Summary

Several *cis* unsaturated 1,4-diketones are shown to be much more susceptible than the *trans* isomers toward furanization through addition and dehydration. A mechanism is suggested to account for this.

The analogy between these furanizations and the formation of 2,3-hydroxyfuranones is considered and new examples of the latter reaction are described.


Basicity Studies of Tertiary Vinyl Amines

BY ROGER ADAMS AND J. E. MAHAN

The introduction of a double bond into a primary or secondary amine lowers the basic strength constant, that is, decreases the degree of ionization.[1] Hixon and co-workers[2] measured the ionization constants of several 2-alkyl substituted 4,5-dihydropyrroles (2-ethyl, 2-benzyl, 2-phenyl, and 2-cyclohexyl-Δ^2-pyrrolines) and of the corresponding saturated compounds (pyrrolidines). The saturated molecules were, in all cases, stronger bases than the unsaturated by 2.4 to 3.3 pK_H units.[2a] In the case of tertiary amines the same general effect as for primary and secondary amines might be expected but no examples were found in the literature. Vinyl tertiary amines, excluding the pseudo bases or anhydro bases formed from pyridinium type salts which are not entirely comparable have also, with one exception, not been studied. The normal assumption would be that they are weaker bases than the corresponding saturated amines.

parative basicity studies[3] of retronecine, desoxyretronecine and their reduction products. These substances were all tertiary amines containing pyrrolizidine rings. For purposes of comparison, a variety of tertiary vinyl amines and the corresponding reduced compounds have been synthesized and their relative basicity measurements made.

A series of 1,2-dialkyl-Δ^2-pyrrolines (I–IV) was first investigated, since such molecules are very closely related in structure to the products under
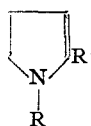
I.	R = CH_3; R' = CH_3
II.	R = CH_3; R' = C_4H_9
III.	R = C_2H_5; R' = CH_3
IV.	R = C_4H_9; R' = CH_3

study. The basic strengths of these pyrrolines and the analogous pyrrolidines are shown in Table I. It is to be noticed that in every case the unsaturated compound is more basic than the

TABLE I

Name	Obs. pK_H	T, °C.	pK_H (25°)[4]	Diff.	Lit.
1,2-Dimethyl-Δ^2-pyrroline	11.94	25	11.94		
1,2-Dimethylpyrrolidine	10.24	26	10.26	1.68	9.8[5]
1-Methyl-2-*n*-butyl-Δ^2-pyrroline	11.88	26	11.90		
1-Methyl-2-*n*-butylpyrrolidine	10.24	25	10.24	1.66	9.8[5]
1-Ethyl-2-methyl-Δ^2-pyrroline	11.88	27	11.92		
1-Ethyl-2-methylpyrrolidine	10.60	27	10.64	1.28	
1-*n*-Butyl-2-methyl-Δ^2-pyrroline	11.90[a]	26			
1-*n*-Butyl-2-methylpyrrolidine	10.43[a]	28		1.47	

[a] Taken in 25% aqueous methanol.

An attempt to locate the relative position of a double bond to the nitrogen atom in retronecine, a base from the plants of the genera *Crotalaria*, *Senecio* and *Trichodesma*, was initiated by com-

saturated. This interesting observation stimulated us to study analogous 6-membered ring compounds, namely, 1,2-dialkyl-Δ^2-tetrahydropyridines and the corresponding piperidines.

(1) Hixon and Johns, THIS JOURNAL, **49**, 1786 (1927).

(2) Craig and Hixon, *ibid.*, **53**, 4367 (1931); Starr, Bulbrook and Hixon, *ibid.*, **54**, 3971 (1932).

(2a) The constant pK_H will be used in this paper to indicate the basic strengths. It is related to the more usual constant K_{Ion}, by the expression $pK_H = pK_w - pK_{Ion}$, where K_w is the ion product for water.

(3) Adams, Carmack, and Mahan, *ibid.*, **64**, 2593 (1942).

(4) Corrected to 25° employing the negative temperature coefficient of the constant as given by Hall and Sprinkle, *ibid.*, **54**, 3469 (1932), for amines of various basicity. Since these data are valid only for aqueous solutions the pK_H constants measured in aqueous methanol were not corrected to 25°.

(5) Craig, *ibid.*, **55**, 2543 (1933).

The results are shown in Table II. Here again the unsaturated tertiary amines are more basic than the saturated.

TABLE II

Name	Obs. pK_H	T, °C.	pK_H (25°)[4]	Lit.
1,2-Dimethyl-Δ^2-tetra-hydropyridine	11.42	25.5	11.43	
1,2-Dimethylpiperidine	10.26	25	10.26	
1-Ethyl-2-methyl-Δ^2-tetrahydropyridine	11.57	25	11.57	
1-Ethyl-2-methylpiperidine	10.70	25	10.70	10.68[4]
ω-Dimethylamino-n-butyl methyl ketone	9.66	24.5	9.67	

A similar comparison has been carried to 1-propenylpiperidine and 1-n-propylpiperidine, as well as to a pair of straight chain compounds, 1-diethylamino-n-heptene-1 and 1-diethylamino-n-heptane (Table III). The basic strength deter-

TABLE III

Name	Obs. pK_H	T, °C.	Diff.
1-Propenylpiperidine	10.66[a]	28	
1-Propylpiperidine	10.23[a]	25	0.43
1-Diethylamino-n-heptene-1	10.38[b]	28	
1-Diethylamino-n-heptane	9.94[b]	26	.44
Piperidine (in 25% methanol which contained over an equivalent of propionaldehyde)	10.77	27	
Diethylamine (in 50% methanol which contained over an equivalent of heptaldehyde)	10.50	27	

[a] In 25% aqueous methanol.   [b] In 50% aqueous methanol.

minations of these two sets of molecules were carried out in the former case in 25% methanol and in the latter in 50% methanol because of the fact that the unsaturated molecules are not sufficiently soluble in water. The phenomenon still holds that the unsaturated molecules are more basic than the saturated, though to a lesser degree than in the Δ^2-pyrroline and Δ^2-tetrahydropyridine series.

In experiments of this kind the question may be raised in the case of the pyrrolines and tetrahydropyridines whether the basic strength as determined is a measure of the molecules in cyclic form or whether of possible open chain hydrolytic products; in the case of the 1-propenylpiperidine and 1-diethylamino-n-heptene-1, whether the basic strength is that of the original molecules or of a mixture of the secondary amine and corresponding aldehyde. The smooth titration curves, described in the experimental part, support the sup-

position that only a single basic molecule is being titrated in each instance. Lipp and Widnmann[6] reported that when a Δ^2-tetrahydropyridine (V) (Table II) is dissolved in water, it is immediately hydrolyzed to some extent to give an open chain secondary amino ketone (VI). This was based

V   VI
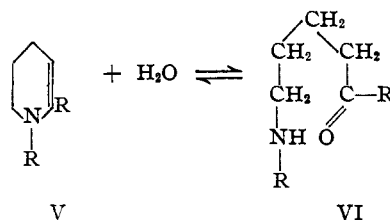
on immediate reaction of the compounds with carbonyl reagents to give derivatives of the open chain amine.

The basic strength of ω-dimethylamino-n-butyl methyl ketone, which is a tertiary amino ketone and thus cannot ring close to a Δ^2-tetrahydropyridine, gave a pK_H value of 9.68, which is relatively low and which led to the deduction that the strong basicity of aqueous solutions of the Δ^2-tetrahydropyridines is not due to the open-chain form of the equilibrium mixture.

Marz[7] observed that 2-methyl-Δ^2-pyrroline would react with hydroxylamine, semicarbazide and phenylhydrazine in aqueous solution, and hence concluded that a similar equilibrium existed in the Δ^2-pyrroline series. Craig,[8] however, prepared and studied several 1-methyl-2-alkyl-Δ^2-pyrrolines and because of their apparent non-reactivity with semicarbazide or phenylhydrazine assumed that hydrolysis did not occur to any great extent in aqueous solution.

Mannich and Davidsen[9] pointed out that vinyl tertiary amines in which the double bond is not a part of a ring are readily hydrolyzed in the presence of mineral acids to the corresponding aldehyde and secondary amine. If rapid hydrolysis occurs during the titration in the present basic strength studies, the resulting curve and pK_H value should be that of piperidine in the case of 1-propenylpiperidine, and that of diethylamine in the case of 1-diethylamino-n-heptene-1. Piperidine and diethylamine were titrated (Table III) in aqueous methanol in the presence of slightly over an equivalent of the appropriate aldehyde, approximating as nearly as possible those conditions used in the titration of the 1-propenylpiperi-

(6) Lipp and Widnmann, *Ann.*, **409**, 79 (1915).
(7) Marz, Diss. Techn. Hochsch., München, 1913.
(8) Craig, THIS JOURNAL, **55**, 295 (1933).
(9) Mannich and Davidsen, *Ber.*, **69**, 2106 (1936).

dine and the 1-diethylamino-heptene-1. The mixture of the aldehyde and base gave a slightly higher basicity than the molecules which were prepared from them, though the difference was far less than expected.

A possible explanation of the increased basicity of the vinyl tertiary amines compared with their saturated homologs lies in the assumption that an equilibrium exists in aqueous solution between the vinyl amine and a hydration product, the corresponding quaternary hydroxide as shown in formulas VII and VIII for 1,2-dimethyl-Δ^2-tetrahydropyridine as a representative of all the vinyl amines studied. The quaternary ammonium
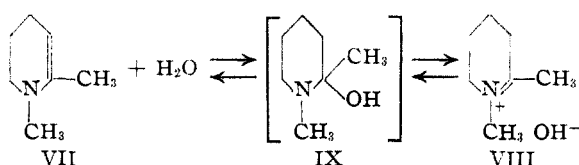
hydroxides are known to be strong bases which exceed in basicity all the tertiary amines. Since pseudo bases in general are weak, no appreciable amount of pseudo base (IX) can be present in the solution when titrated.

Aston[10] studied the action of alkali on 1,2,3,-5,5,6-heptamethyldihydropyrazinium iodide (X) and obtained a strong base (Xa) (pK_H at 25°, 11.6) of a quaternary ammonium type which is in equilibrium in aqueous solution with the tertiary base XI. This coincides with the explanation offered for the basicity of the simple vinyl tertiary amines studied in this investigation.
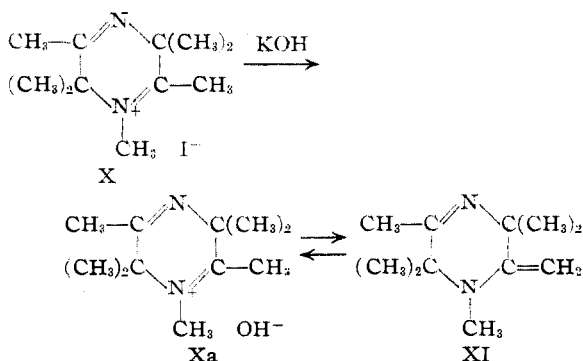
Vinyl primary or secondary amines if they undergo a similar rearrangement would form ammonium bases, not quaternary ammonium bases. Hence a lower basicity of the vinyl primary or secondary amines as compared with the corre-

sponding saturated compounds would be expected and this agrees with the experimental facts. In Table IV, it may be noted that 2-methyl-Δ^2-tetrahydropyridine, a secondary vinyl amine, is less basic than 2-methylpiperidine, a fact which is in harmony with the above statement and the observations of Hixon and co-workers[2] on 2-alkyl-Δ^2-pyrrolines.

TABLE IV

Name	Obs. pK_H	T, °C.	pK_H (25°)[4]	Lit.
2-Methylpiperidine	10.99	25	10.99	10.98[4]
2-Methyl-Δ^2-tetrahydropyridine	9.57	24	9.55	

Although it has been generally assumed that unsaturated tertiary amines with the double bond not in the vinyl position are less basic than the corresponding saturated, it was deemed advisable to test two pairs of such molecules which are related to the amines under investigation. These are shown (Table V) by a comparison of 1-methyl-Δ^3-pyrroline with 1-methylpyrrolidine and 1-allylpiperidine with 1-n-propylpiperidine. The saturated molecules are more basic than the unsaturated.

TABLE V

Name	Obs. pK_H	T, °C.	pK_H (25°)[4]	Diff.	Lit.
1-Methylpyrrolidine	10.36	25	10.36		10.18[5]
1-Methyl-Δ^3-pyrroline	9.92	25	9.92	0.44	
Propylpiperidine	10.45	26.5	10.48		
Allylpiperidine	9.65	27	9.69	.89	

A few effects of substitution were noted in this work which have not been previously mentioned in the literature. When an N-methyl group is replaced by an N-ethyl group on the pyrrolidine or piperidine ring there is an increase in basicity of about 0.4 unit. This effect is exemplified in Table VI; compare 2 with 4, and 8 with 9. However, increasing the size of the alkyl group from ethyl to butyl has little effect on the pK_H value of the resulting base; compare 1 with 2, 7 with 8, 11 with 12 and 13. The close parallel of pK_H values of compounds of the pyrrolidine series with analogous substituted compounds of the piperidine series may be worthy of note; compare 1 with 9, 2 with 10, 4 with 11, and 8 with 16.

Craig, Shedlovsky, Gould and Jacobs[11] assigned the double bond in lysergic acid (XII) to the 5,10-position because this acid and ergome-

(10) Aston, This Journal, 52, 5254 (1930); 53, 1448 (1931); Aston and Montgomery, ibid., 53, 4298 (1931); Aston and Lasselle, ibid., 56, 426 (1934).

(11) Craig, Shedlovsky, Gould and Jacobs, J. Biol. Chem., 125, 289 (1938).

TABLE VI

Name	Obs. pK_H	T, °C.	pK_H (25°)[4]	Lit.
(1) 1-n-Butyl-2-methylpyrrolidine	10.65	27	10.69	
(2) 1-Ethyl-2-methylpyrrolidine	10.61	27	10.64	
(3) 1-Methyl-2-n-butylpyrrolidine	10.24	25	10.24	9.8[5]
(4) 1,2-Dimethylpyrrolidine	10.24	26	10.26	9.8[5]
(5) 1-Methylpyrrolidine	10.36	25	10.36	10.18[5]
(6) Pyrrolidine				11.99[2]
(7) 1-n-Butyl-2-methylpiperidine				10.72[4]
(8) 1-Ethyl-2-methylpiperidine	10.70	25	10.70	10.68[4]
(9) 1,2-Dimethylpiperidine	10.26	25	10.26	
(10) 2-Methylpiperidine	10.99	25	10.99	10.98[4]
(11) 1-Ethylpiperidine				10.41[4]
(12) 1-n-Propylpiperidine	10.45	26.5	10.48	
(13) 1-n-Butylpiperidine	10.47	26	10.49	10.48[4]
(14) Piperidine	11.11	24.5	11.12	11.13[4]

trine, a parent alkaloid, exhibited weaker basic properties than iso-lysergic acid (XIII) and ergometrinine. The double bond in iso-lysergic acid was then assigned to the 9,10-position. In view of the results obtained on the basic strengths of vinyl tertiary amines, it appears questionable whether the deductions of the authors were justified and whether the assignment of the formulas should not possibly be reversed.

XII   XIII
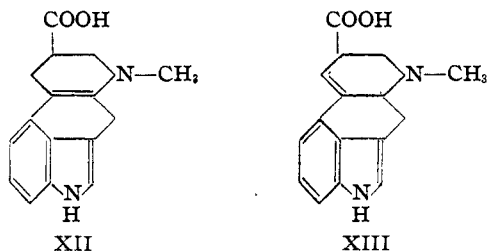
Experimental

Determination of Basic Strength Constants.—A sample of the base calculated to require between 20 to 30 cc. of 0.10 N hydrochloric acid was dissolved in 90 cc. of conductivity water. While the solution was continuously stirred by means of a small air-driven stirrer, the base was titrated by adding appropriate increments of standard 0.1 N hydrochloric acid. After each addition of acid the pH was carefully measured with a Hellige glass electrode pH meter (no. 7040). The pH of the solution when exactly half of the base had been neutralized (pK_H value) was read from the titration curve (pH vs. cc. of acid). Duplicate or triplicate measurements were made in all cases. The curves obtained were smooth and showed only the characteristic sharp break at the end-point. For compounds not sufficiently soluble in water, 90 cc. of an aqueous solution was used which contained the calculated amount of methanol to make a 25 or 50% solution just at the point when half the titer had been added. All of the amines studied were carefully fractionated in a carbon dioxide-free atmosphere immediately before use, and all boiled within a range of 1° or less.

Basicity measurements were made on several compounds for which values have been recorded in the literature by

Hall and Sprinkle[4] who used a hydrogen electrode in their pH determinations. The close agreement (see tables) in all cases with their values indicates that no great error has been introduced by the use of a glass electrode in the basicity studies.[12] Before each titration the electrodes were washed, the half-cell tip flushed with fresh saturated potassium chloride solution, and the meter standardized with 0.05 M potassium acid phthalate. Each day that the pH meter was put in service it was further checked by titration of ammonia (pK_H (25°) 9.27).[4]

Δ^2-**Pyrrolines.**—1,2-Dimethyl-Δ^2-pyrroline and 1-methyl-2-n-butyl-Δ^2-pyrroline were prepared according to the method of Craig.[8] The reaction of methylmagnesium iodide on N-methylpyrrolidone-2 led apparently only to the formation of 1,2-dimethyl-Δ^2-pyrroline, as none of the 1,2,2-trimethylpyrrolidine reported by Lukeš[13] could be found. However, the reversible dimerization mentioned by Craig[8] was encountered. In the synthesis of 1-methyl-2-n-butyl-Δ^2-pyrroline by an analogous reaction using butylmagnesium bromide, 1-methyl-2,2-di-n-butylpyrrolidine was isolated from the mixture of by-products in 14% yield. In preliminary attempts to prepare 1-n-butyl-2-methyl-Δ^2-pyrroline, it was found that the reaction of methylmagnesium iodide on N-n-butylpyrrolidone-2 was incomplete and did not lead to the formation of any appreciable quantity of the desired pyrroline.

A second procedure proved to be more satisfactory for the general preparation of pyrrolines in which alkyl groups larger than methyl were attached to the nitrogen. This consisted in treatment of 3-bromo-n-propyl methyl ketone with the appropriate primary amine[14,15] in aqueous solution. If ethanol instead of water is used as a solvent, the resulting homogeneous mixture undergoes reaction rapidly at room temperature, thus eliminating the necessity of longer periods of agitation. The yields in the case of 1-n-butyl and 1-ethyl-2-methyl-Δ^2-pyrroline were increased from 15% to 40-50% by this modification.

1-Methyl-2-n-butyl-Δ^2-pyrroline and 1-Methyl-2,2-n-dibutylpyrrolidine.—To the Grignard reagent, prepared

(12) It is only in the presence of certain metallic ions that there is a serious error introduced by the use of a glass electrode in alkaline solutions. See Dole, "The Glass Electrode," John Wiley and Sons, Inc., New York, N. Y., 1941, Chapter 7.

(13) Lukeš, Coll. Czechoslov. Chem. Comm., 2, 531 (1930); Chem. Listy, 27, 97, 121 (1933).

(14) Hielscher, Ber., 31, 277 (1898).

(15) Markwalder, J. prakt. Chem., 75, 329 (1907).

from 31.6 g. (1.30 moles) of magnesium, 1200 cc. of dry ether, and 185 g. (1.34 moles) of n-butyl bromide, was added with stirring under nitrogen 63.5 g. (0.642 mole) of N-methylpyrrolidone-2[16] over a period of three hours. The mixture was stirred at room temperature for five hours when it became necessary to stop the stirrer due to the formation of a solid complex. After standing for twenty hours the mixture was hydrolyzed with an excess of 3 N hydrochloric acid. The aqueous layer was separated, made alkaline with 30% aqueous sodium hydroxide and steam distilled. The steam distillate (600–700 cc.) was neutralized with dilute hydrochloric acid, the solvent removed *in vacuo* on a water-bath and the residual sirup taken up in 60 cc. of water. This solution was made basic with sodium hydroxide, extracted with ether, and the ethereal extract dried over anhydrous magnesium sulfate. After removal of ether the product was fractionated. The main portion consisted of 1-methyl-2-n-butyl- Δ²-pyrroline,[s] b. p. 88.5° (30 mm.); yield 48 g. (54%).

A second smaller fraction, 1-methyl-2,2-n-dibutyl-pyrrolidine, boiled at 122° (18 mm.); n^{20}D 1.4567; d^{20}_4 0.846; yield 18 g. (14%). This substance, a colorless liquid, is only slightly soluble in water, but is readily soluble in all common organic solvents.

Anal. Calcd. for $C_{13}H_{27}N$: C, 79.12; H, 13.79. Found: C, 79.53; H, 13.69.

1-Methyl-2,2-dibutylpyrrolidine Methiodide.—This substance was prepared by treating a dry ether solution of the base with the calculated amount of methyl iodide. It was purified by recrystallization from ethanol–ether; white plates, m. p. 211° (cor.), unchanged on further recrystallization from methanol–ether.

Anal. Calcd. for $C_{13}H_{27}N \cdot CH_3I$: C, 49.55; H, 8.91; N, 4.13. Found: C, 49.67; H, 9.09; N, 4.22.

1-Ethyl-2-methyl-Δ²-pyrroline.—To a solution cooled to 0° of 44 g. (0.68 mole) of 70% ethylamine in 110 cc. of absolute ethanol contained in a pressure bottle was added 55.9 g. (0.34 mole) of ω-bromo-n-propyl methyl ketone. The bottle was tightly stoppered and the contents permitted to warm up gradually; at 15° reaction set in and cooling was again necessary as the temperature rose quickly to 50–60°. When the reaction had subsided, as judged by a decrease in temperature, the mixture was shaken for fifteen to twenty minutes and then acidified with dilute hydrochloric acid. The solvent was removed *in vacuo* on a water-bath and the resulting sirup taken up in 100 cc. of water, made strongly alkaline with sodium hydroxide, and steam distilled. A part of the amine fraction would not steam distil as in all runs there was several cc. of very high boiling, brown, viscous oil which remained behind. The clear steam distillate (300–400 cc.) was made more strongly alkaline with 50% sodium hydroxide solution and the pyrroline extracted with ether. After drying and removal of ether the product was fractionated; b. p. 73.5–74.5° (55 mm.); n^{20}D 1.4945; d^{20}_4 0.896; yield 19.5 g. (52%). When water was used as the reaction solvent and the mixture allowed to stand (occasional shaking) for twenty-four to forty-eight hours, the yields were decreased to 10–15%. 1-Ethyl-2-methyl-Δ²-pyrroline is a colorless liquid which turns yellow and deposits an insoluble red viscous oil when

exposed to the air. However, when sealed under nitrogen it will remain colorless indefinitely.

Anal. Calcd. for $C_7H_{13}N$: C, 75.62; H, 11.78. Found: C, 75.54; H, 11.80.

1-n-Butyl-2-methyl-Δ²-pyrroline.—The procedure employed was that as described above for 1-ethyl-2-methyl-Δ²-pyrroline. From 55.3 g. (0.335 mole) of ω-bromo-n-propyl methyl ketone and 49.5 g. (0.68 mole) of n-butyl amine was obtained 18.3 g. (39%) of product; b. p. 82–83.5° (16 mm.); n^{20}D 1.4865; d^{20}_4 0.904. 1-Butyl-2-methyl- Δ²-pyrroline is a colorless liquid which, like all vinyl tertiary amines, soon colors up when exposed to the air. It is only slightly soluble in water (1 part in 300–400 parts water), but is readily miscible with the common organic solvents.

Anal. Calcd. for $C_9H_{17}N$: C, 77.63; H, 12.31. Found: C, 77.50; H, 12.37.

1-Methyl-Δ³-pyrroline.—This was prepared in 80% yield by the partial reduction[17] of 1-methylpyrrole.

Pyrrolidines.—All of the disubstituted pyrrolidines were synthesized by catalytic reduction of the corresponding unsaturated Δ²-pyrrolines in ethanol with Raney nickel and hydrogen at two to three atmospheres pressure. The constants agreed essentially with those in the literature: 1,2-dimethylpyrrolidine,[5] b. p. 98–99°; 1-methyl-2-butyl-pyrrolidine,[5] b. p. 170.5°; 1-ethyl-2-methylpyrrolidine,[18] b. p. 118.5–119.5°; 1-n-butyl-2-methylpyrrolidine,[19] b. p. 86–86.5° (57 mm.). 1-Methylpyrrolidine was obtained by catalytic reduction of 1-methylpyrrole with platinum oxide.[20]

Δ²-Tetrahydropyridines.—The Δ²-tetrahydropyridines and ω-dimethylamino-n-butyl methyl ketone were synthesized from ω-bromo-n-butyl methyl ketone and the appropriate amine according to the directions of Lipp[6,21] and of Ladenburg.[22] Considerable decomposition occurs when ω-bromo-n-butyl methyl ketone is distilled at atmospheric pressure. By distilling under reduced pressure, b. p. 104–106° (17 mm.), this decomposition can be avoided.

1,2-Dialkylpiperidines.—These compounds were prepared by reduction of the corresponding tetrahydropyridines in ethanol with Raney nickel at two to three atmospheres of hydrogen.

1-Propenylpiperidine and 1-Diethylamino-n-heptene-1. —These vinyl tertiary amines were prepared according to the directions of Mannich and Davidsen.[9] 1-Propenyl-piperidine was found to boil at 51–53° (10 mm.) instead of 61–63° (10 mm.) as previously reported.

1-Propylpiperidine and 1-Diethylamino-n-heptane.— These substances resulted when the corresponding vinyl amines were reduced in ethanol with Raney nickel and hydrogen at two to three atmospheres pressure.

1-Allylpiperidine[23] and 1-n-Butylpiperidine.—Refluxing one mole of bromide with two moles of piperidine in benzene solution resulted in good yields of the products.

(16) Spåth and Lintner, *Ber.*, **69**, 2727 (1936).

(17) Andrews and McElvain, THIS JOURNAL, **51**, 887 (1929).
(18) Signaigo and Adkins, *ibid.*, **58**, 715 (1936).
(19) Tsuda, *J. Pharm. Soc. Japan*, **56**, 359 (1936).
(20) Craig and Hixon, THIS JOURNAL, **53**, 187 (1931).
(21) Lipp, *Ann.*, **289**, 209 (1896).
(22) Ladenburg, *ibid.*, **304**, 54 (1899).
(23) Menshutkin, *J. Russ. Phys.-Chem. Soc.*, **31**, 43 (1899); *Chem. Zentr.*, **70**, 1066 (1899).

N-*n*-Butylpyrrolidone-2.—This substance was prepared by the general method of Späth and Lintner.[16] A mixture of 50 g. (0.58 mole) of butyrolactone and 46 g. (0.64 mole) of *n*-butylamine was heated at 280° for four hours. After cooling, the reaction mixture was dissolved in 50 cc. of 6 N hydrochloric acid and the aqueous solution continuously extracted with ether for fifteen hours to remove the N-*n*-butylpyrrolidone-2, which is exceedingly soluble in water. After drying and removal of the ether the product was distilled; b. p. 121° (16 mm.); n^{20}D 1.4650; d^{20}_4 0.964; yield 78 g. (95%).

Anal. Calcd. for $C_8H_{15}ON$: C, 68.04; H, 10.71; N, 9.92. Found: C, 68.03; H, 10.75; N, 10.18.

Summary

1. A variety of cyclic and straight chained vinyl tertiary amines have been synthesized as well as the corresponding saturated molecules.

2. Comparative basicity studies demonstrated that the vinyl tertiary amines were in all cases more basic than the corresponding saturated compounds.

3. This is explained by assuming hydration and rearrangement to a quaternary ammonium base.

URBANA, ILLINOIS   RECEIVED JULY 30, 1942

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Structure of Monocrotaline. VII.[1] Structure of Retronecine and Related Bases

BY ROGER ADAMS, MARVIN CARMACK AND J. E. MAHAN

Structure I, previously suggested for retronecine, was deduced on the basis of (a) the validity of structure II for oxyheliotridane, a stereoisomer[2] of retronecanol, as proposed by Menshikov,[3] and (b) the reduction characteristics of retronecine and the reactivity of the hydroxyls in retronecine and related molecules. No structure other than I will explain as satisfactorily all the available experimental facts. The formulation of platynecine as III, anhydroplatynecine as IV, and desoxyretronecine as V will then result.
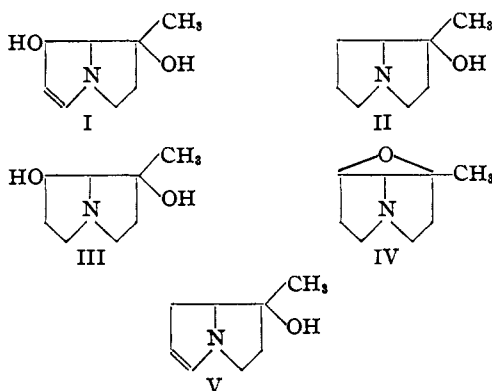
The most objectionable feature to structure I for retronecine, as pointed out in a previous paper, lies in the results obtained upon esterification. One hydroxyl in retronecine esterifies very readily, more readily than would be anticipated from the usual secondary alcohol, and the other esterifies

(1) VI, Adams and Rogers, THIS JOURNAL, **63**, 537 (1941).

(2) Konovalova and Orekhov, *Bull. soc. chim.*, [5] **4**, 1285 (1937); *Ber.*, **69B**, 1908 (1936).

(3) Menshikov, *Bull. acad. sci. U. S. S. R.*, Classe sci. math., Ser. chim., 978 (1936).

with difficulty, but with more facility than is observed with any ordinary tertiary alcohol. Moreover, retronecanol (II) dehydrates more sluggishly than would be expected on the basis of a tertiary hydroxyl group.

Direct chemical proof for the positions of the hydroxyls and double bond in retronecine (I) was undertaken. The evidence for a pyrrolizidine nucleus and for a methyl group in the 1-position is indisputable. A complete assembly of the facts concerning known vinyl tertiary amines revealed that in no instance where the vinyl amine structure was established unequivocally was the molecule stable both to alkali and acid; hydrolysis occurs with one or the other especially when warmed with the reagent. Retronecine is stable to both even on boiling. Further evidence that the presence of a vinyl amine structure is unlikely was obtained through basicity studies. The following table gives the pK_H values for retronecine and its related compounds.

TABLE I

BASICITY OF RETRONECINE AND RELATED COMPOUNDS

Name	pK_H	T, °C.	pK_H (25°)
Retronecine	8.92	26	8.94
Platynecine	10.24	24	10.22
Desoxyretronecine	9.55	25	9.55
Retronecanol	10.92	24.5	10.91
Anhydroplatynecine	9.44	24	9.42
Heliotridane	11.44	27	11.48
Heliotridene	10.59	25.5	10.60
Isoretronecanol[5]	10.87	25.5	10.88

It is to be noted that the saturated molecules on the basis of the postulated structures (I–V)