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5,8′-Dimethoxy-3*H*-1-benzofuran-2-spiro-2′-chroman

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Key indicators

Single-crystal X-ray study
T = 84 K
Mean σ(C–C) = 0.002 Å
R factor = 0.040
wR factor = 0.107
Data-to-parameter ratio = 15.9

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

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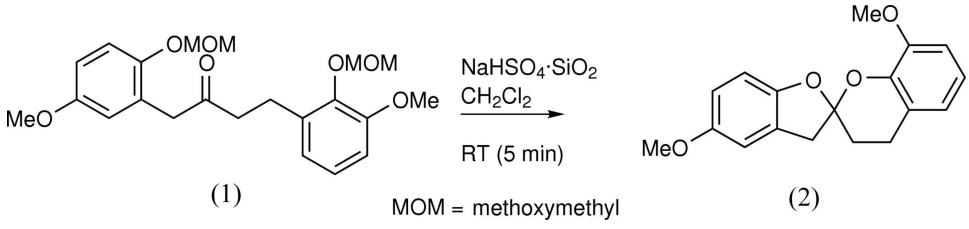
The crystal structure of the title compound, $C_{18}H_{18}O_4$, has been investigated to establish the relative stereochemistry at the spiro ring junction. Each of the O atoms adjacent to the junction is an axial substituent of the neighboring ring; the adoption of this conformation is likely to be due to anomeric effects.

Comment

Telomerase activity is seen as a potential target for cancer therapy. The rubromycins inhibit telomerase and HIV-1 reverse transcriptase and are cytostatically active against certain tumor cell lines. In particular, β-rubromycin (Brockmann *et al.*, 1969; Brockmann & Zeeck, 1970) is a microbial secondary metabolite (Puder *et al.*, 2000) that inhibits human telomerase with 50% inhibitory concentrations of 3 μ*M* (Ueno *et al.*, 2000). It contains naphthoquinone and isocoumarin rings linked to a 5,6 spiroacetal unit. Following on from the synthesis of 5-methoxyspiro[1-benzofuran-2(3*H*),2′-chroman] (Clark *et al.*, 2005), the title compound, (2), was synthesized to explore the ability of various 5,6-aryl spiroacetal units to inhibit human telomerase. The conformation of this 5,6-aryl spiroacetal in the crystal structure is reported here. Bond lengths and angles in the molecule are generally unremarkable. Those near the spiro junction are listed in Table 1, where the major differences from idealized geometry types occur; for example, the angle C7—O2—C10 is 116.61 (10)° whereas C10—O3—C13 is only 107.35 (10)°. Similar values were observed in 5-methoxyspiro[1-benzofuran-2(3*H*),2′-chroman].



(1) (2)

MOM = methoxymethyl

Experimental

To a stirred solution of ketone (1) (0.48 mmol) in dry dichloromethane (10 ml) was added $NaHSO_4{\cdot}SiO_2$ (766 mg) which had been heated at 393 K for 48 h before use (Breton, 1997). After stirring of the reaction mixture at room temperature for 5 min, the catalyst was filtered off and washed with dichloromethane (50 ml). The combined washings were concentrated *in vacuo* to give a yellow residue. Purification by flash column chromatography with hexane–ethyl acetate (80:20) as eluant afforded (2) as an off-white powder that was recrystallized from ethyl acetate to give colorless needles (85 mg, 60%, m.p. 412–414 K). MS (EI, %): 298 (M^+, 43), 209 (9), 161 (100), 137 (47), 135 (14), 118 (6), 91 (3), 77 (4). HR–MS (EI): found M^+,

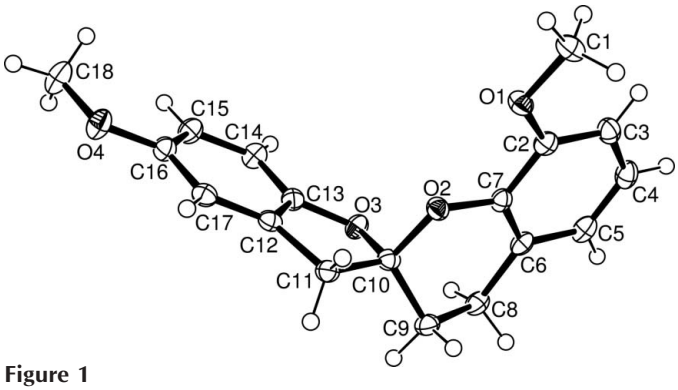


Figure 1
Structure of (2), showing 50% probability displacement ellipsoids for the non-H atoms and arbitrary spheres for the H atoms.

298.12017, $C_{18}H_{18}O_4$ requires 298.12051. IR (film, cm^{-1}): ν_{max} 3053, 2986 (CH, *s*, aromatic), 1586, 1482 (C═C, aromatic), 1421, 1265 (C—O), 1180, 1080, 1030, 1004, 896. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 2.15–2.19 (1H, *m*, H-3′$_{ax}$), 2.29 (1H, *ddd*, $J_{3'eq,4'eq}$ = 2.6 Hz, $J_{3'eq,4'ax}$ = 6.0 Hz and J_{gem} = 13.3 Hz, H-3′$_{eq}$), 2.81 (1H, *ddd*, $J_{4'eq,3'eq}$ = 2.6 Hz, $J_{4'eq,3'ax}$ = 6.0 Hz and J_{gem} = 16.4 Hz, H-4 $_{eq}$), 3.22–3.30 (1H, *m*, H-4′$_{ax}$), 3.28 (1H, *d*, J_{gem} = 16.6 Hz, H_A-3), 3.55 (1H, *d*, J_{gem} = 16.6 Hz, H_B-3), 3.75 (6H, *s*, 2 × OMe), 6.62–6.74 (4H, *m*, H-6, H-7, H-5′ and H-7′), 6.78 (1H, *s*, H-4), 6.84 (1H, *t*, $J_{6',5'}$ = 7.8 Hz and $J_{6',7'}$ = 7.8 Hz, H-6′). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 21.9 (CH_2, C-4′), 30.5 (CH_2, C-3′), 42.3 (CH_2, C-3), 55.9 (CH_3, OMe), 56.0 (CH_3, OMe), 109.2 (quat., C-2), 109.7 (CH, Ar—C), 110.1(CH, Ar—C), 111.0 (CH, Ar—C), 113.0 (CH, Ar—C), 120.7 (CH, Ar—C), 121.1 (CH, Ar—C), 122.4 (quat., C-4′a), 126.3 (quat., C-3a), 142.0 (quat., C-7a), 148.5 (quat., C-8′a), 152.1 (quat., C-8′), 154.5 (quat., C-5).

Crystal data

$C_{18}H_{18}O_4$	Z = 2
M_r = 298.32	D_x = 1.355 Mg m^{-3}
Triclinic, $P\overline{1}$	Mo $K\alpha$ radiation
a = 5.7593 (1) Å	Cell parameters from 5034 reflections
b = 10.6881 (1) Å	θ = 1.9–27.1°
c = 12.3122 (1) Å	μ = 0.10 mm^{-1}
α = 98.857 (1)°	T = 84 (1) K
β = 100.208 (1)°	Plate, colorless
γ = 95.510 (1)°	0.42 × 0.34 × 0.12 mm
V = 731.05 (2) Å^3	

Data collection

Siemens SMART CCD diffractometer	3156 independent reflections
ω scans	2619 reflections with $I > 2\sigma(I)$
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)	R_{int} = 0.040
T_{min} = 0.961, T_{max} = 0.989	θ_{max} = 27.1°
7358 measured reflections	$h = -7 \rightarrow 7$
	$k = -13 \rightarrow 13$
	$l = -15 \rightarrow 15$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0516P)^2 + 0.3055P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)]$ = 0.040	$(\Delta/\sigma)_{max}$ = 0.001
$wR(F^2)$ = 0.107	$\Delta\rho_{max}$ = 0.34 e Å^{-3}
S = 1.02	$\Delta\rho_{min}$ = −0.21 e Å^{-3}
3156 reflections	
199 parameters	
H-atom parameters constrained	

Table 1
Selected geometric parameters (Å, °).

O2—C10	1.4349 (16)	C9—C10	1.5103 (18)
O3—C10	1.4520 (15)	C10—C11	1.5361 (18)
C7—O2—C10	116.61 (10)	O3—C10—C9	107.98 (10)
C13—O3—C10	107.35 (10)	O2—C10—C11	106.24 (10)
O2—C10—O3	107.60 (10)	O3—C10—C11	106.39 (10)
O2—C10—C9	111.10 (11)	C9—C10—C11	117.09 (11)

H atoms were placed in calculated positions and refined using riding constraints [with C—H 0.93–0.97 Å, and U_{iso}(H) = 1.2U_{eq}(C) or 1.5U_{eq}(C)].

Data collection: *SMART* (Siemens, 1995); cell refinement: *SAINT* (Siemens, 1995); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEPIII* (Burnett & Johnson, 1996); software used to prepare material for publication: *SHELXTL* (Siemens, 1995).

References

Breton, G. W. (1997). *J. Org. Chem.* **62**, 8952–8954.
Brockmann, H., Lenk, W., Schwantje, G. & Zeeck, A. (1969). *Chem. Ber.* **102**, 126–151.
Brockmann, H. & Zeeck, A. (1970). *Chem. Ber.* **103**, 1709–1726.
Burnett, M. N. & Johnson, C. K. (1996). *ORTEPIII*. Report ORNL-6895. Oak Ridge National Laboratory, Tennessee, USA.
Clark, G. R., Tsang, K. Y. & Brimble, M. A. (2005). *Acta Cryst.* E**61**, o1123–o1124.
Puder, C., Loya, S., Hizi, A. & Zeeck, A. (2000). *Eur. J. Org. Chem.* pp. 729–735.
Sheldrick, G. M. (1996). *SADABS*. University of Göttingen, Germany.
Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. Release 97-1. University of Göttingen, Germany.
Siemens (1995). *SHELXTL* (Version 5), *SMART* (Version 4.050) and *SAINT* (Version 4.050). Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
Ueno, T., Takahashi, H., Oda, M., Mizunuma, M., Yokoyama, A., Goto, Y., Mizushina, Y., Sakaguchi, K. & Hayashi, H. (2000). *Biochemistry*, **39**, 5995–6002.