Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

6,8′-Dimethoxy-2,2′-spirobichroman

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Key indicators

Single-crystal X-ray study
T = 84 K
Mean σ(C–C) = 0.004 Å
R factor = 0.068
wR factor = 0.173
Data-to-parameter ratio = 14.1

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

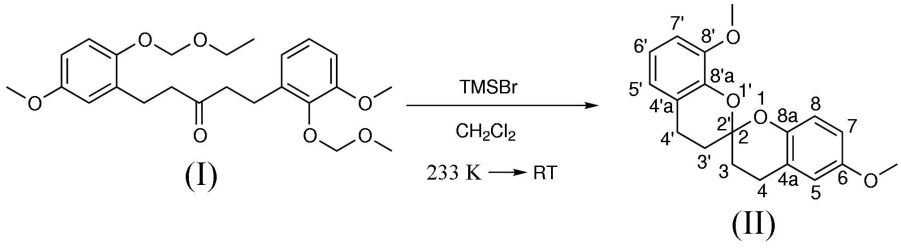
Received 23 February 2005
Accepted 4 March 2005
Online 11 March 2005

The crystal structure of the title compound, $C_{19}H_{20}O_4$, has been determined in order to establish the stereochemistry of aryl-[5,5]spiroacetals related to β-rubromycins.

Comment

β-Rubromycins are potent inhibitors of human telomerase with a micromolar IC_{50} value. These compounds possess a unique aromatic spiroacetal ring system and the fact that α-rubromycin, which lacks the spiroacetal moiety, exhibits substantially decreased inhibitory potency towards telomerase (IC_{50} ∼> 200 μM) suggests that this spiroacetal system plays an essential role in the observed inhibition of telomerase (Ueno *et al.*, 2000). The synthesis of a series of aryl[5.5]acetals homologous to the rubromycins was thus undertaken to probe the mechanism of action of the spiroacetal moiety and the effect of the conformation of the spiroacetal ring system on biological activity.

Spiro systems are unique in that the two core rings are arranged orthogonal about a tetrahedral atom common to both, making the compounds chiral in a similar way to an allene. In spiroacetals, the stereochemistry is predominently driven by the number of anomeric effects contributing to the overall stability of the molecule (Delongchamps *et al.*, 1992). The stereochemistry of an aryl-[5.5]spiroacetal, (II), is reported here. The X-ray analysis shows that each C—O bond at the spiro centre adopts an axial position on the neighbouring benzopyran ring.



(I) (II)

Experimental

To a mixture of ketone (I) (70 mg, 0.15 mmol) and 4 Å molecular sieves (50 mg) in dichloromethane (1.5 ml) at 243 K was added trimethylsilyl bromide (0.20 ml, 1.5 mmol) and the reaction mixture was stirred under nitrogen for 1 h. The reaction mixture was warmed to 273 K, stirred for 1 h, then poured into water (1 ml) and extracted with ethyl acetate (3 × 5 ml). The combined organic extracts were washed with brine (1 ml), dried over magnesium sulfate and concentrated *in vacuo*. The product was purified by flash chromatography (SiO_2, hexane–ethyl acetate 1:1) to give the title compound, (II) (45 mg, 96%) as a white crystalline solid (m.p. 417–420 K). MS (EI, %): 312 (M^+, 80), 188 (6), 176 (55), 174 (32), 161 (100), 137 (40),

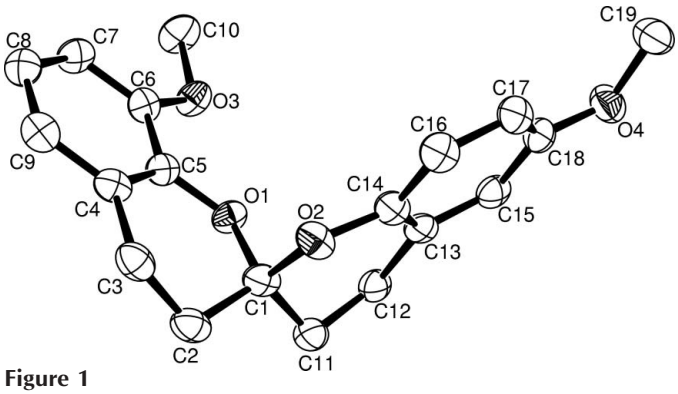


Figure 1
The structure of the title compound, showing 50% probability displacement ellipsoids for non-H atoms (Burnett & Johnson, 1996). H atoms have been omitted.

91 (6), 77 0). HR–MS (found: M^+ 312.1358; $C_{19}H_{20}O_4$ requires 312.1362). IR, ν_{max} (film)/cm^{-1}: 2931, 1482, 1421. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.98 (*ddd*, 2H, ^2J = 13.1, ^3J = 13.1, ^3J = 5.7, 3 and 3′-H_{ax}), 2.1 (*ddd*, 2H, ^2J = 13.1, ^3J = 5.9, ^3J = 2.6, 3 and 3′-H_{eq}), 2.90 (*ddd*, 2H, ^2J = 16.3, ^3J = 5.7, ^3J = 2.6, 4 and 4′-H_{eq}), 3.30 (*ddd*, 2H,^2J = 16.3, ^3J = 13.1, ^3J = 5.9, 4 and 4′-H_{ax}), 3.66 (6H, *s*, 2 × OCH_3), 6.60–7.30 (*m*, 6H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.9, 21.5 (CH_2CH_2Ar), 30.8, 31.2 (CH_2CH_2Ar), 55.6 (6-OCH_3), 56.5 (8′-OCH_3), 96.2 (quat., C2), 111.0, 113.0, 113.6, 117.5, 120.2, 121.3 (Ar–CH), 122.8 (quat., C4a), 123.2 (quat., C4′a), 142.2 (quat., C8′a,), 146.2 (quat., C8a), 148.6 (quat., C8 and C8′), 153.6 (quat., C6).

Crystal data

$C_{19}H_{20}O_4$	Z = 2
M_r = 312.35	D_x = 1.337 Mg m^{-3}
Triclinic, $P\overline{1}$	Mo $K\alpha$ radiation
a = 5.8149 (5) Å	Cell parameters from 2358 reflections
b = 10.9359 (10) Å	θ = 1.6–25.8°
c = 12.9304 (12) Å	μ = 0.09 mm^{-1}
α = 73.684 (2)°	T = 84 (1) K
β = 86.383 (1)°	Needle, colourless
γ = 79.589 (2)°	0.52 × 0.14 × 0.12 mm
V = 776.09 (12) Å^3	

Data collection

Siemens SMART CCD diffractometer	2941 independent reflections
ω scans	1716 reflections with $I > 2\sigma(I)$
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1997)	R_{int} = 0.041
T_{min} = 0.953, T_{max} = 0.989	θ_{max} = 25.8°
7036 measured reflections	$h = -7 \rightarrow 7$
	$k = -12 \rightarrow 13$
	$l = -15 \rightarrow 15$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0803P)^2 + 0.0036P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)]$ = 0.068	$(\Delta/\sigma)_{max} < 0.001$
$wR(F^2)$ = 0.173	$\Delta\rho_{max}$ = 0.49 e Å^{-3}
S = 1.02	$\Delta\rho_{min}$ = −0.21 e Å^{-3}
2941 reflections	
208 parameters	
H-atom parameters constrained	

Table 1
Selected geometric parameters (Å, °).

O1—C5	1.381 (3)	O2—C14	1.386 (3)
O1—C1	1.436 (3)	C2—C3	1.513 (4)
C1—O2	1.426 (3)	C3—C4	1.501 (4)
C1—C11	1.494 (4)	C11—C12	1.526 (4)
C1—C2	1.509 (4)	C12—C13	1.505 (4)
C5—O1—C1	118.0 (2)	C11—C1—C2	115.1 (3)
O2—C1—O1	108.4 (2)	C14—O2—C1	116.7 (2)
O2—C1—C11	111.2 (2)	C1—C2—C3	111.4 (3)
O1—C1—C11	105.0 (2)	C4—C3—C2	110.7 (3)
O2—C1—C2	105.5 (2)	O1—C5—C4	123.7 (3)
O1—C1—C2	111.7 (2)	C13—C12—C11	110.0 (3)

H atoms were placed in calculated positions and refined using a riding model [C—H = 0.93–0.97 Å and 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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