[Contribution from the Noyes Chemical Laboratory, University of Illinois]

Unsaturated Amines. VI. Introduction of α,β-Unsaturation by Means of Mercuric Acetate: Bicyclic Tertiary Amines[1, 2]

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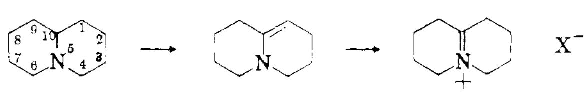
We have studied the mercuric acetate dehydrogenation of the representative bicyclic tertiary amines, octahydropyrrocoline, 1-azabicyclo[5.3.0]decane, 1-azabicyclo[5.4.0]hendecane, and 1-azabicyclo[5.5.0]dodecane, to supplement our study on quinolizidine. A double bond is introduced α,β to the nitrogen in each base, and the bridgehead location of the α,β-double bond has been fixed by following the fate of bridgehead-carbon asymmetry or on analogical grounds.

It has been shown that mercuric acetate introduces α,β-unsaturation into the bicyclic tertiary amine, quinolizidine (I), yielding $\Delta^{1(10)}$-dehydroquinolizidine (II), the salts of which are in the $\Delta^{5(10)}$-dehydroquinolizidinium form (III).[4] It was of considerable interest, in determining the scope of the mercuric acetate dehydrogenation reaction, to study the action of this oxidizing agent upon other representative bicyclic tertiary amines. Tertiary amines having two fused rings comprising combinations of five, six, and seven members were readily available by the general synthetic method provided earlier in this Laboratory.[5]



I II III

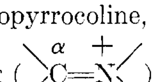
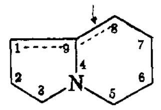
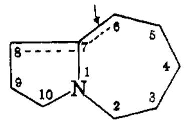
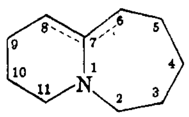
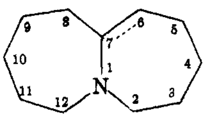
The dehydrogenation of octahydropyrrocoline (1-azabicyclo[4.3.0]nonane), $C_8H_{15}N$, with mercuric acetate in 5% aqueous acetic acid solution gave a hexahydropyrrocoline, $C_8H_{13}N$. That the double bond had entered the molecule α,β to the nitrogen was shown by the shift toward higher infrared frequency observed in going from the unsaturated amine to its perchlorate salt (Table I).[6] A shift of +44 cm.$^{-1}$ had been observed in a similar spectral comparison of $\Delta^{1(10)}$-dehydroquinolizidine with $\Delta^{5(10)}$-dehydroquinolizidinium perchlorate. Further evidence of the α,β-location of the double bond in the hexahydropyrrocoline, and of the ternary iminium grouping ( $\gt\overset{\alpha}{C}=\overset{+}{N}\lt$) in the perchlorate salt, was available from two sources. The perchlorate salt showed zero active hydrogen in the Zerewitinoff determination and was reducible by lithium aluminum hydride to octahydropyrrocoline.[4,7] The location of the α,β-double bond at the bridgehead carbon in hexahydropyrrocoline, which was suggested by analogy with the dehydrogenation of quinolizidine, was established by following the fate of asymmetry at the bridgehead carbon (C-9) during mercuric acetate treatment. A solution of levorotatory octahydropyrrocoline[8] in aqueous acetic acid containing excess mercuric acetate lost

TABLE I
Infrared Spectral Comparison of the Dehydroamines and Their Salts

Dehydro Base	Infrared Maxima, cm.$^{-1\,a}$ Base	Perchlorate	Perchlorate Active H (no.)
 IV	1672 ~1646	1689[b]	0.00
 V	1668	—[c]	—
 VI	1643	1680[b]	0.15
 VII	1638	1662[b]	0.32

[a] Base determined as the liquid, perchlorate salt as the mull. [b] Transparent in the region above 3000 cm.$^{-1}$ [c] Crude hydrochloride showed an absorption maximum at 1680 cm.$^{-1}$

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[3] Sinclair Refining Company Fellow in Organic Chemistry, 1953–1954. Part of this work was done under the sponsorship of the Sinclair Research Laboratories, Inc.

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

[5] N. L. Leonard and W. E. Goode, *J. Am. Chem. Soc.*, **72**, 5404 (1950).

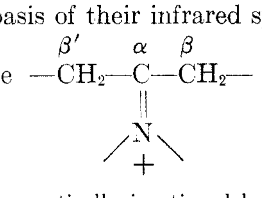
[6] N. J. Leonard and V. W. Gash, *J. Am. Chem. Soc.*, **76**, 2781 (1954).

[7] N. J. Leonard and A. S. Hay, *J. Am. Chem. Soc.*, in press (1956). Article V in this series.

[8] N. J. Leonard and W. J. Middleton, *J. Am. Chem. Soc.*, **74**, 5776 (1952).

its optical activity completely during the course of one hour's heating under reflux, whereas a control solution from which mercuric acetate was omitted retained its optical activity under the same conditions. The perchlorate of the $C_8H_{13}N$ base from levorotatory octahydropyrrocoline was identical with that of the hexahydropyrrocoline obtained by mercuric acetate dehydrogenation of racemic octahydropyrrocoline. Thus, the hydrogen on the asymmetric, bridgehead carbon of octahydropyrrocoline must have been removed by the mercuric acetate treatment, and the perchlorate salt must possess a a 4(9)-double bond ($\Delta^{4(9)}$-hexahydropyrrocolinium perchlorate).[9] The amine obtained *via* basification of either the crude reaction product or the pure perchlorate salt appeared to be a mixture, as judged by the infrared absorption in the 6μ region of the spectrum. From the mixture of $\Delta^{1(9)}$- and Δ^{8}-hexahydropyrrocolines (IV), in which the latter would be expected to predominate[10] (see Table I), the unique perchlorate was formed again.

Mercuric acetate dehydrogenation of 1 azabicyclo[5.3.0]decane, $C_9H_{17}N$, produced a dehydro base, $C_9H_{15}N$, which could not be converted to a stable salt. However, dry hydrogen chloride passed through an ethereal solution of the dehydro base gave colorless crystals, and the crude hydrochloride exhibited an infrared absorption maximum at 1680 cm.$^{-1}$. The shift toward higher frequency from the maximum observed for the dehydro base (Table I), together with the reducibility of the salt under Clemmensen conditions,[11,12] was indication of unsaturation α,β to the nitrogen in the base. By analogy with the dehydroquinolizidine and hexahydropyrrocoline examples, the $C_9H_{15}N$ product is logically a mixture of Δ^6- and Δ^7-dehydro amines (V, arrow indicates probable predominating isomer). The characteristic shift in infrared maxima—unsaturated amine to salt—and reasoning by analogy have been used to arrive at likely structural assignments for the dehydro-1-azabicyclo[5.4.0]-hendecane (VI) and the dehydro-1-azabicyclo-[5.5.0]dodecane (VII) obtained by mild mercuric acetate dehydrogenation of the corresponding saturated bases. Since the perchlorate salts of VI and VII, on the basis of their infrared spectra, are apparently in the



$\overset{\beta'}{\text{—CH}_2}\text{—}\underset{\overset{\|}{\diagup\overset{}{\underset{+}{N}}\diagdown}}{\overset{\alpha}{C}}\text{—}\overset{\beta}{\text{CH}_2}\text{—}$

form, the fraction of one active hydrogen found for each of these perchlorates (Table I) may be due to a competition by the Grignard anion between abstraction of the hydrogen from the β- (or β'-) carbon and nucleophilic attack at the α-carbon.[13]

The mechanism of the mercuric acetate dehydrogenation of the bicyclic bases here considered is regarded as similar to that postulated for the dehydrogenation of quinolizidine,[4] involving initial formation of a mercurated complex through the free pair of electrons on the nitrogen of the saturated tertiary amine, followed by proton removal from the tertiary carbon and a two-electron transfer to give transient Hg^0. (However, a one-electron transfer mechanism has not been excluded.) That the combination, $Hg^0 + Hg^{II} \rightarrow Hg^{I}\downarrow$, giving insoluble mercurous acetate could occur rapidly is further indicated by the recent work of Schwarzenbach and Anderegg.[14]

EXPERIMENTAL[15]

Mercuric acetate dehydrogenation. The mercuric acetate dehydrogenation of octahydropyrrocoline,[5] 1-azabicyclo-[5.3.0]decane,[16] 1-azabicyclo[5.4.0]hendecane,[5] and 1-azabicyclo[5.5.0]dodecane[6] was effected by the same method which had been used for the introduction of $\Delta^{1(10)}$-unsaturation into the quinolizidine nucleus.[4] The time of heating employed was one hour for the first three compounds, 3 hours for the last compound. The yields of dehydro bases were in the range 51–57% for the first three and about 10% for the last example. The properties of the dehydro bases are listed in Table II, along with those of their perchlorate salts. The colorless perchlorates were obtained by addition of perchloric acid to an ethanolic solution of the amine and were recrystallized from ethanol.

Mercuric acetate dehydrogenation of (−)-*octahydropyrrocoline.* Partially racemic (−)-octahydropyrrocoline,[8] $[\alpha]^{25}_{D}$ −1.09°, b.p. 52–53° (14 mm.), was used in both of the following experiments. One-half gram (4 millimoles) was dissolved in 5.0 ml. of 5% acetic acid (95% aqueous), and the solution was heated on the steam-bath one hour under nitrogen. The solution was cooled and the specific rotation was found to be $[\alpha]^{25}_{D}$ −1.00° (c, 10).

To another 0.5 g. of (−)-octahydropyrrocoline in 5 ml. of 5% acetic acid was added 5.1 g. (16 millimoles) of mercuric acetate, and the solution was heated on the steam-bath one hour under nitrogen. The mercurous acetate which separated was removed by filtration, 1.65 g. (80%). The filtrate showed no measurable rotation. Hydrogen sulfide was passed into the filtrate, and the precipitated mercuric sulfide was removed. The liquid was evaporated to small volume under reduced pressure, and the residue was made strongly alkaline with a 40% aqueous solution of potassium hydroxide. Ether extraction was followed by the usual drying and evaporating operations. Absolute ethanol (2 ml.)

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[9] Formation of an optically inactive dehydro product from an optically active precursor by mercuric acetate treatment enabled J. Gadamer (*Arch. Pharm.*, **253**, 274 (1915)) to assign the position of the double bond which was introduced into bulbocapnine methyl ether.

[10] H. C. Brown, J. H. Brewster, and H. Shechter, *J. Am. Chem. Soc.*, **76**, 467 (1954).

[11] M. Ōki, University of Illinois, private communication.

[12] N. J. Leonard, P. D. Thomas, and V. W. Gash, *J. Am. Chem. Soc.*, **77**, 1552 (1955).

[13] Ref. 12, footnote 26.

[14] G. Schwarzenbach and G. Anderegg, *Helv. Chim. Acta*, **37**, 1289 (1954).

[15] All melting points are corrected. The authors are indebted to Miss Elizabeth M. Petersen and Mr. James Brader for determination of the infrared absorption spectra and to Miss Emily Davis, Mrs. Jean Fortney, and Mrs. Katherine Pih for the microanalyses. Zerewitinoff active hydrogen determinations were performed by the Clark Microanalytical Laboratory, Urbana, Illinois.

[16] N. J. Leonard and W. C. Wildman, *J. Am. Chem. Soc.*, **71**, 3089 (1949).

TABLE II

DEHYDROAMINES AND THEIR PERCHLORATES

Dehydroamines	B.p. °C.	Mm.	n_D^{20}	Formula	Carbon Calc'd	Carbon Found	Hydrogen Calc'd	Hydrogen Found	Nitrogen Calc'd	Nitrogen Found
Hexahydropyrrocoline (IV)	68–69	18	1.5090	$C_8H_{13}N$	77.99	78.10	10.64	10.53	11.37	11.30
Dehydro-1-azabicyclo-[5.3.0]decane (V)	78–80	18	1.500	$C_9H_{15}N$	78.77	78.75	11.02	10.92	10.21	10.32
Dehydro-1-azabicyclo-[5.4.0]hendecane (VI)	103	18	1.5167	$C_{10}H_{17}N$	79.40	79.50	11.34	11.36	9.26	9.52
Dehydro-1-azabicyclo-[5.5.0]dodecane (VII)	115–117	18	1.5154	$C_{11}H_{19}N$	79.94	80.05	11.59	11.38	8.48	8.24
Dehydroamine Perchlorates	M.p.[a]	Crystal form								
Hexahydropyrrocoline	218–219	Flakes		$C_8H_{14}ClNO_4$	42.96	42.99	6.31	6.24	6.24	6.18
Dehydro-1-azabicyclo-[5.4.0]hendecane	175–176	Prisms		$C_{10}H_{18}ClNO_4$	47.71	47.52	7.21	6.99	5.57	5.59
Dehydro-1-azabicyclo-[5.5.0]dodecane	226	Needles		$C_{11}H_{20}ClNO_4$	49.72	49.62	7.59	7.72	5.27	5.32

[a] With decomposition.

was added to the ethereal residue, followed by 65% perchloric acid until the solution was just acid to Congo Red paper. The salt which separated was recrystallized from absolute ethanol, m.p. 219–220°, undepressed upon admixture with the perchlorate of the mercuric acetate dehydrogenation product of *dl*-octahydropyrrocoline.

Lithium aluminum hydride reduction of hexahydropyrrocoline perchlorate. A mixture of 2.0 g. of lithium aluminum hydride and 0.70 g. of hexahydropyrrocoline perchlorate in 80 ml. of anhydrous ether was stirred at the reflux temperature for 10 hours. After addition of 25 ml. of a 10% aqueous solution of potassium hydroxide, the ether layer was separated. The aqueous solution was extracted with ether. The combined ether extracts were dried and the volume was reduced. The addition of picric acid in ether caused the separation of the *picrate*, m.p. 228–230°, yield 5.5 g. (52%). Recrystallization from ethanol gave material which did not depress the melting point of an authentic sample of *octahydropyrrocoline picrate*.[5] Lithium aluminum hydride reduction of the perchlorates of VI and VII was not conclusive.

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