aqueous solution was then extracted 3 times with chloroform. The combined chloroform extracts were dried over anhydrous magnesium sulfate. The chloroform solution upon evaporation gave a light yellow oil which crystallized upon addition of ether. The yield was 0.23 g., and additional material was obtained by further chloroform extractions. For analysis the crude product was crystallized from a mixture of benzene and acetone. After the product had been dried at 3 mm. over potassium hydroxide for twenty minutes, it had the approximate composition of a monohydrate, m. p. 50–52°.

Anal. Calcd. for $C_{15}H_{29}N_2S_2Cl \cdot H_2O$:   C, 50.8;   H, 8.80.   Found: C, 51.4;   H, 8.62.

On long drying *in vacuo* at 40°, the above material lost 93% of the calculated weight for 1 molecule of water of hydration. It then melted at 56–57°.

Anal. Calcd. for $C_{15}H_{29}N_2S_2Cl$:   C, 53.5;   H, 8.67;   N, 8.31;   S, 19.03;   Cl, 10.52.   Found: C, 53.1;   H, 8.79;   N, 8.00;   S, 19.50;   Cl, 10.14.

N^α-Benzoyl-L-histidine.—Three grams of N^α-benzoyl-L-histidine[29] was dissolved in 25 cc. of water by addition of 1 N sodium hydroxide with stirring. Then 1.5 cc. of butyl-H was added, and the mixture was stirred for five hours. The pH was maintained at 8–9 by gradual addition of 1 N sodium hydroxide. Methanol (10 cc.) was also added portionwise to increase the solubility of the vesicant. The reaction mixture was evaporated to about one-half volume *in vacuo* and then extracted with ether. The aqueous layer was acidified to pH 4 with 11 cc. of 1 N hydrochloric acid. The oil which separated was removed. The aqueous solution was acidified with 1 cc. of 1 N hydrochloric acid and extracted with chloroform. Evaporation of the chloroform left an oil which was crystallized from ethanol by addition of ether. Recrystallization of the compound from water yielded 200 mg. of rosettes, m. p. 188–190°.

Anal. Calcd. for $C_{19}H_{25}O_3N_3S$:   S, 8.54.   Found: S, 8.37.

Summary

1.   A series of N-substituted derivatives of the simple α-amino acids with benzyl-H (benzyl β-chloroethyl sulfide) and butyl-H (butyl β-chloro-ethyl sulfide) has been prepared by treatment of the various amino acids in alkaline solution with the corresponding vesicant. The following derivatives have been prepared: N-monosubstituted benzyl-H derivatives of glycine, DL-alanine, DL-valine, L-leucine, DL-leucine, DL-isoleucine, DL-threonine, DL-phenylalanine and DL-methionine; N^α-monosubstituted butyl-H derivatives of glycine, DL-leucine, DL-phenylalanine and L-tryptophan; N^α-disubstituted benzyl-H derivatives of glycine and L-tryptophan; N^α-disubstituted butyl-H derivative of glycine.

2.   Treatment of the copper salt of L-lysine in alkaline solution with butyl-H yielded a crystalline monosubstituted derivative. By analogy with benzoylation data this compound is believed to be the N^ϵ-substituted derivative.

3.   S-Substituted derivatives of L-cysteine and DL-homocysteine with benzyl-H have been prepared by reaction of the vesicant with the corresponding sodium mercaptides in liquid ammonia solution.

4.   O,N-Disubstituted derivatives of L-tyrosine with benzyl-H and butyl-H have been prepared.

5.   A trisubstituted butyl-H derivative of L-histidine was obtained by treatment of the amino acid in alkaline solution with the vesicant. Under similar conditions imidazole yielded mono- and disubstituted derivatives, and N^α-benzoyl-L-histidine yielded a monosubstituted derivative.

6.   The data provide a further and direct demonstration that the following groups in amino acids are capable of reacting with H-type vesicants: α-amino group, ε-amino group, imidazolyl group, sulfhydryl group and phenolic hydroxyl group.

(29) Gerngross, Z. physiol. Chem., 108, 50 (1919).

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# N-Phenyl-3,5-diethyl-2-propyl-1,4-dihydropyridine

By David Craig, Laura Schaefgen and Willard P. Tyler

During a study of the reaction of butyraldehyde with aniline in the presence of acetic acid, it has been found possible to isolate a weak base having the formula $C_{18}H_{25}N$. The present paper deals with the structure of this base.

The empirical formula and the method of synthesis suggest dihydropyridine structures I, Ia, or Ib or the open chain anil structure II. The pyrolysis of the compound in the presence of cobaltous chloride forms aniline and 1,3,5-triethylbenzene. The formation of triethylbenzene, $C_{12}H_{18}$, supports these formulations since the linking together of three butyraldehyde residues is thereby indicated. Hydrogenation, depending on conditions, yields di, tetra and decahydro derivatives, in accord with the N-phenyldihydropyridine formulas, but thus far has given no evidence of the
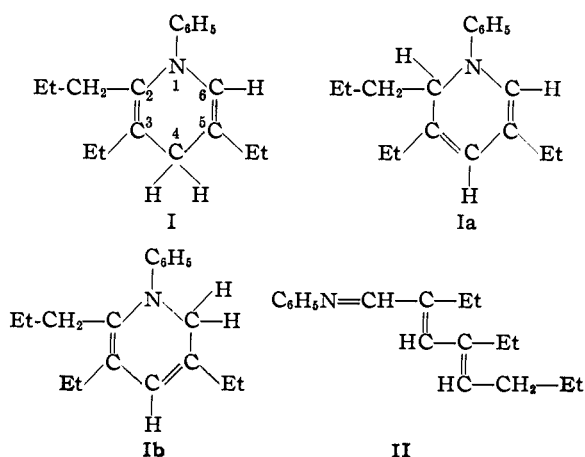
formation of hexahydro or dodecahydro derivatives required of formula II. Dehydrogenation of the new compound occurs upon contact with reduced platinum oxide in acetic acid solution. The product is the corresponding acetate of III. Oxidation with iodine or sulfur in acidic media, containing appropriate anions, produces quaternary salts, e.g., the iodide III. This type of oxidation would be expected of structures I, Ia, or Ib, but would not be expected of the anil II. The anil in such media would be expected to yield hydrolysis products, i.e., aniline and an unsaturated aldehyde. Neither these nor their oxidation products have been observed in the reaction mixtures. Thus oxidation as well as hydrogenation of the new compound supports a dihydropyridine structure and eliminates from consideration an open chain anil structure such as II.
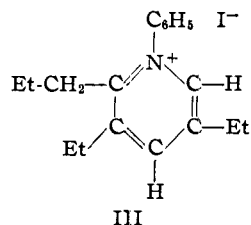
Karrer[1] has studied the formation and behavior of N-phenyl-1,2-dihydropyridine, a compound closely related to the $C_{18}H_{25}N$ base. His assignment of structure was based in part on the prompt reaction of his compound with maleic anhydride[2] although a well characterized reaction product was not reported. In contrast, the reaction of one molecule of the $C_{18}H_{25}N$ base with one of maleic anhydride is comparatively sluggish and a well characterized adduct[3] may be isolated. The N-phenyl-1,2-dihydropyridine also reacted rapidly and irreversibly with hydrochloric acid to form unidentified products. Again in contrast, the $C_{18}H_{25}N$ base reacts immediately only as a weak organic base. However, on long contact with hydrochloric acid it dissolves and then irreversibly undergoes disproportionation. The products are the quaternary chloride corresponding to III and the dihydro derivative obtained by hydrogenation. The N-phenyl-1,2-dihydropyridine is unstable in the atmosphere whereas the $C_{18}H_{25}N$ base has been kept for ten years or more substantially unchanged. The $C_{18}H_{25}N$ base is yellow. Karrer reported and we have confirmed that the 1,2-dihydropyridine is colorless. Neither of these dihydropyridines is fluorescent. The differences and similarities in their behavior constitute the chemical basis for the assignment of the 1,4-dihydro structure I to the $C_{18}H_{25}N$ base.

Knowledge of the structure of the $C_{18}H_{25}N$ base facilitates the identification of some of its derivatives. Thus the decahydro derivative is N-cyclohexyl-3,5-diethyl-2-propylpiperidine and the tetrahydro derivative is the corresponding N-

(1) Karrer, *Helv. Chim. Acta*, **20**, 72 (1937).

(2) Mumm and Diederichsen, *Ann.*, **538**, 198 (1939), reported that 1,2-dihydro-1,2,6-trimethyl-4-phenyl-3,5-dicarbethoxypyridine reacted with maleic anhydride to form a 1:1 adduct and that the corresponding 1,4-dihydro isomer did not react.

(3) The structure of this adduct is the subject of a second paper.

phenylpiperidine IV. The dihydro derivative has been assigned structure V on the basis, (a) that it reacts as a vinylamine toward hydrochloric acid, and (b) that there would be less hindrance to the addition of hydrogen to the Δ^5 double bond than to the Δ^2 bond of compound I.
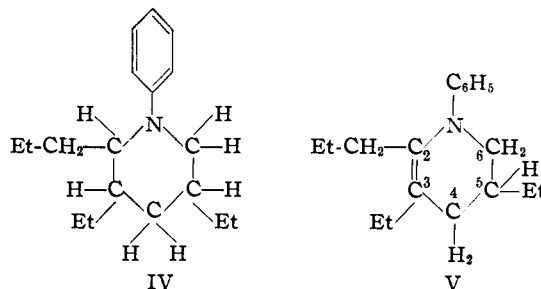
The study of the ultraviolet absorption spectra of compound I and its derivatives supports the assigned structures. Figure 1 shows that the spectrum for compound I is very different from that of N-phenyl-1,2-dihydropyridine but very similar to that of the methyl derivative prepared by the reaction of methylmagnesium iodide with the pyridinium salt III. Compound I and the methyl derivative are therefore considered to be 1,4-dihydropyridines, the methyl group in the latter compound being in the 6 or 4-position.
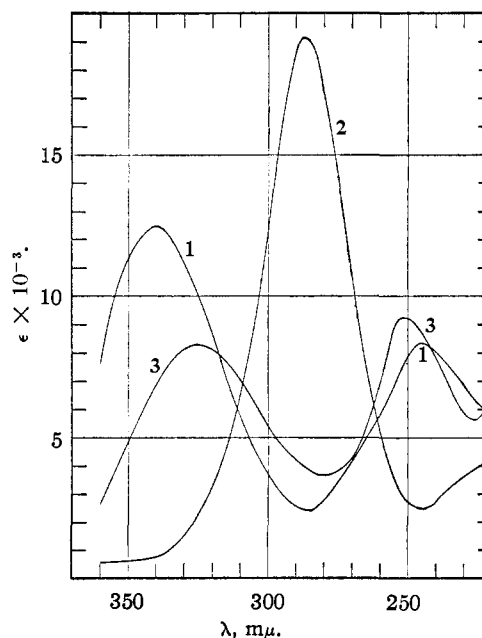

Fig. 1.—Spectra of I (1), N-phenyl-1,2-dihydropyridine (2), and the methyl derivative of I (3).

Figure 2 compares the spectrum of the pyridinium ion of III with the spectra of 3,5-diethyl-2-propylpyridinium ion and N-phenylpyridinium ion. They resemble each other closely. Evidently the tetracovalent nitrogen atom effectively insulates the conjugation of the benzene ring from
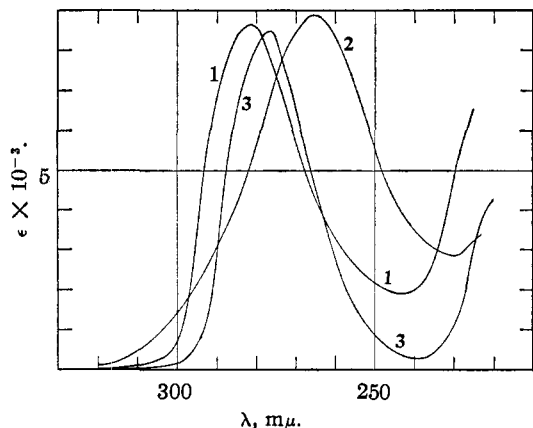
Fig. 2.—Spectrum of the cation of III, obtained by subtraction of the absorption of KI from that of III, (1); spectrum of N-phenylpyridinium chloride (2); spectrum of 3,5-diethyl-2-propylpyridinium ion (3) in 1.2 N HCl in 90% methanol.

that of the pyridine ring. The maxima for the trialkyl pyridinium salts appear at longer wave lengths because of the usual bathochromic effects of the alkyl groups on the pyridine nucleus.

Figure 3 presents the spectrum of N-phenyl-3,5-diethyl-2-propylpiperidine IV along with that of N-phenylpiperidine and di-n-butylaniline. It is of interest to note the similarities and differences among these spectra. The piperidines are, in one sense, dialkylanilines and would be expected to possess a well-defined fundamental band such as the long wave length band of di-n-butylaniline. Extension of the discussion of Remington[4] on steric effects caused by hindrance to ease of for-
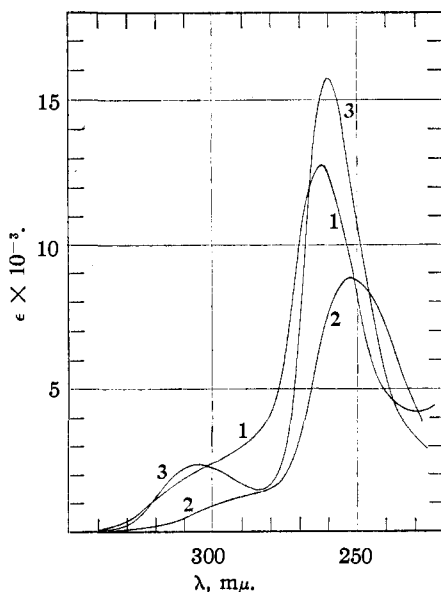

Fig. 3.—Spectra of IV (1), N-phenylpiperidine (2), and di-n-butylaniline (3).

(4) Remington, THIS JOURNAL, **67**, 1838 (1945).

mation of a planar configuration can explain the somewhat distorted shape of the fundamental band in the piperidines. This follows as a result of the tendency of the piperidine ring to be puckered. Further comparison shows the similarity between the spectra of N-phenylpiperidine and of IV which supports the structure assigned to the latter compound as a result of the method used for its preparation.

The absorption spectrum of the tetrahydropyridine V is entirely different from that of the corresponding piperidine IV. The greater intensity and longer wave lengths at which the absorption of V occurs indicates that the double bond must be conjugated with the nitrogen atom.[5] The spectrum observed for V in conjunction with the hydrogenation of the $C_{18}H_{25}N$ base to form V is evidence against structures Ia and Ib for the dihydropyridine since by 3,6- or 2,5-addition such structures would be expected to lead to Δ^4- and Δ^3-tetrahydropyridines.
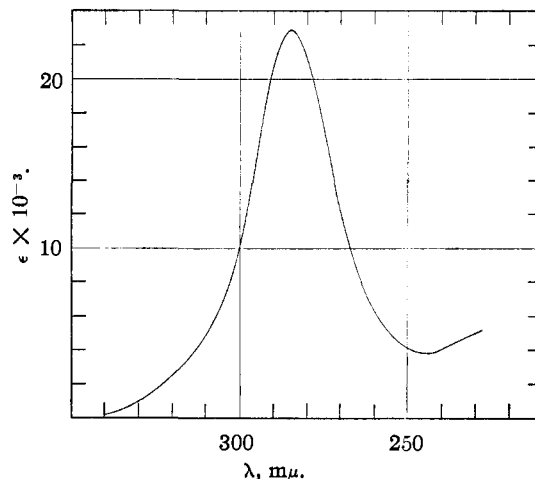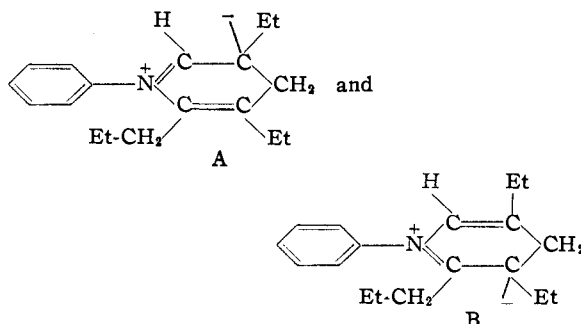

Fig. 4.—Spectrum of V.

Attachment of two vinyl groups to the nitrogen atom as in structure I makes it possible to write, among others, the nearly equivalent resonance forms, A and B, for the first excited state. This

leads to considerable stabilization of the first excited electronic level by resonance, and hence, absorption at a longer wave length than would be

(5) Bowden, Brauda, Jones and Weedon, J. Chem. Soc., 45 (1946).

true for structures Ia and Ib for which the forms contributing to the first excited state would have quite different energies. Thus, the 1,4-dihydropyridine reported here has its first maximum at 340 mμ whereas N-phenyl-1,2-dihydropyridine has a maximum at 286 mμ.

Experimental Part

Absorption Spectra.—The spectra were measured in methanol solution except where specified otherwise using a Beckman quartz spectrophotometer, Model DU.

N-Phenyl-3,5-diethyl-2-propyl-1,4-dihydropyridine, Compound I.—One mole (93 g.) of aniline was added dropwise to a mixture of four moles (288 g.) of butyraldehyde containing 8.7 g. of acetic acid and 6 moles (108 g.) of water during thirty minutes. During this period the mixture was stirred and cooled to about 10° with ice water. The mixture was then heated to reflux and maintained at reflux for five hours. The final liquid temperature was 98°. After removal of the water layer, containing most of the acetic acid, butyraldehyde and 2-ethylhexenal were removed by steam distillation during four hours. The remaining oil was dried at reduced pressure. It was a fluid, light brown oil with a characteristic odor and a refractive index of 1.575^{20}D. The product was distilled to supply a 55% yield of light yellow oil which came over at about 125° at 0.5 mm. pressure. The refractive index of this oil was 1.5725^{20}D. By redistillation the refractive index was raised to 1.5740. This product was nearly odorless.

Anal. Calcd. for C$_{18}$H$_{25}$N: C, 84.64; H, 9.87; N, 5.49; mol. wt., 255. Found: C, 84.56; H, 10.26; N, 5.29; mol. wt. in freezing benzene, 241, 242.

Pyrolysis of Compound I.—A mixture of 150 g. of I and 2 g. of anhydrous cobaltous chloride was placed in a 500-ml. distilling flask equipped with a stirrer. The mixture was heated rapidly with stirring to about 275° when decomposition set in. The temperature was raised to 310° during twenty minutes. The distillate amounted to 115 g. and the residue to 35 g. The distillate was extracted with a mixture of 80 ml. of concd. hydrochloric acid and 160 ml. of water. The oil layer was separated, washed with water, dried over potassium carbonate, and distilled. A yield of 15 g. (16%) of colorless oil was obtained which distilled at 210–212°.

Anal. Calcd. for C$_{12}$H$_{18}$: C, 88.83; H, 11.17. Found: C, 88.99; H, 11.05.

The hydrocarbon was identified by the preparation of the trinitro derivative by the method of Gattermann, *et al.*[6] This derivative melted at 111° alone or when mixed with an authentic specimen of 1,3,5-triethyl-2,4,6-trinitrobenzene.

The acid layer was made basic with strong caustic. The oil which precipitated was dried and distilled. In this way, 14 g. (25%) of aniline and an unidentified oil which distilled at 184–186° at 17 mm. was secured. The aniline was identified by the preparation of the acetyl derivative. The oil analyzed approximately for C$_{18}$H$_{25}$N. After heating with CoCl$_2$ at 300° it was recovered unchanged.

N-Phenyl-3,5-diethyl-2-propyl-1,4,5,6-tetrahydropyridine.—This compound was formed by shaking 25.5 g. of compound I with 10 g. of Raney nickel and 25 ml. of alcohol under 3 atmospheres of hydrogen for three hours. The pressure drop then corresponded to 1.05 moles of hydrogen per mole of I. The product, isolated in 92% yield, distilled at 115 to 120° at 0.2 mm. and had a refractive index of 1.5518^{20}D. It required five minutes of shaking for complete solution in six volumes of 6 N hydrochloric acid.

Anal. Calcd. for C$_{18}$H$_{27}$N: C, 83.98; H, 10.58; N, 5.44. Found: C, 83.87, 83.73; H, 10.87, 10.93; N, 5.41, 5.47.

(6) Gattermann, *et al., Ber.,* **32,** 1124 (1899).

N-Phenyl-3,5-diethyl-2-propylpiperidine.—Hydrogenation of compound I over Raney nickel between 30 and 100° and from 3 to 100 atmospheres produced this derivative quite smoothly although the product contained small quantities of the dihydro base and probably the decahydro derivative as well. In a typical run 13.3 g. of I dissolved in 50 ml. of alcohol was shaken with 12 g. of Raney nickel in a copper lined autoclave for ten hours at 70 atmospheres pressure of hydrogen and 50°. The product was distilled at 0.2 mm. Fraction A distilled at 112–115° and Fraction B at 115–120°. These fractions were almost colorless. The combined yield was 93%. The refractive indices n^{20}D of the fractions were 1.5290 and 1.5350, respectively.

Anal. Calcd. for C$_{18}$H$_{29}$N: C, 83.33; H, 11.27; N, 5.40. Found for A: C, 83.30, 83.40; H, 11.40, 11.32; N, 5.34, 5.40. Found for B: C, 83.46, 83.40; H, 11.24, 11.31; N, 5.42, 5.36.

Although these fractions thus appeared to be analytically pure, their ultraviolet absorption spectra disclosed the presence of the above tetrahydropyridine. It may therefore be inferred that small amounts of some hydrogen rich compound such as the decahydro derivative were present. Extraction with dilute hydrochloric acid removed most of these impurities. The compound thus purified had one absorption maximum (Fig. 3). It had a refractive index of 1.5320^{20}D.

N-Cyclohexyl-3,5-diethyl-2-propylpiperidine.—This compound was secured by heating 64.5 g. of compound I and 10 g. of Raney nickel at 150° for twenty hours under about 100 atmospheres of hydrogen. The main product, which was isolated in 45% yield, distilled at 103–110° at 0.1 mm. and had a refractive index of 1.4868^{20}D. Its ultraviolet absorption spectrum had one low peak at 263 mμ probably due to the presence of a trace of the incompletely reduced phenyl derivative. The compound was colorless.

Anal. Calcd. for C$_{18}$H$_{35}$N: C, 81.42; H, 13.31; N, 5.28. Found: C, 81.37, 81.48; H, 13.15, 13.24; N, 5.29, 5.35.

N-Phenyl-3,5-diethyl-2-propyl-pyridinium Iodide, III.—A turbid mixture containing 2.55 g. (0.01 mole) of compound I, 50 ml. of alcohol, 10 ml. of acetic acid, and 10 ml. of 25% potassium iodide was titrated rapidly with 1 N potassium iodate. Only a small amount of the iodate was required to produce a clear solution. An iodine color was apparent when 17.2 ml. had been added. This color deepened during a period of ten minutes and required 0.1 ml. of 0.1 N thiosulfate solution to reduce it to the color of the iodine end-point. The sample thus is equivalent to 17.1 ml. of the N iodate solution which is 85.5% of the amount (20.0 ml.) required for the reaction

$$C_{18}H_{25}N + I_2 \longrightarrow C_{18}H_{24}NI + HI$$
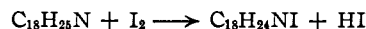
The conditions of titration were investigated in a preliminary way. The reaction is favored by an excess of iodide ion and can be conducted with alcoholic iodine solution instead of iodate solution. Acetic acid is a satisfactory acid and may be used in considerable excess while hydrochloric acid has a strongly inhibitory action. The solutions from four such titrations were evaporated at reduced pressure until all of the alcohol and most of the acetic acid were removed. Excess 48% sodium hydroxide then was added. This precipitated an oil which crystallized on standing overnight. The crystals were dissolved in a little butanol and the solution filtered. The filtrate after being diluted with one liter of cold ether yielded 12.5 g. of brown solid, m. p. 90–95°. This solid was dissolved again in butanol and precipitated with ether to provide a crop of light brown crystals, m. p. 105–106°. The yield of these amounted to 11.5 g. or 75% of the theoretical amount. Solution in dry alcohol and fractional precipitation with ether gave bright yellow plates, m. p. 107–108°.

Anal. Calcd. for C$_{18}$H$_{24}$NI: C, 56.66; H, 6.35; N, 3.67; I, 33.33. Found: C, 56.76, 56.71; H, 6.37, 6.38; N, 3.79, 3.73; I, 33.34, 33.26.

The iodide can be produced in good yield by the action of sulfur on compound I in acetic acid solution followed by the addition of sodium or potassium iodide and working up the mixture as described above.

The iodide is very soluble in water, alcohols, ketones, esters and acetic acid. It is insoluble in hydrocarbons such as benzene and hexane. Three liquid phase systems are formed with benzene and water and a solid addition compound is produced with carbon tetrachloride which is sometimes useful in recovering the salt from aqueous solutions.

The iodine content is quantitatively precipitated with aqueous 0.1 N silver nitrate. The iodide does not react at moderate temperature with maleic anhydride or with hydrogen over Raney nickel. With sulfur no reaction occurs unless a sulfur "acceptor" is present. Suitable "acceptors" are unsaturated compounds such as styrene or rubber. Reaction also occurs readily with sulfur in the presence of alkali.

N-Phenyl-3,5-diethyl-6 or 4-methyl-2-propyl-1,4-dihydropyridine.—One reaction indicating the quaternary nature of the iodide III is the Freund reaction with excess methylmagnesium iodide in ether solution. The product of this reaction, which was obtained in 82% yield, had a refractive index of 1.5510^{20}D and distilled at 105–106° at 0.2 mm. The ultraviolet absorption spectrum of this compound, given in Fig. 1, is similar to that of compound I. The methyl group must be attached to either the 6 or the 4-position of the dihydropyridine ring.

Anal. Calcd. for $C_{19}H_{27}N$: C, 84.69; H, 10.10; N, 5.20. Found: C, 84.44, 84.39; H, 9.83, 9.89; N, 5.54, 5.48.

The reaction of compound I (0.1 mole) with sulfur (0.1 atom) during twenty-four hours on the steam-bath formed hydrogen sulfide and a semicrystalline black mass. Extraction with benzene yielded about 1 g. of nearly colorless crystals which melted at 156–157° after solution in a mixture of acetone and alcohol followed by precipitation with ether.

Anal. Calcd. for $C_{18}H_{25}NSO_4$: C, 61.50; H, 7.18; N, 3.99. Found: C, 61.43, 61.51; H, 7.17, 7.26; N, 4.14, 4.07.

This compound was identified as the acid sulfate corresponding to the quaternary iodide III described above from which it also was prepared by addition of sulfuric acid and distilling off hydroiodic acid at reduced pressure. The product so produced melted at 156–157° alone or when mixed with the analyzed sample. This compound was also secured by shaking I in acetic acid solution with reduced platinum oxide and adding sulfuric acid to the mixture when the evolution of hydrogen had ceased. Most of the acetic acid was evaporated at reduced pressure and the last traces removed by addition of sodium carbonate. The acid sulfate was extracted with warm acetone and precipitated by the addition of ether.

The benzene filtrate from the acid sulfate was evaporated and the resulting solid crystallized twice from alcohol. The yield amounted to 8 g. of bright yellow crystals melting at 127°. The melted product resolidified and then melted again at 132°.

Anal. Calcd. for $C_{18}H_{23}NS$: C, 75.74; H, 8.13; N, 4.91; S, 11.22. Found: C, 75.29, 75.24; H, 8.14, 8.05; N, 5.12, 5.07; S, 11.53, 11.60.

The structure of this compound is believed to be N-phenyl-3,5-diethyl-2-propyl-6-thiopyridone formed by the oxidation of a pseudo form of the pyridinium hydrosulfide.

The Reaction of I with Hydrochloric Acid.—The rate of reaction depends primarily on the concentration of the acid and on the temperature. In the cold and with dilute acid the rate is very slow. A mixture of 12.5 g. of I and 10 g. of 36.5% hydrochloric acid was shaken for twenty minutes at 20°. Gradually solution occurred as might be expected of a vinylamine. The oil precipitated by the addition of caustic to this solution was I. A similar mixture of acid and I was refluxed at 116° for two hours. The product was water soluble. It was neutralized with 6 g.

of sodium carbonate. Then 100 ml. of hexane was added and the mixture shaken with small portions of water until free of water soluble substances. The hexane layer was dried over potassium carbonate and distilled. After the hexane 2.5 g. of light yellow oil distilled at 120–125° at 0.7 mm. It had a refractive index, n^{20}D of 1.5523.

Anal. Calcd. for $C_{18}H_{27}N$: C, 83.98; H, 10.58; N, 5.44. Found: C, 83.82, 83.60; H, 10.55, 10.53; N, 5.43, 5.47.

The analysis and refractive index are in agreement with the supposition that this product is identical with the N-phenyl-3,5-diethyl-2-propyl-1,4,5,6-tetrahydropyridine secured by the hydrogenation of compound I. The substantial identity of the two $C_{18}H_{27}N$ samples finally was established by their ultraviolet absorption spectra. The water layer on evaporation at reduced pressure in the presence of 2.5 g. of potassium iodide yielded a mixture of salts which was extracted with butanol. On addition of ether to the butanol extract there was obtained a crop of yellow crystals which after solution and precipitation melted at 105–107° alone or when mixed with N-phenyl-3,5-diethyl-2-propylpyridinium iodide. The yield was 4.5 g.

Reaction with Maleic Anhydride.—A mixture of 5.1 g. of compound I and 1.8 g. of maleic anhydride was stirred with a thermometer. The immediate formation of a red colored product occurred, usually followed by a temperature rise from 30 to 50° during about twenty minutes. In case the temperature did not rise spontaneously the mixture was heated to about 50°. Reaction then became rapid and it was necessary to cool the mixture in order to keep the temperature from rising above about 60°. During about ten minutes longer a solid began to separate and it soon became impossible to stir the mixture. The temperature was allowed to fall and the mixture was allowed to stand overnight. It melted at 112 to 115°. The product was powdered and extracted with 50 ml. of hexane. The residue melted at 115–117° and weighed 4.7 g. This weight represents a yield of 78%. The melting point was raised to 119–120° by recrystallizing from acetone or alcohol and the product was then colorless.

Anal. Calcd. for $C_{22}H_{27}NO_3$: C, 74.75; H, 7.70; N, 3.96. Found: C, 74.64, 74.70; H, 7.71, 7.74; N, 4.02, 4.00.

Occasionally while working up the reaction products of maleic anhydride with impure samples, a second compound was isolated. This was a white solid melting with decomposition at 153° when recrystallized from alcohol.

Anal. Calcd. for $C_{22}H_{29}NO_4$: C, 71.12; H, 7.87; N, 3.77. Found: C, 71.05, 71.01; H, 8.06, 8.00; N, 3.79, 3.38.

This compound, which is the hydrate of the adduct, melts with almost quantitative loss of water to form the original adduct.

Summary

1. A main product of the condensation of excess butyraldehyde with aniline in the presence of weak acids has been found to be N-phenyl-3,5-diethyl-2-propyl-1,4-dihydropyridine.

2. The reactions of the dihydropyridine which were investigated include pyrolysis, hydrogenation, dehydrogenation, oxidation, reaction with sulfur, vinylamine type behavior toward acids,

and reaction with maleic anhydride. These reactions led to the isolation of some nine new compounds.

3. Vinylamine behavior may be recognized as an important property of some of the new compounds, especially in connection with their ultraviolet absorption spectra.

AKRON, OHIO   RECEIVED OCTOBER 10, 1947

# The Synthesis of Imidazolines from 1,2-Diamines and Carboxylic Acids

BY J. L. RIEBSOMER

Chitwood and Reid[2] prepared a series of 2-alkyl-2-imidazolines by distilling or heating the appropriate diacylethylenediamine with sodium, magnesium, zinc, magnesium oxide or sodium hydroxide. Thus 2-methyl-2-imidazoline was produced in 68% yield when diacetylethylenediamine was heated at 270° with magnesium. The yields were less satisfactory with the other inorganic reagents. When ethylenediamine and acetic acid were heated 2-methyl-2-imidazoline was produced in 19% yield and when monoacetylethylenediamine hydrochloride was heated with sodium hydroxide a 26% yield of the imidazoline formed. Hofmann[3] prepared the same imidazoline upon distillation of a sodium acetate and ethylenediamine hydrochloride mixture.

Hill and Aspinall[4] prepared a series of 2-alkyl and 2-aryl substituted imidazolines by heating monoacylethylenediamines.

The technique employed for the preparation of the imidazolines reported here was to add benzene to a mixture of the 1,2-diamine and carboxylic acid and to distil the benzene through a four-foot packed column. As the benzene distilled, water formed from the reaction was carried out as an azeotropic mixture. The column was equipped with a suitable head so that the benzene returned and the water was separated. It might have been anticipated that the imidazoline would be the only product formed by this process. In nearly all instances studied, however, a higher boiling substance was produced along with the imidazoline. Indeed in some instances the higher boiling product was formed almost exclusively. The course of

most of these reactions may be formulated as
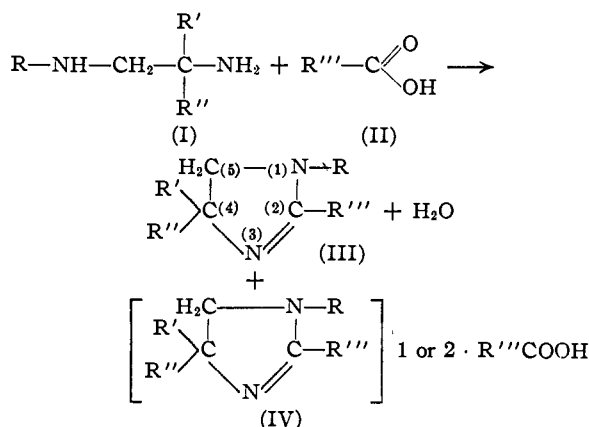
R' and R'' ' were H, alkyl, or aryl. R' and R'' were H or alkyl. The most complete study was made in the case in which R was isopropyl and R' and R'' were methyl. In this instance R'' was H, alkyl groups from CH_3 to $C_{17}H_{35}$ or aryl.

A few exceptions to the general reaction were noted. When 2,3-dimethyl-2,3-butanediamine reacted with acetic acid none of the expected compounds (III) or (IV) were isolated but a low yield of the diacetate was found. Likewise 1,2-butanediamine and acetic acid reacted to form the diacetyl derivative of the amine along with the imidazoline.

A possible mechanism to account for the formation of the imidazolines by this method may be represented as follows:
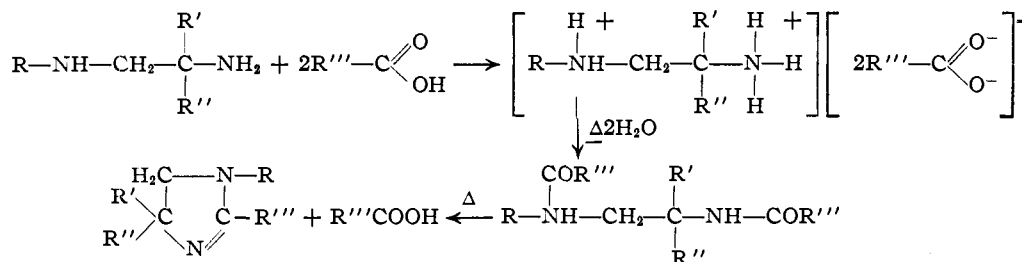
(1) Most of this work was completed while the author was at DePauw University, Greencastle, Indiana.

(2) Chitwood and Reid, THIS JOURNAL, 57, 2424 (1935).

(3) Hofmann, Ber., 21, 2332 (1888).

(4) Hill and Aspinall, THIS JOURNAL, 61, 822 (1939).

The evidence for the existence of the compounds of type (III) seems to be entirely satisfactory. The analyses, neutral equivalents and mode of synthesis all point to the same conclusion.