DOI 10.1007/s10593-016-1881-z

Chemistry of Heterocyclic Compounds **2016**, *52*(5), 299–302

An efficient synthesis of (3-indolyl)acetonitriles by reduction of hydroxamic acids

Alexander V. Aksenov[1]*, Nicolai A. Aksenov[1], Zarema V. Dzhandigova[1], Inna V. Aksenova[1], Leonid G. Voskressensky[2], Alexander N. Smirnov[1], Michael A. Rubin[1,3]*

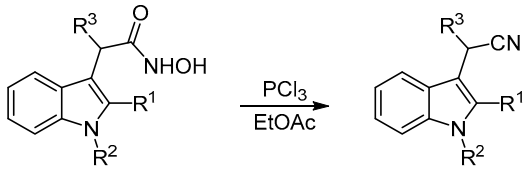
[1] *North-Caucasus Federal University, 1 Pushkina St., Stavropol 355009, Russia; e-mail: alexaks05@rambler.ru*

[2] *People's Friendship University of Russia, 6 Miklukho-Maklaya St., Moscow 117198, Russia; e-mail: lvoskressensky@sci.pfu.edu.ru*

[3] *University of Kansas, 1251 Wescoe Hall Drive, Lawrence, KS 66045-7582, USA; e-mail: mrubin@ku.edu*

Translated from Khimiya Geterotsiklicheskikh Soedinenii, 2016, *52*(5), 299–302

Submitted April 22, 2016
Accepted May 12, 2016

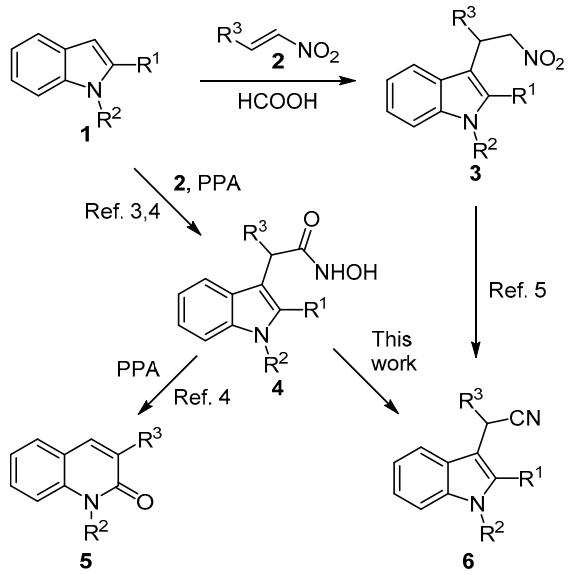


A new, highly efficient method was developed for the synthesis of (3-indolyl)acetonitriles by reduction of readily available (3-indolyl)hydroxamic acids with phosphorus trichloride. The nitriles obtained according to this method are of significant interest for structure-activity studies of potential anticancer agents.

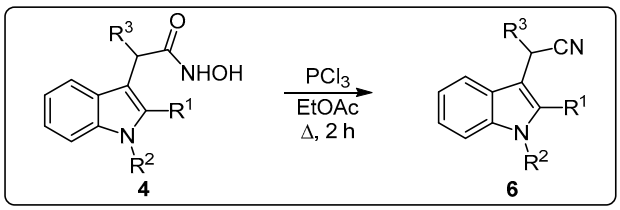
Keywords: hydroxamic acids, indoles, nitriles, reduction.

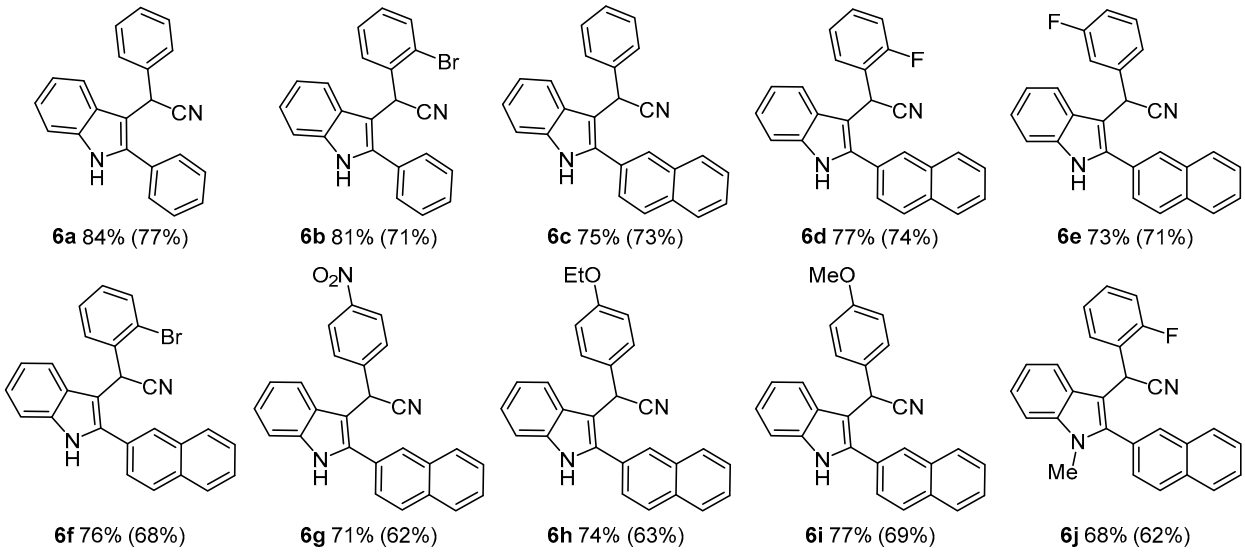
The structural motif of 3-cyanomethylindole, formed as a result of tryptophan metabolism, is quite frequently found in the molecules of natural alkaloids[1] that possess a wide range of useful biological properties.[2] It is not surprising that the development of synthetic approaches to similar structures is among the important tasks of contemporary medicinal chemistry. We have recently reported on unique anticancer activity of (3-indolyl)hydroxamic acids **4**.[3] These acids are formed as stable, isolable intermediates during the synthesis of 2-quinolones **5** according to an ANRORC reaction between indoles **1** and nitroolefins **2** that we previously investigated[4] (Scheme 1) and showed high degree of activity by suppressing the growth of glioma, melanoma, esophageal cancer, and other cancer cell lines stable against apoptosis and therefore resistant against traditional chemotherapy drugs.[3] Furthermore, we identified excellent anticancer activity in one structural analog of hydroxamic acids **4** that contained a nitrile group, compound **6** (R^1 = 2-naphthyl, R^2 = H, R^3 = Ph).[3] In our research program devoted to the discovery of new potential anticancer agents we needed quick access to small libraries of nitriles similar to compound **6** with readily customized structures. One possible method for such syntheses, based on reduction of nitroalkanes **3**, was reported by us in 2015.[5] In the current article we propose an alternative synthetic protocol, using direct reduction of hydroxamic acids **4** (Scheme 1).

Scheme 1



Scheme 2

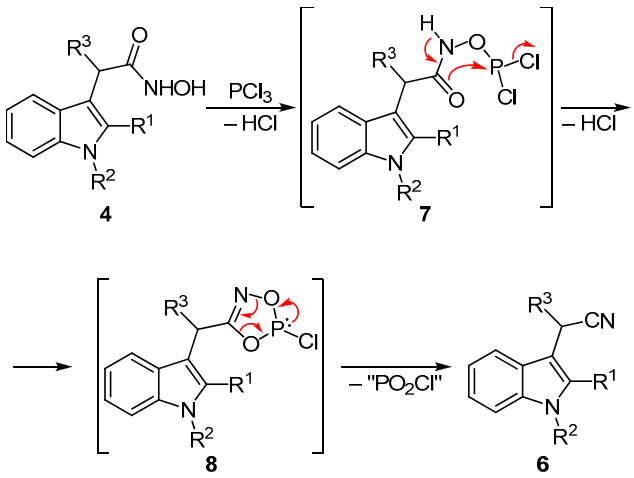




The transformation of hydroxycarbamoyl group to a nitrile is usually achieved employing phosphorus tribromide[6] or thionyl chloride[7] under reflux in nonpolar, aprotic solvents. However, in our case, the reaction under these conditions resulted in substantial resinification of the sensitive indole system. Moreover, partial hydrolysis of the moisture sensitive reagents led to accumulation of strong acids in the reaction mixture, catalyzing the rearrangement of indole to 2-quinolone[4] and substantially decreasing the efficiency of obtaining the desired nitriles. During reaction optimization, we found that these side reactions can be suppressed by using phosphorus trichloride instead of tribromide. Good yields of nitriles were obtained in reactions carried out in refluxing benzene or ethyl acetate, the latter of which was found to be more suitable because it better dissolved the starting hydroxamic acids. Typical reaction results and the obtained preparative yields of purified products are shown in Scheme 2. The yields of nitriles obtained by reducing nitroalkanes **3** according to the procedure[5] published by us in 2015 are indicated in parentheses for comparison (Scheme 1). Clearly, the new synthetic procedure enables preparation of all the studied compounds in better yields. It is also quite apparent that the formation of least sterically hindered nitriles **6a**,**b** with a phenyl substituent at the C-2 atom of the indole ring occurs most readily when the new synthetic procedure is used. Nevertheless, the majority of examples were obtained for indoles with unsubstituted nitrogen atom and 2-naphthyl substituent at the C-2 atom (compounds **6c**–**i**), because this type of molecules presents the greatest interest for investigation of biological activity. Additionally, *N*-methyl-substituted indole **6j** can be obtained as well, although in a somewhat lower yield (Scheme 2).

The likely reaction mechanism is presented in Scheme 3. We assume that heating the hydroxamic acid **4** in the presence of phosphorus trichloride first led to phosphorylation of the hydroxy group, accompanied by cyclocondensation of the intermediate *N*-[(dichlorophosphanyl)oxy]amide **7** to *P*-chlorodioxoazaphosphole **8**. The subsequent elimination of metaphosphoryl chloride resulted in the formation of nitrile **6** (Scheme 3).

Scheme 3



Thus, we have developed a convenient preparative method for obtaining 2-aryl-2-(indol-3-yl)-substituted acetonitriles by direct reduction of readily available hydroxamic acids with phosphorus trichloride. This

method does not rely on heavy metals and is appropriate for the synthesis of small libraries of compounds for biomedical studies, such as those performed at our laboratories for structure optimization of potential anticancer agents.

Experimental

IR spectra were recorded on a Shimadzu IRTracer-100 instrument in NaCl. ^{1}H and ^{13}C NMR spectra were acquired on a Bruker Avance III spectrometer (400 and 100 MHz, respectively) with TMS as internal standard. High-resolution mass spectra were recorded for MeCN/H_2O solutions on a Bruker maXis Impact quadrupole TOF mass spectrometer coupled to HPLC, calibration with HCO_2Na/HCO_2H, electrospray ionization. Melting points were determined on a Stuart SMP30 apparatus. The reaction progress and purity of the obtained compounds were controlled by TLC on Silufol UV-254 plates, with hexane–EtOAc eluent in the indicated proportions. Synthesis of the starting hydroxamic acids **4** was described in our previous work.[3]

Preparation of (2-aryl)-2-(2-aryl-1*H*-indol-3-yl)acetonitriles 6a–j (General method). Phosphorus trichloride (131 μl, 206 mg, 1.50 mmol) was added to a solution of hydroxamic acid **4** (1.0 mmol) in ethyl acetate and the obtained mixture was refluxed for 2 h. The mixture was then cooled and poured into water (50 ml), neutralized with aqueous ammonia, and extracted with benzene (3×10 ml). The combined extracts were concentrated under vacuum, and the dry residue was purified by chromatography on silica gel.

2-Phenyl-2-(2-phenyl-1*H*-indol-3-yl)acetonitrile (6a).[5] Yield 258 mg (84%), white amorphous material, R_f 0.46 (4:1 hexane–EtOAc). IR spectrum, ν, cm^{-1}: 3338, 3070, 3029, 2376, 2349, 1691, 1659, 1498, 1449, 1207, 1072. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 8.28 (1H, s, NH); 7.42–7.31 (9H, m, H Ar); 7.28–7.20 (3H, m, H Ar); 7.16–7.12 (1H, m, H Ar); 7.03–6.98 (1H, m, H Ar); 5.52 (1H, s, CH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 137.0; 136.1; 135.5; 131.6; 129.4 (2C); 129.1 (2C); 128.6 (2C); 128.0; 127.3 (2C); 126.8; 123.2; 120.8; 120.0; 119.7; 111.3; 106.1; 77.2; 33.5. Found, *m*/*z*: 331.1207 [M+Na]$^+$. $C_{22}H_{16}N_2Na$. Calculated, *m*/*z*: 331.1206.

2-(2-Bromophenyl)-2-(2-phenyl-1*H*-indol-3-yl)acetonitrile (6b). Yield 314 mg (81%), colorless crystals, R_f 0.30 (1:1 hexane–EtOAc), mp 148–149°C (benzene) (mp 148–149°C)[5]. IR spectrum, ν, cm^{-1}: 3347, 2363, 2332, 2249, 1458, 1435, 1026, 907, 764, 743. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 8.39 (1H, s, NH); 7.75 (1H, d, *J* = 7.9, H Ar); 7.65 (1H, dd, *J* = 7.8, *J* = 1.6, H Ar); 7.60 (1H, dd, *J* = 7.9, *J* = 1.3, H Ar); 7.50–7.40 (4H, m, H Ar); 7.37–7.34 (2H, m, H Ar); 7.32–7.25 (2H, m, H Ar); 7.23–7.16 (2H, m, H Ar); 5.72 (1H, s, CH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm 137.2; 135.9; 134.9; 133.6; 131.5; 130.0; 129.9; 129.2 (2C); 128.9; 128.3 (2C); 128.0; 127.3; 123.7; 123.0; 120.9; 119.7; 118.7; 111.4; 104.6; 34.5. Found, *m*/*z*: 409.0319 [M+Na]$^+$. $C_{22}H_{15}BrN_2Na$. Calculated, *m*/*z*: 409.0311.

2-[2-(Naphth-2-yl)-1*H*-indol-3-yl]-2-phenylacetonitrile (6c). Yield 304 mg (75%), colorless crystals, mp 146–147°C (benzene) (mp 146–147°C)[5]. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 11.85 (1H, s, NH); 8.11–8.04 (2H, m, H Ar); 8.02–7.92 (2H, m, H Ar); 7.70 (1H, dd, *J* = 8.5, *J* = 1.8, H Ar); 7.62–7.55 (2H, m, H); 7.47 (2H, d, *J* = 8.1, H Ar); 7.42–7.36 (4H, m, H Ar); 7.36–7.28 (1H, m, H Ar); 7.19 (1H, ddd, *J* = 8.2, *J* = 7.1, *J* = 1.1, H Ar); 7.05 (1H, ddd, *J* = 8.0, *J* = .1, *J* = 0.9, H Ar); 6.08 (1H, s, CH).

2-(2-Fluorophenyl)-2-[2-(naphthalen-2-yl)-1*H*-indol-3-yl]-acetonitrile (6d). Yield 289 mg (77%), colorless crystals, mp 186–187°C (benzene) (mp 186–187°C)[5], R_f 0.47 (1:1 hexane–EtOAc). IR spectrum, ν, cm^{-1}: 3451, 2357, 2332, 1485, 1454, 1219, 860, 827, 762, 743. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 8.40 (1H, s, NH); 7.82–7.68 (4H, m, H Ar); 7.64 (1H, d, *J* = 8.0, H Ar); 7.49–7.38 (4H, m, H Ar); 7.31 (1H, d, *J* = 8.1, H Ar); 7.22–7.12 (2H, m, H Ar); 7.06 (1H, t, *J* = 7.3, H Ar); 7.02–6.90 (2H, m, H Ar); 5.70 (1H, s, CH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 171.2; 160.2 (d, $^1J_{CF}$ = 249.3); 136.9; 136.1; 133.3 (d, *J* = 15.2); 130.3; 130.2; 129.4 (d, *J* = 8.2); 129.1 (d, *J* = 2.7); 128.8; 128.3; 128.0 (d, *J* = 3.3); 127.1; 127.0; 126.1; 125.8; 124.6 (d, *J* = 3.7); 123.1; 120.9; 119.7; 118.8; 116.1; 115.9; 111.5; 104.8; 28.2. Found, *m*/*z*: 399.1276 [M+Na]$^+$. $C_{26}H_{17}FN_2Na$. Calculated, *m*/*z*: 399.1268.

2-(3-Fluorophenyl)-2-[2-(naphthalen-2-yl)-1*H*-indol-3-yl]-acetonitrile (6e). Yield 274 mg (73%), colorless crystals, R_f 0.33 (1:1 hexane–EtOAc), mp 92–93°C (benzene) (mp 92–93°C)[5]. IR spectrum, ν, cm^{-1}: 3451, 2357, 2332, 1485, 1454, 1219, 860, 827, 762, 743. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 8.43 (1H, s, NH); 8.00–7.94 (2H, m, H Ar); 7.93–7.85 (2H, m, H Ar); 7.62–7.54 (3H, m, H Ar); 7.48 (2H, dd, *J* = 12.3, *J* = 8.1, H Ar); 7.42 (1H, d, *J* = 1.1, H Ar); 7.38–7.33 (1H, m, H Ar); 7.31–7.26 (3H, m, H Ar); 7.18–7.12 (1H, m, H Ar); 5.65 (1H, s, CH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 160.1 (d, *J* = 247.3); 137.6; 137.2; 136.3; 135.1; 133.4 (d, *J* = 10.8); 130.3; 129.5; 128.6; 128.4; 128.3; 128.1; 128.0; 127.5; 127.3; 126.6; 125.7; 125.5; 123.5; 121.1; 119.8; 119.1; 111.5; 105.9; 77.2; 33.3. Found, *m*/*z*: 399.1276 [M+Na]$^+$. $C_{26}H_{17}FN_2Na$. Calculated, *m*/*z*: 399.1268.

2-(2-Bromophenyl)-2-[2-(naphthalen-2-yl)-1*H*-indol-3-yl]acetonitrile (6f). Yield 336 mg (77%), colorless crystals, R_f 0.27 (1:1 hexane–EtOAc), mp 205–206°C (benzene) (mp 205–206°C)[5]. IR spectrum, ν, cm^{-1}: 3345, 2361, 1497, 1350, 1026, 957, 897, 814, 756, 736, 708. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 8.37 (1H, s); 7.86 (1H, d, *J* = 8.5); 7.84–7.78 (1H, m, H Ar); 7.76–7.72 (2H, m, H Ar); 7.69 (1H, s); 7.63 (1H, dd, *J* = 7.8, *J* = 1.5); 7.55 (1H, dd, *J* = 7.9, *J* = 1.2); 7.50–7.45 (2H, m, H Ar); 7.43–7.38 (2H, m, H Ar); 7.25–7.20 (2H, m, H Ar); 7.16–7.11 (2H, m, H Ar); 5.76 (1H, s, CH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 137.1; 136.0; 135.1; 133.6; 133.3; 133.1; 130.1; 130.0; 129.2; 128.7; 128.3; 128.0; 127.9; 127.7; 127.4; 127.0 (2C); 125.3; 123.7; 123.1; 121.0; 119.8; 118.6; 111.3; 105.1; 34.6. Found, *m*/*z*: 459.0469 [M+Na]$^+$. $C_{26}H_{17}BrN_2Na$. Calculated, *m*/*z*: 459.0467.

2-[2-(Naphthalen-2-yl)-1*H*-indol-3-yl]-2-(4-nitrophenyl)-acetonitrile (6g). Yield 286 mg (71%), light-brown crystals, mp 98–99°C (benzene) (mp 98–99°C)[5], R_f 0.26 (1:1 hexane–EtOAc). IR spectrum, ν, cm^{-1}: 3383, 2920,

2853, 1599, 1518, 1454, 1342, 1242, 1109, 1015, 905, 854, 822, 743, 727, 708. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 8.43 (1H, s, NH); 8.07–8.02 (2H, m, H Ar); 7.89–7.83 (2H, m, H Ar); 7.83–7.74 (2H, m, H Ar); 7.50–7.44 (5H, m, H Ar); 7.37 (1H, d, *J* = 8.2, H Ar); 7.30 (1H, d, *J* = 8.0, H Ar); 7.20 (1H, s); 7.03 (1H, t, *J* = 7.5, H Ar); 5.63 (1H, s, CH). ^{13}C NMR spectrum (100 MHz, $CDCl_3$), δ, ppm: 147.7; 142.7; 137.5; 136.3; 133.4; 133.4; 129.6; 128.3 (3C); 128.1 (2C); 127.4 (2C); 126.3; 125.6; 124.3 (2C); 123.7; 121.3; 119.4; 118.6; 111.7; 105.3; 33.6; 29.8. Found, *m*/*z*: 426.1211 $[M+Na]^+$. $C_{26}H_{17}N_3NaO_2$. Calculated, *m*/*z*: 426.1213.

2-(4-Ethoxyphenyl)-2-[2-(naphthalen-2-yl)-1*H*-indol-3-yl]acetonitrile (6h). Yield 297 mg (74%), light-gray crystals, mp 149–150°C (benzene), R_f 0.28 (1:1 hexane–EtOAc). IR spectrum, ν, cm^{-1}: 3335, 2922, 2237, 1740, 1607, 1508, 1445, 1389, 1346, 1302, 1254, 1236, 1177, 1113, 1043, 957, 903, 816, 758, 739, 704. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 8.43 (1H, s, NH); 7.98–7.80 (4H, m, H Ar); 7.62–7.51 (4H, m, H Ar); 7.44 (1H, d, *J* = 8.1, H Ar); 7.35 (2H, t, *J* = 8.9, H Ar); 7.30–7.21 (1H, m, H Ar); 7.13 (1H, t, *J* = 7.5, H Ar); 6.85 (2H, d, *J* = 8.7, H Ar); 5.63 (1H, s, CH); 4.00 (2H, d, *J* = 7.0, CH_2); 1.40 (3H, t, *J* = 7.0, CH_3). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 158.7; 136.8; 136.3; 133.4; 133.2; 129.3; 128.9; 128.5; 128.3 (2C); 128.0; 127.9; 127.4; 127.1 (2C); 126.9; 125.8; 123.2; 120.9; 120.1; 120.0; 115.0 (2C); 111.3; 106.9; 63.6; 32.9; 14.9. Found, *m*/*z*: 425.1631 $[M+Na]^+$. $C_{28}H_{22}N_2NaO$. Calculated, *m*/*z*: 425.1624.

2-(4-Methoxyphenyl)-2-[2-(naphthalen-2-yl)-1*H*-indol-3-yl]-acetonitrile (6i). Yield 298 mg (77%), light-brown crystals, mp 198–199°C (benzene), R_f 0.24 (1:1 hexane–EtOAc). IR spectrum, ν, cm^{-1}: 3345, 2363, 1508, 1439, 1248, 1179, 1024, 826, 741. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 8.41 (1H, s, NH); 7.96 (2H, d, *J* = 8.9, H Ar); 7.93–7.82 (2H, m, H Ar); 7.60 (1H, dd, *J* = 8.4, *J* = 1.8, H Ar); 7.58–7.51 (3H, m, H Ar); 7.45 (1H, d, *J* = 8.1, H Ar); 7.35 (2H, d, *J* = 8.6, H Ar); 7.29–7.23 (1H, m, H Ar); 7.16–7.10 (1H, m, H Ar); 6.90–6.83 (2H, m, H Ar); 5.63 (1H, s, CH); 3.79 (3H, s, CH_3). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 159.3; 136.8; 136.3; 133.5; 133.3; 129.3; 128.9; 128.5 (2C); 128.3; 128.0; 127.9; 127.6; 127.2; 127.1; 126.9; 125.8; 123.3; 120.9; 120.1; 120.0; 114.5 (2C); 111.3; 106.9; 55.5; 32.9. Found, *m*/*z*: 411.1476 $[M+Na]^+$. $C_{27}H_{20}N_2NaO$. Calculated, *m*/*z*: 411.1468.

2-(2-Fluorophenyl)-2-[1-methyl-2-(naphthalen-2-yl)-1*H*-indol-3-yl]acetonitrile (6j). Yield 265 mg (68%), colorless crystals, mp 65–66°C (benzene), R_f 0.47 (benzene). IR spectrum, ν, cm^{-1}: 2920, 2851, 1742, 1478, 1456, 1364, 1231, 907, 862, 824, 814, 739. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 7.92–7.79 (4H, m, H Ar); 7.71 (1H, d, *J* = 8.0, H Ar); 7.62–7.54 (3H, m, H Ar); 7.45–7.39 (2H, m, H Ar); 7.32 (1H, dd, *J* = 11.2, *J* = 4.1, H Ar); 7.25 (1H, ddd, *J* = 8.7, *J* = 7.5, *J* = 1.7, H Ar); 7.19 (1H, dd, *J* = 11.1, *J* = 4.0, H Ar); 7.09 (1H, dt, *J* = 7.6, *J* = 0.8, H Ar); 6.97 (1H, dd, *J* = 9.8, *J* = 8.8, H Ar); 5.53 (1H, s, CH), 3.64 (3H, s, CH_3). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 160.1 (d, *J* = 249.4); 139.6; 137.4; 133.3 (d, *J* = 21.0); 130.4; 130.1; 129.4; 128.7; 128.4; 128.0; 127.8; 127.7; 127.3; 125.9; 124.4 (d, *J* = 3.6); 123.5; 123.4; 122.6; 120.6; 119.5; 119.0; 116.1; 115.8; 110.0; 105.5; 31.2; 29.9. Found, *m*/*z*: 391.1612 $[M+H]^+$. $C_{27}H_{20}FN_2$. Calculated, *m*/*z*: 391.1605.

This study was performed with financial support from the Russian Science Foundation (grant No. 14-13-01108).

References

1. (a) Yang, L.; Wang, G.; Wang, M.; Jiang, H.; Chen, L.; Zhao, F.; Qiu, F. *Fitoterapia* **2014**, *95*, 175. (b) Zhang, J.; Wang, J.-D.; Liu, C.-X.; Yuan, J.-H.; Wang, X.-J.; Xiang, W.-S. *Nat. Prod. Res.* **2014**, *28*, 431. (c) Pedras, M. S. C.; Yaya, E. E. *Chem. Biodiversity* **2014**, *11*, 910. (d) Chen, M.; Gan, L.; Lin, S.; Wang, X.; Li, L.; Li, Y.; Zhu, C.; Wang, Y.; Jiang, B.; Jiang, J.; Yang, Y.; Shi, J. *J. Nat. Prod.* **2012**, *75*, 1167. (e) Wu, Q.; Bang, M.-H.; Lee, D.-Y.; Cho, J.-G.; Jeong, R.-H.; Shrestha, S.; Lee, K.-T.; Chung, H.-G.; Ahn, E.-M.; Baek, N.-I. *Chem. Nat. Comp.* **2012**, *48*, 281. [*Khim. Prirod. Soedin.* **2012**, 251.]
2. (a) Cho, E.-J.; Shin, J.-S.; Chung, K.-S.; Lee, Y. S.; Cho, Y.-W.; Baek, N.-I.; Chung, H.-G.; Lee, K.-T. *J. Agric. Food Chem*. **2012**, *60*,7398. (b) Wu, Y.; Zhang, Z.-X.; Hu, H.; Li, D.; Qiu, G.; Hu, X.; He, X. *Fitoterapia* **2011**, *82*, 288.
3. Aksenov, A. V.; Smirnov, A. N.; Magedov, I. V.; Reisenauer, M. R.; Aksenov, N. A.; Aksenova, I. V.; Pendleton, A. L.; Nguyen, G.; Johnston, R. K.; Rubin, M.; De Carvalho, A.; Kiss, R.; Mathieu, V.; Lefranc, F.; Correa, J.; Cavazos, D. A.; Brenner,. J.; Bryan, B. A.; Rogelj, S.; Kornienko, A.; Frolova, L. V. *J. Med. Chem*. **2015**, *58*, 2206.
4. (a) Aksenov, A. V.; Smirnov, A. N.; Aksenov, N. A.; Aksenova, I. V.; Frolova, L. V.; Kornienko, A.; Magedov, I. V.; Rubin, M. *Chem. Commun.* **2013**, *49*, 9305. (b) Aksenov, A. V.; Smirnov, A. N.; Aksenov, N. A.; Aksenova, I. V.; Bijieva, A. S.; Rubin, M. *Org. Biomol. Chem.* **2014**, *12*, 9786. (c) Aksenov, A. V.; Smirnov, A. N.; Aksenov, N. A.; Aksenova, I. V.; Matheny, J. P.; Rubin, M. *RSC Adv.* **2015**, *5*, 8647.
5. Aksenov, A. V.; Aksenov, N. A.; Dzhandigova, Z. V.; Aksenov, D. A.; Rubin, M. *RSC Adv.* **2015**, *5*, 106492.
6. (a) Liguori, A.; Sindona, G.; Romeo, G.; Uccella, N. *Synthesis* **1987**, 168. (b) Ashworth, I. W.; Bowden, M. C.; Dembofsky, B.; Levin, D.; Moss, W.; Robinson, E.; Szczur, N.; Virica, J. *Org. Proc. Res. Dev.* **2003**, *7*, 74.
7. (a) Middleton, W. J. *J. Org. Chem.* **1983**, *48*, 3845. (b Thompson, H. W.; Rashid, S. Y. *J. Org. Chem*. **2002**, *67*, 2813. (c) Reiner, J. E.; Siev, D. V.; Araldi, G.-L.; Cui, J. J.; Ho, J. Z.; Reddy, K. M.; Mamedova, L.; Vu, P. H.; Lee, K.-S. S.; Minami, N. K.; Gibson, T. S.; Anderson, S. M.; Bradbury, A. E.; Nolan, T. G.; Semple, J. E. *Bioorg. Med. Chem. Lett*. **2002**, *12*, 1203.