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rac-(1*R*,11*S*,12*R*)-Ethyl 12-hydroxy-15-oxobicyclo[9.3.1]pentadecane-1-carboxylate

Sonia Fresu, Markus Schürmann, Hans Preut* and Peter Eilbracht

Fachbereich Chemie, Universität Dortmund, Otto-Hahn-Straße 6, 44221 Dortmund, Germany

Correspondence e-mail: uch002@uxp1.hrz.uni-dortmund.de

Key indicators

Single-crystal X-ray study
T = 291 K
Mean σ(C–C) = 0.003 Å
R factor = 0.043
wR factor = 0.092
Data-to-parameter ratio = 19.4

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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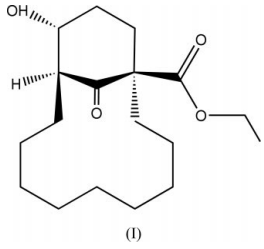
The asymmetric unit of the title compound, $C_{18}H_{30}O_4$, contains two formula molecules, which are described as *trans*-fused bicyclic systems. The carbonyl group lies on the same side as the carbethoxy function, while the OH group is on the opposite side. The six-membered rings have chair conformations and the conformations of the 12-membered rings are similar in the two molecules.

Comment

The title compound, (I), was obtained in a study of the application of the domino Michael addition/aldol condensation procedure to the formation of cycloalkanones with different ring sizes. Here, conversion of ethyl 2-oxocyclododecanoate with acrolein in the presences of DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) gave (I) as the major regio- and diastereoisomer (racemic) in 32% yield. Thus, in contrast to earlier reports of this procedure (Filippini & Rodriguez, 1997), the aldol product starting from cyclododecanone could be isolated, whereas the analogous product from cyclopentanone was not isolated since further conversion *via* retro-Dieckman condensation readily occurred. Stereochemical differences were assumed to be responsible for these observations and the present structure determination shows the title compound to form as the isolable *trans*-fused bicyclic compound, whereas the analogous product from cyclopentanone is interpreted to form as the non-isolated *cis*-fused compound, undergoing further transformation with ring opening (Filippini & Rodriguez, 1997).



(I)

The six-membered rings in the two molecules of (I) have chair conformations. The six-membered rings and the 12-membered rings in the two independent molecules show only slight conformational differences, as indicated by the torsion angles (Table 1).

Four molecules are linked *via* hydrogen bonds and a centrosymmetric 16-membered heterocycle with four O—H···O hydrogen bonds plus six C atoms from two six-membered rings is formed. These four molecules are separated by normal van der Waals interactions from the surroundings.

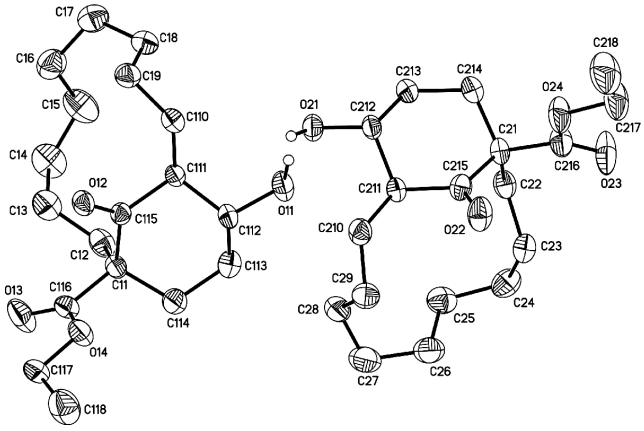


Figure 1
The asymmetric unit of the title compound (*XP*; Sheldrick, 1991) showing the labelling of all non-H atoms. Displacement ellipsoids are shown at the 50% probability level. With the exception of those of the hydroxyl groups, H atoms have been omitted for clarity.

Experimental

To a solution of ethyl 2-oxocyclododecanoate (1 equivalent) in EtOH was added DBU (1 equivalent) in EtOH, and the mixture was stirred for 1 h at room temperature. Acrolein (1 equivalent) in EtOH was slowly added, and the solution was stirred for 18 h at room temperature. The solvent was then evaporated under reduced pressure, the residue was dissolved in diethyl ether, acidified with HCl and the aqueous layer was extracted with ether. The combined organic phases were washed with water and dried over magnesium sulfate. Evaporation of the solvent under reduced pressure yielded a mixture of diastereoisomers. Purification by flash chromatography, using cyclohexane–diethyl ether (2:1) as eluant, gave one diastereoisomer as a crystalline precipitate in 32% yield and, in addition, as an oil, a mixture of two epimers due to different orientations of the 12-hydroxy group. The purity of (I) (m.p. 376–380 K) was confirmed by elemental analysis (calculated: C 69.64, H 9.74%; found: C 69.6, H 9.6%), NMR, IR and mass spectrometry, ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.12 (*q*, 2H, ^3J = 7.23 Hz, CH_2CH_3), 3.45 (*m*, 1H, CH_{ring}), 2.75 (*td*, 1H, ^3J = 10.22 Hz, ^3J = 9.97 Hz, CH_{ring}), 2.13 (*m*, 2H, CH_{2ring}), 1.96 (*s*, 2H, OH), 1.85 (*m*, 6H, CH_{2ring}), 1.34 (*m*, 13H, CH_{2ring}), 1.17 (*t*, 3H, ^3J = 7.23 Hz, CH_2CH_3), 0.86 (*m*, 1H, CH_{2ring}). ^{13}C NMR (100 MHz, $CDCl_3$): δ 209.99 (CO), 174.11 (CO), 74.97 (CH—OH), 63.11 (C_q), 62.24 (CH_2), 52.21 (CH_{ring}), 34.02 (CH_{2ring}), 32.51 (CH_{2ring}), 28.42 (CH_{2ring}), 28.27 (CH_{2ring}), 27.34 (CH_{2ring}), 24.83 (CH_{2ring}), 24.42 (CH_{2ring}), 24.03 (CH_{2ring}), 23.55 (CH_{2ring}), 23.23 (CH_{2ring}), 22.56 (CH_{2ring}), 15.45 (CH_3). MS HR (EI, 70 eV): *m*/*z* (%) = 310 (M^+, 10), 292 (43), 263 (27), 219 (35), 207 (32), 123 (58), 109 (96), 95 (98), 81 (72), 55 (45). IR (Pressling, KBr), ν [cm^{-1}] = 3503 (*s*), 2937 (*s*), 1739 (*s*), 1703 (*s*), 1470 (*m*), 1427 (*s*), 1250 (*m*), 1122 (*m*).

Crystal data

$C_{18}H_{30}O_4$
M_r = 310.42
Triclinic, $P\overline{1}$
a = 12.3829 (3) Å
b = 12.8139 (2) Å
c = 13.2413 (3) Å
α = 68.0725 (9)°
β = 89.2421 (9)°
γ = 65.8290 (10)°
V = 1753.78 (7) Å^3
Z = 4
D_x = 1.176 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 19813 reflections
θ = 3.0–27.5°
μ = 0.08 mm^{-1}
T = 291 (1) K
Plate, colourless
0.50 × 0.15 × 0.03 mm

Data collection

Nonius KappaCCD diffractometer
ω scans
Absorption correction: none
19813 measured reflections
7889 independent reflections
2673 reflections with $I > 2\sigma(I)$
R_{int} = 0.031
θ_{max} = 27.5°
$h = -16 \rightarrow 16$
$k = -14 \rightarrow 16$
$l = -17 \rightarrow 17$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.044
$wR(F^2)$ = 0.092
S = 0.86
7889 reflections
407 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0215P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.26 e Å^{-3}
$\Delta\rho_{min}$ = −0.17 e Å^{-3}

Table 1
Selected torsion angles (°).

C115—C11—C12—C13	−57.2 (2)	C215—C21—C22—C23	−53.4 (2)
C11—C12—C13—C14	153.02 (17)	C21—C22—C23—C24	158.60 (16)
C12—C13—C14—C15	−81.3 (3)	C22—C23—C24—C25	−77.3 (2)
C13—C14—C15—C16	−69.2 (3)	C23—C24—C25—C26	−74.2 (2)
C14—C15—C16—C17	163.1 (2)	C24—C25—C26—C27	162.53 (19)
C15—C16—C17—C18	−62.5 (3)	C25—C26—C27—C28	−64.4 (3)
C16—C17—C18—C19	−63.7 (3)	C26—C27—C28—C29	−62.6 (3)
C17—C18—C19—C110	155.08 (18)	C27—C28—C29—C210	151.78 (17)
C18—C19—C110—C111	−72.5 (2)	C28—C29—C210—C211	−67.9 (2)
C19—C110—C111—C115	−69.9 (2)	C29—C210—C211—C215	−81.8 (2)
C115—C111—C112—C113	62.99 (18)	C215—C211—C212—C213	56.51 (19)
C111—C112—C113—C114	−61.5 (2)	C211—C212—C213—C214	−55.7 (2)
C112—C113—C114—C11	52.0 (2)	C212—C213—C214—C21	52.5 (2)
C115—C11—C114—C113	−43.4 (2)	C215—C21—C214—C213	−48.5 (2)
C110—C111—C115—C11	173.99 (16)	C210—C211—C215—C21	173.64 (16)
C112—C111—C115—C11	−59.5 (2)	C212—C211—C215—C21	−56.5 (2)
C12—C11—C115—C111	−72.5 (2)	C22—C21—C215—C211	−69.1 (2)
C114—C11—C115—C111	48.9 (2)	C214—C21—C215—C211	51.6 (2)

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

D—H···A	D—H	H···A	D···A	D—H···A
O11—H11···O21	1.10 (3)	1.69 (3)	2.771 (2)	167 (2)
O21—H21···O12^{i}	0.84 (2)	1.97 (2)	2.7650 (19)	156 (2)

Symmetry code: (i) $-x, 2-y, -z$.

H atoms, except those of O---H, were placed in calculated positions, with C—H = 0.96--0.98 Å, and were refined as riding, with U_{iso} = 1.5U_{eq}(C) for methyl groups and 1.2U_{eq}(C) for others; the methyl groups were allowed to rotate but not to tip. The O—H H atoms were refined isotropically.

Data collection: *COLLECT* (Nonius, 1998); 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, *PARST*95 (Nardelli, 1995) and *PLATON* (Spek, 2001).

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