By-Products from the Manufacture of 2-Methyl-5-ethylpyridine and 2-Methyl-5-vinylpyridine

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By the catalytic dehydrogenation of 2-methyl-5-ethylpyridine (MEP) 2-methyl-5-vinylpyridine (MVP) is produced commercially in a plant owned by Phillips Chemical Co. at Pasadena, Tex. (*6*). Operation of this plant has afforded a source of by-products more adequate for an extended characterization study than had been available. By-product pyridines are formed in both steps involved in the manufacture of 2-methyl-5-vinylpyridine: the 2-methyl-5-ethylpyridine synthesis reaction and the dehydrogenation of 2-methyl-5-ethylpyridine. These by-products are both lower and higher boiling than the principal products.

In one of the oldest methods for producing pyridines, the Chichibabin synthesis, ammonia is condensed with aldehydes, ketones, unsaturated carbonyl compounds, or derivatives of these compounds (*2,4,5,8,9,13,16*). This method of synthesis, using paraldehyde, was adapted for the commercial scale production of 2-methyl-5-ethylpyridine. The trimerization of acetaldehyde to paraldehyde is catalyzed by sulfuric acid, as indicated by Equation (1). Paraldehyde is condensed with ammonia at elevated temperatures and pressures to give 2-methyl-5-ethylpyridine, which is subsequently converted to 2-methyl-5-vinylpyridine by catalytic dehydrogenation (Equation 2).

$$3\ CH_3CHO \underset{}{\overset{H_2SO_4}{\rightleftharpoons}} (CH_3CHO)_3 \qquad (1)$$

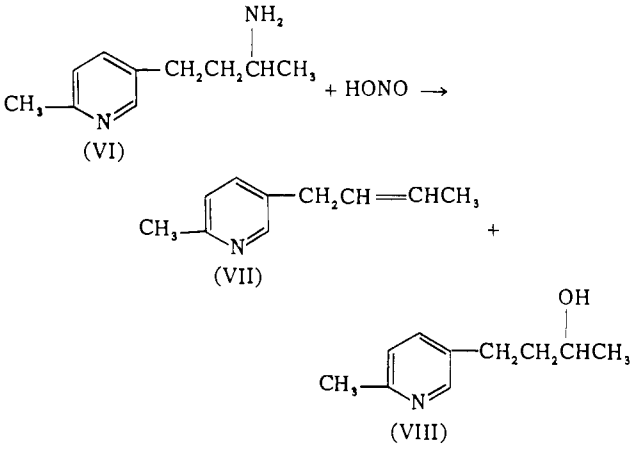
$$4(CH_3CHO)_3 + 3NH_3 \xrightarrow[-12H_2O]{\triangle} 3\ \text{2-methyl-5-ethylpyridine} \xrightarrow{-3H_2} 3\ \text{2-methyl-5-vinylpyridine} \qquad (2)$$

Pyridines may also be made by a number of other procedures, most of which are of laboratory interest only (*13*). Other methods of actual or potential commercial application include the vapor-phase reaction of acetylene with ammonia and the reaction of methyl vinyl ether with ammonia.

The condensation of acetaldehyde or paraldehyde with ammonia produces predominantly 2-methyl-5-ethylpyridine, although significant quantities of by-product pyridines are also formed (*8, 10*). Paraldehyde gives better yields than acetaldehyde, although the yields using acetaldehyde may be improved by slowly adding the acetaldehyde during the course of the reaction (*4*). The amount of by-products formed may be reduced by the proper choice of catalyst and reaction conditions. The lower-boiling derivatives produced are 2- and 4-picoline, the former predominating. The picolines apparently result from the condensation of three molecules of acetaldehyde (or an equivalent amount of a derivative) with ammonia while 2-methyl-5-ethylpyridine is formed from four molecules of acetaldehyde. If more than four molecules of acetaldehyde are involved, higher-boiling pyridines are produced. The exact mode of this condensation is not known, although various mechanisms have been proposed (*9, 13*).

The higher-boiling pyridines, formed during the 2-methyl-5-ethylpyridine synthesis step and previously reported by other investigators, are 3-ethyl-4-methylpyridine (β-collidine) (I), 2-methyl-5-(2-buten-1-yl)pyridine (II), 2-methyl-5-(1-buten-1-yl)pyridine (III), and 2-propenyl-5-ethylpyridine (IV) (*10*). The results of the study reported here confirm the presence of these compounds in the synthesis mixture. The methylbutenylpyridines isolated in this investigation appear to possess trans configurations, based on infrared spectra. They are apparently isomers of the methylbutenylpyridines obtained by Graf, Langer, and Haumeder (*10*), as the picrate melting points differ. Isomerization may have occurred during the prolonged distillation involved in this study.

In addition to the above compounds, two pyridines not previously reported as present were isolated from the 2-methyl-5-ethylpyridine synthesis mixture. One of these is 2-methyl-3-ethylpyridine (V), which boils slightly higher than 2-methyl-5-ethylpyridine. This material is present in very small amounts. The other compound, boiling point, 134° C. (10 mm.), is believed to be 2-methyl-5-(3-amino-1-butyl)pyridine (VI), inasmuch as all of the evidence obtained favors this structure. Infrared spectra and chemical tests indicate a 2,5-disubstituted pyridine containing a primary amino group. Nitrous acid treatment gives an olefin (VII) and an alcohol (VIII).



Based on picrate melting points, this olefin (VII) appears to be the same methyl butenylpyridine as one (II) obtained by Graf and others from the 2-methyl-5-ethylpyridine kettle product. This olefin (VII) hydrogenates to 2-methyl-5-butylpyridine. The alcohol (VIII) gives a positive iodoform test, indicating that the amino group of the amine (VI) is adjacent to a terminal carbon atom.

The proposed structure for the amine (VI) seems reasonable if the imine condensation mechanism for the Chichibabin synthesis is considered (*13*), and this compound may in fact be the precursor of the methyl butenylpyridines found in the 2-methyl-5-ethylpyridine kettle product. This aminoalkyl pyridine apparently is not formed by the addition of ammonia to the methyl butenylpyridines, as evidenced by the fact that an attempt to cause such an addition to occur under 2-methyl-5-ethylpyridine synthesis conditions was unsuccessful. This amine could, presumably, also result from reaction of the analogous alcohol (VIII) with ammonia, if this alcohol is formed during the course of the 2-methyl-5-ethylpyridine synthesis reaction. The olefin (VII) might

be formed by elimination of water from the alcohol or by elimination of ammonia from the amine.

The pyridines discussed above do not include all of the by-products formed in the 2-methyl-5-ethylpyridine synthesis step. In addition to the compounds previously identified and the ones characterized in this study, other unidentified, higher-boiling compounds are produced.

The catalytic dehydrogenation of 2-methyl-5-ethylpyridine produces, in addition to 2-methyl-5-vinylpyridine, small amounts of all of the possible pyridines resulting from removal of part or all of the side chains. These cracking products, which boil below 2-methyl-5-vinylpyridine, are 3-ethylpyridine, 3-vinylpyridine, 2,5-lutidine, 2-picoline, 3-picoline, and pyridine; the latter is present in very small amounts. In addition to these compounds, 2,6-dimethyl-3-ethylpyridine (IX) and 2-methyl-5-isopropenylpyridine (X) were isolated and identified. Because of plant procedures in use at the time that samples were taken for analysis, it was not determined whether these latter two compounds are formed during 2-methyl-5-ethylpyridine synthesis or in the dehydrogenation step. The mechanism by which these two compounds might be formed in either case is not clear.

The initial separations of the various products were made using a column 40 mm. in diameter by 140 cm. in length, packed with Podbielniak Heli-Pak stainless steel packing. Redistillations of the desired fractions were accomplished using a Podbielniak 25-mm. × 36-inch Heligrid column or a Todd precise fractionation assembly. Distillation of the high-boiling by-products from the 2-methyl-5-ethylpyridine synthesis unit is indicated in Figure 1. Infrared data were obtained using a Perkin-Elmer Model 21 spectrometer equipped with a rock salt prism.

2-METHYL-5-ETHYLPYRIDINE BY-PRODUCTS

Samples of 2-methyl-5-ethylpyridine by-products were obtained from forecuts and kettle products from the 2-methyl-5-ethylpyridine fractionator. The low-boiling 2-methyl-5-ethylpyridine by-products, 2- and 4-picoline, have been identified as such (*10*). Their identity has been confirmed in this study by infrared spectra and chemical properties. However, attention was concentrated on high-boiling by-products, which are discussed individually. These materials were isolated by careful fractionation, followed by purification via a derivative, if required.

Isolation and Identification of 2-Methyl-3-ethylpyridine (V). Infrared spectra indicated the presence of an unknown pyridine homolog in fractions boiling slightly above 2-methyl-5-ethylpyridine. A fraction boiling at 178.5°C. was treated with picric acid and after several recrystallizations from methanol, a picrate (melting point, 142.5–3.5°C.) was obtained; literature value, 140–1°C. (*3*). The corresponding chloroplatinate melted at 172–2.5°C. A sample of known 2-methyl-3-ethylpyridine was prepared by the method of Wibaut (*17*) starting with ethyl ethyl acetoacetate. A mixed melting point of the pictrate of 2-methyl-3-ethylpyridine prepared in this manner and that obtained from the 178.5°C. fraction gave no depression.

Isolation and Identification of 3-Ethyl-4-methylpyridine (β-Collidine) (I). Distillation of the 2-methyl-5-ethylpyridine kettle product gave a fraction boiling at 64°C. (7 mm.) or 195–6°C. at atmospheric pressure. To separate the main component from impurities, the oxalate of this material was prepared and recrystallized from ethyl alcohol, melting point 112–14°C. The collidine was regenerated by treatment with caustic. Oxidation with aqueous potassium permanganate gave 3,4-pyridinedicarboxylic acid (cinchomeronic acid), melting point, 260°C. (decomposition). This collidine formed a methiodide, melting point, 154–5°C. The pictrate [melting point, 147–8°C., reported melting point, 147–9°C. (*10*)] gave no melting point depression when mixed with the picrate of a known sample of β-collidine.

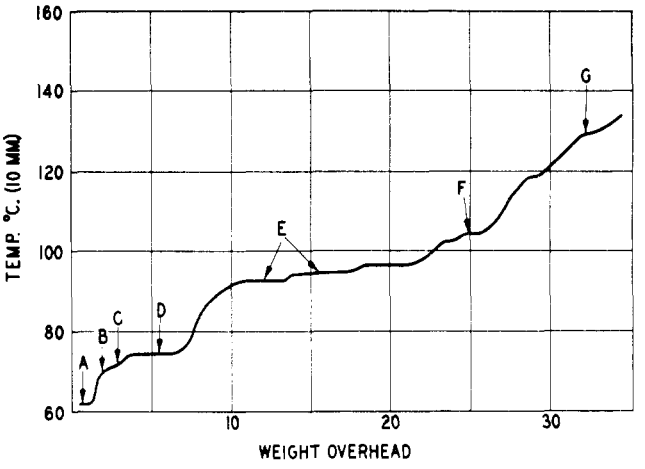


Figure 1. Boiling point curve for products boiling above 2-methyl-5-ethylpyridine

A. 2-Methyl-5-ethylpyridine
B. 2-Methyl-3-ethylpyridine
C. 2,6-Dimethyl-3-ethylpyridine
D. 3-Ethyl-4-methylpyridine
E. 2-Methyl-5-butenylpyridine
F. 2-Propenyl-5-ethylpyridine
G. 2-Methyl-5-(3-amino-1-butyl)pyridine

Isolation and Identification of 2-Methyl-5-butenylpyridines (XI, XII). A mixture of two isomers (XI, XII), boiling in the range 90° to 95°C. (10 mm.) was obtained by distillation of the 2-methyl-5-ethylpyridine kettle products. Infrared data indicated that both compounds possessed a trans configuration. Oxidation with aqueous potassium permanganate gave 2,5-pyridinedicarboxylic acid (isocinchomeronic acid). Treatment of the mixture with picric acid and recrystallization from alcohol yielded two pictrates, melting points, 88–9°C. and 131–3°C. Hydrogenation of the isomeric mixture gave 2-methyl-5-butylpyridine, picrate melting point, 133–4°C.; reported melting point, 135°C. (*10*).

Isolation and Identification of 2-Propenyl-5-ethylpyridine (IV). A fraction boiling at 104–5°C. (10 mm.), n_D^{20} 1.5380, was isolated from the 2-methyl-5-ethylpyridine kettle product. Oxidation with potassium permanganate at 80°C. gave 2,5-pyridinedicarboxylic acid. Titration with perchloric acid gave a neutralization equivalent of 147.6; calculated for $C_{10}H_{13}N$: 147.2. The picrate of this unsaturated alkyl pyridine melted at 129.5–30.5°C. The reported boiling point is 103–4°C. (12 mm.), picrate melting point, 129°C. (*10*). Hydrogenation in ethyl alcohol over 10% palladium on charcoal gave 2-propyl-5-ethylpyridine, boiling point, 104°C. (21 mm.), n_D^{20} 1.4900, picrate melting point 101.5–2°C.; reported picrate melting point 99–100°C. (*10*).

Isolation and Identification of 2-Methyl-5-(3-amino-1-butyl)pyridine (VI). A fraction boiling at 134°C. (10 mm.) from the kettle products was purified via the oxalate, melting point 211–13°C. (from methanol). Regeneration with caustic, and distillation gave a water-soluble liquid (VI), boiling point, 134°C. (10 mm.), n_D^{20} 1.5145, which readily absorbs carbon dioxide from air to form a white solid. Titration of this liquid (VI) with perchloric acid gave a neutralization equivalent of 83.2; calculated for $C_{10}H_{16}N_2$: 82.1. Oxidation with potassium permanganate gave 2,5-pyridinedicarboxylic acid; dimethyl ester melting point 163–5°C; a mixed melting point with a known sample of dimethyl 2,5-pyridinedicarboxylate showed no depression. The compound (VI) gave a positive test for a primary amine but negative unsaturation tests. Infrared spectra (Figure 2) indicate that the compound is an alkyl substituted pyridine possessing a primary amino group.

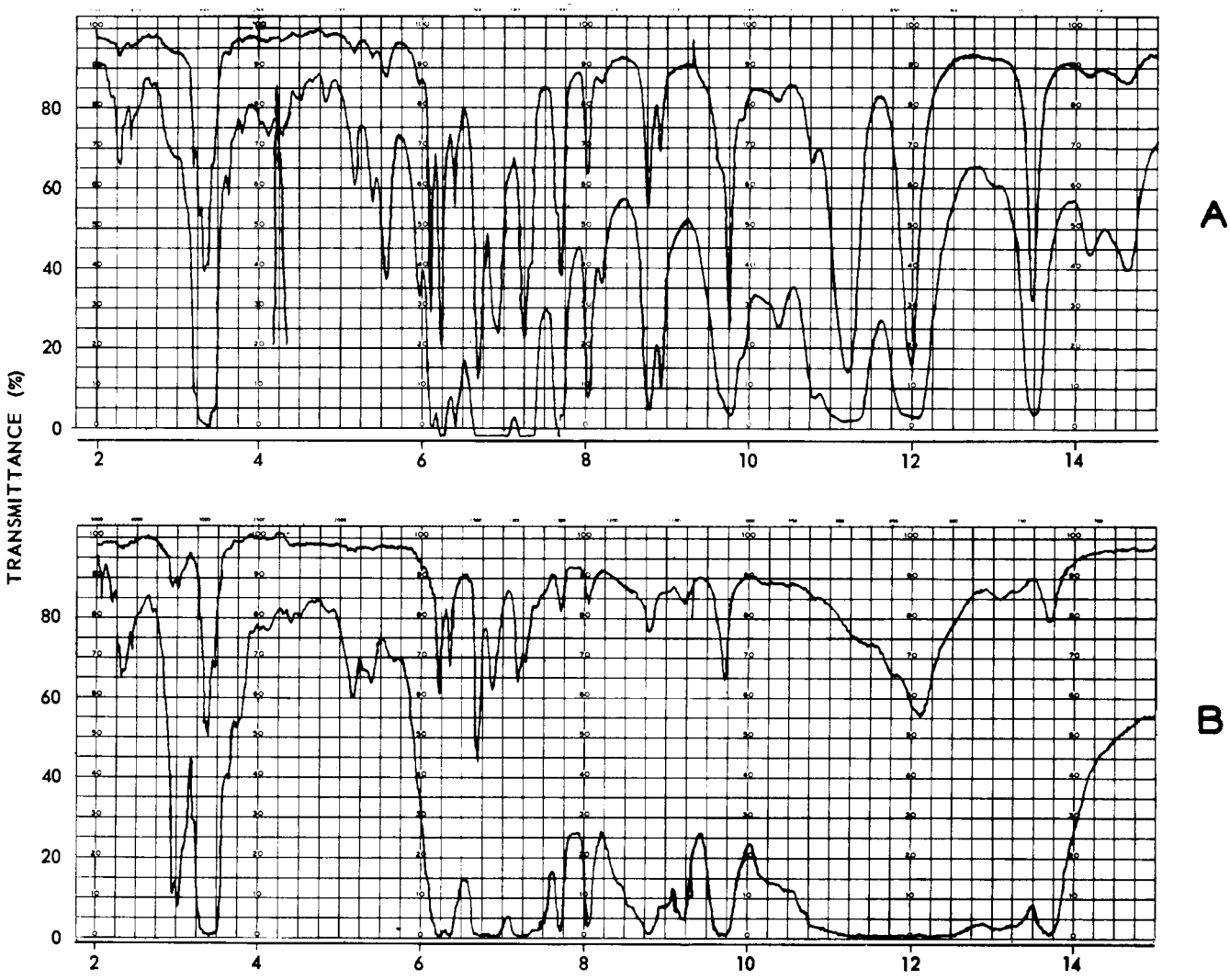


Figure 2. Infrared spectra
A. 2-Methyl-5-isopropenylpyridine
B. 2-Methyl-5-(3-amino-1-butyl)pyridine

This compound (VI) (20 grams, 0.122 mole) was stirred with 300 ml. of water and an equivalent amount of 6*N* hydrochloric acid was added. A saturated solution of sodium nitrite (23 grams, 0.33 mole) in water was slowly added along with 1*N* hydrochloric acid, which was added to maintain acidity. Nitrogen was evolved during this nitrous acid treatment and distillation of an ether extract gave two products. The lower-boiling material (VII, 3.7 grams) boiling point, about 100°C. (10 mm.), picrate melting point, 122–3°C., was hydrogenated over platinum oxide to give 2-methyl-5-butylpyridine, picrate melting point, 135–7°C.; reported value, 135°C. (*10*). The higher-boiling product (VIII, 6.0 grams), boiling point, 160°C. (10 mm.), gave a positive ceric nitrate test for an alcohol and a positive iodoform test. Elemental analyses of the original amine (VI) were erratic, apparently because of carbon dioxide absorption, so analysis was performed on the picrate.

Analysis. Calculated for $C_{10}H_{16}N_2(C_6H_3O_7N_3)_2$: carbon, 42.5; hydrogen, 3.56; nitrogen, 18.0. Found: carbon, 42.3; hydrogen, 3.70; nitrogen, 17.7.

An attempt was made to synthesize this methyl aminobutylpyridine (VI) by causing ammonia to react with methyl butenylpyridines, but none of the desired product was obtained. A mixture of 2-methyl-5-butenylpyridines (177 grams, 1.2 moles), ammonia (115 grams, 6.7 moles), and water (195 grams, 10.85 moles) was charged to a bomb and heated at 260°C. for 30 minutes. Only unchanged methyl butenylpyridines were obtained upon distillation of the organic effluent.

PRODUCTS FROM 2-METHYL-5-ETHYLPYRIDINE DEHYDROGENATION

The low-boiling products obtained in the dehydrogenation step were identified by their physical properties, infrared analyses, and picrate derivatives. The physical properties and melting points of the picrates (from ethyl alcohol) as found are given in Table I.

ADDITIONAL BY-PRODUCTS

Two other pyridines were isolated and identified. Although one was obtained from the 2-methyl-5-ethylpyridine section of the process and the other from the 2-methyl-5-vinylpyridine section, the actual source of each of these could not be determined due to recycle procedures in use when the samples were taken.

Isolation and Identification of 2,6-Dimethyl-3-ethylpyridine

Table I. MEP Dehydrogenation Products

Compound	B.P., °C.	n_D^{20}	d^{20}	Picrate M.P., °C.
2-Picoline	129	1.5007	0.9455	167–168
3-Picoline	145	1.5060	0.9558	151–152
2,5-Lutidine	157	1.5002	0.9301	170–171
3-Ethylpyridine	166	1.5020	0.9408	128–130
3-Vinylpyridine	72 (21 mm.)	1.5530	0.9879	147–148[a]
2-Methyl-5-vinylpyridine	75 (15 mm.)[b]	1.5454	0.9646	158–159

[a] Reported value, 143.5° – 44 °C. (7).
[b] Freezing point, – 12.36° ± 0.03 °C.

(IX). The 2-methyl-5-ethylpyridine kettle products yielded a small fraction boiling at 190°C. This compound contained no unsaturated side chains. Oxidation with potassium permanganate at 80°C. gave two pyridine carboxylic acids which precipitated at pH 3 and pH 2.3. The first acid decomposed at 234°C. and appeared to be a pyridinetricarboxylic acid hydrate. It is reported that 2,3,6-pyridinetricarboxylic acid loses carbon dioxide on heating to give 2,5-pyridinedicarboxylic acid which then decomposes at 236–7°C. (*12*).

Analysis. Calculated for $C_8H_5O_6N \cdot H_2O$: carbon, 42.0; hydrogen, 3.05; nitrogen, 6.12. Found: carbon, 42.5; hydrogen, 2.76; nitrogen, 6.2.

Titration with base indicated that the second acid, melting point, 260–1°C. (decomposition), was a methylpyridinedicarboxylic acid hydrate. Calculated neutralization equivalent, 99.6; found, 99.0.

Analysis. Calculated for $C_8H_7O_4N.H_2O$: carbon, 48.0; hydrogen, 4.5; nitrogen, 7.0. Found: carbon, 48.24; hydrogen, 4.6; nitrogen, 7.1.

This acid formed a methyl ester, melting point, 98.5°–99°C.

The pyridine (IX, 50 grams, 0.37 mole) was condensed with an equimolar amount of benzaldehyde (39.3 grams, 0.37 mole) by refluxing in the presence of acetic anhydride (113.3 grams, 1.11 moles) for 12 hours according to the procedure of Prostenik and Filipovic (*15*). The resulting styryl derivative (XIII, 30 grams) boiled at 219–21°C. (20 mm.), n_D^{20} 1.6408. Calculated neutralization equivalent, 223.3; found, 221.

Analysis. Calculated for $C_{16}H_{17}N$: carbon, 86.05; hydrogen, 7.67; nitrogen, 6.27. Found: carbon, 86.25; hydrogen, 7.78; nitrogen, 6.28.

Oxidation of this styryl derivative (10 grams, 0.049 mole) with potassium permanganate (18.8 grams, 0.119 mole) in acetone (150 ml.) at 0° to 5°C. produced benzoic acid and a pyridine carboxylic acid which was isolated as the mercuric salt. The free acid was regenerated by treatment with hydrogen sulfide. Decarboxylation of this acid was accomplished by heating with calcium oxide and the product was 2-methyl-5-ethylpyridine, picrate melting point, 162°–163°C. A mixed melting point with known 2-methyl-5-ethylpyridine picrate showed no depression. It was thus established that the original pyridine (IX) contained a methyl group in the 2-position and an ethyl group in the 5-position. These results also indicate that the benzaldehyde condensation product (XIII) is 2-styryl-3-ethyl-6-methylpyridine.

The original pyridine (IX) formed a picrate, melting point, 122–3°C.; melting point reported by Dornow and Machens, 122°C. (*3*), and a chloroplatinate, melting point, 204–4.5°C. The melting points for the picrate (162°C.) and chloroplatinate (178°C.) reported by Koenigs and Hoffman (*11*) for 2,6-dimethyl-3-ethylpyridine are close to those well established for 2-methyl-5-ethylpyridine, the starting material for their synthesis of this compound. It thus appears that they obtained derivatives of 2-methyl-5-ethylpyridine, especially since 2-methyl-5-ethylpyridine forms these derivatives more readily than does 2,6-dimethyl-3-ethylpyridine (IX).

A sample of 2,6-dimethyl-3-ethylpyridine was prepared by heating 2-methyl-5-ethylpyridine (552 grams, 4.56 moles) with methyl iodide (119 grams, 0.835 mole) in the presence of copper powder (1.0 gram) at 300°C. for 4 hours. Steam distillation and fractionation gave, after removal of the unreacted 2-methyl-5-ethylpyridine (404 grams, 3.34 moles), a higher-boiling residue from which was obtained a small fraction (8.0 grams), boiling point 190–0°C., n_D^{20} 1.5010.

Analysis. Calculated for $C_9H_{13}N$: carbon, 79.99; hydrogen, 9.69. Found: carbon, 80.1; hydrogen, 9.9.

This prepared sample of 2,6-dimethyl-3-ethylpyridine formed a picrate, melting point, 122–3°C., which gave no depression on mixed melting point with the picrate of the original pyridine (IX) and a chloroplatinate, melting point, 204–4.5°C., which gave no depression on mixed melting point with the chloroplatinate of the original pyridine.

Isolation and Identification of 2-Methyl-5-isopropenylpyridine (X). A small amount of material, boiling point, 116–17°C. (50 mm.), n_D^{20} 1.5360, methiodide melting point 152–3°C., was obtained by fractionation of 2-methyl-5-vinylpyridine kettle products from initial plant operation. Mass analysis indicated that the mass of this material was 133: calculated molecular weight for $C_9H_{11}N$, 133.2. Hydrogenation over platinum oxide gave 2-methyl-5-isopropylpyridine, boiling point, 191°C., picrate melting point, 169–70°C.; reported boiling point, 190–1°C., picrate melting point, 167–8°C. (*14*). A sample of 2-methyl-5-isopropenylpyridine was synthesized from ethyl 6-methylnicotinate using the procedure of Brown and Murphey (*1*). The picrate, melting point, 191–2°C., showed no depression when mixed with that of the material (X) isolated from the kettle products.

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LITERATURE CITED

(1) Brown, H. C., Murphey, W. A., *J. Am. Chem. Soc.* **73**, 3308 (1951).
(2) Chichibabin, A. E., *J. Russ. Phys.-Chem. Soc.* **37**, 1229 (1905); *Chem. Centr.* **77**, I, 1438 (1906); *J. prakt. Chem.* **107**, 109, 122, 129, 132, 138, 145, 154 (1924); *Bull. soc. chim.* (5) **4**, 1826 (1937).
(3) Dornow, A., Machens, H., *Ber.* **73B**, 355 (1940).
(4) Dunn, J. T. (to Union Carbide and Carbon Corp.), U. S. Patent **2,717,897** (Sept. 13, 1955).
(5) Durkopf, E., *Ber.* **20**, 444 (1887); **21**, 294 (1888).
(6) Folz, J. M., Mahan, J. E., White, D. H., *Petroleum Processing* **7**, 1802 (1952).
(7) Frank, R. L., Adams, C. E., Blegen, J. R., Smith, P. V., *Ind. Eng. Chem.* **40**, 879 (1948).
(8) Frank, R. L., Blegen, J. R., Dearborn, R. J., Meyers, R. L., Woodward, F. E., *J. Am. Chem. Soc.* **68**, 1368 (1946).
(9) Frank, R. L., Seven, R. P., *Ibid.*, **71**, 2629 (1949).
(10) Graf, R., Langer, W., Haumeder, K., *J. prakt. Chem.* **150**, 153 (1938).
(11) Koenigs, E., Hoffman, F. K., *Ber.* **58**, 194 (1925).
(12) Kramer, L., *Ibid.*, **24**, 1914 (1891).
(13) Mosher, H. S., in Elderfield's "Heterocyclic Compounds," vol. 1, p. 397, Wiley, New York, 1950.
(14) Oparina, M. P., *J. Russ. Phys.-Chem. Soc.* **61**, 2011 (1929).
(15) Prostenik, M., Filipovic, L., *Arkiv Kemi* **18**, 3 (1946).
(16) Union Carbide & Carbon Corp., Brit. Patent **742,268** (Dec. 21, 1955).
(17) Wibaut, J. P., Kooyman, E. C., *Rec. trav. chim.* **63**, 231 (1944).

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