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TRANSFORMATION OF 5H,11H-INDOLO-[3,2-*b*]CARBAZOLE THROUGH 5,11-DIDEHYDROINDOLO[3,2-*b*]CARBAZOLE

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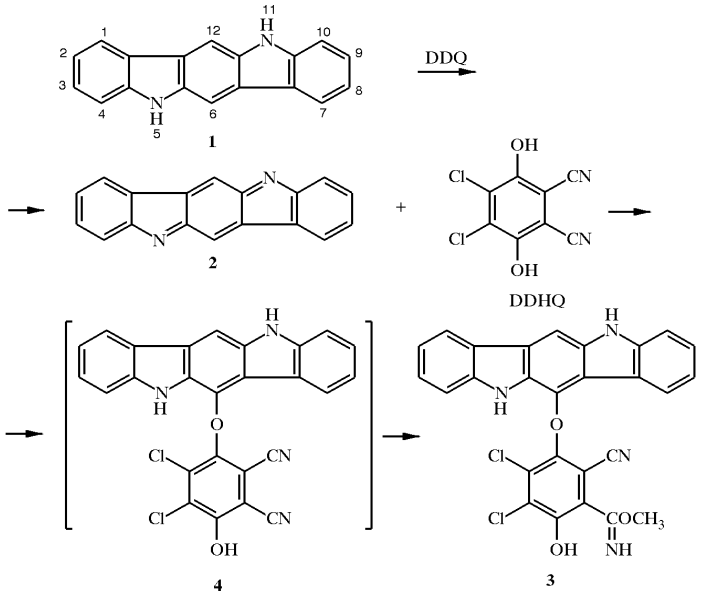
5H,11H-Indolo[3,2-*b*]carbazole (ICZ, **1**) is a natural ligand of the aromatic hydrocarbon receptor (Ah-receptor) and functional analog of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin. Biochemical studies have shown that the ICZ–Ah-receptor complex activates the *CYP1A1* gene of cytochrome P450-dependent oxidase, which leads to enhanced hydroxylation and inactivation of estrogens and several carcinogenic xenobiotics [1]. The chemical properties of ICZ have not yet been studied in detail. Hünig and Steinmetzer [2] have reported the oxidation of ICZ by PbO_2 in ethyl acetate to give 5,11-didehydroindolo[3,2-*b*]carbazole (**2**) in 15% yield. This reaction was carried out in a phase transfer system in light of the low solubility of both components.



We have found previously unreported chemical properties of ICZ, which may be useful for understanding the pathways for its biotransformation and a new method for dehydrogenation based on the reaction of ICZ and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ). We found that compound **2** may participate in both nucleophilic addition and oxidation–reduction reactions. This compound is formed in about 50% yield upon oxidation of a 1-2% suspension of ICZ in ethyl acetate. The ^{13}C NMR spectrum of monoresonance corresponds to a compound with axial symmetry, in which J_{C-H} = 163.1 Hz for $C_{(6)}$ and $C_{(12)}$ suggests the presence of deprotonated $N_{(5)}$ and $N_{(11)}$ in the α-position relative to these carbon atoms.

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6-[2,3-dichloro-6-cyanophenoxy-4-Hydroxy-5-(methoxycarbimidoyl)]-5H,11H-indolo[3,2-*b*]carbazole **3** was isolated in 30% yield upon the oxidation of ICZ by excess DDQ in toluene–methanol. The compound is probably formed through the nucleophilic addition of the DDQ reduction product, namely, 2,3-dichloro-5,6-dicyanohydroquinone (DDHQ), to 5,11-didehydroindolo[3,2-*b*]carbazole **2** formed during the reaction. Subsequent methanolysis of one of the cyano groups in intermediate 6-(2,3-dichloro-5,6-dicyano4-hydroxyphenoxy)-indolo[3,2-*b*]carbazole (**4**) gives indolocarbazole **3**, which was also obtained in the reaction of 5,11-didehydroindolocarbazole with DDHQ. These findings support the proposed reaction mechanism. The reaction of **2** with hydroquinone, tetrachlorohydroquinone, or 4-methoxythiophenol features an oxidation–reduction step to give ICZ and *p*-benzoquinone, chloranil, or bis(4-methoxyphenyl) disulfide, respectively, indicating that the oxidation–reduction potential of **2** is less than the potential of DDQ and higher than the potential of *p*-benzoquinone or chloranil. This hypothesis is also supported by the finding that chloranil does not oxidize ICZ. Thus, the result of the oxidation–reduction reactions involving ICZ (**1**) is a function of the oxidation–reduction potentials of the compounds participating in the reaction.

5,11-Didehydroindolo[3,2-*b*]carbazole (2). A suspension of (30 mg, 0.125 mmol) 5H,11H-indolo[3,2-*b*]-carbazole in dry ethyl acetate (200 ml) was heated at reflux for 1 h. Then, DDQ (52 mg, 0.30 mmol) in ethyl acetate (10 ml) was added dropwise and heating at reflux was continued for 2 h, monitoring the reaction course by thin-layer chromatography using a 2.5:1 mixture of petroleum ether (40-70°C) and ethyl acetate; R_f = 0.40 for **2** and R_f = 0.55 for **1**. The reaction mixture was cooled, washed with 1 N NaOH (2 ×150 ml), and dried over Na_2SO_4. The solvent was evaporated and compound **2** (15 mg, 49%) was obtained as a powder after chromatography on silica gel plates identical in its ^{1}H NMR spectrum and thin-layer chromatography to the sample of **2** obtained by method [2]. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 7.20 (1H, d, J = 7.43 Hz, 1/7-H or 4/10-H); 7.15 (1H, d, J = 8.03 Hz, 4/10-H or 1/7-H); 7.06 (1H, t, 2/8-H or 3/9-H); 6.97 (1H, t, 3/9-H or 2/8-H); 6.83 (1H, s, 6/12-H). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 166.32, 158.93, 142.68, 131.28, 129.69, 128.77, 123.85 (6/12-C), 123.46, 122.20.

6-[2,3-Dichloro-6-cyano-4-hydroxy-5-(C-iminomethoxycarbonyl)phenoxy]-5H,11H-indolo[3,2-*b*]-carbazole (3). A solution of DDQ (52 mg) in methanol was added to a suspension of compound **1** (15 mg) in 1:1 toluene–methanol (15 ml). The reaction mixture was heated at reflux for 1 h and then left at ~20°C for 16 h with stirring. The solvent was evaporated and compound **3** was separated from the residue by chromatography on silica gel plates (eluent $CHCl_3$–MeOH, 20:1). Yield of compound **3** 9 mg (30%); R_f 0.85. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 12.00 (1H, s, 5-H); 10.52 (1H, s, 11-H); 8.83 (1H, d, J = 8.1, 4-H); 8.54 (1H, s, 12-H); 8.38 (1H, d, J = 8.0, 1-H); 8.30 (1H, s, NH(imine)); 8.24 (1H, d, 7-H); 7.67 (1H, d, 10-H); 7.57 (1H, t); 7.53 (1H, t); 7.39 (1H, t, J = 7.7, 2-H); 7.28 (1H, t, 9-H); 4.10 (3H, s, OMe); 3.89 (1H, s, OH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 174.81 [C(OMe)NH], 145.37, 141.36, 139.95, 137.47, 129.33, 129.27, 127.42, 126.89, 124.92, 124.15, 122.49, 121.64, 121.57, 118.93, 118.14, 117.97, 117.90, 114.62, 114.12, 112.07, 111.06, 106.19, 99.78, 86.93 (CN), 80.80, 61.34 (OMe). Found, %: C 62.03; H 3.20; N 11.23. $C_{27}H_{16}N_4Cl_2O_3$. Calculated, %: C 62.09; H 3.24; N 10.94. Electron impact mass spectrum, *m/z*: 514 $[M(^{37}Cl)]^+$, 512 $[M]^+$, 481, $[M - OMe]^+$. IR spectrum, cm^{-1}: 3422 (4-OH), 1718.3, 1707.8, 1654.2 (imine), 1628.1, 1450.1, 1324.0, 1276.1 (C–O–C), 1267.1 (C–O–C), 1126.1, 761.8 (C–Cl).

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