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# Determination of the absolute configuration of (–)-abietic acid *via* its (4*R*,5*R*,9*R*,10*R*)-7,13-abietadien-18-yl *p*-bromobenzoate derivative

## Miguel A. González, Maria J. Gil-Gimeno and Alexander J. Blake

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# Determination of the absolute configuration of (−)-abietic acid *via* its (4*R*,5*R*,9*R*,10*R*)-7,13-abietadien-18-yl *p*-bromobenzoate derivative

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The absolute configuration of the title bromo derivative of abietic acid, $C_{27}H_{35}BrO_2$, has been determined. The structural analysis confirms the absolute stereochemistry for (−)-abietic acid proposed by Bose & Struck [(1959). *Chem. Ind. (London)*, pp. 1628–1630] on the basis of optical rotatory dispersion measurements. The molecule exhibits a *trans anti* 6/6/6 tricyclic hydrocarbon skeleton, with the cyclohexane ring in the expected chair form and the two cyclohexene rings, the double bonds of which are conjugated, in half-chair conformations.

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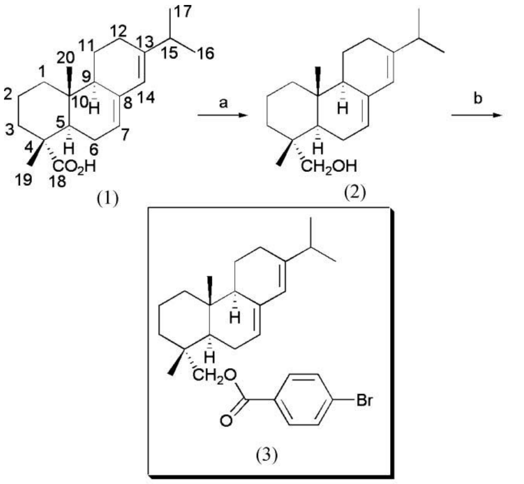
**Key indicators**

Single-crystal X-ray study
*T* = 150 K
Mean σ(C–C) = 0.003 Å
*R* factor = 0.032
*wR* factor = 0.083
Data-to-parameter ratio = 19.2

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

## Comment

Abietic acid (1) is a major acid component of pine rosins which are abundant natural chemicals having many industrial applications, including as paper sizings, polymerization emulsifiers, adhesive tackifiers, printing ink resins and waterproofing materials (McCoy, 2000). Most of the acids in pine rosins have also shown interesting biological properties and are of interest as potential therapeutic agents (Alvarez-Manzaneda *et al.*, 2006). Abietic acid has been widely used as a chiral synthon for the preparation of terpenoids and natural products, confirming their stereochemistry (Arnó *et al.*, 2003). It has been used as a standard of known absolute configuration in circular dichroism experiments by Hartl & Humpf (2000) and Proni *et al.* (2003), but without crystallographic confirmation of the absolute configuration.



**Reagents and Conditions**: a) $LiAlH_4$, THF, reflux, quant.; b) p-BrBzCl, $Et_3N$, $Et_2O$, 76%.

Abietic acid is characterized by a steroid-like carbon skeleton, named 'abietane' in accordance with the IUPAC recommendations, which was chosen as the fundamental parent structure with the numbering pattern as depicted in the

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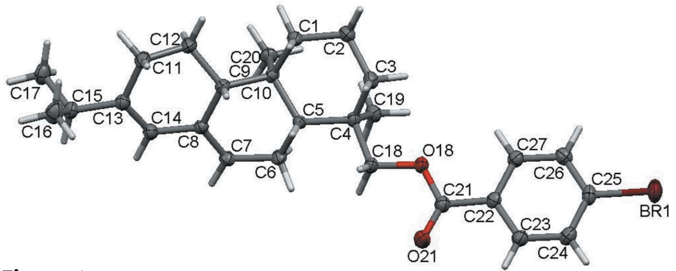

**Figure 1**

A view of the structure of (3), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

scheme. The structure of the title compound (1) has been confirmed by X-ray analysis previously by Okada & Takekuma (1994) and Matsubara *et al.* (1993). However, the only insight into its absolute configuration has been by optical rotatory dispersion experiments (Bose & Struck, 1959). Following our determination of a crystal structure of a compound prepared from abietic acid (Blake *et al.*, 2006), we found a lack of crystallographic evidence for the absolute configuration of abietic acid itself. We therefore decided to embark on such a study by preparing simple derivatives of abietic acid containing significant anomalous scatterers: these include the *p*-bromo ester derivative (3) of the abietanol (2) obtained by standard reduction of abietic acid (1). A single-crystal X-ray study established the connectivity and the absolute configuration of (3) (Fig. 1), thereby confirming the absolute configuration of (−)-abietic acid as 4*R*,5*R*,9*R*,10*R*.

The molecule exhibits a *trans anti* 6/6/6 tricyclic hydrocarbon skeleton in which the cyclohexane ring *A* has a typical chair form. Cyclohexene rings *B* and *C*, containing conjugated double bonds, have half-chair conformations. Thus, the relative stereochemistry is *trans* fusion for the *A*/*B* ring junction, *anti* between C9 hydrogen and C10 methyl (abietane numbering), and coplanar for the *B*/*C* ring junction. The ester linkage is located at C18 and the isopropyl group at C13. The structure is unsolvated. Bond lengths and angles lie in the ranges normally observed for such sterically non-strained molecules (Cambridge Structural Database, Version 5.27, May 2006 update; Allen, 2002).

## Experimental

Compound (3) was synthesized starting from commercially available (−)-abietic acid, so the relative stereochemistry of centres C4, C5, C9 and C10 was fixed from the outset. Reduction of abietic acid under standard conditions, followed by esterification with *p*-bromobenzoyl chloride, afforded the bromo ester derivative (3). Diffraction-quality crystals were obtained by recrystallization from hexane.

*Crystal data*

$C_{27}H_{35}BrO_2$
$M_r = 471.46$
Monoclinic, $P2_1$
$a = 9.4486\ (13)$ Å
$b = 6.0103\ (9)$ Å
$c = 20.616\ (3)$ Å
$\beta = 97.850\ (2)^\circ$
$V = 1159.8\ (5)$ Å$^3$

$Z = 2$
$D_x = 1.350$ Mg m$^{-3}$
Mo $K\alpha$ radiation
$\mu = 1.79$ mm$^{-1}$
$T = 150\ (2)$ K
Lath, colourless
1.00 × 0.23 × 0.05 mm

*Data collection*

Bruker SMART APEX CCD area-detector diffractometer
$\omega$ scans
Absorption correction: multi-scan (*SADABS*; Bruker, 2001)
$T_{\min} = 0.719$, $T_{\max} = 1.000$ (expected range = 0.657–0.914)

10620 measured reflections
5227 independent reflections
4748 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.014$
$\theta_{\max} = 27.5^\circ$

*Refinement*

Refinement on $F^2$
$R[F^2 > 2\sigma(F^2)] = 0.032$
$wR(F^2) = 0.083$
$S = 1.03$
5228 reflections
272 parameters
H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.06P)^2 + 0.099P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} = 0.002$
$\Delta\rho_{\max} = 0.46$ e Å$^{-3}$
$\Delta\rho_{\min} = -0.20$ e Å$^{-3}$
Absolute structure: Flack (1983), 2312 Friedel pairs
Flack parameter: 0.000 (6)

H atoms were positioned geometrically and allowed to ride on their parent C atoms at distances of 0.95, 0.95, 0.98, 0.99 and 1.00 Å for aromatic, alkene, methyl, methylene and methine groups, respectively, and with $U_{\rm iso}({\rm H}) = 1.5U_{\rm eq}({\rm C})$ for methyl groups and $U_{\rm iso}({\rm H}) = 1.2U_{\rm eq}({\rm C})$ for all others.

Data collection: *SMART* (Bruker, 2001); cell refinement: *SAINT* (Bruker, 2001); data reduction: *SAINT* and *SHELXTL* (Bruker, 2001); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *MERCURY* (Macrae *et al.*, 2006); software used to prepare material for publication: *enCIFer* (Allen *et al.*, 2004) and *PLATON* (Spek, 2003).

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