***n*-Hexyllithium.**—The reagent was prepared by a procedure in the literature.[19]

**Inverse Reaction of *n*-Butyllithium with 2-Phenyl-1,3-dioxolane (1a).**—2-Phenyl-1,3-dioxolane (2.25 g., 0.015 mole) was dissolved in 50 ml. of cyclohexane and the system was swept with nitrogen. *n*-Butyllithium (0.0146 mole) in 140 ml. of ether was added dropwise over a 0.5-hr. period (a small rise in temperature was noted). A heavy white precipitate was formed during this period.

The reaction was heated gradually for 2 hr. until the temperature reached 57°. Water (150 ml.) was carefully added to hydrolyze the mixture and additional ether (final volume 250 ml.) was added to dissolve the remaining solids. The organic layer was dried over anhydrous sodium sulfate, and approximately one-half of the sample (*ca.* 100 ml.) was concentrated to a volume of 10 ml. which was used for subsequent g.l.c. analysis.

The water layer was acidified with 6 *N* hydrochloric acid and extracted with three 100-ml. portions of ether. After drying over anhydrous sodium sulfate, 100 ml. of the ether extract was concentrated to 5 ml. and examined by gas chromatography.

G.l.c. analysis was made using a column of SE-30 (5%) on Chromosorb W (80/100), 6 ft. × 0.125 in., on an Aerograph Hy Fi Model A-550 unit with a hydrogen flame ionization detector; the temperature range examined was 112–215°; $H_2$ flow, 20 cc./min.; $N_2$ flow, 30 cc./min. The following compounds were identified by the mixed injection technique: 2-phenyl-1,3-dioxolane, benzaldehyde, valerophenone, ethyl benzoate, benzoic acid, octane, and 5-phenyl-5-nonanol.

**Preparation of 5-Phenyl-5-nonanol.**—The butyl Grignard reagent was prepared in the usual manner from 12.16 g. (0.5 g.-atom) of magnesium, 68.52 g. (0.5 mole) *n*-butyl bromide and 200 ml. of anhydrous ether. To the Grignard reagent was added 37.54 g. (0.25 mole) of ethyl benzoate dissolved in 50 ml. of absolute ether. During addition, which required 0.75 hr., the temperature rose five degrees. After the addition was complete the reaction was heated under reflux for 2 hr.

Hydrolysis was effected with 250 ml. of 20% aqueous ammonium chloride. The mixture was acidified with dilute hydrochloric acid and the organic layer was separated. The aqueous layer was washed with three 100-ml. portions of ether. After the extract had been combined with the organic layer and dried over anhydrous magnesium sulfate, it was distilled to give 33.55 g. (61%) of 5-phenyl-5-nonanol: b.p. 90.8–91.5° (1.5–2 mm.), $n^{25.8}\text{D}$ 1.4993 (lit.[20] b.p. 130–132° at 7–8 mm., $n^{18}\text{D}$ 1.50602); $\lambda_{\max}^{\text{film}}$ 3448 (O–H), 3010 (aromatic C–H), 2915 and 2857 (aliphatic C–H), and 700 cm. ($C_6H_5$–). The n.m.r. (in $CCl_4$) showed resonance frequencies at δ 0.75 (multiplet), 1.12 (multiplet), 1.75 (multiplet), 2.35 (singlet, O–H), and 7.24 (singlet, aromatic protons).

***n*-Valeraldehyde Dimethyl Acetal.**—The procedure was that found in the literature[21]: b.p. 131° (739 mm.); $\lambda_{\max}^{\text{film}}$ 1060 and 1440 cm.$^{-1}$; yield 48%.

**Reaction of *n*-Butyllithium with *n*-Valeraldehyde Dimethyl Acetal.**—*n*-Butyllithium (0.1 mole) and the acetal (2.24 g., 0.02 mole) were heated at reflux in ether–hexane (60°). After 2 hr., the reaction mixture was decomposed with water. Analysis by gas chromatography of the organic solution indicated primarily unreacted acetal.

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(19) H. Gilman, J. A. Beel, C. G. Brannen, M. W. Bullock, G. E. Dunn, and L. S. Miller, *J. Am. Chem. Soc.*, **71**, 1499 (1949).

(20) A. D. Petrov, A. P. Bardanov, N. N. Zakotin, and P. I. Suntsov, *J. Gen. Chem. USSR.*, **9**, 509 (1939); *Chem. Abstr.*, **34**, 388 (1940).

(21) C. Morel, *Soap Perfumery Cosmetics*, **27**, 279 (1954); *Chem. Abstr.*, **48**, 6654 (1954).

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# The Hofmann Elimination of 9-Methyl-3,9-diazabicyclo[4.2.1]nonan-4-one Methiodide. Nature of the Product and Mechanism[1]

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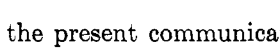
*Received June 24, 1964*

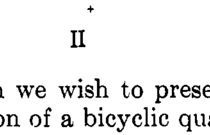
The Hofmann elimination of 9-methyl-3,9-diazabicyclo[4.2.1]nonan-4-one methiodide (IV) has been found to afford the α,β-unsaturated amide VI. Evidence in support of this structure has been obtained from ultraviolet and n.m.r. data, and from studies of the behavior of the monocyclic and tetradeuterated analogs, XV and XX, respectively. The elimination of the quaternary nitrogen center has been shown by proper deuterium labeling to occur most probably *via* an E1cb mechanism.

The thermal decomposition of a quaternary hydroxide to give an olefin and an amine has proven itself not only a useful procedure for degradation and synthesis,[4] but has been found to vary mechanistically upon the demand of the particular system under study. For example, simple alkylammonium hydroxides which possess a β-hydrogen atom that can readily attain *trans* coplanarity with the positively charged nitrogen function in the transition state undergo elimination *via* the E2 mechanism.[5,6] However, the quaternary hydroxide I, wherein the β-hydrogen atom cannot become *trans* and coplanar because of steric factors, has been found to eliminate by the *cis*-ylide mechanism.[7] Additional work has demonstrated that *trans*-2-phenylcyclohexyltrimethylammonium hydroxide (II) reacts exclusively by means of the two-step β-carbanion (E1cb) mechanism to yield only 1-phenylcyclohexene.[8-10]



$$[(CH_3)_3C]_2CH-CH_2\overset{+}{N}(CH_3)_3 \ OH^-$$

I



II

In the present communication we wish to present a study of the Hofmann elimination of a bicyclic quaternary hydroxide wherein the nitrogen function is attached as the bridging atom simultaneously β-oriented to both the carbonyl and nitrogen moieties of an amide group (see IV). Such a system as IV is capable of the normal E2 *trans* elimination, for Dreiding models indicate that the appropriate hydrogens lie *trans* coplanar to the nitrogen function (as illustrated below). Alternatively, one can visualize an E1cb

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(1) Part XI of the series Unsaturated Heterocyclic Systems. For part X, see L. A. Paquette, *J. Org. Chem.*, **29**, 3447 (1964).

(2) Department of Chemistry, The Ohio State University, to whom inquiries should be addressed.

(3) Taken in part from the M.S. Thesis of L. D. W., The Ohio State University, 1964.

(4) For an excellent review of the Hofmann elimination reaction, see A. C. Cope and E. R. Trumbull, *Org. Reactions*, **11**, 317 (1960).

(5) V. G. Shiner and M. L. Smith, *J. Am. Chem. Soc.*, **80**, 4095 (1958).

(6) A. C. Cope, N. A. LeBel, P. T. Moore, and W. R. Moore, *ibid.*, **83**, 3861 (1961).

(7) A. C. Cope and A. S. Mehta, *ibid.*, **85**, 1949 (1963).

(8) J. Weinstock and F. G. Bordwell, *ibid.*, **77**, 6706 (1955).

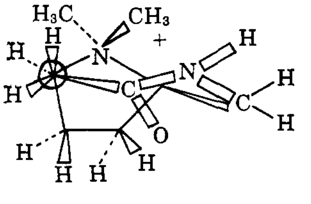
(9) A. C. Cope, G. A. Berchtold, and D. L. Ross, *ibid.*, **83**, 3859 (1961).

(10) G. Ayrey, E. Buncel, and R. N. Bourns, *Proc. Chem. Soc.*, 458 (1961).

TABLE I

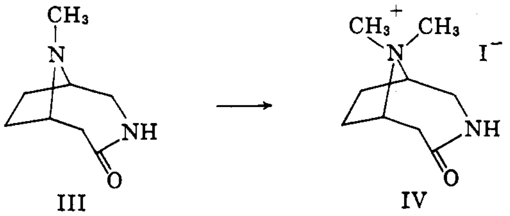
| No. | Compd. | Solvent | $\lambda_{max}$, mμ | ε |
|---|---|---|---|---|
| VII | 5,6-Dihydro-6-methyl-2(1H)-pyridone[a] | EtOH | 252 | 1500 |
| VIII | 5,6-Dihydro-1,6-dimethyl-2(1H)-pyridone[a,b] | EtOH | 252 | 1400 |
| IX | *cis*-2-Methylcrotonamide (angelamide)[c] | $H_2O$ | End absorption | 4660 (200 mμ) |
| X | N-(2-Dimethylaminoethyl)acrylamide[d] | EtOH | 223 | 5050 |
| XI | 3,4,5,6,7,8-Hexahydrocarbostyril[e] | EtOH | 253 | 4900 |
| XII | 4,5-Dihydro-4,4,6-trimethyl-2(3H)-azepinone[f] | MeOH | 237 | 7200 |
| XIII | 6,7-Dihydro-4,6,6-trimethyl-2(5H)-azepinone[f] | MeOH | 218 | 11,800 |
| XIV | α-Obscurine[g] | EtOH | 255 | 5400 |

[a] M. Shamma and P. D. Rosenstock, *J. Org. Chem.*, **26**, 718 (1961). [b] O. E. Edwards and T. Singh, *Can. J. Chem.*, **32**, 683 (1954). [c] A. Castille, *Bull. soc. chim. Belges*, **39**, 417 (1930). [d] The present work. [e] A. D. Campbell and I. D. R. Stevens, *J. Chem. Soc.*, 959 (1956). [f] R. H. Mazur, *J. Org. Chem.*, **26**, 1289 (1961). [g] W. A. Ayer and I. D. R. Stevens, *Tetrahedron Letters*, **No. 10**, 19 (1960).

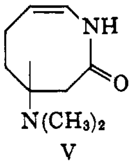


reaction in which the lifetime of the intermediate carbanion could be extended because of interaction with the amide function. On the other hand, however, the β-hydrogen atoms which must be removed in these mechanistic pathways are somewhat more sterically shielded than the methyl groups attached to positive nitrogen. Therefore, if steric factors assume any degree of importance in proceeding to the transition state then an ylid mechanism could be favored.[11]

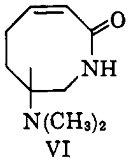
**Nature of the Product.**—Quaternization of 9-methyl-3,9-diazabicyclo[4.2.1]nonan-4-one (III)[12] with methyl iodide in ethanol afforded the corresponding methiodide IV in quantitative yield. A solution of IV in water was passed through a column of Amberlite IRA-400 (hydroxide form)[13] and elution with water was continued until the eluates were neutral. The hydroxide thus obtained was heated *in vacuo;* decomposition commenced at approximately 150° and there was obtained a viscous colorless oil in 86% yield. Our first expectation was that this substance would prove to be the α,β-unsaturated amide VI. However, it remained to distinguish among VI, the enamide isomer V, and several related possibilities.



III IV



V



VI

The product exhibited infrared peaks in carbon tetrachloride solution at 3220 (N–H), 1665 (amide carbonyl), and 1625 cm.$^{-1}$ (conjugated double bond). The ultraviolet spectrum displayed only terminal end absorption. The n.m.r. spectrum (in $CDCl_3$) was fully compatible only with structure V or VI, and definitely removed from consideration alternative isomers which could have resulted by removal of β-protons from the left-hand bridge. Thus, the vinyl protons were found to be the AB portion of an $ABX_2$ system; the least shielded vinyl hydrogen (A) consisted of two sets of triplets centered at $\delta$ 6.11 with $J_{AX} = 5$ and $J_{AB} = 12.5$ c.p.s. while the more shielded vinyl proton (B) was displayed as a broadened doublet[14] ($J = 12.5$ c.p.s.) at $\delta$ 5.70. The vinyl coupling constant of 12.5 c.p.s. confirmed the cisoid nature of the site of unsaturation.[15]

At this point, it was evident that in order to distinguish between V and VI, serious consideration and weight must be given to the ultraviolet datum. The two structures might be expected to display markedly different ultraviolet absorption maxima; however, a discouraging lack of unsaturated azocinones which could serve as model compounds led to the examination of the spectra properties of a group of related structures (see Table I). A comparison of the α,β-unsaturated amides IX, X, and XIII clearly indicates that such systems have low-lying ultraviolet absorption maxima; the exceptions to this general pattern of behavior are the 5,6-dihydro-2(1H)-pyridones (see, for example, VII and VIII) which generally absorb above 240 mμ. Enamides such as XI, XII, and XIV show an ultraviolet absorption maximum in the 235–255-mμ region. The best analogs for the present situation from the standpoint of ring size are the unsaturated seven-membered ring amides XII and XIII. The data indicate that the enamide XII displays absorption about 20 mμ higher than the corresponding α,β-unsaturated lactam (XIII). Extrapolation of this reasoning to the eight-membered ring systems would therefore suggest that the Hofmann elimination

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[11] The influence of steric factors in carbanion reactions has been recognized for sometime; however, the accompanying large electronic effects have made it difficult to assess exactly the precise role of the steric factors. F. G. Bordwell, R. L. Arnold, and J. B. Biranowski [*J. Org. Chem.*, **28**, 2496 (1963)] have recently observed dramatic examples of steric hindrance to carbanion formation and have thus denonstrated that such influences must be considered of fundamental importance in elimination processes.

[12] R. J. Michaels and H. E. Zaugg, *ibid.*, **25**, 637 (1960).

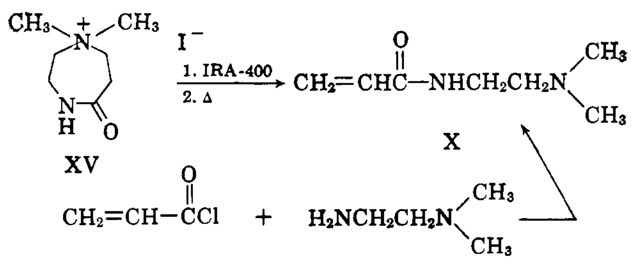
[13] This ion-exchange resin has been utilized previously for this purpose: J. Weinstock and V. Boekelheide, *J, Am. Chem. Soc.*, **75**, 2546 (1953).

[14] This broadened resonance pattern is attributable to spin coupling of the β-proton with the allylic X protons.

[15] The vinyl proton coupling constant of *cis*-cyclooctenes is known to lie in the region of 11.8–12.8 c.p.s.: see O. L. Chapman, *J. Am. Chem. Soc.*, **85**, 2014 (1963); G. V. Smith and H. Kriloff, *ibid.*, **85**, 2016 (1963).

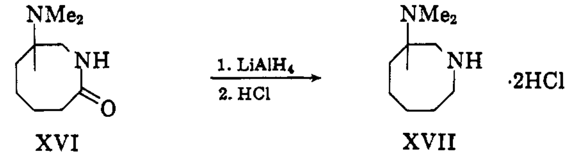
product of IV is indeed VI.[16] However, the possibility cannot be dispelled that absorption in an eight-numbered cyclic enamide such as V might be shifted down from 237 mμ (compound XII) enough to appear as end absorption in many spectrometers.

Further confirmatory evidence in favor of VI was derived from a study of the Hofmann elimination of the monocyclic analog XV which produced exclusively the α,β-unsaturated amide X. The structure of X was confirmed by its independent synthesis from acrylyl chloride and β-dimethylaminoethylamine and by conversion of both samples to identical crystalline methiodides.

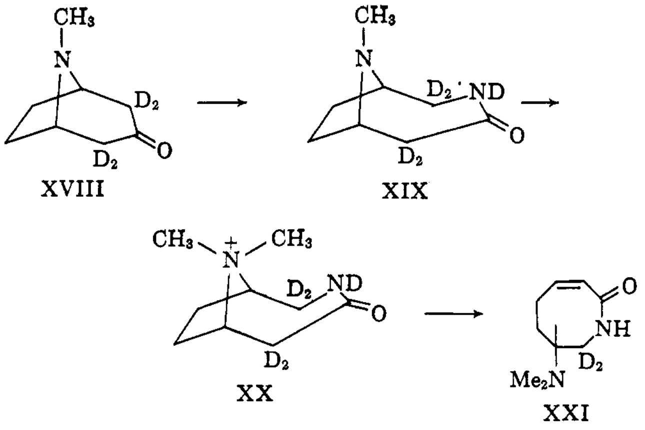


Finally, a strong and conclusive argument for VI was based on the deuterium content and n.m.r. spectrum of the product obtained from the deuterated substrate XX (see below).

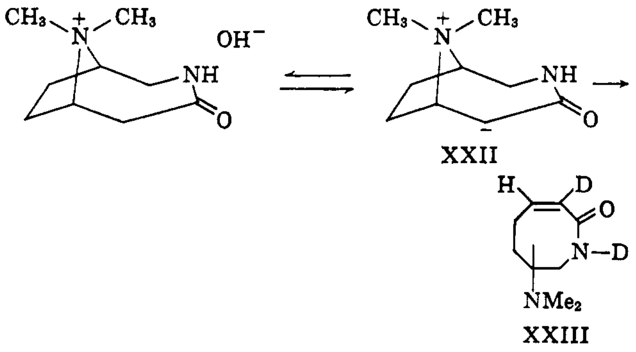
Catalytic hydrogenation of VI occurred with the absorption of 1 mole of hydrogen to yield XVI, characterized as its hydrochloride salt; lithium aluminum hydride reduction of XVI afforded the corresponding diamine isolated as its dihydrochloride salt XVII.



**Mechanism of the Reaction.**—In order to gain further insight into the nature of the olefinic product and, simultaneously, to determine which mechanism was operative, 9,9-dimethyl-4-oxo-3-aza-9-azoniabicyclo[4.2.1]nonane-2,5-$d_4$ iodide (XX) was synthesized. 2,2,4,4-Tetradeuteriotropinone (XVIII) was converted to the ring-enlarged amide XIX with sodium azide in sulfuric deuterioacid–chloroform. Addition of excess methyl iodide to XIX gave the deuterated methiodide XX, which was converted to its hydroxide and pyrolyzed as described earlier. The colorless oil (XXI) which was obtained was found to contain only 2.0 atoms of deuterium. Its n.m.r. spectrum displayed a vinyl proton resonance pattern (relative weight = 2H) superimposable on that of VI; the multiple resonance lines of the methylene group α to the amide nitrogen were totally absent. Complete exchange of hydrogen for deuterium had therefore occurred α to the carbonyl group, and *no* deuterium had become incorporated into the dimethylamino group.



In a further test of the reaction, the nondeuterated methiodide IV was converted to its hydroxide in the usual manner and the dry methohydroxide was equilibrated several times with deuterium oxide at 100° prior to pyrolysis. The colorless oil XXIII obtained in this run was found to contain 2.18 atoms of deuterium. This material gave an n.m.r. spectrum in which the vinyl proton region (relative weight = 1H) was extensively modified and in which the resonance pattern of the methylene group α to the amide nitrogen was retained. The excess 0.18 atom of deuterium was found by integration of the n.m.r. spectrum to reside in the dimethylamino group, a phenomenon readily explained by the known ease of exchange of methyl groups on quaternized nitrogen with active deuterated substrates.



These data are congruent with the E1cb mechanism in which the conjugate acid and conjugate base (XXII) are in equilibrium and in which such reversible proton abstraction is *probably* followed by a unimolecular decomposition of the carbanion to form olefin.[18]

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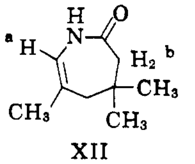
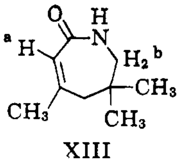
[16] An effort was made to utilize proton n.m.r. chemical shifts as a means of differentiating between V and VI, but the results did not permit a conclusive structural assignment. Thus, vinyl proton a in XII was seen at δ 5.86, while the similarly labeled olefinic hydrogen in XIII was located at δ 5.78.[17] The analogous vinyl proton of VI resonated at δ 5.70. Furthermore, while the methylene group b of XII was displayed at δ 2.92, that of XIII was centered at 2.99 and that of VI at 3.43.



XII



XIII

[17] The authors are indebted to Dr. Robert H. Mazur of the G. D. Searle Co. for providing them with the n.m.r. spectra of XII and XIII.

[18] R. Breslow [*Tetrahedron Letters*, 399 (1964)] has recently elucidated the point that the demonstration of reversible carbanion formation under elimination conditions does not permit a differentiation between an E2 or E1cb process. What we wish to imply in the present instance is that, since a high equilibrium concentration of carbanion can be anticipated especially at the temperature (150–160°) required for elimination, the E1cb mechanism appears the most probable reaction course. In any event, the *cis*-ylide mechanism is definitely removed from consideration.

## Experimental[19]

**9,9-Dimethyl-4-oxo-3-aza-9-azoniabicyclo[4.2.1]nonane Iodide (IV).**—A solution of 30.3 g. (0.196 mole) of III[12] and 85.4 g. (0.6 mole) of methyl iodide in 250 ml. of absolute ethanol was refluxed for 1.5 hr. and cooled. The precipitated solid was filtered and dried to give 57.5 g. (99.1%) of tan solid, m.p. 306° dec. Recrystallization of a sample of this material from aqueous ethanol–ether gave pure IV as small white prisms, m.p. 306° dec., $\nu^{\text{Nujol}}$ 3270 (N-H) and 1650 cm.$^{-1}$ (amide carbonyl).

*Anal.* Calcd. for $C_9H_{17}IN_2O$: C, 36.50; H, 5.79; N, 9.46. Found: C, 36.94; H, 5.89; N, 9.10.

**7-Dimethylamino-5,6,7,8-tetrahydro-2(1H)-azocinone (VI).**—A solution of 29.6 g. (0.10 mole) of IV in water was passed through a column of Amberlite IRA-400 in its hydroxide form. Two liters of eluate were collected and concentrated. The residue was heated *in vacuo* (elimination of water began at approximately 150°) and gave rise to 14.35 g. (85.5%) of a viscous colorless distillate, b.p. 143–144° (0.1 mm.). A center fraction was submitted for analysis.

*Anal.* Calcd. for $C_9H_{16}NO$: C, 64.25; H, 9.59; N, 16.65. Found: C, 64.56; H, 9.98; N, 15.95.

The **methiodide of VI** was obtained in quantitative yield when a solution of VI was refluxed with excess methyl iodide in methanol for 2 hr., giving white solid, m.p. 192–194° (from 95% ethanol). This material invariably yellowed extensively when warmed in 95% ethanol solution.

*Anal.* Calcd. for $C_{10}H_{19}IN_2O$: C, 38.72; H, 6.17; N, 9.03. Found: C, 38.53; H, 6.39; N, 8.77.

**1-Methyl-5-homopiperazinone Methiodide (XV).**—1-Methyl-5-homopiperazinone[20] was converted to its methiodide in 97% average yield by adding excess methyl iodide to an ethanol solution of the base at room temperature and allowing the mixture to stand for 24 hr. Pure XV was obtained by recrystallization from aqueous ethanol, m.p. 236.5–237.5°.

*Anal.* Calcd. for $C_7H_{15}IN_2O$: C, 31.12; H, 5.60; N, 10.37. Found: C 31.39; H, 5.77; N, 10.30.

**N-(2-Dimethylaminoethyl)acrylamide (X). A. Hofmann Elimination of XV.**—A 13.5-g. (0.05-mole) sample of XV in aqueous solution was eluted through a column of Amberlite IRA-400 (basic form). The eluate was collected until no longer basic. The water was evaporated and the residue was pyrolyzed to give 5.4 g. (76.2%) of pale yellow liquid, b.p. 99–100° (0.05 mm.), $n^{23}\text{D}$ 1.4835. Redistillation of this material gave an analytical sample, b.p. 97° (0.3 mm.), $n^{24}\text{D}$ 1.4818.

*Anal.* Calcd. for $C_7H_{14}N_2O$: C, 59.12; H, 9.92; N, 19.70. Found: C, 59.12; H, 10.03; N, 19.79.

A small quantity of this base was converted to its methiodide, white prisms from ethanol–ether, m.p. 127°.

*Anal.* Calcd. for $C_8H_{17}IN_2O$: C, 33.81; H, 6.03; N, 9.86. Found: C, 34.02; H, 6.02; N, 9.65.

**B. From Acrylyl Chloride.**—To a stirred solution of 79.4 g. (0.90 mole) of N,N-dimethylaminoethylamine in 600 ml. of chloroform cooled in an ice bath was added dropwise a solution of 78 g. (0.86 mole) of acrylyl chloride (from glacial acrylic acid and phosphorus trichloride) in 150 ml. of the same solvent at such a rate that the temperature did not exceed 30°. After the addition was completed, the mixture was stirred at room temperature for 4 hr. and treated with an aqueous solution of excess potassium carbonate. The organic layer was separated, dried, and distilled to give 69.0 g. (56.5%) of colorless liquid, b.p. 90–92° (0.1 mm.), $n^{27.5}\text{D}$ 1.4820, identical with the product of part A (infrared, ultraviolet, and n.m.r.).

This base furnished a methiodide, m.p. 126°, also identical with the methiodide of part A.

**7-Dimethylamino-3,4,5,6,7,8-hexahydro-2(1H)-azocinone Hydrochloride (XVI).**—A solution of 16.8 g. (0.10 mole) of VI in 150 ml. of ethyl acetate containing 500 mg. of 10% palladium on charcoal was hydrogenated in a Parr apparatus. The contents were warmed to 60° during 1 hr. and allowed to cool; the absorption of hydrogen ceased after the consumption of 1 mole. The catalyst was separated by filtration and the filtrate was evaporated *in vacuo* to give 16.8 g. (100%) of a colorless viscous oil which was directly converted to its hydrochloride with ethereal hydrogen chloride, m.p. 190.5° (from ethanol–ether), $\nu^{\text{Nujol}}$ 3260 (N-H) and 1650 cm.$^{-1}$ (amide carbonyl).

*Anal.* Calcd. for $C_9H_{19}ClN_2O$: C, 52.59; H, 9.26; N, 13.55. Found: C, 52.03; H, 9.32; N, 13.43.

**3-Dimethylaminooctahydroazocine Dihydrochloride (XVII).**—To a stirred slurry of 3.8 g. (0.10 mole) of lithium aluminum hydride in 75 ml. of ether was added dropwise a solution of 9.3 g. (0.054 mole) of XVI in 65 ml. of ether at such a rate to maintain gentle reflux. When the addition was completed, the stirred mixture was refluxed for 1 hr. and the product was isolated after an alkaline work-up. There was obtained 7.2 g. (86.8%) of colorless liquid, b.p. 98–100° (11 mm.), $n^{25}\text{D}$ 1.4838. A portion of this material was converted to its dihydrochloride, white platelets from ethanol–ether, m.p. 212–213°.

*Anal.* Calcd. for $C_9H_{22}Cl_2N_2$: C, 47.16; H, 9.68; N, 12.22. Found: C, 47.42; H, 9.71; N, 12.24.

**2,2,5,5-Tetradeuterio-9-methyl-3,9-diazabicyclo[3.2.1]nonan-4-one (XIX).**—A solution of 5.2 g. (0.0364 mole) of 2,2,4,4-tetradeuteriotropinone[21] in 50 ml. of chloroform, cooled to −5° in an ice–salt mixture, was treated dropwise with 9 g. of 98% dideuteriosulfuric acid, keeping the temperature below 15°. Sodium azide (4.3 g., 0.0662 mole) was added in small portions over a 1-hr. period below 35°. The reaction mixture was stirred for an additional 2 hr. at 50°. The mixture was poured into 60 g. of deuterium oxide externally cooled in ice and was neutralized portionwise with solid potassium carbonate. The mixture was made strongly alkaline by the addition of 10 g. of solid potassium hydroxide. The alkaline solution was filtered to remove inorganic salts, and the filtrate was extracted with chloroform. The combined organic layers were dried, filtered, and evaporated to yield 5.02 g. (89.4%) of white crystals, m.p. 84–85°.

**9,9-Dimethyl-4-oxo-3-aza-9-azoniabicyclo[4.2.1]nonane-2,5-*d*$_4$ Iodide (XX).**—To 20 ml. of iodomethane cooled in an ice bath was added 5.02 g. (0.0325 mole) of III. After the initial evolution of heat had subsided, the solution was treated with an additional 20 ml. of iodomethane and the mixture was allowed to stand overnight at room temperature. Filtration of the methiodide gave 8.3 g. (87%) of white crystals, m.p. 294–295° dec. Recrystallization from aqueous ethanol gave pure white crystals, m.p. 306° dec.

*Anal.* Calcd. for $C_9H_{13}D_4IN_2O$: 23.5 atom % excess D. Found: 22.4 atom % excess D (94.5% tetradeuteration).

**Hofmann Elimination of XX.**—A solution of 8.3 g. (0.028 mole) of XX in water was passed through Amberlite IRA-400 in its basic form. The aqueous eluate (125 ml.) was collected and concentrated. The residue was pyrolyzed (elimination beginning at about 160°) to give 1.5 g. (35%) of clear viscous liquid, b.p. 170–172° (1.5 mm.). Redistillation of this material gave the analytical sample.

*Anal.* Calcd. for $C_9H_{14}D_2N_2O$: 12.5 atom % excess D. Found: 12.55 atom % excess D (100% dideuterated).

**Preparation of XXIII.**—A solution of 5.0 g. of IV in water was eluted through a column of Amberlite IRA-400 in its basic form. The 175 ml. of solution which was collected was evaporated to dryness under vacuum at 50° to yield a white powder. The methohydroxide was dissolved in 10 ml. of deuterium oxide and the aqueous solution was heated for 1 hr. on a steam bath. The solution was evaporated to dryness at 50°, and the deuterium exchange was repeated under identical conditions. The residue was pyrolyzed (elimination beginning at 150–160°) to give 1.4 g. of viscous, pale yellow liquid, b.p. 133–135° (0.1 mm.). Redistillation gave the analytical sample, b.p. 133° (0.1 mm.).

*Anal.* Calcd. for $C_9H_{14}D_2N_2O$: 12.50 atoms % excess D. Found: 13.60 atom % excess D (2.18 D).

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[19] The melting points and boiling points are uncorrected. Magnesium sulfate was employed throughout as the drying agent. The n.m.r. spectra were determined at 60 Mc. with a Varian Model A-60 spectrometer. The microanalyses were performed by the Physical and Analytical Chemistry Department of The Upjohn Co. and by the Scandinavian Microanalytical Laboratory. Deuterium analyses by combustion were determined by Mr. Josef Nemeth, Urbana, Ill.

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[21] G. L. Closs, *J. Am. Chem. Soc.*, **81**, 5456 (1959).