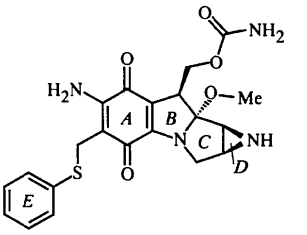
Sheldrick, G. M. (1993). *SHELXL93. Program for the Refinement of Crystal Structures*. University of Göttingen, Germany.
Thuong, N. T. & Hélène, C. (1993). *Angew. Chem. Int. Ed. Engl.* **32**, 666–690.



(I)

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Structural Studies of Mitomycins. IX. 6-Demethyl-6-(phenylthiomethyl)-mitomycin C

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Abstract

The title compound, (1a*S*)-6-amino-8-{[(aminocarbonyl)-oxy]methyl}-1,1a,2,8,8a,8b-hexahydro-8a-methoxy-5-(phenylthiomethyl)azirino[2′,3′:3,4]pyrrolo[1,2-*a*]indole-4,7-dione, $C_{21}H_{22}N_4O_5S$, is a C6-substituted methyl mitomycin C which possesses potent antitumor activities. The N4 atom is more pyramidal than the corresponding atom in both mitomycin C anhydride and mitomycin C dihydrate.

Comment

Mitomycins are potent antitumor antibiotics produced by various *Streptomyces* cultures. Among these compounds, mitomycin C has been extensively used in cancer chemotherapy against a variety of solid tumors. Its use, however, is limited due to detrimental side effects. Many derivatives of mitomycins have been screened from nature and synthesized to obtain less toxic and more potent compounds. A series of C6-substituted methyl mitomycins was synthesized and evaluated for anticellular and antitumor activities (Arai *et al.*, 1994). The results suggested that C6-substituted methyl mitomycins would have a different biological character from that of mitomycin C. We are undertaking the structural analysis of a series of C6-substituted methyl mitomycins in order to understand the structure–activity relationships and present here the structure of the title compound, (I).

An *ORTEP*II (Johnson, 1976) drawing of (I), together with the atomic numbering scheme is shown in Fig. 1. The absolute configuration of the molecule was suggested by referring to that of 1-*N*-(*p*-bromobenzoyl)-mitomycin C (Shirahata & Hirayama, 1983). Most of the bond lengths are in the range observed in other mitomycins. The N1a—C1, N1a—C2 and C1—C2 bonds are significantly shorter than the corresponding bonds in both mitomycin C anhydride (MMCA) (Arora, 1979) and mitomycin C dihydrate (MMCD) (Ogawa, Nomura, Fujiwara & Tomita, 1979). The sum of the bond angles around N4 is 343.9 (6)°, significantly smaller than those around N4 in MMCA and MMCD, and N4 is more pyramidal than the corresponding atoms in MMCA and MMCD. The exocyclic bond angles around atoms C5, C6, C7 and C8 are highly asymmetric. The asymmetry around C6 is greatly increased in the title compound due to the large phenylthiomethyl substituent.

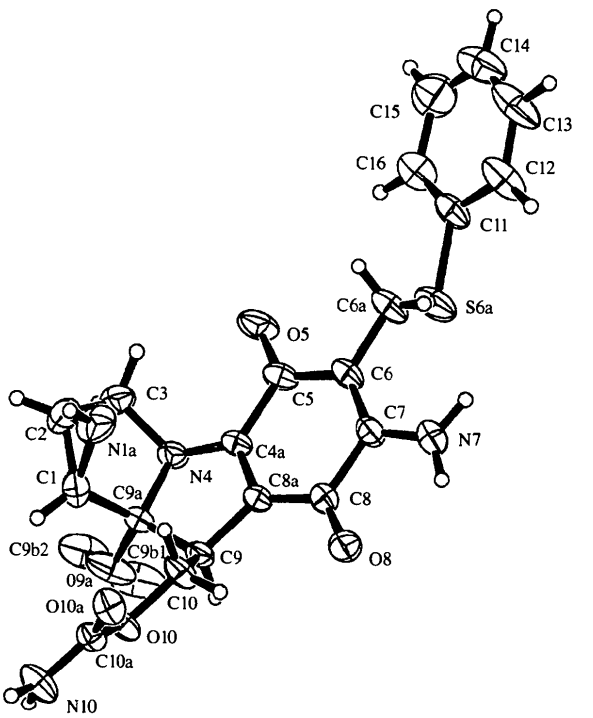

Fig. 1. *ORTEP*II (Johnson, 1976) drawing of the title compound showing the atomic numbering. Displacement ellipsoids are shown at the 30% probability level for non-H atoms and the H atoms are shown as small spheres of arbitrary size.

The carbamoyloxymethyl group has a fully extended conformation. In MMCA and MMCB, the torsion angle C9—C10—O10—C10a is within an anticlinal region and is antiperiplanar in the title compound. The dihedral angles between the least-squares planes of the rings are: 6.1 (6) between rings *A* and *B*, 51.1 (6) between rings *B* and *C*, 85.0 (6) between rings *C* and *D*, and 20.0 (6)° between rings *A* and *E*. The dihedral angle between the least-squares planes of the carbamoyl group and ring *A* is 64.6 (6)°. The mean deviations of the atoms in ring *A* is 0.014 (3) Å. The deviations of the O5 and O8 atoms from the plane are 0.070 (3) and 0.072 (3) Å, respectively. Significant deviations of the quinone ring from planarity are also observed in MMCA and MMCD. The O atoms are located on the same side of the ring in the title compound, MMCA and MMCD. The crystal structure contains the following intermolecular hydrogen bonds: N7—H···O10a($-\frac{1}{2}+x$, $\frac{3}{2}-y$, $1-z$) [N···O 2.957 (4) Å and N—H···O 164°] and N10—H···O10a($\frac{3}{2}-x$, $1-y$, $-\frac{1}{2}+z$) [N···O 2.890 (4) Å and N—H···O 175°].

Experimental

Single crystals were obtained by slow evaporation of a chloroform solution.

Crystal data

$C_{21}H_{22}N_4O_5S$
M_r = 442.5
Orthorhombic
$P2_12_12_1$
a = 14.4649 (9) Å
b = 18.015 (2) Å
c = 8.0881 (8) Å
V = 2107.6 (3) Å^3
Z = 4
D_x = 1.394 Mg m^{-3}
D_m not measured
Cu $K\alpha$ radiation
λ = 1.5418 Å
Cell parameters from 25 reflections
θ = 30–37°
μ = 1.725 mm^{-1}
T = 20.0 K
Rod
0.70 × 0.20 × 0.10 mm
Black

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: none
2468 measured reflections
2468 independent reflections
2118 reflections with $I > 3\sigma(I)$
θ_{max} = 74°
$h = 0 \rightarrow 18$
$k = 0 \rightarrow 22$
$l = -10 \rightarrow 10$
3 standard reflections
every 400 reflections
intensity decay: 0.85%

Refinement

Refinement on F
R = 0.052
wR = 0.080
S = 2.38
2118 reflections
288 parameters
H atoms not refined
$\Delta\rho_{max}$ = 0.32 e Å^{-3}
$\Delta\rho_{min}$ = −0.27 e Å^{-3}
Extinction correction: Zachariasen type 2 Gaussian isotropic
Extinction coefficient: 2.77 (5) × 10^{-6}
$w = 1/[\sigma^2(F)]$
$(\Delta/\sigma)_{max}$ = 0.10
Scattering factors from *International Tables for X-ray Crystallography* (Vol. IV)

Table 1. *Selected geometric parameters (Å, °)*

S6a—C6a	1.836 (4)	C1—C9a	1.505 (5)
S6a—C11	1.788 (4)	C2—C3	1.491 (7)
O5—C5	1.221 (4)	C4a—C5	1.502 (4)
O8—C8	1.226 (4)	C4a—C8a	1.350 (4)
O9a—C9a	1.416 (4)	C5—C6	1.428 (5)
N1a—C1	1.461 (5)	C6—C6a	1.491 (4)
N1a—C2	1.461 (6)	C6—C7	1.366 (5)
N4—C3	1.487 (5)	C7—C8	1.529 (4)
N4—C4a	1.357 (4)	C8a—C8	1.419 (5)
N4—C9a	1.497 (3)	C8a—C9	1.506 (4)
N7—C7	1.333 (5)	C9a—C9	1.545 (4)
C1—C2	1.489 (6)	C9—C10	1.498 (4)
C6a—S6a—C11	100.5 (2)	N7—C7—C6	126.9 (3)
C3—N4—C4a	125.7 (3)	N7—C7—C8	111.2 (3)
C3—N4—C9a	109.7 (3)	C6—C7—C8	121.8 (3)
C4a—N4—C9a	108.5 (2)	C4a—C8a—C8	122.1 (3)
N1a—C1—C9a	110.7 (3)	C4a—C8a—C9	109.9 (3)
C2—C1—C9a	106.8 (3)	C8—C8a—C9	127.9 (3)
N1a—C2—C3	111.7 (4)	O8—C8—C7	118.9 (3)
C1—C2—C3	110.2 (3)	O8—C8—C8a	125.0 (3)
N4—C3—C2	102.2 (3)	C7—C8—C8a	116.1 (3)
N4—C4a—C5	125.1 (3)	O9a—C9a—N4	112.7 (3)
N4—C4a—C8a	113.0 (2)	O9a—C9a—C1	105.9 (3)
C5—C4a—C8a	121.9 (3)	O9a—C9a—C9	111.1 (3)
O5—C5—C4a	120.3 (3)	N4—C9a—C1	103.3 (3)
O5—C5—C6	122.2 (3)	N4—C9a—C9	104.3 (2)
C4a—C5—C6	117.4 (3)	C1—C9a—C9	119.4 (3)
C5—C6—C6a	116.8 (3)	C8a—C9—C9a	102.7 (2)
C5—C6—C7	120.5 (3)	C8a—C9—C10	111.8 (3)
C6a—C6—C7	122.6 (3)	C9a—C9—C10	114.0 (3)
S6a—C6a—C6	110.1 (3)	O10—C10—C9	107.0 (2)
S6a—C6a—C6—C5	−79.7 (4)	C9—C10—O10—C10a	−168.9 (3)
O10—C10—C9—C8a	178.8 (3)	C6—C6a—S6a—C11	159.6 (3)
O10a—C10a—O10—C10	−0.7 (5)	C6a—S6a—C11—C12	73.6 (4)

All non-H atoms were located by direct methods using the program *SAPI*91 (Fan, 1991). The C9b atom is disordered; site occupancies of 0.70 and 0.30 for C9b1 and C9b2 positions, respectively, were determined from the peak heights on a final difference Fourier map and were fixed throughout the refinement. All H atoms except for those on atom C9b were calculated geometrically and their coordinates were not refined.

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989). Cell refinement: *CAD-4 Software*. Data reduction: *PROCESS TEXSAN* (Molecular Structure Corporation, 1992). Program(s) used to solve structure: *SAPI*91. Program(s) used to refine structure: *LS TEXSAN*. Molecular graphics: *ORTEP*II (Johnson, 1976). Software used to prepare material for publication: *FINISH TEXSAN*.

Lists of atomic coordinates, displacement parameters, structure factors and complete geometry have been deposited with the IUCr (Reference: FR1007). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

References

Arai, H., Kanda, Y., Ashizawa, T., Morimoto, M., Gomi, K., Kono, M. & Kasai, M. (1994). *J. Med. Chem.* **37**, 1974–1804.
Arora, S. K. (1979). *Life Sci.* **24**, 1519–1526.
Enraf–Nonius (1989). *CAD-4 Software*. Version 5.0. Enraf–Nonius, Delft, The Netherlands.

Fan, H.-F. (1991). *SAPI91. Structure Analysis Programs with Intelligent Control.* Rigaku Corporation, Tokyo, Japan.
Johnson, C. K. (1976). *ORTEPII.* Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
Molecular Structure Corporation (1992). *TEXSAN. TEXRAY Structure Analysis Package.* MSC, 3200 Research Forest Drive, The Woodlands, TX 77381, USA.
Ogawa, K., Nomura, A., Fujiwara, T. & Tomita, K. (1979). *Bull. Chem. Soc. Jpn*, **52**, 2334–2338.
Shirahata, K. & Hirayama, N.(1983). *J. Am. Chem. Soc.* **105**, 7199–7200.

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A Diastereomeric Pair of Cyclophane Derivatives: Planar–Chiral and *meso*-Dimethylbis([2.2]paracyclophan-4-yl)silane

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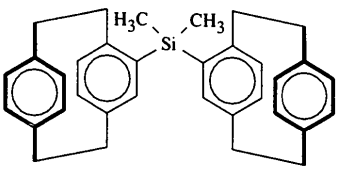
Abstract

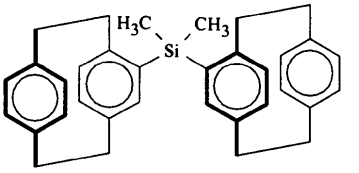
The cyclophane groups of the two title compounds, planar–chiral dimethylbis(tricyclo[8.2.2.2^{4,7}]-tetradeca-4,6,10,12,13,15-hexaen-5-yl)silane, $C_{34}H_{36}Si$, and its *meso* analogue, display similar geometric features to the parent compound [2.2]paracyclophane and also to [2.2]paracyclophane units in other structures; the aromatic rings are distorted in the typical way. The *para*-C atoms are bent out of the plane of the other four approximately coplanar atoms into a boat conformation. The aromatic rings are twisted with respect to one another. The C_{sp^3}—C_{sp^3} bond lengths of the methylene bridges are slightly longer than standard values in unstrained systems.

Comment

As far as we are aware, the two title compounds are the first examples of bis([2.2]paracyclophan-4-yl) compounds of which the chiral and *meso* diastereomers have been isolated and this is the first structural characterization of a diastereomeric pair of such compounds. Both crystallize in centrosymmetric space groups and compound (1) crystallizes with two independent molecules in the asymmetric unit; each molecule displays a *meso* configuration, with one paracyclophanyl group *R* and the other *S*. In contrast, the chiral compound (2) crystallizes with only one independent molecule and the paracyclophanyl groups are either both *R* or both *S*.



(1)



(2)

The paracyclophanyl groups are similar to each other and also to the parent hydrocarbon [2.2]paracyclophane, (3) (Keehn & Rosenfeld, 1983; Stalke, 1996). The aromatic rings are puckered into a boat form whereby the C atoms bearing the methylene bridges are displaced out of the plane of the other four atoms. These planes are not exactly parallel to one another; the interplanar angles within the paracyclophanyl groups range from 1.6 (4) to 4.5 (4)°.

The displacement of the *para*-C atoms from the planes varies from 0.174 (4) to 0.190 (5) Å in the substituted rings and from 0.143 (6) to 0.161 (5) Å in the non-substituted rings of (1). The *para*-C atoms of compound (2) are displaced out of the planes by 0.161 (3)–0.180 (3) Å in the substituted rings and by 0.154 (3)–0.161 (4) Å in the non-substituted rings. The displacement is thus slightly more pronounced in the substituted rings. The rings of the parent non-substituted compound (3) show similar values (0.156 and 0.157 Å; Stalke, 1996).

The displacements are also significantly greater for the C atoms (C3, *etc.*) nearest to the silicon bridges, with values of 0.174 (5)–0.190 (5) Å in (1) and 0.175 (3)–0.180 (3) Å in (2); the Si atoms are displaced by 0.225 (4)–0.473 (6) Å in the opposite direction from the substituted planes.

The planes described by the two sets of four coplanar C atoms are separated by 3.011 (5)–3.222 (5) Å in (1) and 3.036 (3)–3.183 (3) Å in (2). The bridgehead distances C3···C14 and C6···C11 range from 2.766–2.792 Å in (1) and (2) [e.s.d.'s: 0.005 in (1) and 0.003 Å in (2)]. In the parent compound (3), the planes are exactly parallel to one another (crystallographic inversion symmetry), with a bridgehead distance of