The Crystal Structure of [4*R*,7*S*]-7-Isopropyl-4-methyl-2-azepanone [(−)-Menthone Lactam]

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Synopsis. The conformation of the title compound was determined by X-ray crystal analysis. The seven-membered lactam ring is in a quasi-chair conformation with the amide chromophore being approximately coplanar.

We proposed a sign rule (Ogura's sign rule)[1] regarding the relationship between the absolute configuration of the seven-membered lactams and the signs of the n→π* c.d. The Cotton effect of the amide chromophore, indicating that seven-membered lactam rings are classified into two types (A and B) as shown in Fig. 1. The former exibits a positive Cotton effect and the latter a negative one.

Recently, Klyne[2] reported that 7-membered lactam rings connected with a second adjacent ring at the 3,4- or 6,7 positions of the lactam ring showed abnormal CD, and Ogura rule failed to predict the signs of the Cotton effect of several of them. From the results of an X-ray analysis of 2-aza-*A*-homo-5α-cholestan-1-one[3] and ε-caprolactam[4] and on the basis of a study of Dreiding Models, they proposed the hyposesis that the lactam ring A has a positive sign of the C-NH-CO-C torsion angle corresponding to a Cotton effect of the same sign.

We carried out an X-ray analysis of the optical active monocyclic (−)-menthone lactam which obviously has the lactam ring in the conformation depicted in Type B,[5] to confirm the coplanarity of the amide chromophore on which Ogura rule is based. We also wanted to make it clear that (−)-menthone lactam really has a negative C-NH-CO-C torsion angle predicted from the Klyne's hypothesis.

Experimental

A crystal with the dimensions of 0.3×0.4×0.2 mm was used for the structure determination. The density of the crystal was measured by the flotation method using a carbon tetrachloride-light petroleum solution. The cell dimensions and the diffraction intensities were measured on a Rigaku four-circle diffractometer, using graphite monochromated Cu*Kα* radiation at 23°C. Crystal data: $C_{10}H_{19}ON$, orthorhombic, space group $P2_12_12_1$, a=8.837(1), b=40.176(1), c=6.028(1) Å, Z=8. D_c=1.051 g cm^{-3}. 1121 independent reflections within the range of $2\theta<140°$ were collected by the use of the $2\theta-\omega$ scan mode with a scanning rate 4° (2θ)min^{-1}. A total 861 independent reflections with $|F_o|>3\sigma(|F_o|)$ were obtained and corrected for Lorentz and polarization factors but not for absorption factors. The structure was solved by a direct method using MULTAN.[6] The E-map of the phase set with the highest figure of merit showed the skeletons of the molecules.

The structure, thus obtained, was refined by a full-matrix least-squares method with anisotropic temperature factors. After all the hydrogen atoms except those of the methyl group had been located in the difference Fourier map, several cycles of least-squares refinement were carried out including these hydrogen atoms. The atomic scattering factors for C, O, and N were given by Cromer and Mann,[7] and that for H by Stewart *et al.*[8] The final R value was 9.5%, where $R=\Sigma||F_o|-|F_c||/\Sigma|F_o|$.

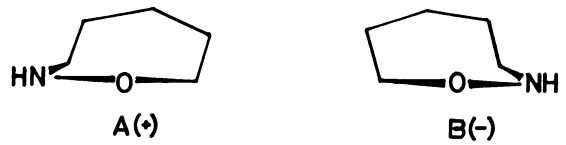

Fig. 1. Projection of a seven-membered lactam ring.

Results and Discussion

The final atomic parameters of crystallographically

TABLE 1. ATOMIC COORDINATES (×10⁴) AND EQUIVALENT ISOTROPIC TEMPERATURE FACTORS OF (−)-MENTHONE LACTAM STANDARD DEVIATIONS ARE GIVEN IN PARENTHESES

Atom	x	y	z	B_{eq}/Å$^{2a)}$
Molecule I				
C(2)	5404(23)	1531(4)	9992(43)	4.9
C(3)	4813(21)	1671(4)	7885(32)	5.8
C(4)	4725(26)	2054(4)	7605(46)	6.2
C(5)	6336(27)	2191(4)	7313(41)	7.0
C(6)	7599(24)	2120(4)	8974(41)	6.5
C(7)	8010(19)	1750(4)	9201(34)	5.3
C(8)	3690(30)	2161(5)	5757(41)	9.3
C(9)	9634(20)	1700(5)	10287(54)	4.8
C(10)	9904(31)	1825(5)	12597(42)	10.0
C(11)	10095(28)	1356(7)	9917(50)	12.5
O(1)	4524(14)	1371(3)	11258(24)	5.7
N(1)	6854(17)	1570(3)	10540(27)	4.8
Molecule II				
C(2)	7015(18)	921(3)	5087(29)	4.7
C(3)	7782(19)	649(4)	6362(35)	4.9
C(4)	7261(24)	600(4)	8853(36)	6.1
C(5)	5704(20)	427(4)	8906(30)	5.2
C(6)	4371(23)	591(4)	7790(33)	5.5
C(7)	4518(19)	620(4)	5211(31)	4.2
C(8)	8473(19)	416(4)	10132(31)	5.9
C(9)	2995(16)	661(4)	4033(33)	5.4
C(10)	2039(19)	336(4)	4099(37)	5.7
C(11)	2057(16)	964(4)	4932(40)	4.1
O(1)	7737(12)	1167(3)	4477(20)	5.7
N(1)	5508(13)	898(3)	4529(23)	3.5

a) W.C. Hamilton, *Acta Crystallogr.*, **12**, 609 (1959).

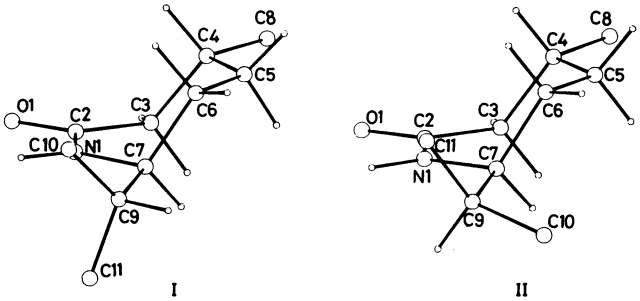

Fig. 2. Perspective view of (−)-menthone lactam (I and II).

Table 2. Bond angles(ϕ/°) and lengths(l/Å) of (−)-menthone lactam standard deviations are given in parentheses

Molecule	I	II		I	II
C(3)-C(2)-O(1)	=120(2)	120(1)	C(2)-C(3)	=1.52(3)	1.50(2)
C(3)-C(2)-N(1)	=120(2)	121(1)	C(2)-O(1)	=1.27(2)	1.23(2)
O(1)-C(2)-N(1)	=120(2)	119(1)	C(2)-N(1)	=1.33(3)	1.38(2)
C(2)-C(3)-C(4)	=117(2)	116(1)	C(3)-C(4)	=1.55(2)	1.58(3)
C(3)-C(4)-C(5)	=109(2)	110(1)	C(4)-C(5)	=1.54(3)	1.54(3)
C(3)-C(4)-C(8)	=112(2)	110(2)	C(4)-C(8)	=1.50(3)	1.51(3)
C(5)-C(4)-C(8)	=112(2)	114(1)	C(5)-C(6)	=1.53(3)	1.51(3)
C(4)-C(5)-C(6)	=122(2)	119(1)	C(6)-C(7)	=1.54(2)	1.56(3)
C(5)-C(6)-C(7)	=114(2)	114(2)	C(7)-C(9)	=1.59(3)	1.53(2)
C(6)-C(7)-C(9)	=112(1)	113(1)	C(7)-N(1)	=1.49(2)	1.48(2)
C(6)-C(7)-N(1)	=111(1)	112(1)	C(9)-C(10)	=1.50(4)	1.56(2)
C(9)-C(7)-N(1)	=110(2)	108(1)	C(9)-C(11)	=1.46(3)	1.57(2)
C(7)-C(9)-C(10)	=119(2)	112(1)			
C(7)-C(9)-C(11)	=108(2)	113(1)			
C(10)-C(9)-C(11)	=115(2)	111(1)			
C(2)-N(1)-C(7)	=126(1)	124(1)			

Table 3. Torsional angles(ϕ/°) of (−)-menthone lactam

Molecule	I	II
N(1)-C(2)-C(3)-C(4)	=−69(2)	−68(2)
O(1)-C(2)-C(3)-C(4)	=113(2)	114(2)
C(2)-C(3)-C(4)-C(5)	=74(2)	75(2)
C(2)-C(3)-C(4)-C(8)	=−162(2)	−159(1)
C(3)-C(4)-C(5)-C(6)	=−56(2)	−60(2)
C(8)-C(4)-C(5)-C(6)	=180(2)	177(2)
C(4)-C(5)-C(6)-C(7)	=63(3)	65(2)
C(5)-C(6)-C(7)-C(9)	=161(2)	158(1)
C(6)-C(7)-C(9)-C(10)	=62(2)	−71(2)
C(6)-C(7)-C(9)-C(11)	=−165(2)	55(2)
N(1)-C(7)-C(9)-C(10)	=−62(2)	164(1)
N(1)-C(7)-C(9)-C(11)	=71(2)	−70(2)
C(6)-C(7)-N(1)-C(2)	=63(2)	61(2)
C(9)-C(7)-N(1)-C(2)	=−173(2)	−173(1)
C(3)-C(2)-N(1)-C(7)	=1(3)	3(2)
O(1)-C(2)-N(1)-C(7)	=180(2)	−178(1)

independent two molecules I and II are listed in Table 1. The complete table of observed and calculated structure factors, thermal parameters and the atomic coordinates of hydrogen atoms are kept as Document No. 8509 at the Office of the Editor of the Bulletin of the Chemical Society of Japan. A perspective drawing of the molecular structure of (−)-menthone lactam is shown in Fig. 2. The bond angles and bond lengths are listed in Table 2, and torsion angles are in Table 3.

The conformation of the lactam ring of (−)-menthone lactam is a quasi-chair with the amide chromophore being approximately coplanar (Table 3). (−)-Menthone lactam belongs to type B, as shown in Fig. 2, and the mean value of the C-NH-CO-C torsion angle is +2°, whose sign is opposite to that of ε-caprolactam (−4.2°). The conformations of the two independent molecules are almost identical except the isopropyl groups. Although the C-NH-CO-C torsion angles in (−)-menthone lactam have the positive sign which is opposite to that predicted by Klyne's hypothesis, this can not be discussed in detail because the values of the torsion angles have large standard deviations.

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