REACTIONS OF THE CONDENSATES OF PICOLYLLITHIUM AND ACROLEIN

by

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REACTIONS OF THE CONDENSATES OF PICOLYLLITHIUM AND ACROLEIN

INTRODUCTION

This investigation was attempted to study the reactions of the condensates of 2-picoline with certain unsaturated aldehydes. The addition of bromine to the condensation products (23, p.2974-2976) produced the cyclization to quinolizinium salts, unsaturated compounds corresponding to quinolizine, a saturated member of the lupin alkaloid, occurring in nature.

Unsaturated alcohols with allylic structure obtained from the condensation of picolyllithium with unsaturated aldehydes were related to a number of compounds prepared by Braude and his co-workers.

In 1950 Braude and Timmons (10, p.2000-2006) condensed isobutenyl bromide with lithium metal in ether, isobutenyllithium was obtained, which was used as a reagent in alkenylation. Carboxylation of iso-butenyllithium, produced the lithium salt of the unsaturated acid (I).

$$(CH_3)_2C{=}CHLi \quad + \quad CO_2 \longrightarrow (CH_3)_2C{=}CHCOOLi$$

I

The additional products also isolated from this reaction were 2,5-dimethyl 2,4-hexadiene (II), formed by this reaction of isobutenyllithium and unreacted isobutenyl bromide, and di(isobutenyl) ketone (III), by the condensation of lithium salt of the unsaturated acid and isobutenyllithium.

$$(CH_3)_2C{=}CHLi + (CH_3)_2C{=}CHBr \longrightarrow (CH_3)_2C{=}CHCH{=}C(CH_3)_2$$
II

$$(CH_3)_2C{=}CHCOOLi + (CH_3)_2C{=}CHLi \longrightarrow (CH_3)_2C{=}CHCOCH{=}C(CH_3)_2$$
III

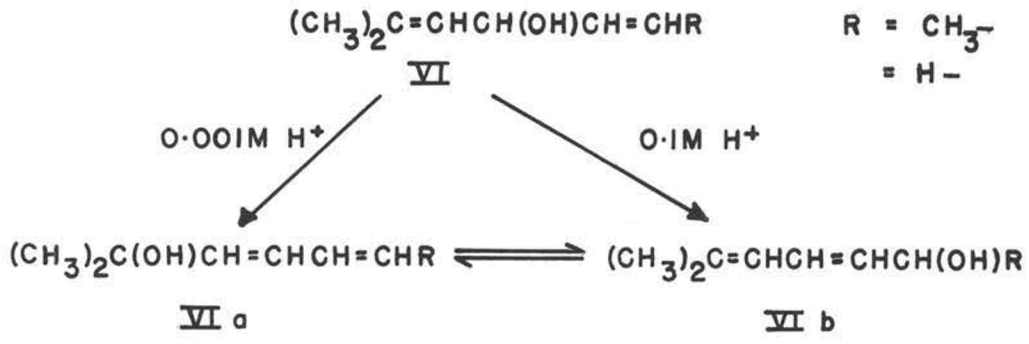
Benzaldehyde and acetone (10, p.2000-2006) condensed with isobutenyllithium formed isobutenyl carbinol (IV) which underwent the oxotropic rearrangement to the conjugated styryl derivative (V) on treatment with dilute acids.

$$Ph{\cdot}CHO + (CH_3)_2C{=}CHLi \longrightarrow Ph{\cdot}CH(OH)CH{=}C(CH_3)_2$$
IV

$$\text{IV} \xrightarrow{H^+} Ph{\cdot}CH{=}CHC(OH)(CH_3)_2$$
V

For their further studies, Braude and Timmons (11, p.2007-2011) condensed isobutenyllithium with acrolein and with crotonaldehyde. The expected carbinols were obtained. They found that in the presence of very dilute mineral acids, the

unsymmetrical substituted divinyl carbinols underwent oxotropic rearrangement. The hydroxyl group migrated to the more substituted γ-carbon atom. Under more strongly acid conditions, an approximately equimolar mixture of two isomers was obtained.



Cyclohexenyllithium was also prepared by Braude and Coles (7, p.2014-2019), using 1-chlorocyclohexene. The condensation of cyclohexenyl lithium with benzaldehyde, benzophenone, acrolein and crotonaldehyde, produced the carbinols in yields of 40%, 65%, 45% and 60% respectively. These carbinols also underwent oxotropic rearrangement under dilute acid conditions. Braude and Coles also prepared propenyllithium (8, p.2078-2084) and studied the oxotropic rearrangement of the condensation products with carbonyl compounds.

Braude and Forbes (9, p.1755-1761) have synthesized cyclopentenyllithium, and studied the reactions of the compound

with various unsaturated aldehydes. They also found that the condensation products underwent the oxotropic rearrangement.

It has been known for many years that picoline can be used as a condensing agent with aldehydes. Spaeth and co-workers (22, p.6961[3]) have prepared a number of 1,4-substituted butanols and butadienes by condensation of cinnamaldehyde with 2-methyl-, 4-methyl-, and 2,5-dimethyl pyridine, by heating equimolecular quantities of aldehyde and base. The reaction occurred in every case but the yields were very small.

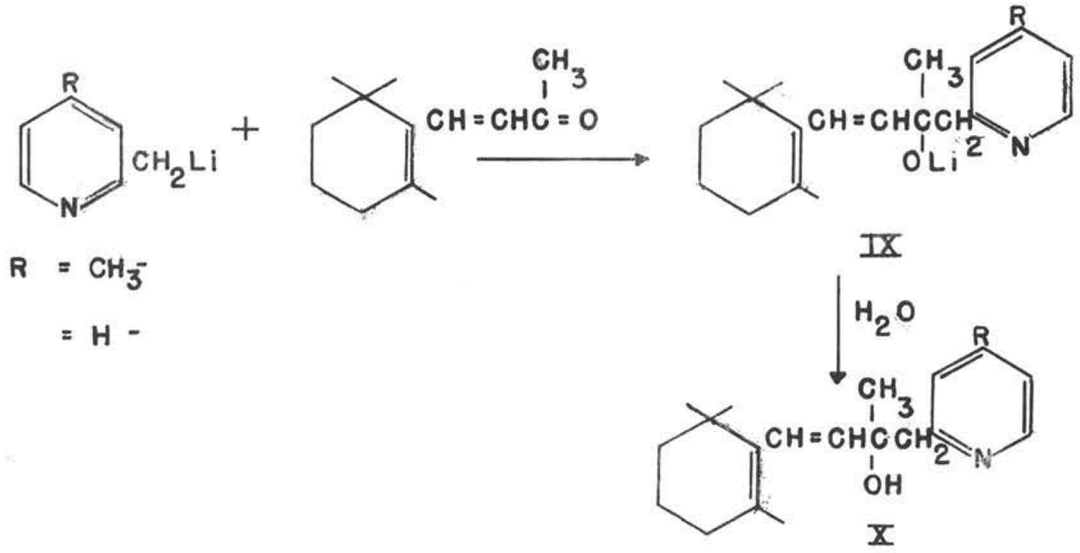
$$RMe + Ph{\cdot}CH{=}CHCHO \longrightarrow \underset{\text{VII}}{RCH_2CH(OH)CH{=}CHPh}$$

$$\text{VII} \xrightarrow{-H_2O} \underset{\text{VIII}}{RCH{=}CHCH{=}CHPh}$$

R = 2 - Pyridyl-, 4 - Pyridyl-, or 5 - Methyl-2-Pyridyl-

Arens and co-workers (1, p.287-294) attempted to synthesize derivatives of vitamin A by hydrolysis of pyridine ring of the carbinols derived from β-ionone condensing with the lithium derivatives of 2-picoline and of 2,4-dimethyl pyridine. The hydrolysis failed to produce vitamin A derivatives but moderate yields of allyl alcohols were obtained. They have

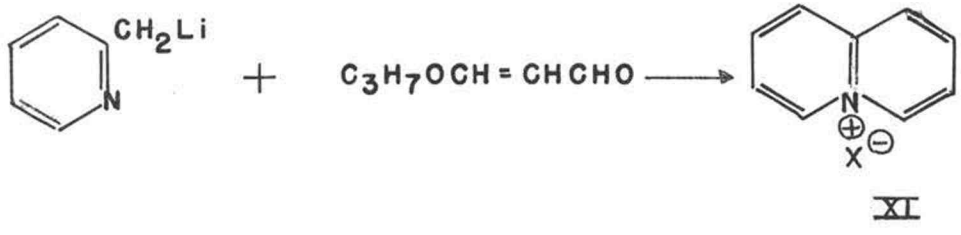
also condensed 2-picoline with crotonaldehyde and sorbic aldehyde.



R = CH_3-

= H -

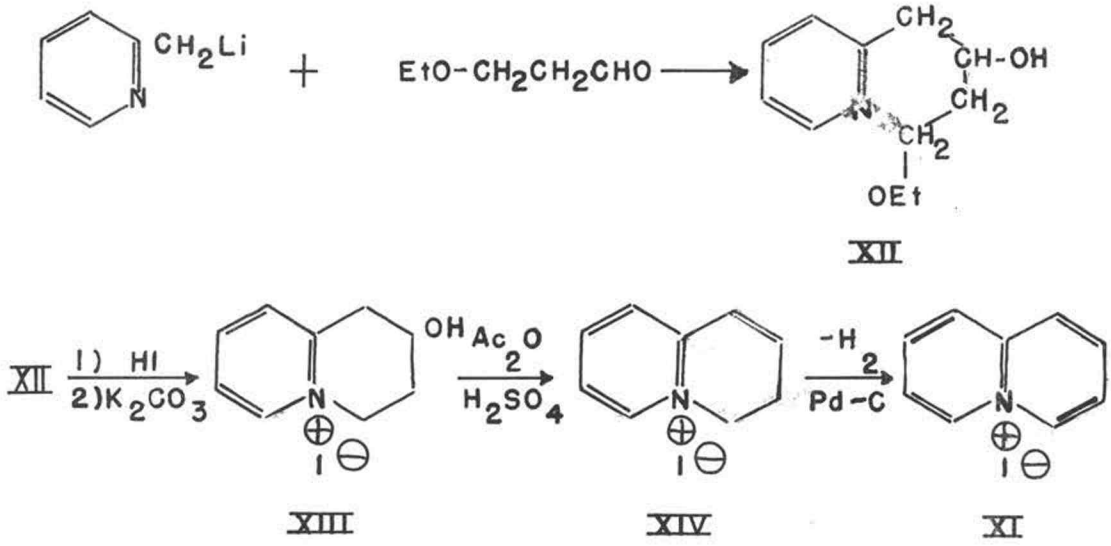
In 1951, Beaman isolated salts of the dehydroquinolizinium ion with great difficult, and in very poor yield, from the reaction of 2-picolyllithium with β-isopropoxyacrolein (2, p.1002)



XI

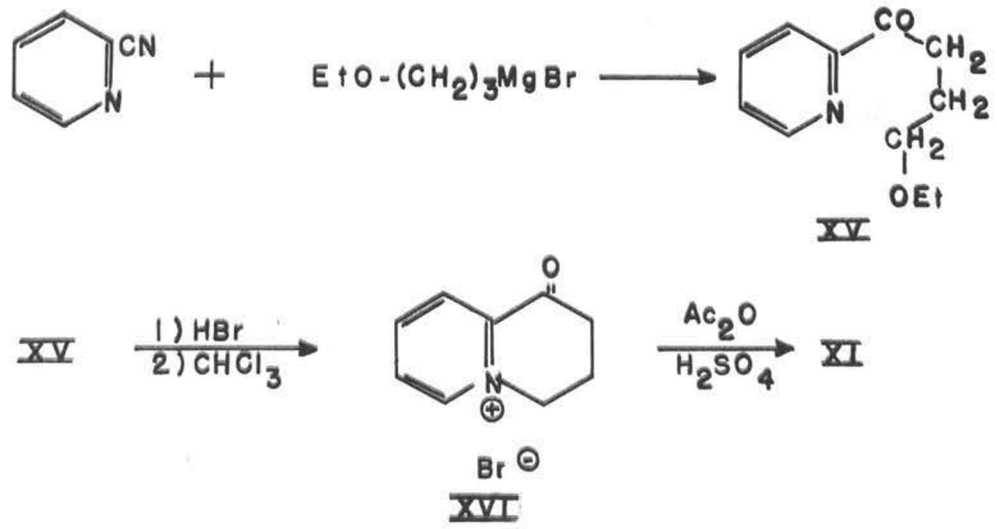
Recently Boekelheide and Gall (3, p.1832-1836) discovered

a method which was suitable for preparing dehydroquinolizinium iodide. 2-Picolyllithium was reacted with β-ethoxypropionaldehyde, producing the corresponding carbinol (XII) in good yield. Treatment of this carbinol with hydriodic acid followed by neutrallization with alkali, the cyclic ammonium iodide dihydroquinolizinium salt (XIII) was formed. Dehydration of the carbinol by means of acetic anhydride containing a drop of sulfuric acid, produced quinolizinium iodide (XIV). The iodide was dehydrogenated to dehydroquinolizinium iodide (XI), in 34% yield by heating the salt in butanol with a palladium-charcoal catalyst (5, p.5691-5693).



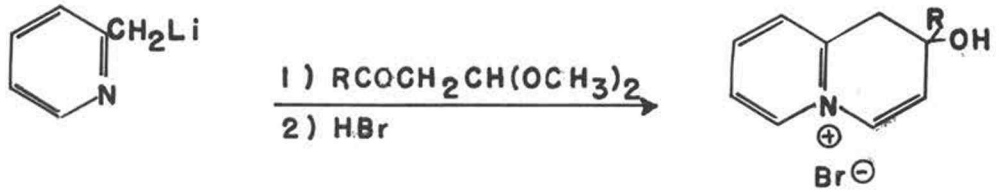
Boekelheide and Ross (5, p.5691-5693) have prepared the 6-methyl homolog of XIV by condensing 2,6-lutidyllithium with β-ethoxypropinaldehyde. The yield in the dehydrogenation step was raised to 42% by means of a platinum catalyst in nitrobenzene.

Glover and Jones have prepared 1,2,3,4-tetrahydro-1-oxo-quinolizinium bromide (16, p.1750-1754) from α-pyridyl α-ethoxypropyl ketone (XV). The ketone was prepared by the condensation of 2-cyanopyridine with 3-ethoxypropyl magnesium bromide (13, p.1144-1147). The ketone (XV) was treated with boiling hydrobromic acid, and the intermediate bromo-ketone was cyclized in boiling chloroform. The bicyclic ketone (XVI) was formed in 79% yield and was converted to dehydroquinolizinium salt (XI) in high yield by treatment with acetic anhydride and a drop of sulfuric acid (17, p.3021-3028).

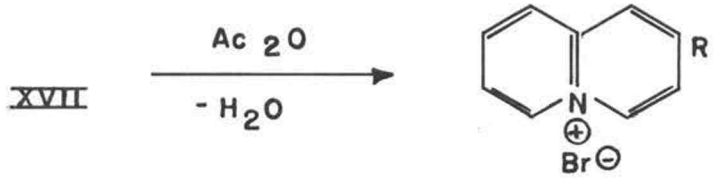


Glover and Jones have also prepared compounds substituted in the 2-,3- and 4-position by using suitable aliphatic precursors (17, p.3021-3028).

An improved synthesis of 2-substituted dehydroquinolizinium salts, was devised by Nesmeyanov and Rybinskaya (20, p.6349d). The condensate of 2-picolyllithium with a β, β-dimethoxyethyl ketone was treated with hydrobromic acid. A carbinol was formed in yield of 21-32%. Dehydration of the carbinol produced dehydroquinolizinium salt (XVIII) in high yield.



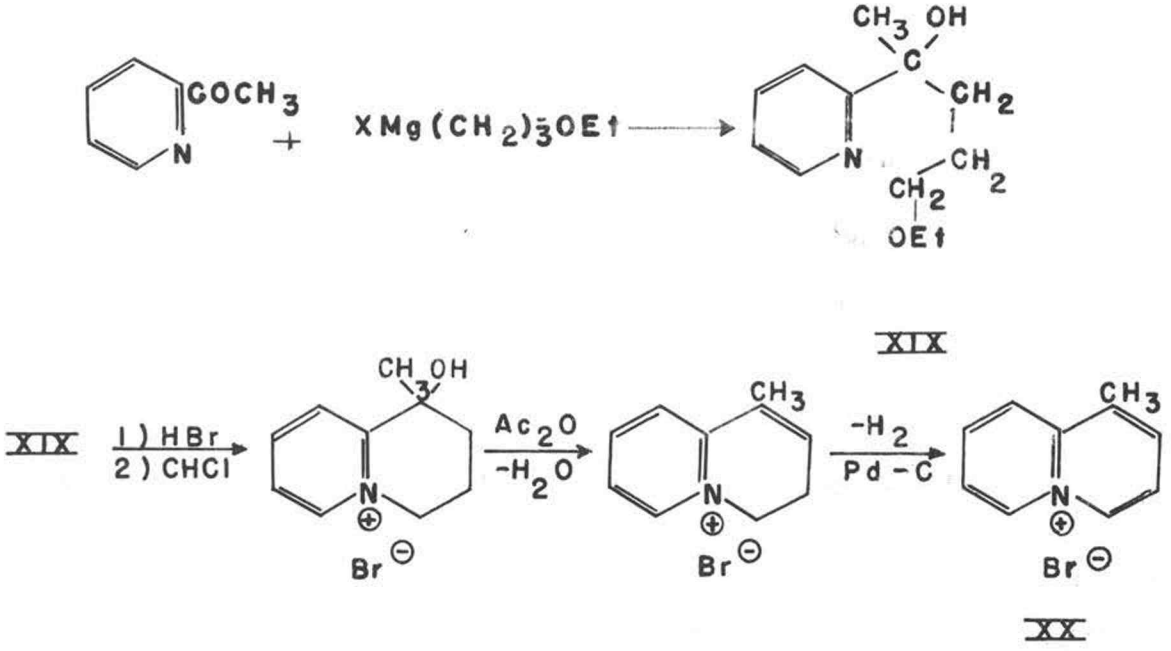
XVII



XVIII

The condensation of 2-acetyl pyridine with 3-ethoxypropyl magnesium bromide or chloride formed a good yield of the

pyridyl alcohol (XIX). The alcohol was cyclized by treatment with hydrobromic acid. The intermediate bromo-amine was heated in chloroform, producing the tetrhydrohydroxy-quinolizinium bromide. The compound was dehydrated and then dehydrogenated, a 1-substituted quinolizinium salt (XX) was obtained (18, p.1686-1691).



Bradsher and Beavers (6, p.4812-4813) prepared benzo [b] quinolizinium salt by the method of aromatic cyclodehydration. The crude quarternary salt obtained by the reaction of pyridine-2-carboxaldehyde and benzyl bromide was cyclized by refluxing with hydrobromic acid for 15 hours. The cyclization

product was obtained in 60% yield. Similarly 0-methyl benzyl bromide and p-methyl benzyl bromide yielded the 7-methyl and 9-methyl benzo[b] quinolizinium salts.

Richard and Stevens (21, p.3067-3073) converted β-oxo-aldehydes or ketones into monoacetals and/or the enol ethers, then treated them with picolyllithium. The resulting alcohols were cyclized by refluxing with alcoholic picric acid, the corresponding dehydroquinolizinium salts were formed. They also studied the reactions of these salts with anionoid reagents.

Doering and Weil (15, p.2461-2466) studied the electrophilic reaction of 2- and 4-vinyl pyridines, the found that α-norlupinone can be prepared by cyclizing γ -(2-piperidyl)-butyric acid in a molecular still.

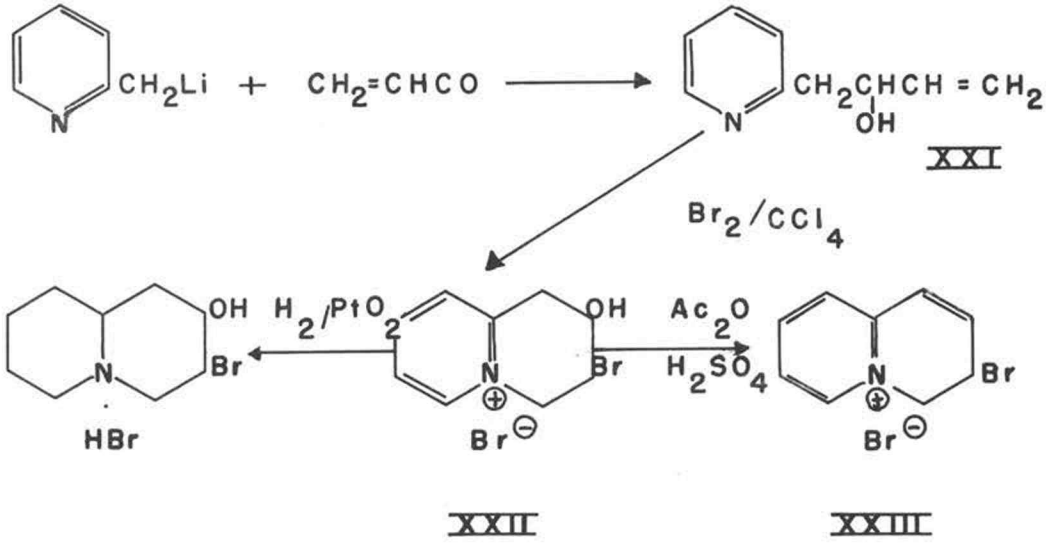
In 1937, Clemo, Morgan and Raper (12, p.965-969) had success in the synthesis of dl-lupinine and dl-iso-lupinine by condensing ethyl pyridyl-2-acetate with γ -phenoxy-n-propyl bromide, yielding ethyl δ-phenoxy-α-2-pyridyl-n-valerate. Upon catalytic reduction, followed by Bouveault reduction, produced a carbinol, which was treated with fuming hydrobromic acid. A dibromo-compound was obtained. Upon treatment with phosphorous pentabromide, a bromo-base resulted. Bromo-base was separated into its two racemic

forms and was hydrolyzed by refluxing with sodium acetate solution, giving two racemate forms, dl-lupinine and di-iso-lupinine.

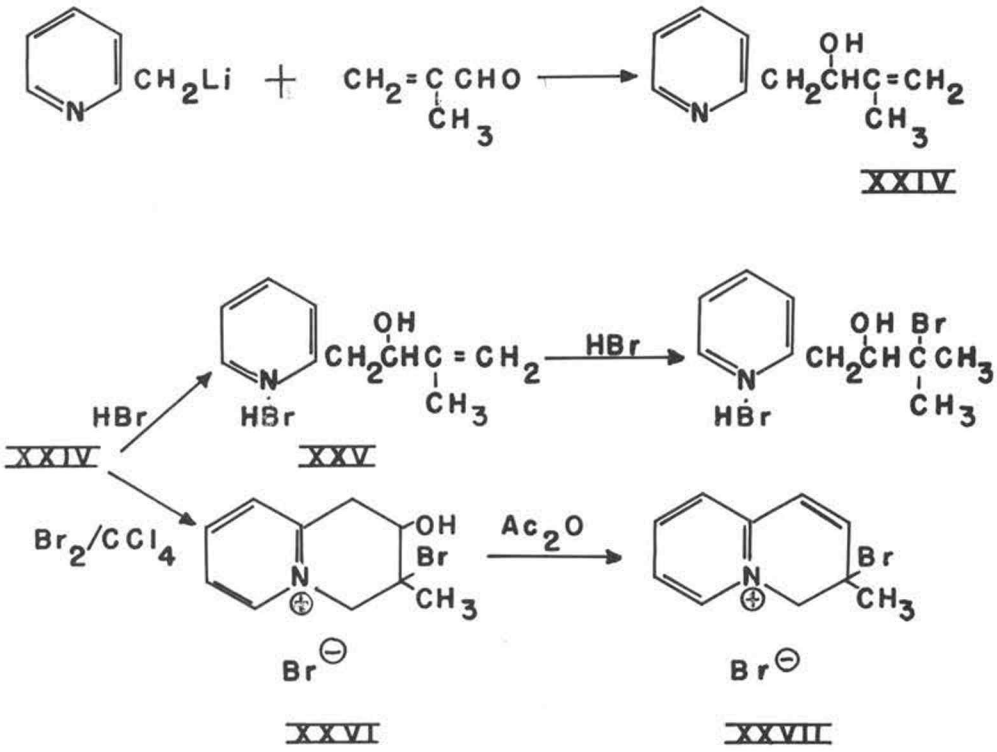
Boekelheide and co-workers (4, p.3243-3248) prepared γ-(2-pyridyl)-butyro nitriles in a good yield from either 2-vinyl pyridine or ethyl 2-pyridyl acetate. Upon mild hydrogenation over platinum in the presence of acid γ-(2-pyridyl)-butyro nitriles underwent cyclization to yield quinolizidine derivatives. They also found that this procedure was particularly useful for preparing 1- and 3-substituted quinolizidine.

Recent work in this laboratory, Wischman (23, p.2794-2796) prepared 1-(2-pyridyl)-3-butene-2-ol (XXI) by the reaction of 2-picolyllithium with acrolein. He found that the resulting allylic alcohol did not undergo oxotropic rearrangement on acid hydrolysis. Cyclization of XXI had occurred when treating with bromine in carbon tetrachloride, forming 2-hydroxy-3-bromo-1,2,3,4-tetrahydroquinolizinium bromide (XXII). Upon a quantitative hydrogenation of XXII, using platinum oxide as a catalyst, 3 1/2 moles of hydrogen were absorbed. Wischman also found that the cyclic alcohol (XXII) could be dehydrated to a purple crystalline compound, 3-bromo-3H,4H-quinolizinium bromide (XXIII), by refluxing with acetic anhydride

and a drop of concentrate sulfuric acid.

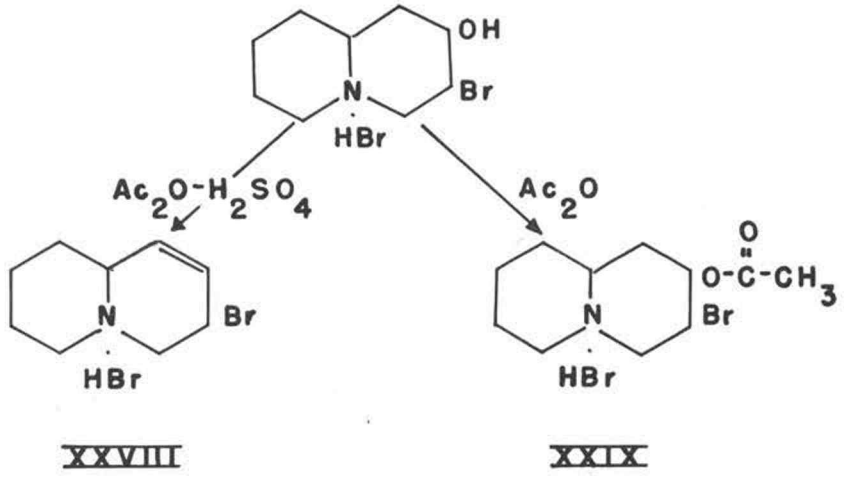


In a similar reaction, Nash (19, p.9-30) condensed 2-picolyllithium with methacrolein, 1-(2-pyridyl)-3-methyl-3-butene-2-ol (XXIV) was produced. He reported the addition reaction of hydrogen bromide across the double bond of 1-(2-pyridyl)3-methyl-3-butene-2-ol hydrogen bromide (XXV). Upon bromination in carbon tetrachloride, 2-hydroxy-3-methyl-3-bromo-1,2,3,4-tetrahydroquinolizinium bromide (XXVI) was obtained. Dehydration of this compound with acetic anhydride alone produced 3-methyl-3-bromo-3,4-dihydroquinolizinium bromide (XXVII).



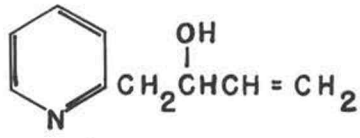
Davis (14, p.22-46) studied the reactions of 2-hydroxy-3-bromo-1,2,3,4-tetrahydroquinolizinium bromide (XXII). He found that XXII reacted with 47% hydriodic acid forming 2-iodo-3-bromo-1,2,3,4-tetrahydroquinolizinium bromide, which showed a similar infrared spectrum to XXII. He also found that 2-hydroxy-3-bromoquinolizidine hydrogen bromide can be dehydrated with acetic anhydride and a drop of concentrated sulfuric acid to 3-bromo- Δ^{1}-dehydroquinolizidine hydrogen bromide (XXVIII). The 2-hydroxy compound treated with

acetic anhydride alone gave 2-acetoxy-3-bromo quinolizidine hydrogen bromide (XXIX).

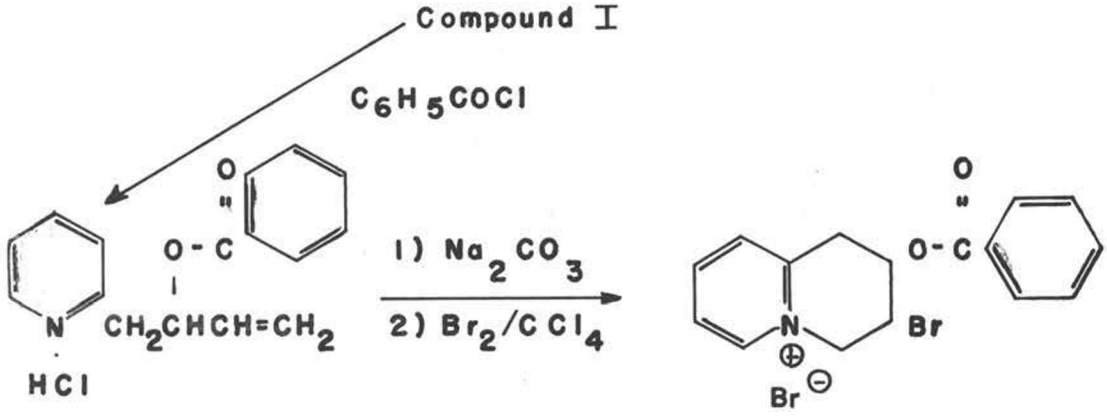


XXVIII XXIX

Figure I COMPOUNDS PREPARED



1-(2 - Pyridyl)-3-butene - 2 - ol



1-(2-Pyridyl hydrochloride)-
-2 - benzoyloxy - 3 - butene

Compound II

2 - Benzoyloxy - 3-bromo -
1,2,3,4 - tetrahydroquino -
- lizinium bromide

Compound III

Figure 2 COMPOUNDS PREPARED

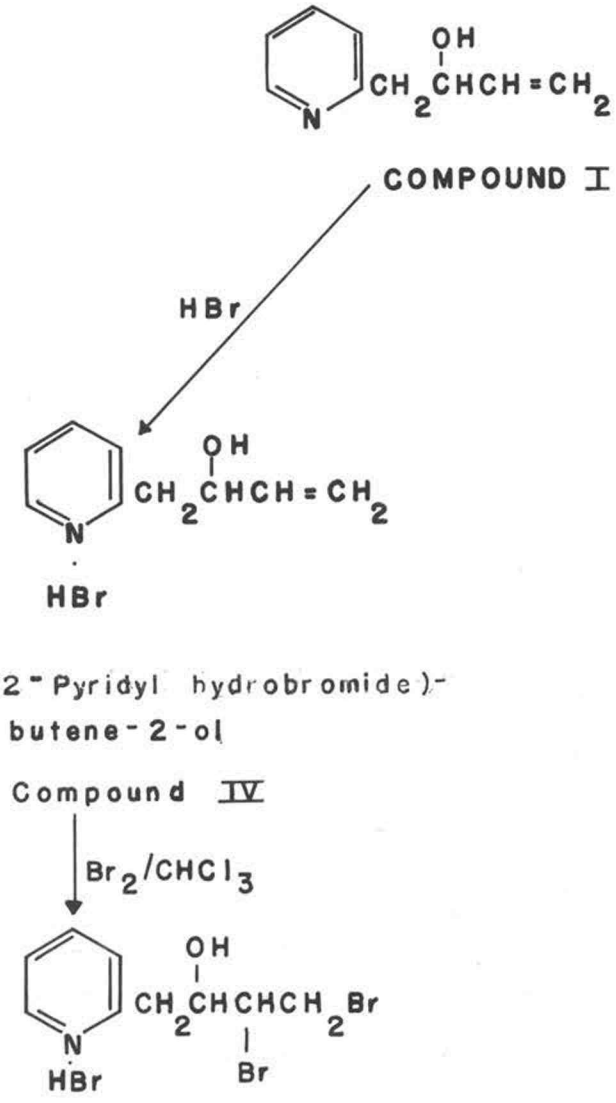
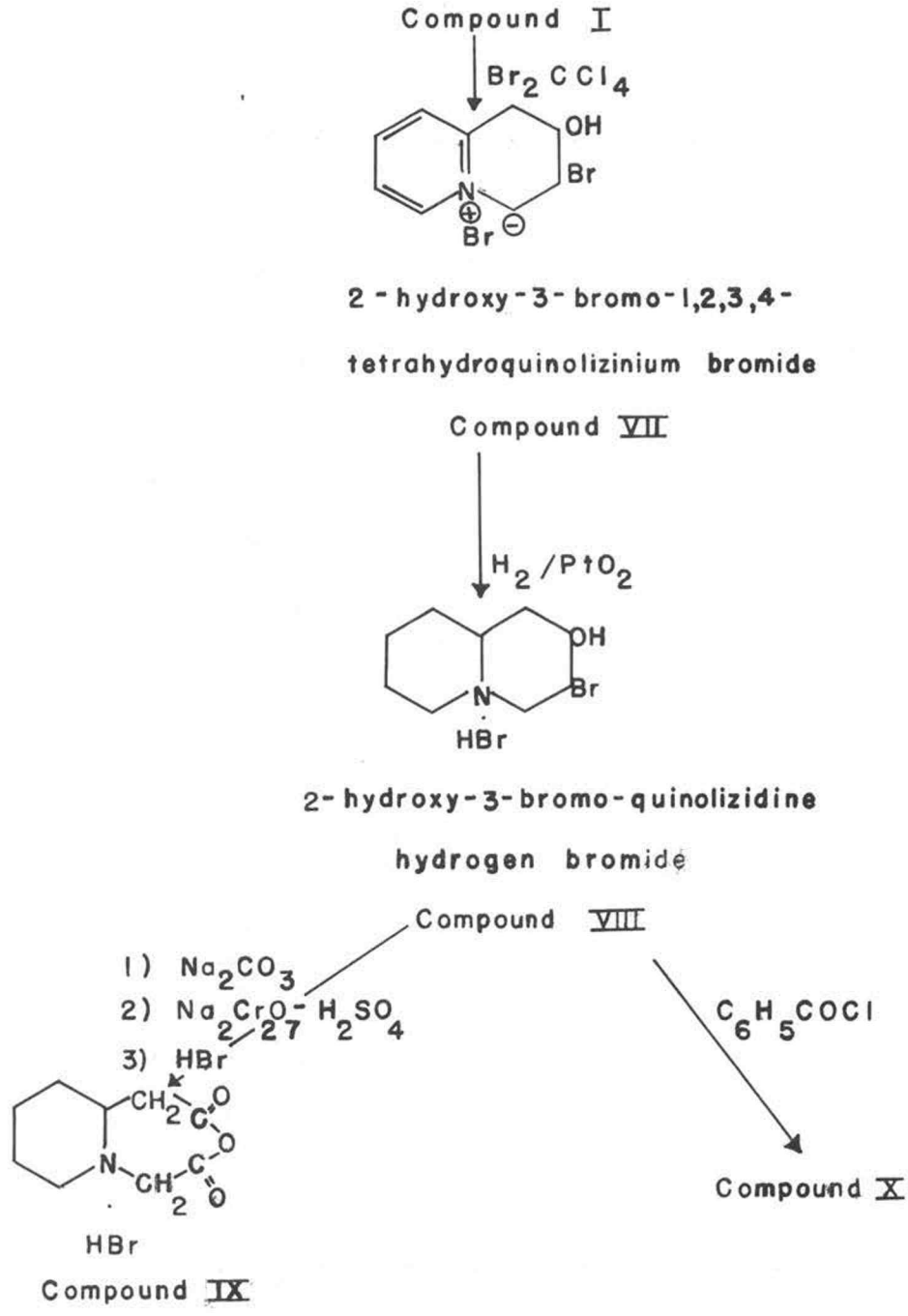


Figure 3 COMPOUNDS PREPARED



DISCUSSION

The condensation of picolyllithium with unsaturated aldehydes has been reported (1, p.287-294). Recently in this laboratory, Wischman (23, p.2794-2796) has investigated the reaction of 2-picolyllithium and acrolein. He prepared 1-(2-pyridyl)-3-butene-2-ol, compound I, and found that no oxotropic rearrangement occurred in acid solution.

Upon bromination of compound I in carbon tetrachloride (23, p.2794-2796), it underwent cyclization and produced a cyclic alcohol, compound VII, 2-hydroxy-3-bromo-1,2,3,4-tetrahydroquinolizinium bromide. Compound VII was very soluble in water and soluble in alcohol and glacial acetic acid, insoluble in acetone, carbon tetrachloride, chloroform and ether. It gave a positive test with silver nitrate. An ultraviolet spectrum gave a maximum absorption at 266 mμ as reported.

In current work compound I, 1-(2-pyridyl)-3-butene-2-ol, was subjected to reaction with benzoyl chloride in etheral solution, following the procedure used by Nash (19, p.26). A crude hydrochloride salt of the ester, 1-(2-pyridyl hydrogen chloride)-2-benzoyloxy-3-butene, compound II, was produced with heat evolved. Recrystallization from the mixture of

chloroform and ether a cyclization product was obtained. The carbon-hydrogen analysis of compound II agreed with the theoretical values. Since no ultraviolet data was reported for this compound, an ultraviolet spectral scan was run, showing peaks at 262 m μ and 234 m μ. Compound II was readily soluble in water and in many polar solvents. Water solution of the salt of the ester gave an acid reaction to pH paper.

To determine whether the salt of the ester could undergo cyclization with bromine, compound II was dissolved in water and treated with sodium carbonate solution. A water-insoluble liquid was formed and separated from the water layer. This material was assumed to be an ester of the free amine. Bromine was added to it, a reddish oily liquid was obtained at the end of the reaction. On the addition of acetone, a white amorphous material was produced. Carbon-hydrogen analysis showed this to be the ester of the cyclic compound, 2-benzoyloxy-3-bromo-1,2,3,4-tetrahydroquinolizinium bromide, compound III. The ultraviolet spectrum showed a 266 m μ peak, which appears to be the characteristic absorption of quinolizinium salt (2, p.1832-1836), and a 234 m μ peak still existed. An infrared spectrum showed a strong peak at 1725-1700 cm^{-1}.

which also indicated the ester was formed. Compound III was found to be soluble in water and gave a positive test with silver nitrate.

In a similar reaction, Nash (19, p.26) attempted to form a cyclic ester salt of 1-(2-pyridyl hydrogen chloride)-3-methyl-3-butene-2-ol benzoate. A white crystalline substance was produced, but the analysis of the isolated product was not established. He also attempted to form the ester of 2-hydroxy-3-bromo-3-methyl-1,2,3,4-tetrahydroquinolizinium bromide (cyclic alcohol) by treating the cyclic alcohol with an acid chloride, he reported that no pure compounds were isolated, perhaps due to the presence of unreacted starting material which could not be separated from the reaction products.

Compound VII, 2-hydroxy-3-bromo-1,2,3,4-tetrahydroquinolizinium bromide, was subjected to hydrogenation over platinum oxide. Compound VIII, 2-hydroxy-3-bromoquinolizidine hydrogen bromide, was produced in a good yield (23, p.2794-2796). In an attempt to form a ketone, compound VIII was oxidized with sodium dichromate and sulfuric acid, a product was isolated as the hydrogen bromide, compound IX. Carbon-hydrogen analysis did not indicate that the ketone had been formed. The infrared spectrum was obtained showing

a peak at 1850-1835 cm^{-1}, which indicates the possible formation of an anhydride. The carbon-hydrogen analysis agreed with the theoretical composition of an anhydride. The formation of compound IX indicated that hydrolysis had occurred during the reaction. It is assumed that a dihydroxy compound was produced as an intermediate, then underwent oxidization, cleaving the ring to give a dicarboxylic acid, which under acid condition was converted to the anhydride. The structure of compound IX was proposed as shown in figure 3. Compound IX was soluble in water and alcohol. It gave a possitive test with silver nitrate and an acid reaction to pH paper.

Recently, Wischman (23, p.2794-2796) had prepared 1-(2-pyridyl hydrogen bromide)-3-butene-2-ol, compound IV. He found that the salt was formed instead of an addition product. It seemed that the ring nitrogen was more nucleophilic than the olefinic double bond. After the salt was obtained the double bond was still present. Compound IV was again subjected to addition of hydrogen bromide, but no compound could be isolated. Compound IV was found to have a maximum absorption at 262 m μ.

Following the procedure used by Nash (19, p.27). Bromine was added to compound IV produced 1-(2-pyridyl

hydrogen bromide)-3,4-dibromo-butane-2-ol, compound V. Analysis showed that bromine had added across the double bond. An ultraviolet spectrum showed a peak at 262 m μ.

An attempt to oxidize compound V was made. An Oppenauer oxidation with aluminum isopropoxide and excess acetone gave a yellow oil, from which a white precipitate was isolated. This compound was expected to be a ketone. An attempt to form a 2,4-dinitrophenylhydrazone derivative was also made. However, an analysis for this compound indicated the starting material was recovered. In this reaction, aluminum isopropoxide was coated with a purple material, it was assumed that an oxidation had occurred. No pure compound could be isolated.

In another attempt to obtain an oxidation product, compound V was oxidized by using potassium permanganate in aqueous solution. Manganese dioxide was removed by filtration at the end of the reaction, and the filtrate was concentrated by evaporation. The solution turned to purple when heated. Again, no compound was isolated.

A dehydration of compound I, 1-(2-pyridyl)-3-butene-2-ol, with acetic anhydride and sulfuric acid was attempted. A yellow oil, which was assumed to be 1-(2-pyridyl)-1,3-

butadiene, was distilled under reduced pressure, and passed into a solution of bromine in carbon tetrachloride. A dark red oil was obtained. The solvent was decanted and the oily liquid turned to green on standing in air. A green powder, compound VI, was obtained on crystallization from chloroform and ether. Analysis indicated 20.24% of carbon, 1.85% of hydrogen, 74.09% of bromine and 3.82% of nitrogen contained in the compound. Upon sublimation, a thin layer of a yellow powder was collected. An ultraviolet spectrum was obtained, showing a peak at 266 mμ, which indicated a possibility of quinolizinium ion was present. The preparations of compound VI were repeated and crystallization was made from acetone. The results of an analysis are about the same values. Compound VI was found to be insoluble in water and soluble in chloroform and acetone. The confusing fact was that if the quinolizinium salt was obtained, the expecting ionic salt should be soluble in water and insoluble in acetone. However no conclusion could be drawn to identify compound VI at this time.

A dehydration of 2-hydroxy-3-bromo-1,2,3,4-tetrahydroquinolizinium bromide was undertaken following the procedure used by Wischman (23, p.2794-2796). Purple crystals were obtained with melting point of 168-170°C as reported. After

many recrystallizations, washing with acetone, the purple colored was removed and only slightly colored crystals remained. The melting point also raised to the same as that of the starting material. An ultraviolet spectrum also showed the same peak at 266 mμ. If the dehydration had occurred as expected, the double bond would have been formed in conjugation with the pyridine ring, and a bathochromic shift should have been found as described by Boekelheide and Gall (3, p.1832-1836) with 3,4-dihydroquinolizinium bromide, and with 3-methyl-3-bromo-3,4-dihydroquinolizinium bromide, observed by Davis (14, p.26). Compound VII was found to react with sulfuric acid and liberated bromine when heated. It was also found that compound VII gave a purple material when reacted with acetic anhydride. More study of this compound should be made in order to identify the material.

In an attempt to esterify compound VIII, 2-hydroxy-3-bromoquinolizidine hydrogen bromide, it was treated with benzoyl chloride. White crystals were isolated, compound X. This material was assumed to be a salt of the ester. The compound was sent to Galbraith Laboratories, Inc. for analysis, showing 48.85% of carbon, 6.27% of hydrogen, 3.59% of nitrogen and 40.74% of bromine contained in the compound.

An infrared analysis was made, showing a peak at 1735 cm^{-1}, which indicated a carbonyl group was present. Since the starting material was a hydrogen bromide salt and reacted with benzoyl chloride, there was a possibility of a mixed salt of hydrogen bromide and hydrogen chloride being formed. A potassium carbonate solution was added to convert the salt to the free amine, a water-insoluble material was isolated with a melting point of 100-101°C. An analysis was made, it indicated 60.10% of carbon and 5.96% of hydrogen contained in the compound. What was assumed to be the free amine was dissolved in chloroform and anhydrous hydrogen bromide gas was passed into the solution. A white precipitate was obtained and analyzed. It showed that the compound contained 49.77% of carbon and 5.46% of hydrogen. Again these values did not agree with the theoretical amount of the salt of the ester. Compound X was found to decolorize bromine water and potassium permanganate solution, indicating double bonds were present. Compound X was assumed to be N-benzoyl-3-bromo-Δ^{1}-dehydroquinolizidine bromide. Since time did not permit, no more evidence was obtained to identify the compound at this time.

EXPERIMENTAL

1-(2-pyridyl)-3-butene-2-ol.

The reaction vessel was a 3-necked one liter flask, equipped with a dropping funnel, a condenser protected by a calcium chloride tube, and a mechanical stirrer. Four hundreds milliliters of anhydrous ether containing 6.9 grams (1 g-atom) of lithium chips were introduced into the flask, while a stream of anhydrous nitrogen gas passed through the flask. From the dropping funnel, 10-15 ml of a mixture containing 79 g. (0.5 mole) of bromobenzene and 100 ml of anhydrous ether were added to start the reaction. If the reaction did not start, the flask was warmed. After the reaction started the remainder of bromobenzene solution was added to maintain a gentle reflux. The mixture was stirred until all the lithium was in the solution. Then 46 g. (0.5 mole) of 2-picoline were added and stirred for one hour. The reaction mixture was then cooled in an ice-salt mixture to 0°C and 35 g. (0.63 mole) of acrolein in 50 ml of anhydrous ether were added slowly. The mixture was stirred for 30 minutes, the red colored solution turned to yellow and the nitrogen train was disconnected.

Hydrolysis of the lithium salt was effected by adding 200 ml of water slowly and stirring for 30 minutes. The ether layer was separated and removed by distillation. The oily residue was distilled at 78-96°C/1 mm.

The yield was 23.5 g. (33.3%). The light yellow oil obtained from the above distillation was cooled and solidified. The solid was recrystallized from petroleum ether to give a white needle crystal with melting point of 36-37°C.

Anal. Cal'd for $C_9H_{11}NO$: C = 72.45 , H = 7.43

Found : C = 72.70 , H = 7.51

1-(2-pyridyl hydrobromide)-3-butene-2-ol.

Four grams (0.027 mole) of 1-(2-pyridyl)-3-butene-2-ol were dissolved in 100 ml of anhydrous benzene in a flask, equipped with mechanical stirrer and a delivery tube. The flask was cooled to 0°C in an ice bath, and anhydrous hydrogen bromide gas was bubbled through this solution. A white solid had precipitated and washed with small amount of acetone. The resulting precipitate was recrystallized from acetone, white needle crystals were obtained, which melted at 96-97°C, yield 4.8 g. (77.6%).

Anal. Cal'd for $C_9H_{12}NOBr$: C = 46.8 , H = 5.22

Found : C = 46.75 , H = 5.17

1-(2-pyridyl hydrobromide)-3,4-dibromo-butane-2-ol.

Two grams (0.0087 mole) of 1-(2-pyridyl hydrobromide)-3-butene-2-ol were dissolved in 150 ml of chloroform. To this solution 1.3 g. of bromine in 10 ml of chloroform were added with stirring. At the end of the reaction, a reddish viscous liquid was formed at the bottom of the flask. Chloroform was decanted. The reddish liquid was dissolved in acetone and ether was added to reduce the solubility of the product in acetone. A white amorphous powder was obtained which melted at 109-110°C.

Anal. Cal'd for $C_9H_{12}NOBr_3$: C = 27.72 , H = 3.102

Found : C = 28.02 , H = 3.21

1-(2-pyridyl hydrochloride)-2-benzoyloxy-3-butene.

Five grams (0.0335 mole) of 1-(2-pyridyl)-3-butene-2-ol were dissolved in 150 ml of anhydrous ether. To this solution, 5.7 g. (0.0399 mole) of benzoyl chloride were added with stirring. The solution was stirred occasionally for several hours, a white precipitate was formed. Filtered and recrystallized from a mixture of chloroform and ether. White crystals were obtained with melting point of 139-140°C. The

yield was 6.9 g. (71.1%).

Anal. Cal'd for $C_{16}H_{16}O_2NCl$: C = 66.32 , H = 5.57

Found : C = 66.75 , H = 5.78

2-benzoyloxy-3-bromo-1,2,3,4-tetrahydroquinolizinium bromide.

Five-tenth gram (0.00173 mole) of 1-(2-pyridyl hydrochloride)-2-benzoyloxy-3-butene in 10 ml of water was treated with 0.092 g. of sodium carbonate in 10 ml of water. A water-insoluble liquid was formed and isolated by extracting with 30 ml of carbon tetrachloride. To this solution, 0.32 g. of bromine in 10 ml of carbon tetrachloride was slowly added with stirring. A reddish oily liquid was formed at the bottom of the flask after the reaction was completed (30 minutes). The solvent was decanted and the oily liquid was dissolved in a small amount of acetone. Ether was added to reduce the solubility. A precipitate was formed and recrystallized in acetone. The yield was 0.36 g. and the melting point 142°C dec.

Anal. Cal'd for $C_{16}H_{15}NO_2Br_2$: C = 46.52 , H = 3.66

Found : C= 46.48 , H = 3.64

2-hydroxy-3-bromo-1,2,3,4-tetrahydroquinolizinium bromide.

In a 300 ml 3-necked round bottom flask, equipped with

a mechanical stirrer, reflux condenser and a dropping funnel, 10 g. (0.07 mole) of 1-(2-pyridyl)-3-butene-2-ol was dissolved in 200 ml of carbon tetrachloride. From a dropping funnel, a solution of 11 g. (0.07 mole) of bromine in 100 ml of carbon tetrachloride was added slowly with stirring to the solution. The solution turned cloudy and a solid formed on the side of the flask. After the reaction was completed, the solvent was decanted. The precipitate was washed with acetone and recrystallized from methanol. Norite was used to decolorize, if necessary. Yield a white crystalline compound in 67% with the melting point of 181-182°C.

Anal. Cal'd for $C_9H_{11}NOBr_2$: C = 34.98 , H = 3.58

Found : C = 34.96 , H = 3.57

2-hydroxy-3-bromoquinolizidine hydrogen bromide.

Five grams (0.0162 mole) of 2-hydroxy-3-bromo-1,2,3,4-tetrahydroquinolizinium bromide were dissolved in 150 ml of absolute ethanol and placed in a Paar hydrogenation apparatus. Five-tenth gram of platinum oxide (Adams catalyst) was added. The hydrogenation took place for two hours. After the hydrogen was absorbed, the catalyst was removed by filtration. The filtrate was evaporated to a volume of 50-

75 ml. The mixture was cooled and a white crystalline compound precipitated. Crystals were filtered and dried. Yield 4.8 g., melting point, decomposition, 206-207°C.

Anal. Cal'd for $C_9H_{17}NOBr_2$: C = 34.3 , H = 5.404

Found : C = 34.07 , H = 5.43

Oxidation of 2-hydroxy-3-bromoquinolizidine hydrogen bromide.

One and a half grams (0.0047 mole) of 2-hydroxy-3-bromoquinolizidine hydrogen bromide were dissolved in 10 ml of water. The aqueous solution was neutralized with 0.5 g. of sodium carbonate in 10 ml of water, and then extracted with chloroform. Two grams of sodium dichromate and 1.0 g. of sulfuric acid were added to the extract and warmed on a steam bath for 30 minutes. The mixture was made alkaline and extracted with chloroform. After the chloroform extract was dried, it was concentrated and treated with anhydrous hydrogen bromide. An oily liquid was obtained. This liquid was dissolved in an absolute ethanol and cooled. White crystals were obtained, melting point 216°C sublimes.

Anal. Cal'd for $C_9H_{14}NBrO_3$: C = 40.93 , H = 5.32

Found : C = 41.01 , H = 5.19

Reaction of 2-hydroxy-3-bromoquinolizidine hydrogen bromide with benzoyl chloride.

In a 50 ml round bottom flask, 1.2 g. (0.0038 mole) of 2-hydroxy-3-bromoquinolizidine hydrogen bromide were dissolved in 10 ml of benzoyl chloride by heating on a steam bath. The solution was allowed to stand overnight at room temperature, protected from the atmosphere. The excess benzoyl chloride was evaporated under vacuum. White crystals were obtained and washed with ether. The crystals were dissolved in water and a potassium carbonate solution was added. A water-insoluble material was formed and separated, and dissolved in chloroform. Anhydrous hydrogen bromide gas was passed into the cooled solution. A white precipitate was obtained. Recrystallization from ethanol formed a white powder with the melting point of 180-182°C.

Anal. Found : C 49.77 , H 5.46

Dehydration of 1-(2-pyridyl)-3-butene-2-ol.

Three grams (0.201 mole) of 1-(2-pyridyl)-3-butene-2-ol was placed in a 50 ml round bottom flask, equipped with a reflux condenser. To this solution, 12 ml of acetic anhydride and 1-2 drops of sulfuric acid were added. The solution

mixture was refluxed for 30 minutes, and then distilled under reduced pressure. The yellow oil was distilled at 140°C under the vacuum of the water pump, and passed into 2.1 ml of bromine in 30 ml of carbon tetrachloride. A dark red oil was produced. This oily liquid was dissolved in chloroform and ether. A green powder was obtained with melting point of 162-164°C dec.

Anal. Found: 1) C 20.24 , H 1.85 , Br 74.09

2) C 21.0 , H 2.0

3) C 20.43 , H 1.95

SUMMARY

The condensation of picolyllithium and acrolein formed 1-(2-pyridyl)-3-butene-2-ol, compound I. It was a free amine contained an allylic type of an alcohol. Esterification of compound I with benzoyl chloride produced 1-(2-pyridyl hydrogen chloride)-2-benzoyloxy-3-butene, compound II, which underwent cyclization to compound III, 2-benzoyloxy-3-bromo-1, 2,3,4-tetrahydroquinolizinium bromide.

Addition of hydrogen bromide to compound I produced compound IV, 1-(2-pyridyl hydrogen bromide)-3-butene-2-ol. Bromine was added across the double bond of compound IV produced 1-(2-pyridyl hydrogen bromide)-3,4-dibromobutane-2-ol, compound V. A dehydration of compound I was attempted and addition of bromine to an intermediate product produced a green precipitate, compound VI, which could not be identified.

Bromination of compound I caused a cyclization, 2-hydroxy-3-bromo-1,2,3,4-tetrahydroquinolizinium bromide, compound VII, was obtained, which upon hydrogenation formed compound VIII, 2-hydroxy-3-bromoquinolizidine hydrogen bromide. Compound VIII was reacted with sodium dichromate and sulfuric acid produced compound IX. An attempt to

esterify compound VIII produced a white precipitate, which could not be identified.

The condensate of picolyllithium and acrolein and of the hydrogen bromide salts have been reported. All the other compounds prepared in this study are new compounds not previously reported in the literature.

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APPENDIX

APPARATUS USED

1. Ultraviolet data were obtained with a Beckman D.B. Spectrophotometer, O.S.U. #77051; #5856.
   (a) Cells used were 1 cm quartz cells manufactured by Beckman.
2. Infrared data were obtained from a Perkin-Elmer Model 21 infrared spectrophotometer.
   (a) Potassium bromide pellets were made of all samples analyzed by infrared.
3. The listed melting points are uncorrected.

TABLE I

Important Peaks for Compounds

Analyzed by Infrared

Compound	Peaks (cm^{-1})
III	3360
	2945
	2300
	1700
	1620
	1585
	1565
	1495
	1450
	1430
	1380
	1310
	1260
	1200
	1165
	1110
	1065
	1045
	1020
	925
	880
	790
	775
	720
	695
	670
VIII	3280
	2880
	2640
	2480

Continued on next page

TABLE I - Cont.

Compound	Peaks (cm^{-1})
	2310
	1450
	1430
	1410
	1385
	1320
	1280
	1225
	1205
	1170
	1145
	1115
	1070
	1060
	1045
	1010
	965
	920
	880
	845
	810
	770
	690
IX	3250
	2800
	2600
	1835
	1560
	1475
	1440
	1400
	1360
	1320
	1270
	1255

Continued on next page

TABLE I - Cont.

Compound	Peaks (cm^{-1})
	1235
	1200
	1160
	1135
	1110
	1090
	1070
	1040
	990
	965
	915
	875
	765
	725
X	3435
	2935
	2475
	1735
	1601
	1581
	1446
	1416
	1396
	1364
	1336
	1311
	1266
	1206
	1173
	1138
	1113
	1068
	1018
	1000
	970

Continued on next page

TABLE I - Cont.

Compound	Peaks (cm^{-1})
	902
	877
	847
	797
	785
	735
	705
	675

TABLE II

Ultraviolet Peaks

Compound	Concentration (mg/l)	λ_{max} (m μ)	Log of Molecular Extinction Coefficient (log ϵ)
I	28	262	3.53
II	11	262	3.84
		234	4.35
III	20	266	3.83
		234	4.18
X	13	272	3.21
		234	4.29