**Electronic supplementary materials** *Mendeleev Commun.*, 2019, **29**, 53–54

# 1,2,5-Oxadiazolo[3,4-*g*]indoles *via* annelation of 6,7-dihydrobenzo[*c*][1,2,5]-oxadiazol-4(5*H*)-one oxime with acetylene

**Arsalan B. Budaev, Andrei V. Ivanov, Aleksei Ya. Tikhonov, Olga V. Petrova, Vladimir A. Samsonov, Igor A. Ushakov, Luybov N. Sobenina and Boris A. Trofimov**

**General Information.** NMR spectra ($^1$H, 400.1 MHz; $^{13}$C, 100.6 MHz; $^{15}$N, 40.55 MHz) were recorded on a “Bruker Avance 400” instrument in $CDCl_3$. The assignment of signals in the $^1$H NMR spectra was made using COSY and NOESY experiments. Resonance signals of carbon atoms were assigned based on $^1$H-$^{13}$C HSQC and $^1$H-$^{13}$C HMBC experiments. The values of the δ $^{15}$N were measured through the 2D NMR $^1$H-$^{15}$N HMBC experiment. The chemical shifts (δ) were referenced to residual deuterated solvent 7.27 ppm ($^1$H) and 77.1 ppm ($^{13}$C) for $CDCl_3$. Coupling constants in hertz (Hz) were measured from onedimensional spectra and multiplicities were abbreviated as following: br (broad), s (singlet), d (doublet), dd (doublet of doublets), t (triplet), m (multiple). The chemical shifts were recorded in ppm, coupling constants (J) in Hz.

IR spectra were obtained on a “Bruker IFS-25” spectrometer (400-4000 cm$^{-1}$, KBr pellets). The (C, H, N) microanalyses were performed on a “Flash EA 1112 CHNS-O/MAS” (CHN Analyzer) instrument. Melting points (uncorrected) were determined with melting point SMP3 (Stuart Scientific).

Column chromatography was conducted on neutral $Al_2O_3$.

*5,8-Dihydro-4H-[1,2,5]oxadiazolo[3,4-g]indole* **2**. A mixture of oxime **1** (4.59 g, 30 mmol), $KOH\cdot 0.5H_2O$ (1.95 g, 30 mmol), DMSO (150 ml) and water (60 ml) was placed in a 1000 ml steel autoclave. The mixture was saturated with acetylene (initial pressure 15 atm) and heated (110 °C) under stirring for 4 h. After cooling to room temperature, the reaction mixture was diluted with saturated solution of NaCl (250 ml), the $NH_4Cl$ was added (2.00 g, 37 mmol) and filtered solution was extracted with chloroform (8x50 ml), the combined extracts were washed with water (5x50 ml) and dried over $CaCl_2$. After removing of the solvent the residue was dissolved in chloroform (15 ml) and the solution was washed with 20% aqueous solution of KOH (for elimination of unreacted oxime **1**, 5x10 ml), washed with water (2x20 ml) and dried over $CaCl_2$. The crystallization from *n*-hexane of the residue, after removing of the solvent, gave indole **2** (1.40 g, 29%) as light-yellow crystals, mp 90-92 $^{o}$C. IR (KBr, ν/cm$^{-1}$): 3268, 2925, 2858, 1717, 1628, 1560, 1526, 1489, 1412, 1359, 1308, 1254, 1213, 1105, 1071, 1035, 986, 904, 850, 756, 698, 649, 690, 514, 441. $^1$H NMR (400 MHz, $CDCl_3$) δ: 9.51 (br s, 1H, NH), 7.04 (dd, *J* 2.5, 2.8 Hz, 1H, H-7), 6.22 (dd, *J* 2.2, 2.8 Hz, 1H, H-6), 3.16 (t, *J* 7.4 Hz, 2H, $CH_2$-5), 3.00 (t, *J* 7.4 Hz, 2H, $CH_2$-4). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 152.7 (C-3a), 144.7 (C-8b), 126.6 (C-7), 123.4 (C-8a), 115.5 (C-5a), 108.9 (C-6), 21.1 (C-5), 19.6 (C-4). Found (%): C, 59.66; H, 4.07; N, 25.81. Calc. for $C_8H_7N_3O$ (%): C, 59.62; H, 4.38; N, 26.07.

*8-Vinyl-5,8-dihydro-4H-[1,2,5]oxadiazolo[3,4-g]indole* **3**. A mixture of oxime **1** (4.59 g, 30 mmol), $KOH\cdot 0.5H_2O$ (1.95 g, 30 mmol), DMSO (150 ml) and water (30 ml) was placed in a 1000 ml steel autoclave. The mixture was saturated with acetylene (initial pressure 15 atm) and heated (110 °C) under stirring for 5 h. After cooling to room temperature, the reaction mixture was diluted with saturated solution of NaCl (250 ml), $NH_4Cl$ (2.00 g, 37 mmol) was added, the precipitate was filtered off, washed with water (170 ml) and dried. The precipitate was then dissolved in chloroform (200 ml), and the solution was filtered. Indole **3** (3.65 g, 65%) was isolated by column chromatography ($Al_2O_3$, eluent – *n*-hexane, gradient *n*-hexane/diethyl ether from 2:1 to 0:1).

The water layer was extracted with chloroform (8x50 ml), the combined extracts were washed with water (5x50 m) and dried over $CaCl_2$. Subsequent column chromatography ($Al_2O_3$, eluent – *n*-hexane/diethyl ether, gradient 1:0-0:1, then ethanol/diethyl ether 1:5, 1:1, 1:0) afforded indole **2** (0.30 g, 6%), vinylindole **3** (0.17 g, 3%) and recovered oxime **1** (0.15 g, conversion 97%). The total yield of product **3** was 68%. Yellow crystals, mp 57-59 ºC (*n*-hexane). IR (KBr, ν/cm$^{-1}$): 3134, 2919, 2851, 1646, 1614, 1551, 1529, 1480, 1446, 1412, 1376, 1292, 1227, 1162, 1080, 975, 910, 854, 736. $^1$H NMR (400 MHz, $CDCl_3$) δ: 7.56 (dd, *J* 8.8, 15.6 Hz, 1H, $H_X$), 7.25 (d, *J* 2.8 Hz, 1H, H-7), 6.23 (d, *J* 2.8 Hz, 1H, H-6), 5.28 (d, *J* 15.6 Hz, 1H, $H_B$), 4.86 (d, *J* 8.8 Hz, 1H, $H_A$), 3.13 (t, *J* 7.2 Hz, 2H, $CH_2$-5), 2.96 (t, *J* 7.2 Hz, 2H, $CH_2$-4). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 152.5 (C-3a), 144.8 (C-8b), 131.5 (Cα), 127.2 (C-5a), 121.3 (C-7), 117.4 (C-8a), 110.4 (C-6), 99.6 (Cβ), 21.2 (C-5), 19.7 (C-4). Found (%): C, 63.98; H, 4.82; N, 22.44. Calc. for $C_{10}H_9N_3O$ (%): C, 64.16; H, 4.85; N, 22.45.

*8H-[1,2,5]Oxadiazolo[3,4-g]indole* **4**. To a solution of dihydroindole **2** (0.100 g, 0.62 mmol) in benzene (15 ml), DDQ (0.282 g, 1.24 mmol) was added and the mixture was kept at room temperature for 7 days. The obtained precipitate was filtered off and washed with benzene (2 mL). The filtrate was concentrated and subjected to column chromatography ($Al_2O_3$, eluent – chloroform) to afford product **4** (0.085 g, 86%) as yellow crystals, mp 142 °C (*n*-hexane). IR (KBr, ν/cm$^{-1}$): 3274, 3030, 2927, 2849, 1635, 1558, 1531, 1522, 1448, 1425, 1395, 1381, 1299, 1205, 1251, 1205, 1098, 1073, 994, 900, 883, 842, 789, 779, 737, 705, 677. $^1$H NMR (400 MHz, $CDCl_3$) δ: 9.76 (br s, 1H, NH), 7.68 (d, *J* 9.3 Hz, 1H, H-5), 7.42 (d, *J* 9.3 Hz, 1H, H-4), 7.34 (dd, *J* 2.6, 2.8 Hz, 1H, H-7), 6.69 (dd, *J* 2.3, 2.8 Hz, 1H, H-6). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 149.4 (C-3a), 141.0 (C-8b), 129.2 (C-7), 126.2 (C-5), 124.5 (C-8a), 117.1 (C-5a), 107.7 (C-6), 106.8 (C-4). Found (%): C, 60.01; H, 3.05; N, 26.12. Calc. for $C_8H_5N_3O$ (%): C, 60.38; H, 3.17; N, 26.40.

*8-Vinyl-8H-[1,2,5]oxadiazolo[3,4-g]indole* **5**. To a solution of dihydroindole **3** (0.200 g, 1.10 mmol) in benzene (30 ml), a solution of DDQ (0.243 g, 1.10 mmol) in benzene (10 ml) was added and the mixture was stirred at room temperature for 20 min. The solvent was then removed under reduced pressure at 50 °C. The residue was kept at room temperature for 24 h and passed through a layer of $Al_2O_3$ (2-3 cm, eluent – $CH_2Cl_2$) to afford product **5** (0.110 g, 55%) as light-yellow crystals, mp 87 °C (*n*-hexane). IR (KBr, ν/cm$^1$): 3138, 2953, 2852, 1646, 1621, 1553, 1526, 1461, 1379, 1360, 1311, 1239, 1205, 1084, 1058, 1033, 984, 965, 872, 795, 727, 695, 656. $^1$H NMR (400 MHz, $CDCl_3$) δ: 7.94 (dd, *J* 8.9, 15.8 Hz, 1H, $H_X$), 7.64 (d, *J* 9.3 Hz, 1H, H-5), 7.57 (d, *J* 3.2 Hz, 1H, H-7), 7.43 (d, *J* 9.3 Hz, 1H, H-4), 6.72 (d, *J* 3.2 Hz, 1H, H-6), 5.50 (d, *J* 15.8 Hz, 1H, $H_B$), 5.07 (d, *J* 8.9 Hz, 1H, $H_A$). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 149.7 (C-3a), 141.4 (C-8b), 131.6 (Cα), 128.9 (C-5), 126.5 (C-5a), 122.6 (C-7), 118.2 (C-8a), 108.5 (C-6), 108.3 (C-4), 101.1 (C-β). Found (%): C, 64.91; H, 3.89; N, 22.81. Calc. for $C_{10}H_7N_3O$ (%): C, 64.86; H, 3.81; N, 22.69.

*Reaction of oxime **1** and acetylene at atmospheric pressure*

A mixture of oxime **1** (1.531 g, 10 mmol) and $KOH \cdot 0.5H_2O$ (0.651 g, 10 mmol) in DMSO (25 ml) was heated to 140 °C, and acetylene was passed under stirring for 13 h. After cooling to room temperature, the reaction mixture was diluted with saturated solution of NaCl (130 ml), and $NH_4Cl$ (0.64 g, 12 mmol) was added. The obtained precipitate was filtered off, washed with water (160 ml) and dried. The precipitate was dissolved in chloroform (300 ml) and the solution was filtered. Column chromatography of the concentrate ($Al_2O_3$, eluent – *n*-hexane, *n*-hexane/diethyl ether gradient 2:1-1:2) afforded compound **3** (0.046 g, 2.5%), compound **4** (0.020 g, 1.3%), indole **5** (0.204 g, 11%) and amine **6** (0.003 g, 0.3%).

The water layer was extracted with chloroform (8x40 ml), the combined extracts were washed with water (5x40 ml) and dried over $CaCl_2$. Column chromatography of the concentrate ($Al_2O_3$, eluent – *n*-hexane, *n*-hexane/diethyl ether 5:1) gave product **3** (0.009 g, 0.5%), product **4** (0.027 g, 1.7%), indole **5** (0.019 g, 1%) and amine **6** (0.037 g, 2.7%). The total yields of compounds: **3** – 3%, **4** – 3%, **5** – 12% and **6** – 3%.

*2,1,3-Benzoxadiazol-4-amine* **6**. Light-yellow crystals, mp 107-108 °C [lit. 109-110 ºC$^{15}$]. Spectral characteristics coincide with the literature [S. Uchiyama, T. Santa, N. Okiyama, K. Azuma and K. Imai, *J. Chem. Soc., Perkin Trans. 2*, 2000, 1199-1207.]. $^1$H NMR (400 MHz, $CDCl_3$) δ: 7.18 (m, 1H, H-7), 7.10 (d, *J* 8.0 Hz, 1H, H-6), 6.33 (d, *J* 8.0 Hz, 1H, H-5), 4.64 (br s, 2H, $NH_2$).