purified by vacuum distillation. The fraction distilling 150–168° at 0.15 mm. was collected as product.

The crude dihydro-6-thioctic acid, wt. 10.5 g. (0.0505 mole), was transferred to a 500-ml. erlenmeyer flask with a few ml. of 3A ethanol and 6.5 g. (0.0505 mole) of potassium carbonate was added. One hundred fifty ml. of water was added, and the *p*H of the resulting solution was adjusted to 7 with a few drops of hydrochloric acid. After the addition of 2 ml. of 1% ferric chloride, the resulting deeply colored solution was transferred to a 250-ml. graduate and a rapid stream of oxygen was bubbled through the solution from a sintered glass inlet tube until the color changed to pale yellow (20 minutes). The solution was acidified and the product extracted with two 150-ml. portions of chloroform. The combined chloroform extracts were dried over sodium sulfate and distilled. The residue, which crystallized, was vacuum distilled. The fraction distilling 150° at 0.1 mm. and crystallizing in the receiver was collected as product. This crude product weighed 6.5 g. and m.p. 58°. A small amount of additional product was obtained by stirring the forerun with cold cyclohexane. Recrystallization of the combined products from cyclohexane gave 5.4 g. of bright yellow crystals m.p. 61°. An additional 1.0 g. of crystals was obtained by concentrating the mother liquors, bringing the total yield to 6.4 g. (0.031 mole) or 30.1% from the ethyl 8-acetylthio-6-hydroxyoctanoate.

Anal. Calcd. for $C_8H_{14}O_2S_2$: neut. equiv., 206; C, 46.57; H, 6.84; S, 31.08. Found: neut. equiv., 202; C, 46.96; H, 6.92; S, 30.68; mol. wt. (Rast camphor), 215.

Acknowledgments.—The authors are indebted to Dr. R. C. Gore and Mr. W. Fulmor for the infrared analyses and to Mr. L. Brancone and staff for the microanalyses.

PEARL RIVER, NEW YORK

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF ROCHESTER]

A Synthesis of Quinolizinium and Dehydroquinolizinium Derivatives[1]

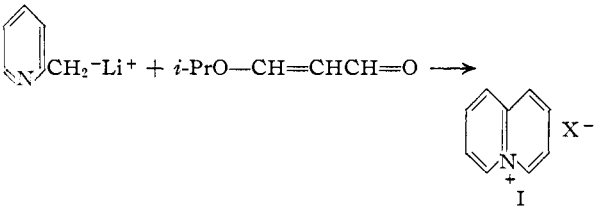
BY V. BOEKELHEIDE AND WALTER G. GALL[2]

RECEIVED AUGUST 11, 1953

A practical preparation of the quinolizinium and dehydroquinolizinium ions is reported. The dehydroquinolizinium ion, which is the parent nucleus of many alkaloids, has been subjected to chemical and spectral studies which substantiate its assigned structure. An attempt to obtain quinolizine, as the free base, gave only 1-(α-pyridyl)-1,3-butadiene.

The dehydroquinolizinium ion (I) represents the nitrogen analog of naphthalene in which the nitrogen atom occurs at a bridgehead position. In contrast to quinoline and isoquinoline, the other two simple nitrogen analogs of naphthalene, the chemistry of the dehydroquinolizinium ion has been little studied and knowledge regarding this ion has been gained almost entirely from investigations of alkaloids containing this nucleus as part of a fairly complex structure. Among the alkaloids, the dehydroquinolizinium nucleus probably occurs most widely as its dihydro derivative, the quinolizinium ion. For example, the dibenzoquinolizinium ion is the parent structure for the various berberine alkaloids,[3-6] palmatine,[7] columbamine,[8] jatrorrhizine,[9] coptisine,[10] worenine,[11] dehydrocorydaline[12] and dehydrothalictrifoline.[13] Here again, although methods for the synthesis of dibenzoquinolizinium derivatives are well described,[7,14] the preparation of the simple quinolizinium ion has not previously been reported.

Actually, the occurrence among alkaloids of the fully unsaturated dehydroquinolizinium ion was first recognized when Woodward and Witkop proposed that sempervirine contained this nucleus.[15] This was immediately confirmed by Woodward and McLamore's synthesis of sempervirine methochloride.[16] Recently, Schwyzer has suggested on the basis of spectral evidence that flavocorynanthyrine also contains the dehydroquinolizinium nucleus.[17]



I

Of the syntheses previously investigated the most promising one for preparing the dehydroquinolizinium ion itself would appear to be that of Woodward and McLamore.[16] For example, by this method these authors were able to prepare 2,3-tetramethylenedehydroquinolizinium picrate in 51% yield. However, when 2-picolyllithium was treated with β-isopropoxyacrolein following this general method as shown below, Beaman found that salts of the dehydroquinolizinium ion could be isolated only with great difficulty and in very poor yield.[18] Since the preparation of the necessary starting material, β-isopropoxyacrolein, is tedious and proceeds in very poor yield, this approach to

(1) Supported in part by the Office of Ordnance Research, Army Ordnance Contract No. DA-30-115-O.R. D-421.

(2) National Science Foundation Predoctoral Fellow, 1952–1953.

(3) W. H. Perkin, Jr., and J. H. Ray, *J. Chem. Soc.*, **127**, 740 (1925).

(4) R. D. Haworth, W. H. Perkin, Jr., and J. Rankin, *ibid.*, **125**, 1686 (1924).

(5) W. H. Perkin, Jr., *ibid.*, **113**, 492 (1918).

(6) J. S. Buck and W. H. Perkin, Jr., *ibid.*, **125**, 1675 (1924).

(7) R. D. Haworth, J. B. Koepfli and W. H. Perkin, Jr., *ibid.*, 548 (1927).

(8) E. Späth and E. Mosettig, *Ber.*, **60**, 383 (1927).

(9) E. Späth and E. Mosettig, *ibid.*, **58**, 2133 (1925).

(10) E. Späth and K. Posega, *ibid.*, **62**, 1029 (1929).

(11) T. A. Henry, "The Plant Alkaloids," 4th Edition, Blakiston Co., Philadelphia, Penna., 1949, p. 344.

(12) J. B. Koepfli and W. H. Perkin, Jr., *J. Chem. Soc.*, 2989 (1928).

(13) R. F. Manske, *Can. J. Research*, **21B**, 111 (1943).

(14) S. Sugasawa and N. Sugimoto, *Ber.*, **72**, 977 (1939).

(15) R. B. Woodward and B. Witkop, THIS JOURNAL, **71**, 379 (1949).

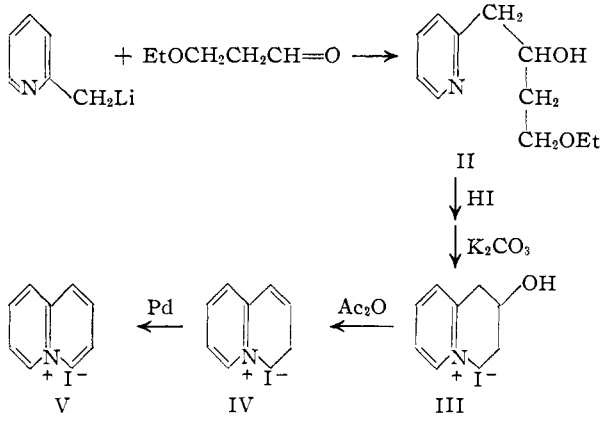
(16) R. B. Woodward and W. M. McLamore, *ibid.*, **71**, 379 (1949).

(17) R. Schwyzer, *Helv. Chim. Acta*, **35**, 867 (1952).

(18) A. G. Beaman, Ph.D. Thesis, Harvard University, 1951. We are much indebted to Professor Woodward for his kindness in sending us a copy of this thesis, since it has permitted us to make a comparison of our products with those prepared previously by Woodward and Beaman.

the synthesis of the dehydroquinolizinium ion would appear, at present, to have serious limitations.

Incidental to another study of quinolizine derivatives, we recently discovered a method which is suitable for preparing dehydroquinolizinium iodide in appreciable quantities. As shown in the reaction scheme below, when 2-picolyllithium was treated with β-ethoxypropionaldehyde, the corresponding carbinol II was produced in good yield. Treatment of II with hydriodic acid followed by neutralization with alkali, readily yielded the cyclic ammonium iodide III. After a number of trials, it was found that dehydration of III could be accomplished in quantitative yield by means of acetic anhydride containing a drop of sulfuric acid. The resulting quinolizinium iodide IV underwent dehydrogenation both catalytically and with chloranil to give the desired dehydroquinolizinium iodide V. Although the yields obtained in the final dehydrogenation step have thus far been low, this is not a serious handicap in view of the ease with which IV can be obtained.



The ionic nature of the dehydroquinolizinium iodide was shown by its solubility in water and by its easy conversion to the corresponding picrate and perchlorate salts. The extent of unsaturation and the nature of the ring system present were demonstrated by the fact that, on catalytic hydrogenation, dehydroquinolizinium iodide absorbed five moles of hydrogen and gave quinolizidine (VIII), as its hydroiodide salt. Therefore, there can be little doubt regarding the correctness of the assigned structure.

As shown in Fig. 1, the ultraviolet absorption spectra of the dehydroquinolizinium iodide and perchlorate salts are identical. The absorption due to the dehydroquinolizinium ion is very characteristic, its aqueous solution showing absorption maxima at the following wave lengths: 226 (log ε 4.25), 272 (3.42), 283 (3.47), 310 (4.03), 316.5 (3.98) and 323.5 mμ (4.23). The spectrum of dehydroquinolizinium picrate, although similar, has higher values for the extinction coefficients throughout this region due to absorption by the picrate anion. It is of interest that N-methylisoquinolinium iodide shows absorption in the same general regions but lacks the fine structure of the more symmetrical dehydroquinolizinium ion. The absorption spectra given by Woodward and Beaman[18] for the dehydroquinolizinium perchlorate and picrate salts are essentially identical with those given here and confirm the identity of the samples produced by the two different preparations.

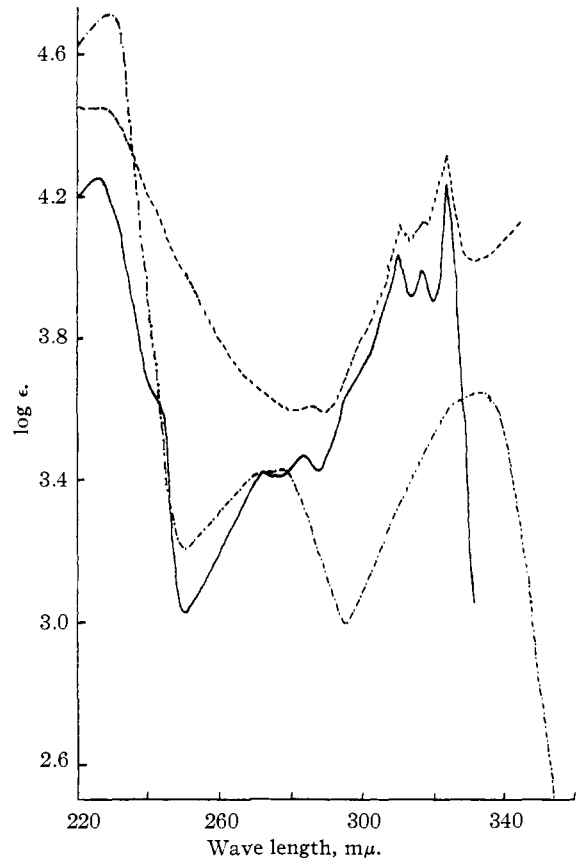


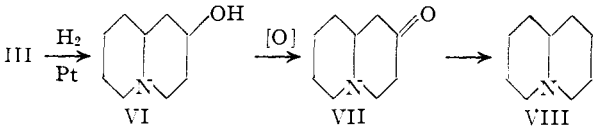
Fig. 1.—Ultraviolet absorption spectra in aqueous solution of dehydroquinolizinium iodide, —; dehydroquinolizinium picrate, – – –; and N-methylisoquinolinium iodide, ··· The spectrum of dehydroquinolizinium perchlorate is identical with that of dehydroquinolizinium iodide.

From a consideration of the reaction scheme employed for the synthesis of dehydroquinolizinium iodide, it is not obvious that the intermediate carbinol III should have the structure assigned. It would seem quite possible that during the treatment of II with hydroiodic acid to effect cleavage of the ether group the secondary carbinol might also be affected. The fact that the resultant product had the composition required for III could readily be explained by alternate formulations. Therefore, in order to establish its structure, III was converted by hydrogenation over Adams catalyst to the corresponding 2-hydroxyquinolizidine VI. Insufficient reference compounds were available to permit identification at this stage, and so the 2-hydroxyquinolizidine was oxidized in turn to the corresponding 2-quinolizidone (VII). Fortunately, the picrates of the 1-, 2- and 3-quinolizidones are all known and have rather different melting points.[19] Thus, the close agreement between the melting point reported for the picrate of 2-quinolizidone[20]

(19) The other possible isomer, 4-quinolizidone, does not form a stable picrate.

(20) G. R. Clemo, W. McG. Morgan and Raper, *J. Chem. Soc.*, 1744 (1935).

and that found for the picrate of our product is good evidence that our product was actually 2 quinolizidone. As additional evidence, our sample of 2-quinolizidone was reduced by the Wolff–Kishner procedure to quinolizidine (VIII), identified as its picrate derivative.



The dehydration of III with acetic anhydride has been assumed to yield 3H,4H-quinolizinium iodide (IV). This assignment is a logical one and best explains the marked shift to longer wave lengths in the ultraviolet absorption spectrum (see Fig. 2) which occurs on going from III to IV. There are, of course, many other structures which can be written for quinolizinium iodide in which the two "extra" hydrogens are variously placed about the ring. However, none of these other isomers would be expected to have the ultraviolet absorption spectrum observed.

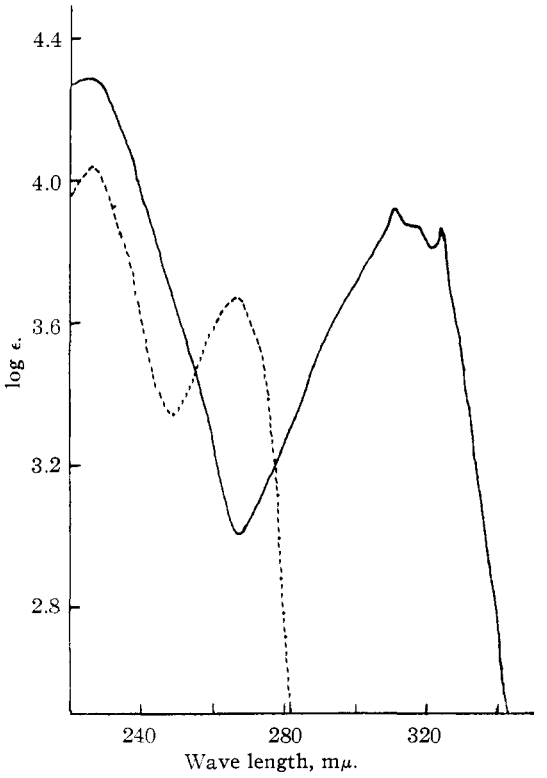
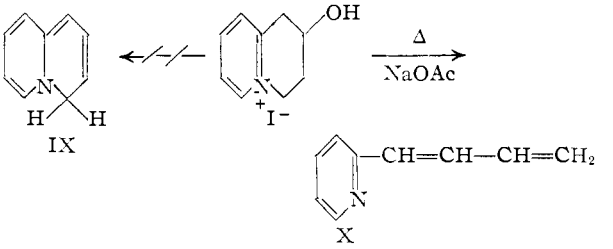


Fig. 2.—Ultraviolet absorption spectra in aqueous solution of 3H,4H-quinolizinium iodide (IV, —) and 2-hydroxy-1,2-dihydro-3H,4H-quinolizinium iodide (III, ---).

Quinolizine (IX), itself, has never been prepared. The claim of Diels and Alder that quinolizine was produced during their degradation studies on adducts of pyridine and acetylenedicarboxylic ester,[21] was later retracted by Diels and Schrum who demonstrated that the compound obtained was actually an isomer, 3-methylindolizine.[22] Because quinolizine might represent an interesting tautomeric system (4H-quinolizine (IX) is only one of the several possible structures which can be written for the molecule), it was of interest to attempt its synthesis utilizing intermediates from the above reaction scheme. The most noteworthy of these attempts was that using III as starting material.

As illustrated in the reaction scheme below, it was hoped that distillation of III from mild base would effect dehydration and removal of hydrogen iodide to give quinolizine (IX). Although the resulting product possessed the correct composition for quinolizine, it soon became evident that the material produced was the isomeric 1-(α-pyridyl)-1,3-butadiene (X). The proof that the compound was indeed 1-(α-pyridyl)-1,3-butadiene rests upon the following observations: (1) its infrared spectrum has absorption peaks at 9.93 and 10.98 μ, indicating a terminal methylene group of the type R—CH=CH_2,[23] (2) on ozonolysis it gave formaldehyde in 29% yield, and (3) on catalytic hydrogenation it absorbed five moles of hydrogen to give 2-*n*-butylpiperidine, identical with an authentic sample. The only previous synthesis reported for 1-(α-pyridyl)-1,3-butadiene is that given by Woodward and Beaman,[18] and the properties which they found for the compound are in good agreement with those of our sample.



Investigations on the chemistry of the dehydroquinolizinium ion and its simple derivatives are being continued.

Experimental[24]

4-Ethoxy-1-(α-pyridyl)-2-butanol (II).—This was prepared following the same procedure used by Walter for preparing 1-(α-pyridyl)-2-propanol.[25] From 50.0 g. of β-ethoxypropionaldehyde there was obtained 44.5 g. (57%) of a yellow oil, b.p. 129–131° at 5.5 mm. This was purified by heating it on a steam-bath for one hour with twice its weight of anhydrous oxalic acid under 20 mm. pressure. The product recovered from this treatment distilled to give a colorless oil (94% recovery); b.p. 130° at 5.5 mm., $n^{20}D$ 1.5060.

Anal. Calcd. for $C_{11}H_{17}NO_2$: C, 67.67; H, 8.78. Found: C, 68.16; H, 8.77.

2-Hydroxy-1,2-dihydro-3H,4H-quinolizinium Iodide (III).—A solution of 15.0 g. of 4-ethoxy-1-(α-pyridyl)-2-butanol in 120 ml. of hydriodic acid was boiled under reflux for four hours.[26] Evaporation of the solution under reduced pressure gave about 30 g. of a light yellow gum. This was dissolved in 100 ml. of water, 100 ml. of chloroform was added and then a 10% aqueous potassium carbonate solution was slowly added with shaking until most of the color

(21) O. Diels and K. Alder, *Ann.*, **498**, 16 (1932); **505**, 103 (1933).
(22) O. Diels and H. Schrum, *ibid.*, **530**, 68 (1937).
(23) N. Sheppard and D. M. Simpson, *Quart. Revs.*, **6**, 1 (1952).
(24) Analyses by Miss Claire King and Miss Viola Williams. All melting points are corrected.
(25) L. A. Walter, *Org. Syntheses*, **23**, 83 (1943).
(26) For reasons unknown, the reaction proceeded in much better yield with J. T. Baker C.P. hydriodic acid than with the other samples of hydriodic acid available to us.

was transferred to the organic layer. The organic layer was removed at this point and 100 ml. of fresh chloroform was added. The addition of the potassium carbonate was then continued dropwise until it no longer gave a transient cloudy precipitate. The chloroform extracts were then combined and warmed on a steam-bath for five minutes. After the chloroform solution had been allowed to stand overnight at room temperature to complete the reaction, the crystals which separated were removed and recrystallized from absolute ethanol containing 5% by volume of ethyl acetate. This gave 13.6 g. (61%) of white plates with m.p. 162–162.5°.

Anal. Calcd. for $C_9H_{12}NOI$: C, 39.01; H, 4.37. Found: C, 39.05; H, 4.57.

3H,4H-Quinolizinium Iodide (IV).—A mixture containing 6.0 g. of 2-hydroxy-1,2-dihydro-3H,4H-quinolizinium iodide (III), 19 ml. of acetic anhydride and one drop of concentrated sulfuric acid was boiled under reflux for five minutes. After the solution had cooled, the precipitated solid was removed and triturated with 25 ml. of ethyl acetate. Recrystallization of the resulting solid from absolute ethanol containing a drop of hydriodic acid gave 5.5 g. (98%) of yellow crystals, m.p. 183–186° dec.

Anal. Calcd. for $C_9H_{10}NI$: C, 41.72; H, 3.89. Found: C, 41.92; H, 4.04.

Dehydroquinolizinium Iodide (V).—A mixture containing 830 mg. of 3H,4H-quinolizinium iodide, 830 mg. of chloranil and 20 ml. of *n*-butyl alcohol was boiled under reflux for one hour. After the mixture had cooled, it was extracted three times with 25-ml. portions of water. Evaporation of the aqueous extracts under reduced pressure gave 80 mg. of a crystalline residue, which was recrystallized four times from an ethanol–ethyl acetate mixture. This gave white crystals that decomposed at 220–230° (indefinite).

Anal. Calcd. for C_9H_8NI: C, 42.05; H, 3.14. Found: C, 42.49; H, 3.36.

Dehydroquinolizinium Picrate.—A mixture consisting of 100 mg. of 3H,4H-quinolizinium iodide, 20 mg. of a 10% palladium-on-charcoal catalyst,[27] and 8 ml. of ethanol was boiled under reflux for one hour. After removal of the catalyst, the filtrate was concentrated and then treated with ethanolic picric acid. The resulting solid was recrystallized three times from ethanol to give 20 mg. (15%) of yellow needles, m.p. 180–181° (Beaman[18] gives 181–181.5°). Although this is typical of the dehydrogenation experiments thus far investigated, we do not feel that optimum conditions have been realized.

Anal. Calcd. for $C_{15}H_{10}N_4O_7$: C, 50.28; H, 2.81. Found: C, 50.52; H, 3.35.

Dehydroquinolizinium Perchlorate.—A solution of 110 mg. of dehydroquinolizinium picrate in 15 ml. of ethanol was passed over a column of Amberlite I.R.A-400 resin which previously had been treated with aqueous perchloric acid. The eluate was collected and concentrated. Recrystallization of the residue from ethanol gave feathery white needles, m.p. 285–288° (Beaman[18] gives 289–289.6°).

Anal. Calcd. for $C_9H_8NO_4Cl$: C, 47.07; H, 3.51. Found: C, 46.82; H, 3.70.

Hydrogenation of Dehydroquinolizinium Iodide (V).—A mixture of 32 mg. of dehydroquinolizinium iodide, 10 mg. of Adams catalyst and 5 ml. of ethanol was subjected to hydrogenation at room temperature and atmospheric pressure using a calibrated microhydrogenation apparatus. The theoretical quantity of hydrogen for 5 molar equivalents was quickly absorbed. Removal of the catalyst and solvent gave a solid residue. This, on recrystallization from an ethanol–ether mixture, gave white crystals, m.p. 189–192°, softening at 178°. An authentic sample of **quinolizidine hydriodide**, prepared from quinolizidine,[28] showed the same melting point behavior as did mixtures of the two samples.

Anal. Calcd. for $C_9H_{18}NI$: C, 40.46; H, 6.79. Found: C, 40.09; H, 6.89.

A sample of the reduction product was converted to the picrate which, after recrystallization from ethanol, melted at 196–198°, both alone and on admixture of an authentic sample of quinolizidine picrate.[28]

(27) R. Mozingo, *Org. Syntheses*, **26**, 78 (1946).

(28) V. Boekelheide and S. Rothchild, THIS JOURNAL, **71**, 879 (1949).

Hydrogenation of 3H,4H-Quinolizinium Iodide (IV).—When a mixture containing 600 mg. of 3H,4H-quinolizinium iodide, 200 mg. of Adams catalyst and 15 ml. of ethanol was subjected to hydrogenation as before, it absorbed four molar equivalents of hydrogen. The reduction product was isolated in high yield as its hydroiodide and picrate salts and these were shown to be identical with the corresponding salts of quinolizidine by the method of mixed melting points.

2-Hydroxyquinolizidine (VI).—A mixture consisting of 5.54 g. of 2-hydroxy-1,2-dihydro-3H,4H-quinolizinium iodide, 50 ml. of ethanol and 500 mg. of Adams catalyst was subjected to hydrogenation at room temperature and atmospheric pressure. Three molar equivalents of hydrogen was absorbed in three hours. After removal of the catalyst and solvent, the residue was dissolved in 10 ml. of water. The aqueous solution was then made alkaline with potassium carbonate and extracted with chloroform. Concentration of the chloroform gave a yellow solid which, on repeated sublimation, gave 2.4 g. of large white crystals, m.p. 92°. This must represent one of the possible racemates of 2-hydroxyquinolizidine.

Anal. Calcd. for $C_9H_{17}NO$: C, 60.63; H, 11.04. Found: C, 70.09; H, 11.17.

Oxidation of VI to 2-Quinolizidone (VII).—A solution containing 865 mg. of 2-hydroxyquinolizidine (VI), 1.20 g. of sodium dichromate and 1.0 g. of sulfuric acid in 6 ml. of ether was warmed on a steam-bath for 25 minutes. The mixture was then made alkaline and extracted with chloroform. After the chloroform extract was dried, it was concentrated to give 710 mg. of an oily residue. Treatment of a portion of this residue with ethanolic picric acid followed by several recrystallizations from ethanol gave small yellow crystals, m.p. 208–210°. The melting point of 2-quinolizidone picrate as recorded by Clemo, Morgan and Raper[29] is 211°. Leonard, Swann and Figueras[29] give 167–168° as the melting point of 1-quinolizidone picrate, and Leonard and Pines[30] give 180–182° for the 3-quinolizidone picrate.

The Wolff–Kishner reduction of 2-quinolizidone was carried out according to the Huang-Minlon modification.[31] A mixture of 460 mg. of the crude ketone, 0.5 ml. of hydrazine hydrate, 0.63 g. of potassium hydroxide and 5 ml. of triethyleneglycol was heated at 140–150° for one hour. Steam distillation of the mixture gave an oil which was converted to the corresponding picrate. This, after recrystallization from ethanol, was obtained as yellow crystals, m.p. 196–198°, alone or mixed with an authentic sample of quinolizidine picrate.[28]

The Conversion of III to 1-(α-Pyridyl)-1,3-butadiene (X).—An intimate mixture of 1.5 g. of 2-hydroxy-1,2-dihydro-3H,4H-quinolizinium iodide (III) and 8 g. of powdered anhydrous sodium acetate (or calcium oxide) under nitrogen was heated under reduced pressure (4 mm.) until no further oil distilled. The reddish-orange oil collected was very unstable and polymerized with great ease. On redistillation in a molecular still it gave 180 mg. of a pale yellow oil, b.p. (pot temperature) 70° at 1 mm.

Anal. Calcd. for C_9H_9N: C, 82.40; H, 6.92. Found: C, 82.08; H, 7.25.

The picrate of 1-(α-pyridyl)-1,3-butadiene was prepared in ethanol and obtained as yellow crystals, m.p. 146.5–147° (Beaman[18] gives 148.2–148.9°).

Anal. Calcd. for $C_{15}H_{12}N_4O_7$: C, 50.00; H, 3.36. Found: C, 49.95; H, 3.69.

Ozonolysis of 1-(α-pyridyl)-1,3-butadiene was carried out in the usual fashion using carbon tetrachloride as solvent. From 70 mg. of 1-(α-pyridyl)-1,3-butadiene there was isolated 45 mg. (29%) of formaldehyde as its dimedon derivative, m.p. 190.5–191° (lit.[32] gives 191–191.5°). The melting point of this sample was not depressed by admixture of an authentic sample of the dimedon derivative of formaldehyde.

Hydrogenation of X to Give 2-*n*-Butylpiperidine.—A mixture of 260 mg. of 1-(α-pyridyl)-1,3-butadiene, 50 mg. of Adams catalyst, 0.5 ml. of concd. hydrochloric acid and 15

(29) N. J. Leonard, S. Swann, Jr., and J. Figueras, Jr., *ibid.*, **74**, 4620 (1952).

(30) N. J. Leonard and S. H. Pines, *ibid.*, **72**, 4931 (1950).

(31) Huang-Minlon, *ibid.*, **68**, 2487 (1946).

(32) E. C. Horning and M. G. Horning, *J. Org. Chem.*, **11**, 96 (1946).

ml. of ethanol was subjected to hydrogenation at room temperature and atmospheric pressure. Approximately 5 moles of hydrogen was absorbed. After removal of the catalyst and solvent, the solid residue was recrystallized from an ethanol-ethyl acetate mixture to give 250 mg. (75%) of white crystals, m.p. 180–183.5°. That this was the hydrochloride of 2-*n*-butylpiperidine was shown by the fact that admixture of an authentic sample of the hydrochloride of 2-*n*-butylpiperidine[22] caused no depression of melting point. As further evidence of the identity of the reduction product, the N-*p*-toluenesulfonyl derivative (m.p. 40–41°) and mercurichloride derivative (m.p. 137–140° dec.) were prepared and found to show no depression of melting point on admixture of samples of these derivatives from authentic 2-*n*-butylpiperidine.

ROCHESTER, N. Y.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF TORONTO]

Hydration of 2-Nitriminoimidazolidine

BY M. W. KIRKWOOD AND GEORGE F WRIGHT

RECEIVED NOVEMBER 25, 1953

The product obtained when nitriminoimidazolidine is decomposed by aqueous alkali has been treated with acetic anhydride and with nitrous acid. One cannot distinguish between 3-β-aminoethylnitrourea or 2-hydroxy-2-nitraminoimidazolidine as the structure of the nitriminoimidazolidine hydration product on the basis of these reactions, and must conclude that either of such ring-chain isomers may be present depending upon the environment. The same behavior is observed upon examination of the acetylation product. It is suggested that, for the purpose of nomenclature, the structure of these ring-chain isomers be assigned in consideration of behavior during potentiometric titration.

It has been shown by potentiometric titration that when 2-nitriminoimidazolidine is dissolved in dilute alkali it is converted slowly to the sodium salt of 2-nitramino-Δ^2-imidazoline.[1] At the same time, although at a slower rate, the hydration product of these tautomers is formed. Two possible structures may be assigned to this hydration product. Barton, Hall and Wright specified these structures as 3-β-aminoethyl-1-nitrourea (I) and 2-hydroxy-2-nitraminoimidazolidine (II) but were unable to discriminate on the basis of their experimental work.

It has been postulated,[2] and more recently proved,[3] that ring-chain isomerism is prevalent among β-substituted-3-ethylnitroureas or 3-ethyl nitroguanidines and their cyclic (imidazolidine) forms. Furthermore, this isomerism is sensitive to reaction environment. The present study seems further to exemplify this same behavior.

When the hydrated nitriminoimidazolidine (I or II) is dissolved in alkali and potentiometrically titrated with acid, it displays a dissociation constant of about 3×10^{-10}. Despite this low acidity the compound forms a well-defined crystalline hydrochloride. This behavior, typical of an amino acid, should designate the structure as 3-β-aminoethylnitrourea (I).

On the other hand, treatment of the hydration product (I or II) with nitrous acid does not yield gaseous nitrogen until at least 15 minutes have elapsed. By contrast a primary amine such as 1,2-diaminoethane evolves gas immediately, while a monoacyl diamine such as 1-acetamino-2-aminoethane, which is easily cyclized[4] evolves gas in about five minutes. Furthermore, the reaction of nitrous acid with the hydration product (I or II) is not simple since the solid and gaseous products differ according to the conditions of nitrosation.

When aqueous sodium nitrite solution is added very slowly to a cold solution of the hydrated nitriminoimidazolidine (I or II) in dilute hydrochloric acid, the gas (which is evolved in the later stages of the reaction) is chiefly nitrous oxide. The solid product isolable from the reaction system is found to be the hitherto-unknown 1-nitrosoimidazolidone-2 (IV) since it can further be nitrosated to give the 1,3-dinitrosoimidazolidone-2 reported by McKay, Park and Viron.[5]

When the aqueous sodium nitrite solution is added rapidly to the cold solution of hydrated nitriminoimidazolidine in hydrochloric acid, the gas, which is mostly evolved during 30 minutes (although two hours is allowed for maximum yield), is found chiefly to be nitrogen. The solid product of this reaction is the 3-β-hydroxyethylnitrourea (VI) which would have been expected if the amino group in 3-β-aminoethylnitrourea had reacted in a normal and rapid manner. Essentially the same type of gas evolution is observed when aqueous acetic rather than hydrochloric acid is used as the reaction medium. However, in this case the isolable solid product is the dehydration product from 3-β-hydroxyethylnitrourea (VI), namely, 2-nitraminooxazoline (VIII).[6] This is the only substance produced in aqueous acetic acid whether nitrite is added over a period of minutes or of hours.

Thus it may be seen that the reaction with nitrous acid cannot specify precisely whether the hydration product of 2-nitriminoimidazolidine is 2-hydroxy-2-nitraminoimidazolidine (II) or whether it is a mixture of II with 3-β-aminoethylnitrourea (I). However, under our conditions of reaction, it does not seem possible that only the chain isomer I is present, because it could not reasonably be a source of 1-nitrosoimidazolidone-2 (IV). On the other hand, the strongly-acid condition involved in slow addition of sodium nitrite in the formation of IV might be expected to promote the loss of nitrous oxide from III after it had been formed from II.

(1) S. S. Barton, R. H. Hall and G. F Wright, THIS JOURNAL, **73**, 2201 (1951).

(2) R. H. Hall, A. F. McKay and G. F Wright, *ibid.*, **73**, 2205 (1951).

(3) M. W. Kirkwood and G. F Wright, *J. Org. Chem.*, **18**, 629 (1953).

(4) A. J. Hill and S. R. Aspinall, THIS JOURNAL, **61**, 822 (1939).

(5) A. F. McKay, W. R. R. Park and S. J. Viron, *ibid.*, **72**, 3659 (1950).

(6) R. H. Hall and G. F Wright, *ibid.*, **73**, 2213 (1951).