

Synthesis and Photoluminescent Properties of 2-(3-Carboxymethylindazol-1-yl)anilines

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Received April 15, 2021; revised May 11, 2021; accepted May 14, 2021

Abstract—A two-stage method for the preparation of 2-(3-carboxymethylindazol-1-yl)anilines using the *N*-arylation reaction of 3-carboxymethylindazoles with *o*-nitrohaloarenes and subsequent reduction of nitro-containing intermediates with tin(II) chloride was developed. The experimental results showed that the use of the synthesized compounds as fluorophores in the visible region of the spectrum is promising.

Keywords: heterocycles, *N*-arylation, reduction, photoluminescence

DOI: 10.1134/S1070363221060049

N-Substituted indazole derivatives have attracted considerable interest of researchers for a long time. They have been found among the alkaloids of black cummin [1, 2]. These compounds are used as antiemetics (granisetron, tropisetron) [3], anticancer drugs (niraparib, pazopanib) [4], anti-inflammatory agents (benzadac, benzydamine) [5, 6]. Biological activity of *N*-substituted indazole derivatives have been reviewed in detail in [7–9].

In addition, a wide range of useful photophysical properties of *N*-substituted indazoles should be noted. They are used in lighting technology, for light-emitting devices production, as well as in study of biochemical processes in living systems using fluorescent trackers [10–13].

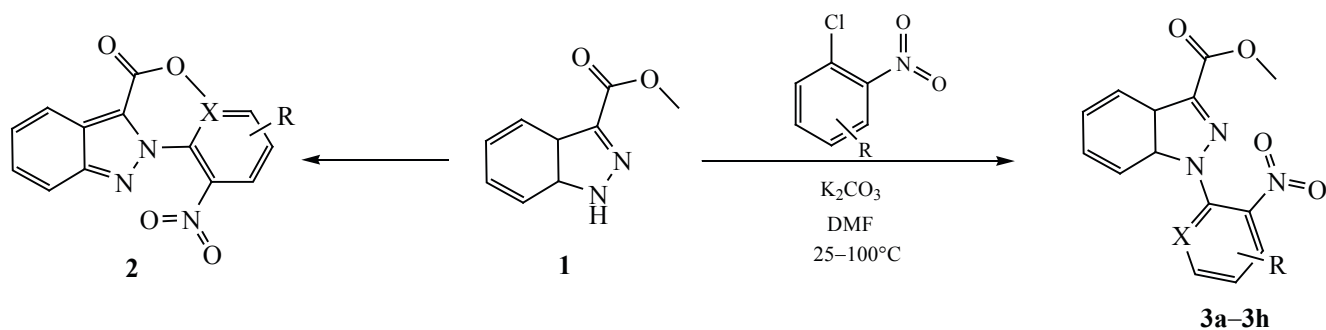
Due to great practical importance of *N*-arylated indazoles, over the past two decades methods for their design have been studied in detail and developed using both base and transition metal catalysis [14–19]. *N*-Arylation reactions of 1*H*-indazoles can proceed at both nitrogen atoms [14–16]. However, as a rule, the reaction proceeds regioselectively at the N¹ atom of the indazole ring [17–19]. At the same time, despite a significant data

on this topic, only a single publication is devoted to the reaction of *N*-arylation of indazole-3-carboxylates [20].

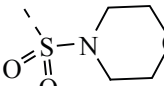
Earlier, we have found unusual regioselectivity in the *N*-arylation reaction of pyrazole-3-carboxylates when using *O*-nitro-substituted haloarenes [21]. Under the reaction conditions, a predominant nucleophilic substitution at the N² atom of the pyrazole ring was observed. Subsequent reduction of the nitro derivative with tin(II) chloride and other reagents [22] in all cases gave *N*-hydroxyquinoxalines as the products of reductive cyclization. The obtained compounds showed the properties of potent and selective inhibitors of human monoamine oxidase [23]. Herein, we attempted to apply this approach to the synthesis of fused systems containing indazole and quinoxaline rings.

To accomplish this task, methyl indazole-3-carboxylate was reacted with a number of electron-deficient *O*-nitrohaloarenes in absolute DMF in the presence of anhydrous potassium carbonate as a deprotonating agent (Scheme 1). However, it was found that the *N*-arylation of indazole-3-carboxylates proceeds at the N¹ atom of the indazole ring to give the corresponding *N*-aryl derivatives **3a–3h**

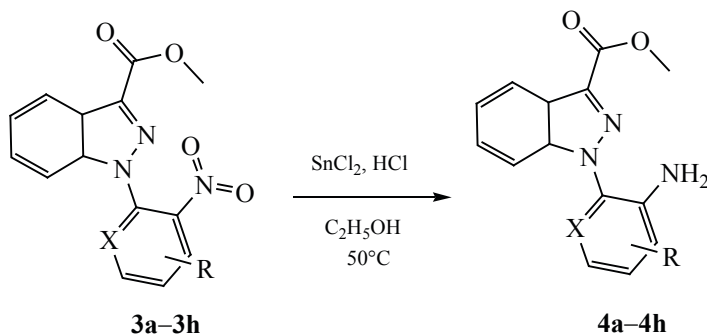
Scheme 1.



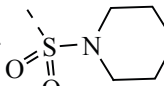
R = H, X = C (**a**, 93%); R = CN, X = C (**b**, 93%); R = 4-NO₂, X = C (**c**, 97%); R = 4-COOEt, X = C (**d**, 82%); R = 4-CF₃,

X = C (**e**, 90%); R = 4-, X = C (**f**, 77%); R = H, X = N (**g**, 77%); R = 5-Br, X = N (**h**, 83%).

Scheme 2.



R = H, X = C (**a**, 84%); R = CN, X = C (**b**, 59%); R = 4-NH₂, X = C (**c**, 61%); R = 4-COOEt, X = C (**d**, 88%); R = 4-CF₃,

X = C (**e**, 58%); R = 4-, X = C (**f**, 81%); R = H, X = N (**g**, 68%); R = 5-Br, X = N (**h**, 76%).

with yields up to 97%. Despite attempts to vary the reaction conditions (temperature, solvent), the use of deprotonating agents of different nature (potassium *tert*-butoxide, triethylamine, 4-*N,N*-dimethylaminopyridine) failed to detect the formation of isomeric compounds **2**.

The obtained series of nitro derivatives **3a–3h** was converted into the corresponding amines **4a–4h** using the previously developed method for the reduction of *N*-nitroarylpyrazole-3-carboxylates with tin(II) chloride in ethanol in the presence of hydrochloric acid [21] (Scheme 2). Compounds **4a–4h** were obtained in yields of 58–88%.

A series of heterocyclic amines **4a–4h** containing various functional groups was investigated for the presence of photoluminescence in the solid state at room temperature using a Fluorolog 3 fluorescence spectrometer. The found emission spectral maxima (λ_{em}^{max}), the excited state lifetime (τ) and the chromaticity diagram parameters (CIE [*x*; *y*]) are given in Table 1. The emission spectra recorded upon irradiation with light λ_{em} 450 nm are shown in Fig. 1.

The obtained data showed that compounds **4a–4h** possess strong yellow-green photoluminescence in the solid state. The emission spectra are mainly represented by a wide band. Luminescence maxima are in the range

from 487 to 540 nm. The largest shift of the maximum occurs when hydrogen (**4a**) is replaced by a nitrile group (**4e**) at position 4. The lifetimes of the excited state for compounds **4b**, **4d–4h** do not differ from each other and are in the range from 0.4 to 4.4 nsec. A sharp difference is observed for compounds **4a** and **4c**, for which the excited state lifetime is 653 and 518 ns, respectively. Such a sharp increase in the excited state lifetime may be explained by more dense molecular packing due to the strong intermolecular dipole-dipole interaction [24, 25].

In conclusion, a series of new 2-(3-carboxymethyl-indazol-1-yl)anilines was synthesized by a two-step method, including *N*-arylation of 3-carboxymethylindazoles with *o*-nitrohaloarenes followed by the reduction of nitro-containing intermediates. The proposed approach provides the overall yield of the target amino derivatives in 62–78% range. The obtained compounds are of interest as organic fluorophores with emission in the yellow-green spectral region.

EXPERIMENTAL

Organic, inorganic reagents and solvents were obtained from commercial sources (Aldrich, Vekton, Ekros) and were used without additional purification. The reaction progress was monitored by thin layer chromatography (TLC) on silica gel on Silufol UV aluminum plates eluting with a mixture of ethyl acetate and petroleum ether (1 : 1). NMR spectra were recorded on a Varian XL-400 instrument (400 MHz) in DMSO-*d*₆ solutions at 25°C. Melting points were determined on a Büchi M-560 melting point and boiling point apparatus. High-resolution mass spectra were recorded on a Bruker Daltonics MicrOTOF-II instrument, the ionization method was electrospray ionisation (ESI), the temperature of the ionization source was 180°C, the eluent was methanol. Photoluminescence spectra, excited state lifetimes were obtained on a Fluorolog 3 fluorescence spectrometer (Horiba Jobin Yvon).

General procedure for the synthesis of methyl 1-(2-nitroaryl)-1*H*-indazole-3-carboxylates **3a–3h.** To a solution of 1*H*-indazole-3-carboxylate (1 mmol) in DMF (1.5 mL) was added the corresponding *o*-nitrohaloarene (1 mmol) and K₂CO₃ (1.3 mmol). The reaction mixture was stirred at 70–100°C for 12 h. After the reaction completed, the resulting suspension was diluted with 7 mL of distilled water, the precipitate was filtered off and washed with 2 mL of water. The resulting product was purified by recrystallization from an ethanol–DMF mixture.

Table 1. Photoluminescent characteristics of compounds **4a–4h**

Comp. no.	$\lambda_{\text{em}}^{\text{max}}$, nm	τ , ns	CIE [x;y]
4a	540	653	0.40; 0.58
4b	487, 520	0.4	0.35; 0.62
4c	535	518	0.41; 0.56
4s	515	4.4	0.37; 0.60
4e	530	3.9	0.39; 0.59
4f	515	4.2	0.38; 0.60
4g	512	3.3	0.35; 0.62
4h	530	2.8	0.43; 0.56

Methyl 1-(2-nitrophenyl)-1*H*-indazole-3-carboxylate (3a**).** Yield 0.276 g (93%), pale yellow crystals, mp 163–165°C. ¹H NMR spectrum, δ , ppm: 3.97 s (3H, CH₃), 7.49 d. t (1H, Ar, *J* 8.4, 2.0 Hz), 7.61 d. d (2H, Ar, *J* 4.0, 2.0 Hz), 7.87 d. t (1H, Ar, *J* 8.8, 2.0 Hz), 7.93–8.07 m (2H, Ar), 8.22 d (1H, Ar, *J* 8.4 Hz), 8.27 d (1H, Ar, *J* 8.4 Hz). ¹³C NMR spectrum, δ , ppm: 52.06, 110.43, 121.68, 123.01, 124.26, 125.92, 128.50, 128.55, 130.64, 130.70, 134.61, 137.18, 140.78, 145.04, 161.81. Mass spectrum, *m/z*: 320.0643 [*M*+Na]⁺ (calcd for C₁₅H₁₁N₃NaO₄: 320.0642).

Methyl 1-(4-cyano-2-nitrophenyl)-1*H*-indazole-3-carboxylate (3b**).** Yield 0.299 g (93%), pale yellow powder, mp 230–232°C. ¹H NMR spectrum, δ , ppm: 3.97 s (3H, CH₃), 7.53 s (1H, Ar), 7.66 s (1H, Ar), 7.76 s (1H, Ar), 8.23 d (1H, Ar, *J* 8.0 Hz), 8.31 d (1H, Ar, *J* 8.4 Hz), 8.49 d (1H, Ar, *J* 8.4 Hz), 8.87 s (1H, Ar). ¹³C NMR spectrum, δ_{C} , ppm:

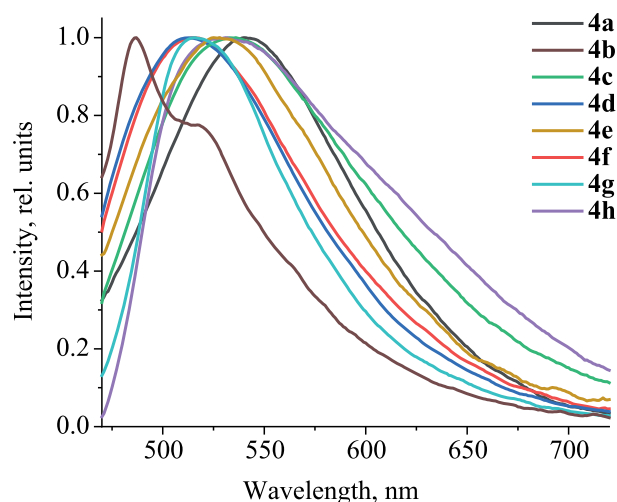


Fig. 1. Photoluminescence spectra of compounds **4a–4h**.

52.36, 110.80, 112.61, 116.51, 121.97, 123.31, 124.86, 128.90, 129.07, 130.36, 134.11, 138.24, 138.36, 140.48, 144.66, 161.62. Mass spectrum, m/z : 345.0596 [$M + Na$]⁺ (calcd for C₁₆H₁₀N₄NaO₄: 345.0594).

Methyl 1-(2,4-dinitrophenyl)-1H-indazole-3-carboxylate (3c). Yield 0.332 g (97%), yellow powder, mp 186–189°C. ¹H NMR spectrum, δ , ppm: 3.98 s (3H, CH₃), 7.54 t (2H, Ar, J 7.6 Hz), 7.68 t (1H, Ar, J 7.6 Hz), 7.78 d (1H, Ar, J 8.0 Hz), 8.24 d (1H, Ar, J 7.6 Hz), 8.37 d (1H, Ar, J 8.8 Hz), 8.75 d (1H, Ar, J 8.4 Hz), 9.00 s (1H, Ar). ¹³C NMR spectrum, δ_C , ppm: 52.28, 110.66, 121.80, 122.00, 123.34, 124.85, 128.85, 129.08, 135.22, 138.57, 140.44, 144.26, 146.65, 161.49. Mass spectrum, m/z : 365.0493 [$M + Na$]⁺ (calcd for C₁₅H₁₀N₄NaO₆: 365.0493).

Methyl 1-[4-(ethoxycarbonyl)-2-nitrophenyl]-1H-indazole-3-carboxylate (3d). Yield 0.302 g (82%), pale yellow powder, mp 158–161°C. ¹H NMR spectrum, δ , ppm: 1.39 t (3H, CH₃, CH₃, J 7.2 Hz), 3.97 s (3H, CH₃), 4.43 q (2H, CH₂, J 7.2 Hz), 7.52 t (1H, Ar, J 7.6 Hz), 7.64 t (1H, Ar, J 7.6 Hz), 7.71 d (1H, Ar, J 8.4 Hz), 8.22 t (2H, Ar, J 8.4 Hz), 8.47 d (1H, Ar, J 8.4 Hz), 8.65 s (1H, Ar). ¹³C NMR spectrum, δ_C , ppm: 14.01, 52.21, 61.95, 110.59, 121.89, 123.23, 124.63, 126.49, 128.66, 128.86, 131.08, 134.07, 134.56, 137.99, 140.51, 144.56, 161.65, 163.33. Mass spectrum, m/z : 392.0850 [$M + Na$]⁺ (calcd for C₁₈H₁₅N₃NaO₆: 392.0853).

Methyl 1-[2-nitrophenyl-4-(trifluoromethyl)]-1H-indazole-3-carboxylate (3e). Yield 0.328 g (90%), beige crystals, mp 182–185°C. ¹H NMR spectrum, δ , ppm: 3.98 s (3H, CH₃), 7.53 t (1H, Ar, J 7.6 Hz), 7.65 t (1H, Ar, J 7.6 Hz), 7.76 d (1H, Ar, J 8.0 Hz), 8.24 d (1H, Ar, J 8.0 Hz), 8.32 d (1H, Ar, J 8.4 Hz), 8.39 d (1H, Ar, J 8.4 Hz), 8.68 s (1H, Ar). ¹³C NMR spectrum, δ_C , ppm: 52.92, 111.33, 122.00, 122.58, 123.92, 125.36, 129.58, 130.82, 131.93, 134.55, 138.83, 145.59, 162.31. Mass spectrum, m/z : 388.0516 [$M + Na$]⁺ (calcd for C₁₆H₁₀F₃N₃NaO₄: 388.0516).

Methyl 1-[4-(morpholin-4-ylsulfonyl)-2-nitrophenyl]-1H-indazole-3-carboxylate (3f). Yield 0.343 g (77%), yellow powder, mp 226–230°C. ¹H NMR spectrum, δ , ppm: 3.10 s (4H, CH₂), 3.69 s (4H, CH₂), 3.98 s (3H, CH₃), 7.54 t (1H, Ar, J 7.6 Hz), 7.66 t (1H, Ar, J 7.6 Hz), 7.81 d (1H, Ar, J 8.4 Hz), 8.18–8.34 m (3H, Ar), 8.49 s (1H, Ar). ¹³C NMR spectrum, δ_C , ppm: 52.29, 110.86, 121.92, 123.26, 124.76, 125.33, 128.87, 129.48, 133.10, 134.25, 135.97, 138.22, 140.57, 144.72, 161.64. Mass spectrum,

m/z : 469.0787 [$M + Na$]⁺ (calcd for C₁₉H₁₈N₄NaO₇S: 469.0788).

Methyl 1-(3-nitropyridin-2-yl)-1H-indazole-3-carboxylate (3g). Yield 0.229 g (77%), pale yellow crystals, mp 143–146°C. ¹H NMR spectrum, δ , ppm: 3.97 s (3H, CH₃), 7.55 t (1H, Ar, J 7.6 Hz), 7.70 t (1H, Ar, J 7.6 Hz), 7.78–7.89 m (1H, Ar), 8.23 d (1H, Ar, J 8.0 Hz), 8.27 d (1H, Ar, J 8.4 Hz), 8.68 d (1H, Ar, J 8.0 Hz), 8.93 d (1H, Ar, J 4.4 Hz). ¹³C NMR spectrum, δ_C , ppm: 52.36, 113.32, 121.76, 123.52, 124.13, 125.13, 129.14, 135.57, 138.41, 139.51, 139.72, 142.64, 151.82, 161.46. Mass spectrum, m/z : 321.0598 [$M + Na$]⁺ (calcd for C₁₄H₁₀N₄NaO₄: 321.0594).

Methyl 1-(5-bromo-3-nitropyridin-2-yl)-1H-indazole-3-carboxylate (3h). Yield 0.312 g (83%), orange crystals, mp 159–162°C. ¹H NMR spectrum, δ , ppm: 3.96 s (3H, CH₃), 7.54 t (1H, Ar, J 7.2 Hz), 7.69 t (1H, Ar, J 8.0 Hz), 8.21 d (1H, Ar, J 8.4 Hz), 8.25 d (1H, Ar, J 8.8 Hz), 9.02 s (1H, Ar), 9.07 s (1H, Ar). ¹³C NMR spectrum, δ_C , ppm: 52.37, 117.90, 121.80, 123.53, 125.25, 137.53, 138.74, 139.08, 139.64, 141.44, 161.32. Mass spectrum, m/z : 398.9705 [$M + Na$]⁺ (calcd for C₁₄H₉BrN₄NaO₄: 398.9699).

General procedure for the synthesis of methyl 1-(2-aminoaryl)-1H-indazole-3-carboxylates 4a–4h. To a mixture of SnCl₂ (3.5 mmol) in conc. HCl (2 mL) and ethanol (2 mL) was added the corresponding 1-(2-nitroaryl)-1H-indazole-3-carboxylate **3** (0.01 mol). The reaction mixture was stirred at 50°C for 3–4 h. The precipitate was filtered off, washed with ethanol, and recrystallized from an ethanol–DMF mixture.

Methyl 1-(2-aminophenyl)-1H-indazole-3-carboxylate (4a). Yield 0.225 g (84%), pale yellow powder, mp 128–130°C. ¹H NMR spectrum, δ , ppm: 3.96 s (3H, CH₃), 5.13 s (2H, NH₂), 6.72 t (1H, Ar, J 7.2 Hz), 6.96 d (1H, Ar, J 8.0 Hz), 7.20 d (1H, Ar, J 7.6 Hz), 7.26 t (1H, Ar, J 7.6 Hz), 7.34 d (1H, Ar, J 8.4 Hz), 7.41 t (1H, Ar, J 7.2 Hz), 7.50 t (1H, Ar, J 7.6 Hz), 8.18 d (1H, Ar, J 8.0 Hz). ¹³C NMR spectrum, δ_C , ppm: 51.75, 111.15, 116.73, 116.93, 121.35, 123.04, 123.48, 127.39, 130.05, 135.76, 140.91, 143.36, 162.32. Mass spectrum, m/z : 290.0908 [$M + Na$]⁺ (calcd for C₁₅H₁₃N₃NaO₂: 290.0900).

Methyl 1-(2-amino-4-cyanophenyl)-1H-indazole-3-carboxylate (4b). Yield 0.169 g (59%), pale yellow powder, mp 176–182°C. ¹H NMR spectrum, δ , ppm: 3.96 s (3H, CH₃), 5.69 s (1H, NH₂), 7.10 d (1H, Ar, J 8.0 Hz), 7.31 s (1H, Ar), 7.38–7.44 m (3H, Ar), 7.53 t (1H, Ar, J 7.6 Hz), 8.19 d (1H, Ar, J 8.0 Hz). ¹³C NMR spectrum,

δ_C , ppm: 51.91, 111.14, 112.44, 118.67, 118.83, 119.27, 121.52, 123.18, 123.77, 125.89, 127.78, 128.86, 136.55, 140.73, 145.07, 162.20. Mass spectrum, m/z : 315.0856 [$M + Na$]⁺ (calcd for C₁₆H₁₂N₄NaO₂: 315.0852).

Methyl 1-(2,4-diaminophenyl)-1H-indazole-3-carboxylate (4c). Yield 0.173 g (61%), white powder, mp 176–180°C. ¹H NMR spectrum, δ , ppm: 3.95 s (3H, CH₃), 4.67 s (2H, NH₂), 5.20 s (2H, NH₂), 5.98 d (1H, Ar, J 8.4 Hz), 6.11 s (1H, Ar), 6.83 d (1H, Ar, J 8.0 Hz), 7.31 d (1H, Ar, J 8.4 Hz), 7.34–7.41 m (1H, Ar), 7.46 t (1H, Ar, J 7.6 Hz), 8.14 d (1H, Ar, J 8.0 Hz). ¹³C NMR spectrum, δ_C , ppm: 51.63, 100.61, 101.02, 104.03, 111.24, 113.73, 121.16, 122.87, 123.22, 127.01, 127.98, 141.29, 144.76, 148.53, 162.42. Mass spectrum, m/z : 305.1014 [$M + Na$]⁺ (calcd for C₁₅H₁₄N₄NaO₂: 305.1009).

Methyl 1-[2-amino-4-(ethoxycarbonyl)phenyl]-1H-indazole-3-carboxylate (4d). Yield 0.299 g (88%), beige powder, mp 130–135°C. ¹H NMR spectrum, δ , ppm: 1.35 t (3H, CH₃, J 6.8 Hz), 3.97 s (3H, CH₃), 4.34 q (2H, CH₂, J 7.2 Hz), 5.49 s (2H, NH₂), 7.28 d (1H, Ar, J 8.0 Hz), 7.33–7.46 m (3H, Ar), 7.53 t (1H, Ar, J 7.6 Hz), 7.61 s (1H, Ar), 8.20 d (1H, Ar, J 8.0 Hz). ¹³C NMR spectrum, δ_C , ppm: 166.17, 162.94, 145.01, 141.44, 136.95, 131.87, 128.40, 128.35, 126.60, 124.37, 123.84, 122.17, 117.84, 117.06, 111.94, 61.49, 52.54, 14.87. Mass spectrum, m/z : 362.1151 [$M + H$]⁺ (calcd for C₁₈H₁₇N₃NaO₄: 362.1111).

Methyl 1-[2-amino-4-(trifluoromethyl)phenyl]-1H-indazole-3-carboxylate (4e). Yield 0.195 g (58%), pale yellow powder, mp 154–157°C. ¹H NMR spectrum, δ , ppm: 3.97 s (3H, CH₃), 4.92 s (2H, NH₂), 6.99 d (1H, Ar, J 8.4 Hz), 7.29 s (1H, Ar), 7.38–7.45 m (3H, Ar), 7.52 t (1H, Ar, J 7.6 Hz), 8.20 d (1H, Ar, J 8.0 Hz). ¹³C NMR spectrum, δ_C , ppm: 52.53, 111.82, 112.48, 113.32, 122.17, 123.85, 124.37, 125.86, 126.09, 128.38, 129.35, 130.98, 131.29, 141.52, 145.68, 162.93. Mass spectrum, m/z : 358.0775 [$M + Na$]⁺ (calcd for C₁₆H₁₂F₃N₃NaO₂: 358.0774).

Methyl 1-[2-amino-4-(morpholin-4-ylsulfonyl)phenyl]-1H-indazole-3-carboxylate (4f). Yield 0.337 g (81%), pale yellow crystals, mp 227–231°C. ¹H NMR spectrum, δ , ppm: 2.98 s (4H, Alk), 3.68 s (4H, Alk), 3.98 s (3H, CH₃), 5.75 s (2H, NH₂), 7.00 d (1H, Ar, J 8.0 Hz), 7.35 s (1H, Ar), 7.41–7.57 m (4H, Ar), 8.21 d (1H, Ar, J 7.6 Hz). ¹³C NMR spectrum, δ_C , ppm: 45.93, 51.86, 65.35, 111.25, 114.21, 115.00, 121.47, 123.15, 123.73, 125.65, 127.70, 128.52, 135.70, 136.47, 140.78, 145.02, 162.21. Mass spectrum, m/z : 439.1053 [$M + Na$]⁺ (calcd for C₁₉H₂₀N₄NaO₅S: 439.1047).

Methyl 1-(3-aminopyridin-2-yl)-1H-indazole-3-carboxylate (4g). Yield 0.183 g (68%), beige powder, mp 145–149°C. ¹H NMR spectrum, δ , ppm: 3.99 s (3H, CH₃), 5.96 s (2H, NH₂), 7.20–7.31 m (1H, Ar), 7.40 d (1H, Ar, J 8.0 Hz), 7.46 t (1H, Ar, J 7.2 Hz), 7.57 t (1H, Ar, J 7.6 Hz), 7.86 d. d (1H, Ar, J 4.4, 2.0 Hz), 8.10 d (1H, Ar, J 8.4 Hz), 8.21 d (1H, Ar, J 8.0 Hz). ¹³C NMR spectrum, δ_C , ppm: 51.97, 113.86, 121.19, 122.80, 124.17, 124.24, 124.74, 127.81, 135.16, 136.21, 137.91, 140.29, 162.01. Mass spectrum, m/z : 291.0854 [$M + Na$]⁺ (calcd for C₁₄H₁₂N₄NaO₂: 291.0852).

Methyl 1-(3-amino-5-bromopyridin-2-yl)-1H-indazole-3-carboxylate (4h). Yield 0.264 g (76%), yellow powder, mp 176–180°C. ¹H NMR spectrum, δ , ppm: 3.99 s (3H, CH₃), 6.23 s (2H, NH₂), 7.47 t (1H, Ar, J 7.6 Hz), 7.54–7.65 m (2H, Ar), 7.92 s (1H, Ar), 8.09 d (1H, Ar, J 8.0 Hz), 8.21 d (1H, Ar, J 7.6 Hz). ¹³C NMR spectrum, δ_C , ppm: 52.01, 113.76, 119.06, 121.26, 122.80, 124.32, 125.85, 128.00, 134.74, 135.04, 135.55, 139.34, 140.23, 161.87. Mass spectrum, m/z : 368.9960 [$M + Na$]⁺ (calcd for C₁₄H₁₁BrN₄NaO₂: 368.9958).

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FUNDING

This work was financially supported by the Russian Science Foundation (project no. 20-73-00203) using the equipment of the Resource Centers “Chemical Analysis and Materials Research Center” and “Center for Optical and Laser Materials Research” of St. Petersburg State University.

CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

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REFERENCES

- Liu, Y.M., Yang, J.S., and Liu, Q.H., *Chem. Pharm. Bull.*, 2004, vol. 52, p. 454.
<https://doi.org/10.1248/cpb.52.454>
- Atta-ur-Rahman Malik, S., Hasan, S.S., Choudhary, M.I., Ni, C.-Z., and Clardy, J., *Tetrahedron Lett.*, 1995, vol. 36, p. 1993.
[https://doi.org/10.1016/0040-4039\(95\)00210-4](https://doi.org/10.1016/0040-4039(95)00210-4)
- Fischer, J. and Ganellin, C.R., *John Wiley & Sons*, 2006, p. 448.
<https://doi.org/10.1002/3527608001>
- Scott, L.J., *Drugs*, 2017, vol. 77, p. 1029.
<https://doi.org/10.1007/s40265-017-0752-y>
- Shen, T.Y., *Ann. Rep. Med. Chem.*, 1968, vol. 3, p. 215.
[https://doi.org/10.1016/S0065-7743\(08\)61326-3](https://doi.org/10.1016/S0065-7743(08)61326-3)
- Gaikwad, D.D., Chapolikar, A.D., Devkate, C.G., Warad, K.D., Tayade, A.P., Pawar, R.P., and Domb, A.J., *Eur. J. Med. Chem.*, 2015, vol. 90, p. 707.
<https://doi.org/10.1016/j.ejmech.2014.11.029>
- Dong, J., Zhang, Q., Wang, Z., Huang, G., and Li, S., *ChemMedChem*, 2018, vol. 13, no. 15, p. 1490.
<https://doi.org/10.1002/cmdc.201800253>
- Wan, Y.C., He, S.Z., Li, W., and Tang, Z.L., *Anti-Cancer Agents Med. Chem.*, 2018, vol. 18, p. 1228.
- Zhang, S.G., Liang, C.G., and Zhang, W.H., *Molecules*, 2018, vol. 23, no. 11, p. 2783.
<https://doi.org/10.3390/molecules23112783>
- Kim, O.S., Jang, J.H., Kim, H.T., Han, S.J., Tsui, G.C., and Joo, J.M., *Org. Lett.*, 2017, vol. 19, no. 6, p. 1450.
<https://doi.org/10.1021/acs.orglett.7b00410>
- Janardhanan, J.C., Mishra, R.K., Das, G., Sini, S., Jayamurthy, P., Suresh, C.H., Praveen, V.K., Manoj, N., and Babu, B.P., *Asian J. Org. Chem.*, 2018, vol. 7, p. 2094.
<https://doi.org/10.1002/ajoc.201800413>
- Pakjoo, V., Roshani, M., Pordel, M., and Hoseini, T., *Arkivoc*, 2012, vol. 9, p. 195.
<https://doi.org/10.3998/ark.5550190.0013.917>
- Cheng, Y., Li, G., Liu, Y., Shi, Y., Gao, G., Wu, D., Lan, J., and You, J., *J. Am. Chem. Soc.*, 2016, vol. 138, no. 14, p. 4730.
<https://doi.org/10.1021/jacs.5b09241>
- Ding, X., Bai, J., Wang, H., Zhao, B., Li, J., and Ren, F., *Tetrahedron*, 2017, vol. 73, p. 172.
<https://doi.org/10.1016/j.tet.2016.11.066>
- Zhang, R., Liu, Z., Peng, Q., Zhou, Y., Xu, L., and Pan, X., *Org. Biomol. Chem.*, 2018, vol. 16, p. 1816.
<https://doi.org/10.1039/c8ob00128f>
- Xu, L., Du, S., Li, Z., and Tian, Z., *Heterocycles*, 2018, vol. 96, no. 1, p. 74.
<https://doi.org/10.3987/com-17-13826>
- Liang, Y., Zhang, X., and MacMillan, D.W.C., *Nature*, 2018, vol. 559, p. 83.
<https://doi.org/10.1038/s41586-018-0234-8>
- Antilla, J.C., Baskin, J.M., Barder, T.E., and Buchwald, S.L., *J. Org. Chem.*, 2004, vol. 69, no. 17, p. 5578.
<https://doi.org/10.1021/jo049658b>
- Gamonal, A., Brunet, E., Juanes, O., and Rodriguez-Ubis, J.C., *J. Photochem. Photobiol. (A)*, 2017, vol. 342, p. 53.
<https://doi.org/10.1016/j.jphotochem.2017.03.037>
- Reddy, A.V., Gogireddy, S., Dubey, P.K., Reddy, M.B., and Veeresh, B., *J. Chem. Sci.*, 2015, vol. 127, p. 433.
<https://doi.org/10.1007/s12039-015-0792-3>
- Panova, V.A., Korsakov, M.K., Shetnev, A.A., and Filimonov, S.I., *Mendeleev Commun.*, 2019, vol. 29, no. 1, p. 114.
<https://doi.org/10.1016/j.mencom.2019.01.039>
- Panova, V.A., Ivanovskii, S.A., Shetnev, A.A., Chirkova, Zh.V., Sudzilovskaya, T.N., and Filimonov, S.I., *Russ. Chem. Bull.*, 2020, vol. 69, p. 1965.
<https://doi.org/10.1007/s11172-020-2986-1>
- Panova, V.A., Filimonov, S.I., Chirkova, Zh.V., Kabanova, M.V., Shetnev, A.A., Korsakov, M.K., Petzer, A., and Petzer, J.P., *Bioorg. Chem.*, 2020, vol. 108, p. 104563.
<https://doi.org/10.1016/j.bioorg.2020.104563>
- Gierschner, J. and Park, S.Y., *J. Mater. Chem. (C)*, 2013, vol. 1, p. 5818.
<https://doi.org/10.1039/C3TC31062K>
- Nishio, S., Higashiguchi, K., and Matsuda, K., *Asian J. Org. Chem.*, 2014, vol. 3, p. 686.
<https://doi.org/10.1002/ajoc.201402024>