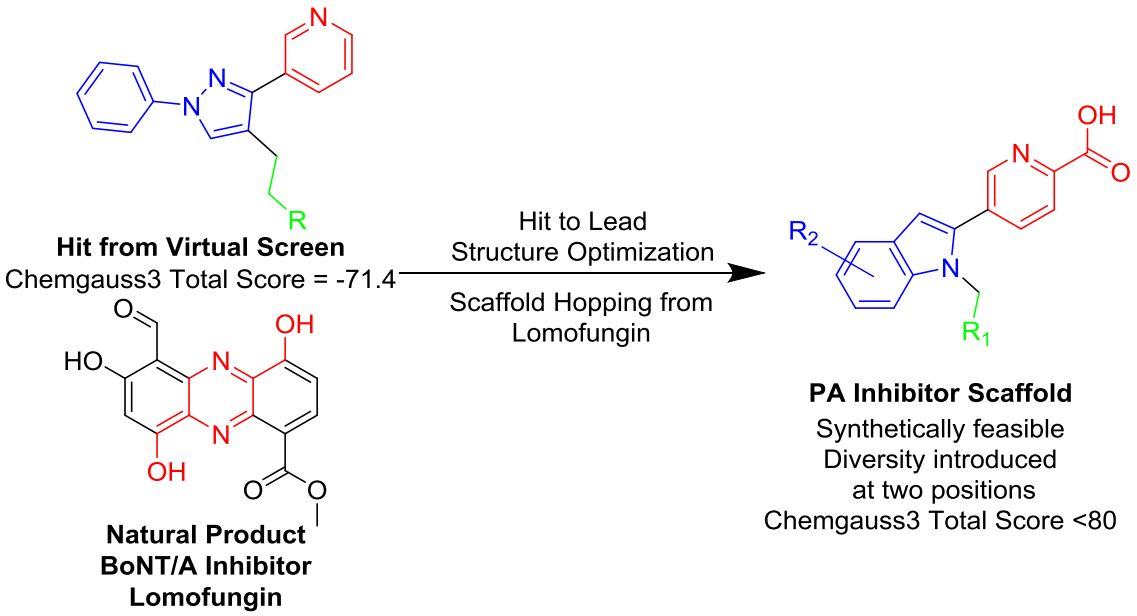
Supporting Information

Picolinic Acids as β-Exosite Inhibitors of Botulinum Neurotoxin A Light Chain

Paul T. Bremer, Song Xue and Kim D. Janda

Fig. S1 Discovery and design of picolinic acid (PA) inhibitors



SAR Tables

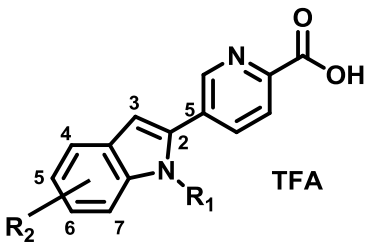


Table S1. Sublibrary 1: Activity of R_1-substituted indolylpicolinates (R_2=H)

Compound	R_1 Substituent	Calculated IC_{50} (μM)
1a-OH	H	57
2a	Et	13
3a	Pr	4.5
4a	Bu	6.3
5	Me-cyclopropane	4.7
6	Bn	14
7	Pr-3-F	NA
8	Et-2-$CONH_2$	NA
9	Et-2-OMe	8.3
10	Et-2-(4-Cl-Ph)	2.5
11	Pr-3-(3-Cl-Ph)	2.7
12	Pr-3-OH	2.8
13	Pr-3-CF_3	9.8
14	Me-benzofuran-2-yl	2.4
15	Me-(4-NH_2CO-oxazol-2-yl)	3.6
16	Me-(4-MeOCO-oxazol-2-yl)	12

NA = Not active at 20 μM

Table S2. Sublibrary 2: Activity of R_2-substituted indolylpicolinates (R_1=Bu)

Compound	R_2	Calculated IC_{50} (μM)
4a	H	6.3
4b	3-Me	2.8
4c	4-Cl	2.9
4d	5-F	3.9
4e	3-CHO	16
4f	3-Et	4.0
4g	3-CN	NA
4h	4-CF_3	3.3
4i	4-F	28
4j	5-Cl	4.4
4k	6-Cl	4.5
4l	7-F	8.1
4m	4-Me	3.3
4n	4-OMe	59
4o	6-OH	7.7
4p	6-F	5.5
4q	6-OME	3.2

NA = Not active at 20 μM

Table S3. Sublibrary 3: Activity effects of simultaneous variation of the R_1 and R_2 groups against full length (448) and truncated (425) BoNT/A LC

Compound	R_1	R_2	Calculated IC_{50} (μM) 425	Calculated IC_{50} (μM) 448
2a	Et	H	22	13
2b	Et	3-Me	7.9	5.8
2c	Et	4-Cl	9.0	3.4
2d	Et	5-F	10	2.8
3a	Pr	H	5.5	4.5
3b	Pr	3-Me	6.9	5.1
4a	Bu	H	6.3	6.2
4b	Bu	3-Me	2.8	0.85
4c	Bu	4-Cl	2.9	2.0
4d	Bu	5-F	3.9	5.3

Fig. S2 Inhibition kinetics of CBIP at low concentrations of lomofungin

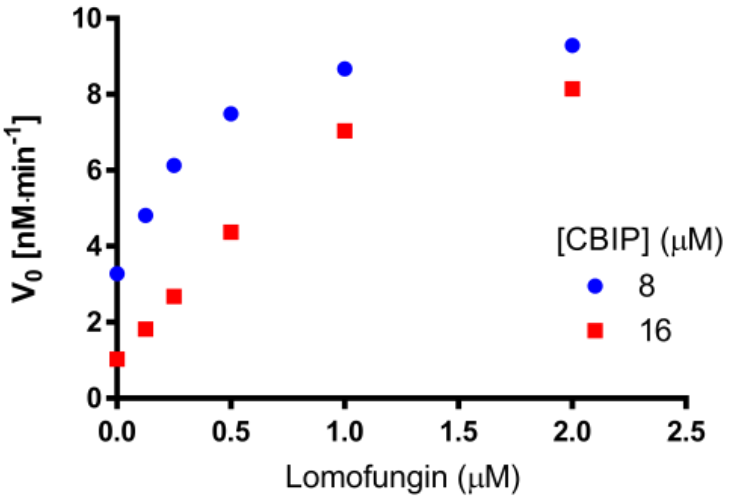
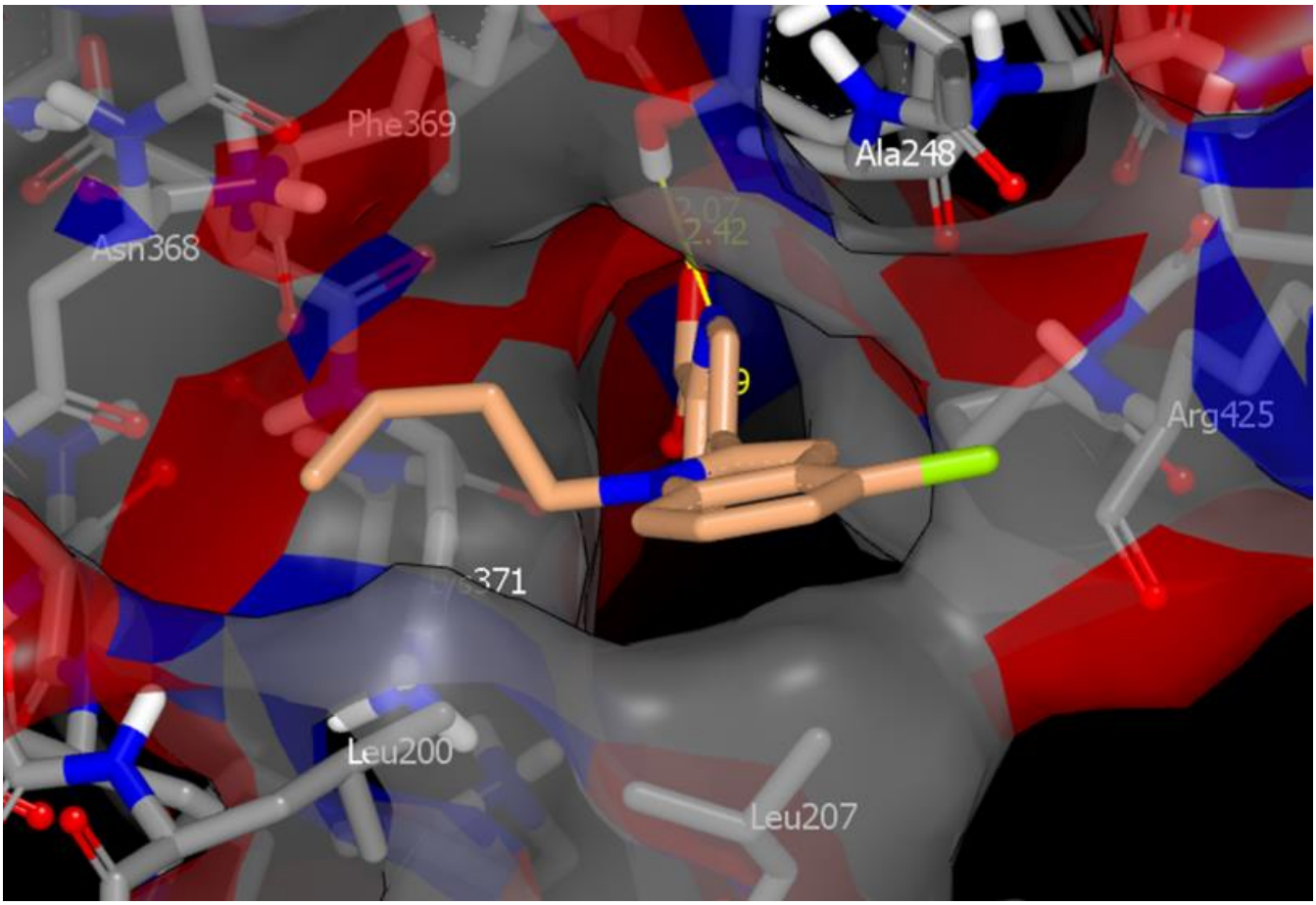


Fig. S3 Predicted pose of CBIP (tan) docked into the β-exosite of BoNT/A LC with rotated view point



Experimental

66-mer Assay.[1] All 66-mer assays were run in 40 mM HEPES pH 7.4 buffer. BoNT/A LC concentrations were 2 nM, 66-mer substrate (prepared in-house via solid phase synthesis) concentrations were 5 μM. All inhibitors were tested in duplicate at two inhibitor concentrations against a 2% DMSO-treated control and substrate cleavage was allowed to occur for 25 min at which point the reaction was quenched with 20% TFA solution. A ^{13}C labelled 9-mer cleavage product was added as an internal standard (IS) and each sample was analyzed by LCMS to quantify the amount of cleavage product relative to the IS. The resulting initial velocities were used to calculate IC_{50} values from equation 1 with V representing enzyme velocity in the presence of inhibitor and V_0 representing enzyme velocity in the presence of DMSO. Kinetic experiments were performed in the same manner using the inhibitors and concentrations as noted in the figures. A global fit of the data was performed using equation 2, derived from previous kinetic studies,[2] which was used to calculate the enhancement factor α represented as mean ± SEM in Fig. 4. Five point inhibition curves were performed for comparison of CBIP and lomofungin and the resulting V_0 values were normalized to 100% activity DMSO controls. The IC_{50}s were then calculated using equation 3 to give the mean ± SEM as represented in Fig 3. Note that CBIP gave a slightly different IC_{50} in using the equation 1 method (2.9 μM) versus the equation 3 method (2.65 μM).

Equation 1: $\mathrm{IC}_{50} = \frac{[\mathrm{I}]\frac{V}{V_0}}{1-\frac{V}{V_0}}$

Equation 2: $V_{1,2} = \frac{V_{max}}{1+\frac{[\mathrm{I}_1]}{K_{i1}}+\frac{[\mathrm{I}_2]}{K_{i2}}+\frac{\alpha[\mathrm{I}_1][\mathrm{I}_2]}{K_{i1}K_{i2}}}$

Equation 3: $V_0 = \frac{100}{1+10^{(\log(IC_{50})-\log([I]))*HillSlope)}}$

Docking. Computer programs were obtained and used under an academic license from Openeye Scientific Software Inc. The receptor file containing the structural information of the β-exosite was generated using a previously reported crystal structure of the BoNT/A LC (PDB ID: 1XTG)[3] and the Make Receptor program.[4] The eMolecules compound database was used as a source of virtual screening molecules (~6000 molecules screened via docking) which served as inspiration for the initial discovery of picolinic acids as lomofungin-like BoNT/A LC inhibitors (Fig. S1). Lowest energy conformers of query molecules e.g. CBIP and lomofungin

were generated with OMEGA,[5] and the rigid conformers were docked with FRED[6] into the BoNT/A LC β-exosite. The docked conformer of each inhibitor with the best fitness score is shown in Fig. 5 and S2, generated using the VIDA GUI.[7] Fitness scores were calculated for the best fit conformer using the Chemgauss3 scoring function which assisted in the selection and design of our inhibitors.

General Chemistry. All starting materials and reagents were purchased from Combi-Blocks or Sigma-Aldrich. Organic solvents were anhydrous or distilled prior to use. Synthesized compounds were purified using preparative thin layer chromatography (pTLC, Merck silica gel 60 F_{254}) using both long and short wave UV lamps for visualization. Amounts of starting materials are specified unless the exact general procedures below were used. NMR spectra were recorded on a Bruker 600 MHz instrument and peaks are reported in ppm, using the solvent peak as a reference. High resolution mass analysis was performed on an Agilent ESI-TOF-MS system. Purity for each compound was judged by NMR and the UV (254 nm) and mass traces from reverse-phase LC-MS. Synthetic procedures were adapted from previously reported conditions from Robbins and Hartwig.[8]

General Procedure for Suzuki Coupling. *Tert*-butyl protected indolylpicolinates (**1a-r**) were synthesized from commercially available 2-indolyl pinacol boronate esters except for (**1f**, **g, h, j, k, l**) in which case the corresponding boronate ester was prepared via C-H borylation of a substituted indole. The substituted indole (0.38 mmol, 1 eq), bis-(pinacolato)diboron (B_2pin_2) (48 mg, 0.5 eq), 4,4'-di-tert-butylbipyridine (dtbpy) (1.0 mg, 0.01 eq) and $[Ir(cod)OMe]_2$ (1.3 mg, 0.005 eq) were dissolved in 0.75 mL dry THF and stirred at 80 °C for 18 h in a sealed vial under inert atmosphere. The resulting crude mixture was allowed to cool and used directly in the next reaction. The corresponding 2-indolyl pinacol boronate ester (0.31 mmol, 1 eq), *tert*-butyl 5-bromopicolinate (80 mg, 1 eq), P(*o*-tol)$_3$ (4 mg, 0.04 eq), $Pd(dba)_2$ (4 mg, 0.02 eq) and Na_2CO_3 (131 mg, 4 eq) were dissolved in 1.0 mL of 1:9 H_2O/THF and stirred at rt for 18 h in a sealed vial under inert atmosphere. The resulting suspension was filtered and purified by pTLC with 1:9 EtOAc/DCM as an eluent (fluorescent product band at $R_f \approx 0.2$), affording the corresponding *tert*-butyl indolylpicolinate (**1a-r**) typically as a white solid.

General Procedure for Indole Alkylation and *tert*-butyl Ester Deprotection. The corresponding *tert*-butyl indolylpicolinate (0.03 mmol, **1a-r**) and alkyl iodide (1.5 eq) or alkyl bromide (4 eq) were dissolved in dry DMF. Cs_2CO_3 (29 mg, 3 eq for iodide; 59 mg, 6 eq for bromide) was added and the mixture was stirred at 80 °C for 1 h (iodide) or 18 h (bromide) in a sealed vial under inert atmosphere. The resulting suspension was allowed to cool, filtered and purified by pTLC with 1:2 EtOAc/hexane as an eluent, yielding the corresponding *tert*-butyl *N*-alkyl indolylpicolinate typically as a colorless oil. *Tert*-butyl deprotection proceeded by stirring the ester in 1 mL 1:1 DCM/TFA for 2 h and evaporating the solvent to quantitatively produce the final picolinic acid as a TFA salt (**2-16, 22**) typically as an orange oil. Product masses and yields are reported for *tert*-butyl esters for higher accuracy.

tert-butyl 5-(1H-indol-2-yl)picolinate (**1a**). The title compound was prepared from indole-2-boronic acid pinacol ester using the general Suzuki coupling procedure as a yellow solid (53 mg, 58% yield). ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.84 (s, 1H), 9.21 (d, *J* = 2.4 Hz, 1H), 8.35 (dd, *J* = 8.2, 2.4 Hz, 1H), 8.06 (d, *J* = 8.2 Hz, 1H), 7.59 (d, *J* = 7.9 Hz, 1H), 7.46 (d, *J* = 8.3 Hz, 0H), 7.19 (s, 1H), 7.18 – 7.15 (m, 1H), 7.05 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H), 1.57 (s, 9H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 163.57, 146.76, 146.05, 137.73, 133.51, 132.33, 128.33, 124.81, 122.84, 120.65, 119.90, 111.61, 101.73, 81.29, 27.79. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 295.1441, *obs.* 295.1442.

5-(1H-indol-2-yl)picolinic acid (**1a-OH**). The title compound was quantitatively produced from TFA deprotection of (**1a**). ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.84 (brs, 1H), 9.22 (dd, *J* = 2.3, 0.8 Hz, 1H), 8.39 (dd, *J* = 8.2, 2.3 Hz, 1H), 8.12 (dd, *J* = 8.2, 0.8 Hz, 1H), 7.62 – 7.58 (m, 1H), 7.45 (dt, *J* = 8.1, 0.9 Hz, 1H), 7.22 (dd, *J* = 2.2, 0.9 Hz, 1H), 7.18 (ddd, *J* = 8.2, 7.0, 1.1 Hz, 1H), 7.05 (ddd, *J* = 7.9, 7.0, 1.0 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 165.83, 146.14, 145.79, 137.72, 133.45, 132.62, 130.90, 128.31, 124.99, 122.84, 120.65, 119.88, 111.60, 101.77. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 239.0815, *obs.* 239.0806

tert-butyl 5-(3-methyl-1H-indol-2-yl)picolinate (**1b**). The title compound was prepared from 3-methylindole-2-boronic acid pinacol ester (0.12 mmol) using the general Suzuki coupling procedure as a yellow solid (30 mg, 81% yield). ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.47 (s, 1H), 9.03 (s, 1H), 8.21 (d, J = 8.3 Hz, 0H), 8.11 (d, J = 8.3 Hz, 1H), 7.60 (d, J = 8.0 Hz, 1H), 7.42 (d, J = 8.1 Hz, 1H), 7.19 (t, J = 7.5 Hz, 1H), 7.06 (t, J = 7.5 Hz, 1H), 2.48 (s, 3H), 1.59 (s, 9H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 163.67, 147.72, 146.32, 136.62, 134.87, 131.74, 129.67, 129.15, 124.59, 122.78, 119.06, 119.00, 111.33, 110.16, 81.35, 27.80, 9.89. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 309.1598, *obs.* 309.1545.

tert-butyl 5-(4-chloro-1H-indol-2-yl)picolinic acid (**1c**). The title compound was prepared from 4-chloroindole-2-boronic acid pinacol ester (0.12 mmol) using the general Suzuki coupling procedure as a white solid (37 mg, 94% yield). ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.19 (s, 1H), 9.26 (dd, J = 2.4, 0.8 Hz, 1H), 8.42 (dd, J = 8.2, 2.3 Hz, 1H), 8.07 (dd, J = 8.2, 0.8 Hz, 1H), 7.44 (dt, J = 8.1, 0.9 Hz, 1H), 7.30 – 7.20 (m, 1H), 7.21 – 7.14 (m, 1H), 7.13 (dd, J = 7.5, 0.9 Hz, 1H), 1.58 (s, 9H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 163.49, 147.24, 146.34, 138.34, 134.56, 132.83, 130.08, 126.93, 124.76, 124.66, 123.56, 119.42, 110.75, 99.66, 81.40, 27.77. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 329.1051, *obs.* 329.1001.

tert-butyl 5-(5-fluoro-1H-indol-2-yl)picolinic acid (**1d**). The title compound was prepared from 5-fluoroindole-2-boronic acid pinacol ester (0.12 mmol) using the general Suzuki coupling procedure as a tan solid (26 mg, 69% yield). ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.15 (s, 1H), 9.25 (dd, J = 2.3, 0.8 Hz, 1H), 8.40 (dd, J = 8.2, 2.3 Hz, 1H), 8.07 (dd, J = 8.2, 0.8 Hz, 1H), 7.31 – 7.29 (m, 1H), 7.29 (s, 1H), 7.15 (td, J = 7.9, 5.3 Hz, 1H), 6.86 – 6.80 (m, 1H), 1.58 (s, 9H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 163.50, 155.58 (d, J_{CF} = 246.15 Hz), 147.13, 146.29, 140.22 (d, J_{CF} = 10.48 Hz), 134.00, 132.68, 130.18, 124.75, 123.36, 117.26 (d, J_{CF} = 20.76 Hz), 108.19, 104.25 (d, J_{CF} = 19.77 Hz), 97.25, 81.36, 27.77. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 313.1347, *obs.* 313.1306.

tert-butyl 5-(3-formyl-1H-indol-2-yl)picolinic acid (**1e**). To a 0.2 mL DCM solution of **1a** (5 mg, 0.017 mmol) was added oxalyl chloride (2 μL, 1.4 eq) and catalytic DMF (1 uL). The reaction was stirred at rt for 20 min and the solvent was evaporated. THF (0.3 mL) and 20% aqueous NH_4OAc solution (0.4 mL) was added and the mixture was stirred for 30 min at 100 °C, then partitioned between EtOAc and water. The organic layer was collected, dried over $MgSO_4$, concentrated and purified by pTLC using 2:5 EtOAc/hexane as an eluent and deprotected with TFA to yield the title compound as a white solid (3.8 mg, 69%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.11 (s, 1H), 10.09 (s, 1H), 8.97 (dd, *J* = 2.2, 0.9 Hz, 1H), 8.41 – 8.39 (m, 1H), 8.17 (dd, *J* = 8.1, 0.8 Hz, 1H), 8.13 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.55 – 7.52 (m, 1H), 7.39 – 7.33 (m, 2H), 1.63 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 185.63, 163.74, 149.79, 149.60, 143.24, 138.20, 136.39, 129.36, 126.32, 125.24, 124.84, 123.73, 122.26, 116.28, 111.89, 83.44, 28.22. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 323.1390, *obs.* 323.1333.

tert-butyl 5-(3-ethyl-1H-indol-2-yl)picolinic acid (**1f**). To a solution of 3-acetylindole (80 mg, 0.50 mmol), Pd/C 5 wt % (106 mg) in cyclopentyl methyl ether (0.5 mL) was added sodium hypophosphite monohydrate (159 mg, 1.5 mmol) and hypophosphorous acid (1 mL, 50% in water), and the mixture was heated at 100 °C for 4 h. The cooled mixture was partitioned between DCM and water and the organic layer was collected, dried over $MgSO_4$ and concentrated. The crude product was purified by pTLC using 1:4 EtOAc/hexane as an eluent to yield 3-ethylindole (30 mg, 41%). The title compound was prepared using the general procedure for the two step, one pot C-H borylation/Suzuki coupling from 3-ethyl indole (0.08 mmol), yielding the product as a white solid (5 mg, 16% over two steps). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.95 (d, *J* = 2.3 Hz, 1H), 8.50 (s, 1H), 8.13 (d, *J* = 8.1 Hz, 1H), 7.96 (dd, *J* = 8.1, 2.3 Hz, 1H), 7.67 (d, *J* = 7.9 Hz, 1H), 7.43 – 7.39 (m, 1H), 7.26 – 7.23 (m, 1H), 7.19 – 7.13 (m, 1H), 2.93 (q, *J* = 7.6 Hz, 2H), 1.65 (s, 9H), 1.34 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.21, 148.49, 147.58, 136.95, 135.17, 132.19, 129.38, 128.87, 124.98, 123.52, 120.07, 119.66, 118.62, 111.38, 82.62, 28.28, 17.99, 15.72. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 323.1754, *obs.* 323.1750.

tert-butyl 5-(3-cyano-1H-indol-2-yl)picolinic acid (**1g**). The title compound was prepared using the general procedure for the two step, one pot C-H borylation/Suzuki coupling from 3-cyanoindole, yielding the product as a tan solid (4 mg, 3% over two steps). ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.25 (dd, J = 2.4, 0.8 Hz, 1H), 8.49 (dd, J = 8.2, 2.3 Hz, 1H), 8.22 (dd, J = 8.2, 0.9 Hz, 1H), 7.71 (dt, J = 8.0, 1.0 Hz, 1H), 7.63 (dt, J = 8.2, 1.0 Hz, 1H), 7.39 (ddd, J = 8.2, 7.1, 1.2 Hz, 1H), 7.31 (ddd, J = 8.1, 7.0, 1.0 Hz, 1H), 1.59 (s, 9H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 163.24, 149.44, 149.00, 147.50, 144.39, 140.47, 136.00, 135.39, 124.87, 124.79, 122.54, 118.74, 116.35, 115.26, 112.97, 81.87, 27.73. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 320.1394, *obs.* 320.1331.

tert-butyl 5-(4-(trifluoromethyl)-1H-indol-2-yl)picolinic acid (**1h**). The title compound was prepared using the general procedure for the two step, one pot C-H borylation/Suzuki coupling from 4-trifluoromethylindole, yielding the product as a tan solid (38 mg, 28% over two steps). ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.38 (s, 1H), 9.28 (s, 1H), 8.51 – 8.43 (m, 1H), 8.08 (dd, J = 8.2, 0.9 Hz, 1H), 7.76 (d, J = 8.2 Hz, 1H), 7.44 (d, J = 7.3 Hz, 1H), 7.34 (t, J = 7.8 Hz, 1H), 7.30 (s, 1H), 1.59 (s, 9H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 163.46, 147.53, 146.48, 138.15, 135.81, 133.25, 129.86, 124.94 (q, J_{CF} = 272.96 Hz), 124.76, 124.00 (q, J_{CF} = 2.04 Hz), 122.01, 120.02 (q, J_{CF} = 31.84 Hz), 117.45 (q, J_{CF} = 5.03 Hz), 116.04, 99.47, 81.46, 27.77. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 363.1315, *obs.* 363.1243.

tert-butyl 5-(4-fluoro-1H-indol-2-yl)picolinic acid (**1i**). The title compound was prepared from 4-fluoroindole-2-boronic acid pinacol ester using the general Suzuki coupling procedure as a tan solid (29 mg, 30% yield). ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.94 (s, 1H), 9.20 (dd, J = 2.4, 0.8 Hz, 1H), 8.34 (dd, J = 8.2, 2.4 Hz, 1H), 8.06 (dd, J = 8.2, 0.8 Hz, 1H), 7.44 (dd, J = 8.8, 4.5 Hz, 1H), 7.35 (dd, J = 9.8, 2.5 Hz, 1H), 7.16 (dd, J = 2.3, 0.9 Hz, 1H), 7.02 (ddd, J = 9.5, 8.8, 2.5 Hz, 1H), 1.57 (s, 9H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 163.52, 157.25 (d, J_{CF} = 228.01 Hz), 147.06, 146.16, 135.37, 134.40, 132.56, 130.41, 128.48 (d, J_{CF} = 10.75 Hz), 124.80, 112.71 (d, J_{CF} = 10.24 Hz), 111.04 (d, J_{CF} = 26.56 Hz), 104.93 (d, J_{CF} = 23.02 Hz), 101.71 (d, J_{CF} = 5.40 Hz), 81.35, 27.78. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 313.1347, *obs.* 313.1327.

tert-butyl 5-(5-chloro-1H-indol-2-yl)picolinic acid (**1j**). The title compound was prepared using the general procedure for the two step, one pot C-H borylation/Suzuki coupling from 5-chlorolindole, yielding the product as a tan solid (17 mg, 14% over two steps). ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.09 (s, 1H), 9.20 (d, J = 2.3 Hz, 1H), 8.36 (dd, J = 8.2, 2.3 Hz, 1H), 8.07 (d, J = 8.2 Hz, 1H), 7.64 (d, J = 2.1 Hz, 1H), 7.47 (d, J = 8.6 Hz, 1H), 7.19 – 7.14 (m, 2H), 1.58 (s, 9H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 163.49, 147.15, 146.23, 136.11, 135.18, 132.70, 130.25, 129.39, 124.79, 124.37, 122.73, 119.65, 113.16, 101.22, 81.38, 27.77. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 329.1051, *obs.* 329.0970.

tert-butyl 5-(6-chloro-1H-indol-2-yl)picolinic acid (**1k**). The title compound was prepared using the general procedure for the two step, one pot C-H borylation/Suzuki coupling from 6-chlorolindole, yielding the product as a tan solid (47 mg, 38% over two steps). ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.00 (s, 1H), 9.19 (dd, J = 2.3, 0.8 Hz, 1H), 8.35 (dd, J = 8.2, 2.3 Hz, 1H), 8.07 (dd, J = 8.2, 0.8 Hz, 1H), 7.61 (d, J = 8.5 Hz, 1H), 7.46 (dt, J = 1.6, 0.7 Hz, 1H), 7.22 (dd, J = 2.2, 0.9 Hz, 1H), 7.07 (dd, J = 8.4, 1.9 Hz, 1H), 1.58 (s, 9H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 163.50, 147.04, 146.16, 138.00, 134.66, 132.53, 130.30, 127.29, 127.09, 124.79, 122.05, 120.33, 111.08, 101.79, 81.36, 27.78. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 329.1051, *obs.* 329.1000.

tert-butyl 5-(7-fluoro-1H-indol-2-yl)picolinic acid (**1l**). The title compound was prepared using the general procedure for the two step, one pot C-H borylation/Suzuki coupling from 7-fluorolindole, yielding the product as a tan solid (23 mg, 19% over two steps). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.91 (s, 1H), 7.76 (d, J = 8.4 Hz, 1H), 7.44 – 7.38 (m, 2H), 7.10 – 7.00 (m, 1H), 6.96 – 6.89 (m, 1H), 6.83 (ddd, J = 10.4, 7.7, 2.2 Hz, 1H), 1.27 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.50, 149.63 (d, J_{CF} = 246.13 Hz), 146.89, 144.45, 134.44, 133.07, 132.13 (d, J_{CF} = 5.38 Hz), 130.71, 126.36 (d, J_{CF} = 13.32 Hz), 124.50, 120.62 (d, J_{CF} = 5.89 Hz), 116.48 (d, J_{CF} = 3.20 Hz), 108.15 (d, J_{CF} = 15.72 Hz), 102.82, 82.53, 27.74. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 313.1347, *obs.* 313.1346.

tert-butyl 5-(4-methyl-1H-indol-2-yl)picolinic acid (**1m**). The title compound was prepared from 4-methylindole-2-boronic acid pinacol ester (0.12 mmol) using the general Suzuki coupling procedure as a yellow solid (35 mg, 94% yield). ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.80 (d, *J* = 2.3 Hz, 1H), 9.23 (dd, *J* = 2.3, 0.8 Hz, 1H), 8.36 (dd, *J* = 8.2, 2.3 Hz, 1H), 8.05 (dd, *J* = 8.2, 0.8 Hz, 1H), 7.28 (d, *J* = 8.1 Hz, 1H), 7.24 (dd, *J* = 2.3, 1.0 Hz, 1H), 7.07 (dd, *J* = 8.2, 7.1 Hz, 1H), 6.83 (dt, *J* = 7.0, 1.0 Hz, 1H), 2.51 (s, 3H), 1.57 (s, 9H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 163.58, 146.58, 145.93, 137.48, 132.81, 132.16, 130.87, 129.69, 128.48, 124.81, 122.98, 119.85, 109.20, 100.54, 81.25, 27.79, 18.56. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 309.1598, *obs.* 309.1598.

tert-butyl 5-(4-methoxy-1H-indol-2-yl)picolinate (**1n**). The title compound was prepared from 4-methoxyindole-2-boronic acid pinacol ester (0.4 mmol) using the general Suzuki coupling procedure as a tan solid (101 mg, 78% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (s, 1H), 7.81 (dd, *J* = 8.4, 2.2 Hz, 1H), 7.40 (d, *J* = 8.5 Hz, 1H), 7.03 (d, *J* = 2.2 Hz, 1H), 6.99 (t, *J* = 7.9 Hz, 1H), 6.74 (d, *J* = 8.2 Hz, 1H), 6.49 (d, *J* = 7.8 Hz, 1H), 4.01 (s, 3H), 1.30 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.73, 153.44, 145.95, 144.00, 139.45, 132.59, 131.90, 131.33, 124.44, 124.21, 119.70, 104.84, 99.77, 99.55, 82.26, 55.36, 27.85. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 325.1547, *obs.* 325.1550.

tert-butyl 5-(6-(benzyloxy)-1H-indol-2-yl)picolinate (**1o**). The title compound was prepared from 6-benzyloxyindole-2-boronic acid (0.18 mmol) using the general Suzuki coupling procedure as a yellow solid (40 mg, 55% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.82 – 8.77 (m, 1H), 8.12 – 8.04 (m, 1H), 7.90 (d, *J* = 2.3 Hz, 1H), 7.81 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.50 – 7.47 (m, 2H), 7.46 (d, *J* = 8.5 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 2H), 7.36 – 7.30 (m, 1H), 7.00 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.60 (s, 1H), 5.17 (s, 2H), 1.38 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.20, 157.72, 150.04, 149.24, 147.84, 138.94, 137.08, 136.27, 134.93, 133.80, 128.68, 128.08,

127.70, 123.91, 123.16, 121.54, 113.65, 112.37, 101.04, 82.41, 70.57, 27.91. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 401.1860, *obs.* 401.1860.

tert-butyl 5-(6-fluoro-1H-indol-2-yl)picolinate (**1p**). The title compound was prepared from 6-fluoroindole-2-boronic acid pinacol ester (0.12 mmol) using the general Suzuki coupling procedure as a tan solid (20 mg, 53% yield). ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.18 (s, 1H), 8.32 (dd, *J* = 8.2, 2.4 Hz, 1H), 8.05 (d, *J* = 8.2 Hz, 1H), 7.60 (dd, *J* = 8.7, 5.4 Hz, 1H), 7.20 (q, *J* = 3.3, 2.3 Hz, 2H), 6.94 – 6.88 (m, 1H), 1.57 (s, 9H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 163.55, 159.62 (d, J_{CF} = 236.73 Hz), 146.79, 145.94, 137.61 (d, J_{CF} = 13.14 Hz), 134.33 (d, J_{CF} = 3.66 Hz), 132.24, 130.50, 125.16, 124.82, 121.87 (d, J_{CF} = 10.99 Hz), 108.59 (d, J_{CF} = 25.42 Hz), 101.82, 97.42 (d, J_{CF} = 25.42 Hz), 81.32, 27.79. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 313.1347, *obs.* 313.1341.

ethyl 3-(4-chloro-1H-indol-2-yl)benzoate (**1q**). The title compound was prepared from 4-chloroindole-2-boronic acid pinacol ester (0.12 mmol) and ethyl 3-bromobenzoate (0.12 mmol) using the general Suzuki coupling procedure as a white solid (26 mg, 72% yield). ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.10 (d, *J* = 2.4 Hz, 1H), 8.48 – 8.44 (m, 1H), 8.20 (ddd, *J* = 7.8, 2.0, 1.1 Hz, 1H), 7.95 – 7.90 (m, 1H), 7.62 (t, *J* = 7.7 Hz, 1H), 7.41 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.15 – 7.07 (m, 2H), 7.03 (dd, *J* = 2.3, 0.9 Hz, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 1.37 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 165.56, 138.02, 137.50, 132.06, 130.78, 130.03, 129.48, 128.40, 127.07, 125.37, 124.30, 122.74, 119.10, 110.61, 97.55, 60.98, 14.22. ESI-TOF-MS (*m*/*z*): $[M+Cl]^-$ *calc*. 300.0791, *obs.* 300.0707.

ethyl 4-(4-chloro-1H-indol-2-yl)benzoate (**1r**). The title compound was prepared from 4-chloroindole-2-boronic acid pinacol ester (0.12 mmol) and ethyl 4-bromobenzoate (0.12 mmol) using the general Suzuki coupling procedure as a white solid (33 mg, 92% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.72 (s, 1H), 8.14 – 8.08 (m, 2H), 7.76 – 7.71 (m, 2H), 7.31 (ddd, *J* = 6.5, 2.4, 0.9 Hz, 1H), 7.18 – 7.09 (m, 2H), 7.04 (dd, *J* = 2.3, 0.9 Hz, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.39, 137.87, 137.25,

135.96, 130.51, 129.77, 128.13, 126.36, 124.99, 123.69, 120.35, 109.83, 100.26, 61.31, 14.49. ESI-TOF-MS (*m*/*z*): $[M+Cl]^-$ *calc*. 300.0791, *obs.* 300.0725.

5-(1-ethyl-1H-indol-2-yl)picolinic acid (**2a**). The title compound was prepared from **1a** (0.015 mmol) and 1-iodoethane using the standard alkylation/deprotection procedure to yield the product as an orange oil (4.5 mg, 88%). ^{1}H NMR (600 MHz, Acetone-d_6) δ 8.92 (brs, 1H), 8.30 (dd, *J* = 8.1, 0.9 Hz, 1H), 8.26 (dd, *J* = 8.0, 2.1 Hz, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.56 (d, *J* = 8.3 Hz, 1H), 7.27 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.13 (ddd, *J* = 7.9, 7.0, 0.9 Hz, 1H), 6.78 (s, 1H), 4.35 (q, *J* = 7.2 Hz, 2H), 1.31 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (151 MHz, Acetone-d_6) δ 165.41, 149.37, 146.97, 139.09, 138.71, 136.81, 133.64, 129.20, 125.05, 123.46, 121.81, 120.99, 111.26, 105.34, 39.64, 15.56. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 267.1128, *obs.* 267.1124.

5-(1-ethyl-3-methyl-1H-indol-2-yl)picolinic acid (**2b**). The title compound was prepared from **1b** (0.021 mmol) and 1-iodoethane using the standard alkylation/deprotection procedure to yield the product as an orange oil (3.3 mg, 47%).^{1}H NMR (600 MHz, $CDCl_3$) δ 8.92 (brs, 1H), 8.51 (d, *J* = 8.0 Hz, 1H), 8.28 (d, *J* = 7.6 Hz, 1H), 7.65 (d, *J* = 7.9 Hz, 1H), 7.41 (d, *J* = 8.3 Hz, 1H), 7.35 (ddd, *J* = 8.2, 6.9, 1.1 Hz, 1H), 7.21 (ddd, *J* = 7.9, 6.9, 0.9 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 2.34 (s, 3H), 1.22 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.29, 145.66, 143.57, 142.37, 137.77, 134.70, 129.76, 128.71, 126.33, 124.16, 120.37, 120.03, 114.24, 110.30, 39.34, 15.24, 9.38. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 281.1285, *obs.* 281.1283.

5-(4-chloro-1-ethyl-1H-indol-2-yl)picolinic acid (**2c**). The title compound was prepared from **1c** (0.023 mmol) and 1-iodoethane using the standard alkylation/deprotection procedure to yield the product as an orange oil (4 mg, 49%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.98 (brs, 1H), 8.45 (d, *J* = 8.0 Hz, 1H), 8.28 (d, *J* = 7.6 Hz, 1H), 7.35 (d, *J* = 8.3 Hz, 1H), 7.27 – 7.24 (m, 1H), 7.20 (dd, *J* = 7.6, 0.8 Hz, 1H), 6.88 (s, 1H), 4.25 (q, *J* = 7.2 Hz, 2H), 1.37 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.08, 146.13, 143.61, 140.50, 139.16, 134.70,

134.10, 127.06, 126.95, 125.79, 124.36, 120.67, 109.13, 104.68, 39.85, 15.53. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 301.0738, *obs.* 301.0717.

5-(1-ethyl-5-fluoro-1H-indol-2-yl)picolinic acid (**2d**). The title compound was prepared from **1d** (0.021 mmol) and 1-iodoethane using the standard alkylation/deprotection procedure to yield the product as an orange oil (1 mg, 14%). ^{1}H NMR (600 MHz, Acetone-d_6) δ 8.97 (s, 1H), 8.34 – 8.31 (m, 2H), 7.41 (d, *J* = 8.3 Hz, 1H), 7.25 (td, *J* = 8.1, 5.3 Hz, 1H), 6.88 – 6.82 (m, 2H), 4.36 (q, *J* = 7.2 Hz, 2H), 1.32 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (151 MHz, Acetone-d_6) δ 165.30, 157.06 (d, J_{CF} = 244.68 Hz), 149.39, 147.21, 141.53 (d, J_{CF} = 11.89 Hz), 139.28, 137.11, 133.13, 125.27, 124.08 (d, J_{CF} = 7.14 Hz), 117.99 (d, J_{CF} = 22.02 Hz), 107.78 (d, J_{CF} = 4.10 Hz), 105.45 (d, J_{CF} = 18.98 Hz), 100.63, 40.17, 15.50. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 285.1034, *obs.* 285.1036.

5-(1-propyl-1H-indol-2-yl)picolinic acid (**3a**). The title compound was prepared from **1a** (0.015 mmol) and 1-iodopropane using the standard alkylation/deprotection procedure to yield the product as an orange oil (3.8 mg, 71%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.20 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.84 (dd, *J* = 8.0, 2.2 Hz, 1H), 7.61 (dt, *J* = 7.9, 1.1 Hz, 1H), 7.37 (dt, *J* = 8.2, 0.9 Hz, 1H), 7.28 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.17 (ddd, *J* = 7.9, 7.0, 1.0 Hz, 1H), 6.69 (s, 1H), 4.00 (t, *J* = 7.5 Hz, 2H), 1.60 (m, *J* = 7.4 Hz, 2H), 0.71 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.22, 151.16, 148.41, 138.50, 137.21, 132.85, 131.68, 128.58, 124.54, 122.74, 119.65, 119.40, 111.38, 110.04, 45.85, 23.47, 11.40. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 281.1285, *obs.* 281.1272.

5-(3-methyl-1-propyl-1H-indol-2-yl)picolinic acid (**3b**). The title compound was prepared from **1b** (0.021 mmol) and 1-iodopropane using the standard alkylation/deprotection procedure to yield the product as an orange oil (5.6 mg, 76%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.49 (d, *J* = 8.0 Hz, 1H), 8.21 (d, *J* = 7.9 Hz, 1H), 7.64 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.40 (dt, *J* = 8.4, 0.9 Hz, 1H), 7.33 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.20 (ddd, *J* = 7.9, 6.9, 1.0 Hz, 1H), 4.05 (t, *J* = 7.4 Hz, 2H), 2.32 (s, 3H), 1.62 (m, *J* = 7.4 Hz, 2H), 0.72 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.72, 146.63, 143.05, 142.73, 137.97, 134.58, 130.55, 128.55,

125.80, 123.88, 120.23, 119.91, 113.60, 110.44, 46.14, 23.51, 11.34, 9.45. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 295.1441, *obs.* 295.1387.

5-(1-butyl-1H-indol-2-yl)picolinic acid (**4a**). The title compound was prepared from **1a** (0.015 mmol) and 1-iodobutane using the standard alkylation/deprotection procedure to yield the product as an orange oil (2.9 mg, 55%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.90 (dd, *J* = 2.2, 0.8 Hz, 1H), 8.16 (dd, *J* = 8.1, 0.8 Hz, 1H), 7.92 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.66 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.41 (dq, *J* = 8.3, 0.9 Hz, 1H), 7.28 (ddd, *J* = 8.3, 7.0, 1.2 Hz, 1H), 7.16 (ddd, *J* = 7.9, 7.0, 0.9 Hz, 1H), 6.64 (d, *J* = 0.8 Hz, 1H), 4.17 (d, *J* = 7.6 Hz, 2H), 1.69 – 1.64 (m, 2H), 1.18 (m, *J* = 7.7 Hz, 2H), 0.81 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.16, 149.80, 148.44, 138.25, 136.99, 136.65, 132.11, 128.14, 124.68, 122.74, 121.15, 120.42, 110.42, 104.45, 44.24, 32.33, 20.16, 13.79. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 295.1441, *obs.* 295.1455.

5-(1-butyl-3-methyl-1H-indol-2-yl)picolinic acid (**4b**). The title compound was prepared from **1b** (0.016 mmol) and 1-iodobutane using the standard alkylation/deprotection procedure to yield the product as an orange oil (2.7 mg, 46%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.88 (s, 1H), 8.48 (d, *J* = 8.0 Hz, 1H), 8.20 (d, *J* = 7.1 Hz, 1H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.40 (d, *J* = 8.3 Hz, 1H), 7.33 (ddd, *J* = 8.2, 7.0, 1.1 Hz, 1H), 7.20 (ddd, *J* = 7.9, 6.9, 1.0 Hz, 1H), 4.08 (t, *J* = 7.5 Hz, 2H), 1.56 (p, *J* = 7.6 Hz, 2H), 1.12 (m, *J* = 7.4 Hz, 2H), 0.78 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.74, 146.67, 143.09, 142.62, 137.89, 134.50, 130.53, 128.55, 125.76, 123.84, 120.19, 119.89, 113.56, 110.40, 44.32, 32.25, 20.09, 13.68, 9.43. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 309.1598, *obs.* 309.1557.

5-(1-butyl-4-chloro-1H-indol-2-yl)picolinic acid (**4c**). The title compound was prepared from **1c** (0.031 mmol) and 1-iodobutane using the standard alkylation/deprotection procedure to yield the product as an orange oil (5.7 mg, 48%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.01 (s, 1H), 8.43 (d, *J* = 8.0 Hz, 1H), 8.28 (d, *J* = 7.9 Hz, 1H), 7.32 (d, *J* = 8.2 Hz, 1H), 7.23 (t, *J* = 7.9 Hz, 1H), 7.17 (d, *J* = 7.5 Hz, 1H), 6.86 (s, 1H), 4.19 (t, *J* = 7.6 Hz, 2H), 1.69

– 1.63 (m, 2H), 1.17 (m, *J* = 7.4 Hz, 2H), 0.82 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.71, 145.51, 143.53, 141.07, 139.44, 134.80, 134.18, 126.88, 126.83, 126.04, 124.26, 120.57, 109.37, 104.69, 44.81, 32.29, 20.03, 13.62. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 329.1051, *obs*. 329.0993.

5-(1-butyl-5-fluoro-1H-indol-2-yl)picolinic acid (**4d**). The title compound was prepared from **1d** (0.021 mmol) and 1-iodoethane using the standard alkylation/deprotection procedure to yield the product as an orange oil (4 mg, 42%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.04 (s, 1H), 8.48 (d, *J* = 8.1 Hz, 1H), 8.37 (d, *J* = 7.9 Hz, 1H), 7.27 – 7.22 (m, 1H), 7.20 (d, *J* = 8.2 Hz, 1H), 6.87 (s, 1H), 6.85 – 6.81 (m, 1H), 4.20 (t, *J* = 7.6 Hz, 2H), 1.68 (p, *J* = 7.7 Hz, 2H), 1.19 (m, *J* = 7.4 Hz, 2H), 0.83 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.12, 156.41 (d, J_{CF} = 250.08 Hz), 144.51, 142.59, 142.11, 141.47 (d, J_{CF} = 10.07 Hz), 134.75, 133.65, 126.65, 124.64 (d, J_{CF} = 6.63 Hz), 117.37 (d, J_{CF} = 23.09 Hz), 106.88, 105.69 (d, J_{CF} = 18.18 Hz), 102.66, 44.90, 32.23, 20.02, 13.58. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 313.1347, *obs.* 313.1348.

5-(1-butyl-3-formyl-1H-indol-2-yl)picolinic acid (**4e**). The title compound was prepared from **1e** (0.012 mmol) and 1-iodoethane using the standard alkylation/deprotection procedure to yield the product as an orange oil (3.2 mg, 70%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.69 (s, 1H), 8.82 (s, 1H), 8.45 (d, *J* = 7.7 Hz, 1H), 8.42 (d, *J* = 7.7 Hz, 1H), 8.12 (d, *J* = 7.7 Hz, 1H), 7.49 – 7.45 (m, 1H), 7.44 – 7.39 (m, 1H), 4.09 (t, *J* = 7.6 Hz, 2H), 1.72 (p, *J* = 7.6 Hz, 2H), 1.21 (m, *J* = 7.5 Hz, 2H), 0.83 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 185.56, 163.78, 149.59, 147.13, 144.70, 140.66, 137.06, 130.05, 125.54, 125.22, 124.18, 123.92, 122.50, 117.18, 110.68, 44.48, 32.08, 20.12, 13.65. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 323.1390, *obs*. 323.1335.

5-(1-butyl-3-ethyl-1H-indol-2-yl)picolinic acid (**4f**). The title compound was prepared from **1f** (0.016 mmol) and 1-iodobutane using the standard alkylation/deprotection procedure to yield the product as an orange oil (4 mg, 68%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.92 (s, 1H), 8.56 (d, *J* = 8.1 Hz, 1H), 8.33 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.70 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.41 (dt, *J* = 8.3, 0.9 Hz, 1H), 7.35 (ddd, *J* = 8.2, 7.0, 1.1 Hz, 1H), 7.20 (ddd, *J* =

7.9, 7.0, 0.9 Hz, 1H), 4.06 (t, *J* = 7.5 Hz, 2H), 2.73 (q, *J* = 7.5 Hz, 2H), 1.61 – 1.54 (m, 2H), 1.26 (t, *J* = 7.5 Hz, 3H), 1.18 – 1.07 (m, 2H), 0.78 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.95, 145.02, 144.50, 142.08, 138.19, 135.21, 129.05, 127.55, 126.74, 124.06, 120.93, 120.32, 120.25, 110.63, 77.16, 44.35, 32.23, 20.08, 17.93, 16.02, 13.64. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 323.1754, *obs.* 323.1755.

5-(1-butyl-3-cyano-1H-indol-2-yl)picolinic acid (**4g**). The title compound was prepared from **1g** (0.023 mmol) and 1-iodoethane using the standard alkylation/deprotection procedure to yield the product as a yellow oil (3.9 mg, 45%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.87 (s, 1H), 8.43 (s, 1H), 8.17 (d, *J* = 7.8 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.49 (d, *J* = 8.4 Hz, 1H), 7.42 (ddd, *J* = 8.3, 7.1, 1.2 Hz, 1H), 7.35 (ddd, *J* = 8.0, 7.0, 0.9 Hz, 1H), 4.16 (t, *J* = 7.6 Hz, 2H), 1.69 (p, *J* = 7.6 Hz, 2H), 1.17 (m, *J* = 7.5 Hz, 2H), 0.80 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.82, 148.63, 146.68, 139.73, 136.58, 132.99, 130.07, 127.56, 125.01, 124.30, 123.07, 120.08, 115.48, 111.33, 88.13, 44.95, 31.97, 19.92, 13.43. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 320.1394, *obs.* 320.1330.

5-(1-butyl-4-(trifluoromethyl)-1H-indol-2-yl)picolinic acid (**4h**). The title compound was prepared from **1h** and 1-iodoethane using the standard alkylation/deprotection procedure to yield the product as an orange oil (10 mg, 79%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.45 (d, *J* = 7.9 Hz, 1H), 8.26 (d, *J* = 8.0 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.49 (dt, *J* = 7.5, 0.9 Hz, 1H), 7.38 (ddd, *J* = 8.3, 7.4, 0.9 Hz, 1H), 6.92 (d, *J* = 1.9 Hz, 1H), 4.23 (t, *J* = 7.4 Hz, 2H), 1.69 (p, *J* = 7.6 Hz, 2H), 1.20 (m, *J* = 7.4 Hz, 2H), 0.83 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.33, 146.82, 144.34, 140.32, 139.05, 136.34, 133.90, 125.48, 124.83 (q, J_{CF} = 271.23 Hz), 124.18 (q, J_{CF} = 2.12 Hz), 122.75 (q, J_{CF} = 33.32 Hz), 122.67, 118.44 (q, J_{CF} = 4.58 Hz), 114.29, 104.42, 44.62, 32.39, 20.09, 13.65. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 363.1315, *obs.* 363.1284.

5-(1-butyl-4-fluoro-1H-indol-2-yl)picolinic acid (**4i**). The title compound was prepared from **1i** (0.019 mmol) and 1-iodobutane using the standard alkylation/deprotection procedure to yield the product as an orange oil (4.2

mg, 60%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.94 (s, 1H), 8.44 (d, *J* = 8.1 Hz, 1H), 8.25 (d, *J* = 8.0 Hz, 1H), 7.35 (dd, *J* = 9.0, 4.2 Hz, 1H), 7.31 (dd, *J* = 9.1, 2.5 Hz, 1H), 7.08 (td, *J* = 9.0, 2.4 Hz, 1H), 6.72 (s, 1H), 4.17 (t, *J* = 7.6 Hz, 2H), 1.67 (p, *J* = 7.5 Hz, 2H), 1.17 (m, *J* = 7.5 Hz, 2H), 0.83 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.96, 158.51 (d, J_{CF} = 236.69 Hz), 145.78, 140.63, 135.78, 135.54, 134.50, 130.65, 128.26 (d, J_{CF} = 11.27 Hz), 125.82, 112.57 (d, J_{CF} = 25.36 Hz), 111.47 (d, J_{CF} = 9.32 Hz), 106.24 (d, J_{CF} = 24.34 Hz), 106.08 (d, J_{CF} = 4.50 Hz), 44.67, 32.34, 20.09, 13.65. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 313.1347, *obs.* 313.1331.

5-(1-butyl-5-chloro-1H-indol-2-yl)picolinic acid (**4j**). The title compound was prepared from **1j** (0.015 mmol) and 1-iodobutane using the standard alkylation/deprotection procedure to yield the product as an orange oil (2.9 mg, 50%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.94 (s, 1H), 8.44 (d, *J* = 7.9 Hz, 1H), 8.22 (d, *J* = 7.8 Hz, 1H), 7.66 (d, *J* = 2.0 Hz, 1H), 7.37 (d, *J* = 8.8 Hz, 1H), 7.30 – 7.28 (m, 1H), 6.71 (s, 1H), 4.19 (t, *J* = 7.5 Hz, 2H), 1.68 (p, *J* = 7.6 Hz, 2H), 1.20 (m, *J* = 7.4 Hz, 2H), 0.84 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.26, 146.66, 144.10, 139.94, 137.15, 136.03, 134.10, 128.96, 126.55, 125.33, 123.95, 120.85, 111.70, 105.37, 44.62, 32.33, 20.10, 13.69. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 329.1051, *obs.* 329.1110.

5-(1-butyl-6-chloro-1H-indol-2-yl)picolinic acid (**4k**). The title compound was prepared from **1k** (0.021 mmol) and 1-iodobutane using the standard alkylation/deprotection procedure to yield the product as an orange oil (6.4 mg, 79%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.91 (s, 1H), 8.30 (dd, *J* = 8.1, 0.8 Hz, 1H), 8.27 (dd, *J* = 8.1, 2.0 Hz, 1H), 7.65 (s, 1H), 7.64 (d, *J* = 5.5 Hz, 1H), 7.12 (dd, *J* = 8.5, 1.8 Hz, 1H), 6.79 (s, 1H), 4.33 (t, *J* = 7.4 Hz, 2H), 1.65 (p, *J* = 7.6 Hz, 2H), 1.18 (m, *J* = 7.4 Hz, 2H), 0.78 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, Acetone-d_6) δ 165.44, 149.54, 147.33, 139.71, 138.79, 138.26, 133.28, 128.81, 127.69, 125.03, 122.94, 121.44, 111.39, 105.34, 44.69, 32.76, 20.42, 13.82. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 329.1051, *obs.* 329.1011.

5-(1-butyl-7-fluoro-1H-indol-2-yl)picolinic acid (**4l**). The title compound was prepared from **1l** (0.016 mmol) and 1-iodobutane using the standard alkylation/deprotection procedure to yield the product as an orange oil (4.3

mg, 73%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.02 (s, 1H), 8.48 (d, *J* = 8.1 Hz, 1H), 8.32 (d, *J* = 7.8 Hz, 1H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.08 (td, *J* = 7.9, 4.4 Hz, 1H), 6.99 (ddd, *J* = 12.8, 7.9, 0.9 Hz, 1H), 6.79 (d, *J* = 1.9 Hz, 1H), 4.30 (t, *J* = 7.5 Hz, 2H), 1.64 (p, *J* = 7.8 Hz, 2H), 1.12 (m, *J* = 7.4 Hz, 2H), 0.79 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.65, 150.18 (d, J_{CF} = 245.76 Hz), 145.34, 143.15, 141.75, 135.45, 134.45, 131.76 (d, J_{CF} = 5.29 Hz), 127.05 (d, J_{CF} = 9.03 Hz), 126.26, 121.26 (d, J_{CF} = 7.49 Hz), 117.47 (d, J_{CF} = 3.74 Hz), 109.69 (d, J_{CF} = 17.84 Hz), 107.45, 46.60, 33.68, 19.81, 13.61. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 313.1347, *obs.* 313.1340.

5-(1-butyl-4-methyl-1H-indol-2-yl)picolinic acid (**4m**). The title compound was prepared from **1m** (0.02 mmol) and 1-iodobutane using the standard alkylation/deprotection procedure to yield the product as an orange oil (2.2 mg, 30%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.94 (s, 1H), 8.42 (d, *J* = 8.1 Hz, 1H), 8.23 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.29 – 7.20 (m, 1H), 7.01 – 6.97 (m, 1H), 6.79 (s, 1H), 4.19 (t, *J* = 7.6, 2H), 2.58 (s, 3H), 1.69 (p, *J* = 7.6 Hz, 2H), 1.20 (m, *J* = 7.4 Hz, 2H), 0.83 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.00, 146.10, 143.23, 139.94, 138.76, 134.88, 133.98, 131.34, 128.08, 125.44, 123.96, 121.04, 108.27, 104.95, 44.57, 32.35, 20.13, 18.75, 13.69. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 309.1598, *obs.* 309.1598.

5-(1-ethyl-4-methoxy-1H-indol-2-yl)picolinic acid (**4n**). The title compound was prepared from **1n** (0.044 mmol) and 1-iodoethane using the standard alkylation/deprotection procedure to yield the product as an orange oil (7 mg, 45%). ^{1}H NMR (600 MHz, Acetone-d_6) δ 8.93 (s, 1H), 8.30 (d, *J* = 8.1 Hz, 1H), 8.27 (d, *J* = 8.0 Hz, 1H), 7.20 (t, *J* = 8.0 Hz, 1H), 7.15 (d, *J* = 8.3 Hz, 1H), 6.81 (s, 1H), 6.62 (d, *J* = 7.6 Hz, 1H), 4.32 (q, *J* = 7.1 Hz, 2H), 3.95 (s, 3H), 1.30 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (151 MHz, Acetone-d_6) δ 165.36, 154.67, 149.13, 140.61, 138.79, 135.13, 133.79, 125.21, 124.71, 119.91, 117.02, 104.49, 102.83, 100.83, 55.57, 39.93, 15.59. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 297.1234, *obs.* 297.1182.

5-(1-butyl-6-hydroxy-1H-indol-2-yl)picolinic acid (**4o**). The title compound was prepared from **1o** (0.02 mmol) and 1-iodobutane using the standard alkylation procedure to yield the benzyl and *t*-butyl protected product as a clear oil (7.3 mg, 53%). The intermediate was deprotected with 10 mg 5% Pd/C in 0.3 mL 1:1 EtOH/THF over 3 h under H_2 atmosphere followed by standard TFA deprotection to quantitatively yield the title compound as an orange oil (5.9 mg). ^{1}H NMR (600 MHz, Acetone-d_6) δ 8.87 (dd, *J* = 2.2, 0.9 Hz, 1H), 8.27 (dd, *J* = 8.1, 0.9 Hz, 1H), 8.21 (dd, *J* = 8.0, 2.2 Hz, 1H), 7.45 (dd, *J* = 8.5, 0.5 Hz, 1H), 6.93 (d, *J* = 2.1 Hz, 1H), 6.75 (dd, *J* = 8.5, 2.1 Hz, 1H), 6.68 (d, *J* = 0.9 Hz, 1H), 4.24 – 4.18 (m, 2H), 1.65 (p, *J* = 7.5 Hz, 2H), 1.19 (m, *J* = 7.4 Hz, 2H), 0.80 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, Acetone-d_6) δ 165.40, 155.32, 148.96, 146.28, 140.93, 138.18, 135.62, 134.10, 125.04, 122.82, 122.47, 111.68, 105.69, 96.70, 44.55, 32.55, 20.49, 13.86. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 311.1390, *obs.* 311.1354.

5-(1-butyl-6-fluoro-1H-indol-2-yl)picolinic acid (**4p**). The title compound was prepared from **1p** (0.013 mmol) and 1-iodoethane using the standard alkylation/deprotection procedure to yield the product as an orange oil (3.4 mg, 71%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.88 (dd, *J* = 2.2, 0.8 Hz, 1H), 8.16 (dt, *J* = 8.1, 0.7 Hz, 1H), 7.90 (dd, *J* = 8.1, 2.3 Hz, 1H), 7.56 (dd, *J* = 8.6, 5.4 Hz, 1H), 7.07 (dd, *J* = 10.0, 2.2 Hz, 1H), 6.92 (td, *J* = 9.1, 2.1 Hz, 1H), 6.61 (d, *J* = 0.8 Hz, 1H), 4.10 (t, *J* = 7.6 Hz, 2H), 1.68 – 1.60 (m, 2H), 1.17 (m, *J* = 7.4 Hz, 2H), 0.82 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.12, 160.36 (d, J_{CF} = 239.28 Hz), 149.71, 148.57, 138.35 (d, J_{CF} = 11.61 Hz), 137.18 (d, J_{CF} = 4.12 Hz), 136.88, 131.78, 124.71, 124.59, 121.96 (d, J_{CF} = 11.61 Hz), 109.40 (d, J_{CF} = 24.34 Hz), 104.46, 96.92 (d, J_{CF} = 25.48 Hz), 44.46, 32.12, 20.14, 13.78. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 313.1347, *obs.* 313.1347.

5-(1-butyl-6-methoxy-1H-indol-2-yl)picolinic acid (**4q**). The title compound was prepared from **1o** (0.02 mmol) and 1-iodobutane using the standard alkylation procedure to yield the benzyl and *t*-butyl product as a clear oil (1.8 mg, 51%). The intermediate was deprotected with 3 mg 5% Pd/C in 0.2 mL 1:1 EtOH/THF over 3 h under H_2 atmosphere to quantitatively produce the 6-OH intermediate (1.8 mg). Methylation proceeded with dimethyl

sulfate (0.5 μL, 1.1 eq) and K_2CO_3 (1.4 mg, 2.2 eq) stirring in 0.3 mL acetone for 4 h at 55 °C, followed by standard TFA deprotection to yield the title compound (1.2 mg, 64%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.85 (s, 1H), 8.35 (d, *J* = 8.0 Hz, 1H), 8.11 (d, *J* = 8.0 Hz, 1H), 7.55 (d, *J* = 8.4 Hz, 1H), 6.87 – 6.86 (m, 1H), 6.85 (s, 1H), 6.68 (s, 1H), 4.14 (t, *J* = 7.6 Hz, 2H), 3.92 (s, 3H), 1.67 (q, *J* = 7.8 Hz, 2H), 1.20 (m, *J* = 7.4 Hz, 2H), 0.83 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.26, 157.53, 146.82, 143.57, 139.91, 138.65, 134.45, 134.26, 124.77, 122.56, 122.25, 110.83, 106.02, 94.09, 55.93, 44.38, 32.05, 20.11, 13.73. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 325.1547, *obs.* 325.1500.

5-(1-(cyclopropylmethyl)-3-methyl-1H-indol-2-yl)picolinic (**5**). The title compound was prepared from **1a** (0.021 mmol) and (bromomethyl)cyclopropane using the standard alkylation/deprotection procedure to yield the product as an orange oil (6 mg, 80%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.52 (d, *J* = 8.1 Hz, 1H), 8.33 (d, *J* = 8.1 Hz, 1H), 7.65 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.46 (dt, *J* = 8.4, 0.9 Hz, 1H), 7.35 (ddd, *J* = 8.2, 6.9, 1.1 Hz, 1H), 7.21 (ddd, *J* = 7.9, 7.0, 0.9 Hz, 1H), 4.01 (d, *J* = 6.4 Hz, 2H), 2.34 (s, 3H), 0.94 – 0.86 (m, 1H), 0.42 – 0.37 (m, 2H), 0.02 – -0.04, (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.87, 145.22, 144.30, 142.08, 138.52, 135.11, 129.78, 128.61, 126.57, 124.20, 120.40, 119.95, 114.71, 110.70, 48.69, 31.07, 11.52, 9.37, 4.24. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 297.1441, *obs.* 297.1430.

5-(1-benzyl-1H-indol-2-yl)picolinic acid (**6**). The title compound was prepared from **1a** (0.02 mmol) and benzyl bromide using the standard alkylation/deprotection procedure to yield the product as an orange oil (3 mg, 39%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.79 (s, 1H), 8.25 (d, *J* = 8.1 Hz, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.74 (d, *J* = 7.9 Hz, 1H), 7.34 – 7.27 (m, 5H), 7.25 – 7.20 (m, 1H), 7.00 (d, *J* = 7.2 Hz, 2H), 6.90 (s, 1H), 5.40 (s, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.23, 146.66, 143.68, 139.57, 139.25, 137.21, 135.38, 134.01, 129.35, 128.03, 125.81, 125.02, 124.16, 121.64, 121.32, 115.86, 113.97, 110.83, 106.26, 48.13. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 329.1285, *obs.* 329.1250.

5-(1-(3-fluoropropyl)-1H-indol-2-yl)picolinic acid (**7**). The title compound was prepared from **1a** (0.016 mmol) and 1-fluoro-3-iodopropane using the standard alkylation/deprotection procedure to yield the product as an orange oil (2.3 mg, 41%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.36 (d, *J* = 7.9 Hz, 1H), 8.12 (d, *J* = 7.8 Hz, 1H), 7.68 (d, *J* = 7.8 Hz, 1H), 7.44 (d, *J* = 8.3 Hz, 1H), 7.32 (t, *J* = 7.5 Hz, 1H), 7.20 (t, *J* = 7.5 Hz, 1H), 6.75 (s, 1H), 4.39 (t, *J* = 7.1 Hz, 2H), 4.29 (t, *J* = 5.4 Hz, 1H), 4.22 (t, *J* = 5.4 Hz, 1H), 2.12 – 2.00 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.25, 147.49, 144.57, 138.89, 138.49, 135.45, 133.71, 128.17, 124.50, 123.62, 121.54, 121.00, 110.41, 105.97, 80.60 (d, J_{CF} = 164.39 Hz), 40.44, 30.75 (d, J_{CF} = 19.61 Hz). ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 299.1190, *obs.* 299.1173.

5-(1-(3-amino-3-oxopropyl)-1H-indol-2-yl)picolinic acid (**8**). Compound **1a** (11 mg, 0.037 mmol) and 3-bromopropanamide (11 mg, 2 eq) were dissolved in 1 mL MeCN and 0.5 mL THF. 82 mg CsF (adsorbed in a 3:5 ratio to Celite) was added and the reaction mixture was stirred at 90 °C for 18 h. Standard pTLC and TFA deprotection procedures yielded the product as an orange solid (4 mg, 30%). ^{1}H NMR (600 MHz, Acetone-d_6) δ 8.92 (s, 1H), 8.29 (d, *J* = 1.9 Hz, 2H), 7.64 (d, *J* = 7.9 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.27 (t, *J* = 7.4 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 1H), 6.77 (s, 1H), 4.60 (t, *J* = 7.4 Hz, 2H), 2.63 (t, *J* = 7.3 Hz, 2H). ^{13}C NMR (151 MHz, Acetone-d_6) δ 172.81, 165.45, 149.51, 146.91, 139.22, 138.96, 137.17, 133.65, 129.25, 124.97, 123.53, 121.78, 121.15, 111.54, 105.66, 41.18, 35.99. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 310.1186, *obs.* 310.1152.

5-(1-(2-methoxyethyl)-1H-indol-2-yl)picolinic acid (**9**). The title compound was prepared from **1a** and 1-bromo-2-methoxyethane using the standard alkylation/deprotection procedure to yield the product as an orange oil (3.3 mg, 31%). ^{1}H NMR (600 MHz, Acetone-d_6) δ 8.99 (dd, *J* = 2.2, 0.9 Hz, 1H), 8.38 (dd, *J* = 8.0, 2.1 Hz, 1H), 8.28 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.65 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.59 (dq, *J* = 8.3, 0.9 Hz, 1H), 7.26 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.14 (ddd, *J* = 7.9, 7.0, 0.9 Hz, 1H), 6.77 (d, *J* = 0.9 Hz, 1H), 4.45 (t, *J* = 5.4 Hz, 2H), 3.72 (t, *J* = 5.4 Hz, 2H), 3.15 (s, 3H). ^{13}C NMR (151 MHz, Acetone-d_6) δ 165.38, 149.81, 146.74, 139.45, 139.37,

137.88, 133.86, 129.14, 124.83, 123.39, 121.72, 121.10, 111.56, 105.27, 71.72, 58.91, 44.93, 29.84. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 297.1234, *obs.* 297.1178.

5-(1-(4-chlorophenethyl)-1H-indol-2-yl)picolinic acid (**10**). To a solution of 2-(4-chlorophenyl)ethan-1-ol (38 mg, 0.24 mmol) in 1 mL DCM was added PBr_3 (22 μL, 1 eq). After 1 h of stirring the reaction mixture was diluted with 25 mL DCM and washed with 25 mL 1 M aqueous NaOH. The organic layer was dried over $MgSO_4$ and concentrated. The resulting crude bromide (a clear oil) was directly reacted with **1a** using the standard alkylation/deprotection procedure to yield the title compound as an orange oil (1.1 mg, 8%). ^{1}H NMR (600 MHz, Acetone-d_6) δ 8.63 (s, 1H), 8.18 (d, *J* = 7.9 Hz, 1H), 7.96 (d, *J* = 8.0 Hz, 1H), 7.65 (d, *J* = 7.8 Hz, 2H), 7.28 (t, *J* = 7.7 Hz, 1H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.08 (d, *J* = 8.1 Hz, 2H), 6.79 (d, *J* = 7.9 Hz, 2H), 6.67 (s, 1H), 4.61 (t, *J* = 7.0 Hz, 2H), 2.98 (t, *J* = 6.9 Hz, 2H). ^{13}C NMR (151 MHz, Acetone-d_6) δ 165.39, 149.43, 148.01, 144.73, 138.39, 135.53, 132.79, 131.30, 129.25, 129.05, 127.85, 124.53, 123.45, 121.82, 121.11, 119.37, 118.52, 111.59, 105.14, 46.06, 35.75. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 377.1051, *obs.* 377.1033.

5-(1-(3-(3-chlorophenyl)propyl)-1H-indol-2-yl)picolinic acid (**11**). To a solution of 3-(3-chlorophenyl)-propan-1-ol (42 mg, 0.24 mmol) in 1 mL DCM was added PBr_3 (22 μL, 1 eq). After 1 h of stirring the reaction mixture was diluted with 25 mL DCM and washed with 25 mL 1 M aqueous NaOH. The organic layer was dried over $MgSO_4$ and concentrated. The resulting crude bromide (a clear oil) was directly reacted with **1a** using the standard alkylation/deprotection procedure to yield the title compound as an orange oil (1.7 mg, 13%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.87 (s, 1H), 8.31 (s, 1H), 8.09 (d, *J* = 7.6 Hz, 1H), 7.68 (d, *J* = 7.9 Hz, 1H), 7.35 – 7.29 (m, 2H), 7.20 (ddd, *J* = 7.9, 6.4, 1.5 Hz, 1H), 7.16 – 7.13 (m, 2H), 6.98 (s, 1H), 6.91 – 6.88 (m, 1H), 6.76 (s, 1H), 4.20 (t, *J* = 7.7 Hz, 2H), 2.49 (t, *J* = 7.2 Hz, 2H), 2.03 (q, *J* = 7.5 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.26, 148.63, 147.11, 142.40, 138.74, 138.67, 135.03, 134.46, 133.88, 129.94, 128.40, 128.16, 126.65, 126.54, 124.70, 123.61, 121.60, 120.94, 110.45, 105.98, 43.51, 32.38, 30.88.

ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 391.1208, *obs.* 391.1090.

5-(1-(3-hydroxypropyl)-1H-indol-2-yl)picolinic acid (**12**). The title compound was prepared from **1a** and (3-bromopropoxy)(tert-butyl)dimethylsilane using the standard alkylation procedure to produce the TBS and *t*-Bu protected product. TBS removal proceeded by stirring the compound with TBAF (10 eq) in 0.5 mL THF for 18 h. After partitioning between water and DCM, the organic layer was dried over $MgSO_4$, concentrated and purified by pTLC with 1:2 EtOAc/hexane to afford the free alcohol. Standard TFA deprotection yielded the final product as an orange solid (3.4 mg, 32%). ^{1}H NMR (600 MHz, Acetone-d_6) δ 8.81 (t, *J* = 1.5 Hz, 1H), 8.16 (d, *J* = 1.5 Hz, 2H), 7.55 (dt, *J* = 7.9, 0.9 Hz, 1H), 7.48 – 7.45 (m, 1H), 7.16 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.03 (ddd, *J* = 7.9, 7.0, 0.9 Hz, 1H), 6.69 (d, *J* = 0.8 Hz, 1H), 4.44 – 4.39 (m, 2H), 4.14 (t, *J* = 6.1 Hz, 2H), 1.93 (p, *J* = 2.2 Hz, 2H). ^{13}C NMR (151 MHz, Acetone-d_6) δ 165.41, 149.54, 147.17, 139.29, 138.72, 137.11, 133.36, 129.23, 124.99, 123.66, 121.96, 121.26, 111.26, 105.88, 66.34, 41.12, 29.16. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 297.1234, *obs*.297.1235.

5-(1-(4,4,4-trifluorobutyl)-1H-indol-2-yl)picolinic acid (**13**). The title compound was prepared from **1a** (0.023 mmol) and 1,1,1-trifluoro-4-iodobutane using the standard alkylation/deprotection procedure to yield the product as an orange oil (1.6 mg, 17%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.37 (d, *J* = 7.9 Hz, 1H), 8.11 (d, *J* = 7.9 Hz, 1H), 7.69 (d, *J* = 7.9 Hz, 1H), 7.40 (d, *J* = 8.3 Hz, 1H), 7.36 – 7.31 (m, 1H), 7.21 (t, *J* = 7.4 Hz, 1H), 6.76 (s, 1H), 4.33 – 4.25 (m, 2H), 1.97 – 1.88 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.32, 147.22, 144.63, 139.02, 138.54, 134.96, 133.71, 128.19, 124.84, 124.59 (q, J_{CF} = 278.41 Hz), 123.89, 121.73, 121.19, 110.23, 106.51, 43.07, 30.91 (q, J_{CF} = 29.81 Hz), 22.76. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 349.1158, *obs.* 349.1129.

5-(1-(benzofuran-2-ylmethyl)-1H-indol-2-yl)picolinic acid (**14**). To a solution of benzofuran-2-ylmethanol (36 mg, 0.24 mmol) in 1 mL DCM was added PBr_3 (22 μL, 1 eq). After 1 h of stirring the reaction mixture was diluted with 25 mL DCM and washed with 25 mL 1 M aqueous NaOH. The organic layer was dried over

$MgSO_4$ and concentrated. The resulting crude bromide (a clear oil) was directly reacted with **1a** using the standard alkylation/deprotection procedure to yield the title compound as an orange oil (2.9 mg, 23%). ^{1}H NMR (600 MHz, Acetone-d_6) δ 8.99 (s, 1H), 8.40 – 8.33 (m, 1H), 8.34 – 8.27 (m, 1H), 7.69 (t, *J* = 7.1 Hz, 2H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.43 (d, *J* = 8.3 Hz, 1H), 7.30 – 7.23 (m, 2H), 7.22 – 7.19 (m, 1H), 7.19 – 7.16 (m, 1H), 6.92 (s, 1H), 6.62 (s, 1H), 5.69 (s, 2H). ^{13}C NMR (151 MHz, Acetone-d_6) δ 165.58, 159.51, 155.81, 149.73, 147.40, 138.81, 132.25, 129.02, 125.27, 124.98, 124.33, 123.87, 123.46, 122.00, 121.87, 121.57, 117.51, 115.62, 111.86, 106.06, 105.45, 99.03, 42.58. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 369.1234, *obs.* 369.1109.

5-(1-((4-carbamoyloxazol-2-yl)methyl)-1H-indol-2-yl)picolinic acid (**15**). To a solution of methyl 2-(chloromethyl)oxazole-4-carboxylate (10.7 mg, 0.06 mmol) in 0.4 mL THF was added potassium iodide (12.2 mg, 1.2 eq), and the mixture was stirred for 30 min. **1a** (15 mg, 0.051 mmol) and 150 mg CsF (adsorbed in a 3:5 ratio to Celite) were added and the reaction was stirred at 75 °C for 18 h. The mixture was filtered and purified by pTLC with 2:5 EtOAc/hexane and deprotected with TFA to yield the title compound as an orange solid (7.2 mg, 30%). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.92 (d, *J* = 2.1 Hz, 1H), 8.25 (dd, *J* = 8.1, 2.3 Hz, 1H), 8.17 (d, *J* = 8.1 Hz, 1H), 7.65 (d, *J* = 7.9 Hz, 1H), 7.58 (s, 1H), 7.55 (d, *J* = 8.3 Hz, 1H), 7.25 (ddd, *J* = 8.3, 7.0, 1.2 Hz, 1H), 7.14 (ddd, 2H), 6.88 (s, 1H), 5.60 (s, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 166.20, 162.00, 160.17, 149.26, 147.49, 142.90, 138.72, 137.79, 136.86, 136.49, 127.97, 125.10, 123.41, 121.23, 116.86, 114.93, 110.89, 105.40, 41.33. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 363.1088, *obs.* 363.1049.

5-(1-((4-(methoxycarbonyl)oxazol-2-yl)methyl)-1H-indol-2-yl)picolinic (**16**). Methyl 2-(chloromethyl)oxazole-4-carboxylate was hydrolyzed with 3 eq LiOH in 1:5 water/THF over 2 h following acidification with 1 M HCl. The aqueous solution was then extracted with EtOAc which was then evaporated to quantitatively produce the corresponding carboxylic acid. To a solution of 2-(chloromethyl)oxazole-4-carboxylic acid (27 mg, 0.17 mmol) in 2 mL 1:1 THF/DCM was added oxalyl chloride (16 μL, 1.1 eq) and catalytic (1 μL) DMF at 0 °C. The mixture was stirred for 18 h, warming to rt. The mixture was cooled to 0 °C and 0.4 mL NH_4OH (30 w/w %)

was added and stirred for 30 min to afford the corresponding primary amide, 2-(chloromethyl)oxazole-4-carboxamide (5 mg, 18%). ^{1}H NMR (600 MHz, Methanol-d_4) δ 8.41 (s, 1H), 4.76 (s, 2H). ^{13}C NMR (151 MHz, Methanol-d_4) δ 164.78, 161.25, 144.41, 137.78, 36.22. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 161.0112, *obs.* 161.0132.

To the amide (5 mg, 0.031 mmol) in 0.4 mL THF was added potassium iodide (6.2 mg, 2.4 eq) and the mixture was stirred for 10 min at 50 °C. **1a** (9 mg, 0.031 mmol) and 150 mg CsF (adsorbed in a 3:5 ratio to Celite) were added and the reaction was stirred at 75 °C for 18 h. The mixture was filtered and purified by pTLC with 9:1 EtOAc/hexane and deprotected with TFA to yield the title compound as an orange solid (1.7 mg, 13%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.01 (dd, *J* = 2.2, 0.8 Hz, 1H), 8.18 (dt, *J* = 8.1, 0.8 Hz, 1H), 8.13 (s, 1H), 8.06 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.67 – 7.63 (m, 1H), 7.46 (dq, *J* = 8.3, 0.9 Hz, 1H), 7.29 – 7.25 (m, 1H), 7.19 (ddt, *J* = 8.0, 7.2, 1.0 Hz, 1H), 6.75 (d, *J* = 0.8 Hz, 1H), 5.39 (d, *J* = 0.8 Hz, 2H), 3.91 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.97, 161.23, 160.24, 150.00, 144.91, 138.69, 137.26, 133.66, 133.05, 132.15, 130.79, 128.28, 125.55, 124.83, 123.73, 121.49, 110.37, 105.70, 52.46, 41.70. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 378.1084, *obs.* 378.1031.

3-(1-butyl-4-chloro-1H-indol-2-yl)benzoic acid (**17**). Compound **1q** (0.038 mmol) and 1-iodoethane were reacted using the standard alkylation procedure to yield the ethyl ester as a clear oil (10 mg, 74%). Hydrolysis proceeded by stirring in 0.25 mL 2 M aqueous KOH, 0.25 mL THF and 0.25 mL MeOH for 18 h. The mixture was acidified with 1 M aqueous HCl and extracted with EtOAc which was dried over $MgSO_4$ and evaporated to give the title compound (5 mg, 54%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.27 (td, *J* = 1.8, 0.6 Hz, 1H), 8.19 (ddd, *J* = 7.8, 1.7, 1.2 Hz, 1H), 7.77 (ddd, *J* = 7.6, 1.9, 1.2 Hz, 1H), 7.64 – 7.58 (m, 1H), 7.30 (ddd, *J* = 7.3, 1.8, 0.8 Hz, 1H), 7.20 – 7.13 (m, 2H), 6.69 (d, *J* = 0.8 Hz, 1H), 4.16 (t, *J* = 7.6 Hz, 2H), 1.72 – 1.64 (m, 2H), 1.22 – 1.14 (m, 2H), 0.81 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.23, 140.60, 138.37, 134.73, 133.38, 131.02, 130.01, 129.79, 129.11, 127.00, 126.17, 122.56, 119.80, 108.95, 101.46, 44.38, 32.23, 20.07, 13.71. ESI-TOF-MS (*m*/*z*): $[M+Cl]^-$ *calc*. 328.1104, *obs.* 328.1049.

4-(1-butyl-4-chloro-1H-indol-2-yl)benzoic acid (**18**). Compound **1q** (0.038 mmol) and 1-iodoethane were reacted using the standard alkylation procedure to yield the ethyl ester as a clear oil (9 mg, 67%). Hydrolysis proceeded by stirring in 0.25 mL 2 M aqueous KOH, 0.25 mL THF and 0.25 mL MeOH for 18 h. The mixture was acidified with 1 M aqueous HCl and extracted with EtOAc which was dried over $MgSO_4$ and evaporated to give the title compound (4 mg, 48%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.25 – 8.21 (m, 2H), 7.65 – 7.61 (m, 2H), 7.31 (ddd, *J* = 7.6, 1.4, 0.8 Hz, 1H), 7.20 – 7.13 (m, 2H), 6.72 (d, *J* = 0.8 Hz, 1H), 4.19 (t, *J* = 7.4 Hz, 2H), 1.69 – 1.62 (m, 2H), 1.17 (m, *J* = 7.4 Hz, 2H), 0.80 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.20, 140.69, 138.70, 138.28, 130.66, 129.42, 128.81, 127.05, 126.31, 122.83, 119.91, 109.03, 102.04, 44.49, 32.20, 20.06, 13.72. ESI-TOF-MS (*m*/*z*): $[M+Cl]^-$ *calc*. 328.1104, *obs.* 328.1051.

(5-(1-butyl-4-chloro-1H-indol-2-yl)pyridin-2-yl)methanol (**19**). Compound **4c-tBu** (3.5 mg, 0.009 mmol) was reduced with lithium aluminum hydride (45 μL 1 M solution, 5 eq) in 0.4 mL THF at 0 °C for 1h. The solution was worked up with 1:1 brine/1 M aqueous NaOH and EtOAc. The organic layer dried over $MgSO_4$, evaporated and purified by pTLC using 1:1 EtOAc/hexane as an eluent to yield the title compound as a clear oil (1.3 mg, 45%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.72 (dd, *J* = 2.3, 0.9 Hz, 1H), 7.82 (dd, *J* = 8.0, 2.2 Hz, 1H), 7.40 (dt, *J* = 8.0, 0.8 Hz, 1H), 7.30 (ddd, *J* = 7.5, 1.5, 0.8 Hz, 1H), 7.19 – 7.13 (m, 2H), 6.68 (d, *J* = 0.8 Hz, 1H), 4.87 (s, 2H), 4.13 (t, *J* = 7.5 Hz, 2H), 1.68 – 1.62 (m, 2H), 1.18 (m, *J* = 7.5 Hz, 2H), 0.82 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 158.98, 148.80, 138.40, 137.49, 127.68, 126.20, 122.79, 122.25, 120.92, 120.34, 119.92, 108.94, 101.94, 64.32, 44.41, 32.31, 20.11, 13.76. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 281.1648, *obs.* 281.1599.

methyl 5-(dibenzo[b,d]furan-4-yl)picolinic acid (**20**). To methyl 5-bromopicolinate (50 mg, 0.23 mmol), dibenzo[b,d]furan-4-ylboronic acid (73 mg, 1.5 eq), $Pd(PPh_3)_4$ (40 mg, 0.15 eq) and K_2CO_3 (127 mg, 4 eq) was added 2.2 mL toluene and 0.8 mL water, and the mixture was stirred at 90 °C for 18 h in a sealed vial. The resulting suspension was filtered, concentrated and purified by pTLC using 1:2 EtOAc/hexane as an eluent,

affording the product as a white solid (32 mg, 46%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.30 (dd, *J* = 2.3, 0.8 Hz, 1H), 8.41 (dd, *J* = 8.2, 2.3 Hz, 1H), 8.30 (dd, *J* = 8.2, 0.8 Hz, 1H), 8.02 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.99 (ddd, *J* = 7.7, 1.4, 0.7 Hz, 1H), 7.65 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.59 (dt, *J* = 8.3, 1.0 Hz, 1H), 7.52 – 7.45 (m, 2H), 7.43 – 7.33 (m, 1H), 4.06 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.77, 156.24, 153.47, 149.65, 146.65, 136.83, 135.65, 127.84, 126.62, 125.53, 125.18, 123.86, 123.65, 123.31, 121.60, 121.25, 120.96, 112.00, 53.08. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 304.0968, *obs.* 304.0968.

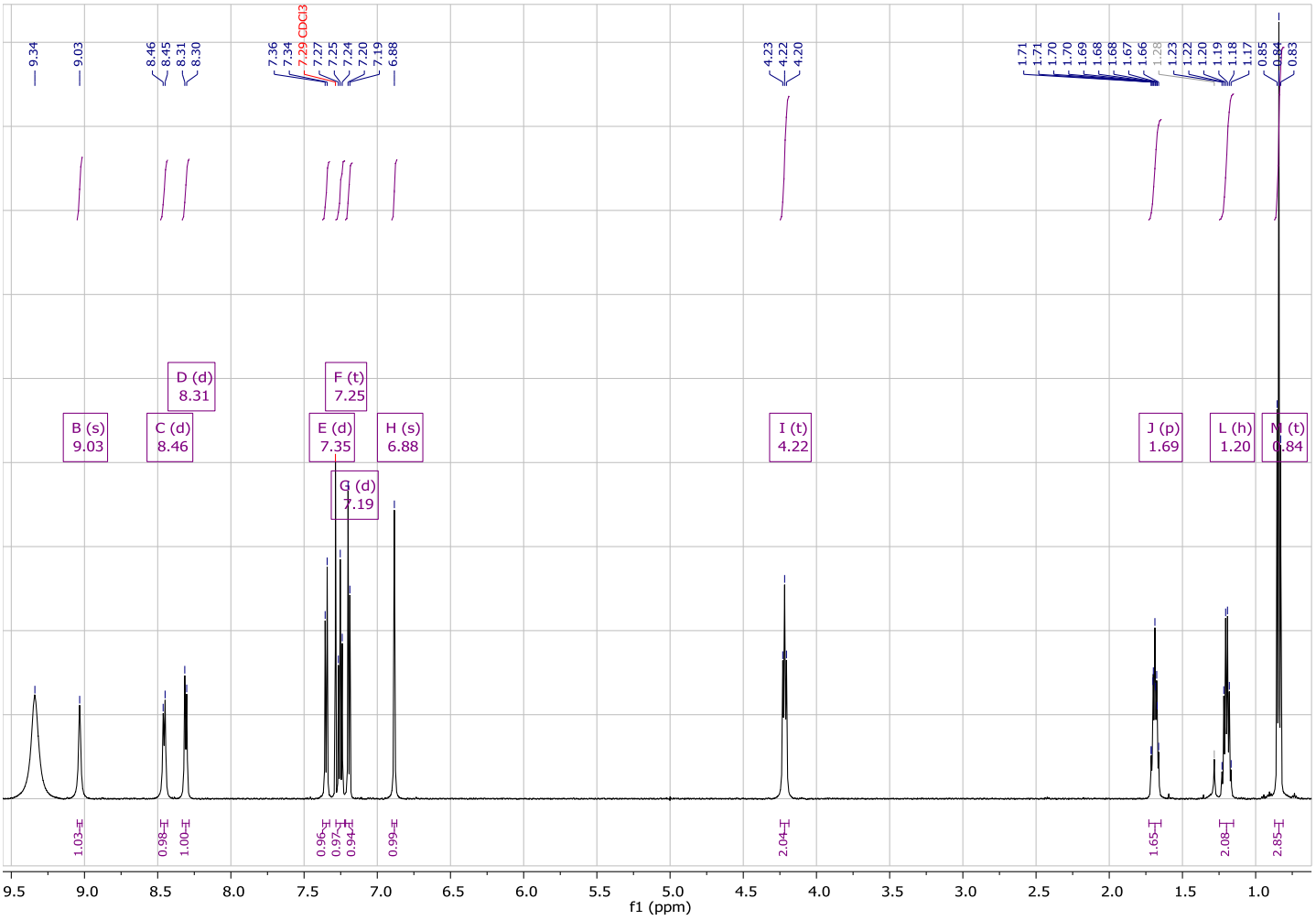
5-(dibenzo[b,d]furan-4-yl)picolinic acid (**21**). Compound **20** (16 mg, 0.053 mmol) was dissolved in 1 mL acetone and 1 mL 1 M aqueous LiOH and stirred for 1 h. The mixture was acidified with 1 M aqueous HCl, diluted with brine and extracted with EtOAc. The organic layer was collected, dried over $MgSO_4$ and concentrated to afford the product as a white solid (12 mg, 81%). ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.27 (m, 1H), 8.52 (dd, *J* = 8.1, 2.2 Hz, 1H), 8.28 – 8.20 (m, 3H), 7.86 (d, *J* = 7.5 Hz, 1H), 7.76 (d, *J* = 8.3 Hz, 1H), 7.57 (t, *J* = 7.6 Hz, 2H), 7.45 (t, *J* = 7.4 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 165.96, 155.44, 152.61, 148.83, 147.35, 136.86, 134.33, 128.01, 127.13, 124.73, 124.64, 123.94, 123.47, 123.22, 121.94, 121.38, 120.77, 111.89. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 290.0812, *obs.* 290.0750.

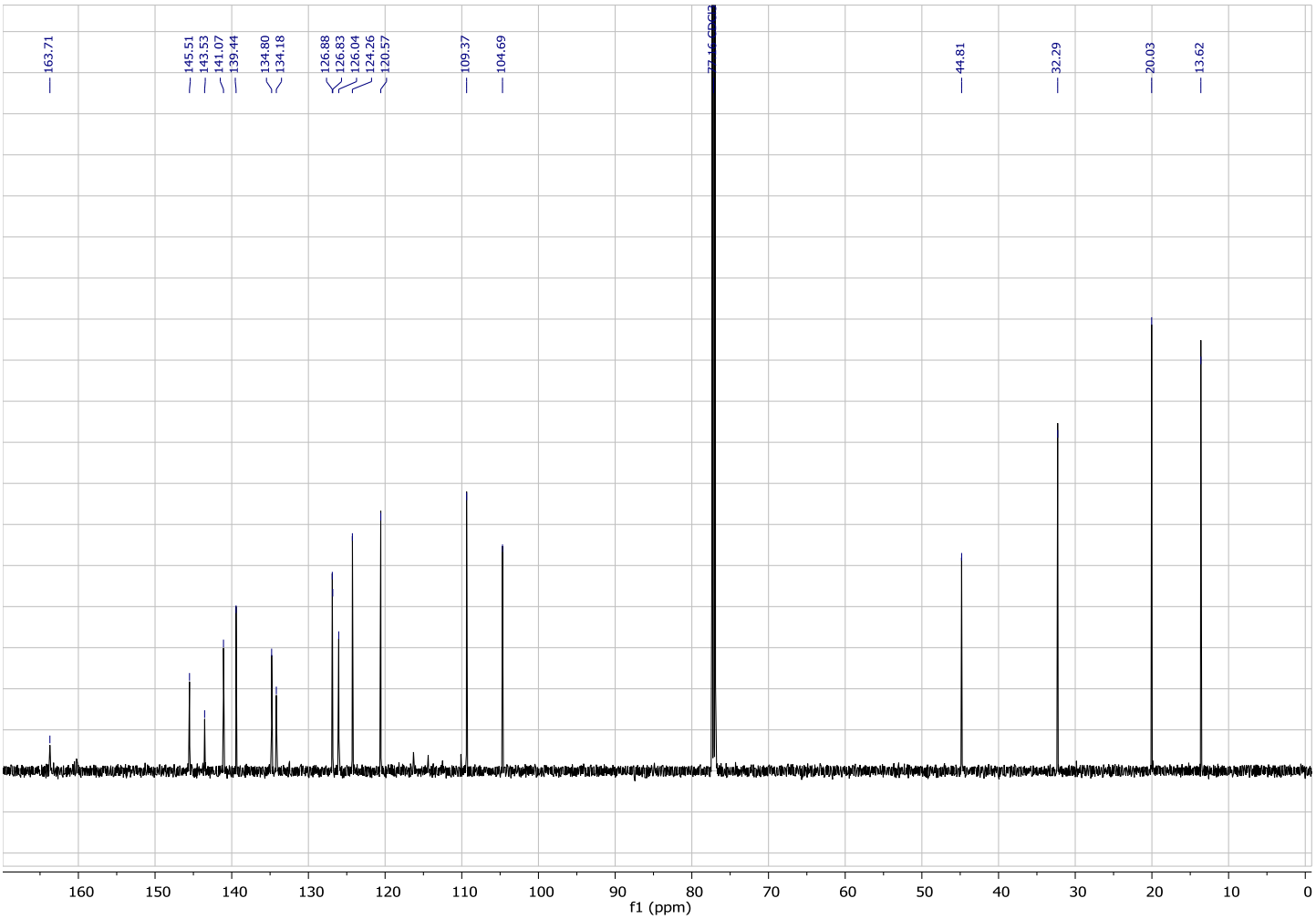
5-(1H-indol-3-yl)picolinic acid (**22**). Compound **23** (6 mg, 0.015 mmol) was deprotected with 1 mL 1:3 DCM/TFA over 6 h to quantitatively yield the title compound as an orange solid. ^{1}H NMR (600 MHz, Acetone-d_6) δ 9.15 (d, *J* = 2.2 Hz, 1H), 8.50 (dd, *J* = 8.2, 2.1 Hz, 1H), 8.28 (d, *J* = 8.1 Hz, 1H), 8.06 – 7.99 (m, 2H), 7.58 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.27 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.23 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H). ^{13}C NMR (151 MHz, Acetone) δ 164.92, 146.25, 143.33, 138.49, 137.75, 136.47, 126.55, 126.39, 125.94, 125.74, 123.47, 121.79, 119.88, 113.25. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 239.0815, *obs.* 239.0803.

tert-butyl 5-(1-(tert-butyloxycarbonyl)-indol-3-yl)picolinate (**23**). To a solution of *tert*-butyl 5-bromopicolinate (19 mg, 0.078 mmol), 1-butyloxycarbonyl-indole-3-boronic acid pinacol ester (29 mg, 1.1 eq), $Pd_2(dba)_3$ (1 mg,

0.01 eq) and PCy_3 (1 mg, 0.024 eq) in 0.25 mL dioxane was added K_3PO_4 (0.1 mL of 1.27 M aqueous solution, 1.7 eq), and the mixture was stirred for 18 h at 80 °C. The cooled mixture was partitioned between water and EtOAc and the organic layer was dried, concentrated and purified by pTLC using 1:9 EtOAc/hexane as an eluent to afford the title compound as a white solid (13 mg, 42%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.04 (dd, *J* = 2.2, 0.8 Hz, 1H), 8.24 (d, *J* = 8.4 Hz, 1H), 8.15 (dd, *J* = 8.1, 0.8 Hz, 1H), 8.06 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.84 (s, 1H), 7.78 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.41 (ddd, *J* = 8.4, 7.2, 1.2 Hz, 1H), 7.33 (ddd, *J* = 8.1, 7.2, 1.0 Hz, 1H), 1.70 (s, 9H), 1.67 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.31, 149.56, 148.76, 147.90, 136.04, 135.44, 132.92, 128.28, 125.30, 125.05, 124.33, 123.62, 119.52, 118.02, 115.84, 84.69, 82.42, 28.32, 28.31. ESI-TOF-MS (*m*/*z*): $[M+H]^+$ *calc*. 395.1965, *obs*. 395.1965.

Fig. S4 NMR spectra of CBIP-TFA (4c)

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104.69
77.16
44.81
32.29
20.03
13.62
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

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