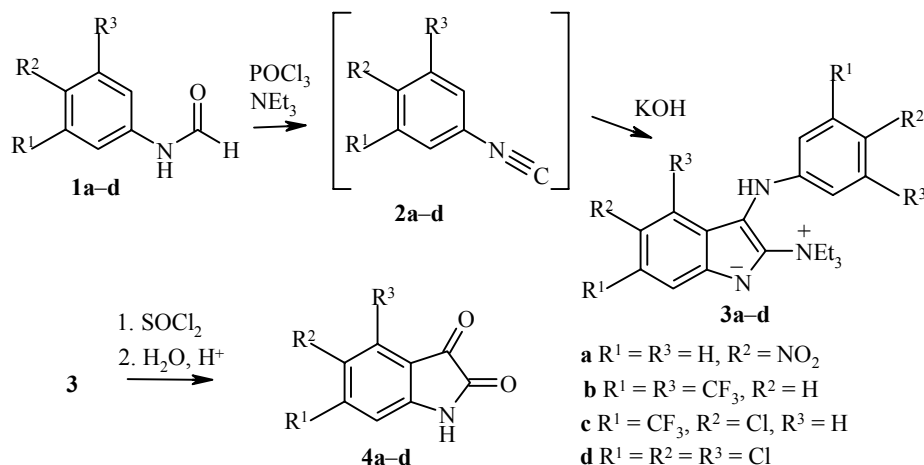


## NOVEL METHOD FOR SYNTHESIS OF ISATINS

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**Keywords:** aromatic isocyanides, 2,3-disubstituted indoles, isatins.

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<sub>2</sub>, Cl, CF<sub>3</sub>. 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<sub>2</sub> 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<sub>2</sub>SO<sub>4</sub>, and boiled for 4 h. Hexane (10 ml) was added, and the precipitate of compound **3a** [2] was filtered off. SOCl<sub>2</sub> (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 ( $2 \times 20$  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).  $^1\text{H}$  NMR spectrum (DMSO- $d_6$ ),  $\delta$ , ppm: 11.52 (1H, s, NH); 7.60 (1H, s, 5-H); 7.42 (1H, s, 7-H). Mass spectrum,  $m/z$ : 283  $[\text{M}]^+$ , 255  $[\text{M} - \text{CO}]^+$ . Found, %: C 42.33; H 1.07; N 5.04.  $\text{C}_{10}\text{H}_3\text{F}_6\text{NO}_2$ . Calculated, %: C 42.42; H 1.06; N 4.95.

**5-Chloro-6-trifluoromethylisatin (4c).** Yield 48%; mp 210-211°C (benzene).  $^1\text{H}$  NMR spectrum (DMSO- $d_6$ ),  $\delta$ , ppm: 11.31 (1H, s, NH); 7.68 (1H, s, 4-H); 7.23 (1H, s, 7-H). Mass spectrum,  $m/z$ : 249  $[\text{M}]^+$ , 221  $[\text{M} - \text{CO}]^+$ . Found, %: C 43.41; H 1.16; N 5.57.  $\text{C}_9\text{H}_3\text{ClF}_3\text{NO}_2$ . 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).  $^1\text{H}$  NMR spectrum (DMSO- $d_6$ ),  $\delta$ , ppm: 11.39 (1H, s, NH); 7.12 (1H, s, 7-H). Mass spectrum,  $m/z$ : 249  $[\text{M}]^+$ , 221  $[\text{M} - \text{CO}]^+$ . Found, %: C 38.29; H 0.76; N 5.44.  $\text{C}_8\text{H}_2\text{Cl}_3\text{NO}_2$ . Calculated, %: C 38.37; H 0.80; N 5.59.

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