Acknowledgments.—This research was supported by grants from the Petroleum Research Fund, administered by the American Chemical Society, and from the Research Foundation of the State of New York. We are pleased to acknowledge gifts of generous quantities of molybdenum and tungsten hexacarbonyls from Climax Molybdenum Co. We are grateful to Ms. R. Cartmell for running spectra on the Varian HA-100 nmr spectrometer. We are indebted to Mr. E. C. H. Keung for carrying out some preliminary experiments.

Selective Metalations of Methylated Pyridines and Quinolines. Condensation Reactions[1a]

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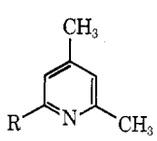
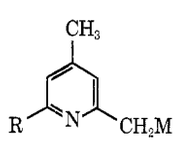
Interactions of 2,4-lutidine, 2,4,6-collidine, and 2,4-dimethylquinoline with *n*-butyllithium in ether–hexane results in exclusive metalation of their 2-methyl groups. In contrast, treatment of these active hydrogen compounds with alkali amides in ammonia or with lithium diisopropylamide in ether–hexane gives exclusive metalation of their 4-methyl groups. Such differences are interpreted in terms of metallic cations and their relative ability to complex with nitrogen atoms, either of the heterocycles or of the solvent or coreagent. Similar selective metalations are not realized on 2,6- or 2,7-dimethylquinolines, presumably because of lack of resonance delocalization of carbanions on the 6- and 7-methyl groups, respectively. All of the carbanions formed, particularly those on the 4-methyl groups, have been condensed with various electrophiles in fair to excellent yields.

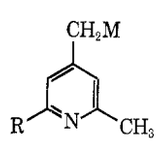
2- and 4-picolyl organometallic reagents, prepared from interaction of the parent picolines with a variety of bases, have been studied rather extensively.[2a,b] However, the related carbanions derived from 2,4-lutidine (**1a**) and 2,4,6-collidine (**1b**) have but rarely been prepared and their reactions are thus relatively unknown. For example, 2-lithiomethyl derivatives **2a,b** have been obtained in a few cases by treatment of **1a,b** with lithiohydrocarbons like phenyllithium; subsequent condensations with various carbonyl compounds are known.[3a-c] On the other hand, 4-alkalimethyl derivatives **3a,b** have been realized only upon treatment of **1a,b** with alkali metal amides in liquid ammonia.[4a,b] Compound **3a** has been methylated in unspecified yield,[4a] and both **3a,b** have been nitrated



1a, R = H
b, R = CH_3



2a, R = H
b, R = CH_3

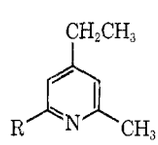


3a, R = H
b, R = CH_3

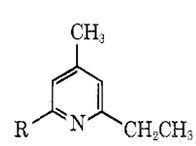
by alkyl nitrates in good yields to afford the corresponding nitromethyl derivatives.[4b]

However, the picture is far from clear, as illustrated by the report by Chichibabin that **1b** is converted to **2b**, not **3b**, by various alkali metal amides.[5] Thus, our involvement with compounds **1a,b** arose not only because of the paucity of data on the 4-lutidyl (**3a**) and 4-collidyl (**3b**) anions, but also on our initial skepticism (and confusion) concerning the above purported different sites of metalation within these molecules (4-methyl *vs.* 2-methyl) as a function of the base (alkali amides *vs.* organolithiums). To our knowledge, such a remarkable dependence upon base had previously not been recognized. Usually, of course, ionization of molecules containing more than a single kind of similarly activated hydrogen atom has resulted in the same hydrogen atom being abstracted regardless of the base employed, though the relative rates of reaction have often been different.

First, to unequivocally ascertain the site of metalation as a function of the base, **1a,b** were allowed to react with three different base systems and the resulting carbanions were subsequently identified by condensations with certain electrophiles. Thus, interaction of **1a,b** with sodium or potassium amides in liquid ammonia (method A) or with lithium diisopropylamide in ether (or THF)–hexane (method B) afforded the 4-alkali methyl derivatives **3a,b** since methylation with methyl iodide gave methylethylpyridines **4a,b** respectively. Similar treatment of



4a, R = H
b, R = CH_3



5a, R = H
b, R = CH_3

1a,b with *n*-butyllithium in ether–hexane (method C) gave the 2-metallomethyl derivatives **2a,b**, since methylation afforded the isomeric methylethylpyridines, **5a,b** respectively. Incidentally, authentic **4b** was prepared by an unequivocal ring closure, thereby providing a standard compound for nmr spectroscopic determinations of other structures.

Methods A and B were then employed to synthesize various other substituted pyridines arising from alkylation of the 4-methyl groups of **1a,b**. Thus, **3a** was *n*-propylated, *n*-butylated, and benzylated to

(1) (a) Supported in part by the Petroleum Research Fund, administered by the American Chemical Society, on Grant 3710-A, and by the National Science Foundation on Grant GY-7281; (b) NSF Undergraduate Research Participant.

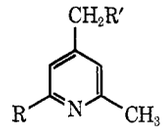
(2) (a) J. M. Mallan and R. L. Bebb, *Chem. Rev.*, **69**, 693 (1969); (b) M. J. Weiss and C. R. Hauser, *J. Amer. Chem. Soc.*, **71**, 2023 (1949).

(3) (a) N. N. Goldberg and R. Levine, *ibid.*, **77**, 3647 (1955), and references cited therein; (b) A. A. Cale, Jr., R. W. McGinnis, Jr., and P. C. Teague, *J. Org. Chem.*, **25**, 1507 (1960); (c) J. I. deJong and J. P. Wibaut, *Recl. Trav. Chim., Pays-Bas*, **70**, 962 (1951).

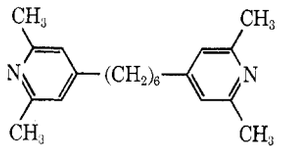
(4) (a) H. L. Lochte and T. H. Cheavens, *J. Amer. Chem. Soc.*, **79**, 1667 (1957); (b) H. Feuer and J. P. Lawrence, *ibid.*, **91**, 1856 (1969).

(5) A. E. Chichibabin, German Patent 676,114 (1939); *Chem. Abstr.*, **33**, 6345 (1939).

give **6a**, **7a**, and **8a**, respectively, in fair to good yields. Also, **3b** was *n*-propylated, *n*-butylated, benzylated and caused to enter into a bis alkylation to afford **6b**, **7b**, **8b**, and **9**, respectively. Parenthetically, a similar bis alkylation on **2b** likewise gave a dipyridyl derivative (**10**).



6a, R = H; R′ = *n*-C_3H_7
b, R = CH_3; R′ = *n*-C_3H_7
7a, R = H; R′ = *n*-C_4H_9
b, R = CH_3; R′ = *n*-C_4H_9
8a, R = H; R′ = $CH_2C_6H_5$
b, R = CH_3; R′ = $CH_2C_6H_5$



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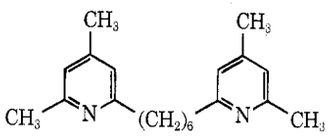

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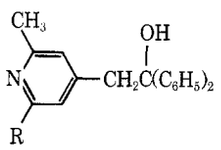
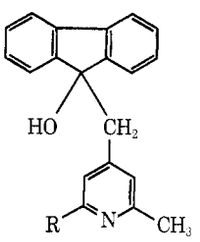
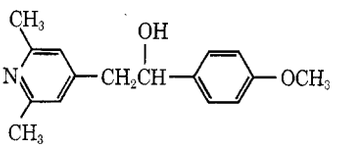
Next, attention was directed toward condensation of the above salts with electrophiles other than alkyl halides. For example, the 4-lutidyl (**3a**) and 4-collidyl (**3b**) anions were condensed with a few aldehydes and ketones to give the expected β-hydroxypyridine derivatives. Thus, **3a,b** were treated with benzophenone and fluorenone by means of method A to afford alcohols **11a–b** and **12a–b**, respectively; adducts **11a–b** were also obtained in THF-hexane (Method B) but in poorer yields. A similar condensation of **3b** with anisaldehyde gave alcohol **13**.



11a, R = H
b, R = CH_3



12a, R = H
b, R = CH_3



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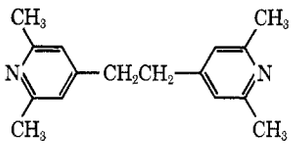
Also, an oxidative dimerization[6] of **3b** was effected by means of potassium permanganate in ammonia to give hydrocarbon **14** in fair yield. It should be mentioned that the 2-lithio derivative **2b** has previously been dimerized by molecular oxygen to give **15**.[7]

Finally, carbanions **2a,b** and **3a,b** were condensed with azobenzene to afford substituted hydrazobenzenes. The specifics of these reactions are reported elsewhere.[8]

(6) E. M. Kaiser, *J. Amer. Chem. Soc.*, **89**, 3659 (1967).
(7) A. M. Jones and C. A. Russell, *J. Chem. Soc. C*, 2246 (1969).
(8) E. M. Kaiser and G. J. Bartling, *J. Org. Chem.*, **37**, 490 (1972).



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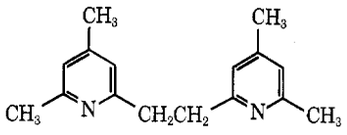
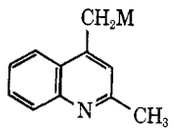


15

Next, attention was directed toward the related base-catalyzed chemistry of three isomeric quinolines, namely the 2,4-, 2,6-, and 2,7-dimethyl isomers. As will be seen, selective metalations were realized on the 2,4-dimethyl system, but not on the others.

First, treatment of the 2,4-dimethyl isomer with sodium amide in ammonia (method A) or lithium diisopropylamide in ether–hexane (method B) resulted in exclusive ionization of the 4-methyl group to give **16**, since subsequent condensations with benzophenone afforded alcohol **17**. Anion **16**, prepared by method A, was also treated with *p*-chlorobenzaldehyde, chalcone, 1,4-dibromobutane, and potassium permanganate to give derivatives **18–21**, respectively.



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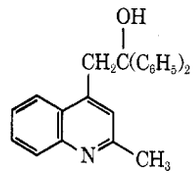

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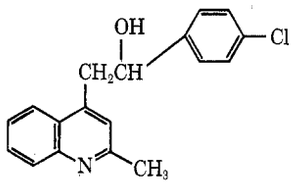

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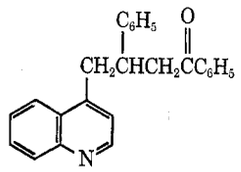

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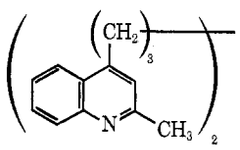

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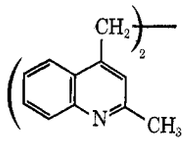
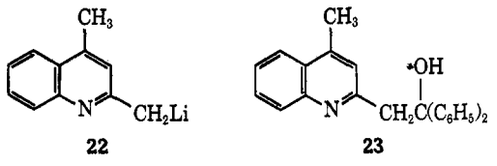


21

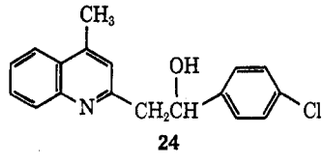
In contrast, treatment of the 2,4-dimethyl isomer with *n*-butyllithium (method C) gave rise only to anion **22** resulting from metalation of the 2-methyl group. Formation of **22** was confirmed by reactions with benzophenone, *p*-chlorobenzaldehyde, and chalcone to give **23**, **24**, and **25**, respectively. Interestingly, in contrast with the chalcone condensation with **16**, which occurs *via* a conjugate addition reaction, that with **22** arises from a 1,2-nucleophilic acyl addition; the importance of metallic cations in such reactions is of course, well known.[9] Compound **22** has previously been dimerized in low yield by molecular oxygen.[7]

Disappointingly, treatment of 2,7-dimethylquinoline with any of the bases described above gave metalation

(9) For example, see E. E. Royals, "Advanced Organic Chemistry," Prentice-Hall, Englewood Cliffs, N. J., 1954, pp 635–637.



22 23



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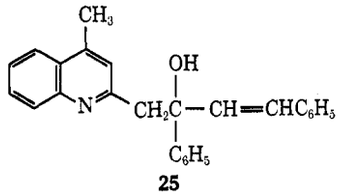

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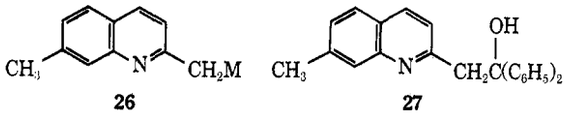
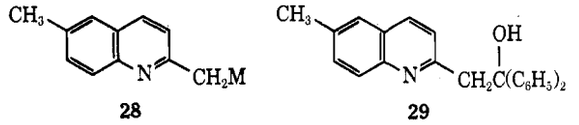
only on the 2-methyl group. Thus, treatment of this isomer by methods A, B, or C afforded only **26**,



26 27



28 29

since condensation with benzophenone gave only **27** in high yields. Similar results were obtained with the 2,6-dimethyl isomer using methods B and C giving anion **28**; addition of benzophenone yielded only alcohol **29**.

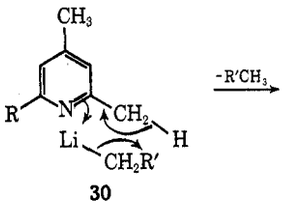
Discussion

The surprising aspect of the above work is not that methyl groups substituted in the 2 and/or 4 positions of pyridine and quinoline moieties undergo facile metalation, since it is well known that the resulting anions are highly resonance stabilized. In fact, even relatively weakly acidic alkyl groups substituted on the 3 position of such molecules can be ionized provided the proper choice of base is made.[10] What is surprising, of course, is that such highly selective metalations can be achieved on these systems at all. This is particularly so if it is realized that the 4-methyl groups are presumably more acidic than those in the 2 position,[11] and thus should undergo exclusive ionization with single molecular equivalents of bases. That *n*-butyllithium (and other lithiohydrocarbons) promotes only ionization of 2-methyl groups can be ascribed to prior complexation of the lithium cation with the ring nitrogen, thereby effectively "locking in" the basic butyl group near that particular methyl group. Metalation then can proceed by a favorable six-membered-ring process (**30**). Similar complexes of organolithium reagents with tertiary amines are well known.[2a]

Metalation of 4-methyl groups in these molecules,

(10) For example, see A. D. Miller, C. Osuch, N. N. Goldberg, and R. Levine, *J. Amer. Chem. Soc.*, **78**, 674 (1956).

(11) H. C. Brown and X. R. Mihm, *ibid.*, **77**, 1723 (1955).



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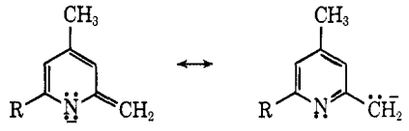
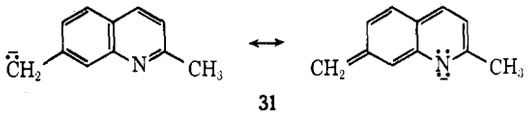


then, can be expected to occur when metallic cations (for example, sodium) are used that are not as effective as lithium in coordinating with nitrogen, or when solvents or coreagents (for example, ammonia or diisopropylamine, respectively) are employed which are more strongly basic, and thus more strongly coordinating, than pyridine or quinoline. For example, in method B, even the use of lithium as cation does not promote lithiation of the 2-methyl groups, since the metal is complexed with the nitrogen of diisopropylamine rather than that of the ring nitrogen. Therefore, the basic reagent is "free" to ionize the more strongly acidic 4-methyl group.

That the 6-methyl group of 2,6-dimethylquinoline is not ionized under any of the conditions described above can be rationalized simply—an anion formed at this position *cannot* be delocalized onto the nitrogen atom. Thus, in this case, only the more acidic 2-methyl group is metalated in this compound. More surprisingly, however, is the fact that the 7-methyl group of 2,7-dimethylquinoline is also unaffected by our systems. Presumably, an anion formed on such a methyl group could be delocalized onto nitrogen provided the aromaticity of the nonheterocyclic ring is destroyed (for example, **31**). Apparently, though,



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this loss of aromaticity offsets the energy gained by delocalizing the charge, so **31** cannot be realized.

The condensations of all the carbanions prepared above seem to be general and could be easily extended to other electrophiles. The structures of the products, most of which are new, were supported by elemental analyses, nmr spectroscopy, and in some cases by the preparation of known picrate or methiodide derivatives (see Table I).

Work is currently in progress to ascertain if other polymethylated heterocycles will similarly be selectively metalated by different bases. Of particular interest is the possible formation of 1,1[12] and other kinds of multiple anions derived from these systems.

Experimental Section[13]

Preparation of Pyridine and Quinoline Derivatives by Means of Alkali Amides in Ammonia (Method A).—In Table I are listed

(12) E. M. Kaiser, L. E. Solter, R. A. Schwarz, R. D. Beard, and C. R. Hauser, *ibid.*, **93**, 4237 (1971).

(13) Infrared spectra were measured on a Perkin-Elmer Model 237 grating infrared spectrometer. Nmr spectra were obtained on a Varian Associates A-60 spectrometer using tetramethylsilane as internal standard. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn.

TABLE I

PRODUCTS PREPARED FROM CONDENSATIONS OF ALKALI DERIVATIVES OF ALKYLATED PYRIDINES AND QUINOLINES WITH ELECTROPHILES

Product	Method[a]	Yield, %[b]	Mp or bp, °C (mm)	Analyses (calcd/obsd) C	H	N	Nmr spectra, δ
4a	A	37	180–182 (760)[c]				8.4[d] (d, 1, ArH), 6.9 (d, 2, ArH), 2.56 (m, 5, CH_2, CH_3), 1, 2 (t, 3, CH_3)
4b	A	47	177–180 (760)[e]				6.7[d] (s, 2, ArH), 2.45 (q, 2, CH_3CH_2), 2.4 (s, 6, CH_3), 1.1 (t, 3, CH_3)
5a	C	40	173–175 (760)[f]				8.0[g] (d, 1, ArH), 6.67 (d, 2, ArH), 2.18 (m, 5, CH_2, CH_3), 0.83 (t, 3, CH_3)
5b	C	60	174–176 (760)[h]				6.7[d] (s, 2, ArH), 2.7 (q, 2, CH_3CH_2), 2.4 (s, 3, CH_3), 2.1 (s, 3, CH_3), 1.2 (t, 3, CH_3CH_2)
6a	A	27	89.5–90 (10)	80.54[i]	10.06	9.40	7.98[d] (d, 1, ArH), 6.04 (d, 2, ArH), 1.93 (m, 5, CH_2,
	B	37	89.5–90 (10)	80.37[j]	10.19		CH_3), 0.79 (m, 7, CH_2, CH_3)
6b	A	57	92–94 (11)	80.98[i]	10.43	8.59	6.25[d] (s, 2, ArH), 1.94 (m, 8, CH_2, CH_3), 0.75 (m, 7, CH_2,
				80.72[j]	10.36		CH_3)
7a	A	44	89–90 (7.5)	80.98[i]	10.43	8.59	7.99[d] (d, 1, ArH), 6.48 (d, 2, ArH), 1.97 (m, 5, CH_2,
				80.70[j]	10.62	8.73	CH_3), 0.70 (m, 9, CH_2, CH_3)
7b	B	42	128–130 (10)	81.35[i]	10.73	7.91	6.26[d] (s, 2, ArH), 1.91 (m, 8, CH_2, CH_3), 0.76 (m, 9,
				81.16[j]	10.81	7.69	CH_2, CH_3)
8a	B	47	149–151 (8)	85.27[i]	7.61	7.11	7.97[g] (d, 1, ArH), 6.79 (m, 5, ArH), 6.35 (m, 2, ArH),
				84.91[j]	7.81	6.76	2.35 (m, 4, CH_2), 2.05 (s, 3, CH_3)
8b	A	34	184–185 (9)	85.30[i]	8.05	6.63	6.80[g] (m, 5, ArH), 6.30 (s, 2, ArH), 2.40 (t, 4, CH_2),
				85.41[j]	8.34	6.48	2.08 (m, 6, CH_3)
9	A	53	186–192 (0.25)[k]	81.03[i]	9.52	9.45	6.77[l] (s, 4, m, ArH), 2.47 (m, 15.9, CH_2, CH_3) 1.4 (m,
				80.79[j]	9.62		8.1, CH_2)
10	C	21	266–271 (1.5)	81.03[i]	9.52	9.45	6.75[l] (s, 4, ArH), 2.69 (m, 4, benzyl, CH_2), 2.23 (s, 6,
				81.26[j]	9.83		benzyl, CH_3), 1.55 (m, 8, CH_2)
11a	A	47	175–177[m]	83.04[i]	6.57	4.84	8.19[l] (d, 1, ArH), 7.35 (m, 10, ArH), 6.67 (d, 2, ArH),
11a	B	26	175–176[m]	83.20[j]	6.47	4.85	3.58 (s, 2, CH_2), 2.41 (s, 3, CH_3)
11b	A	96	141–142[m,n]	78.50[i]	7.17	4.36	7.5[l] (m, 10, ArH), 6.81 (s, 2, ArH), 6.04 (s, 1, OH), 3.8
11b	B	51	141–142[m,n]	78.60[j]	7.16	4.26	(s, 2, OH), 3.63 (s, 2, CH_2), 2.28 (s, 6, CH_3)
12a	A	23	174–175[p]	83.62[i]	5.92	4.88	7.91[l] (d, 1, ArH), 7.41 (m, 8, ArH), 6.64 (d, 2, ArH),
				83.50[j]	5.93	4.79	3.57 (m, 1, OH), 3.24 (s, 2, CH_2), 2.22 (s, 3, CH_3)
12b	A	24	219–221[m]	83.72[i]	6.31	4.65	6.85[o] (m, 10.9, ArH, vinyl), 2.2 (s, 6, CH_3)
				83.49[j]	6.33		
13	A	60	148–149[m]	74.71[i]	7.39	5.49	7.15[l] (q, 4, ArH), 6.86 (s, 2, ArH), 4.91 (t, 1, HCOH),
				74.82[j]	7.41		3.83 (s, 3, OCH_3), 2.89 (m, 3, CH_2, OH), 2.45 (s, 3, CH_3)
14	A	38	144–146 (2.5)[q]	79.95[i]	8.39	11.66	6.7[l] (s, 4, ArH), 2.8 (s, 4, CH_2), 2.48 (s, 12, CH_3)
				79.58[j]	8.28	11.29	
17	A	32	170.5–172[m]	84.95[i]	6.19	4.13	7.34[l] (m, 15, ArH), 4.0 (s, 2, CH_2), 2.48 (m, 4, CH_3, OH)
17	B	57	169–171[m]	85.22[j]	6.23		
18	A	54	192.5–194[r]	72.60[i]	5.38	4.71	7.8[s] (m, 4, ArH), 7.33 (m, 1, ArH), 6.95 (s, 4, ArH),
				72.61[j]	5.47	4.90	5.07 (t, 0.90, CH), 3.6 (m, 1.9, CH_2), 2.6 (s, 3, CH_3)
19	A	80	107.5–109[m,t]	85.48[i]	6.30	3.83	7.5[g] (m, 14, ArH), 6.48 (s, 1, ArH), 3.35 (m, 5, CH_2,
				85.36[j]	6.39	3.80	CH), 2.35 (s, CH_3)
20	A	51	146.5–148[r]	84.78[i]	7.60	7.61	8.2[g] (m, 8, ArH), 7.8 (m, 2, ArH), 3.44 (m, 4, CH_2), 3.05
				84.90[j]	7.45		(s, 6, CH_3)
21	A	37	199–200.5[r]	84.61[i]	6.41	8.97	8.25[g] (m, 10, ArH), 4.06 (s, 4, CH_2), 3.15 (s, 6, CH_3)
				84.90[j]	6.37		
23	C	75	157–159[m]	84.95[i]	6.19	4.13	7.3[l] (m, 15, ArH), 3.98 (s, 2, CH_2), 2.65 (s, 3, CH_3)
				85.06[j]	6.22		
24	C	45	98.5–100[u]	72.60[i]	5.38	4.71	7.54[g] (m, 8, ArH), 6.89 (s, 1, ArH), 5.7 (broad s, 0.8,
				72.46[j]	5.33	4.78	OH), 5.1 (t, 1, OCH), 3.03 (d, 2, CH_2)
25	C	36	120–121.5[m,v]	85.48[i]	6.30	3.83	7.19[g] (m, 18, ArH, OH, vinyl), 3.42 (s, 2, CH_2), 2.44 (s,
				85.26[j]	6.20		3, CH_3)
27	A	89	145.5–148[m]	84.95[i]	6.19	4.13	7.72[l] (m, 15, ArH), 3.86 (s, 2, CH_2), 2.4 (s, 3, CH_3)
27	B	83	145.5–148[m]	84.61[j]	6.44		
27	C	96	145.5–148[m]				
29	B	87	150–152[m]	84.95[i]	6.19	4.13	7.7[l] (m, 15, ArH), 3.83 (s, 2, CH_2), 2.33 (s, 3, CH_3)
29	C	88	150–152[m]	85.02[j]	6.40		

[a] Method A refers to alkali amides in ammonia, method B to lithium diisopropylamide in ether–hexane, and method C to *n*-butyllithium in ether–hexane. [b] Though material balances are not reported, they were found to usually be high; for example, in the preparation of **4b**, *s*-collidine was recovered in 46% yield. [c] Picrate mp 140–141° [lit. mp 141–142°: E. Bamberger and O. Baudisch, *Chem. Ber.*, **42**, 3578 (1909)]. [d] No solvent. [e] Methiodide mp 205° (lit. mp 205°; see ref 15). [f] Picrate mp 116–117° (lit. mp 116–117°; see ref 15). [g] In carbon tetrachloride. [h] Picrate mp 113–115° [lit. mp 117°; F. Engelmann, *Justus Liebigs Ann. Chem.*, **231**, 44 (1885)]. [i] Calculated. [j] Found. [k] Solidified upon standing, mp 47–50°. [l] In deuteriochloroform. [m] Recrystallized from 95% ethanol. [n] This compound was obtained as a monohydrate. All attempts to remove the water were fruitless. [o] In DMSO-d_6. [p] Recrystallized from benzene. [q] Solidified upon standing, mp 103–104°. [r] Recrystallized from methanol. [s] In trifluoroacetic acid. [t] Ir (Nujol) 1675 cm^{-1} (C=O), no OH; 2,4-DNP mp 223–226.5°. [u] Recrystallized from ether. [v] Ir (Nujol) 3100 (broad, OH), 1355 (OH), and 1175 (OH) cm^{-1}; no carbonyl band.

the derivatives of pyridines and quinolines prepared by method A. The following specific examples illustrate the general procedures for alkylations, aldol condensations, and dimerizations, respectively.

A. Preparation of 2,6-Dimethyl-4-ethylpyridine (4b).—To a suspension of 0.3 mol of potassium amide in 700 ml of anhydrous liquid ammonia, prepared from 11.7 g (0.3 g-atom) of potassium metal,[14] was added dropwise a solution of 36.4 g (0.3 mol) of 2,4,6-collidine in 75 ml of anhydrous ether. The dark green mixture was stirred for 30 min; then it was treated with a solution of 42.6 g (0.3 mol) of methyl iodide in 50 ml of ether added during 10 min. After 30 min, the black mixture was neutralized by the addition of excess solid ammonium chloride and the solvents were allowed to evaporate. The residue was treated with 500 ml of water, and the solution was made basic with sodium hydroxide and extracted with ether. The extracts were combined, dried (Na_2SO_4), and concentrated to give crude product which, upon fractionation, afforded 19.5 g (47%) of 2,6-dimethyl-4-ethylpyridine (**4b**), bp 177–181° (760 mm), methiodide mp 205° (lit.[15] mp 205°).

B. Preparation of 2-Methyl-4-(diphenylhydroxymethyl)methylpyridine (11a).—To 0.053 mol of sodium amide in 250 ml of liquid ammonia[14] was added during 5 min a solution of 5.35 g (0.05 mol) of 2,4-lutidine in 50 ml of ether. After 30 min, the mixture was treated with a solution of 9.1 g (0.05 mol) of benzophenone in 50 ml of ether added during 5 min. The resulting mixture was stirred for 5 min, and then it was poured into 250 ml of magnetically stirred ammonia containing 20 g of ammonium chloride. Upon evaporation of the solvents, the residue was hydrolyzed by 100 ml of water. Some product, collected by vacuum filtration, was combined with that obtained by extracting the aqueous phase several times with ether and concentrating the combined extracts. There was thus obtained, after recrystallization from 95% ethanol, 6.4 g (47%) of **11a**, mp 175–177°.

C. Preparation of 4,4′-Bis-γ-collidine (14).—To 0.05 mol of potassium amide in 350 ml of liquid ammonia[14] was added dropwise a solution of 6.1 g (0.05 mol) of *s*-collidine in 30 ml of ether. After 1 hr, the mixture was treated with 7.9 g (0.05 mol) of solid potassium permanganate added in small portions. The resulting blue-green mixture was stirred for 1 hr, then neutralized with excess solid ammonium chloride. The solvents were allowed to evaporate and the residue was extracted overnight with benzene in a Soxhlet extractor. The crude product was recrystallized from aqueous ethanol to give 2.3 g (38%) of 4,4′-bis-γ-collidine (**14**). Distillation of the compound provided the analytical sample, bp 144–146° (2.5 mm), mp 103–104°.

Preparation of Pyridine and Quinoline Derivatives by Means of Lithium Diisopropylamide (Method B).—Table I lists compounds synthesized from alkylated pyridines and quinolines with various electrophiles effected by means of lithium diisopropylamide (method B). Two specific examples follow which may be considered general.

A. Preparation of 2,6-Dimethyl-4-*n*-pentylpyridine (7b).—To a solution of 5.0 g (0.05 mol) of diisopropylamine in 150 ml of anhydrous THF was added *via* a syringe 32.0 ml (0.05 mol) of 1.6 *M* *n*-butyllithium in hexane.[16] After 15 min, the solution was treated during 6 min with a solution of 6.1 g (0.05 mol) of *s*-collidine in 25 ml of THF. The resulting orange mixture was stirred for 1 hr, then treated with a solution of 6.85 g (0.05 mol) of *n*-butyl bromide in 40 ml of THF added during 6 min. After 1 hr, the mixture was cooled to 0° by an ice bath and hydrolyzed by the slow addition of 100 ml of water. Work-up of the reaction mixture and purification of the product were accomplished as described in Part A above.

B. Preparation of 2-(Diphenylhydroxymethyl)methyl-6-methylquinoline (29).—To 0.05 mol of lithium diisopropylamide in 150 ml of THF, prepared as in Part A, was added during 5 min a solution of 7.85 g (0.05 mol) of 2,6-dimethylquinoline in 50 ml of THF. After 1 hr, the resulting intense red solution was cooled to −78° by a Dry Ice–acetone bath, then treated with a solution of 9.1 g (0.05 mol) of benzophenone in 50 ml of THF added during 5 min. After 5 more min, the now green solution was poured into 300 ml of water and the reaction mixture was worked up as in Part B above to afford, after recrystallization from 95% ethanol, 12.1 g (72%) of **29**, mp 150–152°.

Preparation of Pyridine and Quinoline Derivatives by Means of *n*-Butyllithium (Method C).—Table I lists compounds prepared by interacting lithio derivatives of pyridine and quinoline with electrophiles (method C). Except for the absence of diisopropylamine and the use of ether instead of THF, the mechanics of this method are the same as those of Method B. The following preparation of alcohol **23** is illustrative.

Ethyl ether (125 ml) was treated *via* a syringe with 32.0 ml (0.05 mol) of 1.6 *M* *n*-butyllithium in hexane[16] followed immediately with a solution of 7.85 g (0.05 mol) of 2,4-dimethylquinoline in 50 ml of ether added during 5 min. After 1 hr, the mixture was cooled to −78° by a Dry-Ice–acetone bath, then treated during 5 min with a solution of 9.1 g (0.05 mol) of benzophenone in 50 ml of ether. After 5 min, the mixture was poured into 300 ml of water and worked up as above to give 12.0 g (75%) of 2-(diphenylhydroxymethyl)methyl-4-methylquinoline (**23**), mp 158–159.5°.

Preparation of Authentic 2,6-Dimethyl-4-ethylpyridine (4b).—The method of Balaban and Nenitzescu was employed.[17] Acetyl chloride (314.0 g, 4.0 mol), cooled to 0°, was treated with 267.0 g (2.0 mol) of aluminum chloride added with stirring. The thick mass was mixed with 140.3 g (2.0 mol) of 2-methyl-2-butene at 0–10° and stirred for 2 hr while warming to room temperature. The reaction mixture was poured into 2 l. of ice-water and the aqueous solution was made strongly basic with concentrated ammonium hydroxide. The resulting gelatinous yellow mass of aluminum salts was extracted several times with benzene, the combined extracts were concentrated, and the resulting dark red residue was distilled to afford 6.7 g (2.5%) of 2,6-dimethyl-4-ethylpyridine (**4b**): bp 180–183° (760 mm); methiodide mp 205° (lit.[15] mp 205°); nmr (neat) δ 6.75 (s, 2, ArH), 2.45 (q, 2, CH_3CH_2), 2.4 (s, 6, CH_3), and 1.1 (t, 3, CH_3CH_2).

Registry No.—**1a**, 108-47-4; **1b**, 108-75-8; **4a**, 536-88-9; **4b**, 36917-36-9; **5a**, 2150-18-7; **5b**, 1124-35-2; **6a**, 28973-18-4; **6b**, 3044-78-8; **7a**, 36917-41-6; **7b**, 36917-42-7; **8a**, 36917-43-8; **8b**, 36917-44-9; **9**, 36917-45-0; **10**, 36917-46-1; **11a**, 36917-47-2; **11b**, 36917-48-3; **12a**, 36917-49-4; **12b**, 36917-50-7; **13**, 36917-51-8; **14**, 36917-52-9; **17**, 36917-53-0; **18**, 36917-54-1; **19**, 36917-55-2; **20**, 36917-56-3; **21**, 36917-57-4; **23**, 36917-58-5; **24**, 36917-59-6; **25**, 36917-60-9; **27**, 36917-61-0; **29**, 36917-62-1; 2,4-dimethylquinoline, 1198-37-4.

(14) See C. R. Hauser, F. W. Swamer, and J. T. Adams, *Org. React.*, **8**, 122 (1954).

(15) A. Eckert and S. Loria, *Monatsh. Chem.*, **38**, 226 (1917).

(16) Supplied by the Foote Mineral Co., Exton, Pa.

(17) A. T. Balaban and C. D. Nenitzescu, *Justus Liebigs Ann. Chem.*, **625**, 74 (1959).