

spectrophotometrically. In no case was a spectrum obtained that appeared to contain anything but thianthrene and monoxide. Computation on this basis always agreed well with the weight of the portion analyzed. A summary of product balance for solid analyses is given in Table II. A summary of the total products is given in Table I.

The Tan Solids.—Part of each of the solids from runs 10, 12, 13a, 17 and 18 was placed under 95% ethanol and warmed at 50° for several hours. The solids, except that from run 12, did not dissolve completely. The ultraviolet spectra of the ethanol solutions differed from that of VI. Solutions of the solids from runs 10, 12, 13a and 18 had broad shoulders at 312 and 250 m μ and a broad maximum at 239 m μ . The solution of the solid from run 17 had a broad shoulder at 312 m μ , a sharp shoulder at 276.5 m μ , humps at 250 and 239 m μ , and increasing absorption at lower wave lengths. The dioxide VI has sharp shoulders at 269.5 and 276.5 m μ with increasing absorption at lower wave lengths.

Solutions of the solids in 96.9% sulfuric acid were made by weighing 3 mg. of each and dissolving in 25 ml. of acid. Assuming the molecular weight to be 232 (V) these solutions were approx. $5 \times 10^{-4} M$. Absorption spectra were run on solutions diluted to $10^{-4} M$. Each solution had a broad

maximum near 900 and 1000 m μ . Each of the solutions for runs 10, 13a, 17 and 18 had a peak in the range 594–598 m μ and a shoulder at 560 m μ . On the other hand, the solution for run 12 had its maximum at 546 m μ showing signs of absorption on one side of the peak near 590 m μ . The optical densities at the large peaks of the 10, 12, 13a and 18 solutions were about the same and double that of the 17 solution.

E.s.r. Spectra.—A Varian Associates spectrometer was used with 100 Kc. field modulation. Varian Associates aqueous-type cells were used. The spectra were calibrated with a solution of potassium nitrosodisulfonate (K and K Laboratories) in saturated sodium carbonate solution. It is interesting to note that the shape and line width of a freshly made solution of III in sulfuric acid did not differ from a solution that was 17 months old.

Acknowledgments.—This work was generously supported by the Robert A. Welch Foundation, Houston, Texas, and the United States Air Force (AFOSR Grant AF-AFOSR-61-48). Helpful discussions with Dr. Fausto Ramirez are acknowledged with pleasure.

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS, URBANA, ILL.]

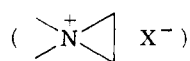
Small Charged Rings. II. The Synthesis of Aziridinium Salts^{1–3}

BY NELSON J. LEONARD AND KLAUS JANN

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In a reaction patterned after the nucleophilic attack of diazomethane on the ketone carbonyl, we have found that a similar attack on a ternary iminium perchlorate (I) or fluoborate can give the corresponding aziridinium salt II in high yield. The prototype for the general method of synthesis of aziridinium salts was the conversion of N-cyclohexylidenepyrrolidinium perchlorate (IV) to 2,2-pentamethylene-1,1-tetramethyleneaziridinium perchlorate (V). Characterization of the three-membered ring was achieved by chemical means, including thiosulfate titration, hydrolysis, alcoholysis and hydrogenolysis, all suggesting new synthetic utility, and by physical methods, including molecular weight determination and infrared and n.m.r. spectroscopy. Other diazoalkanes and ternary iminium salts react in the same manner to give variously substituted aziridinium salts.

The first postulate of the existence of an ethylimonium or aziridinium compound was that of



Marckwald and Frobenius⁴ for the product of treatment of 1- β -chloroethylpiperidine hydrochloride with limited base. The conditions of the reaction and of product purification were such as to suggest a bis-piperizinium salt structure as more reasonable.⁵ Evidence has been provided for the aziridinium cation as an intermediate in the hydrolysis of certain α -bromo- β -3°-aminoketones,^{6–8} and it has been recognized as the key intermediate in chemical reactions of the nitrogen mustards,

β -haloethyl-*tert*.-amines.^{9–18} Moreover, aziridinium cation intermediates (EI-ions) may serve as pharmacologically active species^{9,19–23} in alkylating functional groups of compounds of biological importance, in adrenergic blocking and in antiadrenaline and antihistamine activity.

Thus far, aziridinium intermediates have been trapped only in the form of unwieldy salts.^{10,20,22,24,25}

(1) For the first article in the series, see N. J. Leonard and K. Jann, *J. Am. Chem. Soc.*, **82**, 6418 (1960).

(2) This investigation was supported by a research grant (USPHS-RG5829) from the National Institutes of Health, U. S. Public Health Service.

(3) Presented at the Seventeenth National Organic Chemistry Symposium of the American Chemical Society, June, 1961, Bloomington, Ind.; see Abstracts, pp. 1–10.

(4) W. Marckwald and O. Frobenius, *Ber.*, **34**, 3544 (1901).

(5) H. Bestian in "Methoden der Organischen Chemie (Houben-Weyl)," Georg Thieme Verlag, Stuttgart, Germany, 1958, Vol. XI/2, p. 234.

(6) N. H. Cromwell and D. J. Cram, *J. Am. Chem. Soc.*, **65**, 301 (1943).

(7) N. H. Cromwell and I. H. Witt, *ibid.*, **65**, 308 (1943).

(8) We have recently been able to isolate perchlorate and fluoborate salts containing a ketoaziridinium cation of the type postulated^{4,7} (N. J. Leonard and R. L. Booth, unpublished results).

(9) A. Gilman and F. S. Phillips, *Science*, **103**, 409 (1946).

(10) C. Golumbic, J. S. Fruton and M. Bergmann, *J. Org. Chem.*, **11**, 518 (1946), and following papers.

(11) J. F. Kerwin, G. E. Ulyot, R. C. Fuson and C. L. Zirkle, *J. Am. Chem. Soc.*, **69**, 2961 (1947).

(12) P. D. Bartlett, S. D. Ross and C. G. Swain, *ibid.*, **69**, 2971 (1947).

(13) P. D. Bartlett, J. W. Davis, S. D. Ross and C. G. Swain, *ibid.*, **69**, 2977 (1947).

(14) S. D. Ross, *ibid.*, **69**, 2982 (1947).

(15) P. D. Bartlett, S. D. Ross and C. G. Swain, *ibid.*, **71**, 1415 (1949).

(16) B. Cohen, E. R. Van Artsdalen and J. Harris, *ibid.*, **70**, 281 (1948).

(17) A. W. Hay, A. L. Thompson and C. A. Winkler, *Can. J. Research*, **26B**, 175 (1948).

(18) E. Boyland and R. Nery, *J. Chem. Soc.*, 679 (1961).

(19) F. C. Ferguson, Jr., W. C. Wescoe and P. Theodore, *J. Pharmacol. Exptl. Therap.*, **100**, 100 (1950).

(20) N. B. Chapman and J. W. James, *J. Chem. Soc.*, 2103 (1954).

(21) S. C. Harvey and M. Nickerson, *J. Pharmacol. Exptl. Therap.*, **109**, 328 (1953).

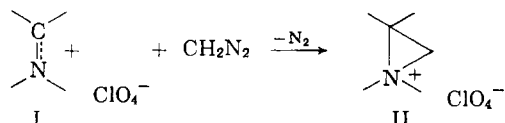
(22) J. D. P. Graham, *Brit. J. Pharmacol.*, **12**, 489 (1957).

(23) B. Belleau, *J. Med. Chem.*, **1**, 327, 343 (1959).

(24) W. E. Hanby, G. S. Hartley, E. O. Powell and H. N. Rydon, *J. Chem. Soc.*, 519 (1947).

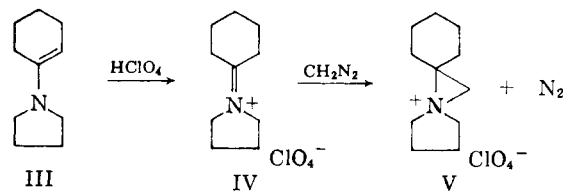
(25) N. B. Chapman, J. W. James, J. D. P. Graham and G. P. Lewis, *Chemistry & Industry*, 805 (1952).

Since the charged three-membered ring is known to open readily in the presence of most anions, including halides,^{12,13,26-28} we felt that a general method of synthesis which would permit the isolation of aziridinium compounds should be guided toward combinations of the aziridinium cation with simple, very weakly nucleophilic anions such as perchlorate and fluoroborate. Ternary iminium perchlorates (I) are readily available as precursors by acidification of the corresponding enamines, and iminium salts are known to undergo nucleophilic attack with a variety of reagents.²⁹⁻³¹ These facts, together with the experience of three-



membered ring formation by the action of diazomethane on certain C=S, C=O and C=C functions,³² led us to the method (I→II), which has proved both general and efficient.

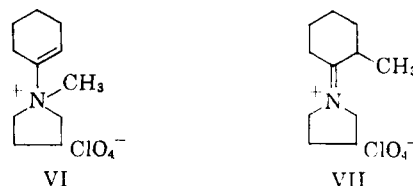
The prototype for aziridinium salt (II) synthesis was N-cyclohexylidene pyrrolidinium perchlorate (IV), obtained in 93% yield by treatment of 1-N-pyrrolidylcyclohexene (III) in ether with aqueous ethanolic perchloric acid. Compound IV reacted



rapidly with diazomethane in methanol-ether solution at -10° , indicated by evolution of nitrogen and decolorization of the solution. When the solution was cooled to -40° , a new compound, $C_{11}H_{20}ClNO_4$, m.p. $133-134^\circ$, was obtained in 93% yield. The product showed no infrared max-

ima corresponding to $-N-H$ and $C=N^+$, and the ultraviolet spectrum in water showed no absorption maximum down to about $192 m\mu$. Although we favored the structure V for the diazomethane product, that is, 2,2-pentamethylene-1,1-tetramethyleneaziridinium perchlorate (or 5-azoniadispiro[4.0.5.1]-dodecane perchlorate),³³ at the outset we

considered the isomeric structures N-(cyclohexen-1-yl)-N-methylpyrrolidinium perchlorate (VI) and N-2-methylcyclohexylidenepyrrolidinium perchlorate (VII) as possible alternatives, since any dissociation



of IV into perchloric acid and base could conceivably result in methylation of the system using diazomethane.³⁴ Compound VII was ruled out

because it would have a typical $>C=N^+<$ absorption maximum in the infrared.³⁵ The double bond in VI would be difficult to detect, by contrast, on the basis of experience in this Laboratory^{36,37} and in that of Opitz,^{38,39} but reliance on other physical evidence, especially n.m.r. spectra, and on chemical behavior clearly established the structure of the diazomethane product as that of 2,2-pentamethylene-1,1-tetramethyleneaziridinium perchlorate (V). The corresponding fluoroborate salt, made from the iminium fluoroborate (IV, BF_4^- in place of ClO_4^-) and diazomethane, possesses properties similar to V and the advantage of greater solubility in organic solvents.

The presence of the aziridinium ring in V was shown first by thiosulfate titration^{10,27} and subsequently by hydrolysis and alcoholysis.⁴⁰ The typical ring-opening reaction of V with thiosulfate proceeded more slowly than that of the nitrogen mustards at room temperature. Reaction was rapid, however, at 50° and pH 5.0. Distinction between the three-membered ring structure and that of a six-membered ring bis-piperazinium salt^{4,41} with the same empirical formula was made possible by the positive thiosulfate titration and by molecular weight determinations in acetone at 30° , utilizing a vapor pressure osmometer employing thermistors, with 1,1-dimethylpyrrolidinium perchlorate as a model. The molecular weight values were constant for $C_{11}H_{20}ClNO_4$ and not for $(C_{11}H_{20}ClNO_4)_2$.

The hydrolysis of 2,2-pentamethylene-1,1-tetramethyleneaziridinium perchlorate (V) was slow at room temperature and led to the development of an amine grouping with $pK_a' 10.2$. The methanolysis was complete in one hour at reflux temperature, and the major product was isolated in pure form, $C_{12}H_{24}ClNO_5$, m.p. $122-123^\circ$, in 87% yield. Analysis showed the presence of a methoxyl group.

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(27) B. Cohen, E. R. Van Artsdalen and J. Harris, *ibid.*, **74**, 1875, 1878 (1952).

(28) It should be mentioned here that a crystalline aziridine hydrochloride $\left(\begin{smallmatrix} H \\ \diagup \end{smallmatrix} N^+ \begin{smallmatrix} \diagdown \\ \end{smallmatrix} \right) Cl^-$ has been isolated by W. A. Skinner, A. P. Martinez, H. F. Gram, L. Goodman and B. R. Baker, *J. Org. Chem.*, **26**, 148 (1961); see also G. F. Hennion and P. E. Butler, *ibid.*, **27**, 2088 (1962).

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(31) N. J. Leonard and A. S. Hay, *ibid.*, **78**, 1984 (1956).

(32) B. Eistert in "Newer Methods of Preparative Organic Chemistry," Interscience Publishers, Inc., New York, N. Y., 1948, p. 513 ff.

(33) International Union of Pure and Applied Chemistry. Definitive Rules for Nomenclature of Organic Chemistry (IUPAC 1957 Rules), *J. Am. Chem. Soc.*, **82**, 5545 (1960), especially p. 5572.

(34) E. Müller, H. Huber-Emden and W. Rundel, *Ann.*, **623**, 34 (1959).

(35) N. J. Leonard and V. W. Gash, *J. Am. Chem. Soc.*, **76**, 2781 (1954); also N. J. Leonard and B. Müller, unpublished results.

(36) N. J. Leonard, A. S. Hay, R. W. Fulmer and V. W. Gash, *J. Am. Chem. Soc.*, **77**, 439 (1955).

(37) N. J. Leonard, C. K. Steinhardt and C. Lee, *J. Org. Chem.*, in press.

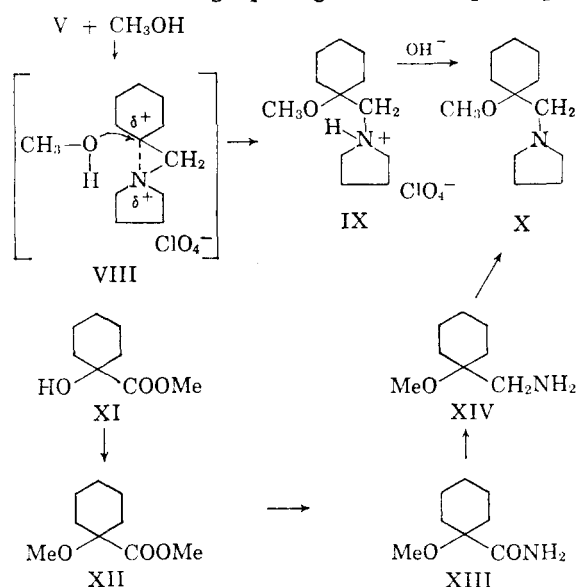
(38) G. Opitz and H. Mildenerberger, *Ann.*, **649**, 26 (1961).

(39) G. Opitz, H. Mildenerberger and H. Suhr, *ibid.*, **649**, 47 (1961).

(40) Reactions of substituted ethylenimines in the presence of acid served as a useful guide in this work, e.g., G. J. Buist and H. J. Lucas, *J. Am. Chem. Soc.*, **79**, 6157 (1957); J. E. Earley, C. E. O'Rourke, L. B. Clapp, J. O. Edwards and B. C. Lawes, *ibid.*, **80**, 3458 (1958).

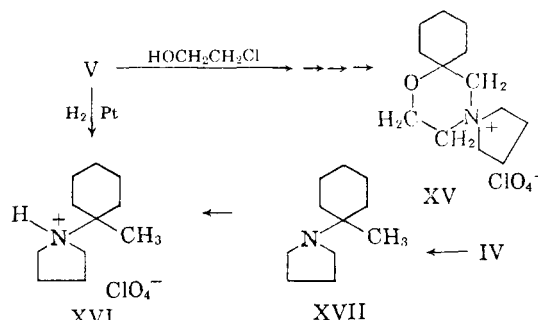
(41) K. H. Slotta and R. Behnisch, *Ann.*, **497**, 170 (1932).

The new $\text{—N}^+\text{—H}$ group, suggested by the pK_a' of 10.0 in water, was indicated by the infrared maximum at 3125 cm^{-1} and underwent exchange to $\text{—N}^+\text{—D}$ (2350 cm^{-1}) with deuterium oxide. The n.m.r. spectrum of the methanolysis product in deuteriochloroform was consistent with the assignment of the structure as N-(1-methoxycyclohexylmethyl)-pyrrolidine perchlorate (IX), but the n.m.r. spectrum of the corresponding base (X) was more definitive since, unlike the $\text{CH}_2\text{—N}^+$ proton signals, the $\text{CH}_2\text{—N}$ signals did not interfere with that of $\text{CH}_3\text{—O}$. The fact that there was no signal at lower field than that for $\text{CH}_3\text{—O}$ (τ value 6.89)⁴² indicated that ring opening had taken place pre-



dominantly in an $\text{S}_{\text{N}}1$ manner (VIII), since attack at the methylene carbon would have produced the grouping $\text{CH}_2\text{—O—CH}_3$, which should have an additional proton signal downfield from that for $\text{CH}_3\text{—O}$.⁴³ The synthesis of N-(1-methoxycyclohexylmethyl)-pyrrolidine (X) by an unequivocal route left no doubt as to its identity with the methanolysis product of V. Methyl 1-hydroxycyclohexanecarboxylate (XI) was methylated by treatment with sodium hydride followed by methyl iodide, and the resulting methyl 1-methoxycyclohexanecarboxylate (XII) was converted to 1-methoxycyclohexanecarboxamide (XIII) with ammonia. Reduction of the amide XIII with lithium aluminum hydride yielded (1-methoxycyclohexyl)-methylamine (XIV), and addition of the pyrrolidine cycle through the use of 1,4-dibromobutane and sodium carbonate gave X. Ethanolysis of the aziridinium salt V proceeded smoothly during refluxing for one hour, and the $\text{C}_{13}\text{H}_{26}\text{ClNO}_5$ product was assigned

the structure N-(1-ethoxycyclohexylmethyl)-pyrrolidine perchlorate by analogy with the methanol product. As further demonstration of the synthetic possibilities of the solvolysis reaction, the aziridinium salt V was heated with ethylene chlorohydrin; sequential liberation of the free base, cyclization and conversion to the perchlorate salt, without isolation of intermediates, yielded 2,2-pentamethylene-4,4-tetramethylenemorpholinium perchlorate (XV).



Since it is possible to open an ethylenimine ring by catalytic hydrogenation,^{44,45} we subjected 2,2-pentamethylene-1,1-tetramethyleniaziridinium perchlorate (V) in methanol to hydrogenation in the presence of platinum oxide. The major hydrogenolysis product, $\text{C}_{11}\text{H}_{22}\text{ClNO}_4$, m.p. $122\text{--}123^\circ$, in 70% yield, exhibited an infrared maximum at

3100 cm^{-1} characteristic of $\text{—N}^+\text{—H}$ in a perchlorate

and a singlet n.m.r. signal at a τ -value of 8.51 indicative that a C—CH_3 group had been formed. Further proof that hydrogenolysis had occurred at the less hindered C—N bond of the three-membered ring, giving N-(1-methylcyclohexyl)-pyrrolidine perchlorate (XVI), was obtained by synthesis of the latter through the addition of methylmagnesium iodide to N-cyclohexylidenepyrrolidinium perchlorate (IV), isolation of the base XVII and conversion to the salt XVI. The perchlorates from the two sources were identical, as were the picrates.⁴⁶

While the chemical proof of structure of the aziridinium salt V was being developed, the n.m.r. spectra began to play a greater role. By comparison of the spectra (in liquid sulfur dioxide) of precursor IV and product V with model compounds, 1,1-dimethylpyrrolidinium perchlorate (XVIII) and isobutylidenepyrrolidinium perchlorate (XIX), assignments could be made corresponding to the broad proton signal areas (Table I). The important spectral features accompanying the chemical conversion of IV to VI were the disappearance of the signal corresponding to the protons at D, the chemical shift for these having been determined by

(44) K. N. Campbell, A. H. Sommers and B. K. Campbell, *J. Am. Chem. Soc.*, **66**, 82 (1944).

(45) J. V. Karabinos and K. T. Serijan, *ibid.*, **67**, 1856 (1945).

(46) Also made in this Laboratory, by Dr. B. Müller, were the following compounds for direct comparison purposes: N-cyclohexylmethylpyrrolidine perchlorate (would have resulted from hydrogenolysis at the more hindered C—N bond in V), m.p. $181.5\text{--}182.5^\circ$; N-cyclohexyl-N-methylpyrrolidinium perchlorate (would have resulted from the catalytic addition of hydrogen to alternative structure VI), m.p. $129\text{--}129.5^\circ$, depressed the melting point of N-(1-methylcyclohexyl)-pyrrolidine perchlorate; N-cyclohexylpyrrolidinium perchlorate, $\text{C}_{10}\text{H}_{18}\text{ClNO}_4$, m.p. $121.5\text{--}122^\circ$.

(42) G. V. D. Tiers, "Table of τ Values for a Variety of Organic Compounds," Minnesota Mining and Manufacturing Co., St. Paul, Minn., 1958; G. V. D. Tiers, *J. Phys. Chem.*, **62**, 1151 (1958).

(43) N-(1-Methoxymethylcyclohexyl)-pyrrolidine has now been made in this Laboratory by J. V. Paukstelis. The n.m.r. spectrum (CDCl_3) has signals at τ -values of 6.72 ($\text{CH}_3\text{—O}$) and 6.65 ($\text{CH}_2\text{—O}$).

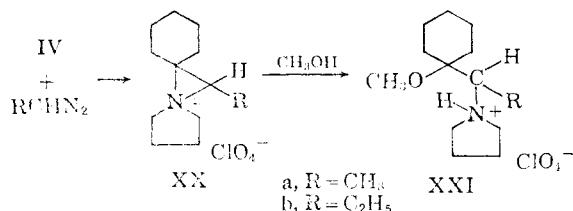
reference to the shift for the single D hydrogen in compound XIX, and the appearance of a new signal, a singlet, at a τ -value of 7.02. The A protons in V and XVIII, adjacent to fully charged nitrogen, were less deshielded than those in XIX and IV, adjacent to partially positive nitrogen of the unsaturated system. The shift of the signal for the E protons in V to higher field than the signal for the A protons in V and XVIII is consistent with their attachment to a three-membered ring.⁴² In order to provide for accurate integration of the n.m.r. signal for the E protons, the fluoroborate salt corresponding to V was used since it was soluble to about 25% in deuteriochloroform compared with 5% for the perchlorate. The integrated n.m.r. spectrum generously provided for us by Prof. J. D. Roberts showed clearly (Fig. 1) that the signal at τ -value 6.98 was due to *two* protons, fully confirming the aziridinium structure.⁴⁷

TABLE I
SIGNAL ASSIGNMENTS (τ -VALUES) IN THE N.M.R. SPECTRA^a

	XIX	IV	V	XVIII
A	5.98 ^b	6.03 ^b	6.55 ^b	6.48 ^b
B	7.80 ^b	7.78 ^b	7.75 ^b	7.70 ^b
C	...	8.15 ^b	8.20 ^b	...
D	7.18 ^b	7.22 ^b
E	7.02	...
F	6.85
G	1.83 ^b
H	8.68 ^b

^a All spectra in liquid SO₂ (compounds recoverable).
^b Center of region.

The accumulation of physical and chemical means for the detection of the aziridinium ring, as in the prototype V, has made it possible to explore the generality of the new method of synthesis, I \rightarrow II. The reaction proceeds with other diazoalkanes. Thus, diazoethane reacted with N-cyclohexylidenepyrrolidinium perchlorate (IV) to give an analogous product, C₁₂H₂₂ClNO₄, m.p. 166–166.5°, having no infrared maxima corresponding to $\text{--}\overset{+}{\text{N}}\text{--H}$ and $\text{>C=}\overset{+}{\text{N}}\text{<}$ but showing a doublet n.m.r. signal at 8.41, 8.51 indicative of methyl



(47) As a corollary, any alternative product, such as VI (as the BF₄⁻ salt), with a new n.m.r. signal corresponding to *three* protons, was ruled out as a possibility.

protons in the grouping CH₃CH< and the total structure 3-methyl-2,2-pentamethylene-1,1-tetramethyleneaziridinium perchlorate (XXa). The signal for the proton on the three-membered ring was located with those for the $\text{N--}\overset{+}{\text{CH}_2}$ protons of the five-membered ring. The additional substitution on the three-membered ring slowed attack at the 3-carbon (thiosulfate, hydrogenolysis). Methanolysis of XXa was slower when compared with V, and the major product was assigned the structure N-[α -(1-methoxycyclohexyl)-ethyl]-pyrrolidine per-

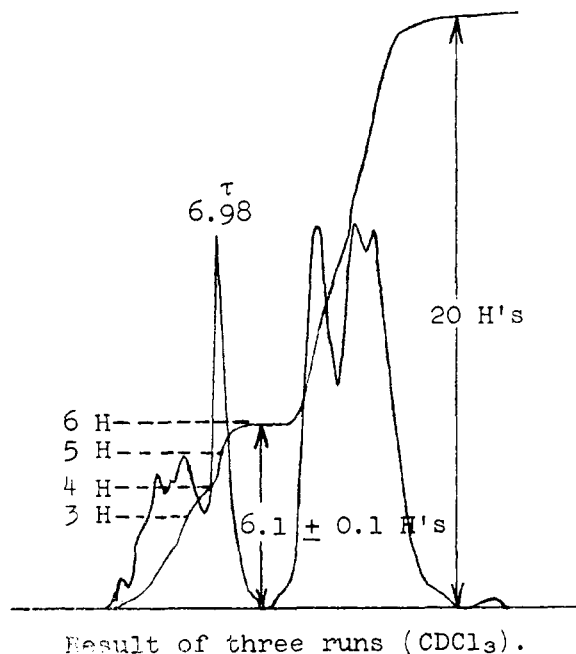


Fig. 1.—Integrated n.m.r. spectrum of C₁₁H₂₀N⁺BF₄⁻. Courtesy of Prof. J. D. Roberts, California Institute of Technology, Pasadena, Calif.

chlorate (XXIa). Diazopropane and IV yielded 3-ethyl-2,2-pentamethylene-1,1-tetramethyleneaziridinium perchlorate (XXb), methanolysis of which yielded N-[α -(1-methoxycyclohexyl)-propyl]-pyrrolidine perchlorate (XXIb) as the probable major product. Another iminium salt which reacted readily with diazomethane was the ring homolog of IV, N-cyclohexylidenepiperidinium perchlorate, prepared in the first instance by treatment of 1-N-piperidylcyclohexene with anhydrous hydrogen bromide in ether and conversion of the bromide salt with silver perchlorate. The product of diazomethane treatment was 1,1-pentamethylene-2,2-pentamethyleneaziridinium perchlorate as indicated by the singlet n.m.r. signal for two protons at a τ -value of 7.03 (in deuteriochloroform) and the absence of infrared maxima corresponding to $\text{--}\overset{+}{\text{N}}\text{--H}$ or $\text{>C=}\overset{+}{\text{N}}\text{<}$. Many additional examples of the reaction of diazoalkanes with ternary iminium salts to yield the corresponding aziridinium salts will be given in succeeding articles, along with further reactions of these three-membered ring compounds, offering wide synthetic utility.

Experimental⁴⁸

N-Cyclohexylenepyrrolidinium Perchlorate (IV).⁴⁹

A 1:1 solution of ethanol-70% perchloric acid was added dropwise to an ice-cooled ether solution of 1-N-pyrrolidylcyclohexene^{50,51} until the mixture was just acid to congo red. The precipitate was recrystallized from absolute ethanol as colorless needles, m.p. 230–231° dec., $\nu_{\text{max}}^{\text{Nujol}}$ 1665 cm.⁻¹,⁵² yield 93%. The n.m.r. spectrum in liquid sulfur dioxide showed peaks at the following τ -values (p.p.m. relative to the internal standard, tetramethylsilane, $\tau = 10$):⁴² 6.03; 7.18; 7.27; 7.78 (pentuplet); 8.15.

Anal. Calcd. for C₁₀H₁₈ClNO₄: C, 47.71; H, 7.21; N, 5.57. Found: C, 47.94; H, 7.26; N, 5.69.

N-Cyclohexylenepyrrolidinium fluoborate, made in similar manner using 1:1 ethanol-48% aqueous fluoboric acid, crystallized as colorless plates from isopropyl alcohol; m.p. 219–221°, $\nu_{\text{max}}^{\text{Nujol}}$ 1670 cm.⁻¹.

Anal. Calcd. for C₁₀H₁₈BF₄N: C, 50.23; H, 7.59; N, 5.86. Found: C, 50.28; H, 7.80; N, 5.80.

2,2-Pentamethylene-1,1-tetramethyleneaziridinium Perchlorate (5-Azoniadispiro[4.0.5.1]dodecane Perchlorate) (V).—A solution of 10.0 g. (0.0397 mole) of N-cyclohexylenepyrrolidinium perchlorate in 700 ml. of absolute methanol maintained at –10° was treated with a slight molar excess of diazomethane in 200 ml. of ether. During the addition nitrogen was evolved and the diazomethane solution was decolorized. The mixture was stirred at –10 to 0° for 30 minutes, then cooled to –40° and filtered, yielding 9.8 g. (93%) of colorless needles, m.p. 132–133°, no infrared

maxima corresponding to $-\text{N}^+-\text{H}$ and $>\text{C}=\text{N}^+<$. A rapid recrystallization from absolute ethanol raised the melting point to 133–134°; n.m.r. τ -values (liquid sulfur dioxide) at: 6.23–6.88; 7.02 (singlet); 7.75; 8.08–8.29. Recently determined values for the aziridinium CH₂-N⁺ proton signal (singlet) of V on the Varian model A-60 are 6.88 (CDCl₃) and 6.91 (CDCl₃ + CH₂Cl₂). The compound was recoverable unchanged from the liquid SO₂. Further treatment of the compound with diazomethane was without effect. The ultraviolet spectrum showed no absorption to about 192 m μ in water (concn. ca. 0.085 mg./ml.).

Anal. Calcd. for C₁₁H₂₀ClNO₄: C, 49.72; H, 7.59; N, 5.27. Found: C, 49.82; H, 7.67; N, 5.28.

Because of the possible action of this aziridinium salt as an alkylating agent, the acute toxicity was determined.⁵³ Fasted mice were dosed per os and observed for 7 days—LD₅₀ \pm SE = 48.96 \pm 2.92 mg./kg. The animals had mild convulsions soon after being treated. Deaths occurred within 2 hours.

2,2-Pentamethylene-1,1-tetramethyleneaziridinium fluoborate⁵⁴ was obtained in similar manner from N-cyclohexylenepyrrolidinium fluoborate in 92% yield, needles from

ethanol, m.p. 110–113°, no infrared maxima corresponding to $-\text{N}^+-\text{H}$ or $>\text{C}=\text{N}^+<$; n.m.r. τ -values (CDCl₃) at:

6.08–6.98; 6.98 (singlet); 7.68, 7.79, 7.90 (multiplet); 8.00–8.81. Recently determined value for the aziridinium CH₂-N⁺ proton signal (singlet) on the Varian model A-60 is 6.93.

Anal. Calcd. for C₁₁H₂₀BF₄N: C, 52.19; H, 7.97; N, 5.53. Found: C, 52.09; H, 8.10; N, 5.65.

Detection of the Three-membered Ring by Titrations.⁵⁵

The titration of 2,2-pentamethylene-1,1-tetramethyleneaziridinium perchlorate with thiosulfate was carried out according to the method of Cohen, Van Artsdalen and Harris.²⁷ The reaction proceeded to the extent of 85% in 10 min. at constant pH 5.0 and 50° with thiosulfate concentration 3.43 $\times 10^{-2}$ molar and the aziridinium salt concentration 6.96 $\times 10^{-3}$ molar. The extent of ring opening was determined by uptake of hydrochloric acid which was added automatically using a Polarad AT-2A titrimeter. Suitable blanks were run. For example, (1) N-cyclohexylenepyrrolidinium perchlorate did not take up thiosulfate under the same conditions; (2) 2,2-pentamethylene-1,1-tetramethyleneaziridinium perchlorate brought to pH 5.0, in the absence of thiosulfate, did not require addition of hydrochloric acid for maintenance of the solution at pH 5.0, nor did thiosulfate alone.

When a solution of 2,2-pentamethylene-1,1-tetramethyleneaziridinium perchlorate in water was maintained at pH \sim 7.1 for 19 days,⁵⁶ a group could be titrated with pKa' 10.2 corresponding to mol. wt. 268 \pm 10 for the initial salt (theor. 265.74) and to hydrolysis of the three-membered ring.

Molecular Weight Determination.—The molecular weight of 2,2-pentamethylene-1,1-tetramethyleneaziridinium perchlorate was determined using thermistors, according to the method of Neumayer.^{57,58} A similar compound, 1,1-dimethylpyrrolidinium perchlorate, mol. wt. 199.64 (see below for characterization), was used as a blank, and since the apparent molecular weight of each ionic compound varied with concentration in acetone, naphthalene was used as the standard substance. The following results were obtained at 30°.

2,2-Pentamethylene-1,1-tetramethyleneaziridinium perchlorate (V)			1,1-Dimethylpyrrolidinium perchlorate (XVIII)		
% by wt. in acetone	Apparent no. av. mol. wt.	α calcd.	% by wt. in acetone	Apparent no. av. mol. wt.	α calcd.
0.375	187	0.42	0.382	137	0.46
1.09	198	.34	1.12	149	.34
2.70	226	.18	2.71	182	.10
5.56	261	.02	5.28	212	..

Graphs of concentration *versus* molecular weight gave virtually parallel plots indicating similar dissociation in acetone. Points obtained by the isothermal distillation method,^{59–61} e.g., 0.020, 183 (for V) and 0.025, 134 (for XVIII), respectively, also fall on the separate curves. The molecular weight values for V are consistent for (C₁₁H₂₀ClNO₄)₁ (265.74) and not for (C₁₁H₂₀ClNO₄)₂ (531.47).

Methanolysis of 2,2-Pentamethylene-1,1-tetramethyleneaziridinium Perchlorate.—A solution of 0.50 g. (1.88 mmoles) of the aziridinium perchlorate in 7.5 ml. of absolute methanol was heated under reflux for 1 hr. Following cooling, ether was added to turbidity. The solid which separated was recrystallized from ethanol-ether yielding colorless plates as the major product, m.p. 122–123°, yield 0.51

(48) All melting points are corrected, boiling points are uncorrected. We are indebted to Mr. Josef Nemeth, Miss Jane Liu, Mr. Gary D. Callahan and Miss Mary Ann Weatherford for the microanalyses. We would also like to thank Mrs. Mary Verkade and Mr. Paul McMahon for the infrared absorption spectra using a Perkin-Elmer model 21 infrared spectrophotometer and Mr. Ben Shoulders and Mr. Oliver W. Norton for the n.m.r. spectra. The n.m.r. spectra were obtained at 60 Mc. with a Varian Associates model V-4300B spectrometer equipped with a superstabilizer. The chemical shifts were determined using tetramethylsilane as an internal standard, obtaining side bands by the application of an audiofrequency signal from an external source. The Varian Associates model A-60 spectrometer was used for some n.m.r. spectra.

(49) A. G. Cook, Ph.D. Thesis, University of Illinois, 1959.

(50) R. C. Terrell, Ph.D. Thesis, Columbia University, 1954.

(51) G. Stork, R. Terrell and J. Szmuszkovicz, *J. Am. Chem. Soc.*, **76**, 2029 (1954).

(52) Mr. J. V. Paukstelis in this Laboratory has found $\nu_{\text{max}}^{\text{MeOH(5.6\%)}}$ 1660 cm.⁻¹ using Connecticut Instrument Corporation IRTRAN matched cells (0.1 mm.).

(53) We are grateful to Dr. K. K. Chen and Dr. R. C. Anderson of Eli Lilly and Co., Indianapolis, Ind., for the pharmacological data.

(54) We are indebted to Dr. J. E. Mulvaney of our Laboratory for this preparation.

(55) Mr. J. V. Paukstelis has verified these experiments and has now determined the products.

(56) We are grateful to Dr. Harold Boaz, Eli Lilly and Co., Indianapolis, Ind., for these observations.

(57) J. J. Neumayer, *Anal. Chim. Acta*, **20**, 519 (1959).

(58) We wish to express our thanks to Dr. J. J. Neumayer for his personal attention to our problem and for the data here recorded.

(59) H. Gysel, W. Padowetz and K. Hamberger, *Mikrochim. Acta*, 192 (1960).

(60) H. Gysel and K. Hamberger, *ibid.*, 254 (1957).

(61) R. Signer, *Ann.*, **478**, 246 (1930).

g. (87%), $\nu_{\text{max}}^{\text{Nujol}}$ 3125 cm^{-1} ($-\text{N}^+-\text{H}$), identified (see below)

as N-(1-methoxycyclohexylmethyl)-pyrrolidine perchlorate (IX); n.m.r. signals at τ -values (CDCl_3): 6.09, 6.16, 6.24 (multiplet); 6.60, 6.70, 6.76; 7.80; 8.08; 8.25; 8.51; $\rho K_a'$ 10.0 (H_2O).

Anal. Calcd. for $\text{C}_{12}\text{H}_{24}\text{ClNO}_5$: C, 48.40; H, 8.12; N, 4.70; OCH₃, 10.42. Found: C, 48.41; H, 8.07; N, 4.63; OCH₃, 10.46.

When the salt was partially exchanged by warming a solution of the perchlorate in deuterium oxide (99.5%), followed by removal of deuterium oxide by freeze-drying, the solid, m.p. 119–122°, showed an $-\text{N}^+-\text{H}$ infrared band reduced in intensity and a new band, $\nu_{\text{max}}^{\text{Nujol}}$ 2350 cm^{-1} ($-\text{N}^+-\text{D}$).

Anal. Calcd. for $\text{C}_{12}\text{H}_{23}\text{DCINO}_5$: C, 48.23; H, 8.09; N, 4.69; atom % D, 4.17. Found: C, 48.21; H, 7.94; N, 4.85; atom % D, 3.35, 3.38.

The free base which was liberated from the methanolysis product, N-(1-methoxycyclohexylmethyl)-pyrrolidine perchlorate, m.p. 122–123°, had b.p. 133° (13 mm.), n_D^{20} 1.4806, with n.m.r. signals at τ -values (CDCl_3) 6.89 for CH_2-O and 7.62 for $\text{O}-\text{C}-\text{CH}_2-\text{N}$.

Anal. Calcd. for $\text{C}_{12}\text{H}_{23}\text{NO}$: C, 73.04; H, 11.75; N, 7.10. Found: C, 73.00; H, 11.79; N, 6.89.

Ethanolysis of 2,2-Pentamethylene-1,1-tetramethyleneaziridinium Perchlorate.—A solution of 0.45 g. (1.69 mmoles) of the aziridinium perchlorate in 10 ml. of absolute ethanol was heated under reflux for 1 hr. Ether was added and the solid which separated on cooling was recrystallized from ethanol-ether as colorless prisms (major product),

m.p. 93–94°, yield 0.39 g. (78%), $\nu_{\text{max}}^{\text{Nujol}}$ 3100 cm^{-1} ($-\text{N}^+-\text{H}$),

by analogy assigned the structure N-(1-ethoxycyclohexylmethyl)-pyrrolidine perchlorate.

Anal. Calcd. for $\text{C}_{13}\text{H}_{26}\text{ClNO}_5$: C, 50.07; H, 8.41; N, 4.49. Found: C, 50.15; H, 8.65; N, 4.44.

Methyl 1-Methoxycyclohexanecarboxylate (XII).—A solution of 35 g. (0.22 mole) of methyl 1-hydroxycyclohexanecarboxylate (XI), b.p. 98–99° (14–15 mm.),⁶² in 150 ml. of pure hexane was treated with 6.0 g. (0.25 mole) of sodium hydride in portions, and the mixture was stirred for 2 hr. at 25°. After the addition of 70 g. (0.5 mole) of methyl iodide, the mixture was heated at reflux for 1 hour. The solvent was removed by filtration, and the hexane was removed *in vacuo*. The residue was dissolved in 150 ml. of pure hexane and remethylated using 1.0 g. of sodium hydride and 15 g. of methyl iodide. After filtration and removal of the hexane the residue was distilled *in vacuo*; b.p. 92–93° (14–15 mm.), n_D^{20} 1.4490, $\nu_{\text{max}}^{\text{film}}$ 1735 ($\text{C}=\text{O}$), yield 15.5 g. (41%).

Anal. Calcd. for $\text{C}_9\text{H}_{18}\text{O}_3$: C, 62.76; H, 9.36. Found: C, 62.38; H, 9.23.

1-Methoxycyclohexanecarboxamide (XIII).—A mixture of 10 g. (0.058 mole) of methyl 1-methoxycyclohexanecarboxylate and 70 ml. of concentrated ammonium hydroxide was heated for 10 hr. at 100° under developed pressure. The colorless plates which separated were recrystallized from ethyl acetate, m.p. 155–156°, yield 5.5 g. (60%); $\nu_{\text{max}}^{\text{Nujol}}$ 3500, 3400 ($\text{N}-\text{H}$), 1675 cm^{-1} ($\text{C}=\text{O}$).

Anal. Calcd. for $\text{C}_8\text{H}_{15}\text{NO}_2$: C, 61.12; H, 9.62; N, 8.91. Found: C, 61.67; H, 9.92; N, 8.55.

(1-Methoxycyclohexyl)-methylamine (XIV).—A solution of 5.5 g. (0.035 mole) of 1-methoxycyclohexanecarboxamide in 150 ml. of absolute ether and 50 ml. of absolute tetrahydrofuran was added to a sludge of 7.4 g. (0.211 mole) of lithium aluminum hydride in 40 ml. of absolute ether during 1.5 hours. After the addition was complete the mixture was heated under reflux for 20 hr. Excess hydride was decomposed by water. The solid was collected by filtration and was washed with ether. The combined ether solutions were cooled and saturated with hydrogen chloride. Colorless needles of the hydrochloride were collected on a sintered

glass funnel and recrystallized from absolute ethanol; m.p. 151–152°, yield 5.57 g. (89%).

Anal. Calcd. for $\text{C}_8\text{H}_{17}\text{ClNO}$: C, 53.47; H, 10.09; N, 7.79. Found: C, 53.06; H, 10.11; N, 7.78.

The amine, obtained by basification of the hydrochloride and extraction with ether, was used directly in the next step.

N-(1-Methoxycyclohexylmethyl)-pyrrolidine (X).—A mixture of 3.5 g. (0.025 mole) of (1-methoxycyclohexyl)-methylamine, 4.2 g. (0.020 mole) of 1,4-dibromobutane and 3.4 g. (0.032 mole) of sodium carbonate in 10 ml. of absolute ethanol was heated on the steam-bath for 60 hr. Water was added, and the solution was extracted four times with ether. The amine was removed from the ether solution by extraction with dilute hydrochloric acid. The acid solution was basified with sodium hydroxide and extracted with ether. The ether was removed, and the residue was distilled through a Holzman column; b.p. 130–131° (13–14 mm.), n_D^{20} 1.4806, yield 2.3 g. (60%). This compound was identical in infrared with the amine liberated from the salt obtained by the methanolysis of 2,2-pentamethylene-1,1-tetramethyleneaziridinium perchlorate.

The perchlorate of N-(1-methoxycyclohexylmethyl)-pyrrolidine was obtained by adding aqueous ethanolic perchloric acid to an ether solution of the amine to congo red. Colorless plates were obtained on recrystallization from ethanol-ether; m.p. 122–123°, identical by mixture m.p., infrared spectrum and paper chromatography with the methanolysis product of 2,2-pentamethylene-1,1-tetramethyleneaziridinium perchlorate (see above).

Anal. Calcd. for $\text{C}_{12}\text{H}_{24}\text{ClNO}_5$: C, 48.40; H, 8.12; N, 4.70; OCH₃, 10.42. Found: C, 48.57; H, 8.15; N, 4.96; OCH₃, 10.55.

Reaction of 2,2-Pentamethylene-1,1-tetramethyleneaziridinium Perchlorate with Ethylene Chlorohydrin.—A solution of 1.0 g. (3.76 mmoles) of 2,2-pentamethylene-1,1-tetramethyleneaziridinium perchlorate in 3 ml. of ethylene chlorohydrin was heated on the steam-bath for 5 hours. The excess ethylene chlorohydrin was removed *in vacuo*, the residue was dissolved in water and made basic with 40% potassium hydroxide. After repeated extraction of the mixture with ether, the combined ether extracts were dried. The ether solution, basic at this time, was refluxed for 24 hours, after which time the ether was neutral and an oil had separated which solidified upon cooling. In ethanol, the addition of perchloric acid caused the separation of colorless plates, m.p. 190–192°, yield 0.50 g. (43%) of 2,2-pentamethylene-4,4-tetramethylenemorpholinium perchlorate (XV), having no infrared maximum corresponding to

$-\text{N}^+-\text{H}$.

Anal. Calcd. for $\text{C}_{13}\text{H}_{24}\text{ClNO}_5$: C, 50.40; H, 7.81; N, 4.52. Found: C, 50.50; H, 7.71; N, 4.48.

Catalytic Hydrogenation of 2,2-Pentamethylene-1,1-tetramethyleneaziridinium Perchlorate.—A solution of 1.0 g. (3.76 mmoles) of 2,2-pentamethylene-1,1-tetramethyleneaziridinium perchlorate in 100 ml. of anhydrous methanol was hydrogenated in the presence of 0.4 g. of platinum oxide. Filtration followed by removal of solvent *in vacuo* yielded an oil which crystallized upon standing. The solid was dissolved in water, the solution was saturated with potassium carbonate and extracted with ether. The dried ether extract was treated with perchloric acid to congo red, and the solid obtained was recrystallized from ethanol-ether as colorless needles, m.p. 122–123°, yield 0.7 g. (70%),

$\nu_{\text{max}}^{\text{Nujol}}$ 3100 cm^{-1} ($-\text{N}^+-\text{H}$); n.m.r. τ -values (in CDCl_3) at:

6.63 (triplet); 7.89 (pentuplet); 8.26; 8.51 (singlet). The structure was established (see below) as that of N-(1-methylcyclohexyl)-pyrrolidine perchlorate (XVI).

Anal. Calcd. for $\text{C}_{11}\text{H}_{22}\text{ClNO}_4$: C, 49.34; H, 8.28; N, 5.23. Found: C, 49.45; H, 8.37; N, 5.23.

The picrate of the major product, N-(1-methylcyclohexyl)-pyrrolidine, was formed in and recrystallized from ethanol as yellow needles, m.p. 184–185°.

Anal. Calcd. for $\text{C}_{17}\text{H}_{24}\text{N}_4\text{O}_7$: C, 51.51; H, 6.10; N, 14.14. Found: C, 51.77; H, 6.17; N, 14.14.

Preparation of N-(1-Methylcyclohexyl)-pyrrolidine Perchlorate (XVI).—To the Grignard reagent prepared from 1.9 g. (0.08 g.-atom) of magnesium and 11.2 g. (0.08 mole) of

(62) P. J. Tarbouriech, *Compt. rend.*, **149**, 605 (1909).

methyl iodide in 100 ml. of ether was added 10 g. (0.04 mole) of N-cyclohexylidenepyrrolidinium perchlorate suspended in 100 ml. of ether (stirrer in the dropping funnel) over a period of 20 min. The mixture was heated under reflux for 2.5 hr. It was then decomposed with a saturated aqueous solution containing 10 g. of ammonium chloride. After addition of sodium fluoride the mixture was filtered and the filtrate was basified with 40% aqueous potassium hydroxide. The ether layer was separated and the basic aqueous layer was extracted five times with ether. After drying and ether removal the residue was distilled through a Holzman column at 114–115° (26–27 mm.), yield 2.6 g. of N-(1-methylcyclohexyl)-pyrrolidine (XVII), following a cyclohexanone fraction.

The perchlorate XVI, colorless needles from ethanol-ether; m.p. 121.5–122.5°, was undepressed in melting point on mixture with the hydrogenolysis product of 2,2-pentamethylene-1,1-tetramethylenearizidinium perchlorate.

The picrate, m.p. 184–185°, was undepressed on mixing with this derivative of the hydrogenolysis product.

Reaction of N-Cyclohexylidenepyrrolidinium Perchlorate with Diazoethane.—A solution of diazoethane in ether was obtained by codistillation from the decomposition of N-nitroso-N-ethylurea in ether with 60% aqueous potassium hydroxide at a water-bath temperature of about 70°. The distillate was dried over sodium hydroxide pellets for 0.5 hour at 0° before use. A solution of 4.5 g. (0.018 mole) of N-cyclohexylidenepyrrolidinium perchlorate in 900 ml. of anhydrous methanol was treated with a solution of diazoethane (prepared from 14 g. of nitrosoethylurea) in 200 ml. of ether. The orange color of the solution disappeared in 10 min., and the solution was kept in the refrigerator for 4 hr. It was then concentrated *in vacuo* at 0° to dryness. The residue was treated with water to which a limited amount of potassium hydroxide had been added to obtain neutrality corresponding to hydrolysis of any ketone iminium salt, and the solution was extracted with ether (discarded). Chloroform extraction furnished, following evaporation of the chloroform, 3-methyl-2,2-pentamethylene-1,1-tetramethylenearizidinium perchlorate (XXa), colorless needles from ethanol, m.p. 166–166.5°, yield ca. 40%, having no infrared maxima corresponding to N^+-H or $>\text{C}=\text{N}^+<$;

n.m.r. signals at τ -values (CDCl_3): 6.37, 6.61, 6.69, 6.81, 6.86; 7.84 (multiplet); 8.17; and 8.41, 8.51 (doublet).

Anal. Calcd. for $\text{C}_{12}\text{H}_{22}\text{ClNO}_4$: C, 51.51; H, 7.93; N, 5.01. Found: C, 51.41; H, 7.98; N, 5.01.

The attempted hydrogenation of 3-methyl-2,2-pentamethylene-1,1-tetramethylenearizidinium perchlorate in absolute methanol with platinum oxide at either 3 atm. or at 300 atm. resulted in at least 75% recovery of the aziridinium perchlorate.

The reaction of 3-methyl-2,2-pentamethylene-1,1-tetramethylenearizidinium perchlorate with thiosulfate proceeded much more slowly than for the compound without the methyl group.

Methanolysis of 3-Methyl-2,2-pentamethylene-1,1-tetramethylenearizidinium Perchlorate (XXa).—A solution of 0.40 g. (1.43 mmoles) of 3-methyl-2,2-pentamethylene-1,1-tetramethylenearizidinium perchlorate in 10 ml. of methanol was heated under reflux for 170 hr. Addition of ether to the cooled methanol solution produced colorless needles, m.p.

158–158.5°, yield 0.37 g. (82%), $\nu_{\text{max}}^{\text{Nujol}}$ 3120 cm^{-1} (N^+-H),

with properties and analysis consistent for N-[α -(1-methoxycyclohexyl)-ethyl]-pyrrolidine perchlorate as the probable major product; n.m.r. τ -values ($\text{CDCl}_3/\text{CH}_2\text{Cl}_2$) at 6.14–6.60; 6.76 (singlet); 7.89; 8.49; 8.64, 8.76 (doublet).

Anal. Calcd. for $\text{C}_{13}\text{H}_{24}\text{ClNO}_5$: C, 50.07; H, 8.41; N, 4.49; OCH_3 , 9.95. Found: C, 50.11; H, 8.32; N, 4.56; OCH_3 , 9.81.

Reaction of N-Cyclohexylidenepyrrolidinium Perchlorate with Diazopropane.—A solution of 5.0 g. (0.02 mole) of N-cyclohexylidenepyrrolidinium perchlorate in 900 ml. of anhydrous methanol was treated at 0° with a solution of diazopropane (prepared from 14 g. of nitrosopropylurea in a manner similar to that described above for obtaining a solution of diazoethane in ether) in 200 ml. of anhydrous ether at 0°. The orange color of the diazopropane disappeared and gas was evolved. The addition was completed in 10 min., and

the solution was allowed to stand in the refrigerator for 4 hr. The solution was concentrated *in vacuo* at 0° to about 40 ml. and ether was added. The colorless needles of 3-ethyl-2,2-pentamethylene-1,1-tetramethylenearizidinium perchlorate (XXb) were recrystallized from isopropyl alcohol, m.p. 204–205°, yield 3.05 g. (52%, or 70% based on unrecovered starting material), no infrared maxima cor-

responding to N^+-H or $>\text{C}=\text{N}^+<$; n.m.r. τ -values

(CDCl_3): 6.36, 6.60, 6.72, 6.78, 6.90, 6.97; 7.85 (multiplet); 8.22, 8.28; 8.72, 8.82, 8.95.

Anal. Calcd. for $\text{C}_{13}\text{H}_{24}\text{ClNO}_4$: C, 53.14; H, 8.23; N, 4.77. Found: C, 53.11; H, 8.40; N, 4.84.

Methanolysis of 3-Ethyl-2,2-pentamethylene-1,1-tetramethylenearizidinium Perchlorate (XXb).—The reaction with refluxing methanol was run as in the case of the 3-methyl compound for 170 hr. The product, obtained as colorless plates from ethanol, m.p. 144–145°, yield 72%, $\nu_{\text{max}}^{\text{Nujol}}$ 3120 cm^{-1} , had properties and analysis consistent for N-[α -(1-methoxycyclohexyl)-propyl]-pyrrolidine perchlorate (XXIb) as the probable major product; n.m.r. τ -values ($\text{CDCl}_3/\text{CH}_2\text{Cl}_2$) at 6.20; 6.69 (singlet); 7.83; 8.46; 8.74, 8.83, 8.96.

Anal. Calcd. for $\text{C}_{14}\text{H}_{26}\text{ClNO}_5$: C, 51.60; H, 8.66; N, 4.30; OCH_3 , 9.52. Found: C, 51.84; H, 8.79; N, 4.41; OCH_3 , 9.35.

Iminium Salts. N-Cyclopentylidenepyrrolidinium Perchlorate.—1-N-Pyrrolidylcyclopentene,⁶⁰ b.p. 71–73° (4.2 mm.), $\nu_{\text{max}}^{\text{Nujol}}$ 1630 cm^{-1} , prepared in 88% yield from cyclopentanone and pyrrolidine,⁶¹ was converted to the perchlorate by treatment of an ether solution with aqueous ethanolic perchloric acid, and the salt was recrystallized from absolute ethanol, colorless needles, m.p. 231–233° dec., $\nu_{\text{max}}^{\text{Nujol}}$ 1705 cm^{-1} ($>\text{C}=\text{N}^+<$), yield 88%.

Anal. Calcd. for $\text{C}_9\text{H}_{15}\text{ClNO}_4$: C, 45.48; H, 6.79; N, 5.89. Found: C, 45.66; H, 6.69; N, 5.89.

N-Cycloheptylidenepyrrolidinium Perchlorate.—1-N-Pyrrolidylcycloheptene, b.p. 84–86° (1.9 mm.), $\nu_{\text{max}}^{\text{Nujol}}$ 1627 cm^{-1} , prepared in 45% yield from cycloheptanone and pyrrolidine,⁶² was converted to the perchlorate by the usual method. Recrystallization from absolute ethanol gave colorless plates, m.p. 234–235° dec., $\nu_{\text{max}}^{\text{Nujol}}$ 1655 cm^{-1} ($>\text{C}=\text{N}^+<$), yield 82%.

Anal. Calcd. for $\text{C}_{11}\text{H}_{19}\text{ClNO}_4$: C, 49.72; H, 7.59; N, 5.27. Found: C, 49.62; H, 7.67; N, 5.20.

N-Cyclooctylidenepyrrolidinium Perchlorate.—1-N-Pyrrolidylcyclooctene,⁶³ b.p. 102–103° (2.2 mm.), $\nu_{\text{max}}^{\text{Nujol}}$ 1625 cm^{-1} , yield 55% from the components, gave a perchlorate which was recrystallized as colorless plates from absolute ethanol; m.p. 140–141°, $\nu_{\text{max}}^{\text{Nujol}}$ 1649 cm^{-1} ($>\text{C}=\text{N}^+<$), yield 69%.

Anal. Calcd. for $\text{C}_{12}\text{H}_{21}\text{ClNO}_4$: C, 51.52; H, 7.93; N, 5.01. Found: C, 51.56; H, 7.90; N, 5.11.

Isobutylidenepyrrolidinium Perchlorate (XIX).⁴⁹—N-Isobutenylpyrrolidine (2-methyl-1-N-pyrrolidyl-1-propene)⁶⁴ (30 g., 0.24 mole) in 200 ml. of anhydrous ether was treated with excess hydrogen bromide. The hydrobromide salt which separated was washed with ether, dissolved in 200 ml. of absolute ethanol, and the ethanol was removed *in vacuo*. The anhydrous residue was redissolved in 200 ml. of absolute ethanol and treated with 53 g. (0.257 mole) of silver perchlorate. The mixture was heated and filtered hot. The silver perchlorate treatment was repeated until no further silver bromide precipitated from the hot solution. The iminium perchlorate⁴⁹ which separated on cooling was recrystallized from ethanol as colorless plates, m.p. 227–229° dec., $\nu_{\text{max}}^{\text{Nujol}}$ 1715 cm^{-1} , yield 26 g. (48%); n.m.r. τ -values (in liquid SO_2) at: 1.70, 1.85; 5.98; 7.06–7.31; 7.80; 8.64, 8.72.

Anal. Calcd. for $\text{C}_8\text{H}_{15}\text{ClNO}_4$: C, 42.57; H, 7.15; N, 6.21. Found: C, 42.54; H, 7.00; N, 6.21.

Reaction of N-Cyclohexylidenepiperidinium Perchlorate with Diazomethane.—To a solution of 28.5 g. (0.34 mole) of dry hydrogen bromide in 350 ml. of anhydrous ether at 0° was added 55 g. (0.34 mole) of 1-N-piperidylcyclohex-

(63) M. E. Kuehne, *J. Am. Chem. Soc.*, **81**, 5400 (1959).

(64) G. Opitz, H. Hellmann and H. W. Schubert, *Ann.*, **623**, 112 (1959).

ene.^{64,65} The colorless precipitate was filtered and washed repeatedly with dry ether under exclusion of moisture. It was then dissolved in 500 ml. of anhydrous ethanol. This solution was treated with a solution of 82 g. (0.35 mole) of anhydrous silver perchlorate in 120 ml. of absolute ethanol. The mixture was filtered. Most of the N-cyclohexylidene-piperidinium perchlorate was found with the silver bromide, from which it could be extracted with hot anhydrous acetone. Upon addition of ether to the acetone solution, 39.5 g. of colorless plates was obtained, m.p. 246–249°. Upon cooling of the ethanol solution (above) and addition of ether 2.8 g. additional iminium perchlorate was obtained; total yield 53%, $\nu_{\text{max}}^{\text{Nujol}}$ 1660 cm^{-1} .

A solution of 5.0 g. (0.019 mole) of N-cyclohexylidene-piperidinium perchlorate in 300 ml. of anhydrous methanol was treated at 0° with a solution of diazomethane, prepared from 5.0 g. (0.049 mole) of nitrosomethylurea, in 70 ml. of anhydrous ether. The yellow color of the diazomethane disappeared and gas was evolved. The addition was complete in 5 min., and the solution was allowed to stand in the refrigerator for 4 hr. After concentration to half-volume *in vacuo* at 0° the solution was cooled to –40°. The 1,1-pentamethylene-2,2-pentamethyleneaziridinium perchlorate separated as colorless needles and was recrystallized from absolute ethanol, m.p. 236–238° dec., yield 3.8 g. (73%), no in-

frared maxima corresponding to $-\text{N}^+-\text{H}$ or $>\text{C}=\text{N}^+<$;

n.m.r. τ -values (CDCl_3): 6.60, 6.68; 7.03 (singlet); 8.00, 8.20.

Anal. Calcd. for $\text{C}_{10}\text{H}_{22}\text{ClNO}_4$: C, 51.51; H, 7.93; N, 5.01. Found: C, 51.24; H, 7.78; N, 5.10.

1-N-Pyrrolidylcyclohexanemethanol.—Formaldehyde condensation with nitrocyclohexane⁶⁶ to give 1-nitrocyclohexanemethanol was followed by reduction to 1-aminocyclohexanemethanol according to Noland, Kneller and Rice⁶⁷;

(65) C. Mannich and H. Davidsen, *Ber.*, **69**, 2106 (1936).

(66) We are grateful to Dr. W. F. Jackson of the Explosives Department, E. I. du Pont de Nemours and Co., Inc., for a generous gift of nitrocyclohexane.

(67) W. E. Noland, J. K. Kneller and D. E. Rice, *J. Org. Chem.*, **22**, 695 (1957).

b.p. 82–83° (1.3–1.4 mm.), n_D^{25} 1.4951 (reported b.p. 84° (1 mm.), n_D^{25} 1.4959). A mixture of 5.7 g. (0.044 mole) of 1-aminocyclohexanemethanol, 13.8 g. (0.065 mole) of 1,4-dibromobutane and 4.9 g. (0.044 mole) of sodium carbonate in 20 ml. of absolute ethanol was heated under reflux for 84 hr. following the general directions for ring formation.^{68,69} After the addition of 50 ml. of water the aqueous ethanolic solution was extracted with ether. The ether extract was washed with dilute aqueous hydrochloric acid. The aqueous layer was strongly basified with sodium hydroxide and extracted with ether. After drying and removal of the ether a pale yellow sludge was obtained. In an attempt to distill it, 1.0 g. of starting material was recovered and the rest solidified. Purification by sublimation at 100° bath temperature and 0.2 mm. yielded 5.3 g. (79% based on unrecovered starting material) of colorless prisms, m.p. 71–72°, $\nu_{\text{max}}^{\text{Nujol}}$ 3400 cm^{-1} (O–H).

Anal. Calcd. for $\text{C}_{11}\text{H}_{21}\text{NO}$: C, 72.08; H, 11.55; N, 7.64. Found: C, 71.85; H, 11.54; N, 7.35.

The perchlorate of 1-N-pyrrolidylcyclohexanemethanol crystallized as colorless prisms from absolute ethanol; m.p.

92–93°; $\nu_{\text{max}}^{\text{Nujol}}$ 3505 (O–H), 3125 cm^{-1} ($-\text{N}^+-\text{H}$).

Anal. Calcd. for $\text{C}_{11}\text{H}_{21}\text{ClNO}_4$: C, 46.56; H, 7.82; N, 4.94. Found: C, 46.72; H, 7.88; N, 4.94.

N.m.r. Model. 1,1-Dimethylpyrrolidinium Perchlorate (XVIII).—A solution of 12.5 g. (0.055 mole) of 1,1-dimethylpyrrolidinium iodide (Aldrich Chemical Co.) in 100 ml. of anhydrous ether was treated with a solution of 12.5 g. (0.060 mole) of anhydrous silver perchlorate in 20 ml. of anhydrous ethanol. Silver iodide was recovered by filtration of the hot solution, ether was added to the filtrate and the precipitate was recrystallized from ethanol as feathery plates, m.p. above 330°, yield 9.5 g. (86%); n.m.r. τ -values (liquid SO_2) at: 6.32, 6.48, 6.65; 6.85 (singlet); 7.70 (broad).

Anal. Calcd. for $\text{C}_6\text{H}_{14}\text{ClNO}_4$: C, 36.10; H, 7.07; N, 7.02. Found: C, 35.98; H, 6.95; N, 7.00.

(68) R. C. Elderfield and H. A. Hageman, *ibid.*, **14**, 605 (1949).

(69) A. T. Bottini and J. D. Roberts, *J. Am. Chem. Soc.*, **80**, 5203 (1958).

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Cationic Catalyzed Polymerization of Styrene at High Conversion¹

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The cationic polymerization of styrene with stannic chloride catalyst has been studied over the conversion range 9.5–97%, in carbon tetrachloride–nitrobenzene solvent mixture at 0°. The cumulative number average molecular weight appears to decrease with increasing conversion, in accord with the behavior shown on varying the initial monomer concentration at low conversion. However, the weight average molecular weight increases markedly, probably due mainly to chain transfer to the polymer. Owing to the attendant increase of branching in the polymers, their intrinsic viscosities show little dependence on the conversion. The limitations of intrinsic viscosity as a measure of molecular weight at high conversion are discussed, and procedures for obtaining reliable data under such conditions are recommended.

Introduction

In the course of an earlier investigation of molecular termination in the cationic polymerization of styrene with stannic chloride catalyst,³ it was observed that the intrinsic viscosities of the isolated polymers showed little dependence on the conversion. It was also found that the intrinsic viscosity at a given conversion was quite markedly dependent

(1) This is the 20th in a series of papers concerned with ionic polymerization; for the previous paper in this series, see C. G. Overberger and A. Schiller, *J. Polymer Sci.*, in press (1962).

(2) This paper comprises a portion of the Dissertation submitted by V. G. Kamath in partial fulfillment of the requirements for the degree of Doctor of Philosophy at the Polytechnic Institute of Brooklyn.

(3) G. F. Endres and C. G. Overberger, *J. Am. Chem. Soc.*, **77**, 2201 (1955).

on the initial monomer concentration. If molecular weights were calculated from these intrinsic viscosities using relationships based on polymers with presumably "most probable" molecular weight distributions, contradictory conclusions could be drawn concerning the dependence of polymer molecular weight on monomer concentration. A possible explanation of this was that it is due to a broadening of the molecular weight distribution with increasing conversion, limiting the validity of these viscosity–molecular weight relationships to low conversions. Such broadening could conceivably be due to at least two causes in the system investigated. The occurrence of "spontaneous" (unimolecular) termination or chain transfer would