Acta Crystallographica Section E
Structure Reports
Online

ISSN 1600-5368

5-Hydroxy-3,3′,4′,5′,7-pentamethoxyflavone (combretol)

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Received 21 November 2003
Accepted 3 December 2003
Online 12 December 2003

The structure of the title compound, $C_{20}H_{20}O_8$, which was extracted from *Rhodomyrtus tomentosa*, confirms the connectivity and is consistent with the results from spectroscopy. The structure, notable for the crowded sequence of (3′,4′,5′) trimethoxy substituents, is compared with that of its previously recorded analogue lacking the methyl at the 4′-oxygen (two polymorphs), and with myricetin which lacks all *O*-methylation (cocrystallized with triphenylphosphine oxide). The latter, interestingly, has a dihedral angle of 36.4 (3)° between its planar aromatic components, but the overall cyclic framework of the title molecule is essentially planar. In the crystal structure, the molecules stack obliquely along the short [4.244 (2) Å] *c* axis of the orthogonal cell.

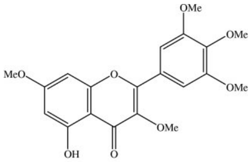
Key indicators

Single-crystal X-ray study
T = 150 K
Mean *σ*(C–C) = 0.009 Å
R factor = 0.053
wR factor = 0.059
Data-to-parameter ratio = 6.1

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

Comment

In continuation of our studies on the constituents of *Rhodomyrtus tomentosa (Ait.) Hassk.* (Dachriyanus *et al.*, 2002), the bark and twigs of this plant were investigated. The ethyl acetate fraction of the extract of these parts showed significant antimicrobial activity. From this fraction the flavonol combretol, (1) (3,3′,4′,5′,7-penta-*O*-methylmyricetin), was isolated. The crystal structure determination and full NMR assignment of this compound are reported.

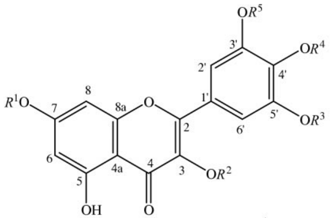


(1)

Compound (1) crystallized in space group $Pna2_1$, one formula unit devoid of crystallographic symmetry comprising the asymmetric unit of the structure which, although noncentrosymmetric, is racemic (Fig. 1). Consisting as it does of extended planar aromatic motifs, it is unsurprizing to find the molecules packing with these planes quasi-normal to a short crystallographic axis (Fig. 2) with, presumably, charge-transfer interactions a significant factor in the stacking. The interplanar dihedral angle between the two aromatic ring systems (O1/C2/C3/C4/C4a/C5/C6/C7/C8/C8a and C1′–C6′) is 6.8 (3)°, these being closely coplanar. This is also the case in the two polymorphs of the variation on (1), compound (2), lacking the methyl at the 4′-oxygen, in which the dihedral angles are 7.8 (*α* polymorph) and 0.4° (*β* polymorph) (Castleden *et al.*, 1985). These contrast with related hydroxylated species such as myricetin, (3) (cocrystallized with triphenylphosphine oxide), in which the angle is 36.4 (3)° (Cody & Luft, 1994) and, further afield, in morin monohydrate (Cody & Luft, 1994) where the

DOI: 10.1107/S1600536803027880

angles are 41.63 (8) and 48.31 (8)° (two molecules). In the latter, intermolecular hydrogen bonding contributes extensively to the structures, but in (2) which is highly methylated, and even more so in (1), for such phenolic residues as remain, intramolecular interactions predominate; here H5···O4 is 1.70 Å. As in (2), most of the methoxy substituents lie coplanar with their associated ring systems; exceptions are found for substituents 3 in each of (1) and (2) and in the present (1) the substituent at 4′ is also out-of-plane, all for steric reasons. Substantial asymmetries are found in the exocyclic angles at C2 and C1′, with H2′···O3 and H6′···O1 = 2.16 and 2.30 Å and C2—C1′ = 1.454 Å. Bond lengths and angles otherwise are in substantial agreement between (1) and (2), but between these and, for example, (3), unsurprisingly, much more substantial differences are found.



	R^1	R^2	R^3	R^4	R^5
(1)	Me	Me	Me	Me	Me
(2)	Me	Me	Me	H	Me
(3)	H	H	H	H	H

Experimental

General procedures have been described previously (Baker *et al.*, 2000). *Rhodomyrtus tomentosa* was collected at Andalas University Campus, Limau Manis, Padang, West Sumatra, Indonesia in December 2001. A voucher specimen (DR-180) was identified by Dr Rusjdi Tamin. The ground air-dried bark and twigs (500 g) were defatted with hexane (3 × 2 l) and then extracted with ethyl acetate (3 × 2 l). The ethyl acetate extract was evaporated *in vacuo* to give a yellow gum (9 g). This fraction showed a significant antimicrobial activity. A portion of the ethyl acetate fraction (5 g) was preadsorbed on to silica gel and chromatographed over a column of silica gel with increasing amounts of ethyl acetate in hexane as eluent. Fractions which exhibited a similar pattern on thin-layer chromatography were combined and subjected to radial chromatography to give combretol, (1) (60 mg), which crystallized from ethyl acetate/hexane as yellow needles, m.p. 419–420 K (417 K; Mongkolsuk *et al.*, 1966).

Found: $[M]^+$ 388.1156; $C_{20}H_{20}O_8$ requires 388.1158; IR (KBr) $\nu_{\max}$: 3419, 1666, 1661, 1590, 1500, 1456, 1246, 1213, 1167, 1162, 1136, 1128 cm^{-1}; UV $\lambda_{\max}$ (CH_3OH): 209 (ε 44,000), 267 (ε 15,800), 344 (ε 14,900); ^1H NMR (500 MHz, $CDCl_3$): δ 3.861 (*s*, 3H, C-3 OMe), 3.864 (*s*, 3H, C-7 OMe), 3.932 (*s*, 6H, C-3′and 5′ 2 × OMe), 3.935 (*s*, 3H, C-4′ OMe), 6.34 (*d*, $J_{6,7}$ = 2.2 Hz, 1 H, 6H), 6.43 (*d*, $J_{7,6}$ = 2.2 Hz, 1H, 7H), 7.35 (*s*, 2H, 2′ and 6′H), 12.56 (*s*, 1H, 5-OH) ^{13}C NMR (125 MHz, $CDCl_3$): δ 55.79 (C-7, OMe), 56.28 (C-3′ and 5′, OMe), 60.27 (C-3, OMe), 60.95 (C-4′, OMe), 92.18 (C-8), 97.87 (C-6), 106.00 (C-10, -2′ and -6′), 125.40 (C-1′), 139.34 (C-3), 140.54 (C-4′), 153.06 (C-3′ and 5′), 155.53 (C-2), 156.65 (C-9), 161.96 (C-5), 165.51 (C-7), 178.70 (C-4); MS *m*/*z* (rel. int.): 388 $[M]^+$ (100), 373 $[M\text{-}CH_3]$ (75), 345 (37).

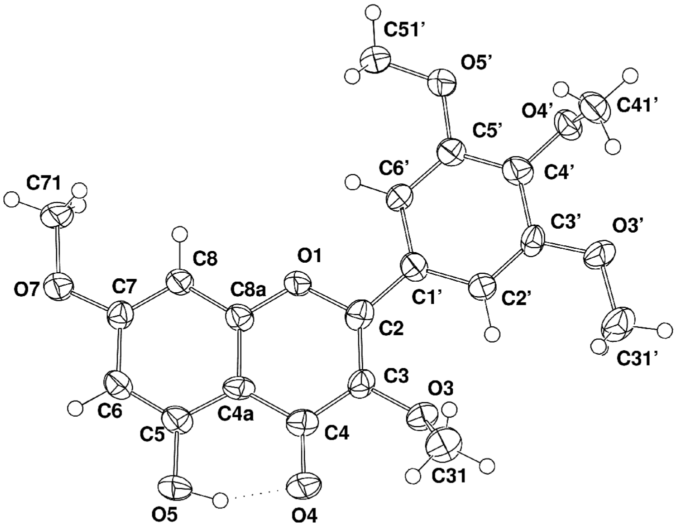


Figure 1
Projection of a single molecule of (1), showing 50% probability displacement ellipsoids for the non-H atoms. H atoms have arbitrary radii of 0.1 Å.

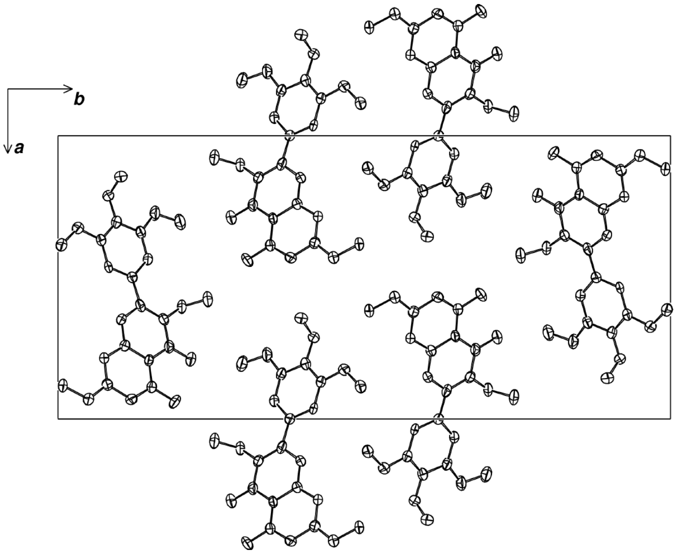


Figure 2
Projection of the unit-cell contents down *c*.

Crystal data

$C_{20}H_{20}O_8$
M_r = 388.37
Orthorhombic, $Pna2_1$
a = 13.827 (6) Å
b = 29.900 (14) Å
c = 4.244 (2) Å
V = 1754.6 (14) $Å^3$
Z = 4
D_x = 1.47 Mg m^{-3}

Mo Kα radiation
Cell parameters from 1050 reflections
θ = 2.4–24.5°
μ = 0.12 mm^{-1}
T = 150 (2) K
Splinter, colourless yellow
0.30 × 0.06 × 0.03 mm

Data collection

Bruker SMART CCD diffractometer
ω scans
Absorption correction: multi-scan *SADABS*; Sheldrick, 1996
$T_{\min}$ = 0.957, $T_{\max}$ = 0.998
13745 measured reflections

1789 independent reflections
1526 reflections with $I > \sigma(I)$
R_{int} = 0.077
$\theta_{\max}$ = 25.2°
$h = -16 \rightarrow 16$
$k = -35 \rightarrow 35$
$l = -5 \rightarrow 5$

Refinement

Refinement on F
$R = 0.053$
$wR = 0.059$
$S = 1.14$
1526 reflections
252 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o) + 0.0013F^2]$
where $\sigma(I) = [\sigma(I)_{\rm meas} + 0.0004(I_{\rm net})^2]^{1/2}$
$(\Delta/\sigma)_{\rm max} = 0.009$
$\Delta\rho_{\rm max} = 0.37$ e Å^{-3}
$\Delta\rho_{\rm min} = -0.36$ e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

O1—C2	1.382 (8)	C7—O7	1.359 (9)
O1—C8a	1.348 (7)	O7—C71	1.447 (7)
C2—C1′	1.454 (9)	C3′—O3′	1.361 (9)
C3—O3	1.381 (10)	O3′—C31′	1.439 (9)
O3—C31	1.461 (9)	C4′—O4′	1.363 (8)
C4—O4	1.267 (8)	C5′—O5′	1.396 (8)
C5—O5	1.370 (8)		
C2—O1—C8a	122.5 (5)	C7—O7—C71	116.6 (5)
O1—C2—C3	118.6 (6)	C2′—C3′—O3′	125.8 (6)
O1—C2—C1′	111.6 (5)	C3′—O3′—C31′	117.0 (5)
C3—C2—C1′	129.7 (7)	C3′—C4′—O4′	120.5 (6)
C3—C4—O4	122.2 (7)	C4′—O4′—C41′	113.4 (6)
C4a—C5—O5	119.6 (6)	O5′—C5′—C6′	123.6 (7)
C6—C7—O7	113.6 (6)	C5′—O5′—C51′	116.9 (5)

The H atoms were located in difference Fourier maps, and placed at idealized positions; C—H = 0.95 Å, and $U_{\rm iso}$(H) = 1.25$U_{\rm eq}$(C) (CH) and 1.5$U_{\rm eq}$(C) (CH_3 and OH).

Data collection: *SMART* (Siemens, 1995); cell refinement: *SAINT* (Siemens, 1995); data reduction: *Xtal*3.5 (Hall *et al.*, 1995); program(s) used to solve structure: *Xtal*3.5; program(s) used to refine structure: *Xtal*3.5 *CRYLSQ*; molecular graphics: *Xtal*3.5; software used to prepare material for publication: *Xtal*3.5 *BONDLA CIFIO*.

We thank Dr Rusjdi Tamin for the identification of the plant material and UNESCO for a travel grant.

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