Br(5a)	−0.3639 (2)	−0.2804	−0.8642 (1)	0.0301 (3)
Br(5b)	0.1380 (2)	−0.2185 (1)	−0.7381 (1)	0.0345 (3)
O(1)	0.111 (1)	−0.4359 (5)	−0.3539 (8)	0.029 (2)
O(3)	0.357 (1)	−0.3295 (6)	−0.2106 (7)	0.028 (2)
N(3b′)	0.515 (2)	−0.0495 (8)	−0.361 (1)	0.043 (3)
C(2)	0.309 (2)	−0.4334 (8)	−0.226 (1)	0.030 (3)
C(2′)	0.254 (2)	−0.4688 (9)	−0.085 (1)	0.036 (3)
C(2″)	0.491 (2)	−0.4889 (9)	−0.265 (1)	0.041 (3)
C(3a)	0.296 (2)	−0.2871 (9)	−0.3606 (10)	0.023 (3)
C(3b)	0.218 (2)	−0.1796 (8)	−0.355 (1)	0.021 (3)
C(3b′)	0.388 (2)	−0.1060 (8)	−0.353 (1)	0.026 (3)
C(4a)	−0.014 (2)	−0.1462 (8)	−0.448 (1)	0.021 (3)
C(4b)	−0.165 (1)	−0.2210 (8)	−0.544 (1)	0.021 (3)
C(4)	0.041 (2)	−0.1498 (8)	−0.282 (1)	0.025 (3)
C(5a)	−0.094 (2)	−0.3279 (8)	−0.552 (1)	0.024 (3)
C(5b)	0.135 (2)	−0.3640 (8)	−0.461 (1)	0.026 (3)
C(5)	−0.124 (1)	−0.2606 (8)	−0.6862 (10)	0.023 (3)

Table 2. *Selected geometric parameters (Å, °)*

Br(4a)—C(4)	1.93 (1)	C(3a)—C(3b)	1.54 (1)
Br(4b)—C(4)	1.910 (10)	C(3a)—C(5b)	1.56 (1)
Br(5a)—C(5)	1.900 (9)	C(3b)—C(3b′)	1.46 (1)
Br(5b)—C(5)	1.930 (9)	C(3b)—C(4a)	1.54 (1)
O(1)—C(2)	1.45 (1)	C(3b)—C(4)	1.51 (1)
O(1)—C(5b)	1.41 (1)	C(4a)—C(4b)	1.49 (1)
O(3)—C(2)	1.43 (1)	C(4a)—C(4)	1.46 (1)
O(3)—C(3a)	1.43 (1)	C(4b)—C(5a)	1.52 (1)
N(3b′)—C(3b′)	1.13 (1)	C(4b)—C(5)	1.50 (1)
C(2)—C(2′)	1.50 (1)	C(5a)—C(5b)	1.53 (1)
C(2)—C(2″	1.50 (2)	C(5a)—C(5)	1.49 (1)
C(2)—O(1)—C(5b)	107.7 (7)	C(4a)—C(4b)—C(5a)	121.4 (8)
C(2)—O(3)—C(3a)	107.9 (8)	C(4a)—C(4b)—C(5)	120.5 (8)
O(1)—C(2)—O(3)	102.1 (8)	C(5a)—C(4b)—C(5)	59.3 (7)
O(1)—C(2)—C(2′)	109.0 (9)	Br(4a)—C(4)—Br(4b)	110.4 (5)
O(1)—C(2)—C(2″)	110.0 (9)	Br(4a)—C(4)—C(3b)	116.0 (7)
O(3)—C(2)—C(2′)	108.8 (9)	Br(4a)—C(4)—C(4a)	117.7 (8)
O(3)—C(2)—C(2″)	110.8 (9)	Br(4b)—C(4)—C(3b)	122.6 (8)
C(2′)—C(2)—C(2″)	115.3 (10)	Br(4b)—C(4)—C(4a)	120.5 (7)
O(3)—C(3a)—C(3b)	110.2 (8)	C(3b)—C(4)—C(4a)	62.4 (6)
O(3)—C(3a)—C(5b)	104.4 (8)	C(4b)—C(5a)—C(5b)	121.6 (9)
C(3b)—C(3a)—C(5b)	119.0 (8)	C(4b)—C(5a)—C(5)	59.6 (6)
C(3a)—C(3b)—C(3b′)	113.4 (8)	C(5b)—C(5a)—C(5)	121.1 (8)
C(3a)—C(3b)—C(4a)	121.5 (8)	O(1)—C(5b)—C(3a)	103.4 (8)
C(3a)—C(3b)—C(4)	123.6 (8)	O(1)—C(5b)—C(5a)	108.7 (8)
C(3b′)—C(3b)—C(4a)	113.0 (9)	C(3a)—C(5b)—C(5a)	118.0 (9)
C(3b′)—C(3b)—C(4)	116.8 (9)	Br(5a)—C(5)—Br(5b)	111.4 (4)
C(4a)—C(3b)—C(4)	57.1 (6)	Br(5a)—C(5)—C(4b)	119.7 (7)
N(3b′)—C(3b′)—C(3b)	175 (1)	Br(5a)—C(5)—C(5a)	119.9 (7)
C(3b)—C(4a)—C(4b)	118.6 (9)	Br(5b)—C(5)—C(4b)	118.9 (7)
C(3b)—C(4a)—C(4)	60.4 (6)	Br(5b)—C(5)—C(5a)	117.6 (6)
C(4b)—C(4a)—C(4)	120.7 (8)	C(4b)—C(5)—C(5a)	61.1 (6)

The θ-scan width used was $(1.30 + 0.3\tan\theta)°$ at a speed of $32.0° \min^{-1}$ (in ω). The weak reflections were rescanned a maximum of four times and the counts accumulated to ensure good counting statistics. Stationary background counts were made on each side of the reflection with a 2:1 ratio of peak to background counting time. H atoms were located from a difference map and fixed at ideal positions with U_{iso} = $1.2U_{eq}$(C). The structure was solved by direct methods using *SIR*92 (Altomare *et al.*, 1994) and expanded using Fourier techniques (Beurskens *et al.*, 1992).

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1991). Cell refinement: *MSC/AFC Diffractometer Control Software*. Data reduction: *TEXSAN* (Molecular Structure Corporation, 1985). Program(s) used to solve structure: *SIR*92 (Altomare *et al.*, 1994); *DIRDIF* (Beurskens *et al.*, 1992). Program(s) used to refine structure: *TEXSAN*. Software used to prepare material for publication: *TEXSAN*.

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: TA1058). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Structural Studies of Mitomycins. VII. Mitomycin G

NORIAKI HIRAYAMA,[a]* HITOSHI ARAI[b] AND MASAJI KASAI[b]

[a]*Department of Biological Science and Technology, Tokai University, 317 Nishino, Numazu, Shizouka 410-03, Japan, and* [b]*Pharmaceutical Research Laboratories, Kyowa Hakko Kogyo Co. Ltd, 1188 Shimotogari, Nagaizumi-cho, Suntogun, Shizuoka 411, Japan*

(*Received 14 November 1995; accepted 16 January 1996*)

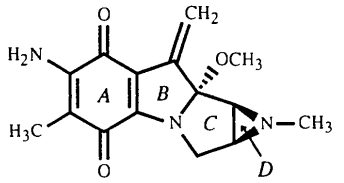
Abstract

The title compound, [1a*S*-(1aα,8aα,8bα)]-6-amino-1,1a,2,8,8a,8b-hexahydro-8a-methoxy-1,5-dimethyl-8-methyleneazirino[2′,3′:3,4]pyrrolo[1,2-*a*]indole-4,7-dione, $C_{15}H_{17}N_3O_3$, is a derivative of the mitomycins, which are antitumor antibiotics. The quinone O atoms deviate significantly from the least-squares plane of the quinone ring.

Comment

Mitomycins are potent antitumor antibiotics and the mitomycin C member of the family has been applied clinically to various tumors successfully. It is important to understand the relationships between the three-

dimensional structures and biological activities of these compounds in order to design better antitumor agents and we have undertaken the structural analysis of a series of mitomycins to gain a better insight into these relationships. The title compound, (I), is one of the minor constituents of the fermentation broth of mitomycin C by *Streptomyces caespitosus*.



(I)

An *ORTEP*II (Johnson, 1976) drawing of the title molecule together with the atomic numbering scheme is shown in Fig. 1. The absolute configuration of the molecule was assigned by reference to that of 1-*N*-(*p*-bromobenzoyl)mitomycin C (Shirahata & Hirayama, 1983). The O5—C5 bond is significantly longer than the O8—C8 bond. In the quinone ring, the C7—C8 bond is the longest and the C4a—C8a bond is the shortest. The exocyclic bond angles around the C5, C7, C8 and C9 atoms are highly asymmetric. The sum of the bond angles around the N4 atom is 345.3 (2)°, indicating that the atom adopts a pyramidal configuration. The dihedral angles between the least-squares planes of the rings are *A*/*B* 7.4 (4), *A*/*C* 55.3 (1) and *A*/*D* 45.8 (1)°. The nonplanarity of the benzoquinone ring, which was observed in the crystal structures of mitomycin C (Arora, 1979) and mitomycin A (Hirayama & Shirahata, 1989), is also found in mitomycin G. The deviations of the O5 and O8 atoms from the least-squares plane of ring *A* are 0.127 (2) and 0.098 (3) Å, respectively. There is an intermolecular hydrogen bond between the N atom of the azirizine ring and the amino group: N7···N1($\frac{3}{2}-x$, $2-y$, $\frac{1}{2}+z$) 2.951 (4) Å and N7—H···N1 146 (1)°.

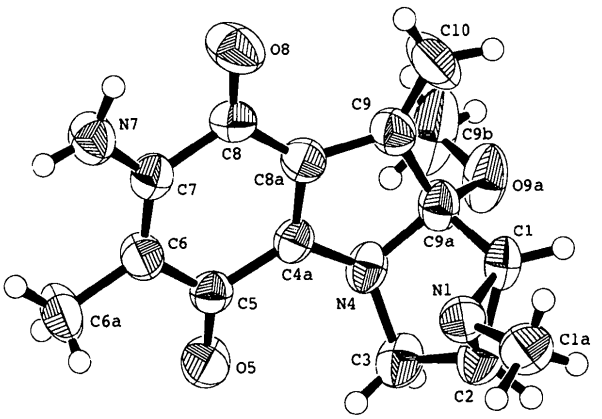


Fig. 1. An *ORTEP*II (Johnson, 1976) drawing of the title compound showing the atomic numbering scheme. Displacement ellipsoids are shown at the 50% probability level for non-H atoms and H atoms are shown as small spheres of arbitrary size.

Experimental

Crystals of mitomycin G were grown from acetone solution.

Crystal data

$C_{15}H_{17}N_3O_3$
$M_r = 287.32$
Orthorhombic
$P2_12_12_1$
$a = 10.387\ (5)$ Å
$b = 17.411\ (7)$ Å
$c = 8.1633\ (8)$ Å
$V = 1476.3\ (7)$ Å^3
$Z = 4$
$D_x = 1.29$ Mg m^{-3}
D_m not measured
Cu $K\alpha$ radiation
$\lambda = 1.54184$ Å
Cell parameters from 25 reflections
$\theta = 30$–$35°$
$\mu = 0.76$ mm^{-1}
$T = 293\ (2)$ K
Prism
$0.3 \times 0.2 \times 0.15$ mm
Deep violet

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: none
1659 measured reflections
1659 independent reflections
1489 observed reflections $[F > 3\sigma(F)]$
$\theta_{max} = 75.0°$
$h = 0 \rightarrow 13$
$k = 0 \rightarrow 21$
$l = 0 \rightarrow 10$
3 standard reflections
frequency: 60 min
intensity decay: 1.92%

Refinement

Refinement on F
$R = 0.043$
$wR = 0.063$
$S = 2.22$
1489 reflections
258 parameters
$w = 1/\sigma^2(F)$
$(\Delta/\sigma)_{max} = 0.01$
$\Delta\rho_{max} = 0.38$ e Å^{-3}
$\Delta\rho_{min} = -0.34$ e Å^{-3}
Extinction correction: none
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters (Å^2)*

$B_{eq} = (4/3)\Sigma_i\Sigma_j\beta_{ij}\mathbf{a}_i.\mathbf{a}_j$.

	x	*y*	*z*	B_{eq}
O5	0.7610 (2)	0.80937 (9)	0.8095 (3)	5.03 (4)
O8	0.4918 (2)	1.0710 (1)	0.8628 (3)	6.51 (5)
O9a	0.2694 (2)	0.8007 (1)	0.6903 (3)	5.68 (4)
N1	0.5010 (2)	0.8577 (1)	0.3803 (3)	4.17 (4)
N4	0.4995 (2)	0.81790 (9)	0.6964 (3)	3.89 (4)
N7	0.7397 (2)	1.0769 (1)	0.9286 (3)	5.06 (4)
C1a	0.4891 (3)	0.8721 (2)	0.2014 (4)	6.20 (7)
C1	0.3794 (2)	0.8325 (1)	0.4561 (3)	4.18 (4)
C2	0.4847 (3)	0.7765 (1)	0.4254 (3)	4.83 (5)
C3	0.5520 (3)	0.7585 (1)	0.5829 (3)	4.89 (5)
C4a	0.5669 (2)	0.8776 (1)	0.7610 (3)	3.28 (4)
C5	0.7041 (2)	0.8717 (1)	0.8142 (3)	3.56 (4)
C6	0.7645 (2)	0.9419 (1)	0.8691 (3)	3.87 (4)
C6a	0.9058 (3)	0.9394 (2)	0.9085 (4)	6.08 (7)
C7	0.6926 (2)	1.0077 (1)	0.8812 (3)	3.75 (4)
C8a	0.4955 (2)	0.9433 (1)	0.7737 (3)	3.51 (4)
C8	0.5499 (2)	1.0110 (1)	0.8412 (4)	4.12 (5)
C9a	0.3731 (2)	0.8469 (1)	0.6379 (3)	3.96 (4)
C9b	0.2552 (4)	0.7957 (2)	0.8648 (4)	8.68 (9)
C9	0.3702 (2)	0.9301 (1)	0.6980 (3)	4.19 (5)
C10	0.2729 (3)	0.9789 (2)	0.6740 (5)	6.99 (8)

Table 2. *Selected geometric parameters (Å, °)*

O5—C5	1.236 (3)	C1—C9a	1.506 (4)
O8—C8	1.219 (3)	C2—C3	1.497 (4)
O9a—C9a	1.410 (3)	C4a—C5	1.493 (3)
O9a—C9b	1.435 (4)	C4a—C8a	1.367 (3)
N1—C1a	1.488 (4)	C5—C6	1.445 (3)
N1—C1	1.473 (3)	C6—C6a	1.504 (4)
N1—C2	1.470 (3)	C6—C7	1.372 (3)
N4—C3	1.492 (3)	C7—C8	1.519 (3)
N4—C4a	1.360 (3)	C8a—C8	1.419 (3)
N4—C9a	1.485 (3)	C8a—C9	1.458 (3)
N7—C7	1.357 (3)	C9a—C9	1.530 (3)
C1—C2	1.486 (4)	C9—C10	1.335 (4)
C9a—O9a—C9b	114.5 (2)	C5—C6—C7	119.5 (2)
C1a—N1—C1	113.0 (2)	C6a—C6—C7	122.7 (2)
C1a—N1—C2	113.5 (2)	N7—C7—C6	124.5 (2)
C1—N1—C2	60.7 (2)	N7—C7—C8	112.3 (2)
C3—N4—C4a	125.7 (2)	C6—C7—C8	123.2 (2)
C3—N4—C9a	111.0 (2)	C4a—C8a—C8	120.5 (2)
C4a—N4—C9a	108.6 (2)	C4a—C8a—C9	108.7 (2)
N1—C1—C2	59.5 (2)	C8—C8a—C9	130.6 (2)
N1—C1—C9a	113.7 (2)	O8—C8—C7	118.9 (2)
C2—C1—C9a	107.9 (2)	O8—C8—C8a	124.8 (2)
N1—C2—C1	59.8 (2)	C7—C8—C8a	116.2 (2)
N1—C2—C3	111.3 (2)	O9a—C9a—N4	112.6 (2)
C1—C2—C3	109.7 (2)	O9a—C9a—C1	103.7 (2)
N4—C3—C2	102.5 (2)	O9a—C9a—C9	115.3 (2)
N4—C4a—C5	123.4 (2)	N4—C9a—C1	102.8 (2)
N4—C4a—C8a	112.9 (2)	N4—C9a—C9	103.7 (2)
C5—C4a—C8a	123.7 (2)	C1—C9a—C9	118.3 (2)
O5—C5—C4a	120.6 (2)	C8a—C9—C9a	105.5 (2)
O5—C5—C6	123.0 (2)	C8a—C9—C10	129.6 (3)
C4a—C5—C6	116.4 (2)	C9a—C9—C10	124.8 (2)
C5—C6—C6a	117.8 (2)		
C9b—O9a—C9a—C9	−57.7 (3)	C1a—N1—C2—C3	154.8 (2)
O9a—C9a—C9—C10	−56.0 (4)		

All H atoms were found from difference Fourier maps. All non-H atoms were refined anisotropically, with all H atoms isotropic.

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989). Cell refinement: *CAD-4 Software*. Data reduction: *CAD-4 Software*. Program(s) used to solve structure: *MULTAN*11/82 (Main *et al.*, 1982). Program(s) used to refine structure: *SDP-Plus* (Frenz, 1985). Molecular graphics: *ORTEP*II (Johnson, 1976).

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates, complete geometry and torsion angles have been deposited with the IUCr (Reference: TA1079). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Acta Cryst. (1996). C**52**, 1808–1810

3-(*m*-Bromophenyl)-1-(3-methyl-2-pyridyl)pyrrolidin-2,5-dione

JANINA KAROLAK-WOJCIECHOWSKA,[a] WITOLD KWIATKOWSKI,[a] JOLANTA OBNISKA[b] AND ALFRED ZEJC[b]

[a]*Institute of General Chemistry, Technical University of Łódź, 90-924 Łódź, Poland, and* [b]*Department of Pharmaceutical Chemistry, Collegium Medicum, Jagiellonian University, Medyczna 5, 31-065 Kraków, Poland. E-mail: jkarolak@lodz1.p.lodz.pl*

(*Received 15 December 1995; accepted 9 February 1996*)

Abstract

The title compound, $C_{16}H_{13}BrN_2O_2$, is one of the 27 phenylsuccinimides for which the correlation between structure and anticonvulsant activity was examined in an earlier study. All of the possible minimum-energy conformations for all of the compounds were found using molecular modelling. For eight of the 27 derivatives the X-ray structures were determined and these were used as a guide to find the correct conformations among the minimum-energy conformations derived from calculations. The results of the present study show that the title compound also has a conformation similar to that calculated previously which confirms that the correct conformation was selected to calculate the structure–activity correlations.

Comment

In our previous paper (Kwiatkowski & Karolak-Wojciechowska, 1993), we studied the correlation between structure and anticonvulsant activity, based on the maximal electrical shock (MES) test, of phenylsuccinimides. The correlation was based on 27 derivatives of which 12 were active, including the title compound (Zejc, Obniska, Chojnacka-Wójcik, Tatarczyńska & Wilczyńska, 1987). Active derivatives could be distinguished from inactive ones based on the sign of the difference between the minima of the molecular electrostatic potential (MEP) at the carbonyl O atoms of the five-membered imide ring. Since this correlation is based on the structural and electronic parameters derived from the geometrical description of the molecule, the three-dimensional conformations of all the investigated compounds had to be determined. We solved the structures of eight derivatives (Kwiatkowski & Karolak-Wojciechowska, 1990, 1991, 1992*a*, 1992*b*; Kwiatkowski, Karolak-Wojciechowska, Obniska & Zejc, 1990) which served as a guide to finding the correct minimum energy conformations from among all the minimum-energy conformations derived