskiego 116, Łódź 90-924, Poland

**Institute of Organic Chemistry, Technical University of Łódź, ul. Żeromskiego 116, Łódź 90-924, Poland

Enantiomerically pure (4a*S*,7*S*,8a*S*)-7-isopropenyl-4a-methyl-3-methyleneperhydro-chromen-2-one, $C_{14}H_{20}O_2$, crystallized in an orthorhombic system: cell constants $a = 6.565(1)$, $b = 10.880(2)$, $c = 17.716(4)$ Å; $V = 1265.5(4)$ Å³; space group $P2_12_12_1$ $Z = 4$. The title compound adopts a *semi*-folded conformation in which the δ -valerolactone and cyclohexane rings are almost perpendicular to one another. Both oxygen atoms are not involved in nonbonding intramolecular contacts with the neighboring atoms.

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The α -methylene- δ -valerolactone moiety has been found in a number of natural products with interesting antibacterial and cytostatic properties. Moreover, enantiomerically pure α -methylene- δ -valerolactones are chiral building blocks that can be applied in organic chemistry. The present study is a continuation of our structural investigations of optically active bicyclic α -methylene- δ -valerolactones, synthesized by an asymmetric Michael reaction.¹ In particular, the title compound is a diastereoisomer of (4a*S*,7*R*,8a*R*)-7-isopropenyl-4a-methyl-3-methyleneperhydro-chromen-2-one, the crystal structure of which was reported by us recently.²

Enantiomerically pure (4a*S*,7*S*,8a*S*)-7-isopropenyl-4a-methyl-3-methylene-perhydro-chromen-2-one (Fig. 1) was obtained in a three-step synthesis involving a highly stereoselective Michael reaction of a chiral enamine derived from (*R*)-1-phenylethylamine and (*S*)-dihydrocarvone with dicyclohexylammonium 2-(diethoxyphosphoryl)acrylate, followed by a chemoselective reduction of the oxoacid obtained with KBH_4 , lactonization and finally the Horner-Wadsworth-Emmons reaction of the resulting 2-(diethoxyphosphoryl)- δ -valerolactone with formaldehyde.³ The absolute structure of this molecule was determined based on this synthetic scheme.

Colorless, prismatic, crystals (mp 55 – 57°C) were grown at room temperature by slow evaporation from a 1:1 mixture of methanol and ethyl acetate. A single crystal with dimensions of $0.15 \times 0.08 \times 0.04$ mm was used for a structure determination. X-ray data were collected with graphite-monochromatized Cu

$K\alpha$ radiation at 20°C. The crystal structure was solved with direct methods and refined on F^2 by a full-matrix least-squares technique. All H atoms were located in a difference Fourier map, calculated after three cycles of anisotropic refinement. Their positional and isotropic displacement parameters were allowed to refine freely [$C-H = 0.94(2) - 1.019(16)$ Å]. Refinement of the Flack parameter $x = 0.0(2)$, indicated that the absolute configuration of the molecules in the crystal is consistent with the reaction mechanism. Relevant crystal and experimental data are summarized in Table 1. The final atomic coordinates and equivalent isotropic displacement parameters for non-H atoms are listed in Table 2. A view of the title compound along with the atom-numbering scheme is shown in

Fig. 1 Chemical structure of the title compound.

† To whom correspondence should be addressed.
E-mail: wmwolf@p.lodz.pl

Table 1 Crystal and experimental data

Formula	$C_{14}H_{20}O_2$
Formula weight	220.30
Crystal system	orthorhombic
Space group	$P2_12_12_1$ $Z = 4$
a	6.565(1) Å
b	10.880(2) Å
c	17.716(4) Å
V	1265.5(4) Å ³
D_x	1.156 g/cm ³
Absorption coefficient	0.594 mm ⁻¹
No. of reflections collected/unique	14212/2414
$2\theta_{max}$	142.32° with Cu $K\alpha$
Final R (all reflections)	0.0286
$(\Delta\sigma)_{max}$	0.00
$(\Delta\rho)_{max}$	0.10 e Å ⁻³
$(\Delta\rho)_{min}$	0.09 e Å ⁻³
Flack parameter	0.0(2), 985 Friedel pairs
Measurement	Bruker SMART APEX CCD
Program system	Bruker SMART (SHELXTL)
Adsorption correction	multi-scan (SADABS)
Structure determination	direct methods (SHELXS)
Refinement	full matrix (SHELXL)
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Table 2 Final atomic coordinates and equivalent isotropic displacement parameters ($\text{\AA}^2$). U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor

Atom	x	y	z	U_{eq}
O1	0.20138(14)	0.11730(8)	0.50658(4)	0.0550(2)
O2	0.35538(17)	-0.02642(12)	0.57106(6)	0.0841(4)
C1	0.10581(17)	0.16164(10)	0.43720(6)	0.0453(2)
C2	0.25632(19)	-0.00086(13)	0.51574(7)	0.0558(3)
C3	0.18566(18)	-0.09323(11)	0.45955(7)	0.0537(3)
C4	0.2141(3)	-0.21031(15)	0.47658(13)	0.0793(5)
C5	0.0811(2)	-0.05038(11)	0.38912(7)	0.0522(3)
C6	-0.03852(17)	0.06815(10)	0.40261(6)	0.0464(3)
C7	-0.1197(2)	0.12332(13)	0.32869(8)	0.0596(3)
C8	0.0433(2)	0.16910(13)	0.27458(7)	0.0595(3)
C9	0.18258(19)	0.26264(11)	0.31230(7)	0.0509(3)
C10	0.27203(18)	0.20601(11)	0.38459(6)	0.0473(3)
C11	-0.2174(2)	0.04172(13)	0.45532(9)	0.0598(3)
C12	0.3513(2)	0.31321(12)	0.26317(7)	0.0611(3)
C13	0.4687(3)	0.41737(18)	0.29543(11)	0.0826(5)
C14	0.3957(3)	0.26840(19)	0.19612(9)	0.0800(5)

Fig. 2 Molecule of title compound with the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level, and H atoms are shown as small spheres of arbitrary radii.

Fig. 2. The molecular conformation can be defined as being *semi*-folded, with the δ -lactone and cyclohexane rings almost perpendicular to one another. The former ring adopts the 5E envelope conformation,⁴ with O1, C1, C2, C3 and C5 being almost coplanar and the C6 atom situated at the flap. The

Table 3 Selected geometric parameters ($\text{\AA}$, $^\circ$)

O1—C2	1.3450 (16)	C3—C5	1.4983 (18)
O1—C1	1.4620 (14)	C5—C6	1.5288 (16)
O2—C2	1.2086 (15)	C9—C12	1.5122 (18)
C1—C6	1.5192 (15)	C12—C14	1.317 (2)
C2—C3	1.4887 (19)	C12—C13	1.485 (2)
C3—C4	1.322 (2)		
C2—O1—C1—C6	36.34 (14)	O2—C2—C3—C5	-174.12 (12)
C1—O1—C2—O2	171.56 (11)	O1—C2—C3—C5	8.49 (16)
C1—O1—C2—C3	-10.88 (15)	C4—C3—C5—C6	146.55 (14)
O2—C2—C3—C4	8.0 (2)	C2—C3—C5—C6	-31.17 (15)
O1—C2—C3—C4	-169.38 (13)		

Cramer & Pople puckering parameters for the ring atom sequence O1/C2/C3/C5/C6/C1 are $Q = 0.476(3)\text{\AA}$, $\theta = 46.2(4)^\circ$ and $\phi = 243.3(4)^\circ$. The cyclohexane ring exists in a chair conformation.

The bond lengths are similar to those observed in the related α -methylene- δ -valerolactones. In particular, two exocyclic double bonds, C2=O2 [1.2086(15) $\text{\AA}$] and C3=C4 [1.322(2) $\text{\AA}$], are shorter than similar bonds in the O=C—C=C moiety⁵ [1.222 and 1.340 $\text{\AA}$]. These bonds are separated by a relatively long C2—C3 bond [1.4887(19) $\text{\AA}$], and are not strictly coplanar, as indicated by the value of the O2—C2—C3—C4 torsion angle [8.0(2) $^\circ$]. These results suggest that the highly polar character of the carbonyl group hinders π electron density delocalization within the O2—C2—C3—C4 moiety. In contrast to the previously published *semi*-folded bicyclic α -methylene- δ -valerolactone,⁶ endocyclic O1 and egzocyclic O2 atoms are not involved in nonbonding intramolecular contacts with neighboring atoms. Additionally, an examination of the crystal packing indicates that all of the intermolecular distances are larger than the sums of the respective van der Waals radii.

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