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8′-Methoxy-3*H*-spiro[1-naphthofuran-2,2′-chroman]

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Key indicators

Single-crystal X-ray study
T = 85 K
Mean σ(C–C) = 0.003 Å
R factor = 0.047
wR factor = 0.124
Data-to-parameter ratio = 16.0

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

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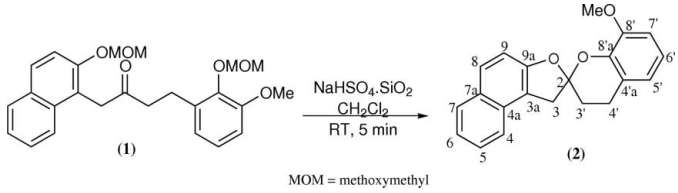
The crystal structure of the title compound, $C_{21}H_{18}O_3$, has been determined to establish the relative stereochemistry at the spiro ring junction. Each O atom adjacent to the junction lies axial to the neighbouring ring; this is presumably due to anomeric effects.

Comment

β-Rubromycin (Brockmann *et al.*, 1969; Brockmann & Zeeck, 1970) is a microbial secondary metabolite (Puder *et al.*, 2000) that inhibits human telomerase with a 50% inhibitory concentration of 3 μ*M* (Ueno *et al.*, 2000). β-Rubromycin contains naphthoquinone and isocoumarin rings linked to a 5,6-spiroacetal unit. We have recently synthesized and determined the crystal structure of 5,8′-dimethoxy-3*H*-benzofuran-2-spiro-2′-chromane in order to examine the ability of the 5,6-aryl spiroacetal unit to inhibit human telomerase (Clark *et al.*, 2005). We now report the crystal structure and synthesis of the naphtho derivative 8′-methoxy-3*H*-spiro[1-naphthofuran-2,2′-chromane], (2), from ketone (1). Bond lengths and angles at the spiro junction are listed in Table 1 and are unremarkable. Comparison with corresponding parameters in the structure of 5,8′-dimethoxy-3*H*-benzofuran-2-spiro-2′-chromane reveals that each pair of listed bonds is statistically equivalent, but each pair of listed angles is statistically different. The maximum variation is, however, only 1.5°, and the variation is most likely due to different crystal packing forces resulting from the presence of the larger naphthalene ring system in the present compound.



MOM = methoxymethyl

Experimental

To a stirred solution of ketone (1) (137 mg, 0.323 mmol) in dichloromethane (2 ml) was added $NaHSO_4{\cdot}SiO_2$ (272 mg) that had been heated at 393 K for 48 h (Breton, 1997). The reaction mixture was stirred at room temperature for 5 min. The catalyst was removed by filtration and washed with dichloromethane (25 ml). The organic portion was concentrated *in vacuo* to give a yellow residue. Purification of the residue by flash column chromatography with hexane–ethyl acetate (95:5) as eluent afforded the title compound, (2), as a white powder which was recrystallized from ethyl acetate to give (2) as colourless needles (yield 42 mg, 41%; m.p. 435–437 K). MS (EI, %): 318 (M^+, 23), 181 (100), 152 (8), 149 (37), 137 (7), 129 (27), 69 (4),

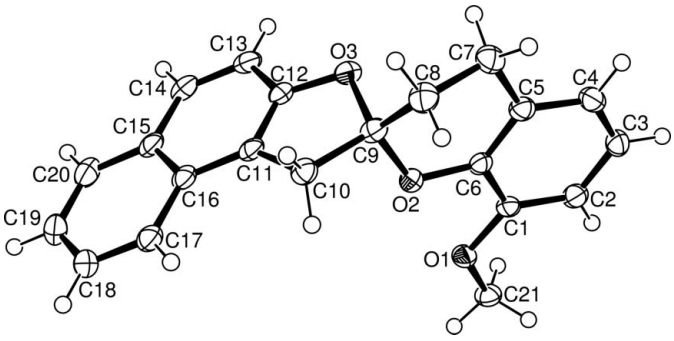


Figure 1
The structure of (2), showing 50% probability displacement ellipsoids for non-H atoms (Burnett & Johnson, 1996).

57 (46), 43 (33). HR–MS (EI): found M^+, 318.12535, $C_{21}H_{18}O_3$ requires 318.12559. ν_{max} (film)/cm^{-1}: 3053, 2978, 2840, 2311, 1739, 1627, 1580, 1476, 1461, 1418, 1265, 1215, 738. δ_H (400 MHz, $CDCl_3$): 2.27 (1H, *ddd*, $J_{3'ax,4'eq}$ = 5.8, $J_{3'ax,4'ax}$ = 12.8, J_{gem} = 13.2 Hz, H-3′$_{ax}$), 2.39 (1H, *ddd*, $J_{3'eq,4'eq}$ = 2.4, $J_{3'eq,4'ax}$ = 5.9, J_{gem} 13.2 = Hz, H-3$_{eq}$), 2.85 (1H, *ddd*, $J_{4'eq,3'eq}$ = 2.4, $J_{4'eq,3'ax}$ = 5.8, J_{gem} = 16.5 Hz, H-4′$_{eq}$) 3.31 (1H, *ddd*, $J_{4'ax,3'eq}$ = 6.0, $J_{4'ax,3'ax}$ = 12.8, J_{gem} = 16.5 Hz, H-4′$_{ax}$), 3.56 (1H, *d*, J_{gem} = 16.6 Hz, H-3a), 3.75 (3H, *s*, OMe), 3.89 (1H, *d*, J_{gem} = 16.6 Hz, H-3 b), 6.73–6.78 (2H, *m*, H-5′ and H-7′), 6.88 (1H, *t*, $J_{6',7'}$ = $J_{6',5'}$ = 7.8 Hz, H-6′), 7.09 (1H, *d*, $J_{9,8}$ = 8.8 Hz, H-9), 7.32 (1H, *dd*, $J_{6,5}$ = 8.1 and $J_{6,7}$ = 8.2 Hz, H-6), 7.47 (1H, *dd*, $J_{5,6}$ = 8.1 and $J_{5,4}$ = 8.2 Hz, H-5), 7.60 (1H, *d*, $J_{4,5}$ = 8.2 Hz, H-4), 7.68 (1H, *d*, $J_{8,9}$ = 8.8 Hz, H-8), 7.80 (1H, *d*, $J_{7,6}$ = 8.2 Hz, H-7). δ_C (100 MHz, $CDCl_3$): 30.7 (CH_2, C-4′), 30.8 (CH_2, C-3′), 40.9 (CH_2, C-3), 55.8 (CH_3, OMe), 109.9 (quat., C-2), 109.9 (CH, C-5′ or C-7′), 112.1 (CH, C-9), 117.1 (quat., C-3a), 120.7 (CH, C-6′), 121.0 (CH, C-5′ or C-7′), 122.3 (quat., C-4′a), 122.7 (CH, C-5), 123.0 (CH, C-6), 126.6 (CH, C-5), 128.6 (CH, C-7), 128.9 (CH, C-8), 129.4 (quat., C-7a), 130.5 (quat., C-4a), 141.9 (quat., C-8′a), 148.4 (quat., C-8′), 155.2 (quat., C-9a).

Crystal data

$C_{21}H_{18}O_3$
M_r = 318.35
Monoclinic, $P2_1/c$
a = 5.9858 (1) Å
b = 13.2104 (2) Å
c = 20.4727 (3) Å
β = 97.066 (1)°
V = 1606.58 (4) Å^3
Z = 4
D_x = 1.316 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 4596 reflections
θ = 1.8–27.1°
μ = 0.09 mm^{-1}
T = 85 (2) K
Fragment cut from needle, colourless
0.38 × 0.20 × 0.18 mm

Data collection

Siemens SMART CCD diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.968, T_{max} = 0.985
9773 measured reflections
3466 independent reflections
2390 reflections with $I > 2\sigma(I)$
R_{int} = 0.040
θ_{max} = 27.1°
$h = -7 \rightarrow 7$
$k = -16 \rightarrow 14$
$l = -17 \rightarrow 25$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.047
$wR(F^2)$ = 0.124
S = 1.02
3466 reflections
217 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0563P)^2 + 0.4607P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.24 e Å^{-3}
$\Delta\rho_{min}$ = −0.23 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

O2—C6	1.3848 (19)	C7—C8	1.527 (3)
O2—C9	1.430 (2)	C8—C9	1.504 (3)
O3—C12	1.385 (2)	C9—C10	1.538 (2)
O3—C9	1.465 (2)	C10—C11	1.506 (2)
C5—C6	1.392 (2)	C11—C12	1.374 (2)
C5—C7	1.510 (2)		
C6—O2—C9	117.34 (13)	O3—C9—C8	109.49 (14)
C12—O3—C9	106.37 (13)	O2—C9—C10	105.54 (14)
O2—C9—O3	106.86 (13)	O3—C9—C10	105.53 (13)
O2—C9—C8	112.24 (14)	C8—C9—C10	116.56 (15)

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

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