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LETTERS TO THE EDITOR

Features of the Reaction of Isatin Derivatives with *ortho*-Phenylenediamine

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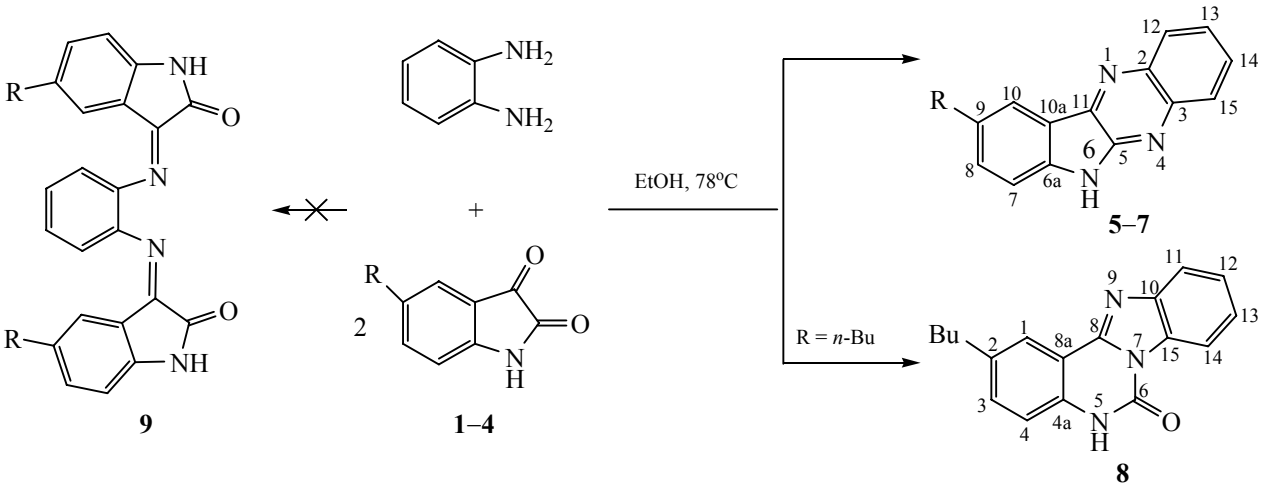
Condensation of isatin with aromatic amines is a convenient method of the synthesis of isatin-3-imines (Schiff bases) having a wide spectrum of biological activity like anticonvulsant, antibacterial, antiviral, and other actions [1–4]. *o*-Phenylenediamine has a special place among the aromatic amines. Depending on the nature of the solvent and pH it can react with isatin derivatives in various ways to give the reaction products with different structure [5–7]. Thus, in an acidic medium only indolo[2,3-*b*]quinoxaline formed; 3-(2'-aminophenyl)quinoxalin-2(1*H*)-one was isolated in 80% yield when using an aqueous alkaline medium. In the case of hexamethylphosporamide the formation of 1,3-dihydrospiro[benzimidazol-2(3*H*),3'-indolin]-2'-one was observed, whereas reaction in THF or benzene afforded 3-(2'-aminophenylimino)indolin-2-one. A mixture of the reaction products mentioned above was obtained when using as solvents methanol or *N*,*N*-dimethylacetamide.

In this work, to obtain bis-Schiff bases we carried out the condensation of 5-substituted isatins **1**–**4** with 1,2-diaminobenzene by procedure described in [8]. However, in all the cases, no target compounds **9** were obtained. Thus, the reaction of 2-fold excess of 5-chloroisatin with 1,2-diaminobenzene afforded solely compound **5** as a reaction product. Its physicochemical characteristics (melting point and ^{1}H NMR data) were identical to the previously described [9]. It was found that, as in the above case, the presence of electron-

Scheme 1.



R = Cl (**1**, **5**), Br (**2**, **6**), NO_2 (**3**, **7**), *n*-Bu (**4**, **8**).

withdrawing substituents (bromine atom, a nitro group) in the position 5 led only to the formation of quinoxaline derivatives **6** and **7** (Scheme 1).

An unexpected result was obtained by reacting *o*-phenylenediamine with isatin **4** containing donor *n*-butyl substituent. In this case, imidazo[1,2-*c*]quinazolinone **8** was obtained in a 79% yield and characterized for the first time. Thus, in contrast to quinoxaline **5** the IR spectrum of compound **8** contained an absorp-tion at 1718 cm^{-1} due to the vibrations of the C=O bonds. In the ^{13}C NMR spectrum the carbonyl carbon atom resonated as a singlet at 146.24 ppm that is characteristic of an urea fragment. In addition, the composition of **8** was confirmed by the mass spectrometry (MALDI).

Finally, the structure of compounds **3** and **8** was proved by X-ray diffraction analysis, whose details will be provided later.

General procedure for the reactions of isatins 1–4 with *o*-phenylenediamine. A solution of 1.08 g (0.01 mol) of *o*-phenylenediamine in anhydrous ethanol (50 mL) was added with stirring (20°C) to a solution of 0.02 mol of the corresponding isatin in 100 mL of anhydrous ethanol. The reaction mixture was maintained at reflux for 2 h. The solvent was evaporated to 1/5 volume. The precipitate was filtered off and heated in anhydrous chloroform to remove impurities. The resulting precipitate was filtered off and dried in a vacuum of 15 mmHg.

9-Chloro-6*H*-indolo[2,3-*b*]quinoxaline (5). Yield 67%, yellow crystals, mp 223°C (mp 222–224°C [9]). IR spectrum, ν, cm^{-1}: 3444, 1615, 1405, 1335, 1239, 1207, 1126, 1107, 1005, 944, 875, 821, 748. ^1H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 7.62 d.d (1H, H^7, $^3J_{HH}$ 8.6, $^4J_{HH}$ 0.5), 7.74 d.d (1H, H^8, $^3J_{HH}$ 8.6, $^4J_{HH}$ 2.2), 7.75 d.d.d (1H, Ar-H, $^3J_{HH}$ 6.9, $^3J_{HH}$ 6.8, $^4J_{HH}$ 1.5), 7.84 d.d.d (1H, Ar-H, $^3J_{HH}$ 6.9, $^3J_{HH}$ 6.8, $^4J_{HH}$ 1.5), 8.09 d.d.d (1H, Ar-H, $^3J_{HH}$ 8.3, $^4J_{HH}$ 1.5, $^5J_{HH}$ 0.5), 8.26 d.d.d (1H, Ar-H, $^3J_{HH}$ 8.3, $^4J_{HH}$ 1.5, $^5J_{HH}$ 0.5), 8.36 d.d (1H, H^{10}, $^4J_{HH}$ 2.2, $^5J_{HH}$ 0.5), 12.19 br.s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm (*J*, Hz) (the data given in parentheses are for the ^{13}C–{^1H} spectra): 146.03 s (s) (C^5), 141.33 d.d (s) (C^3, $^3J_{HC}$ 9.5, $^3J_{HC}$ 9.5), 140.38 d.d (s) (C^{6a}, $^3J_{HC}$ 9.9, $^3J_{HC}$ 9.5), 138.66 m (s) (C^2, C^{11}), 130.91 d.m (s) (CH_{Ar}), 129.19 d.m (s) (CH_{Ar}), 129.09 d.m (s) (CH_{Ar}), 127.53 d.m (s) (CH_{Ar}), 126.27 d.d (s) (C^8, $^1J_{HC}$ 162.1, $^3J_{HCCC}$ 9.2), 124.95 d.d.d (s) (C^9, $^3J_{HC}$ 10.3, $^2J_{HC}$ 4.0, $^2J_{HC}$ 3.3), 121.43 d.d.d (s) (C^{10}, $^1J_{HC}$ 168.0, $^3J_{HC}$ 5.5, $^4J_{HC}$ 1.1), 120.25 d (s) (C^{10a}, $^3J_{HC}$ 5.8), 113.61 d.d (s) (C^7, $^1J_{HC}$ 166.9, $^2J_{HC}$ 0.7). Mass spectrum (MALDI): *m*/*z* 253.8 $[M]^+$.

9-Bromo-6*H*-indolo[2,3-*b*]quinoxaline (6). Yield 77%, yellow powder, mp 289°C (mp >300°C [9]). IR spectrum, ν, cm^{-1}: 3444, 1730, 1614, 1407, 1332, 1240, 1210, 1129, 1110, 1004, 948, 877, 823, 746. ^1H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 7.33 br.d (1H, H^7, $^3J_{HH}$ 8.7), 7.74 d.d.d (1H, ArH, $^3J_{HH}$ 6.9, $^3J_{HH}$ 6.8, $^4J_{HH}$ 1.4), 7.79 d.d (1H, H^8, $^3J_{HH}$ 8.7, $^4J_{HH}$ 2.3), 7.81–7.84 m (1H, ArH), 8.08 br.d.d (1H, ArH, $^3J_{HH}$ 8.3, $^4J_{HH}$ 0.8), 8.24 br.d (1H, ArH, $^3J_{HH}$ 8.3), 8.46 d (1H, H^{10}, $^4J_{HH}$ 1.9), 12.17 br.s (1H, NH). Mass spectrum (MALDI): *m*/*z* 299.8 $[M + H]^+$.

9-Nitro-6*H*-indolo[2,3-*b*]quinoxaline (7). Yield 97%, orange powder, mp 265°C. IR spectrum, ν, cm^{-1}: 3327, 1748, 1716, 1659, 1614, 1518, 1338, 1274, 1165, 1121, 1072, 902, 831, 748, 686. Due to the low solubility of this compound in wide range of the solvents NMR spectra were not recordered. Mass spectrum (MALDI): *m*/*z* 297.3 $[M + Na]^+$. Found, %: C 63.47; H 2.83; N 21.01. Calculated, %: $C_{14}H_8N_4O_2$: C 63.64; H 3.05; N 21.20.

2-Butyl-5*H*-benzo[4,5]imidazo[1,2-*c*]quinazolin-6-one (8). Yield 79%, orange powder, mp 235°C. IR spectrum, ν, cm^{-1}: 3437, 1718, 1615, 1594, 1543, 1498, 1337, 1248, 1200, 1125, 1062, 1009, 933, 829, 801, 758, 743. ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 0.87 t (3H, CH_3, $^3J_{HH}$ 7.4), 1.27–1.36 m (2H, CH_2), 1.56–1.64 m (2H, CH_2), 2.65 t (2H, CH_2, $^3J_{HH}$ 7.5), 7.27 d (1H, $^3J_{HH}$ 8.3), 7.32–7.36 m (2H), 7.38–7.42 m (1H), 7.76 d (1*H*, $^3J_{HH}$ 8.8), 8.11 d (1H, $^4J_{HH}$ 1.4), 8.36 br.d.d (1H, $^3J_{HH}$ 7.8, $^4J_{HH}$ 0.5), 11.65 br.s (1H, NH). ^{13}C NMR spectrum ($CDCl_3$–DMSO-d_6, 6 : 1, δ_C, ppm (*J*, Hz): 147.56 d.d (s) ($^3J_{HC}$ 4.4, $^4J_{HC}$ 0.7), 146.24 s (s) (C=O), 143.24 m (s), 137.53 m (s), 134.74 m (s), 132.19 d.m (s) (CH_{Ar}), 124.53 d.m (s) (CH_{Ar}), 123.16 d.m (s) (CH_{Ar}), 123.12 d.m (s) (CH_{Ar}), 118.51 d.d.t (s) (CH_{Ar}, $^1J_{HC}$ 162.1, $^3J_{HC}$ 8.1, $^3J_{HC}$ 1.5), 115.56 d (s) (CH_{Ar}, $^1J_{HC}$ 163.2), 114.57 d.d.t (s) (CH_{Ar}, $^1J_{HC}$ 168.7, $^3J_{HC}$ 8.1, $^3J_{HC}$ 1.8), 111.27 m (s), 34.30 t.m (s) (CH_2), 32.90 t.m (s) (CH_2), 21.49 t.m (s) (CH_2, $^1J_{HC}$ 120.3, $^3J_{HC}$ 4.0), 13.40 q.t (s) (CH_3, $^1J_{HC}$ 124.7, $^3J_{HC}$ 4.0). Mass spectrum (MALDI): *m*/*z* 291.8 $[M]^+$.

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