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# 6-Dimethoxymethyl-1-methoxycarbonylbicyclo[3.1.0]hex-2-ene-2-carboxylic acid

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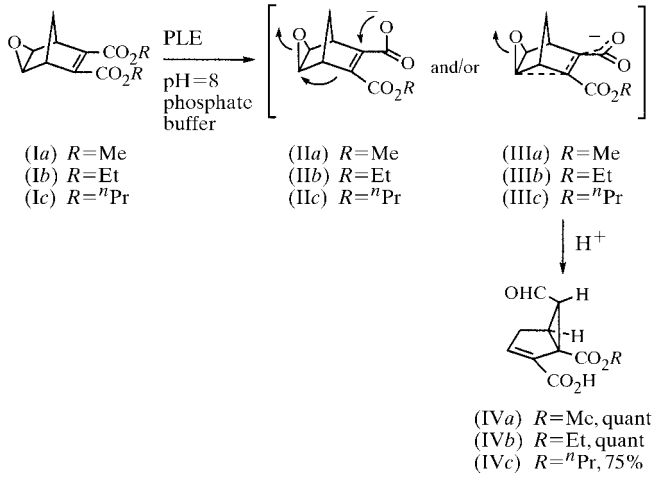
The title compound, $C_{12}H_{16}O_6$, prepared by a standard synthetic method, was determined by single-crystal X-ray crystallography to exist with a cyclopropane ring fused to a cyclopentene ring. Comparison of the unit-cell dimensions and space group of this material with those of a crystal of the same material prepared using a route involving pig liver esterase hydrolysis shows them to be identical.

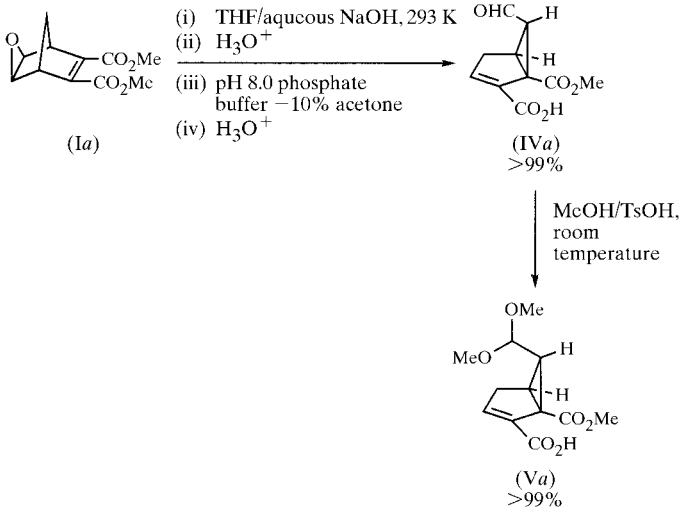
## Comment

Enzymatic reactions have been a powerful tool for the development of elegant methodologies for the syntheses of natural products (Wong & Whitesides, 1994; Drauz & Waldmann, 1995; Ohno & Otuska, 1989; Schoffers *et al.*, 1996). In particular, enzymatic dissymmetrization of symmetric *meso* compounds is a versatile enantio-differentiating reaction as it potentially produces only the desired enantiomer in quantitative yield without the need for separation from the mirror-image molecule.

Most enzymatic reactions, when used in organic synthesis, induce simple chemicoselective conversion of a limited range of functional groups. However, we discovered earlier the first chemicoenzymatic rearrangement which accomplishes skeletal change during enzymatic asymmetric hydrolysis of a *meso* diester (I) to produce the rearranged product (IV) (Niwayama *et al.*, 1993, 1994, 1998). It is initiated by enzymatic reaction, but completed by a subsequent chemical skeletal conversion in one pot in a stereo- and regiospecific manner in a slightly basic aqueous medium. We have observed that diesters (I*a*), (I*b*) and (I*c*) all undergo this rearrangement in quantitative to high yields, although the optical purities of the products are somewhat low under the limited conditions developed up to the present. The structures of rearranged products (IV*a*), (IV*b*) and (IV*c*) were established as 1-alkoxycarbonyl-6-formylbicyclo[3.1.0]hex-2-ene-2-carboxylic acids based on the $^1$H and $^{13}$C NMR, MS and IR spectroscopic data of these materials and their derivatives.




We have treated (IV*a*), isolated as an oil, with methanol and a catalytic amount of *p*-toluenesulfonic acid and obtained a white crystal. This crystal was identical in $^1$H and $^{13}$C NMR, MS and IR spectroscopic data, and in unit-cell dimensions and space group with the material 6-dimethoxymethyl-1-methoxycarbonylbicyclo[3.1.0]hex-2-ene-2-carboxylic acid, (V*a*), prepared by an alternative chemical route and whose crystal structure is reported here. While the material crystallizes in a centrosymmetric space group, indicating the equal presence of both enantiomers, the acetal prepared from (IV*a*) *via* the enzymatic reaction displayed optical activity. Thus, the enzymatic reaction has produced an enantiomeric excess of one form of the racemic mixture present in the crystal.




The acetal derivative has a strained bicyclic structure composed of fused cyclopropane and cyclopentene rings with three consecutive stereocentres including a quaternary carbon. The planes of the cyclopropane and cyclopentene rings subtend an angle of 67.0 (1)°.

Carboxylic acid groups of adjacent molecules are hydrogen bonded in pairs H4*c*···O3($2-x$, $1-y$, $-z$) 1.74 Å, O4—H4*c*···O3 162° and O4···O3 2.668 (3) Å. There is no

hydrogen bonding between the carboxyl group and the carbomethoxy or acetal groups. The hydroxy group of the carboxyl group, which is almost coplanar with the cyclopentene ring (standard deviation from planarity of the five-membered ring is 0.02 Å), is oriented *syn* to the double bond [C3—C2—C9—O4 5.0 (4)°] and the carbonyl group in the carbomethoxy group is at an angle to the cyclopentene ring [C2—C1—C7—O1 34.3 (4)°]. The two methoxy groups in the acetal group are directed away from the bicyclic ring, with the proton at C10 directed over the cyclopentene ring. This orientation in the solid may explain the somewhat shielded chemical shift ($\sigma$ 3.93 p.p.m.) for this acetal proton.

## Experimental

6-Formyl-1-methoxycarbonylbicyclo[3.1.0]hex-2-ene-2-carboxylic acid was prepared as described previously (Niwayama *et al.*, 1998). It was treated with a catalytic amount of *p*-toluenesulfonic acid in approximately 1 ml of methanol at room temperature, to afford the title compound, (V*a*), in crystalline form. The solid material was recrystallized from a hexane/diethyl ether mixture at room temperature to produce a crystal suitable for X-ray diffraction studies. The product showed no optical activity.

*Crystal data*

$C_{12}H_{16}O_6$
$M_r$ = 256.25
Monoclinic, $P2_1/c$
$a$ = 7.537 (4) Å
$b$ = 13.602 (8) Å
$c$ = 12.779 (5) Å
$\beta$ = 94.57 (2)°
$V$ = 1305.9 (12) Å$^3$
$Z$ = 4
$D_x$ = 1.303 Mg m$^{-3}$
Mo $K\alpha$ radiation
Cell parameters from 28 reflections
$\theta$ = 5.6–12.8°
$\mu$ = 0.105 mm$^{-1}$
$T$ = 293 (2) K
Cube, colourless
0.2 × 0.2 × 0.2 mm

*Data collection*

Syntex *P*4 four-circle diffractometer
$\theta/2\theta$ scans
3773 measured reflections
2845 independent reflections
1975 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.126
$\theta_{max}$ = 27.10°
$h = -1 \rightarrow 9$
$k = -1 \rightarrow 17$
$l = -16 \rightarrow 16$
3 standard reflections
every 97 reflections
intensity decay: none

*Refinement*

Refinement on $F^2$
$R(F)$ = 0.067
$wR(F^2)$ = 0.233
$S$ = 0.992
2845 reflections
164 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.1511P)^2 + 0.1243P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.11 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.08 e Å$^{-3}$

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

| | | | |
|---|---|---|---|
| C1—C2 | 1.508 (3) | C7—O1 | 1.212 (3) |
| C1—C7 | 1.513 (4) | C7—O2 | 1.347 (3) |
| C1—C6 | 1.531 (3) | C8—O2 | 1.448 (4) |
| C1—C5 | 1.551 (3) | C9—O3 | 1.228 (3) |
| C2—C3 | 1.353 (4) | C9—O4 | 1.323 (3) |
| C2—C9 | 1.485 (3) | C10—O6 | 1.416 (3) |
| C3—C4 | 1.509 (4) | C10—O5 | 1.422 (3) |
| C4—C5 | 1.548 (4) | C11—O5 | 1.433 (4) |
| C5—C6 | 1.514 (4) | C12—O6 | 1.431 (3) |
| C6—C10 | 1.522 (3) | | |

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

| $D$—H···$A$ | $D$—H | H···$A$ | $D$···$A$ | $D$—H···$A$ |
|---|---|---|---|---|
| O4—H4*c*···O3$^{i}$ | 0.96 | 1.74 | 2.668 (3) | 162 |

Symmetry code: (i) $2-x, 1-y, -z$.

Data collection: *XSCANS* (Siemens, 1991); cell refinement: *XSCANS*; data reduction: *XSCANS*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); software used to prepare material for publication: *SHELXL*97 (Sheldrick, 1997).

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## References

Drauz, K. & Waldmann, H. (1995). In *Enzyme Catalysis in Organic Synthesis*. Weinheim: VCH Publishers.
Niwayama, S., Kobayashi, S. & Ohno, M. (1994). *J. Am. Chem. Soc.* **116**, 3290–3295.
Niwayama, S., Kobayashi, S. & Ohno, M. (1998). *Tetrahedron Lett.* **29**, 6313–6316.
Niwayama, S., Noguchi, H., Ohno, M. & Kobayashi, S. (1993). *Tetrahedron Lett.* **34**, 665–668.
Ohno, M. & Otsuka, M. (1989). *Org. React.* **37**, 1–55.
Schoffers, E., Golebiowski, A. & Johnson, C. R. (1996). *Tetrahedron*, **56**, 3769–3826.
Sheldrick, G. M. (1990). *Acta Cryst.* A**46**, 467–473.
Sheldrick, G. M. (1997). *SHELXL*97. University of Göttingen, Germany.
Siemens (1991). *XSCANS User's Manual.* Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
Wong, C. H. & Whitesides, G. M. (1994). *Enzymes in Synthetic Organic Chemistry*, *Tetrahedron Org. Chem. Ser.* Vol. 12.