[CONTRIBUTION FROM DEPARTMENT OF CHEMISTRY, UNIVERSITY OF TEXAS]

The Emmert Reaction in the Synthesis of Alkyl- and Cycloalkylpyridines[1]

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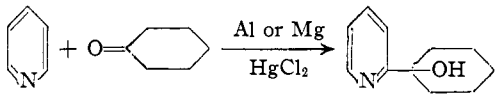
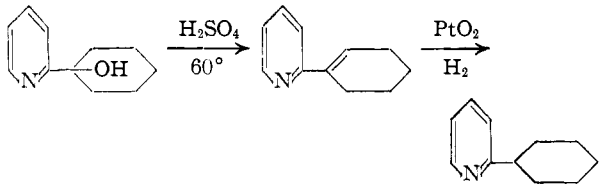
New dehydration procedures for pyridyl alcohols giving better yields have been presented. Five new pyridyl alcohols have been isolated, purified and characterized. Two new alkylpyridines, one new alkenylpyridine, seven new cycloalkylpyridines and six new cycloalkenylpyridines have been synthesized and characterized.

The interesting reaction of pyridines with carbonyl compounds to produce pyridinemethanols reported by Emmert and co-workers,[3] has received little attention in the synthesis of alkyl- and cycloalkylpyridines. The reaction occurs when a ketone is condensed with pyridine in the presence of aluminum or magnesium metal turnings and mercuric chloride. Dehydration of the alcohol and



hydrogenation of the resulting olefin yields the alkyl- or cycloalkylpyridine.



While Emmert reported only 2-pyridyl isomers from the reaction, Tilford and co-workers[4] reported formation of 4-pyridyl isomers in yields up to half the yields of the 2-pyridyl isomer when aluminum was used as the condensing agent. However, all ketones which were used in obtaining the 4-pyridyl isomers by Tilford and co-workers were aromatic ketones, such as acetophenone. When cyclopentanone and cyclohexanone were used in the reaction in the present investigation the amount of 4-pyridyl isomer was extremely small (0.1 to 0.5% yield on ketone). The reaction is therefore not practical in the synthesis of 4-cycloalkylpyridines unless the ketone used is available in large quantities. No 4-pyridyl isomer was isolated from the reaction products of acetone with 3-picoline.

Although attempts were made to improve the yield in this reaction, it was found that careful work in separating the products gave approximately the same yield under widely different reaction conditions. Extremely slow addition of the ketone to the reaction mixture, a large excess of aluminum turnings, and refluxing after all the ketone had been added did not give improved yields. Bachman and Micucci[5] have reported to have improved the published procedure for carrying out the Emmert reaction using acetone and pyridine, but the yield reported from the improved procedure is the same as that reported by Emmert and Asendorf[3] although slightly larger quantities of mercuric chloride and magnesium were used.

Bachman and Micucci,[5] as well as Tilford and co-workers,[4] reported percentage yields based on magnesium or aluminum. In the present report the yields are not based on the aluminum or magnesium whose exact function in the main reaction is not known or on the pyridine which is recovered in good yield, but on the ketone which is completely reacted. This change in basis of reporting yields gives apparently lower yields, but, when figured on the same basic, the yields of other investigators are comparable.

The Emmert reaction when applied to the picolines gives fair yields with the 3- and 4-picolines but very poor yields with 2-picoline. While it might be expected that the yield from 2-picoline would be lower than the yield from pyridine or 4-picoline since the latter have two 2-positions exposed while the 2-picoline has only one, the actual yield from 2-picoline and cyclopentanone is only about one-tenth of the yield from pyridine or 4-picoline with cyclopentanone. It is of interest to note that the reaction of cyclopentanone with 3-picoline gives about three times as much of the 2,5-isomer as of the 2,3-isomer. If the yield of the 2,5-isomer were doubled, the yield would be the same as for the 2-isomer from 4-picoline or pyridine. In the reaction of acetone with 3-picoline it was found that approximately equal quantities of 2,3- and 2,5-isomers were obtained. In the reaction of acetone with 3-picoline and 4-picoline the total yields of product were practically identical. Pertinent data on the reaction of acetone with picolines are shown in Table I, A and B.

The first synthesis of a cycloalkylpyridine using the Emmert reaction was accomplished by Thomas,[6] who synthesized 2-cyclopentylpyridine. Following the dehydration procedure of Emmert and Asendorf he obtained poor yields of 2-(1-cyclopentenyl)-pyridine from 1-(2-pyridyl)-cyclopentanol. The conditions reported by Emmert and Asendorf consisted of heating 1 g. of the alcohol with 3 volumes of concentrated sulfuric acid for 3 hours at 120°. The present investigation has shown that these conditions were much too severe. By slowly adding 2.5 parts by weight of sulfuric acid to one part of pyridyl alcohol while keeping the temperature below 60°, yields of 80–95% have been consistently obtained for the dehydration step. In earlier attempts to modify the dehydration step in this Laboratory a 1:1 mixture (by

(1) From the Ph.D. thesis of Paul F. Kruse, Jr., University of Texas, June, 1951.

(2) Experiments using acetone by P. F. K., using cyclopentanone and cyclohexanone by E. N. W.

(3) B. Emmert and E. Asendorf, *Ber.*, **72B**, 1188 (1939); B. Emmert and E. Pirot, *ibid.*, **74**, 714 (1941).

(4) C. H. Tilford, R. S. Shelton and M. G. Van Campen, THIS JOURNAL, **70**, 4001 (1948).

(5) G. B. Bachman and D. D. Micucci, *ibid.*, **70**, 2381 (1948).

(6) Thomas, M.A. Thesis, University of Texas, 1943; H. L. Lochte, E. D. Thomas and Price Truitt, THIS JOURNAL, **66**, 550 (1944).

TABLE I

A. ACETONE WITH PICOLINES AND PYRIDINE

Reactants, acetone	Moles	Products	Formula	Yield on ketone, %	B.p., °C.	Mm.	Data by
3-Picoline	3.3 3.8	α,α,3-(and α,α,5)-Trimethyl-2-pyridinemethanol	$C_9H_{13}NO$	8.5	119–123.5[a]	23	This paper
4-Picoline	3.3 3.8	α,α,4-Trimethyl-2-pyridinemethanol	$C_9H_{13}NO$	8.5	119–121[b]	23	This paper
Pyridine	2.5 3.44	α,α-Dimethyl-2-pyridinemethanol	$C_8H_{11}NO$	8.5	88–90	12	Ref. 3
2-Picoline	2.15 3.44	α,α,2-Trimethyl-2-pyridinemethanol	$C_9H_{13}NO$	1.9–3.0	98–100	14	Ref. 3
3-Picoline	2.15 3.44	α,α,3-(and α,α,5)-Trimethyl-2-pyridinemethanol	$C_9H_{13}NO$	6.7	106	14	Ref. 3

B. ALKYL- AND ALKENYLPYRIDINES FROM ACETONE AND PICOLINES

Pyridine	B.p., °C.	Mm.	$n^{20}D$	d^{20}_4	Picrate M.p., °C.	Nitrogen, % Found[c]	Calcd.	Formula
2-Isopropyl-3-methyl[e]	181.0–181.5	747	1.4980	0.916	149–151	15.20	15.37	$C_{15}H_{16}N_4O_7$
2-Isopropyl 4-methyl[f]	184.5–185.0	749.5[d]	1.4908	.905	118.5–119.5	15.40	15.37	$C_{15}H_{16}N_4O_7$
2-Isopropenyl 4-methyl[g]	98–101	23	1.5352	...	165–167	15.32	15.47	$C_{15}H_{14}N_4O_7$

[a] B.p. and $n^{20}D$ 1.5095 for mixture. [b] $n^{20}D$ 1.5088. [c] Analyses by micro Dumas. [d] B.p. 81–82° (23 mm.). [e] *Anal.* (by non-aqueous titration) Calcd. for $C_9H_{13}N$: N, 10.36. Found: N, 10.39. [f] *Anal.* (by micro Dumas) Calcd. for $C_9H_{13}N$: N, 10.36. Found: N, 10.18. [g] *Anal.* (by non-aqueous titration) Calcd. for $C_9H_{11}N$: N, 10.52. Found: N, 10.42.

TABLE II

A. EMMERT REACTION PRODUCTS USING CYCLOPENTANONE AND CYCLOHEXANONE

Reactants	Moles	Products[a]	Yield, %	M.p.,[c] °C.	B.p.[c] °C.	Mm.	Formula	Nitrogen, %[d] Found	Calcd.
Cyclohexanone	9	1-(2 Py)-cyclohexanol[e]	29.0	42–43	157	34	$C_{11}H_{15}NO$	7.95	7.91
Pyridine	12	1-(4-Py)-cyclohexanol	0.25	147–148	167	6	$C_{11}H_{15}NO$	7.94	7.91
Cyclopentanone	6	1-(2-Me-6-py)-cyclopentanol	2.3		154	31	$C_{11}H_{15}NO$	7.87	7.91
2-Picoline	8	1-(2-Me-4-py)-cyclopentanol	0.56	[b]					
Cyclopentanone	3	1-(3-Me-2-py)-cyclopentanol	4.0	[b]					
3-Picoline	4	1-(5-Me-2-py)-cyclopentanol	11.0	[b]					
Cyclopentanone	3	1-(4-Me-2-py)-cyclopentanol	23.0	81–82	120	4	$C_{11}H_{15}NO$	7.95	7.91
4-Picoline	4								
Cyclopentanone	6	1-(2-Py)-cyclopentanol[f]	23.0	82.6–83.4	150	32	$C_{10}H_{13}NO$	8.60	8.59
Pyridine	8	1-(4-Py)-cyclopentanol	0.1	[b]					

B. CYCLOALKENYLPYRIDINES

Pyridine	B.p., °C.	Mm.	M.p.,[c] °C.	$n^{20}D$	d^{20}_4	Formula	Nitrogen, %[d] Found	Calcd.
2-(1-Cyclohexenyl)[g]	155	31		1.5737	1.033	$C_{11}H_{13}N$	8.78	8.80
4-(1-Cyclohexenyl)	165	31		1.5733	1.044	$C_{11}H_{13}N$	8.71	8.80
2-(1-Cyclopentenyl)-3-me	148	31		1.5722	1.027	$C_{11}H_{13}N$	8.78	8.80
2-(1-Cyclopentenyl)-4-me	154	30	34–36			$C_{11}H_{13}N$	8.75	8.80
2-(1-Cyclopentenyl)-5-me	156	31	59–60			$C_{11}H_{13}N$	8.86	8.80
2-(1-Cyclopentenyl)-6-me	144	32		1.5702	1.015	$C_{11}H_{13}N$	8.96	8.80
4-(1-Cyclopentenyl)-2-me	157	31		1.5704	1.024	$C_{11}H_{13}N$	8.70	8.80
2-(1-Cyclopentenyl)[h]	141.5	35		1.5795	1.038	$C_{10}H_{11}N$	9.60	9.65

C. CYCLOALKYLPYRIDINES

Pyridine[a]	B.p.,[e] °C.	Mm.	$n^{20}D$	d^{20}_4	Formula	Nitrogen, %[d] Found	Calcd.
2-Cyhex-[i]	245–246	746	1.5246	0.990	$C_{11}H_{15}N$	8.67	8.70
4-Cyhex-	265–266	744	1.5284	.995	$C_{11}H_{15}N$	8.66	8.70
2-Cypen-3-me-	235.5–236.5	744	1.5297	.990	$C_{11}H_{15}N$	8.71	8.70
2-Cypen-4-me-	242–243	744	1.5238	.980	$C_{11}H_{15}N$	8.68	8.70
2-Cypen-5-me-	243–244	744	1.5242	.979	$C_{11}H_{15}N$	8.72	8.70
2-Cypen-6-me-	228–229	746	1.5227	.977	$C_{11}H_{15}N$	8.76	8.70
4-Cypen-2-me-	251–252	747	1.5254	.984	$C_{11}H_{15}N$	8.65	8.70
2-Cypen-[i]	222–223	745	1.5263	.994	$C_{10}H_{13}N$	9.50	9.52

[a] Abbreviations used: me—methyl, py—pyridyl, cyhex—cyclohexyl, cypen—cyclopentyl, d—decomposition. [b] Yield estimated from amount of corresponding cyclopentenylpyridines which were isolated as picrates. [c] All melting points and atmospheric boiling points corrected. [d] All nitrogen analyses by non-aqueous titration of basic nitrogen using method of Fritz, *Anal. Chem.*, **22**, 1028 (1950). [e] Ref. 3b, m.p. 43°, b.p. 143–144° at 13 mm. [f] Ref. 3b, m.p. of base 84°. [g] Ref. 3b, b.p. 259°. [h] Ref. 6, b.p. 238.5–239.5°. [i] Wei-Fa Ho, unpublished research, University of Texas, b.p. 245–246° (752 mm.), $n^{30}D$ 1.5170, d^{30}_4 0.984. [i] Ref. 6, b.p. 217–218° (750 mm.), $n^{20}D$ 1.5205 (n_D taken on unpurified base).

TABLE III

A. PICRATE MELTING POINTS AND ANALYSES

Picrate of	M.p.,[c] °C.	Formula	Nitrogen, %[a] Found	Calcd.
1-(2-Pyridyl)-cyclohexanol[b]	86–87	$C_{11}H_{15}NO \cdot C_6H_3N_3O_6 \cdot H_2O$	12.97, 13.11	13.21
1-(4-Pyridyl)-cyclohexanol	169–170	$C_{11}H_{15}NO \cdot C_6H_3N_3O_6$	14.06	13.79
1-(2-Methyl-6-pyridyl)-cyclopentanol	146–147	$C_{11}H_{15}NO \cdot C_6H_3N_3O_6$	13.77	13.79
1-(4-Methyl-2-pyridyl)-cyclopentanol	125–126	$C_{11}H_{15}NO \cdot C_6H_3N_3O_6$	14.09	13.79
1-(2-Pyridyl)-cyclopentanol	73–74	$C_{10}H_{13}NO \cdot C_6H_3N_3O_6$	13.97	14.28
2-(1-Cyclohexenyl)-pyridine[d]	159–160	$C_{11}H_{13}N \cdot C_6H_3N_3O_6$	14.51	14.41
4-(1-Cyclohexenyl)-pyridine	180–181	$C_{11}H_{13}N \cdot C_6H_3N_3O_6$	14.10, 14.18	14.41
2-(1-Cyclopentenyl)-3-methylpyridine	148–149	$C_{11}H_{13}N \cdot C_6H_3N_3O_6$	14.57	14.41
2-(1-Cyclopentenyl)-4-methylpyridine	204–206d	$C_{11}H_{13}N \cdot C_6H_3N_3O_6$	14.85	14.41
2-(1-Cyclopentenyl)-5-methylpyridine	221–222d	$C_{11}H_{13}N \cdot C_6H_3N_3O_6$	14.65	14.41
2-(1-Cyclopentenyl)-6-methylpyridine	156–157	$C_{11}H_{13}N \cdot C_6H_3N_3O_6$	14.51	14.41
4-(1-Cyclopentenyl)-2-methylpyridine	198d	$C_{11}H_{13}N \cdot C_6H_3N_3O_6$	14.46	14.41
2-(1-Cyclopentenyl)-pyridine	183–184	$C_{10}H_{11}N \cdot C_6H_3N_3O_6$	15.10	14.97
4-(1-Cyclopentenyl)-pyridine	180–182d	$C_{10}H_{11}N \cdot C_6H_3N_3O_6$	15.13	14.97
2-Cyclohexylpyridine[e]	128–129	$C_{11}H_{15}N \cdot C_6H_3N_3O_6$	14.38	14.36
4-Cyclohexylpyridine	154–155	$C_{11}H_{15}N \cdot C_6H_3N_3O_6$	14.47	14.36
2-Cyclopentyl-3-methylpyridine	123–124	$C_{11}H_{15}N \cdot C_6H_3N_3O_6$	14.46	14.36
2-Cyclopentyl-4-methylpyridine	145–146	$C_{11}H_{15}N \cdot C_6H_3N_3O_6$	14.46	14.36
2-Cyclopentyl-5-methylpyridine	114–115	$C_{11}H_{15}N \cdot C_6H_3N_3O_6$	14.50	14.36
2-Cyclopentyl-6-methylpyridine	107–109	$C_{11}H_{15}N \cdot C_6H_3N_3O_6$	14.34	14.36
4-Cyclopentyl-2-methylpyridine	106–107	$C_{11}H_{15}N \cdot C_6H_3N_3O_6$	14.41	14.36
2-Cyclopentylpyridine	105–106	$C_{10}H_{13}N \cdot C_6H_3N_3O_6$	15.03	14.89

B. STYPHNATES AND TRINITRO-*m*-CRESOLATES OF THE CYCLOALKYLPYRIDINES

	Styphnates				Trinitro-*m*-cresolates			
Pyridine[f]	M.p.,[c] °C.	Formula	Nitrogen, %[a] Found	Calcd.	M.p.,[c] °C.	Formula	Nitrogen, %[a] Found	Calcd.
2-Cyhex-	139	$C_{11}H_{15}N \cdot C_6H_3N_3O_7$	13.63	13.79	157	$C_{11}H_{15}N \cdot C_7H_3N_3O_6$	14.00	13.86
4-Cyhex-	154d	$C_{11}H_{15}N \cdot C_6H_3N_3O_7$	13.70	13.79	164	$C_{11}H_{15}N \cdot C_7H_3N_3O_6$	13.57, 13.66	13.86
2-Cypen-3-me-	129	$C_{11}H_{15}N \cdot C_6H_3N_3O_7$	13.71	13.79	139	$C_{11}H_{15}N \cdot C_7H_3N_3O_6$	13.73	13.86
2-Cypen-4-me-	151d	$C_{11}H_{15}N \cdot C_6H_3N_3O_7$	13.90	13.79	137	$C_{11}H_{15}N \cdot C_7H_3N_3O_6$	13.97	13.86
2-Cypen-5-me-	152d	$C_{11}H_{15}N \cdot C_6H_3N_3O_7$	13.92	13.79	121	$C_{11}H_{15}N \cdot C_7H_3N_3O_6$	13.90	13.86
2-Cypen-6-me-	114	$C_{11}H_{15}N \cdot C_6H_3N_3O_7$	13.75	13.79	135	$C_{11}H_{15}N \cdot C_7H_3N_3O_6$	13.82	13.86
4-Cypen-2-me-	145d	$C_{11}H_{15}N \cdot C_6H_3N_3O_7$	13.97	13.79	165	$C_{11}H_{15}N \cdot C_7H_3N_3O_6$	14.01	13.86
2-Cypen-	124	$C_{10}H_{13}N \cdot C_6H_3N_3O_7$	14.23	14.28	134	$C_{10}H_{13}N \cdot C_7H_3N_3O_6$	14.41	14.36

[a] All analyses by the Analytical Laboratory of the Biochemical Institute of The University of Texas; most of the analyses by Miss M. A. Smith. [b] B. R. Brown, Jr., *J. Chem. Soc.*, 2577 (1949); m.p. of picrate 82–83°. [c] All melting points corrected; melting point ranges were usually one degree or less with the highest temperature being recorded. [d] Wei-Fa Ho, unpublished Research, The University of Texas; m.p. of picrate 155–156°. [e] Wei-Fa Ho, *ibid.*, m.p. of picrate 127.5–129°. [f] Abbreviations used: cyhex—cyclohexyl, cypen—cyclopentyl, me—methyl, d—decomposition.

volume) of sulfuric acid and glacial acetic acid was used. Two volumes of this mixture when heated with one volume of the alcohol for three hours gave yields of 67–78% which were better than yields obtained under these conditions using sulfuric acid alone. As already pointed out, milder conditions when using concentrated sulfuric acid gave nearly quantitative yields with pyridylcyclopentanols and pyridylcyclohexanols. Pertinent data on the reaction of these cyclic ketones with pyridines are shown in Table II, A, B and C. Properties and analyses of derivatives of these products are shown in Table III, A and B.

Although the reaction of acetone and 3-picoline had previously been carried out,[3] no attempt had been made to separate the isomers obtained. In this study the pyridinemethanols were dehydrated and the products hydrogenated, as a mixture, and the components of the resulting mixture of isopropylmethylpyridines were separated and identified. Fractional recrystallization of a mixture of 12 g. of picrates (theoretical yield 16 g.) gave 5.5 g. of a picrate melting 149–151°. Oxidation of the base from this picrate gave quinolinic acid which, together with analytical data, showed it to be 2-isopropyl-3-methylpyridine. The presence of 2-isopropyl-5-methylpyridine was confirmed by isolation of the picrate from one of the fractions obtained by amplified distillation[7] of the mixture of bases. A yield of about 3% of 2-isopropyl-4-methylpyridine, probably from 4-picoline impurity in the commercial 3-picoline used, was also isolated by treating the bases with benzaldehyde and isolating the stilbazole, 2-isopropyl-4-styrylpyridine, as the picrate.

The separation of the isomers obtained in the reaction of 3-picoline and cyclopentanone was accomplished by dehydration of the mixture of products and fractional distillation of the mixture of cyclopentenylmethylpyridines. One of the isomers was a solid, so after recrystallization to remove it in pure form the mother liquors were redistilled through an efficient fractionation column. Both compounds isolated were oxidized to the corresponding pyridinedicarboxylic acids to prove the structure.

(7) A. C. Bratton, W. A. Felsing and J. R. Bailey, *Ind. Eng. Chem.*, **28**, 424 (1936).

Although dipyridyls were sought among the different reaction products, none were found so that if formed in the reaction they must have been present in fairly small quantities. When the Emmert reaction mixture was extracted with dilute hydrochloric acid, and the acid layer was extracted three times with benzene to remove neutral materials, cyclopentanol or cyclohexanol, corresponding to the ketone used, was isolated from the benzene extract. Surprisingly, when the hydrochloric acid layer was basified, extracted, and distilled an appreciable yield of the same alcohol was isolated. Apparently this was obtained by cleavage of a basic intermediate as it was heated during distillation. The alcohol obtained from the neutral products was always contaminated with the corresponding ketone while that obtained from the basic products was not.

Experimental

α,α,3-(and α,α,5)-Trimethyl-2-pyridinemethanol (I).—The procedure was adapted from Tilford, Shelton and Van Campen[4] (procedure B) and used 23 g. of magnesium turnings (0.96 mole), 5 g. of dry mercuric chloride, 5 drops of mercury, 220 g. of acetone (3.8 moles) and 307 g. of 3-picoline (3.3 moles). After warming 40 ml. of acetone and 40 ml. of 3-picoline with the magnesium, mercuric chloride and mercury on the steam-bath for a few minutes, a strongly exothermic reaction began. The remainder of the 3-picoline was added at once followed by dropwise addition of the acetone. After heating four hours on the steam-bath, the reaction products were decomposed with 800 ml. of 20% sodium hydroxide solution, extracted with ether, dissolved in 6 *N* hydrochloric acid and steam distilled. The acid solution was basified, dried and distilled yielding 60 g. of azeotrope (b.p. 98–100°), 155 g. of 3-picoline (b.p. 143.0–144.5°), 45.5 g. of pyridinemethanols (b.p. 119–123.5 at 23 mm., $n^{20}D$ 1.5095) and 25 g. of residue.

Conversion of (I) to Isopropylmethylpyridines (II).—To a cold solution of 30 ml. of concentrated sulfuric acid and 30 ml. of glacial acetic acid there was added dropwise with stirring 25 g. of (I). After heating for three hours, with rapid stirring, in an oil-bath at 130°, the base was liberated with ice-cold 20% sodium hydroxide, and extracted with ether. The dried ether extract was distilled and there was obtained 14.7 g. (67% yield) of material boiling 94–102° (22 mm.), $n^{20}D$ 1.5301.

This mixture (14.4 g.) was hydrogenated in glacial acetic acid with Adams catalyst at room temperature and at atmospheric pressure and distilled, yielding 12.1 g. (83% yield) of base having the following properties: b.p. 82–86.5° (22 mm.), $n^{20}D$ 1.4910, and molecular weight of 139 by potentiometric titration (calculated for $C_9H_{13}N$, 135).

Isolation of 2-Isopropyl-3-methylpyridine (III).—Six and two-tenths grams of II was converted to a mixture of picrates yielding 12 g. of picrates (74% yield). By fractional recrystallization from 95% ethanol in the manner described by Tipson,[8] 5.5 g. of picrate melting 149–151° was obtained. Repeated recrystallization from alcohol and dilute acetic acid did not alter the melting range.

Anal. Calcd. for $C_{15}H_{16}N_4O_7$: N, 15.37. Found: N, 15.20.

Decomposition of the picrate with 15% aqueous sodium hydroxide, extraction, and distillation yielded pure III which had the following properties: b.p. 181–181.5° (747 mm.), $n^{20}D$ 1.4980, and d^{20}_4 0.916. Oxidation with potassium permanganate gave quinolinic acid which decomposed and sublimed at 190° to melt at 236.5–237.5°. When mixed with an authentic sample of quinolinic acid no difference in melting behavior was noticed.

Isolation and Identification of 2-Isopropyl-5-methylpyridine (IV).—Ten grams of II was diluted with 150 ml. of purified, dry hydrocarbon oil boiling evenly over the range 163–195°. The solution was fractionated at atmospheric pressure through a 28-inch spinning-band column, operating at a reflux ratio of approximately 30 to 1. Bases were recovered from the various fractions and converted to picrates. There was obtained the picrate of IV melting 111.0–112.5°. An authentic sample of this picrate[9] showed no depression in melting point when the two picrates were mixed and a melting point was taken.

Anal. Calcd. for $C_{15}H_{16}N_4O_7$: N, 15.37. Found: N, 15.25.

Treatment of (II) with Benzaldehyde.[10] Identification of 2-Isopropyl-4-styrylpyridine (V).—One and one-half grams (0.011 mole) of II, 1.18 g. (0.011 mole of freshly distilled benzaldehyde and 0.151 g. (0.0011 mole) of freshly fused and pulverized zinc chloride were heated in a sealed Pyrex tube for ten hours at 210–220°. After cooling, the tube was opened and the discolored contents were rinsed into excess 6 *N* hydrochloric acid. The mixture was steam distilled to remove excess benzaldehyde, made strongly basic with 20% sodium hydroxide, and again steam distilled. In this manner the unchanged pyridines were separated easily from the stilbazole; the minute amount of the latter that steam distilled was collected as a last fraction. This last fraction and the flask contents were extracted with ether, the ether evaporated, and the residual oil diluted with 2 ml. of ethyl alcohol and added to a saturated alcoholic solution of picric acid. The picrate was filtered, washed well with cold ethyl alcohol and air-dried; 160 mg. (equivalent to 48 mg. of 2-isopropyl-4-methylpyridine, or 3.2% of II) was obtained melting 206.5–212.5°. Recrystallization from ethanol and from acetone gave a constant melting point of 216–217°. A mixture melting point with the picrate of 2-isopropyl-4-styrylpyridine (prepared from 2-isopropyl-4-methylpyridine) showed no depression in melting point.

Synthesis of 1-(2-Pyridyl)-cyclohexanol (VI) and 1-(4-Pyridyl)-cyclohexanol (VII).—A mixture of 10 g. of mercuric chloride (0.037 mole) and 150 g. of aluminum turnings was placed in a dry 3-liter three-necked flask and heated in the oven at 120° for 15 minutes. The flask was then fitted with a mercury-seal stirrer, a dropping funnel and a reflux condenser. About 20% of the amount of pyridine and cyclohexanone to be used was then added with vigorous stirring. When the reaction began the remainder of the pyridine (total of 948 g. or 12 moles) was added at once and the ketone was added at a rate that kept the mixture refluxing from the heat of the reaction until a total of 882 g. of cyclohexanone (9 moles) had been added. The period required for the reaction to begin varied from a few minutes to 2 hours, depending on what the reactants were. In some cases (with 2-picoline) as much as 50 g. of mercuric chloride was used to initiate the reaction. External heating to shorten this induction period was sometimes used, but it was always discontinued after the reaction started. After the addition of all the cyclohexanone (1.5 hours), the reaction mixture was allowed to cool for two hours and was then decanted into a liter of 6 *N* sodium hydroxide with vigorous stirring. After sufficient agitation to decompose the hard lumps which first formed, the aqueous layer was drawn off and washed with benzene which had been used to rinse the reaction vessel. When benzene was added to the reaction vessel before decomposing with sodium hydroxide solution the mixture tended to form very stable emulsions. The benzene layer was combined with the other organic layer and the total extracted with 2 liters of 6 *N* hydrochloric acid. The organic layer was extracted twice more with dilute hydrochloric acid and all hydrochloric extracts were extracted three times with fresh benzene. The acid extract was then basified with excess sodium hydroxide, extracted three times with benzene, and the combined extracts dried over sodium hydroxide pellets. Fractional distillation yielded: 500 g. of pyridine, 500 g. of crude VI, 20 g. of cyclohexanol, 4 g. of VII and 70 g. of tar. The neutral products were likewise fractionated and from them were obtained: 15 g. of cyclohexanone, 75 g. of cyclohexanol, 21 g. of high boiling unsaturated ketone (b.p. 150–160° at 36 mm.) and 220 g. of residual tar.

Recrystallization of VI gave 457 g. of the pure compound melting 42–43° and boiling 157° (37 mm.). This is a 29% yield based on the ketone and represents the highest yield obtained in all of these Emmert condensations.

Anal. Calcd. for $C_{11}H_{15}NO$: N, 7.91. Found: N, 7.95.

(8) R. S. Tipson, *Anal. Chem.*, **22**, 628 (1950).

(9) Obtained by S. M. Roberts, Jr. See H. L. Lochte, A. D. Barton, S. M. Roberts and J. R. Bailey, THIS JOURNAL, **72**, 3007 (1950).

(10) Adapted from the method described by J. P. Wibaut, E. C. Kooyam and H. Boer, *Rec. trav. chim.*, **64**, 30 (1945).

From the fraction boiling 167–169° (6 mm.) there was obtained 4 g. (0.25% yield) of VII melting 147–148°.

Anal. Calcd. for $C_{11}H_{15}NO$: N, 7.91. Found: N, 7.94.

A picrate prepared from VI melted 86–87° and a picrate of VII melted at 168.5–169.5°.

1-(2-Piperidyl)-cyclohexanol (VIa).—Adams catalyst (1 g.), 15 g. of VI and 20 ml. of glacial acetic acid were hydrogenated for 40 hours. Filtration and distillation of the viscous product yielded the crystalline acetate salt of VIa which when recrystallized from petroleum ether melted 109–110°.

Anal. Calcd. for $C_{11}H_{21}NO \cdot C_2H_4O_2$: N, 5.76. Found: N, 5.77.

Treatment of the acetate salt with sodium hydroxide solution and recrystallization from petroleum ether yielded pure VIa melting 71–72°.

Anal. Calcd. for $C_{11}H_{21}NO$: N, 7.64. Found: N, 7.68.

Isolation of a $C_{11}H_{21}NO$ Compound from the Emmert Reaction Products.—From the basic fraction boiling 144–167° (6 mm.) there was obtained 3–4 g. of a white crystalline solid melting 120.5–121°. Analysis showed it to be isomeric with VIa. A further study of this compound was not made.

Anal. Calcd. for $C_{11}H_{21}NO$: N, 7.64. Found: N, 7.60.

2-(1-Cyclohexenyl)-pyridine (VIII).—To 164 g. (0.93 mole) of purified VI in a liter erlenmeyer flask was added 392 g. (4 moles) of sulfuric acid. Addition of the acid was done very slowly with vigorous stirring and cooling in tap water. If cooled in ice–water, the material became too viscous for stirring. The temperature was kept below 60°. After addition of all the acid a clear, dark red solution was obtained. After standing for 15 minutes, the solution was poured onto cracked ice and basified with 360 g. (9 moles) of sodium hydroxide dissolved in 800 ml. of water. The oily layer was separated and the water layer washed several times with ether. The ether was evaporated and the combined portions were distilled yielding 138 g. of VIII boiling 97–98° at 3 mm. (89% yield).

Purification of VIII through the picrate (m.p. 159–160°) yielded a liquid having the following constants: b.p. 155° (31 mm.), $n^{20}D$ 1.5737, d^{20}_4 1.033.

Anal. Calcd. for $C_{11}H_{13}N$: N, 8.80. Found: N, 8.78.

2-Cyclohexylpyridine.—Sixteen grams of VIII dissolved in glacial acetic acid was hydrogenated in a low pressure hydrogenator with 150 mg. of Adams catalyst for 1.5 hours. Pressure drop *vs.* time showed when the hydrogenation was complete. There was always a constant pressure drop toward the end due to slow hydrogenation in the pyridine ring. Filtration of the solution and addition of a saturated alcoholic solution of picric acid yielded on the first recrystallization 31 g. (89% yield) of picrate. A second recrystallization failed to raise the m.p. from 128.2–128.8°. Liberation of the 2-cyclohexylpyridine from the picrate with ammonium hydroxide gave a liquid having the properties: b.p. 245–246° (746 mm.), $n^{20}D$ 1.5246, d^{20}_4 0.990.

Anal. Calcd. for $C_{11}H_{15}N$: N, 8.70. Found: N, 8.67.

In addition to the picrate, the following derivatives were prepared in the usual manner: trinitro-*m*-cresolate, m.p. 155.5–156°; styphnate, m.p. 138–138.8°.

Oxidation of 2-(1-Cyclopentenyl)-3-methylpyridine.—The compound oxidized was one of the two compounds isolated by careful fractional distillation of the products resulting from the dehydration of the pyridyl alcohols obtained from the reaction of cyclopentanone with 3-picoline. The oxidation of the second compound is described in the next paragraph.

The method of Jain, Iyer and Guha[11] was adapted for the oxidation procedure. To 30.3 g. of potassium permanganate (0.192 mole, 20% excess) dissolved in 450 ml. of water was added 2.4 g. of the pyridine base (0.015 mole) dropwise during 15 min. Two ml. of concentrated hydrochloric acid was added dropwise during the next four hours. The reaction mixture was kept at 60–70° for 26 hr. The manganese dioxide was filtered off and washed with boiling water. The *p*H of the combined filtrates was adjusted to 4.5 with hydrochloric acid and the carbon dioxide removed by agitation under reduced pressure. The *p*H was then adjusted to 9.0 and the combined filtrates evaporated to dryness using the steam-cone and water aspirator. The residue was rinsed into a 125-ml. erlenmeyer flask with 75 ml. of water and the flask then placed on the steam-bath. Twenty grams of copper sulfate pentahydrate dissolved in 20 ml. of hot water was added slowly with stirring. The solid precipitate was filtered and washed several times with distilled water yielding 2.38 g. of the copper salt (66% yield). The copper salt was suspended in hot 10% hydrochloric acid and the solution was saturated with hydrogen sulfide. After filtration of the copper sulfide the filtrate was evaporated at reduced pressure to a viscous liquid which solidified. The acid was recrystallized from water yielding 0.78 g. of solid acid (45% yield based on copper salt). On slow heating the acid darkened with partial melting at 180–190° with a white solid subliming which melted 234–235°. When the m.p. tube was placed into the m.p. bath at 194° it melted with vigorous evolution of gas and then solidified. Reaction of a water solution of the acid with ferrous sulfate gave a yellowish-red coloration which is given only by 2-pyridinecarboxylic acids.[12] All of the pyridinedicarboxylic acids melt above 248° except 2,3-pyridinedicarboxylic acid which melts 190.5° dec. (rapid heating) and decarboxylates to nicotinic acid (m.p. 236–236.5°). Therefore, the compound oxidized must be 2-(1-cyclopentenyl)-3-methylpyridine.

Oxidation of 2-(1-Cyclopentenyl)-5-methylpyridine.—The same procedure as above was used to oxidize 2.5 g. of the 59–60° melting isomer (0.015 mole). The crude acid obtained weighed 0.70 g. (27% yield based on starting material). The pure acid melted at 256° with decomposition to give a white solid melting at 232°. 2,5-Pyridinedicarboxylic acid is reported[13] to melt at 256–258° with decomposition. Decarboxylation gives nicotinic acid (m.p. 236–236.5°). Reaction of a water solution of the acid with ferrous sulfate gave a yellowish-red coloration. Coupled with the oxidation data for the lower boiling, liquid isomer, the above evidence leaves no doubt that the compound oxidized was 2-(1-cyclopentenyl)-5-methylpyridine.

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(11) B. C. Jain, B. H. Iyer and P. C. Guha, *J. Indian Chem. Soc., Ind. and News Ed.*, **8**, 59 (1945); *C. A.*, **40**, 3453 (1946).

(12) Von Zd. H. Skraup, *Monatsh.*, **7**, 210 (1886).

(13) W. A. Jacobs and L. C. Craig, *J. Biol. Chem.*, **124**, 666 (1938).