1-Phenylsulfonyl-4-phenyl-1,3-butadiene (XIX). Employing the procedure of Chodroff and Whitmore,[26] a solution of phenylsulfonylacetic acid (10.0 g., 0.05 mole), 30 ml. of anhydrous pyridine, cinnamaldehyde (7.76 g., 0.06 mole), and 0.6 ml. of piperidine was heated on a steam bath for 6 hr. The resulting dark red liquid was poured onto a mixture of 35 ml. of concd. hydrochloric acid and 100 g. of ice. The precipitate was isolated and upon crystallization from 100 ml. of methanol gave 5.59 g. (41%) of faintly yellow, lustrous flakes, m.p. 95–97°. An analytical sample was prepared by two further crystallizations from 95% ethanol to give nearly white 1-phenylsulfonyl-4-phenyl-1,3-butadiene, m.p. 97–98°.

Anal. Calcd. for $C_{16}H_{14}O_2S$: C, 71.08; H, 5.22. Found: C, 70.89; H, 5.38.

γ-Phenylmercaptobutyrophenone (XXI). γ-Phenylbutyryl chloride prepared from 75.0 g. (0.38 mole) of the corresponding acid (X) and 60 ml. (0.75 mole) of thionyl chloride was taken up in 200 ml. of dry benzene and added dropwise to a slurry of 80.0 g. (0.60 mole) of aluminum chloride in 250 ml. of benzene at 5–10°. After the mixture was stirred at room temperature for 3 hr. and poured onto 2500 g. of ice, the organic phase was separated, washed with water, 5% sodium hydroxide solution, water, and dried over anhydrous sodium sulfate. The benzene was removed and distillation of the residue gave 52.4 g. of a yellow oil, b.p. 115–180° (0.8 mm.). Redistillation through an 8-inch Vigreux column gave three fractions: I, 11.6 g., b.p. 114–130° (1.0 mm.), n_D^{20} 1.6162; II, 4.4 g., b.p. 130–165° (1.0 mm.), n_D^{20} 16115; III, 34.3 g., b.p. 165–180° (1.0 mm.), n_D^{20} 1.6109. The last fraction was again distilled through a 60-cm. jacketed column, packed with glass helices, and gave 29.1 g. (30%) of γ-phenylmercaptobutyrophenone, b.p. 168–171° (0.7 mm.). The contaminant in the earlier fractions was the cyclic ketone X. A solid was obtained by cooling a solution of the above oil in absolute ethanol to −20°. In this manner 5.0 g. of liquid gave 4.1 g. of crystalline XXI, m.p. 36–38°.

Anal. Calcd. for $C_{16}H_{16}OS$: C, 74.98; H, 6.29. Found: C, 75.01; H, 6.38.

The *semicarbazone* was prepared and after recrystallization from ethanol melted at 126–127° (lit.,[12] m.p. 122°).

1-Phenylmercapto-4-phenylbutane (XXII). A mixture of 150 g. of amalgamated zinc, 200 ml. of concd. hydrochloric acid, 200 ml. of glacial acetic acid, 150 ml. of toluene, and 20.0 g. (0.078 mole) of γ-phenylmercaptobutyrophenone was refluxed vigorously for 40 hr. At intervals of 8, 12, and 30 hr., 60-ml. increments of concd. hydrochloric acid were added. When cooled, the toluene layer was separated and washed with water, saturated sodium bicarbonate solution, water, and dried over anhydrous sodium sulfate. The solvent was removed at atmospheric pressure and the residue distilled through an eight inch asbestos wrapped column to give 12.9 g. (68%) of a pale yellow oil, b.p. 157–160° (1.2 mm.), n_D^{20} 1.5910. An analytical sample was obtained after two distillations of the above material and was colorless 4-phenylbutyl phenyl sulfide b.p. 153–154° (1.0 mm.), n_D^{20} 1.5929.

Anal. Calcd. for $C_{16}H_{18}S$: C, 79.29; H, 7.49. Found: C, 79.26; H, 7.58.

1-Phenylsulfonyl-4-phenylbutane (XX). A solution of 1-phenylmercapto-4-phenylbutane (1.0 g., 41 mmoles), glacial acetic acid (12 ml.) and 30% hydrogen peroxide (5 ml.) was warmed on the steam bath 1 hr., then poured into 50 ml. of water. The precipitate was collected, dried *in vacuo*, and crystallized from petroleum ether (b.p. 60–80°) to give 0.85 g. (76%) of the sulfone, m.p. 65–66°.

Anal. Calcd. for $C_{16}H_{18}O_2S$: C, 70.04; H, 6.61. Found: C, 70.05; H, 6.59.

Hydrogenation of 1-phenylsulfonyl-4-phenyl-1,3-butadiene. A Paar hydrogenation apparatus was charged with 1-phenylsulfonyl-4-phenyl-1,3-butadiene (1.0 g., 3.7 mmoles), methanol (140 ml.) and a catalytic amount of Raney nickel and was shaken under a hydrogen atmosphere (50 p.s.i.) for 1 hr. After the catalyst was filtered and washed with methanol, the filtrate was evaporated under a stream of dry air and gave 0.93 g. (91%) of 1-phenylsulfonyl-4-phenylbutane, m.p. 65–66°. A mixture melting point with a sample of authentic material as prepared above showed no depression and the infrared spectra of the two samples were identical.

An alternate attempt to reduce the above compound using platinum oxide as catalyst and hydrogen at atmospheric pressure was unsuccessful. Only incomplete reduction occurred.

Spectra. The ultraviolet spectra were determined using a Perkin-Elmer Spectracord and Beckman DU instruments. Approximately 10^{-5} molar solutions in 95% ethanol and cyclohexane were used and the data are listed in Table I.

The infrared absorption frequencies listed in Table II were measured using the Perkin-Elmer Model 21 spectrophotometer fitted with sodium chloride optics. Sample solutions were prepared in Spectral grade carbon tetrachloride and cells of 0.050-cm. thickness were used. The absorption bands were frequency calibrated against a film of polystyrene which in turn had been checked against water vapor absorption.

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(26) S. Chodroff and W. F. Whitmore, *J. Am. Chem. Soc.*, 72, 1073 (1950).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF BRITISH COLUMBIA]

Synthesis in the Pyridine Series. I. The Synthesis of 3,4-Dimethyl-5-isopropylpyridine. A General Approach to 3,4,5-Trialkylated Pyridines

JAMES P. KUTNEY AND ROGER C. SELBY

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The synthesis of 3,4-dimethyl-5-isopropylpyridine has been achieved. Modifications of the synthetic scheme provide a general synthetic approach to new and difficultly accessible 3,4,5-trialkylated pyridines.

In connection with the structural elucidation of a new alkaloid isolated from a Chilean plant, it became necessary to consider the identity of several 3,4,5-trialkylpyridine derivatives. The particular compounds which were necessary for our study were the two possible dimethylisopropylpyridines, namely, 3,4-dimethyl-5-isopropylpyridine and 3,5-dimethyl-4-isopropylpyridine. Investigation of the literature soon revealed that 3,4,5-trialkylpyridines are not readily available and in particular, com-

pounds of this type possessing branched alkyl side chains are virtually unknown. It thus became necessary to attempt syntheses of the compounds in question.

Concerning the synthesis of the symmetrical 3,5-dimethyl-4-isopropylpyridine, we first considered a possible extension of the method of Wibaut[1-4] which has been used for the introduction of alkyl substituents into the γ-position of the pyridine nucleus. However, when we treated 3,5-lutidine with acetic anhydride and zinc under the specified conditions, we did not obtain the known 3,5-dimethyl-4-ethylpyridine, but a compound possessing strong carbonyl absorption (5.85 μ) in the infrared. This substance, which we have shown to be 3,5-dimethyl-4-acetylpyridine, could be converted to the expected 4-ethyl compound by much more drastic reduction conditions. Apparently the steric effect of the methyl groups on the adjacent carbon atoms had made it possible for us to isolate the 4-acetylpyridine derivative—an intermediate which could be easily applied in our synthesis of the desired 3,5-dimethyl-4-isopropylpyridine.

An obvious sequence utilizing the now readily accessible 3,5-dimethyl-4-acetylpyridine, could involve conversion of the latter to the requisite tertiary alcohol and removal of the hydroxyl function in a subsequent step. Reaction of the acetylpyridine with methylmagnesium bromide or iodide under various reaction conditions met with failure, the starting ketone being recovered in each case. Similar attempts were also made to react 3,5-dimethyl-4-acetylpyridine with methyllithium but again negative results were obtained. It thus seems that the adjacent methyl groups have sterically hindered the carbonyl group so effectively as to make the latter function completely unreactive to organometallic reagents.

We were also unsuccessful in our attempt to react 3,5-dimethyl-4-acetylpyridine with the Wittig reagent, methyltriphenylphosphonium bromide.[5,6]

We then turned our attention to the work of Vaculik and co-workers,[7] who have recently reported a synthesis of 3,5-dimethyl-4-*n*-alkylpyridines. We felt that a simple modification of this method could lead to the symmetrical dimethylisopropylpyridine. The compound, 1-benzyl-3,5-dimethyl-4-piperidone,[7] was synthesized and treated with isopropylmagnesium bromide under a variety of conditions. We were, however, unable to obtain the desired Grignard product.

Our consistent difficulties in achieving the synthesis of 3,5-dimethyl-4-isopropylpyridine caused us to turn to the preparation of the unsymmetrical dimethylisopropylpyridine, namely 3,4-dimethyl-5-isopropylpyridine. Our first consideration in this direction was an attempt to synthesize the appropriate diethyl α,β,γ-trialkyl-γ-cyanoglutaconate, notably diethyl α,β-dimethyl-γ-isopropyl-γ-cyanoglutaconate, since a synthesis of 3,4,5-trimethylpyridine had been successfully carried out by Rogerson and Thorpe,[8] starting with diethyl α,β,γ-trimethyl-γ-cyanoglutaconate. We were not successful in synthesizing the desired glutaconate. Although we were able to prepare the dialkylated ester, attempts to introduce the third alkyl group resulted in the isolation of lower boiling esters, presumably arising from cleavage of the initial glutaconic ester. Similar difficulties in preparing the higher trialkylcyanoglutaconic esters have been recently reported by Bailey.[9]

In considering another synthetic pathway which has led to the desired 3,4-dimethyl-5-isopropylpyridine, we have developed a general approach to new and otherwise difficulty accessible 3,4,5-trialkylpyridines. Our starting point for this synthesis was 5-cyano-2,6-dihydroxy-3,4-dimethylpyridine, II, a compound which had been previously prepared by Guareschi.[10] The Guareschi type of cyclization has also been employed in other cases by Ruzicka[11] and Hope[12] and recently Bobbitt and co-workers[13] have improved the yield in this type of reaction. We have employed this recent modification[13] to prepare the dihydroxypyridine, II. Condensation of ethyl 2-methylacetoacetate and cyanoacetamide in the presence of a mole of piperidine led to the piperidinium salt, I, which could be conveniently isolated. The dihydroxypyridine, II, was obtained by acidification of the salt, and an over-all yield of 69% of the desired starting material II was achieved. For the purposes of comparison, the starting material was also prepared by the older method[10,11] of condensing the amide of ethyl 2-methylacetoacetate and ethyl cyanoacetate. The product from this latter method was identical in every respect with the material from the first preparation, but the yield was lower and this latter procedure was subsequently abandoned. The conversion of 5-cyano-

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(11) L. Ruzicka and V. Fornasir, *Helv. Chim. Acta*, **2**, 338 (1919).

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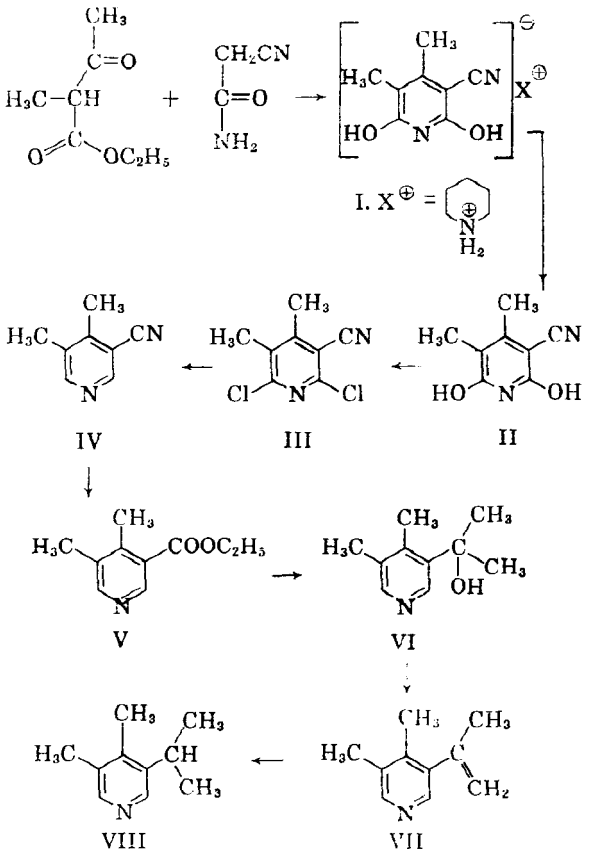
(13) J. M. Bobbitt and D. A. Scola, *J. Org. Chem.*, **25**, 560 (1960).

2,6-dihydroxy-3,4-dimethylpyridine to the corresponding 5-cyano-2,6-dichloro-3,4-dimethylpyridine, III, was effected by the use of an excess of phosphorus oxychloride at an elevated temperature. The halogen atoms were then removed by hydrogenolysis of 5-cyano-2,6-dichloro-3,4-dimethylpyridine, III, in the presence of freshly prepared palladium, to give 5-cyano-3,4-dimethylpyridine, IV, in good yield.

The extension of the synthesis to be desired 3,4-dimethyl-5-isopropylpyridine, utilizing 5-cyano-3,4-dimethylpyridine, IV, as an intermediate, could proceed in a number of ways. We chose to convert the nitrile to ethyl 3,4-dimethyl-5-pyridinecarboxylate, V, by effecting the alcoholysis with sulfuric acid in absolute alcohol at elevated tempera-



tures. Since the preparation of the ester from the nitrile represented the lowest yielding step (45%) in the entire sequence, we attempted to improve the hydrolysis of the nitrile by the use of Amberlite IRA-400.[13] We were, however, not successful in applying this method to any advantage. When ethyl 3,4-dimethyl-5-pyridinecarboxylate was treated with methylmagnesium iodide, a good yield of the expected teritary alcohol, VI, was obtained.

The final step in the synthesis involved removal of the teritary hydroxyl group—a conversion which could also be effected in several ways. One of the most direct methods appeared to be reductive removal of the alcoholic function by means of red phosphorus and hydriodic acid—a reaction frequently employed in the pyridine series.[14,15] The product from the reaction of the tertiary alcohol, VI, with red phosphorus and hydriodic acid, was indeed an oxygen-free pyridine derivative, which showed a typical pyridine absorption in the ultraviolet and which very readily formed a crystalline picrate. Analytical data on the picrate derivative was in good agreement with the values expected for the picrate of the desired 3,4-dimethyl-5-isopropylpyridine, but several carbon and hydrogen analyses of the liquid product consistently yielded low hydrogen values. The infrared spectrum of the product, apart from the characteristic bands attributed to the pyridine nucleus, indicated a band of medium intensity at 6.11 μ which suggested the presence of an olefinic group.[16] These facts suggested the possibility that the product from the reduction was 3,4-dimethyl-5-isopropenylpyridine, VII, resulting from an unexpected dehydration of the tertiary alcohol. The NMR spectrum confirmed our considerations. The NMR[17] of the reduction product showed a doublet in the olefinic proton region[18] (5.24 τ and 5.53 τ).[19]

The highest field signal at 8.66τ arising from the methyl group of the isopropenyl group[20] is split into a quartet by spin interaction with the two olefinic protons. The presence of two methyl substituents attached to the pyridine nucleus was indicated by a strong signal at 8.44 τ. Finally, the presence of a signal at 2.10 τ characteristic[21] of α-protons in the pyridine ring, showed that the above substituents are attached to the ring at the 3,4,5-positions. The relative areas under the signals were in agreement with the requirements for 3,4-dimethyl-5-isopropenylpyridine, VII.

The synthesis of 3,4-dimethyl-5-isopropylpyridine, VIII, was finally achieved when 3,4-dimethyl-5-isopropenylpyridine was reduced by shaking with hydrogen in the presence of platinum oxide in gla-

(14) T. Nakashima, *J. Pharm. Soc. Japan*, **75**, 1010 (1955); *Chem. Abstr.*, **50**, 4944e (1956).

(15) R. Lukes and M. Pergal, *Chem. listy*, **52**, 68 (1958); *Chem. Abstr.*, **52**, 16346e (1958).

(16) L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, John Wiley and Sons, Inc., New York, 1958, p. 34.

(17) The NMR spectrum was run on a Varian 40 Mc. high resolution spectrometer. The spectrum was determined on the pure liquid using hexamethyldisiloxane as an external standard. The calculation of values was done by assigning the reference signal at 10.30 τ. A second spectrum of the compound in carbon tetrachloride was determined under conditions of higher resolution on a 60 Mc. high resolution spectrometer by Dr. H. J. Bernstein, National Research Council, Ottawa. We are very grateful to Dr. Bernstein for his help.

(18) L. M. Jackman, *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, Pergamon Press, Inc., New York, 1959, p. 60.

(19) G. V. D. Tiers, *J. Phys. Chem.*, **62**, 1151 (1958).

(20) Reference 19, p. 58.

(21) W. G. Schneider, H. J. Bernstein, and J. A. Pople, *Can. J. Chem.*, **35**, 1487 (1957).

cial acetic acid. The NMR spectrum[22] was in complete agreement with the assignment of structure VIII to the final product.

The highest field signal arising from the methyl groups of the isopropyl group is split into a doublet (8.70 τ and 8.82 τ) by the tertiary hydrogen atom. The tertiary hydrogen signal in the region of 7.18 τ is split as expected, into a series of lines, and an intense sharp signal at 7.82 τ is assigned to the two methyl groups attached directly to the pyridine ring.[23]

Finally, the low field signal is in the region expected for α-protons in the pyridine ring.[21] It is split by 8 cycles (1.83 τ and 1.94 τ) and indicates that the pyridine is substituted *unsymmetrically* in the 3-, 4-, and 5-positions. The relative areas under the peaks are in good agreement with the requirements for 3,4-dimethyl-5-isopropylpyridine.

It should be pointed out that 5-cyano-3,4-dimethylpyridine, IV, used as an intermediate in the above synthesis represents, in fact, a valuable intermediate for the synthesis of various types of new and otherwise difficulty accessible 3,4-5-trialkylpyridine derivatives. Since numerous modifications of the cyano function are possible, the above compound lends itself to a rather general synthetic approach to pyridines of the type mentioned above. Investigations along some of these lines are currently under study in our laboratories.

EXPERIMENTAL[24]

5-Cyano-2,6-dihydroxy-3,4-dimethylpyridine (II); *piperidine method.*[13] A mixture of ethyl 2-methylacetoacetate[25] (489 g., 3.4 moles), cyanoacetamide[26] (286 g., 3.4 moles), freshly distilled piperidine (340 ml. 3.4 moles) and methyl alcohol (1100 ml.) was refluxed for 29 hr. The mixture was allowed to cool and the white precipitate which resulted was separated by suction filtration and washed thoroughly with methyl alcohol. A second crop of this piperidinium salt was obtained by concentration of the mother liquor and methyl alcohol washings. This salt (m.p. 270–282°) was dissolved in warm water, acidified with concentrated hydrochloric acid and then allowed to cool. The solid, which separated, was removed by suction filtration, washed with methyl alcohol, water and methyl alcohol, and dried at 60° to yield 120 g. of product. A second crop (214 g.) was obtained by concentration of the mother liquors. The total yield of the dihydroxypyridine was 334 g. (69%). A small sample recrystallized three times from methyl alcohol yielded an analytical sample m.p. 294° dec.; infrared; broad, intense bands at 6.13 μ and 6.25 μ due to imide grouping and 4.50 μ medium intensity (CN).

Anal. Calcd. for $C_8H_8O_2N_2$: C, 58.52; H, 4.91; O, 19.48; N, 17.12. Found: C, 58.63; H, 4.96; O, 19.57; N, 17.13.

5-Cyano-2,6-dihydroxy-3,4-dimethylpyridine (II); *older method.*[10,11] Ethyl 2-methylacetoacetate (138.5 g., 0.964 mole) was treated with concentrated ammonium hydroxide (300 ml.) and the mixture was stirred at room temperature for 4 days. At this time some solid had separated but two liquid layers were still present so more concentrated ammonium hydroxide (50 ml.) was added and the mixture stirred at room temperature for another 2 days. The resulting solid (30.5 g.), undoubtedly the undesirable 2-amino-1-methylcrotonate, was removed by suction filtration. To the filtrate, more ammonium hydroxide (50 ml.) was added and the clear solution was stirred at room temperature for a further 8 hr. and then allowed to stand overnight. A second crop (15.5 g.) of solid was removed by suction filtration and the clear filtrate was treated with ethyl cyanoacetate (75.1 g., 0.664 mole). The reaction mixture was allowed to stand at room temperature for 3 days after which time the entire reaction mixture had become solid. The solid, which was the ammonium salt of 5-cyano-2,6-dihydroxy-3,4-dimethylpyridine, was removed by suction filtration, air-dried, and shown to weigh 54.5 g. (m.p. 277–82° dec.).

The desired 5-cyano-2,6-dihydroxy-3,4-dimethylpyridine was obtained by treating the above salt with concentrated hydrochloric acid (200 ml.) and filtering off the resulting solid. This solid was washed with water, dried to yield 29.35 g. (m.p. 284–285° dec.). An additional 2.95 g. (total 32.3 g.) was obtained by concentration of the filtrate. A small sample was recrystallized from methyl alcohol (m.p. 294° dec.) and shown to be identical with the product from the piperidine method, by mixed melting point and infrared comparison.

5-Cyano-2,6-dichloro-3,4-dimethylpyridine (III). Dried 5-cyano-2,6-dihydroxy-3,4-dimethylpyridine (99 g.) was treated with freshly distilled phosphorus oxychloride (225 ml.) and the mixture was sealed in a glass tube and heated at 180° for 6.5 hr. The tube, after allowing to cool, was opened and the contents added cautiously into crushed ice. The brown precipitate was separated by filtration and washed with water. It was then dissolved in hot 95% ethyl alcohol, filtered while hot and the clear filtrate allowed to cool. The first crop of crystals weighed 45 g. and an additional 45 g. (total 90 g.) was obtained by concentration of the mother liquor. Recrystallization from absolute ethyl alcohol yielded an analytical sample m.p. 76–77°; infrared; 4.48 μ weak band (CN) and disappearance of imide bands.

Anal. Calcd. for $C_8H_6N_2Cl_2$: C, 47.78; H, 3.00; N, 13.93; Cl, 35.26. Found: C, 47.71; H, 3.30; N, 13.59; Cl, 35.20.

5-Cyano-3,4-dimethylpyridine IV. To a solution of 5-cyano-2,6-dichloro-3,4-dimethylpyridine (30 g.) in methyl alcohol (300 ml.), anhydrous sodium acetate (30 g.) and freshly prepared palladium chloride[13] were added. The mixture was shaken with hydrogen (50 p.s.i.) for 18 hr. during which time a pressure drop of 27 p.s.i. was recorded. The catalyst was removed by filtration, the solvent evaporated and the residue was dissolved in water (100 ml.). This aqueous solution was made slightly alkaline by addition of solid sodium bicarbonate and the organic material extracted from the aqueous layer by means of ethyl ether. The ether extract was dried over anhydrous sodium sulfate, the solvent evaporated to yield 22 g. of a yellow viscous residue. This residue solidified upon cooling but this gummy solid was difficult to purify. The product formed a picrate very readily and two recrystallizations from ethyl alcohol yielded an analyti-

(22) The NMR spectrum was determined on a Varian 60 Mc. high resolution spectrometer by Dr. J. N. Shoolery and his associates. The compound was run in carbon tetrachloride and the reference compound used as an internal standard was tetramethylsilane. We are most grateful to Dr. Shoolery and his co-workers for running this experiment.

(23) Dr. L. W. Reeves of this department has recently determined the NMR spectrum of 2,3-lutidine and has found the methyl group at the 3-position to give a signal at 7.81 τ. We are grateful to Dr. Reeves for this information prior to publication.

(24) All melting points were taken on a Fisher-Johns Apparatus and are uncorrected. The analyses were performed by Dr. A. Bernhardt and his associates, Mulheim (Ruhr) Germany. Infrared spectra were determined as potassium bromide pellets in the case of solids and as liquid films in the case of liquids.

(25) K. Folkers and H. Adkins, *J. Am. Chem. Soc.*, **53**, 1416 (1931).

(26) B. B. Carson, R. W. Scott, and C. E. Vose, *Org. Syntheses*, Coll. Vol. I, 179 (1941).

cal sample, m.p. 146–147°; infrared; 4.48 μ medium intensity (CN).

Anal. Calcd. for $C_{14}H_{11}N_5O_7$: C, 46.54; H, 3.07; N, 19.38; O, 31.00. Found: C, 46.04; H, 3.30; N, 19.62; O, 30.97.

Ethyl 3,4-dimethyl-5-pyridinecarboxylate (V). A mixture of 5-cyano-3,4-dimethylpyridine (42 g.), concentrated sulfuric acid (51 ml.), and absolute ethyl alcohol (150 ml.) was sealed in a glass tube and maintained at 145° for 21 hr. The tube was then cooled and the contents added to crushed ice (320 g.). The ethyl alcohol was removed by distillation under reduced pressure and the remaining aqueous solution was cautiously neutralized with solid sodium bicarbonate. The resulting solution was extracted several times with ether and the ethereal extract was dried over anhydrous sodium sulfate. After removing the solvent by distillation, the dark green liquid which remained was distilled at a bath temperature 140–160°/0.45 mm. to yield a light yellow liquid (25 g., 45%); lit.[27] 89–91°/0.5 mm. The picrate which was readily prepared, melted at 90–91°; lit.[27] 100–101°; infrared: 5.86 μ intense band (ester).

Anal. Calcd. for $C_{16}H_{16}N_4O_9$: C, 47.06; H, 3.95; N, 13.71; O, 35.26. Found: C, 47.08; H, 3.85; N, 14.41; O, 34.92.

5-(2-Hydroxy-2-propyl)-3,4-dimethylpyridine (VI). To a cold solution of methylmagnesium iodide (0.62 mole) prepared in the usual manner from magnesium turnings (15 g.) and methyl iodide (91.2 g.) in anhydrous ethyl ether (225 ml.), a solution of ethyl 3,4-dimethyl-5-pyridinecarboxylate (25 g., 0.14 mole) in ether (200 ml.) was added dropwise over a period of 1 hr. The reaction was very exothermic and the reaction mixture was kept in ice during addition of the ester. After the addition was complete, the mixture was refluxed for 2 hr. and then allowed to stand overnight at room temperature. The excess Grignard was destroyed by the careful addition of a solution of potassium carbonate (30 g.) in water (80 ml.). The mixture was heated, with stirring, on a steam bath for 30 min. and after this time, the magnesium salts were removed by filtration. These salts were washed with a small portion of ethyl ether and the ether washings combined with the main ether layer from the reaction mixture. The ether extract was washed with water and then dried over anhydrous sodium sulfate. The solvent was evaporated and the dark viscous liquid which remained, solidified upon standing for several hours. The yield of this solid material was 20 g. An analytical sample was prepared by dissolving a small portion of the solid in anhydrous ether, decolorizing once with Norite and then recrystallizing two times from anhydrous ethyl ether. The beautiful, needle-like crystals which were obtained, melted at 107°; infrared; 3.07 μ strong, very broad band (OH).

Anal. Calcd. for $C_{10}H_{15}ON$: C, 72.72; H, 9.09; N, 8.48; O, 9.70. Found: C, 72.79; H, 8.82; N, 8.59; O, 9.97.

3,4-Dimethyl-5-isopropenylpyridine (VII). A mixture of 5-(2-hydroxy-2-propyl)-3,4-dimethylpyridine (20 g.), concentrated hydriodic acid (238 ml., 47%) and red phosphorus (32 g.) was refluxed for 10 hr. After cooling, the phosphorus was removed by filtration and the filtrate concentrated by distillation *in vacuo*. The dark residual oil was taken up in water (150 ml.) and the mixture decolorized by addition of sodium bisulfite. When no further reaction with the bisulfite was noted (approximately a total of 50 g. added), the mixture was made alkaline with potassium hydroxide. The resulting reaction mixture was extracted with several portions of ethyl ether, the etheral extract washed with a small amount of water and then dried over anhydrous sodium sulfate. The ether was removed by distillation and the residual reddish liquid was distilled in vacuo (bath temperature 95–120°/12 mm.). The yield of the distilled liquid was 6.12 g. A second distillation on a small portion yielded an analytical sample (b.p. 222–223°); infrared 6.11 μ medium intensity (C=C).

Anal. Calcd. for $C_{10}H_{13}N$: C, 81.63; H, 8.84; N, 9.52. Found: C, 80.98, 81.64; H, 8.72, 8.86; N, 9.76, 9.39.

A picrate, m.p. 127–129° was prepared in ethanol and recrystallized three times from the same solvent.

Anal. Calcd. for $C_{16}H_{16}N_4O_7$: C, 51.06; H, 4.25; N, 14.89; O, 29.78. Found: C, 51.09; H, 4.80; N, 14.81; O, 29.60.

3,4-Dimethyl-5-isopropylpyridine (VIII). A solution of 3,4-dimethyl-5-isopropenylpyridine (0.90 g.) in glacial acetic acid (20 ml.) was treated with Adams catalyst (200 mg.) and shaken in an atmosphere of hydrogen. An uptake of 0.8 mole of hydrogen was recorded in 3.5 hr., at which time the hydrogen absorption ceased. The catalyst was removed by filtration and the acetic acid was evaporated in vacuo using steam bath temperature. The residue was taken up in water (10 ml.), the aqueous solution made alkaline with sodium hydroxide and then extracted with ethyl ether. The ether extract was dried over anhydrous sodium sulfate, the solvent removed by distillation to yield a nearly colorless liquid. Distillation of this liquid (bath temperature 100–110°/1 mm.) yielded a water-clear liquid (850 mg.). A small portion was distilled once more for an analytical sample (b.p. 232–233°); n_D^{25} 1.5098; infrared; disappearance of band at 6.11 μ.

Anal. Calcd. for $C_{10}H_{15}N$: C, 80.53; H, 10.06; N, 9.39. Found: C, 79.71, 80.13; H, 9.99, 10.05; N, 9.34.

A picrate m.p. 143–144° was prepared in ethanol and recrystallized three times from methanol.

Anal. Calcd. for $C_{16}H_{18}N_4O_7$: C, 50.79; H, 4.80; N, 14.81; O, 29.60. Found: C, 50.68; H, 4.81; N, 14.97; O, 29.34.

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