Makromol. Chem. **177**, *2849–2859 (1976)*

Laboratory of Macromolecular Chemistry
K. Universiteit Leuven, Belgium

Ring Opening Polymerization of L-Methyl 2-(2-Methyl-1-aziridinyl)acetate and Its Racemic Stereoisomer: ^{13}C NMR Study

C. Samyn, S. Toppet, and G. Smets

(Date of receipt: October 30, 1975)

SUMMARY:

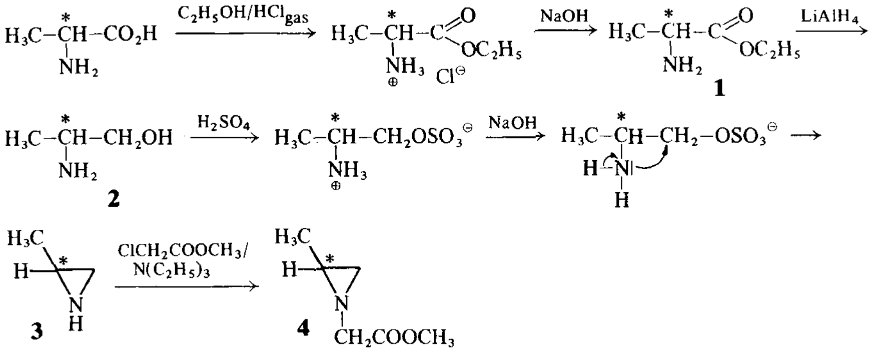
Poly[L(and D, L)-*N*-(methoxycarbonylmethyl)iminopropylene] (**5**) were synthesized by cationic polymerization of methyl 2-(2-methyl-1-aziridinyl)acetate (**4**) in the presence of dimethyl sulfate as initiator. The stereoregularity of the polymer obtained from the L-aziridine **4** was determined by ^{13}C NMR study of the L- and D,L-polyesters **5**. It could be shown that the opening of the aziridine ring proceeds mainly at the unsubstituted methylene carbon atom, retaining the configuration of the asymmetric carbon to at least 85%.

ZUSAMMENFASSUNG:

Poly[L(und D,L)-*N*-(methoxycarbonylmethyl)iminopropylen] (**5**) wurden durch kationische Polymerisation von Methyl-2-(2-methyl-1-aziridinyl)acetat (**4**) mit Dimethylsulfat als Initiator dargestellt. Die Stereoregularität des Polymers, das aus dem L-Aziridin **4** dargestellt wurde, wurde durch ^{13}C NMR-Untersuchungen des L- und D,L-Polyesters **5** bestimmt. Es konnte gezeigt werden, daß die Öffnung des Aziridin-Rings hauptsächlich am unsubstituierten Methylenkohlenstoffatom stattfindet, unter Erhaltung der Konfiguration des asymmetrischen Kohlenstoffs zu mindestens 85%.

Introduction

In order to obtain high molecular weight polyampholytes with well defined alternating structures, we have carried out the ring-opening polymerization of *N*-alkyl aziridine compounds carrying an ester function in the alkyl substituent[1]. The synthesis of the L-isomer was carried out using the following reaction sequence, starting from L-alanine ($[\alpha]_D^{20}$ in 1 M HCl = +14°).

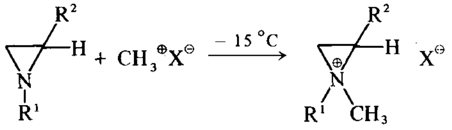


Results and Discussion

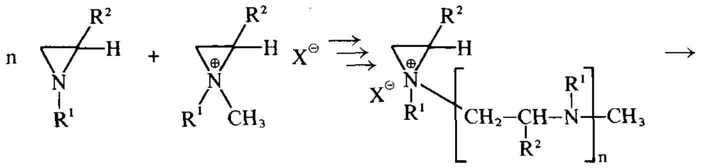
The best results for the polymerization of L and racemic methyl 2-(2-methyl-1-aziridinyl)acetate (**4**) were obtained in mass with dimethyl sulfate (mole fraction $0{,}25 \cdot 10^{-2}$) as initiator at $-15\,°C$ (s. Tab. 1).

On the basis of ring opening reactions of 2-substituted aziridines described in the literature$^{2-4)}$, the polymerization initiated with dimethyl sulfate or boron trifluoride diethyl etherate was expected to propagate mainly by nucleophilic attack of the free aziridine at the methylene carbon of the aziridinium cation, following the scheme.

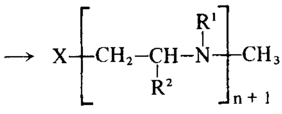
Initation:



Propagation:



Termination:



Tab. 1. Data of the polymerization of methyl 2-(2-methyl-1-aziridinyl)acetate (**4**)

Polymer no.	Monomer (amount in mmol)	Initiator (100 × mole fraction[a])	T/°C	Solvent (volume in cm^3)	$\bar{M}_n$[b]	$\bar{x}_n$[c]
1	DL-	$(CH_3)_2SO_4$ (0,25)	23	none	4300	33
2	DL-	$(CH_3)_2SO_4$ (0,25)	0	none	7750	60
3[d]	DL-	$(CH_3)_2SO_4$ (0,25)	−15	none	17200	133
4	L-	$(CH_3)_2SO_4$ (0,25)	23	none	3150	24
5[d]	L-	$(CH_3)_2SO_4$ (0,25)	−15	none	26000	201
6	L-	$BF_3 \cdot O(C_2H_5)_2$ (5,00)	−15	none	7000	54
7	L (15)	$(CH_3)_2SO_4$ (0,25)	−78	toluene (10)	7400	57
8	DL (20)	$BF_3 \cdot O(C_2H_5)_2$ (5,00)	0	CH_3CN (20)	3500	27
9	DL (30)	$BF_3 \cdot O(C_2H_5)_2$ (5,00)	0	CH_3CN (10)	4000	31
10	DL (20)	$BF_3 \cdot O(C_2H_5)_2$ (5,00)	−15	CH_3CN (2,5)	8000	61
11	DL (20)	$(CH_3)_2SO_4$ (1,00)	23	CH_3CN (50)	2900	22

[a] With respect to monomer concentration.

[b] $\bar{M}_n$ was determined by vapor pressure osmometry (Mechrolab) for molecular weights <8000, by membrane osmometry (Hewlett-Packard) for polymers 3 and 5.

[c] $\bar{x}$ = Degree of polymerization.

[d] For the preparation of polymers 3 and 5 the conversions were 68 and 65%, respectively. Polymer 5 showed $[\alpha]_{D\,HCCl_3}^{25°C} = -49{,}7°$.

In the case of an optically active 2-substituted aziridine, the S_N2 reaction at the ring methylene group CH_2 should leave unaffected the configuration of the asymmetric substituted carbon atom[2,3].

It will be shown in the present paper that the assumption of a stereoregular ring opening reaction is indeed correct; it was proved on the basis of

(1) a comparison of ^{13}C NMR spectra of poly[*N*-(methoxycarbonylmethyl)-iminopropylene]s (**5**), from L- and racemic aziridine **4**, respectively;

(2) a ^{13}C NMR analysis of the ring opening product derived from the optically active monomer with anhydrous hydrochloric acid;

(3) measurements of specific molar rotation after ring reclosure of the salt with base.

^{13}C NMR study of the polyesters **5**

The ^{13}C spectra of polymers **5** obtained from L- and racemic aziridines **4** are shown in Fig. 1. The observed values of the main absorptions of

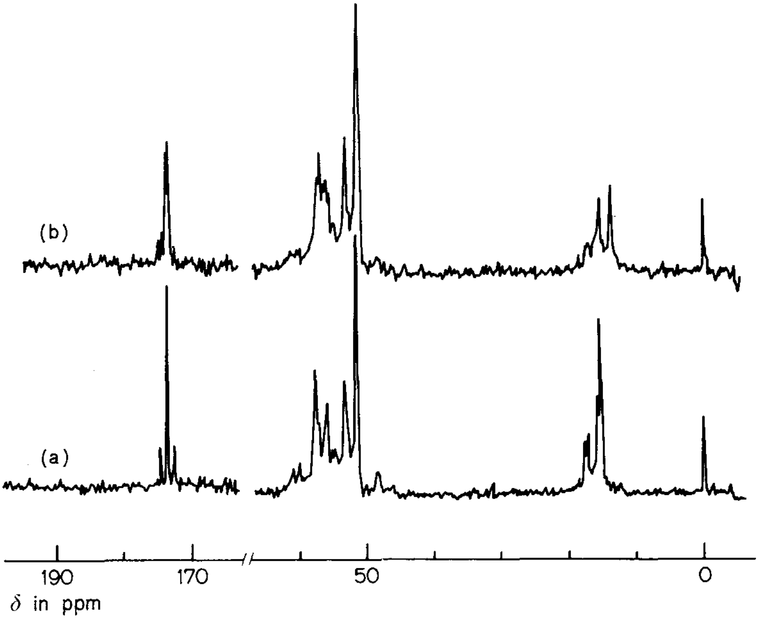
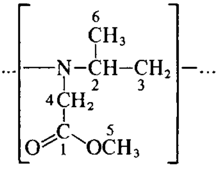
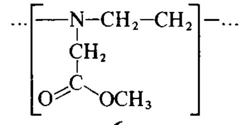


Fig. 1. ^{13}C NMR spectra of L-poly[*N*-(methoxycarbonylmethyl)iminopropylene] (L-**5**) (a) and racemic poly[*N*-(methoxycarbonylmethyl)iminopropylene] (D,L-**5**) (b)

the constitutional repeating unit are given in Tab. 2. For comparison the δ values of the constitutional repeating unit in poly[*N*-(methoxycarbonylmethyl)iminoethylene] (**6**) are also given.



5



6

Tab. 2. Values of ^{13}C chemical shifts of L-**5**, D,L-**5**, and **6** (cf. Fig. 1)

Polymer	^{13}C Chemical shifts δ in ppm of					
	C^1	C^2	C^3	C^4	C^5	C^6
L-**5**	173,4	57,4	55,8	52,9	51,2	15,3
D,L-**5**	173,4	57,4	55,7	52,9	51,2	15,3
	173,2					13,6
6	172,4	53,0	53,0	55,2	51,4	—

The ^{13}C absorptions of carbons 2, 3, 4, and 5 occur between 50 and 58 ppm, and this crowded region of the spectrum is, as a matter of fact, not informative.

On the other hand, the $\underline{C}{=}O$ and $\underline{C}H_3{-}C$ signals are more interesting since each of those carbons displays one main absorption at δ 173,4 and δ 15,3, respectively, in polymer L-**5** and two in racemic **5** at δ 173,4 and 173,2 and δ 15,3 and 13,6. This is a good evidence that the polymer obtained from L-**4** is constituted mainly of the same repeating unit, whereas the polymer obtained from racemic **4** contains an equal amount of two types of diads, the meso diad absorbing at 173,4 and 15,3 and the racemic one with absorptions at 173,2 and 13,6. Besides the main signals of the $\underline{C}{=}O$ and $\underline{C}H_3{-}C$ carbons, smaller peaks are visible. Considering the relatively high degree of polymerization of the two polymers being 133 (D,L-**5**) and 201 (L-**5**), these peaks cannot be attributed to carbons of terminal units. An expansion of the $\underline{C}{=}O$ absorption is shown on Fig. 2.

For polymer L-**5**, two small side signals of comparable intensities are observed at δ 174,3 and 172,4; the integrated areas of the three peaks are

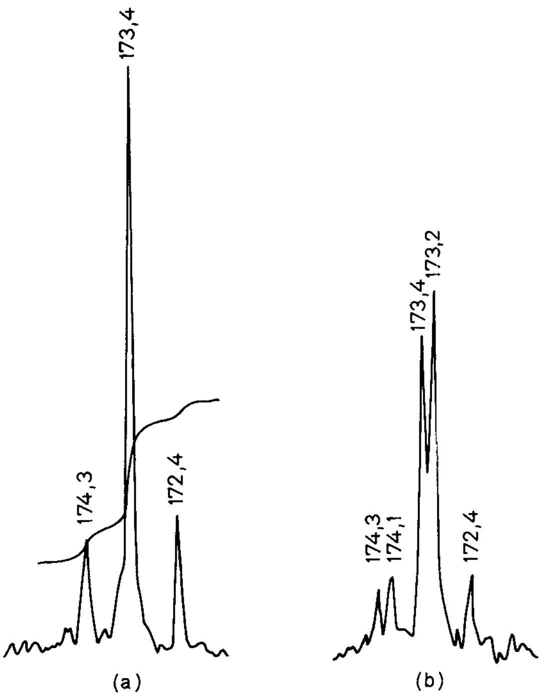


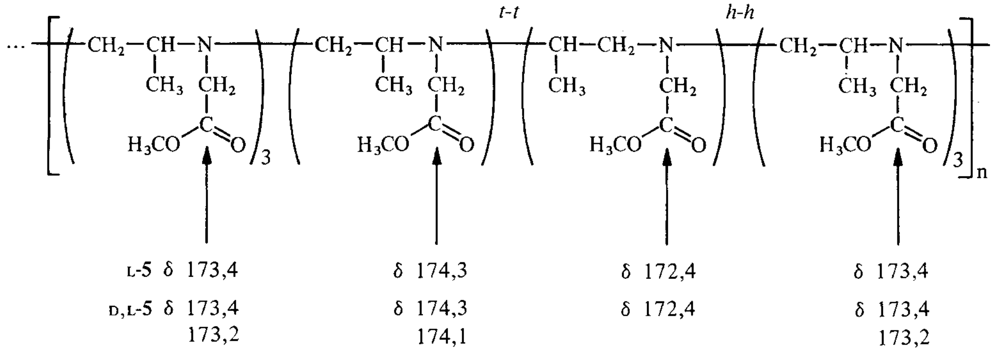
Fig. 2. Expanded ^{13}C NMR spectra of the carbonyl carbon pattern (a): L-polyester **5**; (b): racemic polyester **5**

in a ratio 1/6/1. To rationalize this pattern, we assume an irregularity in the mode of addition:

if the nucleophilic attack of the aziridine occurs once every 7 additions at the substituted methine carbon of the aziridinium cation, tail to tail linkage necessarily must result followed by a head to head junction when the normal S_N2 reaction at the CH_2 again takes place.

The $\underline{C}=O$ absorption of the methoxycarbonylmethyl group linked to the nitrogen is, thus, sensitive to the nature of the carbon (CH_2 or $CH—CH_3$) on both sides of the nitrogen. The $\underline{C}=O$ at δ 172,4 is assigned to the head to head linkage by comparison with the value obtained for the $\underline{C}=O$ in **6** (δ 172,4).

In the racemic polymer **5**, the $\underline{C}=O$ absorption consists of 5 lines (Fig. 2), two small signals at δ 174,3 and 174,1, two main lines at δ 173,4 and δ 173,2 and one small line at δ 172,4. This can be explained in terms of a sensitivity of the $C=O$ not only to the nature of the carbons adjacent to the nitrogen, but also to the configurations (meso or racemic) of the two closest secondary carbons (Fig. 3).



t-t = Tail to tail linkage
h-h = Head to head linkage

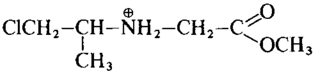
Fig. 3. Assignment of the signals of carbonyl carbon atoms in ^{13}C NMR spectra of L-**5** and D,L-**5** in terms of a sequence of 6 head to tail for 1 tail to tail and 1 head to head linkages

The L polymer **5** shows only one low field signal at δ 174,3 indicating that the nucleophilic attack at the methine carbon does not involve its racemization (excluding S_N1). We can, thus, state that the S_N2 attack of the aziridine at the aziridinium cation occurs to 85–90% at the methylene carbon and to 10–15% at the methine carbon, very likely with inversion of its configuration.

It has been proved indeed that Walden inversion occurs by ring opening of 2,3-disubstituted aziridines with nucleophilic reagents[5-7], the *cis*-aziridines giving rise to *threo* compounds, the *trans*-aziridines to *erythro* compounds. Even hydrolysis of optically active 2-ethylaziridine in concentrated acidic aqueous solution was reported to occur with Walden inversion[8].

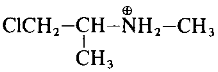
Ring opening with hydrochloric acid in anhydrous diethyl ether

Ring opening reaction of the L-aziridine **4** was carried out with a saturated solution of hydrochloric acid in diethyl ether. In this reaction, the nucleophilic attack of the chloride anion also occurs at the methylene carbon giving rise to *N*-(1-chloromethylethyl)-*N*-(methoxycarbonylmethyl)ammonium salt (**7**) in 85% yield, in agreement with data reported for 2-methylaziridine[9]. The salt **7** was identified by comparing its ^{13}C chemical shift values with the values calculated for *N*-(1-chloromethylethyl)-*N*-methylammonium salt (**8**) and for *N*-(2-chloropropyl)-*N*-methyl ammonium salt (**9**).



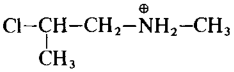
$\mathrm{ClCH_2{-}\underset{CH_3}{CH}{-}\overset{\oplus}{N}H_2{-}CH_2{-}C(=O)OCH_3}$

7



$\mathrm{ClCH_2{-}\underset{CH_3}{CH}{-}\overset{\oplus}{N}H_2{-}CH_3}$

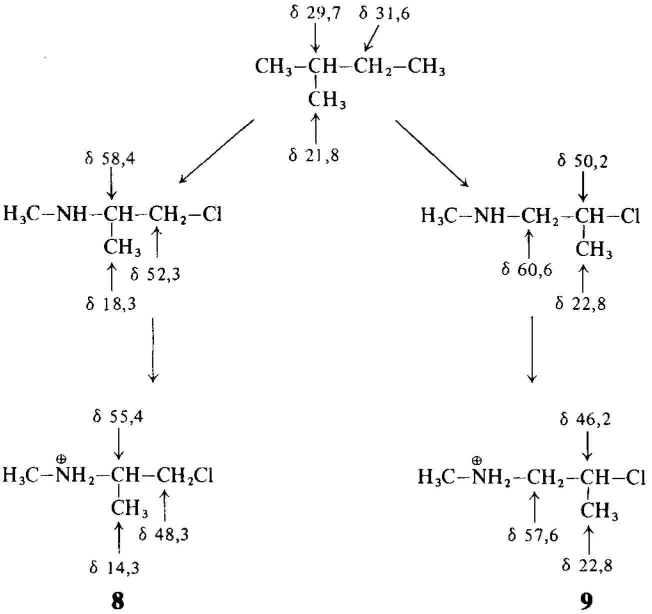
8



$\mathrm{Cl{-}\underset{CH_3}{CH}{-}CH_2{-}\overset{\oplus}{N}H_2{-}CH_3}$

9

The calculations were done by use of empirical additive parameters*), giving the influence of the replacement of a CH_3 group by a polar substituent on the ^{13}C values at carbons α, β, and γ in 2-methylbutane10).

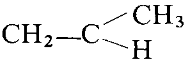


The experimental chemical shift values of salt **7** in D_2O are:

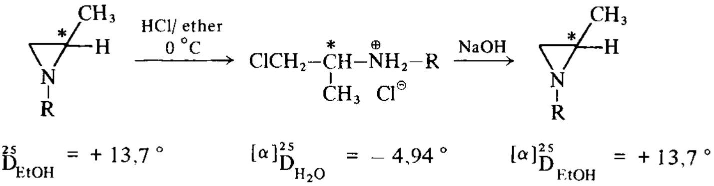
$\underline{C}H_3$—CH: δ 14,5
$\underline{C}$H : δ 55,5
$\underline{C}H_2$: δ 45,5 and 45,2
$\underline{C}$=O: δ 168,5
$O\underline{C}H_3$: δ 54,5

---

*) Replacement of CH_3 by Cl: C_α: +23, C_β: +2, C_γ: −1 ppm; replacement of CH_3 by $NHCH_3$: C_α: +27, C_β: −2,5, C_γ: −1 ppm. Protonation of an amine causes upfield shifts to C_α: −3, C_β: −4 ppm.

The values observed for carbons  $CH_2{-}C\begin{smallmatrix}\diagup CH_3\\ \diagdown H\end{smallmatrix}$ are nearly equal to those calculated for structure **8**.

A further proof that the ring opening reaction of L-aziridine **4** occurs with retention of configuration of the asymmetric carbon was afforded by the ring reclosure of salt **7** in the presence of sodium hydroxide; L-**4** was obtained with the same specific molar rotation as the initial aziridine.



$[\alpha]^{25}_{D_{EtOH}} = +13{,}7°$ $[\alpha]^{25}_{D_{H_2O}} = -4{,}94°$ $[\alpha]^{25}_{D_{EtOH}} = +13{,}7°$

Conclusion

The experimental data reported in the present paper concerning the ring cleavage of an optically active 1-alkyl-2-methyl aziridine, during its polymerization initiated by dimethyl sulfate and in its reaction with anhydrous hydrochloric acid, are consistent with the data mentioned previously by several authors[8,9,11,12].

Our spectroscopic data afford stereochemical evidence for a main S_N2 attack at the methylene carbon atom and only to a small extent at the substituted methine group with Walden inversion.

Experimental Part

NMR Spectroscopy: ^{13}C NMR spectra were recorded with a "VARIAN XL 100-15" equipped for F.T. spectroscopy and working at a frequency of 25,16 MHz. Spectra of the polyesters were taken in hexadeuterobenzene and referred to TMS.

Methyl 2-(2-methyl-1-aziridinyl)acetate (**4**)

(a) *Alanine ethylester* (**1**)[13,14]: Dry HCl gas was passed through a suspension of alanine (1 mol) in 1,5 l absolute ethanol until all the solid was dissolved. The solution was further saturated at 0–5 °C, and then kept at room temp. for 4 h. After evaporation of the solvent (<50 °C) the residue was dissolved in the minimum absolute ethanol and absolute ether added. Yield: 65%. The free base can be isolated by adding a cold solution of sodium hydroxide to the salt suspended in ether. The water layer was extracted several times with ether; the combined ethereal extracts were dried and evaporated; the residue was distilled i. vac.; D,L-**1**: bp 48 °C at ≈11 mbar; L-**1**: bp 61 °C at ≈24 mbar.

(b) *2-Amino-1-propanol* (**2**)¹⁵⁾: Alanine ethylester (1 mol) in absolute ether (1 l) was added under stirring to a suspension of $LiAlH_4$ (75 g) in absolute ether (1,5 l). The mixture was refluxed for 4 h after complete addition. The complex was then decomposed by adding water and extracted. The crude product was purified by distillation.

L-**2**: bp 84–85 °C at ≈23 mbar; $[\alpha]^{25}_{D_{EtOH}} = +21{,}2°$.

D,L-**2**: bp 71–72 °C at ≈11 mbar.

(c) *2-Methylaziridine* (**3**): The sulfate was prepared by adding conc. sulfuric acid (38 g) to **2** (50 g) in 1,2-dichlorobenzene (100 ml) at a temp. <60 °C¹⁶⁾. The solvent was distilled off and the residue treated with 25% NaOH. The crude product was then distilled. By adding KOH to the distillate, **3** separates; bp 66–67 °C for both isomers, L-**3**: $[\alpha]^{25}_{D_{EtOH}} = -12{,}5°$.

(d) *Methyl 2-(2-methyl-1-aziridinyl)acetate* (**4**): Methyl chloroacetate (1 mol) was added dropwise to **3** (1 mol) in triethylamine (1,5 mol) under cooling (0–5 °C) and stirring¹⁷⁾. The precipitated salt was filtered off after 24 h and the solution was distilled.

D,L-**4**: bp 58,7 °C at ≈13 mbar.

L-**4**: bp 57 °C at 14 mbar; $[\alpha]^{25}_{D_{EtOH}} = +13{,}7°$.

Polymerizations: All polymerizations were carried out in a closed tube in an argon atmosphere. The initiator was added at the required temp. and the polymerization was continued for 5 days. The polymers were purified by dissolving in benzene and precipitating in hexane at 0 °C. This procedure was repeated twice. After drying, the polymers are sticky rubbery products.

Ring opening reaction: A saturated solution of hydrochloric acid in anhydrous ether was added dropwise at 0 °C to a solution of L-methyl 2-(2-methyl-1-aziridinyl)acetate in dry acetone. The precipitate was isolated after one night at this temp. and crystallized from methanol/ether; mp 133–134 °C; $[\alpha]^{25}_{D_{H_2O}} = -4{,}94°$; yield 85%.

Acknowledgment is due to the *Service of Scientific Programmation (Belgium)* for a fellowship of one of the authors (C.S.) and for financial support.

---

¹⁾ G. Smets, Pure Appl. Chem. **1**, 1 (1974)

²⁾ Y. Minoura, M. Takeboyashi, C. C. Price, J. Am. Chem. Soc. **81**, 4689 (1959)

³⁾ K. Tsuboyama, S. Tsuboyama, M. Yanagita, Bull. Chem. Soc. Jpn. **40**, 2954 (1967)

⁴⁾ O. C. Dermer, G. E. Ham, "Ethylenimine and other Aziridines", Acad. Press, New York 1969

⁵⁾ R. Ghirardelli, H. J. Lucas, J. Am. Chem. Soc. **79**, 734 (1957)

(6) T. Flogia, L. M. Gregory, G. Maerker, S. F. Osman, J. Org. Chem. **36,** 1068 (1971)

(7) R. Wohl, D. Headly, J. Org. Chem. **37,** 4401 (1972)

(8) H. Wenghoefer, K. Lee, R. Srwastava, G. Srimannarayana, L. B. Clapp, J. Heterocycl. Chem. **7,** 1407 (1970)

(9) H. Kakuichi, T. Iyima, Bull. Chem. Soc. Jpn. **46,** 1568 (1973)

(10) G. Levy, G. Nelson, "^{13}C NMR for Organic Chemists", Wiley, New York 1972

(11) H. Möhle, R. Feil, Tetrahedron **27,** 1033 (1971)

(12) V. R. Gaertner, J. Heterocycl. Chem. **8,** 177 (1971)

(13) Greenstein, Winitz, "Chemistry of Amino Acids", Wiley, New York 1973, vol. 2, p. 926

(14) E. Fischer, Ber. Dtsch. Chem. Ges. **34,** 442 (1901)

(15) P. Karrer, P. Portman, M. Suter, Helv. Chim. Acta **31,** 1617 (1948)

(16) H. Bestian, „Methoden der Organischen Chemie", Houben-Weyl, edited by E. Müller, Thieme Verlag, Stuttgart 1958, vol. XI/2, p. 228

(17) H. Bestian, Justus Liebigs Ann. Chem. **566,** 223 (1950)