C17	0.6731 (6)	0.5120 (5)	0.8071 (3)	0.0753 (18)
C18	0.5215 (5)	0.5211 (4)	0.8068 (3)	0.0561 (15)
C1	0.1058 (4)	0.3083 (3)	0.6678 (2)	0.0423 (11)
C6	0.2221 (6)	0.3510 (4)	0.6278 (3)	0.0561 (15)
C5	0.2054 (8)	0.3713 (4)	0.5530 (3)	0.0703 (18)
C4	0.0770 (9)	0.3493 (4)	0.5189 (3)	0.0847 (25)
C3	−0.0376 (8)	0.3065 (5)	0.5572 (3)	0.0803 (21)
C2	−0.0254 (6)	0.2864 (4)	0.6319 (3)	0.0589 (14)

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

N1—C7	1.320 (5)	C12—C13	1.483 (5)
N1—C9	1.373 (5)	N3—O	1.371 (4)
C7—N2	1.371 (5)	C13—C14	1.389 (6)
C7—C1	1.470 (5)	C13—C18	1.388 (6)
N2—C8	1.394 (5)	C14—C15	1.397 (6)
N2—C12	1.433 (4)	C15—C16	1.352 (8)
C8—C9	1.369 (5)	C16—C17	1.391 (9)
C8—C11	1.487 (6)	C17—C18	1.393 (7)
C9—C10	1.491 (6)	C1—C6	1.392 (6)
C11—C19	1.519 (6)	C1—C2	1.392 (6)
C19—C20	1.387 (7)	C6—C5	1.389 (7)
C19—C24	1.372 (7)	C5—C4	1.35 (1)
C20—C21	1.375 (9)	C4—C3	1.37 (1)
C21—C22	1.37 (1)	C3—C2	1.383 (8)
C22—C23	1.37 (1)	C12—N3	1.261 (4)
C23—C24	1.38 (1)		

C7—N1—C9	107.6 (3)	C21—C22—C23	119.4 (7)
N1—C7—C1	123.8 (3)	C22—C23—C24	120.2 (6)
N1—C7—N2	109.8 (3)	C19—C24—C23	121.1 (5)
N2—C7—C1	126.3 (3)	N2—C12—C13	116.9 (3)
C7—N2—C12	127.5 (3)	N2—C12—N3	122.6 (3)
C7—N2—C8	107.6 (3)	N3—C12—C13	120.5 (3)
C8—N2—C12	124.6 (3)	C12—N3—O	113.1 (3)
N2—C8—C11	124.6 (3)	C12—C13—C18	120.8 (3)
N2—C8—C9	105.5 (3)	C12—C13—C14	120.0 (3)
C9—C8—C11	129.8 (4)	C14—C13—C18	119.2 (4)
N1—C9—C8	109.6 (3)	C13—C14—C15	120.8 (4)
C8—C9—C10	127.6 (4)	C14—C15—C16	119.8 (5)
N1—C9—C10	122.8 (4)	C15—C16—C17	120.3 (5)
C8—C11—C19	113.7 (4)	C16—C17—C18	120.6 (5)
C11—C19—C24	120.8 (4)	C13—C18—C17	119.4 (5)
C11—C19—C20	121.0 (4)	C7—C1—C2	117.9 (4)
C20—C19—C24	118.1 (5)	C7—C1—C6	122.9 (4)
C19—C20—C21	120.7 (5)	C6—C1—C2	119.2 (4)
C20—C21—C22	120.5 (7)	C1—C6—C5	119.6 (5)
C6—C5—C4	120.4 (5)	C4—C3—C2	120.4 (6)
C5—C4—C3	120.8 (5)	C1—C2—C3	119.7 (5)

N1—C7—C1—C2	32.9 (6)	C8—N2—C12—C13	76.2 (4)
N1—C7—N2—C8	−0.8 (4)	N2—C12—C13—C18	−159.0 (4)
C1—C7—N2—C12	5.7 (6)	N2—C12—N3—O	0.9 (5)
C7—N2—C12—N3	67.5 (5)	N3—C12—C13—C14	−156.6 (4)
C7—N2—C12—C13	−111.2 (4)	N3—C12—C13—C18	22.3 (6)
C7—N2—C8—C11	−174.3 (4)	C13—C12—N3—O	179.5 (3)
C8—N2—C12—N3	−105.1 (4)		

Intensity data were corrected for Lorentz and polarization effects. The structure was solved by direct methods with the *MULTAN*80 system (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980); subsequent calculations were performed mainly using the *SHELX*76 (Sheldrick, 1976) and *PARST* (Nardelli, 1983) systems of programs on the VAX3400 computer at the Centro Interdipartimentale di servizi per la Diffrattometria a Raggi-X dell'Università di Messina. The structure was refined anisotropically by full-matrix least-squares methods.

Lists of structure factors, anisotropic displacement parameters and H-atom coordinates have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 71464 (13 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: NA1035]

References

Bruno, G., Foti, F., Grassi, G., Caruso, F. & Risitano, F. (1989). *Acta Cryst.* C**45**, 653–656.

Cromer, D. T. & Mann, J. B. (1968). *Acta Cryst.* A**24**, 321–326.

Diánez, M. J., López-Castro, A. & Márquez, R. (1986). *Acta Cryst.* C**42**, 241–244.

Grassi, G., Foti, F., Risitano, F., Bruno, G., Nicolò, F. & De Munno, G. (1993). *J. Chem. Soc. Perkin Trans.* 1. In the press.

Grassi, G., Foti, F., Risitano, F. & Caruso, F. (1983). *J. Chem. Res.* (*S*), p. 172; (*M*), p. 1680.

Main, P., Fiske, S. J., Hull, S. E., Lessinger, L., Germain, G., Declercq, J.-P. & Woolfson, M. M. (1980). *MULTAN*80. *A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data.* Univs. of York, England, and Louvain, Belgium.

Nagawa, Y., Goto, M., Honda, K. & Nakanishi, H. (1987). *Acta Cryst.* C**43**, 147–149.

Nardelli, M. (1983). *Comput. Chem.* **7**, 95–98.

Sheldrick, G. M. (1976). *SHELX*76. *Program for Crystal Structure Determination.* Univ. of Cambridge, England.

Stewart, R. F. (1970). *J. Chem. Phys.* **53**, 205–213.

Acta Cryst. (1994). C**50**, 430–432

2-Hydroxy-4,4-dimethyl-2-(2-methylphenyl)morpholinium Bromide, $C_{13}H_{20}NO_2^+.Br^-$

J. GABRIEL GARCIA,*† FRANK R. FRONCZEK AND RICHARD D. GANDOUR

Department of Chemistry, Louisiana State University, Baton Rouge, Louisiana 70803-1804, USA

(*Received* 23 *April* 1993; *accepted* 25 *June* 1993)

Abstract

The morpholinium ring adopts a chair conformation with endocyclic torsion angles between 48.3 (4) and 60.7 (5)°. The hydroxyl group is in the axial position of the morpholinium ring, with a C—OH bond distance of 1.406 (5) Å. The hydroxy H atom points towards the Br ion; the interaction has an O···Br distance of 3.241 (3) Å, an H···Br distance of 2.35 (4) Å and an angle at H of 172 (4)°.

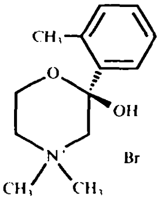
Comment

As part of a larger study on structural changes in reactions involving tetrahedral intermediates as related to substituent effects in the structures of 2-substituted 2-hydroxy-4,4-dimethylmorpholinium salts (Garcia, 1986), the syntheses of some morpholinium bromides (Garcia-Guajardo, Fronczek &

---

† Present address: Lawrence Berkeley Laboratory, UC Berkeley, MS 55-121 Berkeley, CA 94720, USA.

Gandour, 1986; Altbach, Fronczek, Gandour, Garcia, Lin & Watkins, 1988; Garcia, Fronczek & Gandour, 1992) were required. 2-Hydroxy-2-(2-methylphenyl)-4,4-dimethylmorpholinium bromide was prepared by condensing 2-methyl-2′-acetophenone with *N*,*N*-dimethylethanolamine following the procedure described by Garcia (1986). The colorless prisms had an m.p. of 435–437 K. Structural data for 2-(4-cyanophenyl)-2-hydroxy-4,4-dimethylmorpholinium bromide (Altbach *et al.*, 1988), 2-hydroxy-4,4-dimethyl-2-(4-tolyl)morpholinium bromide (Garcia *et al.*, 1992), 2-hydroxy-4,4,6-trimethyl-2-(4-nitrophenyl)morpholinium bromide (Garcia, Fronczek & Gandour, 1993) and 4,4-dimethyl-2-oxomorpholinium bromide (Garcia-Guajardo *et al.*, 1986) are in agreement with those of the title compound.



(I)

The morpholinium ring adopts a chair conformation with the torsion angles ω_1 (O1—C2—C1—N) = −50.3 (4), ω_2 (C2—C1—N—C4) = 48.3 (4), ω_3 (C1—N—C4—C3) = −52.5 (4), ω_4 (N—C4—C3—O1) = 59.5 (5), ω_5 (C4—C3—O1—C2) = −60.7 (5) and ω_6 (C3—O1—C2—C1) = 55.5 (4)°, which are distorted from the ideal chair conformation $\bar{3}$ (D_{3d}) of cyclohexane (Hargittai & Hargittai, 1986), having torsion angles of alternating ±54.4° (Hendrickson, 1967). The pharmacological activities of related compounds are reported by Anderson, Corey, Force, Jensen, Matz & Rivard (1966) and Lee, Stelly, Colucci, Garcia, Gandour & Quinn (1992).

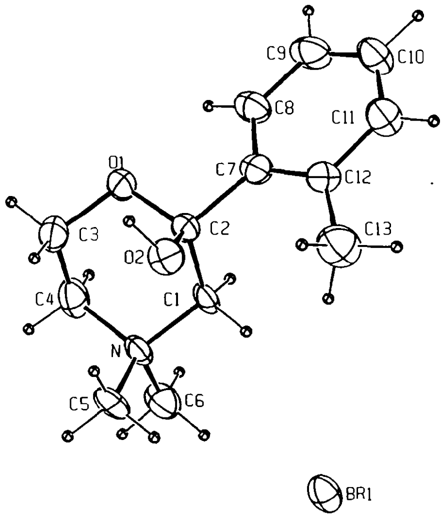


Fig. 1. *ORTEP* drawing (Johnson, 1965) of the molecule, representing heavy atoms as 40% probability ellipsoids and H atoms as circles of arbitrary size.

Experimental

Crystal data

$C_{13}H_{20}NO_2^+.Br^-$
M_r = 302.22
Orthorhombic
$P2_12_12_1$
a = 8.6930 (5) Å
b = 12.3768 (9) Å
c = 12.4624 (9) Å
V = 1340.8 (3) Å^3
Z = 4
D_x = 1.497 Mg m^{-3}
Mo $K\alpha$ radiation
λ = 0.71073 Å

Cell parameters from 25 reflections
θ = 10 - 13°
μ = 3.0 mm^{-1}
T = 298 K
Prism
0.48 × 0.20 × 0.18 mm
Colorless
Crystal source: crystallized from isopropyl alcohol:tetrahydrofuran (1:1)

Data collection

Enraf-Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: empirical
T_{min} = 0.95, T_{max} = 1.00
4871 measured reflections
3081 independent reflections
2144 observed reflections [$I > 3\sigma(I)$]

R_{int} = 0.037
θ_{max} = 27.5°
$h = -11 \rightarrow 11$
$k = 0 \rightarrow 16$
$l = -16 \rightarrow 16$
3 standard reflections
frequency: 167 min
intensity variation: <2%

Refinement

Refinement on F
R = 0.037
wR = 0.037
S = 1.549
2144 reflections
235 parameters
All H-atom parameters refined
$w = 4F_o^2/[\sigma^2(I) + (0.02F_o^2)^2]$

$(\Delta/\sigma)_{max}$ = 0.02
$\Delta\rho_{max}$ = 0.87 e Å^{-3}
$\Delta\rho_{min}$ = −0.42 e Å^{-3}
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV) *Tables* 2.2*B*, 2.3.1

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

$B_{eq} = (8\pi^2/3)\Sigma_i\Sigma_jU_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	B_{eq}
Br1	0.96390 (5)	0.44790 (4)	0.05344 (4)	3.559 (7)
O1	0.7721 (3)	−0.0072 (2)	0.2090 (3)	3.20 (7)
O2	0.9126 (3)	0.1318 (3)	0.2827 (3)	3.25 (7)
N	0.9207 (3)	0.1134 (3)	0.0403 (3)	2.81 (7)
C1	0.7968 (4)	0.1606 (4)	0.1130 (4)	2.51 (9)
C2	0.7831 (4)	0.1061 (3)	0.2201 (4)	2.43 (9)
C3	0.8978 (5)	−0.0526 (4)	0.1493 (4)	3.7 (1)
C4	0.9021 (5)	−0.0074 (4)	0.0394 (4)	3.8 (1)
C5	1.0793 (5)	0.1454 (4)	0.0772 (4)	3.6 (1)
C6	0.8981 (6)	0.1561 (4)	−0.0706 (4)	4.0 (1)
C7	0.6307 (5)	0.1419 (4)	0.2727 (4)	2.84 (9)
C8	0.5004 (5)	0.0752 (4)	0.2572 (4)	3.4 (1)
C9	0.3621 (6)	0.1013 (5)	0.3043 (4)	4.4 (1)

C10	0.3478 (6)	0.1926 (4)	0.3635 (5)	4.5 (1)
C11	0.4698 (6)	0.2601 (4)	0.3749 (4)	4.5 (1)
C12	0.6168 (5)	0.2375 (4)	0.3299 (4)	3.5 (1)
C13	0.7412 (6)	0.3190 (4)	0.3434 (5)	4.9 (1)

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

O1—C2	1.412 (5)	C3—C4	1.480 (7)
O1—C3	1.437 (5)	C7—C8	1.415 (6)
O2—C2	1.406 (5)	C7—C12	1.387 (7)
N—C1	1.524 (5)	C8—C9	1.377 (6)
N—C4	1.504 (6)	C9—C10	1.355 (8)
N—C5	1.507 (5)	C10—C11	1.357 (7)
N—C6	1.492 (6)	C11—C12	1.423 (7)
C1—C2	1.501 (6)	C12—C13	1.488 (7)
C2—C7	1.543 (6)		
C2—O1—C3	112.8 (3)	C1—C2—C7	108.5 (3)
C1—N—C4	108.1 (3)	O1—C3—C4	110.5 (4)
C1—N—C5	111.4 (3)	N—C4—C3	111.8 (4)
C1—N—C6	108.8 (3)	C2—C7—C8	117.5 (4)
C4—N—C5	111.2 (3)	C2—C7—C12	122.5 (4)
C4—N—C6	109.3 (4)	C8—C7—C12	119.9 (4)
C5—N—C6	108.1 (3)	C7—C8—C9	120.2 (4)
N—C1—C2	114.4 (3)	C8—C9—C10	120.6 (5)
O1—C2—O2	109.5 (3)	C9—C10—C11	119.9 (5)
O1—C2—C1	111.4 (4)	C10—C11—C12	122.7 (5)
O1—C2—C7	105.5 (3)	C7—C12—C11	116.6 (4)
O2—C2—C1	109.2 (3)	C7—C12—C13	125.0 (4)
O2—C2—C7	112.8 (3)	C11—C12—C13	118.4 (4)
C2—O1—C3—C4	−60.7 (5)	N—C1—C2—O2	70.7 (4)
C4—N—C1—C2	48.3 (4)	O2—C2—C7—C12	37.6 (6)
N—C1—C2—O1	−50.3 (4)	H2OH—O2—C2—O1	−29.6 (31)

Refinement of the inversion-related structure under identical conditions yielded: $R = 0.060$, $wR = 0.069$, $S = 2.828$. Thus, the absolute configuration of the sample was determined. Programs used were *MolEN* (Fair, 1990) and *ORTEP* (Johnson, 1965).

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 71435 (23 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: HH1076]

References

Altbach, M. I., Fronczek, F. R., Gandour, R. D., Garcia, J. G., Lin, Y. M. & Watkins, S. F. (1988). *Acta Cryst.* C**44**, 1689–1690.

Anderson, E. L., Corey, J. E. Jr, Force, E. E., Jensen, E. M., Matz, R. S. & Rivard, D. E. (1966). *J. Med. Chem.* **9**, 211–213.

Fair, C. K. (1990). *MolEN. An Interactive Intelligent System for Crystal Structure Analysis.* Enraf-Nonius, Delft, The Netherlands.

Garcia, J. G. (1986). MS thesis, Louisiana State Univ., Baton Rouge, Louisiana, USA.

Garcia, J. G., Fronczek, F. R. & Gandour, R. D. (1992). *Acta Cryst.* C**48**, 2231–2233.

Garcia, J. G., Fronczek, F. R. & Gandour, R. D. (1993). Unpublished results.

Garcia-Guajardo, J. G., Fronczek, F. R. & Gandour, R. D. (1986). *Acta Cryst.* C**42**, 1535–1537.

Hendrickson, J. B. (1967). *J. Am. Chem. Soc.* **89**, 7036–7043.

Hargittai, I. & Hargittai, M. (1986). In *Symmetry Through the Eyes of a Chemist*, p. 90. Weinheim: VCH.

Johnson, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee, USA.

Lee, B. H., Stelly, T. C., Colucci, W. J., Garcia, J. G., Gandour, R. D. & Quinn, D. M. (1992). *Chem. Res. Toxicol.* **5**, 411–418.

Acta Cryst. (1994). C**50**, 432–434

Patellamide A, a Cytotoxic Cyclic Peptide from the Ascidian *Lissoclinum patella*

YASUKO IN, MITSUNOBU DOI, MASATOSHI INOUE AND TOSHIMASA ISHIDA*

Osaka University of Pharmaceutical Sciences, 2-10-65 Kawai, Matsubara, Osaka 580, Japan

YASUMASA HAMADA AND TAKAYUKI SHIOIRI

Faculty of Pharmaceutical Sciences, Nagoya City University, Tanabe-dori, Mizuho-ku, Nagoya 467, Japan

(*Received* 22 *March* 1993; *accepted* 17 *September* 1993)

Abstract

The structure of crystals of patellamide A {13-methyl-9,23-bis(1-methylethyl)-2,16-bis(1-methylpropyl)-14,28-dioxa-7,21-dithia-3,10,17,24,29,30,31,32-octaazapentacyclo[24.2.1.$1^{5,8}$.$1^{12,15}$.$1^{19,22}$]dotriaconta-1(29),5,8(30),15(31),19,22(32)-hexaene-4,11,18,25-tetraone methanol solvate monohydrate, $C_{35}H_{49}N_8O_6S_2.CH_4O.H_2O$}, a cytotoxic cyclic peptide having a non-C_2-symmetric methyl group, shows the C_2-symmetric and saddle-shaped rectangular conformation where the methyl group is disordered into two C_2-symmetric positions. The water and methanol solvents were located on the crystallographic diad axis and were held by hydrogen bonds and van der Waals contacts with the polar ring N atoms and non-polar D-Val side-chain atoms, respectively.

Comment

As part of a series of studies on the relationship between the chemical structural symmetry and the molecular conformation in cyclic peptides from marine ascidian, the crystal structure of patellamide A (1), a cytotoxic cyclic peptide from *Lissoclinum patella* (Ireland, Durso, Newman & Hacker, 1982) was determined by X-ray single-crystal analysis. The conformational analysis of this molecule, which has a non-C_2-symmetric methyl group on one side of two C_2-symmetric dihydro oxazole rings, appears to be important in considering the 'active conformation' of cytotoxic cyclic peptides from ascidian, as seen from the C_2-symmetric ascidiacyclamide (2) which takes a rectangular conformation (Ishida, Tanaka, Nabae, Inoue, Kato, Hamada & Shioiri, 1988; Ishida, In, Doi, Inoue, Hamada & Shioiri, 1992). The non-C_2-symmetric patellamide D, in which a benzyl group is attached to only one side, shows a twisted and folded conformation stabilized by four intramolecular

Acta Crystallographica Section C
ISSN 0108-2701 © 1994