were combined, 21 g, since they had nearly identical infrared spectra. The spectra of the composite indicated the presence of high concentrations of a 1,1,4-trisubstituted piperazinium salt (1210–1220 cm^{-1}), $(-CH_2-)_3N$ (1060, 2860 cm^{-1}) characteristic of poly(1-ethylaziridine), and $(-CH_2-)_2NH$ (1110, 2810 cm^{-1}). Since poly(1-ethylaziridine) is soluble in diethyl ether, the composite was thoroughly washed with ether and dried, and its spectra remained unchanged. The ether washed was found to contain no polymer. Analysis of the residue is reported below.

Anal. Found: N, 12.85; C, 42.20; H, 8.78; I, 33.19; >NH, 3.4; $-NH_2$, <0.1; mol wt, 340 (ebulliometrically in 2-butanone) [Calcd: mol wt, 383 (based on iodide), 378 (based on secondary amine)].

Procedure for Rate Determinations.—Into a 100-ml volumetric flask were weighed 2.00 g of phenetole and 3.70 g of 1-ethylaziridine. The flasks were filled with 2-butanone and placed in a 25.0° water bath. To each flask was added 0.50 ml of 6.0 *N* acid and the contents were thoroughly mixed. At predetermined time intervals the reaction mixtures were analyzed by standard glpc techniques using the phenetole as an internal standard. The glpc column previously mentioned was used for these analyses. All runs were made in duplicate.

Preparation of 1,4-Disubstituted Piperazines for Glpc and Infrared Standards.—The diethyl-, di-*n*-butyl-, and diallylpiperazines were prepared by mixing 0.12 mol of the corresponding aziridine and 10 g (0.078 mol) of sodium iodide in 150 ml of 2-butanone followed by the addition of 3.2 g of concentrated hydriodic acid. After remaining at room temperature (24–26°) for 48 hr, the mixtures were shaken for 4 hr with 50 g potassium carbonate and filtered, and the solvent was removed by distillation at atmospheric pressure. The piperazines were isolated from the distillation residues by preparative scale glpc using the aforementioned Carbowax column.

Anal. Calcd for 1,4-diethylpiperazine: N, 19.72. Found: 19.82; $n^{25}D$ 1.4530 (lit.[3] 1.4520).

Anal. Calcd for 1,4-di-*n*-butylpiperazine: N, 14.1. Found: 19.82; $n^{25}D$ 1.4540 (lit.[3] 1.4542).

Anal. Calcd for 1,4-diallylpiperazine: N, 16.87. Found: 16.68; $n^{25}D$ 1.4754 (lit.[4] 1.4761).

The preparation of 1,4-diphenethylpiperazine was the same as above; however the product was isolated by devolatalizing the filtered reaction mixture, washing the residue with water to remove the soluble salts, and recrystallizing the crude product from an acetone–water mixture, mp 79.5–80.5°.

Anal. Calcd: N, 9.52. Found: 9.44.

Attempted Preparation of 1,4-Disubstituted Piperazines Other Than 1,4-Diethylpiperazine.—Using the preceeding procedure, 1-cyanoethylaziridine, 1-(2-hydroxyethylaziridine), 1-allylaziridine, 1-phenethylaziridine, and 1-*n*-butylarizidine were treated with hydriodic acid and sodium iodide in 2-butanone at 25°. After filtering the reaction mixtures in order to remove the potassium salts, the concentrations of the reacted aziridines and of the corresponding piperazines were determined by infrared analysis. The conversions of the aziridines were 99+% in each case.

Anal. % yield for 1,4-substituted piperazine: 1,4-bis(cyanoethyl), <1.0; 1,4-bis(2-hydroxyethyl), <10; 1,4-diallyl, 46; 1,4-diphenethyl, 73; 1,4-di-*n*-butyl, 83.

Registry No.—1-Ethylaziridine, 1072-45-3; 1-*n*-butylaziridine, 1120-85-0; 1-phenethylaziridine, 3164-46-3; 1-allylaziridine, 5536-99-2.

Acknowledgment.—The author gratefully acknowledges the contributions of H. L. Spell who obtained and interpreted the infrared spectra.

(3) J. I. G. Cadogan, *J. Chem. Soc.*, 2971 (1955).

(4) G. B. Butler, and R. L. Bunch, *J. Amer. Chem. Soc.*, **71**, 3120 (1949).

Reactions of Nucleophiles with 1-*tert*-Butyl-3-chloroazetidine and 1-*tert*-Butyl-2-chloromethylaziridine[1]

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These small heterocycles, **1** and **2**, are exceptionally unreactive β-aminoalkyl chlorides. With nucleophiles under vigorous conditions **1** and **2** reacted by simple displacement (mercaptides, alkoxides, and uncatalyzed amines), partial (hydrolysis) or complete (cyanide) ring expansion of **2** to form azetidines, or ring cleavage, recyclization, and reopening (acetic acid, acid-catalyzed amines). Isomerization, **1** ⇄ **2**, occurred with mechanistic duality. Equilibria involving the 1-*tert*-butylazabicyclobutonium and 1-*tert*-butyl-2-aziridinylcarbinyl cations are proposed. Cyclization of β-aminoalkyl mesylates was a versatile route to aziridines carrying functional groups.

A problem of current interest in the chemistry of small heterocycles concerns the nature of nucleophilic substitution of azetidines bearing exophiles in the 3 position. A possible intermediate is the simple carbonium ion (I). The formal relationship of I to the

I II III IV

cyclobutyl–cyclopropylcarbinyl nonclassical cation system[2] suggested a parallel investigation of aziridinylcarbinyl derivatives, perhaps leading to cation II. Nitrogen participation in either case would lead to the strained quaternary 1-azabicyclobutonium ion (III), while the possibility of nonclassical hybridization implies intermediates such as IV.

We recently presented preliminary evidence to support nitrogen assistance in the ionization of the chlorides corresponding to ions I and II (R, *tert*-Bu) and suggested that a common intermediate (such as III alone) could not rationalize the results.[1] Independently Deyrup and Moyer proposed III as an intermediate in solvolysis of the tosylate of 1-*tert*-butyl-3-azetidinol, but they considered unclear the mechanism by which the aziridinylcarbinyl tosylate reacted.[3] The present paper concerns expanded evi-

(1) Preliminary account: V. R. Gaertner, *Tetrahedron Lett.*, 5919 (1968). Presented in part at the 156th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 1968; Abstracts, ORGN 1.

(2) R. H. Mazur, W. N. White, D. A. Semenow, C. C. Lee, M. S. Silver, and J. D. Roberts, *J. Amer. Chem. Soc.*, **81**, 4390 (1959). Review: R. Breslow, in "Molecular Rearrangements," Part 1, P. de Mayo, Ed., Interscience, New York, N. Y., 1963, pp 233–294. J. E. Baldwin and W. D. Foglesong, *J. Amer. Chem. Soc.*, **90**, 4303 (1968), gave a recent summary. See, however, R. E. Davis and A. Ohno, *Tetrahedron*, 2063 (1968), for the view that cyclobutyl cation is classical.

(3) J. A. Deyrup and C. L. Moyer, *Tetrahedron Lett.*, 6179 (1968). We are grateful to Professor Deyrup for initiating an exchange of results with the writer.

dence on reactions of the chlorides and a mechanism consistent with the data on such systems.

Ring expansion and cleavage have been noted in pertinent studies of strained heterocycles. 2-Chloromethylthiirane and 3-chlorothietane were said to ionize with sulfur assistance to give a classical bicyclic sulfonium ion

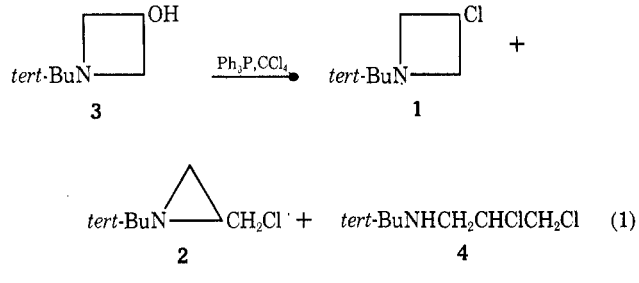
which yielded only 3-substituted thietanes by cross-ring bond cleavage.[4]

In the nitrogen series, the 1-benzenesulfonyl-2-aziridinylmethyl cation expanded to the -2-azetidinyl ion or a nonclassical intermediate, as shown by isotopic tagging, in the Friedel–Crafts alkylation of benzene.[5] Evidence involving ring expansion in tosylate solvolysis has been given recently for the 1-oxabicyclobutonium cation.[6]

Results

Synthesis of Azetidines and Aziridines.—The chlorides, 1-*tert*-butyl-3-chloroazetidine (**1**) and 1-*tert*-butyl-2-chloromethylaziridine (**2**), were chosen for study. Their stabilities were expected to permit more vigorous reaction conditions, and thus yield more varied, revealing results than might the tosylates,[3,7] for example.

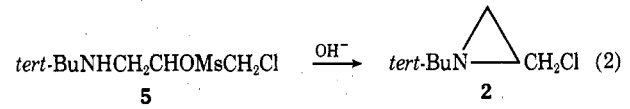
The conversion of 3-azetidinols[8] to 3-chloroazetidines called for mild neutral conditions to avoid ring cleavage or autodehydrochlorination and these requirements were met by the triphenylphosphine–carbon tetrachloride reagent.[9] Although the reaction of 1-*tert*-butyl-3-azetidinol (**3**) was very sluggish (3 days at 76° compared to 10 min for unstrained alcohols[9]), good yields (**1**, 69–72%) were realized. The reaction was unexpectedly complex, two minor products being formed (eq 1). An isomer of **1** formed in 1–4% yield



(1)

was identified as chloromethylaziridine (**2**), and an unstable dichloro amine proved to be *tert*-butyl-2,3-dichloropropylamine (**4**). These secondary products are considered below. 3-Chloro-1-cyclohexylazetidine was prepared similarly. Functionally 3-substituted azetidines were obtainable by displacements on the tosylate[7,3] or, with precautions to be described, from the chloride.

A preparative method for 1-*tert*-butyl-2-chloromethylaziridine (**2**) began with *O*-mesylation of crude 1-*tert*-butylamino-3-chloro-2-propanol.[10] Cyclization[11] of the unstable mesylate (**5**) gave **2** in 55% yield, based on *tert*-butylamine (eq 2). By comparison,

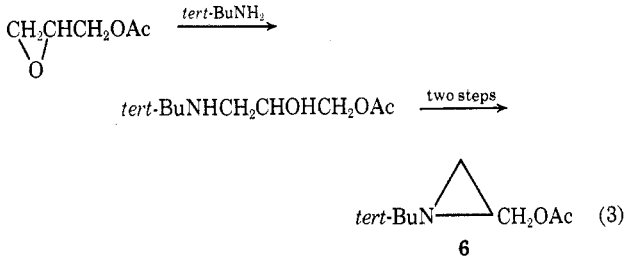


(2)

cyclization of the *O*-sulfuric acid (Wenker aziridine synthesis) gave only a 3% yield of **2**. 1-Cyclohexyl-2-chloromethylaziridine was also prepared.

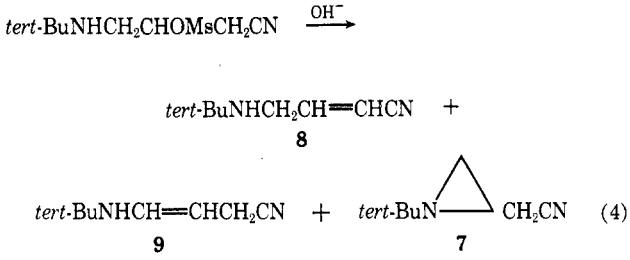
The method is a useful and apparently fairly general synthesis of aziridines. Since either aminochloropropanols or glycidyl derivatives condense with nucleophiles to form 3-substituted aminopropanols,[12,13] it is potentially quite versatile. The preparation of two reference compounds for this work illustrates the probable scope.

1-*tert*-Butyl-2-acetoxymethylaziridine (**6**) was prepared directly, despite its ease of hydrolysis, from glycidyl acetate (eq 3).



(3)

The synthesis of 1-*tert*-butyl-2-cyanomethylaziridine (**7**) involved an unstable mesylate which was sensitive to elimination.[14] 4-*tert*-Butylamino-3-hydroxybutyronitrile, prepared from the aminochloropropanol[10] and cyanide (alkali), was mesylated and cyclized. A mixture of three isomers was isolated (eq 4). The



(4)

two major products were thermally unstable and resinified rapidly in air. The nmr spectra of several mixtures were consistent with 4-*tert*-butylamino-2- (**8**) and -3-butenonitriles (**9**). The third isomer, the

(4) J. C. Martin and D. J. Anderson, Abstracts, 139th National Meeting of the American Chemical Society, St. Louis, Mo., March 1961, p 0-31. See also, E. P. Adams, K. N. Ayad, F. P. Doyle, D. O. Holland, W. H. Hunter, J. H. C. Nayler, and A. Queen, *J. Chem. Soc.*, 2665 (1960); M. Sander, *Monatsh. Chem.*, **96**, 896 (1965).

(5) W. J. Gensler and W. R. Koehler, *J. Org. Chem.*, **27**, 2754 (1962).

(6) H. G. Richey, Jr., and D. V. Kinsman, *Tetrahedron Lett.*, 2505 (1969).

(7) T. Chen, T. Sanjiki, H. Kato, and M. Ohta, *Bull. Chem. Soc. Jap.*, **40**, 2401 (1967), described 1-*tert*-butyl-3-tosyloxyazetidine and the normal displacement by cyanide. Our work on tosylates was discontinued when we became aware of this study and of the work of Deyrup and Moyer,[3] who also prepared chlorides **1** and **2** by displacements on the tosylates.

(8) V. R. Gaertner, *J. Org. Chem.*, **32**, 2972 (1967); *Tetrahedron Lett.*, 4691 (1966).

(9) J. B. Lee and I. M. Downie, *Tetrahedron*, **23**, 359 (1966).

(10) V. R. Gaertner, *ibid.*, **23**, 2123 (1967).

(11) J. Smrt, J. Beránek, and J. Sicher, U. S. Patent Patent 2,958,691 (1960), and K. Okawa, T. Kinutani, and K. Sakai, *Bull. Chem. Soc. Jap.*, **41**, 1353 (1968), described cyclization of sulfonate esters of serine and threonine to aziridine derivatives.

(12) V. R. Gaertner, *J. Org. Chem.*, **33**, 523 (1968).

(13) V. R. Gaertner, *J. Heterocycl. Chem.*, **6**, 273 (1969).

(14) I. Photaki, *J. Amer. Chem. Soc.*, **85**, 1123 (1963), described mesyloxy-amino acid elimination.

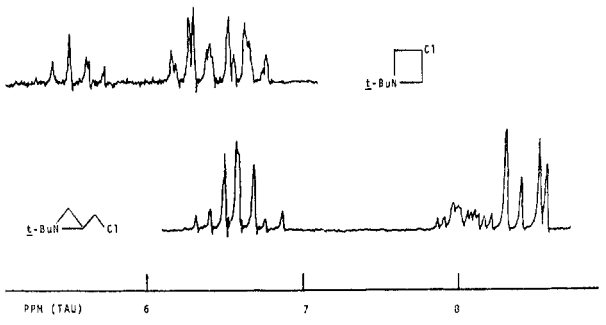


Figure 1.—60-MHz nmr spectra for 1-*tert*-butyl-3-chloroazetidine (1) and 1-*tert*-butyl-2-chloromethylaziridine (2), in deuteriochloroform.

desired aziridine (7), was easily isolated by distillation after thermal resinification of the butenonitriles.

Isomeric azetidines and aziridines were characterized definitively by nmr spectra. Figure 1 illustrates typical features. In addition to the *tert*-butyl singlet at about τ 9 or other usual *N*-alkyl peaks, the 3-substituted azetidines showed two broad triplets (often with further minor splitting) due to the ring methylene protons and downfield a broad pentuplet from the 3 proton. The chemical shifts were little different from those in related strainless heterocycles.

However, aziridine ring-proton multiplets appeared at much higher field (τ 8–9). Also, the substituted methyl protons appeared downfield (τ 5–7) as double AB quartets or collapsed equivalents. Analysis of mixtures involved nmr and vpc methods. Double titration in acetic acid with anhydrous hydrogen bromide and with perchloric acid gave a good estimate of the aziridines present in mixtures. The difference between the 2 titers was due to aziridine cleavage by HBr; azetidines are not cleaved. Aziridines opened more slowly than epoxides.

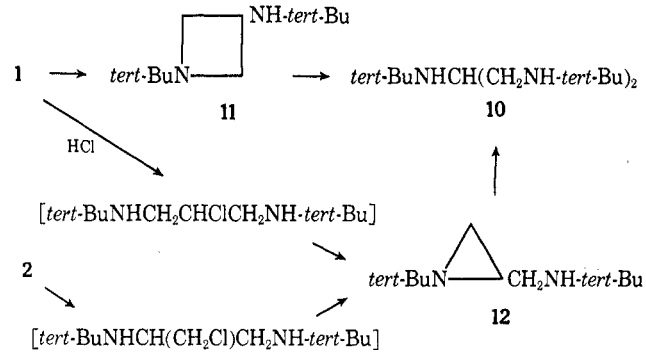
Nucleophilic Displacement Reactions.—The behavior of chlorides **1** and **2** provided evidence for reaction paths ranging from tightly bound SN2 complexes to relatively free rearranging cations. The complication of ring cleavage was foreseeable in displacements with aziridines,[15] but the unexpected ease of azetidine opening was the subject of a parallel investigation.[13]

Simple displacements occurred when both chlorides were treated with good ionic nucleophiles under alkaline conditions. This result was observed with sodium methoxide in methanol, sodium *tert*-butylmercaptide in methanol, potassium *tert*-butoxide in butanol, and *tert*-butylamine in aqueous alkali. The structure of the product corresponded exclusively to that of the starting chloride, ring cleavage being negligible. It is noteworthy that the three bulky reagents, intended as probes for an ionic equilibrium which could be shifted by a large steric requirement of the nucleophile, revealed no such effect.

Initially, *tert*-butylamine in excess gave the same compound from either the chloroazetidine or the chloromethylaziridine. The nmr spectrum and other data indicated that the product was the acyclic triamine **10**. The first cleavage products (Scheme I, in brackets) were undoubtedly chlorodiamines which could not be

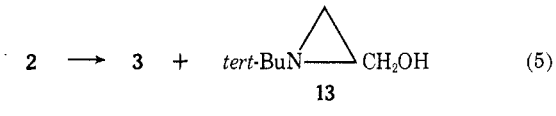
(15) D. H. Powers, Jr., V. B. Schatz, and L. B. Clapp, *J. Amer. Soc.*, **78**, 907 (1956).

SCHEME I



detected in the reaction mixture because both recyclized to the aziridine amine **12**, which was in turn reopened to form **10**. In the presence of anhydrous sodium carbonate, the expected azetidine amine **11** was formed along with **10**; under these conditions **2** gave only **10**. However, when the reaction was conducted in a horizontally rotated bomb with a rolling bar to crush the sodium carbonate and continuously neutralize the hydrogen chloride of reaction, **1** *gave exclusively diamine* **11**, and no triamine, *i.e.*, exclusively chloride displacement and no azetidine ring opening. Similarly, **2** gave diamine **12** by displacement, but aziridine ring cleavage was not completely suppressed and triamine formed slowly from diamine **12**. These reaction conditions were employed to assure the absence of ring opening in azetidine isomerization studies (*vide infra*).

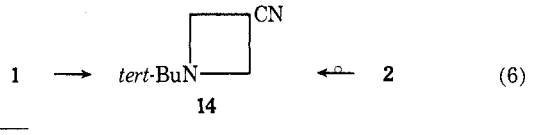
Hydrolysis of β-aminoalkyl chlorides is typically SN1 and may give rearranged products *via* aziridinium cations. Chloroazetidine **1** hydrolyzed to the 3-azetidinol (**3**) as the only monomeric product found, and chloromethylaziridine (**2**) gave both 3-azetidinol and the aziridinylcarbinol (**13**) in a 3:1 ratio (eq 5).



(5)

Kinetics of chloride solvolyses in 50% aqueous ethanol were complex, but specific rate constants could be estimated from the first 10–25% of reaction with adequate accuracy to support qualitative conclusions on relative reactivities. The values for the chloroazetidine were 0.14 hr^{-1} at 35.0° and 0.50 hr^{-1} at 50.0°, and for the chloromethylaziridine about 0.016 hr^{-1} at 70.0°. These data and those of Deyrup and Moyer[3] for the tosylates are consistent, but the order of reactivity is the reverse of comparable data for cyclobutyl and cyclopropylcarbinyl chlorides.[16] Indeed **1** and, especially, **2** are apparently at most a few orders of magnitude more reactive than acyclic secondary and primary alkyl chlorides, respectively.

Cyanide ion gave the same nitrile, 1-*tert*-butyl-3-cyanoazetidine[7] (**14**), from either **1** or **2** (eq 6), the



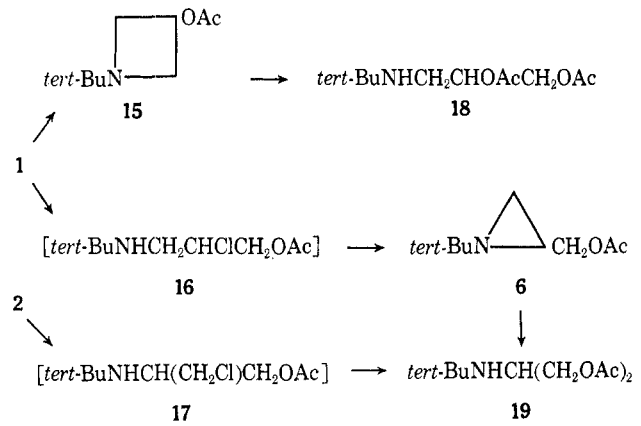
(6)

(16) J. D. Roberts and R. H. Mazur, *ibid.*, **73**, 2509 (1951). At 50°, data for the chlorides were: cyclobutyl, 0.017; cyclopropylcarbinyl, 0.45; allylcarbinyl, >0.0005 hr^{-1}.

second example of ring expansion. The purified nitrile from 2 contained an unstable isomer (probably elimination products 8 and 9) but no cyanomethylaziridine (7).

The acetolysis of chlorides 1 and 2 did not involve ionic intermediates importantly, because acid-catalyzed ring opening intervened. The major reaction paths are summarized in Scheme II.

SCHEME II



Direct displacement on 1 gave the azetidinyl acetate 15, after incomplete reaction, along with the unstable chloro acetate 16, isolated as the impure free amine. Exhaustive reaction produced only 1,2 and 1,3 diacetates 18 and 19, in a 1:1 ratio, from cleavage of 15[13] and 6, respectively. The latter conversion was confirmed separately, a small amount of 1,2 diacetate also being formed.

The reaction of chloromethylaziridine (2) involved ring opening[17] to chloro acetate 17 (also isolated, as an impure hydrochloride), which cyclized to 6 more rapidly than did chloro acetate 16.

Isomerization.—The presence of chloromethylaziridine (2) in chloroazetidine (1) suggested that partial isomerization occurred either during displacement or by isomerization. The amount of 2 increased with extended reaction times, at the expense of 1. Isomerization of 1 proceeded in either carbon tetrachloride or acetonitrile even in the absence of triphenylphosphine. The conversion of 3 to 1 and the isomerization of either 1 or 2 were accompanied by formation of a third unstable compound shown to be dichloro amine 4 (eq 7).

$$1 \text{ or } 2 \longrightarrow \underset{4}{\textit{tert}\text{-BuNHCH}_2\text{CHClCH}_2\text{Cl}} \xrightarrow{\text{DEIPA}} 2 + 1 \quad (7)$$

Experiments indicated that 4 was formed from either 1 or 2 by addition of hydrogen chloride. An added acid scavenger, such as diethylisopropylamine (DEIPA), partially cyclized 4 to a mixture of 2 and 1 in a 10:1 ratio. Aziridine 2 was more stable but slowly isomerized to 1. Similar equilibrium mixtures were obtained by heating either 3-chloro-1-cyclohexylazetidine or 2-chloromethyl-1-cyclohexylaziridine in acetonitrile. Clearly these "equilibria" were attained at least in part by a reversible series of ring cleavage and reclosure sequences initiated by hydrogen chloride from the autodehydrochlorination of the starting chloride.

To determine whether cations I and II (for example) participated in ionic isomerization concomitantly with the above cleavage–recyclization, we employed the conditions under which no ring opening occurred with 1, even with the powerfully nucleophilic amines in excess. Chloroazetidine (1) still slowly isomerized to chloromethylaziridine (2). Although 2 did not generate 1 under these conditions, catalysis by potassium iodide in acetonitrile did promote the reverse reaction, giving up to 0.7% of 1. No dichloro amine or any other product of cleavage was detected. True reversibility was not attained.

Discussion

Clearly 1-*tert*-butyl-3-chloroazetidine (1) and, especially, 1-*tert*-butyl-2-chloromethylaziridine (2) are among the least reactive β-aminoalkyl chlorides known. Their chemistry contains contradictory elements which a successful formulation of cationic intermediates must reconcile.

Qualitatively, preferential formation of azetidines from both chlorides in nucleophilic displacements is understandable in terms of aziridine ring strain relief. On the other hand, the more strained aziridine ionized the more slowly. Thus, ionization is not appreciably concerted with strain relief.

Both ring contraction and expansion were observed in ionic isomerization. Similar reactions occur in relatively strainless systems,[18] but the present case is exceptional in that contraction increases ring strain. This is apparently the first instance of azetidine isomerization to an aziridine.

The simple 3-azetidinyl carbonium ion (I) cannot explain the rate data for 1. A nonclassical carbonium ion of the cyclobutyl type[2] might rationalize the reactivity of 1 to a degree, but this idea does not fit the sluggishness of the more strained 2. The aziridine ring-strain energy (14 kcal/mol;[19] cyclopropane, 25 kcal) is clearly too small to give rise to nonclassical ions, and the unknown azetidine ring strain energy is surely even smaller.

Steric activation of the chlorine at C-3 in 1 may be considered. Steric interaction between N and 3 substituents across the puckered azetidinium ring has been invoked to explain increasingly negative entropies of cyclization.[12] However, *tert*-butyl and chloro groups were not bulky enough to exhibit the effect.

The intermediacy of the 1-*tert*-butyl-1-azabicyclobutonium[20] ion (III) accounts satisfactorily for the reactivity of 1 (or the tosylate[3]). Anchimeric assistance of ionization by the nitrogen lone pair is favored, in the most probable conformational isomer (1a, Scheme III) with a puckered ring,[21] by a shortened N–C-3 distance, a very basic and presumably strongly

(17) This cleavage was originally overlooked[1] and the specific rate constant for appearance of chloride ion was erroneously assigned to solvolysis of 2. The acetolysis constant given for 1 is also incorrect because 1 gave 6 by ring opening and recyclization, not by direct rearrangement. Acetolysis and recyclization of 16 simulated simple first-order kinetics.

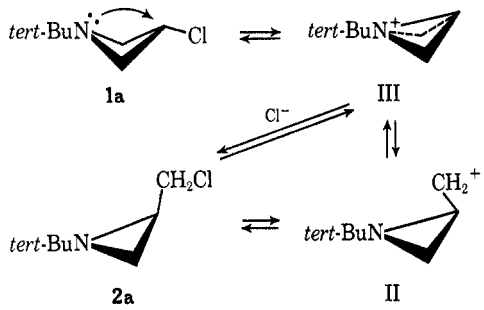
(18) (a) J. F. Kerwin, G. E. Ullyot, R. C. Fuson, and C. L. Zirkle, *J. Amer. Chem. Soc.*, **69**, 2961 (1947); E. M. Schultz and J. M. Sprague, *ibid.*, **70**, 48 (1948); R. C. Fuson and C. L. Zirkle, *ibid.*, **70**, 2760 (1948). (b) See E. M. Fry, *J. Org. Chem.*, **30**, 2058 (1965), and references therein.

(19) R. A. Nelson and R. S. Jessup, *J. Res. Nat. Bur. Stand., A*, **48**, 206 (1952).

(20) A. G. Hortmann and D. A. Robertson, *J. Amer. Chem. Soc.*, **89**, 5974 (1967), synthesized an example of the uncharged ring system.

(21) R. L. VanEtten, personal communication, X-ray crystallographic results on L-azetidine-2-carboxylic acid.

SCHEME III



nucleophilic nitrogen,[22] and a relatively exophilic secondary chlorine. Cation III would be expected, as observed, to add nucleophiles at C-3 by cleavage of the long weak cross-ring bond, on the basis of both heterocyclic[4,6] and bicyclobutane[23a] chemistries.

The simplest pathway for the ring-expanding reactions of chloromethylaziridine 2 involves ionization–rearrangement to III. The relative sluggishness of 2 suggests that ionization to III, if it occurs directly, gains little driving force from rearrangement, however. This may be a result of a long N–CH_2 distance in 2a and of the facts that aziridine nitrogen is less basic[22] and primary exophiles are less easily displaced.

Isomerization of 1 *via* III requires nucleophilic attack at C-2 of III. The closest precedent for this step in heterocyclic chemistry involves openings of the 1-azoniabicyclo[3.1.0]hexane system[18b] in which attack may occur at both the more- and the less-substituted carbon atoms. This system falls far short of III in ring strain energy, however.

A second possibility which avoids C-2 attack on III is ionization of 2 to II, the primary carbonium ion.[23b] Rapid ionic isomerization, II ⇄ III, and recombination of either cation would account for interconversion, 2 ⇄ 1, and for the rearrangements of 2. Cation II, although it should presumably be less stable thermodynamically than III, might be more stable than a simple primary carbonium ion by reason of "internal solvation." In this view, II carries partial single bond character between nitrogen and the exocyclic carbonium carbon atom similar to, and possibly stronger than, that of a polar ionizing solvent.

Experimentally, formation of chloromethylaziridine (2) from 1, counter to ring strain, is undoubtedly detectable only because, under these isomerization conditions, 2 is the more stable thermally and ionizes the more slowly. Many ionization–recombination cycles, each leading to a trace of 2, yield measurable amounts of 2. It is not surprising that 2 did not give 1 detectably; 1 resinified preferentially under these conditions. The stabilities of 1 and 2 were reversed in the presence of potassium iodide, and the formation of 1 from 2 became observable, but 1 did not appear to yield 2, for the same reasons.

(22) Reviews: (azetidines) J. A. Moore, in "Heterocyclic Compounds with Three- and Four-Membered Rings," A. Weissberger, Ed., Part Two, Interscience, New York, N. Y., 1964, pp 885–977; (aziridines) P. E. Fanta, *ibid.*, Part 1, pp 524–575.

(23) (a) Review: K. B. Wiberg, *Rec. Chem. Progr.*, **26**, 143 (1965). (b) In addition to the generally accepted delocalized benzyl, allyl, and cyclopropylcarbinyl primary carbonium ions, support has also been advanced for simple unstabilized examples; see E. S. Gould, "Mechanism and Structure in Organic Chemistry," Holt, Rinehart and Winston, New York, N. Y., 1959, p 254.

The present evidence does not permit a conclusive choice between C-2 attack on III and the stabilized II in equilibrium with III.

Experimental Section[24]

1-*tert*-Butyl-3-chloroazetidine (1).—1-*tert*-Butyl-3-azetidinol,[8] (3, 37.0 g), and 84 g of triphenylphosphine in 700 ml of carbon tetrachloride was stirred and heated under reflux for 3 days as a solid separated. The cooled mixture was filtered, and the filtrates were extracted with excess dilute sulfuric acid, and then washed with water. The combined aqueous extracts were cooled with ice, made strongly alkaline with 50% sodium hydroxide solution, and extracted with ether. Drying ($MgSO_4$) and distillation gave 29.3 g (69%) of chloroazetidine (1): bp 63–64° (25 mm); 45–46° (10 mm); $n^{25}D$ 1.4475; nmr (see Figure 1) except τ 9.0 (s, *tert*-Bu); ir (neat) 3.37 i, 3.50 i, 6.80 m, 7.12 w, 7.36 i, 7.65 w, 7.96 i, 8.13 i, 8.22 i, sh, 9.1 m, 9.24 m, 10.18 m, 11.52 m, 12.53 w, 15.4 i μ.[25]

Anal. Calcd for $C_7H_{14}ClN$: C, 56.94; H, 9.56; Cl, 24.02; N, 9.49; amine neut equiv, 148. Found: C, 56.73; H, 9.35; Cl, 24.25; N, 9.62; amine neut equiv 148.

This product contained usually about 1% of chloromethylaziridine (2), which could be removed by heating with an equal volume of acetic acid at 50° overnight and reisolating pure 1 (vpc, column C, 130°); constants were unchanged.

Longer heating (6 days) gave another higher boiling unstable oil (vpc, column B, 130°, decomposing to 2) which was isolated in up to 11% yields by basifying the iced acidic extracts with aqueous sodium carbonate solution. Distillation gave, after collecting 1 containing up to 4% 2, ***tert*-butyl-2,3-dichloropropylamine** (4): bp 51° (2 mm); $n^{26}D$ 1.4567; nmr τ 8.9 (s, *tert*-bu), 6.9–7.1 (m, CH_2N), 5.6–6.2 (m, $CHClCH_2Cl$). It could not be obtained completely free of 2; crystals separated upon standing.

Anal. Calcd for $C_7H_{15}Cl_2N$: C, 45.66; H, 8.21; Cl, 38.52; N, 7.61; amine neut equiv, 184. Found: C, 46.40; H, 8.25; Cl, 37.41; N, 7.44; amine neut equiv, 187.

Dichloro amine 4 (0.79 g) was also obtained from 5.9 g of 2 by heating with 0.2 g of triphenylphosphine in 10 ml of carbon tetrachloride at 80° for 8 days. The complex multiplets were identical for samples from the two sources.

3-Chloro-1-cyclohexylazetidine.—From 1-cyclohexyl-3-azetidinol[8] (12.0 g) was similarly obtained 6.6 g (49%) of the chloride: bp 62–63° (1 mm); $n^{25}D$ 1.4837; nmr τ 7.7–9.1 (m, cyclohexyl), 6.7–7.0, 6.1–6.4 (basically triplets further split, ring CH_2), 5.4–5.7 (pentuplet, CHCl). A trace of the chloromethylaziridine (below) was detected (vpc, column B, 150°).

Anal. Calcd for $C_9H_{16}ClN$: C, 62.24; H, 9.29; Cl, 20.33; N, 8.07. Found: C, 62.02; H, 9.25; Cl, 20.62; N, 7.91.

1-*tert*-Butyl-2-chloromethylaziridine (2).—Crude 1-*tert*-butylamino-3-chloro-2-propanol[10] (79.1 g from 0.5 mol each of *tert*-butylamine and epichlorohydrin), which had been freshly prepared and carefully freed of starting materials by rotary evaporation at 20° (2 mm), was dissolved in 250 ml of ethanol–free chloroform. The solution was cooled to 0–10° and treated successively with 71 g of anhydrous pyridine, 36.0 g of methanesulfonic acid (75% of theory for salt formation), and then dropwise with 57.3 g of methanesulfonyl chloride. After being stirred as the ice bath melted overnight, the slurry was poured into excess ice and water. The mixture was shaken and treated with 10% sodium carbonate solution in small portions until the pH was about 8, in the presence of ice. All solids dissolved. The cold chloroform layer was dried ($MgSO_4$) in a 10° water bath. The aqueous layer was again extracted with chloroform and the extracts were added to the drying solution.

(24) Melting and boiling points are uncorrected. Three vpc columns used routinely: A, 2 m × 0.25 in., 10% SE-52 on 60–80 mesh Diataport S; B, 2 m × 0.25 in., 10% neopentyl glycol succinate on 30–60 mesh acid-washed Chromosorb W; C, 28 ft × 1/16 in., 1% silver nitrate and 18% Carbowax 20M on 30–60 mesh Chromosorb W. Toluene or xylene was the vpc standard; areas were measured by a disk-integrated recorder on a F & M Model 700 chromatograph (thermal conductivity detector, helium carrier). Nmr spectra were run in deuteriochloroform with internal tetramethylsilane as reference on the Varian A-60 and T-60 spectrometers. Integrations supported the assignments. Pressure reactions were conducted in 100- or 20-ml stainless steel or glass vessels. Some data are based on composites of several experiments. Elemental analyses were by Galbraith Laboratories, Knoxville, Tenn.

(25) Infrared spectra were of little value in distinguishing isomers. Data for 1 and 2 are presented: i, intense; m, medium; w, weak; sh, shoulder.

The cold filtered chloroform layer was concentrated below 15° (2 mm); the crude mesylate was unstable at 25°, warming spontaneously and lowering the yield. The cool mesylate was promptly added to a stirred cold solution of 53 g of Na_2CO_3 and 10 g of diethylenetriamine (a scavenger for epoxide impurities) in 400 ml of water in an ice bath. Stirring was continued overnight as the ice melted. Ether extraction, drying ($MgSO_4$), and distillation (persistent foaming) gave isomerically pure (vpc, column C, 130°) chloromethylaziridine (**2**): bp 47–48° (10 mm); 40.6 g (55%); $n^{26}D$ 1.4454; nmr (see Figure 1) except τ 9.0 (s, *tert*-bu); ir (neat) 3.38 i, 3.49 m, sh, 6.82 m, 6.90 m, sh, 6.94 m, 7.00 m, 7.22 m, 7.36 i, 7.93 i, 8.12 i, 8.32 i, 9.1–9.2 w, 9.78 m, 9.97 w, 10.16 m, 10.73 w, 11.40 w, 12.19 m, 12.3–12.5 w, 13.8 m, 15.02 i. μ [25]

Anal. Calcd for $C_7H_{14}ClN$: C, 56.94; H, 9.56; Cl, 24.02; N, 9.49. Found: C, 57.11; H, 9.50; Cl, 24.06; N, 9.46.

The amine neutralization equivalent was satisfactory (Calcd: 148. Found: 150.) when measured with perchloric acid in acetic acid, but was halved when determined with anhydrous hydrogen bromide in acetic acid (Found: 76.), due to the ring opening by HBr. To avoid overheating the sample can be added to frozen glacial acetic acid, treated with excess HBr in HOAc, allowed to stand 15 min to complete the cleavage, and back-titrated with standard NaOAc in HOAc. The aziridines of this work, and aziridine itself, reacted similarly. The present aziridines were stable to dissolution in 10% aqueous HCl. Crystal violet was a convenient indicator for titrations in acetic acid. Azetidines were not cleaved by HBr at 25°.

1-*tert*-Butylamino-3-chloro-2-propylsulfuric Acid Inner Salt.—Distilled 1-*tert*-butylamino-3-chloro-2-propanol[10] (78.3 g) in 800 ml of carbon tetrachloride was stirred and treated dropwise below 10° with 31.7 ml of chlorosulfonic acid. The gum which separated slowly crystallized and was stirred overnight. Evolution of HCl was completed by heating at 40° for 6 hr. Cooling, filtration, and drying *in vacuo* gave 116 g (99%) of colorless salt. Several recrystallizations from 80:20 ethanol–water gave the pure salt, mp 232–233° dec (placed in bath at 220°).

Anal. Calcd for $C_7H_{16}ClNO_4S$: N, 5.70; S, 13.05. Found: N, 5.70; S, 13.45.

Cyclization with aqueous KOH[26] gave only a 3% yield (vpc) of impure *tert*-butylcdloromethylaziridine (**2**).

2-Chloromethyl-1-cyclohexylaziridine.—From 41.2 g of 1-chloro-3-cyclohexylamino-2-propanol[27] was obtained similarly 20.1 g (54%) of the aziridine: bp 66–67° (2 mm); $n^{25}D$ 1.4814; nmr τ 8.0–8.9 (m, all ring protons), 4.2–4.9 (m, CH_2Cl).

Anal. Calcd for $C_9H_{16}ClN$: C, 62.24; H, 9.29; Cl, 20.41; N, 8.07; amine neut equiv, 174. Found: C, 62.00; H, 9.28; Cl, 20.33; N, 8.18; amine neut equiv, 177.

The modified Wenker synthesis, *via* amine hydrochloride,[26] gave a 3% yield (vpc, column B, 140°) of this aziridine.

2-Acetoxymethyl-1-*tert*-butylaziridine (**6**).—1-Acetoxy-3-*tert*-butylamino-2-propanol,[13] 19.9 g, was mesylated and cyclized overnight at 0–10° to give 5.7 g (32%): bp 45–46° (1 mm); $n^{25}D$ 1.4306; nmr τ 9.0 (s, *tert*-bu), 8.4–8.6 (4 lines, CH_2N), 7.9–8.3 (m, NCH), 7.95 (s, CH_3CO), 5.7–6.4 (overlapping quartets, CH_2OAc).

Anal. Calcd for $C_9H_{17}NO_2$: C, 63.12; H, 10.01; N, 8.18; amine neut equiv, 171. Found: C, 63.03; H, 9.93; N, 8.31; amine neut equiv, 176.

1-*tert*-Butyl-2-hydroxymethylaziridine (**13**).—The acetate, **6**, was hydrolyzed and the distilled carbinol [bp 46–47° (2 mm)] solidified: mp 31–32°; nmr τ 9.0 (s, *tert*-bu), 8.4–8.6 (3 lines, CH_2N), 7.8–8.3 (m, CHN), 6.3–6.6 (t, CH_2OH).

Anal. Calcd for $C_7H_{15}NO$: C, 65.07; H, 11.70; N, 10.84. Found: C, 64.92; H, 11.63; N, 10.82.

4-*tert*-Butylamino-3-hydroxybutyronitrile.—A solution of 150.5 g of crude *tert*-butylaminochloropropanol[10] (from 1.00 mol of amine and epichlorohydrin) in 100 ml of ethanol was added with stirring during 2 hr to a solution of 97.5 g of potassium cyanide in 250 ml of water and 300 ml of ethanol. After stirring another 5 hr, the mixture was treated with 50 ml of 50% NaOH solution, extracted with ether, dried (K_2CO_3), and concentrated. The residual oil crystallized from ethanol: 44.3 g (28%); mp 75–76°; nmr τ 8.9 (s, *tert*-bu), 7.2–7.5 (m, $CH_2CHOHCH_2CN$), 5.9–6.3 (m, CHOH).

Anal. Calcd for $C_8H_{16}N_2O$: C, 61.51; H, 10.32; N, 17.93. Found: C, 61.37; H, 10.75; N, 17.73.

1-*tert*-Butyl-2-cyanomethylaziridine (**7**).—The above nitrile (20.2 g) was mesylated as described for the preparation of **2**, and the crude mesylate was isolated below 10° and added to iced carbonate–diethylenetriamine solution and stirred to 20° overnight. A mixture of three isomers was isolated and kept in a nitrogen atmosphere, 7.6 g (42%), bp 65–72° (2 mm). The cuts ranged from 76 to 87 area % of the unstable overlapping major peaks (column B, 150°). They resinified rapidly in air. Analysis of the last cut and the nmr spectrum were consistent with 50 mol % **4-*tert*-butylamino-2-** and 40 mol % **-3-butenonitrile** containing 13 area % of the cyanomethylaziridine **7** (10 mol %): nmr τ 9.0, 8.9, 8.4 (3 s, *tert*-bu), 8.3–8.6 (m, CH_2N), 6.6–6.8 (4 main lines, CH_2CN), 4.0–4.6, 3.0–3.7 (m, CH=CH).

Anal. Calcd for $C_8H_{14}N_2$: C, 69.45; H, 10.21; N, 20.27. Found: C, 69.39; H, 9.98; N, 20.15.

Further, 24.0 g of hydroxynitrile was mesylated (7% excess methanesulfonic acid, 60% excess mesyl chloride, etc.), and the crude mesylate cyclized as usual. The crude product mixture was heated for 2 days at 70° and distilled and 1.40 g (7%) of **7** collected: bp 59° (2 mm); nmr τ 9.0 (s, *tert*-bu), 8.3–8.6 (4 lines, CH_2N), 7.9–8.3 (m, CHN), 7.5–7.7 (4 lines, CH_2CN).

Anal. Calcd for $C_8H_{14}N_2$: C, 69.45; H, 10.21; N, 20.27. Found: C, 69.55; H, 10.22; N, 20.01.

1-*tert*-Butyl-2-*tert*-butylaminomethylaziridine (**12**).—1,3-Di-*tert*-butylamino-2-propanol,[10] 28.2 g, was mesylated and cyclized as usual: 14.5 g (52%); bp 59–60° (4 mm); nmr τ 9.0 (s, *tert*-buN), 8.9 (s, *tert*-buNH), 7.9–8.8 (m, 3 ring protons), 7.3–7.5 (two broad peaks, CH_2NH).

Anal. Calcd for $C_{11}H_{24}N_2$: C, 71.68; H, 13.12; N, 15.20. Found: C, 71.72; H, 13.14; N, 15.11.

Reactions of Chlorides 1 and 2 with Nucleophiles. 1. Hydrolysis.—The chloride (3.00 g) was heated and rotated in a 90° oven for 6 days with equimolar 10% aqueous sodium carbonate solution. The isolated product mixture was analyzed on columns A and B. The best results, with least tailing, were obtained on column A at 100° using the trimethylsilyl ethers prepared on the 5–10-mg scale with TRI-SIL (Pierce Chemical Co., Rockford, Ill.). From chloroazetidine (**1**) only 1-*tert*-butyl-3-azetidinol (**3**) was obtained in 16% yield. Three minor high boiling impurities were present but no aziridinylcarbinol.

Chloroaziridine (**2**) gave both the azetidinol (11% yield) and 1-*tert*-butyl-2-aziridinylcarbinol (4.4%). The vpc analyses were confirmed by nmr.

In 50:50 v/v aqueous ethanol, specific rate constants were determined by titration of aliquots with 0.1 *N* silver nitrate (HNO_3). For the chloroazetidine (**1**), $k_1^{35.0°}$ was 0.135, 0.146, and 0.130 hr^{-1} in three runs, but the first-order plots were linear through only 11–15% reaction. A 50.0°, the constant was 0.50 hr^{-1} and addition of 1 vol % of triethylamine gave a value of 0.79. (Deyrup and Moyer found no effect on the tosylate hydrolysis rates with triethylamine addition.[3]) 3-Chloro-1-cyclohexylazetidine gave rates of 0.087 and 0.086 hr^{-1} at 35.0°.

The chloromethylaziridine (**2**) hydrolyzed too slowly to measure accurately by the above method but the initial constant at 70.0° was about 0.016 hr^{-1}; the plots were linear up to about 10% reaction.

2. Potassium Cyanide.—The chloroazetidine (**1**, 1.56 g) and 6.5 g of KCN in 10 ml of acetonitrile were heated in the bomb at 100° for 18 hr, when no **1** remained (vpc). 1-*tert*-Butyl-3-cyanoazetidine (0.68 g) was isolated in 42% yield, bp 66–68° (4 mm). After 6 days at 100° chloromethylaziridine (**2**) gave the same nitrile in 27% conversion and 79% yield (vpc). The nmr and ir spectra were identical with those of the compound prepared from the tosylate as described by Ohta *et al.*[7] No aziridine was detected in either mixture. Similar but inferior results were obtained in methanol. A second product, previously identified as chloroazetidine (**1**),[1] has now been shown by vpc on another column (C, 130°) and by nmr to be 1-*tert*-butyl-2-methoxymethylaziridine (below).

3. Sodium *tert*-Butylmercaptide.—Chloroazetidine (**1**), 1.49 g, in 4 ml of methanol containing 4.86 meq of sodium methoxide was treated with 0.90 g of *tert*-butyl mercaptan and heated in the bomb at 100° for 18 hr, giving **1-*tert*-butyl-3-*tert*-butylthioazetidine**: bp 68–69° (2 mm); 1.42 g (71%); nmr τ 9.0 (s, *tert*-buN), 8.7 (s, *tert*-buS), 6.2–7.0 (m, ring protons). Two minor impurities persisted (vpc, column B, 150°), but neither was the aziridine.

Anal. Calcd for $C_{11}H_{23}NS$: C, 65.61; H, 11.45; N, 6.96; S, 15.92. Found: C, 64.89; H, 11.49; N, 7.33; S, 16.55.

(26) R. C. Elderfield and H. A. Hageman, *J. Org. Chem.*, **14**, 605 (1949).
(27) J. B. McKelvey, B. G. Webre, and E. Klein, *ibid.*, **24**, 614 (1959).

Pure **1-*tert*-butyl-2-*tert*-butylthiomethylaziridine** was formed from **2** in 73% yield: bp 52–54° (1 mm); nmr τ 9.0 (s, *tert*-buN), 8.7 (s, *tert*-buS), 8.0–8.6 (m, ring protons), 7.3–7.6 (m, CH_2S).

Anal. Calcd for $C_{11}H_{23}NS$: C, 65.61; H, 11.45; N, 6.96; S, 15.92. Found: C, 65.57; H, 11.46: H, 7.03; S, 16.17.

4. Potassium *tert*-Butoxide in *tert*-Butyl Alcohol.—In a nitrogen-filled glove bag, 5.9 g of **1** in 10 ml of anhydrous *tert*-butyl alcohol and 4.2 g of *tert*-buOK (MSA Research Corp., Evans City, Pa.) were sealed in a 20-ml bomb. After being rotated in a 70° oven for 11 days, water and ether were added. After a forerun containing unchanged **1** (0.6 g, column C, 130°), 4.7 g (64%) of **1-*tert*-butyl-3-*tert*-butoxyazetidine** was collected: bp 56–58° (4 mm); nmr τ 9.0 (s, *tert*-buN), 8.8 (s, *tert*-buO), 6.5–7.1 (m, ring protons), 5.7 (pentuplet, CHO).

Anal. Calcd for $C_{11}H_{23}NO$: C, 71.27; H, 12.50; N, 7.60. Found: C, 71.22; H, 12.68; N, 7.64.

Similarly (6 days, 70°) **2** gave 49% yield of isomer-free (vpc, column C, 150°) **1-*tert*-butyl-2-*tert*-butoxymethylaziridine**: bp 35–36° (1 mm partial decomposition); nmr τ 9.0 (*tert*-buN), 8.8 (s, *tert*-buO), 8.0–8.7 (m, ring protons), 6.3–7.1 (m, CH_2O).

Anal. Calcd for $C_{11}H_{23}NO$: C, 71.27; H, 12.50; N, 7.60. Found: C, 70.42; H, 12.38; N, 8.29.

5. Sodium Methoxide in Methanol.—A solution of 3.00 g of **1** in 6 g of methanol containing 20 mequiv of sodium methoxide was heated at 100° for 6 days. Pure **1-*tert*-butyl-3-methoxyazetidine** (2.04 g, 71%) was isolated: bp 45–46° (10 mm); vpc, column B, 90°; nmr τ 9.0 (s, *tert*-bu), 6.7 (s, CH_3O), 6.4–7.1 (m, ring CH_2), 5.7–6.2 (m, $CHOCH_3$).

Anal. Calcd for $C_8H_{17}NO$: C, 67.08; H, 11.97; N, 9.78. Found: C, 67.40; H, 11.88; N, 9.70.

From chloroaziridine (**2**), after 4 days at 70°, **1-*tert*-butyl-2-methoxymethylaziridine** (88%) was obtained: bp 41–42° (10 mm); nmr τ 9.0 (s, *tert*-bu), 8.3–8.8 (5 lines, ring CH_2), 7.9–8.3 (m, ring CH), 6.3–6.8 (m, CH_2O), 6.7 (s, CH_3O). An impurity persisted (vpc, column B, 90°); it was not an azetidine.

Anal. Calcd for $C_8H_{17}NO$: C, 67.08; H, 11.97; N, 9.78. Found: C, 66.04; H, 11.70; N, 9.61.

6. *tert*-Butylamine.—Either of the chlorides gave the same triamine when heated at 100° for 24 hr with 100% excess amine, 0.01 mol of chloride, 5 ml of acetonitrile, and 1.5 g of potassium carbonate. The carbonate became caked during the reaction. **1,2,3-Tris-(*tert*-butylamino)propane** (**10**), bp 71–72° (1 mm), 55–57% yield, was a viscous oil: nmr τ 8.9, 8.8 (uot resolved, 2 s, *tert*-bu), 7.3–7.5 [two broad peaks, $(NCH_2)_2CHN$].

Anal. Calcd for $C_{15}H_{35}N_3$: C, 69.98; H, 13.70; N, 16.32; amine neut equiv, 86; mol wt, 257. Found: C, 69.92; H, 13.81; N, 16.40; amine neut equiv, 88; mol wt, 269 (osmometric, in benzene).

Under milder conditions the above method gave a forerun containing a diamine, along with the triamine. It was the sole monomeric product when a similar mixture was heated at 70° in a horizontally rotated bomb containing a Teflon-coated magnetic stirring bar which continually crushed the carbonate and maintained it in a finely divided suspension. After 10 days, 24% of the chloride remained (**1**) and a 39% yield of **1-*tert*-butyl-3-*tert*-butylaminoazetidine** (**11**) was isolated but no triamine was detected. The diamine had bp 59–60° (2 mm); nmr τ 9.0 (s, *tert*-bu), 8.9 (s, *tert*-buNH), 7.0–7.3 (m, ring CH_2); 6.2–6.7 (m, ring CH_2, CHNH).

Anal. Calcd for $C_{11}H_{24}N_2$: C, 71.68; H, 13.12; N, 15.20; amine neut equiv, 92; mol wt, 184. Found: C, 71.44; H, 13.26; N, 15.28; amine neut equiv, 94; mol wt, 199 (benzene).

Similarly, chloromethylaziridine (**2**) without the rolling bar gave only the triamine **10**. When the bar was used with **2**, after 12 days at 70°, analysis (vpc, column C, 130°) indicated that 13% of **2** remained, and 1.08 g (23%) of a diamine (**12**) was isolated, along with 1.37 g (21%) of triamine. The diamine was identical (nmr and ir spectra, vpc, and constants) with **12** prepared from di-*tert*-butylaminopropanol and analyzed correctly.

1-*tert*-Butyl-3-methylaminoazetidine.—Using sodium carbonate with a rolling bar, chloroazetidine (**1**) and excess anhydrous methylamine at 75° for 4 days gave the diamine (66% yield): bp 62–64° (10 mm); nmr τ 9.0 (s, *tert*-buN), 7.6 (s, CH_3NH), 6.3–7.2 (m, 5 ring protons).

Anal. Calcd for $C_8H_{18}N_2$: C, 67.55; H, 12.75; N, 19.69. Found: C, 67.18; H, 12.88; N, 19.76.

1-*tert*-Butyl-3-dimethylaminoazetidine.[28]—Chloroazetidine (**1**) did not react appreciably with dimethylamine at 75° in 18 hr. A solution of 3.7 g of **1** and 5.1 g of silver tetrafluoroborate (Ozark-Mahoning Co., Tulsa, Okla.) in 10 ml of acetonitrile was cooled and treated with 19 g of dimethylamine, then sealed in the bomb and heated at 75° for 20 hr. Evaporation and dissolution in water, filtration, addition of excess 50% alkali and filtration, ether extraction, drying over NaOH pellets, and concentration gave the crude amine. It was precipitated from acetic acid as the **diperchlorate** salt, which did not melt, but decomposed at 210–225°.

Anal. Calcd for $C_9H_{22}Cl_2N_2O_8$: C, 30.26; H, 6.21; Cl, 19.85; N, 7.84. Found: C, 30.43; H, 6.27; Cl, 19.73; N, 7.84.

The free amine was obtained with alkali: bp 62° (10 mm); $n^{25}D$ 1.4384; nmr and ir spectra were identical with those of Ohta, *et al.*,[28] *via* the tosylate.

7. Acetolysis.—A mixture of 7.4 g of chloroazetidine (**1**) and 9.8 g of anhydrous potassium acetate in 40 ml of glacial acetic acid heated at 100° in a bomb for 4 days gave *tert*-butyldiacetoxypropylamines (7.9 g, 68%), bp 85–87° (1 mm), $n^{25}D$ 1.4355.

Anal. Calcd for $C_{11}H_{21}NO_4$: C, 57.12; H, 9.15; N, 6.06. Found: C, 57.31; H, 9.22; N, 6.02.

The nmr and ir spectra were additive combinations for the ***tert*-butyl-1,3-diacetoxy-2-propyl- and -2,3-diacetoxy-1-propylamines.**[13] The aminodiols obtained by alkaline hydrolysis were present in equal amounts as indicated by nmr integration of the two *tert*-butyl singlets. This was confirmed by vpc analysis of the trimethylsilylated diols (TRI-SIL, Pierce Chemical Co., Rockford, Ill.) separated on column B at 125°.

The 1,3-diacetate was separated by heating the mixed amines with equimolar acetic anhydride at 80° overnight. Distillation gave ***tert*-butyl-1,3-diacetoxypropylamine** (**19**): bp 89–90° (1 mm); $n^{26}D$ 1.4372; nmr τ 8.9 (s, *tert*-bu), 8.0 (s, CH_3CO), 6.7–7.1 (pentuplet, CHN), 5.9–6.1 (2 d, $2CH_2OAc$).

Anal. Calcd for $C_{11}H_{21}NO_4$: C, 57.12; H, 9.15; N, 6.06. Found: C, 57.10; H, 9.64; N, 5.89.

Hydrolysis of the diester gave **2-*tert*-butylamino-1,3-propanediol**, crystallized from ethanol–hexane: mp 107–108°; nmr τ 8.9 (s, *tert*-bu), 6.9–7.3 (m, NCH), 6.4, 6.5 (broad lines, $2CH_2OH$).

Anal. Calcd for $C_7H_{17}NO_2$: C, 57.11; H, 11.64; O, 21.74. Found: C, 57.25; H, 11.72; O, 22.00.

A partial acetolysis run (3.00 g of **1**, 60°, 20 days) was quickly worked up with iced carbonate solution and extracted with ether. Rapid distillation gave 0.39 g of an unstable oil, bp 63–66° (1 mm). It contained (vpc, column B, 100–150°) 3-acetoxy-1-*tert*-butylazetidine,[8] the diacetoxyamines **18** and **19**, and a new chlorine-containing compound (75 area %) decomposing on the column to 2-acetoxymethyl-1-*tert*-butylaziridine (**6**). It was impure (80 mol %) **3-*tert*-butylamino-2-chloro-1-propyl acetate** (**16**): nmr τ 8.9 (s, *tert*-bu), 7.9 (s, CH_3CO), 7.0–7.4 (m, NCH_2), 5.8–6.1 (m, CHCl), 5.5–5.7 (m, CH_2OAc).

Anal. Calcd for $C_9H_{18}ClNO_2$: Cl, 17.07. Found: Cl, 13.77.

The impure amine (**16**, 75 area %, 82 mg) and 65 mg of diisopropylethylamine in 2 ml of acetonitrile was heated at 60° for 18 hr. Analysis (column A) indicated 38% conversion to acetoxymethyl-*tert*-butylaziridine (**6**).

Acetolysis of chloroaziridine **2** (90°, 18 hr) gave only the 1,3- and 1,2-diacetoxyamines, **19** and **18**, in a 95:5 ratio, determined by nmr and confirmed by selective acetylation and acid extraction.

Solutions of **2** made by adding it to partially frozen glacial acetic acid were unstable at 20°. A solution, which initially required 1.98 mequiv of HBr–HOAc/mmole, after 18 hr used only 1.12 mequiv/mmol, but potentiometric titration with silver perchlorate (0.1 *M* in HOAc) indicated only 3.9% ionization of chloride. A similar solution after 3 days was iced, quickly basified with carbonate and extracted, and an oil isolated below 20°. The oil was too unstable to distil (giving only acetoxymethyl-*tert*-butylaziridine **6**) and contained **6**, diacetoxyamine **19**, and an unstable peak (column A, 100–130°) decomposing to **6**. The oil deposited a white salt, which was purified by dissolution in chloroform and reprecipitation by ether, mp 157–159°. It was ***tert*-butyl-1,3-diacetoxypropylamine** (**19**) **hydrochloride**, as shown by regeneration of the free amine and charcterization by nmr and vpc.

(28) T. Chen, H. Kato, and M. Ohta, *Bull. Chem. Soc. Jap.*, **41**, 712 (1968).

Acetolysis of 1.5 g of **2** in 10 ml of acetic acid, for 16 hr at 20°, was followed by titration to the crystal violet endpoint with 1.6 *M* hydrogen chloride in HOAc. Evaporation of the solvent at 20° left a gum which crystallized partially after several precipitations from chloroform with ether. It was impure **1-*tert*-butylamino-3-chloro-2-propyl acetate (17) hydrochloride**, 0.30 g.

Anal. Calcd for $C_9H_{19}Cl_2NO_2$: C, 44.27; H, 7.84; Cl, 29.04. Found: C, 46.81; H, 7.53; Cl, 25.09.

1-*tert*-Butyl-3-tosyloxyazetidine[7] (5.67 g) was heated in buffered acetic acid 4 days at 60°; under these conditions 1-*tert*-butyl-3-acetoxyazetidine[8] did not react detectably. Basification with iced carbonate and ether extraction gave an oil from which 2.9 g of the unchanged tosylate was recovered by Dry Ice cooling of the solution in *n*-pentane. The purity of the tosylate was confirmed by nmr. The remaining oil (0.79 g) contained only 1-*tert*-butyl-3-acetoxyazetidine and *tert*-butyl-1,3-diacetoxypropylamine (**19**) in a mole ratio of 91:9, determined by nmr. Although it may be inferred that ionization and ring contraction were followed by formation of acetoxymethylaziridine (**6**) which was then cleaved to give **19**, it is possible that opening by acetic acid occurred first; then the acetoxy tosylate, *tert*-$BuNHCH_2CHOTsCH_2OAc$, may have cyclized to **6**.

1,3-Diacetoxypropyldimethylamine.—1,3-Benzylideneglycerol[29] was prepared and converted to the tosylate[30] and to the mesylate, **5-mesyloxy-2-phenyl-1,3-dioxane** (66% yield), mp 132–133°, from methanol.

Anal. Calcd for $C_{11}H_{14}O_5S$: C, 51.15; H, 5.46; S, 12.41. Found: C, 51.22; H, 5.59; S, 12.55.

Neither the mesylate nor the tosylate reacted with *tert*-butylamine at 100° in acetonitrile, but the tosylate with excess dimethylamine in acetonitrile at 130° in a bomb gave **5-dimethylamino-2-phenyl-1,3-dioxane** (46% yield): bp 103–104° (1 mm); $n^{26}D$ 1.5320; nmr τ 7.8 [s, $(CH_3)_2N$], 7.2–7.6 (m, CHOMs), 6.1–6.6 (*m*, 2CHO), 5.5–5.8 (m, 2CHO), 4.7 (s, $O_2CHC_6H_5$), 2.4–2.8 (m, C_6H_5).

Anal. Calcd for $C_{12}H_{17}NO_2$: C, 69.53; H, 8.27; amine neut equiv, 207. Found: C, 69.90; H, 8.15; amine neut equiv, 207.

The dioxane was hydrolyzed with dilute sulfuric acid at 60–70°; the aminodiol was prepared by alkali, dried, and acetylated with acetic anhydride to give **1,3-diacetoxy-2-propyldimethylamine**: bp 73–74° (1 mm); $n^{26}D$ 1.4467; nmr τ 8.0 (s, $2CH_3CO_2$), 7.7 [s, $(CH_3)_2N$], 7.3–6.9 (m, NCH), 5.7–5.9 (2 d, $2CH_2OAc$).

Anal. Calcd for $C_9H_{17}NO_4$: C, 53.18; H, 8.43; N, 6.89. Found: C, 53.33; H, 8.41; N, 7.00.

The nmr and ir spectra showed the expected resemblances to data for *tert*-butyl-1,3-diacetoxy-2-propylamine (**19**).

Isomerization.—The two chlorides isomerized under a variety of conditions. When subjected to vpc on a 10 ft × 0.25 in. column packed with 1% mercuric chloride and 20% Carbowax 20M on Gas Chrom (60–80 mesh), chloroazetidine **1**, programmed at 7.5°/min from 75 to 220°, eluted at about 166° and was followed by chloromethylaziridine **2** (22% from **1**) at 177°. Under these conditions, **2** was stable.

A series of runs was carried out in bombs and glass pressure vessels. The contents were analyzed periodically by vpc (toluene standard, column C, 130°). The isomer ratios were not self-consistent but in a few runs were essentially stable for several days. For the following runs are listed starting chloride, solvent-catalyst, days at temperature, total isomeric chlorides based on starting chloride, and ratio of **1**:**2**: (1) **1**, CCl_4–4% Ph_3P based on **1**, 8–90°, 76%, 41:59; (2) **1**, CH_3CN–, 2.7–90°, 41%, 62:38; (3) **1**, CCl_4–1% Ph_3P, 5–90°, 16%, 78:22; (4) **1**, CH_3CN–, 7 to 16–90°, 49–21%, 54:46 (stable 8 d); (5) **1**, CH_3CN–10% $HgCl_2$, 1–80°, 18%, 98:2; (6) **2**, CH_3CN–, 3–90°, 77%, 5:95; (7) **2**, CCl_4–4% Ph_3P, 4–90°, less than 1% **1**; (8) 3-chloro-1-cyclohexylazetidine, CH_3CN–, 2–90°, 44%, 33:67 azetidine:aziridine; (9) 2-chloromethyl-1-cyclohexylaziridine, CH_3CN–17–90°, 7%, 30:70 (stable for several days).

In runs 1–4 above, up to 15 mol % of *tert*-butyl-2,3-dichloropropylamine (**4**), based on **1**, was detected. It was also isolated from **2** in a run similar to run 8. An equimolar mixture of **4** and diisopropylethylamine in acetonitrile after 4 hr at 80° gave in 80% conversion a mixture of **1** and **2** in a 9:91 ratio.

Runs were conducted in acetonitrile using **1** and an equal weight of anhydrous sodium carbonate with a Teflon-covered stirring bar in a horizontally rotated bomb at 80°. Under these conditions *no* ring opening of **1** by excess *tert*-butylamine or even methylamine was observed. During 6 days, the **1**:**2** ratio gradually reached 93.5:6.5 while the total of the two isomers slowly dropped to 53.4% of **1** charged; no **4** was detected but poorly resolved higher boiling by-products (eluted at 200° from column C) were formed.

Similar runs with **2** showed it to be more stable, decreasing only a few per cent per day, but no trace of **1** or **4** was detected. The results do not exclude formation of **1** but reflect its poorer stability toward resinification. This was shown by rotating a solution of 1.61 g of **2**, 0.154 g of **1**, and 2.5 g of anhydrous Na_2CO_3 in 5 ml of acetonitrile with a bar at 70°. After 2 days, for instance, analysis indicated that 88.9% **2** and 86.3% **1** remained. Thus the initial loss of **1** was over 20% greater for **1** than for **2**.

Catalysis by potassium iodide (0.20 g and 1.5 g of **1** or **2**) in the presence of sodium carbonate and acetonitrile was studied at 75°. After 18 hr, **2** gave 0.71% **1** and 66% of the original **2** was found. In 2 days, **1** remained constant, but **2** decreased to 56%. No other volatile products were detected. With KI, **1** did not isomerize to **2** detectably, but it was shown that **2** was less stable than **1** under these conditions. A third compound, eluting between xylene and **1**, was probably an elimination product.

1-*tert*-Butyl-3-azetidinol (**3**) was not opened detectably with diethylamine in 10 days at 100° in the presence of carbonate and a rolling bar, although this reaction did occur at 150° in the absence of carbonate.[13]

Registry No.—**1**, 21452-71-1; **2**, 21452-72-2; **4**, 17027-01-9; **6**, 26146-47-4; **7**, 26146-48-5; **10**, 26146-49-6; **11**, 26146-50-9; **12**, 26146-51-0; **13**, 25665-28-5; **16**, 26146-53-2; **18**, 22741-50-0; **19**, 26146-54-3; **19** HCl, 26146-55-4; 3-chloro-1-cyclohexylazetidine, 26146-56-5; 1-*tert*-butylamino-3-chloro-2-propylsulfuric acid inner salt, 26146-57-6; 2-chloromethyl-1-cyclohexylaziridine, 26146-58-7; 4-*tert*-butylamino-3-hydroxybutyronitrile, 26146-59-8; 1-*tert*-butyl-3-*tert*-butylthioazetidine, 26146-60-1; 1-*tert*-butyl-2-*tert*-butylthiomethylaziridine, 26146-61-2; 1-*tert*-butyl-3-*tert*-butoxyazetidine, 26146-62-3; 1-*tert*-butyl-2-*tert*-butoxymethylaziridine, 26146-63-4; 1-*tert*-butyl-3-methoxyazetidine, 26146-64-5; 1-*tert*-butyl-2-methoxymethylaziridine, 25662-25-3; 1-*tert*-butyl-3-methylaminoazetidine, 26146-66-7; 1-*tert*-butyl-3-dimethylaminoazetidine, 18713-65-0; 1-*tert*-butyl-3-dimethylaminoazetidine diperchlorate, 26146-68-9; 2-*tert*-butylamino-1,3-propanediol, 26146-70-3; 5-mesyloxy-2-phenyl-1,3-dioxane, 26146-71-4; 5-dimethylamino-2-phenyl-1,3-dioxane, 26146-72-5; 1,3-diacetoxy-2-propyldimethylamine, 26146-73-6.

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