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5-Methoxyspiro[1-benzofuran-2(3*H*),2′-chroman]

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Key indicators

Single-crystal X-ray study
T = 200 K
Mean σ(C–C) = 0.003 Å
R factor = 0.030
wR factor = 0.080
Data-to-parameter ratio = 7.6

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

The crystal structure of the title compound, $C_{17}H_{16}O_3$, has been determined to establish the relative stereochemistry at the spiro ring junction. Both O atoms adjacent to the junction adopt axial positions because of anomeric effects.

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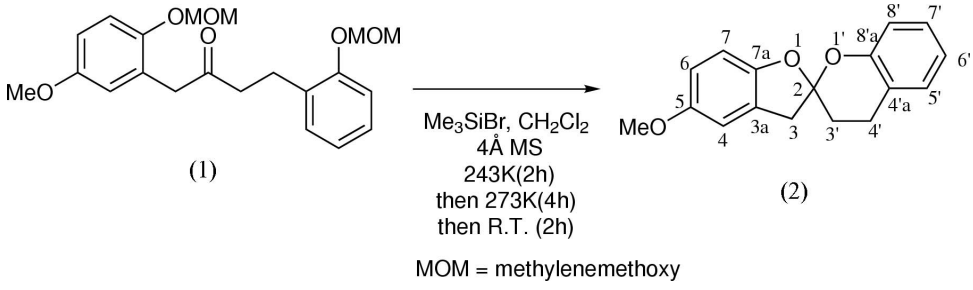
Comment

The rubromycins (Brockmann *et al.*, 1969; Brockmann & Zeeck, 1970) are microbial secondary metabolites (Puder *et al.*, 2000) that exhibit antibacterial and cytostatic activity. β-Rubromycin contains naphthoquinone and isocoumarin rings linked to a 5,6 spiroacetal system. β-Rubromycin is one of the most potent human telomerase inhibitors, with 50% inhibitory concentrations (IC_{50}) of about 3 μ*M* (Ueno *et al.*, 2000). It also exhibits inhibitory activity towards retroviral reverse transcriptase and human immunodeficiency virus type 1 reverse transcriptase. In order to examine the ability of the 5,6-aryl spiroacetal unit to inhibit human telomerase, the analogue of rubromycin, 5-methoxyspiro[1-benzofuran-2(3*H*),2-chroman], (2), was synthesized. The conformation of this 5,6-aryl spiroacetal was determined and is reported here. The title molecule is shown in Fig. 1 and selected bond lengths and angles are given in Table 1. The geometry at the spiro ring junction reflects the constraints of fusing five-membered and six-membered rings together, *i.e.* the angles O1—C1—C2 and O2—C1—C10 are 111.6 (2) and 117.1 (2) ° respectively.



Experimental

A solution of ketone (1) (0.27 mmol) in dry dichloromethane (1.5 ml) containing 4 Å molecular sieves (75 mg) was treated with bromotrimethylsilane (2.47 mmol) at 243 K. After 2 h, the reaction mixture was warmed to 273 K for 4 h then warmed to room temperature for another 2 h. The reaction mixture was poured into a solution of saturated sodium bicarbonate (2 ml) and extracted with diethyl ether (4 × 2 ml). The combined organic extracts were washed with brine (5 ml), dried over magnesium sulfate and concentrated under reduced pressure to give a white solid. Purification by flash column

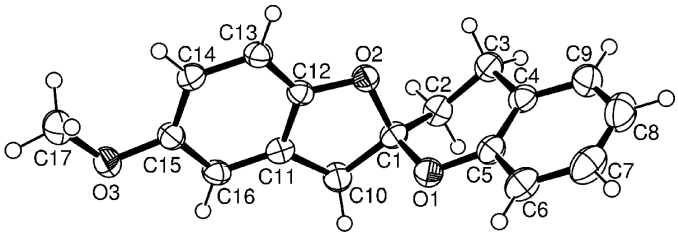


Figure 1
The structure of (I) (Burnett & Johnson, 1996), showing 50% probability displacement ellipsoids. H atoms are shown as spheres of arbitary radius.

chromatography using hexane- ethyl acetate (80:20) afforded the title compound (2), as a white solid that was recrystallized from ethyl acetate to give colourless needles (37 mg, 51%, m.p. 363–365 K. MS (EI, %) 268 (M^+, 32), 161 (100), 131 (6), 107 (12), 77 (6), 65 (3), 45 (3). HR–MS (EI) Found M^+, 268.10970, $C_{17}H_{16}O_3$ requires 268.10994. ν_{max} (film)/cm^{-1} 3054, 2986, 2959, 2930, 2305, 1584, 1488, 1457, 1466, 1433, 1422, 1265, 1222, 1209, 1177, 736, 705. δ_H (300 MHz, $CDCl_3$) 2.17 (1H, *ddd,* $J_{3'ax,4'eq}$ 6.0, $J_{3'ax,4'ax}$ 13.3 Hz and J_{gem} 13.3 Hz, H-3′$_{ax}$), 2.31 (1H, *ddd,* $J_{3'eq,4'eq}$ 2.8, $J_{3'eq,4'ax}$ 6.0 and J_{gem} 13.3 Hz, H-3′$_{eq}$), 2.81 (1H, *ddd,* $J_{4'eq,3'eq}$ 2.8, $J_{4'eq,3'ax}$ 6.0 and J_{gem} 16.4 Hz, H-4′$_{eq}$), 3.17–3.27 (1H, *m*, H-4′$_{ax}$), 3.26 (1H, J_{gem} 16.6 Hz, H_A-3), 3.41 (1H, J_{gem} 16.6 Hz, H_B-3), 3.76 (3H, *s*, OMe), 6.69 (2H, *m*, H-4 and H-6), 6.77–6.82 (2H, *m*, H-7 and H-8′), 6.90 (1H, *dt, J* 1.1 and 7.9 Hz, H-6′), 7.07–7.13 (2H, *m*, H-5′ and H-7′). δ_C(75 MHz, $CDCl_3$) 21.9 (CH_2, C-4′), 30.4 (CH_2, C-3′), 42.3 (CH_2, C-3), 56.0 (CH_3, OMe), 109.2 (quat., C-2), 109.8 (CH, C-6), 111.2 (CH, C-8′), 113.0 (CH, C-4), 117.1 (CH, C-7), 121.1 (CH, C-6′), 121.4 (quat., C-4′a), 126.3 (quat., C-3a), 127.4 (CH, C-7′), 129.1 (CH, C-5′), 152.0 (quat., C-7a), 152.3 (quat., C-8′a), 154.6 (quat., C-5).

Crystal data

$C_{17}H_{16}O_3$
M_r = 268.30
Monoclinic, *Pc*
a = 10.3982 (7) Å
b = 5.7749 (4) Å
c = 11.2480 (8) Å
β = 96.132 (1)°
V = 671.56 (8) Å^3
Z = 2
D_x = 1.327 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 3003 reflections
θ = 3.5–26.4°
μ = 0.09 mm^{-1}
T = 200 (2) K
Block, colourless
0.34 × 0.30 × 0.24 mm

Data collection

Bruker SMART CCD diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1997)
T_{min} = 0.970, T_{max} = 0.979
3951 measured reflections
1367 independent reflections
1250 reflections with $I > 2\sigma(I)$
R_{int} = 0.017
θ_{max} = 26.4°
$h = -12 \rightarrow 12$
$k = -7 \rightarrow 7$
$l = -14 \rightarrow 14$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.030
$wR(F^2)$ = 0.080
S = 1.02
1367 reflections
181 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0556P)^2 + 0.0273P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.11 e Å^{-3}
$\Delta\rho_{min}$ = −0.16 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

O1—C5	1.384 (3)	C2—C3	1.518 (3)
O1—C1	1.421 (2)	C3—C4	1.506 (3)
O2—C12	1.381 (2)	C4—C5	1.395 (3)
O2—C1	1.454 (2)	C10—C11	1.506 (3)
C1—C2	1.507 (3)	C11—C12	1.394 (3)
C1—C10	1.535 (3)		
C5—O1—C1	117.56 (16)	C1—C2—C3	110.20 (18)
C12—O2—C1	107.62 (15)	C4—C3—C2	110.06 (18)
O1—C1—O2	107.49 (15)	C5—C4—C3	119.54 (18)
O1—C1—C2	111.63 (18)	O1—C5—C4	123.44 (18)
O2—C1—C2	107.36 (17)	C11—C10—C1	102.72 (17)
O1—C1—C10	106.41 (17)	C12—C11—C10	107.80 (19)
O2—C1—C10	106.37 (16)	O2—C12—C11	112.73 (17)
C2—C1—C10	117.11 (18)		

H atoms were placed in calculated positions [C—H 0.93–0.97 Å] and refined using a riding model, with U_{iso}(H) = 1.2 or 1.5 times U_{eq}(C). In the absence of significant anomalous dispersion effects, the Friedel pairs were merged before refinement.

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).

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