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6,7-Dimethoxy-1-(4-methoxyphenyl)isochroman

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Key indicators

Single-crystal X-ray study
T = 120 K
Mean σ(C–C) = 0.002 Å
R factor = 0.053
wR factor = 0.106
Data-to-parameter ratio = 18.4

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

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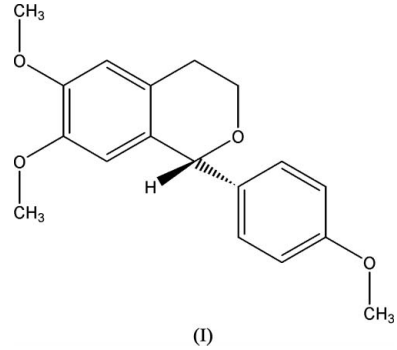
In the title compound, $C_{18}H_{20}O_4$, a rare example of a crystallographically characterized 6,7-dimethoxyisochroman, the packing is determined by intermolecular C(methyl)–H···O(pyran) hydrogen bonds.

Comment

Isochroman (3,4-dihydro-1*H*-benzo[*c*]pyran) derivatives are found in nature; for example 1,6,8-trihydroxy-3-heptyl-7-carboxyisochroman, an antibiotic and topoisomerase II inhibitor from *Penicillum sp*. (Imamura *et al.*, 2000), pseudodeflectusin, a selective human cancer cytotoxin from *Aspergillus pseudodeflectus*, (Ogawa *et al.*, 2004) in softwood lignin (Peng *et al.*, 1999) and in the male wing gland pheromone of *Aphomia sociella* (Kunesch *et al.*, 1987), or as part of complex natural products such as stephaoxocanine (Kashiwaba *et al.*, 1996) and glucoside B (Cameron *et al.*, 1964). 1-Phenyl- and 1-(3-methoxy-4-hydroxy)phenyl-6,7-dihydroxyisochromans have been identified in extra-virgin olive oil and shown to exhibit beneficial antioxidant effects (Lorenz *et al.*, 2005) and antiplatelet activity (Togna *et al.*, 2003). Isochroman derivatives also exhibit plant-growth regulatory and herbicidal activities (Bianchi *et al.*, 2004; Cutler *et al.*, 1997), they are oestrogen receptors (Liu *et al.*, 2005), dopamine receptor ligands (TenBrink *et al.*, 1996), and fragrances, such as galaxolide (Fráter *et al.*, 1999). 1-Aryl-6,7-dimethoxyisochromans have shown a wide range of biological activities such as analgesic, muscle relaxant, antidepressant, anti-inflammatory, antihistaminic and anticoagulant, hypotensive with peripheral and central activities and are adrenergic antagonists (Dobson & Humber 1975; Yamato *et al.*, 1985; McCall *et al.*, 1982). The oxa-Pictet–Spengler reaction is a variation of the Pictet–Spengler reaction in which a phenethyl alcohol reacts with a carbonyl compound to give a 1-substituted isochroman derivative (Guiso *et al.*, 2001).



(I)

The title compound, (I), is one of the rare examples of crystallographically characterized 6,7-dimethoxyisochromans

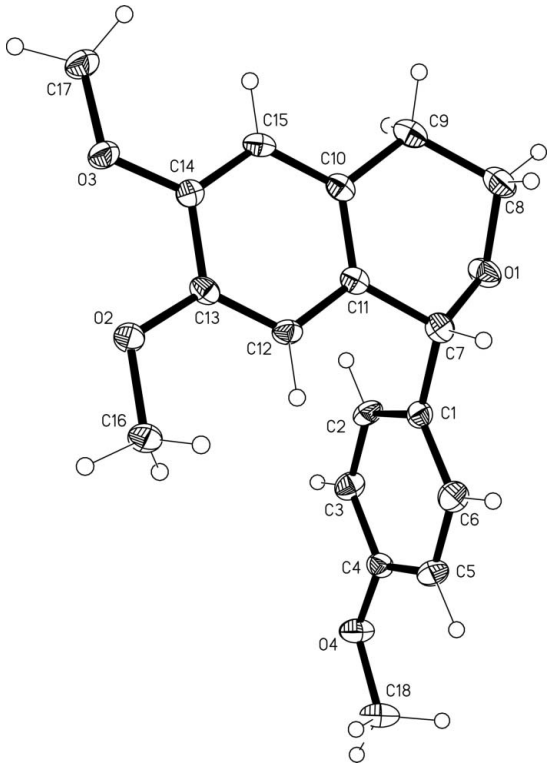


Figure 1
Molecular structure of (I). Displacement ellipsoids are drawn at the 50% probability level.

(TenBrink & Kamdar, 1979; Venkateswarlu *et al.*, 2001). The pyran ring is puckered with O1 and C8 lying −0.328 (1) and 0.441 (2) Å, respectively, below and above the isochroman plane. The methyl C atoms of both methoxy groups are slightly bent out of this plane, pointing to different sides with deviations of 0.137 (2) and −0.324 (2) Å for C16 and C17, respectively. The angle formed by the aromatic isochroman and benzene planes is 85.49 (5)°; the methoxy group O4–C18 is almost coplanar with the benzene plane, as shown by the C18—O4—C4—C3 torsion angle of −174.0 (2)°. The packing shows stacking of the molecules *via* intermolecular C—H···O(pyran) hydrogen bonds (see Table 2). There are no π–π interactions between the molecules.

Experimental

To a mixture of 2-(3,4-dimethoxyphenyl)ethanol (0.182 g, 1 mmol) and 4-methoxybenzaldehyde (0.136 g, 0.12 ml, 1 mmol), a catalytic amount of *p*-toluenesulfonic acid monohydrate was added. The reaction mixture was homogenized and irradiated for 2.5 min. On completion of the reaction, as monitored by TLC (every 30 s) using petroleum ether and ethyl acetate (7:2) the reaction mixture was purified by thick layer chromatography. The product obtained was recrystallized from ethyl acetate (0.29 g, 0.98 mmol, 98%) TLC (R_f): 0.38; Mp.: 361–362 K; ^{1}H NMR ($CDCl_3$): δ 6.74 (1H, *s*, H-5), 6.26 (1H, *s*, H-8), 5.61 (1H, *s*, H-1), 3.98 and 3.74 (2*H*, *m*, 2 × H-3), 3.74 (6H, *s*, 2 × OCH_3), 2.64, 2.83 (2H, *m*, 2 × H-4), 1-*p*-methoxyphenyl group: 7.19 (2H, *d*, *J* = 8.4, H-2′, H-6′); 6.84 (2H, *d*, *J* = 8.4, H-3′, H′); 3.78 (OCH_3). Analysis calculated for $C_{18}H_{20}O_4$: C, 71.98%, H, 6.71% found, 72.1%, H, 5.97%.

Crystal data

$C_{18}H_{20}O_4$	D_x = 1.326 Mg m^{-3}
M_r = 300.34	Mo $K\alpha$ radiation
Monoclinic, $P2_1/c$	Cell parameters from 1871 reflections
a = 17.567 (2) Å	θ = 2.3–27.3°
b = 5.3580 (7) Å	μ = 0.09 mm^{-1}
c = 16.153 (2) Å	T = 120 (2) K
β = 98.202 (3)°	Prism, colourless
V = 1504.8 (3) Å^3	0.45 × 0.20 × 0.18 mm
Z = 4	

Data collection

Bruker SMART CCD area-detector diffractometer	3656 independent reflections
	2247 reflections with $I > 2\sigma(I)$
φ and ω scans	R_{int} = 0.064
Absorption correction: multi-scan *SADABS* (Bruker, 2002)	θ_{max} = 28.1°
	$h = -23 \rightarrow 23$
T_{min} = 0.949, T_{max} = 0.974	$k = -7 \rightarrow 7$
14429 measured reflections	$l = -21 \rightarrow 19$

Refinement

Refinement on F^2	H-atom parameters constrained
$R[F^2 > 2\sigma(F^2)]$ = 0.053	$w = 1/[\sigma^2(F_o^2) + (0.0391P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2)$ = 0.106	$(\Delta/\sigma)_{max} < 0.001$
S = 1.00	$\Delta\rho_{max}$ = 0.28 e Å^{-3}
3656 reflections	$\Delta\rho_{min}$ = −0.25 e Å^{-3}
199 parameters	

Table 1
Selected geometric parameters (Å, °).

O1—C8	1.4317 (19)	C1—C7	1.506 (2)
O1—C7	1.437 (2)		
C8—O1—C7	112.12 (13)	O1—C7—C11	111.44 (14)
O1—C7—C1	106.57 (13)	C1—C7—C11	113.44 (14)
C18—O4—C4—C3	−173.96 (16)	C17—O3—C14—C13	−167.32 (14)
C16—O2—C13—C14	−174.94 (15)		

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

D—H···A	D—H	H···A	D···A	D—H···A
C18—H18A···O1^{i}	0.98	2.61	3.349 (2)	132
C16—H16B···O1^{ii}	0.98	2.58	3.540 (2)	167

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

Hydrogen atoms were placed at idealized positions (C—H = 0.95–0.99Å) and refined as riding, with U_{iso}(H) = 1.2U_{eq}(C) or 1.5U_{eq}(methyl-C).

Data collection: *SMART* (Bruker, 2002); cell refinement: *SAINT* (Bruker, 2002); data reduction: *SAINT*; program(s) used to solve structure: *SHELXTL* (Bruker, 2002); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*.

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