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Studies on Tertiary Amine Oxides. LXIX.[1] Reactions of 2-Chloromethylquinoline Derivatives with 2-Nitropropane

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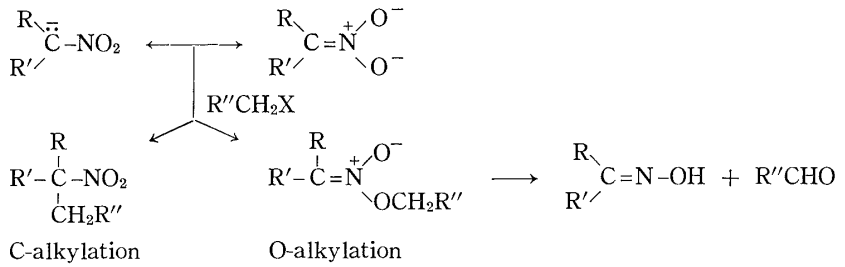
Reactions of 2-chloromethylquinoline (**1**), its N-oxide (**2**) and their nitro derivatives with the sodium salt of 2-nitopropane were investigated. O-Alkylation occurred with **1** and **2**, giving 2-quinolinecarboxyaldehyde (**5**: 11%) and its N-oxide (**6**: 10%). The reaction of 2-chloromethyl-5-nitroquinoline (**3b**) gave both the O-alkylation product, 5-nitro-2-quinolinecarboxyaldehyde (**7**: 21%), and the C-alkylation products, 2-(2-methyl-2-nitropropyl)-5-nitroquinoline (**8b**: 24%) and 2-(2-methyl-1-propenyl)-5-nitroquinoline (**9b**: trace). In the reactions of the 6-nitro (**3c**) and 8-nitro (**3d**) derivatives of **1**, the 2-(2-methyl-2-nitropropyl)quinolines (**8c**: 86% and **8d**: 63%) were predominantly formed. In contrast, the reactions of the 4-nitro (**4a**), 5-nitro (**4b**) and 6-nitro (**4c**) derivatives of **2** produced the corresponding 2-(2-methyl-1-propenyl)quinoline N-oxides (**11a**: 53%, **11b**: 20% and **11c**: 66%) as main products, accompanied by small amounts of the 2-(2-methyl-2-nitropropyl) compounds (**10a**: 20% and **10b**: 17%).

Keywords——nucleophilic substitution; radical anion-free radical chain process; $S_{RN}1$ mechanism; C-alkylation; O-alkylation; nitro derivatives of 2-chloromethylquinoline; nitro derivatives of 2-chloromethylquinoline 1-oxide; 2-(2-methyl-2-nitropropyl)quinolines and their N-oxides; 2-(2-methyl-1-propenyl)quinolines and their N-oxides

The alkylations of nitroalkane monoanions with alkyl halides may occur on either oxygen or carbon, depending upon the nature of the alkyl halide and the reaction conditions.[3]



O-Alkylations are more usual and give the carbonyl compound derived from the alkyl halide and the oxime derived from the nitroalkane. In 1966, Kornblum[4] and Russell[5] and their respective co-workers disclosed that the C-alkylations proceed by a chain process involving radical anions and free radicals, as illustrated below for the typical reaction of the sodium salt of 2-nitropropane with *p*- and *o*-nitrobenzyl[6] chlorides.

1) Part LXVIII: M.M. Yousif, S. Saeki, and M. Hamana, *J. Heterocycl. Chem.*, **17**, in press.
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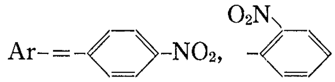
3) R.G. Coombes, "Comprehensive Organic Chemistry," Vol. 2, ed. by Sir D. Barton and W.D. Ollis, Pergamon Press Ltd., Oxford, 1979, Chapter 7.
4) *a*) N. Kornblum, R.E. Michael, and R.C. Kerber, *J. Am. Chem. Soc.*, **88**, 5660, 5662 (1966); *b*) N. Kornblum and F.W. Stuchal, *J. Am. Chem. Soc.*, **92**, 1804 (1970); *c*) N. Kornblum, *Angew. Chem. Int. Ed. Engl.*, **14**, 734 (1975).
5) *a*) G.A. Russell and W.C. Danen, *J. Am. Chem. Soc.*, **88**, 5663 (1966); *b*) *Idem, ibid.*, **90**, 347 (1968).
6) R.C. Kerber, G.W. Urry, and N. Kornblum, *J. Am. Chem. Soc.*, **87**, 4520 (1965).

$$ArCH_2Cl + [Me_2CNO_2]^- \longrightarrow [ArCH_2Cl]^{\dot{-}} + Me_2\dot{C}{-}NO_2$$

$$[ArCH_2Cl]^{\dot{-}} \longrightarrow ArCH_2\cdot + Cl^-$$

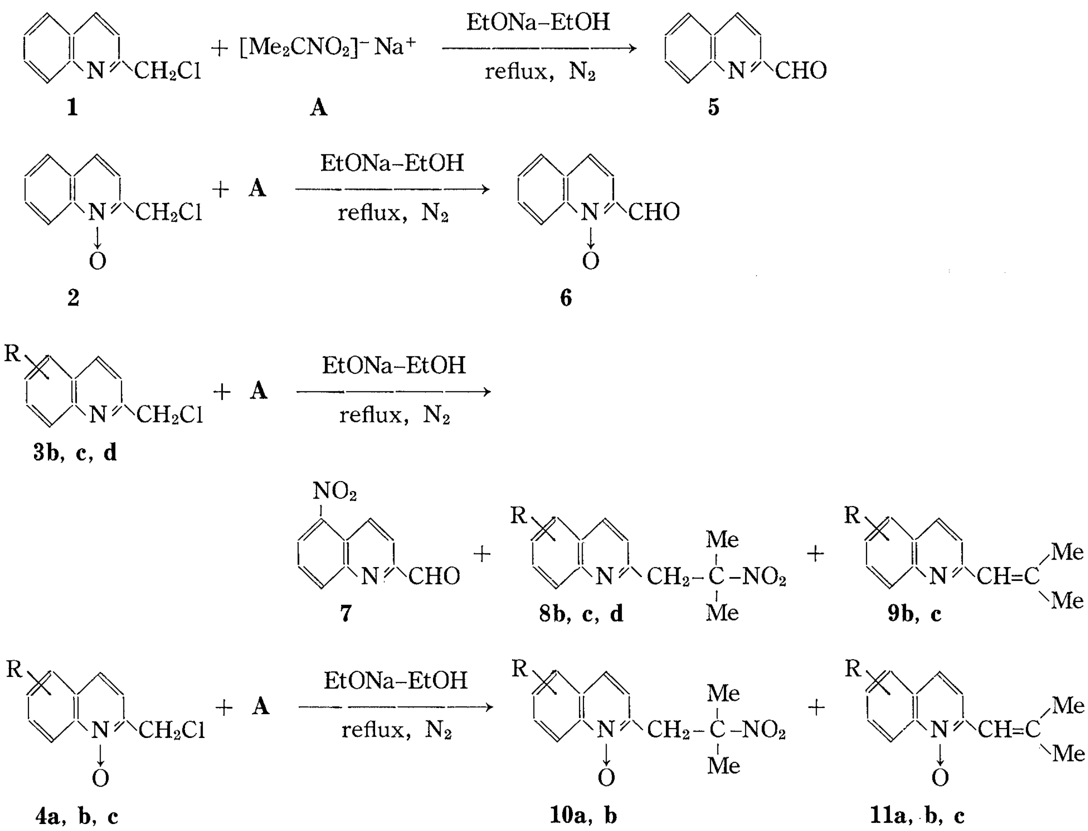
$$ArCH_2\cdot + [Me_2CNO_2]^- \longrightarrow \left[ArCH_2{-}C(Me)_2{-}NO_2\right]^{\dot{-}}$$

$$\left[ArCH_2{-}C(Me)_2{-}NO_2\right]^{\dot{-}} + ArCH_2Cl \longrightarrow ArCH_2{-}C(Me)_2{-}NO_2 + [ArCH_2Cl]^{\dot{-}}$$



In 1970, Bunnett and Kim[7] found aromatic substitutions which progress by a radical anion-free radical chain mechanism of the same pattern, and proposed the designation "$S_{RN}1$" for this type of reaction.

$S_{RN}1$ reactions at both aliphatic and aromatic sites are now attracting much attention as a new type of nucleophilic substitution of considerable synthetic values.[4c,8] We have studied these reactions of aromatic N-oxide derivatives of the pyridine and benzopyridine series, and have obtained some interesting results. This paper deals with our observations on the reactions of 2-chloromethylquinoline, its N-oxide and thier nitro derivatives with the sodium salt of 2-nitropropane. The results obtained are summarized in Chart 1 and Table I.



a: R=4-NO$_2$, **b**: R=5-NO$_2$, **c**: R=6-NO$_2$, **d**: R=8-NO$_2$

Chart 1

7) J.K. Kim and J.F. Bunnett, *J. Am. Chem. Soc.*, **92**, 7463, 7464 (1970).
8) J.F. Bunnett, *Accts. Chem. Res.*, **11**, 413 (1978).

First, the reactions of 2-chloromethylquinoline (**1**) and its N-oxide (**2**) were investigated. Using the procedure of Hass and Bender,[9] 1.4 eq. of ethanolic sodium ethoxide was added dropwise to a solution of **1** or **2** and 5 eq. of 2-nitropropane in ethanol, and the reactants were refluxed for 20 min in a stream of nitrogen. Only O-alkylation occurred in each case, and 2-quinolinecarboxyaldehyde (**5**)[10] and its N-oxide (**6**)[11] were isolated in poor yields of 11 and 10%, respectively, accompanied by extensive resinification.

Next, some nitro derivatives of **1** and **2** were treated with 2-nitropropane under the same conditions.

Table I. Reaction of 2-Chloromethylquinoline Derivatives with the 2-Nitropropane Anion

2-Chloromethyl quinolines	O-Alkylation product (%)	C-Alkylation products (%)	
		2-(2-Methyl-2-nitropropyl)-quinoline	2-(2-Methyl-1-propenyl)-quinoline
1	**5**: 11	—	—
2	**6**: 10	—	—
4a	—	**10a**: 22	**11a**: 53
3b	**7**: 21	**8b**: 24	**9b**: trace
4b	—	**8b**: 17	**11b**: 20
3c	—	**8c**: 86	**9c**: trace
4c	—	—	**11c**: 66
3d	—	**8d**: 63	—

The reaction of 2-chloromethyl-4-nitroquinoline 1-oxide (**4a**) afforded 2-(2-methyl-2-nitropropyl)-4-nitroquinoline 1-oxide (**10a**) and 2-(2-methyl-1-propenyl)-4-nitroquinoline 1-oxide (**11a**) in 22 and 53% yields, respectively. Taking accout of the potential susceptibility of the 4-nitro group in quinoline 1-oxides to nucleophilic displacement with ethoxide, the high reactivity of the 2-chloromethyl group for C-alkylation of the sodium salt of 2-nitropropane (**A**) is very noteworthy.

While the reaction of 2-chloromethyl-5-nitroquinoline (**3b**) gave both the O-alkylation product (**7**, 21%) and the C-alkylation products (**8b**, 24%; **9b**, a trace), only the C-alkylation products (**10b**, 17%; **11b**, 20%) were obtained from the N-oxide of **3b** (**4b**). Both 5-nitroquinoline derivatives, **3b** and **4b**, seem to be somewhat less reactive than **4a**.

2-Chloromethyl-6-nitroquinoline (**3c**) readily reacted with **A** to give the 2-(2-methyl-2-nitropropyl)quinoline (**8c**) in high yield (86%) accompained by a trace amount of the 2-(2-methyl-1-propenyl)quinoline (**9c**). From the reaction of 2-chloromethyl-6-nitroquinoline 1-oxide (**4c**), the 2-(2-methyl-1-propenyl) product (**11c**) was isolated as the sole product in 66% yield.

The reaction of 2-chloromethyl-8-nitroquinoline (**3d**) also progressed readily and the 2-(2-methyl-2-nitropropyl)quinoline (**8d**) was formed as the sole product in 63% yield.

In order to confirm that the above C-alkylation proceeds by the $S_{RN}1$ mechanism, an ethanol solution of **4a**, **A** and a small amount (0.1 eq) of *p*-dinitrobenzene, a strong radical anion scavenger,[4c] were refluxed for 20 min in the dark. In spite of careful examination, no C-alkylation products (**10a** and **11a**) were detected; intractable substance were formed.

The structure of the products thus obtained was established by elemental analyses and spectral examinations; the nuclear magnetic resonance (NMR) data for the C-alkylation products are listed in Table II.

9) H.B. Hass and M.L. Bender, *J. Am. Chem. Soc.*, **71**, 1767, 3842 (1949).
10) H. Kaplan, *J. Am. Chem. Soc.*, **63**, 2654 (1930).
11) M. Hamana, S. Saeki, Y. Hatano, and M. Nagakura, *Yakugaku Zasshi*, **83**, 348 (1963).

Table II. NMR Data for C-Alkylation Products

Compd. No.	Chemical shifts: δ ($CDCl_3$)
8b	1.74 (6H, s, $2CH_3$), 3.64 (2H, s, $-CH_2-$), 7.45 (1H, d, $J=8.0$ Hz, C_3–H), 7.75 (1H, dd, $J=8.0$, 8.0 Hz, C_7–H), 8.30 (2H, d, $J=8.0$ Hz, C_6–H, C_8–H), 8.90 (1H, d, $J=8.0$ Hz, C_4–H)
8c	1.72 (6H, s, $2CH_3$), 3.64 (2H, s, $-CH_2-$), 7.36 (1H, d, $J=8.0$ Hz, C_3–H), 8.11 (1H, d, $J=9.0$ Hz, C_8–H), 8.14 (1H, d, $J=8.0$ Hz, C_4–H), 8.24 (1H, dd, $J=9.0$, 3.0 Hz, C_7–H), 8.74 (1H, d, $J=3.0$ Hz, C_5–H)
8d	1.67 (6H, s, $2CH_3$), 3.59 (2H, s, $-CH_2-$), 7.31 (1H, d, $J=9.0$ Hz, C_3–H), 7.61 (1H, dd, $J=8.0$, 8.0 Hz, C_6–H), 7.99 (2H, d, $J=8.0$ Hz, C_5–H, C_7–H), 8.12 (1H, d, $J=9.0$ Hz, C_4–H)
9b	2.04 (3H, d, $J=1.0$ Hz, CH_3), 2.25 (3H, d, $J=1.0$ Hz, CH_3), 6.50 (1H, m, $-CH=C<$), 7.49 (1H, d, $J=8.0$ Hz, C_3–H), 7.73 (1H, dd, $J=8.0$, 8.0 Hz, C_7–H), 8.26 (2H, d, $J=8.0$ Hz, C_6–H, C_8–H), 8.75 (1H, d, $J=8.0$ Hz, C_4–H)
9c	2.06 (3H, d, $J=1.0$ Hz, CH_3), 2.28 (3H, d, $J=1.0$ Hz, CH_3), 6.49 (1H, m, $-CH=C<$), 7.38 (1H, d, $J=8.0$ Hz, C_3–H), 8.06 (1H, d, $J=9.0$ Hz, C_8–H), 8.15 (1H, d, $J=8.0$ Hz, C_4–H), 8.37 (1H, dd, $J=9.0$, 3.0 Hz, C_7–H), 8.67 (1H, d, $J=3.0$ Hz, C_5–H)
9d	2.03 (3H, d, $J=1.0$ Hz, CH_3), 2.35 (3H, d, $J=1.0$ Hz, CH_3), 6.44 (1H, m, $-CH=C<$), 7.31 (1H, d, $J=9.0$ Hz, C_3–H, 7.46 (1H, dd, $J=8.0$, 8.0 Hz, C_6–H), 7.84—7.99 (2H, m, C_5–H, C_7–H), 8.07 (1H, d, $J=9.0$ Hz, C_4–H)
10a	1.75 (6H, s, $2CH_3$), 3.89 (2H, s, $-CH_2-$), 7.76—7.90 (2H, m, C_6–H, C_7–H), 8.13 (1H, s, C_3–H), 8.64—8.80 (2H, m, C_5–H, C_8–H)
10b	1.79 (6H, s, $2CH_3$), 3.65 (2H, s, $-CH_2-$), 7.40—7.81 (2H, m, C_3–H, C_7–H), 8.21—8.53 (2H, m, C_4–H, C_6–H), 9.08 (1H, d, $J=9.0$ Hz, C_8–H)
11a	2.04 (3H, d, $J=1.0$ Hz, CH_3), 2.15 (3H, d, $J=1.0$ Hz, CH_3), 6.70 (1H, m, $-CH=C<$), 7.70—7.90 (2H, m, C_6–H, C_7–H), 8.23 (1H, s, C_3–H), 8.62—8.81 (2H, m, C_5–H, C_8–H)
11b	2.60 (3H, d, $J=1.0$ Hz, CH_3), 2.12 (3H, d, $J=1.0$ Hz, CH_3), 6.74 (1H, m, $-CH=C<$), 7.51—7.90 (2H, m, C_3–H, C_7–H), 8.24—8.40 (2H, m, C_4–H, C_6-H), 9.08 (1H, dd, $J=9.0$, 1.0 Hz, C_8–H)
11c	2.02 (3H, d, $J=1.0$ Hz, CH_3), 2.10 (3H, d, $J=1.0$ Hz, CH_3), 6.80 (1H, m, $-CH=C<$), 7.55 (1H, d, $J=8.0$ Hz, C_3–H), 7.80 (1H, d, $J=8.0$ Hz, C_4–H), 8.44 (1H, dd, $J=9.0$, 4.0 Hz, C_7–H) ,8.76 (1H, d, $J=4.0$ Hz, C_5–H), 8.92 (1H, d, $J=9.0$ Hz, C_8–H)

The starting materials of the above reactions were prepared by the reactions shown in Chart 2. The nitration of **2** to **4a** was achieved in 61% yield by warming **2** with a mixture of potassium nitrate and 85% sulfuric acid at 50°, whereas the yield of **4a** decreased to 29% when 95% sulfuric acid was used.[12]

The above results demonstrate that the C-alkylation of 2-nitropropane occurs not with **1** and **2** but with their nitro derivatives **3b,c,d** and **4a,b,c**. Thus, not only the nitrogen of the quinoline ring but also its N-oxide function are not effective for the initiation of $S_{RN}1$ reaction at the *ortho*-chloromethyl group with the 2-nitropropane anion, in contrast to the case of *o*-nitrobenzyl chloride. It is readily understandable that the 6- and 8-nitro derivatives (**3c**, **4c**, and **3d**) are highly reactive as regards C-alkylation, since transmission of the polar effect of the nitro groups to the 2-position is possible. However, the finding that the reaction also proceeds with the 4- and 5-nitro derivatives (**4a**, **3b**, and **4b**) is rather surprising, because the positions of the nitro groups in these compounds can be regarded as being equivalent to the β-position of the 2-chloromethyl function. Although it is conceivable that an interaction between the 4-nitro group, for instance, and the nitrogen atom or the N-oxide group may promote the $S_{RN}1$ reaction, the capacity of the compound as a whole for accepting an electron seems more important. The phenomenon remains to be studied in detail.

Considerable differences were observed in the composition of the C-alkylation products from the nitroquinolines (**3b**, **3c**, and **3d**) and the nitroquinoline 1-oxides (**4a**, **4b**, and **4c**). Only trace amounts of 2-(2-methyl-1-propenyl)quinolines (**9b** and **9c**) were obtained from the reactions of **3b** and **3c**; **3d** did not give the corresponding product. On the other hand,

12) *cf.* M. Hamana and T. Nagayoshi, *Chem. Pharm. Bull.*, **14**, 319 (1966).

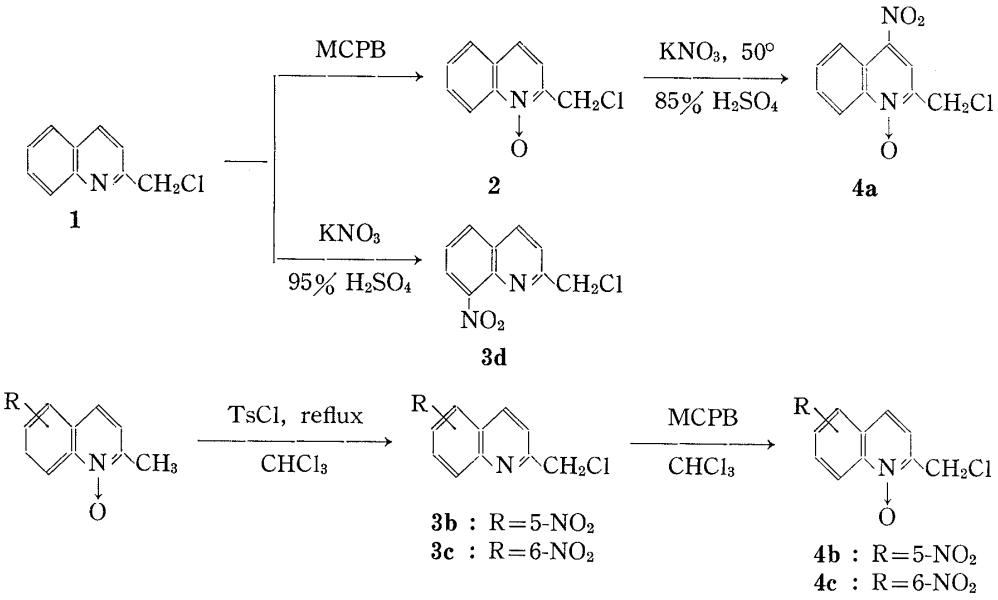
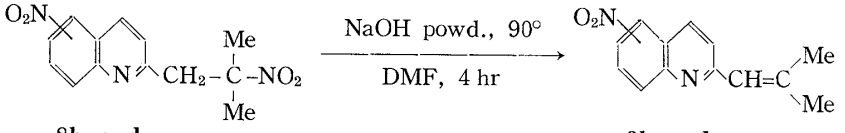


Chart 2

the formation of the 2-(2-methyl-1-propenyl)quinoline 1-oxides (**11a**, **11b**, and **11c**) was always predominant or exclusive in the reactions of **4a**, **4b**, and **4c**. Such easy formation of **11a**, **b**, **c** can be accounted for by the strong electron-withdrawing effect of the N-oxide function in the 2-(2-methyl-2-nitropropyl)quinoline 1-oxides (**10a**, **10b**, and **10c**), which would considerably accelerate the base-catalyzed elimination of nitrous acid; this is not the case for 2-(2-methyl-2-nitropropyl)quinolines (**8b**, **8c**, and **8d**). Nevertheless, **8b**, **8c**, and **8d** could be converted into the corresponding 2-(2-methyl-1-propenyl)quinolines (**9b**, **9c**, and **9d**) in good yields by heating them in the dimethylformamide (DMF) solution at 90° for 4 hr in the presence of sodium hydroxide powder.



8b, c, d **9b, c, d**

Experimental[13]

N-Oxidation of 2-Chloromethylquinolines with *m*-Chloroperbenzoic Acid (MCPB)——1) A solution of 2-chloromethylquinoline (**1**) (1.00 g) and MCPB (1.07 g, *ca.* 1.1 eq) in $CHCl_3$ (10 ml) was stirred at room temperature for 12 hr. Deposited benzoic acid was filtered off and the filtrate was washed with saturated Na_2CO_3 solution and dried over $MgSO_4$. The residue from the $CHCl_3$ solution was chromatographed on alumina with *n*-C_6H_{14}–benzene (1: 1) to give 0.75 g (69%) of 2-chloromethylquinoline 1-oxide (**2**), colorless pillars, mp 126.5—128° (benzene). *Anal.* Calcd for $C_{10}H_8ClNO$: C, 62.03; H, 4.17; N, 7.23. Found: C, 62.21; H, 4.19; N, 7.41. MS *m/e*: 195 (M^++2), 193 (M^+). NMR ($CDCl_3$) δ: 5.05 (2H, s, CH_2Cl), 7.57—7.97 (5H, m, aromatic protons), 8.75 (1H, dd, J=8.0, 1.0 Hz, C_8–H).

2) Similar treatment of 2-chloromethyl-5-nitroquinoline (**3b**, 1.1 g) gave 0.59 g (51%) of 2-chloromethyl-5-nitroquinoline 1-oxide (**4b**), yellow needles, mp 137—139° (MeOH–H_2O). *Anal.* Calcd for $C_{10}H_7ClN_2O_3$: C, 50.33; H, 2.96; N, 11.74. Found: C, 50.46; H, 2.84; N, 11.56. MS *m/e*: 240 (M^++2), 238 (M^+). IR ν_{max}^{Nujol} cm^{-1}: 1530, 1355 (NO_2). NMR ($CDCl_3$) δ: 5.00 (2H, s, CH_2Cl), 7.63—7.99 (2H, m, C_3–H, C_7–H), 8.30—8.54 (2H, m, C_4–H, C_6–H), 9.12 (1H, d, J=9.0 Hz, C_8–H).

3) Similar treatment of 2-chloromethyl-6-nitroquinoline (**3c**, 0.81 g) gava 0.62 g (72%) of 2-chloromethyl-6-nitroquinoline 1-oxide (**4c**), yellow needles, mp *ca.* 265° (dec.) (MeOH). *Anal.* Calcd for $C_{10}H_7$-

13) All melting and boiling points are uncorrected. IR spectra were recorded on a JASCO IR-E spectrophotometer. NMR spectra were measured with a JEOL PS-100 spectrometer at 100 MHz using TMS as an internal reference. Mass spectra were obtained on a JMS 01SG spectrometer.

ClN_2O_3: C, 50.33; H, 2.96; N, 11.74. Found: C, 50.21; H, 2.81; N, 11.86. MS *m/e*: 240 (M^++2), 238 (M^+). IR ν_{max}^{Nujol} cm^{-1}: 1540, 1355 (NO_2). NMR ($CDCl_3$) δ: 5.01 (2H, s, CH_2Cl), 7.64 (1H, d, J=8.0 Hz, C_3–H), 8.14 (1H, d, J=8.0 Hz, C_4–H), 8.48 (1H, dd, J=9.0, 3.0 Hz, C_7–H), 8.79 (1H, d, J=3.0 Hz, C_5–H), 9.15 (1H, d, J=8.0 Hz, C_8–H).

2-Chloromethyl-4-nitroquinoline 1-Oxide (4a)——A solution of **2** (1.00 g) and KNO_3 (0.57 g, 1.1 eq) in 85% H_2SO_4 (10 ml) was stirred at 50° for 5 hr. The reactants were poured into ice-water and kept at room temperature for 12 hr. Precipitated crystals were filtered off, washed with water and recrystallized from $CHCl_3$–MeOH to give 0.75 g (61%) of **4a**, yellow needles, mp 160—161.5°. *Anal.* Calcd for $C_{10}H_7ClN_2O_3$: C, 50.33; H, 2.96; N, 11.74. Found: C, 50.12; H, 2.84; N, 11.96. MS *m/e*: 240 (M^++2), 238 (M^+). IR ν_{max}^{Nujol} cm^{-1}: 1530, 1330 (NO_2). NMR ($CDCl_3$) δ: 5.00 (2H, s, CH_2Cl), 7.80—7.95 (2H, m, C_6–H, C_7–H), 7.50 (1H, s, C_3–H), 8.70—8.85 (2H, m, C_5–H, C_8–H).

2-Chloromethyl-5-nitroquinoline (3b)——A solution of 5-nitroquinaldine 1-oxide[14] (1.00 g) and TsCl (1.03 g, 1.1 eq) in $CHCl_3$ (100 ml) was refluxed for 6 hr.[15] The reaction mixture was concentrated and the residue was chromatographed on alumina with benzene and $CHCl_3$. The fraction eluted with benzene–$CHCl_3$ (*ca.* 2: 1) gave 0.39 g (33%) of **3b**, yellow needles, mp 89—90° (MeOH–H_2O). *Anal.* Calcd for $C_{10}H_7ClN_2O_2$: C, 53.95; H, 3.17; N, 12.58. Found: C, 53.61; H, 3.01; N, 12.40. MS *m/e*: 224 (M^++2), 222 (M^+). IR ν_{max}^{Nujol} cm^{-1}: 1510, 1350 (NO_2). NMR ($CDCl_3$) δ: 4.85 (2H, s, CH_2Cl), 7.75 (1H, d, J=8.0 Hz, C_3–H), 7.82 (1H, d, J=9.0 Hz, C_7–H), 8.35 (2H, d, J=9.0 Hz, C_6–H, C_8–H), 9.02 (1H, d, J=8.0 Hz, C_4–H).

6-Nitroquinaldine 1-Oxide and 2-Chloromethyl-6-nitroquinoline (3c)——1) A solution of 6-nitroquinaldine (3.4 g) and MCPB (3.43 g, 1.1 eq) in $CHCl_3$ (30 ml) was stirred at room temperature for 12 hr. Deposited benzoic acid was filtered off, and the filtrate was washed with saturated $NaHCO_3$ solution then dried over $MgSO_4$. The residue from the $CHCl_3$ solution was chromatographed on alumina with benzene to give 3.13 g (85%) of 6-nitroquinaldine 1-oxide, yellow fine crystals, mp *ca.* 252° (dec.) (MeOH–H_2O). *Anal.* Calcd for $C_{10}H_8N_2O_3$: C, 58.82; H, 3.95; N, 13.72. Found: C, 59.19; H, 4.21; N, 13.69. IR ν_{max}^{Nujol} cm^{-1}: 1535, 1350 (NO_2). NMR ($CDCl_3$) δ: 3.78 (3H, s, CH_3), 7.50 (1h, d, J=8.0 Hz, C_3–H), 7.85 (1H, d, J=8.0 Hz, C_4–H), 8.45 (1H, dd, J=9.0, 3.0 Hz, C_7–H), 8.78 (1H, d, J=3.0 Hz, C_5–H), 8.93 (1H, d, J=9.0 Hz, C_8–H).

2) 6-Nitroquinaldine 1-oxide (1.00 g) was refluxed with TsCl (1.30 g)–$CHCl_3$ (100 ml) for 6 hr. Chromatography on alumina with benzene–$CHCl_3$ gave 0.34 g (29%) of **3c**, yellow pillars (MeOH–H_2O). *Anal.* Calcd for $C_{10}H_7ClN_2O_2$: C, 53.95; H, 3.17; N, 12.58. Found: C, 54.34; H, 3.21; N, 12.48. MS *m/e*: 224 (M^++2), 222 (M^+). IR ν_{max}^{Nujol} cm^{-1}: 1535, 1350 (NO_2). NMR ($CDCl_3$) δ: 4.84 (2H, s, $CHCl_2$), 7.74 (1H, d, J=8.0 Hz, C_3–H), 8.15 (1H, d, J=9.0 Hz, C_8–H), 8.34 (1H, d, J=8.0 Hz, C_4–H), 8.45 (1H, dd, J=9.0, 3.0 Hz, C_7–H), 8.76 (1H, d, J=3.0 Hz, C_5–H).

2-Chloromethyl-8-nitroquinoline (3d)——A solution of **1** (1.5 g) and KNO_3 (0.94 g, 1.1 eq) in 95% H_2SO_4 (10 ml) was stirred with ice-cooling for 2 hr. The reaction mixture was poured over ice (120 g), adjusted to pH 1—2 with K_2CO_3 solution and kept at room temperature for 12 hr. Precipitated crystals were filtered off, washed with water and recrystallized from MeOH–$CHCl_3$ to gave 0.79 g (42%) of **3d**, pale yellow needles, mp 156—156.5°. *Anal.* Calcd for $C_{10}H_7ClN_2O_2$: C, 53.95; H, 3.17; N, 12.58. Found: C, 53.81; H, 3.01; N, 12.64. MS *m/e*: 224 (M^++2), 222 (M^+). IR ν_{max}^{Nujol} cm^{-1}: 1530, 1370 (NO_2). NMR ($CDCl_3$) δ: 5.01 (2H, s, CH_2Cl), 7.78 (1H, dd, J=8.0, 8.0 Hz, C_6–H), 7.88 (1H, d, J=8.0 Hz, C_3–H), 8.31 (2H, d, J=8.0 Hz, C_5–H, C_7–H), 8.65 (1H, d, J=8.0 Hz, C_4–H).

Reaction of 1 with the Sodium Salt of 2-Nitropropane (A)——An EtOH solution of NaOEt, prepared from Na (0.18 g) and EtOH (10 ml), was added under a stream of N_2 to a solution of **1** (1.00 g) and 2-nitropropane (2.50 g, 5eq) in EtOH (10 ml). The reactants were refluxed under a stream of N_2 for 20 min. After cooling, the precipitate was filtered off and the filtrate was concentrated. The residue was chromatographed on alumina with benzene and $CHCl_3$. The fraction eluted with benzene–$CHCl_3$ (2: 1) was recrystallized from *n*-C_6H_{14} to give 0.09 g (11%) of 2-quinolinecarboxyaldehyde (**5**), pale yellow prisms, mp 68°. This was identical with an authentic sample[10] as judged by mixed melting point determination and comparison of their IR spectra.

Reaction of 2 with A——A similar reaction of **2** (1.00 g) with 2-nitropropane (2.29 g, 5 eq), Na (0.166 g) and EtOH (20 ml) gave 0.09 g (10%) of 2-quinolinecarboxyaldehyde 1-oxide (**6**),[11] yellow needles, mp 121—122° (benzene–*n*-C_6H_{14}).

Reaction of 3b with A——An EtOH solution of NaOEt, prepared from Na (0.02 g) and EtOH (2 ml), was added under a stream of N_2 to a solution of **3b** (0.20 g) and 2-nitropropane (0.08 g, 5 eq) in EtOH (4 ml). The whole was refluxed under a stream of N_2 for 20 min. After cooling, a precipitate was filtered off and the filtrate was concentrated. The residue was chromatographed on alumina with *n*-C_6H_{14}, benzene and $CHCl_3$. The first fraction eluted with *n*-C_6H_{14} gave a trace amount of 2-(2-methyl-1-propenyl)-5-nitroquinoline (**9b**). This was identical with a sample prepared from 2-(2-methyl-2-nitropropyl)-5-nitroquinoline (**8b**) as judged by comparison of their NMR spectra. The second fraction eluted with *n*-C_6H_{14}–benzene (2: 1) gave 0.06 g (24%) of **8b**, yellow oil, bp 195° (0.9 mmHg) (bath temp.). *Anal.* Calcd for $C_{13}H_{13}N_3O_4$: C, 56.72;

14) E. Ochiai and K. Satake, *Yakugaku Zasshi*, **71**, 1078 (1951).
15) *cf.* M. Hamana and M. Yamazaki, *Chem. Pharm. Bull.*, **11**, 415 (1963).

H, 4.76; N, 15.27. Found: C, 56.61; H, 4.60; N, 15.54. MS *m/e*: 279 (M^+-NO_2). IR ν_{max}^{Nujol} cm^{-1}: 1530, 1350 (NO_2). The last fraction eluted with benzene–$CHCl_3$ (1: 1) gave 0.04 g (21%) of 5-nitro-2-quinolinecarboxyaldehyde (**7**), colorless fine crystals, mp 164° (MeOH–H_2O). *Anal.* Calcd for $C_{10}H_6N_2O_3$: C, 59.41; H, 2.99; N, 13.86. Found: C, 59.30; H, 2.81; N, 13.71. MS *m/e*: 202 (M^+). IR ν_{max}^{Nujol} cm^{-1}: 1710 (CHO), 1520, 1350 (NO_2). NMR ($CDCl_3$) δ: 7.91 (1H, dd, $J=8.0$, 8.0 Hz, C_7–H), 8.19 (1H, d, $J=9.0$ Hz, C_3–H), 8.51 (2H, m, C_6–H, C_8–H), 9.15 (1H, d, $J=9.0$ Hz, C_4–H), 10.21 (1H, s, CHO).

Reaction of 3c with A——The 6-nitro derivative **3c** (0.20 g) was treated with **A** as described above. The resulting mixture of products was chromatographed on alumina with *n*-C_6H_{14}, benzene and $CHCl_3$. The fraction eluted with *n*-C_6H_{14} gave a trace amount of 2-(2-methyl-1-propenyl)-6-nitroquincline (**9c**). Its identity was confirmed by NMR spectral examination. The fraction eluted with *n*-C_6H_{14}–benzene (2: 1) afforded 0.21 g (86%) of 2-(2-methyl-2-nitropropyl)-6-nitroquinoline (**8c**), yellow prisms, mp 221—222° (MeOH–H_2O). *Anal.* Calcd for $C_{13}H_{13}N_3O_4$: C, 56.72; H, 4.76; N, 15.27. Found: C, 56.64; H, 4.77; N, 15.22. MS *m/e*: 229 (M^+-NO_2). IR ν_{max}^{Nujol} cm^{-1}: 1530, 1350 (NO_2).

Reaction of 3d with A——The 8-nitro derivative **3d** (0.20 was treated with **A** as described above. Chromatography on alumina with *n*-C_6H_{14} gave 0.155 g (63%) of 2-(2-methyl-2-nitropropyl)-8-nitroquinoline (**8d**), yellow needles, mp 109—112° (MeOH). *Anal.* Calcd for $C_{13}H_{13}N_3O_4$: C, 56.72; H, 4.76; N, 15.27. Found: C, 56.20; H, 4.48; N, 15.57.

Reaction of 4a with A——2-Chloromethyl-4-nitroquinoline 1-oxide (0.20 g) was treated with 2-nitropropane (0.075 g), Na (0.02 g) and EtOH (6 ml) as described above. The resulting mixture of products was chromatographed on alumina with *n*-C_6H_{14} and benzene. The fraction eluted with *n*-C_6H_{14} gave 0.11 g (53%) of 2-(2-methyl-1-propenyl)-4-nitroquinoline 1-oxide (**11a**), yellow prisms, mp 67—69° (MeOH–H_2O). *Anal.* Calcd for $C_{13}H_{12}N_2O_3$: C, 63.92; H, 4.95; N, 11.47. Found: C, 64.19; H, 4.69; N, 11.26. MS *m/e*: 244 (M^+). IR ν_{max}^{Nujol} cm^{-1}: 1530, 1335 (NO_2). The fraction eluted with *n*-C_6H_{14}–benzene (1: 1) gave 0.055 g (22%) of 2-(2-methyl-2-nitropropyl)-4-nitroquinoline 1-oxide (**10a**), yellow needles, mp 141—144° (MeOH–H_2O). *Anal.* Calcd for $C_{13}H_{12}N_2O_3$: C, 53.61; H, 4.50; N, 14.43. Found: C, 53.41; H, 4.49; N, 14.45. MS *m/e*: 244 (M^+). IR ν_{max}^{Nujol} cm^{-1}: 1530, 1330 (NO_2).

Reaction of 4b with A——The 6-nitro derivative **4b** (0.20 g) was similarly treated with 2-nitropropane (0.075 g), Na (0.02 g) and EtOH (4 ml). Chromatography on alumina with *n*-C_6H_{14}–benzene (3: 1) gave 0.082 g of a crystalline substance. The NMR spectrum clearly showed that this was a mixture of 2-(2-methyl-2-nitropropyl)- and 2-(2-methyl-1-propenyl)-5-nitroquinoline 1-oxide (**10b** and **11b**). The ratio of **10b** to **11b** was determined to be *ca.* 1: 1 from the integrated areas of the methyl signals at δ 1.79 in **10b** and δ 2.02 and 2.10 in **11b**. The yields of **10b** and **11b** were 17 and 20%, respectively. Attemped separation of this mixture into **10b** and **11b** failed because their *Rf* values were practically the same. NaOH powder (0.01 g) was added to a solution of the mixture in DMF (1 ml), and the whole was stirred at 90° for 4 hr. The reaction mixture was then poured into water and extracted with $CHCl_3$. The residue from the $CHCl_3$ extract was chromatographed on alumina with *n*-C_6H_{14}–benzene (3: 1) to give 0.06 g of **11b**, yellow needles, mp 107—110° (MeOH–H_2O). *Anal.* Calcd for $C_{13}H_{12}N_2O_3$: C, 63.92; H, 4.95; N, 11.47. Found: C, 63.96; H, 4.86; N, 11.43. MS *m/e*: 244 (M^+). IR ν_{max}^{Nujol} cm^{-1}: 1545, 1350 (NO_2).

Reaction of 4c with A——Similar treatment of **4c** (0.02 g) gave 0.135 g (66%) of 2-(2-methyl-1-propenyl)-6-nitroquinoline 1-oxide (**11c**), yellow scales, mp 198—200° (MeOH–H_2O). *Anal.* Calcd for $C_{13}H_{12}N_2O_3$: C, 63.92; H, 4.95; N, 11.39. Found: C, 63.58; H, 4.93; N, 11.39. MS *m/e*: 244 (M^+). IR ν_{max}^{Nujol} cm^{-1}: 1540, 1355 (NO_2).

Formation of 9b, c, d from 8b, c, d——1) A mixture of **8b** (0.20 g), NaOH powder (0.044 g) and DMF (1.5 ml) was stirred at 90° for 4 hr. Water (10 ml) was added to the reaction mixture and the whole was extracted four times with $CHCl_3$ (4 ml). The residue from the $CHCl_3$ extract was chromatographed on alumina with *n*-C_6H_{14} to give 0.118 g (71%) of **9b**, a yellow oil, bp 181° (0.7 mmHg) (bath temp.). *Anal.* Calcd for $C_{13}H_{12}N_2O_2$: C, 68.41; H, 5.30; N, 12.27. Found: C, 68.30; H, 5.29; N, 12.48. MS *m/e*: 228 (M^+). IR ν_{max}^{Nujol} cm^{-1}: 1530, 1345 (NO_2).

2) Similar treatment of **8c** (0.20 g) gave 0.132 g (79%) of **9c**, red plates, mp 108.5—109.5° (MeOH). *Anal.* Calcd for $C_{13}H_{12}N_2O_2$: C, 68.41; H, 5.30; N, 12.27. Found: C, 68.30; H, 5.21; N, 12.11. MS *m/e*: 228 (M^+). IR ν_{max}^{Nujol} cm^{-1}: 1530, 1340 (NO_2).

3) Similar treatment of **8d** (0.20 g) gave 0.116 g (69%) of **9d**, colorless pillars, mp 91.5—92.5° (MeOH). *Anal.* Calcd for $C_{13}H_{12}N_2O_2$: C, 68.41; H, 5.30; N, 12.27. Found: C, 68.38; H, 5.24; N, 12.01. MS *m/e*: 228 (M^+). IR ν_{max}^{Nujol} cm^{-1}: 1530, 1380 (NO_2).

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