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(±)-5-Ethyl-*endo*-4-(4-methoxyphenyl)-2,2,*anti*-8-trimethyl-6-oxabicyclo[3.2.1]-octan-7-one, a bicyclic γ-lactone

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Key indicators

Single-crystal X-ray study
T = 296 K
Mean σ(C–C) = 0.002 Å
R factor = 0.038
wR factor = 0.113
Data-to-parameter ratio = 14.6

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

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The title bicyclic γ-lactone, $C_{19}H_{26}O_3$, (II), the thermodynamically favored lactone, was formed in the reaction of (±)-*cis*-2,6,6-trimethyl-*trans*-3-ethyl-4-oxocyclohexanecarboxylic acid with *p*-methoxyphenylmagnesium bromide, following prolonged treatment under acidic conditions. The kinetically favored isomeric (±)-δ-lactone is described in the preceding paper [Xie *et al.* (2003). *Acta Cryst.* E59, o403–o405]. In lactone (II), basically composed of an aromatic ring appended to a [3.2.1] bicyclic system, the O—C(O)—C group is asymmetric, its O—C═O angle being 120.80 (15)° and its O═C—C angle being 130.46 (16)°.

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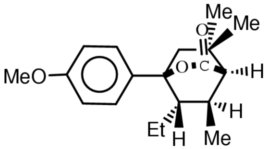
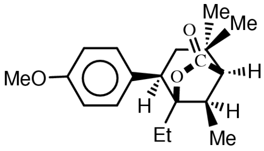
Lactone precursors of prostate therapy agents. II.

Comment

We recently described the preparation, isolation and X-ray analysis of bicyclic δ-lactone (I) (Xie *et al.*, 2003), which is the kinetically favored lactone formed in the reaction of (±)-*cis*-2,6,6-trimethyl-*trans*-3-ethyl-4-oxocyclohexanecarboxylic acid with *p*-methoxyphenylmagnesium bromide, followed by acidification with excess 3N HCl, and the mixture worked up within an hour. When the acidified mixture was worked up after several days, the thermodynamically favored isomeric bicyclic γ-lactone, namely (±)-5-ethyl-*endo*-4-(4-methoxyphenyl)-2,2,*anti*-8-trimethyl-6-oxabicyclo[3.2.1]octan-7-one, (II), was obtained as the major product. This reaction is described in detail in the preceding paper (Xie *et al.*, 2003).



(**I**) racemic



(**II**) racemic

The structure and atom numbering of (II) are shown in Fig. 1. Lactone (II) is basically composed of an aromatic ring appended to a [3.2.1] bicyclic system. The O—C(O)—C group is asymmetric, its O—C═O angle being 120.80 (15)° and its O═C—C angle being 130.46 (16)°. The four atoms comprising the lactone moiety, C1/C7/O6/C5, are essentially coplanar, as evidenced by the torsion angle (Table 1), and the least-squares plane of this moiety is nearly perpendicular to the cyclohexane ring, the angle being 89.48 (8)°. Geometric values of interest are given in Table 1.

Experimental

Compound (II) was prepared by the procedure described for (I) (Xie *et al.*, 2003), except that the brown pasty solid obtained after the addition of 3N HCl was left untouched for several days before being

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treated with *p*-TsOH·H_2O. The resulting solid product was purified by recrystallization (ethyl acetate-hexane; m.p. 410.6–411.4 K) and shown to be (II). GC–MS: M^+ 302, *w.w.* calculated: 302; NMR ($CDCl_3$), ^1H (300 MHz): δ 0.73 (*t*, *J* = 7.5 Hz, 3H), 1.02 (*d, J* = 6.9 Hz, 3H), 1.12 (*s*, 3H),1.18 (*s*, 3H), 1.53 (*m*, *J* = 7.2 Hz, 2H), 1.66 (*d, J* = 10.5 Hz, 1H), 1.67 (*d, J* = 7.5 Hz, 1H), 2.06 (*s*, 1H), 2.44 (*q*, *J* = 6.9 Hz, 1H), 2.92 (*dd*, *J* = 7.8 Hz, 10.5 Hz, 1H), 3.79 (*s*, 3H), 6.83 (*d*, *J* = 9.0 Hz, 2H), 7.24 (*d*, *J* = 9.0 Hz, 2H); ^{13}C (75 MHz): δ 6.72, 14.30, 23.68, 25.99, 28.30, 31.80, 39.49, 44.49, 44.95, 55.16, 59.84, 91.52, 113.69, 129.66, 133.67 (2C), 158.33 (2C), 177.72.

Crystal data

$C_{19}H_{26}O_3$
$M_r = 302.40$
Monoclinic, $P2_1/c$
$a = 18.318$ (2) Å
$b = 7.597$ (3) Å
$c = 12.0935$ (13) Å
$\beta = 91.860$ (10)°
$V = 1682.2$ (7) Å^3
$Z = 4$

$D_x = 1.194$ Mg m^{-3}
Mo Kα radiation
Cell parameters from 25 reflections
$\theta = 19.6$–21.3°
$\mu = 0.08$ mm^{-1}
$T = 296$ K
Prism, colorless
0.48 × 0.46 × 0.27 mm

Data collection

Rigaku AFC-5*S* diffractometer
ω scans
Absorption correction: none
3069 measured reflections
2971 independent reflections
2145 reflections with $I > 2\sigma(I)$
$R_{int} = 0.008$

$\theta_{max} = 25.1°$
$h = 0 \rightarrow 21$
$k = 0 \rightarrow 9$
$l = -14 \rightarrow 14$
3 standard reflections every 100 reflections intensity decay: 1.6%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.038$
$wR(F^2) = 0.113$
$S = 1.01$
2971 reflections
204 parameters
H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0574P)^2 + 0.3918P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.14$ e Å^{-3}
$\Delta\rho_{min} = -0.19$ e Å^{-3}

Table 1
Selected geometric parameters (°).

O1—C7—C1	130.46 (16)	C5—O6—C7	108.97 (11)
C1—C7—O6	108.74 (14)		
C1—C7—O6—C5	3.11 (17)	C3—C4—C14—C15	−62.6 (2)
C3—C4—C14—C19	115.85 (17)		

The rotational orientations of the methyl H atoms were refined by the circular Fourier method available in *SHELXL*97 (Sheldrick, 1997). All H atoms were refined as riding, with C—H distances ranging from 0.93 to 0.98 Å.

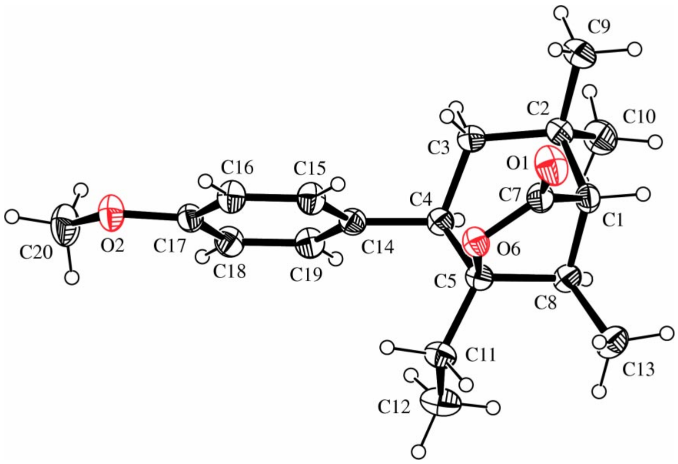

Figure 1
The molecular structure and atom-numbering scheme for (II), with displacement ellipsoids at the 30% probability level.

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1996); cell refinement: *MSC/AFC Diffractometer Control Software*; data reduction: *PROCESS* in *TEXSAN* (Molecular Structure Corporation, 1997); program(s) used to solve structure: *SIR*92 (Burla *et al.*, 1989); program(s) used to refine structure: *LS* in *TEXSAN* and *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*-3 (Farrugia, 1997); software used to prepare material for publication: *TEXSAN, SHELXL*97 and *PLATON* (Spek, 2000).

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