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SYNTHESIS OF CINNOLINE 1,2-DIOXIDE

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Recently, Palmer and Russell (1) have reported that 4-methylcinnoline afforded 4-methylcinnoline 1,2-dioxide by the action of hydrogen peroxide and acetic acid, and the structure of the latter was elucidated by n.m.r., mass, UV, IR spectrometry. We have also independently succeeded in the synthesis of cinnoline 1,2-dioxide.

When cinnoline (I) was heated with hydrogen peroxide in acetic acid at 65-70° for 8 hours, cinnoline 1-oxide (II), cinnoline 2-oxide (III) (2), cinnoline 1,2-dioxide (IV) and indazole were isolated in 25.9%, 49.4%, 0.3% and 3.0% yields, respectively. Heating of I at 110-120° for 8 hours gave IV in 12.8% yield. Indazole was proved to be identical with the authentic sample synthesized by a known method (3). However, the mechanism of this contraction reaction has not been made clear as yet (4). IV gave correct analytical data for cinnoline dioxide (white needles, Anal. Calcd. for $C_8H_6N_2O_2$: C, 59.26; H, 3.73; N, 17.28. Found : C, 59.49; H, 3.91; N, 17.12.).

Benzo(c)cinnoline monoxide obtained from the sodium sulfide reduction of 2,2'-dinitrobiphenyl afforded benzo(c)cinnoline 5,6-dioxide (5) on treatment with hydrogen peroxide in acetic acid at 110-120°. A similar oxidation of II and III gave cinnoline dioxide in 25% and 3.6% yields, respectively.

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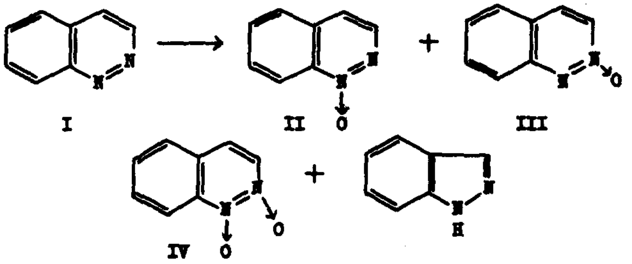
Catalytic hydrogenation of IV over palladium charcoal gave known dihydrocinnoline (6), m.p. 83°, after three molar equivalents of hydrogen uptake. When the catalytic hydrogenation of IV was stopped after about one molar equivalent of hydrogen uptake, the formation of I, II, III and dihydrocinnoline was observed in 3.9%, 17.5%, 64.6% and 3.4% yields, respectively.

The treatment of IV with 1.7 mole of phosphorus trichloride in chloroform for 40 hours resulted in the formation of III in 10.1% yield, and in the recovery of the starting material in 72.7% yield.



I II III

IV

$$\begin{tikzcd}
II \arrow[dr, "H_2O_2 \text{ in AcOH}"] & & III \\
& IV \arrow[ur, "PCl_3 \text{ in } CHCl_3"] \arrow[dr, "H_2\text{, Pd-C}"'] & \\
III \arrow[ur, "H_2O_2 \text{ in AcOH}"'] & & I + II + III
\end{tikzcd}$$

The polarographic reduction of I, II, III and IV was studied in aqueous solution and the values of the half-wave potential, $-E_{\frac{1}{2}}$ are summarized in Table I. As shown in Table I, cinnoline more easily reduced than its monoxides, and the waves obtained with cinnoline monoxides may correspond to reduction of cinnoline monoxide to dihydrocinnoline. Further, IV was reduced more easily than the base itself, and the first half-wave potential for IV may correspond to the reduction of dioxide to monoxide (probably 2-N-oxide). The half-wave potential of the second wave nearly coincides with the half-wave potential of cinnoline 2-oxide, and the ratio of the step hights observed is 1 : 2. In view of these results, it is probable that IV was first reduced to 2-N-oxide (2-electron step) which was then reduced to dihydrocinnoline (4-electron step).

Table I.

Half-wave Potentials and UV Absorption Maximum of Cinnoline Oxides

	$-E_{\frac{1}{2}}$(V) at pH 7.0 (S.C.E.)	max(mμ), (log ε)
Cinnoline (I)	0.78	
1-oxide (II)	0.83	230(4.4),303(3.7),315(4.0),351(3.9),367(3.9)
2-oxide (III)	0.86	262(4.5),310(3.7),352(3.7),361(3.7)
dioxide (IV)	0.63 0.85	234(4.3),258(4.4),273(4.6),340(3.8)

As shown in Table I, the ultraviolet spectrum of IV shows strictly different curve from the spectra of monoxides, and the blue shift for IV increases characteristically with increasing of solvent polarity, as already known in other N-oxides (7).

In benzo(c)cinnoline 5,6-dioxide, the 1399 cm^{-1} and 1342 cm^{-1} bands were assigned to the N-O streching vibration by investigating a number of cis nitroso dimers (8). Consequently, two bands at 1403 cm^{-1} and 1343 cm^{-1} in cinnoline dioxide may be assigned to N-O streching vibration.

Nuclear magnetic resonance spectral parameters obtained are listed in Table II. Since the protons H_8 and H_3 in IV are affected by the anisotropic effect on the 1-oxide and 2-oxide groups, the signal peaks of H_8 and H_3 appear at lower field than other signal peaks. On the other hand, in the n.m.r. spectra of quinoline 1-oxide and its derivatives, the chemical shifts were assigned in the order $8 < 2 < 4 < 3$ by Tori (9). This order is believed to be retained in cinnoline dioxide. Therefore, the peaks at 1.66τ and 1.92τ in the spectrum of IV can be assigned to the proton H_8 and H_3 , respectively. The π-electron charge density on the C_4 atom in IV may be increased by the mesomeric effect of the 1-oxide group, accordingly, the signal peak of 2.55τ can be assigned to the proton H_4. The values of the coupling constant $J_{3,4}$ are resonable for ortho coupling of the ring protons, and support the above mentioned assignment.

Table II.

Nuclear Magnetic Resonance Spectral Parameters* for Cinnoline Oxides

	H_3	H_4	H_8	$J_{3,4}$	$J_{7,8}$	$J_{4,8}$
Cinnoline (I)	0.72	-	1.47	5.5	-	1.0
1-Oxide (II)	1.75	2.61	1.41	6.0	6.0	1.0
2-oxide (III)	1.85	2.05	-	7.0	-	1.0
dioxide (IV)	1.92	2.55	1.66	7.5	9.6	1.0

* In $CDCl_3$ (1-4% solutions). The chemical shifts are expressed on τ-units (100 Mc./sec.) and coupling constants were in c.p.s.

From the evidence obtained by chemical and physicochemical data stated above, we concluded that IV was cinnoline 1,2-dioxide.

Although the di-N-oxide is sometimes referred to as dinitroso compound (4), the chemical and physical properties of IV, that is, inertness towards phosphorus trichloride, formation of dioxide from its base and monoxides by N-oxidation, its high melting point, and lack of color in the solid state and in solution, are incompatible with the presence of free nitroso groups.

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