3-phenylsulfonyl cyclohexane, 35925-50-9; 4-*tert*-butylcyclohexene-1-carboxamide, 35906-02-6.

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The Direct Acylation of Pyridine 1-Oxides

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The reaction of pyridine 1-oxides with BuLi at low temperature in nonprotic solvents gives the 2-lithiopyridine 1-oxides, which react with carbon dioxide to give acids and with esters to give ketones. Some interesting by-products are obtained when *N*,*N*-dimethylacetamide and benzonitrile are used as the electrophiles.

Though the direct introduction of an acyl group into the pyridine nucleus is possible *via* the Emmert reaction (a nucleophilic attack at the α positions[1]), the direct electrophilic acylation of pyridine derivatives has not been feasible until recently, since these π-deficient rings do not undergo the Friedel–Crafts reaction. In an earlier paper, we reported the base-catalyzed deprotonation of pyridine 1-oxides in nonprotic solvents and the trapping of the carbanion so formed with aldehydes and ketones to give 2- and 2,6-dialkylated pyridine 1-oxides.[2] We now report the reaction of these 1-oxido-2-pyridyllithium derivatives with carbon dioxide, esters, amides, and nitriles to give acids and ketones.[3]

The 2-pyridyl 1-oxide anions were generated by the addition of *n*-butyllithium to a solution of the *N*-oxide in ether or tetrahydrofuran at −65°, and trapped by the addition of the electrophile. The results of the carboxylation of the anions are summarized in Table I.

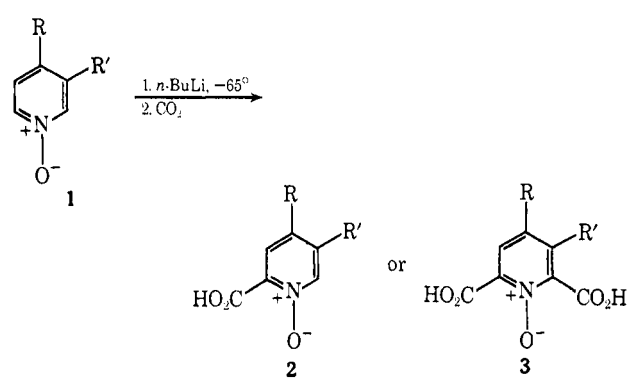
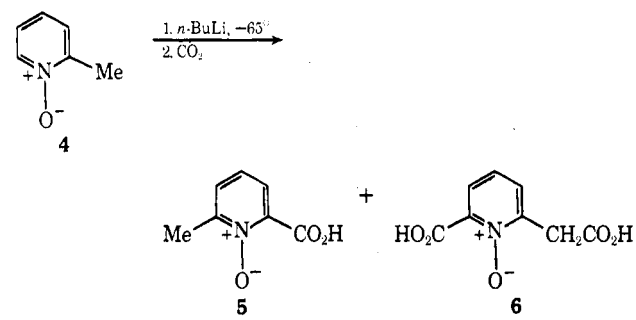


TABLE I

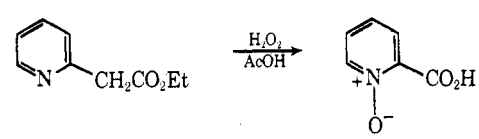
CARBOXYLATION OF 1-OXIDO-2-PYRIDYLLITHIUM DERIVATIVES (1)

1	Product (%)	Registry no.
R = Cl; R′ = H	2 (49.0)	35895-54-6
R = Me; R′ = H	3 (48.0)	35895-55-7
R = Cl; R′ = Me	2 (23.8)	17117-05-4
R = R′ = Me	2 (17.9)	35895-57-9

Authentic **2** (R = Cl; R′ = Me) was synthesized by nitration of 5-methylpicolinic acid 1-oxide to yield the nitro compound, followed by treatment with acetyl chloride. As before,[2] a 3-methyl substituent directs deprotonation preferentially para to itself. Only one example of 2,6 dilithiation was observed here, and that in the case of 4-picoline 1-oxide. Methyl groups at C_3 or C_4 are not affected. On the other hand, as observed previously in the alkylation reactions, a 2-methyl substituent does undergo some deprotonation as well. Thus, when 2-picoline 1-oxide (**4**) was lithiated and then treated with CO_2, both 6-methyl-2-picoline 1-oxide (**5**) and 2-picoline-6,α-dicarboxylic acid 1-oxide (**6**) were obtained.



For possible comparison with **5** an attempt was made to synthesize authentic 2-pyridylacetic acid 1-oxide from **4** *via* the ethyl pyruvate as reported by Adams and Miyano[4] or by oxidation of ethyl 2-pyridylacetate with 30% H_2O_2 in glacial acetic acid. In both cases, picolinic acid 1-oxide was the final product obtained instead of the desired acetate.



6-(1-Hydroxycyclohexyl)-3,4-dimethylpyridine 1-oxide (**7**) could only be metalated and carbonated in very low yield to give **8**, the main product formed apparently being that of addition of butyllithium to the azomethine linkage (**9**).

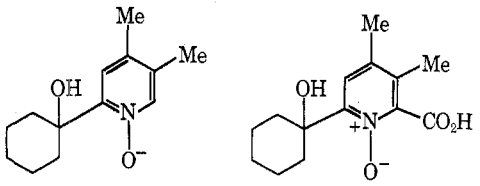
Various carbonyl compounds were used to effect the acylation of the 2-lithio 1-oxides, and esters were found to give the best results, though yields of ketones were generally low. Reaction of 3,4-lutidine 1-oxide with *n*-butyllithium followed by ethyl acetate and work-

(1) R. A. Abramovitch and A. R. Vinutha, *J. Chem. Soc. C*, 2104 (1969).

(2) R. A. Abramovitch, E. M. Smith, E. E. Knaus, and M. Saha, *J. Org. Chem.*, **37**, 1690 (1972).

(3) Preliminary communication: R. A. Abramovitch, M. Saha, E. M. Smith, and R. T. Coutts, *J. Amer. Chem. Soc.*, **89**, 1537 (1967).

(4) R. Adams and S. Miyano, *ibid.*, **76**, 3168 (1954).



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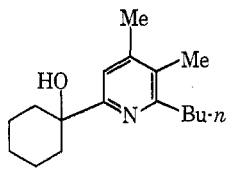

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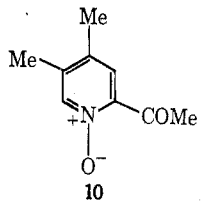
up of the reaction mixture by vacuum distillation gave a respectable yield (65%) of 2-acetyl-4,5-dimethylpyridine 1-oxide (**10**). On the other hand, if a similar reaction mixture was resolved by chromatography, **10** (19.6%) and 2-acetyl-3,4-dimethylpyridine 1-oxide (**11**) (6.3%) were obtained. Reaction of lithio-4-ethoxypyridine 1-oxide with ethyl butyrate gave a



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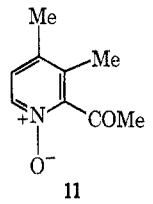

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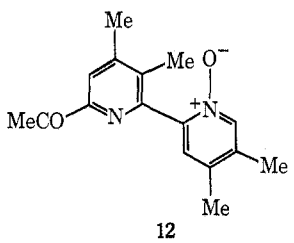

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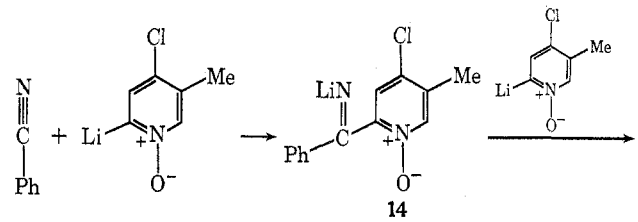
mixture of the 2-mono- and 2,6-dibutyryl derivatives. The use of *N*-acetylmorpholine as the carbonyl electrophile *in lieu* of ethyl acetate gave a much lower yield of **10** from **1** (R = R′ = Me). When *N*,*N*-dimethylacetamide was used none of the simple acylated product was obtained; instead the product formed was 6′-acetyl-3′,4,4′,5-tetramethyl-2,2′-dipyridyl 1-oxide (**12**). A similar result was obtained when the anion of **1** (R = Cl; R′ = Me) was treated with benzonitrile; the product isolated was 6′-benzoyl-4,4′-dichloro-3′,5-dimethyl-2,2′-dipyridyl 1-oxide (**13**). The structures of these dipyridyl mono-*N*-oxides were confirmed by high-resolution mass spectrometry and by nmr. **13** exhibited the isotopic cluster expected for 2Cl. Formation of these products involves initial reaction of the pyridyllithium derivative with the amide or nitrile function to give the expected intermediate (**14**) which undergoes subsequent *addition* of another pyridyllithium 1-oxide molecule at C_2 (addition ortho to the 3-methyl group is facile as expected[5a]) followed by elimination of LiOH (and hydrolysis on work-up) to give the product.

In a preliminary series of experiments to test the acylation procedure[5b] 2-pyridyllithium was treated with ethyl butyrate and with D-(−)-ethyl 2-methoxypropionate



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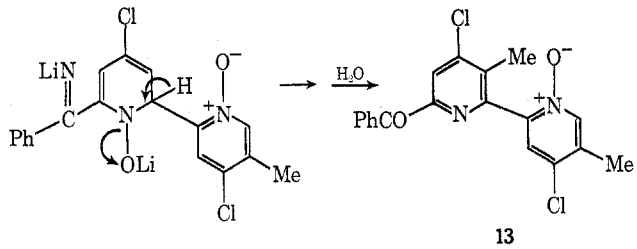

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(kindly supplied by Professor G. Fodor), and gave 1-(2-pyridyl)-1-butanone (55%) and D-2-methoxy-1-(2-pyridyl)-1-propanone (56%), respectively.

Experimental Section

Melting points are uncorrected. In most cases only the main infrared bands are reported.

Reaction of Pyridyl 1-Oxide Carbanions with Carbonyl Compounds. General Procedure.—To a stirred solution (or suspension) of the substituted pyridine 1-oxide (0.007 mol) in anhydrous ether (or tetrahydrofuran) (40–60 ml) at −78° under a dry nitrogen atmosphere, *n*-butyllithium (0.96 g in hexane solution, 0.015 mol) was added dropwise. After the solution was stirred for 15 min, a solution of the carbonyl compound (0.015 mol) in ether (or tetrahydrofuran) (10 ml) was added dropwise to give a dark red to brown solution. The reaction mixture was stirred for 1–3 hr at −78°, and then warmed to room temperature. It was decomposed with water (10 ml) and the excess solvent was evaporated *in vacuo*. The products were isolated from the aqueous solution as described in individual cases.

Reaction of 4-Chloro-2-pyridyl 1-Oxide Carbanion with Carbon Dioxide.—*n*-Butyllithium (1.92 g in hexane, 0.03 mol) was added to a suspension of 4-chloropyridine 1-oxide (1.899 g, 0.014 mol) in anhydrous ether (50 ml) and the mixture was treated with gaseous carbon dioxide at −65° for 3 hr. The aqueous solution was carefully acidified with dilute hydrochloric acid to pH 2–3 to give a tan precipitate. The acidic solution was extracted with chloroform (4 × 75 ml) and the dried ($MgSO_4$) chloroform solution was evaporated *in vacuo* to give a brown oil. Trituration of the oil with acetone gave **4-chloropyridine-2-carboxylic acid 1-oxide** (1.25 g, 49.0%) (from acetone): mp 136° (lit.[6] mp 144°); ir (KBr) 1710 cm^{-1} (s); nmr (DMSO-d_6) τ 1.70–2.20 (m, 2, C_3H, C_5H), 1.37 (d, 1, C_6H).

Anal. Calcd for $C_6H_4ClNO_3$: C, 41.52; H, 2.32; N, 8.07. Found: C, 41.35; H, 2.23; N, 7.73.

Reaction of 4-Methyl-2-pyridyl 1-Oxide Carbanion with Carbon Dioxide.—4-Methylpyridine 1-oxide (1.50 g, 0.0138 mol) in anhydrous tetrahydrofuran (60 ml) was treated with *n*-butyllithium (1.92 g in hexane, 0.03 mol) as usual, and then with gaseous carbon dioxide at −65° for 3 hr. The aqueous layer was carefully acidified to pH 2–3 with dilute HCl, the solution was extracted with $CHCl_3$ (4 × 75 ml), and the dried ($MgSO_4$) extract was evaporated *in vacuo* to give a brown oil which, on tritration with acetone, gave **4-methylpyridine-2,6-dicarboxylic acid 1-oxide** (1.30 g, 48.0%): mp 160° (from acetone); ir (KBr) 3080 (m), 1730 (s), 1485 (s), 1380 (m), 1230 (m), 1145 (w), 910 (m), 795 (m), 770 (m), and 600 cm^{-1} (m); nmr (DMSO-d_6) τ 7.45 (s, 3, $ArCH_3$), 1.83 (s, 2, C_3H, C_5H), −1.17 (s, 2, OH, disappears on addition of D_2O).

Anal. Calcd for $C_8H_7NO_5$: C, 48.74; H, 3.58; N, 7.15. Found: C, 48.73; H, 3.71; N, 7.60.

4-Chloro-5-methylpyridine-2-carboxylic Acid 1-Oxide.—4-Chloro-3-methylpyridine 1-oxide (2.04 g, 0.014 mol) in anhydrous ether (50 ml) was treated with *n*-butyllithium (1.92 g in hexane,

(5) (a) R. A. Abramovitch and C. S. Giam, *Can. J. Chem.*, **42**, 1627 (1964); (b) R. H. Mizzoni in "Pyridine and Its Derivatives," Part 4, E. Klingsberg, Ed., Interscience, New York, N. Y., 1964, p 153.

(6) E. Profft and W. Steinke, *J. Prakt. Chem.*, **13**, 85 (1961); *Chem. Abstr.*, **56**, 10091*a* (1962).

0.03 mol) at −65° and then with gaseous carbon dioxide for 3 hr. Acidification of the aqueous solution to pH 2–3 with dilute HCl and extraction of the aqueous solution with $CHCl_3$ (4 × 75 ml) followed by evaporation of the dried ($MgSO_4$) chloroform solution gave a brown oil which, on tritration with acetone, gave the 2-carboxylic acid 1-oxide (0.56 g, 23.8%): mp 160° (from acetone); ir (KBr) 1700 (s), 1660 cm^{-1} (s); nmr ($CDCl_3$) τ 7.60 (s, 3, $ArCH_3$), 1.83 (s, 1, C_3H), 1.17 (s, 1, C_6H).

Anal. Calcd for $C_7H_6ClNO_3$: C, 44.82; H, 3.22; N, 7.74. Found: C, 44.77; H, 3.31; N, 7.66.

5-Methylpyridine-2-Carboxylic Acid 1-Oxide.—5-Methyl-2-pyridylmethanol (5.0 g) (prepared from 2,5-dimethylpyridine 1-oxide and acetic anhydride[7]) was dissolved in concentrated nitric acid (30 ml) and fuming nitric acid (6 ml) and kept at room temperature for 72 hr. The reaction mixture was diluted with water, and the solution was made basic with solid sodium carbonate and then acidified to pH 4 with dilute hydrochloric acid. It was continuously extracted with $CHCl_3$ for 48 hr. Evaporation of the $CHCl_3$ solution gave 5-methylpyridine-2-carboxylic acid (3.41 g, 61.3%), mp 165° (from acetone) (lit.[8] mp 167–168°).

The acid (6.0 g) was oxidized in glacial acetic acid (150 ml) and 30% hydrogen peroxide (60 ml) at 80–90° for 18 hr to give 5-methylpyridine-2-carboxylic acid 1-oxide (5.20 g, 77.6%), mp 162–163° (lit.[9] mp 162–163°).

5-Methyl-4-nitropyridine-2-carboxylic Acid 1-Oxide.—Concentrated nitric acid (5 ml) was slowly added to a solution of 5-methylpyridine-2-carboxylic acid 1-oxide (1.0 g) in concentrated sulfuric acid (5 ml) at 10–15°. The reaction mixture was heated under reflux at 90–110° for 4 hr, and was then poured into ice water (20 ml). The solution was made basic with Na_2CO_3 and then acidified to pH 4–5 with dilute HCl to give 5-methyl-4-nitropyridine-2-carboxylic acid 1-oxide (0.35 g, 27.1%): mp 145° (from acetone); ir (KBr) 3140 (w), 3050 (m), 1703 (s), 1610 (s), 1525 (s), 1445 (s), 1350 (s), 1288 (s), 1276 (s), 1167 (m), 1110 (w), 1040 (m), 1010 (m), 956 (m), 878 (m), 862 (w), 788 (s), 758 (w), 696 (m), 660 (s), and 635 cm^{-1} (m); nmr (DMSO-d_6) τ 7.07 (s, 3, $ArCH_3$), 1.06 (s, 1, C_3H), 0.72 (s, 1, C_6H); mass spectrum (no M^+ at *m/e* 198) *m/e* (rel intensity) 154 (12.2) ($M^+ - CO_2$), 138 (6.4), 108 (2.9), 92 (8.1), 65 (16.8), 39 (20.9).

Anal. Calcd for $C_7H_6N_2O_5$: C, 42.46; H, 3.26. Found: C, 42.75; H, 3.56.

Unreacted 5-methylpyridine-2-carboxylic acid 1-oxide (0.41 g) was isolated from the acidic solution.

Authentic 4-Chloro-5-methylpyridine-2-carboxylic Acid 1-Oxide.—4-Nitro-5-methylpyridine-2-carboxylic acid 1-oxide (0.100 g) and acetyl chloride (3 ml) were warmed briefly to give a yellow solid which was dissolved in chloroform (5 ml). The chloroform solution was filtered and evaporated *in vacuo* to give 4-chloro-5-methylpyridine-2-carboxylic acid 1-oxide (0.023 g, 26.4%), mp 155°, identical with the sample obtained from the pyridyl oxide carbanion.

4,5-Dimethylpyridine-2-carboxylic Acid 1-Oxide.—This was prepared from 3,4-dimethylpyridine 1-oxide (0.86 g, 0.007 mol) in anhydrous tetrahydrofuran (30 ml) and *n*-butyllithium (0.96 g, 0.015 mol), followed by gaseous carbon dioxide at −78° for 3 hr to give a brown oil. Trituration of the oil with acetone gave 4,5-dimethylpyridine-2-carboxylic acid 1-oxide (0.20 g, 17.9%): mp 180–181° (recrystallized from acetone); ir (KBr) 1700 (s), 1630 cm^{-1} (s); nmr (DMSO-d_6) τ 7.85 (s, 6, $2ArCH_3$), 2.07 (s, 1, C_3H), 1.58 (s, 1, C_6H).

Anal. Calcd for $C_8H_9NO_3$: C, 57.48; H, 5.43; N, 8.38. Found: C, 57.81; H, 5.66; N, 8.38.

Reaction of 2-Methylpyridyl 1-Oxide Carbanions with Carbon Dioxide.—Using the method outlined previously, 2-methylpyridine 1-oxide (1.50 g, 0.014 mol) was treated with *n*-butyllithium (1.92 g in hexane, 0.03 mol) and the resulting solution was treated with gaseous carbon dioxide at −78° for 3 hr. The aqueous solution was acidified to pH 2–3 with dilute HCl. The acidic solution was extracted with $CHCl_3$ (4 × 75 ml) and the dried ($MgSO_4$) extract was evaporated *in vacuo* to give an orange oil which solidified to give 6-methylpyridine-2-carboxylic acid 1-oxide (0.28 g, 13.5%): mp 181–182° (lit.[10] mp 177°) (recrystallized from acetone); ir (KBr) 1675 cm^{-1} (s); nmr (C_5D_5N) τ 7.64 (s, 3, $ArCH_3$), 2.82 (m, 3, C_3H, C_4H, C_5H).

Anal. Calcd for $C_7H_7NO_3$: C, 54.90; H, 4.60; N, 9.10. Found: C, 55.33; H, 4.66; N, 9.21.

After the aqueous solution was allowed to stand for 12 hr, **2-methylpyridine 1-oxide α,6-dicarboxylic acid** (0.27 g, 10.1%), mp 177° (from acetone), separated: ir (KBr) 3200–3800 (m), 1705 (s), 1600 (m), 1495 (w), 1395 (s), 1310 (m), 1250 (m), 1195 (m), 1155 (m), 1070 (m), 915 (m), 835 (w), 810 (w), 755 (m), and 600 cm^{-1} (m); nmr (DMSO-d_6) τ 5.92 (s, 2, $ArCH_2CO_2H$), 1.50–2.30 (m, 3, C_3H, C_4H, C_5H).

Anal. Calcd for $C_8H_7NO_5$: C, 48.74; H, 3.58. Found: C, 48.79; H, 3.76.

Oxidation of Ethyl 2-Pyridylacetate.—Ethyl 2-pyridylacetate (0.9 g) dissolved in glacial acetic acid (10 ml) and 30% hydrogen peroxide (1 ml) was heated under reflux at 70° for 10 hr. The colorless solution was basified with sodium carbonate, and the solution was acidified to pH 2 with 10% HCl and then extracted with $CHCl_3$, evaporation of which *in vacuo* gave pyridine-2-carboxylic acid 1-oxide (0.16 g, 21.4%), mp 160° (lit.[6] mp 162°).

6-(1-Hydroxycyclohexyl)-3,4-dimethylpyridine-2-carboxylic Acid 1-Oxide.—Prepared from 6-(1-hydroxycyclohexyl)-3,4-dimethylpyridine 1-oxide, butyllithium, and CO_2, the acid (7%) had mp 97°.

Anal. Calcd for $C_{14}H_{19}NO_4$: C, 63.38; H, 7.22. Found: C, 63.94; H, 7.39.

The main product appeared to be 2-*n*-butyl-6-(1-hydroxycyclohexyl)-3,4-dimethylpyridine: ir (KBr) 3600–3000 (m), 2930 (s), 2860 (m), 1600 (m), 1450 (m), 1400 (w), 1260 (m), 1168 (w), 1039 (m), 968 (m), 800 cm^{-1} (w); mass spectrum *m/e* 261 (M^+).

Reaction of 3,4-Dimethylpyridyl 1-Oxide Carbanion with Ethyl Acetate. A.—3,4-Dimethylpyridine 1-oxide (0.86 g, 0.007 mol) in tetrahydrofuran (60 ml) was treated with *n*-butyllithium [0.96 g in hexane (6 ml)] and the mixture was treated with ethyl acetate (1.23 g, 0.015 mol) for 1 hr. The aqueous solution was extracted with $CHCl_3$ (3 × 75 ml), and the dried (K_2CO_3) $CHCl_3$ extract was evaporated *in vacuo* to give a yellow oil (1.29 g), distillation of which at 108° (0.01 mm) gave a white solid (0.795 g) which was washed with ether to give **2-acetyl-4,5-dimethylpyridine 1-oxide** (0.75 g, 65.1%): mp 61–62°; ir (KBr) 1685 (s), 1250 cm^{-1} (s); nmr ($CDCl_3$) τ 7.80 (s, 6, $2ArCH_3$), 7.28 (s, 3, $COCH_3$), 2.65 (s, 1, C_3H), 2.10 (s, 1, C_6H); mass spectrum *m/e* 165 (M^+), 149 ($M^+ - O$).

Anal. Calcd for $C_9H_{11}NO_2$: C, 65.44; H, 6.71; N, 8.48. Found: C, 65.50; H, 6.92; N, 8.80.

B.—3,4-Dimethylpyridine 1-oxide (0.96 g, 0.0078 mol) dissolved in anhydrous tetrahydrofuran (60 ml) was treated with *n*-butyllithium (1.03 g in hexane, 0.016 mol) and the mixture was treated with ethyl acetate (1.50 g, 0.017 mol) at −78° for 1 hr. The aqueous solution was extracted with $CHCl_3$ (3 × 75 ml) and the dried (K_2CO_3) $CHCl_3$ extract was evaporated to give a yellow-orange oil (1.531 g) which was chromatographed on a silica gel column (18 g, 1 × 8 in.). Elution with benzene–ether (3:1 v/v, 300 ml) gave a noncrystalline material which was not further investigated. Elution with benzene–ether (1:1 v/v, 300 ml) gave 2-acetyl-4,5-dimethylpyridine 1-oxide (0.25 g, 19.6%), mp 61–62°. Elution with benzene–ether (1:3 v/v, 300 ml) gave **2-acetyl-3,4-dimethylpyridine 1-oxide** (0.81 g, 6.3%): mp 109–110° (recrystallized from acetone–light petroleum); ir (KBr) 1700 (s), 1269 (s), 1243 cm^{-1} (s); nmr ($CDCl_3$) τ 7.70 (m, 6, $2ArCH_3$), 7.40 (s, 3, $COCH_3$), 2.94 (d, 1, C_5H), 2.10 (d, 1, C_6H); mass spectrum *m/e* 165 (M^+), 149 ($M^+ - O$).

Anal. Calcd for $C_9H_{11}NO_2$: C, 65.44; H, 6.71. Found: C, 65.31; H, 6.82.

Elution with ether–absolute ethanol (19:1 v/v, 200 ml) gave a yellow oil (0.06 g) which was not further investigated. Elution with ether–absolute ethanol (3:1 v/v, 300 ml) gave 3,4-dimethylpyridine 1-oxide (0.095 g).

Reaction of 3,4-Dimethylpyridyl 1-Oxide Carbanion with *N,N*-Dimethylacetamide.—3,4-Dimethylpyridine 1-oxide (0.86 g, 0.007 mol) in tetrahydrofuran (60 ml) was treated with *n*-butyllithium (0.96 g in hexane, 0.015 mol) and then with *N,N*-dimethylacetamide (1.22 g, 0.0145 mol) at −65° for 1 hr. The aqueous solution was extracted with $CHCl_3$ (3 × 75 ml) and the dried (K_2CO_3) extract was evaporated *in vacuo* to give a yellow oil (0.90 g) which was chromatographed on alumina (45 g, 2.5 × 18 cm). Elution with benzene–ether (1:3 v/v, 200 ml) and ether (100 ml) gave **6′-acetyl-3′,4,4′,5-tetramethyl-2,2′-dipyridyl 1-oxide** (0.12 g, 12.9%): mp 217°; ir (KBr) 3070 (w), 3000–2920 (w), 1795 (s), 1580 (w), 1550 (w), 1505 (w), 1485 (w), 1465 (w), 1345 (w), 1315 (w), 1260 (m), 1230 (w), 1190 (w), 1160 (m),

(7) E. Hardegger and E. Nikles, *Helv. Chim. Acta*, **40**, 2428 (1957).
(8) F. C. Uncle, J. E. Krugger, and A. E. Rogers, *J. Amer. Chem. Soc.*, **78**, 1932 (1956).
(9) R. M. Acheson and G. A. Taylor, *J. Chem. Soc.*, 1691 (1960).
(10) J. Suzzko and M. Szafran, *Rocz. Chem.*, **38**, 1793 (1964).

1095 (w), 1020 (w), 890 (w), 865 (w), 785 (w), 755 (w), and 740 cm^{-1} (w); nmr ($CDCl_3$) τ 7.55–7.80 (m, 12, 4ArCH_3), 7.36 (s, 3, Ar$COCH_3$), 2.80 (s, 1, C_5H), 2.13 (s, 1, C_3H), 1.88 (s, 1, C_6H); mass spectrum *m/e* (rel intensity) 270 (M^+) (35), 254 ($M^+ - O$) (33), 253 ($M^+ - OH$) (100).

Anal. Calcd for $C_{16}H_{18}N_2O_2$: C, 71.09; H, 6.71; N, 10.36. Found: C, 70.75; H, 6.65; N, 10.62.

Reaction of 3,4-Dimethylpyridyl 1-Oxide Carbanion with *N*-Acetylmorpholine.—3,4-Dimethylpyridine 1-oxide (0.86 g, 0.03 mol) in anhydrous tetrahydrofuran (100 ml) was treated with *n*-butyllithium (0.96 g in hexane, 0.015 mol), and the mixture was then treated with *N*-acetylmorpholine (1.85 g, 0.0145 mol) at −78° for 1 hr. The reaction mixture was decomposed with a saturated solution of ammonium chloride (75 ml). The organic layer was separated and evaporated to give an oil (1.50 g). A white solid was obtained from this oil and identified as 2-acetyl-4,5-dimethylpyridine 1-oxide (0.04 g, 2.8%).

Reaction of 4-Ethoxypyridine 1-Oxide Carbanion and Ethyl Butyrate.—4-Ethoxypyridine 1-oxide (1.00 g, 0.077 mol) suspended in tetrahydrofuran (40 ml) was treated with *n*-butyllithium (0.96 g in hexane, 0.015 mol) and then with ethyl butyrate (1.62 g, 0.015 mol), as outlined in the general procedure, to give an orange-red oil (1.76 g) which was column chromatographed on silica gel (15 g, 2.5 × 15 cm). Elution with light petroleum (bp 30–60°)–benzene (3:1 v/v, 300 ml) gave a noncrystalline material (0.023 g) which was not further investigated. Elution with light petroleum–benzene (1:3 v/v, 300 ml), benzene (300 ml), and benzene–ether (3:1 v/v, 300 ml) gave an oily solid (0.749 g) which, after recrystallization from light petroleum, gave **2,6-di-*n*-butyryl-4-ethoxypyridine 1-oxide** (0.33 g, 16.5%): mp 64–65°; ir (KBr), 1680 cm^{-1} (s); nmr ($CDCl_3$) τ 9.04 (t, 6, 2-$CH_2CH_2CH_3$), 8.60 (t, 3, -OCH_2CH_3), 8.15–8.40 (m, 4, 2CH_2-CH_2CH_3), 6.88 (t, 4, 2 -$COCH_2$), 5.94 (q, 2, -CH_2CH_3), 2.94 (s, 2, C_3H, C_5H).

Anal. Calcd for $C_{15}H_{21}NO_4$: C, 64.50; H, 7.58. Found: C, 64.59; H, 7.56.

Benzene–ether (1:3 v/v, 300 ml) and ether (300 ml) were used as eluents to give a noncrystalline material (0.054 g) which was not investigated further. Elution with ether–absolute ethanol (3:1 v/v, 300 ml) gave **2-butyryl-4-ethoxypyridine 1-oxide** (0.28 g, 18.5%) as an oil which decomposed on attempted purification: ir (film) 1710 (s), 1640 (s), 1460 (s), 1240 cm^{-1} (s); nmr ($CDCl_3$) τ 9.03 (t, 3, -$CH_2CH_2CH_3$), 8.58 (t, 3, -OCH_2-CH_3), 8.16–8.40 (q, 2, -$CH_2CH_2CH_3$), 6.82 (t, 2, -$COCH_2$–), 5.80–6.08 (q, 2, -OCH_2CH_3), 3.08–3.24 (q, 1, C_5H), 3.96 (d, 1, C_3H), 1.94 (d, 1, C_6H).

Reaction of 4-Chloro-3-methylpyridyl 1-Oxide Carbanion with Benzonitrile.—4-Chloro-3-methylpyridine 1-oxide (1.00 g, 0.007 mol) suspended in anhydrous ether (20 ml) was treated with *n*-butyllithium (0.96 g in hexane, 0.015 mol) and the mixture was treated with benzonitrile (1.00 g, 0.01 mol) at −78° for 3 hr. The aqueous solution was extracted with chloroform (3 × 75 ml). Evaporation of the dried (K_2CO_3) chloroform solution gave a brown oil (0.75 g) which was chromatographed on an alumina column (40 g, 2.5 × 15 cm). Elution with benzene–absolute ethanol (19:1 v/v, 200 ml) gave **6′-benzoyl-4,4′-dichloro-3′,5-dimethyl-2,2′-dipyridyl 1-oxide** (0.15 g, 11.5%): mp 235° (recrystallized from acetone); ir (KBr) 3020 (m), 1656 (s), 1594 (m), 1547 (s), 1490 (m), 1445 (m), 1390 (m), 1381 (m), 1350 (w), 1310 (s), 1275 (w), 1255 (m), 1225 (m), 1178 (s), 1140 (m), 1080 (w), 1005 (m), 972 (m), 922 (m), 895 (m), 870 (w), 845 (m), 810 (m), 796 (m), 770 (m), 740 (s), 710 (s), 700 (s), and 690 cm^{-1} (s); nmr (C_5D_5N) τ 7.94 (s, 3, ArCH_3), 7.64 (s, 3, ArCH_3), 2.88 (s, 2, $C_5'H$, C_3H), 2.42–2.76 (m, 3, 3ArH), 1.85 (m, 3, C_6H, ArH).

Anal. Calcd for $C_{19}H_{14}Cl_2N_2O_2$: C, 61.14; H, 3.78; N, 7.51; mol wt (2 ^{35}Cl), 372.0432. Found: C, 61.03; H, 3.94; N, 7.63; mol wt, 372.0423 (mass spectrum).

D-2-Methoxy-1-(2-pyridyl)-1-propanone.—2-Bromopyridine (1.10 g, 0.007 mol) in anhydrous ether (40 ml) at −65° was treated with *n*-butyllithium (0.48 g in hexane) and then with a solution of D-(−)-ethyl 2-methoxypropionate (1.848 g, 0.014 mol) in anhydrous ether (10 ml) and worked up as usual to give an oil which, on distillation at 66° (0.05 mm), gave D-2-methoxy-1-(2-pyridyl)-1-propanone (0.64 g, 55.9%): mp 40–45°; ir (film) 1704 cm^{-1} (s); nmr ($CDCl_3$) τ 8.52 (d, J = 7 Hz, 3, $CHCH_3$), 6.57 (s, 3, -OCH_3), 4.62 (q, 1, CH), 1.77–2.60 (m, 3, C_3H, C_4H, C_5H), 1.27 (d, J = 5 Hz, 1, C_6H); mass spectrum *m/e* 165 (M^+).

Anal. Calcd for $C_9H_{11}NO_2$: C, 65.44; H, 6.71; N, 8.48. Found: C, 65.24; H, 6.70; N, 8.56.

Registry No.—2 (R = NO_2, R′ = Me), 35895-58-0; **5**, 1125-34-4; **6**, 35895-59-1; **8**, 35895-60-4; **10**, 35895-61-5; **11**, 35895-62-6; **13**, 35895-63-7; 2-*n*-butyl-6-(1-hydroxycyclohexyl)-3,4-dimethylpyridine, 35895-64-8; 2,6-di-*n*-butyryl-4-ethoxypyridine 1-oxide, 35895-65-9; 2-butyryl-4-ethoxypyridine 1-oxide, 35895-66-0; 6′-acetyl-3′,4,4′,5-tetramethyl-2,2′-dipyridyl 1-oxide, 35895-67-1; D-2-methoxy-1-(2-pyridyl)-1-propanone, 33169-01-6.

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