TABLE II (*Continued*)

Amine used	M.p., °C.	Yield, %	Formula	Nitrogen, % Calcd.	Found
Methylamine[b]	216–218	67	$C_{19}H_{15}N_3O_4$	12.03	11.92
Octadecylamine	77–79	49	$C_{36}H_{49}N_3O_4$	7.15	7.04
3-Isopropoxypropylamine	120.5–121	55	$C_{24}H_{25}N_3O_5$	9.65	9.48
n-Propylamine	145.5–146.5	60	$C_{21}H_{19}N_3O_4$	11.13	11.16
Isopropylamine	166–167.5	58	$C_{21}H_{19}N_3O_4$	11.13	11.04
Tetradecylamine	78.5–79	38	$C_{37}H_{41}N_3O_4$	7.90	7.83

[a] Recrystallized from 95% ethanol. [b] Recrystallized from dioxane–petroleum ether (65–110°).

and the product collected. Several amines required refluxing periods of one hour. These are indicated in Table I.

The reaction medium was thoroughly chilled, and the product was filtered and dried. Many of the derivatives precipitated in a high state of purity and were brightly colored compounds. The majority of the derivatives were recrystallized from 95% ethanol. Those derivatives which were only slightly soluble in this solvent were best recrystallized from a mixture of dioxane and petroleum ether (65–110°) or some other solvent pair, as indicated in Table I.

Bis-(phthalimidomethyl)-alkylamines.—The same procedure as described above was followed except that 0.0105 mole of the primary aliphatic amine and only 10 ml. of 95% ethanol was employed. Also the reaction mixture was refluxed only 15 minutes. If the reactants did not dissolve readily when refluxing began then more ethanol was added in 5-ml. portions until the mixture was homogeneous. The reaction mixture was then chilled overnight, filtered and dried. Recrystallization of the bis derivatives was best accomplished by dissolving the compound (usually 2–3 g.) in 10 ml. of hot acetone, filtering while hot, and adding petroleum ether (65–110°) to the hot solution until a faint cloudiness persisted. The solution was then chilled overnight and the recrystallized product filtered and dried.

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LEWISBURG, PENNSYLVANIA

[CONTRIBUTION NO. 955 FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF PITTSBURGH]

The Synthesis of Nitrogen-containing Ketones. V. The Direct Acylation of 3-Picoline[1,2,3]

BY ALFRED D. MILLER, CARL OSUCH, NEWTON N. GOLDBERG AND ROBERT LEVINE

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The direct acylation of 3-picoline with aromatic and heterocyclic esters using potassium amide as the condensing agent is described. The structure of one of the ketones, 3-phenacylpyridine, was established by reducing it to 3-(2-phenylethyl)-pyridine, authentic samples of which were prepared by two independent routes.

In previous work we reported[4] that the phenyllithium-effected acylations of 2-picoline with aliphatic, aromatic and heterocyclic esters give high yields of the corresponding 2-picolyl ketones.

The present paper is concerned with the direct acylation of 3-picoline—a reaction which has not been reported previously. Apparently the only 3-picolyl ketone recorded in the literature is 3-acetonylpyridine. This ketone has been synthesized by two routes: (1) the reaction of 3-pyridylacetic acid (prepared from 3-picoline in six steps) with acetic anhydride and sodium acetate[5] and (2) the reaction of 3-pyridylmagnesium bromide with 2-methyl-3-chloropropene followed by ozonolysis of the resulting olefin.[6]

In the present study it has been found that phenyllithium cannot be used to metalate the methyl group of 3-picoline since the interaction of these reagents in the presence (or absence) of an acylating agent such as methyl benzoate gives only the azomethine addition product, 2-phenyl-5-methylpyridine, and none of the desired 3-phenacylpyridine.[7] The use of methyllithium in place of phenyllithium gave an extremely complex mixture from which we were unable to isolate any pure compounds.

Since Brown and Murphey[8] recently demonstrated that it is possible to alkylate 3-picoline with alkyl halides, using a suspension of sodium amide in liquid ammonia as the condensing agent, it was desirable to attempt acylations under similar conditions. Using methyl benzoate as the acylating agent, 3-phenacylpyridine (isolated as its picrate) was indeed obtained, but in only 10% yield. Further study showed that considerably higher yields

(1) For paper IV in this series, see N. N. Goldberg and R. Levine, THIS JOURNAL, **77**, 4926 (1955).

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

(3) Presented before the Organic Division of the 128th National ACS Meeting, Minneapolis, Minn., September 11–16, 1955.

(4) N. N. Goldberg, L. B. Barkley and R. Levine, THIS JOURNAL, **73**, 4301 (1951).

(5) A. Burger and C. R. Walter, Jr., *ibid.*, **73**, 1988 (1950); the yield in the last step is 40% of theory.

(6) J. P. Wibaut and H. G. P. van der Voort, *Rec. trav. chim.*, **71**, 798 (1952); the over-all yield of ketone based on 3-bromopyridine is 15%.

(7) When the tar base was rapidly added to the phenyllithium (Standard Addition Technique), a 30.8% yield of 2-phenyl-5-methylpyridine was obtained; when the phenyllithium was added slowly to the tar base (Reverse Addition Technique), the yield of addition product dropped to 18.1%. The structure of the 2-phenyl-5-methylpyridine was established by oxidizing it to pyridine-2,5-dicarboxylic acid.

(8) H. C. Brown and W. A. Murphey, THIS JOURNAL, **73**, 3308 (1951).

TABLE I

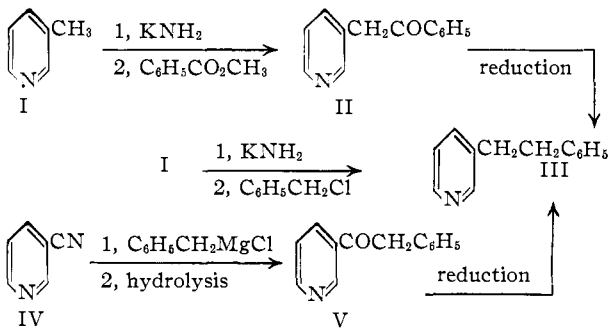
3-PICOLYL KETONES, 3-$C_5H_4NCH_2COR$, BY ACYLATING 3-PICOLINE WITH METHYL ESTERS IN THE PRESENCE OF POTASSIUM AMIDE

R	Yield, %	M.p. or b.p. °C.	Mm.	Formula	Carbon, % Calcd.	Found	Hydrogen, % Calcd.	Found
C_6H_5	38.2	170–175 48.6–49.5	3	$C_{13}H_{11}NO$	79.16	79.07	5.62	5.34
p-$CH_3OC_6H_4$[a]	31	174–179 75–75.6	4	$C_{14}H_{13}NO_2$	74.00	73.83	5.72	5.57
3-C_5H_4N[c]	13.2	169–173 79.8–80.6	3	$C_{12}H_{10}N_2O$	72.73	72.38	5.05	4.80
4-C_5H_4N[e]	27.8	167–170 65.8–66.8	3	$C_{12}H_{10}N_2O$	72.73	72.52	5.05	4.91
C_4H_3O[f]	35.1	157–160	3	$C_{11}H_9NO_2$	70.56	70.32	4.86	4.75
C_4H_3S[h]	21.7	176–180	4	$C_{11}H_9NOS$	64.98	64.88	4.47	4.40
				Derivatives				
Picrate[i]		168.8–169.6		$C_{19}H_{14}N_4O_8$	53.52	53.81	3.24	3.07
Oxime[i]		154.2–155.2		$C_{13}H_{12}N_2O$	73.56	73.86	5.70	5.61
Picrate		135.2–136.2		$C_{20}H_{16}N_4O_9$[b]	52.63	52.41	3.54	3.26
Dipicrate		199.5–200		$C_{24}H_{16}N_8O_{15}$[d]	43.90	44.12	2.44	2.39
Dipicrate		174.3–175		$C_{24}H_{16}N_8O_{15}$	43.90	44.24	2.44	1.92
Picrate		158–158.8		$C_{17}H_{12}N_4O_9$[g]	49.03	49.26	2.88	2.86
Picrate		150–150.5		$C_{17}H_{12}N_4O_8S$	47.22	47.16	2.80	2.68

[a] Ethyl ester used. [b] N, calcd.: 12.27; found: 12.00. [c] 3-C_5H_4N is the 3-pyridyl radical. [d] N, calcd.: 17.07; found: 16.68. [e] 4-C_5H_4N is the 4-pyridyl radical. [f] C_4H_3O is the 2-furyl radical. [g] N, calcd.: 13.46; found: 13.14. [h] C_4H_3S is the 2-thienyl radical. [i] Both of these derivatives were prepared from the compound where R = C_6H_5.

of the desired ketone may be obtained by using either the *ether-soluble lithium diisopropylamide* (37%) or the *liquid ammonia-soluble potassium amide* (38%) as the condensing agent. The results of the acylation of 3-picoline with several aromatic and heterocyclic esters are found in Table I. These reactions were effected using a 2:2:1 molar ratio of tar base, potassium amide and ester. When 3-picoline was benzoylated using a 1:1:1 molar ratio of reactants, the yield of 3-phenacylpyridine dropped to 19.2%.[9] Potassium amide rather than lithium diisopropylamide was used as the condensing agent for the synthesis of the ketones listed in the table since the former base may be prepared in considerably less time than the latter base. To date we have not been able to acylate 3-picoline with aliphatic esters.

To elucidate the orientation of the acyl groups in the ketonic products, the structure of 3-phenacylpyridine was established. This was done by reducing 3-phenacylpyridine (II) to 3-(2-phenylethyl)-pyridine (III) of which authentic samples were prepared by the alkylation of 3-picolylpotassium with benzyl chloride and by the reduction of benzyl 3-pyridyl ketone (V) prepared from 3-cyanopyridine (IV) and benzylmagnesium chloride.



We are continuing to investigate the reactions of the methyl group of 3-picoline.

Experimental[10,11]

Reaction of 3-Picoline with Phenyllithium. The Preparation of 2-Phenyl-5-methylpyridine.—3-Picoline (0.2 mole, 18.6 g.) was added to an ether solution of 0.2 mole of phenyllithium over a ten-minute period and the reaction mixture was then refluxed for 30 minutes and processed as described earlier[4] to give 10.4 g. (30.8%) of 2-phenyl-5-methylpyridine, b.p. 241–245° at 2.0 mm., m.p. 137–139° (from 60–70° petroleum ether). *Anal.* Calcd. for $C_{12}H_{11}N$: C, 85.17; H, 6.55; N, 8.28. Found: C, 84.95; H, 6.75; N, 8.14.

The last reaction was repeated except that the phenyllithium (0.4 mole in 400 ml. of anhydrous ether) was added over a 2.5- to 3-hour period to 0.4 mole (37.2 g.) of 3-picoline dissolved in 200 ml. of anhydrous ether. The reaction mixture was then refluxed for 30 minutes and processed to give 12.2 g. (19.1%) of 2-phenyl-5-methylpyridine.

Oxidation of 2-Phenyl-5-methylpyridine to Pyridine-2,5-dicarboxylic Acid.—To 125 ml. of water containing 2 ml. of concentrated sulfuric acid, 0.003 mole (0.5 g.) of 2-phenyl-5-methylpyridine was added with stirring. When all the solid had dissolved, 6.0 g. of potassium permanganate was added in 2-g. portions, waiting until the violet color of the solution was discharged before the next addition of permanganate. During the addition and for five hours afterwards, the solution was heated at 75–85° with constant stirring. The precipitated manganese dioxide was filtered from the hot solution and washed with hot water. The combined aqueous phases were acidified with concentrated hydrochloric acid to a *p*H of 1.4 (Beckman *p*H meter). The solution was then concentrated and cooled to room temperature. After two days a white solid precipitated which on recrystallization from hot water gave 0.2 g. (50%) of pyridine-2,5-dicarboxylic acid, m.p. 235–236.5° dec., uncor.[12]

(9) These yields are calculated on the assumption that the ketones formed are converted to their anions by 3-picolylpotassium as previously suggested in the 2-picoline series by M. J. Weiss and C. R. Hauser [THIS JOURNAL, **71**, 2023 (1949)] and Goldberg, Barkley and Levine.[4]

(10) All boiling and melting points are uncorrected.

(11) All the pyridine derivatives were supplied through the courtesy of Dr. F. E. Cislak, Reilly Tar and Chemical Corp.

(12) G. Black, E. Depp and B. B. Corson, *J. Org. Chem.*, **14**, 14 (1949).

Preparation of 3-Phenacylpyridine.—To a solution of potassium amide, prepared from potassium (0.4 mole, 15.6 g.) dissolved in 350–400 ml. of anhydrous liquid ammonia, was added 3-picoline (0.4 mole, 37.2 g.) over a 15-minute period. The resulting blood-red mixture was stirred for two hours and then methyl benzoate (0.2 mole, 27.2 g.), diluted with an equal volume of anhydrous ether, was added over a 20-minute period. After the ester was added, the reaction mixture, which was violet in color, was stirred for an additional hour and then the reaction was quenched by the addition of solid ammonium chloride (22.0 g., 0.41 mole). The liquid ammonia was replaced by the addition of 200–300 ml. of ether and warming the reaction mixture on a water-bath until the ether started to reflux. Then the mixture was cooled, poured onto crushed ice, made strongly acid with concentrated hydrochloric acid, and extracted with several portions of ether. The combined ether extracts were dried over Drierite. The aqueous phase was made basic by the addition of solid sodium carbonate, extracted with chloroform, and the extracts dried over sodium carbonate. The solvent was removed from the combined ether extracts to give 3.3 g. of benzoic acid, m.p. 121–122° alone and when mixed with an authentic sample, and 1.4 g. of benzamide, m.p. 129–130° alone and when mixed with an authentic sample. The chloroform extracts were distilled at atmospheric pressure to remove the solvent and recovered 3-picoline (22.0 g., b.p. 135–143°). The residue was then distilled in vacuum to give 18.0 g. of a white solid mixture of 3-phenacylpyridine and benzamide, b.p. 141–175° at 2 mm. The mixture was washed with cold ether in which the benzamide (3.0 g., m.p. 130° alone and when mixed with an authentic sample) is insoluble and the 3-phenacylpyridine is soluble. The ether washings were distilled to give 15.0 g. (38.2%) of 3-phenacylpyridine, b.p. 170–175° at 3 mm., m.p. 48.6–49.5° (from 30–60° petroleum ether); picrate, m.p. 168.6–169.6° (from 95% ethanol); oxime, m.p. 154.2–155.2° (from ethanol–benzene).

Alkylation of 3-Picolylpotassium with Benzyl Chloride.—Benzyl chloride (0.2 mole, 25.3 g.), dissolved in an equal volume of anhydrous ether, was added to 3-picolylpotassium (0.4 mole), prepared as described above, and the reaction mixture was then stirred for one hour, quenched with solid ammonium chloride, and processed to give 2.8 g. (7.7%) of 3-(2-phenylethyl)-pyridine, b.p. 126–130° at 3 mm. (*Anal.* Calcd. for $C_{13}H_{13}N$: C, 85.20; H, 7.15. Found: C, 85.23; H, 7.42. Picrate m.p. 144.2–145.2° (from 95% ethanol). *Anal.* Calcd. for $C_{19}H_{16}N_4O_7$: C, 55.53; H, 3.88; N, 13.59. Found: C, 55.11; H, 4.04; N, 13.81) and 5.0 g. of what is probably slightly impure dibenzyl-3-pyridylmethane, b.p. 198–201° at 3 mm. *Anal.* Calcd. for $C_{20}H_{19}N$: C, 87.86; H, 7.00. Found: C, 87.09; H, 8.18.

Wolff–Kishner Reduction of 3-Phenacylpyridine.—A solution of 3-phenacylpyridine (0.057 mole, 11.2 g.), hydrazine hydrate (4.7 ml. of an 85% solution), sodium hydroxide (4.7 g.) and diethylene glycol (75.0 ml.) was refluxed for six hours, cooled to room temperature, and extracted with several portions of benzene. The solvent was removed and the residue distilled in vacuum to give 4.8 g. (46.2%) of 3-(2-phenylethyl)-pyridine, b.p. 126–130° at 2.75 mm. This material gave a picrate, m.p. 144.2–145.2° alone and when mixed with a sample prepared from the compound obtained by the benzylation of 3-picolylpotassium.

Preparation and Wolff–Kishner Reduction of Benzyl 3-Pyridyl Ketone.—3-Cyanopyridine (0.18 mole, 18.3 g.), dissolved in 200 ml. of anhydrous ether, was added over a one-hour period to 0.18 mole of benzylmagnesium chloride. A yellow solid precipitated and the solution refluxed during the addition of the 3-cyanopyridine. The reaction mixture was stirred for 24 hours at room temperature and then 50 g. of ammonium chloride in 200 ml. of water and 50 ml. of concentrated hydrochloric acid were added. Stirring was continued for an additional 24 hours and the phases separated. The aqueous phase was refluxed for an additional two hours, cooled to room temperature, and extracted with ether. The combined ether extracts were dried over sodium sulfate and the solvent removed. Distillation of the residue gave 5.0 g. (12.7%) of benzyl 3-pyridyl ketone, b.p. 155–158° at 3 mm.; oxime, m.p. 124.5–125.5°[5]; picrate, m.p. 126–126.8°. *Anal.* Calcd. for $C_{19}H_{14}N_4O_8$: C, 53.52; H, 3.24. Found: C, 53.62; H, 3.43. When this ketone was treated with hydrazine hydrate, sodium hydroxide, and diethylene glycol and processed as described in the previous experiment, there was obtained 1.7 g. of an oil which gave a picrate, m.p. 144.2–145.2° alone and when mixed with a sample of the picrate obtained from the reduction product of 3-phenacylpyridine and from the benzylation of 3-picolylpotassium.

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[CONTRIBUTION FROM THE RESEARCH INSTITUTE OF TEMPLE UNIVERSITY]

The Copolymerization of Highly Fluorinated Olefins with Ethylene Oxide[1]

BY MURRAY HAUPTSCHEIN[2a] AND JOSEPH M. LESSER[2b]

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The copolymerizations of perfluoropropene and trifluorochloroethylene with ethylene oxide have been effected and studied in the presence of ultraviolet light or di-*t*-butyl peroxide (DTBP) as the initiators. Vinylidene fluoride did not copolymerize with ethylene oxide using DTBP as the initiator but the conversion to vinylidene fluoride homopolymer has been shown to be increased greatly by the presence of ethylene oxide. Perfluoropropene and vinylidene fluoride in the presence of DTBP react with ethyl ether to form telomers.

The purpose of this research was to investigate the possibility of synthesizing highly fluorinated polyether type polymers by the interpolymerization of fluorinated olefins with ethylene oxide. The only references to olefin–alkylene oxide copolymers are in the recent patent literature.[3a,b] Ethylene and vinylidene chloride formed copolymers with aliphatic epoxides utilizing azine catalysts at 200–300° in the former case, and using persulfate or peroxide aqueous emulsion systems in the latter case. In general, the copolymers contained a relatively small percentage of alkylene oxide units, which in the case of ethylene were shown to be joined together rather than to be interspersed among ethylene units.

Perfluoropropene, chlorotrifluoroethylene and vinylidene fluoride were the olefins investigated in

(1) The work herein reported was carried out on Project NR 055.354 between the Office of Naval Research and the Research Institute of Temple University. Reproduction in whole or in part is permitted for any purpose of the United States Government.

(2) (a) Pennsylvania Salt Mfg. Co., Whitemarsh Research Laboratories, Chestnut Hill P. O. Box 4388, Philadelphia 18, Pa.; (b) part of a thesis to be submitted to Temple University in partial fulfillment of the requirements for the Masters degree.

(3) (a) D. D. Coffman, U. S. Patent 2,516,960 (August 1, 1950); (b) G. W. Stanton and C. E. Lowry, U. S. Patent 2,556,048 (June 5, 1951).