2-Methyl-7-nitro-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepine (13). The residue left after separation of the 3-methyl isomer[9] was treated with methanolic hydrogen chloride and ether and fractionally crystallized to yield the hydrochloride of **11**, mp 276–277°, in 2% yield. The free base was obtained by ether extraction of an aqueous solution of the hydrochloride which had been made basic. The residue left after concentrating the dried extract was recrystallized from ether to give **13** as yellow prisms, mp 152–153°.

Anal. Calcd for $C_{16}H_{15}N_3O_2$: C, 68.31; H, 5.38. Found: C, 68.24; H, 5.71.

Acknowledgment. We thank Dr. E. Billeter and Dr. T. Williams for the nmr spectra, Mr. S. Traiman for the infrared spectra, Dr V. Toome for the ultraviolet spectra, and Dr. A. Steyermark for the microanalyses.

Alkyl Migration to Electron-Deficient Nitrogen

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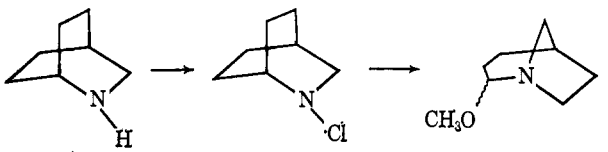
Abstract: Although aryl migration has been well documented in the rearrangement of aryl-substituted N-chloramines, the lack of alkyl migration has remained an anomaly. We have shown that such alkyl migrations can occur in high yield. The N-chloro derivatives of 2-azabicyclo[2.2.2]octane (**1**) and 6-azabicyclo[3.2.1]octane (**2**) have been prepared through the reaction of **1** and **2** with *t*-butyl hypochlorite. The N-chloro derivatives, **3** and **4**, respectively, rearrange with alkyl migration to nitrogen under solvolytic conditions in the presence of silver nitrate. When methanol was the solvent, **3** rearranged to 2-methoxy-1-azabicyclo[3.2.1]octane (**5**) in greater than 60% yield. By comparison, **4** gave the ring cleavage product, 3-(2,2-dimethoxyethyl)piperidine (**6**), on reaction with methanolic silver nitrate. The formation of **6** also requires alkyl migration to nitrogen. The silver ion catalyzed and thermal decompositions of **3** and **4** are compared.

Although the Stieglitz rearrangement of tritylhydroxylamines and the related rearrangement of aryl-substituted N-chloramines have been investigated in some detail, it have been noted[2] that there are no existing examples of such rearrangements involving alkyl migration. In fact, the failure of N-methyl-N-chlorotritylamine to rearrange has been used as evidence for a mechanism which involves initial loss of a proton from the amine followed by loss of chloride ion[2,3] as shown below. It was also proposed[2] that

$$Ar_3\overset{\overset{H}{|}}{C}NCl \xrightarrow{-H^+} Ar_3CN\overset{-}{Cl} \xrightarrow{-Cl^-} Ar_2C{=}NAr$$

with N,N-dichloramines the initial step was loss of positively charged chloride. The results discussed below demonstrate: (1) that alkyl migration can occur in rearrangements of N-chloramines, (2) that N,N-disubstituted chloramines do undergo rearrangement and, consequently, (3) that the mechanism of N-chloramine rearrangements can involve loss of chloride anion as the initial step.

Since bicyclic molecules are known to undergo rearrangement with particular ease, our initial efforts in the study of N-chloramine rearrangements have been restricted to the azabicyclic area. Thus, 2-azabicyclo[2.2.2]octane (**1**) was prepared according to the method of Schneider and Dillman[4] and subsequently converted to 2-chloro-2-azabicyclo[2.2.2]octane (**3**) with *t*-butyl hypochlorite. Refluxing of **3** with a methanolic solution of silver nitrate for 2 hr gave a 60% yield of 2-methoxy-1-azabicyclo[3.2.1]octane (**5**).[5]



1 **3** **5**

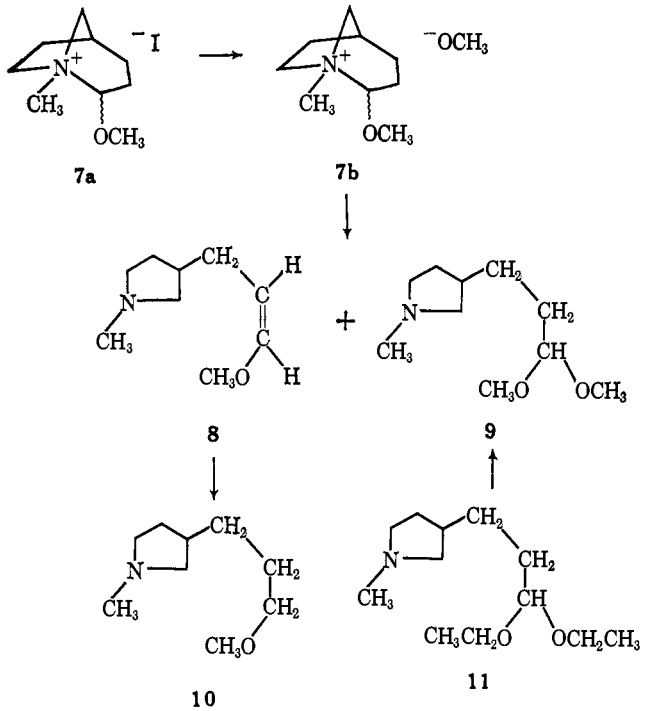
Compound **5** was a clear, colorless liquid which possessed unusual stability for an α-amino ether. It was completely resistant to acid hydrolysis under conditions which normally cause rapid hydrolysis of α-amino ethers.[6–8] Furthermore, it was stable to reductive conditions such as lithium aluminum hydride described by Eliel and Daignault[9] for the reductive cleavage of α-amino ethers. The unusual stability of **5** may be due to the inability of **5** to yield an intermediate with a double bond to the bridgehead, which would be in violation of Bredt's rule.

In view of the failure of **5** to undergo reactions normally associated with α-amino ethers, it was deemed desirable to prove unequivocally that **5** had the proposed structure. This was accomplished by partial degradation, coupled with synthesis of the degradation products.

The rearrangement product, **5**, was converted to the quaternary methiodide, **7a**, followed by passage of a methanolic solution of **7a** through IRA 400 ion-ex-

(1) Esso Fellow, summer 1964; American Cyanamid Fellow, 1964-1965; Goodyear Foundation Fellow, 1965–1966.
(2) For a recent discussion of developments in this area, see P. A. S. Smith in "Molecular Rearrangements," Vol. 1, P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, pp 479–483.
(3) J. Stieglitz and I. Vosburgh, *J. Am. Chem. Soc.*, **38**, 2081 (1916).
(4) W. Schneider and R. Dillman, *Chem. Ber.*, **96**, 2377 (1963).
(5) For a preliminary report of part of this work see P. G. Gassman and B. L. Fox, *Chem. Commun.*, 153 (1966).
(6) C. M. McLeod and G. M. Robinson, *J. Chem. Soc.*, 1470 (1921).
(7) G. M. Robinson and R. Robinson, *ibid.*, 532 (1923).
(8) R. H. Harradence and F. Lions, *J. Proc. Roy. Soc. N. S. Wales*, **73**, 22 (1939).
(9) E. L. Eliel and R. A. Daignault, *J. Org. Chem.*, **30**, 2450 (1965).

change resin to produce the syrupy quaternary ammonium methoxide, **7b**. Pyrolysis of **7b** yielded a mixture of **8** and **9**.



The vinyl ether, **8**, was assigned the *cis* stereochemistry on the basis of the nmr coupling constant for the olefinic protons of 6.3 cps.[10] This assignment was substantiated by the infrared absorption at 13.55 μ.[11] The structure of the skeleton was verified by catalytic hydrogenation to yield the previously synthesized[12] 1-methyl-3-(3-methoxypropyl)pyrrolidine (**10**). The dimethyl acetal, **9**, was synthesized from the known[12] diethyl acetal **11** *via* an acid-catalyzed exchange reaction in methanol. The nmr spectra of **8** and **9** were consistent with the assigned structures.

Isolation of **8** and **9** requires the rearrangement product, **5**, to have the structure shown since no other arrangement of atoms could give the Hofmann products obtained.

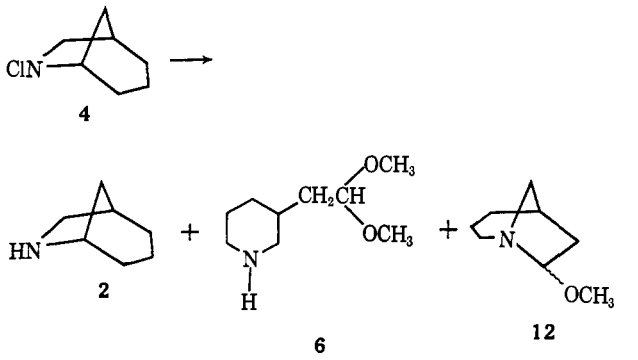
A second example of alkyl migration to electron-deficient nitrogen was provided by the reaction of 6-chloro-6-azabicyclo[3.2.1]octane (**4**) with methanolic silver nitrate. The reaction of *t*-butyl hypochlorite with 6-azabicyclo[3.2.1]octane (**2**) provided **4** in good yield. When **4** was refluxed with methanolic silver nitrate, a large amount (36%) of the secondary amine, **2**, was recovered. In addition, two rearrangement products were obtained. The major product of skeletal rearrangement was 3-(2,2-dimethoxyethyl)piperidine (**6**) which was obtained in 8% yield. In addition, a second rearrangement product was present in 1% yield. This compound has tentatively been assigned structure **12** on the basis of elemental analysis and nmr and infrared spectra.[13]

(10) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, Inc., New York, N. Y., 1959, p 85.

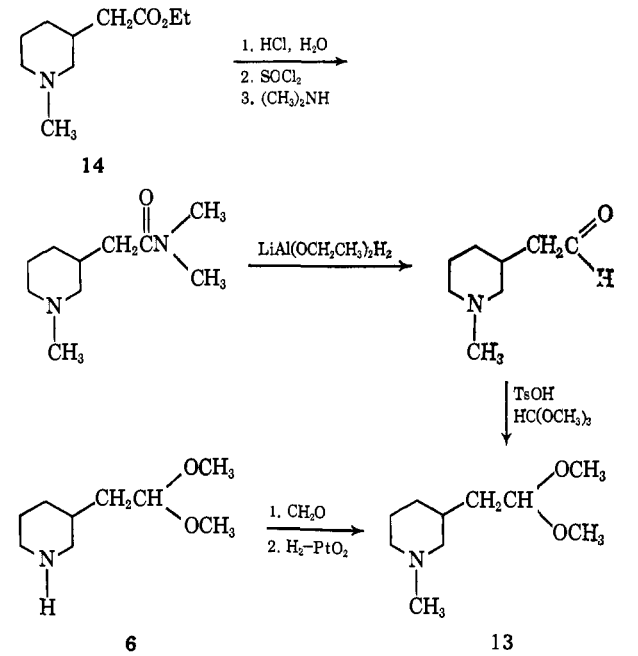
(11) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1964, p 48.

(12) P. G. Gassman and B. L. Fox, *J. Org. Chem.*, **31**, 982 (1966).

(13) Owing to the lack of sufficient material, an unequivocal structure proof could not be carried out.



The structure of **6** was consistent with nmr and infrared data. In addition, **6** was converted to the N-methyl derivative, **13**, *via* reaction with formaldehyde followed by catalytic reduction over Adams catalyst. As shown below, **13** was also prepared from **14** in a straightforward manner.

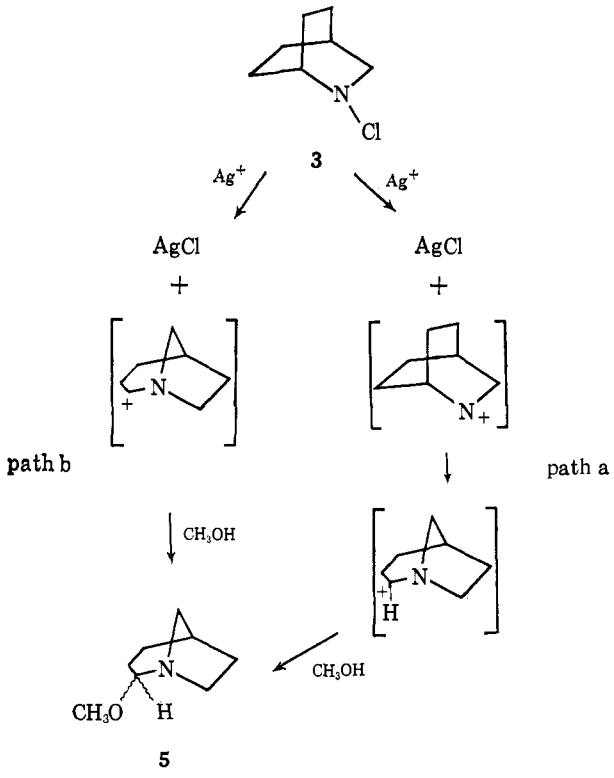


The contrasting behavior of **3** and **4** in methanolic silver nitrate prompted us to investigate the thermal decomposition of these isomeric N-chloramines. The N-chloramine derived from 6-azabicyclo[3.2.1]-octane was considerably less stable than the corresponding N-chloramine derived from **1**. In refluxing methanol in the absence of silver nitrate, **3** had a half-life of 65 hr while **4** had a half-life of 10 hr. In refluxing methanolic silver nitrate, the reactivities were reversed in that **3** was completely reacted (precipitation of silver chloride complete) after 2 hr while **4** took about 12 hr for complete reaction. This represents a difference of a factor of 36 between the two compounds under the conditions described. The thermal nonsilver-catalyzed decompositions of both **3** and **4** were very complex from a product standpoint. Refluxing **3** with methanol gave 20% of the starting amine, **1**, 11% of the rearrangement product, **5**, and 11 other components which amounted to *ca.* a 30% yield. In addition, considerable decomposition was noted. This is to be contrasted with the silver ion catalyzed reaction of **3** which gave *only* **5** and **1**.

Thermolysis of **4** in refluxing methanol gave only trace amounts of **12** and no detectable amount of **6**. The major product was the starting amine, **2**.

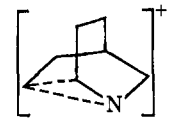
The data described above clearly indicate that the silver nitrate catalyzed decomposition of N-chloramines differs drastically from the thermal decomposition. This may be due to predominant homolytic cleavage of the N–Cl bond on thermolysis *vs.* predominant heterolytic cleavage in the reaction with silver nitrate. In the case of the 6-chloro-6-azabicyclo[3.2.1]octane (**4**), the rates of the two reactions were competitive. For 2-chloro-2-azabicyclo[2.2.2]octane (**3**), the rate of the silver ion catalyzed reaction was *ca.* 200 times faster than the thermolysis. This would indicate that the products from the silver ion catalyzed reaction of **3** were those of predominant heterolytic cleavage while the products observed from **4** would be a mixture resulting from silver ion catalyzed and thermal decomposition.

The two examples of alkyl migration from carbon to nitrogen cited above represent a reaction of N-chloramines which has heretofore been considered unlikely.[2] The exact mechanism of this silver-catalyzed reaction is not known. Two possibilities appear attactive: (a) a nitrenium ion[14] could be formed followed by rearrangement,[15] or (b) a concerted alkyl migration with loss of chloride ion could be occurring. Neither of these mechanisms can be eliminated or verified on the basis of the present evidence. The formation of the stereo-



5

chemically pure ether, **5**, can be used as evidence of a completely concerted loss of halide ion, alkyl migration, and solvent addition. An alternate possibility would involve the formation of a delocalized ion such as **15** which would collapse with stereospecific addition of solvent.



15

The rearrangement of **3** to **5** can be compared to other reactions in which carbon–nitrogen bonds were formed from nitrenium ion precursors.[16,17] In these cases the reaction pathway probably involved hydride abstraction by a nitrenium ion prior to C–N bond formation.[16] The nature of our products precludes a similar mechanistic route in the rearrangement of **3** to **5** and in the rearrangement of **4** to **6**.

Experiments designed to determine the scope and detailed mechanism of alkyl migration to electron-deficient nitrogen in N-chloramine solvolyses are in progress.

Experimental Section

2-Azabicyclo[2.2.2]octane (Isoquinuclidine, 1). Isoquinuclidine was synthesized from *p*-aminobenzoic acid following the procedure of Schneider and Dillman.[4]

2-Chloro-2-azabicyclo[2.2.2]octane (3). To a cold solution of 3.14 g (28.3 mmoles) of **1** in 50 ml of diethyl ether containing 0.5 g of sodium bicarbonate was added dropwise with stirring at 10° in the dark 3.14 g (29.1 mmoles) of distilled *t*-butyl hypochlorite.[18] After stirring in the dark for 1 hr at 10°, the salts were removed by filtration to give an ethereal solution of the N-chloramine.

Solvolysis of 2-Chloro-2-azabicyclo[2.2.2]octane. The above solution of N-chloramine was taken up in 200 ml of absolute methanol and 6.80 g (40 mmoles) of silver nitrate was added. The reaction was refluxed with stirring in diffuse light for 2 hr, cooled, the silver chloride removed by filtration and rinsed thoroughly with methanol. The combined filtrate and rinses were concentrated to *ca.* 15 ml on a steam bath by distilling off the solvent through a short column packed with glass helices. The residue was made basic with 2 *N* sodium hydroxide solution, saturated with sodium chloride, and continuously extracted with ether for 36 hr. After drying the extract over anhydrous magnesium sulfate, the desiccant was removed by filtration and the ether distilled off. A small amount of dry benzene was added to the concentrate and the benzene distilled off to assure the removal of any last trace of water. Distillation of the residue afforded 2.41 g (60.4%) of 2-methoxy-1-azabicyclo[3.2.1]octane (**5**), bp 69–71° (18 mm), as a clear colorless colorless liquid; $n^{25}D$ 1.4722.

Anal. Calcd for $C_8H_{15}NO$: C, 68.04; H, 10.71; N, 9.92. Found: C, 67.83; H, 10.76; N, 10.09.

Treatment of a few drops of this material with a saturated solution of picric acid in 95% ethanol produced a picrate, mp 175–178° (95% ethanol).

Anal. Calcd for $C_{14}H_{18}N_4O_8$: C, 45.41; H, 4.90; N, 15.13. Found: C, 45.33; H, 4.86; N, 15.15.

The nmr spectrum of the rearrangement product had a sharp singlet at τ 6.64 which integrated for three protons (OCH_3) and a broad peak at τ 6.34 integrating for one proton which was assigned to the proton on the 2 position. The remainder of the spectrum consisted of complex envelopes.

Hofmann Degradation of 2-Methoxy-1-azabicyclo[3.2.1]octane. To a solution of 0.53 g (3.75 mmoles) of 2-methoxy-1-azabicyclo[3.2.1]octane in 1.4 ml of methanol was added excess methyl iodide. After standing for 6 hr at room temperature, the solvent was evaporated *in vacuo* and the yellow residue taken up in a minimum amount

(14) The term "nitrenium ion" will be used here to signify a divalent, positively charged nitrogen species of the type R–N–R.

(15) For recent reviews of rearrangements involving charged nitrogen intermediates, see R. A. Abramovitch and B. A. Davis, *Chem. Rev.*, 64, 149 (1964), and P. A. S. Smith in "Molecular Rearrangements," Vol. 1, P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, pp 457–483.

(16) O. E. Edwards, D. Vocelle, J. W. ApSimon, and F. Haque, *J. Am. Chem. Soc.*, 87, 678 (1965).

(17) G. Adam and K. Schreiber, *Angew. Chem.*, 76, 752 (1964).

(18) H. M. Teeter and E. W. Bell, "Organic Syntheses," Coll. Vol. IV, N. Rabjohn, Ed., John Wiley and Sons, Inc., New York, N. Y., 1963, p 125. See note of caution: C. P. C. Bradshaw and A. Nechvatal, *Proc. Chem. Soc.*, 213 (1963).

of acetone and precipitated with ether to give 0.95 g (89%) of methiodide, mp 200–203° dec as a white powder. A 10 × 0.5 in. chromatography column filled with 19 g of Amberlite IRA 400 ion-exchange resin was rinsed with 240 ml of 10% sodium hydroxide solution, followed by distilled water until the eluent was neutral, and finally 150 ml of absolute methanol. Through this column was passed a solution of the methiodide in 60 ml of methanol. The column was washed with absolute methanol, and the portion of the eluent which was basic to pH indicator paper was collected. This fraction was evaporated *in vacuo* without the application of heat to give a clear syrup. Pyrolysis of the syrup in a molecular still was carried out between 65 and 90° (30 mm) and afforded a mixture containing two major components. Preparative vapor phase chromatography using a 5 ft × 3/8 in. column of 20% (4:1) Apiezon L-KOH on 60–80 Firebrick at 130° gave as the more rapidly eluted component 1-methyl-3-(*cis*-3-methoxyprop-2-enyl)-pyrrolidine (**8**); n^{24}D 1.4618.

Anal. Calcd for $C_9H_{17}NO$: C, 69.63; H, 11.04; N, 9.02. Found: C, 69.73; H, 11.09; N, 9.02.

The component having the longer retention time proved to be 1-methyl-3-(3,3-dimethoxypropyl)pyrrolidine (**9**); n^{24}D 1.4438.

Anal. Calcd for $C_{10}H_{21}NO_2$: C, 64.13; H, 11.30; N, 7.48. Found: C, 64.02; H, 11.34; N, 7.45.

The nmr spectrum of the enol ether showed the following integrated intensities and multiplicities: τ 4.16, 1 H (doublet showing *cis*-vicinal coupling,[10] J = 6.3 cps, being split further by allylic coupling, J = 1.2 cps); τ 5.75, 1 H (quartet, J = 6.3 cps); τ 6.52, 3 H (singlet); τ 7.78, singlet in the center of a complex envelope which integrated for a total of 12 protons. The nmr spectrum of the acetal had integrated intensities and multiplicities as follows: τ 5.72, 1 H (triplet, J = 5.3 cps); τ 6.78, 6 H (singlet); τ 7.82, singlet in a broad complex envelope which integrated for a total of 14 protons.

1-Methyl-3-(3-methoxypropyl)pyrrolidine (10). A solution of 106 mg (0.684 mmole) of 1-methyl-3-(*cis*-3-methoxyprop-2-enyl)-pyrrolidine (**8**) in 11 ml of thiophene-free benzene was hydrogenated at room temperature and atmospheric pressure using 75 mg of 5% palladium-on-carbon catalyst. The theoretical amount of hydrogen was taken up in 10 min. The catalyst was removed by filtration, the solvent distilled off, and finally a gentle stream of dry nitrogen was passed over the residue to remove as much solvent as possible. The nmr and infrared spectra of this material were identical with those of authentic 1-methyl-3-(3-methoxypropyl)-pyrrolidine prepared by a known procedure.[12]

1-Methyl-3-(3,3-dimethoxypropyl)pyrrolidine (9). A solution of 1.0 g (4.65 mmoles) of 1-methyl-3-(3,3-diethoxypropyl)pyrrolidine[12] in 50 ml of anhydrous methanol was saturated with hydrogen chloride gas and allowed to stand at room temperature for 40 hr. Concentration to dryness *in vacuo* afforded white crystals which were taken up in 10 ml of 1 *N* sodium hydroxide solution and extracted eight times with 10-ml portions of ether. After drying over anhydrous magnesium sulfate, the ethereal solution was concentrated on a steam bath, and the residue was purified by preparative vapor phase chromatography to give 1-methyl-3-(3,3-dimethoxypropyl)pyrrolidine. n^{24}D 1.4442, which gave nmr and infrared spectra identical with that of the material from degradation of 2-methoxy-1-azabicyclo[3.2.1]octane.

6-Azabicyclo[3.2.1]octane. Lithium aluminum hydride reduction of 6-azabicyclo[3.2.1]octan-7-one according to the known procedure[19] afforded the corresponding amine, mp 132–135°, in 47.5% yield.

Solvolysis of 6-Chloro-6-azabicyclo[3.2.1]octane (4). To the N-chloramine, **4**, prepared from 4.30 g (38.7 mmoles) of 6-azabicyclo[3.2.1]octane in the same manner as outlined above, was added 250 ml of anhydrous methanol and 6.80 g (0.40 mole) of silver nitrate. The reaction was stirred at reflux in diffuse light for 12 hr and then worked up as described above. Distillation afforded starting material, bp 100° (10 mm), which solidified in the distillation apparatus, followed by 1.06 g of a mixture, bp 110–112° (19 mm), which was shown to be principally 3-(2,2-dimethoxyethyl)piperidine (**6**) by vapor phase chromatography on 20% (4:1) Apiezon L–KOH on 60–80 Firebrick at 160°. Preparative vapor phase chromatography on the same absorbent at 140° produced an analytical sample, n^{27}D 1.4568.

Anal. Calcd for $C_9H_{19}NO_2$: C, 62.39; H, 11.05; N, 8.09. Found: C, 62.58; H, 11.14; N, 8.23.

The nmr spectrum displayed a sharp singlet at τ 6.79 which integrated for six protons, a poorly resolved triplet (J = 5.0 cps) at τ 5.64 of correct intensity for one proton, and a broad envelope at τ 6.93–9.22 which integrated for 12 protons.

6-Methoxy-1-azabicyclo[3.2.1]octane (12). Small amounts of **12** could be isolated in addition to **5** by preparative vapor phase chromatography; $n^{5.5}$D 1.4768.

Anal. Calcd for $C_8H_{15}NO$: C, 68.04; H, 10.71; N, 9.92. Found: C, 68.09; H, 10.81; N, 10.08.

The nmr spectrum showed peaks having the following integrated intensities and multiplicities: τ 5.72, 1 H (triplet J = 4.0 cps); τ 6.80, 3 H (singlet); τ 7.25, 4 H (complex multiplet); τ 7.53–9.06, envelope integrating for seven protons.

Vapor Phase Chromatographic Analysis of Solvolysis Products from 4. The products from an 8-hr solvolysis of **4** in methanolic silver nitrate were analyzed using *p*-methylanisole as an internal standard by vapor phase chromatography on a column of 10% (4:1) Carbowax 20M–KOH on 60–80 Chromosorb W at 126°. This analysis showed the presence of 1% of **12**, 8% of **5**, and 38% of **2**.

Ethyl 2-(1-Methyl-3-piperidyl)acetate. A solution of 10 g (60.6 mmoles) of ethyl 3-pyridylacetate[20] and 10 g (70.4 mmoles) of methyl iodide in 75 ml of ether was stirred at room temperature for 8 hr, an additional 5.0 g (35.2 mmoles) of methyl iodide added, and stirring continued for 4 hr. The ether was decanted from the red oil which was then taken up in 200 ml of absolute ethanol and hydrogenated at 40 psi using 0.5 g of Adams catalyst. The catalyst was removed by filtration and the filtrate concentrated *in vacuo* to a yellow oil. This oil was taken up in saturated potassium bicarbonate solution and extracted with six 40-ml portions of chloroform. After drying over anhydrous magnesium sulfate, the solvent was removed by distillation and the residue vacuum distilled to give 5.48 g (49%) of ethyl 2-(1-methyl-3-piperidyl)acetate as a clear colorless liquid, bp 87–89° (5 mm); n^{16}D 1.4546 [lit.[21] bp 115–116° (15 mm); n^{18}D 1.4540].

N,N-Dimethyl-2-(1-methyl-3-piperidyl)acetamide. A solution of 5.03 g (27.2 mmoles) of ethyl 2-(1-methyl-3-piperidyl)acetate in 100 ml of 6 *N* hydrochloric acid was refluxed for 8 hr, the solvent removed on a rotary evaporator, and the residue dried by azeotropic distillation with benzene and absolute ethanol. The residual white amino acid hydrochloride was refluxed for 1 hr in 50 ml of thionyl chloride. The thionyl chloride was removed on a rotary evaporator, the last traces being removed by codistillation with dry benzene. The residual yellow solid was suspended in 100 ml of dry benzene and stirred with excess anhydrous dimethylamine for 12 hr at room temperature. After concentration to *ca.* 50 ml on a steam bath, the residue was made basic with saturated potassium bicarbonate solution, the benzene layer separated and saved, and the aqueous layer extracted with six 50-ml portions of chloroform. The benzene and chloroform layers were combined, and after drying and evaporation of the solvent, yielded upon distillation 3.67 g (73.4%) of the desired amide, bp 78–80° (0.19 mm). This material readily formed a picrate, mp 166–167°.

Anal. Calcd for $C_{16}H_{23}N_5O_8$: C, 46.49; H, 5.61; N, 16.94. Found: C, 46.62; H, 5.79; N, 16.85.

1-Methyl-3-(2,2-dimethoxyethyl)piperidine. To 2 ml of 0.92 *M* lithium aluminum hydride solution (1.84 mmoles) at 0° was added with stirring over a period of 10 min 92 mg (2.0 mmoles) of absolute ethanol[22] in 1 ml of dry ether. After stirring for 0.5 hr, this reagent was transferred with a hypodermic syringe to a dropping funnel and added dropwise with stirring under nitrogen to 0.6945 g (3.53 mmoles) of N,N-dimethyl-2-(1-methyl-3-piperidyl)acetamide in 2 ml of dry ether at 0° over a period of 0.5 hr. Stirring was continued for 1 hr, 1.5 ml of saturated sodium potassium tartrate solution was added, and, after stirring for 0.5 hr, the ether decanted and dried over anhydrous magnesium sulfate. The desiccant was removed by filtration, the solvent distilled off, and the residue distilled through a short-path distillation apparatus to give 0.14 g (28%) of aldehyde, bp 78° (6 mm). A solution of this material and 0.2 g of *p*-toluenesulfonic acid in 2 ml of trimethyl orthoformate was stirred at room temperature for 6 hr, then at 60–70° for an additional 6 hr. After cooling, 5 ml of ether and 3 ml of water were added; the aqueous layer was neutralized with 10 ml of saturated postassium bicarbonte solution, and the organic layer extracted with two 1-ml portions of cold 4 *N* hydrochloric acid, the

(19) F. R. Hewgill and P. R. Jefferies, *J. Chem. Soc.*, 2767 (1955).

(20) This material was purchased from the Aldrich Chemical Co. and was used without further purification.

(21) A. D. Yanina and M. V. Rubstov, *Zh. Obshch. Khim.*, **30**, 526 (1960).

(22) L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., Boston, Mass., 1957, p 286.

Table I. Thermal Decomposition of 2-Chloro-2-azabicyclo[2.2.2]octane (3)

Time, hr	Sodium thiosulfate, 0.0101 *N*, ml	Unreacted N-chloramine, mmoles
0	33.63	8.50
15	26.16	6.60
31	21.42	5.41
37	20.30	5.12
61	17.20	4.35

Table II. Thermal Decomposition of 6-Chloro-6-azabicyclo[3.2.1]octane (4)

Time, hr	Sodium thiosulfate 0.101 *N*, ml	Unreacted N-chloramine, mmoles
0	23.80	2.40
1	20.73	2.09
2	19.40	1.96
4	18.30	1.85
8	14.59	1.47
12	10.86	1.10

acid extracts being added to the bicarbonate solution referred to above. Extraction of the bicarbonate solution with six 10-ml portions of ether gave, after drying and evaporation of the solvent, the desired 1-methyl-3-(2,2-dimethoxyethyl)piperidine. Purification by preparative vapor phase chromatography on a 10-ft column of 10% (4:1) Carbowax 20M–KOH on 60–80 Chromosorb W at 140° gave pure acetal, having the same vpc retention time on Carbowax 20M and infrared spectrum as the material prepared by methylation of **6**.

1-Methyl-3-(2,2-dimethoxyethyl)piperidine (13). A solution of 62 mg (0.36 mmole) of **6** and 0.050 ml of formalin in 2 ml of methanol was stirred at room temperature for 10 hr. The solution was diluted with 10 ml of methanol and hydrogenated at atmospheric pressure over 200 mg of Adams catalyst. The catalyst was removed by filtration, and the solvent was removed by fractional distillation. Vapor phase chromatography on a 6 ft × 0.5 in. column of 10% (4:1) Carbowax 20M–KOH on 60–80 Chromosorb W at 135° using propiophenone as an internal standard showed the presence of 59 mg (87%) of 1-methyl-3-(2,2-dimethoxyethyl)piperidine (**13**). Isolation of **13** *via* vpc on the same column gave an analytical sample, $n^{31}D$ 1.4770.

Anal. Calcd for $C_{10}H_{21}NO_2$: C, 64.13; H, 11.30; N, 7.48. Found: C, 64.03; H, 11.02; N, 7.64.

Thermal Decomposition of N-Chloramines. Methanolic solutions of **3** and **4** were prepared as described above with silver nitrate being omitted. The solutions were refluxed in the dark, and the reaction rates were followed by removing 5-ml aliquots. Each aliquot was treated with 2 ml of 1 *N* sulfuric acid and 5 ml of 5% potassium iodide. The liberated iodine was then titrated with 0.0101 *N* sodium thiosulfate using a starch indicator. The results are given in Tables I and II.

Product analyses were carried out by vpc on a 5 ft × ⅛ in. column containing 20% (4:1) Apiezon L–KOH on 60–80 Chromosorb P at 118° with diethylaniline as an internal standard.

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The Thermal Rearrangement of 1,5-Hexadiyne and Related Compounds[1]

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Abstract: 1,5-Alkadiynes undergo intramolecular rearrangement at elevated temperatures to give dimethylenecyclobutenes. Thus, at 335° in a flow system, 1,5-hexadiyne rearranges rapidly to 3,4-dimethylenecyclobutene. 1,5-Heptadiyne rearranges somewhat more slowly, giving 1-methyl-3,4-dimethylenecyclobutene at 377°, while 1,2-dimethyl-3,4-dimethylenecyclobutene is formed from 2,6-octadiyne at 410°. Evidence pertinent to the stereochemistry of the reaction was obtained from a study of the rearrangement of the stereoisomeric 3,4-dimethyl-1,5-hexadiynes. Rearrangement of *meso*-3,4-dimethyl-1,5-hexadiyne gives *syn,anti*-3,4-diethylidenecyclobutene (**13**), while *rac*-3,4-dimethyl-1,5-hexadiyne gives a symmetrical cyclic product, believed to be the *anti,anti* isomer **14**. Thus the rearrangement involves a conrotatory process. From kinetics data obtained for the rearrangement of 1,5-hexadiyne over the temperature range 210–297° the energy and entropy of activation are calculated to be 34.4 kcal/mole and −9.4 eu, respectively. Two possible mechanisms are presented and the origin of retardation by methyl groups is discussed.

Although there is a wealth of literature on thermal rearrangements of molecules containing olefinic linkages,[3] little has been reported on similar reactions of acetylenic analogs. As a result of the finding that 6-octen-1-yne (**1**) rearranges to 1-methylene-2-vinylcyclopentane (**2**) even more rapidly than the olefinic counterpart **3** rearranges to **4**,[4] it was decided to study the thermal behavior of other acetylenic derivatives. Results of an investigation of 1,5-hexadiyne (**5**) and some of its methyl-substituted homologs are presented in this paper.

The behavior of 1,5-hexadiyne was investigated over the temperature ranges 210–232° in a static system and

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(2) Taken in part from the Ph.D. dissertation of H. J. Wristers, June 1965.

(3) Review articles which provide leading references are: S. J. Rhoads in "Molecular Rearrangements," P. de Mayo, Ed., Part 1, Interscience Publishers, Inc., New York, N. Y., 1963; W. von E. Doering and W. R. Roth, *Angew. Chem. Intern. Ed. Engl.*, 2, 115 (1963).

(4) W. D. Huntsman and R. P. Hall, *J. Org. Chem.*, 27, 1988 (1962).