

### Summary

Tetraphenyl-di-*tert.*-butylethynylethane has been prepared and characterized. It has been found to be easily oxidized by gaseous oxygen, easily rearranged to an isomeric hydrocarbon on standing and easily cleaved by alkali metals.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF STANFORD UNIVERSITY]

## SALTS OF THE AMMONO ENOLIC MODIFICATION OF PYRIDINES AND QUINOLINES ALKYLATED IN THE 2- AND 4-POSITIONS<sup>1</sup>

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RECEIVED JULY 15, 1931

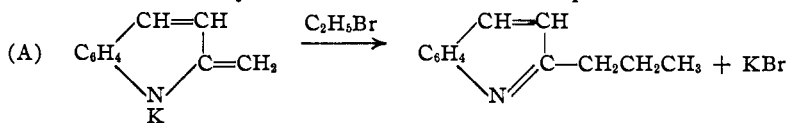
PUBLISHED NOVEMBER 5, 1931

### Introduction

In previous articles it has been shown that 2-methylquinoline (quinaldine) and 2,3-dimethylquinoxaline are cyclic ketone-acetals of the ammonia system<sup>2</sup> because of the  $\begin{matrix} \text{CH}_3 \\ \diagdown \\ \text{C}=\text{N}- \end{matrix}$  group which is a part of their structure.

In conformity with this view both of these compounds have been shown to react with potassium amide, a base of the ammonia system, to form highly colored (red or reddish-brown) salts of the corresponding ammono enolic modification,<sup>3</sup> that is to say, salts which contain the grouping  $\begin{matrix} \text{CH}_2 \\ \diagdown \\ \text{C}-\text{NK}- \\ \diagup \\ \text{R} \end{matrix}$ .

In chemical reactivity these salts have been found to resemble in many respects the salts of the enolic modification of acetoacetic ester and related ketones of the water system. Thus, 2-methylquinoline and 2,3-dimethylquinoxaline may be alkylated by treating the potassium salt of the ammono enolic form with an alkyl halide in the sense of the equation



The resemblance of this reaction to the alkylation of acetoacetic ester has been pointed out by Ziegler and Zeiser.<sup>3b,2b,2c</sup>

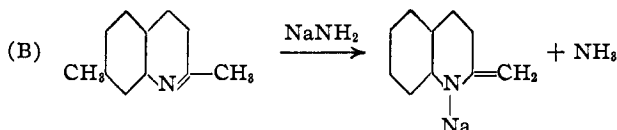
<sup>1</sup> Presented at the Pasadena Meeting of the A. A. A. S., June, 1931.

<sup>2</sup> (a) Ogg and Bergstrom, *THIS JOURNAL*, **53**, 1846 (1931); (b) Bergstrom, *ibid.*, **53**, 3027 (1931); (c) *Science*, **72**, 402 (1930).

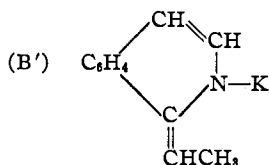
<sup>3</sup> (a) Ref. 2(a-c); (b) Ziegler and Zeiser, *Ann.*, **485**, 178 (1931), have made an examination of reactions of this type in connection with their very interesting work on the chemical reactivity of the lithium alkyls and aryls. Thus, lithium phenyl reacts with quinaldine to form benzene and the lithium salt of the ammono enol of quinaldine. 2-Picoline (2-methylpyridine) is likewise converted without difficulty to the lithium salt of the corresponding ammono enol.

In continuation of this work, a study has been made of the chemical reactivity of other cyclic ammono ketone acetals, that is, of derivatives of quinoline, isoquinoline and pyridine alkylated in the alpha position.

**Salts of the Ammono Enolic Modification of Alkylated Pyridines, Quinolines and Isoquinolines.**—It was found in the present work that all pyridine and quinoline derivatives with an alkyl group in the 2-position, in so far as investigated, react with potassium amide or sodium amide in liquid ammonia to form strongly colored (deep red or brownish-red) salts of the ammono enolic modification, in accordance with the type equation



1-Ethylisoquinoline, likewise a cyclic ammono ketone acetal, readily reacts with sodium amide to form a salt of the probable constitution



4-Methylquinoline (lepidine), although a cyclic ammono aldehyde acetal, nevertheless forms a potassium and a sodium salt which appear to possess the quinoid structure of the first formula in equation (J).<sup>4</sup>

The salts so obtained, together with the results of their analyses, are recorded in Table I. The experimental technique required for their preparation will best be understood from a description of the isolation of the sodium and potassium salts of 2,4-dimethylquinoline.

In one leg of a two-legged reaction tube<sup>5</sup> was placed 0.21 g. of sodium (1.4 equivalents) together with a coil of iron wire to act as a catalyst for the conversion of the liquid ammonia solution of the metal to sodium amide. Into the other leg was pipetted 0.9 cc. of 2,4-dimethylquinoline (1.0 equivalent). After the lapse of a few days, when the reaction between sodium and solvent was complete, the dimethylquinoline was washed over into the leg containing the sparingly soluble sodium amide and the resulting deep brownish-red solution concentrated to a volume of 2 or 3 cc. After standing overnight this solution was carefully decanted into the other leg of the reaction tube, leaving the unused sodium amide behind. The ammonia was evaporated from the tube, leaving the sodium salt as a reddish amor-

<sup>4</sup> Mills and Smith, *J. Chem. Soc.*, 121, 2730 (1922), have shown that the methyl group in the 4-position of quinoline is second only to the 2-methyl group in reactivity.

<sup>5</sup> (a) Franklin, *THIS JOURNAL*, 27, 831 (1905); (b) 29, 1275 (1907); 35, 1460 (1913); *J. Phys. Chem.*, 15, 510 (1911); 16, 694 (1912); Bohart, *ibid.*, 19, 539 (1915).

phous solid.<sup>6</sup> The leg containing this material was sealed off and evacuated at 20°. The specimen, after hydrolysis with water vapor, was dissolved in dilute hydrochloric acid and analyzed. One aliquot of this solution was evaporated to dryness and gently ignited to carbonize the organic matter. Thereupon sulfuric acid was added and the sodium weighed as sulfate after further ignition. A second aliquot was made alkaline with sodium hydroxide, the liberated base extracted with ether and converted to picrate. A mixed melting point of this picrate (m. p. 194–195.2°) with known 2,4-dimethylquinoline picrate was 194–195°, showing their identity. It is worthy of mention, however, that very little dimethylquinoline was recovered from the products of the hydrolysis of the heated specimens of the sodium or potassium salts. Therefore these salts are thermally unstable.

The potassium salt of 2,4-dimethylquinoline was isolated by treating its liquid ammonia solution—prepared from potassium amide and an excess of dimethylquinoline—with twice the volume of absolute ether.<sup>7</sup> The solvent ammonia was evaporated from the reaction tube, leaving a precipitate of the potassium salt under absolute ether. The dimethylquinoline not used in the reaction was removed by washing the crude potassium salt with ether in the same manner that a solid is washed with liquid ammonia in a reaction tube.<sup>8</sup> The purified salt was then dissolved in dilute hydrochloric acid and analyzed.

The barium salt of 2,4-dimethylquinoline, alone of all the salts in Table I, was purified by repeated crystallization from liquid ammonia at –40°.

The sodium salts of the ammono enolic modifications of 2-methyl-, 2,4-dimethyl- and 2,4,6-trimethylpyridine could not readily be prepared by the methods outlined above, because the reactions were slow and incomplete. In view of the ease and completeness with which 2-methyl- and 2,4-dimethylquinoline react with sodium amide in liquid ammonia, it must be concluded that the 2-methylated pyridines are weaker “acids”<sup>8a</sup> than the

<sup>6</sup> It was not possible to crystallize any of the salts described in this paper even by cooling their liquid ammonia solutions to –78°. The barium salt of 2,4-dimethylquinoline is an exception.

<sup>7</sup> The reaction tube (Fig. 1) was cooled in a bath of liquid ammonia, the side tube A broken open and ether introduced, after which A was resealed. A current of ammonia from the supply tank passed through the stopcock and out of A while the ether was introduced.

<sup>8</sup> The ammonia gas in the reaction tube necessarily interferes with the free transference of the ether from one leg to the other. Therefore it was imperative first to boil the ether for a few moments under diminished pressure (water-pump) to insure removal of the ammonia.

<sup>8a</sup> Only in the sense that the enolic modification of an aquo ketone may be regarded as an extremely weak acid. The reaction of potassium amide with quinaldine is not necessarily a reaction analogous to the neutralization of an acid by a base. We may follow the suggestions of Ziegler and Zeiser [Ref. 3b, *Ber.*, **63B**, 1847 (1930)] and say that potassium amide first adds to the double bond between the carbon and nitro-

2-methylated quinolines, as would be anticipated as a result of the negative influence of the benzene ring in the latter.

Lithium amide, which is probably a weaker ammonio base than sodium amide, reacts very sluggishly with a liquid ammonia solution of 2-methylpyridine, the resulting reddish-brown solution remaining transparent even after the lapse of three months. The almost insoluble calcium amide does not react with 2,4-dimethylquinoline.

The lithium and sodium salts of the methylated pyridines, being salts of very weak acids, are undoubtedly partly ammonolyzed in liquid ammonia solution to the pyridine base and the free metal amide. This ammonolysis must necessarily be the greater because of the low solubility of these amides in liquid ammonia. Therefore one should expect the readily soluble potassium amide to react more completely with the methylated pyridines, and this proved to be the case, because it was possible to have a sufficient excess of amide in solution to drive the reactions approximately to completion. Conversely, an excess of 2-methylpyridine was found to convert a limited quantity of potassium amide almost entirely to the potassium salt of the ammono enol, in liquid ammonia solution at 20°. The reaction tube, prepared for analysis in the customary manner, was well evacuated at room temperature to remove the excess methylpyridine. The analysis of the crude potassium salt so obtained is given in Table I (No. 16).

In view of the lack of a thoroughly satisfactory method of analysis for nitrogen in the salts listed in Table I, the change in weight that occurs when a quinoline or pyridine derivative reacts with sodium or potassium amide has been determined and from this has been calculated the number of molecules of ammonia retained by the salts of the ammono enol form. Naturally, before this method can be used with assurance, it must have been demonstrated that the anticipated chemical reaction occurs. This has been done by showing that the 2-substituted quinolines and pyridines react with the alkali metal amides to form salts which can be isolated and analyzed (see Table I).

The determination of the amount of ammonia retained by the sodium salt of 2,4-dimethylquinoline will serve as an example of the method followed.

For convenience in manipulation, the customary liquid ammonia reaction tube has been slightly modified, as shown in Fig. 1. With the opening of the small tube A closed by a stopper, legs B and C were sealed off in the usual manner in a current of ammonia. Leg B was left empty; leg C contained a few tenths of a gram of sodium (50 % in excess of the theoretical; see equation B), together with a coil of iron wire to serve as a catalyst gen of quinaldine in such a way that the methyl and amino groups are both attached to the same carbon atom. The subsequent loss of ammonia between the amino and methyl groups would give a potassium salt of the ammono enol.

for the conversion of the sodium to sodium amide. A weighed amount (approximately a gram) of 2,4-dimethylquinoline was introduced into the reaction tube through A by means of a small weight pipet. Tube A was sealed off close to the stopcock, ammonia distilled into the reaction tube and then evaporated off again when all of the sodium had been converted to sodium amide.<sup>9</sup> The reaction tube was evacuated at room temperatures and weighed on an ordinary analytical balance. Under these conditions the sodium amide retains no ammonia of crystallization. The legs of the tube had purposely been shortened to allow of the suspension of the apparatus in a vertical position from one of the pan supports of the balance. Ammonia was now distilled into the tube, all dimethylquinoline washed over into the sodium amide leg and the resulting opaque reddish-brown solution concentrated. After a day—at the end of which time the reaction was adjudged complete—the solution of the sodium

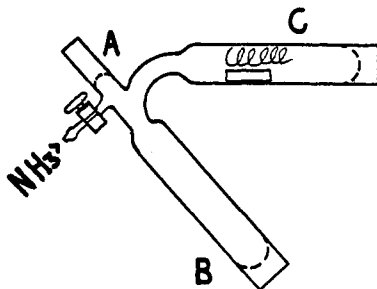


Fig. 1.

ammonio enolate was decanted into the clean leg of the reaction tube and the ammonia evaporated off. The weight of the evacuated tube, subtracted from the weight of the same evacuated tube before the reaction had taken place, gave the weight of ammonia lost in the reaction. Thus it was found that the sodium ammonio enolate from 0.9956 g. of 2,4-dimethylquinoline lost 0.0534 g. of ammonia, corresponding to a retention of 0.505 molecule of ammonia per mole of the salt. It must be remembered that, in accordance with equation B, one molecule of ammonia would be lost if the product of the reaction retains no ammonia of crystallization.<sup>10</sup>

The reaction tube was attached to a source of ammonia and the stopcock slowly opened to destroy the vacuum. The legs of the tube, now full of gaseous ammonia, were sealed apart and the sodium amide leg (C) discarded. The specimen of the sodium ammonio enolate was then dried in a vacuum at 25 and 150° and analyzed.<sup>5a,b</sup>

In a similar manner, 1.0867 g. of 2,4-dimethylquinoline, in reacting with

<sup>9</sup> The procedure described is not quite as convenient as the method of Kraus and Greer, *THIS JOURNAL*, 45, 3079 (1923), in which the gain or loss in weight during a reaction at  $-33^{\circ}$  is determined. However, when reactions take place too slowly at  $-33^{\circ}$ , it is advisable to employ the present manipulation. Furthermore, working in the manner described, one may purify and analyze a substance in the familiar manner developed by Dr. E. C. Franklin,<sup>5</sup> after the change in weight resulting from the reaction is determined.

<sup>10</sup> A further quantity of ammonia was lost when one of these tubes was heated *in vacuo* at 150° (both legs heated), the loss corresponding to the formation of the approximately anammonous salt.

1.75 equivalents of potassium amide, lost 0.1129 g. or 0.957 mole of ammonia at 20°. This would correspond to the formation of the approximately anammonous salt. The last traces of ammonia were very difficult to remove at room temperature. On heating this specimen, a small amount of dimethylquinoline, undoubtedly formed by ammonolysis of its salt by the small amount of remaining ammonia, was removed by the vacuum pump.

Likewise, a loss in weight of 0.0140 g. occurred after 1.2535 g. of lepidine had reacted with a 50% excess of sodium amide at room temperature. The sodium salt of lepidine, therefore, retains 0.906 or practically one molecule of ammonia. When heated at 150°, all except 0.17 molecule of this ammonia was given off. Perhaps some aminolepidine is formed, since this would account for the retained ammonia.

It was necessary to determine the ammonia retained by the potassium salt of collidine in a slightly different manner—the procedure as described above being inapplicable because of the volatility of collidine in a vacuum at room temperatures.

0.6445 g. of potassium (3.1 equivalents)<sup>11</sup> and a coil of iron wire to convert the ammonia solution of the metal to potassium amide were placed in one leg of a shortened ammonia reaction tube; 0.6458 g. of dry collidine (2,4,6-trimethylpyridine) was pipetted into the other leg. Liquid ammonia was distilled into the tube, the potassium solution shortly being converted to potassium amide, which was all transferred to the leg containing the collidine. After the lapse of two days, the reaction was adjudged to be complete. The ammonia was evaporated, leaving a reddish-brown mass of the potassium salt admixed with the excess potassium amide used in the reaction. The reaction tube was evacuated at 18 and 125°, weighing after each evacuation. The precipitate was hydrolyzed with water, then dissolved in alcohol and removed from the reaction tube, which was dried and evacuated. The loss of ammonia during the reaction was found by subtracting the weight of the material removed from the reaction tube (1.4700 g. at 18°, 1.4610 g. at 125°) from the sum of the weights of the collidine and the potassium amide (0.6458 g. + 0.9082 g. or 1.5540 g.). The weight of the latter was calculated from the known weight of potassium used in the reaction. The loss of ammonia during the reaction and subsequent evacuations was therefore 0.0840 g. at 18° and 0.0930 g. at 125°. That is, 0.923 and 1.02 moles of ammonia were lost per mole of collidine, corresponding to the formation of the anammonous salt at 125°.

### Discussion

Since the sodium salts enumerated in the above table were prepared by treating an excess of sodium amide with a substituted quinoline or iso-

<sup>11</sup> Kraus and Chiu, *THIS JOURNAL*, **44**, 2001 (1922); Peck, *ibid.*, **40**, 338 (1918).

TABLE I  
 EXPERIMENTAL DATA

No.	Quinoline derivative	Ammonio base	Dried in vacuo, 20° % Metal		Calcd. for salt ( )NH <sub>2</sub> % Metal	Heated in vacuo ( )° % Metal		Calcd. for salt ( )NH <sub>2</sub> % Metal
1	2,6-Dimethyl <sup>a</sup>	NaNH <sub>2</sub> <sup>a</sup>	12.1	12.2	11.7 (1)	13.7 (140°)	12.9 (0)	
2	2,4-Dimethyl	KNH <sub>2</sub>	19.9		19.9 (0)	20.4 (120°)	19.9 (0)	
3	2,4-Dimethyl	NaNH <sub>2</sub>	12.3		12.3 (1/2)	13.1 (125°)	12.9 (0)	
4	2,4-Dimethyl	LiNH <sub>2</sub>	Reaction not quite complete, 1 month at 20°					
5	2,4-Dimethyl <sup>a</sup>	Ba(NH <sub>2</sub> ) <sub>2</sub> <sup>a</sup>	28.6 (110°)	28.4 (2)		29.6 (110°)	29.5 (1)	
			29.2			30.0 (110°)		
6	2,4-Dimethyl	Ca(NH <sub>2</sub> ) <sub>2</sub>	No appreciable reaction					
7	2- <i>n</i> -Propyl-3-ethyl	NaNH <sub>2</sub>	(Viscous liquid)		(Solid) →	10.9 (110°)	10.4 (0)	
8	2-Ethyl	NaNH <sub>2</sub>	12.4		11.7 (1)	13.0 (130°)	12.9 (0)	
9	2- <i>n</i> -Propyl	LiNH <sub>2</sub>	Incomplete reaction					
10	2- <i>n</i> -Propyl	NaNH <sub>2</sub>	11.8		11.9 (0)	12.3 (150°)	11.9 (0)	
11	2- <i>n</i> -Amyl	Ba(NH <sub>2</sub> ) <sub>2</sub>	Slight reaction					
		LiNH <sub>2</sub>	Reaction not quite complete, 3 months at 20°					
12	2- <i>n</i> -Amyl	NaNH <sub>2</sub>	10.7			11.0 (150°)	10.4 (0)	
13	4-Methyl	NaNH <sub>2</sub>	13.3		12.6 (1)			
14	4-Methyl	Ba(NH <sub>2</sub> ) <sub>2</sub>	Reaction a trifle slow, salt not obtained pure, brown solution					
15	β-Naphthoquinaldine	NaNH <sub>2</sub>	11.3			11.5 (135°)	10.7 (0)	
16	2-Methyl pyridine	KNH <sub>2</sub>	24.6		23.6 (2)	26.6 (115°)	26.4 (1)	
		NaNH <sub>2</sub>	Incomplete reaction					
		LiNH <sub>2</sub>	Slight reaction, brownish-red solution					
17	2,4-Dimethylpyridine and 2,6-Dimethylpyridine	KNH <sub>2</sub>	Reaction a trifle slow					
18	Sym.-collidine	KNH <sub>2</sub>	Reaction a trifle slow					
		NaNH <sub>2</sub>	Reaction slow and incomplete, red solution					
		Ba(NH <sub>2</sub> ) <sub>2</sub>	Slight reaction, red solution					
19	1-Ethylisoquinoline	NaNH <sub>2</sub>	12.8			13.1 (135°)	12.8 (0)	
20	2-Phenylethylquinoline	NaNH <sub>2</sub>	Rapid reaction, opaque maroon red solution					

<sup>a</sup> Two preparations.

## PREPARATION OF THE COMPOUNDS IN COLUMN II

(1) *Ber.*, 23, 3483 (1890). Prepared by Mr. D. M. Morgan. (2), (13), (15) Obtained from Eastman Kodak Co. (7) Doebner and Miller, *Ber.*, 17, 1718 (1884). Prepared by Mr. V. Bowles. (8), (9), (11), (20) *THIS JOURNAL*, 53, 3032 (1931). (18) Obtained from the Gesellschaft für Teerverwertung, Duisberg-Meiderich. (19) Bergstrom and McAllister, *THIS JOURNAL*, 52, 2848 (1930).

quinoline, and since the liquid ammonia solutions of the salts so formed contained some dissolved sodium amide (solubility about a gram a liter at room temperatures), it is apparent why most of the sodium analyses reported are slightly higher than the theoretical. The salts were not crystallized, but were obtained by evaporating their ammonia solutions to dryness.

It will be noted that some of the salts of Table I still contain ammonia after being dried in a vacuum at 20°, although it is often possible that this

is not held as true solvent of crystallization. Thus it seems peculiar that the sodium salt of 2,4-dimethylquinoline retains only one-half molecule of ammonia in a vacuum at room temperatures. On the other hand, many of the salts retain very little ammonia under ordinary conditions (Nos. 2, 10, 12, 15).

The alkylated quinolines from which the above salts were prepared could always be recovered from the products of water hydrolysis of the unheated salts, although usually not in quantitative yield.<sup>12</sup> Most of the salts, on the other hand, appear to have suffered some decomposition on heating.<sup>13</sup> It was thus impossible to recover the parent quinoline base as the picrate from the products of hydrolysis of the heated potassium or sodium salts of 2,6-dimethyl- or 4-methylquinoline (lepidine). 2,4-Dimethylquinoline was recovered in greatly lessened yield by the water hydrolysis of its heated potassium salt and very little methyl-*n*-propylquinoline was obtained from it by the action of ethyl bromide. Conversely, an almost quantitative yield of the free  $\beta$ -naphthoquinaldine resulted from the hydrolysis of its heated sodium salt. (Identification by mixed melting point with authentic  $\beta$ -naphthoquinaldine.) The other salts mentioned in Table I were partially decomposed by heating.

It is worthy of note that lithium amide, and particularly barium amide, react only to a slight extent with 2-*n*-amylquinoline in liquid ammonia, forming red solutions. Remembering that the corresponding reactions between 2-methylquinoline and these amides are almost or entirely complete<sup>2b</sup> under the same experimental conditions, it would appear that the ammono enol of 2-*n*-amylquinoline is a poorer "acid" than the ammono enol of 2-methylquinoline because of the longer aliphatic side chain of the former. In agreement with this view, 2-*n*-propylquinoline was found to react less completely with lithium amide than did 2-methylquinoline.

### The Preparation of 2- and 4-Alkylated Quinolines

**Homologs of 2,4-Dimethylquinoline. 2-*n*-Propyl-6-methylquinoline.**—Following the method<sup>2b</sup> used in a previous article for the preparation of 2-*n*-propylquinoline, 2-*n*-propyl-6-methylquinoline was obtained by the reaction of a liquid ammonia solution (at  $-33^\circ$ ) of the potassium salt of 2,6-dimethylquinoline with ethyl bromide; yield, 12.2 g. from 12.0 g. of 2,6-dimethylquinoline, or 86%; b. p. 131–134.5° at 3–4 mm. (uncorr.).

*Anal.* 0.2177 g. gave 13.25 cc. of nitrogen under standard conditions. 0.1616 g. gave 0.1184 g. of H<sub>2</sub>O and 0.4989 g. of CO<sub>2</sub>. Calcd. for C<sub>13</sub>H<sub>15</sub>N: C, 84.26; H, 8.17; N, 7.57. Found: C, 84.19; H, 8.20; N, 7.61.

*Picrate*, yellow crystals which appear to decompose on repeated crystallization. *2,4,6-Trinitromelacresolate*, from alcohol solution of base and alcohol solution of 2,4,6-trinitro-*m*-cresol, m. p. 172.5–173.5° corrected.

<sup>12</sup> Identification as the picrate. Identification confirmed by the unchanged mixed melting points with picrates of authentic origin.

<sup>13</sup> The potassium salt of quinaldine thus appears to be completely decomposed at 150° in a vacuum.<sup>2b</sup>

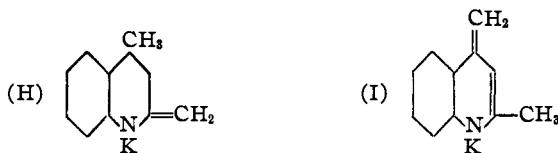


Homologs of 2,4-Dimethylquinoline. 4-Methyl-2-ethylquinoline (?).—2,4-Dimethylquinoline was regenerated by the reaction of a liquid ammonia solution of its potassium salt with methyl iodide or ethyl bromide.<sup>14</sup> It was therefore necessary, in order to effect the preparation of the expected methylethyl- and methyl-*n*-propylquinolines to make use of the ammonia reaction tube technique described in a previous article.<sup>2b</sup> As an example the preparation of methylethylquinoline is described. The product of the action of a 10% excess of potassium amide on 2 g. of dimethylquinoline in liquid ammonia was freed from the solvent by evaporation of the latter, the reaction tube evacuated at room temperatures and ether admitted,<sup>15</sup> followed by an ethereal solution of methyl iodide in slight excess of the calculated amount. The ether-soluble material, freed by filtration from the potassium halide formed in the reaction, was treated with alcoholic picric acid and the precipitated picrate crystallized until the melting point did not change; m. p. 167–168° corr.

*Anal.* 0.1862 g. (dried *in vacuo* over H<sub>2</sub>SO<sub>4</sub>) gave 20.64 cc. of nitrogen under standard conditions. (Dumas) N, 13.85. 0.1840 g. gave 0.0705 g. H<sub>2</sub>O and 0.3669 g. CO<sub>2</sub>. Calcd. for C<sub>18</sub>H<sub>18</sub>N<sub>4</sub>O<sub>7</sub>: C, 53.98; H, 4.03; N, 14.00. Found: C, 54.31; H, 4.29; N, 13.85.

(4,2)-Methyl-*n*-propylquinoline (?).—This was prepared as above from ethyl bromide and the potassium salt of 2,4-dimethylquinoline. *Picrate*, m. p. 196–198° corr.; mixed melting point with known 2,4-dimethylquinoline picrate (m. p. 195–196° corr.) is 170–180°, showing that they are not the same. 0.1603 g. gave 17.25 cc. of nitrogen under standard conditions. (Dumas) N, 13.47. Calcd. for C<sub>19</sub>H<sub>18</sub>N<sub>4</sub>O<sub>7</sub>: N, 13.52.

The barium salt of 2,4-dimethylquinoline, which formed a brownish solution in liquid ammonia not altogether similar in color to the more reddish solution of the potassium or sodium salt, was converted by the same series of operations outlined above to a liquid which yielded a picrate melting at 197–198.5° (corr.). The gold chloride double salt, prepared from a dilute hydrochloric acid solution of the base, melted at about 130°, dec. Found: Au, 37.7. Calcd. for C<sub>13</sub>H<sub>15</sub>N.HAuCl<sub>4</sub>: Au, 37.6. 2,4,6-Trinitro-*m*-cresolate, m. p. 181.7–182.2° (corr.). It would appear then that the difference in the color of the solutions of the barium and alkali metal salts of 2,3-dimethylquinoline is not connected with a marked difference in their structure.<sup>16</sup> Due to the greater reactivity of the methyl group in the 2-position of the heterocyclic ring of quinoline,<sup>4</sup> one would expect these salts to correspond to the structure (H) rather than to (I).



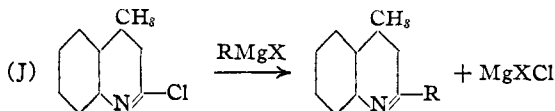
An unsuccessful attempt was made to determine the orientation of the methylethyl- and methyl-*n*-propylquinolines that resulted from the reactions just described, by an independent synthesis from 2-chlorolepidine in accordance with the type equation<sup>17</sup>

<sup>14</sup> The potassium salt of quinaldine reacts with a number of paraffin polyhalides in the same fashion.<sup>2b</sup>

<sup>15</sup> The potassium salt was almost insoluble in ether.

<sup>16</sup> Salts of 4-methylquinoline form brown colored solutions.

<sup>17</sup> A similar synthesis was successfully carried out by heating 2,3-dichloroquinoxaline with the Grignard reagent (Ogg and Bergstrom, Ref. 2 a). It will be noted that 2-chlorolepidine is formally an acid chloride (and at the same time an ester) of the ammonia system, but its reactivity, while greater than that of 3-chloroquinoline, is much less



However, by refluxing 5 g. of 2-chlorolepidine<sup>18</sup> for eight hours with a 10% excess of *n*-propylmagnesium bromide<sup>19</sup> there was obtained some tar, together with 1.8 g. of a liquid with an odor of lepidine (etheral solution hydrolyzed, ether evaporated and the residue steam distilled, when this liquid came over). That this liquid was principally lepidine was shown by conversion to the picrate, which melted by itself at 214–216.5° corr. and at 214–215° corr. when mixed with authentic lepidine picrate, m. p. 215–216° corr.; yield of the crude lepidine, based on the chlorolepidine, 45%. 2-Chlorolepidine refluxed with twice the theoretical amount of a filtered etheral solution of ethylmagnesium iodide for six hours gave much tarry material and some lepidine. (Most of the ether was evaporated off so that the refluxing mixture would attain a higher temperature.) It is hoped to investigate reactions of this type more completely at a later date.

Homologs of 2-Ethylquinoline. 2-Isopropylquinoline.—2-Isopropylquinoline was made by the action of methyl bromide upon the potassium salt of the ammono enol of 2-ethylquinoline. In carrying out this preparation, 3.0 g. of 2-ethylquinoline<sup>20</sup> was allowed to react overnight with the potassium amide from 0.85 g. of potassium (1.13 equivalents) at 20° in an ammonia reaction tube. The solvent having been evaporated from the tube, the latter was evacuated to remove as much ammonia as possible.<sup>21</sup> Then, with the end of the stopcock capillary dipping under absolute ether in a small beaker, the stopcock was opened so as to admit a few cc. of ether to the evacuated tube. Most of the potassium salt dissolved to form a deep red solution. Then, in the same manner, an absolute etheral solution of an excess of methyl bromide (methyl iodide can also be used) was drawn into the tube. A rather rapid reaction ensued; the solution decolorized and potassium bromide was precipitated. The tube was broken open, the precipitate filtered off, and the etheral solution distilled: b. p. of base, 124–125.5°, uncorr., at 7 mm.; yield, 2.3 g. or 70%. 0.1738, 0.1617 g. gave 0.5362, 0.4990 CO<sub>2</sub> and 0.1205, 0.1141 H<sub>2</sub>O. 0.1871 g. gave 12.46 cc. N<sub>2</sub> (Dumas) under standard conditions. Calcd. for C<sub>12</sub>H<sub>13</sub>N: C, 84.16; H, 7.66; N, 8.19. Found: C, 84.14, 84.16; H, 7.76, 7.89; N, 8.32. M. p. of picrate, 153.5–154.5°, corr.; mixed m. p. with the picrate of 2-ethylquinoline (m. p. 150°) is 136–145°, showing that the picrates differ. 0.1775 g. gave 19.88 cc. of nitrogen under standard conditions. (Dumas) Calcd. for C<sub>14</sub>H<sub>15</sub>N<sub>4</sub>O<sub>7</sub>: N, 14.0. Found: N, 14.0.

Döbner<sup>22</sup> gives 150° as the melting point of 2-isopropylquinoline picrate.<sup>23</sup>

than that of typical aliphatic acid chlorides. The chlorine in 4-chloroquinoline is somewhat mobile. Marckwald, *Ber.*, **26**, 2188 (1893); Marckwald, Klemm and Trabert, *ibid.*, **33**, 1556 (1900). Mills and Smith, Ref. 4.

<sup>18</sup> Obtained from the Eastman Kodak Company.

<sup>19</sup> The excess magnesium used in the preparation of the Grignard reagent was not removed.

<sup>20</sup> Prepared according to the directions of Ref. 2b.

<sup>21</sup> Ammonia decreases the yields of many of the products formed by the action of alkyl halides upon the salts of quinaldine. In some cases none of the expected product is formed but the quinoline base is regenerated.<sup>2b</sup>

<sup>22</sup> Döbner, *Ann.*, **242**, 299 (1887).

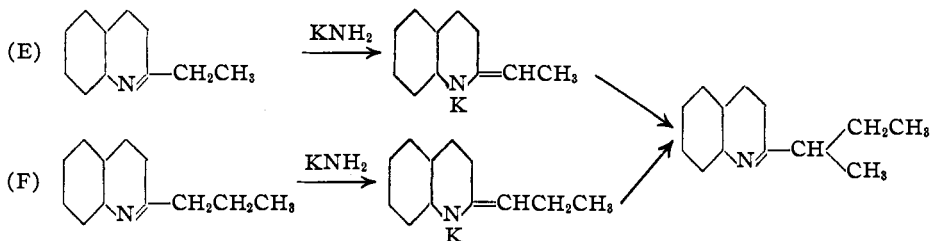
<sup>23</sup> Mulliken, "The Identification of Pure Organic Compounds," Vol. II, page 155, also gives 155–157° as the melting point [undocumented reference, probably W. Knöigs, *Ber.*, **32**, 227 (1899)].

**2-Sec.-butylquinoline.**—In a similar fashion, ethyl bromide was allowed to react with an ethereal solution of the potassium salt of 2-ethylquinoline. The reaction followed equation (E) below and gave as the reaction product 2-sec.-butylquinoline: picrate, m. p. 164–165° corr.; mixed m. p. with the picrate of 2-*n*-propylquinoline (m. p. 163–164° corr.) is 148–150°, showing that the picrates differ. 0.2621 g. gave 27.95 cc. of nitrogen, standard conditions. Calcd. for  $C_{19}H_{18}N_4O_7$ : N, 13.5. Found: N, 13.3.

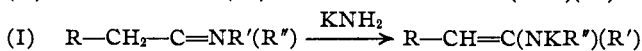
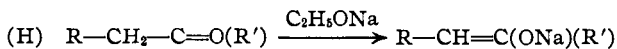
**Homologs of 2-*n*-Propylquinoline. 2-Sec.-butylquinoline.**—The potassium salt of the ammono enol of 2-*n*-propylquinoline<sup>24</sup> was treated in a large ammonia reaction tube with an absolute ethereal solution of an excess (5 g.) of methyl iodide, in accordance with the directions of the preceding section.<sup>25</sup> The filtered ethereal solution was distilled, the ether at atmospheric pressure and the product in a vacuum; yield, 2.7 g. (57%) of a light yellow oil, b. p. 118–121° uncorr. at 3–5 mm. Although this product boiled at almost the same temperature as the 2-*n*-propylquinoline used as a starting material, and although the picrate of the reaction product melted at 163.5–164.5° corr. (picrate of 2-*n*-propylquinoline, 163–164° corr.), the two substances were not identical since the m. p. of a mixture of the picrates was 145–155°.

**Analysis** of picrate of the reaction product. 0.1552 g. gave 16.48 cc. of nitrogen, standard conditions. Calcd. for  $C_{19}H_{18}N_4O_7$ : N, 13.5. Found: N, 13.3. **Analysis** of the free base: 0.1581 g. gave 0.4881 g. of  $CO_2$  and 0.1187 g. of  $H_2O$ . 0.1300 g. gave 7.67 cc. of nitrogen, standard conditions. Calcd. for  $C_{13}H_{13}N$ : C, 84.26; H, 8.17; N, 7.57. Found: C, 84.20; H, 8.40; N, 7.38.

The identity of the products formed by the action of ethyl bromide on the potassium salt of 2-ethylquinoline and by the action of methyl iodide on the potassium salt of 2-*n*-propylquinoline (see equations E and F, respectively) was shown by determining the mixed m. p. (163.5–164.8°) of their respective picrates, which was the same as the melting points of the individual compounds.



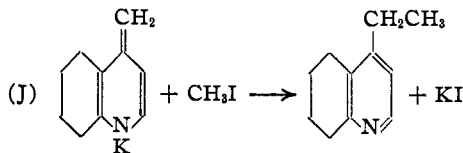
Although it is possible to write structural formulas for the potassium salts of 2-ethyl- and 2-*n*-propylquinolines other than the above, these formulas are in themselves improbable and do not afford a satisfactory explanation of the reactions expressed by equations (E) and (F), nor of the formation of isopropylquinoline from the potassium salt of ethylquinoline and methyl iodide. Therefore it may be concluded that the enolization of ketones of the water and ammonia systems takes place in a strictly analogous fashion, that is, in accordance with the equations



<sup>24</sup> From 1.1 g. (1.1 equivalents) of potassium and 4.4 g. of 2-*n*-propylquinoline, prepared as in Ref. 2 b.

<sup>25</sup> The rather vigorous reaction made it necessary to cool the tube from time to time to prevent the pressure within from rising above atmospheric.

**Homologs of Lepidine.**—The potassium salt of lepidine (4-methylquinoline) described in Table I presumably has the structure of the first formula below.<sup>4,26</sup>



The reaction of this salt with alkyl halides might be expected to follow the course of equation (J) and yield homologs of lepidine with a lengthened side chain in the 4-position.

To test this supposition, lepidine was submitted to the same series of operations that were described in the preceding section to convert it to the potassium salt and then by the action of methyl iodide to 4-ethylquinoline.<sup>27</sup> The picrate of the oily reaction product melted at 191–192° dec., that is, much above the value of Reher,<sup>28</sup> but in agreement with the melting point of Blaise and Maire (191°),<sup>29</sup> whose method of preparation probably yielded the purer product.

*Anal.* 0.2737 g. gave 31.35 cc. of nitrogen under standard conditions. Calcd. for  $\text{C}_{17}\text{H}_{14}\text{N}_4\text{O}_7$ : N, 14.5. Found: N, 14.3.

In the same manner, the potassium salt of lepidine, in reacting with an absolute ethereal solution of ethyl bromide was converted to an oil, the picrate of which melted at 204–205°, corr., rapid determination.<sup>30</sup>

*Anal.* 0.1802 g. gave 20.25 cc. of nitrogen under standard conditions (Dumas). 0.1262 g. gave 0.2504 g. of  $\text{CO}_2$  and 0.0488 g. of  $\text{H}_2\text{O}$ . Calcd. for  $\text{C}_{18}\text{H}_{16}\text{N}_4\text{O}_7$ : C, 53.98; H, 4.03; N, 14.00. Found: C, 54.11; H, 4.33; N, 14.03.

*Chloroplatinate*, m. p. 198–199°, dec.; *bromocadmiate*, m. p. 147–148° corr. (dec.).<sup>30</sup> These latter two salts appeared to decompose slowly on crystallization.

**Homologs of 2-Methylpyridine, 2,4,6-Trimethylpyridine and 2,6-Dimethylpyridine.**—Attempts to prepare homologs of the pyridine derivatives named above by the action of ethyl bromide upon the potassium salts of the corresponding ammonio enols in liquid ammonia solution resulted in failure. The reaction products were clear colorless liquids of rather sharp odor, whose picrates were precipitated as uncrystallizable yellow tars. It is hoped that these will be more fully investigated in the future. The expected alkylated pyridines were not formed in appreciable quantities (compare equation A). Ziegler and Zeiser<sup>3b</sup> have however prepared 2-( $\beta$ -phenylethyl)-pyridine by the action of benzyl chloride on the lithium salt of 2-methylpyridine in absolute ether.

It was of especial interest to find that 2-methylpyridine reacts with an excess of potassium amide in liquid ammonia either at room temperatures or at 130°<sup>31</sup> to form the

<sup>26</sup> Compare the pyridine methides of Mumm and co-workers, *Ann.*, **443**, 272 (1925); *Ber.*, **56**, 2301 (1923). Chichibabin, *ibid.*, **60B**, 1607 (1927), explains certain reactions of lepidine on the basis of formula (J). (Potassium replaced by hydrogen.)

<sup>27</sup> One cc. of lepidine was used. Lepidine seems to react more slowly with the alkali amides than quinaldine.

<sup>28</sup> Reher, *Ber.*, **19**, 2999 (1886), gives 178–180° dec. as the melting point of the picrate.

<sup>29</sup> Blaise and Maire, *Bull. soc. chim.*, [4] **3**, 668 (1908).

<sup>30</sup> The melting point depends upon the rate of heating. Blaise and Maire,<sup>29</sup> p. 670, give 204° as the melting point of 4-*n*-propylquinoline picrate, 198° as the m. p. of the chloroplatinate, and 148° as the melting point of the bromocadmiate.

<sup>31</sup> Cf. Blair, *THIS JOURNAL*, **48**, 91 (1926).

salt of the ammono enol modification but no 2-methyl-6-aminopyridine, as in the reaction between solid sodium amide and 2-methylpyridine in boiling xylene.<sup>32</sup>

### Summary

1. It has been shown that quinolines with an alkyl group in the 2-position may be regarded as cyclic ammono ketone acetals. Particularly is this true because all of the substituted quinolines and pyridines examined react with a liquid ammonia solution of potassium or sodium amide to form highly colored (red or reddish-brown) salts of an ammono enolic modification. Lepidine likewise reacts with the alkali amides to form salts.

2. Salts of the ammono enols of the 2-alkylquinolines, in so far as investigated, react with alkyl halides to form homologous quinolines with a lengthened side chain. It was shown that the potassium salts of the ammono enols of 2-ethyl- and 2-*n*-propylquinolines react with ethyl bromide and methyl iodide, respectively, to form the same product, 2-*sec*-

butylquinoline. The group,  $\begin{array}{c} \text{RCH}_2 \\ \diagdown \\ \text{C}=\text{N}- \\ \diagup \\ \text{R} \end{array}$ , is therefore converted by potassium amide to the group,  $\begin{array}{c} \text{RCH} \\ \diagdown \\ \text{C}=\text{NK}- \\ \diagup \\ \text{R} \end{array}$ , as would be expected from

the known mode of enolization of the ketones of the water system. 4-Methylquinoline (lepidine) was converted, through its potassium salt, into 4-ethyl- and 4-*n*-propylquinoline.

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

## THE ALPHA-CHLOROETHYL NORMAL ALKYL ETHERS<sup>1</sup>

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RECEIVED JULY 16, 1931

PUBLISHED NOVEMBER 5, 1931

Although the preparation of the  $\alpha$ -chloromethyl normal alkyl ethers has been reported by a large number of investigators, the series being complete through the amyl derivative,<sup>2</sup> the syntheses of only three of the  $\alpha$ -chloroethyl normal alkyl ethers have been recorded, namely, the methyl,<sup>3</sup> ethyl,<sup>4</sup>

<sup>32</sup> Seide, *J. Russ. Phys.-Chem. Soc.*, 50, 534 (1920).

<sup>1</sup> An abstract of the dissertation submitted by J. T. Murchison to the Faculty of the University of Texas, in partial fulfillment of the requirements for the degree of Master of Arts, August, 1930.

<sup>2</sup> J. Bliss Norton, "Dissertation," University of Texas, 1930.

<sup>3</sup> (a) Rübenkamp and Geuther, *Ann.*, 225, 269-270 (1884); (b) Favre, *Bull. soc. chim.*, [3] 11, 1096 (1894); (c) Gauthier, *Ann. chim.*, [8] 16, 311-313 (1909); (d) Madinaveitin and Puyal, *Anales soc. españ. fis. quim.*, 16, 329-337 (1918), (through *C. A.*, 13, 2677 (1919)).

<sup>4</sup> (a) Wurtz and Frapolli, *Ann.*, 108, 226-227 (1858); (b) Geuther and Bachmann, *ibid.*, 218, 39 (1883); (c) Jacobson, *Ber.*, 4, 215 (1871); (d) Fritsch and Schumacher, *Ann.*, 279, 302-303 (1894); (e) Geuther and Laatsch, *ibid.*, 218, 21 (1883);