Palladium Catalyzed Cross-coupling Reactions of Potassium N-Methyltrifluoroborate Isoindolin-1-one with Aryl and Heteroaryl Chlorides

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Supplementary Material

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EXPERIMENTAL

General Experimental Considerations

All starting materials were obtained from commercial suppliers and used without further purification unless otherwise noted. All reactions were carried out under nitrogen. All solvents and deionized water were degassed with N₂ each time prior to use for cross-coupling reactions. Standard bench-top techniques were employed for handling air-sensitive reagents. NMR spectra were recorded on a 400 spectrometer. Data are represented as follows: chemical shifts (ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, br = broad), coupling constant *J* (Hz). Analytical thin-layer chromatography (TLC) was performed on TLC silica gel plates pre-coated with fluorescent indicator. Standard flash chromatography procedures were followed using silica gel 60 (230-400 mesh). Visualization was performed with ultraviolet light. Melting points are uncorrected. IR spectra were taken on FT-IR spectrophotometer.

Potassium *N*-Methyltrifluoroborate Isoindolin-1-one (6). To a 2-neck round bottom flask was added sodium hydride 60% in mineral oil (0.750 mg, 30.0 mmol) and dry THF (150 ml). Isoindolin-1-one (**5**) (2.50 g, 18.8 mmol) was added to the suspension at 0 °C under N₂. The reaction mixture was stirred for 30 min at 0 °C, then potassium bromomethyl trifluoroborate (3.00 g, 15.0 mmol) was added to the reaction mixture in one portion and stirred for 30 min at 0 °C. The reaction mixture was warmed to room temperature and refluxed for 48 h. The reaction mixture was cooled to 0 °C, and mixture quenched by KHF₂ (3.0 M) in H₂O (14 mL). The reaction mixture was stirred at room temperature for 2 h. The solvents were removed under vacuum and residue was dissolved in ethyl acetate (100 mL) and filtered. The solid obtained was triturated with boiling acetone (3 x 50 mL) and the resulting white powder was washed with cold ether (3 x 20 mL) and

dried to give the potassium *N*-methyltrifluoroborate isoindolin-1-one (**6**) as white solid (2.54 g, 65 %): mp: 229-234 °C; IR (KBr, neat): 3032, 2936, 2897, 2879, 1658, 1590, 1473, 1455, 1426, 1415, 1306, 1228, 1210, 1099, 1069, 1011, 996, 760, 726, 538 cm⁻¹; ¹H NMR (DMSO-d₆, 400 MHz) δ = 7.59 (d, *J* = 8.0 Hz, 1H), 7.53–7.46 (m, 2H), 7.42–7.39 (m, 1H), 4.38 (s, 2H), 2.47 (s, 2H); ¹³C NMR (DMSO-d₆, 100 MHz) δ = 169.9, 144.0, 131.5, 131.2, 127.5, 123.7, 122.7, 44.8; ¹¹B NMR (DMSO-d₆, 128.37 MHz) δ = 3.46 (br s); ¹⁹F NMR (DMSO-d₆, 376.49 MHz): δ = -138.67; HRMS (ESI-TOF) *m/z* calcd. for C₉H₈BNOF₃⁻ (M - K) 214.0651, found 214.0661.

General procedure for the cross-coupling reaction of Potassium *N*-Methyltrifluoroborate Isoindolin-1-one (6**) with Aryl and Heteroaryl Electrophiles (**7a-q**; **9a-l**; **11a-e**).** In a microwave vial equipped with a stirring bar were successively introduced potassium *N*-methyltrifluoroborate isoindolin-1-one (**6**) (80.1 mg, 0.316 mmol), potassium carbonate (104 mg, 0.752 mmol), Pd(MeCN)₂Cl₂ (4.9 mg, 7.5 mol %), and XPhos (17.9 mg, 15.0 mol %). The vial was capped and put under inert atmosphere (3 x vacuum/N₂ cycles). The electrophile was then introduced using a micro syringe (0.25 mmol, 1.0 equiv.) followed by 0.8 mL of degassed *t*-BuOH and 0.2 mL of degassed distilled water. The resulting mixture was then placed in an oil bath or a hotplate-magnetic stirrer system preheated at 100 °C and stirred at this temperature for overnight (reactions followed by TLC). After cooling to room temperature, the vial was uncapped and the reaction mixture was diluted with dichloromethane (5 mL) and water (5 mL). The aqueous layer was extracted with dichloromethane (3 x 15 mL). Organic layers were combined, washed with brine solution and dried over Na₂SO₄, and the solvent was removed under vacuum to yield the crude product. The crude product was purified by flash column chromatography on silica gel using 30% ethyl acetate/hexane as the eluent.

2-(4-Methoxybenzyl)isoindolin-1-one (8a).^[1] White solid (52.5 mg, 83%): mp: 98-100 °C; IR (KBr, neat): 3056, 2964, 2925, 2837, 1769, 1673, 1511, 1468, 1411, 1241, 1178, 1028, 979 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ = 7.89 (d, J = 8.8 Hz, 1H), 7.50-7.45 (m, 2H), 7.37 (d, J = 4.0 Hz, 1H), 7.25 (d, J = 8.0 Hz, 2H), 6.87 (d, J = 8.0 Hz, 2H), 4.74 (s, 2H), 4.25 (s, 2H), 3.78 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ = 169.6, 160.7, 142.7, 134.3, 132.8, 131.1, 129.4, 125.2, 124.1, 115.7, 56.7, 50.7, 47.3; HRMS (ESI-TOF) m/z calcd. for C₁₆H₁₅NO₂⁺ (M + Na⁺) 276.1000, found 276.1004.

2-(2-Methoxybenzyl)isoindolin-1-one (8b). White solid (50.0 mg, 79%): mp: 93-96 °C; ¹H NMR (CDCl₃, 400 MHz) δ = 7.88 (d, J = 8.0 Hz, 1H), 7.51-7.42 (m, 2H), 7.38 (d, J = 8.0 Hz, 1H), 7.25 (t, J = 8.0 Hz, 2.0 Hz, 2H), 6.90 (t, J = 8.0 Hz, 2H), 4.85 (s, 2H), 4.31 (s, 2H), 3.87 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ 168.4, 157.2, 141.5, 132.9, 130.8, 130.0, 129.1, 127.8, 125.1, 123.6, 122.7, 120.6, 110.3, 55.3, 49.8, 40.9; HRMS (ESI-TOF) m/z calcd. for C₁₆H₁₅NO₂⁺ (M + Na⁺) 276.1000, found 276.1011.

2-(3-Methoxybenzyl)isoindolin-1-one (8c).^[2] Pale yellow oil (51.9 mg, 82%): ¹H NMR (CDCl₃, 400 MHz) δ = 7.90 (d, J = 8.8 Hz, 1H), 7.54-7.45 (m, 2H), 7.39 (d, J = 4.0 Hz, 1H), 7.26 (d, J = 8.0 Hz, 1H), 6.88 (d, J = 8.0 Hz, 1H), 6.81 (t, J = 8.0 Hz, 2H), 4.77 (s, 2H), 4.27 (s, 2H), 3.78 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ 168.5, 160.0, 141.2, 138.6, 132.6, 131.4, 129.9, 128.1, 123.9, 122.8, 120.5, 113.8, 113.2, 55.2, 49.5, 46.4; HRMS (ESI-TOF) m/z calcd. for C₁₆H₁₅NO₂⁺ (M + Na⁺) 276.1000, found 276.0983.

2-(3,5-Dimethoxybenzyl)isoindolin-1-one (8d). Colorless oil (44.6 mg, 63%): ¹H NMR (CDCl₃, 400 MHz) δ = 7.90 (d, J = 8.8 Hz, 1H), 7.53-7.41 (m, 2H), 7.39 (d, J = 8.0 Hz, 2H), 6.45 (d, J = 2.0 Hz, 1H), 6.37 (t, J = 2.0 Hz, 1H), 4.73 (s, 2H), 4.28 (s, 2H), 3.75 (s, 6H); ¹³C NMR (CDCl₃,

100 MHz) δ 168.6, 161.2, 141.1, 139.4, 132.7, 131.2, 128.4, 124.0, 123.0, 106.1, 99.5, 55.2, 49.7, 46.7; HRMS (ESI-TOF) m/z calcd. for $C_{17}H_{17}NO_3^+$ ($M + Na^+$) 306.1106, found 306.1119.

2-Benzylisoindolin-1-one (8e).^[3] White solid (51.9 mg, 93%): mp: 86-89 °C, lit.^[3] 87-89 °C; 1H NMR ($CDCl_3$, 400 MHz) δ = 7.90 (d, J = 8.8 Hz, 1H), 7.53-7.44 (m, 2H), 7.38-7.25 (m, 6H), 4.83 (s, 2H), 4.27 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.5, 141.2, 137.4, 132.8, 132.6, 131.4, 129.0, 128.3, 128.1, 128.0, 127.7, 123.7, 122.7, 49.5, 46.4; HRMS (ESI-TOF) m/z calcd. for $C_{15}H_{13}NO^+$ ($M + Na^+$) 246.0895, found 246.0886.

2-(4-Methylbenzyl)isoindolin-1-one (8f).^[2] White solid (55.2 mg, 93%): mp: 70-73 °C; IR (KBr, neat): 3007, 2920, 1675, 1514, 1470, 1409, 1273, 1211, 1191, 1108, 1024, 943 cm^{-1} ; 1H NMR ($CDCl_3$, 400 MHz) δ = 7.89 (d, J = 8.0 Hz, 1H), 7.52-7.43 (m, 2H), 7.38 (d, J = 4.0 Hz, 1H), 7.20 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 8.0 Hz, 2H), 4.77 (s, 2H), 4.25 (s, 2H), 2.33 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 168.5, 141.4, 137.2, 134.1, 132.7, 131.3, 129.6, 128.1, 127.9, 123.8, 122.6, 49.4, 46.2, 21.1; HRMS (ESI-TOF) m/z calcd. for $C_{16}H_{15}NO^+$ ($M + Na^+$) 260.1051, found 260.1049.

2-(2-Methylbenzyl)isoindolin-1-one (8g).^[4] Colorless oil (36.2 mg, 61%): 1H NMR ($CDCl_3$, 400 MHz) δ = 7.90 (d, J = 8.2 Hz, 1H), 7.53-7.44 (m, 2H), 7.37 (d, J = 8.0 Hz, 1H), 7.21-7.17 (m, 4H), 4.83 (s, 2H), 4.18 (s, 2H), 2.35 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.2, 141.2, 136.8, 134.7, 132.6, 131.3, 130.7, 129.0, 128.0, 127.9, 126.2, 123.8, 122.7, 49.3, 44.6, 19.0; HRMS (ESI-TOF) m/z calcd. for $C_{16}H_{15}NO^+$ ($M + Na^+$) 260.1051, found 260.1049.

2-(3-Methylbenzyl)isoindolin-1-one (8h).^[5] Colorless oil (47.4 mg, 80%): 1H NMR ($CDCl_3$, 400 MHz) δ = 7.91 (d, J = 8.2 Hz, 1H), 7.53-7.44 (m, 2H), 7.39 (d, J = 8.0 Hz, 1H), 7.24 (t, J = 8.0 Hz, 1H), 7.12-7.08 (m, 3H), 4.79 (s, 2H), 4.25 (s, 2H), 2.33 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz)

δ 168.4, 141.1, 138.5, 136.9, 133.1, 131.3, 129.1, 128.6, 128.1, 128.0, 125.3, 124.1, 122.8, 49.5, 46.3, 21.1; HRMS (ESI-TOF) m/z calcd. for $C_{16}H_{15}NO^+$ ($M + Na^+$) 260.1051, found 260.1070.

2-(2,6-Dimethylbenzyl)isoindolin-1-one (8i).^[3] White solid (39.6 mg, 63%): mp: 143-146 °C; 1H NMR ($CDCl_3$, 400 MHz) δ = 7.88 (d, J = 8.0 Hz, 1H), 7.50-7.43 (m, 2H), 7.32 (d, J = 8.0 Hz, 1H), 7.15-7.11 (m, 1H), 7.06 (d, J = 4.0 Hz, 2H), 4.89 (s, 2H), 4.04 (s, 2H), 2.39 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 168.0, 141.4, 138.0, 132.6, 131.0, 128.4, 128.0, 123.8, 122.4, 48.4, 40.3, 20.0; HRMS (ESI-TOF) m/z calcd. for $C_{17}H_{17}NO^+$ ($M + H^+$) 252.1388, found 252.1396.

Methyl 4-((1-oxoisoindolin-2-yl)methyl)benzoate (8j). White solid (60.1 mg, 89%): mp: 118-120 °C; IR (KBr, neat): 3006, 2929, 1727, 1674, 1473, 1276, 1186, 1103, 1023, 956 cm^{-1} ; 1H NMR ($CDCl_3$, 400 MHz) δ = 8.01 (d, J = 8.0 Hz, 2H), 7.92 (d, J = 8.0 Hz, 1H), 7.55-7.46 (m, 2H), 7.40 - 7.35 (m, 3H), 4.86 (s, 2H), 4.28 (s, 2H), 3.92 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.3, 166.4, 141.7, 140.4, 131.8, 131.1, 129.6, 128.8, 127.7, 127.5, 123.6, 122.1, 51.7, 48.9, 45.7; HRMS (ESI-TOF) m/z calcd. for $C_{17}H_{15}NO_3^+$ ($M + Na^+$) 304.0950, found 304.0928.

2-(4-Acetylbenzyl)isoindolin-1-one (8k). White solid (57.0 mg, 86%): mp: 111-114 °C; IR (KBr, neat): 3009, 2923, 1679, 1608, 1470, 1407, 1352, 1265, 1108, 1019, 954 cm^{-1} ; 1H NMR ($CDCl_3$, 400 MHz) δ = 7.91 (t, J = 8.0 Hz and 2.0 Hz, 3H), 7.56 - 7.46 (m, 2H), 7.40 (d, J = 8.0 Hz, 3H), 4.87 (s, 2H), 4.28 (s, 2H), 2.59 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 197.3, 167.9, 141.9, 140.6, 136.1, 131.8, 131.0, 128.4, 127.4, 123.6, 122.3, 49.1, 45.6, 26.1; HRMS (ESI-TOF) m/z calcd. for $C_{17}H_{15}NO_2^+$ ($M + Na^+$) 288.1000, found 288.1017.

2-(2-Methylbenzophenone)isoindolin-1-one (8l). Pale yellow oil (49.1 mg, 60%); IR (neat): 3060, 2987, 2929, 2855, 1684, 1660, 1596, 1448, 1408, 1265, 1209, 1153, 1098, 976, 930 cm^{-1} ; 1H NMR ($CDCl_3$, 400 MHz) δ = 7.85 - 7.81 (m, 3H), 7.59 (t, J = 4.0 Hz, 1H), 7.52 - 7.32 (m, 9H),

4.86 (s, 2H), 4.32 (s, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 197.8, 168.7, 145.6, 141.9, 138.3, 137.5, 136.6, 133.3, 132.3, 131.1, 130.3, 130.0, 128.8, 127.8, 126.8, 124.1, 122.5, 120.3, 50.1, 43.6; HRMS (ESI-TOF) m/z calcd. for $\text{C}_{22}\text{H}_{17}\text{NO}_2^+$ ($\text{M} + \text{Na}^+$) 350.1157, found 350.1137.

2-(4-(1H-Pyrrol-1-yl)benzyl)isoindolin-1-one (8m). White solid (51.2 mg, 71%): mp: 156-158 °C; IR (KBr, neat): 3102, 2910, 1680, 1527, 1410, 1327, 1209, 1069, 913 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ = 7.90 (d, J = 8.0 Hz, 1H), 7.58 - 7.48 (m, 2H), 7.39 (bs, 1H), 7.35 (m, 4H), 7.07 (t, J = 2.0 Hz, 2H), 6.34 (t, J = 2.0 Hz, 2H), 4.82 (s, 2H), 4.31 (s, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 168.1, 140.9, 139.9, 134.1, 132.2, 130.8, 129.1, 128.0, 123.6, 122.5, 120.4, 118.9, 110.2, 49.2, 45.4; HRMS (ESI-TOF) m/z calcd. for $\text{C}_{19}\text{H}_{16}\text{N}_2\text{O}^+$ ($\text{M} + \text{Na}^+$) 311.1160, found 311.1180.

4-((1-Oxoisindolin-2-yl)methyl)benzaldehyde (8n). White solid (35.2 mg, 56%): mp: 77-80 °C; IR (KBr, neat): 3038, 2924, 1702, 1673, 1472, 1393, 1209, 1172, 1087, 974 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ = 10.0 (s, 1H), 7.93 (d, J = 8.0 Hz, 1H), 7.84 (d, J = 8.0 Hz, 2H), 7.56-7.46 (m, 4H), 7.42 (d, J = 8.0 Hz, 1H), 4.90 (s, 2H), 4.30 (s, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 192.0, 168.7, 144.1, 141.1, 135.6, 132.1, 131.6, 130.3, 128.6, 124.3, 122.8, 49.8, 46.1; HRMS (ESI-TOF) m/z calcd. for $\text{C}_{16}\text{H}_{13}\text{NO}_2^+$ ($\text{M} + \text{Na}^+$) 274.0844, found 274.0862.

4-((1-Oxoisindolin-2-yl)methyl)benzonitrile (8o).^[6] White solid (39.1 mg, 63%): mp: 137-139 °C, Lit.^[6] 130-135 °C; IR (KBr, neat): 3054, 2923, 2225, 1681, 1469, 1404, 1281, 1210, 1115, 986, 921 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ = 7.91 (d, J = 8.0 Hz, 1H), 7.64 (d, J = 8.0 Hz, 2H), 7.57-7.47 (m, 2H), 7.42 (d, J = 8.0 Hz, 3H), 4.86 (s, 2H), 4.31 (s, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 168.7, 142.7, 141.0, 132.7, 132.1, 131.8, 128.8, 128.2, 124.1, 123.0, 118.6, 111.7, 49.7, 46.3; HRMS (ESI-TOF) m/z calcd. for $\text{C}_{16}\text{H}_{12}\text{N}_2\text{O}^+$ ($\text{M} + \text{Na}^+$) 271.0847, found 271.0860.

2-(4-Nitrobenzyl)isoindolin-1-one (8p). Yellow solid (34.9 mg, 52%): mp: 147-149 °C; IR (KBr, neat): 3036, 2927, 1692, 1525, 1448, 1343, 1209, 1152, 1100, 942 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ = 8.20 (d, J = 8.0 Hz, 2H), 7.92 (d, J = 8.0 Hz, 1H), 7.61-7.41 (m, 5H), 4.92 (s, 2H), 4.33 (s, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 168.8, 147.7, 144.6, 141.1, 132.0, 131.8, 128.7, 128.3, 124.1, 122.9, 49.8, 46.0; HRMS (ESI-TOF) m/z calcd. for $\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}_3^+$ ($\text{M} + \text{Na}^+$) 291.0746, found 291.0756.

2-(4-Fluorobenzyl)isoindolin-1-one (8q).^[2] White solid (45.2 mg, 75%): mp: 93-95 °C; IR (KBr, neat): 3004, 2954, 2925, 1672, 1510, 1471, 1221, 1192, 1094, 973 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ = 7.90 (d, J = 8.0 Hz, 1H), 7.54-7.45 (m, 2H), 7.39 (d, J = 4 Hz, 1H), 7.30-7.26 (m, 2H), 7.04-6.99 (m, 2H), 4.77 (s, 2H), 4.26 (s, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 168.5, 163.6, 161.2, 141.2, 132.9, 132.6, 131.4, 129.9, 128.1, 124.0, 122.8, 115.8, 115.5, 49.4, 45.6; ^{19}F NMR (CDCl_3 , 376.49 MHz) δ = -114.6; HRMS (ESI-TOF) m/z calcd. for $\text{C}_{15}\text{H}_{12}\text{FNO}^+$ ($\text{M} + \text{Na}^+$) 264.0801, found 264.0814.

2-((6-Methoxypyridin-3-yl)methyl)isoindolin-1-one (10a). White solid (37.5 mg, 59%): mp: 97-99 °C; IR (KBr, neat): 3020, 2927, 1680, 1613, 1497, 1471, 1311, 1298 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ = 8.12 (d, J = 4.0 Hz, 1H), 7.88 (d, J = 4.0 Hz, 1H), 7.58-7.44 (m, 3H), 7.39 (d, J = 8.0 Hz, 1H), 6.73 (d, J = 8.0 Hz, 1H), 4.74 (s, 2H), 4.26 (s, 2H), 3.92 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 168.6, 164.0, 146.3, 140.9, 139.0, 132.6, 131.8, 128.4, 125.5, 124.0, 122.8, 111.3, 53.6, 49.4, 43.4; HRMS (ESI-TOF) m/z calcd. for $\text{C}_{15}\text{H}_{14}\text{N}_2\text{O}_2^+$ ($\text{M} + \text{Na}^+$) 277.0953, found 277.1094.

2-((6-Fluoropyridin-3-yl)methyl)isoindolin-1-one (10b). White solid (32.1 mg, 53%): mp: 121-124 °C; IR (KBr, neat): 3045, 2925, 1674, 1594, 1473, 1397, 1294, 1243, 1117, 1026, 956 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ = 8.20 (d, J = 4.0 Hz, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.80 (dt, J = 4.0 Hz, 1H), 7.56 (dt, J = 8.0 and 2 Hz, 1H), 7.54 (t, J = 6.0 Hz, 1H), 7.43 (d, J = 8.0 Hz, 1H), 6.92 (dd, J = 8.0 Hz, 2.0 Hz 1H), 4.81(s, 2H), 4.30 (s, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 168.8, 164.7, 162.5, 147.1, 141.5, 132.0, 130.7, 128.6, 124.1, 123.0, 110.3, 49.65, 43.2; ^{19}F NMR (CDCl_3 , 376.49 MHz) δ = -68.8, HRMS (ESI-TOF) m/z calcd. for $\text{C}_{14}\text{H}_{11}\text{FN}_2\text{O}^+$ ($\text{M} + \text{Na}^+$) 265.0753, found 265.0740.

2-((5-Acetylthiophen-2-yl)methyl)isoindolin-1-one (10c). White solid (44.7 mg, 66%): mp: 123-126 °C; IR (KBr, neat): 3058, 2953, 2853, 1680, 1654, 1468, 1355, 1274, 1120, cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ = 7.88 (d, J = 8.0 Hz, 1H), 7.56-7.45 (m, 3H), 7.43 (d, J = 8.0 Hz, 1H), 7.06 (d, J = 4.0 Hz, 1H), 4.96 (s, 2H), 4.39 (s, 2H), 2.52 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 190.5, 167.9, 148.9, 144.4, 141.1, 132.6, 132.0, 131.7, 128.1, 127.3, 124.1, 122.8, 49.6, 41.1, 26.5; HRMS (ESI-TOF) m/z calcd. for $\text{C}_{15}\text{H}_{13}\text{NO}_2\text{S}^+$ ($\text{M} + \text{H}^+$) 272.0745, found 272.0738.

5-((1-Oxoisindolin-2-yl)methyl)thiophene-2-carbaldehyde (10d). Pale yellow solid (30.2 mg, 47%): mp: 45-48 °C; IR (neat): 3054, 2924, 2854, 1773, 1680, 1620, 1532, 1469, 1455, 1407, 1301, 1210, 1177, 1045, 981 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ = 9.85 (s, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.50 (t, J = 4.0 Hz, 1H), 7.45 (t, J = 4.0 Hz, 1H), 7.15 (d, J = 4.0 Hz 1H), 5.03 (s, 3H), 4.42 (s, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 182.6, 168.3, 150.2, 143.4, 141.6, 141.0, 136.5, 131.8, 128.2, 127.5, 123.9, 122.8, 49.5, 41.3; HRMS (ESI-TOF) m/z calcd. for $\text{C}_{14}\text{H}_{11}\text{NO}_2\text{S}^+$ ($\text{M} + \text{Na}^+$) 280.0408, found 280.0428.

2-((Thiophen-2-yl)methyl)isoindoline-1-one (10e).^[7] White solid in (34.9 mg 61%): mp: 89-92 °C, Lit.^[7] 92-94 °C; IR (neat): 3093, 2927, 2855, 1680, 1620, 1469, 1454, 1406, 1328, 1299, 1209, 1151, 1086, 986 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ = 7.89 (d, J = 8.0 Hz, 1H), 7.54 (dt, J = 8.0 Hz, 2.0 Hz, 1H), 7.47 (t, J = 8.0 Hz, 1H), 7.41 (d, J = 8.0 Hz, 1H), 7.26 (dd, J = 8.0, 4.0 Hz, 1H), 7.06 (d, J = 4.0 Hz, 1H), 7.00–6.97 (m, 1H), 4.82 (s, 2H), 4.28 (s, 2H); ¹³C NMR (CDCl₃, 100 MHz) δ 168.1, 141.2, 139.4, 132.4, 131.4, 128.0, 127.0, 126.7, 125.7, 124.0, 122.8, 49.2, 40.8; HRMS (ESI-TOF) m/z calcd. for C₁₃H₁₁NOS⁺ (M + Na⁺) 252.0459, found 252.0472.

3-((Thiophen-2-yl)methyl)isoindoline-1-one (10f).^[7] White solid (39.5 mg, 69%): mp: 62-65 °C, Lit.^[7] 65-66 °C; ¹H NMR (CDCl₃, 400 MHz) δ = 7.88 (d, J = 8.0 Hz, 1H), 7.54 (dt, J = 8.0 Hz, 2.0 Hz, 1H), 7.46 (t, J = 8.0 Hz, 1H), 7.39 (d, J = 8.0 Hz, 1H), 7.30–7.28 (m, 1H), 7.21 (d, J = 4.0 Hz, 1H), 7.06 (dd, J = 8.0 Hz, 4.0 Hz, 1H), 4.98 (s, 2H), 4.35 (s, 2H); ¹³C NMR (CDCl₃, 100 MHz) δ 168.2, 141.2, 137.8, 132.7, 131.3, 128.0, 127.6, 126.5, 123.9, 123.0, 122.7, 49.4, 41.3; HRMS (ESI-TOF) m/z calcd. for C₁₃H₁₁NOS⁺ (M + Na⁺) 252.0459, found 252.0476.

5-((1-Oxoisindolin-2-yl)methyl)furan-2-carbaldehyde (10g). Pale yellow solid (31.9 mg, 53 %): mp: 54-57 °C; IR (neat): 3117, 2924, 2852, 1674, 1620, 1519, 1455, 1404, 1366, 1300, 1209, 1021, 968 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ = 9.59 (s, 1H), 7.86 (d, J = 8.0 Hz, 1H), 7.56 (t, J = 8.0 Hz, 4.0 Hz, 1H), 7.49–7.44 (m, 2H), 7.20 (d, J = 4.0 Hz, 1H), 6.52 (d, 1H), 4.88 (s, 2H), 4.49 (s, 2H); ¹³C NMR (CDCl₃, 100 MHz) δ 177.5, 168.4, 157.2, 152.7, 141.2, 131.9, 128.3, 124.1, 123.0, 111.0, 50.2, 39.3; HRMS (ESI-TOF) m/z calcd. for C₁₄H₁₁NO₃⁺ (M + Na⁺) 264.0637, found 264.0623.

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¹H NMR (DMSO-d₆, 400 MHz) spectrum of potassium N-methyltrifluoroborate isoindolin-1-one
(**6**)

^{13}C NMR (DMSO- d_6 , 100 MHz) spectrum of potassium N-methyltrifluoroborate isoindolin-1-one (**6**)

^{11}B NMR (DMSO- d_6 , 128.37 MHz) spectrum of potassium N-methyltrifluoroborate isoindolin-1-one (**6**)

^{19}F NMR (DMSO- d_6 , 376.49 MHz) spectrum of potassium N-methyltrifluoroborate isoindolin-1-one (**6**)

^1H NMR (CDCl_3 , 400 MHz) spectrum of 2-(4-methoxybenzyl)isoindolin-1-one (**8a**)

^{13}C NMR (CDCl_3 , 100 MHz) spectrum of 2-(4-methoxybenzyl)isoindolin-1-one (**8a**)

^1H NMR (CDCl_3 , 400 MHz) spectrum of 2-(2-methoxybenzyl)isoindolin-1-one (**8b**)

^{13}C NMR (CDCl_3 , 100 MHz) spectrum of 2-(2-methoxybenzyl)isoindolin-1-one (**8b**)

^1H NMR (CDCl_3 , 400 MHz) of 2-(3-methoxybenzyl)isoindolin-1-one (**8c**)

^{13}C NMR (CDCl_3 , 100 MHz) spectrum of 2-(3-methoxybenzyl)isoindolin-1-one (**8c**)

^1H NMR (CDCl_3 , 400 MHz) of 2-(3,5-dimethoxybenzyl)isoindolin-1-one (**8d**)

^{13}C NMR (CDCl_3 , 100 MHz) spectrum of 2-(3,5-dimethoxybenzyl)isoindolin-1-one (**8d**)

^1H NMR (CDCl_3 , 400 MHz) spectrum of 2-benzylisoindolin-1-one (**8e**)

8e

c1ccc(cc1)CN2Cc3ccccc3C2=O

16.57
12.71
12.68
12.63
12.60
12.58
12.44
12.44
12.07
12.07
12.03
12.01
11.70
11.70
11.70
11.70
11.70
11.70
77.19
77.04
76.71
48.52
46.42

170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

Chemical structure of **8f** is shown in the inset:

Cc1ccc(cc1)CN2C(=O)c3ccccc32

The ¹H NMR spectrum (CDCl₃) shows the following chemical shifts (ppm):

- 7.898, 7.881, 7.528, 7.524, 7.510, 7.505, 7.491, 7.487, 7.476, 7.460, 7.439, 7.380, 7.360, 7.209, 7.191, 7.146, 7.127
- 4.775
- 4.250
- 2.326

The spectrum displays a complex aromatic region (7.1-7.9 ppm), a methine doublet (4.250 ppm), a methoxy singlet (3.8 ppm), a methoxy singlet (3.7 ppm), a methoxy singlet (3.6 ppm), a methoxy singlet (3.5 ppm), a methoxy singlet (3.4 ppm), a methoxy singlet (3.3 ppm), a methoxy singlet (3.2 ppm), a methoxy singlet (3.1 ppm), a methoxy singlet (3.0 ppm), a methoxy singlet (2.9 ppm), a methoxy singlet (2.8 ppm), a methoxy singlet (2.7 ppm), a methoxy singlet (2.6 ppm), a methoxy singlet (2.5 ppm), a methoxy singlet (2.4 ppm), a methoxy singlet (2.3 ppm), a methoxy singlet (2.2 ppm), a methoxy singlet (2.1 ppm), a methoxy singlet (2.0 ppm), a methoxy singlet (1.9 ppm), a methoxy singlet (1.8 ppm), a methoxy singlet (1.7 ppm), a methoxy singlet (1.6 ppm), a methoxy singlet (1.5 ppm), a methoxy singlet (1.4 ppm), a methoxy singlet (1.3 ppm), a methoxy singlet (1.2 ppm), a methoxy singlet (1.1 ppm), a methoxy singlet (1.0 ppm), a methoxy singlet (0.9 ppm), a methoxy singlet (0.8 ppm), a methoxy singlet (0.7 ppm), a methoxy singlet (0.6 ppm), a methoxy singlet (0.5 ppm), a methoxy singlet (0.4 ppm), a methoxy singlet (0.3 ppm), a methoxy singlet (0.2 ppm), a methoxy singlet (0.1 ppm).

^{13}C NMR (CDCl_3 , 100 MHz) spectrum of 2-(4-methylbenzyl)isoindolin-1-one (**8f**)

^1H NMR (CDCl_3 , 400 MHz) spectrum of 2-(2-methylbenzyl)isoindolin-1-one (**8g**)

^{13}C NMR (CDCl_3 , 100 MHz) spectrum of 2-(2-methylbenzyl)isoindolin-1-one (**8g**)

^1H NMR (CDCl_3 , 400 MHz) spectrum of 2-(3-methylbenzyl)isoindolin-1-one (**8h**)

^{13}C NMR (CDCl_3 , 100 MHz) spectrum of 2-(3-methylbenzyl)isoindolin-1-one (**8h**)

^1H NMR (CDCl_3 , 400 MHz) spectrum of 2-(2,6-dimethylbenzyl)isoindolin-1-one (**8i**)

^{13}C NMR (CDCl_3 , 100 MHz) spectrum of 2-(2,6-dimethylbenzyl)isoindolin-1-one (**8i**)

^1H NMR (CDCl_3 , 400 MHz) spectrum of methyl 4-((1-oxoisindolin-2-yl)methyl) benzoate (**8j**)

^{13}C NMR (CDCl_3 , 100 MHz) spectrum of methyl 4-((1-oxoisindolin-2-yl)methyl) benzoate (**8j**)

^1H NMR (CDCl_3 , 400 MHz) spectrum of 2-(4-acetylbenzyl)isoindolin-1-one (**8k**)

^{13}C NMR (CDCl_3 , 100 MHz) spectrum of 2-(4-acetylbenzyl)isoindolin-1-one (**8k**)

^1H NMR (CDCl_3 , 400 MHz) spectrum of 2-(2-methylbenzophenone)isoindolin-1-one (**8l**)

^{13}C NMR (CDCl_3 , 100 MHz) spectrum of 2-(2-methylbenzophenone)isoindolin-1-one (**8I**)

^1H NMR (CDCl_3 , 400 MHz) spectrum of 2-(4-(1H-pyrrol-1-yl)benzyl)isoindolin-1-one (**8m**)

^{13}C NMR (CDCl_3 , 100 MHz) spectrum of 2-(4-(1H-pyrrol-1-yl)benzyl)isoindolin-1-one (**8m**)

^1H NMR (CDCl_3 , 400 MHz) spectrum of 4-((1-oxoisindolin-2-yl)methyl) benzaldehyde (**8n**)

^{13}C NMR (CDCl_3 , 100 MHz) spectrum of 4-((1-oxoisindolin-2-yl)methyl)benzaldehyde (**8n**)

^1H NMR (CDCl_3 , 400 MHz) spectrum of 4-((1-oxoisindolin-2-yl)methyl)benzonitrile (**8o**)

^{13}C NMR (CDCl_3 , 100 MHz) spectrum of 4-((1-oxoisindolin-2-yl)methyl)benzonitrile (**8o**)

^1H NMR (CDCl_3 , 400 MHz) spectrum of 2-(4-nitrobenzyl)isoindolin-1-one (**8p**)

^{13}C NMR (CDCl_3 , 100 MHz) spectrum of 2-(4-nitrobenzyl)isoindolin-1-one (**8p**)

^1H NMR (CDCl_3 , 400 MHz) spectrum of 2-(4-fluorobenzyl)isoindolin-1-one (**8q**)

^{13}C NMR (CDCl_3 , 100 MHz) spectrum of 2-(4-fluorobenzyl)isoindolin-1-one (**8q**)

^{19}F NMR (DMSO- d_6 , 376.49 MHz) spectrum of 2-(4-fluorobenzyl)isoindolin-1-one (**8q**)

^1H NMR (CDCl_3 , 400 MHz) spectrum of 2-((6-methoxypyridin-3-yl)methyl)isoindolin-1-one (**10a**)

^{13}C NMR (CDCl_3 , 100 MHz) spectrum of 2-((6-methoxypyridin-3-yl)methyl)isoindolin-1-one (**10a**)

^1H NMR (CDCl_3 , 400 MHz) spectrum of 2-((6-fluoropyridin-3-yl)methyl)isoindolin-1-one (**10b**)

^{13}C NMR (CDCl_3 , 100 MHz) spectrum of 2-((6-fluoropyridin-3-yl)methyl)isoindolin-1-one
(**10b**)

^{19}F NMR (CDCl_3 , 376.49 MHz) spectrum of 2-((6-fluoropyridin-3-yl)methyl)isoindolin-1-one (**10b**)

^1H NMR (CDCl_3 , 400 MHz) spectrum of 2-((5-acetylthiophen-2-yl)methyl)isoindolin-1-one (**10c**)

^{13}C NMR (CDCl_3 , 100 MHz) spectrum of 2-((5-acetylthiophen-2-yl)methyl)isoindolin-1-one
(**10c**)

^1H NMR (CDCl_3 , 400 MHz) spectrum of 5-((1-oxoisindolin-2-yl)methyl)thiophene-2-carbaldehyde (**10d**)

^{13}C NMR (CDCl_3 , 100 MHz) spectrum of 5-((1-oxoisindolin-2-yl)methyl)thiophene-2-carbaldehyde (**10d**)

^1H NMR (CDCl_3 , 400 MHz) spectrum of 2-((thiophen-2-yl)methyl)isoindolin-1-one (**10e**)

7.890
7.872
7.540
7.520
7.503
7.481
7.462
7.442
7.403
7.383
7.303
7.295
7.291
7.283
7.204
7.197
7.056
7.050
7.043
7.038

— 4.827

— 4.285

^{13}C NMR (CDCl_3 , 100 MHz) spectrum of 2-((thiophen-2-yl)methyl)isoindolin-1-one (**10e**)

^1H NMR (CDCl_3 , 400 MHz) spectrum of 3-((thiophen-2-yl)methyl)isoindolin-1-one (**10f**)

^{13}C NMR (CDCl_3 , 100 MHz) spectrum of 3-((thiophen-2-yl)methyl)isoindolin-1-one (**10f**)

^1H NMR (CDCl_3 , 400 MHz) spectrum of 5-((1-oxoisindolin-2-yl)methyl)furan-2-carbaldehyde (**10g**)

^{13}C NMR (CDCl_3 , 400 MHz) spectrum of 5-((1-oxoisindolin-2-yl)methyl)furan-2-carbaldehyde (**10g**)