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Studies on Pyrimidine Derivatives. V.[1] Reaction of 2,4-Dimethylazines with Ethyl Benzoate under Basic Conditions

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Benzoylation of 2,4-dimethyl- (Ia), 2,4,6-trimethyl-pyrimidine (Ib), 2,4-dimethylquinazoline (Ic), 2,4-dimethyl- (Id), 2,4,6-trimethyl-pyridine (Ie), and 2,4-dimethylquinoline (If) with ethyl benzoate under basic conditions were performed. In analogy with the nitrosation with ethyl nitrite, methyl groups on the 4-position of IIa—f were preferentially benzoylated to give 4-phenacyl derivatives. Structures of all the products were determined by chemical derivatization.

Keywords——benzoylation of 2,4-dimethyldiazines; 4-phenacylpyridines; 4-phenacylpyrimidines; 2-methyl-4-phenacylquinoline; 2-methyl-4-phenacylquinazoline; 4-ethyl-2-methylpyrimidines

In a previous work of this series,[3] the authors reported that 2,4-dimethylpyrimidine was nitrosated with ethyl nitrite and potassium amide in liquid ammonia to give 2-methylpyrimidine-4-aldoxime as the sole product. Similar results were obtained in all cases of pyridine, quinoline, pyrimidine and quinazoline homologues containing 2,4-dimethyl groups giving 4-aldoximes preferentially.

In order to reconfirm relative reactivity of the methyl groups, benzoylation of 2,4-dimethylazines with ethyl benzoate was examined under basic conditions. And it was concluded that, in analogy with the nitrosation, the benzoylation of 2,4-dimethylazines occurred at 4-methyl groups.

The reactivity of 2,4-dimethyldiazine series was at first tested. A benzene solution of 2,4-dimethylpyrimidine (Ia) and ethyl benzoate was heated in the presence of potassium ethoxide to give α-(2-methyl-4-pyrimidinyl)acetophenone (IIa). In general, the chemical

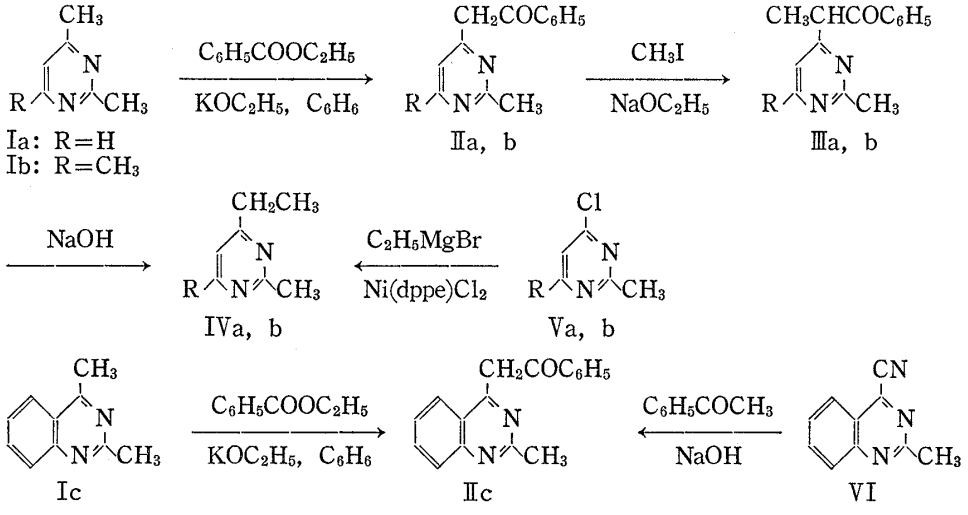

Chart 1

1) Part IV: T. Sakamoto, K. Kanno, T. Ono, and H. Yamanaka, *Heterocycles*, **6**, 525 (1977).
2) Location: *Aobayama, Sendai 980, Japan.*
3) H. Yamanaka, H. Abe, T. Sakamoto, H. Hiranuma, and A. Kamata, *Chem. Pharm. Bull.* (Tokyo), **25**, 1821 (1977).

shift of the 2-methyl group on the pyrimidine ring is close to that of the 4-methyl group. The nuclear magnetic resonance (NMR) spectra, therefore, is not enough for the structural assignment of the product.

The structural determination of IIa by chemical reactions was performed as follows: IIa was treated with methyl iodide to give α-(2-methyl-4-pyrimidinyl)propiophenone (IIIa), whose NMR spectrum reveals a doublet (1.58 ppm, 3H, J=7.0 Hz) assignable to a methyl group on the side chain, along with a singlet (2.76 ppm, 3H, $-CH_3$). Alkaline hydrolysis of IIIa afforded an oily product (IVa) which was identical with authentic specimen of 4-ethyl-2-methylpyrimidine. The authentic specimen of IVa was synthesized by the coupling reaction[4] of ethylmagnesium bromide with 4-chloro-2-methylpyrimidine in the presence of catalytic amount of dichloro[1,2-bis(diphenylphosphino)ethane]nickel II (Ni(dppe)Cl_2).

Following the similar fashion given for Ia, 2,4,6-trimethylpyrimidine (Ib) was allowed to react with ethyl benzoate to give α-(2,6-dimethyl-4-pyrimidinyl)acetophenone (IIb)[5] whose structure was also determined as shown in Chart 1.

2,4-Dimethylquinazoline (Ic) seemed to be very reactive toward this benzoylation and was converted to 4-phenacyl derivative (IIc) in good yield under milder conditions. According to the method reported by Higashino,[6] 2-methylquinazoline-4-carbonitrile (VI)[3] was allowed to stand with acetophenone and 50% sodium hydroxide yielding α-(2-methyl-4-quinazolinyl)acetophenone which was identical with IIc.

Then the reactivity of the 2,4-dimethylmonoazine series were investigated. Although 2,4-dimethylpyridine (Id) was recovered under identical conditions given for Ia, b, the reaction of Id with ethyl benzoate in the presence of potassium amide in liquid ammonia afforded α-(2-methyl-4-pyridyl)acetophenone (IId)[7] in a yield of 20%. Methylation and subsequent hydrolysis of IId gave an oily product (IVd) which was identical with authentic 4-ethyl-2-methylpyridine prepared by the following reactions. 4-Ethylpyridine was heated with ammonium peroxydisulfate in aqueous methanol[8] to give 4-ethyl-2-pyridinemethanol (VIII). On treatment with phosphoryl chloride, VIII was transformed into 2-chloromethyl-4-ethylpyridine (IX). Hydrogenolysis of IX over palladium-charcoal afforded IVd.

Similarly, the benzoylation of 2,4,6-trimethylpyridine (Ie) gave α-(2,6-dimethyl-4-pyridyl)acetophenone (IIe) of which structure was proved as shown in Chart 2. 2,4-Dimethylquinoline (If) was also benzoylated to α-(2-methyl-4-quinolyl)acetophenone (IIf). The infrared (IR) spectrum of IIf shows a strong absorption band assignable to a carbonyl group at 1695 cm^{-1}. Hamana, *et al.*[9] reported that in the IR spectrum of α-(2-quinolyl)acetophenone no band due to the carbonyl group is observed at 1700 cm^{-1} region, which is caused by the tautomerism of the 2-phenacyl group. On the basis of these spectral data, it could be presumed that IIf contained a phenacyl group at the 4-position. This presumption was supported by the following chemical determination. When IIf was reduced by the Wolff-Kishner reaction, 2-methyl-4-phenethylquinoline (XI) was obtained which was identical with the authentic specimen prepared by the homolytic phenethylation[10] of 2-methylquinoline.

4) K. Tamano, S. Kodama, I. Nakajima, T. Nakatsuka, A. Minato, and M. Kumada, Abstracts of the 8th Congress of Heterocyclic Chemistry, Kyoto, Japan, 1975, p. 174.
5) H.R. Sullivan and W.T. Caldwell have already reported the reaction of Ib with ethyl benzoate to give IIb. However, they did not determined the structure of the product (IIb) by chemical reactions. [*J. Am. Chem. Soc.*, 77, 1159 (1955)].
6) T. Higashino, *Chem. Pharm. Bull.* (Tokyo), **10**, 1048 (1962).
7) R. Levine, D.A. Dinning, and W.M. Kadunce reported the benzoylation of Id with ethyl benzoate to give IId. However, as well as the case of IId, some ambiguity still remained in their conclusion on the structure of the product (IId). [*J. Org. Chem.*, **39**, 3834 (1974)].
8) W. Buratti, G.P. Gardini, J. Minisci, F. Bertini, R. Galli, and M. Perchinunno, *Tetrahedron*, **27**, 3655 (1971).
9) M. Yamazaki, K. Noda, and M. Hamana, *Chem. Pharm. Bull.* (Tokyo), **18**, 908 (1970).
10) F. Minisci, R. Bernardi, R. Galli, and M. Perchinunns, *Tetrahedron*, **27**, 3585 (1971).

In conclusion, those experiments described above, showed not merely the preferential activity of 4-methyl groups on the azine rings under basic conditions, but the application for the syntheses of the derivatives containing a phenacyl group at the 4-position of aromatic azine rings.

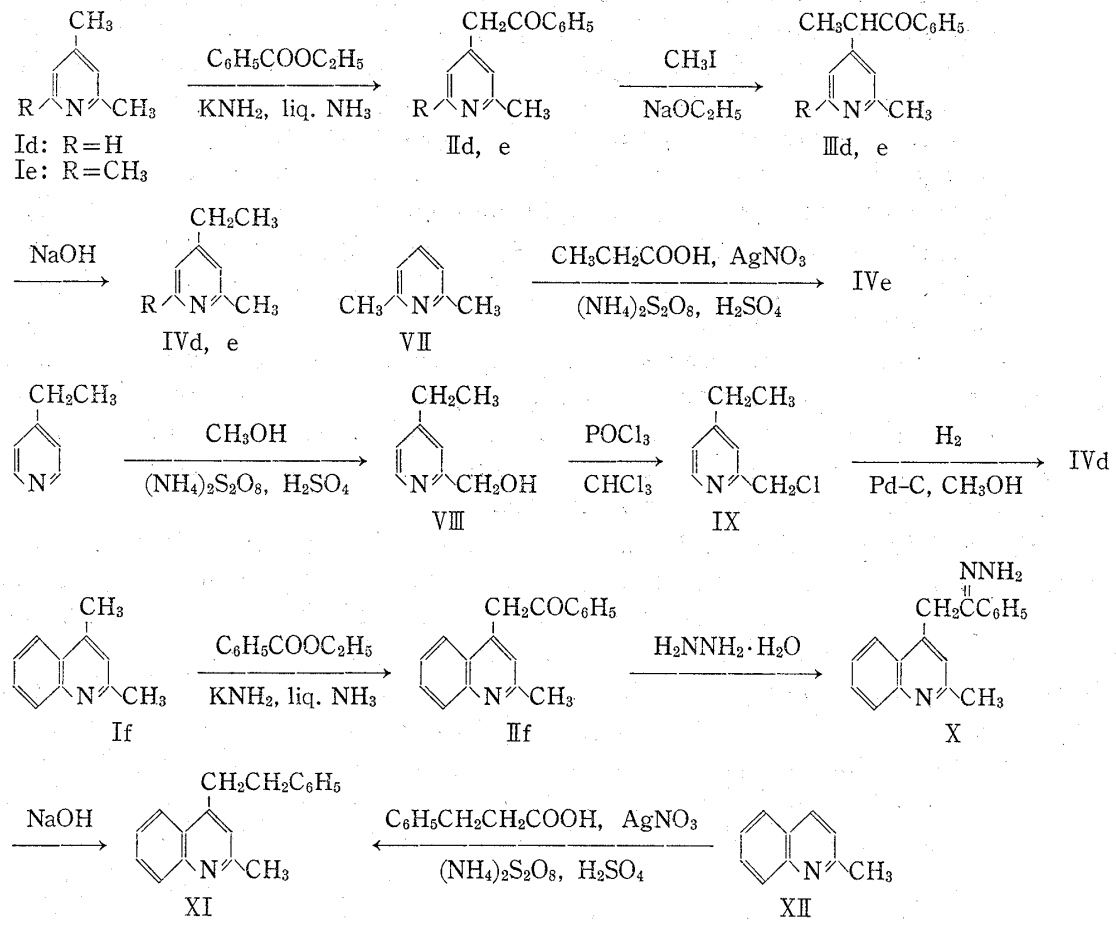

Chart 2

Experimental[11]

α-(2-Methyl-4-pyrimidinyl)acetophenone (IIa)[12]——To a solution of Ia (1.08 g, 0.01 mol) and ethyl benzoate (3.0 g, 0.02 mol) in dry C_6H_6 (10 ml), was added powdered KOEt prepared from metallic potassium (0.78 g, 0.02 g·atom) and abs. EtOH (20 ml). The mixture was refluxed for 72 hr with stirring and extracted with 20% HCl. The HCl layer was made alkaline with $NaHCO_3$ (solid) and extracted with $CHCl_3$. The $CHCl_3$ extract was passed through an alumina column (C_6H_6) for decolorization. Recrystallization from ether gave pale yellow needles. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1630. NMR ($CDCl_3$): 2.61 (s, 2.25H, $-CH_3$), 2.70 (s, 0.75H, $-CH_3$), 4.38 (s, 0.5H, $-CH_2-$), 5.97 (s, 0.75H, $-CH=C\langle$), 6.66 (d, 0.75H, $J=6.0$, pyrimidine ring proton), 7.12 (d, 0.25H, $J=6.0$, pyrimidine ring proton), 7.30—8.05 (m, 5H, C_6H_5), 8.21 (d, 0.75H, $J=6.0$, pyrimidine ring proton), 8.56 (d, 0.25H, $J=6.0$, pyrimidine ring proton), 15.30—15.62 (b, 0.75H, NH or OH).

α-(2,6-Dimethyl-4-pyrimidinyl)acetophenone (IIb)[12]——According to the similar manner described above, Ib (1.22 g, 0.01 mol) was treated with ethyl benzoate (3.0 g, 0.02 mol) to give a pale yellow liquid.

11) All melting points and boiling points are uncorrected. The IR spectra were taken with a JASCO IRA-1 spectrometer and the NMR spectra with a Hitachi-Perkin Elmer R-20 spectrometer. The chemical shifts are expressed by the ppm downfield from tetramethylsilane used as an internal standard and the coupling constants by Herz (Hz). Following abbreviations are used: singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), and broad (b).

12) The spectral data of IIa, b suggested that these compounds were consisted of two kinds of tautomers. On the contrary, any equilibrium of the tautomers was not observed on IIc. Further assignment on the structure of the tautomers, however, has not yet been performed.

IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1680, 1630. NMR ($CDCl_3$): 2.34 (s, 2.25H, $-CH_3$), 2.42 (s, 0.75H, $-CH_3$), 2.56 (s, 2.25H, $-CH_3$), 2.65 (s, 0.75H, $-CH_3$), 4.31 (s, 0.5H, $-CH_2-$), 5.85 (s, 0.75H, $-CH=C\langle$), 6.48 (s, 0.75H, pyrimidine ring proton), 6.92 (s, 0.25H, pyrimidine ring proton), 7.2—7.5 (m, 3H, $-C_6H_5$), 7.6—8.1 (m, 2H, $-C_6H_5$), 13.5—15.5 (b, 0.75H, NH or OH).

α-(2-Methyl-4-quinazolinyl)acetophenone (IIc)[12]——To a dry C_6H_6 solution of Ic (1.58 g, 0.01 mol) and ethyl benzoate (3.0 g, 0.02 mol), was added powdered KOEt prepared from metallic potassium (0.78 g, 0.02 g·atom) and abs. EtOH (20 ml). The mixture was heated at 80° for 24 hr, and worked up in a similar manner as for the preparation of IIa. Recrystallization from acetone gave pale yellow needles. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1608. NMR ($CDCl_3$): 2.51 (s, 3H, $-CH_3$), 6.66 (s, 1H, $-CH=C\langle$). 7.31—8.1 (m, 9H, ring proton), 14.6—15.5 (b, 1H, NH or OH).

α-(2-Methyl-4-pyridyl)acetophenone (IId)——In a three necked flask fitted with a dry-ice condenser and a mechanical stirrer, were placed liq. NH_3 (150 ml), metallic potassium (1.30 g, 0.033 g·atom) and a catalytic amount of anhyd. $FeCl_3$ to prepare KNH_2 in liquid NH_3. After adding Id (3.21 g, 0.03 mol), this solution was stirred for 1 hr at a boiling point of liq. NH_3 (−33°). Then ethyl benzoate (6.0 g, 0.04 mol) was dropwise added and the resulting solution was stirred for additional 2 hr at −33°. The solution was neutralized with NH_4Cl (solid) and concentrated to dryness. The residue was treated with 10% HCl and the HCl layer was made alkaline with $NaHCO_3$ (solid) followed by extracting with ether. After removal of ether and the starting material (Id) under reduced pressure, the residue was purified as described in the case of IIa and recrystallized from ether to give pale yellow needles. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1695. NMR ($CDCl_3$): 2.57 (s, 3H, $-CH_3$), 4.24 (s, 2H, $-CH_2-$), 7.10 (s, 1H, pyridine ring proton), 7.30—7.70 (m, 4H, pyridine and benzene ring proton), 7.90—8.20 (2H, C_6H_5), 8.50 (d,d, 1H, $J=4.5$, 1.5, pyridine ring proton).

α-(2,6-Dimethyl-4-pyridyl)acetophenone (IIe)——Compound Ie (4.63 g, 0.03 mol) was treated with ethyl benzoate (6.0 g, 0.04 mol) and KNH_2 in liquid NH_3. Recrystallization from ether gave pale yellow needles. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1695. NMR ($CDCl_3$): 2.49 (s, 6H, $2\times-CH_3$), 4.18 (s, 2H, $-CH_2-$), 6.87 (s, 2H, pyridine ring proton), 7.4—7.65 (m, 3H, C_6H_5), 7.2—8.1 (m, 2H, C_6H_5).

α-(2-Methyl-4-quinolyl)acetophenone (IIf)——Compound If (4.71 g, 0.03 mol) was treated with ethyl benzoate (6.0 g, 0.04 mol) and KNH_2 (0.033 mol) in liquid NH_3. Recrystallization from acetone gave pale yellow needles. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1695. NMR ($CDCl_3$): 2.70 (s, 3H, $-CH_3$), 4.66 (s, 2H, $-CH_2-$), 7.16 (s, 1H, quinoline ring proton), 7.4—8.2 (m, 9H, quinoline and benzene ring proton). Hydrazone: mp 171—174° (EtOH). Melting points, yields, and the results of elemental analysis of IIa—f were summerized in Table I.

Table I. Melting Points, Yields and Elemental Analyses of IIa—f

Compd.	mp or bp (mmHg) (°C)	Yield (%)	Formula	Analysis (%) Calcd. C	H	N	Found C	H	N
IIa	74— 76	39	$C_{13}H_{12}N_2O$	73.56	5.70	13.24	73.53	5.76	13.64
IIb	[160—162(3)]	34	$C_{14}H_{14}N_2O$	74.31	6.24	12.38	74.40	6.51	12.05
IIc	123—125	62	$C_{17}H_{14}N_2O$	77.84	5.38	10.68	77.43	5.64	10.40
IId	79—81	20	$C_{14}H_{13}NO$	79.59	6.20	6.63	79.54	6.32	6.79
IIe	77—79	25	$C_{15}H_{15}NO$	79.97	6.71	6.22	79.91	6.77	6.06
IIf	159—161	32	$C_{18}H_{15}NO$	82.73	5.79	5.36	82.97	5.94	5.32

Methylation of α-Substituted Acetophenones (IIa, b, d, e) with Methyl Iodide——General Procedure: To a solution of NaOEt in EtOH (prepared from 0.002 g·atom of metallic sodium and 2 ml of abs·EtOH) were dissolved IIa, b, d, e (0.002 mol) and CH_3I (0.004 mol). The solution was heated for 1—2 hr on a boiling water bath. Then the solution was concentrated to dryness under reduced pressure. The residue was dissolved in $CHCl_3$ and the $CHCl_3$ layer was washed with a small amount of water. After removal of $CHCl_3$, the crude product was purified by vacuum distillation or recrystallization.

α-(2-Methyl-4-pyrimidinyl)propiophenone (IIIa): pale yellow liquid, yield 35%.

α-(2,6-Dimethyl-4-pyrimidinyl)propiophenone (IIIb): pale yellow needles (petr. ether), yield 60%.

α-(2-Methyl-4-pyridyl)propiophenone (IIId): pale yellow liquid, yield 71%.

α-(2,6-Dimethyl-4-pyridyl)propiophenone (IIIe): pale yellow needles (ether), yield 54%.

The physical constants, spectral data and the results of elemental analysis of IIIa, b, d, e were summarized in Table II.

Alkaline Hydrolysis of α-Substituted Propiophenones (III)——General Procedure: A mixture of IIIa, b, d, e (0.002 mol), 30% NaOH (5 ml) and EtOH (5 ml) was refluxed for 3 hr. EtOH was removed under reduced pressure and anhyd. K_2CO_3 (*ca.* 1 g) was added to the residue. The resulting solution was extracted with ether. The extract was purified by vacuum distillation to give IV. Benzoic acid was obtained from the aqueous layer by usual work-up.

Table II. Physical Constant, Spectral Data and Elemental Analyses of III

Compd.	mp or bp (mmHg) (°C)	IR $\nu_{max}^{CHCl_3}$ cm^{-1} >C=O	NMR[a] $\underline{CH_3}CH<$	NMR[a] $CH_3\underline{CH}<$	Formula	Analysis (%) Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
IIIa	165—170 (16)	1695	1.58 (d, J=7.0)	4.84 (q, J=7.0)	$C_{14}H_{14}N_2O$	74.31	6.24	12.38	74.09	6.47	12.62
IIIb	96—96.5	1697	1.53 (d, J=7.0)	4.78 (q, J=7.0)	$C_{15}H_{16}N_2O$	74.97	6.71	11.66	75.25	6.82	11.73
IIId	169—171 (16)	1695	1.51 (d, J=6.5)	4.62 (q, J=6.5)	$C_{15}H_{15}NO$	79.97	6.71	6.22	78.19	6.71	6.16
IIIe	81—83	1695	1.48 (d, J=7.0)	4.57 (q, J=7.0)	$C_{16}H_{17}NO$	80.30	7.16	5.88	80.14	6.99	5.88

a) The chemical shifts in $CDCl_3$ are expressed in ppm downfield from tetramethylsilane as an internal standard and the coupling constants in Hz.

Table III. Physical Constants, Spectral Data and Elemental Analysis of IV

Compd.	bp (°C) (mmHg)	mp (°C) (Picrate)	NMR[a] $\underline{CH_3}CH_2-$	NMR[a] $CH_3\underline{CH_2}-$	Formula (Picrate)	Analysis (%) Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
IVa	57—58 (16)	111—112.5	1.26 (t, J=7.0)	2.67 (q, J=7.0)	$C_{13}H_{13}N_5O_7$	44.45	3.73	19.94	44.73	3.73	19.94
IVb	66 (12)	85—87	1.22 (t, J=7.0)	2.60 (q, J=7.0)	$C_{14}H_{15}N_5O_7$	46.03	4.14	19.17	46.13	4.07	19.14
IVd	62—63 (12)	140—142	1.20 (t, J=7.0)	2.53 (q, J=7.0)	$C_{14}H_{14}N_4O_7$	48.00	4.03	16.00	47.73	4.23	16.12
IVe	95—97 (50)	94—96	1.17 (t, J=7.0)	2.48 (q, J=7.0)	$C_{15}H_{16}N_4O_7$	49.45	4.43	15.38	49.24	4.45	15.16

a) The chemical shifts in $CDCl_3$ are expressed in ppm downfield from tetramethylsilane as an internal standard and the coupling constants in Hz.

4-Ethyl-2-methylpyrimidine (IVa): colorless liquid, yield 24%, picrate, yellow needles (ether), mp 111—112.5°.

4-Ethyl-2,6-dimethylpyrimidine (IVb): colorless liquid, yield 80%, picrate, yellow needles (ether), mp 85—87°.

4-Ethyl-2-methylpyridine (IVd): colorless liquid, yield 33%, picrate, yellow needles (EtOH), mp 140—142°.

4-Ethyl-2,6-dimethylpyridine (IVe): coreless liquid, yield 33%, picrate, yellow needles (EtOH), mp 94–96°.

The physical constants, spectral data, and the results of elemental analysis of IV were summerized in Table III.

4-Ethyl-2-methylpyrimidine (IVa) from 4-Chloro-2-methylpyrimidine (Va)——An ethereal solution of Va (0.7 g, 0.0054 mol), EtMgBr (prepared from 0.01 mol of EtBr) and Ni(dppe)Cl_2 (25 mg) was heated for 24 hr with stirring. After cooling, 10% HCl was added to the reaction mixture. The HCl layer was neutralized with K_2CO_3 (solid) and extracted with ether. The extract was distilled under reduced pressure to give a colorless liquid (0.52 g, 72%), bp 57—58° (16 mmHg). This compound was identical with IVa obtained from IIIa.

4-Ethyl-2,6-dimethylpyrimidine (IVb) from 4-Chloro-2,6-dimethylpyrimidine (Vb)——Vb (2.9 g, 0.02 mol), EtMgBr (0.04 mol) and Ni(dppe)Cl_2 (108 mg) were treated as above to give colorless liquid (1.7 g, 63%), bp 66—67° (12 mmHg). This compound was identical with IVb obtained from IIIb.

***α*-(2-Methyl-4-quinazolinyl)acetophenone (IIc) from 2-Methylquinazoline-4-carbonitrile (VI)**——A mixture of acetophenone (1.7 ml), 2-methylquinazoline-4-carbonitrile (0.17 g, 0.01 mol) and 50% NaOH (0.3 ml) was stirred at 20° for 2.5 hr. The resulting solution was treated with 10% HCl to afford precipitate. The precipitate was collected, washed with ether and dissolved in H_2O. The H_2O solution was made alkaline with $NaHCO_3$ (solid) and extracted with $CHCl_3$. After removal of $CHCl_3$, the residue was recrystallized

from acetone to give pale yellow needles (0.12 g, 45%), mp 123—125°. This compound was identical with IIc obtained from the benzoylation of Ic.

4-Ethyl-2,6-dimethylpyridine (IVe) from 2,6-Dimethylpyridine (VII)——To a warm (70—75°) solution of 2,6-dimethylpyridine (1.07 g, 0.01 mol), propionic acid (2.96 g, 0.04 mol) and $AgNO_3$ (0.17 g, 0.001 mol) in 10% H_2SO_4 (10 ml), a solution of $(NH_4)_2S_2O_8$ (2.3 g, 0.01 mol) in H_2O (10 ml) was dropwise added, and the resulting mixture was warmed at 70° for additional 1 hr. The mixture was made alkaline with conc. NH_4OH and extracted with $CHCl_3$. The extract was purified by vacuum distillation to give a colorless liquid (0.23 g, 17%), bp 95—97° (50 mmHg). This compound was identical with IVe obtained from IIIe.

4-Ethyl-2-pyridinemethanol (VIII)——A solution of 4-ethylpyridine (10.7 g, 0.1 mol), $(NH_4)_2S_2O_8$ (45.6 g, 0.2 mol), and conc. H_2SO_4 (4.5 ml) in aqueous MeOH (H_2O 70 ml, MeOH 150 ml) was refluxed for 24 hr. The mixture was concentrated to 100 ml, neutralized with 3 N NaOH and extracted with $CHCl_3$. The extract was distilled under reduced pressure to give a colorless liquid (2.1 g, 15%), bp 132—133° (15 mmHg). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3370. NMR ($CDCl_3$): 1.22 (t, 3H, J=7.0, $\underline{CH_3}CH_2$–), 2.65 (q, 2H, J=7.0, $CH_3\underline{CH_2}$–), 3.95—4.30 (b, 1H, –OH), 4.72 (s, 2H, –$\underline{CH_2}$OH), 6.95—7.20 (m, 2H, pyridine ring proton), 8.40 (d, 1H, J=5.0, pyridine ring proton). *Anal.* Calcd. for $C_8H_{11}NO$: C, 70.04; H, 8.08; N, 10.21. Found: C, 69.72; H, 8.06; N, 10.19.

2-Chloromethyl-4-ethylpyridine (IX)——To a solution of $POCl_3$ (5 ml) in $CHCl_3$ (5 ml) was added VIII (1.3 g, 0.01 mol) under ice-cooling and the mixture was refluxed for 3 hr. After removal of $CHCl_3$ and $POCl_3$ under reduced pressure, the residue was poured into ice-cooled conc. NH_4OH. The H_2O layer was extracted with ether and the extract was distilled under reduced pressure to give a colorless liquid (1.4 g, 93%), bp 102° (3 mmHg). NMR ($CDCl_3$): 1.25 (t, 3H, J=7.0, $\underline{CH_3}CH_2$–), 2.63 (q, 2H, J=7.0, $CH_3\underline{CH_2}$–), 4.54 (s, 2H, –CH_2Cl), 6.96 (d, 1H, J=5.0, pyridine ring proton), 7.26 (s, 1H, pyridine ring proton), 8.30 (d, 1H, J=5.0, pyridine ring proton). *Anal.* Calcd. for $C_8H_{10}ClN$: C, 61.74; H, 6.43; Cl, 22.83; N, 9.00. Found: C, 61.53; H, 6.61; Cl, 22.56; N, 8.81.

Hydrogenolysis of 2-Chloromethyl-4-ethylpyridine (IX)——To a solution of IX (1.25 g, 0.008 mol) in MeOH (10 ml), 5% Pd-charcoal was added and the mixture was shaken under H_2 stream (1 atm.) at room temperature. After H_2 absorption ceased (180 ml), the catalyst was removed by filtration and the solvent was removed under reduced pressure. The residue was made alkaline with 1 N $NaHCO_3$ and extracted with ether. The extract was distilled under reduced pressure to afford a colorless liquid (0.8 g, 82%), bp 69° (16 mmHg). This compound was identical with IVd obtained from IIId.

Wolff-Kishner Reduction of α-(2-Methyl-4-quinolyl)acetophenone (IIf)——Hydrazone of IIf (0.275 g, 0.001 mol) and NaOH (0.2 g, 0.005 mol) were dissolved in triethyleneglycol (3 ml) and the mixture was refluxed for 6 hr. After cooling, H_2O (3 ml) was added and the H_2O solution was extracted with C_6H_6. The C_6H_6 layer was extracted with 10% HCl, the HCl layer was made alkaline with 3 N Na_2CO_3 and the separated oil was extracted with ether. After removal of the solvent, the residue was recrystallized from petr. ether to give colorless prisms (0.11 g, 44%), mp 61—63°. NMR (CCl_4): 2.58 (s, 3H, CH_3–), 2.76—3.38 (m, 4H, –$\underline{CH_2}\underline{CH_2}$–), 6.90 (s, 1H, quinoline ring proton), 7.12 (s, 5H, C_6H_5), 7.22—8.05 (m, 4H, quinoline ring proton). *Anal.* Calcd. for $C_{18}H_{17}N$: C, 87.41; H, 6.93; N, 5.66. Found: C, 87.22; H, 6.87; N, 5.73.

2-Methyl-4-phenethylquinoline (XI) from 2-Methylquinoline (XII)——To a warm (70—75°) solution of 2-methylquinoline (1.43 g, 0.01 mol), 3-phenylpropionic acid (5.7 g, 0.038 mol) and $AgNO_3$ (0.17 g, 0.001 mol) in 10% H_2SO_4, a solution of $(NH_4)_2S_2O_8$ (2.3 g, 0.01 mol) in H_2O (10 ml) was dropwise added and the mixture was treated as described in the case of VI. The crude product was decolorlized by passing through an alumina column (ether) and recrystallized from petr. ether to give colorless prisms (0.7 g, 67%), mp 61—62.5°. This compound was identical with XI obtained by the Wolff-Kishner reduction of X.

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