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Studies on Tertiary Amine Oxides. XLIV.[1] Reactions of Aromatic N-Oxides with N-Acylmethylpyridinium Salts in the Presence of Acylating Agents

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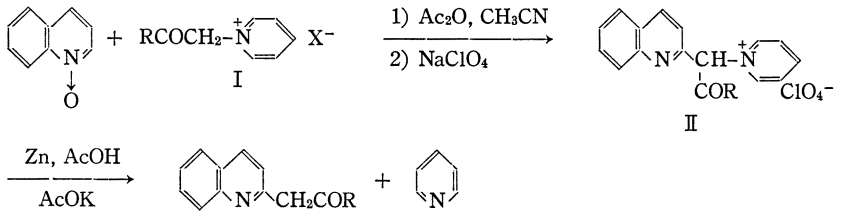
N-Acylmethylpyridinium salts (Ia—c) were applied to some pyridine and quinoline N-oxides in the presence of acetic anhydride. 4-Methoxyquinoline 1-oxide (IV) readily reacted with Ia—c to give N-(α-acyl-4-methoxy-2-quinolylmethyl)pyridinium compounds (Va—c) in good yields. Whereas N-oxides of lepidine (VIII), pyridine (XII) and 4-picoline (XV) reacted similarly with N-acetonylpyridinium chloride (Ia). Quinaldine and 2-picoline N-oxides did not react even with Ia.

The pyridinium salts thus obtained afforded smoothly the corresponding quinaldyl (XVIIIa,b; XIX) or α-picolyl ketones (XXI, XXII) upon treatment zinc powder and acetic acid.

The tautomeric structures of the quinaldyl ketones (XVIIIa,b; XIX) were discussed.

Previous papers of this series[3] have shown that quinoline 1-oxide reacts with N-acylmethylpyridinium salts (I) in the presence of acetic anhydride to give N-(α-acyl-2-quinolylmethyl)pyridinium salts (II) in good yields, and the reduction of II with zinc powder and acetic acid affords the corresponding quinaldyl ketones(III). These reactions have opened a new route to the preparation of various quinaldyl ketones, III, from quinoline 1-oxide.



III: R=Me, C_6H_5, *p*-Cl-C_6H_4, *etc.*

In exploring the scope of reaction we examined the reaction of some derivatives of quinoline and pyridine N-oxides with N-acylmethylpyridinium salts in the presence of acetic anhydride and also the reduction of the resultant products with zinc powder and acetic acid.

The Reaction of Aromatic N-Oxides with Pyridinium Salts

At first, the reaction of 4-methoxyquinoline 1-oxide(IV) was carried out. When a solution of IV, N-acetonylpyridinium chloride (Ia)[4] and acetic anhydride in acetonitrile was refluxed for 5 hours and treated with sodium perchlorate, N-(α-acetyl-4-methoxy-2-quinolylmethyl)pyridinium perchlorate (Va) was obtained as yellow needles of mp 230—232°(decomp.) in 66% yield.

1) Part XLIII: M. Hamana and I. Kumadaki, *Chem. Pharm. Bull.* (Tokyo), **19**, 1669 (1971).
2) Location: *a*) *Nanakuma. Nishi-ku, Fukuoka*; *b*) *Katakasu, Higashi-ku, Fukuoka.*
3) *a*) M. Yamazaki, K. Noda, and M. Hamana, *Chem. Pharm. Bull.* (Tokyo), **18**, 901 (1970); *b*) *Idem, ibid.*, **18**, 908 (1970).
4) F. Kröhnke, *Ber.*, **66**, 604 (1933).

Similar reactions with N-phenacylpyridinium-(Ib) and N-(*p*-methylphenacyl)pyridinium iodides (Ic)[5] gave N-(α-benzoyl-4-methoxy-2-quinolymethyl)- and N-(α-*p*-methylbenzoyl-4-methoxy-2-quinolylmethyl)pyridinium perchlorates (Vb and Vc) in 55 and 66% yields, respectively. The structures of Va—c were evident from the elementary analysis, the infrared (IR) spectra and their conversion by alkaline hydrolysis to N-(4-methoxy-2-quinolylmethyl) pyridinium perchlorate (VI), colorless plates of mp 197—198°, and the corresponding carboxylic acids; VI was proved to be identical with an authentic sample prepared from 4-methoxyquinaldine by the Ortoleva–King reaction[6] followed by treating the resulting N-(4-methoxy-2-quinolymethyl)pyridinium iodide (VII) with sodium perchlorate.

Lepidine 1-oxide (VIII) reacted with Ia in the same manner to give N-(α-acetyl-4-methyl-2-quinolylmethyl)pyridinium perchlorate (IX), yellow needles of mp 197—199°, in 43% yield. The alkaline hydrolysis of IX yielded N-(4-methyl-2-quinolylmethyl)pyridinium perchlorate (X), which was proved identical with an authentic sample obtained from 2-chloromethyllepidine (XI)[7] as shown in Chart 1.

On the other hand the attempted reaction of VIII with Ib failed, Ib being recovered as its perchlorate (Id) upon treating the reaction mixture with sodium perchlorate.

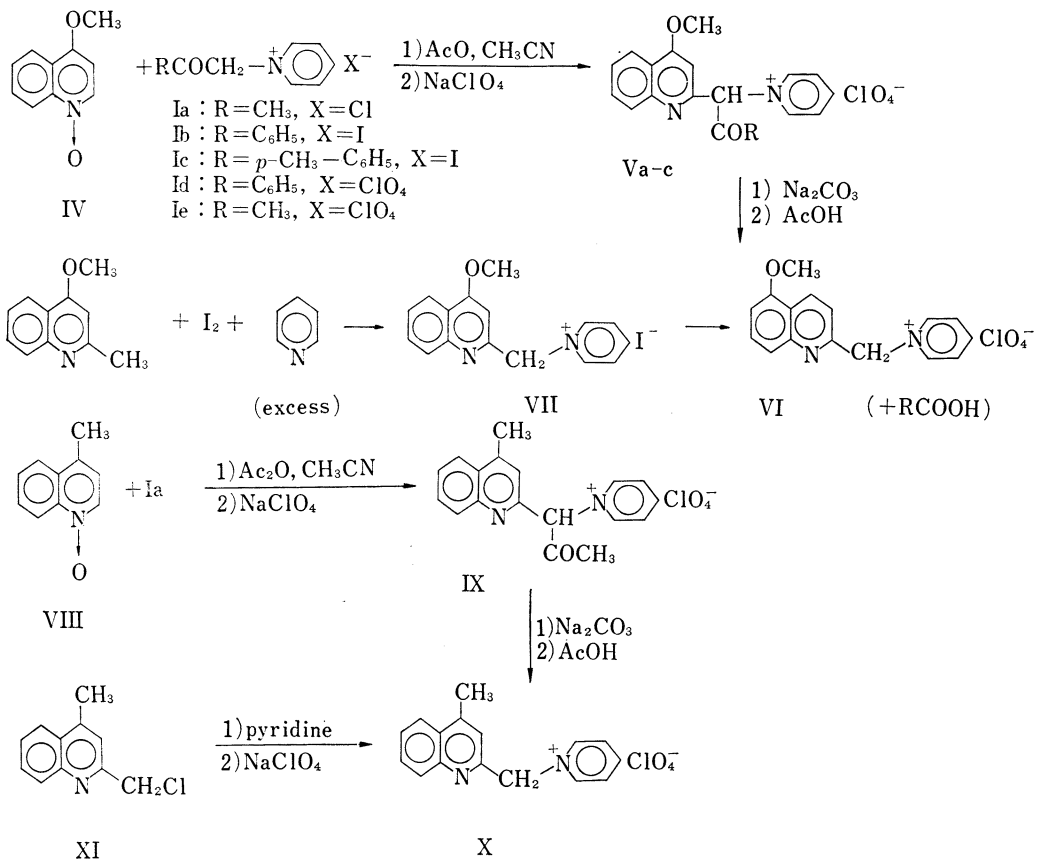


Chart 1

5) L.C. King, M. McWhirter, and R.L. Rowland, *J. Am. Chem. Soc.*, **70**, 239 (1948).
6) L.C. King and S.V. Abrano, *J. Org. Chem.*, **23**, 1609 (1958).
7) M. Hamana and M. Yamazaki, *Chem. Pharm. Bull.* (Tokyo), **11**, 415 (1963).

Further, quinaldine 1-oxide was subjected to similar reactions with Ia and Ib, but no visible signs of formation of 4-or ω-substituted quinaldine was obtained and the pyridinium salts(Ia and Ib) were recovered as their perchlorates(Ic and Id).

These results are shown in Chart 1. The IR spectra of Va—c and IX thus obtained exhibit a strong chelated carbonyl band near 1635 cm^{-1}.

Subsequently the reaction of pyridine 1-oxides was examined. Pyridine 1-oxide(XII) reacted similarly with Ia and afforded N-(α-acetyl-2-pyridylmethyl)pyridinium perchlorate (XIII), yellow pillars of mp 171—172°, in 55% yield. The structure of XIII was confirmed by its conversion to N-(2-pyridylmethyl)pyridinium dipicrate (XIV)[8] as shown in Chart 2. However the reactivity of XII is somewhat lower and XII did not react with Ib, Ib being recovered as Id.

Upon treatment of 4-picoline 1-oxide (XV) with Ia under the same condition, N-(α-acetyl-4-methyl-2-pyridylmethyl)pyridinium perchlorate (XVI), yellow needles of mp 198—200°, was obtained in 21% yield accompanied by the recovery of Ia as its perchlorate (Ie) in 39% yield. Alkaline hydrolysis of XVI, followed by treatment with picric acid afforded N-(4-methyl-2-pyridylmethyl)pyridinium dipicrate (XVII), which was proved identical with the dipicrate of the product obtained from 4-methyl-2-chloromethylpyridine[9] and pyridine. Therefore the substitution occured apparently at the 2-position of XV (Chart 2).

Although a similar reaction of 2-picoline 1-oxide was well expected to give a 6-substituted product in view of the above mentioned results, no reaction was observed even with Ia, Ia being recovered as its perchlorate Ie.

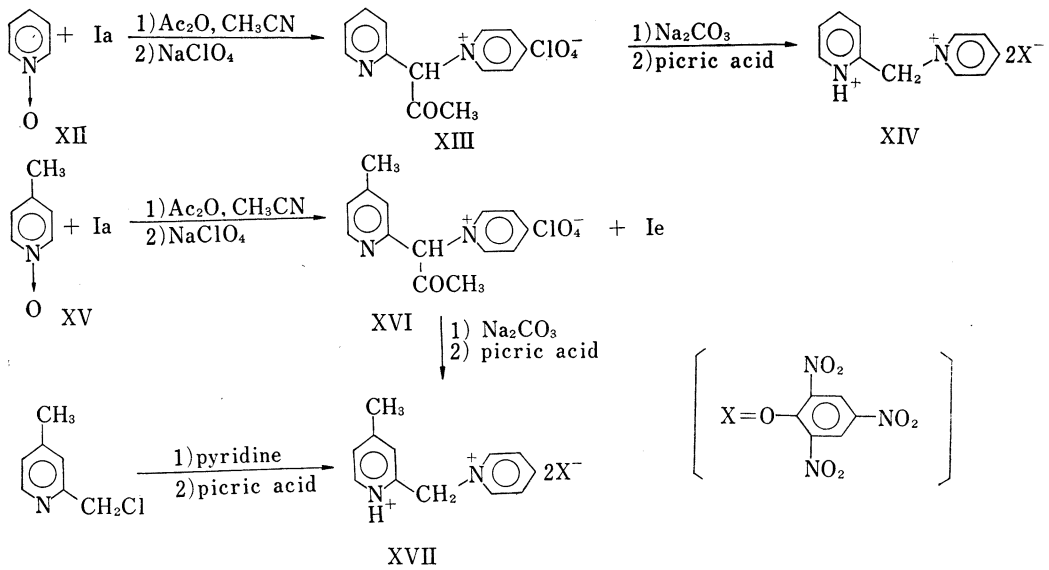


Chart 2

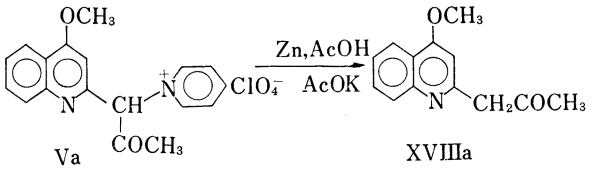
These results demonstrated that N-acetonylpyridinium chloride(Ia) is more reactive than N-phenacylpyridinium iodide (Ib), and the rough order of reactivity of the aromatic N-oxides is as follows: quinoline 1-oxide, 4-methoxyquinoline 1-oxide (IV), lepidine 1-oxide (VIII), pyridine 1-oxide (XII), 4-picoline 1-oxide (XV); quinaldine 1-oxide, 2-picoline 1-oxide.

8) M. Hamana and M. Yamazaki, *Chem. Pharm. Bull.* (Tokyo), **11**, 415 (1963).
9) S. Furukawa, *Chem. Pharm. Bull.* (Tokyo), **3**, 413 (1955).

Reduction of the Pyridinium Salts

The reduction of Vb with zinc powder and acetic acid in the presence of potassium acetate proceeded smoothly at room temperature in the similar manner to the cases described in a previous paper,[3b] giving 4-methoxy-2-phenacylquinoline (XVIIIb), yellow needles of mp 130—131°, in 55% yield. On the other hand the reduction of Va under the similar condition was found to afford only a very small amount of 4-methoxy-2-acetonylquinoline(XVIIIa) as yellow needles of mp 139—140°. Then, the reduction of Va was re-examined under various conditions and it was revealed that the elevated reaction temperature was more favorable in this case contrary to the results previously reported[3b] as shown in Table I.

TABLE I. Reduction of N-(α-Acetyl-4-methyl-2-quinolylmethyl)-pyridinium Perchlorate (Va)



Va XVIIIa

Exper. No.	Reaction temp.(°C)	Reaction time(min)	Yield of XVIIIa (g) (%)
1	below 30	60	trace
2	below 30	120	0.14 (6)
3	50	40	0.17 (26)
4	50	60	0.23 (36)
5	70	60	0.31 (47)
6	70	120	0.33 (52)
7	90	60	0.38 (59)

Similarly the reaction at 90° was required for reduction of IX to 4-methyl-2-acetonylquinoline (XIX), yellow needles of mp 113—114°; however its yield (37%) was somewhat unsatisfactory. The oxidation of XIX with peracetic acid produced 4-methylquinaldic acid 1-oxide (XX).[10]

The reduction of pyridine derivatives, XIII and XVI, was also temperature-dependent and the somewhat elevated temperatures were found favorable similarly to the reduction of Va. Table II shows the results of reduction of XIII with zinc powder and acetic acid under various conditions; the best yield of 2-acetonylpyridine (XXI)[11] (72%) was obtained when the reaction was carried out at 90° for 1 hour. Treatment of XVI under the same condition afforded 4-methyl-2-acetonylpyridine (XXII), a pale yellow oil, in 76% yield. When XXII was heated with peracetic acid, 4-methylpicolinic acid 1-oxide (XXIII)[10] was formed.

These results are shown in Chart 3.

Mondellie and Merlini[12] have investigated the tautomeric structures of 2-acetonylquinoline (XXIVa) by the ultraviolet (UV) and nuclear magnetic resonance (NMR) spectroscopies and revealed that XXIVa appears as a tautomeric mixture composed of 75% of the enamine-form (XXIVa-B) and 25% of the keto-form (XXIVa-A), the enolic species (XXIVa-C) being not noticed. We have also carried out the detailed studies on the tautomeric structures of aryl quinaldyl ketones (XXIVb, c) and demonstrated that 2-phenacylquinoline (XXIVb) and some aryl quinaldyl ketones (XXIVc: R=*p*-tolyl, *p*-anisyl, α-thienyl *etc.*) exist as an

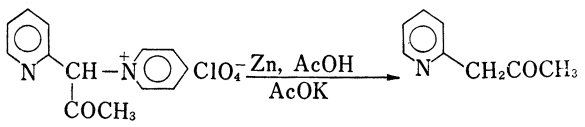
10) M. Hamana and H. Noda, *Chem. Pharm. Bull.* (Tokyo), **14**, 762 (1966).
11) N.N. Goldberg, L.B. Barkley, and R. Levine, *J. Am. Chem. Soc.*, **73**, 4301 (1951).
12) R. Mondelli and L. Merlini, *Tetrahedron*, **22**, 3253 (1966).

equilibrium mixture of the enamine-form (XXIVb,c-B) and the keto-form (XXIVb,c-A), in which the former dominates (95—65%) and the latter is minor (5—35%).[3b] Further, some quinaldyl ketones (XXIVc: R=*p*-chlorophenyl, *p*-bromophenyl, α- and β-naphthyl) were shown to exist exclusively in the enamine structures (XXIVc-B).

Similar spectroscopic examination was carried out on the tautomeric structures of the quinaldyl ketones XVIIIa, b and XIX, obtained above.

The UV spectra of both XVIIIa and XIX were similar to that of XXIVa and show the strong bands near 400 mμ which is attributed to the enamine structure (XVIIIa-B, XIX-B)

Table II. Reduction of N-(α-Acetyl-2-pyridylmethyl)-pyridinium Perchlorate(IX)



XIV XXIII

Exper. No.	Reaction temp.(°C)	Reaction time(min)	Yield of XXIII (g) (%)
1	below 30	120	0.05 (15)
2	50	30	0.15 (44)
3	50	60	0.20 (59)
4	70	30	0.19 (56)
5	70	60	0.23 (68)
6	90	30	0.24 (70)
7	90	60	0.25 (72)

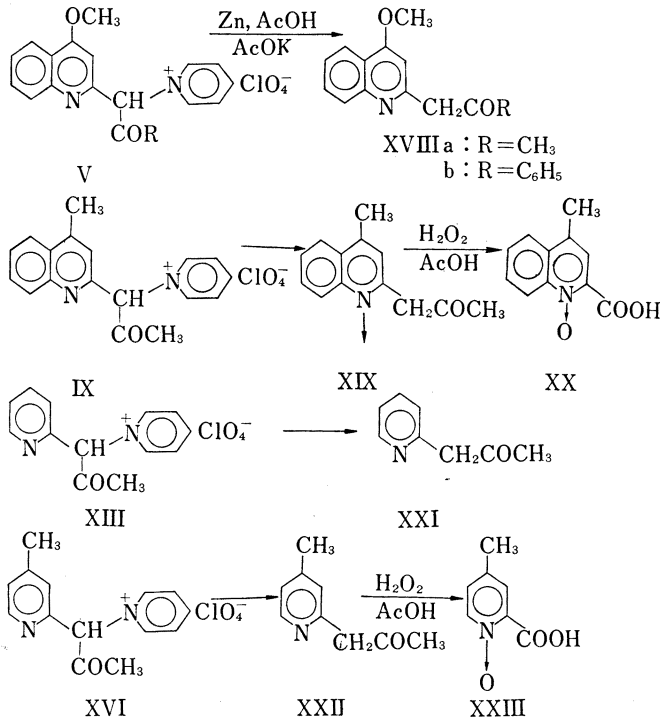


Chart 3

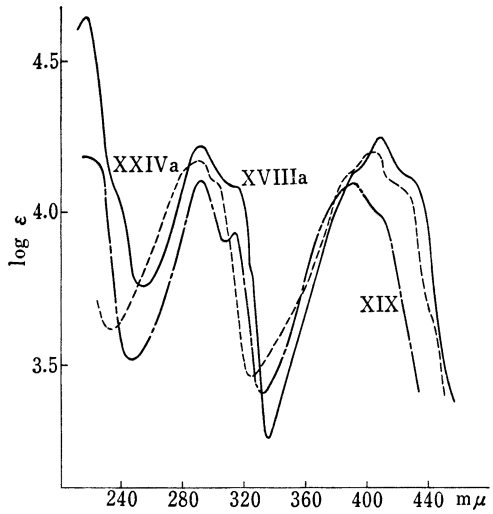


Fig. 1. UV Spectra of XXIVa, XVIIIa and XIX

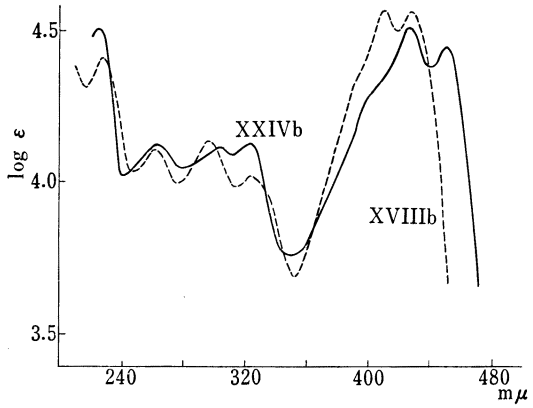


Fig. 2. UV Spectra of XXIVb and XVIIIb

(Fig. 1). The UV spectrum of XVIIIb is closely similar to that of XXIVb, showing a strong absorption band at 420 mμ (Fig. 2).

The NMR spectra of XVIIIa and XIX in deuteriochloroform show the signals of the methylene protons of the keto-form (XVIIIa-A, XIX-A) at 5.89 and 5.87 τ, respectively, and the signals of Cα-H of the enamine structures (XVIIIa-B, XIX-B) are noticed at 4.65 and 4.71 τ, respectively. On the other hand, the NMR spectrum of XVIIIb shows only the signal of Cα-H at 3.77 or 3.85 τ, no signal attributable to the methylene protons being detected (Table III).

The IR spectra of XVIIIa, XVIIIb and XIX in the solid state exhibit the chelated carbonyl bands near 1640 cm^{-1} in the same way with those of XXIVa and XXIVb.[3b] Whereas

Table III. NMR Spectra of XVIII and XIX ($CDCl_3$)

	NH	C_3-H	Cα-H	CH_2	OCH_3	CH_3	$COCH_3$	(%)
XVIIIa-A				5.89	5.77		7.66	25
XVIIIa-B	−5.4	4.01	4.65		6.00		7.86	75
XIX-A				5.87		7.33	7.71	25
XIX-B	−5.5	3.50	4.71			7.60	7.86	75
XVIIIb-A	−6.2	3.77 or 3.85	3.85 or 3.77		5.95			100

Table IV. IR Spectra of XXIV, XVIII and XIX

	νC=O (cm^{-1}) In Nujol mull enamine-form (B)	In solution enamine-form (B)	Keto-form (A)	Solvent
XXIVa	1640	1633	1718	$CHCl_3$
XVIIIa	1645	1642	1718	CCl_4
XIX	1643	1636	1718	CCl_4
XXIVb	1639	1631		$CHCl_3$
XVIIIb	1634	1637		CCl_4

those of XVIIIa and XIX as well as XXIVa in solution show the normal ketonic carbonyl bands in addition to the chelated carbonyl band, no band indicative of a normal ketone being observed in those of XVIIIb and XXIVb.

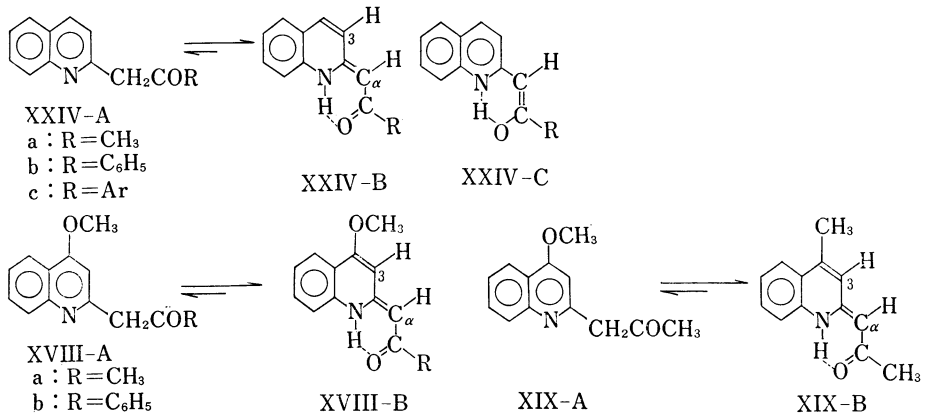


Chart 4

From these observations, it may be well concluded that the acetonyl derivatives, XVIIIa and XIX, exist as an equilibrium mixture of the enamine-form (XVIIIa-B, XIX-B) and the keto-form (XVIIIa-A, XIX-A), in which the former is predominant, while the 2-phenacyl compound (XVIIIb) exists exclusively as the enamine-form (XVIIIb-B).

Experimental[13]

Reaction of 4-Methoxyquinoline 1-Oxide(IV) with N-Acetonylpyridinium Chloride (Ia)——A solution of IV (0.88 g), Ac_2O (5 ml) and Ia (0.86 g) in MeCN (30 ml) was refluxed for 5 hr. The reaction mixture was evaporated *in vacuo* and the residue was dissolved in a small amount of MeOH, to which was added 20% $NaClO_4$ (10 ml), and the whole was kept in a refrigerator overnight. Recrystallization of the resultant precipitates from MeOH gave 1.36 g (66%) of N-(α-acetyl-4-methoxy-2-quinolylmethyl) pyridinium perchlorate (Va), yellow needles, mp 230—232° (decomp.). *Anal.* Calcd. for $C_{18}H_{17}O_6N_2Cl \cdot H_2O$: C, 52.62; H, 4.66; N, 6.82. Found: C, 52.45; H, 4.46; N, 7.30. IR ν_{max}^{Nujol} cm^{-1}: 1645 (C=O).

Reaction of IV with N-Phenacylpyridinium Iodide (Ib)——A solution of IV (1.93 g), Ac_2O (8 ml) and Ib (3.3 g) in MeCN (50 ml) was refluxed for 5 hr. Processing as the foregoing experiment afforded 2.68 g (55%) of N-(α-benzoyl-4-methoxy-2-quinolylmethyl) pyridinium perchlorate (Vb), yellow needles, mp 251—252° (decomp.). *Anal.* Calcd. for $C_{23}H_{19}O_6N_2Cl$: C, 60.72; H, 4.21: N, 6.16. Found: C, 60.64; H, 4.22; N, 6.21. IR ν_{max}^{Nujol} cm^{-1}: 1636 (C=O).

Reaction of IV with N-(*p*-Methylphenacy) pyridinium Iodide(Ic)——A solution of IV (2.64 g), Ac_2O (5 ml) and Ic (5.09 g) in MeCN (90 ml) was refluxed for 7 hr, and the silmiar treatment of the reaction mixture gave 4.32 g (61%) of N-(α-*p*-methylbenzoyl-4-methoxy-2-quinolylmethyl)pyridinium perchlorate (Vc); pale yellow needles, mp 205—207°. *Anal.* Calcd. for $C_{24}H_{21}O_6N_2Cl$: C, 61.47; H, 4.51; N, 5.97. Found: C, 61.45; H, 4.56; N, 6.27. IR ν_{max}^{Nujol} cm^{-1}: 1633 (C=O).

Hydrolysis of Va——To a solution of Va (0.41 g) in H_2O (10 ml)–EtOH (5 ml) was added 20% Na_2CO_3 (3 ml), and the whole was warmed on a water-bath for 15 min. The reaction mixture was neutralized with 60% $HClO_4$ and kept standing in a refrigerator overnight. The precipitates were recrystallized from aqueous EtOH to give 0.24 g (69%) of N-(4-methoxy-2-quinolylmethyl)pyridinium perchlorate (VI) colorless plates, mp 197—198°. It was identified by admixture with a sample prepared as described below.

N-(4-Methoxy-2-quinolylmethyl)pyridinium Perchlorate (VI)——Iodine (5.1 g) was added in small portions to a solution of 4-methoxyquinaldine (3.46 g) in pyridine (8 ml) under heating on a water-bath, and heating was continued further 2 hr. The resultant precipitates were collected, washed with acetone and

13) All melting points are uncorrected. IR spectra were recorded on a Koken DS-301 spectrophotometer and UV spectra were taken on a Shimadzu SU-50A spectrophotometer. NMR spectra were measured in $CDCl_3$ on Varian A-60 spectrophotometer at 60 MC using TMS as an internal reference.

recrystallized from EtOH to afford 1.94 g (26%) of N-(4-methoxy-2-quinolylmethyl)pyridinium iodide (VII), colorless prisms, mp 190—191° (decomp.). *Anal.* Calcd. for $C_{16}H_{15}ON_2I$: C, 50.82; H, 4.00; N, 7.41. Found: C, 50.73; H, 3.99; N, 7.83. The corresponding perchlorate (VI) was recrystallized from 80% EtOH to colorless plates, mp 197—198°. *Anal.* Calcd. for $C_{16}H_{15}O_5N_2Cl$: C, 54.79; H, 4.31; N, 7.99. Found: C, 54.64; H, 4.31; N, 8.03.

Hydrolysis ob Vb——To a suspension of Vb (0.46 g) in H_2O (20 ml)–EtOH (10 ml) was added 20% Na_2CO_3 (4 ml), and the whole was warmed on a water-bath for 15 min. After neutralization with 60% $HClO_4$, the reaction mixture was extracted with ether. The extract gave 0.1 g (80%) of benzoic acid, colorless plates, mp 121—122°. The residual solution was kept in a refrigerator overnight to give precipitates, which was recrystallized from EtOH to afford 0.13 g (37%) of VI, colorless plates, mp 195—197°.

Hydrolysis of Vc——To a suspension of Vc (0.47 g) in H_2O (20 ml)–EtOH (10 ml) was added 20% Na_2CO_3 (4 ml), and the whole was warmed on a water-bath for 15 min. The reaction mixture was similarly worked up to yield 0.07 g (51%) *p*-toluic acid, colorless plates, mp 176—177°, and 0.22 g (63%) of VI.

Reaction of Lepidine 1-Oxide (VIII) with Ia——The hemihydrate (0.84 g) VIII was azeotropically dehydrated with $CHCl_3$ and dissolved in MeCN (30 ml), to which Ac_2O (5 ml) and Ia (0.86 g) was added, and the whole was refluxed for 5 hr. The usual treatment of the reaction mixture gave 0.84 g (43%) of N-(α-acetyl-4-methyl-2-quinolylmethyl)pyridinium perchlorate (IX), yellow needles, mp 197—199°. *Anal.* Calcd. for $C_{18}H_{17}O_5N_2Cl \cdot \frac{1}{2}H_2O$: C, 56.03; H, 4.70; N, 7.26. Found: C, 55.69; H, 4.76; N, 6.94. IR ν_{max}^{Nujol} cm^{-1}: 1636 (C=O).

Hydrolysis of IX——To a solution of IX (0.38 g) in H_2O (10 ml)–EtOH (5 ml) was added 20% Na_2CO_3 (3 ml), and the whole was warmed on a water-bath for 15 min. The reaction mixture was neutralized with AcOH and kept in a refregerator overnight to give precipitates, which was recrystallized from 85% EtOH to afford 0.27 g (71%) of N-(4-methyl-2-quinolylmethyl)pyridinium perchlorate (X), colorless plates, mp 171—173°. *Anal.* Calcd. for $C_{16}H_{15}O_4N_2Cl$: C, 57.40; H, 4.52; N, 8.37. Found: C, 57.15; H, 4.33; N,8.22.

Reaction of VIII with Ib——The hemihydrate (0.84 g) was dehydrated and treated with MeCN (30 ml), Ac_2O (5 ml) and Ib (1.63 g) under reflux for 5 hr as mentioned above. The similar processing resulted in the recovery of Ib as 0.92 g (62%) of its perchlorate (Id), colorless plates, mp 188—189°.

Reaction of Pyridine 1-Oxide (XII) with Ia——A solution of XII (2.28 g), Ac_2O (6 ml) and Ia (3.4 g) in MeCN (50 ml) was refluxed for 10 hr. The reaction mixture was evaporated *in vacuo*, and the residue was dissolved in MeOH (40 ml) and allowed to stand with 20% $NaClO_4$ (20 ml) in a refrigerator overnight. The resultant precipitates were collected and washed with $CHCl_3$ and recrystallized from MeOH to give 3.45 g (55%) of N-(α-acetyl-2-pyridylmethyl)pyridinium perchlorate (XIII), yellow pillars, mp 171—172°. *Anal.* Calcd. for $C_{13}H_{13}O_5N_2Cl$: C, 49.96; H, 4.19; N, 8.96. Found: C, 49.68; H, 4.15; N, 8.63. IR ν_{max}^{Nujol} cm^{-1}: 1631 (C=O). UV λ_{max}^{EtOH} mμ (log ε): 256 (3.81, shoulder), 261 (3.86), 266 (3.76, shoulder).

Hydrolysis of XIII——A mixture of XIII (0.31 g), H_2O (10 ml)–EtOH (5 ml) and 20% Na_2CO_3 (4 ml) was warmed on a water-bath for 15 min. After neutralization with 60% $HClO_4$, the reaction mixture was kept in a refrigerator overnight and the hygroscopic precipitates were derived to 0.38 g (60%) of N-(2-pyridylmethyl)pyridinium dipicrate (XIV),[7] yellow needles mp 169—170° (MeOH). *Anal.* Calcd. for $C_{23}H_{16}O_{14}N_8$: C, 43.94; H, 2.54; N, 17.83. Found: C, 43.80; H, 2.43; N, 17.76.

Reaction of XII with Ib——A solution of XII (0.95 g), Ac_2O (5 ml) and Ib (3.3 g) in MeCN (50 ml) was refluxed for 5 hr. The reaction mixture was evaporated *in vacuo* and the residue was treated with MeOH and 20% $NaClO_4$ (10 ml) under ice-cooling. Recrystallization of the resultant precipitates from MeOH afforded 2.1 g (68%) of Id, colorless plates, mp 189—190°.

Reaction of 4-Picoline 1-Oxide (XV) with Ia——A solution of XV (2.6 g), Ac_2O (10 ml) and Ia (3.4 g) in MeCN (40 ml) was refluxed for 10 hr. The reaction mixture was evaporated *in vacuo* and the residue was dissolved in MeOH (40 ml) and allowed to stand with 20% $NaClO_4$ (20 ml) in a refrigerator overnight. The resultant precipitates were recrystallized from MeOH to give 1.39 g (21%) of N-(α-acetyl-4-methyl-2-pyridylmethyl)pyridinium perchlorate (XVI), yellow needles, mp 198—200°. *Anal.* Calcd. for $C_{14}H_{15}O_5N_2Cl$: C, 51,42; H, 4.63; N, 8.57. Found: C, 51.23; H, 4.58; N, 8.62. IR ν_{max}^{Nujol} cm^{-1}: 1640 (>C=O). UV λ_{max}^{EtOH} mμ (log ε): 260 (3.90), 265 (3.84, shoulder). To the mother liquor from the above precipitate was added H_2O and the whole was kept in a refrigerator to give again precipitates, which was recrystallized from MeOH to yield 1.38 g (30%) of Ie, colorless plates, mp 119—120°.

Hydrolysis of XVI——A mixture of XVI (0.33 g), H_2O (10 ml)–EtOH (5 ml) and 20% Na_2CO_3 (4 ml) was heated on a water-bath for 30 min. The reaction mixture was acidified with 10% HCl, evaporated *in vacuo* and treated with MeOH. Insoluble substances were filtered and the filtrate was treated with picric acid to afford 0.07 g (11%) of N-(4-methyl-2-pyridylmethyl)pyridinium dipicrate (XVII), yellow plates, mp 178—179° (MeOH). *Anal.* Calcd. for $C_{24}H_{18}O_{14}N_8$; C, 44.85; H, 2.82; N, 17.44. Found: C, 44.49; H, 2.71; N, 17.64. It was identified with an authentic sample prepared as described below.

N-(4-Methyl-2-pyridylmethyl)pyridinium Dipicrate (XVII)——A solution of 4-methyl-2-pyridinemethanol (0.4 g) and PCl_3 (0.6 ml) in benzene (10 ml) was refluxed for 5 min. The reaction mixture was poured on ice and made alkaline with solid K_2CO_3 and extracted with benzene. Pyridine (3 ml) was added to the dried benzene solution and the whole was refluxed for 1 hr. The solution was evaporated *in vacuo* and the residue was treated with solution of picric acid to afford 0.71 g (33%) of XVII, yellow plates, mp 178—179°

(MeOH). *Anal.* Calcd. for $C_{24}H_{18}O_{14}N_8$: C, 44.85; H, 2.82; N, 17.44. Found: C, 45.06; H, 2.82; N, 17.27.

Reduction of Vb——To a solution of Vb (1.14 g) and AcOK (0.5 g) in AcOH (30 ml) was added Zn powder (1 g) in small portions, and the mixture was stirred at room temperature for 1 hr. The deposited inorganic substances were filtered, and the filtrate was evaporated *in vacuo*. The residue was dissolved in H_2O made alkaline with solid K_2CO_3 and extracted with $CHCl_3$. The extract was evaporated under reduced pressure and residue was chromatographed on Al_2O_3 with benzene. The effluent was treated with MeOH and insoluble substances were filtered. The filtrate was evaporated and the residue was recrystallized from petroleum benzine to yield 0.39 g (55%) of 4-methoxy-2-phenacylquinoline (XVIIIb), yellow needles, mp 130—131°. *Anal.* Calcd. for $C_{18}H_{15}O_2N$: C, 77.96; H, 5.45; N, 5.05. Found: C, 78.31; H, 5.38; N, 5.27.

Reduction of Va——General Procedure: To a solution of Va (1.23 g) and AcOK (0.5 g) in AcOH (30 ml) was added Zn powder (1.2 g) in small portions, and the mixture was stirred at 30—90° for 40—120 min (Table I). The reaction was processed as described above to afford 4-methoxy-2-acetonylquinoline (XVIIIa), yellow needles of mp 139—140° (petroleum benzine). The yields are shown in Table I. *Anal.* Calcd. for $C_{13}H_{13}O_2N$: C, 72.54; H, 6.09; N, 6.51. Found: C, 72.26; H, 6.06; N, 6.61.

Reduction of IX——To a solution of IX (0.96 g) and AcOK (0.5 g) in AcOH (30 ml) was added Zn powder (1 g) in small portions, and the mixture was heated at 90° with occasional stirring for 1 hr. Similar processing gave 0.19 g (37%) of 4-methyl-2-acetonylquinoline (XIX), yellow needles, mp 113—114°. *Anal.* Calcd. for $C_{13}H_{13}ON$: C, 78.36; H, 6.58; N, 7.03. Found: C, 78.36; H, 6.81; N, 7.19

Oxidation of XIX——A solution of XIX (0.20 g) and 30% H_2O_2 (3 ml) in AcOH (5 ml) was heated at 80—90° for 2 hr, then another 30% H_2O_2 (2 ml) was added and the heating was continued further 3 hr. The solvent was removed under reduced pressure, and the residue was recrystallized from MeOH to give 0.10 g (50%) of 4-methylquinaldic acid 1-oxide (XX), pale yellow needles, mp 171—172° (decomp.). *Anal.* Calcd. for $C_{11}H_9O_3N$: C, 65.02; H, 4.46; N, 6.89. Found: C, 64.58; H, 4.43; N, 7.20. It was identified by direct comparison with an authentic sample.[11]

Reduction of XIII——General Procedure: The mixture of XIII (0.78 g), AcOK (0.5 g), AcOH (20 ml) and Zn powder (1 g) was warmed at 30—90° for 30—120 min (Table II). The deposited inorganic substances were filtered, and the filtrate was evaporated *in vacuo*. The residue was treated with 20% K_2CO_3 and extracted with $CHCl_3$. The extracted product was distilled under reduced presure to yield, 2-acetonylpyridine (XXI), a pale yellow oil, bp 110—120° (2 mmHg) (bath temperature). The yields are shown in Table II. Picrate: yellow needles, mp 139—140° (MeOH). *Anal.* Calcd. for $C_{14}H_{12}O_8N_4$: C, 46.16; H, 3.32; N, 15.38. Found: C, 46.02; H, 3.33; N, 15.58. This picrates was identified by admixture with an authentic sample.[12]

Reduction of XVI——To a solution XVI (0.82 g) and AcOK (0.5 g) in AcOH (20 ml) was added Zn powder (1 g) and the mixture was heated at 90° with occasional stirring for 1 hr. Similar processing afforded 0.28 g (76%) of 4-methyl-2-acetonylpyridine (XXII), a pale yellow oil, bp 110—130° (2 mmHg) (bath temperature). Picrate: Yellow plates, mp 141—142° (MeOH). *Anal.* Calcd. for $C_{15}H_{14}O_8N_4$: C, 47.62; H, 3.73; N, 14.81. Found: C, 47.73; H, 3.91; N, 15.00.

Oxidation of XXII——A solution of XXII (0.15 g) and 30% H_2O_2 (3 ml) in AcOH (5 ml) was heated at 80—90° for 2 hr, and then another 30% H_2O_2 (2 ml) was added and the heating was continued further 3 hr. After evaporation of the solution under reduced presure, the residue was recrystallized from EtOH to give 0.12 g (80%) of 4-methylpicolinic acid 1-oxide (XXIII),[11] colorless needles, mp 166—167° (decomp.). *Anal.* Calcd. for $C_7H_7O_3N$: C, 54.90; H, 4.61; N, 9.15. Found: C, 55.22; H, 4.70; N, 9.32.