Acta Crystallographica Section E
Structure Reports
Online

ISSN 1600-5368

Absolute configuration of 3α-feruloyltaraxerol dichloromethane solvate

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Received 21 October 2003
Accepted 29 October 2003
Online 8 November 2003

The title compound, $C_{40}H_{58}O_4.CH_2Cl_2$, was isolated for the first time from *Bruguiera cylindrica* (*Rhizophoraceae*), and for the first time from natural product resources. The structure contains five fused six-membered rings, with two rings in chair, two in twist-boat and one in a slightly twisted boat conformation. The *D* and *E* rings are *cis*-fused. The feruloyl substituent group is axially attached to the skeleton. O—H···O hydrogen bonds and C—H···O interactions are observed in the structure. The absolute configuration was established on the basis of anomalous scattering effects of the solvent.

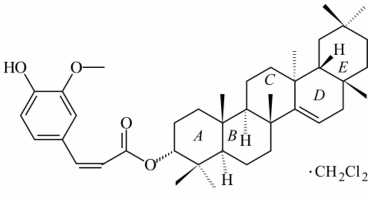
Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.005 Å
Disorder in solvent or counterion
R factor = 0.062
wR factor = 0.152
Data-to-parameter ratio = 16.2

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

Comment

Bruguiera cylindrica (*Rhizophoraceae*), a mangrove plant, is found in South-East Asia. This plant has been used as a traditional medicine in the treatment of diarrhea and in the healing of wounds (Boonyapraphat & Chockchaicharaenphom, 1998). The ethanol extract of the leaves has shown antiviral activity (Premanthan *et al.*, 1995). The isolation of sulfur compounds, brugierol, isobrugierol and brugine from the $CHCl_3$ extract of the stem bark of *Bruguiera cylindrica* has been reported (Kato & Takanishi, 1975, 1976).



(I)

We have isolated the title compound, (I), for the first time from *Bruguiera cylindrica*, and also for the first time from natural product resources. It is found to exhibit cytotoxicity against human small lung-cancer cell lines. In order to establish the absolute configuration of this important naturally occurring triterpenoid, we have used a novel method (Fun *et al.*, 2003) of incorporating heavy-atom-containing solvent molecules (in this case dichloromethane) into the crystal structure of the compound. Although the strict and demanding criteria of Flack & Bernardinelli (2000) are not met in this study, it confirms the absolute configuration with a reasonable confidence. The present X-ray study shows that (I) is in the α-form.

The structure of (I) contains five fused six-membered rings, *A*/*B*/*C*/*D*/*E*, as a taraxerol skeleton and a feruloyl substituent (O1–O4/C31–C40), axially attached to ring *A* (Fig. 1). In the taraxerol skeleton, rings *D* and *E* are *cis* fused and other junctions show *trans*-fusion. The cyclohexane *A* and *B* rings adopt chair conformations, while the cyclohexane ring *C* and

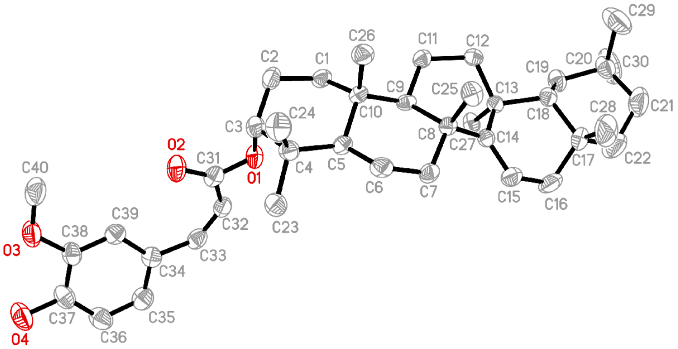


Figure 1
The structure of (I), showing 50% probability displacement ellipsoids and the atom-numbering scheme. For clarity, the dichloromethane molecule and H atoms have been omitted.

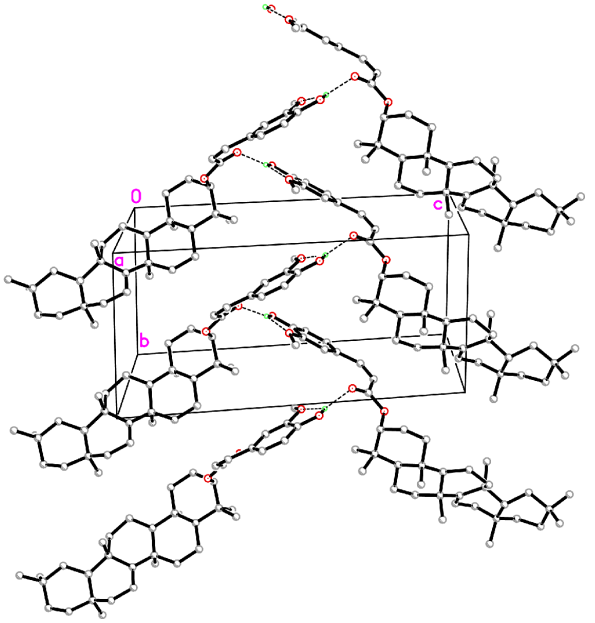


Figure 2
A view of the O—H···O hydrogen-bonded chain. For clarity, H atoms attached to C atoms have been omitted.

cyclohexene ring *D* have twist-boat conformations. The cyclohexane ring *E* adopts a slightly twisted boat conformation (Cremer & Pople, 1975).

The bond lengths and angles in the taraxerol skeleton are comparable with the corresponding values in taraxerol acetate (Billodeaux *et al.*, 1999). The C14—C15 distance of 1.328 (4) Å confirms its double-bond character. The feruloyl substituent is attached axially to ring *A* [C1—C2—C3—O1 = −67.4 (3)°] and the C31—O1—C3—C2 torsion angle of −121.4 (3)° indicates a (−)-anticlinal conformation. The C40—O3—C38—C39 torsion angle of −10.8 (5)° shows that the methoxy group is slightly twisted out of the benzene ring plane.

The methoxy and carbonyl O atoms are involved in O—H···O hydrogen bonding and C—H···O weak interactions, respectively. The molecules are interlinked through O4—H4···O2^{i} hydrogen bonds (see Table 2 for details) into chains parallel to the *b* axis (Fig. 2).

Experimental

The air-dried fruits of *Bruguiera cylindrica* (6 kg) were milled and extracted with hexane (20 l × 2). The filtered solution was then evaporated to dryness under reduced pressure to afford 35 g of crude hexane extract. This extract was subjected to quick column chromatography (QCC) over silica gel and eluted with a gradient of hexane–acetone to afford 15 fractions (A1–A15, each fraction collecting 300 ml). Fraction A9 (2.80 g) was recrystallized from acetone–hexane (3:7 *v*/*v*, 50 ml) to give a white powder of compound (I). The white powder were recrystallized from CH_2Cl_2–CH_3OH (9:1 *v*/*v*) to give colourless single crystals of compound (I) after a few days (m.p. 458–459 K).

Crystal data

$C_{40}H_{58}O_4 \cdot CH_2Cl_2$
$M_r = 687.79$
Monoclinic, $P2_1$
$a = 12.5558$ (10) Å
$b = 8.5131$ (7) Å
$c = 18.6076$ (15) Å
$\beta = 104.834$ (1)°
$V = 1922.7$ (3) Å^3
$Z = 2$

$D_x = 1.188$ Mg m^{-3}
Mo *Kα* radiation
Cell parameters from 4263 reflections
$\theta = 2.3$–26.0°
$\mu = 0.21$ mm^{-1}
$T = 293$ (2) K
Needle, colourless
0.48 × 0.18 × 0.14 mm

Data collection

Siemens SMART CCD area-detector diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
$T_{min} = 0.907$, $T_{max} = 0.972$
10423 measured reflections

7198 independent reflections
5897 reflections with $I > 2\sigma(I)$
$R_{int} = 0.020$
$\theta_{max} = 26.0°$
$h = -15 \rightarrow 15$
$k = -9 \rightarrow 10$
$l = -14 \rightarrow 22$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.062$
$wR(F^2) = 0.152$
$S = 1.11$
7198 reflections
445 parameters
H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0698P)^2 + 0.5197P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.002$
$\Delta\rho_{max} = 0.34$ e Å^{-3}
$\Delta\rho_{min} = -0.48$ e Å^{-3}
Absolute structure: Flack (1983), 3171 Friedel pairs
Flack parameter = 0.12 (13)

Table 1
Selected geometric parameters (Å, °).

O1—C31	1.349 (4)	O3—C40	1.410 (4)
O1—C3	1.457 (4)	O4—C37	1.357 (4)
O2—C31	1.211 (4)	C14—C15	1.328 (4)
O3—C38	1.369 (4)	C32—C33	1.324 (5)
C31—O1—C3—C2	−121.4 (3)	C32—C33—C34—C39	21.8 (6)
O1—C31—C32—C33	164.0 (3)	C40—O3—C38—C39	−10.8 (5)
C31—C32—C33—C34	3.2 (7)	C40—O3—C38—C37	171.3 (3)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O4—H4···O3	0.82	2.19	2.651 (4)	115
O4—H4···O2^{i}	0.82	2.04	2.768 (4)	147
C3—H3···O2	0.98	2.27	2.724 (4)	107
C39—H39···O2	0.93	2.18	2.932 (4)	137

Symmetry code: (i) $1 - x, y - \frac{1}{2}, 1 - z$.

Acta Cryst. (2003). E**59**, o1864–o1866 Suchada Chantrapromma *et al.* • $C_{40}H_{58}O_4 \cdot CH_2Cl_2$ **o1865**

H atoms were placed in calculated positions with an O—H distance of 0.82 Å and C—H distances in the range 0.93–0.98 Å. The $U_{\rm iso}$ values were constrained to be $1.5U_{\rm eq}$ of the carrier atom for hydroxyl and methyl H atoms and $1.2U_{\rm eq}$ for the remaining H atoms. One of the Cl atoms, Cl2, in the dichloromethane solvent molecule was found to be disordered over three positions and the occupancies of the disordered positions Cl2*A*, Cl2*B* and Cl2*C* were refined to 0.216 (4), 0.529 (11) and 0.255 (12), respectively. The C—Cl distances involving the disordered Cl atoms were restrained to be equal with an effective standard deviation of 0.01. The absolute configuration was determined by refining the Flack parameter, exploiting the anomalous scattering effect of chlorine in the solvent (Flack & Bernardinelli, 1999). Owing to the large fraction of weak data at higher angles, the 2θ maximum was limited to 52°.

Data collection: *SMART* (Siemens, 1996); cell refinement: *SAINT* (Siemens, 1996); data reduction: *SAINT*; program(s) used to solve structure: *SHELXTL* (Sheldrick, 1997); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL, PARST* (Nardelli, 1995) and *PLATON* (Spek, 2003).

The authors thank the Prince of Songkla University for a research grant. SL thanks the Natural Products from Mangrove Plants and Synthetic Materials Research Unit, PSU, and the Royal Golden Jubilee PhD Program (grant No. PHD/0007/2546). The authors also thank the Malaysian Government and Universiti Sains Malaysia for research grant R&D No. 305/PFIZIK/610961.

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o1866 Suchada Chantrapromma *et al.* • $C_{40}H_{58}O_4\cdot CH_2Cl_2$ *Acta Cryst.* (2003). E**59**, o1864–o1866