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Phyllanthin from the plant *Phyllanthus amarus*

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Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.005 Å
R factor = 0.066
wR factor = 0.181
Data-to-parameter ratio = 12.1

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

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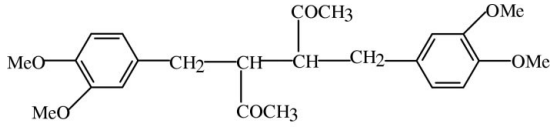
In the title compound, $C_{24}H_{34}O_6$, the molecule resides on a crystallographic twofold axis, which runs through the central C—C bond. The crystal packing is stablized by C—H···O intramolecular and C—H···π intermolecular interactions.

Comment

Phyllanthus amarus is a predominant plant species in South India, especially in Tamilnadu. The plant has been used traditionally in the treatment of jaundice, gastropathy, diarrhoea, dysentry, scabies, ulcers and wounds. *Phyllanthus amarus* has shown profound antiviral activity against the hepatitis B virus, as reported by Thyagarajan *et al.* (1982), Venkateswaran *et al.* (1987), Mehrotra *et al.* (1991), Lee *et al.* (1996) and Ott *et al.* (1997). *Phyllanthus amarus* has various constituents such as lignans, terpenes, alkaloids, flavanoids, phenols and tannins. Lignans form the major component of the plant. Phyllanthin and hypophyllanthin are the two major constituents, belonging to the group of lignans which have been extensively investigated by Krishnamurthi & Seshadri (1946), Ramachandra Row *et al.* (1966), Anjaneyulu *et al.* (1973) and Houghton *et al.* (1996).



(I)

The present study deals with the molecular structure of phyllanthin, (I), from the South Indian variety of *Phyllanthus amarus*. The molecular structure of (I) and the atom-numbering scheme are shown in Fig. 1. The bond distance C10—C10^{i} of 1.558 (5) Å [symmetry code: (i) $-x, y, -z$] confirms the C—C single-bond character. All the C—C and C—O bond lengths are comparable to the reported mean values of C_{phenyl}—C_{phenyl} = 1.380 Å, C_{phenyl}—O = 1.362 Å and C—C = 1.530 Å (Allen *et al.*, 1987).

The exocyclic angles around atoms C2 and C3 show considerable asymmetry, with O1—C2—C1 [124.8 (3)°] being wider than O1—C2—C3 [115.7 (2)°] and C4—C3—O2 [124.5 (3)°] being wider than O2—C3—C2 [115.3 (3)°]. This may be due to the substitution of methoxy groups and the steric repulsion between the phenyl rings and methyl groups. A similar effect has also been reported in related structures (Lerbscher *et al.*, 1977; Hough, 1976).

The torsion angles about the bonds C2—O1 and C11—O3 [C1—C2—O1—C7 = 0.8 (5)°, C3—C2—O1—C7 =

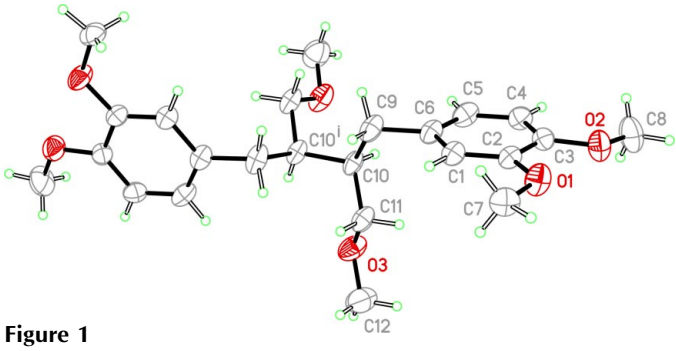


Figure 1
The molecular structure of (I), showing 30% probability displacement ellipsoids.

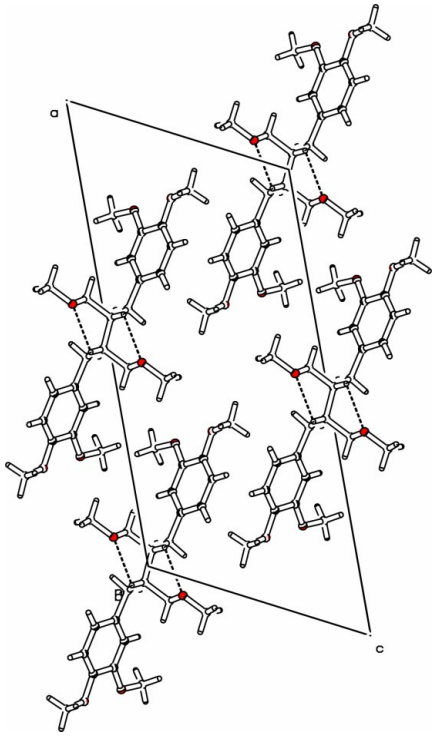


Figure 2
Packing of the molecules, viewed down the *b* axis.

−179.2 (3)° and C10—C11—O3—C12 = 178.7 (3)°] cofirm the energetically favourable *trans* conformation. The torsion angles C4—C3—O2—C8 [−6.6 (5)°] and C2—C3—O2—C8 [172.1 (3)°] indicate that the methoxy group deviates slightly from coplanarity with the phenyl ring; atom C8 deviates by 0.21 (1) Å. The values of the torsion angles C5—C6—C9—C10 and C1—C6—C9—C10 [64.7 (4) and −115.3 (3)°, respectively] show the +synclinal and -anticlinal conformations around these atoms.

The structure is stabilized by a pair of C—H···O intramolecular hydrogen bonds (C10—H10···O3^{i}), where the C···O^{i} distance is 2.943 (4) Å, H···O is 2.54 Å and the C—H···O3^{i} angle is 105° [symmetry code: (i) $-x, y, -z$]. Symmetry-related molecules are linked by intermolecular C—H···π contacts, so that H7 is 2.80 Å from the centroid of the phenyl ring with an angle of 157° for C7—H7···*Cg*, where *Cg* is the centroid of C1^{ii}/C2^{ii}/C3^{ii}/C4^{ii}/C5^{ii}/C6^{ii} [symmetry code: (ii) $x, -1+y, z$] (Selvanayagam *et al.*, 2002).

Experimental

Fresh plant (14 g) was ground and was extracted three times with methanol. The combined extract was concentrated to a semi-solid mass. It was then purified by removing fatty material and carotenoids, by extracting it with methanol and petroleum ether alternately. The extract was then subjected to column chromatography with silica gel (60–80 mesh) as stationary phase and *n*-hexane, with an increasing amount of ethyl acetate, as mobile phase. Online thin-layer chromatography was performed for each fraction, phyllanthin was identified by the blue–green colour it gave when sprayed with 10% methanolic sulfuric acid, heated at 358 K for 5 min and compared with a reference. Phyllanthin was recrystallized from *n*-hexane.

Crystal data

$C_{24}H_{34}O_6$
M_r = 418.51
Monoclinic, *C*2
a = 22.6091 (7) Å
b = 5.3506 (2) Å
c = 11.0871 (4) Å
β = 117.328 (1)°
V = 1191.54 (7) Å^3
Z = 2
D_x = 1.166 Mg m^{-3}
Mo *K*α radiation
Cell parameters from 2451 reflections
θ = 2.9–25.1°
μ = 0.08 mm^{-1}
T = 293 (2) K
Block, colourless
0.20 × 0.20 × 0.20 mm

Data collection

Siemens SMART CCD diffractometer
ω scans
Absorption correction: none
4350 measured reflections
1651 independent reflections
1138 reflections with $I > 2\sigma(I)$
R_{int} = 0.072
θ_{max} = 29.4°
h = −29 → 26
k = −7 → 5
l = −15 → 13

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.066
$wR(F^2)$ = 0.181
S = 1.02
1651 reflections
136 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.1P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.22 e Å^{-3}
$\Delta\rho_{min}$ = −0.24 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

C1—C2	1.381 (4)	C6—C9	1.524 (4)
C1—C6	1.387 (4)	C7—O1	1.411 (4)
C2—O1	1.369 (4)	C8—O2	1.417 (6)
C2—C3	1.395 (4)	C9—C10	1.539 (4)
C3—C4	1.365 (4)	C10—C11	1.504 (4)
C3—O2	1.386 (3)	C10—C10^{i}	1.558 (5)
C4—C5	1.399 (4)	C11—O3	1.411 (5)
C5—C6	1.377 (4)	C12—O3	1.397 (5)
O1—C2—C1	124.8 (3)	C4—C3—O2	124.5 (3)
O1—C2—C3	115.7 (2)	O2—C3—C2	115.3 (3)
C5—C6—C9—C10	64.7 (4)	C3—C2—O1—C7	−179.2 (3)
C1—C6—C9—C10	−115.3 (3)	C4—C3—O2—C8	−6.6 (5)
C10^{i}—C10—C11—O3	60.6 (3)	C2—C3—O2—C8	172.1 (3)
C1—C2—O1—C7	0.8 (5)	C10—C11—O3—C12	178.7 (3)

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

The H atoms were positioned geometrically and were treated as riding on their parent C atom, with an aromatic C—H distance of 0.93 Å, methoxy C—H distance 0.96 Å and methylene C—H distance of 0.97 Å. Due to the lack of anomalous scatterers the absolute configuration was not determined from the X-ray diffraction data and Friedels pairs were merged. The absolute configuration of (I) is unknown.

Data collection: *SMART* (Siemens, 1996); cell refinement: *SAINT* (Siemens, 1996); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*-3 (Farrugia, 1997) and *PLATON* (Spek, 1990); software used to prepare material for publication: *SHELXL*97 and *PARST* (Nardelli, 1995).

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