

CYCLIC TETRAMERS OF OPTICALLY ACTIVE AZIRIDINES:

1,4,7,10-TETRABENZYL-2,5,8,11-TETRA-(R)-ETHYL-1,4,7,10-TETRAAZACYCLODODECANE

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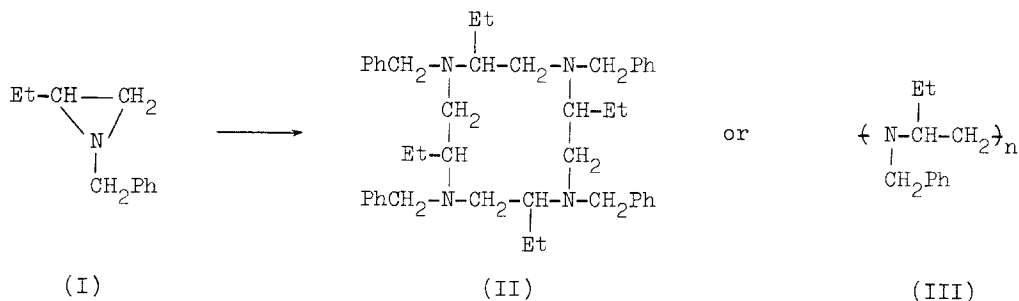
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Although several cyclic oligomers containing hetero atoms have been synthesized recently (1,2), little is known about optically active cyclic tetramer of aziridines. Hansen and Burg (3) reported that twelve-membered ring compound from 1-benzylaziridine was isolated in good yield, but other N-substituted aziridines such as 1-methyl and 1-phenylaziridines gave only the corresponding polymers.

We have now found that 1-benzyl-2-(R)-ethylaziridine (I) (4) in the presence of $\text{BF}_3 \cdot \text{Et}_2\text{O}$ reacts to give a cyclic oligomer or the corresponding polymer depending on the reaction temperature. The former proved to be a cyclic tetramer, 1,4,7,10-tetrabenzyl-2,5,8,11-tetra-(R)-ethyl-1,4,7,10-tetraazacyclododecane (II), which had no end groups. The cyclic tetramer has shown a tendency to include, in the crystalline state, a molecule used as recrystallization solvent.

As described by Katnik and Schaefer (1) concerning cyclic tetramers from propylene oxide, there are four structural and twenty-three geometrical (cis and trans) isomers of these types of compound depending on the position of ring cleavage. If the ring-opening in an optically active aziridine takes place at the primary carbon, only one structural isomer (head-to-tail) should be obtained and the configuration of the isomer must retain that of the starting material. The experimental result with regard to stereochemistry on ring rupture of unsymmetrical C-substituted (5) or optically active aziridines (6), strongly suggests that the ring-opening in this case also occurs exclusively at the primary carbon under the reaction condition employed. This means that the monomer units



of the tetramer are head-to-tail and, their configuration are all *cis* and (R)-form.

Treatment of I (2 g) with $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (0.1 g) for 20 hr at room temperature yields, after removal of the catalyst, 0.4 g (20%) of II. II was also synthesized by refluxing I in benzene or ethanol for 24 hr by the same catalyst in 30% yield. Purification of II was carried out by recrystallization in benzene and then dried at 140° under reduced pressure over 20 hr. II: mp $189-190^\circ$; IR KBr_{max} 13.44μ ; $[\alpha]_{\text{D}}^{25} +336^\circ$ (c 0.11, benzene), $[\alpha]_{\text{D}}^{25} +220^\circ$, $[\alpha]_{220(\text{max})}^{25} +19000^\circ$ (c 0.01, dioxane); NMR (CDCl_3) τ 2.85 (s, 20, aromatic), 6.68 (q, 8, CH_2Ph , $J_{\text{AB}} = 14.2$ cps*), 6.80-7.20 (m, 8, ring CH_2), 7.65-8.90 (m, 12, CH , CH_3CH_2), 9.04 (t, 12, CH_3CH_2); m/e 644 (M^+), 553 ($\text{M} - \text{C}_6\text{H}_5\text{CH}_2$) $^+$. Anal. Calcd for $(\text{C}_{11}\text{H}_{15}\text{N})_4$: C, 81.93; H, 9.38; N, 8.69. Found: C, 82.06; H, 9.26; N, 8.60.

When the reaction mixture was kept at -70° in a nitrogen-filled tube over 5-6 hr and the temperature was raised gradually until 100° , and then kept at this temperature for 48 hr, the corresponding polymer, poly(1-benzyl-2-(R)-ethylaziridine) (III), was formed as pale yellow powder after freeze-drying (1.2 g, 60%); softening point $60-88^\circ$; IR KBr_{max} 14.31μ ; $[\alpha]_{\text{D}}^{25} +170^\circ$ (c 0.51, benzene), $[\alpha]_{\text{D}}^{25} +149^\circ$, $[\alpha]_{220(\text{max})}^{25} +7500^\circ$ (c 0.10, dioxane); mol. wt. 2640 (vapor pressure method). Anal. Calcd for $(\text{C}_{11}\text{H}_{15}\text{N})_n$: C, 81.93; H, 9.38; N, 8.69. Found: C, 81.71; H, 9.03; N, 8.64.

* The discussion on such magnetic non-equivalence in the diastereoisomeric methylene hydrogens of the N-benzyl groups in cyclic systems is given by R. E. Lyle and J. J. Thomas in Tetrahedron Letters, No. 11, 897 (1969).

Crystallization of II from benzene gave a clathrate type compound containing the solvent (II-B) [mp 183-185°; NMR (CDCl_3) τ 2.65 (s, 6, benzene); m/e 644 (M^+), 78 (benzene). Anal. Calcd for $(\text{C}_{11}\text{H}_{15}\text{N})_4 \cdot \text{C}_6\text{H}_6$: C, 83.05; H, 9.20; N, 7.75. Found: C, 83.21; H, 9.27; N, 7.68]. A slow loss of the guest component occurred over several weeks at room temperature under a reduced pressure. Similarly, thermogravimetric analysis of the clathrate showed a discrete weight loss below the melting point. After removal of the guest molecule, the host lattice had reverted to the original crystal structure. Since pure II did not give a single crystal but was in a polycrystalline state, the comparison of the crystal forms was carried out with their X-ray powder diffraction patterns. The pattern of II-B was distinctly different from that of pure II, which indicated that a crystal transformation had taken place. These results support formation of molecular inclusion compound.

The transparent plate-like crystals of II-B are tetragonal, with $a = b = 12.06$, $c = 30.89 \text{ \AA}$; space group, P4_1 or P4_3 , number of II-B molecule per unit cell = 4. The observed density measured by flotation method (NaCl aqueous solution) was 1.04 g/cm^3 . The sample crystallized from toluene, which had the composition of $(\text{C}_{11}\text{H}_{15}\text{N})_4 \cdot \text{C}_6\text{H}_5\text{CH}_3$ (II-T), was found to be essentially isomorphous with the crystals II-B; the unit cell constants, $a = b = 12.01$, $c = 31.52 \text{ \AA}$, the same space group.

(S)-Enantiomer of II has shown the same constants and behavior as its (R)-isomer except for the opposite sign of optical rotation. (S)-II: mp 188-189°; $[\alpha]_D^{23} -325^\circ$ (c 0.11, benzene). (S)-II-B: mp 182-185°.

An equal amount of mixture of (R)-II and (S)-II formed new racemic crystals (II-(R+S)) which were sparingly soluble in benzene and did not contain the solvent [mp 221-223°. Anal. Found: C, 82.20; H, 9.25; N, 8.53]. Columnar single crystals of the racemic compound are monoclinic, with cell dimensions of $a = 11.85$, $b = 14.68$, $c = 22.69 \text{ \AA}$, and $\beta = 89.3^\circ$. The space group is $\text{P2}_1/\text{C}$.

Twelve-membered ring compounds were also derived from the racemic I: mp 199-205°. Glpc analysis of the sample showed that this product consisted of two materials. These two could separate by fractional recrystallization in benzene. The crystals of the first crop were identified as II-(R+S) by X-ray and other

spectral data, and mixed mp with the authentic sample. A more soluble product in the second crop gave single crystals from ligroin [mp 201-203°; m/e 644 (M)⁺. Anal. Found: C, 82.03; H, 9.40; N, 8.31]. The crystals were triclinic with cell dimensions of $a = 9.41$, $b = 13.48$, $c = 9.24$ Å, $\alpha = 113.5^\circ$, $\beta = 102.0^\circ$, and $\gamma = 64.0^\circ$. Because of showing no optical power, this compound seems likely to correspond to either 1:1 mixture of (c) and (d), or (e), or (f) as described below.

As for the cyclic tetramer, six possible stereoisomers are considered. Assuming that a propagating terminal of oligomer reacts with R- or S-monomer in the same conditional probability and that the resulting linear tetramer cyclizes with the same probability, the ratio of cyclic stereoisomers formed is as follows:

stereo- isomer	$\begin{array}{c} \text{R} - \text{R} \\ \quad \\ \text{R} - \text{R} \end{array}$	$\begin{array}{c} \text{S} - \text{S} \\ \quad \\ \text{S} - \text{S} \end{array}$	$\begin{array}{c} \text{R} - \text{R} \\ \quad \\ \text{R} - \text{S} \end{array}$	$\begin{array}{c} \text{S} - \text{S} \\ \quad \\ \text{S} - \text{R} \end{array}$	$\begin{array}{c} \text{R} - \text{R} \\ \quad \\ \text{S} - \text{S} \end{array}$	$\begin{array}{c} \text{R} - \text{S} \\ \quad \\ \text{S} - \text{R} \end{array}$
	(a)	(b)	(c)	(d)	(e)	(f)
ratio of formation	1	1	4	4	4	2

In spite of low possibility of formation, the relative accessibility of II-(R+S) (1:1 mixture of (a) and (b)) from racemic I might be responsible not only to the solubility for the solvent, but to the ease of cyclization depending on the stereostructure of the linear tetramer. Further studies on this problem are currently in progress.

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References

- 1) R. J. Katnik and J. Schaefer, J. Org. Chem., **33**, 384 (1968).
- 2) R. J. Kern, ibid., **33**, 388 (1968).
- 3) G. R. Hansen and T. E. Burg, J. Heterocyclic Chem., **5**, 305 (1968).
- 4) S. Tsuboyama, A. Ohta and M. Yanagita, Tetrahedron Letters, 3921 (1969).
- 5) L. B. Clapp, J. Am. Chem. Soc., **70**, 184 (1948).
- 6) K. Tsuboyama, S. Tsuboyama and M. Yanagita, Bull. Chem. Soc. Japan, **40**, 2954 (1967).