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Color Reaction Mechanism of Chinoform by Quinonedichlorodiimide[1)]

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Quinonedichlorodiimide (I) reacts with chinoform (5-chloro-7-iodo-8-hydroxyquinoline (II)) as well as with 7-iodo-8-hydroxyquinoline-5-sulfonic acid (III) to yield a colored compound. The chemical structure of this compound is investigated from the spectral (infrared, ultraviolet, nuclear magnetic resonance, Mass) data and the elemental analysis. The fact that both the reactions of I+II and I+III give the same compound suggests that I replaces chlorine atom and sulfonic acid group at 5-positions of II and III, respectively.

The spectral data supports that the reaction product is 5-quinonediimino-7-iodo-8-hydroxyquinoline.

Keywords——chinoform; quinonedichlorodiimide; structure of colored compound; quinoline derivatives; NMR; mass spectrum; IR spectrum

In the preceding paper,[3)] it was reported that quinonedichlorodiimide (I) reacted with chinoform (5-chloro-7-iodo-8-hydroxyquinoline) (II) to produce a blue color (λ_{max}^{EtOH} 611 nm) on heating in the presence of potassium hydrogenphthalate and this coloration could be applied to the determination of II.

In the present paper, the chemical structure of this color compound is discussed on the basis of the spectral data (infrared, ultraviolet, nuclear magnetic resonance and mass spectrum) and the results of the elemental analysis.

Quinoline derivatives having hydroxy group at the 8-position reacted with I to produce color compounds similar to II. The color compounds produced by II, 7-iodo-8-hydroxyquinoline-5-sulfonic acid (III) or 5,7-dichloro-8-hydroxyquinoline (IV) showed positive Beilstain test but those produced by the quinoline derivatives not halogenated, for example, 8-hydroxyquinoline or 8-hydroxyquinoline-5-sulfonic acid, showed negative. These results suggest that the two chlorines of I were lost by the reaction.

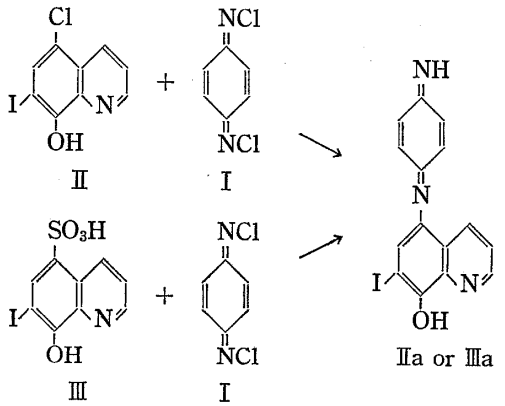

Chart 1

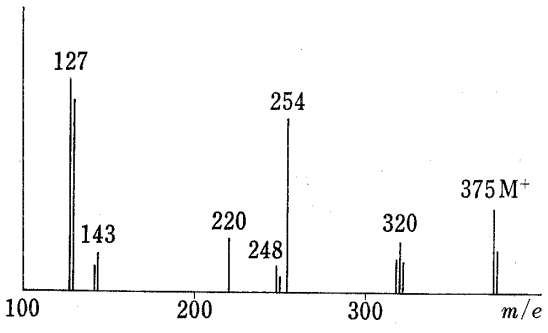

Fig. 1. Mass Spectrum of Colored Compound (IIa)

1) This work was presented at the 96th Annual Meeting of the Pharmaceutical Society of Japan, Nagoya, April, 1976.
2) Location: *a) Mizuho-cho, Mizuho-ku, Nagoya*: *b) Yoshidashimoadachi-cho, Sakyo-ku, Kyoto.*
3) T. Uno and M. Yamamoto, *Bunseki Kagaku*, **22**, 1417 (1973).

The reaction product of I and II(IIa) and that of I and III(IIIa) were purified by recrystallization in ethanol to give the violet blue needles. Both of them showed the same infrared (IR) and ultraviolet (UV) spectra and the same *Rf* values (0.79) on the thin-layer chromatography (TLC). These results suggest that IIa and IIIa are the same compound and the reaction of I with II or III occurs at the 5-position of II or III.

The mass spectrum of IIIa showed the expected molecular ion peak at *m/e* 375 (Fig. 1) and the same molecular weight was obtained from the vapor pressure depression. Also 374.990 was measured by high resolution mass spectrum. Therefore, it was found that I reacted with II or III at the rate of 1: 1.

As shown in Fig. 2, IIIa showed the nuclear magnetic resonance (NMR) signals for the quinone ring having four hydrogens (δ 6.70—7.05, 4H quartet) and for protons of the quinoline skeleton, that is, the C_2-hydrogen (δ 8.89, 1H), the C_4-hydrogen situated *para* position of nitrogen (δ 8.70—8.80, 1H), the C_6-hydrogen (δ 8.22, 1H), the C_3-hydrogen (δ 7.70—7.83, 1H).

The above facts lead to the conclusion that the ring hydrogens of III are not substituted. The signal for hydroxyl group of quinolinol and imino group of quinoneimine (δ 5.80—6.00, 2H) was also observed. The presence of hydroxyl group of quinoline skeleton of IIIa was confirmed by positive $FeCl_3$-test.

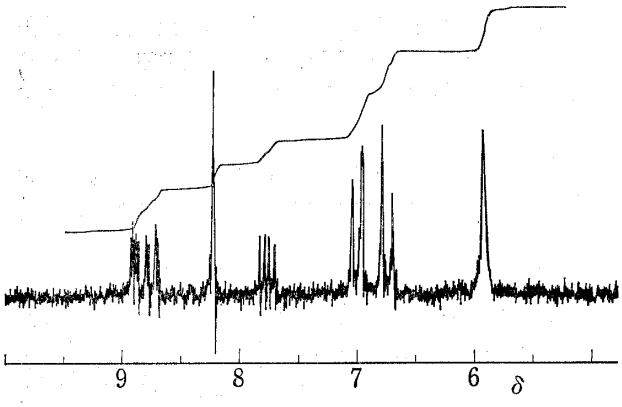

Fig. 2. NMR Spectrum of Colored Compound (IIIa)

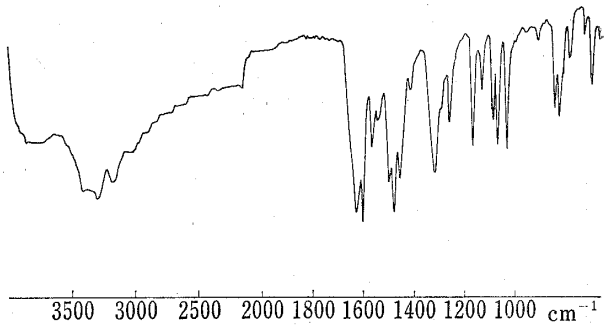

Fig. 3. Infrared Absorption Spectrum of Colored Compound (IIIa)

The IR spectrum of IIIa exhibited strong bands due to conjugated C=C and C=N double bonds (1480—1625 cm^{-1}) and C–O group (1185 cm^{-1} and 1320 cm^{-1}) (Fig. 3). The IR spectrum of the reaction product of I and IV (IVa) is similar to that of IIIa except that the aromatic C–Cl band (850 cm^{-1}) is observed only for the former.

In the mass spectrum the fragmentation of IIa was studied. The peak at *m/e* 320 is the ion by losses of CO (28) and HCN (27) from the molecular ion and the fragment *m/e* 248 is the ion by loss of iodine (127) and the *m/e* 220 is the ion by losses of iodine and CO (28) from the molecular ion. Moreover the peak at *m/e* 143 is thought to be 8-hydroxyquinoline ion by losses of iodine (127) and the quinone ring. The *m/e* 127 and *m/e* 128 is iodine ion and hydrogen iodide ion. By the measurement of the high resolution mass spectrum, the peak at *m/e* 254 was firmed to be iodine molecular ion. Probably this peak is that of iodine as impurity formed during the reaction of I and II.

From the results of above spectral data and elemental analysis, the reaction mechanism was proved as shown in Chart 1 and IIa and IIIa are 5-quinonediimino-7-iodo-8-hydroxyquinoline ($C_{15}H_{10}ON_3I$).

Experimental[4]

Preparation of IIa——A water solution (100 ml) of potassium hydrogen phthalate (3.47 g) was added to the mixture of quinonedichlorodiimide (I) (175 mg) and 5-chloro-7-iodo-8-hydroxyquinoline (II) (91 mg) in ethanol solution (300 ml). The mixture was refluxed in a water bath at 95° for 35 min. After cooling, water was added to the mixture, and the product was extracted with 100 ml of $CHCl_3$. The $CHCl_3$ solution was washed with water for three times. To this extract, EtOH (30 ml) was added and the solution was placed under reduced pressure to remove $CHCl_3$. The precipitate formed was dissolved by adding EtOH (50 ml). This solution was chromatographed on Kieselgel 60 and then on Sephadex-LH 20. The violet blue ethanol eluate was collected and the solvent was evaporated. Recrystallization from EtOH gave violet blue needles (IIa), mp over 300°.

Preparation of IIIa——A solution of potassium hydrogenphthalate (3.47 g) in water (100 ml) was added to a solution of I (175 mg) and 7-iodo-8-hydroxyquinoline-5-sulfonic acid (III) in EtOH (300 ml). The mixture was refluxed in a water bath (95°) for 15 min. The product (IIIa) was chromatographed and recrystallized in the same manner as given for IIa: Violet blue needles, mp over 300°. IIIa was proved to be identical with IIa by the comparison of the spectral data and TLC. $FeCl_3$-Test for IIa and IIIa: green. TLC (the thin layer plates: Kieselgel, solvent: EtOH): *Rf* 0.79. UV λ_{max}^{EtOH} 255 nm. IR cm^{-1} (KBr): 1625 (C=C), 1600 (C=N), 1320 and 1185 (C–O). NMR δ (DMSO-d_6): 5.80—6.00 (2H, O–H and N–H), 6.70—7.05 (4H quartet, quinone ring), 7.70—7.83 (1H multiplet, quinoline skeleton C_3–H), 8.22 (1H singlet, C_6–H), 8.70—8.80 (1H multiplet, C_4–H), 8.89 (1H multiplet, C_2–H). Mass Spectrum: *m/e* 375 (M^+). *Anal.* Calcd. for $C_{15}H_{10}ON_3I$: C, 48.02; H, 2.69; N, 11.20; I, 33.82. Found: C, 48.26; H, 2.76; N, 11.03; I, 33.73.

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4) The infrared spectra were measured in KBr discs using a Hitachi-215 spectrometer and the ultraviolet spectra were measured on a Hitachi-124 spectrophotometer. The NMR spectra were taken on a Varian HA-100 spectrometer in DMSO-d_6 solution using TMS as the internal reference. The mass spectra were taken on a Hitachi RMU-6C and a Hitachi Dataanalyzer.