# A Cinnoline 2-Oxide from 2-Nitrosobenzophenone

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Base catalyzed cyclization of the 2-methylazoxybenzophenone (**4B**) obtained by condensation of the 2-nitrosobenzophenone (**2a**) with methylhydroxylamine led to the cinnoline 2-oxide (**7**) which is the major product of the peracid oxidation of the corresponding cinnoline (**5**).

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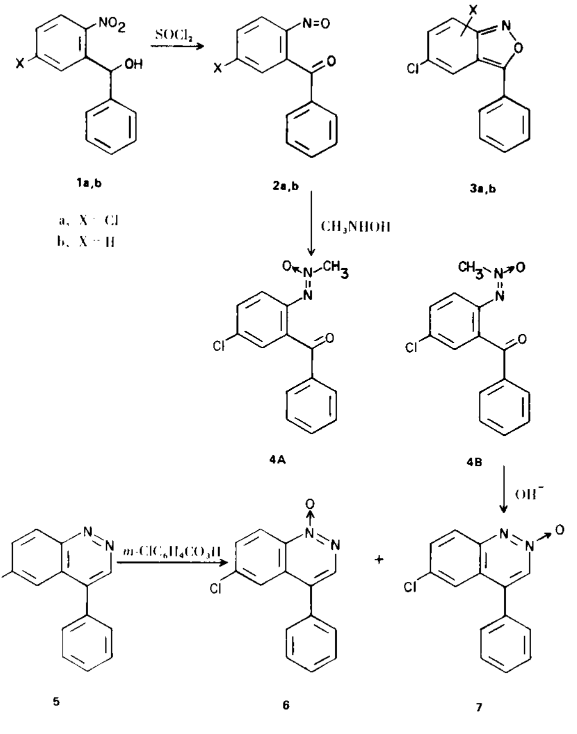
Oxidation of 6-chloro-4-phenylcinnoline (**5**) (1) (prepared according to Stoermer and Fincke (2) with *m*-chloroperbenzoic acid gave a mixture of the *N*-oxides (**6**) and (**7**). The 2-oxide (**7**) was the major product and was readily obtained by fractional crystallization while the 1-oxide (**6**) had to be isolated by chromatography. The structures of these oxides were assigned on the basis of their nmr spectra. In the 1-oxide (**6**) the proton in position 8 is markedly deshielded. We would like to report now a novel and unambiguous synthesis of the 2-oxide (**7**) starting from 5-chloro-2-nitrobenzhydrol (**1a**) (3).



Dickinson (4) has described the conversion of the 2-nitrobenzhydrol (**1b**) to the 2-nitrosobenzophenone (**2b**) using *p*-toluenesulfonyl chloride and pyridine. He also reported that thionyl chloride in refluxing chloroform transformed **1b** into the 5-chloro-3-phenyl-2,1-benzisoxazole (**3b**). In our hands, reaction of the chloro substituted analog **1a** with thionyl chloride at 75° gave almost exclusively the nitrosobenzophenone (**2a**). The chlorinated benzisoxazole (**3a**) was not formed in detectable amounts. Condensation of the nitrosobenzophenone (**2a**) with methylhydroxylamine gave a mixture of two isomeric azoxy derivatives **4A** and **4B** which were partially separated by chromatography. The major more polar isomer **B** was found to cyclize to the cinnoline 2-oxide (**7**) upon treatment with methanolic potassium hydroxide. The facile cyclization of the azoxy compound **4B** indicates that it has the required stereochemistry and demonstrates that carbanions in an *alpha* position to an oxazo group are generated with ease. Such carbanions may be used more frequently for the formation of carbon-carbon bonds.

## EXPERIMENTAL

### 5-Chloride-2-nitrosobenzophenone (**2a**).

5-Chloro-2-nitrobenzhydrol (3), 5.3 g. (0.02 mole), was added with stirring to 40 ml. of thionyl chloride. Following the addition the solution was gradually warmed to 75° and kept at this temperature for 10 minutes. The thionyl chloride was evaporated under reduced pressure at the end of the reaction azeotropically with benzene. The residue was crystallized from methylene chloride/hexane to yield 2.8 g. (81%) of cream-colored crystals with m.p. 91-94° which form green solutions typical for nitroso compounds. The analytical sample was recrystallized from methylene chloride/hexane, m.p. 92-94°; uv (2-propanol): $\lambda$ max 245 m$\mu$ ($\epsilon$, 16,850) 292 (9,650) 319 (9,350); ir (chloroform): 1670 cm$^{-1}$ (C=O); nmr (deuteriochloroform) $\delta$: 7.2-8 ppm (m, 8, aromatic H).

*Anal.* Calcd. for $C_{13}H_8ClNO_2$: C, 63.6; H, 3.3; N, 5.7; Cl, 14.4. Found: C, 63.8; H, 3.1; N, 5.9; Cl, 14.5.

### 2-Benzoyl-4-chloro-(*N*-methyl-*N*-oxyazo)benzene (**4A** and **4B**).

A mixture of 2.46 g. (0.01 mole) of **2a**, 1.66 g. (0.02 mole) of methylhydroxyamine hydrochloride, 1.64 g. (0.02 mole) of sodium acetate and 50 ml. of ethanol was heated on the steam bath for 5 minutes. The ethanol was evaporated under reduced pressure and the residue was partitioned between methylene chloride and saturated sodium bicarbonate solution. The organic phase was dried over sodium sulfate and evaporated. The residue was chromatographed over 70 g. of silica gel (Merck 70-230 mesh) using methylene chloride/hexane 1:1 (v/v). The fractions containing the less polar isomer **4A** were combined and evaporated. Crystallization of the residue from ether/hexane gave 130 mg. of colorless crystals with m.p. 79-80°; uv (2-propanol): λ max 250 mμ (ε, 22,000) infl 290 (3,420); ir (chloroform): 1680 $cm^{-1}$ (C=O); nmr (deuteriochloroform): δ 3.03 ppm (s, 3, $CH_3$) 7.2-7.8 (m, 7, aromatic H), 8.01 (d, 1, J = 8 Hz, $C_6$-H); ms, m/e 274 ($M^+$).

Crystallization of the following mixed fractions gave 670 mg. of crystals with m.p. 57-60°, which according to thin layer chromatofram consisted mainly of isomer **4B** contaminated with **4A**. Pure isomer **4B**, 390 mg., was obtained from the combined later fractions, crystallized from ether/hexane, m.p. 57-58°, yield of both isomers, 1.19 g. (43%). The analytical sample was recrystallized from aqueous methanol, m.p. 57-60°; uv (2-propanol): λ max 236 mμ (ε, 18,520) sh 290 (8,310); ir (chloroform): δ 3.91 ppm (s, 3, $CH_3$) 7.2-8.0 (m, 8, aromatic H).

*Anal.* Calcd. for $C_{14}H_{11}ClN_2O_2$: C, 61.2; H, 4.0; N, 10.2. Found: C, 61.0; H, 4.0; N, 10.1.

### 6-Chloro-4-phenylcinnoline 2-Oxide (**7**).

A mixture of 0.275 g. (1 mmole) of **4B**, 0.2 g. of potassium hydroxide, 1 ml. of water and 10 ml. of ethanol was heated to reflux for 10 minutes. The reaction mixture was initially dark brown and became lighter with progressing reaction. The ethanol was partially evaporated under reduced pressure and the product was crystallized by diluting with water. The crystals were collected and dissolved in methylene chloride. The solution was dried and evaporated. Crystallization of the residue from ether yielded 185 mg. (72%) of yellowish crystals with m.p. 192-194°. The analytical sample was recrystallized from methylene chloride/petroleum ether, m.p. 195-197°; uv (2-propanol): λ max 217 mμ (ε, 27,750) 270 (31,250) 315 (8,220) 365 (4,920) infl 380 (4, 620); nmr (deuteriochloroform): 7.3-8 ppm (m, 8, aromatic H) 8.14 (s, 1, $C_3$-H).

*Anal.* Calcd. for $C_{14}H_9ClN_2O$: C, 65.5; H, 3.5; N, 10.9. Found: C, 65.7; H, 3.4; N, 11.2.

### Compound **7** and 6-Chloro-4-phenylcinnoline 1-Oxide (**6**) by Oxidation.

A mixture of 48 g. (0.2 mole) of 6-chloro-4-phenylcinnoline (**5**), 41.6 g. (0.24 mole) of *m*-chloroperbenzoic acid and 3 l. of methylene chloride was stirred at room temperature for 1½ hours. The solution was washed with 1*N* aqueous sodium hydroxide, dried over sodium sulfate and partially evaporated. Fractional crystallization by addition of ether yielded 17 g. of pure **7** with m.p. 194-197°. The remaining mixture (19 g.) was chromatographed over 400 g. of silica gel (Merck 70-230 mesh) using 20% (v/v) ethyl acetate in methylene chloride. The fractions containing the less polar compound only were combined and evaporated. Crystallization from methylene chloride/methanol gave 2.3 g. of **6** as pale yellow needles with m.p. 165-167°; uv (2-propanol): λ max 235 mμ (ε, 27,600) 283 (7,750) infl 295 (6,600) infl 336 (7,500) max 367 (12,100); nmr (deuteriochloroform): δ 7.51 ppm (s, 5, $C_6H_5$), 7.66 (q, 1, $J_{AB}$ = 9 Hz, $J_{AX}$ = 2 Hz, $C_7$-H) 7.85 (d, 1, J = 2 Hz, $C_5$-H), 8.25 (s, 1, $C_3$-H) 8.65 (d, 1, J = 9 Hz, $C_8$-H).

*Anal.* Calcd. for $C_{14}H_9ClN_2O$: C, 65.5; H, 3.5; N, 10.9. Found: C, 65.4; H, 3.5; N, 10.9.

The later fractions yielded 10 g. of the mixture and 3 g. of pure **7**.

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