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NOVEL METHOD FOR SYNTHESIS OF ISATINS

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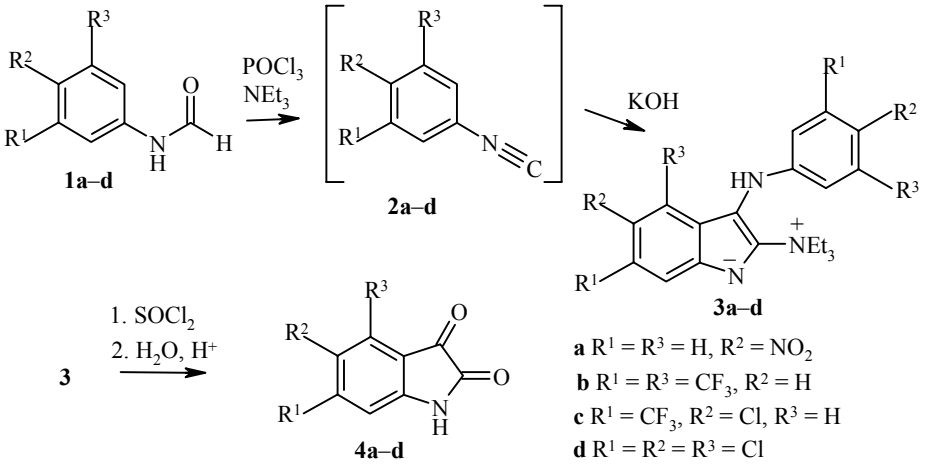
Isatins, which are a basis for obtaining antiviral drugs, pesticides, dyes, and analytical reagents, have attracted the attention of researchers for many decades [1]. We propose a novel method for synthesis of difficultly accessible isatins containing electron-acceptor groups NO_2, Cl, CF_3. The method is based on the reaction we have found out between aromatic isocyanides and tertiary amines [2], and includes two steps. In the first step, we obtain 2-triethylammonio-3-arylaminoindolates **3** from the corresponding aromatic formamide **1** without isolation of the intermediate isocyanides **2**. Heating compounds **3** with excess $SOCl_2$ followed by hydrolysis of the reaction products leads to the target isatins **4**. The total yield of isatins, calculated on the basis of the formamide, is 40%-55%. The mechanism of this reaction will be the subject of further studies.



5-Nitroisatin (4a). 4-Nitroformylaniline (0.83 g, 5 mmol) was added to a mixture of dry benzene (20 ml), triethylamine (2 ml), and phosphorus oxychloride (0.56 ml, 6 mmol). This was stirred for 1 h at 10°C, then with cooling the reaction mixture was washed with a 10% KOH solution (12 ml). The organic layer was removed and it was dried over Na_2SO_4, and boiled for 4 h. Hexane (10 ml) was added, and the precipitate of compound **3a** [2] was filtered off. $SOCl_2$ (8 ml) was added to the precipitate (0.84 g) and boiled for 5 h, the excess thionyl chloride was driven off, and then water (1 ml) and concentrated hydrochloric acid (15 ml) was

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added and it was boiled for another 2 h. The excess acid was driven off, the residue was washed with water (2 × 20 ml), and extracted with hot ethanol, from which on evaporation yellow crystals of the product precipitated. Yield 0.2 g (42%); mp 245°C. Lit. mp 245°C [1].

The following compounds were obtained similarly.

4,6-Ditrifluoromethylisatin (4b). Yield 57%; mp 193-194°C (benzene). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 11.52 (1H, s, NH); 7.60 (1H, s, 5-H); 7.42 (1H, s, 7-H). Mass spectrum, *m*/*z*: 283 $[M]^+$, 255 $[M - CO]^+$. Found, %: C 42.33; H 1.07; N 5.04. $C_{10}H_3F_6NO_2$. Calculated, %: C 42.42; H 1.06; N 4.95.

5-Chloro-6-trifluoromethylisatin (4c). Yield 48%; mp 210-211°C (benzene). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 11.31 (1H, s, NH); 7.68 (1H, s, 4-H); 7.23 (1H, s, 7-H). Mass spectrum, *m*/*z*: 249 $[M]^+$, 221 $[M - CO]^+$. Found, %: C 43.41; H 1.16; N 5.57. $C_9H_3ClF_3NO_2$. Calculated, %: C 43.32; H 1.20; N 5.61.

4,5,6-Trichloroisatin (4d). Yield 46%; mp 112-113°C (1:1 benzene–hexane). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 11.39 (1H, s, NH); 7.12 (1H, s, 7-H). Mass spectrum, *m*/*z*: 249 $[M]^+$, 221 $[M - CO]^+$. Found, %: C 38.29; H 0.76; N 5.44. $C_8H_2Cl_3NO_2$. Calculated, %: C 38.37; H 0.80; N 5.59.

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