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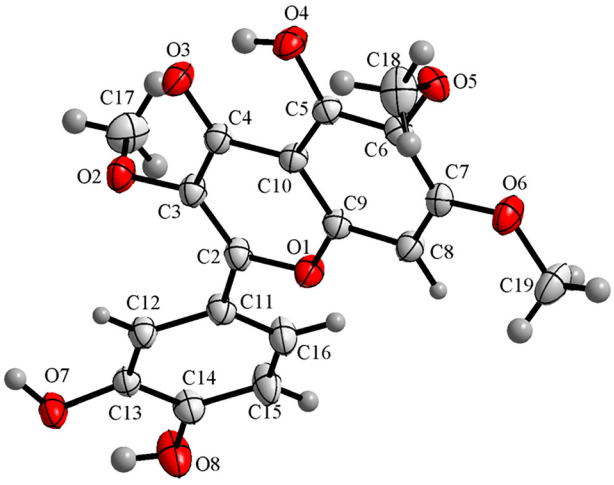
The crystal structure of Chrysosplenol D, $C_{18}H_{16}O_8$



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Abstract

$C_{18}H_{16}O_8$, monoclinic, $P2_1/n$ (no. 14), a = 14.5762(6) Å, b = 6.6791(3) Å, c = 17.4240(7) Å, β = 103.5820(10)°, V = 1648.89(12) Å^3, Z = 4, $R_{gt}(F)$ = 0.0436, $wR_{ref}(F^2)$ = 0.1218, T = 293(2) K.

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The molecular structure is shown in the figure. Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

Table 1: Data collection and handling.

Crystal:	Yellow needle
Size:	0.22 × 0.17 × 0.13 mm
Wavelength:	Mo $K\alpha$ radiation (0.71073 Å)
μ:	0.12 mm^{-1}
Diffractometer, scan mode:	Bruker APEX-II, φ and ω
θ_{max}, completeness:	30.6°, 98%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	26,956, 4974, 0.028
Criterion for I_{obs}, $N(hkl)_{gt}$:	I_{obs} > 2 σ(I_{obs}), 4066
$N(param)_{refined}$:	246
Programs:	Bruker [1], SHELX [2, 3]

Source of material

The whole plants of *Caryopteris terniflora* collected from Santai County, Sichuan Province were extracted with 95% ethanol for three times (once for seven days) at room temperature. The combined filtrate was concentrated to give the brown residue, which was suspended in water and extracted with petroleum ether, ethyl acetate, and *n*-butanol successively. The ethyl acetate fraction (0.219 kg) was then separated over silica gel column chromatography eluted with petroleum ether/ethyl acetate and dichloromethane/methanol in gradient, affording six fractions of E1–E6. The title compound (131.8 mg) was obtained from the E4 fraction *via* repeated silica gel column chromatography. Yellow needle shaped crystals were obtained by recrystallization in ethyl acetate for two days. The structure was further comfirmed by NMR analysis with its systematic name as 2-(3,4-dihydroxyphenyl)-5-hydroxy-3,6,7-trimethoxy-4*H*-chromen-4-one.

Experimental details

A Bruker APEX-II CCD diffractometer was employed to perform the diffraction experiments of a single crystal selected carefully. The data was collected using APEX 2 [1] data collection software at 293 K. The structure was solved and refined using the Bruker SHELXTL software package [2, 3].

Comment

Flavonoids, a common class of natural products widely distributed in plants and ferns, are characterized by their

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Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2).

Atom	*x*	*y*	*z*	U_{iso}^*/U_{eq}
O1	0.67411 (6)	0.37707 (13)	0.47987 (5)	0.03476 (18)
O2	0.78874 (6)	0.25446 (13)	0.32164 (5)	0.03709 (19)
O3	0.90108 (6)	0.55706 (14)	0.39832 (5)	0.0398 (2)
O4	0.94321 (6)	0.81128 (15)	0.51429 (6)	0.0405 (2)
O5	0.89493 (6)	0.97839 (12)	0.64258 (5)	0.03456 (18)
O6	0.74024 (7)	0.86607 (14)	0.68375 (5)	0.0422 (2)
O7	0.50979 (7)	−0.12550 (14)	0.20154 (5)	0.0396 (2)
H7	0.5469 (11)	−0.066 (3)	0.1725 (7)	0.059*
O8	0.45890 (8)	−0.36848 (16)	0.30770 (6)	0.0542 (3)
H8A	0.4522 (13)	−0.383 (2)	0.2579 (14)	0.081*
C2	0.69411 (8)	0.28595 (16)	0.41562 (6)	0.0310 (2)
C3	0.76907 (8)	0.34384 (16)	0.38656 (6)	0.0309 (2)
C4	0.83054 (7)	0.50306 (16)	0.42306 (6)	0.0296 (2)
C5	0.86423 (7)	0.74856 (16)	0.53425 (6)	0.0287 (2)
C6	0.83902 (8)	0.83410 (15)	0.59814 (6)	0.0285 (2)
C7	0.75824 (8)	0.76715 (16)	0.62150 (6)	0.0299 (2)
C8	0.70351 (8)	0.61126 (17)	0.58245 (6)	0.0320 (2)
H8	0.651550	0.563469	0.599227	0.038*
C9	0.72943 (7)	0.52961 (16)	0.51738 (6)	0.0288 (2)
C10	0.80759 (7)	0.59516 (16)	0.49085 (6)	0.0283 (2)
C11	0.62949 (8)	0.12028 (17)	0.38662 (6)	0.0318 (2)
C12	0.60149 (8)	0.07936 (17)	0.30565 (6)	0.0314 (2)
H12	0.622033	0.161017	0.269816	0.038*
C13	0.54364 (7)	−0.08138 (16)	0.27893 (6)	0.0291 (2)
C14	0.51408 (9)	−0.20721 (18)	0.33272 (7)	0.0352 (2)
C15	0.54088 (10)	−0.1654 (2)	0.41268 (7)	0.0438 (3)
H15	0.520808	−0.247764	0.448553	0.053*
C16	0.59745 (9)	−0.0013 (2)	0.43945 (7)	0.0403 (3)
H16	0.614086	0.027568	0.493154	0.048*
C17	0.83729 (11)	0.0663 (2)	0.33716 (10)	0.0519 (3)
H17A	0.851323	0.016904	0.289449	0.078*
H17B	0.798009	−0.028368	0.355880	0.078*
H17C	0.894982	0.084574	0.376523	0.078*
C18	0.88594 (13)	1.1704 (2)	0.60732 (9)	0.0513 (4)
H18A	0.896200	1.160883	0.555000	0.077*
H18B	0.931818	1.259098	0.638408	0.077*
H18C	0.823700	1.221443	0.604635	0.077*
C19	0.65910 (11)	0.8102 (2)	0.71101 (9)	0.0525 (4)
H19A	0.604113	0.818154	0.668153	0.079*
H19B	0.652004	0.899301	0.752467	0.079*
H19C	0.666467	0.675578	0.730773	0.079*
H9	0.9458 (15)	0.744 (4)	0.4711 (13)	0.079 (6)*

diversified structural skeleton and bioactivities [4–6]. *C. terniflora* was used as folk medicine to relieve swelling and pain, which were associated with inflammation [7]. The title compound belongs to the flavonols, the structural subtype of flavonoids. It also pocessed various biological effects including anti-inflammatory and antioxidant activity [8–10], indicating it may act as the anti-inflammatory ingredient of *C. terniflora*.

There is one molecule in the asymmetric unit (see the figure). The bond lengths and angles are all in the expected ranges [11, 12]. Detailed analysis of its crystal structure revealed that the methoxyl groups located at C-3 and C-6 are turned out from the plane of chromone skeleton, which is in accordance with that of casticin, the methyl etherified derivative at 4′-OH of the title compound [11, 13]. The phenyl group at C-2 position deviated from the plane of chromone skeleton with a dihedral angle of 36.7°, which was unfavorable for the conjugation in cinnamoyl unit associated with characteristic UV absorption band. Thus, the conformation of phenyl group in combination with methyl etherification of 3-OH may contribute to the blue shift of band I in UV spectrum when compared with that of 3,5,3′,4′-tetrahydroxy-6,7-dimethoxyflavone (345 vs 374 nm) [14, 15].

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References

1. Bruker. *APEX2 Ver 2.0-1*; Bruker AXS Inc.: Madison, WI, 2005.
2. Sheldrick G. M. *SHELXTL* – integrated space-group and crystal-structure determination. *Acta Crystallogr.* 2015, *A71*, 3–8.
3. Sheldrick G. M. Crystal structure refinement with SHELXL. *Acta Crystallogr.* 2015, *C71*, 3–8.
4. Guven H., Arici A., Simsek O. Flavonoids in our foods: a short review. *J. Basic Clin. Health Sci.* 2019, *3*, 96–106.
5. Williamson G., Kay C. D., Crozier A. The bioavailability, transport, and bioactivity of dietary flavonoids: a review from a historical perspective. *Compr. Rev. Food Sci. Food Saf.* 2018, *17*, 1054–1112.
6. Gentile D., Fornai M., Pellegrini C., Colucci R., Blandizzi C., Antonioli L. Dietary flavonoids as a potential intervention to improve redox balance in obesity and related co-morbidities: a review. *Nutr. Res. Rev.* 2018, *31*, 239–247.
7. Zhong G. Y., Qin S. Y. Pharmacognostical identification of traditional ethnic use of *Caryopteris* plants in Qiang nationality. *China J. Chin. Mater. Med.* 1993, *18*, 392–394.
8. Hsieh M. J., Lin C. C., Lo Y. S., Chuang Y. C., Ho H. Y., Chen M. K. Chrysosplenol D triggers apoptosis through heme oxygenase-1 and mitogen- activated protein kinase signaling in oral squamous cell carcinoma. *Cancers* 2021, *13*, 4327.
9. Lang S. J., Schmiech M., Hafner S., Paetz C., Werner K., Gaafary M. E., Schmidt C. Q., Syrovets T., Simmet T. Chrysosplenol D, a flavonol from *Artemisia annua*, induces ERK1/2-mediated apoptosis in triple negative human breast cancer cells. *Int. J. Mol. Sci.* 2020, *21*, 4090.

10. Zhang Q., Feng A., Zeng M., Zhang B., Shi J., Lv Y., Cao B., Zhao C., Wang M., Ding Y., Zheng X. Chrysosplenol D protects mice against LPS-induced acute lung injury by inhibiting oxidative stress, inflammation, and apoptosis via TLR4–MAPKs/NF-?B signaling pathways. *Innate Immun.* 2021, *27*, 514–524.
11. Asker E., Akin S., Hökelek T. 5,3′-Dihydroxy-3,6,7,4′-tetramethoxyflavone. *Acta Crystallogr.* 2006, *E62*, o4159–o4161.
12. Sosa A., Rosquete C., Bruno J., Rojas L., Pouysegu L., Quideau S., Leger J.-M., Massip S., Lacaille-Dubois M.-A., Mitaine-Offer A.-C. Crystal structure analysis of 6,7-di-*O*-methyl-quercetagetin-3-*O*-β-D-glucopyranoside dihydrate isolated from *Urena sinuata* L. *Av. en Quimica* 2011, *6*, 55–59.
13. Han X., Ma X., Zhang T., Zhang Y., Liu Q., Ito Y. Isolation of high-purity casticin from *Artemisia annua* L. by high-speed counter-current chromatography. *J. Chromatogr. A* 2007, *1151*, 180–182.
14. Lai J. P., Lim Y. H., Su J., Shen H. M., Ong C. N. Identification and characterization of major flavonoids and caffeoylquinic acids in three *Compositae* plants by LC/DAD–APCI/MS. *J. Chromatogr. B* 2007, *848*, 215–225.
15. Horie T., Kawamura Y., Tsukayama M., Yoshizaki S. Studies of the selective O-alkylation and dealkylation of flavonoids. XII. A new, convenient method for synthesizing 3,5-dihydroxy-6,7-dimethoxyflavones from 3,5,6,7-tetramethoxyflavones. *Chem. Pharm. Bull.* 1989, *37*, 1216–1220.