

## Agatholic acid

Robert B. Bates,<sup>a\*</sup> Sheng Cai,<sup>a</sup>  
 Ryan S. Cantor,<sup>b</sup> Michael D.  
 Carducci,<sup>a</sup> Anthony K. Irvine,<sup>c</sup>  
 Beth V. Jiorle,<sup>a</sup> Pichaya  
 Nakkiew,<sup>a</sup> William N. Setzer<sup>b</sup>  
 and Long N. Trinh<sup>a</sup>

<sup>a</sup>University of Arizona, Department of Chemistry, 1306 E. University, Tucson, AZ 85721-0041, USA, <sup>b</sup>Department of Chemistry, The University of Alabama in Huntsville, Huntsville, AL 35899, USA, and <sup>c</sup>Cooperative Research Centre for Tropical Rainforest Ecology and Management, CSIRO., Atherton, Queensland, Australia

Correspondence e-mail: batesr@u.arizona.edu

## Key indicators

Single-crystal X-ray study

$T = 170\text{ K}$

Mean  $\sigma(\text{C}-\text{C}) = 0.010\text{ \AA}$

$R$  factor = 0.051

$wR$  factor = 0.126

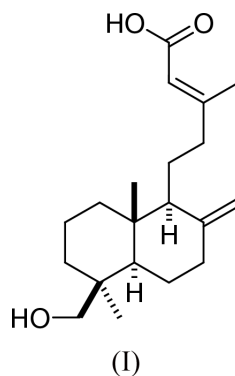
Data-to-parameter ratio = 6.2

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

In agatholic acid,  $\text{C}_{20}\text{H}_{32}\text{O}_3$ , the two molecules in the asymmetric unit have essentially the same conformation. The molecules are linked by  $\text{O}-\text{H}\cdots\text{O}$  hydrogen bonds between the carboxyl and alcohol groups.

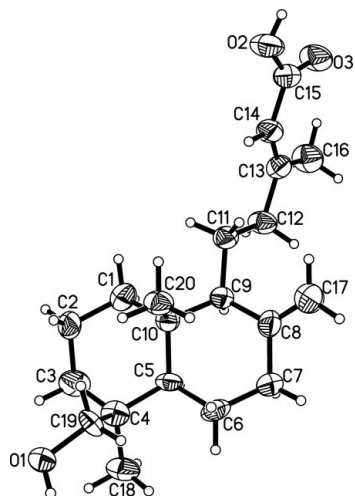
## Comment

The resin from the Queensland kauri pine, *Agathis atropurpurea* B. Hyland (Araucariaceae), oozes profusely from wounds on the tree trunk and is used by aborigines to start fires. Collecting the resin from Longlang's Gap (near Atherton) and applying flash chromatography on silica gel, eluting with hexane/ethyl acetate, gave crystals which NMR spectra indicated to be agatholic acid, (I). This substance is known only from other trees of this family: in Manila copal resin from *Agathis* species (Enzell, 1961), in the resin of the Australian tree *Araucaria bidwillii* (Caputo & Mangoni, 1974), in the Brazilian tree *Araucaria angustifolia* (De Paiva Campello & Ferreira Fonseca, 1975), and in the New Caledonian tree *Agathis lanceolata* (Manh *et al.*, 1983). We undertook an X-ray study of (I) to confirm the structure.



This X-ray study confirms the previously proposed molecular structure and shows the conformation of the side chain (Fig. 1), which is essentially the same in the two independent molecules in the asymmetric unit. The molecules are held in a three-dimensional lattice by hydrogen bonds between the carboxyl groups and the alcohol groups, as listed in Table 1.

The X-ray study did not conclusively determine the absolute configuration, but the positive optical rotation showed this compound to be in the labdane series as depicted (De Paiva Campello & Ferreira Fonseca, 1975), rather than in the *ent*-labdane series, which occurs naturally in other plants. Since extensive NMR parameters are available only for the methyl ester of (I), we report the parameters of the natural acid itself below.



**Figure 1**  
View of one of the molecules in the asymmetric unit of (I). Ellipsoids are drawn at the 50% probability level.

## Experimental

Crystals of (I) were grown from hexane/ethyl acetate by solvent diffusion. Optical rotation:  $[\alpha]_D^{25} +47^\circ$  ( $c = 1$ , EtOH);  $+46^\circ$  was reported (De Paiva Campello & Ferreira Fonseca, 1975).  $^1\text{H NMR}$  (600 MHz;  $\text{CD}_3\text{OD}$ ; assignments aided by a COSY spectrum; coupling constants in Hz in parentheses):  $\delta$  0.69 (*s*, H20), 0.94 (*td*, 13, 3.5, H3 $\alpha$ ), 0.95 *s* (H18), 1.08 (*td*, 13, 3.5, H1 $\alpha$ ), 1.27 (*dd*, 13, 2, H5), 1.34 (*qd*, 12.5, 3.5, H6 $\beta$ ), 1.49 (*m*, 2 $\alpha$ ), 1.52 (*m*, H11), 1.58 (*qt*, 13.5, 3.5, H2 $\beta$ ), 1.63 (*br d*, 11, H9), 1.71 (*dt*, 13, 8, H11'), 1.80 (*br d*, 13, H1 $\beta$ ), 1.84 (*m*, 6 $\alpha$ ), 1.86 (*br d*, 13, H3 $\beta$ ), 1.95 (*td*, 12.5, 5, H7 $\alpha$ ), 2.00 (*dt*, 13.5, 8, H12), 2.12 (*d*, 1, H16), 2.28 (*ddd*, 13.5, 9.5, 4, H12'), 2.40 (*ddd*, 12.5, 3.5, 2.5, H7 $\beta$ ), 3.27 (*d*, 11, H19), 3.71 (*d*, 11, H19'), 4.53 (*br s*, H17), 4.85 (*br s*, H17'), 5.60 (*q*, 1, H14).

### Crystal data

$\text{C}_{20}\text{H}_{32}\text{O}_3$   
 $M_r = 320.46$   
Monoclinic,  $P2_1$   
 $a = 7.7955$  (14) Å  
 $b = 23.362$  (4) Å  
 $c = 10.6973$  (19) Å  
 $\beta = 102.297$  (3)°  
 $V = 1903.4$  (6) Å<sup>3</sup>  
 $Z = 4$

$D_x = 1.118$  Mg m<sup>-3</sup>  
Mo  $K\alpha$  radiation  
Cell parameters from 2540 reflections  
 $\theta = 2.6$ – $22.5^\circ$   
 $\mu = 0.07$  mm<sup>-1</sup>  
 $T = 170$  (2) K  
Plate, white  
 $0.5 \times 0.4 \times 0.2$  mm

### Data collection

Bruker SMART CCD diffractometer  
 $\varphi$  and  $\omega$  scans  
Absorption correction: none  
15289 measured reflections  
2580 independent reflections

1596 reflections with  $I > 2\sigma(I)$   
 $R_{\text{int}} = 0.114$   
 $\theta_{\text{max}} = 22.5^\circ$   
 $h = -8 \rightarrow 8$   
 $k = -25 \rightarrow 25$   
 $l = -11 \rightarrow 11$

### Refinement

Refinement on  $F^2$   
 $R[F^2 > 2\sigma(F^2)] = 0.051$   
 $wR(F^2) = 0.126$   
 $S = 1.00$   
2580 reflections  
419 parameters

H-atom parameters constrained  
 $w = 1/[\sigma^2(F_o^2) + (0.0582P)^2]$   
where  $P = (F_o^2 + 2F_c^2)/3$   
 $(\Delta/\sigma)_{\text{max}} = 0.002$   
 $\Delta\rho_{\text{max}} = 0.16$  e Å<sup>-3</sup>  
 $\Delta\rho_{\text{min}} = -0.21$  e Å<sup>-3</sup>

**Table 1**

Hydrogen-bonding geometry (Å, °).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
$\text{O1A}-\text{H1A}\cdots\text{O3}^{\text{i}}$	0.84	1.88	2.694 (7)	164
$\text{O2}-\text{H32}\cdots\text{O1}^{\text{ii}}$	0.84	1.76	2.582 (7)	166
$\text{O2A}-\text{H32A}\cdots\text{O1A}^{\text{iii}}$	0.84	1.79	2.603 (6)	163
$\text{O1}-\text{H1}\cdots\text{O3A}$	0.84	1.84	2.673 (7)	174

Symmetry codes: (i)  $2 + x, y - 1, z$ ; (ii)  $1 - x, \frac{1}{2} + y, 2 - z$ ; (iii)  $3 - x, \frac{1}{2} + y, 2 - z$ .

While data were initially collected to  $55^\circ 2\theta$ , significant diffraction was only observed to  $45^\circ$  and higher angle data were discarded. As mentioned above, the absolute configuration could not be determined crystallographically and the choice of enantiomer was based on comparison of the optical rotation with that of related compounds with known stereochemistry. All H atoms were positioned geometrically. Those attached to C atoms were refined with fixed bond lengths and angles, while those attached to O atoms were given fixed bond lengths and free angles, to account for intermolecular hydrogen bonds.

Data collection: *SMART* (Bruker, 1997); cell refinement: *SMART*; data reduction: *SAINT* (Bruker, 1997) and *SHELXTL* (Bruker, 1997); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1990); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*.

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## References

- Bruker (1997). *SMART*, *SAINT* and *SHELXTL*. Versions 5.0. Bruker AXS Inc., Madison, Wisconsin, USA.  
Caputo, R. & Mangoni, L. (1974). *Phytochemistry*, **13**, 467–470.  
De Paiva Campello, J. & Ferreira Fonseca, S. (1975). *Phytochemistry*, **14**, 2299–2300.  
Enzell, C. (1961). *Acta Chem. Scand.* **15**, 1303–1312.  
Manh, D. D. K., Bastard, J., Fetizon, M. & Sevenet, T. (1983). *J. Nat. Prod.* **46**, 262–273.  
Sheldrick, G. M. (1997). *SHELXL97* and *SHELXS97*. University of Göttingen, Germany.