

L'Abbé Rearrangement Enables Access to N-Amino-1,2,3-Triazoles from Pyridotriazole Carbaldehydes with Hydrazine Derivatives

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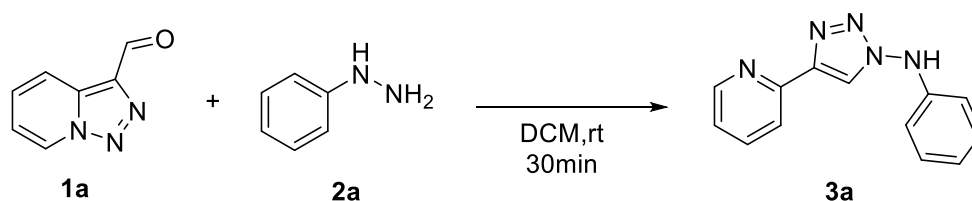
Context

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General information

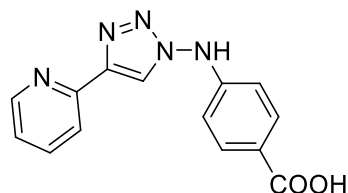
Unless otherwise stated, all reagents were used directly without further purification. Silica gel was purchased from Qing Dao Hai Yang Chemical Industry Co. All melting points were determined on a Beijing Science Instrument Dianguang Instrument Factory XT4B melting point apparatus and uncorrected. ^1H and ^{13}C NMR spectra were measured on a 400 MHz Bruker spectrometer (^1H 400 MHz, ^{13}C 100 MHz), using CDCl_3 or $\text{DMSO}-d_6$ as the solvent with tetramethylsilane (TMS) as the internal standard at room temperature. HRMS-ESI spectra were equipped with an ESI source and a TOF detector. PE is petroleum ether (60–90 °C). [1,2,3]triazolo[1,5-a]pyridine-3-carbaldehyde **1a**, 1-([1,2,3]triazolo[1,5-a]pyridin-3-yl)ethan-1-one **4a**, 1-([1,2,3]triazolo[1,5-a]quinolin-3-yl)ethan-1-one **4b** and [1,2,3]triazolo[1,5-a]quinolin-3-yl(phenyl)methanone **4c** were prepared by known procedures.^{[1][2]}

A Typical Procedure for the Synthesis of N-phenyl-4-(pyridin-2-yl)-1H-1,2,3-triazol-1-amine (3a).



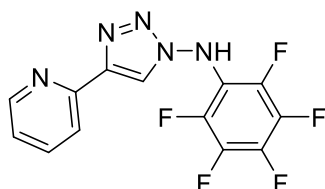
A suspension of [1,2,3]triazolo[1,5-a]pyridine-3-carbaldehyde **1a** (0.5 mmol, 74 mg) and phenylhydrazine **2a** (0.55 mmol, 59 mg) in DCM (2 mL) was stirred at rt for 30 min. After **1a** was exhausted completely (monitored by TLC), saturated aqueous brine (20 mL) was added. The mixture was stirred for 10 min and then was extracted by CH_2Cl_2 (3 X 10 mL). The combined organic layers were dried over Na_2SO_4 . Removal of the solvent gave a residue, which was purified by a column chromatography (silica gel, PE/EtOAc = 3/1) to afford **3a** as white solid, 111 mg, 94% yield; mp 182–185 °C. ^1H NMR (400 MHz, CDCl_3) δ 8.61–8.60 (m, 1H), 8.34 (s, 1H), 8.20 (d, J = 8.0, 1H), 7.95 (s, 1H), 7.81 (td, J = 7.8, 1.8 Hz, 1H), 7.28–7.26 (m, 1H), 7.25–7.21 (m, 2H), 7.02–6.98 (m, 1H), 6.64 (d, J = 7.5 Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 150.0, 149.4, 147.1, 145.6, 137.1, 129.4 (2C), 123.9, 123.2, 123.1, 120.2, 114.3 (2C). HRMS m/z (ESI) calcd for $\text{C}_{13}\text{H}_{11}\text{N}_5$, ($\text{M}+\text{H}$)⁺ 238.1093; found, 238.1093.

The similar procedure was used for the preparation of products **3b-3ac**.

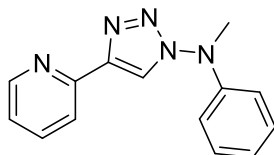


4-((4-(pyridin-2-yl)-1H-1,2,3-triazol-1-yl)amino)benzoic acid (3b) The compound was purified by column chromatography (silica gel, PE/EtOAc = 1/1 v/v): 138 mg, 98% yield; brown solid, mp 243–247 °C. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 12.60 (s, 1H), 10.84 (s, 1H), 8.88 (s, 1H), 8.63 (d, J = 4.0 Hz, 1H), 8.11 (d, J = 7.9 Hz, 1H), 7.97–7.92 (m, 1H), 7.85 (d, J = 8.4 Hz, 2H), 7.41–7.38 (m, 1H), 6.57 (d, J = 8.5 Hz, 2H); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$) δ 167.5, 151.0, 150.1, 150.0, 149.3, 147.1, 132.6, 131.0 (2C), 124.4, 123.8, 113.4 (2C), 111.9. HRMS m/z (ESI)

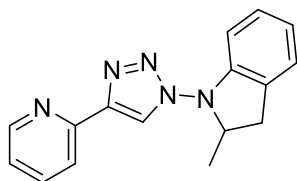
calcd for $C_{14}H_{11}N_5O_2$, $(M+H)^+$ 282.0991; found, 282.0992.



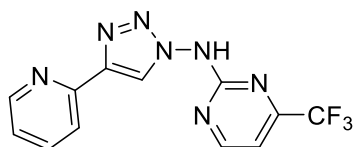
N-(perfluorophenyl)-4-(pyridin-2-yl)-1H-1,2,3-triazol-1-amine (3c) The compound was purified by column chromatography (silica gel, PE/EtOAc = 3/1 v/v): 134 mg, 82% yield; white solid, mp 141–143 °C. ^1H NMR (400 MHz, DMSO- d_6) δ 10.71 (s, 1H), 8.91 (s, 1H), 8.63–8.61 (m, 1H), 8.06 (dt, J = 7.8, 1.1 Hz, 1H), 7.92 (td, J = 7.7, 1.8 Hz, 1H), 7.39 (ddd, J = 7.5, 4.8, 1.2 Hz, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 150.2, 149.9, 146.6, 137.8, 124.6, 123.9, 119.9. HRMS m/z (ESI) calcd for $C_{13}H_6F_5N_5$, $(M+H)^+$ 328.0622; found, 368.0621.



N-methyl-N-phenyl-4-(pyridin-2-yl)-1H-1,2,3-triazol-1-amine (3d) The compound was purified by column chromatography (silica gel, PE/EtOAc = 3/1 v/v): 119 mg, 92% yield; yellow liquid, ^1H NMR (400 MHz, $CDCl_3$) δ 8.59–8.57 (m, 1H), 8.29 (s, 1H), 8.23 (d, J = 8.0 Hz, 1H), 7.80 (t, J = 7.7 Hz, 1H), 7.28–7.23 (m, 3H), 7.00 (t, J = 7.4 Hz, 1H), 6.68–6.65 (m, 2H), 3.55 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.9, 149.4, 148.5, 147.0, 136.9, 129.3 (2C), 123.1, 122.53, 122.50, 120.0, 114.8 (2C), 42.8. HRMS m/z (ESI) calcd for $C_{14}H_{13}N_5$, $(M+Na)^+$ 274.1069; found, 274.1067.

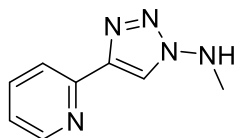


2-methyl-1-(4-(pyridin-2-yl)-1H-1,2,3-triazol-1-yl)indoline (3e) The compound was purified by column chromatography (silica gel, PE/EtOAc = 3/1 v/v): 130 mg, 94% yield; yellow liquid, ^1H NMR (400 MHz, $CDCl_3$) δ 8.61–8.59 (m, 1H), 8.35 (s, 1H), 8.24 (d, J = 8.0 Hz, 1H), 7.81 (td, J = 7.8, 1.8 Hz, 1H), 7.27–7.24 (m, 1H), 7.21 (d, J = 7.3 Hz, 1H), 7.08 (t, J = 7.7 Hz, 1H), 6.96 (td, J = 7.4, 1.1 Hz, 1H), 6.31 (d, J = 7.8 Hz, 1H), 4.48–4.41 (m, 1H), 3.33 (dd, J = 15.2, 7.9 Hz, 1H), 2.86–2.79 (m, 1H), 1.38 (d, J = 6.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.94, 149.91, 149.4, 146.8, 137.0, 127.72, 127.70, 124.9, 123.1, 123.0 (2C), 120.0, 110.7, 67.2, 36.0, 18.2. HRMS m/z (ESI) calcd for $C_{16}H_{15}N_5$, $(M+Na)^+$ 300.1225; found, 300.1227.

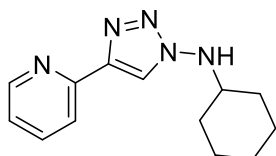


N-(4-(pyridin-2-yl)-1H-1,2,3-triazol-1-yl)-4-(trifluoromethyl)pyrimidin-2-amine (3f) The compound was purified by column chromatography (silica gel, PE/EtOAc = 3/1 v/v): 143 mg, 93% yield; white solid, mp 213–215 °C. ^1H NMR (400 MHz, DMSO- d_6) δ 12.24 (s, 1H), 8.87 (s, 1H), 8.85 (d, J = 5.0 Hz, 1H), 8.63–8.61 (m, 1H), 8.09 (dt, J = 7.9, 1H), 7.94 (td, J = 7.7, 1.8 Hz, 1H),

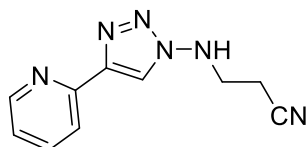
7.51 (d, $J = 5.0$ Hz, 1H), 7.39 (ddd, $J = 7.5, 4.8, 1.2$ Hz, 1H); ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 163.1, 162.2, 155.4, 150.2, 150.1, 147.0, 137.9, 125.7, 123.8, 119.9, 110.7 (2C). HRMS m/z (ESI) calcd for $\text{C}_{12}\text{H}_8\text{F}_3\text{N}_7$, $(\text{M}+\text{Na})^+$ 330.0691; found, 330.0693.



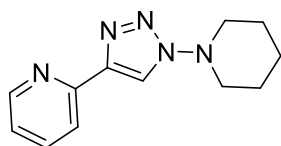
N-methyl-4-(pyridin-2-yl)-1H-1,2,3-triazol-1-amine (3g) The compound was purified by column chromatography (silica gel, PE/EtOAc = 1/1 v/v): 87 mg, 99% yield; white solid, mp 116–117 °C. ^1H NMR (400 MHz, CDCl_3) δ 8.57–8.55 (m, 1H), 8.15–8.12 (m, 2H), 7.76 (td, $J = 7.7, 1.8$ Hz, 1H), 7.23–7.20 (m, 1H), 5.78–5.76 (m, 1H), 3.09 (d, $J = 5.6$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 150.1, 149.3, 146.9, 136.9, 122.9, 121.2, 119.9, 40.8. HRMS m/z (ESI) calcd for $\text{C}_8\text{H}_9\text{N}_5$, $(\text{M}+\text{Na})^+$ 198.0756; found, 198.0755.



N-cyclohexyl-4-(pyridin-2-yl)-1H-1,2,3-triazol-1-amine (3h) The compound was purified by column chromatography (silica gel, PE/EtOAc = 3/1 v/v): 118 mg, 97% yield; white solid, mp 116–119 °C. ^1H NMR (400 MHz, CDCl_3) δ 8.57–8.55 (m, 1H), 8.14 (d, $J = 8.0$, 1H), 8.09 (s, 1H), 7.75 (td, $J = 7.7, 1.8$ Hz, 1H), 7.21 (ddd, $J = 7.5, 4.9, 1.2$ Hz, 1H), 5.67 (d, $J = 3.4$ Hz, 1H), 3.38–3.32 (m, 1H), 1.77–1.58 (m, 5H), 1.27–1.19 (m, 5H); ^{13}C NMR (100 MHz, CDCl_3) δ 150.2, 149.3, 146.4, 136.9, 122.82, 122.80, 119.9, 60.3, 30.8 (2C), 25.6, 23.9 (2C). HRMS m/z (ESI) calcd for $\text{C}_{13}\text{H}_{17}\text{N}_5$, $(\text{M}+\text{Na})^+$ 266.1382; found, 266.1385.

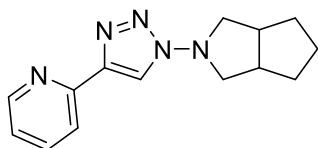


3-((4-(pyridin-2-yl)-1H-1,2,3-triazol-1-yl)amino)propanenitrile (3i) The compound was purified by column chromatography (silica gel, PE/EtOAc = 3/1 v/v): 100 mg, 93% yield; brown liquid, ^1H NMR (400 MHz, CDCl_3) δ 8.58–8.56 (m, 1H), 8.21 (s, 1H), 8.11 (dt, $J = 7.9, 1.1$ Hz, 1H), 7.77 (td, $J = 7.8, 1.8$ Hz, 1H), 7.24 (ddd, $J = 7.6, 4.9, 1.2$ Hz, 1H), 6.34 (t, $J = 4.8$ Hz, 1H), 3.67–3.63 (m, 2H), 2.62 (t, $J = 6.6$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 149.6, 149.4, 147.0, 137.0, 123.2, 122.8, 120.0, 117.3, 48.1, 17.1. HRMS m/z (ESI) calcd for $\text{C}_{10}\text{H}_{10}\text{N}_6$, $(\text{M}+\text{Na})^+$ 237.0865; found, 237.0867.

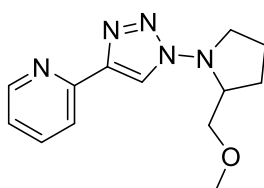


2-(1-(piperidin-1-yl)-1H-1,2,3-triazol-4-yl)pyridine (3j) The compound was purified by column chromatography (silica gel, PE/EtOAc = 3/1 v/v): 110 mg, 96% yield; white solid, mp 126–128 °C. ^1H NMR (400 MHz, CDCl_3) δ 8.57–8.55 (m, 1H), 8.19–8.14 (m, 2H), 7.76 (td, $J = 7.7, 1.8$ Hz, 1H), 7.21 (ddd, $J = 7.6, 4.9, 1.2$ Hz, 1H), 3.32–3.29 (m, 4H), 1.84–1.79 (m, 4H), 1.60–1.54 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 150.3, 149.3, 146.1, 136.9, 122.8, 120.0, 119.9,

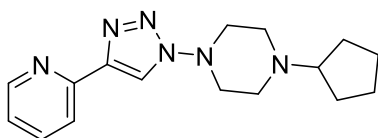
57.4 (2C), 25.7 (2C), 23.1. HRMS m/z (ESI) calcd for $C_{12}H_{15}N_5$, $(M+Na)^+$ 252.1225; found, 252.1227.



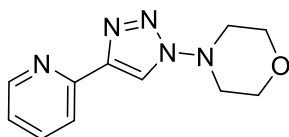
2-(4-(pyridin-2-yl)-1H-1,2,3-triazol-1-yl)octahydrocyclopenta[c]pyrrole (3k) The compound was purified by column chromatography (silica gel, PE/EtOAc = 3/1 v/v): 125 mg, 98% yield; white solid, mp 101–103 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.57–8.55 (m, 1H), 8.18–8.13 (m, 2H), 7.76 (td, J = 7.7, 1.8 Hz, 1H), 7.21 (ddd, J = 7.5, 4.9, 1.2 Hz, 1H), 3.66–3.58 (m, 2H), 3.14 (dd, J = 8.8, 4.5 Hz, 2H), 2.83–2.76 (m, 2H), 1.84–1.74 (m, 3H), 1.62–1.50 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 149.3, 146.2, 136.8, 122.8, 120.5, 119.9, 62.8 (2C), 40.6 (2C), 32.8 (2C), 26.0. HRMS m/z (ESI) calcd for $C_{14}H_{17}N_5$, $(M+Na)^+$ 278.1382; found, 278.1383.



2-(1-(2-(methoxymethyl)pyrrolidin-1-yl)-1H-1,2,3-triazol-4-yl)pyridine (3l) The compound was purified by column chromatography (silica gel, PE/EtOAc = 3/1 v/v): 128 mg, 99% yield; yellow liquid, ^1H NMR (400 MHz, $CDCl_3$) δ 8.56–8.54 (m, 1H), 8.17–8.14 (m, 2H), 7.75 (td, J = 7.8, 1.8 Hz, 1H), 7.20 (ddd, J = 7.5, 4.9, 1.2 Hz, 1H), 3.89–3.82 (m, 1H), 3.65–3.58 (m, 1H), 3.55–3.50 (m, 1H), 3.35–3.28 (m, 2H), 3.24 (s, 3H), 2.25–2.16 (m, 1H), 2.13–2.04 (m, 1H), 2.01–1.91 (m, 1H), 1.87–1.78 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 149.3, 146.0, 136.8, 122.7, 122.5, 119.9, 73.6, 65.6, 59.1, 57.1, 26.3, 22.1. HRMS m/z (ESI) calcd for $C_{13}H_{17}N_5O$, $(M+Na)^+$ 282.1331; found, 282.1333.

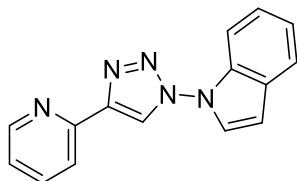


1-cyclopentyl-4-(4-(pyridin-2-yl)-1H-1,2,3-triazol-1-yl)piperazine (3m) The compound was purified by column chromatography (silica gel, PE/EtOAc = 3/1 v/v): 140 mg, 94% yield; white solid, mp 206–208 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.56–8.55 (m, 1H), 8.18–8.15 (m, 2H), 7.76 (td, J = 7.7, 1.8 Hz, 1H), 7.21 (ddd, J = 7.6, 4.9, 1.2 Hz, 1H), 3.42 (t, J = 5.0 Hz, 4H), 2.75 (s, 4H), 2.63–2.55 (m, 1H), 1.92–1.84 (m, 2H), 1.75–1.65 (m, 2H), 1.62–1.51 (m, 2H), 1.48–1.38 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 149.3, 146.4, 136.9, 122.9, 119.9, 119.7, 66.9, 55.9 (2C), 51.6 (2C), 30.5 (2C), 24.1 (2C). HRMS m/z (ESI) calcd for $C_{16}H_{22}N_6$, $(M+H)^+$ 299.1984; found, 299.1985.



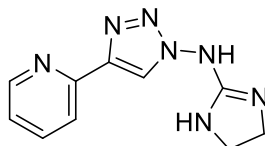
4-(4-(pyridin-2-yl)-1H-1,2,3-triazol-1-yl)morpholine (3n) The compound was purified by column chromatography (silica gel, PE/EtOAc = 3/1 v/v): 106 mg, 92% yield; white solid, mp

175–178 °C. ^1H NMR (400 MHz, CDCl_3) δ 8.58–8.56 (m, 1H), 8.19–8.16 (m, 2H), 7.78 (td, J = 7.7, 1.8 Hz, 1H), 7.23 (ddd, J = 7.6, 4.8, 1.2 Hz, 1H), 3.93–3.91 (m, 4H), 3.42–3.39 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 150.1, 149.3, 146.4, 137.0, 123.0, 120.1, 120.0, 66.6 (2C), 56.3 (2C). HRMS m/z (ESI) calcd for $\text{C}_{11}\text{H}_{13}\text{N}_5\text{O}$, $(\text{M}+\text{Na})^+$ 254.1018; found, 254.1020.

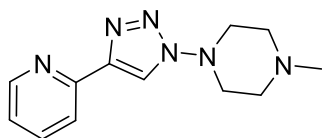


1-(4-(pyridin-2-yl)-1H-1,2,3-triazol-1-yl)-1H-indole (3o) The compound was purified by column chromatography (silica gel, PE/EtOAc = 3/1 v/v): 121 mg, 93% yield; white solid, mp 143–146 °C. ^1H NMR (400 MHz, CDCl_3) δ 8.61–8.59 (m, 1H), 8.49 (s, 1H), 8.27 (d, J = 7.9, 1H), 7.83 (td, J = 7.8, 1.8 Hz, 1H), 7.70–7.66 (m, 1H), 7.36 (d, J = 3.5 Hz, 1H), 7.30–7.23 (m, 3H), 7.09–7.06 (m, 1H), 6.73 (dd, J = 3.6, 0.9 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 149.6, 149.3, 147.6, 137.1, 136.4, 126.7, 126.5, 124.2, 123.5, 123.1, 122.2, 121.6, 120.3, 108.7, 104.4. HRMS m/z (ESI) calcd for $\text{C}_{15}\text{H}_{11}\text{N}_5$, $(\text{M}+\text{Na})^+$ 284.0912; found, 284.0914.

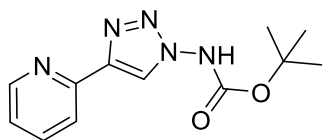
For **3o** (gram-scale), a mixture of [1,2,3]triazolo[1,5-*a*]pyridine-3-carbaldehyde **1a** (1.0 mmol, 1.47 g) and 1H-indol-1-amine **2o** (11 mmol, 1.45g) in DCM (20 mL) was stirred at rt for 5 h. After completion of the reaction (monitored by TLC), the resulting solution was poured into water (100 mL), and extracted with DCM (3 X 50 mL). The combined DCM extracts were dried over Na_2SO_4 and concentrated. Then the solvent was evaporated, and the residue was purified by chromatography (silica gel, PE/EtOAc = 3/1 v/v) to give **3o** in 95% yield (2.48 g).



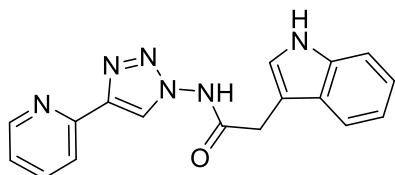
N-(4,5-dihydro-1H-imidazol-2-yl)-4-(pyridin-2-yl)-1H-1,2,3-triazol-1-amine (3p) The compound was purified by column chromatography (silica gel, PE/EtOAc = 1/1 v/v): 89 mg, 78% yield; white solid, mp 216–217 °C. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.57–8.56 (m, 1H), 8.12 (s, 1H), 8.01 (d, J = 7.9, 1H), 7.86 (td, J = 7.7, 1.8 Hz, 1H), 7.30 (ddd, J = 7.5, 4.8, 1.2 Hz, 1H), 6.86 (s, 1H), 6.74 (s, 1H), 3.41 (s, 4H); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$) δ 164.3, 151.1, 149.9, 145.8, 137.5, 123.1, 120.6, 119.5, 43.3, 42.1. HRMS m/z (ESI) calcd for $\text{C}_{10}\text{H}_{11}\text{N}_7$, $(\text{M}+\text{Na})^+$ 252.0974; found, 252.0974.



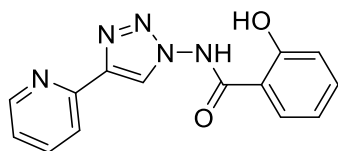
1-methyl-4-(4-(pyridin-2-yl)-1H-1,2,3-triazol-1-yl)piperazine (3q) The compound was purified by column chromatography (silica gel, PE/EtOAc = 1/1 v/v): 111 mg, 91% yield; white solid, mp 130–136 °C. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.70 (s, 1H), 8.60 (d, J = 4.8 Hz, 1H), 8.04 (d, J = 7.9 Hz, 1H), 7.89 (t, J = 7.7 Hz, 1H), 7.37–7.33 (m, 1H), 3.37–3.34 (m, 4H), 2.70 (s, 4H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$) δ 150.3, 150.1, 146.3, 137.7, 123.7, 121.1, 119.8, 55.3 (2C), 54.3 (2C), 45.2. HRMS m/z (ESI) calcd for $\text{C}_{12}\text{H}_{16}\text{N}_6$, $(\text{M}+\text{Na})^+$ 267.1334; found, 267.1336.



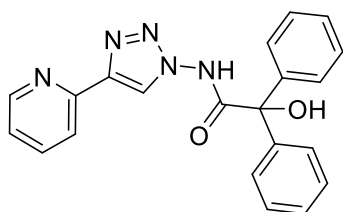
tert-butyl (4-(pyridin-2-yl)-1H-1,2,3-triazol-1-yl)carbamate (3r) The compound was purified by column chromatography (silica gel, PE/EtOAc = 3/1 v/v): 117 mg, 90% yield; white solid, mp 147–150 °C. ^1H NMR (400 MHz, CDCl_3) δ 9.70 (s, 1H), 8.59–8.58 (m, 1H), 8.19 (s, 1H), 8.11 (d, J = 8.0, Hz, 1H), 7.78 (td, J = 7.8, 1.8 Hz, 1H), 7.27–7.24 (m, 1H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 153.1, 149.6, 149.2, 146.6, 137.2, 124.3, 123.2, 120.5, 83.7, 28.0 (3C). HRMS m/z (ESI) calcd for $\text{C}_{12}\text{H}_{15}\text{N}_5\text{O}_2$, $(\text{M}+\text{Na})^+$ 284.1123; found, 284.1125.



2-(1H-indol-3-yl)-N-(4-(pyridin-2-yl)-1H-1,2,3-triazol-1-yl)acetamide (3s) The compound was purified by column chromatography (silica gel, PE/EtOAc = 3/1 v/v): 153 mg, 96% yield; yellow solid, mp 206–208 °C. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 11.03 (s, 1H), 8.75 (s, 1H), 8.61 (d, J = 4.5 Hz, 1H), 8.06 (d, J = 8.0 Hz, 1H), 7.91 (td, J = 7.7, 1.8 Hz, 1H), 7.65 (d, J = 7.9 Hz, 1H), 7.41–7.34 (m, 3H), 7.14–7.03 (m, 2H), 3.86 (s, 2H); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$) δ 170.6, 150.3, 150.0, 146.7, 137.9, 136.7, 127.7, 125.4, 124.9, 123.9, 121.8, 120.0, 119.2, 119.1, 112.1, 107.3, 31.2. HRMS m/z (ESI) calcd for $\text{C}_{17}\text{H}_{14}\text{N}_6\text{O}$, $(\text{M}+\text{H})^+$ 319.1307; found, 319.1308.

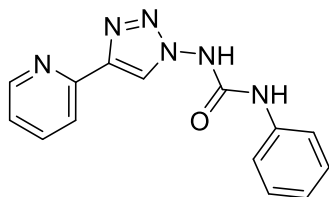


2-hydroxy-N-(4-(pyridin-2-yl)-1H-1,2,3-triazol-1-yl)benzamide (3t) The compound was purified by column chromatography (silica gel, PE/EtOAc = 3/1 v/v): 121 mg, 86% yield; white solid, mp 190–192 °C. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 11.54 (s, 1H), 8.84 (s, 1H), 8.64–8.63 (m, 1H), 8.10 (dt, J = 8.0, 1.1 Hz, 1H), 7.94 (td, J = 7.7, 1.8 Hz, 1H), 7.90 (dd, J = 8.0, 1.8 Hz, 1H), 7.53–7.49 (m, 1H), 7.39 (ddd, J = 7.6, 4.8, 1.2 Hz, 1H), 7.07–6.99 (m, 2H); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$) δ 166.5, 158.4, 150.2, 150.1, 146.6, 137.9, 135.2, 130.5, 125.8, 123.8, 119.99, 119.96, 117.7, 116.0. HRMS m/z (ESI) calcd for $\text{C}_{14}\text{H}_{11}\text{N}_5\text{O}_2$, $(\text{M}+\text{H})^+$ 282.0991; found, 282.0993.

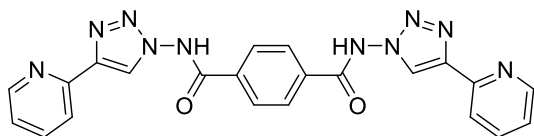


2-hydroxy-2,2-diphenyl-N-(4-(pyridin-2-yl)-1H-1,2,3-triazol-1-yl)acetamide (3u) The compound was purified by column chromatography (silica gel, PE/EtOAc = 3/1 v/v): 169 mg, 91% yield; white solid, mp 244–245 °C. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 12.65 (s, 1H), 8.76 (s, 1H), 8.63–8.61 (m, 1H), 8.05 (d, J = 7.9, 1H), 7.92 (td, J = 7.7, 1.8 Hz, 1H), 7.49–7.46 (m, 4H), 7.42–7.33 (m, 7H), 7.29 (s, 1H); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$) δ 173.1, 150.2, 150.0, 146.7, 143.5

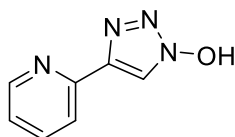
(2C), 137.8, 128.4 (4C), 128.3 (2C), 128.0 (4C), 125.6, 123.8, 120.0, 81.4. HRMS m/z (ESI) calcd for $C_{21}H_{17}N_5O_2$, $(M+H)^+$ 372.1460; found, 372.1458.



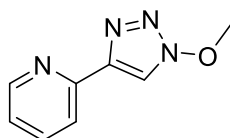
1-phenyl-3-(4-(pyridin-2-yl)-1H-1,2,3-triazol-1-yl)urea (3v) The compound was purified by column chromatography (silica gel, PE/EtOAc = 1/1 v/v): 123 mg, 88% yield; brown solid, mp 227–228 °C. ^1H NMR (400 MHz, DMSO- d_6) δ 10.74 (s, 1H), 9.57 (s, 1H), 8.73 (s, 1H), 8.63–8.61 (m, 1H), 8.08 (d, J = 7.9, 1H), 7.92 (td, J = 7.7, 1.8 Hz, 1H), 7.51–7.48 (m, 2H), 7.37 (ddd, J = 7.6, 4.8, 1.2 Hz, 1H), 7.32–7.29 (m, 2H), 7.05–7.01 (m, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 153.9, 150.24, 150.21, 146.5, 139.3, 137.8, 129.4 (2C), 126.2, 123.7, 123.4, 119.9, 119.6 (2C). HRMS m/z (ESI) calcd for $C_{14}H_{12}N_6O$, $(M+H)^+$ 281.1151; found, 281.1152.



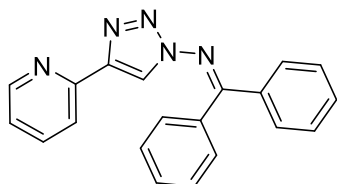
N^1,N^4 -bis(4-(pyridin-2-yl)-1H-1,2,3-triazol-1-yl)terephthalamide (3w) A suspension of [1,2,3]triazolo[1,5- a]pyridine-3-carbaldehyde **1a** (1.1 mmol, 162 mg) and terephthalohydrazide **2w** (0.5 mmol, 97 mg) in DCM (2 mL) was stirred at rt for 6 h. After **2w** was exhausted completely (monitored by TLC), saturated aqueous brine (20 mL) was added. The mixture was stirred for 10 min and then was extracted by CH_2Cl_2 (3 X 10 mL). The combined organic layers were dried over Na_2SO_4 . Removal of the solvent gave a residue, which was purified by a column chromatography (silica gel, PE/EtOAc = 3/1) to afford **3w** as white solid, 192 mg, 85% yield; mp 310–312 °C. ^1H NMR (400 MHz, DMSO- d_6) δ 13.21 (s, 2H), 8.95 (s, 2H), 8.65 (d, J = 4.1 Hz, 2H), 8.23 (s, 4H), 8.11 (d, J = 7.9 Hz, 2H), 7.95 (td, J = 7.7, 1.8 Hz, 2H), 7.41 (ddd, J = 7.5, 4.8, 1.1 Hz, 2H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 165.3 (2C), 150.3 (2C), 150.0 (2C), 146.9 (2C), 137.9 (2C), 135.0 (2C), 129.0 (4C), 125.6 (2C), 123.9 (2C), 120.0 (2C). HRMS m/z (ESI) calcd for $C_{22}H_{16}N_{10}O_2$, $(M+H)^+$ 453.1536; found, 453.1537.



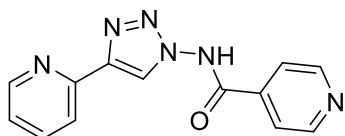
4-(pyridin-2-yl)-1H-1,2,3-triazol-1-ol (3x) The compound was purified by column chromatography (silica gel, PE/EtOAc = 1/3 v/v): 77 mg, 95% yield; white solid, mp 133–134 °C. ^1H NMR (400 MHz, DMSO- d_6) δ 10.38 (s, 1H), 9.06 (s, 1H), 8.75–8.73 (m, 1H), 8.45 (td, J = 7.8, 1.6 Hz, 1H), 8.37 (d, J = 8.1 Hz, 1H), 7.82–7.79 (m, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 145.0 (2C), 144.4, 139.7, 125.8, 122.9, 120.7. HRMS m/z (ESI) calcd for $C_7H_6N_4O$, $(M+H)^+$ 163.0620; found, 163.0619.



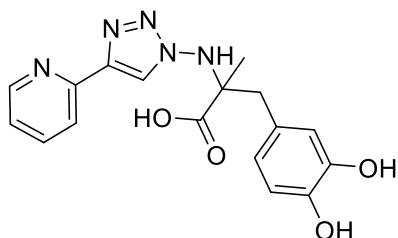
2-(1-methoxy-1*H*-1,2,3-triazol-4-yl)pyridine (3y) The compound was purified by column chromatography (silica gel, PE/EtOAc = 3/1 v/v): 85 mg, 97% yield; white solid, mp 133–134 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.15 (s, 1H), 8.69–8.67 (m, 1H), 8.21–8.14 (m, 2H), 7.58 (ddd, *J* = 7.0, 5.1, 1.6 Hz, 1H), 4.32 (s, 3H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 147.7, 147.5, 143.5, 141.0, 124.9, 121.2, 118.9, 69.3. HRMS *m/z* (ESI) calcd for C₈H₈N₄O, (M+Na)⁺ 199.0596; found, 199.0595.



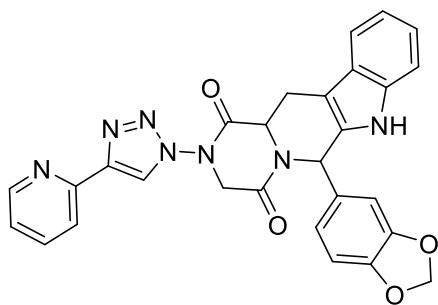
1,1-diphenyl-*N*-(4-(pyridin-2-yl)-1*H*-1,2,3-triazol-1-yl)methanimine (3z) The compound was purified by column chromatography (silica gel, PE/EtOAc = 1/1 v/v): 146 mg, 90% yield; white solid, mp 145–147 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.53–8.52 (m, 1H), 8.09 (d, *J* = 7.9 Hz, 1H), 8.00 (s, 1H), 7.79–7.76 (m, 2H), 7.71 (td, *J* = 7.7, 1.8 Hz, 1H), 7.58–7.54 (m, 1H), 7.47–7.32 (m, 5H), 7.22–7.16 (m, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 173.7, 150.0, 149.3, 147.0, 136.7, 135.9, 133.5, 132.5, 130.2, 130.0 (2C), 128.6 (2C), 128.5 (2C), 128.2 (2C), 122.8, 120.0, 119.2. HRMS *m/z* (ESI) calcd for C₂₀H₁₅N₅, (M+H)⁺ 326.1406; found, 326.1408.



***N*-(4-(pyridin-2-yl)-1*H*-1,2,3-triazol-1-yl)isonicotinamide (3aa)** The compound was purified by column chromatography (silica gel, PE/EtOAc = 3/1 v/v): 122 mg, 92% yield; white solid, mp 213–214 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.93 (s, 1H), 8.89 (d, *J* = 6.1 Hz, 2H), 8.64 (d, *J* = 4.5 Hz, 1H), 8.10 (d, *J* = 8.0 Hz, 1H), 7.97–7.91 (m, 3H), 7.42–7.38 (m, 1H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 164.8, 151.3 (2C), 150.3, 149.9, 147.0, 138.4, 138.0, 125.5, 124.0, 122.1 (2C), 120.0. HRMS *m/z* (ESI) calcd for C₁₃H₁₀N₆O, (M+H)⁺ 267.0994; found, 267.0992.

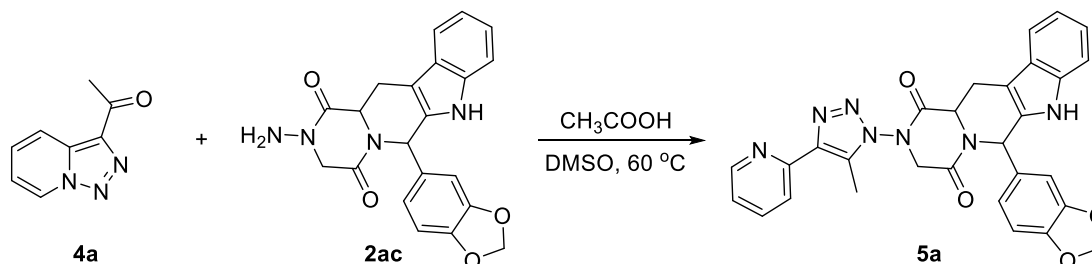


3-(3,4-dihydroxyphenyl)-2-methyl-2-((4-(pyridin-2-yl)-1*H*-1,2,3-triazol-1-yl)amino)propionic acid (3ab) The compound was purified by column chromatography (silica gel, PE/EtOAc = 1/2 v/v): 149 mg, 84% yield; white solid, mp 150–153 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.79 (s, 2H), 8.59–8.57 (m, 1H), 8.30 (s, 1H), 8.04–8.02 (m, 2H), 7.88 (td, *J* = 7.7, 1.8 Hz, 1H), 7.35–7.32 (m, 1H), 6.70 (d, *J* = 2.1 Hz, 1H), 6.65 (d, *J* = 8.0 Hz, 1H), 6.52 (dd, *J* = 8.1, 2.1 Hz, 1H), 2.97 (d, *J* = 13.3 Hz, 1H), 2.75 (d, *J* = 13.3 Hz, 1H), 1.01 (s, 3H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 175.3, 150.3, 150.2, 145.9, 145.3, 144.7, 137.8, 126.9, 124.3, 123.7, 121.9, 119.8, 118.4, 115.7, 66.7, 43.0, 19.8. HRMS *m/z* (ESI) calcd for C₁₇H₁₇N₅O₄, (M+H)⁺ 356.1359; found, 356.1360.



6-(benzo[d][1,3]dioxol-5-yl)-2-(4-(pyridin-2-yl)-1H-1,2,3-triazol-1-yl)-2,3,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione (3ac) The compound was purified by column chromatography (silica gel, PE/EtOAc = 2/1 v/v): 234 mg, 90% yield; white solid, mp 269–272 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.11 (s, 1H), 9.00 (s, 1H), 8.66–8.65 (m, 1H), 8.11 (d, *J* = 7.9 Hz, 1H), 7.95 (td, *J* = 7.8, 1.8 Hz, 1H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.41 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.11–7.07 (m, 1H), 7.04–7.00 (m, 2H), 6.96–6.94 (m, 1H), 6.84 (d, *J* = 8.0 Hz, 1H), 6.24 (s, 1H), 5.96 (d, *J* = 2.1, 2H), 4.94 (d, *J* = 15.6 Hz, 1H), 4.86 (dd, *J* = 11.7, 4.4 Hz, 1H), 4.64 (d, *J* = 15.8 Hz, 1H), 3.63 (dd, *J* = 15.7, 4.5 Hz, 1H), 3.20 (dd, *J* = 15.7, 11.7 Hz, 1H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 166.9, 165.7, 150.4, 149.7, 147.7, 146.8, 146.7, 138.0, 137.1, 136.8, 134.4, 126.2, 124.7, 124.1, 121.9, 120.2, 120.0, 119.5, 118.8, 111.9, 108.5, 107.6, 104.7, 101.5, 56.3 (2C), 54.6, 23.6. HRMS *m/z* (ESI) calcd for C₂₈H₂₁N₇O₄, (M+H)⁺ 520.1733; found, 520.1736.

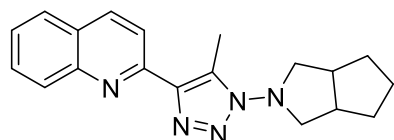
A Typical Procedure for the Synthesis of 6-(benzo[d][1,3]dioxol-5-yl)-2-(5-methyl-4-(pyridin-2-yl)-1H-1,2,3-triazol-1-yl)-2,3,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione (5a).



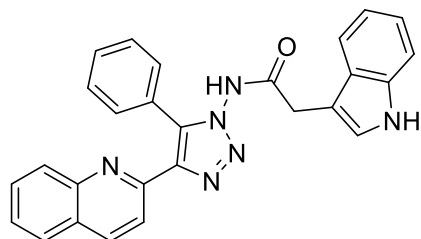
A suspension of 1-([1,2,3]triazolo[1,5-a]pyridin-3-yl)ethan-1-one **4a** (0.5 mmol, 81 mg), aminotadalafil **2ac** (0.55 mmol, 214 mg) and AcOH (0.5 mmol, 30 mg) in DMSO (2 mL) was stirred at 60 °C for 12 h. After **4a** was exhausted completely (monitored by TLC), saturated aqueous brine (20 mL) was added. The mixture was stirred for 10 min and then was extracted by CH₂Cl₂ (3 X 10 mL). The combined organic layers were dried over Na₂SO₄. Removal of the solvent gave a residue, which was purified by a column chromatography (silica gel, PE/EtOAc = 2/1) to afford **3a** as white solid, 208 mg, 78% yield; mp 238–240 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.12 (s, 1H), 8.68–8.66 (m, 1H), 8.14 (d, *J* = 8.0 Hz 1H), 7.94 (td, *J* = 7.7, 1.8 Hz, 1H), 7.58 (d, *J* = 7.7 Hz, 1H), 7.38 (ddd, *J* = 7.6, 4.9, 1.2 Hz, 1H), 7.34 (d, *J* = 8.0 Hz 1H), 7.11–7.07 (m, 1H), 7.04–6.98 (m, 2H), 6.92–6.89 (m, 1H), 6.85 (d, *J* = 8.1 Hz, 1H), 6.27 (d, *J* = 6.6 Hz, 1H), 5.97–5.95 (m, 2H), 5.01–4.92 (m, 2H), 4.76–4.53 (m, 1H), 3.66–3.59 (m, 1H), 3.25–3.18 (m, 1H), 2.62 (d, *J* = 26.0 Hz, 3H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 167.4, 166.0, 151.4, 150.0, 147.7, 146.8, 137.8, 137.3, 136.8, 134.3, 133.8, 126.2, 123.3, 122.0, 120.6, 119.8, 119.5, 118.8, 111.9, 108.6, 107.4, 104.6, 101.5, 56.2, 56.1, 53.9, 23.5, 9.3, 9.1. HRMS *m/z* (ESI) calcd for

C₂₉H₂₃N₇O₄, (M+H)⁺ 534.1890; found, 534.1889.

The similar procedure was used for the preparation of products **5b** & **5c**.



2-(1-(hexahydrocyclopenta[c]pyrrol-2(1H)-yl)-5-methyl-1H-1,2,3-triazol-4-yl)-1,4-dihydroquinoline (5b) The compound was purified by column chromatography (silica gel, PE/EtOAc = 3/1 v/v): 120 mg, 75% yield; white solid, mp 130–136 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.35 (d, *J* = 8.6 Hz, 1H), 8.20 (d, *J* = 8.7, 1H), 8.07 (d, *J* = 8.4, 1H), 7.80 (d, *J* = 8.1, 1H), 7.68 (ddd, *J* = 8.5, 6.9, 1.5 Hz, 1H), 7.49 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 3.66–3.62 (m, 1H), 3.12 (dd, *J* = 8.8, 3.6 Hz, 2H), 2.85–2.78 (m, 5H), 1.91–1.79 (m, 4H), 1.65–1.51 (m, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 152.4, 147.8, 141.8, 136.3, 132.9, 129.3, 129.2, 127.6, 127.1, 126.0, 119.2, 62.1 (2C), 40.6 (2C), 33.3 (2C), 26.4, 9.5. HRMS *m/z* (ESI) calcd for C₁₉H₂₁N₅, (M+Na)⁺ 342.1695; found, 342.1697.



2-(1H-indol-3-yl)-N-(5-phenyl-4-(quinolin-2-yl)-1H-1,2,3-triazol-1-yl)acetamide (5c) The compound was purified by column chromatography (silica gel, PE/EtOAc = 3/1 v/v): 115 mg, 52% yield; gray solid, mp 172–179 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.95 (s, 1H), 8.43 (d, *J* = 8.6 Hz, 1H), 8.11 (d, *J* = 8.6 Hz, 1H), 7.96 (d, *J* = 8.1 Hz, 1H), 7.72–7.68 (m, 1H), 7.64 (d, *J* = 8.5 Hz, 1H), 7.59–7.48 (m, 4H), 7.41–7.36 (m, 3H), 7.32 (d, *J* = 7.9 Hz, 1H), 7.11–7.07 (m, 2H), 6.96 (t, *J* = 7.5 Hz, 1H), 3.74 (s, 2H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 170.7, 150.7, 147.6, 142.6, 137.4, 137.3, 136.7, 130.7 (2C), 130.5, 130.2, 129.2, 128.4 (2C), 127.6, 127.5, 127.3, 126.1, 124.8, 121.7, 119.9, 119.1, 118.9, 111.9, 107.0, 31.0. HRMS *m/z* (ESI) calcd for C₂₇H₂₀N₆O, (M+H)⁺ 445.1777; found, 445.1779.

References

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- [2] G. P. da Costa, M. F. Bach, M. C. de Moraes, T. Barcellos, E. J. Lenardão, M. S. Silva, D. Alves, *Adv. Synth. Catal.*, 2020, **362**, 5044–5055.

^1H NMR and ^{13}C NMR spectra of products **3a-3ac** and **5a-5c**

