Highly Regioselective C–N Bond Formation through C–H Azolation of Indoles Promoted by Iodine in Aqueous Media

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Supporting Information

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General Information

Commercial solvents and reagents were used directly without further purification, and tap water was used for the reaction.

Indole was purchased from Alfa Aesar; 1-methylindole, pyrazole, 1,2,4-triazole and ammonium formate were purchased from Aladdin Chemistry Co., Ltd. in China; 3-methylindole, 5-bromoindole, 5-nitroindole, indole-6-carboxylic acid, 2-methylimidazole, 1H-1,2,3-triazole and 7-azaindole were purchased from J&K Scientific Ltd. in China; 5-methoxyindole was purchased from Matrix Scientific; Imidazole was purchased from Tianjin Yuanhang Chemicals Co., Ltd. in China. 1,3-Dimethylindole, 5-bromo-1-methylindole, 5-nitro-1-methylindole, 5-methoxy-1-methylindole were prepared following the procedure of Shieh[1]. 1-acetylindole was prepared using the method described by Yoon[2]. 1-methylindole-6-carboxylic acid were prepared following the procedure of Szczepankiewicz and Liu[3]. And all the spectra data matched literature values.

Analytical thin layer chromatography (TLC) plates and the silica gel (200−300 mesh) for column chromatography were phased from Qingdao Haiyang Chemical and Special Silica Gel Co, Ltd.

Proton nuclear magnetic resonance (^{1}H NMR) and carbon nuclear magnetic resonance (^{13}C NMR) spectroscopy were performed on Bruker Advance III-400 spectrometers (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR). Chemical shifts of ^{1}H NMR and ^{13}C NMR spectra are reported as in units of parts per million (ppm) downfield from $SiMe_4$ (δ 0.0 ppm) and relative to the signal of chloroform-d (δ 7.26 ppm for ^{1}H NMR and δ 77.1 ppm for ^{13}C NMR) or DMSO-d_6 (δ 2.50 ppm for ^{1}H NMR and δ 39.5 ppm for ^{13}C NMR). Multiplicities were given as: s (singlet); br s (broad singlet); d (doublet); t (triplet); q (quartet); dd (doublet of doublets); m (multiplets), etc. The number of protons (n) for a given resonance is indicated by nH.

IR spectra were recorded on Bruker Tensor 27 FTIR spectrometer and only major peaks are reported in cm^{-1}.

The pH values were measured by PHS-25 pH-meter with E-201C electrode (Shanghai Leici Corporation, Shanghai, China).

Melting points were recorded on SWG X-4 melting point apparatus (Shanghai Precision & Scientific Instrument Co., Ltd.) without correction.

HRMS data were collected on Q-star Elite, ELI-LC-MS/MS (product from ABI, America).

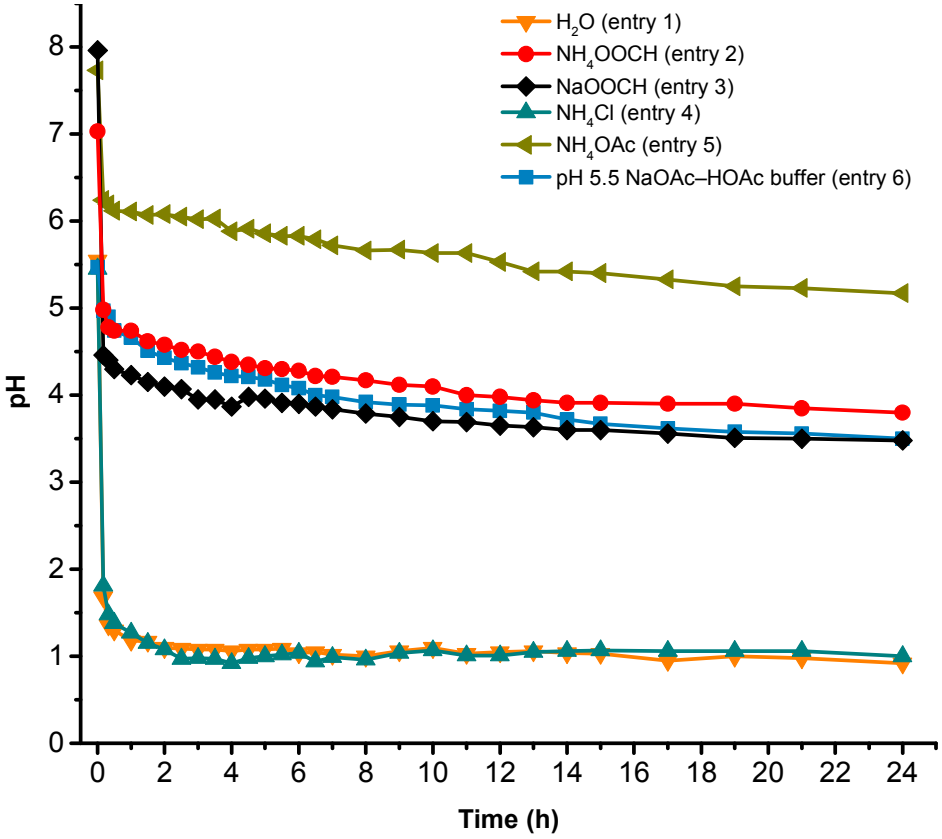
References

(1) Shieh, W.-C.; Dell, S.; Bach, A.; Repič, O.; Balcklock, T. J. *J. Org. Chem.* **2003**, *68*, 1954.

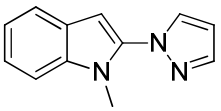
(2) Benkovics, T.; Guzei, I. A.; Yoon, T. P. *Angew. Chem. Int. Ed.* **2010**, *49*, 9153.

(3) Szczepankiewicz, B. G.; Liu, G.; Jae, H.-S.; Tasker, A. S.; Gunawardana, I. W.; von Geldern, T. W.; Gwaltney, S. L., II; Wu-Wong, J. R.; Gehrke, L.; Chiou, W. J.; Credo, R. B.; Alder, J. D.; Nukkala, M. A.; Zielinski, N. A.; Jarvis, K.; Mollison, K. W.; Frost, D. J.; Bauch, J. L.; Hui, Y. H.; Claiborne, A. K.; Li, Q.; Rosenberg, S. H. *J. Med. Chem.* **2001**, *44*, 4416.

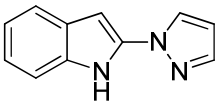
Figure S1. Monitoring the pH values of the reaction mixtures in different solutions for 24 hours.



Synthesis and characterization of products

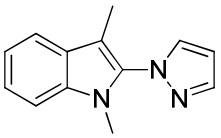


1-Methyl-2-pyrazol-1-yl-1H-indole (3a) (General Procedure): To the mixture of 1-methylindole (63 μL, 0.5 mmol) and pyrazole (85 mg, 1.25 mmol) in 1,4-dioxane (0.3 mL) was added a saturated aqueous NH_4OOCH solution (0.3 mL), and then I_2 (254 mg, 1.25 mmol) was added at rt. The reaction mixture was stirred at room temperature for 24 hours, and then a saturated aqueous $Na_2S_2O_3$ solution (1 mL) was added. The mixture was extracted with ethyl acetate (2 × 20 mL). The combined organic layer was washed with brine (10 mL) and dried over anhydrous magnesium sulfate, filtered and concentrated in vacuo. The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 20/1) to give **3a** as white solid (94 mg, 95%). Mp 59-60 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (d, 1H, *J* = 1.2 Hz), 7.76 (d, 1H, *J* = 2.4 Hz), 7.67 (d, 1H, *J* = 8.0 Hz), 7.40-7.31 (m, 2H), 7.24-7.20 (m, 1H), 6.55 (s, 1H), 6.50 (t, 1H, *J* = 2.0 Hz), 3.71 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.9, 135.8, 132.4, 126.1, 122.6, 121.0, 120.4, 109.7, 106.8, 95.9, 30.0; IR (thin film, cm^{-1}): 3053, 2940, 1583, 1477, 1395, 1347, 1099, 1021, 939, 746; HRMS (ESI): *m/z* ($M+H^+$) calcd. for $C_{12}H_{12}N_3$ 198.1031, found 198.1034.



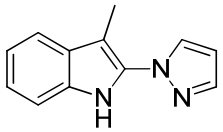
2-Pyrazol-1-yl-1H-indole (3b): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 8/1) to give **3b** as white solid (85 mg, 93%). Mp 153-155 °C (reported: 153-155 °C); ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.98 (s, 1H), 8.42 (d, 1H, *J* = 2.0 Hz), 7.82 (s, 1H), 7.57 (d, 1H, *J* = 7.6 Hz), 7.51 (d, 1H, *J* = 8.0 Hz), 7.16 (t, 1H, *J* = 7.6 Hz), 7.09 (t, 1H, *J* = 7.6 Hz), 6.64 (s, 1H), 6.55 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 140.9, 136.0, 134.0, 128.6, 127.6, 121.3, 120.0, 119.9, 111.6, 107.9, 87.5.

Reference: Poirier, M.; Goudreau, S.; Poulin, J.; Savoie, J.; Beaulieu, P. L. *Org. Lett.* **2010**, *12*, 2334.



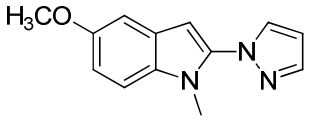
1,3-Dimethyl-2-pyrazol-1-yl-1H-indole (3c): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 20/1) to give **3c** as white solid (98 mg, 93%). Mp 102-103 °C (reported: 100-102 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, 1H, *J* = 1.2 Hz), 7.74-7.70 (m, 2H), 7.44-7.38 (m, 2H), 7.32-7.28 (m, 1H), 6.58 (t, 1H, *J* = 2.0 Hz), 3.57 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.5, 134.7, 132.8, 132.0, 126.4, 122.7, 119.5, 119.3, 109.2, 106.4, 105.2, 29.1, 7.8.

Reference: Poirier, M.; Goudreau, S.; Poulin, J.; Savoie, J.; Beaulieu, P. L. *Org. Lett.* **2010**, *12*, 2334.

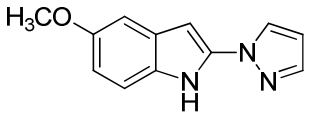


3-Methyl-2-pyrazol-1-yl-1H-indole (3d): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1) to give **3d** as white solid (94 mg, 95%). Mp 114-116 °C (reported: 114-115 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.70 (br s, 1H), 7.95 (d, 1H, *J* = 2.4 Hz), 7.79 (d, 1H, *J* = 1.2 Hz), 7.60 (d, 1H, *J* = 7.2 Hz), 7.33-7.31 (m, 1H), 7.25-7.17 (m, 2H), 6.54 (dd, 1H, *J* = 2.4Hz, 2.0Hz), 2.45 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 140.6, 133.0, 131.5, 130.5, 127.9, 121.7, 119.1, 118.5, 111.2, 107.0, 98.6, 8.3.

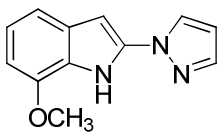
Reference: Poirier, M.; Goudreau, S.; Poulin, J.; Savoie, J.; Beaulieu, P. L. *Org. Lett.* **2010**, *12*, 2334.



5-Methoxy-1-methyl-2-pyrazol-1-yl-1H-indole (3e): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10/1) to give **3e** as white solid (111 mg, 98%). Mp 100-101 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, 1H, *J* = 1.2 Hz), 7.73 (d, 1H, *J* = 2.0 Hz), 7.25 (d, 1H, *J* = 8.8 Hz), 7.10 (d, 1H, *J* = 2.4 Hz), 6.97 (dd, 1H, *J* = 8.8 Hz, 2.4 Hz), 6.47 (t, 1H, *J* = 2.0 Hz), 6.45 (s, 1H), 3.87 (s, 3H), 3.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.7, 141.8, 136.1, 132.3, 131.0, 126.4, 112.9, 110.5, 106.8, 102.7, 95.6, 55.9, 30.1; IR (thin film, cm^{-1}): 3134, 2944, 2832, 1581, 1485, 1349, 1029, 937, 840, 760, 617; HRMS (ESI): *m/z* ($M+H^+$) calcd. for $C_{13}H_{14}N_3O$ 228.1137, found 228.1131.

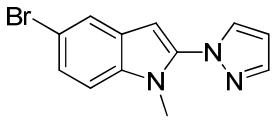


5-Methoxy-2-pyrazol-1-yl-1H-indole (3f): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1) to give **3f** as pale yellow solid (102 mg, 96%). Mp 142-145 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.78 (s, 1H), 8.37 (d, 1H, *J* = 2.0 Hz), 7.80 (s, 1H), 7.37 (d, 1H, *J* = 8.8 Hz), 7.05 (d, 1H, *J* = 1.6 Hz), 6.81 (dd, 1H, *J* = 8.8 Hz, 2.0 Hz), 6.55 (s, 1H), 6.53 (s, 1H), 3.77 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 154.1, 140.9, 136.4, 128.9, 128.4, 128.1, 112.3, 111.1, 107.8, 102.0, 87.6, 55.3; IR (thin film, cm^{-1}): 2831, 1595, 1495, 1398, 1309, 1229, 1154, 1054, 972, 841, 770; HRMS (ESI): *m/z* ($M+H^+$) calcd. for $C_{12}H_{12}N_3O$ 214.0980, found 214.0974.

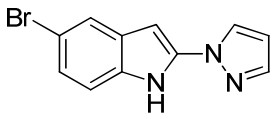


7-Methoxy-2-pyrazol-1-yl-1H-indole (3g): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10/1) to give **3g** as white solid (95 mg, 89%). Mp 87-88 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.00 (br s, 1H), 7.92 (d, 1H, *J* = 1.2 Hz), 7.80 (s, 1H), 7.31 (d, 1H, *J* = 8.0 Hz), 7.18 (t, 1H, *J* = 8.0 Hz), 6.74 (d, 1H, J = 7.6 Hz), 6.48 (s, 1H), 6.46 (d,

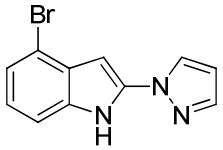
1H, J = 0.8 Hz), 3.94 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.0, 140.8, 135.3, 129.0, 127.4, 123.7, 120.9, 112.9, 107.6, 102.2, 87.7, 55.2; IR (thin film, cm^{-1}): 2935, 2836, 1593, 1474, 1394, 1328, 1260, 1095, 1046, 974, 786, 755, 729; HRMS (ESI): *m/z* ($M+H^+$) calcd. for $C_{12}H_{12}N_3O$ 214.0980, found 214.0971.



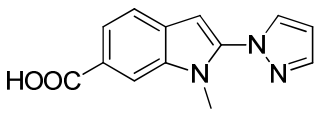
5-Bromo-1-methyl-2-pyrazol-1-yl-1H-indole (3h): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10/1) to give **3g** as white solid (125 mg, 90%). Mp 118-120 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (s, 1H), 7.71 (s, 2H), 7.33 (dd, 1H, J = 8.8 Hz, 1.6Hz), 7.15 (d, 1H, J = 8.8 Hz), 6.47 (s, 1H), 6.40 (s, 1H), 3.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.9, 136.4, 134.2, 132.1, 127.5, 125.2, 123.1, 113.4, 111.1, 107.0, 94.8, 30.1; IR (thin film, cm^{-1}): 3116, 2939, 1575, 1470, 1404, 1329, 1101, 938, 901, 753; HRMS (ESI): *m/z* ($M+H^+$) calcd. for $C_{12}H_{11}BrN_3$ 276.0136, found 276.0131.



5-Bromo-2-pyrazol-1-yl-1H-indole (3i): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 8/1) to give **3h** as white solid (125 mg, 95%). Mp 164-166 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.19 (br s, 1H), 8.40 (d, 1H, J = 1.2 Hz), 7.81 (s, 1H), 7.70 (s, 1H), 7.41 (d, 1H, J = 8.8 Hz), 7.24 (d, 1H, J = 8.4 Hz), 6.59 (s, 1H), 6.55 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 141.2, 137.0, 132.6, 129.4, 128.6, 123.7, 122.0, 113.4, 112.5, 108.1, 86.9; IR (thin film, cm^{-1}): 3231, 1582, 1490, 1450, 1396, 1047, 969, 897, 743, 604; HRMS (ESI): *m/z* ($M+H^+$) calcd. for $C_{11}H_9BrN_3$ 261.9980, found 261.9969.

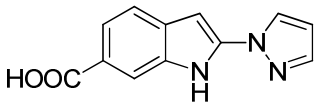


4-Bromo-2-pyrazol-1-yl-1H-indole (3j): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10/1) to give **3j** as white solid (136 mg, 86%). Mp 113-114 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.73 (s, 1H), 8.03 (d, 1H, J = 2.4 Hz), 7.79 (s, 1H, J = 1.6 Hz), 7.31 (d, 1H, J = 7.6 Hz), 7.22 (d, 1H, J = 8.0 Hz), 7.01 (t, 1H, J = 8.0 Hz), 6.55 (t, 1H, J = 2.0 Hz), 6.51 (d, 1H, J = 1.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.2, 135.8, 133.9, 128.7, 128.1, 123.5, 122.9, 114.0, 110.3, 108.4, 87.6; IR (thin film, cm^{-1}): 3428, 3244, 1620, 1589, 1561, 1428, 1394, 1330, 1177, 1048, 971, 919, 755; HRMS (ESI): *m/z* ($M+H^+$) calcd. for $C_{11}H_9BrN_3$ 261.9980, found 261.9968.

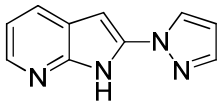


1-Methyl-2-pyrazol-1-yl-1H-indole-6-carboxylic acid (3k): The crude product was recrystallized with ethyl ether to give **3i** as white solid (108 mg, 90%). Mp 181-186 °C (decomposed); ^{1}H NMR (400

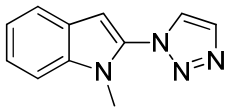
MHz, DMSO-d_6): δ 8.25 (d, 1H, *J* = 2.0 Hz), 8.16 (s, 1H), 7.90 (s, 1H), 7.74 (d, 1H, *J* = 8.4 Hz), 7.67 (d, 1H, *J* = 8.4 Hz), 6.70 (s, 1H), 6.61 (s, 1H), 3.77 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.1, 142.1, 138.3, 134.7, 133.0, 129.2, 124.4, 121.1, 120.2, 112.3, 107.4, 95.2, 30.4; IR (thin film, cm^{-1}): 2990, 2923, 1766, 1676, 1599, 1470, 1374, 1242, 1050, 947, 740; HRMS (ESI): *m/z* ($M+H^+$) calcd. for $C_{13}H_{11}N_3O_2$ 242.0930, found 242.0925.



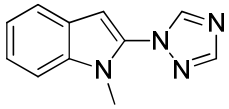
2-Pyrazol-1-yl-1H-indole-6-carboxylic acid (3l): The crude product was recrystallized with ethyl ether to give **3j** as white solid (80 mg, 70%). Mp 244-247 °C (decomposed); ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.52 (br s, 1H), 12.29 (s, 1H), 8.49 (s, 1H), 8.07 (s, 1H), 7.84 (s, 1H), 7.68 (d, 1H, *J* = 8.0 Hz), 7.57 (d, 1H, *J* = 8.0 Hz), 6.71 (s, 1H), 6.60 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.2, 141.5, 138.5, 133.2, 131.2, 128.9, 123.2, 121.1, 119.3, 113.5, 108.4, 87.6; IR (thin film, cm^{-1}): 3168, 1682, 1627, 1583, 1507, 1407, 1284, 1233, 1053, 975, 771; HRMS (ESI): *m/z* ($M+H^+$) calcd. for $C_{12}H_{10}N_3O_2$ 228.0773, found 228.0766.



2-Pyrazol-1-yl-1H-pyrrolo[2,3-b]pyridine (3o): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1) to give **3m** as white solid (85 mg, 92%). Mp 233-236 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.60 (br s, 1H), 8.48 (d, 1H, *J* = 2.4 Hz), 8.21 (dd, 1H, *J* = 4.8 Hz, 0.8 Hz), 7.92 (dd, 1H, *J* = 8.0 Hz, 1.2 Hz), 7.83 (d, 1H, *J* = 1.2 Hz), 7.10 (dd, 1H, *J* = 7.6 Hz, 4.8 Hz), 6.60-6.59 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 146.7, 142.2, 141.6, 136.5, 128.7, 127.6, 120.2, 116.5, 108.1, 86.2; IR (thin film, cm^{-1}): 3198, 3058, 1569, 1481, 1397, 1321, 1275, 1108, 1041, 958, 905, 796, 751; HRMS (ESI): *m/z* ($M+H^+$) calcd. for $C_{10}H_9N_4$ 185.0827, found 185.0825.

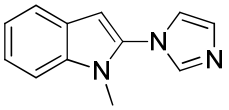


1-Methyl-2-[1,2,3]triazol-1-yl-1H-indole (4a): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 5/1) to give **4a** as white solid (80 mg, 81%). Mp 75-76 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (s, 1H), 7.87 (s, 1H), 7.66 (d, 1H, *J* = 8.0 Hz), 7.40-7.33 (m, 2H), 7.23-7.20 (m, 1H), 6.63 (s, 1H), 3.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.0, 133.5, 131.5, 126.6, 125.7, 123.5, 121.4, 120.9, 109.9, 97.3, 30.0; IR (thin film, cm^{-1}): 3055, 2943, 1570, 1482, 1347, 1235, 1087, 1017, 785, 744; HRMS (ESI): *m/z* ($M+H^+$) calcd. for $C_{11}H_{11}N_4$ 199.0984, found 199.0983.

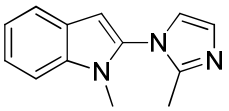


1-Methyl-2-[1,2,4]triazol-1-yl-1H-indole (4b): The crude product was purified by column

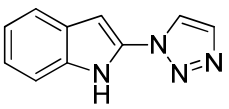
chromatography on silica gel (petroleum ether/ethyl acetate = 4/1) to give **4b** as pale yellow solid (80 mg, 81%). Mp 88-90 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 (s, 1H), 8.21 (s, 1H), 7.66 (d, 1H, *J* = 8.0 Hz), 7.39-7.33 (m, 2H), 7.23-7.19 (m, 1H), 6.61 (s, 1H), 3.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.2, 145.6, 136.1, 131.2, 125.7, 123.5, 121.4, 120.9, 109.9, 97.5, 29.9; IR (thin film, cm^{-1}): 3054, 2947, 1572, 1492, 1324, 1274, 1207, 1136, 984, 745; HRMS (ESI): *m/z* ($M+H^+$) calcd. for $C_{11}H_{11}N_4$ 199.0984, found 199.0984.



2-Imidazol-1-yl-1-methyl-1H-indole (4c): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1) to give **4c** as yellow solid (63 mg, 64%). Mp 81-82 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (s, 1H), 7.60 (d, 1H, *J* = 8.0 Hz), 7.32-7.28 (m, 2H), 7.22-7.21 (m, 1H), 7.18-7.14 (m, 1H), 7.11 (s, 1H), 6.49 (s, 1H), 3.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.8, 135.7, 132.2, 130.1, 126.0, 123.1, 121.4, 121.2, 120.8, 109.8, 97.9, 29.3; IR (thin film, cm^{-1}): 3054, 2933, 1583, 1472, 1406, 1328, 1225, 1100, 1049, 969, 901, 742, 655; HRMS (ESI): *m/z* ($M+H^+$) calcd. for $C_{12}H_{12}N_3$ 198.1031, found 198.1033.

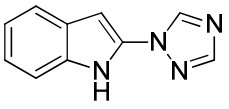


1-Methyl-2-(2-methyl-imidazol-1-yl)-1H-indole (4d): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1) to give **4d** as yellow solid (64 mg, 61%). Mp 75-76 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (d, 1H, *J* = 8.0 Hz), 7.32-7.27 (m, 2H), 7.18-7.14 (m, 1H), 7.07 (d, 1H, *J* = 1.2 Hz), 6.95 (d, 1H, *J* = 1.2 Hz), 6.47 (s, 1H), 3.36 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.6, 135.1, 131.5, 127.9, 125.7, 122.6, 121.2, 120.8, 120.3, 109.4, 98.4, 28.5, 12.7; IR (thin film, cm^{-1}): 3053, 2931, 1582, 1445, 1406, 1308, 1165, 1133, 985, 787, 742; HRMS (ESI): *m/z* ($M+H^+$) calcd. for $C_{13}H_{14}N_3$ 212.1188, found 212.1179.



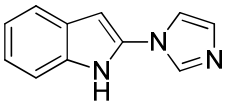
2-[1,2,3]Triazol-1-yl-1H-indole (4e): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1) to give **4e** as white solid (86 mg, 93%). Mp 174-176 °C (reported: 168-171 °C); ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.40 (br s, 1H), 8.78 (s, 1H), 8.03 (s, 1H), 7.63 (d, 1H, *J* = 7.6 Hz), 7.54 (d, 1H, *J* = 8.0 Hz), 7.22 (t, 1H, *J* = 7.6), 7.12 (t, 1H, *J* = 7.2), 6.87 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 134.4, 134.2, 131.9, 126.9, 123.8, 122.5, 120.7, 120.4, 112.0, 91.2.

Reference: Poirier, M.; Goudreau, S.; Poulin, J.; Savoie, J.; Beaulieu, P. L. *Org. Lett.* **2010**, *12*, 2334.



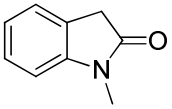
2-[1,2,4]Triazol-1-yl-1H-indole (4f): The crude product was purified by column chromatography on

silica gel (petroleum ether/ethyl acetate = 2/1) to give **4f** as pink solid (74 mg, 80%). Mp 136-138 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.24 (s, 1H), 8.33 (s, 1H), 7.58 (d, 1H, *J* = 7.6), 7.46 (d, 1H, *J* = 8.0 Hz), 7.17 (t, 1H, *J* = 7.6 Hz), 7.08 (t, 1H, *J* = 7.6 Hz), 6.76 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 152.4, 143.1, 134.1, 132.1, 127.0, 122.2, 120.4, 120.3, 111.8, 90.5; IR (thin film, cm^{-1}): 3113, 1587, 1492, 1408, 1320, 1270, 1230, 1142, 1005, 780, 746, 670; HRMS (ESI): *m/z* (M+H$^+$) calcd. for $C_{10}H_9N_4$ 185.0827, found 185.0833.



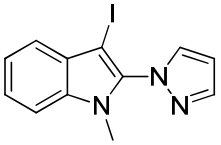
2-Imidazol-1-yl-1H-indole (4g): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1) to give **4d** as white solid (82 mg, 90%). Mp 162-163 °C (reported: 162.5-163 °C); ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.94 (br s, 1H), 8.30 (s, 1H), 7.76 (s, 1H), 7.54 (d, 1H, *J* = 8.0 Hz), 7.42 (d, 1H, *J* = 8.0 Hz), 7.17-7.13 (m, 2H), 7.09-7.05 (m, 1H), 6.60 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 135.8, 133.9, 132.7, 129.7, 127.4, 121.7, 120.2, 120.0, 118.4, 111.4, 89.9;

Reference: Poirier, M.; Goudreau, S.; Poulin, J.; Savoie, J.; Beaulieu, P. L. *Org. Lett.* **2010**, *12*, 2334.



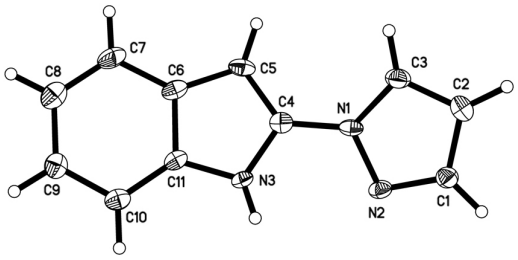
1-Methylindolin-2-one (5)[5]**:** White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30-7.23 (m, 2H), 7.04 (t, 1H, *J* = 7.6 Hz), 6.81 (d, 1H, *J* = 7.6 Hz), 3.51 (s, 2H), 3.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.2, 145.3, 127.9, 124.4, 122.4, 108.1, 35.8, 26.2.

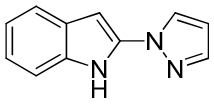
Reference: Liégault, B.; Petrov, I.; Gorelsky, S. I.; Fagnou, K. *J. Org. Chem.* **2010**, *75*, 1047.



3-Iodo-1-methyl-2-pyrazol-1-yl-1H-indole (6): White solid; Mp 87-88 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, 1H, *J* = 1.2 Hz), 7.82 (d, 1H, *J* = 2.4 Hz), 7.51 (d, 1H, *J* = 8.0 Hz), 7.40-7.36 (m, 1H), 7.34-7.28 (m, 2H), 6.56 (t, 1H, *J* = 2.0 Hz), 3.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.3, 136.3, 135.7, 133.4, 128.5, 124.1, 121.9, 121.3, 110.1, 107.0, 54.4, 30.4; IR (thin film, cm^{-1}): 2931, 1739, 1575, 941, 749; HRMS (ESI): *m/z* (M+H$^+$) calcd. for $C_{12}H_{11}IN_3$ 323.9998, found 323.9992.

X-ray Crystallography Structure of 3b





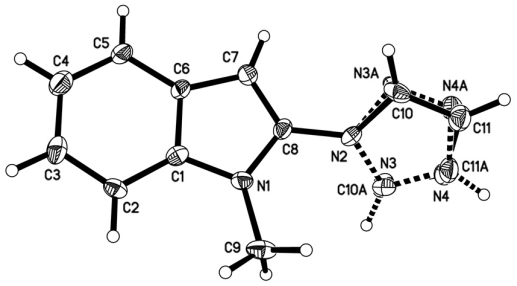
3b

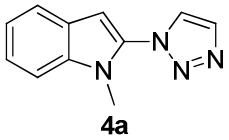
CCDC 891118 contains the supplementary crystallographic data for product **3b**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk/data_request/cif.

Table S1. Crystal data and structure refinement of **3b**

Empirical formula	C11 H9 N3	
Formula weight	183.21	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	C222(1)	
Unit cell dimensions	a = 10.7653(4) Å	α= 90°.
	b = 11.5943(4) Å	β= 90°.
	c = 29.2492(10) Å	γ = 90°.
Volume	3650.8(2) $Å^3$	
Z	16	
Density (calculated)	1.333 Mg/m^3	
Absorption coefficient	0.084 mm^{-1}	
F(000)	1536	
Crystal size	0.40 x 0.40 x 0.38 mm^3	
Theta range for data collection	1.39 to 28.31°.	
Index ranges	0<=h<=14, 0<=k<=15, 0<=l<=38	
Reflections collected	3460	
Independent reflections	3460 [R(int) = 0.0000]	
Completeness to theta = 28.31°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9689 and 0.9673	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3460 / 2 / 261	
Goodness-of-fit on F^2	1.108	
Final R indices [I>2sigma(I)]	R1 = 0.0603, wR2 = 0.1605	
R indices (all data)	R1 = 0.0748, wR2 = 0.1725	
Largest diff. peak and hole	0.309 and -0.275 $e.Å^{-3}$	

X-ray Crystallography Structure of 4a



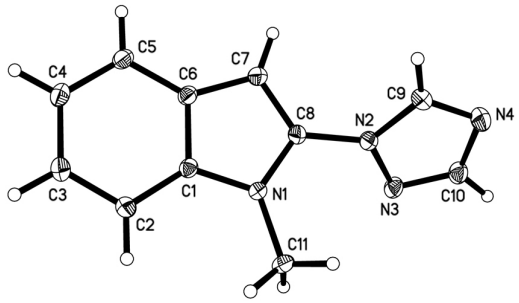


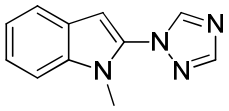
CCDC 900318 contains the supplementary crystallographic data for product **4a**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk/data_request/cif.

Table S2. Crystal data and structure refinement of **4a**

Empirical formula	C11 H10 N4	
Formula weight	198.23	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 6.8519(5) Å	α= 93.122(4)°.
	b = 8.8049(6) Å	β= 102.154(4)°.
	c = 16.1947(12) Å	γ = 93.106(4)°.
Volume	951.55(12) $Å^3$	
Z	4	
Density (calculated)	1.384 Mg/m^3	
Absorption coefficient	0.089 mm^{-1}	
F(000)	416	
Crystal size	0.22 x 0.20 x 0.14 mm^3	
Theta range for data collection	1.29 to 30.47°.	
Index ranges	-9<=h<=8, -12<=k<=10, -23<=l<=19	
Reflections collected	18166	
Independent reflections	5673 [R(int) = 0.0599]	
Completeness to theta = 26.00°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9877 and 0.9807	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5673 / 434 / 357	
Goodness-of-fit on F^2	0.855	
Final R indices [I>2sigma(I)]	R1 = 0.0617, wR2 = 0.1441	
R indices (all data)	R1 = 0.1648, wR2 = 0.2075	
Extinction coefficient	0.034(4)	
Largest diff. peak and hole	0.559 and -0.454 $e.Å^{-3}$	

X-ray Crystallography Structure of 4b





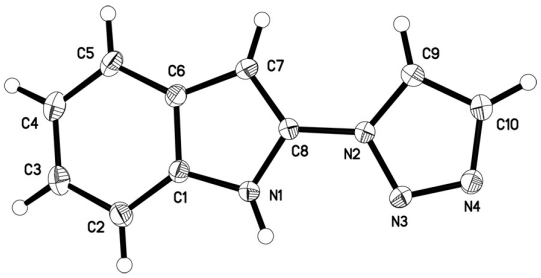
4b

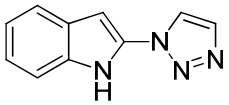
CCDC 891119 contains the supplementary crystallographic data for product **4b**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk/data_request/cif.

Table S3. Crystal data and structure refinement of **4b**

Empirical formula	C11 H10 N4	
Formula weight	198.23	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 6.9749(3) Å	α= 88.458(2)°.
	b = 8.2033(4) Å	β= 73.953(2)°.
	c = 8.5227(4) Å	γ = 87.824(2)°.
Volume	468.24(4) $Å^3$	
Z	2	
Density (calculated)	1.406 Mg/m^3	
Absorption coefficient	0.090 mm^{-1}	
F(000)	208	
Crystal size	0.40 x 0.30 x 0.20 mm^3	
Theta range for data collection	2.48 to 31.03°.	
Index ranges	-10<=h<=10, -11<=k<=11, -7<=l<=12	
Reflections collected	6479	
Independent reflections	2927 [R(int) = 0.0224]	
Completeness to theta = 25.00°	98.4 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9822 and 0.9648	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2927 / 0 / 137	
Goodness-of-fit on F^2	1.070	
Final R indices [I>2sigma(I)]	R1 = 0.0439, wR2 = 0.1145	
R indices (all data)	R1 = 0.0500, wR2 = 0.1215	
Largest diff. peak and hole	0.625 and -0.295 $e.Å^{-3}$	

X-ray Crystallography Structure of 4e





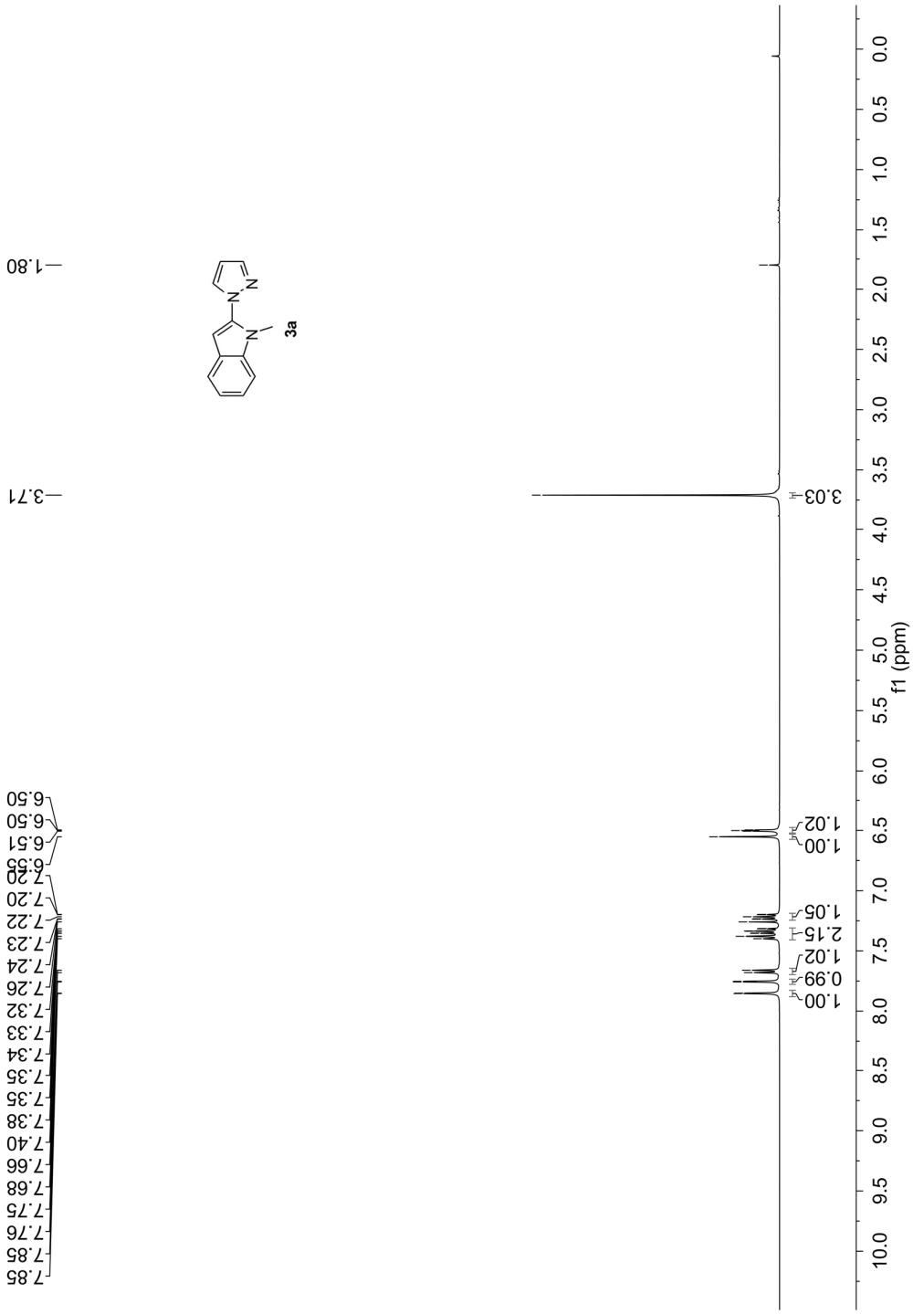
4e

CCDC 891119 contains the supplementary crystallographic data for product **4e**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk/data_request/cif.

Table S4. Crystal data and structure refinement of **4e**

Empirical formula	C10 H8 N4	
Formula weight	184.20	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 7.4156(5) Å	α= 90°.
	b = 8.8137(6) Å	β= 90°.
	c = 13.4503(9) Å	γ = 90°.
Volume	879.10(10) $Å^3$	
Z	4	
Density (calculated)	1.392 Mg/m^3	
Absorption coefficient	0.090 mm^{-1}	
F(000)	384	
Crystal size	0.40 x 0.38 x 0.05 mm^3	
Theta range for data collection	2.76 to 34.95°.	
Index ranges	-11<=h<=11, -13<=k<=12, -13<=l<=20	
Reflections collected	7313	
Independent reflections	2047 [R(int) = 0.0296]	
Completeness to theta = 25.00°	98.4 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9951 and 0.9648	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2047 / 0 / 127	
Goodness-of-fit on F^2	1.055	
Final R indices [I>2sigma(I)]	R1 = 0.0368, wR2 = 0.0984	
R indices (all data)	R1 = 0.0399, wR2 = 0.1007	
Largest diff. peak and hole	0.373 and -0.240 $e.Å^{-3}$	

Copies of NMR spectra of products



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30.0
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7.07
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6.55
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0.98
0.96
f1 (ppm)

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127.6
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120.0
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111.6
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87.5
3b
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39.7
39.5
39.3
39.1
38.9
f1 (ppm)

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2.33
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2.02
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3.21
f1 (ppm)

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119.3
109.2
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77.1
76.8
29.1
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3c
f1 (ppm)

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2.15
1.05
1.04
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1.03
3.11
f1 (ppm)

8.3
38.9
39.1
39.3
39.5
39.7
39.9
40.1
98.6
107.0
111.2
118.5
119.1
121.7
127.9
130.5
131.5
133.0
140.6
3d
f1 (ppm)

7.82
7.82
7.73
7.72
7.26
7.24
7.10
7.10
6.48
6.47
6.47
6.45
3.87
3.66
3e
0.96
1.00
1.57
1.01
1.00
0.97
1.02
3.14
3.11
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

154.7
141.8
136.1
132.3
131.0
126.4
112.9
110.5
106.8
102.7
95.6
77.4
77.1
76.8
55.9
30.1
H3CO
3e
f1 (ppm)

11.78
8.37
8.37
7.80
7.38
7.35
7.05
7.05
6.82
6.81
6.80
6.79
6.55
6.53
3.77
3.55
2.50
H3CO
3f
H2O
0.98
3.00
1.00
0.99
1.01
1.03
1.06
1.99
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

154.1
140.9
136.4
128.9
128.4
128.1
112.3
111.1
107.8
102.0
87.6
55.3
40.1
39.9
39.7
39.5
39.3
39.1
38.9
H3CO
3f
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

3g
OCH3
10.00
7.92
7.91
7.80
7.32
7.30
7.26
7.20
7.18
7.16
6.75
6.73
6.48
6.46
6.46
3.94
0.96
1.01
0.98
1.01
1.00
1.02
1.00
0.94
3.04
f1 (ppm)

146.0
140.8
135.3
129.0
127.4
123.7
120.9
112.9
107.6
102.2
87.7
77.4
77.1
76.8
55.2
OCH3
3g
f1 (ppm)

3h
Br
7.82
7.71
7.34
7.32
7.26
7.16
7.14
6.47
6.40
3.64
0.98
2.00
1.03
1.04
1.02
1.01
3.09
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

141.9
136.4
134.2
132.1
127.5
125.2
123.1
113.4
111.1
107.0
94.8
77.4
77.1
76.8
30.1
Br
3h
f1 (ppm)

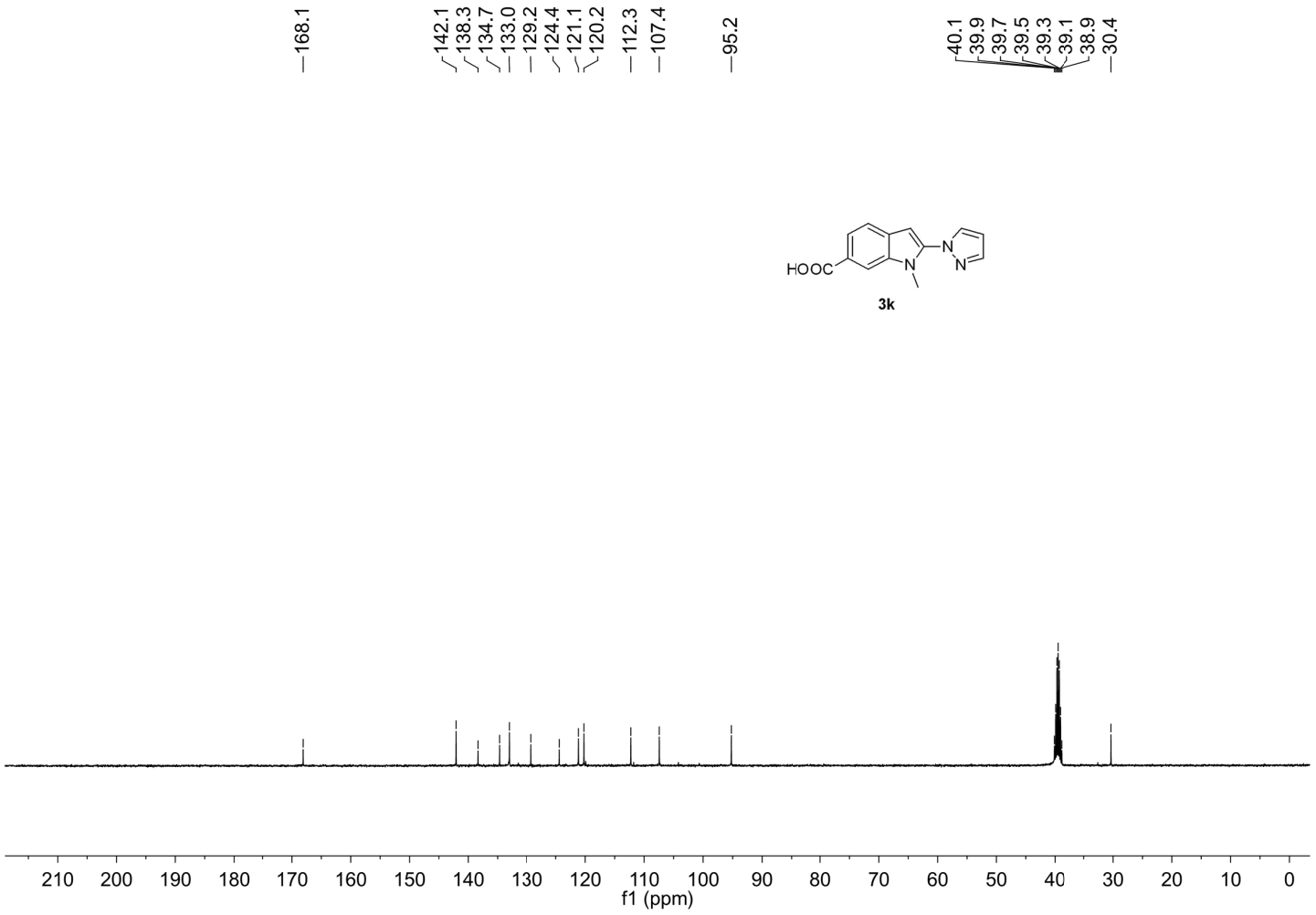
12.19
8.40
8.40
7.81
7.70
7.42
7.40
7.25
6.59
6.55
2.50
3i
Br
N
N
H
1.01
2.02
0.98
1.08
1.00
1.06
1.05
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

141.2
137.0
132.6
129.4
128.6
123.7
122.0
113.4
112.5
108.1
86.9
40.1
39.9
39.7
39.5
39.3
39.1
38.9
Br
N
N
H
3i
f1 (ppm)

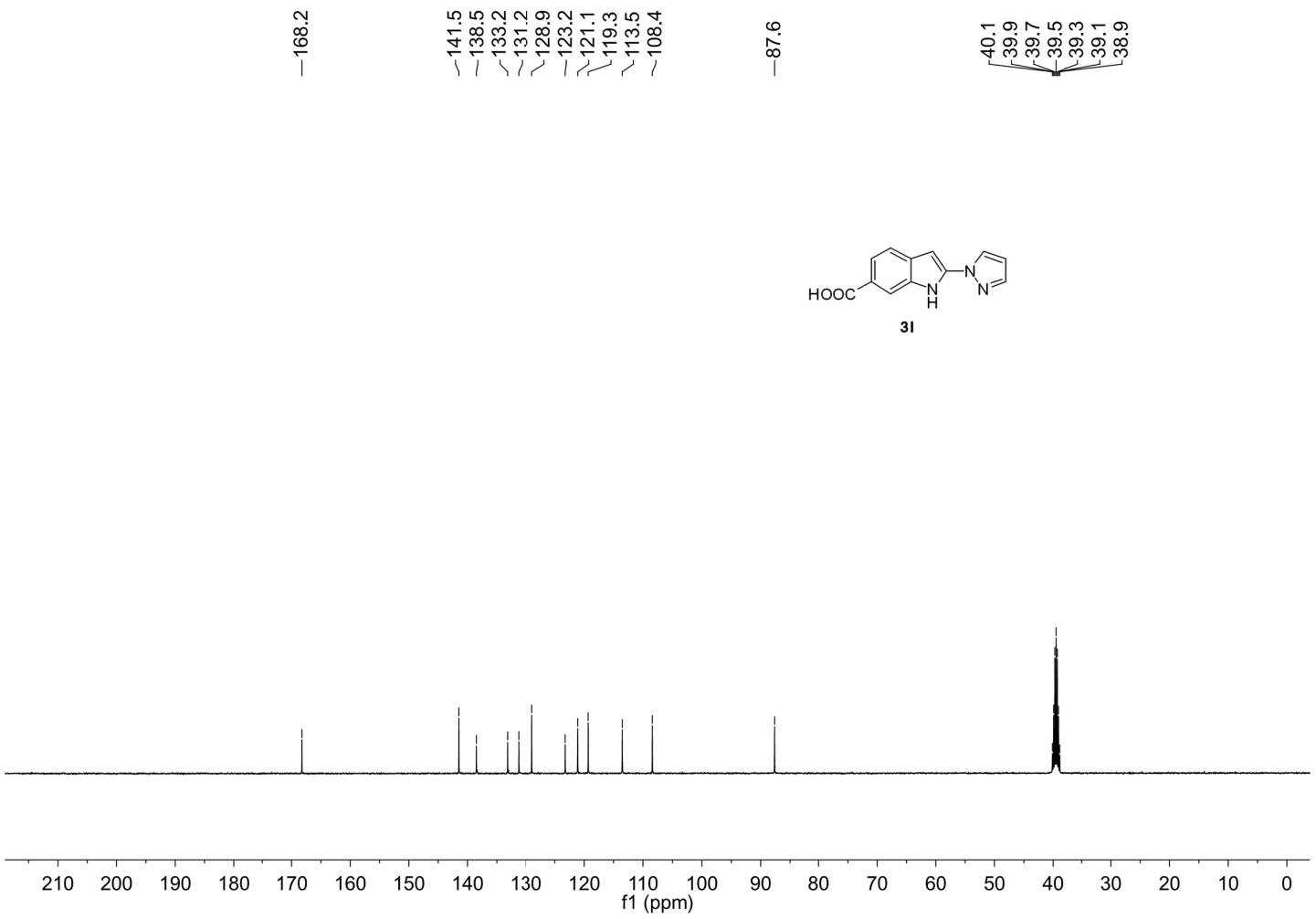
10.73
8.03
8.03
7.79
7.78
7.32
7.30
7.26
7.23
7.21
7.03
7.01
6.99
6.55
6.55
6.54
6.51
6.50
Br
N
H
N
N
3j
0.99
1.00
1.00
1.00
1.01
1.03
1.00
1.00
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

141.2
135.8
133.9
128.7
128.1
123.5
122.9
114.0
110.3
108.4
87.6
77.4
77.1
76.8
Br
N
H
N
N
3j
f1 (ppm)

8.25
8.24
8.16
7.90
7.75
7.73
7.68
7.66
6.70
6.61
3.77
3.39
2.50
HOOC
3k
1.00
0.98
1.00
1.03
0.97
0.99
0.97
3.06
H2O
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


168.1
142.1
138.3
134.7
133.0
129.2
124.4
121.1
120.2
112.3
107.4
95.2
40.1
39.9
39.7
39.5
39.3
39.1
38.9
30.4
HOOC
N
N
N
3k
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

12.52
12.29
8.49
8.07
7.84
7.69
7.67
7.58
7.56
6.71
6.60
3.45
2.50
HOOC
3l
1.71
1.00
1.00
0.96
1.00
1.00
0.98
0.99
H2O
14.0
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)


168.2
141.5
138.5
133.2
131.2
128.9
123.2
121.1
119.3
113.5
108.4
87.6
40.1
39.9
39.7
39.5
39.3
39.1
38.9
HOOC
N
H
N
N
3l
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

12.60
8.48
8.48
8.21
8.20
7.93
7.93
7.91
7.83
7.83
7.11
7.10
7.09
7.08
6.60
3o
3.37
2.50
H2O
1.07
1.97
0.99
0.94
1.05
1.02
1.00
f1 (ppm)

146.7
142.1
141.6
136.5
128.7
127.6
120.2
116.5
108.1
86.2
40.1
39.9
39.7
39.5
39.3
39.1
38.9
3o
f1 (ppm)

7.89
7.87
7.67
7.65
7.40
7.38
7.37
7.35
7.33
7.26
7.23
7.23
7.22
7.20
6.63
3.65
0.96
0.97
1.00
2.03
1.01
0.95
3.02
4a
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

136.0
133.5
131.5
126.6
125.7
123.5
121.4
120.9
109.9
97.3
77.4
77.1
76.8
30.0
4a
f1 (ppm)

8.39
8.21
7.67
7.65
7.37
7.37
7.35
7.26
7.21
6.61
3.66
0.95
0.96
1.02
2.12
1.06
1.00
3.08
4b
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

153.2
145.6
136.1
131.2
125.7
123.5
121.4
120.9
109.9
97.5
77.4
77.1
76.8
29.9
4b
f1 (ppm)

7.65
7.61
7.59
7.32
7.30
7.28
7.26
7.22
7.21
7.18
7.16
7.14
7.11
6.49
3.48
4c
1.00
0.98
1.97
1.20
1.05
0.93
0.96
2.97
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

29.3
77.4
77.1
76.8
97.9
109.8
120.8
121.2
121.4
123.1
126.0
130.1
132.2
135.7
138.8
4c
f1 (ppm)

7.63
7.61
7.32
7.30
7.29
7.29
7.27
7.27
7.26
7.18
7.18
7.17
7.16
7.16
7.15
7.14
7.07
7.07
6.95
6.94
6.47
3.36
2.23
4d
1.00
2.04
1.00
0.98
0.98
0.98
3.02
3.04
f1 (ppm)

146.6
135.1
131.5
127.9
125.7
122.6
121.2
120.8
120.3
109.4
98.4
77.4
77.1
76.8
28.5
12.7
4d
f1 (ppm)

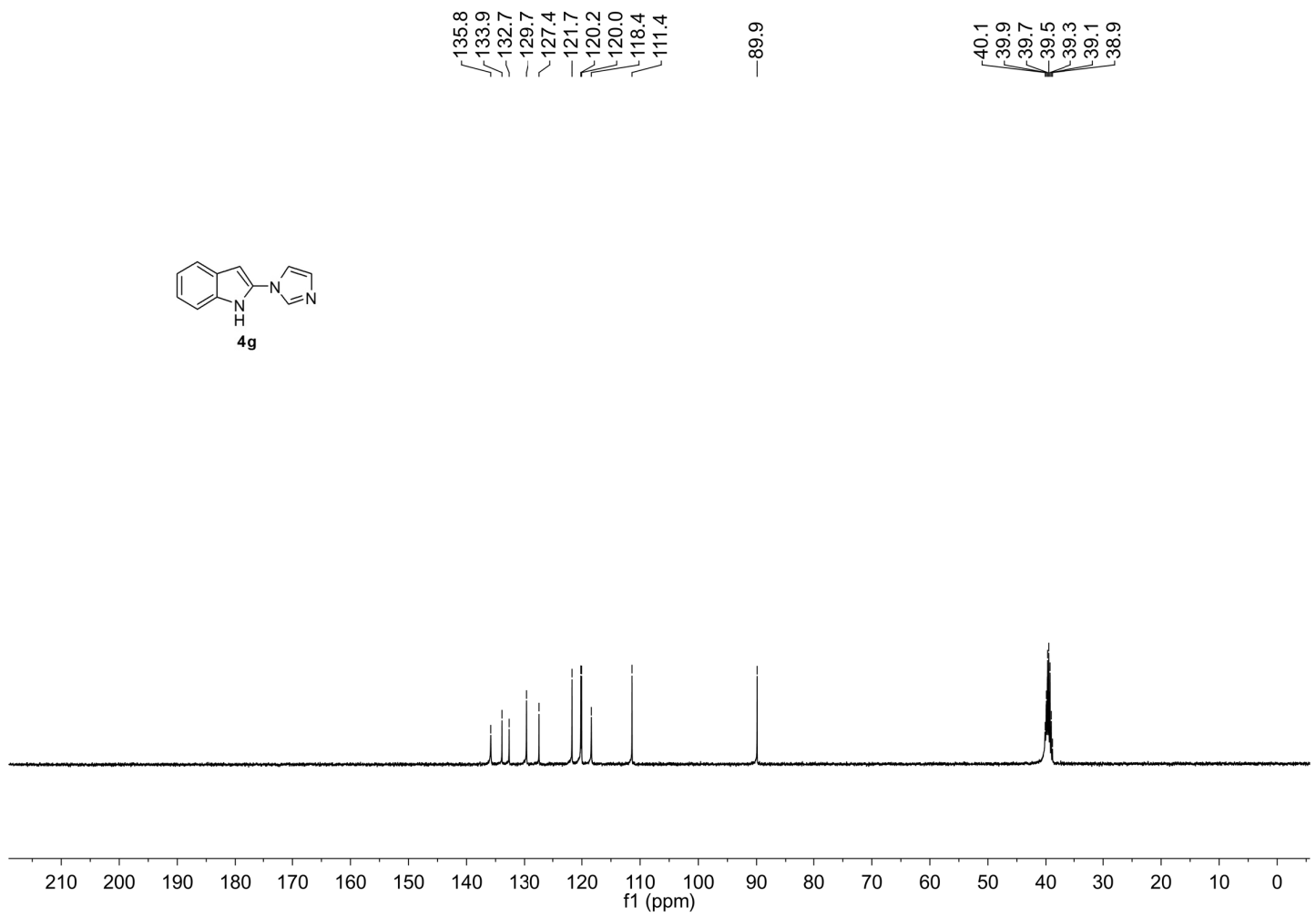
12.40
8.78
8.03
7.64
7.62
7.55
7.53
7.24
7.22
7.21
7.14
7.12
7.10
6.87
2.50
4e
1.00
1.04
1.09
1.00
1.04
1.01
1.00
1.00
14.0
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

134.4
134.2
131.9
126.9
123.8
122.5
120.7
120.4
112.0
91.2
40.1
39.9
39.7
39.5
39.3
39.1
38.9
4e
f1 (ppm)

9.24
8.33
7.59
7.57
7.47
7.44
7.19
7.17
7.15
7.10
7.08
7.06
6.76
2.50
4f
1.00
0.94
1.04
1.03
1.07
1.01
0.97
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

152.4
143.1
134.1
132.1
127.0
122.2
120.4
120.3
111.8
90.5
40.1
39.9
39.7
39.5
39.3
39.1
38.9
4f
f1 (ppm)

11.94
8.30
7.76
7.55
7.53
7.43
7.41
7.17
7.15
7.15
7.13
7.09
7.07
7.05
6.60
3.46
2.50
4g
1.00
1.03
1.03
1.04
2.04
0.99
0.97
1.04
H2O
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)


135.8
133.9
132.7
129.7
127.4
121.7
120.2
120.0
118.4
111.4
89.9
40.1
39.9
39.7
39.5
39.3
39.1
38.9
N
N
H
4g
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)