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Stereoregularity of Poly-(R)-2-ethylaziridine

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Poly-(R)-2-ethylaziridine (I) was obtained by three different procedures: (A) the polymerization of (R)-2-ethylaziridine (II) by boron trifluoride-etherate, (B) the polymerization of the aziridine in the presence of ammonium chloride in liquid ammonia, and (C) the reaction of (R)-2-amino-1-bromobutane hydrobromide (III) with caustic alkali. The stereoregularity of the polymer I may be assumed to be fairly high as a result of comparing the specific rotations of the above polymers. In order to evaluate this assumption, the addition reaction of the aziridine and diethylamine was carried out as a model experiment under experimental conditions similar to those of the polymerization (A). On the basis of the data as analyzed by gas chromatography, it is concluded that the ring opening at the primary carbon takes place over 99.4%. This implies that the ring cleavage at the primary carbon in the polymerization occurs over 180 units successively. Considering the molecular weight of the polymer I (3500—5000, 50—70 monomer units), one can assume that the configuration of the polymers obtained here perfectly retains that of the monomer and that the polymer is "isotactic."

In their studies of aziridine polymerization, both Jones and his co-workers⁽¹⁾ and Barb⁽²⁾ established some facts bearing on the mechanism. Jones⁽³⁾ pointed out that the mechanism of 2, 2-dimethylaziridine polymerization may be regarded as a S_N2 process and the ring opening at the primary carbon. This was supported by Minoura *et al.* with respect to the polymerization of both optically active and optically inactive 2-methylaziridines.⁽⁴⁾ We have also assumed that the stereoregularity of the backbone in various optically active polyaziridines, which were capable of catalyzing in asymmetric cyanohydrin syntheses, was markedly high on the basis of the view on their physical and chemical properties.⁽⁵⁾ However, very few data offering direct evidence relating to the problem have been reported. This work was, therefore, undertaken in order to clarify the stereoregularity of poly-(R)-2-ethylaziridine (I).

The polymer I was obtained by three different procedures:

(A) The polymerization of (R)-2-ethylaziridine (II) by boron trifluoride-etherate. Polymerization was carried out under nitrogen atmosphere in the presence of boron trifluoride-etherate as the catalyst. The polymer obtained was pale yellow and viscous, and its molecular weight was 3500—5000. The specific rotation of the polymer in benzene was −120—−130° and was inclined to increase with increases in the degree of polymerization.

(B) The polymerization of the aziridine II in liquid ammonia by ammonium chloride. The molecular weight of the polymer thus obtained was low (810), and the specific rotation was −109° in benzene.

(C) The reaction of (R)-2-amino-1-bromobutane hydrobromide (III) with caustic alkali. The product was similar to that yielded by method (B) (mol wt 820, $[\alpha]_D$ −109° in benzene).

The stereoregularity of these polymers depends on the orientation of the ring opening during polymerization. If the breaking occurs exclusively at

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1) G. D. Jones, A. Langsjoen, M. M. C. Neumann and J. Zomlefer, *J. Org. Chem.*, **9**, 125 (1944).

2) W. G. Barb, *J. Chem. Soc.*, **1955**, 2564.

3) G. D. Jones, *J. Org. Chem.*, **9**, 484 (1944).

4) Y. Minoura, M. Takebayashi and C. C. Price, *J. Am. Chem. Soc.*, **81**, 4690 (1959).

5) S. Tsuboyama, This Bulletin **35**, 1004 (1962); *ibid.*, **39**, 698 (1966).

TABLE 1. POLY-(R)-2-ETHYLAZIRIDINE

Method	Configuration of monomer	Yield %	Molecular weight	$[\alpha]_D$[*1] degree
A	R	92	5000	−129.0
A	R	92	4650	−127.4
A	R			−123.5
A	R		3300, 3550[*2]	−122.1
A	R			−117.2
A	R			−106.5
A	S	97		+120.2
A	S			+119.5
A	RS		3770, 3650[*2]	0
A	RS		2000	0
B	R	34	810	−108.9
B	R	77		−90.9
C	R	63		−112.1[*3]
C	R		820	−109.2[*4]
C	R			−89.2[*5]

[*1] c 0.5—2 in benzene.

[*2] Molecular weights of these two were measured by vapor pressure method with a Hitachi 115-type instrument, and the others were determined by cryoscopic method.

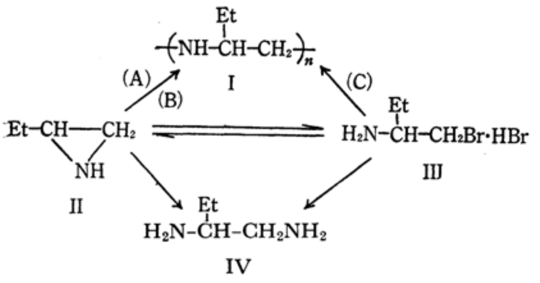
[*3] III/NaOH=0.5

[*4] III/NaOH=1

[*5] A large excess of NaOH was used.

the primary carbon, the polymer to be expected must retain the same configuration as the monomer, whereas at the opposite side racemization or inversion may occur.

When II was treated in liquid ammonia in the presence of ammonium chloride at room temperature, I was obtained, at 100°C the main product isolated was optically pure (R)-1, 2-diaminobutane (IV) which was also derived from the reaction of III with methanolic ammonia.[6] Both of the diamines obtained, as well their diacetyl and di-(phenylthiourea) derivatives, showed the same characteristics. This means that if in liquid ammonia both reactions, the diamine formation and the polymerization, proceed by the same mechanism, regardless of the reaction temperature, the configuration of the polymer will be identical with that of II.



The reaction of the salt III with a large excess of an alkaline solution gave the corresponding aziridine II, whereas when an alkaline solution was added portion by portion to the salt III and then the resulting mixture was warmed gently, the polymer I was found to be given mainly. In the intermolecular condensation, a polymer may be expected, while intramolecular dehydrobromination gives an aziridine which may polymerize with a small amount of the cation species partially present. In the former case, the configuration of the polymer may be expected to be identical with that of the starting material. However, there is no evidence at present as to whether intra- or intermolecular condensation takes place in the above reaction.

As is shown in Table 1, the polymers obtained indicate the corresponding optical rotations in spite of the fact that they are polymerized under different experimental conditions. This result suggests that polymerization occurs in every case independently of the asymmetric carbon, even if in the method (C) the polymerization takes place through aziridine-ring formation. This supports the assumption regarding the position of ring opening during polymerization and the stereoregularity of the polymer mentioned before.

There have been many papers concerning the stereochemistry of ring opening reactions in aziridine. In the reaction of aziridine with a nucleophilic reagent, HY, by an acid catalyst, the three-membered ring cleaves in two possible directions. The hydrolysis or alcoholysis of C-substituted unsymmetrical aziridine gives product of the type V indicating a break in the ring at the

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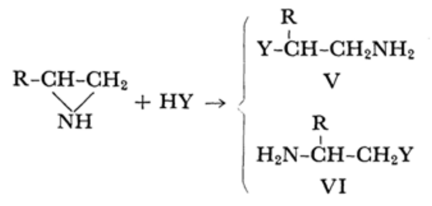
[6] L. B. Clapp, *J. Am. Chem. Soc.*, **70**, 184 (1948).

secondary carbon than at the primary carbon.[7,8] In reactions other than hydrolysis, the break preferentially occurs on the opposite side to form an amine of the type VI[6,9-11]



The data, when analyzed by gas chromatography, showed that the addition reaction of II with diethylamine gave 2-amino-1-diethylaminobutane (VII, R=Et, Y=NEt_2 in VI) exclusively; this conclusion is based on the break at the primary carbon. The diamine VII was identified by the use of authentic samples derived from the reaction of III with an excess of diethylamine. 1-Amino-2-diethylaminobutane (VIII, R=Et, Y=NEt_2 in V) was synthesized by the reduction of α-diethylaminobutyronitrile with lithium aluminum hydride. The ratio of the areas of the two peaks corresponding to the amines VII/VIII was about 180/1. On the basis of this finding, it can be said that there is little possibility of involving another configuration in the backbone of the polymer. This indicates that the ring cleavage at the primary carbon in the polymerization occurs over 180 units successively. All the data obtained so far are compatible with this conclusion. Since the molecular weight of the polymer is 3500—5000, corresponding to 50—70 units of the monomer, it can be stated that the polymer I completely retains the same configuration as the monomer and that it is "isotactic."

Experimental

Poly-(R)-2-ethylaziridine (I). *Method (A). Polymerization of (R)-2-ethylaziridine (II) by Boron Trifluoride-etherate.* Polymerization was carried out by Minoura's procedure.[4] Boron trifluoride - etherate (2.5 m*l*) was added to II ($[\alpha]_D^{18}+17.6°$ (neat), 26.0 g) which was placed in a nitrogen-filled tube cooled at about −75°C. The tube, after being flushed again with nitrogen and sealed, was allowed to stand overnight at room temperature and then heated at 100°C for 48 hr. The contents were dissolved in 3 N hydrochloric acid (150 m*l*), and then the solution was alkalized with an excess of sodium hydroxide under cooling. The separated polymer was extracted with ether, and the extracts were washed with a dilute sodium hydroxide solution to remove low-molecular-weight materials and then dried over potassium hydroxide pellets. The polymer obtained by removal of the solvent under reduced pressure was colorless and viscous; $[\alpha]_D^{30}-88.40°$ (*c* 2.85, dioxane), $[\alpha]_D^{23}$ −127.40° (*c* 0.53, benzene), n_D^{20} 1.4926, mol wt, 4650 (cryoscopic method in benzene). It weighed 24.0 g (92.3%).

Found: C, 67.24; H, 12.94; N, 19.55%. Calcd for $(C_4H_9N)_n$: C, 67.55; H, 12.76; N, 19.70%.

Method (B). Polymerization of (R)-2-Ethylaziridine (II) in Liquid Ammonia by Ammonium Chloride. A mixture of II (3.5 g. 0.05 mol), ammonium chloride (0.3 g), and liquid ammonia (50 m*l*) was placed in a bomb and stirred at 25°C for 72 hr. After ammonia had been allowed to escape, the reaction mixture was filtered and distilled under reduced pressure. (A fraction, bp 80—110°C/5 mmHg, was obtained.) The residue was purified by the same precedure as in method (A) to give 1 g of I ($[\alpha]_D^{16}$ −108.9° (*c* 1.33, benzene), mol wt, 810), whose infrared spectrum was essentially identical with that of the above polymer.

Found: C, 67.21; H, 12.82; N, 19.68%.

Method (C). Polymer from (R)-2-Amino-1-bromobutane Hydrobromide (III) with Alkali. To a solution of III (12 g, 0.05 mol) in water (12 m*l*) a 40% sodium hydroxide solution (0.1 mol) was gradually added; the mixture was then slowly heated to 85°C and left as it was for 2 hr. The organic layer which separated was worked up in the usual manner. The resulting solution was filtered over carbon, and the filtrate was evaporated to dryness under reduced pressure to give the polymer I; $[\alpha]_D^{16}$ −109.2° (*c* 0.86, benzene), mol wt, 820. The infrared spectrum was identical in detail with that of the polymer obtained by method (A).

Found: C, 67.46; H, 13.55: N, 19.21%.

(R)-2-Amino-1-bromobutane Hydrobromide (III). (R)-2-Aminobutanol[13] (135 g, 1.5 mol) was dissolved in 47% hydrobromic acid (600 g, 2.5 mol), and the solution was distilled with a fractionating column in an oil bath heated at 180—190°C. The first fraction, distilled at 100°C, was removed, and the second fraction at 110—125°C collected. When the distillation was over, the second fraction was returned to the distillation flask and distillation was performed again. After this treatment had been repeated five times, the contents were evaporated to dryness under reduced pressure. Acetone (500 m*l*) was poured into the solidified residue. The crushed precipitate was filtered and washed with acetone. Crude bromoamine salt III weighing 265 g resulted. An additional 28 g of the product was obtained by the evaporation of the filtrate and washings. The total yield was 293 g (83.8%). It melted at 177—179°C after recrystallizations from acetone; $[\alpha]_D^{18}$ −12.09° (*c* 3.13, water), $[\alpha]_D^{15}$ −5.3° (*c* 4.5, ethanol).

Found: C, 20.64; H, 4.54; N, 6.22; Br, 68.73%. Calcd for $C_4H_{11}NBr_2$: C, 20.62; H, 4.76; N, 6.01; Br 68.61%.

(R)-1, 2-Diaminobutane (IV). *From (R)-2-Amino-1-bromobutane Hydrobromide (III).* The procedure of Amundsen[12] was used with a slight modification. A mixture of 20 g (0.086 mol) of III and 200 m*l* of

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[7] T. L. Cairns, *ibid.*, **63**, 871 (1941).

[8] D. S. Tarbell and P. Noble, Jr., *ibid.*, **72**, 2657 (1950).

[9] S. Gabriel and H. Ohle, *Ber.*, **50**, 804 (1917).

[10] G. Meguerian and L. P. Clapp, *J. Am. Chem. Soc.*, **73**, 2121 (1951).

[11] U. Harder, E. Pfeil and K-F. Zenner, *Chem. Ber.*, **97**, 510 (1964).

[12] L. H. Amundsen and K. W. Krantz, *ibid.*, **63**, 305 (1941).

[13] F. H. Radke, R. B. Fearing and S. W. Fox, *J. Am. Chem. Soc.*, **76**, 2801 (1954).

ammonia-saturated methanol was allowed to stand for six days with stirring. After small amounts of water had been added, the residue was concentrated *in vacuo*. An organic layer was separated by saturation with potassium hydroxide and dried. Distillation gave 2.2 g (29%) of IV; bp 140—141°C, n_D^{18} 1.4508, $[\alpha]_D^{18}$ $-20.80°$ (*c* 1.25, ethanol).

Found: C, 54.48; H, 13.41; N, 31.68%. Calcd for $C_4H_{12}N_2$: C, 54.50; H, 13.72; N, 31.78%.

Diacetyl compound; recrystallization from ethanol-ether afforded silky crystals, mp 169—170°C, $[\alpha]_D^{17}$ $+51.88°$ (*c* 0.51, ethanol).

Found: C, 55.75; H, 9.15; N 16.42%. Calcd for $C_8H_{16}N_2O_2$: C, 55.79; H, 9.36; N, 16.27%.

Di(phenylthiourea) derivative; recrystallization from ethanol gave needle crystals, mp 177—178°C (racemic compound, mp 174°C[6]), $[\alpha]_D^{16}$ $+2.17°$ (*c* 2.76, dioxane).

Found: C, 60.33; H, 6.06; N, 15.93%. Calcd for $C_{18}H_{22}N_4S_2$: C, 60.30; H, 6.19; N, 15.63%.

From (R)-2-Ethylaziridine (II). The diamine IV was obtained from II by the procedure of Clapp.[6] 3.5 g (0.05 mol) of II afforded 2.5 g (57%) of the diamine; bp 139—140°C, $[\alpha]_D^{17}$ $-19.70°$ (*c* 0.97, ethanol).

This compound was determined as diacetyl or di(phenylthiourea) derivatives. The melting points of both compounds corresponded with those for the derivatives obtained from III, and no depression in melting point was observed upon the admixture of any pair of these derivatives.

(R)-2-Amino-1-diethylaminobutane (VII). *From (R)-2-Amino-1-bromobutane Hydrobromide (III) and Diethylamine.* III (23.5 g, 0.1 mol) was added to a mixture of diethylamine (40 g, 0.55 mol) and water (20 m*l*) under cooling. The mixture was stirred at room temperature for 2 days, heated slowly to 100°C, and then maintained at the same temperature for 5 hr. After the excess diethylamine had been removed, the residue was treated with sodium hydroxide. The diamine separated was extracted with tetrahydrofuran and dried over potassium hydroxide pellets. Distillation gave VII in a yield of 9.4 g (65%); bp 76—77°C/30 mmHg, n_D^{20} 1.4347, $[\alpha]_D^{27}$ $-92.30°$ (*c* 2.43, ethanol).

Found: C, 66.69; H, 13.79; N, 19.41%. Calcd for $C_8H_{20}N_2$: C, 66.60; H, 13.98; N, 19.42%.

The second fraction was its dimer, 8-(R)-amino-3-ethyl-5-(R)-ethyl-3, 6-diazadecane. The yield was 2.4 g (22%); bp 87—89°C/2 mmHg, n_D^{20} 1.4543, $[\alpha]_D^{27}$ $-100.5°$ (*c* 1.71, ethanol).

Found: C, 66.66; H, 13.21; N, 19.63%. Calcd for $C_{12}H_{29}N_3$: C, 66.91; H, 13.57; N, 19.52%.

From (R)-2-Ethylaziridine (II) and Diethylamine. Boron trifluoride - etherate (1.5 m*l*) was added to a mixture of II (15 g, 0.2 mol) and diethylamine (39 g, 0.5 mol) placed in a pressure ampoule cooled at −30— −50°C. The mixture was allowed to stand at room temperature overnight and was then heated under conditions similar to those used in the polymerization of the aziridine II. The resulting mixture was treated with potassium hydroxide pellets and filtered. The distillable products were collected over a wide range of temperatures, 70—95°C/40 mmHg, and the fraction was analyzed by gas chromatography in order to determine the orientation of the ring rupture in the aziridine. The diamine VII was redistilled to give 18.5 g (64.3%); bp 85—86°C/40 mmHg, n_D^{20} 1.4352, $[\alpha]_D^{27}$ $-92.40°$ (*c* 2.47, ethanol), $[\alpha]_D^{27}$ $-84.90°$ (*c* 2.83, benzene).

Gas chromatography was carried out under the following conditions: apparatus, Shimadzu GC-1A type; column liquid, 25% of carbowax 1000 and 12.5% of KOH (6 mm 1.5 m); temperature, 110°C; helium flow, 100 m*l*/min; results, retention time, 8.5 min for VII and 11.6 min for VIII.

2-Diethylaminobutyronitrile. A mixture of potassium cyanide (19 g, 0.28 mol) and water (25 m*l*) was added drop by drop to a mixture of diethylamine (73 g, 1.0 mol), diethylamine hydrochloride (33 g, 0.3 mol), propionaldehyde (15 g, 0.25 mol), and water (20 m*l*) at a temperature below 20°C; the reaction mixture was then held at room temperature overnight. The contents were extracted twice with ether, and the extracts were dried over potassium carbonate. After the removal of the ether, the aminonitrile was collected under reduced pressure; bp 78—82°C/20 mmHg. Redistillation gave a colorless liquid; bp 96—97°C/45 mmHg, n_D^{20} 1.4263. The yield was 23.2 g (66.3%).

Found: C, 68.84; H, 11.50; N, 20.53%. Calcd for $C_8H_{16}N_2$: C, 68.52; H, 11.50; N, 19.98%.

1-Amino-2-diethylaminobutane (VIII). A mixture of the nitrile obtained (22 g, 0.15 mol) and dry ether (30 m*l*) was added, drop by drop to a suspension of lithium aluminum hydride (8 g, 0.21 mol) in ether. After the mixture had been allowed to stand overnight, it was treated in the usual manner. VIII was obtained in a 75.0% yield (16.2 g) and boiled at 83—84°C/30 mmHg, n_D^{20} 1.4405.

Found: C, 66.61; H, 13.69; N, 19.68%. Calcd for $C_8H_{20}N_2$: C, 66.60; H, 13.98; N, 19.42%.

Part of the expenses for this investigation have been defrayed by Kakenkagaku Co., Inc.