for 0.5 hour and the solution, after cooling and filtering, was made basic to phenolphthalein with 10 *N* sodium hydroxide. The crude product resulting was crystallized twice from isooctane (with charcoal decoloration); yield 20.0 g., m.p. 190.5–191.5°, λ_{max} 295 mμ, E^1_1 1184 in ethanol.

Anal. Calcd. for $C_9H_{10}N_2O$: C, 66.65; H, 6.21; N, 17.28. Found: C, 66.67; H, 6.29; N, 17.23, 17.32.

3,4-Dihydro-3-methyl-4-methylene-2,1(H)quinazolinethione (Provisional Identification).—A solution of 10 g. of *o*-aminoacetophenone[38] (0.074 mole) and 5.4 g. of methyl isothiocyanate (0.074 mole) in 40 ml. of ethanol was refluxed 3 hours. The product, which began separating after approximately 1.5 hours, was collected and dried. A yield of 7.7 g. (50%) of crude product, m.p. 215–218°, was obtained. A sample for analysis, obtained by crystallization successively from ethanol, 1–1 ethanol–Cellosolve and ethanol, melted at 223–225°.

(38) N. J. Leonard and S. N. Boyd, Jr., *J. Org. Chem.*, **11**, 409 (1946).

Anal. Calcd. for $C_{10}H_{19}N_2S$: C, 63.12; H, 5.30; N, 14.73; S, 16.85. Found: C, 62.79, 62.74; H, 5.51, 5.54; N, 14.78; S, 16.62, 16.66.

The infrared spectrum (KBr disk) exhibits a band at 6.05 μ characteristic of a carbon–carbon double bond and a bond at 3.09 μ for a N–H band. In the ultraviolet the compound absorbs in three regions: λ_{max} 279 mμ, E^1_1 1344; λ_{max} 240 mμ, E^1_1 663; λ_{max} 215, E_1' 338 in ethanol.

Acknowledgment.—We wish to thank Mr. Charles Childs and co-workers for the microanalyses; Mr. Bruce Scott, Dr. J. M. Vandenbelt and co-workers for the ultraviolet and infrared determinations; and Mr. Richard Kavanaugh for technical help in the performance of the *in vivo* tests.

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

Amine Oxides. Cyclic Quaternary Salts and their Decomposition[1]

BY V. BOEKELHEIDE AND WAYNE FEELY[2]

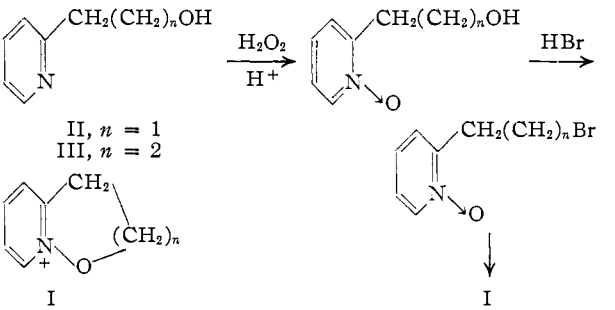
RECEIVED DECEMBER 4, 1957

The synthesis of 2,3-dihydro-4H-oxazino[2,3-a]pyridinium bromide (IV) and its alkaline decomposition to 2-vinylpyridine and formaldehyde is described. The preparation of 2,3-dihydroisoxazolo[2,3-a]pyridinium bromide (VI) also is given but its alkaline decomposition yields products of unknown structure. The quaternization of 2-(β-bromoethyl)-pyridine results in dimerization and the product has structure XI rather than the simple azobicycloöctane structure previously assigned by Löffler.

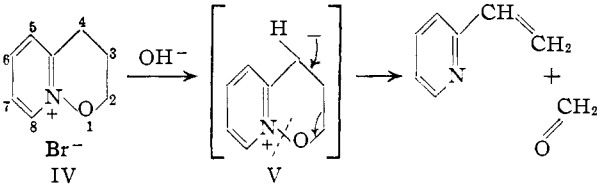
Since the time of Meisenheimer's experiments on quaternary salts of amine oxides,[3] it has been known that the decomposition of such salts would yield aldehydes. Although the yield of aldehyde obtained from such decompositions usually is poor, recent work has demonstrated that under the proper circumstances the yield of aldehydes may be quite high and the reaction may have general usefulness in preparative work.[4] A possible extension of this method would be the introduction of a carbonyl function into the side chain of simple pyridine derivatives. With this in mind we undertook to synthesize and study the properties of some simple cyclic quaternary salts of pyridine-N-oxide as shown by I.

The synthesis of the simple salts corresponding to I, where *n* was 1 and 2, followed in a straightforward fashion. As shown below, the commercially available alcohols 2-(β-hydroxyethyl)-pyridine (II) and 2-(γ-hydroxypropyl)-pyridine (III) were oxidized to the corresponding N-oxides, these were converted to the bromides with hydrobromic acid, and the bromides readily cyclized to the desired quaternary salts.

In support of the assigned structures it was found that catalytic hydrogenation of 2,3-dihydro-4H-oxazino[2,3-a]pyridinium bromide (IV) over Adams catalyst gave the crystalline hydrobromide of 3-(2'-piperidyl)-propan-1-ol. This was identical in all respects with an authentic sample prepared by the hydrogenation of III. Likewise, catalytic hydrogenation of 2,3-dihydroisoxazolo[2,3-a]pyridinium bromide (VI) gave the hydrobromide of 2-(2'-piperidyl)-ethanol, identical in all respects with a sample prepared by the hydrogenation of II.



When these cyclic salts were treated with alkali, reaction occurred readily, but the products were not the expected pyridine aldehydes. Instead, the aqueous alkaline decomposition of IV gave 2-vinylpyridine in 85% yield. If it is presumed that the first stage is the removal of a proton at the 4-position to give V, it becomes understandable how the formation of 2-vinylpyridine could readily occur with accompanying elimination of formaldehyde. When the aqueous solution from the reaction was steam distilled, formaldehyde was isolated from the distillate as its dimedon derivative.



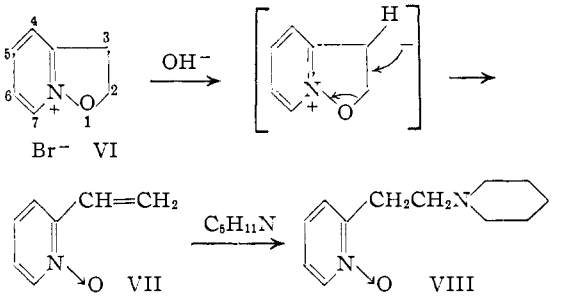
(1) This investigation was aided by a grant from the National Science Foundation.

(2) Union Carbide and Carbon Predoctoral Fellow, 1955–1956.

(3) J. Meisenheimer, *Ann.*, **397**, 273 (1913).

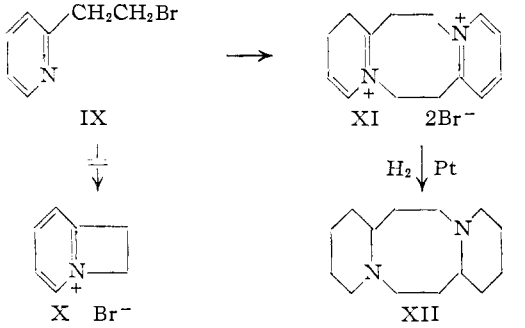
(4) W. Feely, W. L. Lehn and V. Boekelheide, *J. Org. Chem.*, **22**, 1135 (1957).

In the case of VI, treatment with aqueous alkali led to intractable tars. By analogy to the previous example, it seemed likely that VI, after loss of a proton, would be converted to 2-vinylpyridine-N-oxide (VII), a compound which would be expected to polymerize very readily. In an attempt to establish the presence of 2-vinylpyridine-N-oxide, the reaction of VI with aqueous piperidine was investigated. Under these conditions it was anticipated that the addition of piperidine to 2-vinylpyridine-N-oxide would successfully compete with the polymerization reaction. A crystalline product, m.p. 124–126°, separated directly from the reaction mixture and, as expected, its composition was in agreement with that required for the adduct (VIII) of piperidine and 2-vinylpyridine-N-oxide.



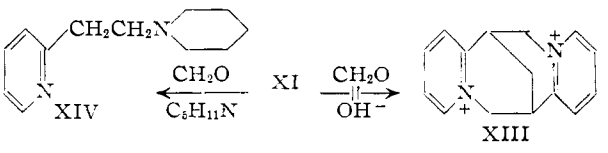
However, a closer inspection of the physical properties and chemical behavior of the product melting at 124–126° makes the assignment of structure VIII untenable. Its ultraviolet absorption spectrum in alcohol shows a maximum at 340 mμ (ε 43,000) which is shifted irreversibly by acid to 248 mμ (ε 15,000). Hydrogenation over platinum in ethyl acetate proceeded extremely rapidly with the uptake of four moles of hydrogen. Since the catalytic hydrogenation of VIII would be expected to yield 2-(1′-piperidyl)-ethylpiperidine, a sample of this was prepared by independent synthesis and by comparison was shown to be quite different. Actually the oily hydrogenation product had a composition in accord with the empirical formula $(C_7H_{15}NO)_x$, corresponding to a loss of the piperidine moiety. With the evidence at hand it is not yet possible to assign a satisfactory structure to this unusual product from the reaction of VI with piperidine.[5]

The possibility of preparing salts such as I with smaller ring size, where $n = 0$, was considered as an alternate route for the preparation of 2-pyridine aldehyde. In the early work of Löffler there is described the cyclization of 2-(β-haloethyl)-pyridines (IX) to give pyridinum salts for which structure X was assigned.[6] A number of such compounds appear in the literature[7–10] and their structural assignments have been generally accepted even in recent publications.[11] However, in the case of the next lower homolog, α-bromomethylpyridine, Sorm and Sedivy have shown that the quaternary salt is a dimer.[12] Therefore, it seemed advisable to obtain definite evidence regarding the structures of Löffler's compounds before undertaking the synthesis of I, where $n = 0$.



When the "pyridonium" bromide, prepared as described by Löffler,[6] was subjected to hydrogenation over platinum, it gave an oil, b.p. 100° at 0.2 mm., having a composition corresponding to $(C_7H_{13}N)_x$. The high boiling point indicated that the product was a dimer ($x = 2$) and a molecular weight determination confirmed this. Thus, the most reasonable structure for Löffler's "pyridonium" bromide is XI and the structures assigned to the various methyl analogs prepared in his studies[7–10] must be reconsidered.

The behavior of XI toward base was of interest since Löffler had reported that such solutions turned red but did not yield 2-vinylpyridine, the expected Hofmann decomposition product. This observation, which we were able to confirm, indicated that the corresponding methine base possessed fair stability and suggested the possibility that XI might undergo base-catalyzed condensation with aldehydes to give XIII. This would produce in a very simple way the carbon skeleton present in various lupin alkaloids. Although this hope could not be realized, it was found, during attempts to effect condensation using piperidine as catalyst, that XI underwent a smooth reaction with piperidine to give β-(N-piperidino)-ethylpyridine (XIV). Whether 2-vinylpyridine is an intermediate or whether the reaction proceeds by a simple direct displacement was not determined.



The ease with which XI underwent cleavage to give products related to 2-vinylpyridine suggested that the reverse reaction might also occur. This was found to be true. When 2-vinylpyridine hydrobromide was heated at elevated temperatures, it gave XI in 68% yield and this is probably the most convenient method for preparing XI. Whether 2-(β-bromoethyl)-pyridine is an actual intermediate in this case is uncertain.

(5) Publication of these observations is included in the present work because this research has been unavoidably interrupted.
(6) K. Löffler, *Ber.*, **37**, 161 (1904).
(7) K. Löffler, *ibid.*, **42**, 948 (1909).
(8) K. Löffler and A. Grosse, *ibid.*, **40**, 1325 (1907).
(9) K. Löffler and F. Thiel, *ibid.*, **42**, 132 (1909).
(10) K. Löffler and P. Plocker, *ibid.*, **40**, 1310 (1907).
(11) F. Bohlmann, N. Ottawa and R. Keller, *Ann.*, **587**, 162 (1954).
(12) F. Šorm and L. Sedivy, *Coll. Czech. Chem. Comm.*, **13**, 289 (1948).

Experimental[13]

2,3-Dihydro-4H-oxazino[2,3-a]pyridinium Bromide (IV).—A solution of 68.0 g. of 3-(2′-pyridyl)-propan-1-ol-N-oxide[14] in 1 l. of 48% hydrobromic acid was boiled under reflux for 24 hours. After concentration under reduced pressure, the residue was taken up in 1 l. of water and passed over an ion-exchange column (300 g. of Amberlite-IR-4B-OH). Concentration of the eluate under reduced pressure gave a brown solid. This was crystallized from acetonitrile to give 55.0 g. (57%) of white crystals, m.p. 151–153°.

Anal. Calcd. for $C_8H_{10}NOBr$: C, 44.46; H, 4.66. Found: C, 44.37; H, 4.86.

3-(2′-Piperidyl)-propan-1-ol Hydrobromide. (A) By Hydrogenation of IV.—A mixture containing 1.5 g. of 2,3-dihydro-4H-oxazino[2,3-a]pyridinium bromide (IV) and 100 mg. of Adams catalyst in 75 ml. of water was subjected to hydrogenation at room temperature and atmospheric pressure. Four moles of hydrogen was absorbed in 3 hours. After removal of the catalyst, the aqueous filtrate was concentrated under reduced pressure. The white solid residue, after recrystallization from acetone, gave in high yield white crystals, m.p. 126–128°.

Anal. Calcd. for $C_8H_{18}NOBr$: C, 42.86; H, 8.04. Found: C, 43.16; H, 8.36.

(B) By Hydrogenation of 3-(2′-Pyridyl)-propan-1-ol Hydrobromide.—A solution of 1.0 g. of 3-(2′-pyridyl)-propan-1-ol dissolved in 25 ml. of 5% hydrobromic acid was added to a suspension prepared by reducing 100 mg. of Adams catalyst in 20 ml. of water. The hydrogenation, conducted at room temperature and atmospheric pressure, stopped when 3 moles of hydrogen had been absorbed. Evaporation of the solution under reduced pressure gave a white solid which, after recrystallization from acetone, gave white crystals, m.p. 125–127°. A comparison of these crystals with a sample obtained as in (A), both by the method of mixed melting points and by use of their infrared spectra, confirmed their identity.

Treatment of IV with Alkali.—To a solution of 10 g. of 2,3-dihydro-4H-oxazino[2,3-a]pyridinium bromide (IV) in 50 ml. of water was added 20 ml. of a 10% sodium hydroxide solution. The resulting turbid mixture was extracted with ether, the combined ether extracts were dried, and the ethereal solution was concentrated in a nitrogen atmosphere. Distillation of the residual oil gave 3.94 g. (85%) of a clear liquid, b.p. 68–70° at 15 mm. The infrared and ultraviolet absorption spectra of this oil were identical with those of an authentic sample of 2-vinylpyridine. The picrate readily formed and, after recrystallization from ethanol, melted at 157–159° (lit.[5] gives 157–159°), undepressed by admixture of an authentic sample of the picrate of 2-vinylpyridine.

The aqueous layer was steam distilled and the distillate was treated with 5,5-dimethyldihydroresorcinol (dimedon). The white crystals (12% yield) which separated melted at 185–188°, undepressed by admixture of an authentic sample of the dimedon derivative of formaldehyde.

2-(2′-Pyridyl)-ethanol-N-oxide was prepared in the same manner previously described for the preparation of 3-(2′-pyridyl)-propan-1-ol-N-oxide.[14] From 123.0 g. of 2-(2′-pyridyl)-ethanol there was obtained, after recrystallization from dry ethyl acetate, 120.0 g. (86%) of white needles, m.p. 93–95°.

Anal. Calcd. for $C_7H_9NO_2$: C, 60.42; H, 6.52. Found: C, 60.51; H, 6.77.

The picrate of 2-(2′-pyridyl)-ethanol-N-oxide formed readily and was obtained, after recrystallization from absolute ethanol, as yellow needles, m.p. 96-98°.

Anal. Calcd. for $C_{13}H_{12}N_4O_9$: C, 42.40; H, 3.28. Found: C, 42.35; H, 3.55.

2,3-Dihydroisoxazolo[2,3-a]pyridinium Bromide (VI).—A solution of 20.0 g. of 2-(2′-pyridyl)-ethanol-N-oxide in 500 ml. of 48% hydrobromic acid was boiled under reflux for 10 hours. After the resulting solution had been concentrated under reduced pressure, the residual solid was taken up in 500 ml. of water and passed over an ion-exchange column (300 g. of Amberlite-IR-4B-OH). Concentration of the eluate gave a tan solid which, after recrystallization from acetonitrile, yielded 17.2 g. (60%) of white crystals, m.p. 152–155°.

Anal. Calcd. for C_7H_8NOBr: C, 41.61; H, 3.99. Found: C, 41.58; H, 3.92.

The picrate of the 2,3-dihydroisoxazolo[2,3-a]pyridinium ion was prepared in ethanol and, after recrystallization from the same solvent, was isolated as yellow needles, m.p. 94–97°.

Anal. Calcd. for $C_{14}H_{12}N_4O_8$: C, 44.58; H, 2.89. Found: C, 44.73; H, 3.04.

2-(2′-Piperidyl)-ethanol Hydrobromide. (A) By Hydrogenation of VI.—A solution of 1.2 g. of 2,3-dihydroisoxazolo[2,3-a]pyridinium bromide in 30 ml. of water was added to a suspension of 100 mg. of prereduced Adams catalyst in 20 ml. of water. Hydrogenation was conducted at room temperature and atmospheric pressure until 4 moles of hydrogen was absorbed (4.5 hours). Removal of the catalyst and evaporation of the filtrate gave a white solid which, after recrystallization from dry acetone, yielded white needles, m.p. 108–110°.

Anal. Calcd. for $C_7H_{16}NOBr$: C, 40.01; H, 7.68. Found: C, 40.13; H, 7.48.

(B) By Hydrogenation of 2-(2′-Pyridyl)-ethanol Hydrobromide.—A solution of 1.0 g. of 2-(2′-pyridyl)-ethanol in 25 ml. of 5% hydrobromic acid was added to a suspension of 100 mg. of prereduced Adams catalyst in 20 ml. of water. After hydrogenation at room temperature and atmospheric pressure, the catalyst and solvent were removed. The residual solid, when recrystallized from acetone, gave 1.0 g. of white needles, m.p. 108–110°.

A comparison of the samples from (A) and (B) by infrared spectra and the method of mixed melting points showed the two to be identical.

Reaction of VI with Piperidine.—A solution of 10.0 g. of 2,3-dihydroisoxazolo[2,3-a]pyridinium bromide (VI) in 100 ml. of water was added to 100 ml. of piperidine. The resulting homogeneous solution was warmed on a steam-bath for 15 minutes and then allowed to cool slowly. The yellow crystals, which separated from the solution, were collected and recrystallized from ethanol to give 4.45 g. (42%) of yellow plates, m.p. 124–126°. The ultraviolet absorption spectrum of the crystals in ethanol showed maxima at 238 mμ (ε 2,900) and 340 mμ (ε 43,000). When aqueous acid was added to the solution, a single maximum was observed at 248 mμ (ε 15,000). Addition of base left the spectrum unaffected and did not regenerate the original spectrum observed in neutral solution. While the crystals could be dissolved in alcohol without change, their benzene and chloroform solutions showed rapid decomposition on warming.

Anal. Calcd. for $C_{12}H_{18}N_2O$: C, 69.89; H, 8.80; N, 13.58. Found: C, 69.93; H, 8.89; N, 13.57.

When a solution of 2.0 g. of these crystals in 20 ml. of ethyl acetate was subjected to hydrogenation over 100 mg. of Adams catalyst at room temperature and atmospheric pressure, 4 moles of hydrogen was absorbed very rapidly. Removal of the catalyst and solvent and then distillation of the residual gum gave a colorless, viscous oil, b.p. 130° at 1 mm. The high boiling point of this oil would suggest that it is a dimer (*i.e.*, $x = 2$).

Anal. Calcd. for $(C_7H_{15}NO)_x$: C, 65.07; H, 11.70; N, 10.84. Found: C, 65.17; H, 11.88; N, 10.52.

3,4,7,8-Tetrahydrodibenzo[a,e]-1,5-diazocinium Dibromide (XI).—A solution of 12.3 g. of 2-(2′-pyridyl)-ethanol in 150 ml. of 48% hydrobromic acid was boiled under reflux for 12 hours. After concentration, the white crystalline solid, 2-(β-bromoethyl)-pyridine hydrobromide, was taken up in 100 ml. of water, neutralized with sodium carbonate, and extracted with ether. The combined ether extracts were dried and concentrated to give a white solid which, after recrystallization from ethanol–water, yielded 13.5 g. (73%) of white needles, m.p. 238–240°.[15]

Anal. Calcd. for $C_{14}H_{16}N_2Br_2$: C, 45.18; H, 4.54. Found: C, 44.98; H, 4.41.

The dipicrate of XI was prepared in aqueous solution and was obtained, after recrystallization from water, as yellow needles, m.p. 179–181°.

Anal. Calcd. for $C_{26}H_{20}N_8O_{14}$: C, 46.71; H, 3.02. Found: C, 46.76; H, 3.35.

(13) All melting points are corrected. Analyses by Miss A. Smith and Micro-Tech Laboratories.

(14) V. Boekelheide and W. Feely, *J. Org. Chem.*, **22**, 589 (1957).

(15) Löffler[5] gives 226–227°.

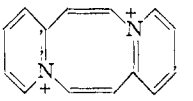
The diiodide of XI was prepared by adding potassium iodide to an aqueous solution of XI. After recrystallization from water it gave pale yellow crystals, m.p. 230–231°.[16]

Anal. Calcd. for $C_{13}H_{16}N_2I_2$: C, 36.07; H, 3.46. Found: C, 36.09; H, 3.76.

When an attempt was made to oxidize XI with dichromate in the hope of preparing the parent substance XV, the only reaction was the precipitation of the dichromate salt of XI. This, after recrystallization from water, yielded orange needles, m.p. 170–175° dec.

Anal. Calcd. for $C_{14}H_{16}N_2O_7Cr_2$: C, 39.26; H, 3.77. Found: C, 39.05; H, 3.89.

Similarly, attempts to oxidize XI using bromine water simply precipitated an unstable, yellow di-perbromide.



XV

1,2,5,6-Bis-(tetramethylene)-octahydro-1,5-diazocine (XII).—A solution of 1.60 g. of 3,4,7,8-tetrahydrodibenzo-[a,e]-1,5-diazocinium bromide (XI) in 25 ml. of water was subjected to hydrogenation at room temperature and atmospheric pressure using 100 mg. of Adams catalyst. When 6 moles of hydrogen had been absorbed, the hydrogenation was stopped and the catalyst removed. Neutralization of the filtrate followed by extraction with chloroform and concentration gave 600 mg. of a colorless oil; b.p. 105° at 0.2 mm., $n^{24}D$ 1.5800.

The infrared spectrum of the oil showed a strong band at 3.63 μ in addition to the usual absorption at 3.45 μ. As has been pointed out by Wenkert and Roychaudhuri,[17] strong absorption in this region probably is due to an axial hydrogen at the bridgehead carbon.

Anal. Calcd. for $C_{14}H_{26}N_2$: C, 75.61; H, 11.79; mol. wt., 220. Found: C, 75.25; H, 11.58; mol. wt. (Rast), 208.

The dimethiodide of XII formed readily and, after recrystallization from a water–ethanol mixture, was obtained as white needles, m.p. 282–283° dec.

Anal. Calcd. for $C_{16}H_{28}N_2I_2$: C, 38.26; H, 5.62. Found: C, 37.87; H, 5.61.

Reaction of XI with Piperidine.—To a solution of 2.0 g. of XI in 4 ml. of water was added 1 ml. of piperidine. After the mixture had been boiled under reflux for 3 hours, it was concentrated under reduced pressure to give a tan solid. This, after recrystallization from a benzene–ethanol mixture, yielded 2.9 g. (89%) of N-(β-(2-pyridyl)-ethyl)-piperidine hydrobromide as white crystals, m.p. 173–175°.

Anal. Calcd. for $C_{12}H_{19}N_2Br$: C, 53.14; H, 7.06. Found: C, 53.99; H, 7.45.

Conversion of the above crystals to the corresponding dipicrate gave yellow crystals, m.p. 160–161.5°.[18] A mixture melting point determination with an authentic sample of the dipicrate of N-(β-(2-pyridyl)-ethyl)-piperidine showed no depression of melting point.

N-(2-(2'-Piperidyl)-ethyl)-piperidine.—A solution of 19.0 g. of N-(β-(2-pyridyl)-ethyl)-piperidine[18] in 200 ml. of a 10% hydrobromic acid solution containing 500 mg. of Adams catalyst was subjected to hydrogenation at room temperature and atmospheric pressure. After 3 moles of hydrogen had been absorbed, the catalyst was removed and the solution was made basic. Extraction with ether followed by concentration and distillation of the residue gave 18.0 g. (93%) of a colorless oil, b.p. 107° at 1 mm., $n^{23}D$ 1.4886. This was prepared for comparison with the reduction product from VI and was shown by comparison of spectra and other physical properties to be different.

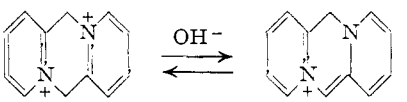
Anal. Calcd. for $C_{12}H_{24}N_2$: C, 73.41; H, 12.33. Found: C, 73 51; H, 11.90.

Preparation of XI from 2-Vinylpyridine Hydrobromide.—A sample of 4.0 g. of 2-vinylpyridine hydrobromide was heated in a sealed tube at 160° for 3 hours. The resulting solid was washed from the tube with absolute ethanol and collected by filtration. After recrystallization from an ethanol–water mixture, it yielded 2.7 g. (68%) of crystals, m.p. 238–240°. A comparison of these crystals with the sample of XI previously prepared showed them to have identical infrared spectra and a mixture of the two showed no depression of melting point.

3,6-Dihydrodibenzo[a,d]-1,4-diazinium Dichloride (XV).—In studying the behavior of XI toward alkali we were interested in repeating the observations of Šorm and Sedivy[12] on the analogous system XVI for comparison. When a solution of 2-chloromethylpyridine in dry acetonitrile was boiled under reflux for 5 days, a white solid separated. This, after recrystallization from an ethanol–water mixture, gave white needles, m.p. 253–255°.

Anal. Calcd. for $C_{12}H_{12}N_2Cl_2$: C, 56.48; H, 4.74. Found: C, 56.81; H, 5.02.

When an aqueous solution of these crystals was treated with dilute alkali, an intense red color developed and the colored substance could not be extracted from the aqueous solution with organic solvents. However, with stronger alkali, a highly unstable, dark red compound, soluble in organic solvents, did separate. It would appear that the intense red color formed in dilute alkali is due to XVII and only in strong alkali is the non-ionic, free base produced.



XVI 2 Cl^- XVII Cl^-

(16) Löffler[6] gives 211–213°.

(17) E. Wenkert and D. K. Roychaudhuri, THIS JOURNAL, **78**, 6417 (1956).

(18) W. E. Doering and R. A. N. Weil, *ibid.*, **69**, 2461 (1947), give 159-160° as the melting point of the dipicrate of N-(β-(2-pyridyl)-ethyl)piperidine.

ROCHESTER, NEW YORK

[CONTRIBUTION FROM THE RESEARCH LABORATORIES, THE UPJOHN CO.]

Preparation and Reactions of 11-Substituted 1,3,5(10)-Estratrienes.[1] I. 11-Oxygenated Estrones and Estradiols

BY BARNEY J. MAGERLEIN AND JOHN A. HOGG

RECEIVED DECEMBER 26, 1957

The aromatization of steroidal 3-keto-1,4-dienes containing 11α-hydroxy, 11α-acetoxy and 11β-hydroxy substituents or 9,11-unsaturation is reported. The conversion of these products to the 11-oxygenated 19-nortestosterones is the first reported synthesis of this type of compound wherein the 11-hydroxyl group is present during the chemical modification of ring A. A novel compound obtained by a Birch-type reduction is described.

The pyrolytic method for the aromatization of 3-keto-1,4-dienes announced by Inhoffen in 1940,[2] has been used for the preparation of a variety of aromatic A ring steroids unsubstituted at C-11.[3] The pyrolysis of 11β-hydroxy, 11α-hydroxy, 11α-

(1) A preliminary announcement of this work was made in a Communication to the Editor, THIS JOURNAL, **79**, 1508 (1957).

(2) H. H. Inhoffen, *Angew. Chem.*, **53**, 471 (1940).

(3) See B. J. Magerlein and J. A. Hogg, *Tetrahedron* (in press), for a brief review of this reaction.