ylation with acetic anhydride and pyridine at room temperature and exhibited the same melting point (m.p. 92–94°) as the unlabeled material XXXIIb.[47]

5α,6α-Oxidoandrostan-3β-ol-7β-d$_1$ (*XXXVIIa*). The acetate XXXIIa (80 mg.) in 2 cc. of chloroform was left at room temperature for 1 hr. with 80 mg. of *m*-chloroperbenzoic acid, ether was then added, and the excess peracid was removed by washing with dilute sodium carbonate solution. After washing with water and drying, the ether was evaporated and the crystalline oxide XXXVIIIa shown to be identical in terms of melting point and thin layer chromatographic mobility with a sample of the unlabeled analog XXXVIIIb, m.p. 111–112°, $[\alpha]_D$ −80°.

Anal. Calcd. for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 75.72; H, 9.49.

Saponification of the acetate XXXVIIIa was effected by heating under reflux for 2 hr. with 1% methanolic potassium hydroxide solution. Crystallization from hexane yielded the pure 5α,6α-oxidoandrostan-3β-ol-7β-*d*$_1$ (XXXVIIa), whose melting point (152–153°) was not depressed upon admixture with an authentic sample[49] of the unlabeled oxide XXXVIIb ($[\alpha]_D$ −92°).

(49) A. Butenandt and L. A. Suranyi, *Ber.*, **75**, 597 (1942).

Anal. Calcd. for $C_{19}H_{30}O_2$: C, 78.57; H, 10.41. Found: C, 78.36; H, 10.16.

5β,6β-Oxidoandrostan-3β-ol-7β-d$_1$ (*XLa*). Δ^5-Androsten-3β-ol-7β-*d*$_1$ acetate (XXXIIa) (140 mg.) in 7 cc. of dioxane and 1.5 cc. of water was left at room temperature for 1 hr. with 0.46 cc. of 9% perchloric acid and 76 mg. of N-bromoacetamide, and then poured into sodium thiosulfate solution. Extraction with ether, washing, drying, and evaporation afforded the crude crystalline bromohydrin XXXIXa[50] which was dissolved in 15 cc. of methanol and heated under reflux for 2 hr. with 300 mg. of potassium hydroxide dissolved in 1 cc. of water. Isolation with ether and preparative chromatography on one silica gel H plate (20 × 20 cm.) in ether yielded 75 mg. of the β-oxide XLa, m.p. 172–174°. Recrystallization from ethyl acetate provided 48 mg. of the pure substance, whose melting point (m.p. 183–185°) was not depressed when mixed with a sample of unlabeled β-oxide XLb (m.p. 182–183°, $[\alpha]_D$ −16°).

Anal. Calcd. for $C_{19}H_{30}O_2$: C, 78.57; H, 10.41. Found: C, 78.39; H, 10.22.

(50) In the nondeuterated series, 5α-bromoandrostane-3β,6β-diol 3-acetate (XXXIXb) was purified by recrystallization from methanol; m.p. 173–174°, $[\alpha]_D$ −61°. *Anal.* Calcd. for $C_{21}H_{33}BrO_3$: C, 61.01; H, 8.05. Found: C, 60.68; H, 7.89.

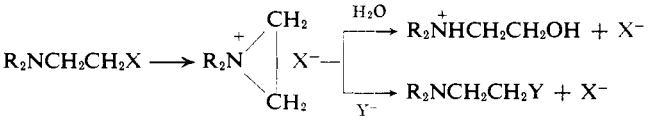
A Nuclear Magnetic Resonance Study of the 2-Haloethylamines

P. L. Levins and Z. B. Papanastassiou

Contribution from Arthur D. Little, Inc., Cambridge, Massachusetts 02140.
Received October 7, 1964

The rates and mechanism of solvolysis of 2-fluoroethylamine (II) and bis(2-fluoroethyl)amine (IV) in basic deuterium oxide solution have been studied by nuclear magnetic resonance and compared with their chloro analogs. The fluoroethylamines solvolyze by first-order kinetics through the same aziridinium intermediates as the chloroethylamines, but the chloro amines are 16–128 times more reactive than the fluoro amines. Application of n.m.r. techniques to 2,2'-dichloro-N-methyldiethylamine (VI) allowed us to observe simultaneously the disappearance of starting amine, formation and reaction of the aziridinium intermediate, and formation of the piperazinium product.

In connection with our studies on potential carcinolytic agents[1] we have found nuclear magnetic resonance to be a valuable aid in interpreting the *in vitro* reactions of 2-haloethylamines which involve aziridines as reactive intermediates or as products. The widespread use of 2-haloethylamines in biological studies as alkylating agents has led to extensive studies of their chemistry and biochemistry.[2–5] When the halogen is chlorine, bromine, or iodine, the reactions proceed under many conditions through an intermediate aziridinium ion to hydrolysis or alkylation products. The chemistry of the fluoro analogs was not clearly defined. Chapman and James[6] found that 2-fluoroethylamines did not solvolyze under the conditions of their experiments whereas the chlorine and bromine analogs reacted normally. Although Nemetz and Tzybaeva[7] observed solvolysis of 2-fluoroethylamines, they were unable to decide whether the solvolysis proceeded by a normal SN2 mechanism or through an aziridinium intermediate.



(1) Z. B. Papanastassiou and R. J. Bruni, Abstracts, 144th National Meeting of the American Chemical Society, Los Angeles, Calif., April 1963, p. 42L.

(2) J. D. P. Graham in "Progress in Medicinal Chemistry," Vol. 2, G. P. Ellis and G. B. West, Ed., Butterworth and Co., London, 1962, Chapter 4.

(3) W. C. J. Ross, "Biological Alkylating Agents," Butterworth and Co., London, 1962.

(4) C. C. Price, *Ann. N. Y. Acad. Sci.*, **68**, 657 (1958).

(5) P. D. Bartlett, S. D. Ross, and C. G. Swain, *J. Am. Chem. Soc.*, 71, 1415 (1949), and previous papers.

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

(7) V. G. Nemetz and G. G. Tzybaeva, *Tr. Leningr. Tekhnol. Inst. im. Lensoveta*, **60**, 56 (1960); *Chem. Abstr.*, **56**, 7111*b* (1962).

Table I. Nuclear Magnetic Resonance Spectra of $XCH_2CH_2NH_2$ (A B)

	X	State	δ_A[a]	δ_B	
I	Cl	Base	3.65 (t)	2.92 (t)	J_{AB}[b] = 6
Ia	Cl	HCl salt	3.90 (c)	3.43 (c)	
II	F	Base	4.60 (dt)	2.91 (dt)	$J_{FA} = 47, J_{FB} = 30, J_{AB} = 5$
IIa	F	HCl salt	4.91 (dt)	3.43 (dt)	$J_{FA} = 48, J_{FB} = 28, J_{AB} = 5$

[a] s = singlet, d = doublet, t = triplet, dt = pair of triplets, m = center of multiplet, c = centers of A_2B_2 mirror image multiplet. [b] In c.p.s.

Table II. Nuclear Magnetic Resonance Spectra of $XCH_2CH_2\underset{\displaystyle R}{N}CH_2CH_2X'$ (A B C D)

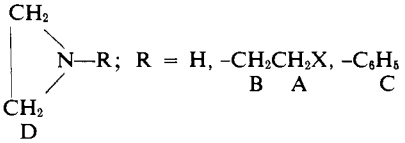
	X	X′	R	State	δ_A	δ_B	
III	Cl	Cl	H	Base	3.55 (t)	2.77 (t)	$J_{AB} = 6$
IIIa	Cl	Cl	H	HCl salt	3.97 (c)[a]	3.57 (c)[a]	$J_{AB} = 6$
IV	F	F	H	Base	4.60 (dt)	2.92 (dt)	$J_{FA} = 47, J_{FB} = 30, J_{AB} = 5$
IVa	F	F	H	HCl salt	4.86 (dt)	3.55 (dt)	$J_{FA} = 46.5, J_{FB} = 27.5, J_{AB} = 4.5$
V	F	Cl	H	HCl salt	4.91 (dt)	3.72 (m) (B + C + D)	$J_{FA} = 47, J_{AB} = 5$
VI	Cl	Cl	CH_3	Base[b]	3.75 (t)	2.88 (t)	$\delta_{CH_3} = 2.35$ (s)
VIa	Cl	Cl	CH_3	HCl salt[c]	4.08 (c)	3.75 (c)	$\delta_{CH_3} = 3.10$ (s)

[a] This spectrum contains 18 of the maximum 24 possible A_2B_2 lines. [b] 1.0 *M* NaCl, 60 sec. after neutralization. [c] 1.0 *M* NaCl.

Table III. Nuclear Magnetic Resonance Spectra of $XCH_2CH_2NHC_6H_5$ (A B C)

	X	State	δ_A	δ_B	δ_C
VII	Cl	HCl salt[a]	3.75 (m)		7.4 (m)
VIII	Br	Base	3.50 (s)		6.65 (m) + 7.15 (m)
VIIIa	Br	HBr salt	3.90 (c)	3.60 (c)	7.52 (s)

[a] Solvent CH_3OH.

Table IV. Nuclear Magnetic Resonance Spectra of  R = H, $-CH_2CH_2X$, $-C_6H_5$ (B A C; D)

	R	State	δ_A	δ_B	δ_C	δ_D
IX	$ClCH_2CH_2$	Base	3.55 (t)	2.41 (t)		1.41 + 1.21 (c)
IXa	$ClCH_2CH_2$	HCl salt	3.63 (t)	3.16 (t)		2.59 + 2.70 (c)
X	FCH_2CH_2	Base	4.63 (dt)	2.54 (dt)		$J_{FA} = 47, J_{FB} = 30, J_{AB} = 5$; 1.34 + 1.76 (c)
XI	C_6H_5	Base[a]			7.1 (m)	2.10 (s)
XII	H	Base				1.60 (s)
XIIa	H	HCl salt				2.70 (s)

[a] Solvent CH_3OH.

In previous studies on 2-haloethylamines a variety of analytical techniques have been used to follow the course of the reaction and determine the nature of the intermediates involved. Friedman and Boger[8] have extended the technique of Epstein, which uses colorimetry for determining the concentration of alkylating agents in solution. Bartlett, Ross, and Swain,[5] in their extensive investigations, used acid titration and Volhard chloride determinations. Golumbic, Fruton, and Bergmann[9] developed a thiosulfate titration method for aziridinium ions, and recently Wagner and Berg[10] have reported on the use of a polarographic catalytic wave technique for measuring aziridinium ion concentrations. The recent paper by Nemetz and Tzybaeva[7] demonstrates the limitations of the pH and chloride ion techniques in interpreting the reactions of 2-fluoroethylamines. The technique of Friedman[8] suffers from similar deficiencies.

Using n.m.r. we have studied the reactivity of a number of 2-chloro- and 2-fluoroethylamines and have been able to follow simultaneously the disappearance of starting materials and the formation of aziridine products. In the case of 2,2′-dichloro-N-methyldiethylamine, we were able, in addition, to follow the formation and reaction of the aziridinium intermediate. During the progress of this work, Beroza and Borkovec[11] have reported the use of n.m.r. in studying the reactions of some aziridine chemosterilants. Pettit and Smith[12,12a] have recently referred to an n.m.r. investigation of bis(2-haloethyl)amines.

(8) O. M. Friedman and E. Boger, *Anal. Chem.*, **33**, 906 (1961).
(9) C. Golumbic, J. S. Fruton, and M. Bergmann, *J. Org. Chem.*, 11, 518, 536 (1946).
(10) H. Wagner and H. Berg, *J. Electroanal. Chem.*, **2**, 452 (1961).
(11) M. Beroza and A. B. Borkovec, *J. Med. Chem.*, 7, 44 (1964).

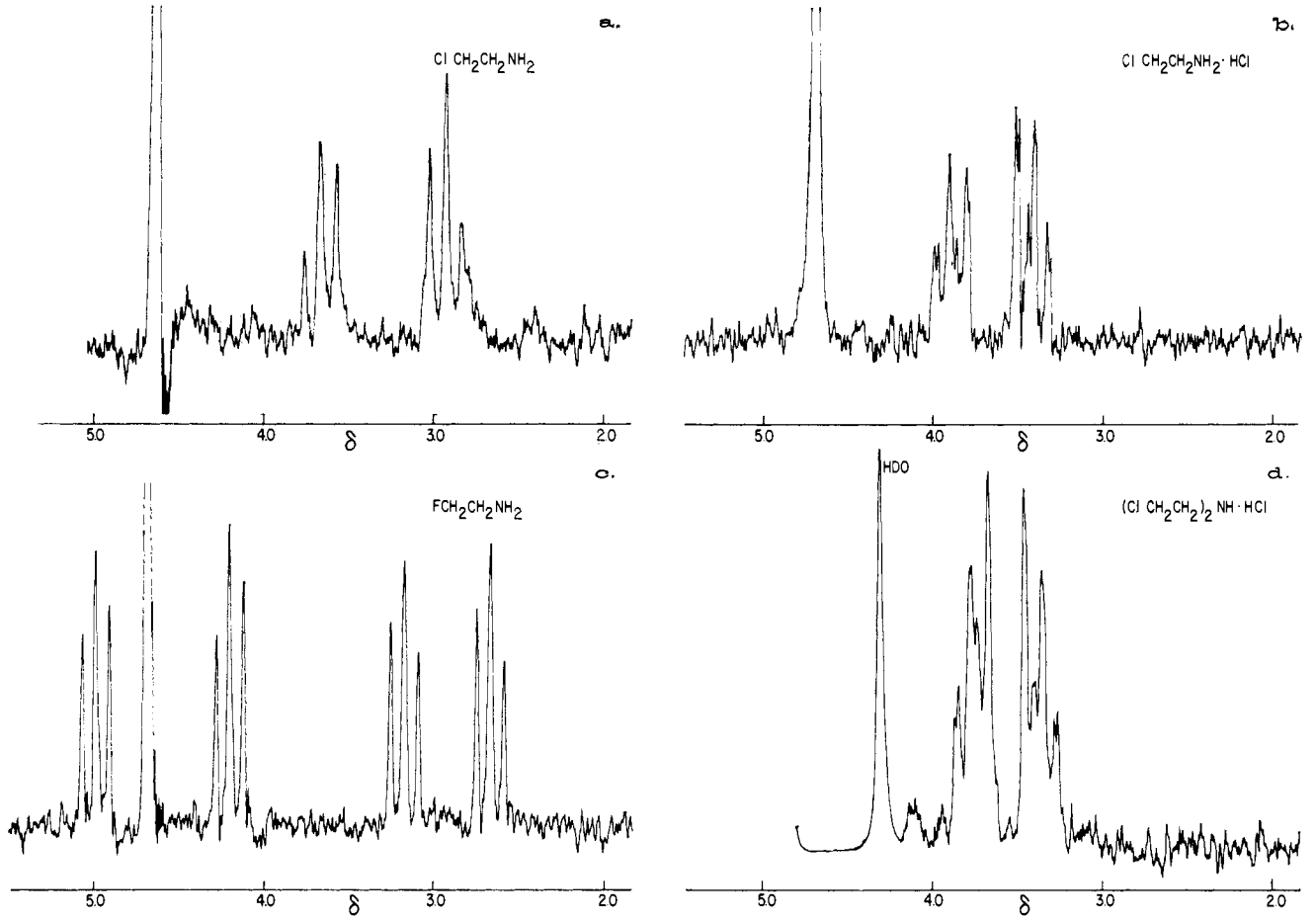


Figure 1. Nuclear magnetic resonance spectra of representative 2-haloethylamines.

Experimental

2,2'-Dichloro-N-methyldiethylamine hydrochloride (m.p. 108–110°, lit. 110°[13]) was generously supplied by Merck and Company. *2-Chloroethylamine hydrochloride* (m.p. 142–143°, lit. 144°[14]) was purchased from Aldrich. *Bis(2-chloroethyl)amine hydrochloride* (m.p. 212–214°, lit. 216–217°) was prepared by a modification of the method of Mann.[15] *2-Fluoroethylamine* (b.p. 63.5–64.5°, n^{25}D 1.3705), *bis(2-fluoroethyl)amine* (b.p. 120–122°, n^{25}D 1.3823), and *2-chloro-2'-fluorodiethylamine hydrochloride* (m.p. 193–194°) were prepared by the method of Papanastassiou and Bruni.[16] *N-(2-Bromoethyl)aniline hydrobromide* (m.p. 137–139°, lit. 135–139°) was prepared by Dr. G. R. Handrick of these laboratories according to the method of Pearlman.[17] *N,N-Diphenylpiperazine* (m.p. 165°, lit. 164°[18]) was isolated by Dr. Handrick as a product of the reaction between N-(2-bromoethyl)aniline hydrobromide, trifluoroacetic anhydride, and sodium carbonate. *N-Phenylaziridine* (b.p. 65° (10 mm.), lit. 70° (13 mm)) was prepared according to the method of Heine, Kapur, and Mitch.[19] A solution of *N-(2-chloroethyl)aniline* was prepared by the addition of 1 equiv. of hydrochloric acid to an aqueous solution of N-phenylaziridine.

Spectra were obtained on a Varian Associates A-60 spectrometer equipped with a V-6040 variable temperature controller and probe. The chart paper and temperature controller were carefully calibrated prior to each study. Except where noted, all spectra were obtained in deuterium oxide solutions using sodium 2,2-dimethyl-2-silapentane-5-sulfonate (DSS) as an internal reference or external reference. The CH_3–Si shifts of DSS and tetramethylsilane (TMS) are identical, and shift values are reported in p.p.m.; downfield values from TMS are taken as positive.

Solutions of the free base were prepared, immediately before use, either by addition of solvent to the base or by neutralization of the combined acid in the hydrochloride (or hydrobromide) salt with a predetermined amount of sodium hydroxide. Solutions of 10 *N* hydrochloric acid and sodium hydroxide in deuterium oxide were used and were handled with Hamilton syringes. Unless noted otherwise, all runs were conducted at the probe temperature of 37°. Relative concentrations of materials were obtained from measurement of peak heights. The reactions occurred too rapidly to allow accurate use of the integrator for

(12) G. R. Pettit and R. L. Smith, *Can. J. Chem.*, **42**, 572 (1964).
(12a) NOTE ADDED IN PROOF. Exchange of prepublication manuscripts with Dr. G. R. Pettit (G. R. Pettit, J. A. Settepani, and R. A. Hill, submitted for publication) reveals that the conclusions of our studies are in agreement.
(13) Heilbron, "Dictionary of Organic Compounds," Vol. 3, Oxford University Press, New York, N. Y., p. 364.
(14) Ref. 13, Vol. 1, p. 500.
(15) F. G. Mann, *J. Chem. Soc.*, 461 (1934).
(16) Z. B. Papanastassiou and R. J. Bruni, *J. Org. Chem.*, **29**, 2870 (1964).
(17) W. M. Pearlman, *J. Am. Chem. Soc.*, 70, 871 (1948).
(18) D. S. Pratt and C. O. Young, *ibid.*, **40**, 1428 (1918).
(19) H. W. Heine, B. L. Kapur, and C. S. Mitch, *ibid.*, **76**, 1173 (1954).

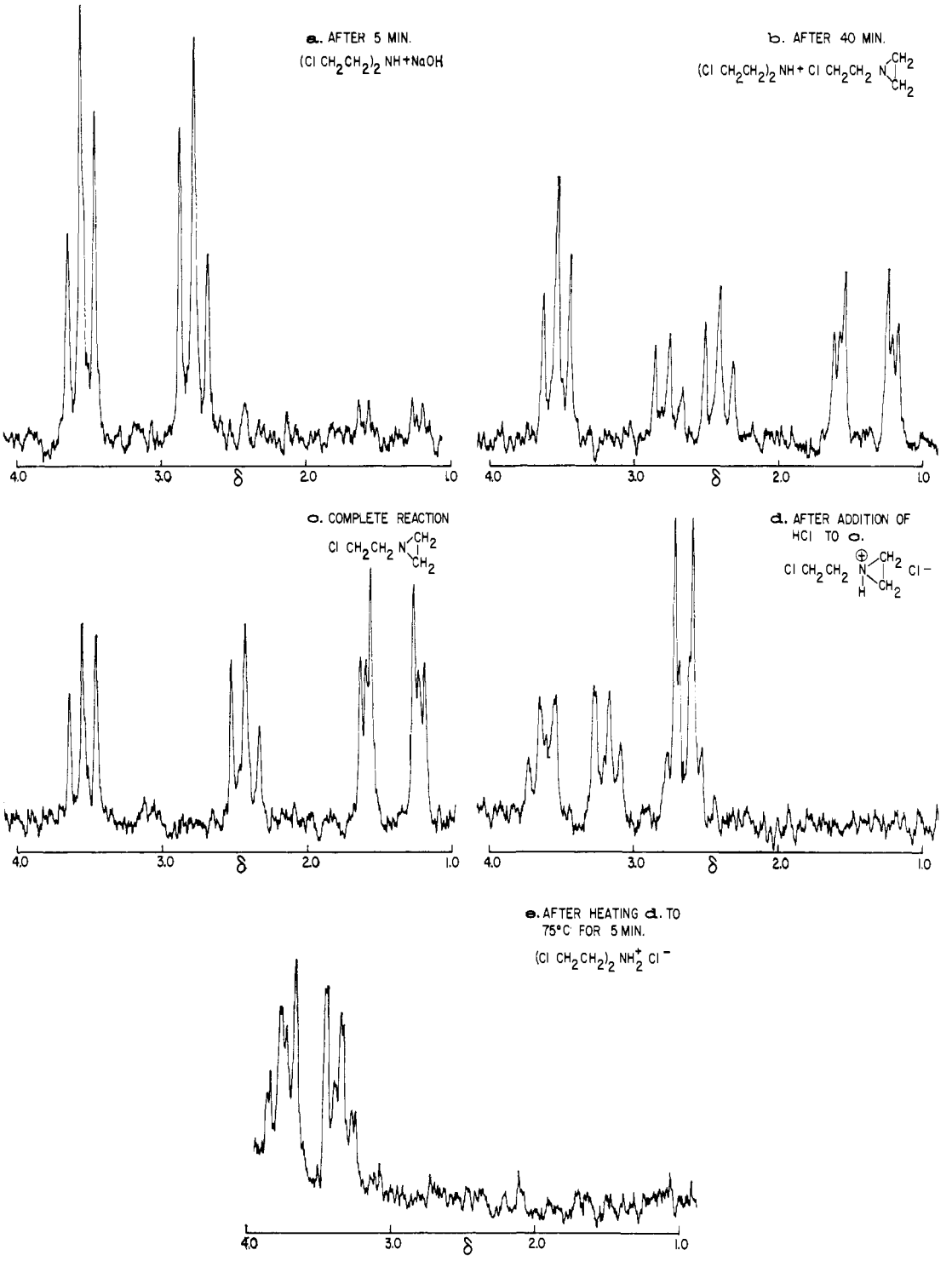


Figure 2. Nuclear magnetic resonance spectra of bis(2-chloroethyl)amine in basic D_2O at various stages of reaction at 37°.

measurement of peak area, but the peaks were sharp singlets in most cases so that a linear relationship exists between peak height and peak area.

Results and Discussion

Nuclear Magnetic Resonance Spectra. The n.m.r. spectra of the compounds involved in this study have been analyzed in detail. The analyses are presented in Tables I–IV.

The unique F^{19} splitting pattern in these compounds has made n.m.r. a useful tool for qualitatively identifying fluoroethyl compounds during syntheses, as well as for quantitative analysis. The spectra of 2-chloroethylamine (I), 2-chloroethylamine hydrochloride (Ia), 2-fluoroethylamine (II), and bis(2-chloroethyl)amine hydrochloride (IIIa) are shown in Figure 1 as being representative (in appearance) of all the compounds studied. The A_2B_2 complexities observed in IIIa are removed when the $\Delta\delta/J$ values are increased either by substitution of fluorine for chlorine or by neutralization of the acid salt.

The spectrum of N,N-diphenylpiperazine consists

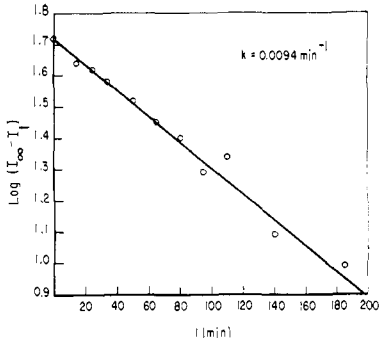
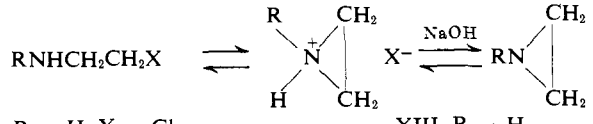


Figure 3. First-order rate plot for the formation of aziridine from 2-fluoroethylamine: [amine] = 0.10 *M*, [NaOH] = 0.20 *M*, temperature = 90°.

of aromatic multiplets centered at δ = 6.8 and 7.2 p.p.m. and a methylene singlet at δ = 4.32 p.p.m. (benzene-d_6 solution).

Reaction Mechanism. The solvolysis of amines I to VIII was observed in neutral and basic solutions in order to determine the mechanism of reaction and compare the n.m.r. kinetic data with those obtained by other methods.[2-5]

The reactions of all the compounds obeyed good first-order kinetics in neutral or basic solutions with the exception of the mustard (VI) which was not evaluated in kinetic detail. Figure 2a–c represents various stages of reaction of bis(2-chloroethyl)amine (III) in a 0.15 *M* solution of amine and 0.20 *M* solution of sodium hydroxide in deuterium oxide at 37°. Figure 2d was obtained after the addition of hydrochloric acid to the final reaction product of III, and Figure 2e was obtained after heating the hydrochloride solution to 75° for 10 min. Through the alternate addition of base and acid we were able to repeat this cycle a number of times, demonstrating the lack of competing reactions under these conditions. The formation of aziridines has been observed in basic solution for all of the mono- and bis(2-haloethyl)amines involved in this study, and the rate constants obtained for these compounds under our conditions are given in Table V. The temperatures were chosen to give reasonable half-lives for use with the spectrometer.



I, R = H, X = Cl
II, R = H, X = F
III, R = CH_2CH_2Cl, X = Cl
IV, R = CH_2CH_2F, X = F

XIII, R = H
IX, R = CH_2CH_2Cl
X, R = CH_2CH_2F

Since the rate-determining reaction in these studies is the internal SN2 neighboring nitrogen displacement, it is unlikely that the H_2O/D_2O kinetic isotope effect would be greater than a maximum of 10%.[20] The first-order rate plot for formation of aziridine (XIII) from 2-fluoroethylamine (II) is shown in Figure 3. The rate constant obtained for bis(2-chloroethyl)-amine (III) was the same when determined from disappearance of starting material or from formation of product. The rate constants obtained for I and III were comparable to those obtained by Bartlett, Ross, and Swain[5] when reasonable temperature and solvent adjustments were made. N-(2-Bromoethyl)aniline (VIII) was not studied quantitatively; it was completely converted in 5 hr. to N-phenylaziridine (XI) in basic methanol solution at 50° in agreement with the kinetic studies of Heine and Kapur.[21]

Table V. Rate of Formation of Aziridines in Basic Deuterium Oxide[a]

Amine	Product	[Amine]	[NaOH]	*T*, °C.	*k*, min.$^{-1}$	$t_{1/2}$, min.
I	XIII	0.40	0.30	50	0.0080	86.6
II	XIII	0.10	0.20	90	0.0094	73.7
III	IX	0.20	0.20	37	0.037	18.7
IV	X	0.15	0.20	80	0.045	15.4

[a] Determined from the intensity of aziridine peaks.

N-Alkylaziridines and -aziridinium ions are stable in solution at temperatures up to 40–50°, and have been isolated as stable salts.[9] In contrast, N-phenylaziridine (XI) is extremely reactive as demonstrated by the absence of any aziridine or aziridinium ion spectra as soon as 15 sec. after hydrochloric acid had been added to solutions of the aziridine at 10° in methanol, *t*-butyl alcohol, and acetone-d_6–deuterium oxide solvents. The primary reaction product was polymeric. Although N-(2-haloethyl)anilines do react through aziridinium ion intermediates *in vitro*, it may be quite reasonable to conclude, in agreement with Ross,[8] that no important concentrations of the aziridinium ion exist in the *in vivo* reactions of these compounds.

Our studies indicate that the same reactions occur with fluoroethyl compounds as with chloroethyl compounds, differing only in rate as a result of the increased strength of the C–F bond. If it is assumed that the reactions have a normal Arrhenius temperature dependence of rate doubling or trebling with a 10° rise in temperature,[22] it can be calculated from Table V that the chloro compounds are approximately 16–128 times more reactive than the corresponding fluoro compounds in neighboring nitrogen reactions, since a 40° temperature increase gives the same rate for the fluoro amine as the chloro amine.

Our findings on the stability of aziridine and aziridine hydrochloride in solutions of deuterium oxide are in agreement with those of Beroza and Borkovec.[11] The half-life of aziridine hydrochloride in deuterium oxide (pH *ca.* 2) at 37° was about 270 min. (k = 0.0026 min.$^{-1}$). The N-alkylaziridines and -aziridinium ions exhibited comparable stability. The spectrum of N-(2-chloroethyl)aziridine hydrochloride was unchanged after 24 hr. in deuterium oxide at room temperature. However, the aziridinium ion was quickly converted to bis(2-chloroethyl)amine (III) upon heating the solution to 75°.

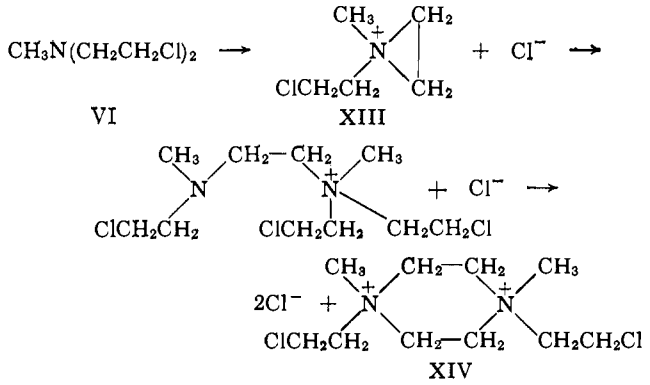
The nitrogen mustard (VI) represents a case of special interest since we were able to observe simultaneously the changes in concentration of starting amine VI, intermediate aziridinium ion XIII, and product piperazinium ion XIV (Figure 4). The ordinate is arbitrary in terms of concentration since the

(20) L. Melander, "Isotopes Effects on Reaction Rates," The Ronald Press, New York, N. Y., 1960.

(21) H. W. Heine and B. L. Kapur, *J. Am. Chem. Soc.*, 77, 4892 (1955).

(22) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons, Inc., New York, N. Y., 1958, p. 23.

peak height does not necessarily have the same relation to concentration for each species.



VI XIII XIV

Observations were begun 1 min. after neutralization of the hydrochloride salt. The amount of mustard VI was measured from the N–CH_3 singlet height at δ = 2.35 p.p.m.; the aziridinium ion XIII from the N–CH_3 singlet at δ = 3.17 p.p.m.; and the piperazinium ion XIV from the ring methylenes at δ = 4.1 p.p.m. Although Bartlett, *et al.*,[5] attempted to use the thiosulfate titration technique for estimation of the aziridinium ion concentrations in their studies of this compound, the rate of reaction with the ring was too slow to be useful. The n.m.r. technique has the advantage that intermediates which accumulate are easily observed. There is the added advantage that any change in mechanism with changing conditions may also be observed, as well as any side reactions.

In a study of a series of halogenoethyl-N-alkyl-1-naphthylmethylamines, Graham[2] found that the fluoro compounds were inactive as antagonists of adrenaline, noradrenaline, and histamine in contrast to the chloro, bromo, and iodo analogs. However, it is possible that *in vivo* the fluoro compounds are oxidized to precursors of fluoroacetic acid by amine oxidase and their toxicity masks any adrenergic blocking action.[23]

(23) F. L. M. Pattison, "Toxic Aliphatic Fluorine Compounds," Elsevier Publishing Company, New York, N. Y., 1959.

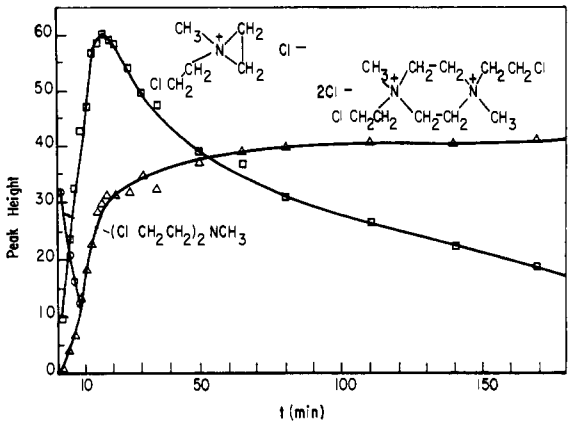


Figure 4. Change in concentration of the species involved in the solvolysis of N-methylbis(2-chloroethyl)amine in D_2O at 37°.

Recently, Russian investigators[24] have reported that some 2-fluoroethylamine derivatives are active as antitumor agents, and Pettit and Smith[12] have found that bis(2-fluoroethyl)amine inhibited the growth of Walker 256 carcinoma at near-toxic levels; similar results were obtained in our laboratory with 2-chloro-2′-fluorodiethylamine.[25] Since it has been shown that many tumors are not inhibited by fluoroacetate, it is possible that the antitumor activity of these compounds is due to their action as biological alkylating agents.

Acknowledgment. We wish to thank the research committee of Arthur D. Little, Inc., for their support of this work, Mr. R. J. Bruni for assistance in preparation of the compounds, and Mrs. Nancy L. King for assistance in obtaining the n.m.r. spectra and kinetic data.

(24) See, for example, L. S. Erukhinov, V. P. Zolotsev, and S. V. Kagramanov, *Urologiia*, **27**, 54 (1962); *Cancer Chemotherapy Abstr.*, **3**, 487 (1962).

(25) Z. B. Papanastassiou, R. J. Bruni, and P. L. Levins, paper in preparation.

On the Role of Electrophilic Catalysis in Competitive Reductions of Ketones by Lithium Tetrakis(N-dihydropyridyl)aluminate and Metal Borohydrides

Peter T. Lansbury[1] and Ronald E. MacLeay[2]

Contribution from the Department of Chemistry, State University of New York at Buffalo, Buffalo 14, New York. *Received September 26, 1964*

Benzophenone is more reactive than phenyl t-butyl ketone toward reduction by lithium tetrakis(N-dihydropyridyl)aluminate (LDPA), but the opposite order was observed when sodium borohydride in isopropyl alcohol was the reducing agent. It is proposed that electrophilic catalysis is minimized in the LDPA reactions, in which case aryl groups conjugate less effectively with the carbonyl function, thus magnifying their normally masked −I effects. Even sodium borohydride itself shows different relative reactivities with ketones in going from alcohol to pyridine solvents. The relative rates of reduction of a series of benzophenones by LDPA correlate with Hammett constants better than σ^+ constants and give $\rho = +1.5$. All four dihydropyridyl groups in LDPA show comparable reactivity as hydride donors and there is no rate difference in reduction of 2,4′-dichlorobenzophenone by 1,2- and 1,4-dihydropyridyl groups in LDPA.

(1) Alfred P. Sloan Foundation Fellow, 1963–1965.
(2) National Institutes of Health Predoctoral Fellow, 1963–1964.