peridine-2-carboxamide-6-carboxylate was also recovered.

EXPERIMENTAL[3]

2,6-Dicyanopiperidine. A solution consisting of 12.0 g. of sodium cyanide (0.24 mole) and 13.0 g. of ammonium chloride (0.24 mole) in 50 ml. of water was cooled to 0°. To this was added with stirring 50 ml. of 20% aqueous glutaraldehyde (0.1 mole) during 60 min.; the temperature was kept below 5°. After another 6.0 g. of sodium cyanide and 6.5 g. of ammonium chloride had been added, the solution was allowed to stand at 5° for 10 days. The dark-colored, crystalline solid which had separated was removed by filtration and dried. This solid was then extracted several times with hot benzene and the combined benzene solutions evaporated to leave 3.8 g. of yellow needles, m.p. 110–115°. A small quantity (0.3 g.) was also recovered by extracting the aqueous mother liquors with four 100-ml. portions of ether and two 100-ml. portions of benzene, combining, drying, and evaporating. The total recovery corresponded to a 30% yield.

Recrystallization from benzene after decolorization gave long, flat, white needles, m.p. 114–115°.

Anal. Calcd. for $C_7H_9N_3$: C, 62.20; H, 6.71; N, 31.09. Found: C, 62.41; H, 6.71; N, 30.90.

The *hydrochloride* was prepared by dissolving some of the compound in benzene and saturating the solution with dry hydrogen chloride. The product turns dark and shrinks between 235–250° but does not melt up to 250°; it is very poorly soluble in 2-propanol and absolute ethanol, fairly soluble in 95% ethanol, and readily soluble in water. Hot solutions in 90% ethanol exhibit a strong hydrogen cyanide odor.

Anal. Calcd. for $C_7H_{10}N_3Cl$: N, 24.48. Found: N, 24.03.

The *N-nitroso* derivative was obtained as pale yellow, felted needles after recrystallization from benzene-heptane (2:1); m.p. 143.5–144.5°.

Anal. Calcd. for $C_7H_8N_4O$: C, 51.21; H, 4.91; N, 34.13. Found: C, 51.04; H, 4.83; N, 34.08.

Piperidine-2,6-dicarboxamide. Recrystallized dicyano compound (0.5 g.) was added in small portions to 5 g. of 95% sulfuric acid chilled in an ice-water bath. Each increment was allowed to dissolve before adding the next because too rapid addition caused a fume-off. The yellow colored solution was allowed to stand overnight at room temperature, poured over ice, neutralized to the bromophenol blue end point with aqueous sodium hydroxide, and cooled to 5°. The solid was removed and washed with cold water; 0.45 g., m.p. 228–230°. Recrystallization from water did not change the melting point. Fischer[1] reported 228–229° for the diamide from the low-melting isomer of 2,6-piperidine dicarboxylic acid.

Anal. Calcd. for $C_7H_{13}N_3O_2$: C, 49.11; H, 7.65; N, 24.55. Found: C, 49.32; H, 7.80; N, 24.66.

2,6-Dicyanopiperidine (*ca.* 1 g.) was dissolved in 25 ml. of absolute methanol; the solution was cooled to 5° and saturated with hydrogen chloride. Initially the hydrochloride separated, but it dissolved in the excess hydrogen chloride. During the 5 days that the solution stood at 5° a fine white powder separated; the latter was removed by filtration and retained (A). The methanolic filtrate was evaporated to dryness, the solid residue dissolved in 5 ml. of water, and neutralized with sodium bicarbonate. Evaporation of this aqueous solution on the steam bath left a residue which was first extracted several times with chloroform (B) and then with absolute ethanol (C); the remaining residue was sodium chloride. Extract B was evaporated and the solid residue twice recrystallized from carbon tetrachloride, white needles, m.p. 110.5–111.5°. The analyses are consistent with those required for *methyl piperidine-2-carboxamide-6-carboxylate.*

Anal. Calcd. for $C_8H_{14}N_2O_3$: C, 51.59; H, 7.58; N, 15.05. Found: C, 51.65; H, 7.79; N, 14.82.

(3) All melting points are uncorrected.

The solid, m.p. 210–215°, recovered by evaporating extract C, was once recrystallized from methyl ethyl ketone plus ethanol and once from water, coarse prisms, m.p. 227–229° (dec.). Admixture with the piperidine-2,6-dicarboxamide prepared above did not depress the melting point.

Fraction A was dissolved in methanol-water, neutralized with bicarbonate, and worked up as before. A chloroform-soluble fraction melting at 75–80° was obtained but was not successfully purified.

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Participation of 3-Picoline in Aldol-Type Condensations[1,2]

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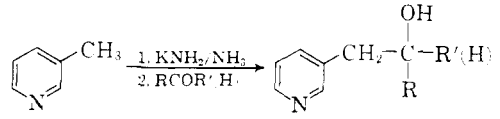
In 1951 Brown and Murphey[3] elegantly demonstrated that the methyl group of 3-picoline shows prototropic activity, when they found that the reaction of 3-picoline, methyl chloride, and sodium amide in liquid ammonia solution gave a mixture of 3-ethyl-, 3-isopropyl- and 3-*t*-butylpyridine. More recently we reported that 3-picolylpotassium, prepared from the tar base and potassium amide in liquid ammonia, can be acylated[4] with aromatic and heterocyclic esters to give a series of 3-picolylketones, $3\text{-}C_5H_4NCH_2COR$, (R = aryl and heterocyclic) and alkylated[5] with a series of alkyl halides to give a number of 3-alkylpyridines, $3\text{-}C_5H_4NCH_2R$ (R = alkyl).

We have now found that 3-picolylpotassium will undergo aldol-type condensations with aldehydes and ketones to give a series of carbinols containing the 3-picolyl radical.



In order to arrive at the best reaction conditions, a study was made of the reaction of benzophenone with 3-picolylpotassium. It was found that the interaction of a 1:1:1 molar ratio of 3-picoline:potassium amide:ketone, using two hours to prepare the anion of the tar base and stirring the reaction mixture for one or two hours after the ketone

(1) This work was performed under Contract No. At(30-1)-670 between the U. S. Atomic Energy Commission and the University of Pittsburgh.

(2) Based on part of the thesis presented by A.D.M. to the Graduate Faculty of the University of Pittsburgh in partial fulfillment of the requirements for the Ph.D. degree.

(3) H. C. Brown and W. A. Murphey, *J. Am. Chem. Soc.*, **73**, 3308 (1951).

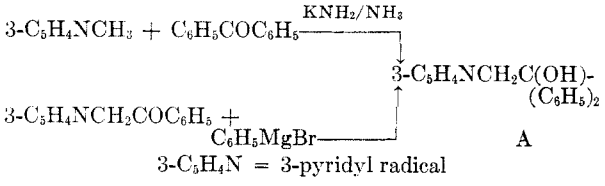
(4) A. D. Miller, C. Osuch, N. N. Goldberg, and R. Levine, *J. Am. Chem. Soc.*, **78**, 674 (1956).

(5) A. D. Miller and R. Levine, *J. Org. Chem.*, **22**, 168 (1957).

was added gave 27% and 28% yield, respectively, of diphenyl-3-picolylcarbinol. When a 2:2:1 molar ratio[6] of tar base:potassium amide:ketone was employed the yield of carbinol was 27%. Therefore, a 1:1:1 molar ratio of 3-picoline:potassium amide:carbonyl compound and a total reaction time of three hours were used to prepare the carbinols which are found in Table I. It should be pointed out that prior to our study, Nunn and Schofield[7] reported that the interaction of 3-picoline, sodium amide, and 2-amino-4′-methoxybenzophenone gave a 14.5% yield of 1-(*o*-aminophenyl)-1-(*p*-methoxyphenyl)-2-(3-pyridyl)ethanol. Also, Tilford and Van Campen[8] had used the procedure of Nunn and Schofield[7] to condense 3-picoline with benzophenone and obtained a 7% yield of 1,1-diphenyl-2-(3-pyridyl)ethanol as compared with the 27% yield which was obtained in the present study.

Although all the alcohols listed in Table I were obtained in only low yield by the present method, the simplicity of the route to these difficultly accessible compounds compensates to some extent for the low yields. It should be noticed that the product obtained from the reaction of 3-picolylpotassium with *p,p′*-bis(dimethylamino)benzophenone is the olefin, 1,1-bis(*p*-dimethylaminophenyl)-2-(3-pyridyl)ethene, which undoubtedly arises from the dehydration of the initially formed carbinol, 1,1-bis(*p*-dimethylaminophenyl)-2-(3-pyridyl)ethanol.

It was established that the carbinols appearing in Table I contain the 3-picolyl radical by elucidating the structures of three representative examples. The product from the reaction of 3-picoline with benzophenone was shown to be 1,1-diphenyl-2-(3-pyridyl)ethanol, A, since it was identical with an authentic sample which was prepared in 65% yield from the reaction of 3-phenacylpyridine[4] with phenylmagnesium bromide.



Similarly, the properties of an authentic sample of 1-(3-pyridyl)-2-phenyl-2-propanol, B, 3-$C_5H_4NCH_2C(OH)(CH_3)(C_6H_5)$, which was prepared in 88% yield from 3-phenacylpyridine[4] and methylmagnesium iodide, were shown to be identical with those of the alcohol which was obtained from the reaction of 3-picoline with acetophenone.

(6) Earlier[4,5] it was found that the use of a 2:2:1 molar ratio of tar base:potassium amide:ester or alkyl halide gave considerably higher yields of products than were obtained using a 1:1:1 molar ratio of reactants.

(7) A. J. Nunn and K. Schofield, *J. Chem. Soc.*, 716 (1953).

(8) C. H. Tilford and M. G. Van Campen, Jr., *J. Am. Chem. Soc.*, **76**, 2431 (1954).

TABLE I

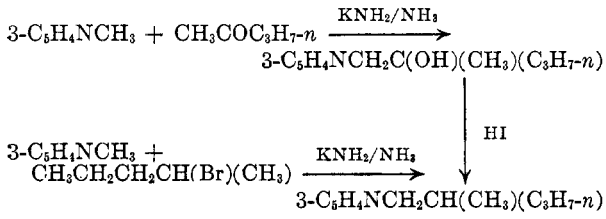
3-PICOLYLCARBINOLS, $3\text{-}C_5H_4NCH_2C(OH)RR'$, BY CONDENSING 3-PICOLINE WITH ALDEHYDES AND KETONES IN THE PRESENCE OF POTASSIUM AMIDE

Carbonyl Compound	R	R′	Yield, %	B.P. or M.P., °C.	Mm.	Formula	Carbon, %		Hydrogen, %	
							Calcd.	Found	Calcd.	Found
i-C_3H_7CHO	*i*-C_3H_7	H	6	122–125	2	$C_{10}H_{15}NO$	72.69	72.71	9.15	8.97
C_6H_5CHO	C_6H_5	H	17	180–185	3	$C_{13}H_{13}NO$	78.36	78.45	6.59	6.34
				120.6–121[a]						
$CH_3COC_2H_5$	CH_3	C_2H_5	10	111–112	2	$C_{10}H_{15}NO$	72.69	72.44	9.15	9.26
$CH_3COC_3H_7$-*n*	CH_3	*n*-C_3H_7	9	128–130	3	$C_{11}H_{17}NO$	73.69	73.51	9.56	9.44
2-$C_4H_3SCOCH_3$[b]	CH_3	2-C_4H_3S	12	160–164	2	$C_{12}H_{13}NOS$	65.72	66.12	5.97	6.18
				98.4–98.8[a]						
$CH_3COC_6H_5$	CH_3	C_6H_5	11	164–167	3	$C_{14}H_{15}NO$[c]	78.84	79.35	7.09	7.24
$C_2H_5COC_2H_5$	C_2H_5	C_2H_5	10	118–120	2	$C_{11}H_{17}NO$	73.69	73.92	9.56	9.74
$C_2H_5COC_6H_5$	C_2H_5	C_6H_5	14	165–168	3	$C_{15}H_{17}NO$	79.26	79.56	7.54	7.82
n-$C_3H_7COC_3H_7$-*d*	*n*-C_3H_7	*n*-C_3H_7	10	133–136	2	$C_{13}H_{21}NO$	75.31	75.41	10.21	10.38
$C_6H_5COC_6H_5$	C_6H_5	C_6H_5	27	143.8–144.4[d]		$C_{19}H_{17}NO$	82.92	82.72	6.18	6.19
$[p\text{-}(CH_3)_2NC_6H_4]_2CO$	*p*-$(CH_3)_2NC_6H_4$	*p*-$(CH_3)_2NC_6H_4$	25	129.4–130[e]		$C_{23}H_{25}N_3$[f]	80.42	80.45	7.34	7.23

[a] Recrystallized from 60–70° petroleum ether. [b] This is methyl 2-thienyl ketone. [c] This compound gave a *picrate*, m.p. 147.2–147.8; *Anal.* calcd. for $C_{20}H_{18}N_4O_8$: C, 54.30; H, 4.10. Found: C, 54.54; H, 4.35. [d] Recrystallized from methanol. [e] Recrystallized from 95% ethanol. [f] This is 1,1-bis(*p*-dimethylaminophenyl)-2-(3-pyridyl)ethene.

Since 3-phenacylpyridine, which was prepared in 38% yield[4] from the reaction of 3-picolylpotassium with methyl benzoate, has been converted to carbinol B in 88% yield by reaction with methylmagnesium bromide, the over-all yield of B is 37%. Thus, this synthesis appears to be superior to the 3 - picolylpotassium – acetophenone route which gives only an 11% yield of B. However, since the carbinol A was obtained in essentially the same over-all yield, 27% and 25% respectively, by the 3-picolylpotassium–benzophenone and the 3 - phenacylpyridine – phenylmagnesium bromide routes, the first method is preferable to the second since it does not involve the initial synthesis of 3-phenacylpyridine.

The structure of 1-(3-pyridyl)-2-methyl-2-pentanol, which was obtained from 3-picoline and methyl *n*-propyl ketone, was elucidated by reducing it with hydrogen iodide to 1-(3-pyridyl)-2-methylpentane and comparing this 3-alkylpyridine with an authentic sample which was prepared in 86% yield by alkylating 3-picolylpotassium with 2-bromopentane.



EXPERIMENTAL[9]

General procedure for preparing 3-picolylcarbinols from 3-picoline, aldehydes, and ketones. With the exceptions noted below, the following procedure was used for effecting these reactions.

3-Picoline (0.2 mole, 18.6 g.) was added over a 15-min. period to a liquid ammonia solution of potassium amide, prepared from potassium (0.2 mole, 7.8 g.) in 350–400 ml. of anhydrous liquid ammonia, and the mixture was stirred for 2 hr. The aldehyde or ketone (0.2 mole in an equal volume of anhydrous ether) was added, the mixture was stirred for 1 hr. and then the reaction was quenched by the addition of solid ammonium chloride (0.41 mole, 22.0 g.). The ammonia was replaced by 200 ml. of ether and the mixture was poured onto crushed ice, made strongly acidic with concentrated hydrochloric acid, and extracted with several portions of ether. The combined ether extracts were dried over Drierite. The aqueous solution was made basic by the addition of solid sodium carbonate, was extracted with several portions of chloroform and the combined extracts were dried over sodium carbonate. Distillation of the ether extracts gave recovered aldehyde or ketone and distillation of the chloroform extracts gave recovered 3-picoline and the 3-picolylcarbinol.

When the reaction mixture from 3-picoline (0.2 mole), potassium amide (0.2 mole), and benzophenone (0.2 mole) was quenched with ammonium chloride and poured onto ice and hydrochloric acid a solid, consisting of benzophenone and 1,1-diphenyl-2-(3-pyridyl)ethanol hydrochloride precipitated. This solid was filtered and washed with several portions of cold anhydrous ether, in which the benzophenone is soluble and the carbinol hydrochloride is insoluble, to give 22.0 g. of recovered benzophenone, m.p. 48–49° alone and when mixed with an authentic sample, and 16.7 g. (27%) of 1,1-diphenyl-2-(3-pyridyl)ethanol hydrochloride, m.p. 240–243°. The carbinol hydrochloride was recrystallized from methanol.

Anal. Calcd. for $C_{19}H_{18}NOCl$: C, 73.19; H, 5.78. Found: C, 72.87; H, 5.86.

Refluxing the carbinol hydrochloride with 20% methanolic sodium hydroxide solution for 2 hr. converted it quantitatively to 1,1-diphenyl-2-(3-pyridyl)ethanol, m.p. 143.8–144.4° (from methanol).

When the reaction mixture from 0.2 mole each of 3-picoline, potassium amide, and *p,p'*-bis(dimethylamino)benzophenone was quenched with ammonium chloride and was poured onto ice without adding any hydrochloric acid, a solid precipitated which was fractionally crystallized from 95% ethanol to give 19.5 g. of recovered ketone, m.p. 172.5–174°, and 17.2 g. (25.0%) of 1,1-bis(*p*-dimethylaminophenyl)-2-(3-pyridyl)ethene, m.p. 129.4–130°.

Preparation of authentic sample of 1,1-diphenyl-2-(3-pyridyl)-ethanol. 3-Phenacylpyridine[4] (0.055 mole, 11.0 g.), dissolved in 100 ml. of anhydrous ether, was added over 90 min. to phenylmagnesium bromide (0.06 mole) in 200 ml. of anhydrous ether. The reaction mixture was refluxed for 4 hr., was cooled to room temperature, and was then poured onto a mixture of ice and concentrated hydrochloric acid. The white precipitate which was present was filtered and recrystallized from methanol to give 11.0 g. (65%) of 1,1-diphenyl-2-(3-pyridyl)ethanol hydrochloride, m.p. 240–243°. Using the procedure described above the carbinol hydrochloride was converted quantitatively to 1,1-diphenyl-1,1-diphenyl-2-(3-pyridyl)ethanol, m.p. 143.9–144.4° alone and when mixed with the material prepared from the reaction of 3-picolylpotassium with benzophenone.

Reduction of 1-(3-pyridyl)-2-methyl-2-pentanol. The procedure used was modeled after that employed by French and Sears[10] for the reduction of diphenyl-3-pyridylcarbinol to diphenyl-3-pyridylmethane.

A solution of 1-(3-pyridyl)-2-methyl-2-pentanol (0.039 mole, 6.9 g.), glacial acetic acid (28.0 ml.), concentrated hydrochloric acid (7.0 ml.), and hydriodic acid (23.0 ml. of 47% aqueous solution) was refluxed for 2 min. and poured onto 100 ml. of water containing 10.0 g. of sodium bisulfite. The mixture was made strongly basic with 40% sodium hydroxide solution and was extracted with several portions of ether. The combined ether extracts were dried over anhydrous sodium sulfate and distilled to give 4.1 g. (65.0%) of 1-(3-pyridyl)-2-methylpentane, b.p. 120–122° at 25 mm.; picrate, m.p. 75–76° alone and when mixed with an authentic sample prepared from the product obtained by alkylating 3-picoline with 2-bromopentane (see below).

Synthesis of 1-(3-pyridyl)-2-methylpentane. Using the previously described procedure[5] for the synthesis of similar compounds, 1-(3-pyridyl)-2-methylpentane (28.0 g., 86%, b.p. 120–122° at 25 mm.) was prepared from potassium amide (0.4 mole), 3-picoline (0.4 mole, 37.2 g.), and 2-bromopentane (0.2 mole, 30.2 g.).

Anal. Calcd. for $C_{11}H_{17}N$: C, 80.92; H, 10.50. Found: C, 80.70; H, 10.29.

This compound gave a *picrate*, m.p. 75–76° (from ethanol-water).

Anal. Calcd. for $C_{17}H_{20}N_4O_7$: C, 52.03; H, 5.14. Found: C, 51.80; H, 5.06.

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(9) The 3-picoline used in this study was supplied through the courtesy of Dr. F. E. Cislak, Reilly Tar and Chemical Corp.

(10) H. E. French and K. Sears, *J. Am. Chem. Soc.*, **73**, 469 (1951).