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Activation-free one-pot alkynylation–cyclization synthesis of 2-substituted 4-azaindoles and indoles

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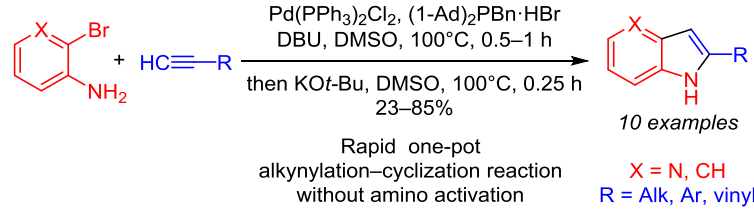


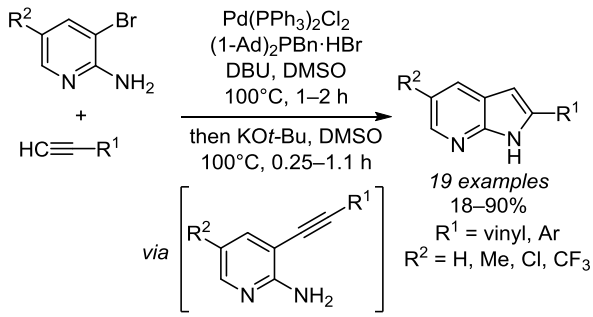
2-Substituted 4-azaindoles and indoles are rapidly and efficiently prepared in an activation-free Pd-catalyzed alkynylation–cyclization sequence starting from 3-amino-2-bromopyridine or *o*-bromoaniline and terminal alkynes in a one-pot fashion.

Keywords: 4-azaindoles, heterocycles, indoles, alkynylation, cyclization, one-pot reaction.

Indole[1] takes a most prominent position as a heterocyclic core element, and it can be found in numerous both natural and synthetic biologically active compounds[2–6] as well as in dyes.[7] As a consequence, indole syntheses have become an evergreen topic in synthetic chemistry.[8–13] In particular, Pd-catalyzed routes starting from *o*-haloanilines[14] are elegant annulation strategies. Furthermore, multicomponent syntheses of heterocycles initiated by transition metal catalysis[15–17] as one-pot processes have received increasing attention in the past decade. Azaindoles, i.e., pyrrolopyridines, are the isoelectronic congeners of indoles, where a CH unit in the benzene ring is formally replaced by a nitrogen atom. Since kinases have been identified to be most promising targets[18] in controlling cancer metabolism, privileged scaffolds[19–22] for anticancer agents evolved.[23–25] In this capacity, azaindole derivatives[26] have turned out to be promising potent inhibitors of various kinases.[27–34] This justifies why, like for indoles, catalytic, organometallic routes to azaindoles are a constant endeavor in synthetic chemistry.[35–38]

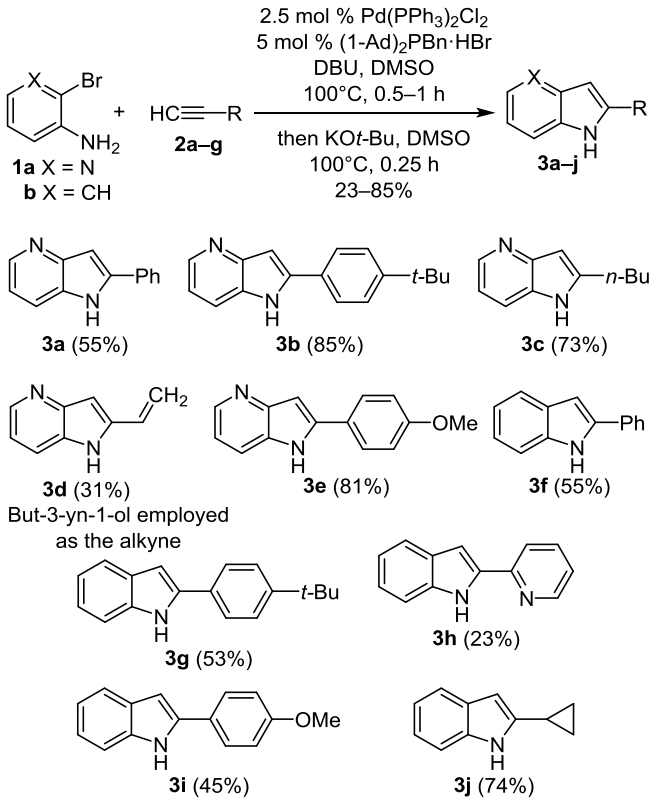
Just recently, taking advantage of our copper-free Pd-catalyzed alkynylation protocol applicable to consecutive multicomponent syntheses of heterocycles,[39–41] we disclosed a rapid and efficient activation-free access to 2-substituted 7-azaindoles in a one-pot alkynylation–cyclization sequence starting from 2-aminopyridyl halides and terminal alkynes (Scheme 1).[42] This sequence was then developed further into an alkynylation–cyclization–alkylation three-component synthesis of 1,2,5-trisubstituted 7-azaindoles.[43] Herein, we report the exemplary activating group-free one-pot alkynylation–cyclization synthesis of 2-substituted 4-azaindoles and indoles.

Scheme 1. 2-Substituted 7-azaindoles by one-pot Cu-free Pd-catalyzed alkynylation–cyclization synthesis



Based on the optimized protocol for the synthesis of 2-substituted 7-azaindoles[19] we applied the developed conditions, maintaining $PdCl_2(PPh_3)_2$ as a Pd source and cataCXium® ABn·HBr ($(1\text{-Ad})_2$PBn·HBr, di(1-adamantyl)-benzylphosphonium hydrobromide) as a ligand,[44,45] for reacting 3-amino-2-bromopyridine (**1a**) or *o*-bromoaniline (**1b**) with various terminal alkynes **2a–g**. The process proceeds smoothly and furnishes ten 2-substituted 4-azaindoles and indoles **3a–j** in moderate to good yields after isolation (Scheme 2).

Scheme 2. 2-Substituted 4-azaindoles and indoles **3a**–**j** by one-pot Cu-free Pd-catalyzed alkynylation–cyclization synthesis



The structures of all compounds **3a**–**j** were unambiguously assigned by spectroscopic methods (^{1}H and ^{13}C NMR, IR spectra) and elemental analyses or HRMS. The yields of 4-azaindoles are higher, presumably due to the acidification of the amino group in the terminal base-mediated cyclization. As previously shown for 7-azaindoles, it is very likely that a broad substitution pattern on both *o*-bromoaniline and 3-amino-2-bromopyridine is tolerated as well. Methodological studies to expand this approach to decorated 4-azaindoles and indoles are currently underway.

Aliphatic and (hetero)aromatic terminal alkynes can be successfully employed as substrates for both 4-azaindole and indole syntheses in an activation-free Pd-catalyzed alkynylation–cyclization reaction starting from 3-amino-2-bromopyridine or *o*-bromoaniline.

Experimental

IR spectra were recorded on a Shimadzu IRAffinity-1 apparatus using ATR technique. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AVIII 300 (300 and 75 MHz, respectively, compounds **3a**,**d**,**c**,**h**) or Bruker AVIII 600 spectrometers (600 or 150 MHz, respectively, compounds **3b**,**c**,**f**,**g**,**i**,**j**) in $CDCl_3$ (compounds **3c**,**d**,**e**–**h**,**j**) or DMSO-d_6 (compounds **3a**,**b**,**i**). 17% CS_2 was added to the solution of compound **3d** in $CDCl_3$. Residual solvent peaks (7.26 ppm for ^{1}H nuclei, 77.16 ppm for ^{13}C nuclei in $CDCl_3$; 2.50 ppm for ^{1}H nuclei, 39.52 ppm for ^{13}C nuclei in DMSO-d_6) or TMS were used as internal standards. The type of carbon nuclei was determined by 135-DEPT NMR spectroscopy. Mass spectra (EI, 70 eV) were obtained on a Finnigan TSQ 7000 apparatus. HRMS were performed on a Bruker maxis 4G apparatus (ESI). Elemental analyses were performed on an Elementar vario MICRO cube. Melting points were measured on a Büchi Melting Point B-540 and are uncorrected. The progress of the reactions was monitored using TLC on silica gel 60 F254 aluminum sheets supplied by Merck KGaA (Darmstadt). The spots were visualized with UV light (254 nm) and aqueous potassium permanganate solution. Crude products were adsorbed on Celite® 545 for flash chromatography. Flash chromatographic purification was performed on a Biotage SP1 Flash Chromatography Purification system using SNAP 100 g cartridges and silica gel 60 M (0.040–0.063 mm), supplied by Macherey Nagel (Düren).

All reactions were performed using Schlenk tubes, septa, and syringes under nitrogen atmosphere. Reagents were purchased from ABCR GmbH & Co. KG, Alfa Aesar GmbH & Co. KG, Fisher Scientific GmbH, Merck KGaA, Sigma-Aldrich Chemie GmbH, VWR International GmbH and used without further purification.

Synthesis of 2-substituted 4-azaindoles and indoles 3a–j *via* one-pot alkynylation–cyclization (General method). 3-Amino-2-bromopyridine (**1a**) (87 mg, 0.5 mmol) or 2-bromoaniline (**1b**) (172 mg, 1.00 mmol), $Pd(PPh_3)_2Cl_2$ (9.0 mg, 13 mmol or 17.5 mg, 25.0 mmol), and $(1\text{-Ad})_2PBn\cdot HBr$ (12 mg, 25 mmol or 23.6 mg, 50.0 mmol) were placed into a dry screw-cap Schlenk tube with a magnetic stirring bar, and the vessel was evacuated. After flushing the vessel with nitrogen, dry DMSO (1.0 or 1.5 ml), the corresponding alkyne **2a**–**j** (0.6 mmol or 1.2 mmol), and DBU (225 mg, 1.50 mmol or 457 mg, 3.00 mmol) were added. The reaction mixture was stirred at 100°C under nitrogen for 1 h until the bromide was completely consumed (monitored by TLC). After cooling to room temperature, KO*t*-Bu (253 mg, 2.25 mmol or 281 mg, 2.50 mmol) and DMSO (0.50 or 1.00 ml) were added to the reaction mixture, and the mixture was stirred at 100°C under nitrogen for 0.25 h. After cooling to room temperature, deionized water or brine (20 ml) was added to the mixture. The aqueous layer was extracted several times with EtOAc or CH_2Cl_2. The combined organic phases were dried over anhydrous Na_2SO_4 and after filtration, the solvents were removed under reduced pressure. The residue was purified by flash chromatography on silica gel to give the analytically pure products **3a**–**j**.

2-Phenyl-1*H*-pyrrolo[3,2-*b*]pyridine (3a) was synthesized from 3-amino-2-bromopyridine (**1a**) (87 mg, 0.5 mmol) and phenylacetylene (**2a**) (61 mg, 0.6 mmol), eluent for flash chromatography EtOAc–*n*-hexane, 3:2. Yield 53 mg (55%), beige solid, mp 249°C. IR spectrum, ν, cm^{-1}: 3082 (w), 3053 (w), 3011 (w), 2969 (w), 2932 (w), 1603 (w), 1568 (w), 1537 (w), 1481 (w), 1456 (m), 1414 (m), 1362 (m), 1343 (m), 1289 (w), 1275 (m), 1227 (w), 1200 (w), 1173 (w), 1157 (w), 1119 (w), 1096 (w), 1074 (w), 1053 (w), 1030 (w), 988 (w), 924 (m), 910 (w), 833 (w), 810 (w), 785 (m), 766 (s), 735 (m), 687 (s). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.06 (1H, s, H-3); 7.10 (1H, dd, *J* = 8.0, *J* = 4.6, H-6); 7.37–7.38 (1H, m, H Ph); 7.48–7.50 (2H, m, H Ph); 7.77 (1H, d,

J = 8.0, H-7); 7.92–7.93 (2H, m, H Ph); 8.31–8.32 (1H, m, H-5); 11.82 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 99.2 (CH); 116.8 (CH); 118.3 (CH); 125.5 (CH); 128.4 (CH); 129.2 (CH); 130.1 (C); 131.7 (C); 141.1 (C); 142.9 (CH); 146.9 (C). Mass spectrum, *m*/*z* (I_{rel}, %): 195 (14), 194 $[M]^+$ (100), 193 (25), 192 (7), 167 (6), 166 (8), 97 (11). Found, *m*/*z*: 195.0920 $[M+H]^+$. $C_{13}H_{11}N_2$. Calculated, *m*/*z*: 195.0917.

2-(4-*tert*-Butylphenyl)-1*H*-pyrrolo[3,2-*b*]pyridine (3b) was synthesized from pyridine **1a** (87 mg, 0.5 mmol) and 1-(*tert*-butyl)-4-ethynylbenzol (**2b**) (95 mg, 0.6 mmol), eluent for flash chromatography EtOAc–*n*-hexane, 3:2. Yield 106 mg (85%), beige solid, mp 290°C (decomp.). IR spectrum, ν, cm^{-1}: 3061 (w), 2965 (w), 2901 (w), 2868 (w), 1493 (m), 1443 (w), 1410 (m), 1354 (w), 1275 (m), 1267 (m), 1242 (w), 1059 (w), 928 (w), 835 (m), 777 (s). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.32 (9H, s, $C(CH_3)_3$); 6.98–6.99 (1H, m, H-3); 7.08 (1H, dd, *J* = 8.1, *J* = 4.6, H-7); 7.49–7.52 (2H, m, H Ar); 7.72 (1H, dd, *J* = 8.1, *J* = 1.0, H-6); 7.83–7.86 (2H, m, H Ar); 8.29 (1H, dd, *J* = 4.6, *J* = 1.4, H-5); 11.72 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 31.1 (CH_3); 34.5 (C); 98.6 (CH); 116.5 (CH); 118.1 (CH); 125.2 (CH); 125.8 (CH); 128.9 (C); 129.9 (C); 141.1 (C); 142.7 (CH); 147.0 (C); 151.0 (C). Mass spectrum, *m*/*z* (I_{rel}, %): 251 (14), 250 $[M]^+$ (65), 234 (5), 220 (10), 219 (9), 207 (17), 206 (11), 194 (6), 117 $[M–C_{10}H_{13}]^+$ (6), 103 (32), 91 (6). Found, *m*/*z*: 251.1545 $[M+H]^+$. $C_{17}H_{19}N_2$. Calculated, *m*/*z*: 251.1543.

2-Butyl-1*H*-pyrrolo[3,2-*b*]pyridine (3c) was synthesized from pyridine **1a** (87 mg, 0.5 mmol) and hex-1-yne (**2c**) (50 mg, 0.6 mmol), eluent for flash chromatography EtOAc–*n*-hexane, 3:2. Yield 64 mg (73%), beige solid, mp 121°C. IR spectrum, ν, cm^{-1}: 3121 (w), 3026 (w), 2957 (w), 2930 (w), 1566 (w), 1549 (w), 1414 (m), 1358 (w), 1277 (w), 953 (w), 907 (w), 835 (w), 814 (w), 779 (s). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.94 (3H, t, *J* = 7.3, CH_3); 1.38–1.45 (2H, m, CH_2); 1.69–1.76 (2H, m, CH_2); 2.79–2.84 (2H, t, *J* = 7.7, CH_2); 6.45 (1H, s, H-3); 7.04 (1H, dd, *J* = 8.1, *J* = 4.8, H-7); 7.60–7.63 (1H, m, H-6); 8.38 (1H, dd, *J* = 4.8, *J* = 1.3, H-5); 8.82 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 13.9 (CH_3); 22.5 (CH_2); 28.5 (CH_2); 31.2 (CH_2); 99.8 (CH); 115.7 (CH); 117.8 (CH); 129.4 (C); 142.1 (CH); 145.3 (C); 147.3 (C). Mass spectrum, *m*/*z* (I_{rel}, %): 175 (6), 174 $[M]^+$ (38), 145 $[M–C_2H_5]^+$ (9), 132 (66), 131 $[M–C_3H_7]^+$ (100), 104 (7), 77 (5), 39 (6). Found, *m*/*z*: 175.1231 $[M+H]^+$. $C_{11}H_{15}N_2$. Calculated, *m*/*z*: 175.1230.

2-Ethenyl-1*H*-pyrrolo[3,2-*b*]pyridine (3d) was synthesized from pyridine **1a** (87 mg, 0.5 mmol), but-3-yn-1-ol (**2d**) (43 mg, 0.6 mmol), and KO*t*-Bu (196 mg, 1.75 mmol, 3.5 equiv), eluent for flash chromatography EtOAc–*n*-hexane, gradient from 1:1 to 4:1. Yield 22 mg (31%), beige solid, mp 176°C. IR spectrum, ν, cm^{-1}: 3127 (w), 3077 (w), 3036 (w), 3011 (w), 2967 (w), 2901 (w), 2874 (w), 1613 (w), 1549 (w), 1493 (m), 1460 (w), 1447 (w), 1437 (w), 1416 (w), 1375 (w), 1358 (w), 1289 (w), 1271 (m), 1246 (m), 1209 (w), 1179 (m), 1109 (w), 1063 (w), 1028 (m), 924 (w), 912 (w), 831 (m), 824 (m), 775 (s). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 5.36 (1H, d, *J* = 11.2, =CH_2); 5.82 (1H, d, *J* = 17.7, =CH_2); 6.68 (1H, s, H-3); 6.79 (1H, dd, *J* = 17.7, *J* = 11.2, CH=); 7.07 (1H, dd, *J* = 8.1, *J* = 4.5, H-7); 7.62 (1H, d, *J* = 8.1, H-6); 8.42 (1H, d, *J* = 4.5, H-5); 10.32 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 102.6 (CH); 115.1 (CH_2); 117.3 (CH); 118.4 (CH); 127.6 (CH); 130.4 (C); 140.4 (C); 142.9 (CH); 146.7 (C). Mass spectrum, *m*/*z* (I_{rel}, %): 145 (11), 144 $[M]^+$ (100), 143 (27), 142 (6), 118 (20), 117 $[M–C_2H_3]^+$ (11), 116 (13), 90 (7), 89 (8). Found, *m*/*z*: 145.0761 $[M+H]^+$. $C_9H_9N_2$. Calculated, *m*/*z*: 145.0760.

2-(4-Methoxyphenyl)-1*H*-pyrrolo[3,2-b]pyridine (3e) was synthesized from pyridine **1a** (87 mg, 0.5 mmol) and 1-ethynyl-4-methoxybenzene (**2e**) (79 mg, 0.6 mmol), eluent for flash chromatography EtOAc–*n*-hexane, gradient from 1:1 to 4:1). Yield 89 mg (81%), gray solid, mp 242°C. IR spectrum, ν, cm^{-1}: 3069 (w), 3044 (w), 3021 (w), 2978 (w), 2911 (w), 1614 (w), 1566 (w), 1516 (w), 1493 (w), 1449 (w), 1414 (m), 1395 (w), 1343 (m), 1283 (w), 1263 (m), 1209 (w), 1194 (w), 1155 (w), 1115 (w), 1086 (w), 1038 (w), 986 (m), 963 (w), 912 (m), 839 (w), 820 (w), 801 (w), 783 (s). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.86 (3H, s, OCH_3); 6.90 (1H, s, H-3); 6.98–7.00 (2H, m, H Ar); 7.06–7.08 (1H, m, H-7); 7.65–7.66 (3H, m, H Ar, H-6); 8.43 (1H, d, *J* = 3.8, H-5); 8.78 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 55.5 (CH_3); 99.6 (CH); 114.7 (CH); 116.7 (CH); 117.8 (CH); 124.5 (C); 127.0 (CH); 130.0 (C); 141.8 (C); 143.5 (CH); 147.7 (C); 160.2 (C). Mass spectrum, *m*/*z* (I_{rel}, %): 278 (15), 277 (46), 225 (17), 224 $[M]^+$ (100), 210 (13), 209 $[M–CH_3]^+$ (86), 201 (5), 199 (10), 183 (7), 182 (6), 181 (38), 180 (5), 179 (8), 154 (8), 153 (8), 152 (8), 149 (9), 135 (7), 128 (7), 127 (13), 112 (8), 77 (8), 43 (6). Found, *m*/*z*: 225.1026 $[M+H]^+$. $C_{14}H_{13}N_2O$. Calculated, *m*/*z*: 225.1022.

2-Phenyl-1*H*-indole (3f)[46] was synthesized from 2-bromoaniline (**1b**) (172 mg, 1.00 mmol) and acetylene **2a** (122 mg, 1.20 mmol), eluent for flash chromatography EtOAc–*n*-hexane, 1:20. Yield 106 mg (55%), yellow solid, mp 187°C. IR spectrum, ν, cm^{-1}: 3443 (w), 3050 (w), 3024 (w), 2969 (w), 2957 (w), 2920 (w), 1595 (w), 1491 (w), 1481 (w), 1456 (w), 1447 (w), 1404 (w), 1368 (w), 1348 (w), 1339 (w), 1298 (w), 1260 (w), 1240 (w), 1231 (w), 1202 (w), 1188 (w), 1163 (w), 1123 (w), 1115 (w), 1074 (w), 1049 (w), 1028 (w), 990 (w), 968 (w), 932 (w), 907 (w), 880 (w), 855 (w), 824 (w), 797 (m), 762 (m), 743 (s), 689 (s). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 6.82 (1H, d, *J* = 1.3, H-3); 7.09–7.22 (2H, m, H Ph); 7.28–7.45 (4H, m, H indole, H Ph); 7.61–7.65 (3H, m, H indole, H Ph); 8.30 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 100.1 (CH); 111.0 (CH); 120.4 (CH); 120.8 (CH); 122.5 (CH); 125.3 (CH); 127.8 (CH); 129.2 (CH); 129.4 (C); 132.5 (C); 136.9 (C); 138.0 (C). Mass spectrum, *m*/*z* (I_{rel}, %): 194 (16), 193 $[M]^+$ (100), 192 (18), 191 (6), 166 (6), 165 (27), 164 (5), 97 (8), 96 (5), 90 (5), 89 (7), 97 (8), 96 (5), 90 (5), 89 (7).

2-(4-*tert*-Butylphenyl)-1*H*-indole (3g) was synthesized from aniline **1b** (172 mg, 1.00 mmol) and acetylene **2b** (189 mg, 1.20 mmol), eluent for flash chromatography EtOAc–*n*-hexane, 1:20. Yield 131 mg (53%), gray solid, mp 190°C. IR spectrum, ν, cm^{-1}: 3431 (w), 3051 (w),

3032 (w), 2955 (w), 2901 (w), 2866 (w), 1611 (w), 1497 (w), 1454 (w), 1425 (w), 1393 (w), 1352 (w), 1300 (w), 1269 (w), 1242 (w), 1231 (w), 1202 (w), 1186 (w), 1123 (w), 1111 (w), 1049 (w), 1022 (w), 1013 (w), 1005 (w), 963 (w), 924 (w), 887 (w), 835 (m), 789 (m), 739 (s). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.35 (9H, s, $C(CH_3)_3$); 6.78 (1H, d, *J* = 1.3, H-3); 7.08–7.20 (2H, m, H Ph); 7.37–7.39 (1H, d, *J* = 7.7, H indole); 7.43–7.47 (2H, m, H Ph); 7.57–7.63 (3H, m, H indole); 8.27 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 31.4 (CH_3); 34.8 (C); 99.6 (CH); 111.0 (CH); 120.3 (CH); 120.7 (CH); 122.2 (CH); 125.0 (CH); 126.1 (CH); 129.5 (C); 129.7 (C); 136.9 (C); 138.1 (C); 151.0 (C). Mass spectrum, *m*/*z* (I_{rel}, %): 250 (14), 249 $[M]^+$ (70), 235 (20), 234 $[M–CH_3]^+$ (100), 233 (6), 219 (16), 218 (8), 217 (8), 206 (18), 205 (7), 204 (9), 193 (9), 191 (5), 165 (5), 117 (7), 109 (5), 103 (28), 102 (11), 90 (5), 89 (5). Found, %: C 86.76; H 7.85; N 5.52. $C_{18}H_{19}N$. Calculated, %: C 86.70; H 7.68; N 5.62.

2-(Pyridin-2-yl)-1*H*-indole (3h)[47] was synthesized from aniline **1b** (172 mg, 1.00 mmol) and 2-ethynylpyridine (**2f**) (121 mg, 1.20 mmol), eluent for flash chromatography *n*-hexane. Yield 45 mg (23%), yellow solid, mp 190°C. IR spectrum, ν, cm^{-1}: 3202 (w), 3071 (w), 3053 (w), 3021 (w), 2974 (w), 2951 (w), 1597 (m), 1532 (w), 1545 (w), 1468 (w), 1443 (w), 1412 (w), 1368 (w), 1341 (w), 1304 (m), 1262 (w), 1227 (w), 1190 (w), 1144 (w), 1071 (w), 1047 (w), 999 (w), 936 (w), 808 (w), 777 (s), 748 (s), 735 (s). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.05 (1H, s, H-3); 7.13 (1H, td, *J* = 7.6, *J* = 2.3, H indole); 7.18 (1H, dd, *J* = 6.9, *J* = 5.3, H indole); 7.22 (1H, t, *J* = 7.6, H indole); 7.37–7.38 (1H, m, H indole); 7.68 (1H, dd, *J* = 7.8, *J* = 2.7, H pyridine); 7.72 (1H, td, *J* = 7.8, *J* = 1.6, H pyridine); 7.82–7.83 (1H, m, H pyridine); 8.59–8.60 (1H, m, H pyridine); 10.04 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 100.8 (CH); 111.6 (CH); 120.1 (CH); 120.2 (CH); 121.3 (CH); 122.1 (CH); 123.3 (CH); 129.2 (C); 136.8 (3C); 149.2 (CH); 150.6 (C). Mass spectrum, *m*/*z* (I_{rel}, %): 195 (15), 194 $[M]^+$ (100), 193 (42), 192 (11), 168 (6), 167 (12), 166 (11), 139 (5), 97 (7), 89 (7), 84 (6), 70 (7), 43 (22). Found, %: C 80.10; H 5.37; N 14.12. $C_{13}H_{10}N_2$. Calculated, %: C 80.39; H 5.19; N 14.42.

2-(4-Methoxyphenyl)-1*H*-indole (3i)[23] was synthesized from aniline **1b** (172 mg, 1.00 mmol) and acetylene **2e** (159 mg, 1.20 mmol), eluent for flash chromatography gradient from *n*-hexane to EtOAc–*n*-hexane, 1:9. Yield 101 mg (45%), beige solid, mp 226°C. IR spectrum, ν, cm^{-1}: 3429 (w), 3005 (w), 2965 (w), 2895 (w), 2837 (w), 1607 (w), 1541 (w), 1499 (m), 1485 (w), 1452 (w), 1431 (m), 1398 (w), 1350 (w), 1287 (w), 1242 (m), 1229 (m), 1180 (m), 1113 (w), 1049 (w), 1026 (m), 934 (w), 914 (w), 889 (w), 833 (m), 781 (s), 747 (s), 739 (s). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.80 (3H, s, OCH_3); 6.75–6.76 (1H, m, H-3); 6.95–7.09 (4H, m, H indole, H Ph); 7.36–7.39 (1H, m, H indole); 7.48–7.51 (1H, m, H indole); 7.77–7.82 (2H, m, H Ph); 11.40 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 55.2 (CH_3); 97.3 (CH); 111.1 (CH); 114.3 (CH); 119.2 (CH); 119.7 (CH); 121.0 (CH); 124.9 (C); 126.4 (CH); 128.8 (C); 136.9 (C); 137.8 (C); 158.8 (C). Mass spectrum, *m*/*z* (I_{rel}, %): 224 (17), 223 $[M]^+$ (100), 209 (16), 208 $[M–CH_3]^+$ (97), 181 (8), 180 (53), 179 (11), 178 (13), 153 (8), 152 (24), 151 (9), 127 (6), 112 (11), 95 (6), 77 (6).

2-Cyclopropyl-1*H*-indole (3j)[48] was synthesized from aniline **1b** (344 mg, 2.00 mmol) and cyclopropylacetylene (**2g**) (157 mg, 2.40 mmol), eluent for flash chromatography *n*-hexane. Yield 233 mg (74%), yellow solid, mp 57°C. IR spectrum, ν, cm^{-1}: 3396 (w), 3082 (w), 3046 (w), 3003 (w), 2696 (w), 2913 (w), 1915 (w), 1614 (w), 1580 (w), 1553 (w), 1456 (m), 1414 (w), 1393 (w), 1341 (m), 1308 (m), 1281 (w), 1236 (w), 1204 (w), 1152 (w), 1146 (w), 1094 (w), 1067 (w), 1049 (w), 1023 (m), 1013 (w), 970 (w), 928 (w), 899 (w), 878 (m), 783 (w), 774 (m), 745 (s), 737 (s). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.73–0.77 (2H, m, CH_2); 0.93–0.96 (2H, m, CH_2); 1.93 (1H, tt, *J* = 8.4, *J* = 5.1, CH); 6.14 (1H, m, H-3); 7.05–7.10 (2H, m, H indole); 7.23–7.24 (1H, m, H indole); 7.48–7.50 (1H, m, H indole); 7.90 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 7.4 (CH_2); 9.0 (CH); 97.8 (CH); 110.3 (CH); 119.8 (2CH); 121.1 (CH); 128.8 (C); 135.9 (C); 141.8 (C). Mass spectrum, *m*/*z* (I_{rel}, %): 158 (11), 157 $[M]^+$ (93), 156 (82), 155 (7), 154 (17), 131 (11), 130 (100), 129 $[M–C_2H_4]^+$ (30), 128 (30), 127 (10), 117 (5), 115 (6), 103 (7), 102 (6), 89 (6), 78 (5), 77 (12), 65 (5), 63 (5).

Supplementary information file containing ^{1}H and ^{13}C NMR spectra and 135-DEPT experiments of synthesized compounds is available at the journal website http://hgs.osi.lv

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