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cis-5-Bromo-2,2,6-trimethyl-trans-6-phenyl-tetrahydropyran-3-carboxylic acid

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Key indicators

Single-crystal X-ray study
$T = 303$ K
Mean σ(C–C) = 0.015 Å
R factor = 0.069
wR factor = 0.217
Data-to-parameter ratio = 17.6

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

Centrosymmetric hydrogen-bonding between carboxy substituents links enantiomers of the title compound, $C_{15}H_{19}BrO_3$, into dimers. Close contacts that originate from axially arranged methyl substituents in positions 2 and 6 induce distortions, which are evident from a widening of the endocyclic bond angle at the ring O atom [122.6 (6)°] and a flattening of the tetrahydropyran chair.

Comment

cis-5-Bromo-2,2,6-trimethyl-trans-(6-phenyl)tetrahydropyran-3-carboxylic acid, (I), is a valuable starting material for the synthesis of the marine natural product aplysiapyranoid A (Hartung & Greb, 2003). By mistake, an incorrect diastereomeric ratio of cis:trans = 34:66 for the minor cyclization product, i.e. methyl 2,2-dimethyl-5-(1-phenylethenyl)tetrahydrofuran-3-carboxylate, was given in that report; the correct diastereomeric ratio for the latter product is cis:trans = 66:34. The racemate of compound (I) has been crystallized and investigated by X-ray diffraction in order to verify its relative trans configuration at C5 and C6.

(I)
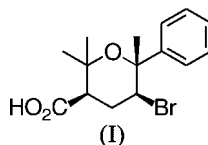
Substituents at C3 (CO_2H), C5 (Br) and C6 (C_6H_5) are attached in equatorial positions of the tetrahydropyran ring, thus leading to a relative 3,5-cis and 5,6-trans configuration of (I) (Fig. 1). Axially arranged methyl groups at C2 and C6 cause steric repulsions, since the C7···C10 distance [3.222 (9) Å] falls below the sum of the van der Waals radii (1.70 Å for C; Bondi, 1964). The distortion imposed by these close contacts is evident from a widening of the bond angle at O1 [122.6 (6)°] and from the magnitude of the endocyclic torsion angles of the tetrahydropyran subunit (Table 1).

The cyclic ether adopts a $^4C_1$ conformation, with atoms O1 [−0.505 (10) Å] and C4 [0.673 (12) Å] offset in opposite directions from the plane of atoms C2/C3/C5/C6. This geometry corresponds to the most significantly populated conformer of (I) in $CDCl_3$ solution (298 K), as established on the basis of H,H coupling constants (^{1}H NMR).

Short intermolecular distances [O2···O3^i 2.622 (10) Å; symmetry code: (i) $1 - x, -1 - y, 1 - z$] were interpreted as O—H···O hydrogen bonds (Table 2 and Fig. 2) which link neighbouring molecules into centrosymmetric dimers (Fig. 2). Although the carboxy H atom was not located in the differ-
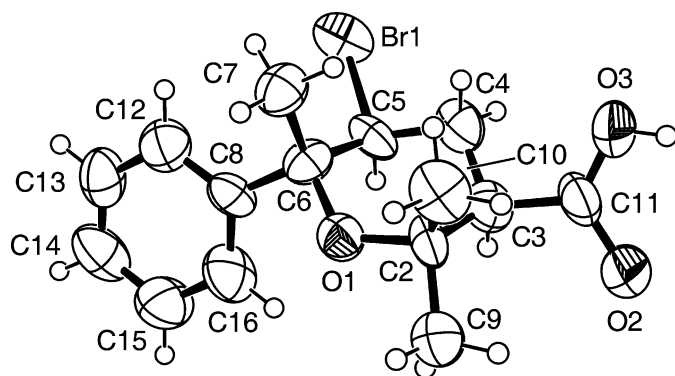
Figure 1
The molecular structure of (I). Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres.
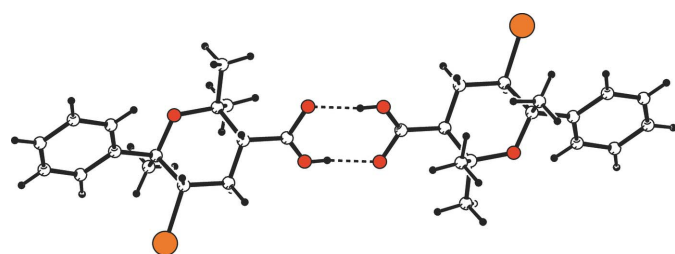

Figure 2
The hydrogen-bonded (dashed lines) centrosymmetric dimer of (I). O atoms are depicted as red and Br atoms as orange.

ence Fourier map, the NMR spectroscopic data for (I) leave no doubt of atom C11 being a carboxy C atom.

Experimental

A solution of methyl 5-bromo-2,2,6-trimethyl-6-phenyltetrahydro-pyran-3-carboxylate (3,5-*cis*,5,6-*trans*:3,5-*trans*,5,6-*trans* = 80:20; Hartung & Greb, 2003) (3.00 g, 8.79 mmol) and LiOHxH$_2$O (5.94 mg, 142 mmol) in dimethoxyethane (120 ml) and H$_2$O (180 ml) was stirred for 2 d at 293 K. Afterwards, the solution was acidified with aqueous HCl (pH 2). The mixture was extracted with CH$_2$Cl$_2$ (4 × 80 ml). The organic washings were combined, dried (MgSO$_4$) and concentrated under reduced pressure to furnish 5-bromo-2,2,6-trimethyl-6-phenyltetrahydropyran-3-carboxylic acid, (I), as a brownish solid (2.67 g, 93%; 3,5-*cis*,5,6-*trans*:3,5-*trans*,5,6-*trans* = 80:20). Colourless prisms, suitable for X-ray diffraction, were grown by slowly concentrating a saturated solution of (I) in CH$_2$Cl$_2$–diethyl ether (3:1 *v/v*) (m.p. 421 K). Elemental analysis calculated for C$_{15}$H$_{19}$BrO$_3$: C 55.06, H 5.85%; found C 57.52, H 6.54%.

Crystal data

C$_{15}$H$_{19}$BrO$_3$	$Z = 4$
$M_r = 327.21$	$D_x = 1.431$ Mg m^{-3}
Monoclinic, $P2_1/n$	Mo $K\alpha$ radiation
$a = 9.955$ (2) Å	$\mu = 2.71$ mm^{-1}
$b = 9.875$ (3) Å	$T = 303$ (2) K
$c = 15.896$ (2) Å	Plate, colourless
$\beta = 103.62$ (1)°	0.80 × 0.32 × 0.05 mm
$V = 1518.7$ (6) Å^3	

Data collection

Enraf–Nonius CAD-4 diffractometer	2977 independent reflections
$\omega/2\theta$ scans	1024 reflections with $I > 2\sigma(I)$
Absorption correction: ψ scan (North *et al.*, 1968)	$R_{int} = 0.252$
	$\theta_{max} = 26.0°$
$T_{min} = 0.221$, $T_{max} = 0.877$	3 standard reflections
3621 measured reflections	frequency: 120 min
	intensity decay: 10.0%

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0855P)^2 + 2.55P]$
$R[F^2 > 2\sigma(F^2)] = 0.069$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.217$	$(\Delta/\sigma)_{max} = 0.004$
$S = 0.96$	$\Delta\rho_{max} = 0.83$ e Å^{-3}
2977 reflections	$\Delta\rho_{min} = -0.56$ e Å^{-3}
169 parameters	
H-atom parameters constrained	

Table 1
Selected geometric parameters (Å, °).

Br1—C5	1.965 (9)	C6—C5	1.518 (10)
O1—C6	1.444 (10)	C2—C3	1.518 (11)
O1—C2	1.455 (10)	C4—C3	1.486 (13)
O3—C11	1.214 (10)	C4—C5	1.508 (12)
O2—C11	1.320 (11)		
C6—O1—C2	122.6 (6)	C3—C4—C5	108.7 (7)
O1—C6—C5	106.2 (7)	O3—C11—O2	119.3 (9)
O1—C2—C3	108.4 (7)	C4—C3—C2	113.7 (8)
C2—O1—C6—C5	50.3 (9)	O1—C2—C3—C4	48.5 (10)
C6—O1—C2—C3	−48.5 (10)	C3—C4—C5—C6	58.7 (10)
C5—C4—C3—C2	−55.7 (10)	O1—C6—C5—C4	−53.0 (9)

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

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
O2—H2$\cdots$O3^i	0.82	1.81	2.622 (10)	174

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

All H atoms were positioned geometrically and treated as riding atoms, with C—H distances in the range 0.95–1.00 Å and with U_{iso}(H) set at $1.2U_{eq}$ (aromatic, CH$_2$, CH) or $1.5U_{eq}$ (CH$_3$ and OH) of the parent atom. A free rotating-group refinement was used for the CH$_3$ groups. The high value of R_{int} probably originates from the large number of weak data, which also might lower the precision of the structure.

Data collection: *CAD-4 Diffractometer Control Software* (Enraf–Nonius, 1993); cell refinement: *CAD-4 Diffractometer Control Software*; data reduction: *CAD-4 Diffractometer Control Software*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *PLATON2002* (Spek, 2003) and *ORTEP-3* (Farrugia, 1997); software used to prepare material for publication: *SHELXL97*.

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