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3-(3,4,5-Trimethoxyphenyl)-1*H*-isochromen-1-one

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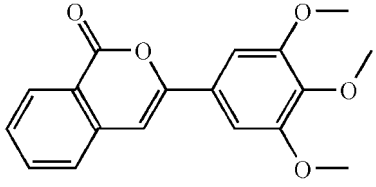
Key indicators: single-crystal X-ray study; T = 100 K; mean σ(C–C) = 0.002 Å; R factor = 0.044; wR factor = 0.115; data-to-parameter ratio = 14.2.

The title compound, $C_{18}H_{16}O_5$, is a biologically active isocoumarin. The molecule is almost planar. No hydrogen bonding is found in the crystal structure.

Related literature

For related literature, see: Barry (1964); Meepagala *et al.* (2002); Powers *et al.* (2002); Rossi *et al.* (2003). For bond-length data, see: Allen (2002); Bruno *et al.* (2004).



Experimental

Crystal data

$C_{18}H_{16}O_5$
M_r = 312.31
Monoclinic, $P2_1/n$
a = 9.1496 (11) Å
b = 12.8426 (15) Å
c = 12.6835 (14) Å
β = 100.592 (2)°
V = 1465.0 (3) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.10 mm^{-1}
T = 100 (2) K
0.60 × 0.50 × 0.40 mm

Data collection

Bruker SMART CCD area-detector diffractometer
Absorption correction: none
8307 measured reflections
2994 independent reflections
2278 reflections with $I > 2\sigma(I)$
R_{int} = 0.037

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.044
$wR(F^2)$ = 0.115
S = 1.05
2994 reflections
211 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.34 e Å^{-3}
$\Delta\rho_{min}$ = −0.17 e Å^{-3}

Data collection: *SMART* (Bruker, 1998); cell refinement: *SAINT* (Bruker, 1999); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL* (Bruker, 1999); software used to prepare material for publication: *SHELXTL*.

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: HK2289).

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supplementary materials

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3-(3,4,5-Trimethoxyphenyl)-1*H*-isochromen-1-one

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Comment

The isocoumarin nucleus is an abundant structural motif in natural products (Barry, 1964). Many constituents of the steadily growing class of known isocoumarins exhibit valuable biological properties such as antifungal (Meepagala *et al.*, 2002), anti-tumor or cytotoxic, anti-inflammatory, anti-allergic (Rossi *et al.*, 2003) and enzyme inhibitory activity (Powers *et al.*, 2002). In view of the importance of this class of compounds, the title compound, (I), has been synthesized and its crystal structure is reported here.

In the molecule of the title compound, (I), (Fig. 1) the bond lengths and angles can be regarded as normal (Cambridge Structural Database, Version 5.28, November 2006; Allen, 2002; Mogul, Version 1.1; Bruno *et al.*, 2004). The molecules are essentially planar (r.m.s. deviation for all non-H atoms = 0.033 Å). No hydrogen bonding is found within the crystal lattice.

Experimental

A mixture of 3,4,5-trimethoxybenzoic acid (5.9 g, 28 mmol) and thionyl chloride (2.94 ml, 34 mmol) was heated for 30 min in the presence of a few drops of DMF under reflux at 343 K to give 3,4,5-trimethoyxbenzoyl chloride. Completion of reaction was indicated by the disappearance of gas evolution. Removal of excess thionyl chloride was carried out under reduced pressure to afford 3,4,5-tri- methoxybenzoyl chloride. Homophthalic acid (1.5 g, 7.2 mmol) was then added and the solution was refluxed for 6 h at 473 K with stirring. The reaction mixture was extracted with ethyl acetate (3 times 100 ml), an aqueous solution of sodium carbonate (5%, 200 ml) was added to remove the unreacted homophthalic acid. The organic layer was separated, concentrated and chromatographed on silica gel using petroleum ether (313–353 K fractions) as eluent to afford the title compound (yield; 72%; m.p. 437–438 K). Colorless single crystals suitable for X-ray analysis were obtained by slow evaporation of an ethyl acetate solution.

Refinement

H atoms were positioned geometrically, with C—H = 0.95 and 0.98 Å, for aromatic and methyl H atoms, and constrained to ride on their parent atoms, with $U_{iso}(H) = xU_{eq}(C)$, where $x = 1.5$ for methyl H, and $x = 1.2$ for all other H atoms.

Figures

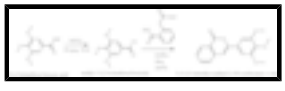


Fig. 1. The reaction scheme.

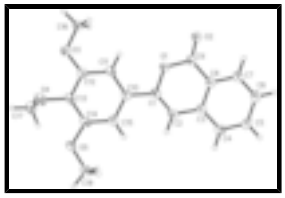


Fig. 2. The molecular structure of the title molecule, with the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

3-(3,4,5-trimethoxyphenyl)-1*H*-isochromen-1-one

Crystal data

$C_{18}H_{16}O_5$	F_{000} = 656
M_r = 312.31	D_x = 1.416 Mg m^{-3}
Monoclinic, $P2_1/n$	Melting point: 437(1) K
Hall symbol: -P 2yn	Mo $K\alpha$ radiation λ = 0.71073 Å
a = 9.1496 (11) Å	Cell parameters from 2460 reflections
b = 12.8426 (15) Å	θ = 2.3–26.3º
c = 12.6835 (14) Å	μ = 0.10 mm^{-1}
β = 100.592 (2)º	T = 100 (2) K
V = 1465.0 (3) Å^3	Irregular, colorless
Z = 4	0.60 × 0.50 × 0.40 mm

Data collection

Bruker CCD area-detector diffractometer	2278 reflections with $I > 2\sigma(I)$
Radiation source: fine-focus sealed tube	R_{int} = 0.037
Monochromator: graphite	θ_{max} = 26.4º
T = 100(2) K	θ_{min} = 2.3º
φ and ω scans	h = −7→11
Absorption correction: none	k = −13→16
8307 measured reflections	l = −15→10
2994 independent reflections	

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map
Least-squares matrix: full	Hydrogen site location: inferred from neighbouring sites
$R[F^2 > 2\sigma(F^2)]$ = 0.044	H-atom parameters constrained
$wR(F^2)$ = 0.115	$w = 1/[\sigma^2(F_o^2) + (0.0558P)^2 + 0.0317P]$ where $P = (F_o^2 + 2F_c^2)/3$
S = 1.05	$(\Delta/\sigma)_{max} < 0.001$
2994 reflections	$\Delta\rho_{max}$ = 0.34 e Å^{-3}
211 parameters	$\Delta\rho_{min}$ = −0.17 e Å^{-3}

Primary atom site location: structure-invariant direct methods

Extinction correction: none

Special details

Geometry. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

Refinement. Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit S are based on F^2, conventional *R*-factors *R* are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

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

	x	*y*	*z*	U_{iso}*/U_{eq}
O1	0.06795 (13)	−0.09566 (8)	0.90108 (9)	0.0233 (3)
O2	−0.02138 (14)	−0.25646 (9)	0.89341 (10)	0.0318 (3)
O3	0.48183 (13)	0.05277 (9)	1.16745 (9)	0.0260 (3)
O4	0.49911 (13)	0.25376 (9)	1.12205 (9)	0.0257 (3)
O5	0.33372 (14)	0.33656 (9)	0.94506 (9)	0.0276 (3)
C1	0.07078 (19)	0.00454 (12)	0.86049 (13)	0.0219 (4)
C2	−0.02265 (19)	0.03254 (13)	0.77178 (14)	0.0242 (4)
H2	−0.0177	0.1011	0.7446	0.029*
C3	−0.13180 (19)	−0.03967 (13)	0.71586 (13)	0.0224 (4)
C4	−0.2329 (2)	−0.01390 (14)	0.62211 (14)	0.0270 (4)
H4	−0.2305	0.0535	0.5916	0.032*
C5	−0.33525 (19)	−0.08564 (14)	0.57447 (13)	0.0257 (4)
H5	−0.4019	−0.0680	0.5104	0.031*
C6	−0.34238 (19)	−0.18538 (14)	0.61976 (14)	0.0266 (4)
H6	−0.4145	−0.2343	0.5868	0.032*
C7	−0.24555 (19)	−0.21133 (13)	0.71088 (14)	0.0246 (4)
H7	−0.2511	−0.2781	0.7420	0.029*
C8	−0.13848 (19)	−0.14039 (13)	0.75854 (13)	0.0226 (4)
C9	−0.03234 (19)	−0.17074 (13)	0.85328 (14)	0.0241 (4)
C10	0.18687 (19)	0.06831 (13)	0.92672 (13)	0.0211 (4)
C11	0.27868 (19)	0.02571 (13)	1.01638 (13)	0.0222 (4)
H11	0.2680	−0.0453	1.0345	0.027*
C12	0.38595 (19)	0.08734 (13)	1.07925 (13)	0.0216 (4)
C13	0.39979 (18)	0.19212 (13)	1.05433 (13)	0.0220 (4)
C14	0.30928 (19)	0.23387 (12)	0.96341 (14)	0.0222 (4)
C15	0.20359 (19)	0.17299 (13)	0.89984 (14)	0.0232 (4)
H15	0.1425	0.2020	0.8382	0.028*
C16	0.4738 (2)	−0.05468 (13)	1.19420 (14)	0.0276 (4)
H16A	0.3743	−0.0704	1.2083	0.041*
H16B	0.5481	−0.0700	1.2584	0.041*
H16C	0.4933	−0.0975	1.1343	0.041*

C17	0.6300 (2)	0.27931 (15)	1.08026 (15)	0.0326 (5)
H17A	0.6817	0.2151	1.0669	0.049*
H17B	0.6961	0.3223	1.1324	0.049*
H17C	0.6018	0.3179	1.0129	0.049*
C18	0.2489 (2)	0.38220 (13)	0.85078 (15)	0.0319 (5)
H18A	0.2674	0.3443	0.7875	0.048*
H18B	0.2782	0.4552	0.8459	0.048*
H18C	0.1429	0.3785	0.8542	0.048*

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0270 (7)	0.0168 (6)	0.0253 (6)	−0.0011 (5)	0.0024 (5)	0.0009 (5)
O2	0.0363 (8)	0.0227 (7)	0.0328 (7)	−0.0039 (6)	−0.0033 (6)	0.0045 (5)
O3	0.0300 (7)	0.0209 (7)	0.0266 (7)	−0.0029 (5)	0.0038 (5)	−0.0007 (5)
O4	0.0275 (7)	0.0243 (7)	0.0275 (7)	−0.0071 (5)	0.0105 (6)	−0.0039 (5)
O5	0.0334 (8)	0.0176 (6)	0.0320 (7)	−0.0035 (5)	0.0062 (6)	0.0003 (5)
C1	0.0238 (10)	0.0174 (9)	0.0270 (10)	0.0002 (7)	0.0108 (8)	−0.0006 (7)
C2	0.0266 (10)	0.0183 (9)	0.0298 (10)	0.0007 (7)	0.0104 (8)	0.0019 (7)
C3	0.0230 (9)	0.0226 (9)	0.0231 (9)	0.0026 (7)	0.0078 (7)	−0.0016 (7)
C4	0.0296 (10)	0.0246 (10)	0.0271 (10)	0.0042 (8)	0.0061 (8)	0.0014 (7)
C5	0.0223 (10)	0.0320 (10)	0.0221 (9)	0.0033 (8)	0.0024 (7)	−0.0030 (8)
C6	0.0214 (9)	0.0319 (10)	0.0273 (9)	0.0009 (8)	0.0067 (8)	−0.0077 (8)
C7	0.0250 (10)	0.0232 (10)	0.0269 (10)	0.0018 (7)	0.0086 (8)	−0.0021 (7)
C8	0.0212 (9)	0.0232 (9)	0.0247 (9)	0.0002 (7)	0.0076 (7)	−0.0032 (7)
C9	0.0229 (9)	0.0215 (10)	0.0287 (10)	−0.0013 (7)	0.0066 (8)	−0.0016 (8)
C10	0.0220 (9)	0.0196 (9)	0.0236 (9)	0.0006 (7)	0.0091 (7)	−0.0028 (7)
C11	0.0254 (10)	0.0169 (9)	0.0272 (9)	−0.0008 (7)	0.0122 (8)	−0.0021 (7)
C12	0.0235 (9)	0.0238 (10)	0.0194 (8)	0.0021 (7)	0.0086 (7)	−0.0011 (7)
C13	0.0229 (9)	0.0208 (9)	0.0244 (9)	−0.0045 (7)	0.0100 (7)	−0.0065 (7)
C14	0.0265 (10)	0.0169 (9)	0.0261 (9)	0.0008 (7)	0.0126 (8)	−0.0016 (7)
C15	0.0229 (9)	0.0221 (9)	0.0260 (9)	0.0020 (7)	0.0086 (8)	−0.0002 (7)
C16	0.0333 (11)	0.0204 (9)	0.0284 (10)	0.0005 (8)	0.0041 (8)	0.0006 (7)
C17	0.0261 (10)	0.0366 (11)	0.0364 (11)	−0.0061 (8)	0.0093 (9)	−0.0020 (8)
C18	0.0359 (11)	0.0230 (10)	0.0370 (11)	−0.0028 (8)	0.0070 (9)	0.0061 (8)

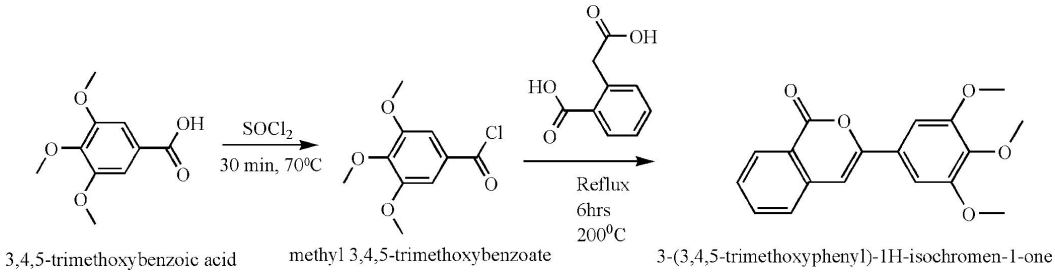
Geometric parameters (Å, °)

O1—C1	1.3880 (19)	C7—C8	1.392 (2)
O1—C9	1.391 (2)	C7—H7	0.9500
O2—C9	1.209 (2)	C8—C9	1.453 (2)
O3—C12	1.363 (2)	C10—C11	1.395 (2)
O3—C16	1.426 (2)	C10—C15	1.402 (2)
O4—C13	1.3796 (19)	C11—C12	1.392 (2)
O4—C17	1.434 (2)	C11—H11	0.9500
O5—C14	1.3648 (19)	C12—C13	1.393 (2)
O5—C18	1.426 (2)	C13—C14	1.397 (2)
C1—C2	1.331 (2)	C14—C15	1.382 (2)
C1—C10	1.475 (2)	C15—H15	0.9500

C2—C3	1.449 (2)	C16—H16A	0.9800
C2—H2	0.9500	C16—H16B	0.9800
C3—C4	1.405 (2)	C16—H16C	0.9800
C3—C8	1.408 (2)	C17—H17A	0.9800
C4—C5	1.372 (2)	C17—H17B	0.9800
C4—H4	0.9500	C17—H17C	0.9800
C5—C6	1.410 (2)	C18—H18A	0.9800
C5—H5	0.9500	C18—H18B	0.9800
C6—C7	1.362 (2)	C18—H18C	0.9800
C6—H6	0.9500		
C1—O1—C9	122.47 (13)	C12—C11—C10	119.96 (15)
C12—O3—C16	117.18 (13)	C12—C11—H11	120.0
C13—O4—C17	113.61 (13)	C10—C11—H11	120.0
C14—O5—C18	117.34 (13)	O3—C12—C11	124.38 (15)
C2—C1—O1	120.73 (15)	O3—C12—C13	115.41 (15)
C2—C1—C10	127.91 (16)	C11—C12—C13	120.20 (15)
O1—C1—C10	111.35 (14)	O4—C13—C12	119.33 (15)
C1—C2—C3	121.23 (16)	O4—C13—C14	121.09 (15)
C1—C2—H2	119.4	C12—C13—C14	119.54 (15)
C3—C2—H2	119.4	O5—C14—C15	124.49 (15)
C4—C3—C8	118.25 (16)	O5—C14—C13	114.88 (15)
C4—C3—C2	123.42 (16)	C15—C14—C13	120.63 (15)
C8—C3—C2	118.33 (15)	C14—C15—C10	119.77 (16)
C5—C4—C3	120.28 (17)	C14—C15—H15	120.1
C5—C4—H4	119.9	C10—C15—H15	120.1
C3—C4—H4	119.9	O3—C16—H16A	109.5
C4—C5—C6	120.63 (16)	O3—C16—H16B	109.5
C4—C5—H5	119.7	H16A—C16—H16B	109.5
C6—C5—H5	119.7	O3—C16—H16C	109.5
C7—C6—C5	119.76 (17)	H16A—C16—H16C	109.5
C7—C6—H6	120.1	H16B—C16—H16C	109.5
C5—C6—H6	120.1	O4—C17—H17A	109.5
C6—C7—C8	120.29 (17)	O4—C17—H17B	109.5
C6—C7—H7	119.9	H17A—C17—H17B	109.5
C8—C7—H7	119.9	O4—C17—H17C	109.5
C7—C8—C3	120.75 (15)	H17A—C17—H17C	109.5
C7—C8—C9	119.59 (15)	H17B—C17—H17C	109.5
C3—C8—C9	119.66 (15)	O5—C18—H18A	109.5
O2—C9—O1	116.78 (15)	O5—C18—H18B	109.5
O2—C9—C8	125.70 (16)	H18A—C18—H18B	109.5
O1—C9—C8	117.50 (15)	O5—C18—H18C	109.5
C11—C10—C15	119.86 (16)	H18A—C18—H18C	109.5
C11—C10—C1	120.59 (15)	H18B—C18—H18C	109.5
C15—C10—C1	119.55 (15)		
C9—O1—C1—C2	−1.0 (2)	C2—C1—C10—C15	2.5 (3)
C9—O1—C1—C10	179.63 (14)	O1—C1—C10—C15	−178.16 (14)
O1—C1—C2—C3	1.1 (3)	C15—C10—C11—C12	0.4 (2)
C10—C1—C2—C3	−179.65 (16)	C1—C10—C11—C12	−178.83 (15)

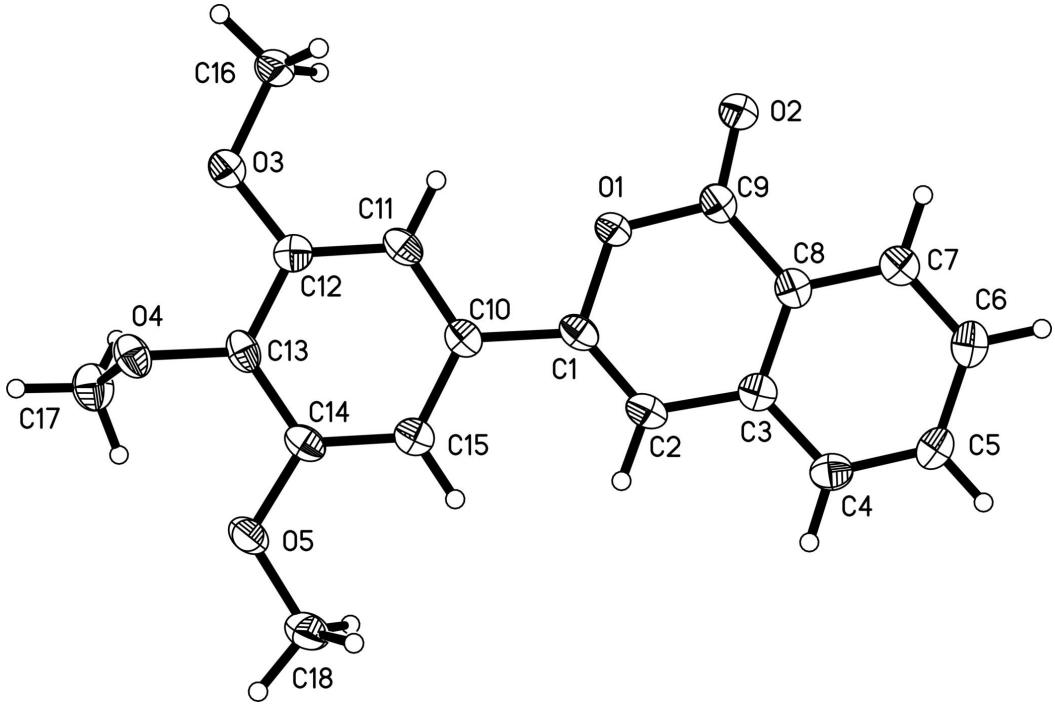
C1—C2—C3—C4	179.91 (17)	C16—O3—C12—C11	2.1 (2)
C1—C2—C3—C8	0.9 (3)	C16—O3—C12—C13	−178.50 (15)
C8—C3—C4—C5	0.2 (3)	C10—C11—C12—O3	−179.23 (15)
C2—C3—C4—C5	−178.76 (16)	C10—C11—C12—C13	1.4 (3)
C3—C4—C5—C6	1.2 (3)	C17—O4—C13—C12	106.40 (17)
C4—C5—C6—C7	−0.9 (3)	C17—O4—C13—C14	−75.9 (2)
C5—C6—C7—C8	−0.9 (3)	O3—C12—C13—O4	−4.2 (2)
C6—C7—C8—C3	2.3 (3)	C11—C12—C13—O4	175.20 (15)
C6—C7—C8—C9	−177.59 (16)	O3—C12—C13—C14	178.08 (15)
C4—C3—C8—C7	−2.0 (3)	C11—C12—C13—C14	−2.5 (2)
C2—C3—C8—C7	177.06 (16)	C18—O5—C14—C15	−3.2 (2)
C4—C3—C8—C9	177.94 (16)	C18—O5—C14—C13	177.38 (15)
C2—C3—C8—C9	−3.0 (2)	O4—C13—C14—O5	3.6 (2)
C1—O1—C9—O2	177.54 (15)	C12—C13—C14—O5	−178.75 (14)
C1—O1—C9—C8	−1.1 (2)	O4—C13—C14—C15	−175.88 (14)
C7—C8—C9—O2	4.5 (3)	C12—C13—C14—C15	1.8 (2)
C3—C8—C9—O2	−175.39 (17)	O5—C14—C15—C10	−179.39 (16)
C7—C8—C9—O1	−176.98 (15)	C13—C14—C15—C10	0.0 (2)
C3—C8—C9—O1	3.1 (2)	C11—C10—C15—C14	−1.1 (2)
C2—C1—C10—C11	−178.24 (17)	C1—C10—C15—C14	178.13 (15)
O1—C1—C10—C11	1.1 (2)		

Fig. 1



3,4,5-trimethoxybenzoic acid methyl 3,4,5-trimethoxybenzoate 3-(3,4,5-trimethoxyphenyl)-1H-isochromen-1-one

Fig. 2


C16
O3
O2
C9
O1
C11
C8
C7
C12
C10
C6
O4
C13
C1
C17
C14
C3
C15
C2
C5
C4
O5
C18