Aziridinemethanols

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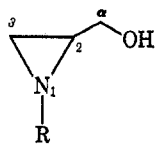
Procedures for the synthesis of substituted aziridinemethanols from aziridine esters have been developed. The stereochemistry of hydride reductions leading to α-phenylaziridinemethanols is highly dependent on the solvent and hydride reagent. Stereochemistry of these hydride reductions is assigned by independent chemical means and discussed in terms of models for asymmetric induction. A number of transformations of aziridine alcohols in which the aziridine ring remains intact are described. The mass spectra of aziridinemethanols are also discussed.

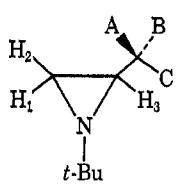
Our interest in the interaction of the aziridine ring with incipient positive charge[2] necessitated the preparation of a series of α-substituted aziridinemethanols and their derivatives. Although there are a number of



known routes to substituted aziridinemethanols,[3] our desire to study a homologous set of compounds and the availability of aziridine esters led to developing the high yield sequence of reactions shown in Scheme I. General structures were assigned to these compounds on the basis of their nmr spectra (Table I) as well as infrared, mass spectral (see below), and elemental analyses.

TABLE I

NMR SPECTRAL PROPERTIES OF *t*-BUTYLAZIRIDINE DERIVATIVES[a]

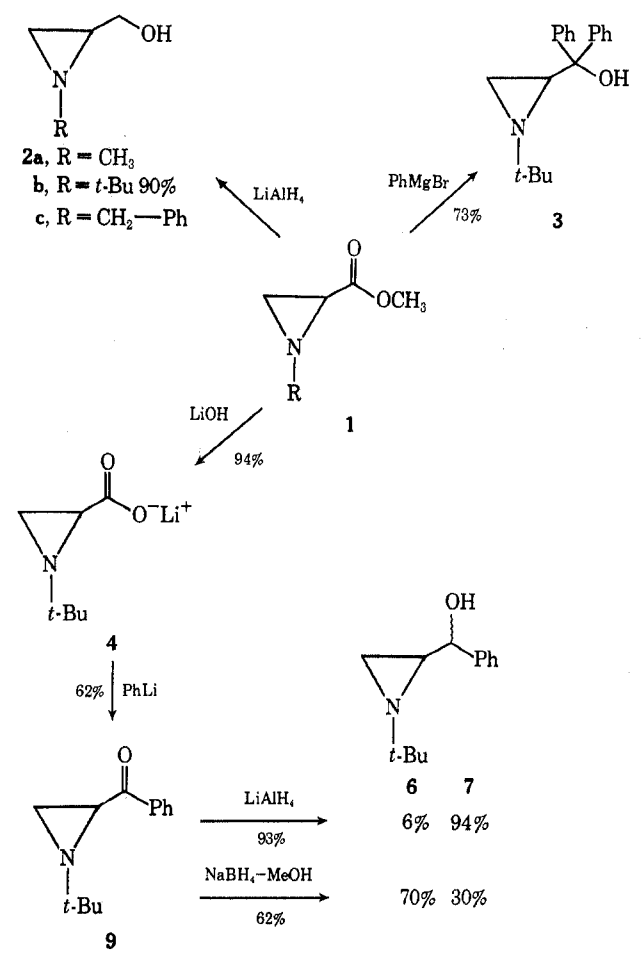


Compd	H_1	H_2	H_3	A	B	*t*-Bu
1b[b]	1.67	1.85	2.12			0.97
2b	1.33–1.50		1.80	3.43		0.97
6	1.37–1.57		1.83	4.25		0.84
7	1.34	1.55	1.97		4.60	0.85
3	1.60–1.75		2.59			0.77
4	1.82	2.04	2.93			1.03

[a] Values are expressed in parts per million (δ) downfield from TMS. [b] R = *t*-Bu.

It will be noted from Scheme I that a change in the hydride donor and solvent resulted in an inversion of stereoselectivity. Although this result allows investigation of the stereochemical consequences of aziridine interactions with a carbinyl center, an unambiguous stereochemical assignment must precede such study.

SCHEME I



Various models have been invoked to explain and predict the stereochemistry of addition to carbonyl groups adjacent to asymmetric carbon atoms.[4] In the absence of interaction between the carbonyl and the asymmetric center, attack apparently occurs on the most stable conformation and from the least hindered side (open chain model). Additions for which this model is valid seldom display high stereoselectivity. Presence of a heteroatom at the asymmetric carbon offers potential coordination of the heteroatom and the carbonyl group with a metal species (cyclic model). Additions to which this model is applicable usually are highly stereoselective. A third model in which the conformational preference is dominated by repulsion between the carbonyl oxygen and heteroatom has been proposed (and criticized[4b]).

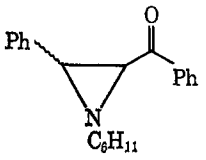
(1) Support of this research by National Science Foundation Grants GP-5531 and GP-8044 is gratefully acknowledged.

(2) J. A. Deyrup and C. L. Moyer, *Tetrahedron Lett.*, 6179 (1968).

(3) (a) R. V. Capeller, R. Griot, M. Haring, and T. Wagner-Jauregg, *Helv. Chim. Acta*, **40**, 1652 (1957); (b) N. H. Cromwell, *J. Amer. Chem. Soc.*, **69**, 258 (1947); (c) N. H. Cromwell, J. H. Anglin, Jr., F. W. Olsen, and N. G. Barker, *ibid.*, **73**, 2803 (1951); (d) D. K. Wall, J. L. Imbach, A. E. Pohland, R. C. Badger, and N. H. Cromwell, *J. Heterocycl. Chem.*, **5**, 77, 1968.

(4) (a) D. J. Cram and D. R. Wilson, *J. Amer. Chem. Soc.*, **85**, 1245 (1963); (b) G. J. Karabatsos, *ibid.*, **89**, 1367 (1967).

The stereochemistry of reduction of several aziridinyl ketones (**8**) has recently been studied by Cromwell.[3d]



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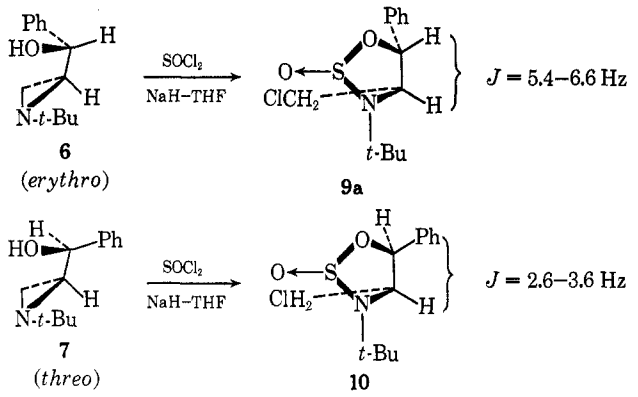
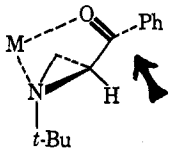
In contrast to our results, both $LiAlH_4$ and $NaBH_4$ yielded the same isomer as the major product. The stereochemistry of this major product was assigned the *erythro* configuration on the basis of the open chain model. The high stereoselectivity observed in both studies with $LiAlH_4$ is, however, suggestive of the cyclic model which also predicts preferential formation of the erythro isomer. Reductions with $NaBH_4$ were of diminished stereoselectivity in the case of **8** and of inverted stereoselectivity in the case of **5**. The different selectivity exhibited by $NaBH_4$ toward **8** and **5** clearly indicates the delicate balance between those factors which govern orientation of addition. Attempts to apply current theories concerning asymmetric induction and reagent size failed to explain convincingly the difference between the two ketones. This failure casts a certain amount of doubt on the validity of stereochemical assignments based solely on these models.

Fortunately, it was possible to obtain independent chemical evidence for the stereochemistry of **6** and **7**. Reaction of **6** with $SOCl_2$ gave oxathiazolidine **9a**.[5] Similarly, **7** yielded **10**. The stereochemistry of these



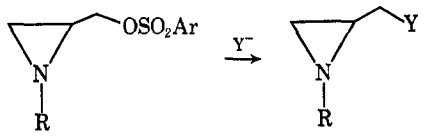
compounds can readily be assigned from the magnitude of the coupling constants in these relatively rigid heterocycles. Since oxathiazolidine formation does not affect the configuration at either asymmetric carbon, the stereochemistry can be assigned as shown. The erythro isomer (**6**) is, therefore, probably formed by attack from the least hindered side of the carbonyl group as shown in the following structure.



(5) J. A. Deyrup, C. L. Moyer, and P. S. Dreifus, *J. Org. Chem.*, **35**, 3428 (1970).

Chemistry of the Aziridinemethanols.—Our study of the properties of the aziridine ring as a neighboring group necessitated the conversion of these alcohols into esters which would serve as suitable leaving groups.[2] The conventional procedure for tosylate preparations from alcohols using tosyl chloride and pyridine was unsuccessful. This failure presumably arises from the greater base strength of the aziridine (relative to pyridine) and results in open chain products *via* chloride ion attack on the protonated aziridine ring. Use of triethylamine or sodium hydride as proton scavengers overcame this problem. In this manner, tosylates of **2a**, **2b**, and **2c** as well as the nosylate of **2b** could be prepared in good yield. The sulfonate esters with R = *t*-Butyl were relatively stable and could be obtained in analytical purity. The other sulfonate esters (R = CH_3 and CH_2Ph) were stable in solution. These solutions could be analyzed spectrally and used for further reactions. Removal of solvent, however, resulted in exothermic polymerization. It appears probable that the *t*-butyl group inhibits intermolecular alkylation. Attempts to prepare esters of **3**, **6**, and **7** have been unsuccessful. In all cases, conditions required for formation of these derivatives proved too drastic or unselective.

The sulfonate esters described above underwent facile displacement in poor ionizing solvents.[2] In each case, the displacement product, **11**, was obtained in



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good yield and uncontaminated by ring-opened or ring-expanded by-products. Although only halide and alcoxide nucleophiles were investigated, it seems certain that such nucleophilic displacements offer quite general procedures for connecting the aziridine methyl system to various groups.

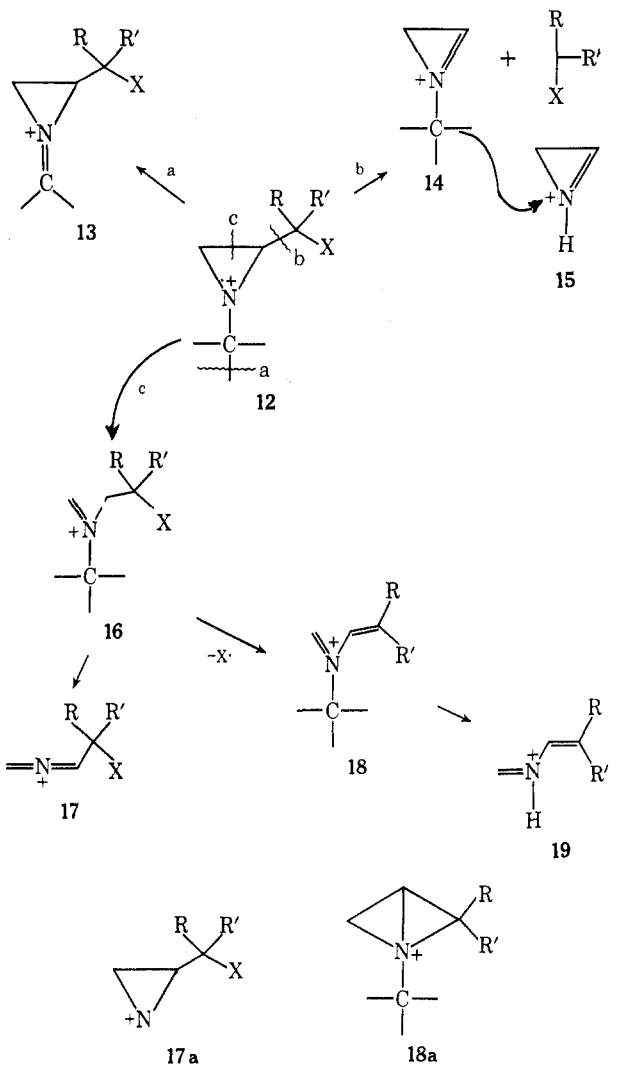
Mass Spectra of Aziridinemethanols.—The closely related series of compounds available from the synthetic work described in this paper prompted us to examine their mass spectral behavior. In addition to providing precedent for future aziridine mass spectral structural assignments, the mass spectra of these compounds offered the potentially interesting features of interplay between the nitrogen atom and the exocyclic heteroatom. The lower ionization potential of nitrogen relative to oxygen generally results in the predominance of molecular ions formed by the removal of an electron from nitrogen when both nitrogen and oxygen are present.[6] In the case of aziridines, the high s character of the unshared electron pair results in a higher ionization potential (relative to larger nitrogen heterocycles)[7] and thus might diminish the effectiveness of nitrogen in directing fragmentation. In spite of this fact, it seems quite clear that the important fragmentation pathways can best be rationalized in terms of initial ionization at the nitrogen atom.

(6) K. Biemann, "Mass Spectrometry," McGraw-Hill, New York, N. Y., 1962, pp 87–90; H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, 1967, pp 9–26.

(7) H. C. Brown and M. Gerstein, *J. Amer. Chem. Soc.*, **72**, 2926 (1950)

Although space does not allow depiction of all the mass spectra and discussion of their detailed interpretation, certain common fragmentation patterns and trends dominate the spectra.[8] These patterns are summarized in Scheme II. It is reasonable to expect

SCHEME II



those aziridine fragmentations which are directed by nitrogen will be similar to the facile fragmentations which are characteristic of other amines. In the case of **12**, three different types (a, b, and c) of α cleavage are possible. Fragments from type a cleavage are present in all *t*-butylaziridines. Type b cleavage is only important when X = OH and/or R = phenyl. Apparently, considerable stabilization of the expelled radical is required to overcome the instability of ion **14**. The third type of α cleavage (c) cannot be directly verified by experiment since the product is isomeric with the molecular ion. Nevertheless, the strain relief of this process and potential resonance stabilitization make it an attractive possibility. This possibility is strengthened by the facility with which it allows rationalization of a large number of peaks. In addition, it offers reasonable alternatives to **18a** and the even more improbable **17a**.

(8) The mass spectra of these and related compounds are reproduced in the Ph.D. thesis of C. L. Moyer, Harvard University, Cambridge, Mass., 1968.

Experimental Section

Melting points and boiling points are uncorrected. Liquid samples of less than 5 g were molecularly distilled using a hot air bath and the boiling point reported was the temperature of the air bath. Routine infrared spectra were recorded on a Perkin-Elmer 137 spectrophotometer and the expanded infrared spectra were run on a Perkin-Elmer 337 spectrophotometer. All nmr spectra were recorded on a Varian A-60A spectrometer. Chemical shifts of nmr spectra run in organic solvents are reported in parts per million downfield from internal TMS (δ). Chemical shifts run in D_2O are reported in parts per million downfield from a point 4.99 ppm upfield from the DOH peak. Mass spectra were obtained on a RMU 6E mass spectrometer for all compounds reported in this paper except **4**. In each case molecular weights in agreement with theory were obtained. Fragments are reported as *m/e* (relative intensity). Microanalyses were obtained from Galbraith Laboratories, Inc., Knoxville, Tenn. Reductions with $LiAlH_4$ were worked up according to the procedure of Micovic and Mihailovic.[9] Solvents such as THF, dimethoxyethane, and 1,4-dioxane were distilled from $LiAlH_4$ just prior to use.

Methyl 1-*t*-Butyl-2-aziridinecarboxylate.—Triethylamine (230 g, 2.28 mol) was added to methyl 2,3-dibromopropionate[10] (520 g, 2.11 mol) in 3 l. of benzene over 0.5 hr with stirring in an ice-water bath. The mixture was stirred for 1 hr at room temperature and additional *t*-butylamine (200 g, 2.74 mol) added over 0.25 hr. The mixture was refluxed for 24 hr, *t*-butylamine (73 g, 1.0 mol) added, and reflux continued for 24 hr. The reaction mixture was cooled to room temperature, filtered, and evaporated to a crude oil which was distilled without washing to give the aziridine ester (293 g, 88%): bp 58–59° (4 mm); $n^{25}D$ 1.4379; ir (CCl_4)[11,12] 1735 and 1755 cm^{-1}.

Anal. Calcd for $C_8H_{15}NO_2$: C, 61.12; H, 9.62; N, 8.91. Found: C, 60.95; H, 9.70; N, 9.01.

1-*t*-Butyl-2-aziridinemethanol.—A solution of methyl 1-*t*-butyl-2-aziridinecarboxylate (95 g, 0.61 mol) in 100 ml of ether was added over 0.25 hr to lithium aluminum hydride (20 g, 0.52 mol) suspended in 1 l. of ether. The reaction was stirred at room temperature for 3 hr. Excess lithium aluminum hydride was destroyed; the metal salts were removed by filtration and washed with two 100-ml portions of ether. The combined filtrate and washings were evaporated and distilled to give aziridinol (71.5 g, 90%): bp 58–59° (4 mm); mp 36–37°; $n^{25}D$ 1.4516.

Anal. Calcd for $C_7H_{15}NO$: C, 65.07; H, 11.70; N, 10.84. Found: C, 65.04; H, 11.73; N, 10.94.

1-Methyl-2-aziridinemethanol.—Methyl 1-methyl-2-aziridinecarboxylate[13] (30.4 g, 264 mmol) was added in 50 ml of ether to a suspension of lithium aluminum hydride (15 g, 0.40 mol) in 500 ml of ether over 0.25 hr and the reaction mixture stirred for 4 hr at room temperature. Excess lithium aluminum hydride was destroyed; the metal salts were removed by filtration and washed with several 50-ml portions of ether. The combined filtrate and washings were evaporated to a crude oil (36% of the expected aziridinol). Continuous extraction of the metal salts with ether in a Soxhlet extractor for 6 hr yielded an additional 34% of the aziridinol (total yield 15.9 g, 70%). A macro "kugelrohr" distillation gave 14 g of the aziridinol. This material, however, still contained a small amount (~10%) of an impurity. The entire sample was redistilled through an annular Teflon spinning-band column and a center cut obtained of pure (97% by analysis of the nmr spectrum) 1-methyl-2-aziridinemethanol: nmr (CCl_4) δ 1.0–1.7 (m, 3, ring H's), 2.30 (s, 3, CH_3), 3.0–3.8 (m, 2, CH_2–O), 5.15 (6 hr, 1, OH); bp 40° (2.5 mm).

(9) V. M. Micovic and M. L. Mihailovic, *J. Org. Chem.*, **18**, 1190 (1953).

(10) C. S. Marvel, J. Dec, H. G. Cooke, Jr., and J. C. Cowan, *J. Amer. Chem. Soc.*, **62**, 3495 (1940).

(11) Similar spectra have been obtained from other aziridine esters. Two carbonyl frequencies have been reported for some α-halo esters. They have been interpreted in terms of rotational isomers. L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," Wiley, New York, N. Y., 1958, p 183.

(12) A. Rosowsky in "Heterocyclic Compounds with Three- and Four-Membered Rings," Part 1, A. Weissberger, Ed., Interscience, New York, N. Y., 1964, p 17.

(13) Prepared from methyl 2,3-dibromopropionate and 30% aqueous methylamine in an equal volume of methanol in a reaction similar to that of Antonov and Berlin.[14]

(14) V. K. Antonov and A. Y. Berlin, *Zh. Obshch. Khim.*, **30**, 151 (1960); *J. Gen. Chem. USSR*, **30**, 161 (1960); *Chem. Abstr.*, **54**, 22552*b* (1960).

Anal. Calcd for C_4H_9NO: C, 55.14; H, 10.41; N, 16.08. Found: C, 54.94; H, 10.54; N, 15.91.

1-*t*-Butyl-α,α-diphenyl-2-aziridinemethanol.—Methyl 1-*t*-butyl-2-aziridinecarboxylate (39 g, 0.25 mol) in 100 ml of ether was added over 0.25 hr to a solution of phenylmagnesium bromide prepared from magnesium (12 g, 0.5 g-atom) and bromobenzene (78.5 g, 0.5 mol) in 225 ml of ether. The mixture was stirred at room temperature for 1 hr and then a solution of ammonium chloride (30 g) in 250 ml of ice water was added slowly with stirring. The ether layer was decanted and the aqueous layer stirred with two 200-ml portions of ether which were also decanted. Evaporation of the combined ether layers yielded a crude solid (68 g, 97%) which was recrystallized from aqueous ethanol to give 1-*t*-butyl-α,α-diphenyl-2-aziridinemethanol (51 g, 73% recrystallized): mp 124–125°.

Anal. Calcd for $C_{19}H_{23}NO$: C, 81.10; H, 8.24; N, 4.98. Found: C, 81.01; H, 8.30; N, 5.09.

1-*t*-Butyl-2-aziridinecarboxylic Acid Lithium and Sodium Salts.—Lithium hydroxide monohydrate (13 g, 0.31 mol) was added in four portions over 0.5 hr to a solution of methyl 1-*t*-butyl-2-aziridinecarboxylate (47 g, 0.30 mol) in 150 ml of water and stirred at room temperature overnight. Evaporation gave a viscous syrup which solidified when triturated with ether. The salt was dried at 70° for 2 hr, ground to a fine powder, and redried at 70° (0.01 mm) overnight (42 g, 94%): nmr (D_2O) δ 1.20 [s, 9, $C(CH_3)_3$], 1.9–2.1 (m, 2, AB of ABX, $H_{b,c}$), and 2.47 ppm (m, 1, X of ABX, H_a). The sodium salt has been prepared in the same way from sodium hydroxide.

1-*t*-Butyl-2-aziridinyl Phenyl Ketone.—Phenyllithium (200 ml of an ether solution[15] (~130 g or ~0.30 mol) was added to a solution of lithium 1-*t*-butyl-2-aziridinecarboxylate (45 g, 0.30 mol) in 600 ml of dimethoxyethane. The mixture was stirred for 1 hr at room temperature and evaporated to an oil which was taken up in 500 ml of ether and 500 ml of water. The ether layer was washed with saturated sodium chloride solution, dried (K_2CO_3), and evaporated to a crude oil (47.5 g, 80% aziridinyl ketone by analysis of the nmr spectrum, 62% yield) which contained some biphenyl[16] (8% by analysis of the nmr spectrum). On standing in the ice chest overnight, the ketone crystallized. The crystals were filtered, washed with low boiling (20–40°) petroleum ether, and dried to give 1-*t*-butyl-2-aziridinyl phenyl ketone (22 g, 36%): mp 41–44°; bp 100° (0.2 mm); ir (CCl_4) 1675 cm^{-1}.

Anal. Calcd for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.89. Found: C, 76.66; H, 8.25; N, 7.02.

Reduction of 1-*t*-Butyl-2-aziridinyl Phenyl Ketone to *erythro*- and *threo*-1-*t*-Butyl-α-phenyl-2-aziridinemethanol (6 and 7, Respectively). (1) Sodium Borohydride.—1-*t*-Butyl-2-aziridinyl phenyl ketone (10 g, 95% pure, 47 mmol) was dissolved in 100 ml of methanol and enough water added (~5 ml) to turn the solution cloudy. Sodium borohydride (3.0 g, 70 mmol) was then added in small portions with stirring over 0.5 hr at room temperature. The reaction was refluxed for 0.25 hr, cooled to room temperature, and evaporated to an oil. This oil was extracted with 50 ml of ether, washed with two 25-ml portions of water and 25 ml of saturated sodium chloride solution, dried (K_2CO_3), and evaporated to a solid (6.0 g, 62%). This solid was identified (by analysis of its nmr spectrum) as a mixture of the two diastereomeric α-phenylaziridinemethanols (70%; **6**, 30%). This mixture, when recrystallized from hexane (6 g in 10 ml), gave pure **7** (1.7 g, 28%; no **6** was detected in the nmr spectrum). The filtrate was evaporated to a slush (4.0 g) which was fractionally sublimed with no separation of the two diastereomers. An analytical sample of **7** was prepared by recrystallization from low boiling (20–40°) petroleum ether: mp 86–87°; mixture melting point with **6**, 65–80°.

Anal. Calcd for $C_{13}H_{19}NO$: C, 76.05; H, 9.33; N, 6.82. Found: C, 76.19; H, 9.23; N, 6.64.

(2) **Lithium Aluminum Hydride.**—1-*t*-Butyl-2-aziridinyl phenyl ketone (20 g, 80%, 78 mmol) in 60 ml of ether was added over 0.25 hr to lithium aluminum hydride (3.0 g, 79 mmol) suspended in 500 ml of ether and the reaction stirred overnight at room temperature. Excess lithium aluminum hydride was destroyed in the usual way; the metal salts were removed by filtration and washed with two 50-ml portions of ether and the combined filtrate and washings evaporated to a crude solid (15 g, 93%). The solid was identified (by analysis of the nmr spectrum) as a mixture of the two diastereomeric α-phenylaziridinemethanols (**7**, 6%; **6**, 94%). This solid, when recrystallized from low boiling (20–40°) petroleum ether (15 g in 75 ml), yielded the pure **6** (56%; no **7** was detected in the nmr spectrum). A second crop was also obtained (2 g, 12%). An analytical samples of **6** was prepared by recrystallization from low boiling petroleum ether: mp 85–86°.

Anal. Calcd for $C_{13}H_{19}NO$: C, 76.05; H, 9.33; N, 6.82. Found: C, 75.89; H, 9.21; N, 6.82.

1-*t*-Butyl-2-aziridinemethyl Tosylate.—A solution of 1-*t*-butyl-2-aziridinemethanol (7.5 g, 58 mmol) and tosyl chloride (10.6 g, 56 mmol) in 125 ml of triethylamine was kept at 0° for 3 days. Triethylamine hydrochloride was then removed by filtration and washed with two 10-ml portions of triethylamine. The combined filtrate and washings were evaporated to an oil which was dissolved in 100 ml of carbon tetrachloride or methylene chloride, washed with two 50-ml portions of water, dried (K_2CO_3), and evaporated to give an oil (10.2 g, 65%) which would not crystallize. Rotary evaporation under high vacuum (1.0 mm) for 6 hr produced an analytical sample of the tosylate: nmr (CCl_4) δ 0.90 (s, 9, $C(CH_3)_3$), 1.28 (d, 1, H_1) 1.85 (m, 1, H_3), 2.43 (s, 3, CH_3Ar), 3.55–4.05 (m, 2, CH_2–O), 7.1–7.8 (9, 4, Ar).

Anal. Calcd for $C_{14}H_{21}NO_3S$: C, 59.35; H, 7.47; N, 4.94. Found: C, 59.24; H, 7.35; N, 4.99.

1-*t*-Butyl-2-aziridinemethyl Nosylate.—Nosyl chloride (11.0 g, 45 mmol) was stirred at 0° in 250 ml of triethylamine for several minutes until most of it had dissolved. 1-*t*-Butyl-2-aziridinemethanol (7.0 g, 54 mmol) was added in one portion and stirred for 1 hr. The entire reaction mixture was evaporated to a thick paste and extracted with 250 ml of methylene chloride and 250 ml of water. The organic layer was washed with 100 ml of saturated sodium bicarbonate solution and two 150-ml portions of water, dried (K_2CO_3), and evaporated. The resultant solids were dissolved in 100 ml of carbon tetrachloride, filtered, and evaporated twice, then dried at room temperature for 48 hr (0.01 mm) to give the aziridine nosylate:[17] mp 81–81.5°; nmr ($DCCl_3$) δ 0.93 [s, 9, $C(CH_3)_3$], 1.38 (d, 1, H_2), 1.60 (d, 1, H_1), 193 (m, 1, H_2), 3.7–4.3 (m, 2, CH_2–O), 8.0–8.5 (9, 4, Ar).

Anal. Calcd for $C_{13}H_{18}N_2O_5S$: C, 49.68; H, 5.77; N, 8.91. Found: C, 49.45; H, 5.71; N, 8.85.

1-Methyl-2-aziridinemethyl Toylate.—Tosyl chloride (4.0 g, 21 mmol) was added in several portions over a period of 0.5 hr to a mixture of sodium hydride (1.5 g, 50% in mineral oil, 31 mmol, washed with three 20-ml portions of hexane) and 1-methyl-2-aziridinemethanol (2.0 g, 23 mmol) in 75 ml of benzene. The mixture was stirred at 5–10° for 2 hr, washed with two 40-ml portions of water, dried (K_2CO_3), and evaporated to a crude solution with a volume of 25 ml. The nmr spectrum showed only one broad methyl peak at 2.0 ppm. About 30 ml of tetrachloroethylene was added and the mixture evaporated to a volume of ~25 ml: nmr ($Cl_2C{=}CCl_2$) 1.08 (d, 1, H_1), 1.4–1.5 (m, 2, H_2 and H_3), 2.18 (s, 1, N–CH_3), 2.41 (s, 1, $ArCH_3$), 3.8–4.0 (m, 2, CH_2–O), 7.25–7.90 (9, 4, Ar). The nmr spectrum of the crude material showed a considerable amount of benzene present (~45 mol%) and a small amount (~5 mol %) of a material which no longer retained the aziridine ring. Evaporation, even at 0°, gave an oil which quickly polymerized with frothing and could not be extracted with hexane or tetrachloroethylene. The original crude solution in benzene could be kept several days in the ice chest without extensive loss due to polymerization. This crude solution was used directly in the preparation of 1-methyl-2-aziridinemethyl bromide.

1-Benzyl-2-aziridinemethyl Tosylate.—Tosyl chloride (3.8 g, 20 mmol) was added in several portions over a 0.5-hr period with stirring to a solution of sodium hydride (1.5 g, 50% in mineral oil, 31 mmol, washed with three 20-ml portions of hexane) and 1-benzyl-2-aziridinemethanol[18] (3.3 g, 20 mmol) in 100 ml of benzene at room temperature. After stirring for 20 hr, the reaction mixture was washed with two 50-ml portions of water and dried (K_2CO_3) to give a crude solution of the tosylate in benzene: nmr (CCl_4), δ 1.28 (d, 1, H_1), 1.5–1.7 (m, 2, H_2, H_3), 2.31 (s, 1,

(15) A. I. Vogel, "Practical Organic Chemistry," 3rd ed, Wiley, New York, N. Y., 1962, p 931.

(16) Biphenyl could be removed from the ketone by recrystallization with considerable loss (40–50%) of ketone. Since the biphenyl was easily removed from the aziridinemethanols by recrystallization, the ketone–biphenyl mixture was usually analyzed for ketone content and used directly in the carbinol syntheses.

(17) The nosylate could be recrystallized from benzene or cyclohexane, but it was not possible to completely remove these solvents without decomposing some of the nosylate.

(18) Prepared from methyl 1-benzyl-2-aziridinecarboxylate by the method of Capeller and coworkers.[3a]

$ArCH_3$), 3.27 (9, 2, CH_2–Ph), 3.88 (m, 2, CH_2–O), 7.1–7.8 (m, 9, Ar). This crude solution could be kept for several days in the ice chest without appreciable polymerization and was used directly in the preparation of 1-benzyl-2-aziridinemethyl bromide. Evaporation of the crude benzene solution gave an oil which would not crystallize and after standing at room temperature overnight, had polymerized.

1-*t*-Butyl-2-aziridinemethyl Bromide.—1-*t*-Butyl-2-aziridinemethyl tosylate (7.0 g, 25 mmol, as a crude oil) and tetrabutylammonium bromide (10.0 g, 31 mmol) were refluxed in 100 ml of benzene for 12 hr. After cooling to room temperature, the reaction mixture was washed with two 100-ml portions of water, dried (K_2CO_3), and evaporated to an oil (4.0 g, 97% pure by analysis of the nmr spectrum, 81% yield) which was distilled to give an analytical sample of the aziridinemethyl bromide: bp 75–80° (0.3–0.5 mm); nmr (CCl_4) δ 0.97 [s, 9, $C(CH_3)_3$], 1.38 (d, 1, H_1), 1.62 (d, 1, H_2), 1.95 (m, 1, H_3), 2.96–3.44 (m, 2, CH_2–Br).

Anal. Calcd for $C_7H_{14}BrN$: C, 43.78; H, 7.34; N, 7.29. Found: C, 43.95; H, 7.47; N, 7.00.

1-Methyl-2-aziridinemethyl Bromide.—Tetrabutylammonium bromide (7.0 g, 22 mmol) was added with stirring to a solution of 1-methyl-2-aziridinemethyl tosylate (85 mg, ~18 mmol, freshly prepared from 1-methyl-2-aziridinemethanol) in 20 ml of benzene. Within 5 min, the nmr spectrum showed that ~50% of tosylate had been converted to the corresponding aziridinemethyl bromide. The reaction mixture was allowed to stand overnight, washed with two 25-ml portions of water, dried (K_2CO_3), and evaporated to an oil which was distilled with some decomposition to yield the 1-methyl-2-aziridinemethyl bromide (100 mg, 36%): bp 80–90° (40–50 mm); nmr (CCl_4) δ 1.24 (δ, 1, H_1), 1.3–1.7 (m, 2, H_2, H_3), 2.31 (s, 3, CH_3), 3.25–3.45 (m, 2, CH_2–Br).

1-Benzyl-2-aziridinemethyl Bromide.—Tetrabutylammonium bromide (7.0 g, 22 mmol) was added to a crude solution of 1-benzyl-2-aziridinemethyl tosylate (~10 mmol) in 35 ml of benzene. This mixture was stirred for 12 hr, then washed with two 25-ml portions of water, dried (K_2CO_3), and evaporated to an oil which was distilled to give 1-benzyl-2-aziridinemethyl bromide (1.2 g, 53%): bp 100° (0.5 mm); nmr (CCl_4) δ 1.3–2.0 (m, 3, H_1, H_2, H_3), 2.9–3.7 (m, 4, CH_2), 7.22 (s, 5, Ar).

1-*t*-Butyl-2-aziridinemethyl Methyl Ether.—1-*t*-Butyl-2-aziridinemethyl tosylate (5.6 g, 20 mmol) in 20 ml of methanolic sodium hydroxide (1 *N*, 20 mmol) was allowed to stand at room temperature and the reaction followed by observation of the *t*-butyl peaks in the nmr spectra. The reaction was approximately 50% completed in 22 hr. After 2 days, in order to complete the reaction, an additional 2 ml of methanolic sodium hydroxide (15% wt/total vol, 7.5 mmol) was added and the reaction allowed to stand for several additional days. The aziridinemethyl ether was the only product observed in the nmr spectrum of the crude reaction mixture which was filtered and evaporated to an oil. This oil was dissolved in 15 ml of ether, washed with 3 ml of water, dried (K_2CO_3), evaporated, and distilled to give an analytical sample of the aziridinyl ether (2.0 g, 65%): bp 85° (water aspirator); $n^{25}D$ 1.425; nmr (CCl_4) δ 0.95 [s, 9, $C(CH_3)_3$], 1.24 (d, 1, J = 3.0 Hz, H_c), 1.42 (d, 1, J = 6.5 Hz, H_b), 1.5–1.9 (m, 1, H_a), 3.20 (d, 2, CH_2), and 3.32 ppm (s, 3, OCH_3).

Anal. Calcd for $C_8H_{17}NO$: C, 67.09; H, 11.69; N, 9.78. Found: C, 67.16; H, 11.91; N, 9.69.

1-*t*-Butyl-2-aziridinemethyl Ethyl Ether from 1-*t*-Butyl-2-aziridinemethyl Tosylate.—Sodium (0.50 g, 22 g-atoms) in 70 ml of absolute ethanol was allowed to stand until all of the sodium had reacted. 1-*t*-Butyl-2-aziridinemethyl tosylate (1.25 g, 4.4 mmol) was added and the reaction mixture refluxed overnight under nitrogen. Flash evaporation gave an oil which was extracted with ether, washed with water, dried (K_2CO_3), flash evaporated, and distilled to give the aziridinemethyl ethyl ether (~0.4 g, ~50%), bp 60° (10 mm).

Anal. Calcd for $C_9H_{19}NO$: C, 68.75; H, 12.15; N, 8.92. Found: C, 69.02; H, 12.39; N, 9.08.

Registry No.—**1a**, 25662-13-9; **1b**, 25662-14-0; **2a**, 25662-15-1; **2a** (tosylate), 25662-16-2; **2b**, 25665-28-5; **2b** (tosylate), 23398-26-7; **2b** (nosylate), 25716-11-4; **2c** (tosylate), 25662-19-5; **3**, 25665-26-3; **4**, 25662-21-9; **6**, 25662-70-8; **7**, 25662-73-1; **9**, 25662-27-5; 1-*t*-butyl-2-aziridinemethyl bromide, 25662-22-0; 1-methyl-2-aziridinemethyl bromide, 25662-23-1; 1-benzyl-2-aziridinemethyl bromide, 25662-24-2; 1-*t*-butyl-2-aziridinemethyl methyl ether, 25662-25-3; 1-*t*-butyl-2-aziridinemethyl ethyl ether, 25662-26-4.

Reaction of Aziridinemethanols with Thionyl Chloride[1]

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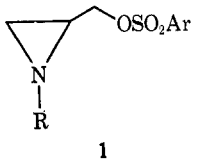
Aziridinemethanols react with thionyl chloride in the presence of base to yield aziridinemethyl chlorides (both rearranged and unrearranged), dihalamines, and 1,2,3-oxathiazolidines. The distribution among these products is a function of structure of the aziridinemethanol and the base used. The mechanisms of these reactions are discussed.

We have recently reported the investigation of the solvolytic behavior of primary aziridinemethyl sulfonates (**1**).[2] Our study of these compounds suggested



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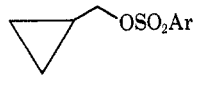

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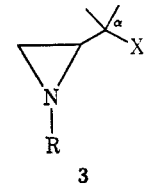
that reactivity was probably derived from classical (albeit sluggish) participation by the annular nitrogen, and thus little charge was developed on the primary carbon. These aziridines thus differ markedly from their cyclopropyl carbinyl analogs (**2**) in which participation is characterized by extensive charge delocalization. In hopes of obtaining more information concerning the interaction of the aziridine ring with adjacent cationic centers, we sought to prepare a variety of aziridinemethyl derivatives (**3**) substituted



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at the α position by groups which would facilitate positive charge development. This paper describes various attempts to prepare these derivatives by the

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(2) J. A. Deyrup and C. L. Moyer, *Tetrahedron Lett.*, 6179 (1968).