Anal. Calcd. for $C_{27}H_{44}O_2$: C, 80.94; H, 11.07. Found: C, 80.87; H, 11.12.

Dehydration with Phosphorus Pentoxide.—A mixture of 148 mg. of the hydroxy acid, 0.70 g. of phosphorus pentoxide, and 35 ml. of anhydrous decalin was boiled under reflux for 1.5 hr. The liquid was then decanted from solid material, concentrated to a small volume under reduced pressure, and diluted with moist ether. The ether solution was extracted with four 25-ml. portions of 0.2 *N* potassium hydroxide, concentrated to 50 ml., and extracted twice more with 10-ml. portions of the potassium hydroxide solution. The alkaline extracts and the flocculent material from the interface were combined, acidified with dilute hydrochloric acid, and the resulting mixture was extracted with 70 ml. of ether. The ether extract was dried and evaporated to give 91 mg. of a semisolid residue, which was dissolved in a benzene–petroleum ether mixture (1 part to 2 parts). This solution was then chromatographed on a column of 5 g. of silica gel and 5 g. of Supercel. Elution with benzene gave 25 mg. of an oil. Elution with more polar solvents (finally 0.3% acetic acid in methanol) gave 62 mg. (68%) of crystalline unsaturated acid, m.p. 197–207°. Three recrystallizations from ether–petroleum ether gave needles, m.p. 217–218.5°, m.m.p. with the material obtained by pyrolysis, 218–219°.

The methyl ester was prepared by treatment of the acid with diazomethane in ether as described above, and had, after three recrystallizations from methanol, m.p. 85.5–87°, $[\alpha]_D$ +49° (1.1% in $CHCl_3$), λ_{max}^{KBr} 5.84, 6.24 μ, λ_{max}^{MeOH} 227 mμ (log ϵ 4.01).

Anal. Calcd. for $C_{28}H_{46}O_2$: C, 81.10; H, 11.18. Found: C, 80.87; H, 11.05.

A solution of 25 mg. of the methyl ester and 1 g. of sodium hydroxide in 50 ml. of methanol was allowed to stand at room temperature for 40 hr., and then was acidified with dilute hydrochloric acid and extracted with ether. The ether extract was dried, the ether was evaporated and the residue was triturated with petroleum ether to give 9 mg., m.p. 215.5–217°. One recrystallization from ether–petroleum ether gave 6 mg., m.p. 217–218°, m.m.p. with the unsaturated acid described above, 218–219°.

A-Norcholestan-2-one (V).—A solution of 34 mg. (0.081 mmole) of A-norcholestan-2-ol-2-carboxylic acid (m.p. 257–257.5°) and 102 mg. of lead tetraacetate in 17 ml. of acetic acid was allowed to stand at room temperature in a sealed tube for 40 hr. The contents of the tube were added to 20 ml. of water and the mixture was extracted with one 20-ml. and two 15-ml. portions of ether. The ether extract was washed once with 10 ml. of water, four times with 15-ml. portions of half-saturated potassium bicarbonate solution, and once with water, and then was dried over anhydrous sodium sulfate. The ether was evaporated to give 29 mg. (97%) of A-norcholestan-2-one, m.p. 97–98°, $[\alpha]_D$ +135° (0.8% in $CHCl_3$). One half of the product was recrystallized from alcohol and water to give 11 mg., m.p. 102–102.5°, m.m.p. with an authentic sample (m.p. 99–99.5°) 102–102.5°.

The second half was converted to the oxime, 15 mg., m.p. 194–196°, after recrystallization from alcohol and water 9 mg., m.p. 203.5–205°, m.m.p. with an authentic sample (m.p. 201–202°) 203.5–205.5°.

Attempted Decarboxylation of Δ^1- or Δ^2-Cholesten-2-carboxylic Acid. (a) With Cupric Oxide.—A mixture of 70 mg. of the unsaturated acid, 40 mg. of cupric oxide (wire), and 10 ml. of quinoline was heated at 230° for 3 hr. under a nitrogen atmosphere. The liquid was decanted from the cupric oxide and 50 ml. of ether was added. This solution was washed well with dilute hydrochloric acid and with water, the ether solution was then dried, and evaporated to give 50 mg. of a brown oil. The oil was dissolved in benzene–petroleum ether and chromatographed on 3 g. of alumina. None of the seven fractions could be obtained crystalline and the largest fraction had $\lambda_{max}^{CHCl_3}$ 2.90, 5.81, and 6.32 μ.

(b) By Distillation of the Barium Salt.—A solution of 300 mg. of the unsaturated acid in 2 ml. of ether was mixed with a solution of 130 mg. of barium hydroxide in 2 ml. of water. The ether was evaporated, the water was decanted from the precipitate, and the solid was washed with 1 ml. of water and with 1 ml. of ether, and dried. It did not melt below 340°. The salt was then heated in a small distillation flask at 340–360° (16 mm.) and 75 mg. of oily material distilled, which could not be obtained crystalline and had $\lambda_{max}^{CHCl_3}$ 2.80, 5.75, 5.88 (sh.), and 6.16 μ.

Unsaturated Amines. XVII. Preparation of Enamines by a Reductive Process[1–3]

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Hydrolytically stable enamines can be isolated from the lithium-*n*-propylamine reduction of aromatic amines. The synthesis is illustrated in the preparation of Δ^5-tetrahydrojulolidine (II) from julolidine (I) and 1-methyl-Δ^8-(V) and 1-methyl-Δ^9-octahydroquinoline (IV) from 1-methyltetrahydroquinoline (III). These enamines—*i.e.*, II and IV—undergo N- rather than C-methylation, and physical and chemical proof is provided for the structures of the corresponding methiodides and methoperchlorates (X and IX).

The reductive route to enamines from compounds of the tetrahydroquinoline type offers the possible advantage of avoiding the attendant hydroxylation in the oxidative route from decahydroquinoline types.[4–6] We therefore turned to the lithium–primary amine reducing system, which has been found capable of producing enamine *intermediates* during reduction of aromatic amines.[7,8] Enamine

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[1] For article XVI in this series, see N. J. Leonard and W. K. Musker, *J. Am. Chem. Soc.*, **82**, 5148 (1960).

[2] This investigation was supported by a research grant (USPHS-RG5829) from the National Institutes of Health, U. S. Public Health Service.

[3] Presented at the Seventeenth National Organic Chemistry Symposium of the American Chemical Society, June, 1961, Bloomington, Indiana.

[4] N. J. Leonard, L. A. Miller, and P. D. Thomas, *J. Am. Chem. Soc.*, **78**, 3463 (1956).

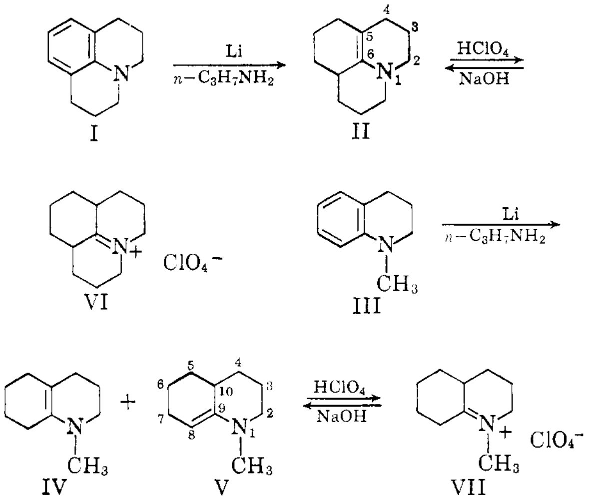
[5] P. D. Thomas, Ph.D. thesis, University of Illinois, 1954.

[6] F. Bohlmann and C. Arndt, *Ber.*, **91**, 2167 (1958).

[7] R. A. Benkeser, R. F. Lambert, P. W. Ryan, and D. G. Stoffey, *J. Am. Chem. Soc.*, **80**, 6573 (1958).

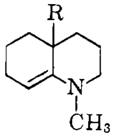
[8] R. A. Benkeser, J. J. Hazdra, R. F. Lambert, and P. W. Ryan, *J. Org. Chem.*, **24**, 854 (1959).

intermediates have also been detected in metal–ammonia reducing systems.[9-11] We considered that the method could be of preparative value if the enamine grouping being produced were contained in a bicyclic or tricyclic system and accordingly were resistant to hydrolysis. Our examples illustrate this point and suggest generality. We have found that Δ^5-tetrahydrojulolidine (II) can be prepared from julolidine (I) (66% yield) and that a mixture of the enamines, 1-methyl-Δ^8-octahydroquinoline (V) and 1-methyl-Δ^9-octahydroquinoline (IV), is obtained from 1-methyltetrahydroquinoline (III) (87% yield) by lithium-*n*-propylamine reduction.

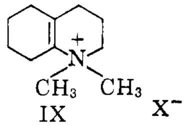


In the case of the reduction of 1-methyl-1,2,3,4-tetrahydroquinoline (III), our findings are at variance with the conclusions of Gray and Heitmeier,[12] who decided that there was not very much enamine in the product of the lithium-*n*-propylamine reduction of III on the basis of the absence of absorption ascribable to the iminium ($\rangle C{=}\overset{+}{N}\langle$) group in the infrared spectrum of the methiodide. The infrared spectrum of the methiodide salt, as employed by Gray and Heitmeier, is not a diagnostic test for the presence of enamine.[4,13-15] We have obtained clear evidence that the product of the reduction of 1-methyl-1,2,3,4-tetrahydroquinoline (III) is a mixture of the two enamine isomers 1-methyl-Δ^8-octahydroquinoline (V) and 1-methyl-Δ^9-octahydroquinoline (IV). The infrared spectrum of the reduction product shows absorption maxima at 1663 cm.$^{-1}$ and 1642 cm.$^{-1}$ which indicate the presence of two enamines,[16] with the compound corresponding to the former in greater amount. Acidification with perchloric acid produced a single perchlorate salt (VII), which exhibited strong infrared absorption at 1668 cm.$^{-1}$ ($\rangle C{=}\overset{+}{N}\langle$).[13] When the perchlorate was reconverted to the free base, the n.m.r. and infrared spectra were identical with those for the original mixture of enamines. The perchlorate was readily converted to 9-cyano-1-methyldecahydroquinoline upon treatment with aqueous potassium cyanide, confirming the presence of the iminium structure.[4,17] Another confirmation of the enamine structures in the mixture, IV and V, was the reducibility of the mixture, with formic acid, to a mixture of *cis* and *trans* isomers of 1-methyldecahydroquinoline.[18]

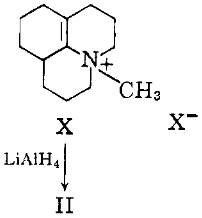
In order to decide which enamine, IV or V, exhibits the 1663-cm.$^{-1}$ infrared maximum and which the 1642-cm.$^{-1}$ maximum, model compounds were compared: 10-hydroxy-1-methyl-Δ^8-octahydroquinoline (VIIIa), ν_{max} 1643 cm.$^{-1}$,[4] and



VIIIa. R = OH
b. R = C_6H_5



IX



X

1-methyl-10-phenyl-Δ^8-octahydroquinoline (VIIIb), ν_{max} 1638 cm.$^{-1}$.[19] The iminium salts corresponding to these enamines absorb at 1668 and 1671 cm.$^{-1}$, respectively. Thus, the absorption at 1642 cm.$^{-1}$ in the mixture of IV and V is by analogy contributed by 1-methyl-Δ^8-octahydroquinoline (V) and that at 1663 cm.$^{-1}$, by 1-methyl-Δ^9-octahydroquinoline (IV). Parcell has reported the same enamine mixture (IV and V) to result from the treatment with base of the iminium bromide formed by the reaction of 3-bromopropylmethylamine hydrobromide and 1-*N*-piperidylcyclohexene.[20] The ratio of the 1-methyl-(Δ^8 and Δ^9)-octahydroquinoline isomers was determined by integration of the n.m.r. spectrum of the mixture by two methods: (1) integration of the area under the *N*-methyl signals at τ values[21] (neat) of 7.53 (Δ^9-isomer) and 7.56 (Δ^8-isomer); (2) integration of the olefinic proton signal of V at τ =

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(9) A. J. Birch, *J. Chem. Soc.*, 593 (1946).

(10) G. Stork and W. N. White, *J. Am. Chem. Soc.*, **78**, 4604 (1956).

(11) B. B. Millward, *J. Chem. Soc.*, 26 (1960).

(12) A. P. Gray and D. E. Heitmeier, *J. Am. Chem. Soc.*, **80**, 6274 (1958).

(13) N. J. Leonard and V. W. Gash, *ibid.*, **76**, 2781 (1954).

(14) N. J. Leonard, A. S. Hay, R. W. Fulmer, and V. W. Gash, *ibid.*, **77**, 439 (1955).

(15) G. Stork, R. Terrell, and J. Szmuszkovicz, *ibid.*, **76**, 2029 (1954).

(16) R. Lukeš, V. Dědek, and L. Novotný, *Collection Czech. Chem. Commun.*, **24**, 1117 (1959).

(17) N. J. Leonard and A. S. Hay, *J. Am. Chem. Soc.*, **78**, 1984 (1956).

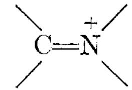
(18) N. J. Leonard and R. R. Sauers, *ibid.*, **79**, 6210 (1957).

(19) C. F. Koelsch and D. L. Ostercamp, *J. Org. Chem.*, **26**, 1104 (1961).

(20) R. F. Parcell, *J. Am. Chem. Soc.*, **81**, 2596 (1959).

(21) G. V. D. Tiers, "Table of τ Values for a Variety of Organic Compounds," Minnesota Mining and Manufacturing Company, St. Paul, Minnesota, 1958; G. V. D. Tiers, *J. Phys. Chem.*, **62**, 1151 (1958).

5.62[22] and comparison with either the total methyl signal or the total signal from the methylene protons α to the nitrogen at $\tau = 7.24$. By these methods it was determined that there is 22 ± 2% of 1-methyl-Δ^8-octahydroquinoline (V) in the usual mixture, from which it might be argued, if the rate of basification of VII were slow enough to allow for equilibration between IV and V *via* the salt VII during the process, that compound IV is the more stable by roughly 0.7 kcal./mole (ΔF°_{25}).

Returning to the problem of the methiodide, $C_{11}H_{20}IN$, obtained from the enamine mixture (IV and V), the possibility of C- or N-alkylation existed.[14, 23–25] The methiodide that was isolated in pure form, m.p. 215.5–216°, absorbed in neither the 1600–1700 nor the 3100–4000-cm.$^{-1}$ region of the infrared. This was true also of the methoperchlorate, m.p. 185°, obtained by treatment of the methiodide with silver perchlorate in acetone. The lack of strong absorption in the 6 μ region ruled against C-methylation, which would have been accompanied by generation of the  function, and was suggestive of an N-methylated product, since other α,β-unsaturated quaternary ammonium salts have been reported as lacking 6 μ absorption.[14,24] The possibility that the methoperchlorate (or methiodide) was dimeric was eliminated on the basis of the apparent molecular weight of the perchlorate salt in water. Positive proof of N-methylation was obtained from the n.m.r. spectrum of the methoperchlorate, which exhibited no proton signal corresponding to $C—C\underline{H}_3$ but instead showed a six-proton singlet at $\tau = 6.77$ ($CDCl_3$) indicative of two $N^+—C\underline{H}_3$ groups in the molecule. 1,1-Dimethylpyrrolidinium perchlorate, as a model, had a proton signal for $N^+—C\underline{H}_3$ at $\tau = 6.85$ (liquid SO_2).[26] Moreover, the N-methoperchlorate which had been isolated could be assigned the structure 1,1-dimethyl-Δ^9-octahydroquinolinium perchlorate (IX. $X^- = ClO_4^-$), since no proton signal below $\tau = 6.35$, corresponding to a vinyl proton in the alternative Δ^8-structure, was observed. Any Δ^8-isomer was probably removed during purification of the salts. Compound IX did not decolorize bromine in chloroform, gave no yellow color with tetranitromethane, but did decolorize neutral permanganate (1,1-dimethylpyrrolidinium perchlorate did not). The double bond in IX was detectable by ultraviolet.[27–29] It showed significant absorption near 200 mμ ($\lambda_\epsilon^{H_2O}{}_{1000}$ 207.7 mμ, $\epsilon_\lambda^{H_2O}{}_{200\ m\mu}$ 4.2×10^3) whereas the saturated quaternary ammonium salt 1,1-dimethylpyrrolidinium perchlorate showed no appreciable absorption in the ultraviolet above 190 mμ.

The reduction of julolidine (I) by lithium and *n*-propylamine yielded Δ^5-tetrahydrojulolidine (II), ν_{max} 1655 cm.$^{-1}$, as the major product, together with hexahydrojulolidine. Acidification of II with perchloric acid gave the known iminium salt, $\Delta^{1(6)}$-tetrahydrojulolidinium perchlorate (VI), ν_{max} 1680 cm.$^{-1}$. Treatment of II with methyl iodide produced 1-methyl-Δ^5-tetrahydrojulolidinium iodide (X, $X^- = I^-$) $C_{13}H_{22}IN$, the structure of which was established as follows. Neither the methiodide nor the corresponding methoperchlorate derived from it showed infrared absorption in the 1600–1700-cm.$^{-1}$ region[14,24]; hence these could not be C-methylated salts. The singlet n.m.r. signal at $\tau = 6.69$ (CH_2Cl_2) was indicative of $N^+—C\underline{H}_3$ protons, and this group could be removed by treatment of the methiodide with lithium aluminum hydride in tetrahydrofuran,[30,31] resulting in the regeneration of the original tetrahydrojulolidine (II). The presence of the double bond in the methoperchlorate (X, $X^- = ClO_4^-$) was confirmed by the ultraviolet absorption spectrum,[27–29] showing $\lambda_\epsilon^{H_2O}{}_{1000}$ 213.8 mμ and $\epsilon_{200\ m\mu}^{H_2O}$ 7.2×10^3. The compound was resistant to hydrogenation at low pressures using platinum oxide as a catalyst and at high pressures using Raney nickel or rhodium-on-alumina. Opitz *et al.* have noted a similar resistance to hydrogenation of some α,β-unsaturated quaternary ammonium compounds.[24]

In summary, the chemistry here described provides an efficient route to cyclic enamines and to certain ene-quaternary-ammonium salts.

Experimental[32]

Reduction of 1-Methyltetrahydroquinoline (III).—A slight modification of the method of Gray and Heitmeier[12] was used. A mixture of 21.3 g. (0.145 mole) of 1-methyl-1,2,3,4-tetrahydroquinoline,[33] 415 ml. of *n*-propylamine and 10.15 g. (1.45 g.-atoms) of chopped lithium wire was

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[22] For reference, the single proton on the enamine double bond in the model compound 1-*N*-pyrrolidylcyclohexane shows resonance at $\tau = 5.87$.

[23] R. Lukeš and V. Dědek, *Collection Czech. Chem. Commun.*, **23**, 2046 (1958).

[24] G. Opitz and H. Mildenberger, *Ann.*, **649**, 26 (1961); G. Opitz, H. Mildenberger, and H. Suhr, *ibid.*, **649**, 47 (1961).

[25] G. Stork, Abstracts of the Sixteenth National Organic Chemistry Symposium of the American Chemical Society, June, 1959, Seattle, Washington, p. 48.

[26] N. J. Leonard and K. Jann, *J. Am. Chem. Soc.*, in press.

[27] K. Stich, B. Rotzler, and T. Reichstein, *Helv. Chim. Acta*, **42**, 1480 (1959).

[28] D. W. Turner, *J. Chem. Soc.*, 30 (1959).

[29] P. S. Ellington and G. D. Meakins, *ibid.*, 697 (1960).

[30] A. C. Cope, E. Ciganek, L. J. Fleckenstein, and M. A. P. Meisinger, *J. Am. Chem. Soc.*, **82**, 4651 (1960).

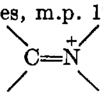
[31] G. W. Kenner and M. A. Murray, *J. Chem. Soc.*, 406 (1950).

[32] Infrared spectra were determined using a Perkin-Elmer automatic recording infrared spectrophotometer, Model 21, except as noted. We are indebted to Mr. Josef Nemeth and his associates for microanalyses. The ultraviolet absorption spectra were determined using a Bausch and Lomb Spectronic 505 spectrophotometer. The n.m.r. spectra were obtained at 60 Mc. with a Varian Associates Model V-4300B spectrometer equipped with a superstabilizer or with a Varian Associates Model A-60 spectrometer. The chemical shifts were determined using tetramethylsilane as an internal standard ($\tau = 10$), obtaining side bands by the application of an audiofrequency signal from an external source. We wish to thank Mr. Oliver W. Norton and Mr. Dick H. Johnson for determining the n.m.r. spectra.

[33] A. N. Kost and L. C. Yodin, *Zh. Obshch. Khim.*, **26**, 1720 (1956).

stirred under nitrogen for 16.5 hr. Unchanged lithium was removed and excess propylamine was distilled from the flask. The semisolid residue was cooled in an ice bath, overlaid with ether and neutralized slowly with solid ammonium chloride. The mixture was diluted cautiously with water, the ether layer was separated, and the aqueous layer was extracted four times with ether. The ether extracts were combined, dried over magnesium sulfate, and the ether was evaporated. The residue was distilled through a Vigreux column, and the material boiling at 60–75°/1.5–1.7 mm. was collected, crude yield, 19.82 g. (90.5%). A sample of this material was gas-chromatographed at 147° on a 10-ft. silicone-on Fluoropak column. Integration of the areas under the peaks indicated that 96% of this sample was enamine. The impure base was redistilled through a modified Holzman column and the material boiling at 63–65°/1.5 mm. (17.3 g., 79% yield) was collected, n^{25}D 1.5138. The infrared spectrum (liquid film) determined on a Beckman IR-7 showed absorption at 1663 cm.$^{-1}$ and 1642 cm.$^{-1}$. The n.m.r. spectrum at 60 Mc. on the Varian A-60 showed peaks at τ = 7.56, 7.53, 7.24, 5.62, and an unresolved region from τ = 8.20 to 8.44; $\lambda_{\max}^{\text{ether}}$ 226 mμ (ϵ 6000)[34]; picrate, m.p. 128–129° (reported[12] 126–127°).

Anal. Calcd. for $C_{10}H_{17}N$: C, 79.40; H, 11.33; N, 9.26. Found: C, 79.27; H, 11.58; N, 9.40.

1-Methyl-$\Delta^{1(9)}$-octahydroquinolinium Perchlorate (VII).—To a solution of 16.6 g. (0.11 mole) of 1-methyloctahydroquinoline (IV and V) in anhydrous ether was added dropwise a 1:1 mixture of 70% perchloric acid and absolute ethanol until the ether solution was acid to Congo Red. The perchlorate salt was filtered, washed with ether, and recrystallized twice from ethanol, colorless needles, m.p. 196–197°, yield 22.3 g. (81%), $\nu_{\max}^{\text{Nujol}}$ 1668 cm.$^{-1}$ () (determined using a Beckmann IR-7 instrument); n.m.r. signal at τ value 6.39 ($CDCl_3$) for $N^+—C\underline{H}_3$.

Anal. Calcd. for $C_{10}H_{18}ClNO_4$: C, 47.80; H, 7.17; N, 5.57. Found: C, 47.62; H, 6.98; N, 5.72.

A sample of 2.62 g. (0.0104 mole) of 1-methyl-$\Delta^{1(9)}$-octahydroquinolinium perchlorate was treated with aqueous sodium hydroxide, and the solution was extracted with ether. After evaporation of the ether, 1.44 g. (92%) of enamine remained. The enamine was distilled, and the n.m.r. and infrared spectra were found to be identical to those of the enamine obtained from the reduction mixture (IV and V).

9-Cyano-1-methyldecahydroquinoline.—An aqueous solution of 5.00 g. (0.02 mole) of 1-methyl-$\Delta^{1(9)}$-octahydroquinolinium perchlorate was overlaid with ether, and to it was added 2.6 g. (0.04 mole) of potassium cyanide The mixture was shaken immediately in a separatory funnel, the ether layer separated, and the aqueous phase extracted twice more with ether. The ether extracts were combined, dried, and evaporated. The residue was distilled, b.p. 92–96°/2.2 mm., yield 2.98 g. (83%), n^{25}D 1.4912 constant. Upon standing in the refrigerator, the material solidified. The infrared spectrum showed the maximum at 2218 cm.$^{-1}$ characteristic of the cyano group.

Anal. Calcd. for $C_{11}H_{18}N_2$: C, 74.11; H, 10.18; N, 15.71. Found: C, 74.10; H, 9.95; N, 16.00.

Formic Acid Reduction of 1-Methyloctahydroquinoline (IV and V).—Addition of 0.1 g. (0.002 mole) of 98% formic acid to 0.46 g. (0.003 mole) of 1-methyloctahydroquinoline resulted in gas evolution. Additional formic acid was added until the reaction ceased. The solution was kept at 60–75° for 15 min. and then made basic with potassium hydroxide and extracted three times with ether. The ether extracts were dried, filtered, and the ether was evaporated. The residue was distilled and the infrared spectrum was compared with those of the *cis* and *trans* isomers of 1-methyldecahydroquinoline. Gas chromatography showed only two peaks, whose retention time corresponded to those of the separate authentic *cis* and *trans* isomers.

Anal. Calcd. for $C_{10}H_{19}N$: C, 78.36; H, 12.50; N, 9.14. Found: C, 77.95; H, 12.45; N, 9.06.

1,1-Dimethyloctahydroquinolinium Iodide.—To an ether solution of 10.0 g. (0.04 mole) of 1-methyloctahydroquinoline (IV and V) was added 4 ml. of methyl iodide, and the mixture was allowed to stand for 2 days protected from moisture. The yellowish precipitate was removed by filtration, m.p. 198–199°, yield 9.85 g. (84%). A portion was purified several times by precipitation from an ethanol solution with low boiling petroleum ether, colorless powder, m.p. 215.5–216° (reported[12] 200–201°), no infrared absorption in the 1600–1700 cm.$^{-1}$ region or in the 3100–4000 cm.$^{-1}$ region.

Anal. Calcd. for $C_{11}H_{20}IN$: C, 45.06; H, 6.88; N, 4.78. Found: C, 45.03; H, 6.97; N, 4.72.

1,1-Dimethyl-Δ^9-octahydroquinolinium Perchlorate (IX, X^- = ClO_4^-).—To an acetone solution of 7.25 g. (0.0245 mole) of 1,1-dimethyloctahydroquinolinium iodide was added an acetone solution of 5.1 g. (0.0246 mole) of silver perchlorate. The silver iodide was removed by filtration, and the filtrate was evaporated to dryness. The residue was recrystallized four times from ethanol, twice using Darco, yield 3.81 g. (58%) of very pure material, m.p. 185°; no infrared absorption (in either potassium bromide or Nujol mull) in the 1600–1700-cm.$^{-1}$ region or in the 3100–4000-cm.$^{-1}$ region; $\lambda_{\epsilon\,1000}^{H_2O}$ 207.7 mμ, $\epsilon_{\lambda\,200\,\text{m}\mu}^{H_2O}$ 4.2 × 10^3. The compound did not decolorize bromine in chloroform, and no yellow color was formed with tetranitromethane. However, it decolorized neutral potassium permanganate, forming a brown precipitate. The n.m.r. spectrum (CH_2Cl_2) showed peaks at τ = 6.35 (multiplet), 6.77 (singlet), and broad absorption near τ = 7.88 and 8.30 from the ring protons.

Anal. Calcd. for $C_{11}H_{20}ClNO_4$: C, 49.71; H, 7.58; N, 5.27. Found: C, 49.54; H, 7.66; N, 5.38.

A solution of 0.129 g. (0.487 mmole) of 1,1-dimethyl-Δ^9-octahydroquinolinium perchlorate in 5 ml. of deuterium oxide was lyophilized to dryness. Analysis of the residue showed no deuterium. The infrared spectrum was identical with that of the starting material.

The calculated molecular weight of the monomeric perchlorate salt is 265.74, and the apparent molecular weight assuming complete dissociation is 132.87 for the monomer and 177.16 for a dimer. The apparent molecular weight in water at a concentration of 4.6 mg./ml. was 124, as determined by means of a vapor pressure osmometer employing thermistors.[35,36] Sucrose and mannitol were used as calibration compounds.

Since the compound is related to neurine in structure, the acute toxicity was of interest and was determined for us at Eli Lilly and Company, Indianapolis, Indiana: LD_{50} = 27.02 ± 1.6 mg./kg. in fasted mice by intravenous route.

$\Delta^{1(6)}$-Tetrahydrojulolidinium Perchlorate (VI).—A mixture of 25.1 g. (0.145 mole) of julolidine dissolved in *n*-propylamine and 10.15 g. (1.45 g.-atoms) of ether-washed chopped lithium wire was diluted to 400 ml. with *n*-propylamine and stirred under nitrogen (Dry Ice condenser) for 12.5 hr. The reaction mixture was worked up as described above. The residue after evaporation of the ether extracts was distilled through a Vigreux column, yielding impure tetrahydrojulolidine (23.7 g., 92%). This crude material was gas-chromatographed on a 6-ft., ¼ in. o.d. column of 20% Carbowax 20-M on 80–100 mesh acid-washed Chromosorb which had been washed with methanolic potassium hydroxide. Integration of the areas under the curves showed that the enamine was present to the extent of

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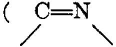
[34] N. J. Leonard and D. M. Locke, *J. Am. Chem. Soc.*, **77**, 437 (1955).

[35] J. J. Neumayer, *Anal. Chim. Acta*, **20**, 519 (1959).

[36] Mechrolab Inc., Vapor Pressure Osmometer Model 301 A.

72% and the hexahydrojulolidine to about 22%. None of the other peaks accounted for more than 2% of the total.

The crude bases from three batches were combined (69.8 g.) and redistilled through a Cason column. The fractions boiling at 83–85°/1.5–1.6 mm. were combined (44.5 g.) and converted to the perchlorate salt by adding a 1:1 mixture of ethanol and 70% perchloric acid to an ether solution of the bases. Recrystallization of the perchlorate twice from ethanol yielded 53.6 g. (44% on the basis of 75.3 g. of julolidine) of colorless needles that melted (>280°) with decomposition at a point which depended upon the rate of heating. The infrared spectrum was identical with that of an authentic sample kindly supplied by Prof. F. Bohlmann,[6] ν_{max}^{Nujol} 1680 cm.$^{-1}$ ().

Anal. Calcd. for $C_{12}H_{20}ClNO_4$: C, 51.89; H, 7.26; N, 5.04. Found: C, 52.07; H, 7.21; N, 4.92.

Pure tetrahydrojulolidinium perchlorate was converted to the free base in 83% yield, b.p. 62° (0.04 mm.), n^{25}D 1.5369, $\nu_{max}^{CCl_4}$ 1645 cm.$^{-1}$; ν_{max}^{film} 1655 cm.$^{-1}$.

Anal. Calcd. for $C_{12}H_{19}N$: C, 81.30; H, 10.80; N, 7.90. Found: C, 81.09; H, 11.00; N, 7.97.

1-Methyl-Δ^5-tetrahydrojulolidinium Iodide (X, $X^- = I^-$).—To a solution of 5.0 g. (0.0282 mole) of tetrahydrojulolidine in 25 ml. of acetone was added about 5.7 g. (0.0403 mole) of methyl iodide. After standing about 5 min., beautiful white needles formed. The crystals were removed by filtration and washed with a small amount of acetone and a small amount of ether, m.p. 221–222° dec., yield 7.42 g. (83%), no infrared absorption in the 1600–1700-cm.$^{-1}$ region. A small sample was recrystallized from acetone for analysis.

Anal. Calcd. for $C_{13}H_{22}IN$: C, 48.91; H, 6.95; N, 4.38. Found: C, 48.98; H, 6.95; N, 4.30.

1-Methyl-Δ^5-tetrahydrojulolidinium Perchlorate (X, $X^- = ClO_4^-$).—To a warm acetone solution of 2.0 g. (0.00627 mole) of tetrahydrojulolidinium iodide was added dropwise an acetone solution of silver perchlorate until no more precipitate was formed. The silver iodide was removed by filtration and the filtrate was evaporated to dryness, m.p. 138–140°, yield 1.34 g. (73%). The residue was recrystallized from isopropyl alcohol, irregular prisms, m.p. 140–140.5°. No infrared absorption was present in the 1600–1700-cm.$^{-1}$ region. The ultraviolet spectrum of 1-methyltetrahydrojulolidinium perchlorate was measured in water after a baseline using water in both sample and reference beams was determined in duplicate. The sample run at a concentration of 6.86 × 10^{-5} mole/l. was also made in duplicate. The instrument was calibrated using mercury lines and the corrections were applied to the wave length values. The following values are significant: $\lambda_{\epsilon\,1000}^{H_2O}$ 213.8 mμ; $\epsilon_{\lambda\,200\ m\mu}^{H_2O}$ 7.2 × 10^3. 1,1-Dimethylpyrrolidinium perchlorate served as a saturated model. A solution in water at 6.52 × 10^{-5} mole/l. showed no appreciable absorption in the ultraviolet down to 200 mμ. The calculated apparent molecular weight of the monomer is 145.88. The apparent molecular weight in water was determined as 137.[35,36] The n.m.r. spectrum in methylene chloride showed a singlet signal at τ = 6.69 for the N^+—$C\underline{H}_3$, complex absorption at τ = 6.34 and 6.39 for four ring protons next to nitrogen and broad signals at τ = 7.81 and 8.42 for other ring protons.

Anal. Calcd. for $C_{13}H_{22}ClNO_4$: C, 53.51; H, 7.60; N, 4.80. Found: C, 53.33; H, 7.52; N, 4.84.

The acute toxicity of this compound was found to be LD_{50} = 15.43 ± 0.95 mg./kg. in fasted mice by intravenous route. As in the case of 1,1-dimethyl-Δ^9-octahydroquinolinium perchlorate, mild tonic convulsions which lasted 5 min. were observed immediately after injection on all doses. Deaths were immediate.

Demethylation of 1-Methyl-Δ^5-tetrahydrojulolidinium Iodide.[30,31]—Anhydrous tetrahydrofuran (75 ml.) freshly distilled from lithium aluminum hydride was heated under reflux with 3.0 g. (0.0792 mole) of lithium aluminum hydride for 1 hr. Then 4.0 g. (0.0125 mole) of finely crystalline 1-methyltetrahydrojulolidinium iodide was added. Gas evolution ceased after 3 hr., when 77% of the theoretical amount of methane had been collected. The heating was stopped, and the mixture was stirred overnight. The reaction mixture was cautiously hydrolyzed with water and sodium hydroxide solution, and the solution was extracted with ether. The dried ether extracts were evaporated to leave 2.0 g. (90%) of crude tetrahydrojulolidine. A perchlorate salt had an infrared spectrum identical with that of tetrahydrojulolidinium perchlorate. The crude tetrahydrojulolidine was distilled (78°/0.3 mm.) and afforded 1.25 g. of pure tetrahydrojulolidine, the infrared spectrum of which was identical with that of tetrahydrojulolidine originally prepared.

Steric Effects in Methyl-substituted 1-Tetralones

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The combined effects of four methyl groups at positions 4, 5, 7, and 8 in the 1-tetralone moiety strongly inhibited addition of the Grignard reagent to the carbonyl group. This was in contrast to corresponding dimethyl- and trimethyl-1-tetralones, having two or three methyl groups at these positions, showing that the steric hindrance is not due to substitution at any one position. Molecular models indicate that the most favorable conformation of 4,5,7,8-tetramethyl-1-tetralone is with the 4-methyl group axial and the alicyclic ring in the boat form, causing considerable shielding of the carbonyl group by the 4-methyl group. The resulting lack of coplanarity of the carbonyl group with the aromatic ring was confirmed by ultraviolet spectral studies. This effect of 4,5-dimethyl crowding appears to be greater than the steric effect of a methyl group at position 2.

While preparing a series of polymethylnaphthalenes, we have had occasion to employ the reaction of methyl-substituted 1-tetralones with the methyl Grignard reagent, followed by dehydration and dehydrogenation of the tertiary alcohols. This generally good method was unsuccessful in one case, because of strikingly low reactivity of 4,5,7,8-tetramethyl-1-tetralone with the Grignard reagent.

Two of the ketones, 5,8-dimethyl-1-tetralone (I)[1] and 5,7,8-trimethyl-1-tetralone (II)[2] were

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[1] E. de B. Barnett and F. G. Sanders, *J. Chem. Soc.*, 434 (1933).

[2] W. Cocker, B. E. Cross, and J. McCormick, *ibid.*, 72 (1952).