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A NOVEL REARRANGEMENT PRODUCED BY THE PHOTOLYSIS OF 3-(3'-CHLORO-2'-OXOPROPYL)-3-HYDROXYOXINDOLE

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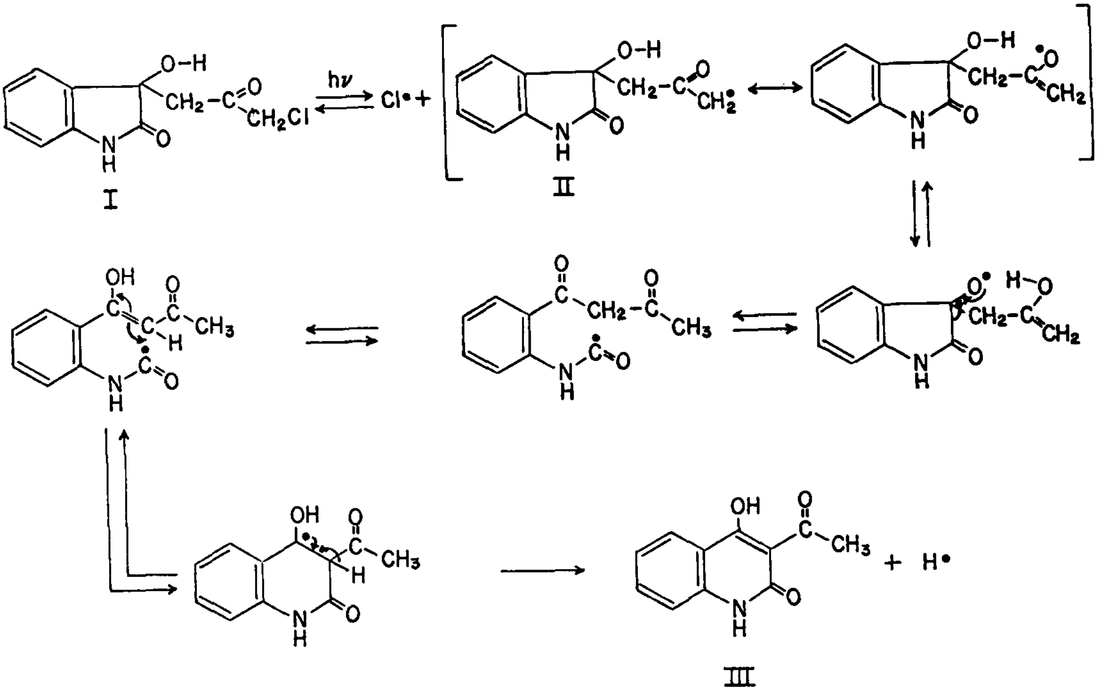
Because of the utility of 3-(3'-chloro-2'-oxopropyl)-3-hydroxyoxindole (I) as a model compound for anticipated studies of certain derivatives of isatin and related compounds, I was synthesized and then photolyzed with a low-pressure mercury-vapor lamp. From this reaction the product of a novel deep-seated rearrangement has been isolated in 20% yield and characterized.

The condensation of chloro-2-propanone with isatin in ethanol solution with diethylamine as a catalyst[2] afforded I in poor yields. It was subsequently found that a reversal of the condensation takes place in solutions of I in aqueous organic solvents and in primary alcohols (studied by means of tlc and uv spectroscopy). The stability of I in alcohols increases in going from primary to secondary to tertiary alcohols. The condensation of isatin (0.08 mole) with a large excess of chloro-2-propanone (0.49 mole) in the presence of 1 ml of diethylamine produced I as cream-colored crystals (60% yield), mp 135-150° dec. Recrystallization from EtOAc produced white crystals, mp 140-150° dec; uv max (Et_2O) 251 mμ (log ε 3.67), 296 (3.09); nmr (CD_3OD, 60 MHz) δ 2.47 (s, 2H, $-\underline{CH_2}\overset{O}{\overset{\|}{C}}CH_2Cl$), 4.71 (s, 2H, $-CH_2\overset{O}{\overset{\|}{C}}\underline{CH_2}Cl$), 6.75-7.50 (aromatic multiplet, 4H); mass spectrum, molecular ion $^m/e$ 239. <u>Anal</u>. Calcd for $C_{11}H_{10}NO_3Cl$: C, 55.15; H, 4.20; N, 5.84. Found: C, 55.41; H, 3.94; N, 5.60. All preparations of I displayed a broad melting range. This property has been observed previously for condensation products of isatin.[2,3]

A solution of 1 g of I in 200 ml of tetrahydrofuran was placed in two quartz semi-circular cells with inner radii of 4 cm. The cells were arranged about a Hanovia No. 87A-45 20 watt U-shaped low-pressure mercury-vapor lamp. After 16 hr of irradiation the substrate had been transformed. Concentration of the reaction mixture in vacuo and treatment of the residue with MeOH produced a 20% yield of pale yellow needles, mp 258-9°. Recrystallization from MeOH afforded colorless needles (III), mp 258-9°; uv max (MeOH) 234 mμ (log ε 4.47), 301 (4.08), 307 sh (4.07), 352 (3.65); uv max (2 ml MeOH soln plus 0.05 ml 2N NaOH), 228 (4.50), 266 (4.08), 310 (4.05); nmr ($(CD_3)_2SO$, 100 MHz) δ 2.68 (s, 3H, $CH_3\overset{O}{\overset{\|}{C}}-$), 7.10-8.10 (aromatic multiplet, 4H), 11.20 (broad singlet, $-\overset{O}{\overset{\|}{C}}\cdot\overset{H}{\overset{|}{N}}-$, removed on D_2O treatment); mass spectrum, molecular ion $^m/e$ 203. Anal. Calcd for $C_{11}H_9NO_3$: C, 65.02; H, 4.46; N, 6.89. Found: C, 65.06; H, 4.40; N, 6.88. These data indicated that III had been formed with the loss of only the elements of HCl and that a simple photocyclodehydrohalogenation had not taken place - the uv spectrum indicated that the oxindole chromophore was no longer present and the nmr spectrum revealed the presence of only three aliphatic protons, as a methyl group. The changes in the uv spectrum on alkalinization were reversed completely on acidification with hydrochloric acid. The pK_a of III was found to be 5.3 in ethanol-water (1:9, v/v) by a spectrophotometric determination.[4] The following treatments of III resulted only in the recovery of III: hydrogenation over 5% Pd/C in EtOH at 1 atm; hydrogenation over 5% Rh/Al_2O_3 in EtOH at 2 atm; Ac_2O/pyridine for 3 days at room temp; boiling for 30 hr with HCl, 2.2 N in EtOH-HOH (1:1); boiling for 1 hr with 1 N Na_2CO_3 solution followed by acidification. Consideration of these data and observations and consideration of the routes of rearrangement open to the free radical II produced by the homolysis of the C-Cl bond of I led to the realization that III might be 3-acetyl-4-hydroxycarbostyril. The lit. mp 255-6°[5] and 259°[6] and uv data[5] agreed with those of III. 3-Acetyl-4-hydroxycarbostyril was synthesized by the procedure described by Lacey.[6] Its mp, uv, ir, nmr and mass spectra are identical with those of III and confirmed the correctness of the structure indicated for III. Photolysis of I in *tert*-butanol also produced III.

We believe that a reasonable mechanism for the reaction is the one indicated in Scheme 1, in which photolysis results in homolysis of the carbon-chlorine bond of I to produce the free radical II. II could rearrange in a straight forward manner to produce III, with a major part of the driving force for the rearrangement being the increased delocalization of electrons of the product III.



SCHEME I

Work on the scope and mechanism of this rearrangement is in progress. Two additional products have been isolated from the photolysis mixture in substantial amounts by silica gel chromatography. However, these compounds have not yet been purified sufficiently to permit characterization.

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