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Synthesis of 4-Azidoquinoline 1-Oxides and Related Compounds[1]

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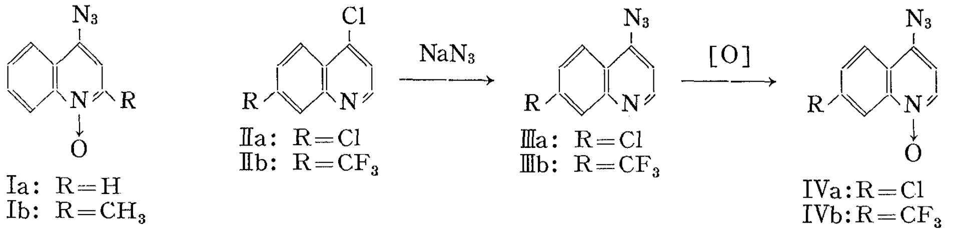
4-Azidoquinoline 1-oxides with methyl, cyano and carbamoyl groups at the 2 position, and chloro and trifluoromethyl groups at the 7 position were prepared. 4-Azidocinnoline 1-oxide and 2-oxide were also prepared. Their antitumor and mutagenic activities were tested in comparison with those of a carcinogenic, carcinostatic and mutagenic compound, 4-nitroquinoline 1-oxide.

Keywords——4-azidoquinoline 1-oxide; 4-azidocinnoline 1-oxide; 4-azidocinnoline 2-oxide; 4-azido-7-chloroquinoline 1-oxide; 4-azido-7-trifluoromethylquinoline 1-oxide; 4-azido-2-cyanoquinoline 1-oxide; 4-azido-2-carbamoylquinoline 1-oxide; 2,2′-dicarboxy-7,7′-dichloro-4,4′-azoquinoline 1,1′-dioxide; antitumor activity; mutagenic activity

4-Azidoquinoline 1-oxide reacts with sodium alkoxides to give 4-alkoxyquinoline 1-oxides, and, in boiling benzene, it gives 4,4′-azoquinoline 1,1′-dioxide accompanied by evolution of molecular nitrogen. However, 4-azidoquinoline itself is unreactive in both cases. Thus, the azido group of 4-azidoquinoline 1-oxide is very reactive, in contrast to usual aromatic azides.[3]

We synthesized 4-azidoquinoline 1-oxides and their derivatives in order to examine some of their biological activities.

4-Azidoquinoline 1-oxide (Ia) was previously synthesized by the reaction of 4-hydrazinoquinoline 1-oxide with nitrous acid.[4] This time, Ia was directly synthesized in 98% yield by heating 4-nitroquinoline 1-oxide (4-NQO) and sodium azide in aqueous ethanol. 4-Azido-2-methylquinoline 1-oxide (Ib) was prepared in 56% yield by treating 2-methyl-4-nitroquinoline 1-oxide with sodium azide. This compound was also prepared in 50% yield by the reaction of 4-hydrazino-2-methylquinoline 1-oxide with nitrous acid.



Ia: $R=H$
Ib: $R=CH_3$

IIa: $R=Cl$
IIb: $R=CF_3$

IIIa: $R=Cl$
IIIb: $R=CF_3$

IVa: $R=Cl$
IVb: $R=CF_3$

Chart 1

When 4,7-dichloroquinoline (IIa) and 4-chloro-7-trifluoromethylquinoline (IIb) were heated with sodium azide in aqueous ethanol, the corresponding azides, IIIa and IIIb, were obtained in 94% and 87% yields, respectively. The N-oxidation of IIIa and IIIb using a

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1) S. Kamiya, M. Anzai, T. Nakashima, S. Sueyoshi, M. Tanno, I. Suzuki, M. Ishidate, Jr. and S. Odashima, *Chem. Pharm. Bull.*, **25**, 504 (1977).
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3) S. Kamiya, *Chem. Pharm. Bull.*, **10**, 471 (1962).
4) T. Itai and S. Kamiya, *Chem. Pharm. Bull.*, **9**, 87 (1961).

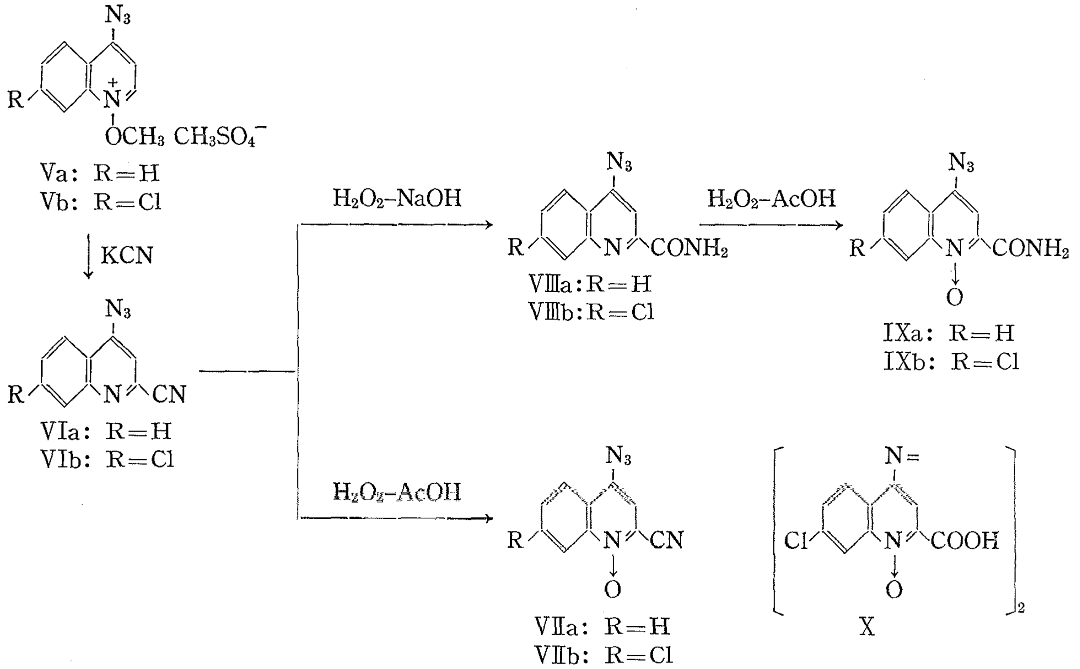


Chart 2

mixture of acetic acid and 30% hydrogen peroxide gave 4-azido-7-chloroquinoline 1-oxide (IVa) and 4-azido-7-trifluoromethylquinoline 1-oxide (IVb), both in yields of over 80% (Chart 1).

Treatment of Ia and IVa with dimethyl sulfate gave the methosulfates (Va, Vb) quantitatively. When these methosulfates were treated potassium cyanide, 4-azido-2-cyanoquinoline (VIa) and 4-azido-7-chloro-2-cyanoquinoline (VIb) were obtained in 63% and 39% yields, respectively. The corresponding 1-oxides (VIIa, VIIb) were prepared by heating VIa and VIb in a mixture of 30% hydrogen peroxide and acetic acid.

Heating VIa and VIb in a mixture of hydrogen peroxide and sodium hydroxide gave the corresponding 2-carbamoyl derivatives, VIIIa and VIIIb, and their N-oxidation using a mixture of 30% hydrogen peroxide and acetic acid gave the 1-oxides (IXa, IXb). In the latter case, 2,2′-dicarboxy-7,7′-dichloro-4,4′-azoquinoline 1,1′-dioxide (X) was isolated as a minor product (6%).

Subsequently, 4-azidocinnoline 1-oxide and 2-oxide were synthesized (Chart 3). The reaction of 4-chlorocinnoline with sodium azide in boiling aqueous ethanol gave 4-azidocin-

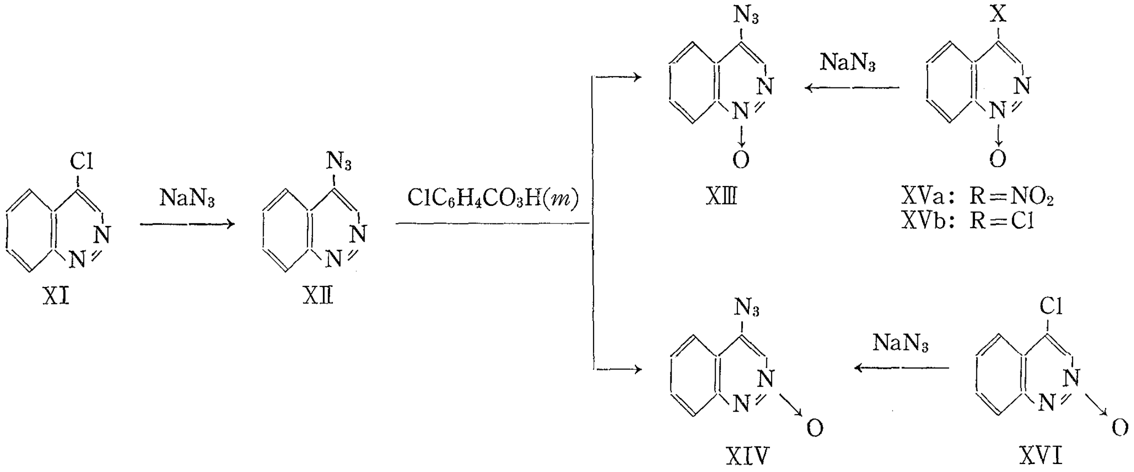


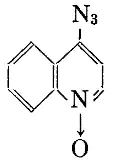
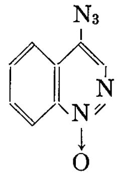
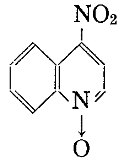
Chart 3

noline (XII). The N-oxidation of XII with *m*-chloroperbenzoic acid in chloroform at room temperature gave a mixture of the 1-oxide (XIII) and the 2-oxide (XIV). They were separated by recrystallization from ethanol to give XIII in 21% yield and XIV in 53% yield. Compound XIII could also be prepared by the reaction of 4-nitrocinnoline 1-oxide (XVa) or 4-chlorocinnoline 1-oxide (XVb) with sodium azide, both in good yields.

The reaction of 4-chlorocinnoline 2-oxide (XVI) and sodium azide also gave XIV in 86% yield. These 4-azidocinnoline N-oxides were very sensitive to light and developed color on standing. For instance, the photolysis of XIII in benzene under sunlight gave 4,4'-azocinnoline 1,1'-dioxide.

The antitumor activity of these 4-azidoquinoline 1-oxides (Ia, Ib, IVa, IVb, VIIa, VIIb, IXa, IXb) and 4-azidocinnoline N-oxides (XIII, XIV) was tested against rat ascites hepatoma AH-13 cells, but they were ineffective.

Table I. Mutagenic Activity of 4-Azidoquinoline 1-Oxide and Related Compounds

Compounds	Concentration (μg/ml)	Treatment (min)	Survival (%)	Number of surviving bacteria	Mutants per 10^8
Ia 	0	0	100.0	7.0×10^8	
	0	15	90.0	6.3×10^8	3.2
	50	15	82.9	5.8×10^8	5.2
	100	15	78.6	5.5×10^8	14.5
	200	15	68.6	4.8×10^8	25.0
	500	15	38.6	2.7×10^8	51.9
XIII 	0	0	100.0	8.5×10^8	
	0	15	83.5	7.1×10^8	1.4
	100	15	72.9	6.2×10^8	1.6
	200	15	72.9	6.2×10^8	1.6
	500	15	85.9	7.3×10^8	1.4
4-NQO 	0	0	100.0	8.2×10^8	
	0	15	86.6	7.1×10^8	1.4
	20	15	85.4	7.0×10^8	118.5

(Mutation from streptomycin-dependent to streptomycin-nondependent in *E. coli* Sd-841 was tested.)

The mutagenicity of Ia and XIII was tested using reverse mutation[5] of a streptomycin-dependent strain of *E. coli* Sd-841 to streptomycin-nondependent. As shown in Table 1, Ia is hardly mutagenic and XIII is nonmutagenic in this test system. This may be mainly due to their chemical properties; thus, 4-NQO is slowly reduced to nonmutagenic 4-aminoquinoline 1-oxide through 4-hydroxyaminoquinoline 1-oxide, which is the proximate form showing mutagenic and carcinogenic actions, whereas Ia is reduced directly to 4-aminoquinoline 1-oxide. Compound Ia was reported to show no carcinogenicity upon subcutaneous or intravenous administration to mice.[6]

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5) S. Iwahara, K. Yanagimachi, S. Kamiya, M. Nakadate, and I. Suzuki, *Chem. Pharm. Bull.*, **19**, 1914 (1971); *Eisei Shikenjo Hokoku*, **88**, 118 (1970).

6) Y. Shirasu, *Gann*, **54**, 487 (1963).

Experimental[7]

4-Azidoquinoline 1-Oxide (Ia) and 4-Azido-2-methylquinoline 1-Oxide (Ib)——4-Azidoquinoline 1-Oxide (Ia): A mixture of 9.5 g (0.05 mol) of 4-NQO, 5.20 g (0.08 mol) of sodium azide and 100 ml of 60% aqueous ethanol was heated in a boiling water bath for 1 hr. The ethanol was evaporated off under reduced pressure. The resulting crystals were gathered by filtration and recrystallized from acetone. Pale brown needles, mp 141° (dec.). Yield, 9.11 g (98%).

4-Azido-2-methylquinoline 1-Oxide (Ib): 1) Ib was similarly prepared in 50% yield by heating 2-methyl-4-nitroquinoline 1-oxide and sodium azide. Reddish pillars (from acetone), mp 132—133° (dec.). IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1}: 2160 (N_3). NMR ($CDCl_3$, δ): 2.72 (3H, s, CH_3), 7.01 (1H, s, C_3–H), 7.5—8.7 (4H, m, aromatic-H). *Anal.* Calcd for $C_{10}H_8N_4O$: C, 59.99; H, 4.03; N, 27.99. Found: C, 59.94; H, 3.75; N, 27.75. 2) Ib was also prepared in 56% yield by the reaction of 4-hydrazino-2-methylquinoline 1-oxide and nitrous acid. 4-Hydrazino-2-methylquinoline 1-oxide was obtained by directly heating 4-chloro-2-methylquinoline 1-oxide[8] with 80% hydrazine hydrate. Yellow granules (from ethanol), mp 164° (dec.). *Anal.* Calcd for $C_{10}H_{11}N_3O$: C, 63.47; H, 5.86; N, 22.21. Found: C, 63.49; H, 5.79; N, 22.25.

Treatment of Ib with phosphorus trichloride gave 4-azido-2-methylquinoline in 50% yield. Hydrochloride: Yellow prisms (from ethanol), mp 166—167° (dec.). *Anal.* Calcd for $C_8H_8N_4 \cdot HCl \cdot 1/2H_2O$: C, 52.29; H, 4.39; N, 24.40. Found: C, 52.83; H, 4.15; N, 24.63.

4-Azido-7-chloroquinoline (IIIa) and 4-Azido-7-trifluoromethylquinoline (IIIb)——4-Azido-7-chloroquinoline (IIIa): A mixture of 1.98 g (0.01 mol) of 4,7-dichloroquinoline (IIa), 1.30 g (0.02 mol) of sodium azide, 10 ml of ethanol and 10 ml of water was heated in a boiling water bath for 2 hr. The reaction mixture was evaporated to dryness under reduced pressure, the residue was extracted with $CHCl_3$, and the $CHCl_3$ layer was dried over anhyd. Na_2SO_4. The extract was evaporated to dryness and the residue was recrystallized from diisopropyl ether to give colorless leaflets, mp 115°. Yield, 1.92 g (94%). IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1}: 2160 (N_3). NMR (DMSO-d_6, δ): 7.48 (1H, d, $J=5$ Hz, C_3–H), 7.64 (1H, q, $J=2$ and 9 Hz, C_6–H), 8.00 (1H, d, $J=9$ Hz, C_5–H), 8.05 (1H, d, $J=2$ Hz, C_8–H), 8.86 (1H, d, $J=5$ Hz, C_2–H). *Anal.* Calcd for $C_9H_5ClN_4$: C, 52.82; H, 2.46; N, 27.43. Found: C, 52.64; H, 2.29; N, 28.68. Hydrochloride: Brown dices (from ethanol), mp 178° (dec.).

4-Azido-7-trifluoromethylquinoline (IIIb): This compound was similarly prepared by treating 4-chloro-7-trifluoromethylquinoline (IIb) with sodium azide in 87% yield. Pale yellow needles (from ethanol), mp 118°. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1}: 2140 (N_3). NMR (DMSO-d_6, δ): 7.23 (1H, d, $J=6$ Hz, C_3–H), 7.70 (1H, q, $J=$ 2 and 8 Hz, C_6–H), 8.20 (1H, d, $J=8$ Hz, C_5–H), 8.38 (1H, d, $J=2$ Hz, C_8–H), 8.93 (1H, d, $J=6$ Hz, C_2–H). *Anal.* Calcd for $C_{10}H_5F_3N_4$: C, 50.42; H, 2.12; N, 23.53. Found: C, 49.71; H, 2.09; N, 23.53.

4-Azido-7-chloroquinoline 1-Oxide (IVa) and 4-Azido-7-trifluoromethylquinoline 1-Oxide (IVb)——4-Azido-7-chloroquinoline 1-Oxide (IVa): A mixture of 6.12 g (0.03 mol) of IIIa, 200 ml of acetic acid and 20 ml of 30% hydrogen peroxide solution was heated at 65—70° for 3 hr. The reaction mixture was diluted with 100 ml of water and concentrated under reduced pressure. The concentrated solution was neutralized with sodium bicarbonate, and the crystals that separated were filtered off and recrystallized from acetone. Straw yellow needles, mp 152—153° (dec.). Yield, 5.27 g (80%). IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1}: 2140 (N_3). NMR ($CDCl_3$, δ): 7.08 (1H, d, $J=7$ Hz, C_3–H), 7.64 (1H, q, $J=2$ and 9 Hz, C_6–H), 8.06 (1H, d, $J=9$ Hz, C_5–H), 8.52 (1H, d, $J=7$ Hz, C_2–H), 8.75 (1H, d, $J=2$ Hz, C_8–H). *Anal.* Calcd for $C_9H_5ClN_4O$: C, 49.00; H, 2.24; N, 25.39. Found: C, 48.77; H, 2.06; N, 25.80. Hydrochloride: Reddish plates (from ethanol), mp 180° (dec.).

4-Azido-7-trifluoromethylquinoline 1-Oxide (IVb): *m*-Chloroperbenzoic acid [85% purity, 5.0 g (0.024 mol)] was added to a solution of 5.0 g (0.02 mol) of IIIb with stirring under ice-cooling, and the mixture was allowed to stand at room temperature for 30 hr. The reaction mixture was extracted with saturated sodium bicarbonate solution, washed with water, and dried over anhyd. Na_2SO_4. The solvent was evaporated off, and the residue was recrystallized from ethanol to give orange needles, mp 149° (dec.). Yield, 4.5 g (84%). IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1}: 2140 (N_3). NMR ($CDCl_3$, δ): 7.18 (1H, d, $J=6$ Hz, C_3–H), 7.82 (1H, q, $J=2$ and 6 Hz, C_6–H), 8.24 (1H, d, $J=8$ Hz, C_5–H), 8.60 (1H, d, $J=6$ Hz, C_2–H), 9.02 (1H, d, $J=2$ Hz, C_8–H). *Anal.* Calcd for $C_{10}H_5F_3N_4O$: C, 47.25; H, 1.98; N, 22.04. Found: C, 47.25; H, 1.89; N, 22.24.

4-Azido-2-cyanoquinoline (VIa) and 4-Azido-7-chloro-2-cyanoquinoline (VIb)——4-Azido-2-cyanoquinoline (VIa): Dimethyl sulfate (2.52 g, 0.02 mol) was added to a solution of 2.72 g (0.02 mol) of Ia in 25 ml of $CHCl_3$, and the mixture was allowed to stand overnight. The $CHCl_3$ was evaporated off and the residue was recrystallized from acetone to give a methosulfate (Va), mp 159—160° (dec.). Yield, 5.74 g (92%). A solution of 0.78 g (0.012 mol) of potassium cyanide in 5 ml of water was added to a solution of 3.12 g (0.01 mol) of Va in 20 ml of 80% aqueous dioxane under ice-cooling with stirring. The crystals that

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7) The following instruments were used to obtain physical data. Infrared (IR) spectra, JASCO IR-S spectrophotometer; ultraviolet (UV) spectra, Shimadzu UV 210 double-beam spectrophotometer; NMR spectra, Varian 360A spectrometer (with tetramethylsilane as an internal standard). All melting points are uncorrected.

8) E. Ochiai and K. Satake, *Yakugaku Zasshi*, **71**, 1078 (1951).

separated were filtered off and recrystallized from a mixture of acetone and diisopropyl ether. Pink needles, mp 172—173°. Yield, 2.46 g (63%). IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 2170 (N_3), 2260 (CN). NMR ($CDCl_3$, δ): 7.40 (1H, s, C_3–H), 7.6—8.2 (4H, m, aromatic-H). *Anal.* Calcd for $C_{10}H_5N_5$: C, 61.53; H, 2.58; N, 35.88. Found: C, 61.23; H, 2.39; N, 35.48.

4-Azido-7-chloro-2-cyanoquinoline (VIb): This compound was similarly prepared by treating the corresponding methosulfate (Vb) with potassium cyanide. Colorless needles (from a mixture of acetone and diisopropyl ether), mp 188—189° (dec.). Yield, 39%. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 2160 (N_3), 2260 (CN). NMR ($CDCl_3$, δ): 7.38 (1H, s, C_3-H), 7.60 (1H, q, $J=2$ and 9 Hz, C_6-H), 8.03 (1H, d, $J=9$ Hz, C_5-H), 8.10 (1H, d, $J=2$ Hz, C_8-H). *Anal.* Calcd for $C_{10}H_4ClN_5$: C, 52.30; H, 1.73; N, 30.50. Found: 52.60; H, 1.95; N, 30.40.

4-Azido-2-cyanoquinoline 1-Oxide (VIIa) and 4-Azido-7-chloro-2-cyanoquinoline 1-Oxide (VIIb)——4-Azido-2-cyanoquinoline 1-Oxide (VIIa): A mixture of 1.05 g (0.01 mol) of VIa, 75 ml of acetic acid and 12 ml of 30% hydrogen peroxide solution was heated in a boiling water bath for 3 hr. A further 6 ml of 30% hydrogen peroxide solution was then added, and the mixture was heated for another 2 hr. The reaction mixture was diluted with 40 ml of water, then the mixture was concentrated under reduced pressure, and this procedure was repeated twice. The crystals that separated were filtered off and recrystallized from acetone. Reddish needles, mp 154—155° (dec.). Yield, 1.20 g (57%). IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 2160 (N_3), 2260 (CN). *Anal.* Calcd for $C_{10}H_5N_5O$: C, 56.87; H, 2.39; N, 33.17. Found: C, 56.94; H, 2.32; N, 32.37.

4-Azido-7-chloro-2-cyanoquinoline 1-Oxide (VIIb): This compound was similarly prepared from VIb. Reddish needles (from acetone), mp 170° (dec.). Yield, 48%. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 2150 (N_3), 2260 (CN). *Anal.* Calcd for $C_{10}H_4ClN_5O$: C, 48.81; H, 1.64; N, 28.51. Found: C, 48.50; H, 1.58; N, 28.46.

4-Azido-2-carbamoylquinoline (VIIIa) and 4-Azido-2-carbamoyl-7-chloroquinoline (VIIIb)——4-Azido-2-carbamoylquinoline (VIIIa): A solution of 1.2 g (0.006 mol) of VIa in 60 ml of acetone was mixed with 60 ml of 15% hydrogen peroxide solution and 1 ml of 6N sodium hydroxide solution. The mixture was warmed at 50—60° for 2 hr. The crystals that separated were filtered off and recrystallized from ethanol. White needles, mp 207—208° (dec.). Yield, 1.2 g (92%). IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 3380, 3140, 1696 ($CONH_2$), 2150 (N_3). *Anal.* Calcd for $C_{10}H_7N_5O \cdot 1/4H_2O$: C, 55.17; H, 3.47; N, 32.17. Found: C, 55.52; H, 3.11; N, 32.36.

4-Azido-2-carbamoyl-7-chloroquinoline (VIIIb): This compound was similarly prepared from VIb. Grayish-white needles (from ethanol), mp 202—203° (dec.). Yield, 86%. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 3400, 3140, 1700 ($CONH_2$), 2150 (N_3). *Anal.* Calcd for $C_{10}H_6ClN_5O$: C, 48.50; H, 2.44; N, 28.28. Found: C, 48.39; H, 2.27; N, 28.10.

4-Azido-2-carbamoylquinoline 1-Oxide (IXa) and 4-Azido-2-carbamoyl-7-chloroquinoline 1-Oxide (IXb)——4-Azido-2-carbamoylquinoline 1-Oxide (IXa): A mixture of 0.4 g (0.002 mol) of VIIIa, 5 ml of 30% hydrogen peroxide solution and 10 ml of acetic acid was heated at 75° for 4 hr. A small amount of water was added to the reaction mixture, and the crystals that separated were filtered off. Yellow needles (from acetone), mp 182—183° (dec.). Yield, 0.1 g (23%). IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 3200, 1690 ($CONH_2$), 2140 (N_3). *Anal.* Calcd for $C_{10}H_7N_5O_2$: C, 52.40; H, 3.08; N, 30.56. Found: C, 52.71; H, 3.10; N, 30.05.

4-Azido-2-carbamoyl-7-chloroquinoline 1-Oxide (IXb): A mixture of 0.7 g (0.003 mol) of VIIIb, 10 ml of 30% hydrogen peroxide solution and 20 ml of acetic acid was heated at 75° for 4 hr. The crystals that separated were filtered off, washed with water and dried. This product was 2,2′-dicarboxy-7,7′-dichloro-4,4′-azoquinoline 1,1′-dioxide (X), brown leaflets, mp>300°. Yield, 80 mg (6%). IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 3160 (OH), 1680 (CO). *Anal.* Calcd for $C_{20}H_{10}Cl_2N_4O_4 \cdot H_2O$: C, 48.90; H, 2.46; N, 11.41. Found: C, 49.26; H, 2.68; N, 11.86. The filtrate was diluted with water. The crystals that separated were filtered off and recrystallized from ethanol. 4-Azido-2-carbamoyl-7-chloroquinoline 1-oxide (IXb), yellow needles, mp 200° (dec.). Yield, 0.26 g (35%). IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 3200, 1695 ($CONH_2$), 2160 (N_3). *Anal.* Calcd for $C_{10}H_6ClN_5O_2$: C, 45.55; H, 2.29; N, 26.57. Found: C, 45.77; H, 2.16; N, 26.66.

4-Azidocinnoline (XII)——A mixture of 1.65 g (0.01 mol) of 4-chlorocinnoline[9] (XI), 1.30 g (0.02 mol) of sodium azide and 80% aqueous ethanol was heated in a boiling water bath for 3 hr. The reaction mixture was concentrated under reduced pressure, and the crystals that separated were filtered off. Yellow needles (from ethanol), mp 145—146° (dec.). Yield, 1.23 g (72%). IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 2140 (N_3). NMR ($CDCl_3$, δ): 9.20 (1H, s, C_3–H), 7.9—8.6 (4H, m, aromatic-H). *Anal.* Calcd for $C_8H_5N_5$: C, 56.13; H, 2.94; N, 40.92. Found: C, 56.03; H, 2.91; N, 40.70.

N-Oxidation of 4-Azidocinnoline (XII)——*m*-Chloroperbenzoic acid [85% purity, 2.1 g (0.01 mol)] was added to a solution of 1.5 g (0.009 mol) of XII in 30 ml of $CHCl_3$ with stirring under ice-cooling. After stirring at room temperature for 20 hr, the $CHCl_3$ layer was extracted with saturated sodium bicarbonate solution, washed with water, and dried over anhyd. Na_2SO_4. The $CHCl_3$ extract was evaporated to dryness and the residue was recrystallized from ethanol. The first crop was 4-azidocinnoline 2-oxide (XIV); this was identical with authentic XIV derived from 4-chlorocinnoline 2-oxide[10] (XVI). Yellow-brown needles

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9) N.J. Leonard and S.N. Boyd, Jr., *J. Org. Chem.*, **11**, 419 (1946).

10) I. Suzuki and T. Nakashima, *Chem. Pharm. Bull.*, **12**, 619 (1964).

(from ethancl), mp 184—185° (dec.). Yield, 0.86 g (53%). IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1}: 2160 (N_3). NMR ($CDCl_3$, δ): 8.20 (1H, s, C_3–H), 7.4—8.1 (4H, m, aromatic-H). *Anal.* Calcd for $C_8H_5N_5O$: C, 51.34; H, 2.69; N, 37.42. Found: C, 51.17; H, 2.84; N, 37.02. The second crop from the filtrate was 4-azidocinnoline 1-oxide (XIII); this was identical with authentic XIII derived from 4-nitro- (XVa) and 4-chlorocinnoline 1-oxide[9] (XVb). Pale yellow needles (from ethanol), mp 129° (dec.). Yield, 0.34 g (21%). IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1}: 2160 (N_3). NMR ($CDCl_3$, δ): 8.16 (1H, s, C_3–H), 7.7—8.7 (4H, m, aromatic-H). *Anal.* Calcd for $C_8H_5N_5O$: C, 51.34; H, 2.69; N, 37.42. Found: C, 51.49; H, 2.58; N, 37.73.

The authentic XIII was obtained in 81% yield by treating XVa with sodium azide and also in 21% yield by treating XVb with sodium azide. The authentic XIV was obtained in 86% yield by treating XVI with sodium azide.

4,4′-Azocinnoline 1,1′-Dioxide——A solution of 50 mg of XIII in 10 ml of benzene was exposed to the sun for 4.5 hr. The solvent was evaporated off under reduced pressure and the residue was recrystallized from ethanol. Dark-brown powder, mp>300°. Yield, 25 mg (29%). IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1}: 1365 (N–O). *Anal.* Calcd for $C_{16}H_{10}N_6O_2 \cdot 1/2H_2O$: C, 58.71; H, 3.39; N, 25.68. Found: C, 59.10; H, 3.42; N, 24.84.

The screening method using AH-13 cells and the reverse mutation test method are described in our previous papers.[1,5]