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Reaction of Methyl N-Oxido-quinolyl and -isoquinolyl Ketone Oximes with Tosyl Chloride

YOSHINOBU TAGAWA, NORIKO HONJO, and YOSHINOBU GOTO*

Faculty of Pharmaceutical Sciences, Fukuoka University, Nanakuma, Jonan-ku, Fukuoka 814-01, Japan

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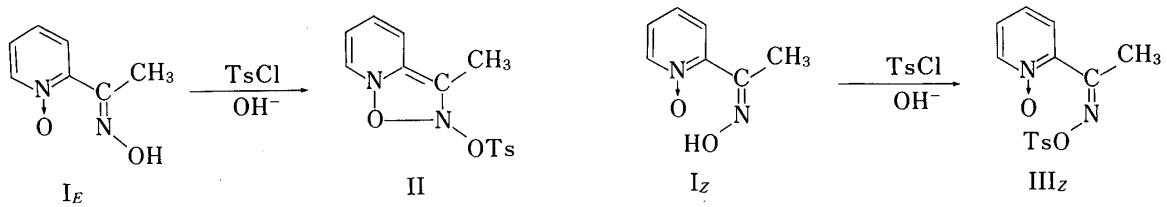
The reactions of (*E*)-methyl 1-oxido-2-quinolyl ketone oxime (V_E), (*E*)- and (*Z*)-methyl 1-oxido-4-quinolyl ketone oxime (VII_E and VII_Z) and (*Z*)-methyl 2-oxido-1-isoquinolyl ketone oxime (IX_Z) with tosyl chloride in the presence of NaOH were investigated to compare the reactivity of the N-oxide with that of the oxime group in the same molecule. In the reaction of V_E, 1-hydroxy-2-(1*H*)-quinolinone (XII) and 2(1*H*)-quinolinone (XIII) were obtained by the elimination of the acetoxime group. The mechanism of the formation of XII and XIII is discussed in detail. In the reaction of VII_E, Beckmann rearrangement occurred to afford 4-acetylaminoquinoline 1-oxide (XVIII), while the reactions of VII_Z and IX_Z gave only the tosylates of the oximes. These results demonstrate that there is a large difference of reactivity between the *E*-form and the *Z*-form, and further that V_E and VII_E show markedly different chemical behavior.

Keywords——methyl 1-oxido-quinolyl ketone oxime; methyl 2-oxido-1-isoquinolyl ketone oxime; *E*-form; *Z*-form; steric compression effect; ^{13}C-NMR; acetoxime group elimination; tosylation; Beckmann rearrangement

In the previous paper,[1] it was reported that in the reaction of (*E*)-methyl 1-oxido-2-pyridyl ketone oxime (I_E) with tosyl chloride (TsCl), neighboring group participation by the N-oxide group occurred, and the 1,2,5-oxadiazole derivative (II) was obtained as the sole product. On the other hand, the reaction of (*Z*)-methyl 1-oxido-2-pyridyl ketone oxime (I_Z) with TsCl resulted only in the formation of the tosylate (III_Z) of the oxime group of I_Z.



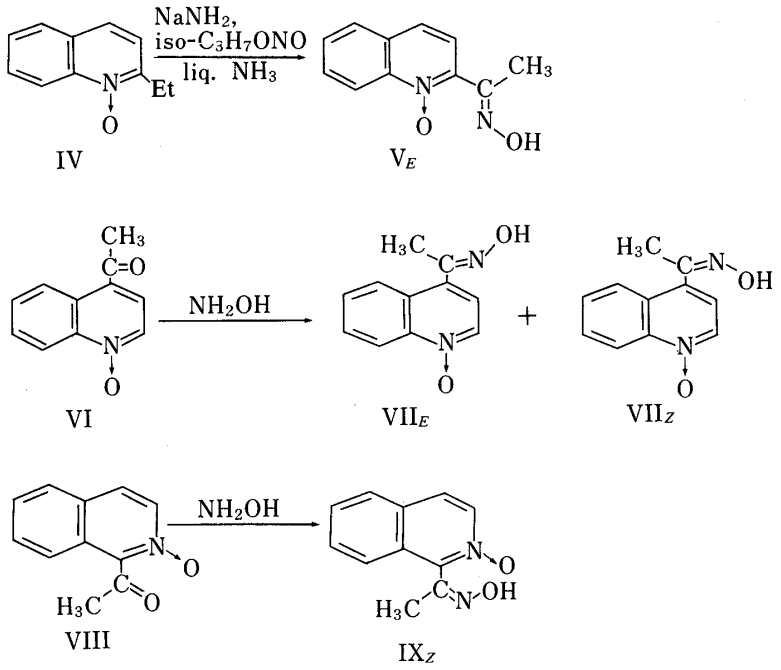
I_E II I_Z III_Z

Chart 1

As a continuation of our studies on the reaction of the oximes with TsCl, we investigated in the present work the reactions of methyl N-oxido-quinoyl and -isoquinolyl ketone oximes with TsCl in the presence of sodium hydroxide (NaOH).

(*E*)-Methyl 1-oxido-2-quinolyl ketone oxime (V_E) was prepared from the reaction of 2-ethylquinoline 1-oxide (IV) with isopropyl nitrite in the presence of $NaNH_2$ in liquid ammonia.[2] On the other hand, the corresponding 4-isomer (VII) and isoquinolyl derivative (IX) could not be obtained in satisfactory yields by the same method, but abnormal reactions occurred.[3] Therefore VII_E, VII_Z and IX_Z were prepared by the reaction of the corresponding acetyl derivatives with hydroxylamine under conventional conditions.

The configurations of the oximes V, VII, IX and X were determined by using the



IV V_E VI VII_E VII_Z VIII IX_Z

Chart 2

differences between the chemical shifts of the parent ketones and the corresponding oximes in the ^{13}C nuclear magnetic resonance (NMR) spectra described by Roberts *et al.*[4] and by using the OH proton chemical shifts in the ^{1}H-NMR spectra in deuterated dimethyl sulfoxide (DMSO-d_6) solution.[5] The results are summarized in Table I. The configurations have already been confirmed for methyl 1-oxido-2-pyridyl ketone oxime (I_E and I_Z)[6] and methyl phenyl ketone oxime (XI_E and XI_Z)[7] by other methods. The Δ values of the ^{13}C chemical shifts of the isomers of the oximes I, V, VII, IX, X and XI were calculated by using the equation $\Delta = \delta_{\text{ketone}} - \delta_{\text{ketoxime}}$ (ppm), where δ_{ketone} and δ_{ketoxime} are the ^{13}C-NMR chemical shifts for the parent ketones and the corresponding ketoximes, respectively. The subscripts 1, 2 and 3 represent the numbers on the carbons depicted in Table I. All the Δ_3 values of the *E*-forms are larger than those of the *Z*-forms, because of the steric compression effect. The opposite tendency is found in the case of the Δ_1 and Δ_2 values.

As shown in Table I, the OH proton chemical shifts for the *E*-forms (*syn*-methyl forms) of the oximes are larger than those for the *Z*-forms (*anti*-methyl forms) in all cases.

Although there is only one isomer in the cases of V and X, the Δ_3 values and the OH proton chemical shifts of these compounds are similar to the values for the known *E*-form compounds. Therefore it is assumed that the configurations of V and X are *E*-forms.

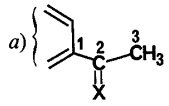
In the case of IX, the major isomer was purified by fractional recrystallization, but the minor isomer could not be isolated. The chemical shifts of IX in Table I were obtained from the NMR spectra of the mixture of these isomers. As judged from the values in Table I, the major isomer is *Z*-form and the minor one is *E*-form.

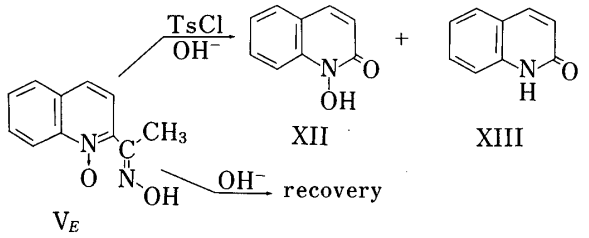
(*E*)-Methyl 1-oxido-2-quinolyl ketone oxime (V_E) reacted with TsCl in the presence of NaOH at room temperature to give unexpected products, *i.e.* 1-hydroxy-2(1*H*)-quinolinone (XII) and 2(1*H*)-quinolinone (XIII) in *ca.* 50% and *ca.* 25% yields, respectively, and no cyclic compound such as II could be detected. Compounds XII and XIII were identical in terms of the infrared (IR) spectra with authentic samples.[8] In order to confirm whether TsCl took part in this elimination reaction of the acetoxime group or not, V_E was treated with NaOH alone at room temperature, but V_E was recovered quantitatively (Chart 3-1).

From these results, it is clear that TsCl takes part in the formation of XII and XIII. We

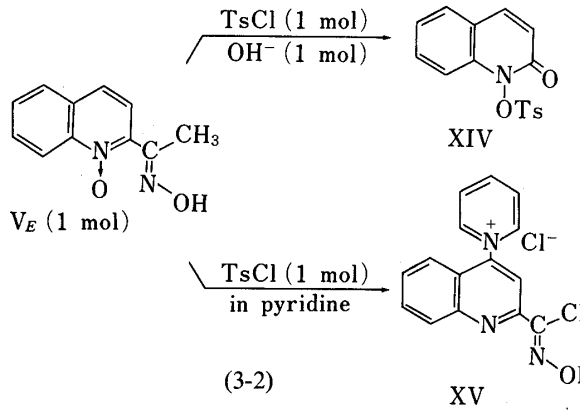
TABLE I. ^{13}C Substituent Shift Parameters ($\Delta = \delta_{ketone} - \delta_{ketoxime}$ (ppm)) for Conversion of Ketones to Ketoximes, and OH Proton Chemical Shifts (δ (ppm))

Parameter	Compound									
	XI_E	XI_Z	I_E	I_Z	V_E	VII_E	VII_Z	IX_E	IX_Z	X_E
Δ_1 [a]	0.60	3.1	0.49	2.13	0.12	0.34	0.82	—[b]	3.74	−1.65
Δ_2 [a]	41.70	43.3	44.95	48.30	44.35	46.35	48.78	—[b]	53.64	44.76
Δ_3 [a]	13.90	4.9	16.75	11.70	17.11	14.28	7.98	18.02	13.98	15.35
OH (δ (ppm))	—[c]	—[c]	11.53	10.90	11.73	11.79	10.82	11.68	10.97	11.66

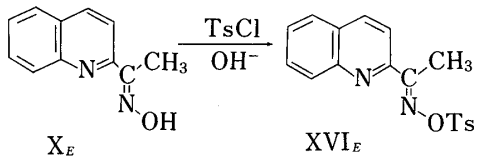
a)  X=O or NOH. b) These Δ values were not obtained. c) No data.



(3-1)



(3-2)



(3-3)

Chart 3

next investigated whether TsCl reacts with the oxygen atoms of both the N-oxide group and the oxime group or with only one.

The reactions of V_E with TsCl at reactant ratios of (a) 1 : 1, (b) 1 : 1.5, and (c) 1 : 2 were quantitatively investigated in the presence of excess NaOH. In all cases, XII and XIII were obtained in *ca.* 50% and *ca.* 25% yields, respectively, *i.e.* there was no significant difference among the yields of the products under these three conditions. These results indicate that TsCl does not attack both the oxygen atom of the N-oxide group and that of the oxime group, but only one of them.

Moreover, the reaction of V_E with TsCl in the presence of NaOH (at a reactant ratio of 1 : 1 : 1) gave 1-tosyloxy-2(1*H*)-quinolinone (XIV)[9] in 20% yield. Compound XIV is easily hydrolyzed in aqueous NaOH solution at room temperature to give XII in quantitative yield. In the case of a 1 : 1 ratio of V_E to TsCl in pyridine solution,[10] the reaction proceeded with the introduction of a pyridine ring at the 4-position of the quinoline nucleus accompanied with deoxygenation to give 1-[2-(α-hydroxyiminoethyl)quinolin-4-yl]pyridinium chloride (XV) in

84% yield. In this reaction the oxime group remained intact (Chart 3-2).

From these results, it is clear that TsCl attacks predominantly the oxygen atom of the N-oxide group in the initial step of the reaction of V_E.

In contrast, the reaction of (*E*)-methyl 1-oxido-2-pyridyl ketone oxime (I_E) with TsCl in the presence of NaOH (at a reactant ratio of 1 : 1 : 1) yielded only the cyclic compound (II).[1] This result in the case of I_E suggests that the tosylation occurred predominantly at the oxime group rather than at the oxygen of the N-oxide group. In the case of the reaction of (*E*)-methyl 2-quinolyl ketone oxime (X_E)[11] with TsCl in the presence of excess NaOH, only the corresponding tosylate (XVI_E) of the oxime group was obtained in 92% yield, and no products arising from the attack of hydroxide ion on the 2-position of the quinoline nucleus were formed (Chart 3-3). These results can be rationalized in terms of the fact that the electron-withdrawing effect of the N-oxide group is very much larger than that of nitrogen in the parent heterocyclic ring.

From the above results, the reaction of V_E with TsCl is supposed to proceed according to the scheme in Chart 4. First, tosylation of the oxygen atom of the N-oxide group of V_E by TsCl occurs, and subsequently a hydroxide ion attacks the carbon at the 2-position of the quinoline ring to form an intermediate (XVII). The intermediate XVII undergoes elimination of the acetoxime group followed by hydrolysis of XIV to form XII as indicated by the solid arrows in the structure XVII shown in Chart 4 (path A). This hypothesis is supported by the following observations. First, acetonitrile was detected in the reaction mixture by gas chromatography (GC). Second, 1-tosyloxy-2(1*H*)-quinolinone (XIV) was readily hydrolyzed by aqueous NaOH solution at room temperature to give XII in quantitative yield.

On the other hand, the formation of XIII can be rationalized in terms of path B. In the intermediate XVII, fission of the N–O bond of the N-tosyloxy group occurs with elimination of the acetoxime group according to the dotted arrows to give XIII. From the following experimental results, it seems reasonable to assume that the formation of XIII proceeds *via* path B. The reaction of V_E with TsCl in the presence of excess NaOH gave XII and XIII in a ratio of 2 : 1, while XIV was readily hydrolyzed under the same conditions to give only XII in quantitative yield. Consequently, it is evident that XIII is obtained not from the hydrolysis of XIV, but directly from the intermediate (XVII).

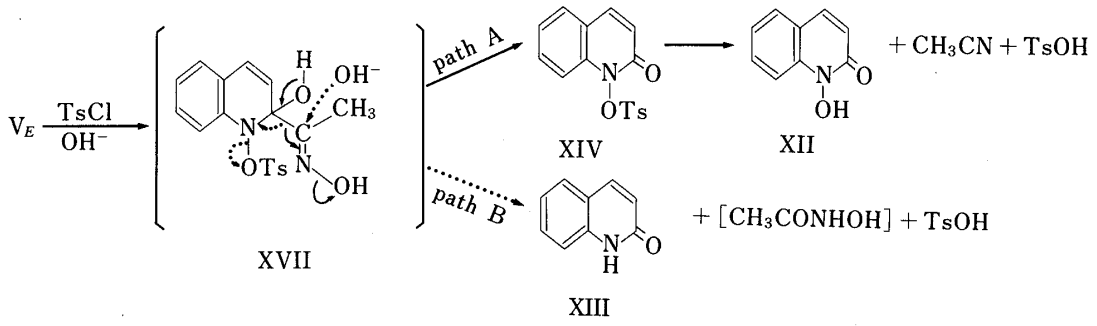


Chart 4

As regards the 4-isomer, (*Z*)-methyl 1-oxido-4-quinolyl ketone oxime (VII_Z) reacted with TsCl in the presence of NaOH under cooling with ice-salt to give only the tosylate (XIX_Z) quantitatively, while the *E*-form of the oxime (VII_E) afforded the rearranged product, 4-acetylaminoquinoline 1-oxide (XVIII),[12] in 30% yield under the same conditions. In the case of the isoquinoline derivative, the *Z*-form of the oxime (IX_Z) gave the tosylate of the oxime group (XX_Z) in 60% yield.

From all the results described above, it is considered that in the case of the reaction of N-oxide derivatives, the *Z*-forms of the oximes always give only the tosylates of the oxime

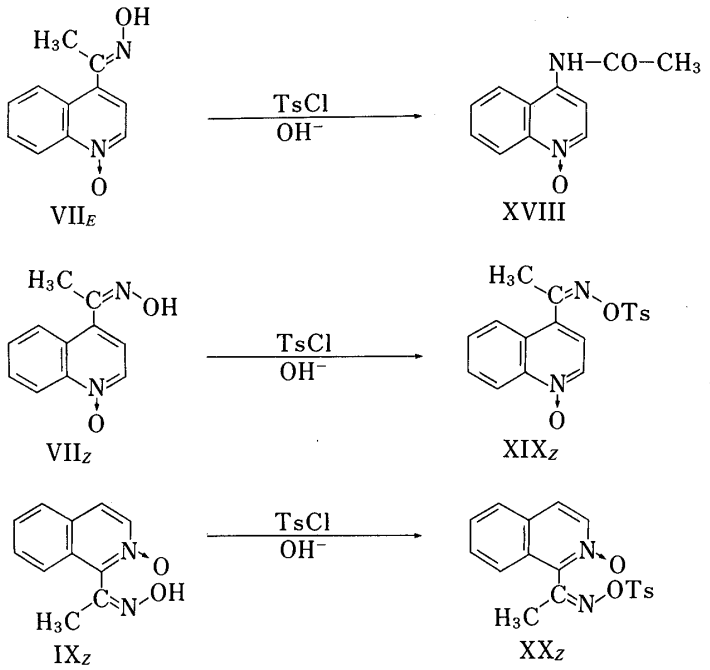


Chart 5

groups under the conditions described in this report. On the other hand, the *E*-forms of the oximes showed specific chemical behavior, *i.e.* I_E gave the cyclic 1,2,5-oxadiazole derivative (II), and V_E underwent elimination of the acetoxime group to give XII and XIII, while VII_E afforded the Beckmann rearrangement product (XVIII). It is assumed that the carbon at the 2-position of quinoline 1-oxide derivatives is strongly activated by the N-oxide group, while the effect of the N-oxide group on the carbon at the 4-position is not large, so that the Beckmann rearrangement occurs predominantly.

Further work is in progress.

Experimental

Melting points were measured on a Yanagimoto micro melting point apparatus and are uncorrected. Spectral data were recorded on the following spectrometers: ultraviolet (UV) spectra, Hitachi 556; IR spectra, Hitachi 295; ^{1}H-NMR spectra, Hitachi R-22 (90 MHz) and JEOL FX-100 (100 MHz); ^{13}C-NMR spectra, JEOL FX-100 (25.1 MHz); mass spectra (MS), JEOL JMS-DX300. High-performance liquid chromatography (HPLC) was conducted on a JASCO TRI ROTAR-II liquid chromatograph. Gas chromatographic analyses were performed on a Shimadzu GC-6AM gas chromatograph equipped with a flame ionization detector using nitrogen gas.

Oximation of 2-Ethylquinoline 1-Oxide (IV) and 2-Ethylquinoline. General Procedure——Reactions were carried out as described in the previous paper[2] but using isopropyl nitrite instead of amyl nitrite. Work-up of the products as described below gave V_E and X_E.

Methyl 1-Oxido-2-quinolyl Ketone Oxime (V_E): Recrystallization from pyridine–$CHCl_3$ or 95% EtOH gave pale yellow prisms, mp 237—238 °C (dec.) (56% yield). *Anal.* Calcd for $C_{11}H_{10}N_2O_2$: C, 65.35; H, 4.95; N, 13.86. Found: C, 65.37; H, 5.07; N, 13.85. UV λ_{max}^{EtOH} nm (log ε): 234.2 (4.39). IR ν_{max}^{KBr} cm^{-1}: 3000, 2810 (OH), 1635 (C=N), 1255 (N→O). ^{1}H-NMR (DMSO-d_6, 90 MHz) δ: 2.24 (3H, s, CH_3), 7.51—8.67 (6H, m, Ar-H), 11.73 (1H, s, OH). ^{13}C-NMR (DMSO-d_6) δ: 13.2 (q, CH_3), 118.7 (d, Ar), 122.5 (d, Ar), 124.6 (d, Ar), 128.5 (d, Ar), 128.7 (d, Ar), 129.8 (d, Ar), 130.4 (s, Ar), 141.1 (s, Ar), 142.3 (s, Ar), 151.8 (s, C=N). MS Calcd for $C_{11}H_{10}N_2O_2$: M^+, 202.074. Found *m/z*: M^+, 202.075.

Methyl 2-Quinolyl Ketone Oxime (X_E): The residue was chromatographed on a silica gel column with $CHCl_3$ to give pale yellow prisms (from ether), mp 147—148 °C (lit.[10] mp 143.5 °C) (12.4% yield). UV λ_{max}^{EtOH} nm (log ε): 247.2 (4.53). IR ν_{max}^{KBr} cm^{-1}: 3240, 2920 (OH). ^{1}H-NMR (DMSO-d_6, 90 MHz) δ: 2.40 (3H, s, CH_3), 7.49—8.40 (6H, m, Ar-H), 11.67 (1H, s, OH). ^{13}C-NMR (DMSO-d_6) δ: 9.9 (q, CH_3), 117.6 (d, Ar), 126.7 (d, Ar), 127.5 (s, Ar), 127.7 (d, Ar), 129.0 (d, Ar), 129.6 (d, Ar), 136.0 (d, Ar), 146.7 (d, Ar), 154.3 (s, Ar), 154.7 (s, C=N). MS Calcd for $C_{11}H_{10}N_2O$: M^+, 186.079. Found *m/z*: M^+, 186.079.

Oximation of 4-Acetylquinoline 1-Oxide (VI) and 1-Acetylisoquinoline 2-Oxide (VIII). General Procedure——A mixture of an acetyl derivative (0.01 mol) in 99% EtOH and hydroxylamine hydrochloride (0.012 mol dissolved in the minimum amount of water) was heated in the presence of sodium acetate (0.012 mol) for 2 h at the reflux temperature. The EtOH was evaporated off, cold water was added, and the resulting precipitate was filtered off and washed with water.

Methyl 1-Oxido-4-quinolyl Ketone Oxime (VII_E): The crude oxime was recrystallized from acetone to give a mixture of VII_E and VII_Z (1 : 1) (62% yield). VII_E was separated by fractional recrystallization (from 99% EtOH : H_2O = 4 : 1) or obtained by isomerization of VII_Z in the following manner.

A mixture (0.6 g) of VII_E and VII_Z was dissolved in 99% EtOH and then hydrogen chloride was bubbled into the solution with stirring under ice-cooling for *ca.* 30 min. The solvent was evaporated off as completely as possible under reduced pressure on a steam bath. A little water was added to the residue, and the aqueous solution was neutralized with aq. NH_3 and extracted with $CHCl_3$. The extract was dried over anhyd. Na_2SO_4 and the solvent was evaporated off. The residue was recrystallized from acetone to give VII_E, 0.4 g. Colorless prisms, mp 203—204 °C. *Anal.* Calcd for $C_{11}H_{10}N_2O_2$: C, 65.35; H, 4.95; N, 13.86. Found: C, 65.35; H, 5.00; N, 13.80. UV λ_{max}^{EtOH} nm (log ε): 233.6 (4.47). IR ν_{max}^{KBr} cm^{-1}: 3020, 2760 (OH), 1215 (N→O). ^{1}H-NMR (DMSO-d_6, 100 MHz) δ: 2.34 (3H, s, CH_3), 7.48—8.80 (6H, m, Ar-H), 11.79 (1H, s, OH). ^{13}C-NMR (DMSO-d_6) δ: 15.0 (q, CH_3), 119.1 (d, Ar), 121.2 (d, Ar), 127.1 (d, Ar), 127.4 (s, Ar), 128.9 (d, Ar), 130.1 (d, Ar), 132.3 (s, Ar), 134.6 (d, Ar), 140.9 (s, Ar), 152.1 (s, C=N). MS Calcd for $C_{11}H_{10}N_2O_2$: M^+, 202.074. Found *m/z*: M^+, 202.071.

Methyl 1-Oxido-4-quinolyl Ketone Oxime (VII_Z): VII_Z was also obtained by fractional recrystallization (from 99% EtOH: H_2O = 4 : 1). Colorless prisms, mp 217—218 °C. *Anal.* Calcd for $C_{11}H_{10}N_2O_2$: C, 65.35; H, 4.95; N, 13.86. Found: C, 65.38; H, 5.07; N, 13.78. UV λ_{max}^{EtOH} nm (log ε): 232.5 (4.49). IR ν_{max}^{KBr} cm^{-1}: 3000, 2810 (OH), 1640 (C=N), 1210 (N→O). ^{1}H-NMR (DMSO-d_6, 90 MHz) δ: 2.22 (3H, s, CH_3), 7.29—8.78 (6H, m, Ar-H), 10.82 (1H, s, OH). ^{13}C-NMR (DMSO-d_6) δ: 21.3 (q, CH_3), 119.0 (d, Ar), 119.8 (d, Ar), 126.3 (s, Ar), 126.8 (d, Ar), 128.7 (d, Ar), 130.2 (d, Ar), 132.2 (s, Ar), 134.6 (d, Ar), 140.5 (s, Ar), 149.7 (s, C=N). MS Calcd for $C_{11}H_{10}N_2O_2$: M^+, 202.074. Found *m/z*: M^+, 202.071.

Methyl 2-Oxido-1-isoquinolyl Ketone Oxime (IX_Z): The crude oxime was recrystallized from acetone containing a little 99% EtOH to give colorless prisms, mp 262—263 °C (dec.) (32% yield). *Anal.* Calcd for $C_{11}H_{10}N_2O_2$: C, 65.35; H, 4.95; N, 13.86. Found: C, 65.32; H, 4.93; N, 13.75. UV λ_{max}^{EtOH} nm (log ε): 258.4 (4.43). IR ν_{max}^{KBr} cm^{-1}: 3440, 3180 (OH), 1690 (C=N), 1260 (N→O). ^{1}H-NMR (DMSO-d_6, 90 MHz) δ: 2.19 (3H, s, CH_3), 7.33—8.33 (6H, m, Ar-H), 10.97 (1H, s, OH). ^{13}C-NMR (DMSO-d_6) δ: 17.1 (q, CH_3), 123.8 (d, Ar), 124.2 (d, Ar), 126.2 (s, Ar), 127.1 (d, Ar), 127.6 (s, Ar), 128.0 (d, Ar), 128.1 (d, Ar), 129.5 (d, Ar), 136.8 (s, Ar), 140.7 (s, C=N). MS Calcd for $C_{11}H_{10}N_2O_2$: M^+, 202.074. Found *m/z*: M^+, 202.075.

Reaction of V_E with TsCl——Run (a): TsCl (0.0025 mol) in tetrahydrofuran (THF) (6 ml) was added dropwise to a solution of V_E (0.0025 mol) in aqueous NaOH solution (0.01 mol of NaOH in 4 ml of H_2O) with stirring under water-cooling. The resulting solution was further stirred for 2 h at room temperature. After removal of the THF, the aqueous solution was neutralized with 10% HCl and extracted with $CHCl_3$. The solution was dried over anhyd. Na_2SO_4 and then evaporated completely. The residue was dissolved in CH_3CN–MeOH (10 : 1) and the yields of XII and XIII were determined by HPLC. The yields of XII and XIII were 0.2 g (50%) and 0.09 g (25%), respectively. HPLC conditions: column, Sorbax CN (4.6 × 250 mm); flow rate, 1.0 ml/min; detection, UV at 242 nm; eluent, CH_3CN–MeOH (10 : 1). CH_3CN was detected in the reaction mixture by GC. GC conditions: column, 5% Triton X-305, 3 mm × 2 m; column temperature 55 °C; t_R 7 min.

Run (b): Carried out as described for run (a) but using TsCl (0.00375 mol) and NaOH (0.0125 mol). The yields of XII and XIII were 0.18 g (46%) and 0.085 g (24%), respectively.

Run (c): Carried out as described for run (a) but using TsCl (0.005 mol) and NaOH (0.015 mol). The yields of XII and XIII were 0.2 g (51%) and 0.098 g (27%), respectively.

Reaction of V_E with TsCl in the Presence of NaOH at a Reactant Ratio of 1 : 1 : 1——TsCl (0.48 g, 0.0025 mol) in THF (6 ml) was added dropwise to a solution of V_E (0.5 g, 0.0025 mol) in aqueous NaOH solution (NaOH 0.1 g, 0.0025 mol and H_2O 4 ml) with stirring under ice-cooling. The resulting mixture was further stirred for 2 h at room temperature. After removal of THF, the aqueous solution was extracted with $CHCl_3$. The $CHCl_3$ layer was dried over anhyd. Na_2SO_4 and then evaporated completely. The residue was recrystallized from acetone–petr. ether to give XIV (0.15 g, 20%) and the starting material (0.05 g, 10%).

Reaction of I_E with TsCl in the Presence of NaOH at a Reactant Ratio of 1 : 1 : 1——TsCl (0.63 g, 0.0033 mol) in THF (6 ml) was added dropwise to a solution of I_E (0.5 g, 0.0033 mol) in aqueous NaOH solution (0.13 g (0.0033 mol) of NaOH in 4 ml of H_2O) with stirring under ice-cooling. The resulting mixture was further stirred for 2 h at room temperature. After removal of THF, the aqueous solution was extracted with $CHCl_3$. The $CHCl_3$ layer was dried over anhyd. Na_2SO_4 and then evaporated completely. The residue was recrystallized from acetone–petr. ether to give II 0.25 g (25%).

Reaction of V_E with TsCl at a Reactant Ratio of 1 : 1 in Pyridine——TsCl (0.48 g, 0.0025 mol) was added in small portions to a solution of V_E (0.5 g, 0.0025 mol) in pyridine (10 ml) with stirring under ice-cooling. The resulting solution was further stirred for 2 h at room temperature. The precipitated crystals were filtered off, the pyridine in the

filtrate was largely evaporated off under reduced pressure, and the residue was dissolved in water and extracted with $CHCl_3$. A small amount of starting material was obtained from the $CHCl_3$ layer. From the aqueous layer the same crystals as above were obtained. Recrystallization from acetone–95% EtOH gave colorless prisms XV, mp 218 °C, 0.63 g (84% yield). *Anal.* Calcd for $C_{16}H_{14}N_3O \cdot C_6H_2N_3O_7$ (picrate): C, 53.66; H, 3.25; N, 17.07. Found: C, 53.69; H, 3.30; N, 17.03. UV λ_{max}^{EtOH} nm (log ε): 249 (4.79). IR ν_{max}^{KBr} cm^{-1}: 3400 (OH), 1620 (C=N). ^{1}H-NMR (DMSO-d_6, 100 MHz) δ: 2.40 (3H, s, CH_3), 7.40—9.50 (9H, m, Ar-H), 8.45 (1H, s, Ar-H), 12.10 (1H, s, OH). ^{13}C-NMR (DMSO-d_6) δ: 9.7 (q, CH_3), 115.4 (d, Ar), 121.3 (s, Ar), 121.3 (d, Ar), 128.3 (d, Ar), 129.1 (d, Ar), 129.4 (d, Ar), 131.4 (d, Ar), 145.8 (s, Ar), 145.8 (d, Ar), 147.6 (s, Ar), 147.9 (d, Ar), 153.7 (s, Ar), 154.7 (s, C=N). MS Calcd for $C_{16}H_{14}ClN_3O$: $(M-Cl)^+$, 264. Found *m/z*: $(M-Cl)^+$, 264.

Reaction of V_E with NaOH——A mixture of V_E (0.5 g, 0.0025 mol) in aqueous NaOH solution (NaOH 0.5 g, 0.0125 mol and H_2O 4 ml) and THF (5 ml) was stirred for 2 h at room temperature. After removal of the THF, the aqueous solution was neutralized with 10% HCl and extracted with $CHCl_3$. The extract was dried over anhyd. Na_2SO_4 and the solvent was evaporated off. The residue was recrystallized from pyridine–$CHCl_3$ to give the starting material, 0.4 g (80% recovery).

Reaction of IX_Z (or X_E) with TsCl. General Procedure——TsCl (0.003 mol) in THF (10 ml) was added dropwise to a solution of IX_Z (or X_E) (0.002 mol) in aqueous NaOH solution (NaOH 0.008 mol and H_2O 5 ml) with stirring under ice-cooling. The resulting solution was further stirred for 2 h at room temperature. After removal of the THF, the aqueous solution was cooled in an ice bath to give the crude product.

(*Z*)-1-(α-Tosyloxyiminoethyl)isoquinoline 2-Oxide (XX_Z): Recrystallization from 99% EtOH gave colorless prisms, mp 189—190 °C, 0.4 g (57% yield). *Anal.* Calcd for $C_{18}H_{16}N_2O_4S$: C, 60.67; H, 4.49; N, 7.87. Found: C, 60.45; H, 4.49; N, 7.80. UV λ_{max}^{EtOH} nm (log ε): 223.7 (4.55). IR ν_{max}^{KBr} cm^{-1}: 1365, 1330, 1180, 1190 (SO_2), 1230 (N→O). ^{1}H-NMR ($CDCl_3$, 90 MHz) δ: 2.38 (3H, s, CH_3), 2.47 (3H, s, tolyl-CH_3), 7.22—8.13 (10H, m, Ar-H). ^{13}C-NMR ($CDCl_3$) δ: 17.9 (q, CH_3), 21.7 (q, tolyl-CH_3), 123.0 (d, Ar), 125.0 (d, Ar), 125.9 (s, Ar), 127.4 (d, Ar), 128.5 (s, Ar), 128.9 (d, Ar), 129.0 (s, Ar), 129.6 (d, Ar), 130.4 (d, Ar), 132.1 (s, Ar), 136.5 (d, Ar), 145.3 (s, Ar), 157.2 (s, C=N). MS Calcd for $C_{18}H_{16}N_2O_4S$: M^+, 356.083. Found *m/z*: M^+, 356.083.

(*E*)-2-(α-Tosyloxyiminoethyl)quinoline (XVI_E): Recrystallization from ether gave colorless prisms, mp 137—138 °C (dec.), 1.54 g (92% yield). *Anal.* Calcd for $C_{18}H_{16}N_2O_3S$: C, 63.53; H, 4.71; N, 8.24. Found: C, 63.39; H, 4.70; N, 8.04. UV λ_{max}^{EtOH} nm (log ε): 245 (4.60). IR ν_{max}^{KBr} cm^{-1}: 1375, 1190, 1180 (SO_2). ^{1}H-NMR ($CDCl_3$, 90 MHz) δ: 2.44 (3H, s, CH_3), 2.59 (3H, s, tolyl-CH_3), 7.22—8.18 (10H, m, Ar-H). ^{13}C-NMR (C_5D_5N) δ: 12.3 (q, CH_3), 21.3 (q, tolyl-CH_3), 118.6 (d, Ar), 128.1 (d, Ar), 128.2 (d, Ar), 128.9 (s, Ar), 129.3 (d, Ar), 130.1 (d, Ar), 130.3 (d, Ar), 130.3 (d, Ar), 133.0 (s, Ar), 137.0 (d, Ar), 145.9 (s, Ar), 147.6 (s, Ar), 151.5 (s, Ar), 165.0 (s, C=N). MS Calcd for $C_{18}H_{16}N_2O_3S$: M^+, 340.089. Found *m/z*: M^+, 340.089.

1-Tosyloxy-2(1*H*)-quinolinone (XIV)——A mixture of XII (0.4 g, 0.0025 mol) and TsCl (0.95 g, 0.005 mol) was stirred for 5 h in pyridine (*ca.* 20 ml) at room temperature. Practically all the pyridine was evaporated off at 40 °C under reduced pressure, then the residue was dissolved in $CHCl_3$. The $CHCl_3$ solution was dried over anhyd. Na_2SO_4 and evaporated to dryness. The resulting product was recrystallized from 99% EtOH to give colorless prisms, mp 142—143 °C, 0.57 g (72% yield). *Anal.* Calcd for $C_{16}H_{13}NO_4S$: C, 60.95; H, 4.13; N, 4.44. Found: C, 60.83; H, 4.09; N, 4.40. UV λ_{max}^{EtOH} nm (log ε): 230 (4.61). IR ν_{max}^{KBr} cm^{-1}: 1690 (C=O), 1380, 1190, 1180 (SO_2). ^{1}H-NMR ($CDCl_3$, 90 MHz) δ: 2.51 (3H, s, CH_3), 6.56—8.13 (10H, m, Ar-H). MS Calcd for $C_{16}H_{13}NO_4S$: M^+, 315.056. Found *m/z*: M^+, 315.056.

Hydrolysis of XIV——XIV (0.1 g, 0.32 mmol) in THF (10 ml) was added dropwise to a 10% aqueous NaOH solution (1.28 ml) with stirring under ice-cooling. The resulting solution was further stirred for 2 h at room temperature. After removal of the THF, the aqueous solution was neutralized with 10% HCl and then extracted with $CHCl_3$. The $CHCl_3$ solution was dried over anhyd. Na_2SO_4 and evaporated to dryness. The residue was recrystallized from 99% EtOH to give XII, 0.05 g (98% yield).

Reactions of VII_E and VII_Z with TsCl. General Procedure——TsCl (0.0052 mol) in THF (20 ml) was added dropwise to a solution of VII_E (or VII_Z) (0.0035 mol) in aqueous NaOH solution (NaOH 0.014 mol and H_2O 10 ml) with stirring under cooling with ice-salt mixture. The resulting solution was continuously stirred for 2 h, then extracted with $CHCl_3$. The $CHCl_3$ solution was dried over anhyd. Na_2SO_4 and evaporated under reduced pressure to give the crude product.

4-Acetylaminoquinoline 1-Oxide (XVIII): The crude product was chromatographed on a silica gel column with benzene–MeOH (10 : 1) to give colorless needles (from ether–petr. ether), mp 247—248 °C, 0.21 g (30% yield). The mp and IR spectrum coincided with those of an authentic sample.[11]

(*Z*)-4-(α-Tosyloxyiminoethyl)quinoline 1-Oxide (XIX_Z): Recrystallization from ether–petr. ether gave colorless prisms, mp 154—155 °C, 0.33 g (95% yield). *Anal.* Calcd for $C_{18}H_{16}N_2O_4S$: C, 60.67; H, 4.49; N, 7.87. Found: C, 60.56; H, 4.57; N, 7.77. UV λ_{max}^{EtOH} nm (log ε): 232.2 (4.61). IR ν_{max}^{KBr} cm^{-1}: 1680 (C=N), 1370, 1190, 1180 (SO_2), 1210 (N→O). ^{1}H-NMR ($CDCl_3$, 90 MHz) δ: 2.33 (3H, s, CH_3), 2.48 (3H, s, tolyl-CH_3), 6.89—8.87 (10H, m, Ar-H). ^{13}C-NMR ($CDCl_3$) δ: 21.7 (q, CH_3), 22.3 (q, tolyl-CH_3), 118.5 (d, Ar), 120.3 (d, Ar), 125.3 (d, Ar), 125.8 (s, Ar), 128.8 (d, Ar), 129.6 (d, Ar), 130.8 (d, Ar), 132.1 (s, Ar), 134.6 (d, Ar), 141.4 (s, Ar), 145.3 (s, Ar), 161.7 (s, C=N). MS Calcd for $C_{18}H_{16}N_2O_4S$: M^+, 356.083. Found *m/z*: M^+, 356.081.

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