double bond. It will therefore be subjected to a negative (deshielding) effect from the anisotropy of this bond.[20] The resonance at −2.285 p.p.m. is therefore assigned to the methyl at C-1 and that at −2.225 p.p.m. to the methyl at C-1′.

Our ultraviolet spectral data in methanol solution agree with those of McEntee and Pinder.[21]

(20) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, New York, N. Y., 1959, pp. 124, 129.

(21) M. E. McEntee and A. R. Pinder, *J. Chem. Soc.*, 4419 (1957).

Preparation of 1-Azabicycloalkanes by Reductive Cyclization

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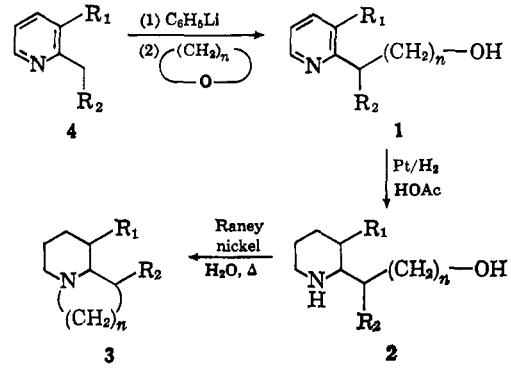
Indolizidine, quinolizidine, and several of their methyl derivatives have been prepared in 80–90% yield by the two-step reductive cyclization of readily available 2-pyridyl alcohols. Under similar conditions, the corresponding 3- and 4-pyridyl alcohols failed to undergo cyclization. The probable stereochemistry of the 8-methylindolizidines produced in this cyclization is discussed.

In connection with another problem in this laboratory we recently required substantial quantities of various indolizidines and quinolizidines. Although several methods for synthesizing compounds of this type had been reported in the literature,[2] for the most part these proceeded in low over-all yields from readily available starting materials. The most attractive method in this regard seemed to be the high-pressure, high-temperature, reductive cyclization of various 2-(3′-hydroxypropyl)pyridines such as **1a** to the corresponding indolizidines. In the case of indolizidine itself (**3a**) a 78% yield was reported[3] although with slightly more complex molecules it was much lower.[4] Repeated attempts to prepare indolizidine by this method in our laboratory, however, led only to complex mixtures containing, at best, 15% of the desired product.[5]

A related method which was considered was that of Lavagnino, *et al.*,[6] in which indolizidine (**3a**) was obtained in 73% yield by simply distilling an aqueous solution of 2-(3′-hydroxypropyl)piperidine (**2a**) from Raney nickel. Since the piperidine **2a** is easily prepared by catalytic reduction[3] of the commercially available pyridine **1a**, it appeared that this sequence of two reactions (reduction followed by cyclization) might be used for the preparation of the desired compounds. This paper reports the synthesis of a variety of indolizidines and quinolizidines in 80–90% over-all yield by this two-step reductive cyclization of readily available pyridyl alcohols of the type **1**.

Results and Discussion

The starting pyridyl alcohols **1** were obtained either commercially (**1a**), or by treatment of the appropriate alkylpyridyllithium reagent[7] with ethylene oxide[8] (**1c, 1e–g**) or propylene oxide[9] (**1b** and **1d**). Reduction of the pyridine ring of **1a–g** proceeded in 92–96% yield at room temperature and moderate pressure according to the method of Prelog.[10] The saturated alcohols **2a–g** produced in this reaction were partially esterified by the glacial acetic acid used as a solvent and therefore were saponified before isolation and purification. In those preparations where only the final quinolizidines or indolizidines were desired, the crude mixture of piperidyl alcohols **2a–g** and their acetate esters could be used without prior saponification since hydrolysis apparently took place under the conditions of the cyclization described below.



Cyclization of the piperidyl alcohols **2a–g** to the desired indolizidines and quinolizidines **3a–g** took place in high yield (85–95%) by a procedure very similar to that of Lavagnino, *et al.*[6] The 15% higher yields in our cyclizations may be due to the repeated use of the same portion of Raney nickel, since the ability of the catalyst to irreversibly adsorb either the reactants or the products[11] would be greatly reduced after the first prep-

(1) (a) Department of Chemistry, Texas Christian University, Fort Worth, Texas; (b) National Science Foundation Summer Teaching Fellow, 1963; National Institutes of Health Predoctoral Fellow in Chemistry, 1963–1964.

(2) For a recent summary of the syntheses of compounds with bridgehead nitrogen atoms, see W. L. Mosby, "The Chemistry of Heterocyclic Compounds," Vol. 15, parts 1 and 2, A. Weissburger, Ed., Interscience Publishers, Inc., New York, N. Y., 1961.

(3) V. Boekelheide and S. Rothchild, *J. Am. Chem. Soc.*, **70**, 864 (1948).

(4) J. Sam, J. Plampin, and D. Alwani, *J. Org. Chem.*, **27**, 4543 (1962).

(5) The reason for the failure of this synthesis in our hands is not clear, although the exact nature of the Raney nickel catalyst used may be responsible. The identities of the products obtained from this attempted reductive cyclization are under investigation and will be reported elsewhere.

(6) E. R. Lavagnino, R. R. Chauvette, W. N. Cannon, and E. C. Kornfeld, *J. Am. Chem. Soc.*, **82**, 2609 (1960).

(7) The successful preparation of at least a 25% yield (see Table I) of the lithium reagent of 2-isopropylpyridine is surprising in view of the failure of C. Osuch and R. Levine [*J. Org. Chem.*, **21**, 1099 (1956)] and W. von E. Doering and V. Z. Pasternak [*J. Am. Chem. Soc.*, **72**, 143 (1950)] to metalate 2-isopropyl- and 2-*sec*-butylpyridine, respectively, with phenyllithum under essentially identical conditions (see Experimental).

(8) L. A. Walter, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 757.

(9) K. Winterfeld and W. Haring, *Arch. Pharm.*, **295**, 615 (1962).

(10) V. Prelog and O. Metzler, *Helv. Chim. Acta*, **29**, 1163 (1946).

(11) For examples of the irreversible adsorption of certain amines on Raney nickel, see (a) A. Bendich, P. Russell, Jr., and J. Fox, *J. Am. Chem. Soc.*, **76**, 6073 (1954); and (b) M. G. Reinecke and L. R. Kray, unpublished results.

aration. By cyclizing the crude mixtures of the piperidyl alcohols **2** and their corresponding acetates without saponification or purification (see above), the time and effort necessary to carry out the over-all conversion **1** → **3** was greatly reduced and the yield of final product (**3**) increased by about 5%. The yields of the various reactions discussed above are summarized in Table I.

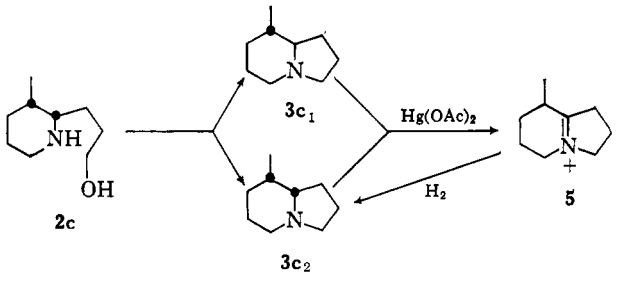
TABLE I

YIELDS OF 1-AZABICYCLOALKANES (**3**), 2-(ω-HYDROXYALKYL)-PIPERIDINES (**2**), AND 2-(ω-HYDROXYALKYL)PYRIDINES (**1**) OBTAINED FROM VARIOUS ALKYLPYRIDINES (**4**)

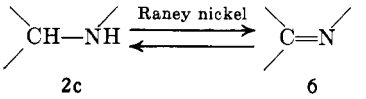
	Compounds			% yield in conversion of		
	R_1	R_2	n	**4** → **1**	**1** → **2**	**2** → **3**
a	H	H	2	*a*	94	85
b	H	H	3	46	95	89
c	CH_3	H	2	63	92	85
d	CH_3	H	3	43	93	95
e	H	CH_3	2	39	96	92
f	CH_3	CH_3	2	35	92	92
g	H	$(CH_3)_2$	2	25	95	90

[a] 2-(3′-Hydroxypropyl)pyridine (**1a**) was obtained commercially.

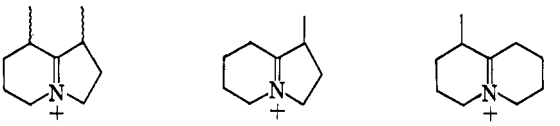
The 8-methylindolizidine (**3c**) produced by the above method proved to be a 5:1 mixture of the two possible diastereoisomers (**3c**$_1$ and **3c**$_2$) that could be readily separated by preparative vapor phase chromatography. The diastereoisomeric relationship of these two compounds was indicated by the similarity of their analyses and infrared spectra and proven by the mercuric acetate oxidation[12] of their mixture to a single quaternary immonium salt (**5**) which on catalytic reduction produced only that isomer which had been obtained in lesser amount from the original cyclization reaction



If preferential *cis* hydrogenation from the least-hindered side of the immonium salt **5** is assumed,[13] then the stereochemical assignment which logically follows indicates that the major product of the cyclization of the piperidyl alcohol **2c** is **3c**$_1$ and the minor product **3c**$_2$. This assignment is not necessarily inconsistent with the expected[14] predominantly *cis* orientation of the alkyl groups in the piperidyl alcohol **2c**, since epimerization at C-2 could occur under the conditions of the cyclization by means of a reversible dehydrogenation to the imine **6**.[15]

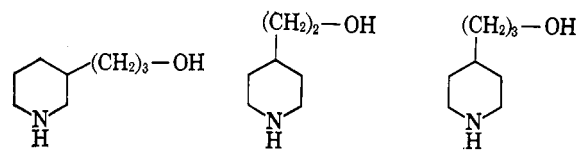


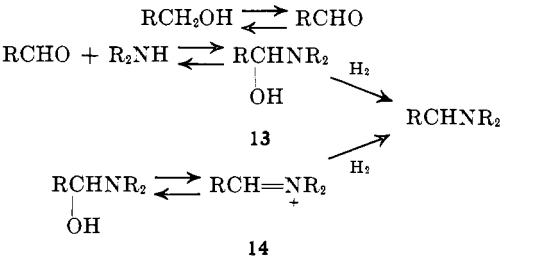
Cyclization of the piperidyl alcohol **1f** also led to a mixture which according to a vapor phase chromatogram contained only two of four possible diastereoisomers of 1,8-dimethylindolizidine, **3f**$_1$ and **3f**$_2$, in a ratio of 7:3, respectively. Oxidation of this mixture with mercuric acetate[12] produced the immonium salt **7** which on catalytic reduction gave predominantly a single isomer of 1,8-dimethylindolizidine (**3f**$_3$) different from the two products of cyclization. At present, insufficient evidence is available for the assignment of the relative stereochemistry of these isomers.



Vapor phase chromatography indicated that 1-methylindolizidine (**3e**) and 1-methylquinolizidine (**3d**) also were obtained as diastereoisomeric mixtures from the cyclization reaction. In these cases, however, no separation was attempted since the properties of these mixtures agreed with those reported in the literature, and in both cases single quaternary immonium salts (**8** and **9**, respectively) were obtained upon oxidation with mercuric acetate.[12]

The 3- and 4-substituted piperidyl alcohols **10**, **11**, and **12** were prepared by catalytic reduction of the corresponding commercially available pyridyl alcohols. Attempted cyclization by the procedure employed for the 2-substituted isomers (**2**) gave only small amounts of volatile material which in the case of **10** was wholly the dehydroxymethylation product,[16] 3-ethylpiperidine, and which in the case of **11** and **12** were complex and not easily separable mixtures whose infrared spectra indicated the presence of substantial quantities of olefins and secondary amines. The failure of these three piperidyl alcohols to cyclize to the expected bridged bicyclic tertiary amines is probably due to prohibitive strain in one or more of the proposed[17] intermediates of this reaction, *i.e.*, the carbinolamine **13** and/or most certainly the immonium salt **14**. A similar reason





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

(13) R. P. Linstead, W. E. Doering, S. B. Davis, P. Levine, and R. R. Whetstone, *ibid.*, **64**, 1985 (1942).

(14) Catalytic reduction of 1,2-dialkylbenzenes gives predominantly *cis* products at room temperature: see R. L. Burwell, *Chem. Rev.*, **57**, 895 (1957).

(15) K. Kindler, G. Melamed, and D. Matthies, *Ann.*, **644**, 23 (1961).

(16) Dehydroxymethylation is also the primary process which occurs during the attempted cyclization[6] of 2-(2′-hydroxyethyl)piperidine.

(17) R. G. Rice and E. J. Kohn, *J. Am. Chem. Soc.*, **77**, 4052 (1955).

doubtless accounts for the failure of 2-(2′-hydroxyethyl)piperidine to cyclize under these conditions.[6]

Experimental[18]

Preparation of Pyridyl Alcohols Ib–g. General Procedure.[8,9]—To 6 g. of finely cut lithium wire and 400 ml. of anhydrous ether under nitrogen in a 2-l. Morton flask equipped with a reflux condenser, dropping funnel, and mechanical stirrer was added 68.2 g. of freshly distilled bromobenzene over a period of 20 min. with rapid stirring. After all the lithium had dissolved (2 hr.), 0.43 mole of the freshly distilled alkylpyridine[19] was added in a 30-min. period and the resulting red-brown solution stirred at room temperature for an additional hour at which time the flask was cooled in an ice bath and 0.43 mole of ethylene oxide or propylene oxide in 75 ml. of ether was slowly added. The pale yellow solution thus formed was stirred for an hour, 200 ml. of 6 *M* hydrochloric acid added, and the aqueous layer separated, made basic with a solution of 111 g. of sodium carbonate in 150 ml. of water, and extracted with four 100-ml. portions of chloroform. After the chloroform extracts were dried over anhydrous potassium carbonate, the chloroform was removed by distillation and the remaining oil distilled through a small Vigreux column under reduced pressure.

The pyridyl alcohols obtained in this way were generally viscous, colorless to pale yellow oils which darkened on standing and gave poor analytical results. In most cases the only satisfactory derivatives were the **2,4,6-trinitrobenzenesulfonates (TNBS)** which were prepared as sharp-melting, pale yellow to white, crystalline solids by the dropwise addition of an ethanol solution of the free base to an ethanol solution of 2,4,6-trinitrobenzenesulfonic acid,[22] followed by precipitation with ether and recrystallization from ethanol–ether.

The properties of the pyridyl alcohols **Ib–g** and their derivatives are summarized in Table II.

TABLE II

PROPERTIES OF PYRIDYL ALCOHOLS AND THEIR DERIVATIVES

Compound	M.p. or b.p. (mm.), °C.	Analyses, % Calcd. C	Calcd. H	Found C	Found H
1b	98–100 (0.05)[a]				
1b·CH_3I	98–99[b]				
1c	125–126 (0.2)				
1c·TNBS	150–151	40.54	3.63	40.74	3.96
1d	152–153 (0.5)				
1d·TNBS	135–136	41.92	3.95	42.29	3.80
1e	112–113 (0.09)	71.48	8.66	71.19	8.69
1e·TNBS	137–138	40.54	3.63	40.17	3.77
1f	128–130 (0.09)				
1f·TNBS	138–139	41.92	3.95	41.61	3.61
1g	123–125 (0.1)				
1g·TNBS	146–148	41.92	3.95	42.00	4.24

[a] Lit.[9] b.p. 98–100° (0.04). [b] Lit.[9] m.p. 98–99°.

Preparation of Piperidyl Alcohols 2a–g, 10, 11, and 12. General Procedure.—A solution of 0.12–0.17 mole of the appropriate pyridyl alcohol[23] in 150 ml. of glacial acetic acid containing 0.4–0.5 g. of platinum oxide was hydrogenated in a medium-pressure Paar apparatus with an initial pressure of *ca.* 60 p.s.i. After the theoretical pressure drop had been realized (15–20 hr.), the catalyst was removed by filtration and the solvent evaporated at reduced pressure with a rotary evaporator. A vapor phase chromatogram of the remaining residue displayed two peaks of varying proportions depending on the particular pyridyl alcohol being reduced. Infrared spectra indicated that the material of higher retention time contained ester carbonyl (1746 cm.$^{-1}$) and NH (3100 cm.$^{-1}$, broad) groups while that of lower retention time contained only the latter. In those preparations where only the final 1-azabicycloalkanes were desired, this mixture could be used directly in the cyclization reaction (*vide infra*); if the pure piperidyl alcohol was to be isolated, however, this mixture was heated until reflux with 100 ml. of a 25% sodium hydroxide solution for 2–3 hr. and the resulting mixture saturated with potassium carbonate and extracted with three 100-ml. portions of ether. The combined ether extracts were dried over anhydrous potassium carbonate, the ether removed by distillation, and the remaining oil distilled under nitrogen at reduced pressure.

The piperidyl alcohols prepared in this manner were viscous, colorless oils some of which darkened on standing and gave poor analyses. Once again the most satisfactory derivatives were the 2,4,6-trinitrobenzenesulfonates.

The properties of the piperidyl alcohols **2a–g, 10, 11,** and **12** and their derivatives are summarized in Table III.

TABLE III

PROPERTIES OF PIPERIDYL ALCOHOLS AND THEIR DERIVATIVES

Compound	M.p. or b.p. (mm.), °C.	Analyses, % Calcd. C	Calcd. H	Found C	Found H
2a	94–95 (0.6)[a,b]				
2a·HCl	128–129[c]				
2b	46–48[d] / 92–93 (0.1)[e]				
2c	112–113 (2.0)	68.74	12.10	69.14	12.17
2c·TNBS	134–135	39.99	4.92	39.98	5.09
2d	104–105 (0.6)				
2d·TNBS	147–148	41.37	5.21	41.43	5.02
2e	110–111 (0.05)				
2e·TNBS	164–165	39.99	4.92	40.28	4.83
2f	113–115 (0.05)				
2f·TNBS	201–203 dec.	41.37	5.21	41.72	5.33
2g	111–112 (0.05)				
2g·TNBS	200–202 dec.	41.37	5.21	41.16	5.25
10	107–108 (0.04)				
10·TNBS	166–167	38.51	4.58	38.93	4.88
11	99–100 (0.06)[f,g]				
12	64–65 / 109–110 (0.06)				
12·TNBS	184–185	38.51	4.58	38.35	4.99

[a] Lit.[3] 101–102° (3.0). [b] Observed $n^{25}D$ 1.4880, lit.[3] $n^{21.5}D$ 1.4882. [c] Lit.[3] 128–129°. [d] Lit.[9] 47–49°. [e] Lit.[9] 90–92° (0.1). [f] J. Meisenheimer, J. Neresheimer, O. Finn, and W. Schneider, [*Ann.*, **420**, 190 (1920)] give b.p. 140–141° (13 mm.). [g] Observed $n^{23.8}D$ 1.4903; S. Wawzonek, M. F. Nelson, Jr., and P. S. Thelen [*J. Am. Chem. Soc.*, **74**, 2894 (1952)] give $n^{23}D$ 1.4902.

Preparation of 1-Azabicycloalkanes 3a–g. General Procedure—A mixture of 500 ml. of water, 60 g. of wet, W-5 Raney nickel,[24] and 25 g. of the piperidyl alcohol **2**, either pure or as originally obtained from the reduction of the corresponding pyridyl alcohol **1** (*i.e.*, contaminated with the acetate ester of **2**), was placed in a 1-l., three-necked flask equipped with a mechanical stirrer, dropping funnel, Claisen head, with condenser arranged for distillation. The reaction mixture was heated to boiling with stirring and water added from the dropping funnel to keep the level of liquid in the flask constant. When the distillate was no longer strongly basic to pH paper, the heating was stopped (about 500–800 ml. of distillate had been collected at this point) and the distillate saturated with potassium carbonate and extracted with three 100-ml. portions of ether. The combined ether extracts were dried over potassium carbonate, the ether removed by distillation, and the remaining colorless oil distilled through a Vigreux

(18) All melting points and boiling points are corrected; analyses were performed by Mr. C. F. Geiger of Ontario, Calif.

(19) All the alkyl pyridines were obtained commercially with the exception of 2-ethyl-3-methylpyridine[20] and 2-isopropylpyridine[21] which were prepared in 49% yields from 2,3-dimethylpyridine and 2-ethylpyridine, respectively, by a procedure identical with that described above for the preparation of the pyridyl alcohols **1b-g** except that methyl iodide was used in place of the ethylene or propylene oxides.

(20) H. L. Lochte and T. H. Cheavens, *J. Am. Chem. Soc.*, **79**, 1667 (1957).

(21) H. C. Brown and W. A. Murphey, *ibid.*, **73**, 3308 (1951).

(22) D. J. Pettitt and G. K. Helmkamp, *J. Org. Chem.*, **28**, 2939 (1963).

(23) The pyridyl alcohols used in addition to those (**1a–g**) prepared above were 2-(3′-hydroxypropyl)pyridine (**1a**), 3-(3′-hydroxypropyl)pyridine, 4-(3′-hydroxypropyl)pyridine, and 4-(2′-hydroxyethyl)pyridine which were obtained from Reilly Tar and Chemical Co., Indianapolis, Ind.

(24) H. R. Billica and H. Adkins, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 176.

TABLE IV

PROPERTIES OF 1-AZABICYCLOALKANES AND THEIR DERIVATIVES

Compound	M.p. or b.p. (mm.), °C.	Analyses, % Calcd. C	Calcd. H	Found C	Found H
3a	156–157 (745)[a]				
3a·picrate	230–231[b]				
3a·H_2PtCl_6	218–219[c]				
3b	164.5 (735)[d,e]				
3b·picrate	199–200[f]				
3b·$HClO_4$	149–150[g]				
3c$_1$	179 (733)[d]				
3c$_1$·picrate	218–219	48.91	5.47	49.07	5.73
3c$_2$	175 (733)[d]				
3c$_2$·picrate	203–204	48.91	5.47	48.82	5.65
3c$_2$·$HClO_4$	154–155	45.07	7.56	45.39	7.56
3d	193.5 (735)[d]				
3d·picrate	170–172[h]				
3e	175.5 (735)[d]				
3e·picrate	192–193[i]				
3f$_1$	188.0 (736)[d]				
3f$_1$·picrate	187–189 dec.	50.13	5.75	49.88	5.85
3f$_2$	195.0 (736)[d]				
3f$_2$·picrate	230–234 dec.	50.13	5.75	50.42	5.73
3f$_3$[j]	187.5 (737.6)[d]				
3f$_3$·picrate	197–198 dec.	50.13	5.75	50.38	5.88
3f$_3$·$HClO_4$	162–163	47.39	7.89	47.48	7.78
3g	178.5 (735)[d]				
3g·picrate	191–192	50.13	5.75	50.35	5.91
3g·$HClO_4$	209–210	47.39	7.89	47.49	8.17

[a] C. W. Tullock and S. M. McElvain [*J. Am. Chem. Soc.*, **61**, 961 (1939)] report b.p. 156–158°. [b] Lit.[3] 228–229. [c] E. Ochiai and K. Tsuda [*Chem. Ber.*, **67**, 1011 (1934)] report m.p. 215°. [d] Microboiling point determination (R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 4th Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 32). [e] N. J. Leonard and W. E. Goode [*J. Am. Chem. Soc.*, **72**, 5404 (1950)] report b.p. 165–169° (748 mm.). [f] G. R. Clemo, G. R. Ramage, and R. Raper [*J. Chem. Soc.*, 2959 (1932)] report m.p. 199–200°. [g] Lit.[12] 149–150°. [h] N. J. Leonard, R. W. Fulmer, and A. S. Hay [*J. Am. Chem. Soc.*, **78**, 3457 (1956)] report m.p. 171.5–172.5°. [i] G. R. Clemo and T. P. Metcalfe [*J. Chem. Soc.*, 1518 (1937)] report m.p. 191° dec. [j] Obtained by catalytic hydrogenation of **7** (*vide infra*).

column. The Raney nickel was recovered from the distillation pot, washed thoroughly with distilled water, and used for subsequent cyclizations.

Vapor phase chromatograms indicated that **3d**, **3e**, **3f**, and **3g** each consisted of two substances, presumably diastereoisomers. In the case of **3d** and **3e** separation was neither feasible nor necessary, since the physical properties of these mixtures and their derivatives had been reported previously (see Table IV). The mixtures of **3c** and **3f**, however, were easily separated by preparative v.p.c. into **3c**$_1$ and **3c**$_2$ (5:1) and **3f**$_1$ and **3f**$_2$ (7:3), each of which was characterized.

The physical properties of the 1-azabicycloalkanes **3a–g** and their derivatives are summarized in Table IV.

Mercuric Acetate Oxidation of Stereoisomeric Mixtures of 1-Azabicycloalkanes 3d, 3e, 3f, and 3g. General Procedure.[12]—In a 500-ml., three-necked flask fitted with an efficient mechanical stirrer, gas inlet valve, and a serum cap was placed 50 g. (0.38 mole) of mercuric acetate and 200 ml. of 5% aqueous acetic acid. After the apparatus had been evacuated and refilled with nitrogen several times, it was placed on a steam bath until all of the mercuric acetate had dissolved. Upon addition of 0.036 mole of the stereoisomeric 1-azabicycloalkane mixture through the serum cap by means of a syringe, an immediate precipitate of mercurous acetate formed. The reaction mixture was stirred on the steam bath for an hour, cooled, and the mercurous acetate removed by filtration. The filtrate was saturated with hydrogen sulfide and the resulting black precipitate removed by centrifugation. The resulting clear centrifugate was treated with sodium hydroxide, saturated with potassium carbonate, and extracted with three 100-ml. portions of ether which were dried over anhydrous potassium carbonate. After the drying agent had been removed by filtration, the ether extracts were concentrated to 100 ml. on a rotary evaporator, diluted with 50 ml. of absolute ethanol, and acidified (to litmus) with a 50% (v./v.) solution of 70% perchloric acid in absolute ethanol. The precipitated immonium perchlorate salt was recrystallized from ethanol–ether with the aid of some Norit.

The yields, properties, and analyses of these immonium salts are summarized in Table V.

TABLE V

PROPERTIES AND YIELDS OF IMMONIUM PERCHLORATES FROM MERCURIC ACETATE OXIDATION OF MIXTURES OF STEREOISOMERIC 1-AZABICYCLOALKANES **3d–g**

Compound	Yield, %	M.p., °C.	Analyses, % Calcd. C	Calcd. H	Found C	Found H
5	53	258–260 dec.	45.48	6.78	45.20	6.68
7	54	238–239 dec.	47.72	7.16	47.57	7.12
8	62	235–237 dec.	45.48	6.78	45.65	6.56
9	49	253–255[a]				

[a] N. J. Leonard, R. W. Fulmer, and A. S. Hay [*J. Am. Chem. Soc.*, **78**, 3457 (1956)] report m.p. 252–253°.

Catalytic Reduction of the Immonium Perchlorates 5 and 7. A. 8-Methyl-$\Delta^{4(9)}$-dehydroindolizidinium Perchlorate (5).—A methanol solution of 1 g. of the immonium salt **5** was hydrogenated at atmospheric pressure and room temperature in the presence of about 10 mg. of platinum oxide catalyst. After 1 equivalent of hydrogen had been taken up (10 min.), the reaction was stopped, the catalyst removed by filtration, and the solvent evaporated at reduced pressure to leave 1.0 g. of a white crystalline solid, m.p. 150–153° (153–155° after recrystallization from ethanol–ether), which on treatment with base and ether extraction gave 0.5 g. of a colorless oil whose vapor phase chromatogram gave a single peak with a retention time identical with that of **3c**$_2$.

B. 1,8-Dimethyl-$\Delta^{4(9)}$-dehydroindolizidinium Perchlorate (7).—A vapor phase chromatogram of the colorless oil obtained by reduction and work-up of **7** in the same manner as employed for **5**, showed the presence of three substances. Separation of the major component (80–90%) by preparative v.p.c. gave a colorless oil (**3f**$_3$) whose infrared spectrum, boiling point, and the melting point of its picrate (see Table IV) indicated that it was different from **3f**$_2$ and **3f**$_1$.

Attempted Cyclization of 3-(3′-Hydroxypropyl)piperidine (10).—Treatment of 8 g. of the piperidyl alcohol **10** by the general procedure described above led to 1 l. of aqueous distillate which after the usual work-up yielded 0.5 g. of a colorless oil, identified as 3-ethylpiperidine by its b.p. 152° (745 mm.) (lit.[25] b.p. 154–155°), and by the melting points of its picrate, m.p. 62–63° (lit.[25] m.p. 63°), and chloroplatinate, m.p. 182–183° (lit.[25] m.p. 181°).

Attempted Cyclization of 4-(2′-Hydroxyethyl)piperidine (11).—Treatment of 9 g. of the piperidyl alcohol **11** in the same manner as above gave about 1 g. of an oil whose vapor phase chromatogram indicated the presence of at least five components and whose infrared spectrum showed strong absorption in the N–H,O–H and C=O regions. The distillation pot residue was filtered, saturated with sodium carbonate, and extracted with three 50-ml. portions of chloroform. After being dried over anhydrous potassium carbonate, the combined chloroform extracts were freed of chloroform by distillation through a Vigreux column to leave 4 g. of an oily residue whose vapor phase chromatogram and infrared spectrum were as complex as those of the oil which had distilled over during the attempted cyclization.

Attempted Cyclization of 4-(3′-Hydroxypropyl)piperidine (12).—Treatment of 9 g. of the piperidyl alcohol **12** in the same manner as above gave about 0.5 g. of an oil whose vapor phase chromatogram indicated the presence of at least three components and whose infrared spectrum showed strong absorption in the NH,OH and C=C regions. In the same way as above, the distillation pot residue yielded 6 g. of an oil whose infrared spectrum was quite similar to that of the starting piperidyl alcohol **12**.

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(25) A. Gunther, *Chem. Ber.*, **31**, 2140 (1898).