Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

(1*S*,2*S*)-1-{2-[(4-Methoxybenzyl)oxy]ethyl}-2-methyl-3-butenyl (1*S*,4*R*)-4,7,7-trimethyl-3-oxo-2-oxabicyclo[2.2.1]heptane-1-carboxylate

Kai T. Meilert, George R. Clark,* Tania Groutso and Margaret A. Brimble

Chemistry Department, University of Auckland, Private Bag 92019, Auckland, New Zealand

Correspondence e-mail: g.clark@auckland.ac.nz

Key indicators

Single-crystal X-ray study
T = 83 K
Mean σ(C–C) = 0.004 Å
R factor = 0.041
wR factor = 0.092
Data-to-parameter ratio = 9.0

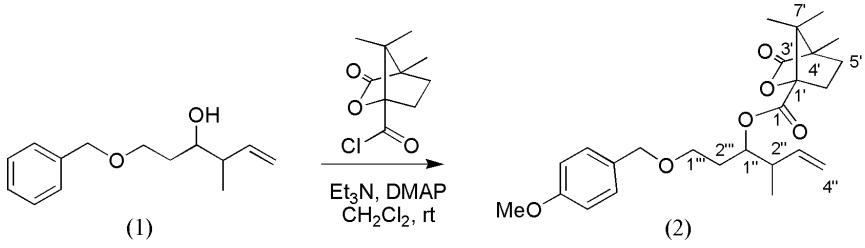
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Received 1 November 2004
Accepted 25 November 2004
Online 4 December 2004

The title compound, $C_{25}H_{34}O_6$, crystallizes in the orthorhombic space group $P2_12_12_1$. The crystal structure has been determined to establish the absolute configuration of the parent compound by introducing a chiral auxiliary of known structure.

Comment

The spirolides *A*–*D* comprise a novel family of pharmacologically active macrocyclic imines that cause potent and characteristic symptoms in the mouse bioassay (spirolide *A*: LD_{100} 250 µg kg^{-1}) and are activators of type *L* calcium channels (Hu *et al.*, 1995, 1996, 2001; Cembella & Lewis, 1999). 1-[(4-Methoxybenzyl)oxy]-4-methylhex-5-en-3-ol, (1) (see scheme), is a synthetic intermediate for these compounds. In order to establish the absolute configuration at C1″ and C2″, the camphanoate derivative, *i.e.* the title compound, (2), has been synthesized by authentic methods (Gerlach, 1978; Fourneron *et al.*, 1989). As the stereochemistry at C1′ and C4′ in the camphanoate moiety is known to be 1*S*,4*R*, the absolute configuration at C1″ and C2″ (C15, C13 in the crystallographic numbering scheme; Fig. 1) has been assigned as 1*S*,2*S*.



(1) (2)

Experimental

To a solution of 1-[(4-methoxybenzyl)oxy]-4-methylhex-5-en-3-ol (0.91 mmol), (1), in dry dichloromethane (1 ml) was added triethylamine (1.27 mmol) and 4-dimethylaminopyridine (0.091 mmol), followed by (1*S*)-(−)-camphanic chloride (1.36 mmol). After 2 h the solution was diluted with CH_2Cl_2 (5 ml) and 1 *N* HCl was added (5 ml). After phase separation the organic layer was further extracted with saturated $NaHCO_3$ (5 ml) and the organic layer was dried over $MgSO_4$. Flash chromatography (SiO_2, *n*-hexane/ether 4:1) afforded 327 mg of the title compound, (2), as a white solid that was recrystallized from diethyl ether to give colorless needles (yield 83%, m.p. 337 K). MS (EI): 430 (5, [M^+]), 294 (4), 203 (10), 176 (17), 137 (23), 121 (100), 109 (5), 95 (12), 83 (15). HR–MS (EI): calculated for $C_{25}H_{34}O_6$ 430.23554; found 430.23516 (Δ p.p.m. = 0.9). IR (NaCl): ν 2965, 1790, 1750, 1610, 1515, 1465, 1305, 1265, 1250, 1175, 1100, 1060, 1035, 930, 820. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23 (*d*, 2H, ^3J = 8.6 Hz, H—C_{arom}), 6.86 (*d*, 2H, ^3J = 8.6 Hz, H—C_{arom}), 5.76 (*ddd*, 1H, ^3J = 7.2 Hz, ^3J = 10.0 Hz, ^3J = 17.4 Hz, H—C3″), 5.18 (*ddd*, 1H, ^3J = 3.2 Hz,

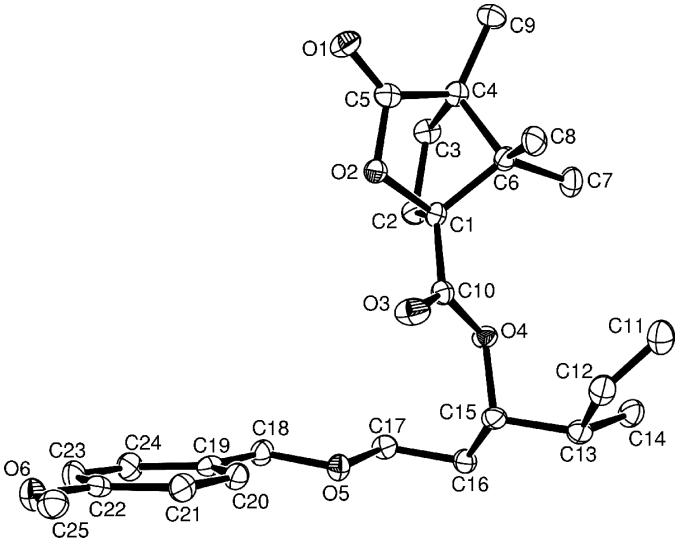


Figure 1
The structure of (2), showing 50% probability displacement ellipsoids for non-H atoms. H atoms have been omitted.

^3J = 5.5 Hz, ^3J = 9.1 Hz, H—C1″), 5.08–5.03 (*m*, 2H, H—C4″), 4.46 (*d*, 1H, ^2J = 11.6 Hz, CH_2C_{arom}), 4.36 (*d*, 1H, ^2J = 11.6 Hz, CH_2C_{arom}), 3.79 (*s*, 3H, CH_3OC_{arom}), 3.49–3.35 (*m*, 2H, H—C1‴), 2.48 (*m*, 1H, H—C2″), 2.31 (*m*, 1H, H_a–C6′), 1.98–1.77 (*m*, 4H, 2*H*—C2‴, H_a—C5′, H_b—C6′), 1.64 (*m*, 1H, H_b—C5′), 1.09, 1.03 [2*s*, 6H, $(CH_3)_2$—C7′], 1.04 (*d*, ^3J = 6.8 Hz, CH_3—C2″), 0.91 (*s*, 3H, CH_3—C4′). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 178.1 (*s*, C3′), 166.9 (*s*, C1), 159.1 (*s*, C_{arom}), 139.1 (*d*, C3″), 130.1 (*s*, C_{arom}), 129.3 (*d*, 2C, C_{arom}), 115.8 (*d*, C4″), 113.7 (*d*, 2C, C_{arom}), 91.1 (*s*, C1′), 75.7 (*d*, C1″), 72.3 (*t*, CH_2C_{arom}), 66.0 (*t*, C1‴), 55.2 (*q*, CH_3OC_{arom}), 54.7 (*s*, C4′), 53.8 (*s*, C7′), 41.2 (*d*, C2″), 31.5 (*d*, C5′), 30.7 (*d*, C6′), 28.9 (*d*, C2‴), 16.7, 16.6 [*q*, 2C, $(CH_3)_2$C7′], 14.7 (*q*, CH_3C4′), 9.6 (*q*, CH_3C2″).

Crystal data

$C_{25}H_{34}O_6$
M_r = 430.52
Orthorhombic, $P2_12_12_1$
a = 6.8297 (1) Å
b = 12.0970 (2) Å
c = 27.8762 (4) Å
V = 2303.10 (6) Å^3
Z = 4
D_x = 1.242 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 4366 reflections
θ = 2.2–25.7°
μ = 0.09 mm^{-1}
T = 83 (2) K
Needle, colorless
0.42 × 0.16 × 0.10 mm

Data collection

Bruker SMART CCD diffractometer
ω scans
Absorption correction: multi-scan (Blessing, 1995)
T_{min} = 0.964, T_{max} = 0.992
4366 measured reflections
2511 independent reflections
2171 reflections with $I > 2\sigma(I)$
R_{int} = 0.057
θ_{max} = 25.7°
$h = -8 \rightarrow 8$
$k = -14 \rightarrow 14$
$l = -33 \rightarrow 33$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.041
$wR(F^2)$ = 0.092
S = 1.08
2511 reflections
280 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0387P)^2 + 0.8019P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.22 e Å^{-3}
$\Delta\rho_{min}$ = −0.21 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

C1—C10	1.516 (4)	C13—C14	1.532 (4)
O3—C10	1.206 (3)	C13—C15	1.541 (4)
O4—C10	1.341 (3)	C15—C16	1.515 (4)
O4—C15	1.480 (3)	C16—C17	1.509 (4)
O5—C17	1.425 (3)	C18—C19	1.506 (4)
O5—C18	1.427 (3)	C19—C20	1.385 (4)
C11—C12	1.322 (4)	C19—C24	1.401 (4)
C12—C13	1.508 (4)		
C10—O4—C15	117.4 (2)	C12—C13—C15	109.6 (2)
C17—O5—C18	110.79 (19)	C14—C13—C15	113.3 (2)
C22—O6—C25	118.1 (2)	O4—C15—C16	106.9 (2)
O3—C10—O4	125.9 (2)	O4—C15—C13	107.8 (2)
O3—C10—C1	124.5 (2)	C16—C15—C13	116.1 (2)
O4—C10—C1	109.6 (2)	C17—C16—C15	113.4 (2)
C11—C12—C13	127.3 (3)	O5—C17—C16	109.4 (2)
C12—C13—C14	114.1 (2)	O5—C18—C19	110.3 (2)

H atoms were placed in calculated positions (C—H = 0.93–0.98 Å) and refined using the riding model, with U_{iso}(H) = 1.2 or 1.5 times U_{eq}(C). Friedel pairs were merged before the final refinement; the absolute configuration is known from the synthesis.

Data collection: *SMART* (Siemens, 1995); cell refinement: *SAINT* (Siemens, 1995); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *SHELXTL* (Siemens, 1994); software used to prepare material for publication: *SHELXL*97.

References

Blessing, R. H. (1995). *Acta Cryst.* A**51**, 33–38.
Cembella, A. D. & Lewis, N. I. (1999). *Nat. Toxins*, **7**, 197–206.
Fourneron, J. D., Archelas, A. & Furstoss, R. (1989). *J. Org. Chem.* **54**, 4686–4689.
Gerlach, H. (1978). *Helv. Chim. Acta*, **61**, 2773–2776.
Hu, T., Burton, I. W., Cembella, A. D., Curtis, J. M., Quilliam, M. A., Walter, J. A. & Wright, J. L. C. (2001). *J. Nat. Prod.* **64**, 308–312.
Hu, T., Curtis J. M., Oshima Y., Quilliam, M. A., Walter, J. A., Watson-Wright, W. M. & Wright, J. L. C. (1995). *J. Chem. Soc. Chem. Commun.* pp. 2159–2161.
Hu, T., Curtis, J. M., Walter, J. A. & Wright, J. L. C. (1996). *Tetrahedron Lett.* **37**, 7671–7674.
Sheldrick, G. M. (1997). *SHELXS*97 and *SHELXL*97. University of Göttingen, Germany.
Siemens (1994). *SHELXTL*. Siemens Analytical Instruments Inc., Madison, Wisconsin, USA.
Siemens (1995). *SMART* and *SAINT*. Siemens Analytical Instruments Inc., Madison, Wisconsin, USA.