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Reduction of N-(α-Acyl-2-quinolylmethyl)pyridinium Perchlorate

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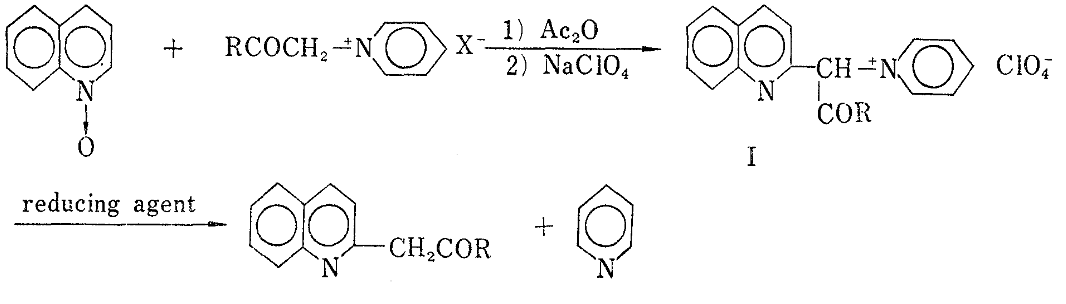
The reductive cleavage of pyridinium group from N-(α-acyl-2-quinolylmethyl)-pyridinium perchlorate (I) was found to be effected by treatment of I with zinc powder in the presence of potassium acetate in acetic acid under relatively mild conditions to give quinaldyl ketone (II). The tautomeric structures (II-A, II-B and II-C) of aryl quinaldyl ketones (IIb—IIk) were examined by UV, NMR and IR spectroscopies, and it was made clear that II existed chiefly as the enaminic form (II-C) rather than the chelated enolic form (II-B), differently from the case of aryl 2-picolyl ketones (IV).

The preceeding paper[2] has shown that N-acylmethylpyridinium salts readily react with quinoline 1-oxide in the presence of acetic anhydride, producing the corresponding N-(α-acyl-2-quinolylmethyl)pyridinium perchlorate (I) in good yields upon treatment with sodium perchlorate. If the reductive cleavage of pyridinium group from I could be effected, the reaction would open a new and promising route to the preparation of various quinaldyl ketones (II) from quinoline 1-oxide.



I

II

The present paper deals with the reduction of I to II, and also with the spectroscopic studies on the tautomeric structures of II thus obtained.

The Reduction of N-(α-Acyl-2-quinolylmethyl)pyridinium Perchlorate (I) to Quinaldyl Ketones (II)

There have been only a few reports recorded on the reductive cleavage of pyridinium group as pyridine from N-substituted pyridinium compounds. Kröhnke[3] found that N-phenacylpyridnium bromide was reduced with zinc powder in acetic acid at 60° to acetophenone, and Hamana, Umezawa and Noda[4] showed that N-(1-oxido-2-pyridylmethyl)pyridnium iodide yielded 2-picoline and pyridine under the same condition.

At first, the reduction of N-(α-benzoyl-2-quinolylmethyl)pyridinium perchlorate (Ib) with zinc powder in acetic acid was carried out under similar conditions, but the expected

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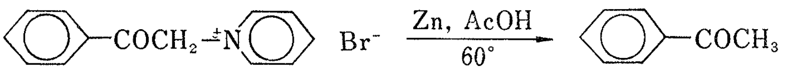
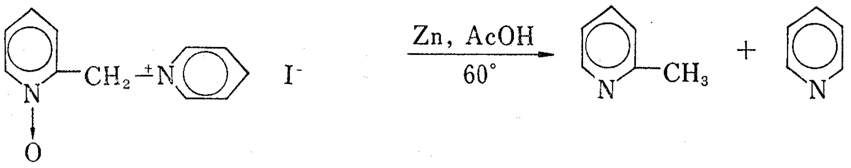
[1] Location: *a*) *Nanakuma, Fukuoka*; *b*) *Katakasu, Fukuoka*.

[2] M. Yamazaki, K. Noda, and M. Hamana, *Chem. Pharm. Bull.* (Tokyo), **18**, 899 (1970).

[3] F. Kröhnke, *Ber.*, **67**, 656 (1934).

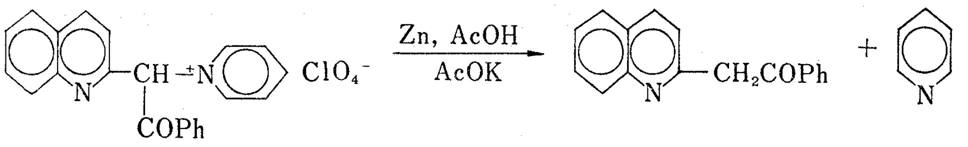
[4] M. Hamana, B. Umezawa, and K. Noda, *Chem. Pharm. Bull.* (Tokyo), **11**, 694 (1963).





2-phenacylquinoline (IIb) was not isolated, an untractable mixture being formed. Then, the reaction conditions were re-examined in some detail, and it was found that the presence of potassium acetate and the relatively mild conditions were favorable for a smooth progressing of the reaction, the prolonged heating or the elavated reaction temperatures promoting, on the contrary, the formation of resinous substances. The representative results are shown in Table I.

Table I. Recudtion of N-(α-Benzoyl-2-quinolylmethyl) pyridinium Perchlorate (Ib)



Ib IIb

Exper. No.	Reaction temp (°C)	Reaction time (min)	Yield of IIb (%)
1	below 30	30	74
2	below 30	60	71
3	below 30	90	71
4	50	15	69
5	50	30	61
6	70	15	45

Subsequently, other ten kinds of N-(α-acyl-2-quinolylmethyl)pyridinium perchlorate (Ia, Ic—k) described in the preceeding paper[2] were subjected to the reduction using the condition which afforded the best result in that of Ib, and the corresponding quinaldyl ketones (II) were obtained in moderate to good yields. These results are given together with some properties of II in Table II.

The structures of II, except that of IIg, were confirmed by direct comparison with the authentic samples prepared from quinaldyllithium (III) and the methyl esters of the corresponding acids according to the procedure of Goldberg and Levine.[5] On the reduction of N-(α-*p*-nitrobenzoyl-2-quinolylmethyl)pyridinium perchlorate (Ig), the nitro group was also reduced to afford *p*-aminophenyl quinaldyl ketone (IIg), which was identified with the authentic sample similarly prepared by the reaction of ethyl *p*-acetamidobenzoate with III, followed by acid hydrolysis of the resultant *p*-acetamidophenyl quinaldyl ketone (III).

The Tautomeric Structure of Quinaldyl Ketones (II)

In 2-picolyl ketone (IV) and quinaldyl ketone (II), three tautomeric structures, the ketonic, the enolic and the enaminic forms (A, B and C, respectively), are possible.

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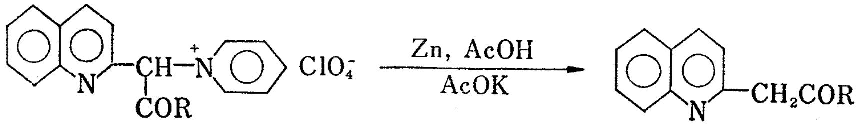
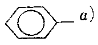
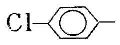
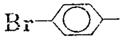
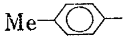
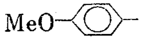
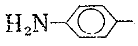
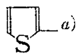
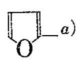
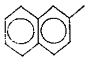
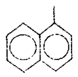
[5] N.N. Goldberg and R. Levine, *J. Am. Chem. Soc.*, **74**, 5217 (1952).

Table II. Reduction of N-(α-Acyl-2-quinolylmethyl)pyridinium Perchlorates(I) and Some Properties of Quinaldyl Ketones (II)



I II

II	R	Yield (g) (%)	Appearance	mp (°C)	Recrystn. solvent	Formula	Analysis (%) Calcd. C	H	N	Found C	H	N
a	Me- [a]	0.20(43)	pale yellow needles	78—80	petr. ether	$C_{18}H_{14}O_8N_4$[b]	52.18	3.41	13.52	52.01	3.37	13.41
b	 [a]	0.46(74)	yellow leaflets	116—117	petr. benzine	$C_{17}H_{13}ON$	82.57	5.30	5.66	83.04	5.43	5.61
c		0.46(65)	yellow plates	162—163	MeOH	$C_{17}H_{12}ONCl$	72.49	4.29	4.97	72.26	4.14	5.35
d		0.50(62)	yellow plates	167—168	MeOH	$C_{17}H_{12}ONBr$	62.59	3.71	4.29	62.81	3.66	4.39
e		0.44(68)	yellow plates	172—173	MeOH	$C_{18}H_{15}ON$	82.73	5.79	5.36	82.26	5.70	5.34
f		0.42(61)	yellow plates	155—156	MeOH	$C_{18}H_{15}O_2N$	77.96	5.45	5.05	77.84	5.79	5.12
g		0.42(64)	orange-yellow prisms	174—175	benzene	$C_{17}H_{14}ON_2$	77.84	5.38	10.68	78.16	5.52	10.47
h	 [a]	0.44(70)	yellow prisms	124—126	petr. benzine	$C_{15}H_{11}ONS$	71.14	4.37	5.53	71.07	4.30	5.51
i	 [a]	0.32(54)	yellow needles	103—104	petr. benzine	$C_{15}H_{11}O_2N$	75.93	4.67	5.90	76.19	4.44	5.68
j		0.37(50)	yellow leaflets	196—197	EtOH	$C_{21}H_{15}ON$	84.82	5.09	4.71	84.96	5.19	4.69
k		0.27(36)	yellow needles	149—151	petr. benzine	$C_{21}H_{15}ON$	84.82	5.09	4.71	84.98	5.22	4.63

[a] lit. 5 [b] picrate of 2-acetonylquinoline, yellow needles, mp 185—186° (decomp.)

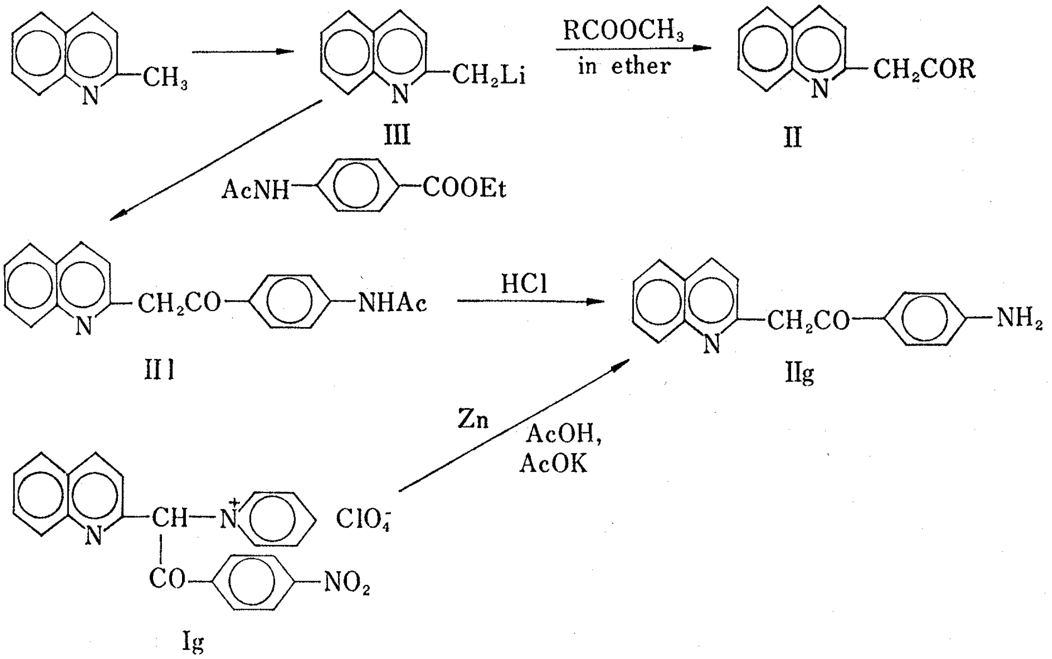
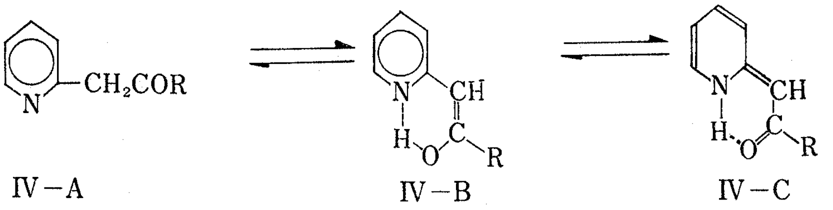
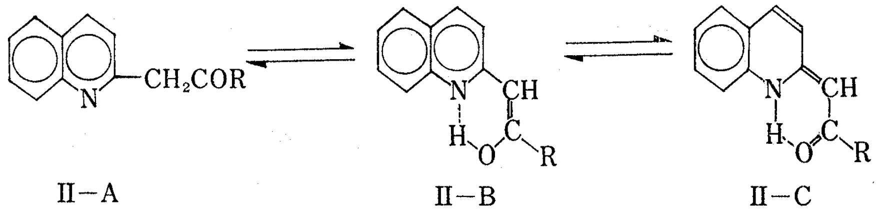


Chart 1

It has been previously deduced mainly from the ultraviolet (UV) spectroscopic examinations that 2-acetonylquinoline (IIa) and 2-phenacylquinoline (IIb) exist chiefly in the chelated enolic form (II-B)[6] in the same manner with 2-phenacylpyridine (IV: R=Ph).[7]





IIa : R=CH_3, IIb : R=Ph, IIm : R=COOEt

Recently, the UV and nuclear magnetic resonance (NMR) spectroscopic studies have revealed that the enolic form (IV-B) is more favorable over the enaminic form (IV-C) in the pyridine series (IV),[8] but on the contrary in the quinoline series, the enaminic form (II-C) is more preferable to the enol structure (II-B).[9]

Thus, in deuteriochloroform solution, IIa appears as a tautomeric mixture composed of 75% of the enaminic form (IIa-C) and 25% of the keto form (IIa-A), and ethyl 2-quinolylpyruvate (IIm) exists exclusively in the enaminic form (IIm-C).

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6) T. Okamoto and H. Takayama, *Chem. Pharm. Bull.* (Tokyo), **11**, 514 (1963).
7) R.F. Branch, A.H. Beckett, and D.B. Cowell, *Tetrahedron*, **19**, 401 (1963).
8) G. Klose and E. Uhlemann, *Tetrahedron*, **22**, 1373 (1966).
9) R. Mondelli and L. Merlini, *Tetrahedron*, **22**, 3253 (1966).

Now, we investigated the tautomeric structures of aryl quinaldyl ketones (IIb—k) by the UV, NMR and infrared (IR) spectroscopies, and it became apparent that the enaminic form (II-C) was the most predominant species among the three tautomeric structures in IIb—k.

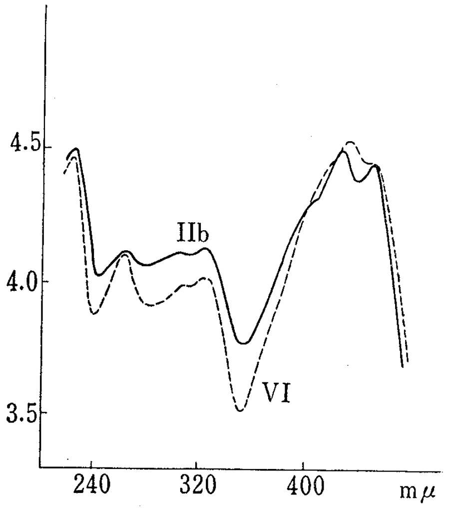
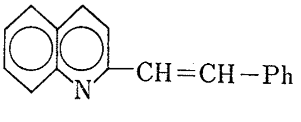


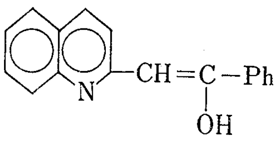
Fig. 1. UV Spectra of IIb and VI

The UV spectrum of 2-phenacylquinoline (IIb) shows a strong absorption band at 428 mμ (log ε: 4.51) in the visible region (Fig. 1). This absorption band is not ever explicable only by the keto form (IIb-A), which should show a similar UV spectrum to that of quinaldine ($\lambda_{\max}^{\mathrm{CHCl_3}}$: 316 mμ).[9] As the enol structure (IIb-B) corresponds to 2-(α-hydroxystyril)quinoline, it might be expected to exhibit an absorption in the region about 15—45 mμ longer compared with the maximum absorption of 2-styrilquinoline (V) ($\lambda_{\max}^{\mathrm{CHCl_3}}$: 320 mμ).[10,11]

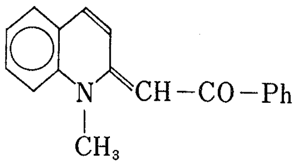
The observed absorption band apparently occurs in a much longer wave-length region. On the other hand, the UV spectrum of IIb is quite alike that of 1-methyl-2-phenacylidene-1,2-dihydroquinoline (VI)[14] in which only the enaminic structure is possible (Fig. 1). Therefore, it may be reasonably considered that IIb exists predominantly in the enaminic form (IIb-C) in alcoholic solution.



V



IIb−B



VI

Other aryl quinaldyl ketones (IIc—k) also showed the UV absorption closely similar to that of 2-phenacylquinoline (IIb), and it may be well assumed that the enaminic structures (II-C) are predominant in these cases, too.

Mondelli and Merlini[9] have described that the signals of C_3-H and C_4-H in the NMR spectrum of the enaminic form of 2-acetonylquinoline (IIa-C) are shifted *ca.* 0.6 ppm upfield (3.39 and 2.49 τ) and their coupling constant increases by *ca.* 1.0 cps ($J_{3,4}$=9—9.2 cps) compared with those of the keto form (IIa-A) (2.4—2.8 and 1.90 τ; $J_{3,4}$=8.0—8.5 cps) as well as those of quinaldine and 2-cyanomethylquinoline,[15] and this may be due to the loss of the ring current contribution of the pyridine nucleus because of the enaminic structure (IIa-C). However, they did not studied on the spectra of an aryl quinaldyl ketones.

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10) C. Compton and W. Bergmann, *J. Org. Chem.*, **12**, 363 (1947).

11) In conjugated enones or similar conjugated system, it is generally noticed that the introduction of a hydroxyl group into α- or β-position leads to the bathochromic shift of the π-π^* absorption band by 15—45 mμ (lit. 9, 12). For example, 2-styrilpyridine (lit. 13) and 2-phenacylpyridine (IV-B, R=Ph) (lit. 7) have a maximum at 315 and 337 mμ, respectively.

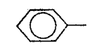
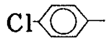
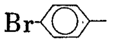
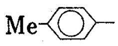
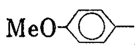
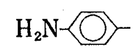
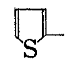
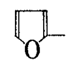
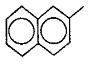
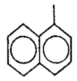
12) A.E. Gillam and E.S. Stern, "Electronic Absorption Spectroscopy," E. Arnold, London, 1957.

13) J.L. Bills and C.R. Noller, *J. Am. Chem. Soc.*, **70**, 957 (1948).

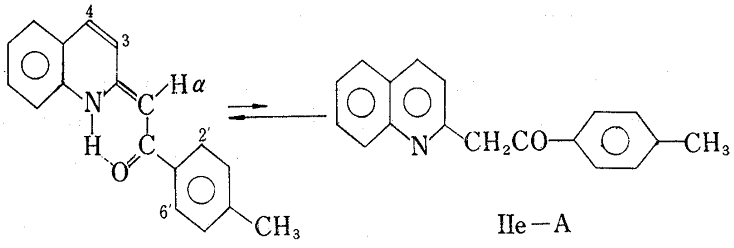
14) E. Vongerichten and W. Rotta, *Ber.*, **44**, 1419 (1911).

15) The chemical shifts of C_3–H and C_4–H of quinaldine appear at 2.79 and 2.03 τ ($J_{3,4}$=8.0—8.5 cps), and those of 2-cyanomethylquinoline do at 2.55 and 1.84 τ ($J_{3,4}$=8.0—8.5 cps) (lit. 9).

Table III. UV and IR Spectra of Quinaldyl Ketones (II)

II	R	UV λ_{max}^{EtOH} mμ (log ε)							IR $\nu_{C=O}^{Nujol}$ (cm^{-1})
a	Me−	216 (4.46)	275a) (3.96)	300 (4.18)	315 (4.10)	396a) (4.12)	415 (4.21)	435 (4.07)	1640
b		225 (4.51)	263 (4.13)	304 (4.12)	326 (4.13)	408a) (4.33)	428 (4.51)	453 (4.45)	1639
c		225 (4.42)	268 (4.07)	304 (3.96)	326 (3.98)	408a) (4.29)	428 (4.51)	453 (4.47)	1623
d		225 (4.45)	269 (4.23)	304 (4.13)	326 (4.15)	408a) (4.25)	428 (4.48)	453 (4.44)	1630
e		224 (4.51)	266 (4.11)	303 (4.13)	326 (4.17)	410a) (4.37)	432 (4.54)	457 (4.48)	1623
f		225 (4.55)	266a) (4.18)	302 (4.29)	327 (4.33)	409 (4.46)	431 (4.59)	456 (4.53)	1630
g		222 (4.16)	—	—	334 (4.18)	420a) (4.33)	442 (4.52)	467 (4.45)	1633
h		226 (4.45)	270 (4.06)	303 (4.07)	332 (4.06)	413 (4.35)	434 (4.57)	461 (4.57)	1628
i		224 (4.53)	—	304 (4.16)	325 (4.16)	413a) (4.37)	433 (4.72)	458 (4.72)	1640
j		219 (4.96)	284 (4.32)	—	330 (4.13)	412 (4.37)	433 (4.54)	459 (4.51)	1627
k		216 (4.76)	289 (4.23)	—	322 (4.15)	—	428 (4.50)	453a) (4.41)	1627

a) inflection



IIe−C IIe−A

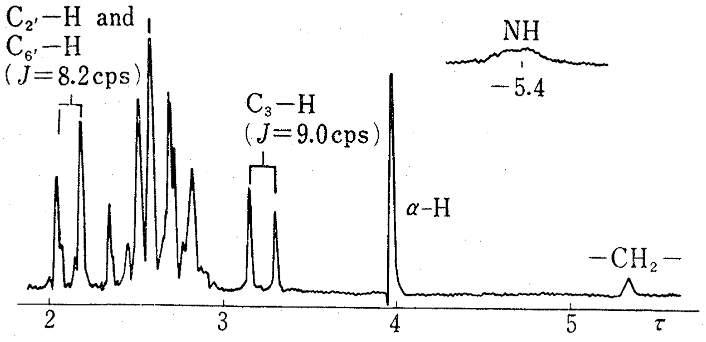


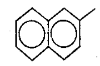
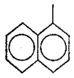
Fig. 2. NMR Spectrum of IIe

In the NMR spectra of IIb—k, the similar features were observed in all cases. The signals of C_4-H and also those of C_3-H of the ketonic form could not be detected by the overlapping with those of the other aromatic protons, but the peak of C_3-H in the enaminic structures was easily recognized because of the upfield shift to 3.1—3.37 τ (AB pattern) with $J_{3,4}=ca.$ 9.0 cps (Table IV). As an example, the NMR spectrum measured in deuteriochloroform of *p*-toluyl quinaldyl ketone (IIe) is shown in Fig. 2.

Moreover, the NMR spectra of 2-phenacylquinolines (IIb—g) showed the doublets corresponding two protons at 1.9—2.2 τ ($J=ca.$ 8—9 cps), which might be assigned to $C_{2'}$-H and $C_{6'}$-H of the phenyl ring as shown in Table IV and Fig. 2. These appreciably down-field shifts also support that the presence of a carbonyl group (not an enol group) adjacent to the phenyl moiety.[16)]

[16)] In acetophenone (Varian Catalog No. 192) and 1-methyl-2-phenacylidene-1,2-dihydroquinoline (VI), the signals of two α-protons of the phenyl ring have been observed at 2.09 and 1.8 τ (multiplet), respectively.

Table IV. Chemical Shifts[a] of Aryl Quinaldyl Ketones (IIb—k)

II	R	NH (broad,s) II-C	Aromatic protons (m)	$C_{2'}$ and $C_{6'}$-H	C_3-H (d)[c] II-C	C_α-H (s) II-C	CH_2 (s) II-A	Others (s)
b		—[b]	2.0—3.1	2.1(m)	3.3	4.02	5.25[d]	
c	Cl-	−5.5	1.9—3.0	2.1(d)	3.2	4.00		
d	Br-	−5.4	2.0—3.0	2.2(d)	3.2	4.02		
e	Me-	−5.4	2.0—3.0	2.1(d)	3.2	3.98	5.33[e]	Me: 7.64
f	MeO-	−5.4	1.8—3.2	2.1(d)	3.2	4.02	5.36[f]	MeO: 6.20
g	H_2N-	—[b]	1.7—3.2	1.9(d)	3.1	3.81	5.18[g]	H_2N: 5.78
h		−4.9	2.3—3.1		3.3	4.12	5.36[e]	
i		−5.1	2.2—3.6		3.2	4.01	5.37[e]	
j		−5.2	1.5—3.0		3.1	3.80		
k		−5.0	1.4—3.0		3.3	4.25		

a) NMR spectra were taken by Varian A-60 Spectrometer at 60 mc in $CDCl_3$ (*ca.* 50 mg in 0.4 ml) using TMS as an internal reference (τ-values).
b) not detectable c) $J_{3,4}=9.0$ cps d) *ca.* 5% e) *ca.* 10% f) *ca.* 15% g) *ca.* 35%
(m: multiplet, d: doublet, s: singlet)

The NMR spectrum of 2-acetonylquinoline (IIa) in deuteriochloroform has been shown to have both a signal due to the methylene protons of the keto form (IIa-A) at 5.88 τ (*ca.* 25%) and that due to the olefinic proton (α–H) of the enaminic form (IIa-C) at 4.68 τ (*ca.* 75%).[9]

The spectra of IIb,e,f,g,h,i showed similarly the olefinic proton at 3.1—3.3 τ as well as the methylene protons at 5.18—5.37 τ, but the signal of the methylene protons was not observed in the spectra of IIc,d,j,k. Consequently, it may be well concluded that IIc,d,j,k exist exclusively in the enaminic structures (II-C), and IIb,e,f,g,h,i exist as an equilibrium mixture of the enaminic form (II-C) and the ketonic form (II-A), in which the former dominates (95—65%), the latter being minor (5—35%) (Table IV).

The IR spectral data also support that the predominant tautomeric forms of aryl quinaldyl ketones (IIb—k) are always the enaminic forms. The chelated carbonyl band was shown at 1623—1640 cm^{-1} in nujol mull (Table III) in all cases, but the carbonyl band of keto form (II-A) was not observed near 1720 cm^{-1}. The IR spectrum of IIb in chloroform was shown to be quite similar to that in a solid state.

From the observations described above, it may be well concluded that aryl quinaldyl ketone (II) exists chiefly as the enaminic form (II-C) rather than the chelated enolic form (II-B), differently from the case of aryl 2-picolyl ketone (IV).

Experimental[17]

Reduction of N-(α-Benzoyl-2-quinolylmethyl)pyridinium Perchlorate (Ib)——(Exper. No. 1 in Table I): To a solution of Ib (1.06 g) and AcOK (0.5 g) in AcOH (25 ml), Zn powder (1 g) was added gradually below

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[17] 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.

30° with stirring, and the reaction mixture was stirred for 30 min at room temperature. The inorganic precipitates were removed by filtration, and the filtrate was concentrated under reduced pressure. After addition of H_2O to the residue, the solution was made alkaline with solid K_2CO_3 and extracted with $CHCl_3$. The extract was dried over Na_2SO_4 and evaporated under reduced pressure. Treatment of the distilate with a solution of picric acid in ether afforded the picrate of pyridine, yellow needles, mp 166—167°, 0.37 g (48%). The residue obtained from the $CHCl_3$ extract was chromatographed on Al_2O_3 with benzene. The eluted benzene was evaporated, and MeOH was added to the residue. After removal of an insoluble substance[18] by filtration, the filtrate was evaporated to dryness, and the residual crystals were recrystallized from petroleum benzine to yellow plates, mp 116—117°. This was identified as 2-phenacylquinoline (IIb)[5] by direct comparison with the authentic sample.

(Exper. No. 2—6): These experiments were carried out by essentially the same way as mentioned above except that pyridine was not isolated.

Reduction of N-(α-Acyl-2-quinolylmethyl)pyridinium Perchlorate (I)——(General Procedure): To a solution of I (0.0025 mole) and AcOK (0.5 g) in AcOH (25 ml), Zn powder (1 g) was added slowly with stirring below 30°, and the whole was stirred for 30 min at room temperature. The inorganic precipitates were filtered off, and the filtrate was evaporated to almost dryness under reduced pressure. The residue was disolved in H_2O, and the solution was made alkaline with solid K_2CO_3, and extracted with $CHCl_3$. The $CHCl_3$ extract was dried over Na_2SO_4 and evaporated under reduced pressure to dryness. The residue was chromatographed over Al_2O_3 with benzene. To the effluent, MeOH was added, and an insoluble substance was removed by filtration. The filtrate was evaporated to dryness and the crude product was recrystallized from an appropriate solvent to afford quinaldyl ketones (II) (Table II). The structure of products, except *p*-aminophenyl quinaldyl ketone (IIg), were confirmed by direct comparison with the authentic samples prepared by the method of Goldberg and Levine.[5] The structure of IIg was determined by the comparison with the synthesized sample by an another route as described below.

Synthesis of IIg——*p*-Acetamidophenyl quinaldyl ketone (III) was synthesized from quinaldyllithium (III) and ethyl *p*-acetamidobenzoate by the method of Goldberg and Levine. Recrystallization of the product from MeOH afforded III, yellow plates, mp 223—224°. *Anal.* Calcd. for $C_{19}H_{16}O_2N_2$: C, 74.98; H, 5.30; N, 9.21. Found: C, 74.85; H, 5.18; N, 9.19.

The suspension of III (0.1 g) in 10% HCl (10 ml) was refluxed for 1 hr and evaporated under reduced pressure to dryness. The residue was disolved in H_2O, the solution was made alkaline with solid K_2CO_3 and extracted with $CHCl_3$. The extract was dried over Na_2SO_4 and evaporated to dryness. The residue was recrystallized from benzene to IIg, orange-yellow prisms, mp 175—176°, 0.08 g (91%).

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[18] This was recrystallized from benzene-EtOH as yellow needles, mp 255—257°, 0.02 g, of which the structure was not determined.