

Obacunone

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Key indicators

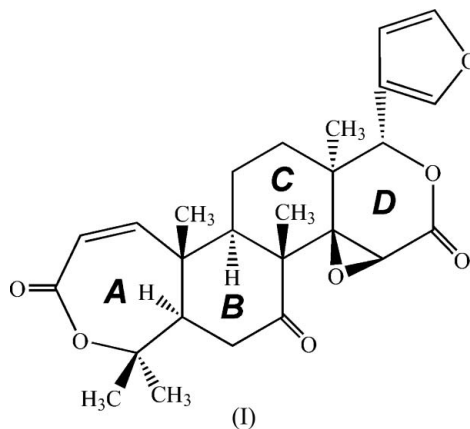
Single-crystal X-ray study
T = 293 K
Mean $\sigma(\text{C}-\text{C}) = 0.007 \text{ \AA}$
R factor = 0.045
wR factor = 0.112
Data-to-parameter ratio = 7.3

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

The title compound, $\text{C}_{26}\text{H}_{30}\text{O}_7$, crystallizes with three independent molecules in the asymmetric unit. The crystal structure is stabilized by intra- and intermolecular $\text{C}-\text{H}\cdots\text{O}$ hydrogen-bonding interactions.

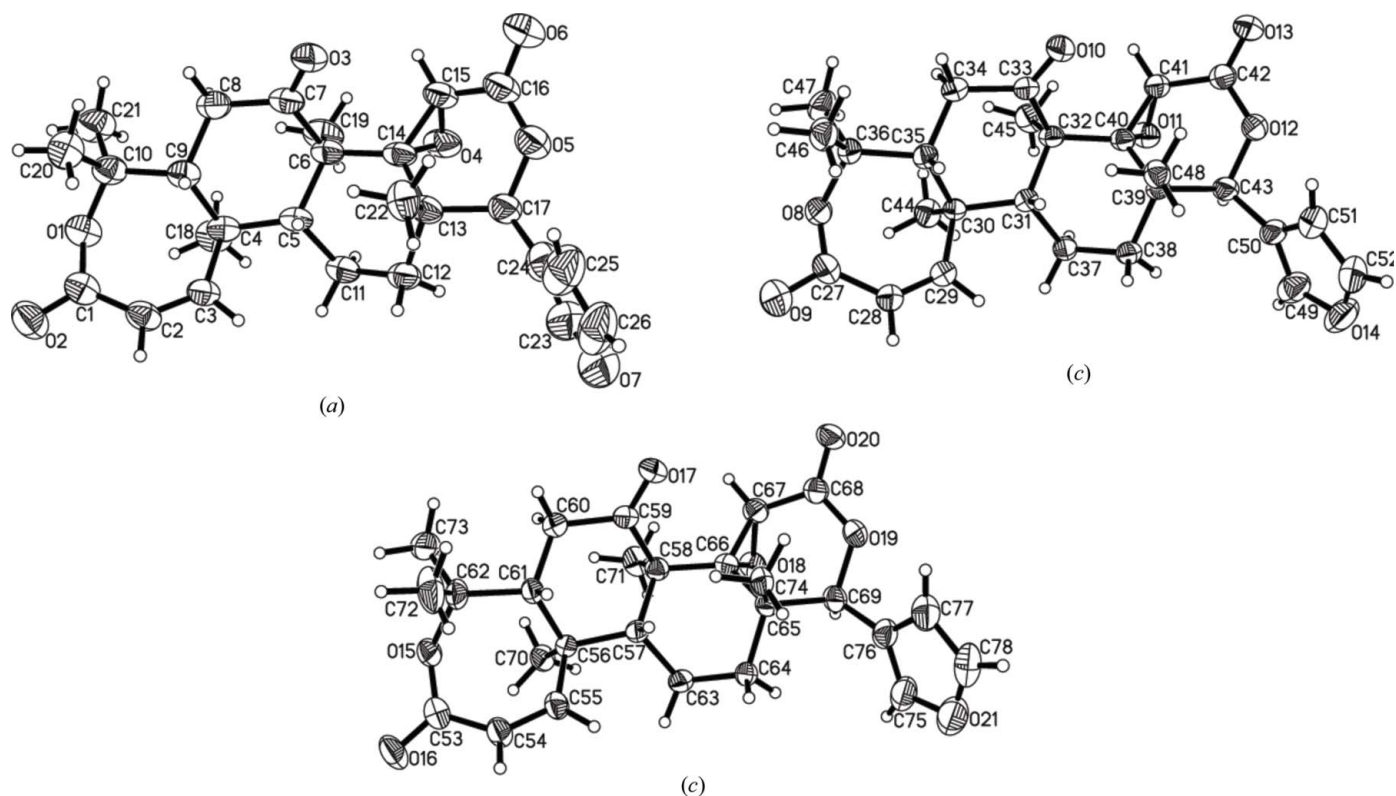
Comment

Cortex dictamni, bai-xian-pi in Chinese, is the dry root bark of *Dictamnus dasycarpus* Turcz (Rutaceae). It is officially listed in the Chinese pharmacopoeia (Chinese Pharmacopoeia Commission, 1995) and widely used for the treatment of jaundice, coughs and rheumatism (Jiangsu New Medical College, 1986). A number of phytochemical studies have been made of its constituents and various compounds, including furoquinoline alkaloids (Ishii *et al.*, 1974; Deshpande & Shastri, 1977), limonoids (Zhao, Wolfender, Hostettmann, Xu & Qin, 1998) and sesquiterpenes (Chang *et al.*, 2001; Takeuchi *et al.*, 1993; Zhao, Wolfender, Hostettmann, Li *et al.*, 1998), have been reported. Within the frame of a research project aimed at finding natural products with a selective immunosuppressive activity for drug discovery, we have reported that the aqueous extract of cortex dictamni possesses an attenuating effect on both cellular and humoral immune responses in mice (Wang *et al.*, 1992). Here we report the crystal structure of obacunone, 14,15:21,23-diepoxy-4,4,8-trimethyl-*A*,*D*-dihomo-24-nor-4,17-dioxachola-1,20,22-triene-3,7,16-trione, (I), a main component of cortex dictamni, which has recently attracted much attention because of its wide variety of biological activities (Lee *et al.*, 2005; Ruberto *et al.*, 2002; Tanaka *et al.*, 2001).



The asymmetric unit of (I) consists of three crystallographically independent molecules (molecule 1: O1–O7/C1–C26; molecule 2: O8–O14/C27–C52; molecule 3: O15–O21/

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**Figure 1**

The structures of (a) molecule 1, (b) molecule 2 and (c) molecule 3 in the asymmetric unit of (I), showing 30% probability displacement ellipsoids and the atom-numbering scheme.

C53–C78; Fig. 1a, 1b and 1c). All bond lengths and angles in (I) are within normal ranges (Allen *et al.*, 1987). The A/B, B/C and C/D ring junctions are all *trans*-fused. The five-membered ring is equatorially attached to ring D. The seven-membered heterocyclic ring A adopts a twist-boat conformation (Cremer & Pople, 1975; Table 2). The six-membered ring B assumes a chair conformation, while rings C and D show twist-boat conformations (Table 2). The crystal packing of (I) is stabilized by an extended three-dimensional network of intra- and

intermolecular C–H...O hydrogen-bonding interactions (Table 1, Fig. 2).

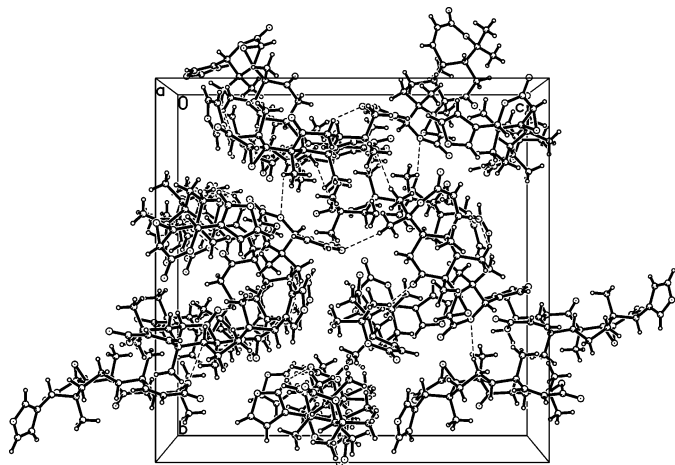
Experimental

All the solvents and reagents were commercial and purified according to standard laboratory techniques. Powdered root bark (5.0 kg) of *D. dasycarpus* was extracted three times with 60% EtOH under reflux. The total filtrate was evaporated under reduced pressure to remove EtOH; the extract was suspended in distilled water and partitioned with CH₂Cl₂ and EtOAc successively, to yield CH₂Cl₂ (148 g) and EtOAc (18 g) extracts, respectively. The CH₂Cl₂ extract (100 g) was subjected to silica gel column chromatography, eluted with CH₂Cl₂/MeOH (10:1 and 2:1), and further purified by flash column chromatography (silica gel) using a gradient of CH₂Cl₂–MeOH to afford the title compound (1.0 g). The structure of (I) was confirmed by comparison of MS, ¹H NMR, ¹³C NMR and physical data with those reported in the literature (Dreyer, 1965; Pailer, *et al.*, 1965; Kang, *et al.*, 1986; Zhang, *et al.*, 2005). Single crystals of (I) suitable for X-ray crystallographic analysis were obtained by slow evaporation of an MeOH–CH₂Cl₂ (2:1 *v/v*) solution (yield 65%).

Crystal data

C₂₆H₃₀O₇
M_r = 454.50
 Orthorhombic, *P*2₁2₁2₁
a = 12.531 (2) Å
b = 23.041 (5) Å
c = 23.649 (5) Å
V = 6828 (2) Å³

Z = 12
D_x = 1.326 Mg m⁻³
 Mo *K*α radiation
 μ = 0.10 mm⁻¹
T = 293 (2) K
 Block, colourless
 0.30 × 0.25 × 0.20 mm

**Figure 2**

The crystal packing of (I), viewed along the *a* axis. Intermolecular hydrogen bonds are shown as dashed lines.

Data collection

Bruker SMART APEX area-detector diffractometer
 φ and ω scans
 Absorption correction: multi-scan (SADABS; Sheldrick, 1996)
 $T_{\min} = 0.972$, $T_{\max} = 0.981$

34845 measured reflections
 6625 independent reflections
 3328 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.098$
 $\theta_{\text{max}} = 25.0^\circ$

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.045$
 $wR(F^2) = 0.113$
 $S = 0.84$
 6625 reflections
 909 parameters
 H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0501P)^2]$
 where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\text{max}} < 0.001$
 $\Delta\rho_{\text{max}} = 0.20 \text{ e } \text{Å}^{-3}$
 $\Delta\rho_{\text{min}} = -0.21 \text{ e } \text{Å}^{-3}$
 Extinction correction: SHELXL97
 Extinction coefficient: 0.00153 (17)

Table 1

Hydrogen-bond geometry (Å, °).

| D—H...A | D—H | H...A | D...A | D—H...A |
|------------------------------|------|-------|-----------|---------|
| C18—H18A...O1 | 0.96 | 2.46 | 3.041 (7) | 119 |
| C22—H22A...O5 | 0.96 | 2.55 | 2.970 (6) | 107 |
| C44—H44B...O8 | 0.96 | 2.49 | 3.033 (6) | 116 |
| C55—H55...O13 | 0.93 | 2.52 | 3.312 (5) | 143 |
| C61—H61...O10 | 0.97 | 2.57 | 3.448 (4) | 149 |
| C64—H64B...O13 | 0.97 | 2.57 | 3.403 (6) | 144 |
| C70—H70C...O15 | 0.96 | 2.56 | 2.925 (5) | 103 |
| C74—H74A...O19 | 0.96 | 2.55 | 2.964 (5) | 106 |
| C9—H9...O17 ⁱ | 0.98 | 2.53 | 3.460 (6) | 159 |
| C22—H22C...O17 ⁱ | 0.96 | 2.58 | 3.439 (6) | 149 |
| C23—H23...O2 ⁱⁱ | 0.93 | 2.48 | 3.188 (8) | 133 |
| C37—H37B...O19 ⁱ | 0.97 | 2.57 | 3.424 (5) | 147 |
| C37—H37B...O20 ⁱ | 0.97 | 2.58 | 3.299 (5) | 131 |
| C72—H72A...O8 ⁱⁱⁱ | 0.96 | 2.56 | 3.409 (7) | 148 |
| C73—H73B...O21 ^{iv} | 0.96 | 2.55 | 3.430 (7) | 152 |

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

Table 2

Puckering parameters (Å, °) for seven- and six-membered rings.

| | q_2 | q_3 | φ_2 | φ_3 | Q | θ_2 |
|------------|-----------|------------|-------------|-------------|-----------|------------|
| Molecule 1 | | | | | | |
| Ring A | 0.821 (4) | 0.273 (4) | -20.1 (3) | 75.6 (10) | 0.866 (4) | 71.6 (3) |
| Ring B | 0.053 (4) | 0.528 (4) | 103 (5) | | 0.503 (4) | 5.8 (4) |
| Ring C | 0.755 (5) | -0.102 (5) | -159.5 (3) | | 0.764 (5) | 97.7 (4) |
| Ring D | 0.495 (6) | -0.190 (6) | 97.4 (6) | | 0.530 (6) | 111.0 (7) |
| Molecule 2 | | | | | | |
| Ring A | 0.816 (4) | 0.301 (5) | -16.2 (4) | 70.8 (8) | 0.870 (4) | 69.8 (3) |
| Ring B | 0.100 (4) | 0.527 (4) | 87 (3) | | 0.536 (4) | 10.7 (4) |
| Ring C | 0.778 (5) | -0.108 (4) | -152.0 (3) | | 0.786 (5) | 97.9 (3) |
| Ring D | 0.480 (5) | -0.200 (4) | 96.6 (6) | | 0.520 (5) | 112.7 (5) |
| Molecule 3 | | | | | | |
| Ring A | 0.901 (4) | 0.240 (4) | -36.3 (3) | 78.2 (10) | 0.932 (4) | 75.1 (2) |
| Ring B | 0.085 (4) | 0.536 (4) | 76 (3) | | 0.542 (4) | 9.0 (4) |
| Ring C | 0.757 (4) | -0.099 (4) | -154.7 (3) | | 0.763 (4) | 97.5 (3) |
| Ring D | 0.537 (4) | -0.166 (4) | 95.7 (4) | | 0.562 (4) | 107.2 (4) |

Owing to the lack of significant anomalous scattering, Friedel pairs were merged before the final refinement and the absolute configuration could not be assigned. All H atoms were placed in geometrically idealized positions and constrained to ride on their parent atoms, with C—H = 0.93–0.98 Å, and with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$, or $U_{\text{iso}}(\text{H}) = 1.5U_{\text{eq}}(\text{C})$ for methyl H atoms.

Data collection: SMART (Bruker, 2003); cell refinement: SAINT (Bruker, 2003); data reduction: SAINT; program(s) used to solve structure: SHELXS97 (Sheldrick, 1997a); program(s) used to refine structure: SHELXL97 (Sheldrick, 1997a); molecular graphics: SHELXTL (Sheldrick, 1997b); software used to prepare material for publication: SHELXL97.

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