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# CYCLIC TETRAMERS OF CHIRAL AZIRIDINES. III. RING CONFORMATION.

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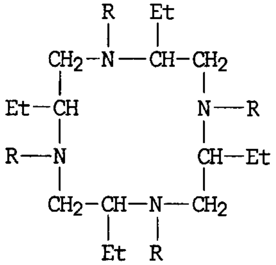
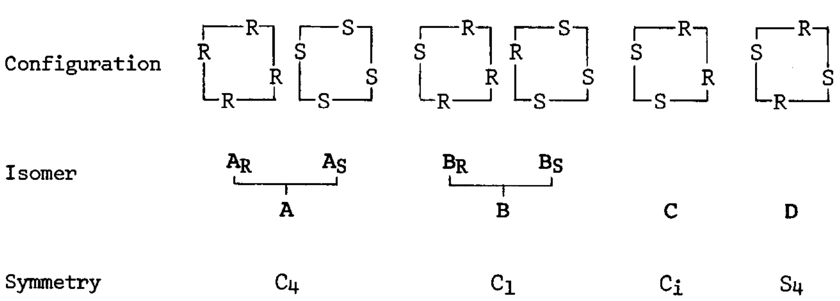
In the course of our studies on polymerization of chiral aziridines, four stereoisomers (**I-A** ~ **I-D**) of the cyclic tetramer obtained from racemic 1-benzyl-2-ethylaziridine have been isolated and identified.1,2)



I : R = $CH_2Ph$
II: R = H



We report that $^{13}$C-NMR spectra of the cyclic tetramers I and II were symmetry-dependent and temperature-independent and that an analysis of these spectra and $^1$H-spectra together with conformational energy calculations3) lent support to a square type [3333] ring conformation with methylene corner. X-Ray crystallography on 2,5,8,11-tetra-(R)-ethyl-1,4,7,10-tetraazacyclododecane (II-$A_R$, Table 1) obtained by debenzylation4) of **I-$A_R$** confirmed that the square ring conformation predicted by NMR data and has essentially $C_4$ symmetry.

Table 1. Characterization of the debenzylated tetramer, **II-$A_R$**.

Mp; 105 ~ 106 °C.
Anal. Calcd.; C 67.55, H 12.76, N 19.70:
Found; C 67.61, H 12.64, N 19.55%.
Mass spectrum; m/e 285 $(M+1)^+$.
IR (KBr); 3270 $cm^{-1}$ ($\nu_{NH}$).
ORD; [α] -310°(589 nm), -1537°(256 nm, min), +1093°(222 nm, max) (c 0.128, MeOH).
CD; [θ] +41400°(205 nm, max) (c 0.128, MeOH).
Crystal data; orthorhombic, $P2_12_12_1$, a = 9.390, b = 9.414, c = 43.139 Å, U = 3813 $Å^3$, Dm = 1.00, Dc = 0.99, Z = 8.

$^{13}$C-NMR spectra are shown in Fig. 1, except for the aromatic signals. Their signals were assigned using gated-decoupling technique. In agreement with $^1$H-NMR data (Fig. 2) described already in a preceding paper,2) each $^{13}$C-NMR spectrum reflects its respective symmetry. The isomers **I-A** and **I-D**, which belong to the symmetry $C_4$ and $S_4$,

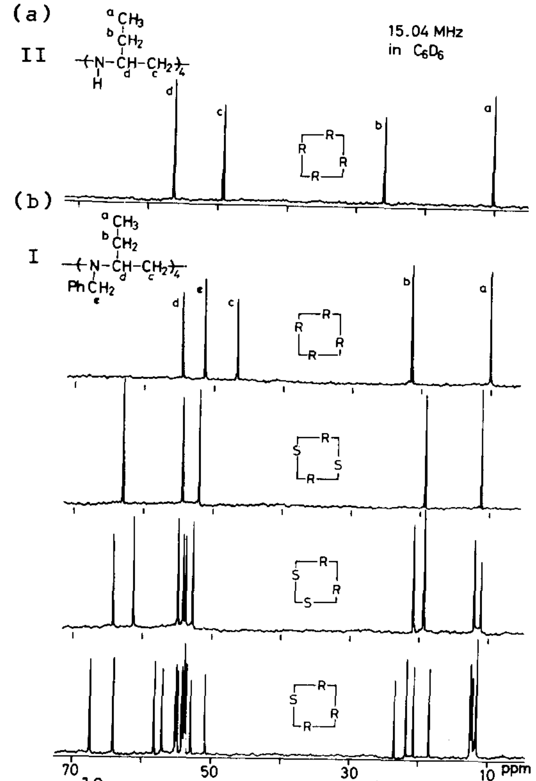


Fig. 1. $^{13}$C-NMR spectra of II-A$_R$(a) and isomers of I(b) except aromatic carbons. The chemical shifts are in ppm from internal TMS at 55 °C.

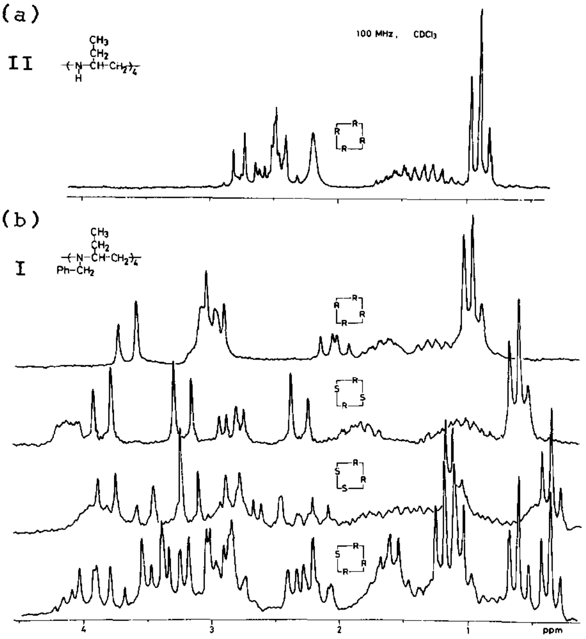


Fig. 2. $^{1}$H-NMR spectra of II-A$_R$(a) and I(b) except aromatic signals with 100 MHz in CDCl$_3$. Chemical shifts are in ppm from internal TMS at room temperature.

respectively, have five resonances in the upfield region as shown in Fig. 1. Only four lines are observed in the spectrum of II-A$_R$. These results mean that four monomeric units in these three molecules are equivalent conformationally and magnetically. In the spectra of the isomers I-C and I-B, double and four sets of signals are observed, respectively. The observations convinced us that the former has a pair of enantiotopic groups in the molecule and the latter has no symmetry. The corresponding sets of resonances were also observed in the aromatic regions of the four stereoisomers, I-A ~ I-D.

The signals of all methylene and methine carbons in the debenzylated cyclic tetramer, II-A$_R$, are shifted downfield, compared with those in the parent compound, I-A$_R$. While no chemical shift difference is observed for the methyl carbons between the two compounds. The facts suggest that the methyl groups are flexible even in I-A$_R$ having each four N- and C-substituents and the other corbons are subjected to a steric compression effect.

No temperature dependence of the signals of ring protons and carbons was observed in the various NMR solvents. The coalescence temperature (Tc) concerning the nonequivalence of methylene geminal protons in the ethyl groups[6] was observed at 90° for I-A and 60° for II-A and, however, in the other isomers the corresponding signals of the geminal protons did not coalesce even 180°. The higher Tc and the temperature-independence of the ring protons and carbons are likely to be due to rigidity of the ring skeleton. Thus, each of these compounds probably exists in a single kind of conformation based on the symmetry of molecule itself in wide range of temperature.

Generally, it has been known that the saturated 12-membered ring compounds exist in a square [3333] conformation and the conformational properties depend more on the ring size than on whether the ring contains simple hetero atoms or has simple substituents.7) When the cyclic tetramer of aziridines also adopts the same square type conformation as cyclododecane, the conformations of **I-A** and **I-D** are consistent with their NMR data. If the chiral carbons were at corner position, $^3J_{HH}$ value of the ring protons should be near 4, but the observed value of $^3J_{HH}$ were 9.5 and 1.0 for **I-A** and 6.0 and 0.5 for **I-D**. Although both the nitrogen and the methylene corner forms are consistent with the dihedral angles of the ring protons, the former form, which has eight transannular H-H repulsive interactions above and below with respect to the ring plane, should be highly unfavored over the latter form, which has four such interactions. Hence, the methylene groups of the ring must occupy the corner positions of the square conformation with or without bulky substituents.

Conformational energy estimates also indicated that "the methylene corner form" is of lowest energy. On the basis of the above consideration on the NMR data, the molecular models were built so that their conformational energies were minimized by rotation of N- and C-substituents. In the conformation of **I-A** obtained by this method, the ring has a square type with (anti - gauche(±) - gauche (±)) monomer units of the same sign (minus sign to R-configuration as in Fig. 3 and vice versa) for the repeating linkage. The C- and N-substituents in **I-A** must be situated outside of the ring skeleton owing to a limited space in the ring and

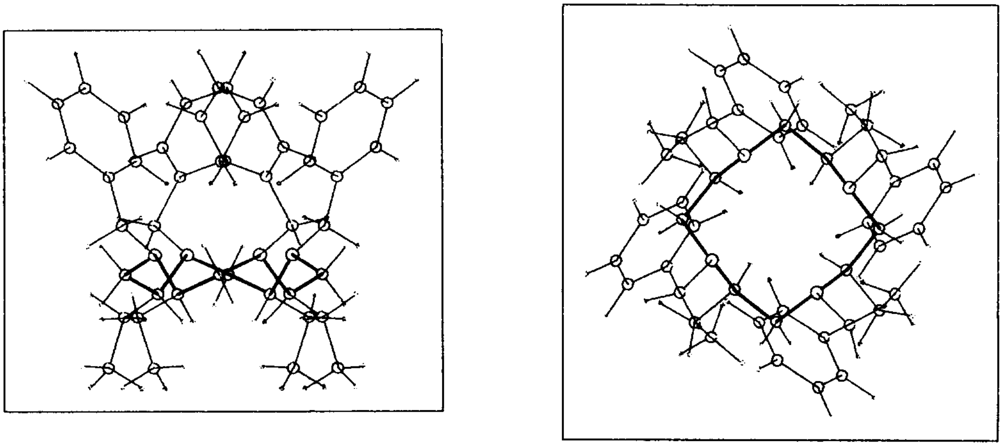


Fig. 3. Plots of the molecular model of **I-A**R obtained by computation of the conformational energy.

keep separately at the opposite side of the ring plane each other in order to reduce the steric hindrance.

The ring conformations of the cyclic tetramers were unequivocally established by X-ray crystallography using the simple form of this series, **II-A**$_R$.[8] As shown in stereo drawing of the molecule in Fig. 4, the ring structure has essentially $C_4$ symmetry, and the square [3333] conformation with the methylene at the corner position. The torsion angles of the ring of **II-A**$_R$ are listed with the calculated values in Table 2, in which the data resemble each other very well. The square conformation seems to be adoptable to the series of compound **I**.

Table 2. Torsion angles of the ring in **A**.

| | Observed[a)] in **II-A**$_R$ | Calculated[b)] for **A** |
|---|---|---|
| C—N—C—C | 166.0°<br>166.1 | 164.0° |
| C—N—C<br>│<br>C | -74.5<br>-75.5 | -74.5 |
| N—C—C<br>│<br>N | -63.6<br>-62.6 | -63.6 |

a) The crystal contains two molecules in the asymmetric unit.[8)]

b) Bond length, 1.53 Å for C-C and 1.47 Å for C-N; all bond angles, 111.5°.[9)]

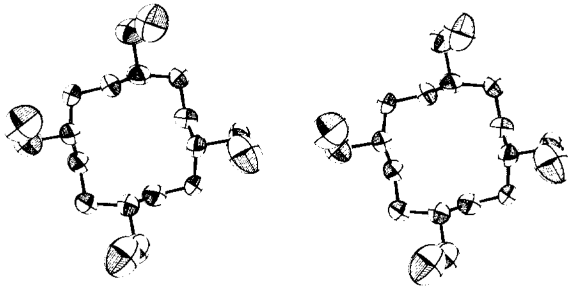


Fig. 4. A stereo drawing of 2,5,8,11-tetra-(R)-ethyl-1,4,7,10-tetraazacyclododecane, **II-A**$_R$.

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## References and Footnotes

1) S. Tsuboyama, K. Tsuboyama, I. Higashi and M. Yanagita, *Tetrahedron Letters*, 1970, 1367.

2) K. Tsuboyama, S. Tsuboyama, J. Uzawa and I. Higashi, *Chem. Letters*, 1974, 1367.

3) T. Sakurai and K. Kobayashi, *Reports Inst. Phys. Chem. Research*, 48, 133 (1972).

4) Debenzylation of I-A$_R$ was carried out by 10% Pd-C under hydrogen (4 atm), for 72 hrs in quantitative yield.

5) Usually, 10% solution of the tetramers was used for measurement.

6) Two multipletes ($\delta$ 1.0 ~ 1.8 ppm for I-A and $\delta$ 0.6 ~ 2.0 ppm for I-D) corresponded to the geminal protons in methylenes of the ethyl groups. The signals of II-A$_R$ in $CD_3OD$ were revealed separately at $\delta$ 1.25 and 1.60 ppm.

7) J. Dale, "*Topics in Stereochemistry*", Vol. 9, p. 199, E. L. Eliel and N. L. Allinger, Eds., Interscience, New York (1976).

8) T. Sakurai, K. Kobayashi, K. Tsuboyama and S. Tsuboyama, *Acta Cryst.*, B, (1977), in press.

9) The torsion angles were obtained from the model constructed with bond lengths 1.53 Å for C-C and 1.47 Å for C-N and with all bond angles 111.5°, which are observed in the various 12-membered ring compounds. Only one set of the torsion angles is possible for the ring with methylene corner.