Supporting Information

Non-nucleoside Inhibitors of BasE, An Adenylating Enzyme in the Siderophore Biosynthetic Pathway of the Opportunistic Pathogen *Acinetobacter baumannii*

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Preparative reverse-phase HPLC conditions:

mobile phases:

solvent A: 10 mM NH_4HCO_3

solvent B: MeOH

Elution with solvent A and a linear gradient of solvent B

Method 1: 20 to 60% of B in 20 min;

Method 2: 40-100% of B in 20 min;

Method 3: 20-80% of B in 20 min;

Method 4: 20-60% of B in 15 min;

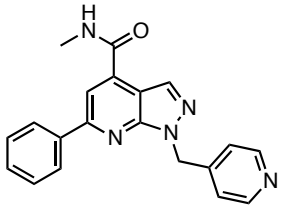
Method 5: 10-40% of B in 15 min;

Method 6: 30-60% of B in 20 min;

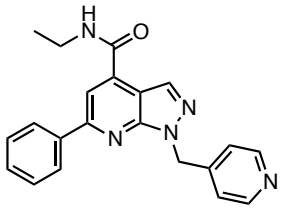
Method 7: 10-80% of B in 30 min.

Method 8: 10-40% of B in 20 min

Experimental Procedures and Data for Compounds 23–25, 27–28, 37–41, 43–62, 66-90.

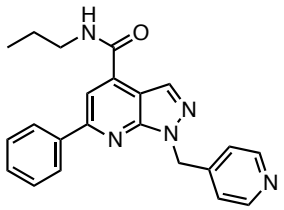


***N*-Methyl-6-phenyl-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxamide (23).** The title compound was prepared using the general procedure for the synthesis of 4-carboxamide analogues, using a 2 M methylamine solution in THF (300 μL, 0.60 mmol, 12 equiv). Purification by preparative reverse-phase HPLC using method 2 afforded the title compound (9.7 mg, 56%) as a white solid: R_T 13.7 min; ^{1}H NMR (600 MHz, CD_3OD) δ 3.04 (s, 3H), 5.87 (s, 2H), 7.31 (d, *J* = 6.0 Hz, 2H), 7.48 (t, *J* = 7.2 Hz, 1H), 7.52 (t, *J* = 7.2 Hz, 2H), 8.09 (s, 1H), 8.21 (d, *J* = 7.2 Hz, 2H), 8.43 (s, 1H), 8.47 (d, *J* = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, CD_3OD) δ 26.9, 50.4, 113.1, 113.8, 124.2, 128.6, 130.0, 131.1, 134.6, 138.6, 139.7, 149.0, 150.4, 153.0, 159.0, 168.2; HRMS (ESI–) calcd for $C_{20}H_{18}N_5O$ $[M + H]^+$ 344.1511, found 344.1504 (error 2.0 ppm).

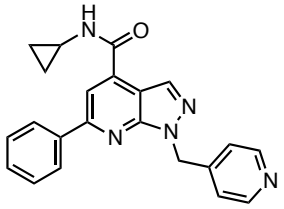


***N*-Ethyl-6-phenyl-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxamide (24).** The title compound was prepared using the general procedure for the synthesis of 4-carboxamide analogues, using a 70% (w/w) ethylamine solution in water (202 μL, 0.25 mmol, 5.6 equiv). Purification by preparative reverse-phase HPLC using method 2 afforded the title compound (6.5 mg, 40%) as a white solid: R_T 15.2 min; ^{1}H NMR (600 MHz, CD_3OD) δ 1.32 (t, *J* = 7.2 Hz, 3H), 3.53 (q, *J* = 7.2 Hz, 2H), 5.88 (s, 2H), 7.32 (d, *J* = 6.0 Hz, 2H), 7.49 (t, *J* = 7.2

Hz, 1H), 7.53 (t, J = 7.2 Hz, 2H), 8.10 (s, 1H), 8.22 (d, J = 7.2 Hz, 2H), 8.43 (s, 1H), 8.47 (d, J = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, CD_3OD) δ14.7, 36.0, 50.4, 113.1, 113.8, 124.1, 128.7, 130.0, 131.1, 134.6, 138.9, 139.8, 149.0, 150.4, 153.0, 159.0, 167.5; HRMS (ESI–) calcd for $C_{21}H_{20}N_5O$ $[M + H]^+$ 358.1668, found 358.1675 (error 2.0 ppm).

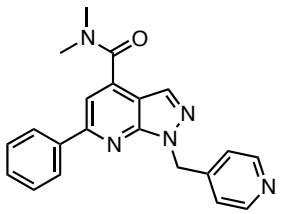


6-Phenyl-*N*-propyl-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxamide (25). The title compound was prepared using the general procedure for the synthesis of 4-carboxamide analogues, using propylamine (149 mg, 207 μL, 0.25 mmol, 5.6 equiv). Purification by preparative reverse-phase HPLC using method 2 afforded the title compound (6.5 mg, 40%) as a white solid: R_T 16.8 min; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.05 (t, J =7.2 Hz, 3H), 1.73 (sext, J = 7.2 Hz, 2H), 3.54 (q, J = 7.2 Hz, 2H), 5.80 (s, 2H), 6.41 (br s, 1H), 7.21 (d, J = 5.4 Hz, 2H), 7.48 (t, J = 7.2 Hz, 1H), 7.52 (t, J = 7.2 Hz, 2H), 7.89 (s, 1H), 8.12 (d, J = 7.2 Hz, 2H), 8.36 (s, 1H), 8.54 (d, J = 5.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 11.7, 23.1, 42.2, 49.9, 111.6, 112.9, 122.7, 127.7, 129.1, 130.2, 132.8, 137.5, 138.5, 145.8, 150.3, 151.8, 157.7, 165.6; HRMS (ESI–) calcd for $C_{22}H_{22}N_5O$ $[M + H]^+$ 372.1824, found 372.1830 (error 1.6 ppm).

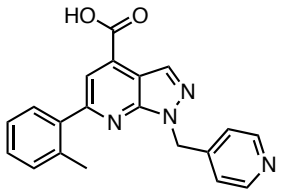


***N*-Cyclopropyl-6-phenyl-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-b]pyridine-4-carboxamide (27).** The title compound was prepared using the general procedure for the synthesis of 4-carboxamide analogues, using cyclopropylamine (144 mg, 175 μL, 0.25 mmol,

5.6 equiv). Purification by preparative reverse-phase HPLC using method 2 afforded the title compound (4.7 mg, 28%) as a white solid: R_T 15.3 min; ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.72–0.74 (m, 2H), 0.95–0.99 (m, 2H), 2.99–3.04 (m, 1H), 5.79 (s, 2H), 6.57 (br s, 1H), 7.20 (d, *J* = 6.0 Hz, 2H), 7.48 (t, *J* = 7.2 Hz, 1H), 7.51 (t, *J* = 7.2 Hz, 2H), 7.84 (s, 1H), 8.10 (d, *J* = 7.2 Hz, 2H), 8.37 (s, 1H), 8.53 (d, *J* = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 7.1, 23.5, 49.9, 111.6, 112.7, 122.7, 127.7, 129.1, 130.2, 133.0, 136.9, 138.5, 145.8, 150.3, 151.8, 157.6, 166.9; HRMS (ESI–) calcd for $C_{22}H_{20}N_5O$ $[M + H]^+$ 370.1668, found 370.1673 (error 1.4 ppm).

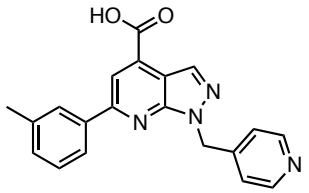


***N*,*N*-Dimethyl-6-phenyl-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxamide (28).** The title compound was prepared using the general procedure for the synthesis of 4-carboxamide analogues, using a 2 M dimethylamine solution in methanol (1.26 mL, 0.25 mmol, 5.6 equiv). Purification by preparative reverse-phase HPLC using method 2 afforded the title compound (6.5 mg, 40%) as a white solid: R_T 14.4 min; ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.02 (s, 3H), 3.24 (s, 3H), 5.79 (s, 2H), 7.23 (d, *J* = 6.0 Hz, 2H), 7.48 (t, *J* = 7.2 Hz, 1H), 7.51 (t, *J* = 7.2 Hz, 2H), 7.65 (s, 1H), 8.06 (s, 1H), 8.10 (d, *J* = 7.2 Hz, 2H), 8.55 (d, *J* = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 35.7, 39.2, 49.8, 111.4, 113.0, 122.8, 127.7, 129.1, 130.1, 132.3, 138.6, 138.8, 145.8, 150.3, 151.3, 157.6, 167.9; HRMS (ESI–) calcd for $C_{21}H_{20}N_5O$ $[M + H]^+$ 358.1668, found 358.1662 (error 1.7 ppm).



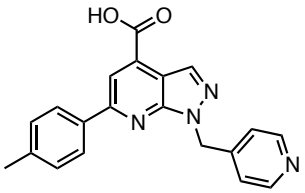
1-(Pyridin-4-ylmethyl)-6-*o*-tolyl-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (37). Ethyl 1-(pyridin-4-ylmethyl)-6-*o*-tolyl-1H-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with *o*-tolylboronic acid (91.1 mg, 0.67 mmol, 2 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (77 mg, 58%) as a white solid: R_f 0.41 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.48 (t, J = 7.2 Hz, 3H), 2.35 (s, 3H), 4.52 (q, J = 7.2 Hz, 2H), 5.76 (s, 2H), 7.15 (d, J = 6.0 Hz, 2H), 7.29–7.36 (m, 3H), 7.48 (d, J = 7.2 Hz, 1H), 7.94 (s, 1H), 8.51 (s, 1H), 8.52 (d, J = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.4, 20.6, 49.9, 62.1, 111.7, 119.4, 122.5, 126.2, 129.2, 130.1, 131.3, 131.9, 133.9, 136.4, 139.3, 145.9, 150.2, 151.4, 160.2, 165.1.

Ethyl 1-(pyridin-4-ylmethyl)-6-*o*-tolyl-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50 mg, 0.134 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 2 afforded the title compound (45 mg, 97%) as a white solid: R_T 10.8 min; ^{1}H NMR (600 MHz, CD_3OD) δ 2.29 (s, 3H), 5.81 (s, 2H), 7.35 (d, J = 6.0 Hz, 2H), 7.27–7.34 (m, 3H), 7.46 (d, J = 7.2 Hz, 1H), 7.76 (s, 1H), 8.44 (d, J = 6.0 Hz, 2H), 8.58 (s, 1H); ^{13}C NMR (150 MHz, CD_3OD) δ 20.6, 50.5, 114.4, 119.6, 123.9, 127.0, 129.7, 130.9, 131.9, 135.9, 137.4, 141.4, 142.8, 149.3, 150.3, 152.5, 161.8, 172.2; HRMS (ESI–) calcd for $C_{20}H_{15}N_4O_2$ $[M - H]^-$ 343.1195, found 343.1203 (error 2.3 ppm).



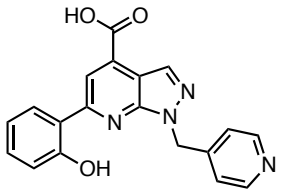
1-(Pyridin-4-ylmethyl)-6-*m*-tolyl-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (38). Ethyl 1-(pyridin-4-ylmethyl)-6-*m*-tolyl-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with 3-tolylboronic acid (91 mg, 0.67 mmol, 2.0 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (96.0 mg, 71%) as a pale brown solid: R_f 0.38 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.50 (t, J = 7.2 Hz, 3H), 2.45 (s, 3H), 4.53 (q, J = 7.2 Hz, 2H), 5.79 (s, 2H), 7.20 (d, J = 6.0 Hz, 2H), 7.27 (d, J = 7.2 Hz, 1H), 7.39 (t, J = 7.2 Hz, 1H), 7.93 (ovlp d, J = 7.2 Hz, 1H), 7.94 (ovlp s, 1H), 8.24 (s, 1H), 8.43 (s, 1H), 8.53 (d, J = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.4, 21.6, 49.7, 62.1, 112.0, 115.9, 122.6, 124.8, 128.2, 128.9, 130.8, 132.2, 133.9, 138.2, 138.7, 145.9, 150.1, 151.9, 157.6, 165.2.

Ethyl 1-(pyridin-4-ylmethyl)-6-*m*-tolyl-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50.0 mg, 0.134 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 4 afforded the title compound (43.2 mg, 94%) as a white solid: R_T 11.2 min; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.42 (s, 3H), 5.85 (s, 2H), 7.21 (d, J = 6.0 Hz, 2H), 7.32 (d, J = 7.6 Hz, 1H), 7.43 (t, J = 7.6 Hz, 1H), 8.01 (ovlp d, J = 7.6 Hz, 1H), 8.02 (ovlp s, 1H), 8.23 (s, 1H), 8.45 (s, 1H), 8.51 (d, J = 6.0 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 21.1, 49.0, 111.9, 115.0, 122.3, 124.5, 127.8, 128.9, 130.1, 133.3, 133.8, 137.7, 138.3, 146.1, 149.9, 151.4, 156.4, 166.1; HRMS (ESI–) calcd for $C_{20}H_{15}N_4O_2$ $[M - H]^-$ 343.1200, found 343.1207 (error 2.0 ppm).



1-(Pyridin-4-ylmethyl)-6-*p*-tolyl-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (39). Ethyl 1-(pyridin-4-ylmethyl)-6-*p*-tolyl-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with *p*-tolylboronic acid (91.1 mg, 0.67 mmol, 2 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (70 mg, 56%) as a white solid: R_f 0.39 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.50 (t, J = 7.2 Hz, 3H), 2.42 (s, 3H), 4.53 (q, J = 7.2 Hz, 2H), 5.79 (s, 2H), 7.20 (d, J = 6.0 Hz, 2H), 7.31 (d, J = 7.8 Hz, 2H), 8.05 (d, J = 7.8 Hz, 2H), 8.24 (s, 1H), 8.43 (s, 1H), 8.54 (d, J = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.5, 21.5, 49.8, 62.1, 111.9, 115.7, 122.7,127.5, 129.8, 132.3, 133.9, 135.6, 140.4, 145.9, 150.2, 151.9, 157.4, 165.3.

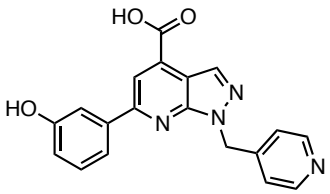
Ethyl 1-(pyridin-4-ylmethyl)-6-*p*-tolyl-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50 mg, 0.134 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 2 afforded the title compound (45.9 mg, 99%) as a white solid: R_T 12.3 min; ^{1}H NMR (600 MHz, CD_3OD) δ 2.41 (s, 3H), 5.85 (s, 2H), 7.35 (d, J = 6.0 Hz, 2H), 7.29 (d, J = 6.0 Hz, 2H), 7.31 (d, J = 7.8 Hz, 2H), 8.07 (d, J = 7.8 Hz, 2H), 8.17 (s, 1H), 8.45 (d, J = 6.0 Hz, 2H), 8.51 (s, 1H); ^{13}C NMR (150 MHz, CD_3OD) δ 21.3, 50.3, 114.5, 115.9, 124.1, 128.5, 130.5, 135.9, 137.6, 141.0, 143.0, 149.3, 150.3, 153.2, 159.0, 172.5; HRMS (ESI–) calcd for $C_{20}H_{15}N_4O_2$ $[M - H]^-$ 343.1195, found 343.1202 (error 2.0 ppm).



6-(2-Hydroxyphenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (40). Ethyl 6-(2-hydroxyphenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with 2-hydroxybenzeneboronic acid (92 mg, 0.67 mmol, 2.0 equiv). After initial extraction with CH_2Cl_2 the aqueous phase was back extracted with EtOAc (15 mL) and the organic extracts were combined and concentrated. Purification by flash chromatography afforded the ethyl ester of the title compound (108.5 mg, 87%) as a yellow solid: R_f 0.47 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.51 (t, J = 7.2 Hz, 3H), 5.55 (q, J = 7.2 Hz, 2H), 5.68 (s, 2H), 6.95–6.98 (m, 1H), 7.02 (dd, J = 8.4 Hz, 1.2 Hz, 1H), 7.18 (d, J = 6.0 Hz, 2H), 7.34–7.37 (m, 1H), 7.94 (dd, J = 8.4, 1.8 Hz, 1H), 8.35 (s, 1H), 8.44 (s, 1H), 8.55 (d, J = 6.0 Hz, 2H), 12.90 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.4, 50.6, 62.5, 112.4, 114.9, 118.7, 118.9, 119.8, 122.4, 127.9, 132.8, 133.4, 134.4, 144.7, 148.7, 150.5, 157.9, 159.6, 164.6.

Ethyl 6-(2-hydroxyphenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50.0 mg, 0.134 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 4 afforded the title compound (43.7 mg, 94%) as a yellow solid: R_T 9.7 min; ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.82 (s, 2H), 6.95–7.01 (m, 2H), 7.18 (d, J = 6.0 Hz, 2H), 7.32–7.36 (m, 1H), 8.00 (d, J = 8.0 Hz, 1H), 8.40 (s, 1H), 8.48 (s, 1H), 8.51 (d, J = 6.0 Hz, 2H), 11.66 (br s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 49.4, 112.2, 116.5, 117.4, 119.6, 121.9,

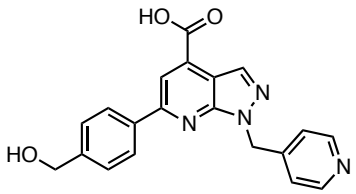
122.1, 129.5, 131.6, 133.8, 135.9, 145.9, 149.6, 150.0, 156.4, 157.3, 166.1; HRMS (ESI–) calcd for $C_{19}H_{13}N_4O_3$ $[M - H]^-$ 345.0993, found 345.0996 (error 0.9 ppm).



6-(3-Hydroxyphenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (41). Ethyl 6-(3-hydroxyphenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with 3-hydroxyphenylboronic acid (92 mg, 0.67 mmol, 2.0 equiv). The aqueous phase was back extracted with CH_2Cl_2 (4 × 10 mL) and the organic extracts were combined and concentrated. Purification by flash chromatography afforded the ethyl ester of the title compound (26.5 mg, 21%) as a pale brown solid: R_f 0.38 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.50 (t, J = 7.2 Hz, 3H), 4.54 (q, J = 7.2 Hz, 2H), 5.74 (s, 2H), 6.99 (dd, J = 7.8, 1.8 Hz, 1H), 7.21 (d, J = 6.0 Hz, 2H), 7.37 (t, J = 7.8 Hz, 1H), 7.63 (d, J = 7.8 Hz, 1H), 7.82 (t, J = 1.8 Hz, 1H), 8.27 (s, 1H), 8.44 (s, 1H), 8.57 (d, J = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.5, 49.6, 62.3, 112.2, 114.3, 116.0, 117.8, 119.4, 123.1, 130.3, 132.4, 134.2, 139.5, 146.8, 149.6, 151.9, 157.2, 157.6, 165.2.

Ethyl 6-(3-hydroxyphenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (20.0 mg, 0.0534 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 4 afforded the title compound (16.2 mg, 88%) as a white solid: R_T 8.7 min; ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.84 (s, 2H), 6.91 (dd, J = 8.0, 1.6 Hz, 1H), 7.20 (d, J = 6.0 Hz, 2H), 7.35 (t, J = 8.0 Hz, 1H), 7.62–7.63 (m, 2H), 8.16 (s, 1H), 8.45 (s, 1H), 8.51 (d, J = 6.0 Hz, 2H), 9.68 (br s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 49.0, 111.9, 113.9, 115.0, 117.2,

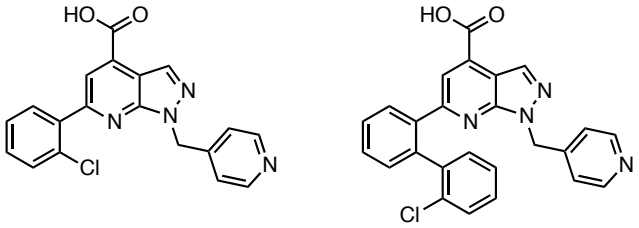
118.1, 122.3, 130.1, 133.3, 133.7, 139.0, 146.0, 149.9, 151.4, 156.3, 157.9, 166.0; HRMS (ESI–) calcd for $C_{19}H_{13}N_4O_3$ $[M - H]^-$ 345.0993, found 345.0996 (error 0.9 ppm).



6-[4-(Hydroxymethyl)phenyl]-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (43). Ethyl 6-[4-(hydroxymethyl)phenyl]-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with 4-(hydroxymethyl)phenylboronic acid (102 mg, 0.67 mmol, 2.0 equiv). After initial extraction with CH_2Cl_2 the aqueous phase was back extracted with EtOAc (15 mL) and the organic extracts were combined and concentrated. Purification by flash chromatography afforded the ethyl ester of the title compound (40.7 mg, 31%) as a brown solid: R_f 0.19 (EtOAc); ^{1}H NMR (600 MHz, DMSO-d_6) δ 1.44 (t, J = 7.2 Hz, 3H), 4.50 (q, J = 7.2 Hz, 2H), 4.59 (d, J = 5.4 Hz, 2H), 5.33 (t, J = 5.4 Hz, 1H), 5.87 (s, 2H), 7.20 (d, J = 6.0 Hz, 2H), 7.50 (d, J = 8.4 Hz, 2H), 8.21 (d, J = 8.4 Hz, 2H), 8.26 (s, 1H), 8.46 (s, 1H), 8.50 (d, J = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 14.1, 49.1, 62.0, 62.5, 111.3, 114.8, 122.3, 127.0, 127.2, 132.2, 133.3, 135.9, 145.0, 146.1, 149.9, 151.4, 156.3, 164.5.

Ethyl 6-[4-(hydroxymethyl)phenyl]-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (24.0 mg, 0.0618 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 4 afforded the title compound (5.8 mg, 26%) as a pale yellow solid: R_T 8.4 min; ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.58 (s, 2H), 5.84 (s, 2H), 7.21 (d, J = 6.0 Hz, 2H), 7.48 (d, J = 8.4 Hz, 2H), 8.18–8.21 (m, 3H), 8.45–8.51 (m, 3H); ^{13}C NMR (150 MHz, DMF-d_7)

δ 50.4, 64.3, 113.4, 116.1, 123.6, 128.1, 128.4, 134.6, 135.0, 137.8, 146.2, 147.5, 151.2, 153.0, 157.9, 167.4; HRMS (ESI–) calcd for $C_{20}H_{15}N_4O_3$ $[M - H]^-$ 359.1150, found 359.1148 (error 0.6 ppm).

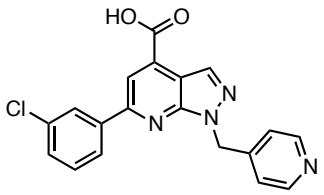


6-(2-Chlorophenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (44) and 6-(2′-Chlorobiphenyl-2-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (74). 2-Chlorophenylboronic acid (105 mg, 0.67 mmol, 2.0 equiv) was coupled to **109** (100 mg, 0.335 mmol, 1.0 equiv) using the general procedure for Suzuki coupling. Purification by flash chromatography afforded a mixture of the ethyl esters of the two title compounds (confirmed by APCI+ MS) as a brown oil (99 mg), which was not purified further. The mixture was converted to the title compounds using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 2 afforded the title compounds **44** (18 mg, 15%) as a white solid and **74** (7 mg, 5%) as a light orange solid.

Data for **44**: R_T 9.8 min; ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.80 (s, 2H), 7.18 (d, J = 6.0 Hz, 2H), 7.49–7.55 (m, 2H), 7.62–7.69 (m, 2H), 7.91 (s, 1H), 8.50 (d, J = 6.0 Hz, 2H), 8.53 (s, 1H); ^{13}C NMR (150 MHz, DMF-d_7) δ 50.4, 110.9, 114.0, 120.1, 123.5, 128.6, 130.8, 131.3, 131.6, 132.9, 133.2, 135.2, 140.0, 147.6, 151.1, 152.6, 157.5; HRMS (ESI–) calcd for $C_{19}H_{12}ClN_4O_2$ $[M - H]^-$ 363.0654, found 363.0655 (error 0.3 ppm).

Data for **74**: R_T 12.1 min; ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.38 (s, 2H), 6.93 (d, J = 6.0 Hz, 2H), 7.08–7.13 (m, 1H), 7.21–7.25 (m, 3H), 7.35–7.37 (m, 1H), 7.55–7.61 (m, 2H), 7.66 (s, 1H),

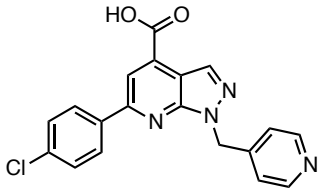
7.80–7.82 (m, 1H), 8.38 (s, 1H), 8.47 (d, J = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, DMF-d_7) d 49.8, 119.5, 119.6, 123.4, 123.5, 127.8, 129.5, 129.9, 130.0, 130.1, 131.2, 132.3, 133.0, 133.5, 134.8, 139.8, 140.3, 141.8, 147.4, 151.0, 151.1, 152.2, 159.5.; HRMS (ESI–) calcd for $C_{25}H_{16}ClN_4O_2$ $[M - H]^-$ 439.0967, found 439.0971 (error 0.9 ppm).



6-(3-Chlorophenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (45). Ethyl 6-(3-chlorophenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with 3-chlorophenylboronic acid (105 mg, 0.67 mmol, 2 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (83 mg, 63%) as a white solid: R_f 0.45 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.51 (t, J = 7.2 Hz, 3H), 4.55 (q, J = 7.2 Hz, 2H), 5.80 (s, 2H), 7.19 (d, J = 5.4 Hz, 2H), 7.43 (d, J = 5.4 Hz, 2H), 7.99–8.01 (m, 1H), 8.15 (s, 1H), 8.22 (s, 1H), 8.46 (s, 1H), 8.54 (d, J = 5.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.5, 49.9, 62.3, 112.5, 115.7, 122.6, 125.7, 127.7, 130.0, 130.3, 132.6, 134.0, 135.2, 140.1, 145.7, 150.3, 151.8, 155.8, 165.0.

Ethyl 6-(3-chlorophenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50 mg, 0.127 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 2 afforded the title compound (45.9 mg, 99%) as a white solid: R_T 13.1 min; ^{1}H NMR (600 MHz, CD_3OD) δ 5.87 (s, 2H), 7.30 (d, J = 5.4 Hz, 2H), 7.45 (d, J = 7.8 Hz, 1H), 7.49 (t, J = 7.8 Hz, 1H), 8.10 (d, J = 7.8 Hz, 1H), 8.19 (s, 1H), 8.29 (s, 1H), 8.46 (d, J = 5.4 Hz, 2H), 8.55 (s,

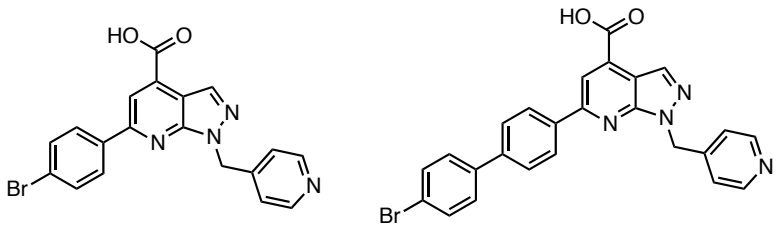
1H); ^{13}C NMR (150 MHz, CD_3OD) δ 50.4, 115.1, 115.9, 124.1, 126.8, 128.4, 130.5, 131.4, 135.9, 136.0, 142.4, 143.4, 149.3, 150.3, 153.1, 157.0, 172.1; HRMS (ESI–) calcd for $C_{19}H_{12}ClN_4O_2$ $[M - H]^-$ 363.0649, found 363.0654 (error 1.7 ppm).



6-(4-Chlorophenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (46). Ethyl 6-(4-chlorophenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with 4-chlorophenylboronic acid (105 mg, 0.67 mmol, 2 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (90 mg, 70%) as a white solid: R_f 0.43 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.51 (t, J = 7.2 Hz, 3H), 4.55 (q, J = 7.2 Hz, 2H), 5.80 (s, 2H), 7.20 (d, J = 4.8 Hz, 2H), 7.49 (d, J = 8.4 Hz, 2H), 8.10 (d, J = 8.4 Hz, 2H), 8.23 (s, 1H), 8.46 (s, 1H), 8.55 (d, J = 4.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.5, 49.9, 62.3, 112.3, 115.5, 122.6, 128.9, 129.3, 132.6, 134.1, 136.4, 136.8, 145.8, 150.3, 151.9, 156.2, 165.1.

Ethyl 6-(4-chlorophenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (15 mg, 0.038 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 2 afforded the title compound (10 mg, 72%) as a white solid: R_T 13.4 min; ^{1}H NMR (600 MHz, CD_3OD) δ 5.86 (s, 2H), 7.29 (d, J = 6.0 Hz, 2H), 7.51 (d, J = 8.4 Hz, 2H), 8.18 (s, 1H), 8.19 (d, J = 8.4 Hz, 2H), 8.46 (d, J = 6.0 Hz, 2H), 8.53 (s, 1H); ^{13}C NMR (150 MHz, CD_3OD) δ 50.3, 114.9, 115.8, 124.1, 129.98, 130.05, 135.9, 136.8, 139.0, 143.3, 149.3, 150.3, 153.1, 157.4,

172.2; HRMS (ESI–) calcd for $C_{19}H_{12}ClN_4O_2$ $[M - H]^-$ 363.0649, found 363.0658 (error 2.5 ppm).

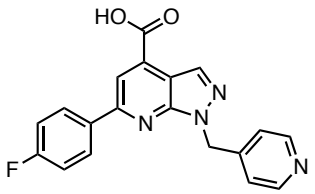


6-(4-Bromophenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (47) and 6-(4′-Bromobiphenyl-4-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (73). The ethyl esters of the title compounds were prepared using the general procedure for Suzuki coupling of **109** with 4-bromophenylboronic acid (135 mg, 0.67 mmol, 2 equiv). Purification by flash chromatography afforded a mixture of the esters of the two title compounds as a white solid, which was not purified further. The esters mixture (40 mg) was converted to the title compounds using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 2 afforded the two title compounds as white solids **47** (13 mg, 9.5%) and **73** (12 mg, 7.4 %).

Data for **47**: R_T 13.6 min; ^{1}H NMR (600 MHz, CD_3OD) δ 5.85 (s, 2H), 7.29 (d, J = 6.0 Hz, 2H), 7.66 (d, J = 8.4 Hz, 2H), 8.11 (d, J = 8.4 Hz, 2H), 8.18 (s, 1H), 8.46 (d, J = 6.0 Hz, 2H), 8.53 (s, 1H); ^{13}C NMR (150 MHz, CD_3OD) δ 50.3, 114.9, 115.7, 124.1, 125.0, 130.3, 133.0, 135.9, 139.4, 143.3, 149.3, 150.3, 153.1, 157.5, 172.2; HRMS (ESI–) calcd for $C_{19}H_{12}BrN_4O_2$ $[M - H]^-$ 409.0144, found 409.0137 (error 1.7 ppm).

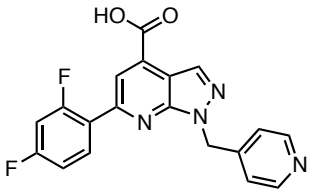
Data for **73**: R_T 17.4 min; ^{1}H NMR (600 MHz, CD_3OD) δ 5.87 (s, 2H), 7.31 (d, J = 5.4 Hz, 2H), 7.59–7.64 (m, 4H), 7.76 (d, J = 8.4 Hz, 2H), 8.25 (s, 1H), 8.28 (d, J = 8.4 Hz, 2H), 8.46 (d, J = 5.4 Hz, 2H), 8.54 (s, 1H); ^{13}C NMR (150 MHz, CD_3OD) δ 50.3, 114.8, 116.0, 122.8, 124.1,

128.2, 129.2, 129.8, 133.0, 135.9, 139.6, 140.7, 142.2, 143.1, 149.3, 150.3, 153.2, 158.2, 172.3; HRMS (ESI–) calcd for $C_{25}H_{16}BrN_4O_2$ $[M - H]^-$ 483.0457, found 483.0469 (error 2.5 ppm).



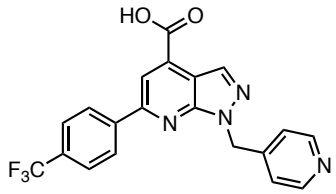
6-(4-Fluorophenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (48). Ethyl 6-(4-fluorophenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with 4-fluorophenylboronic acid (94 mg, 0.67 mmol, 2.0 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (85.3 mg, 68%) as a gray solid: R_f 0.42 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.50 (t, J = 7.2 Hz, 3H), 4.54 (q, J = 7.2 Hz, 2H), 5.79 (s, 2H), 7.16–7.20 (m, 4H), 8.12–8.15 (m, 2H), 8.20 (s, 1H), 8.44 (s, 1H), 8.54 (d, J = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.4, 49.8, 62.2, 112.0, 115.5, 116.0, 116.1, 122.6, 129.5, 129.6, 132.5, 134.0, 146.0, 150.0, 151.9, 156.3, 165.1.

Ethyl 6-(4-fluorophenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50.0 mg, 0.133 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 4 afforded the title compound (40.8 mg, 88%) as a white solid: R_T 10.7 min; ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.80 (s, 2H), 7.18 (d, J = 6.0 Hz, 2H), 7.32–7.37 (m, 2H), 8.07 (s, 1H), 8.22–8.25 (m, 2H), 8.48–8.50 (m, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 48.8, 113.3, 114.1, 115.7, 115.9, 122.2, 129.35, 129.43, 134.5, 135.1, 146.5, 149.8, 151.4, 154.7, 166.7; HRMS (ESI–) calcd for $C_{19}H_{12}FN_4O_2$ $[M - H]^-$ 347.0950, found 347.0964 (error 4.0 ppm).



6-(2,4-Difluorophenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (49). Ethyl 6-(2,4-difluorophenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with 2,4-difluorophenylboronic acid (106 mg, 0.67 mmol, 2 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (87 mg, 66%) as a white solid: R_f 0.39 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.50 (t, J = 7.2 Hz, 3H), 4.54 (q, J = 7.2 Hz, 2H), 5.80 (s, 2H), 6.95-6.99 (m, 1H), 7.02-7.05 (m, 1H), 7.18 (d, J = 6.0 Hz, 2H), 8.00-8.04 (m, 1H), 8.25 (d, J = 1.8 Hz, 1H), 8.49 (s, 1H), 8.54 (d, J = 6.0 Hz, 2H).

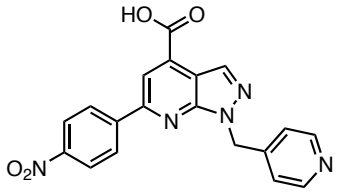
Ethyl 6-(2,4-difluorophenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50 mg, 0.127 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 2 afforded the title compound (45 mg, 97%) as a white solid: R_T 11.2 min; ^{1}H NMR (600 MHz, CD_3OD) δ 5.84 (s, 2H), 7.09–7.12 (m, 2H), 7.28 (d, J = 6.0 Hz, 2H), 8.02–8.06 (m, 1H), 8.08 (d, J = 2.4 Hz, 1H), 8.45 (d, J = 6.0 Hz, 2H), 8.56 (s, 1H); HRMS (ESI–) calcd for $C_{19}H_{11}F_2N_4O_2$ $[M - H]^-$ 365.0850, found 365.0863 (error 3.6 ppm).



1-(Pyridin-4-ylmethyl)-6-[4-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (50). Ethyl 1-(Pyridin-4-ylmethyl)-6-[4-(trifluoromethyl)phenyl]-1*H*-

pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with 4-(trifluoromethyl)phenylboronic acid (127.3 mg, 0.67 mmol, 2 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (92 mg, 62%) as a white solid: R_f 0.46 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.53 (t, J = 7.2 Hz, 3H), 4.57 (q, J = 7.2 Hz, 2H), 5.84 (s, 2H), 7.25 (d, J = 6.0 Hz, 2H), 7.79 (d, J = 8.4 z, 2H), 8.27 (d, J = 8.4 z, 2H), 8.30 (s, 1H), 8.50 (s, 1H), 8.56 (d, J = 6.0 Hz, 2H).

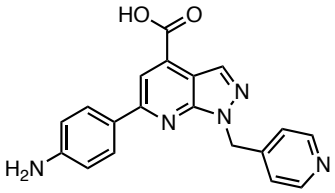
Ethyl 1-(pyridin-4-ylmethyl)-6-(4-(trifluoromethyl)phenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (90 mg, 0.211 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 2 afforded the title compound (40 mg, 48%) as a white solid: R_T 13.9 min; ^{1}H NMR (600 MHz, CD_3OD) δ 5.88 (s, 2H), 7.31 (d, J = 6.0 Hz, 2H), 7.81 (d, J = 8.4 Hz, 2H), 8.25 (s, 1H), 8.39 (d, J = 8.4 Hz, 2H), 8.47 (d, J = 6.0 Hz, 2H), 8.56 (s, 1H); ^{13}C NMR (150 MHz, CD_3OD) δ 50.3, 115.2, 116.1, 124.0, 125.7, 126.58, 126.61, 129.0, 135.9, 143.8, 149.0, 150.2, 153.0, 156.8, 172.0; HRMS (ESI–) calcd for $C_{20}H_{12}F_3N_4O_2$ $[M - H]^-$ 397.0912, found 397.0907 (error 0.3 ppm).



6-(4-Nitrophenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (51). Ethyl 6-(4-nitrophenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with 4-nitrophenylboronic acid (112 mg, 0.67 mmol, 2.0 equiv). After initial extraction with CH_2Cl_2 the aqueous phase was back extracted with EtOAc (15 mL) and the organic extracts were combined and concentrated.

Purification by flash chromatography afforded the ethyl ester of the title compound (67.0 mg, 50%) as a brown solid: R_f 0.39 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.52 (t, J = 7.2 Hz, 3H), 4.57 (q, J = 7.2 Hz, 2H), 5.83 (s, 2H), 7.21 (d, J = 6.0 Hz, 2H), 8.32–8.37 (m, 5H), 8.51 (s, 1H), 8.55 (d, J = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.5, 50.0, 62.5, 113.1, 116.0, 122.6, 124.3, 128.5, 133.0, 134.2, 144.2, 145.6, 148.8, 150.2, 151.9, 154.6, 164.8.

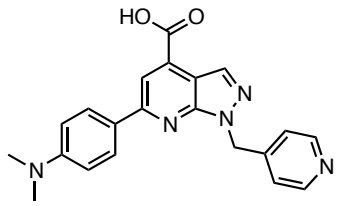
Ethyl 6-(4-nitrophenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (47 mg, 0.117 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 2 afforded the title compound (38 mg, 88%) as a white solid: R_T 11.2 min; ^{1}H NMR (150 MHz, DMSO-d_6) δ 5.81 (s, 2H), 7.19 (d, J = 6.0 Hz, 2H), 8.17 (s, 1H), 8.36 (d, J = 9.0 Hz, 2H), 8.45 (d, J = 9.0 Hz, 2H), 8.50 (d, J = 6.0 Hz, 2H), 8.56 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 48.9, 114.6, 114.8, 122.3, 124.0, 128.3, 135.1, 145.0, 145.4, 146.4, 147.8, 149.9, 151.5, 153.0, 166.3; HRMS (ESI–) calcd for $C_{19}H_{12}N_5O_4$ $[M - H]^-$ 374.0889, found 374.0884 (error 1.3 ppm).



6-(4-Aminophenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (52). Ethyl 6-(4-aminophenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** (50 mg, 0.168 mmol, 1.0 equiv) with 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (74 mg, 0.34 mmol, 2 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (27 mg, 43%) as a yellow solid: R_f 0.25 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.50 (t, J = 7.2 Hz, 3H), 4.53 (q, J = 7.2 Hz, 2H), 5.77 (s, 2H), 6.77 (d, J = 8.4 Hz, 2H), 7.19 (d, J = 6.0 Hz, 2H),

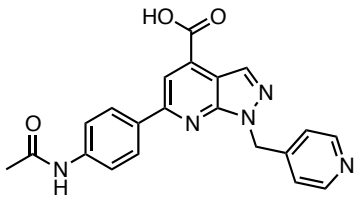
8.01 (d, J = 8.4 Hz, 2H), 8.18 (s, 1H), 8.34 (s, 1H), 8.53 (d, J = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.5, 49.7, 62.1, 111.2, 115.11, 115.12, 122.7, 128.4, 129.0, 132.1, 134.0, 146.1, 146.7, 150.2, 152.0, 157.5, 165.5.

Ethyl 6-(4-aminophenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (20 mg, 0.054 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 6 afforded the title compound (8.1 mg, 44%) as a yellow solid: R_T 6.5 min; ^{1}H NMR (150 MHz, CD_3OD) δ 5.82 (s, 2H), 6.78 (d, J = 9.0 Hz, 2H), 7.29 (d, J = 6.6 Hz, 2H), 7.97 (d, J = 9.0 Hz, 2H), 8.08 (s, 1H), 8.45–8.46 (m, 3H); HRMS (ESI–) calcd for $C_{19}H_{14}N_5O_2$ [M - H]$^-$ 344.1147, found 344.1150 (error 0.6 ppm).



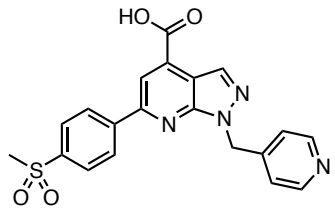
6-[4-(Dimethylamino)phenyl]-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (53). Ethyl 6-[4-(dimethylamino)phenyl]-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with 4-(dimethylamino)phenylboronic acid (166 mg, 0.67 mmol, 2 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (130 mg, 97%) as a white solid: R_f 0.35 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.51 (t, J = 7.2 Hz, 3H), 3.06 (s, 6H), 4.53 (q, J = 7.2 Hz, 2H), 5.78 (s, 2H), 6.80 (d, J = 9.0 Hz, 2H), 7.21 (d, J = 6.0 Hz, 2H), 8.10 (d, J = 9.0 Hz, 2H), 8.21 (s, 1H), 8.37 (s, 1H), 8.53 (d, J = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.5, 40.4, 49.7, 62.0, 111.1, 112.2, 115.1, 122.8, 125.9, 128.7, 131.9, 134.0, 146.2, 150.2, 151.8, 152.2, 157.7, 165.6.

Ethyl 6-[4-(dimethylamino)phenyl]-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50 mg, 0.125 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 2 afforded the title compound as a white solid (41 mg, 88%): R_T 11.8 min; ^{1}H NMR (600 MHz, CD_3OD) δ 3.02 (s, 6H), 5.82 (s, 2H), 6.83 (d, J = 9.0 Hz, 2H), 7.29 (d, J = 6.0 Hz, 2H), 8.08 (d, J = 9.0 Hz, 2H), 8.12 (s, 1H), 8.44–8.45 (m, 3H); ^{13}C NMR (150 MHz, CD_3OD) δ 40.5, 50.2, 113.2, 113.6, 115.2, 124.1, 127.8, 129.5, 135.8, 142.5, 149.5, 150.3, 153.2, 153.3, 159.5, 172.8; HRMS (ESI–) calcd for $C_{21}H_{18}N_5O_2$ $[M - H]^-$ 372.1460, found 372.1470 (error 2.7 ppm).



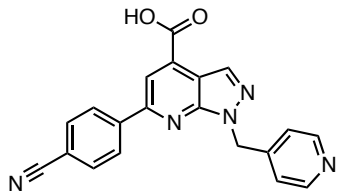
6-(4-Acetamidophenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (54). Ethyl 6-(4-acetamidophenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with 4-acetamidophenylboronic acid (120 mg, 0.67 mmol, 2 equiv). Purification by flash chromatography afforded the ester (77 mg, 55%) as a white solid: R_f 0.09 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.50 (t, J = 7.2 Hz, 3H), 2.20 (s, 3H), 4.53 (q, J = 7.2 Hz, 2H), 5.78 (s, 2H), 7.20 (d, J = 6.0 Hz, 2H), 7.69 (d, J = 9.0 Hz, 2H), 8.05 (br s, 1H), 8.11 (d, J = 9.0 Hz, 2H), 8.21 (s, 1H), 8.42 (s, 1H), 8.52 (d, J = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.5, 24.8, 49.8, 62.2, 111.9, 115.5, 120.0, 122.8, 128.4, 132.4, 133.8, 134.0, 140.1, 146.1, 150.1, 151.9, 156.7, 165.2, 169.0.

Ethyl 6-(4-acetamidophenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50 mg, 0.120 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 2 afforded the title compound as a white solid (35 mg, 75%): R_T 8.6 min; ^{1}H NMR (600 MHz, DMSO-d_6) δ 2.08 (s, 3H), 5.80 (s, 2H), 7.20 (d, J = 4.8 Hz, 2H), 7.75 (d, J = 8.4 Hz, 2H), 8.11 (s, 1H), 8.15 (d, J = 8.4 Hz, 2H), 8.46 (s, 1H), 8.50 (d, J = 4.8 Hz, 2H), 10.20 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 24.2, 48.8, 112.6, 114.0, 119.0, 122.3, 127.7, 132.8, 134.2, 140.8, 146.5, 149.9, 151.5, 155.5, 156.5, 166.7, 168.6; HRMS (ESI–) calcd for $C_{21}H_{16}N_5O_3$ [M – H]$^-$ 386.1253, found 386.1262 (error 2.3 ppm).



6-[4-(Methylsulfonyl)phenyl]-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (55). Ethyl 6-[4-(methylsulfonyl)phenyl]-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with 4-(methylsulfonyl)phenylboronic acid (134 mg, 0.67 mmol, 2 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (85 mg, 58%) as a white solid: R_f 0.22 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.52 (t, J = 7.2 Hz, 3H), 3.11 (s, 3H), 4.57 (q, J = 7.2 Hz, 2H), 5.83 (s, 2H), 7.19 (d, J = 6.0 Hz, 2H), 8.09 (d, J = 8.4 z, 2H), 8.30 (s, 1H), 8.35 (d, J = 8.4 z, 2H), 8.50 (s, 1H), 8.55 (d, J = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.6, 44.8, 50.1, 62.6, 113.1, 116.1, 122.7, 128.3, 128.7, 133.0, 134.2, 141.7, 143.5, 145.6, 150.4, 152.0, 155.1, 165.0.

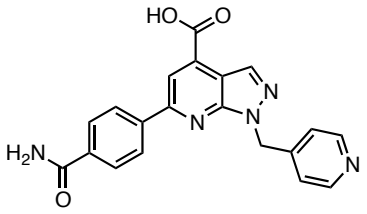
Ethyl 6-[4-(methylsulfonyl)phenyl]-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50 mg, 0.115 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 2 afforded the title compound (46 mg, 98%) as a white solid: R_T 8.0 min; ^{1}H NMR (600 MHz, CD_3OD) δ 3.18 (s, 3H), 5.88 (s, 2H), 7.30 (d, J = 5.4 Hz, 2H), 8.08 (d, J = 8.4 Hz, 2H), 8.27 (s, 1H), 8.44 (d, J = 8.4 Hz, 2H), 8.46 (d, J = 5.4 Hz, 2H), 8.57 (s, 1H); ^{13}C NMR (150 MHz, CD_3OD) δ 44.4, 50.4, 115.4, 116.3, 124.1, 128.9, 129.4, 136.0, 142.6, 143.6, 145.4, 149.2, 150.4, 153.1, 156.4, 171.9; HRMS (ESI–) calcd for $C_{20}H_{15}N_4O_4S$ $[M - H]^-$ 407.0814, found 407.0818 (error 1.0 ppm).



6-(4-Cyanophenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (56). Ethyl 6-(4-cyanophenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with 4-cyanophenylboronic acid (98 mg, 0.67 mmol, 2 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (67 mg, 52%) as a white solid: R_f 0.37 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.52 (t, J = 7.2 Hz, 3H), 4.57 (q, J = 7.2 Hz, 2H), 5.82 (s, 2H), 7.19 (d, J = 6.0 Hz, 2H), 7.81 (d, J = 8.4 Hz, 2H), 8.28 (d, J = 8.4 Hz, 2H), 8.29 (s, 1H), 8.50 (s, 1H), 8.55 (d, J = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.5, 50.0, 62.5, 113.0, 113.5, 115.8, 118.7, 122.6, 128.2, 132.8, 132.9, 134.2, 142.4, 145.5, 150.4, 151.9, 155.0, 164.9.

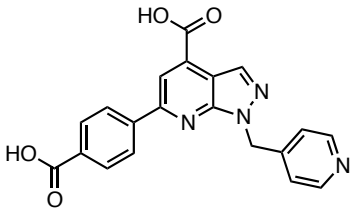
Ethyl 6-(4-cyanophenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50 mg, 0.130 mmol, 1.0 equiv) prepared above was converted to the title compound using the

general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 2 afforded the title compound (34 mg, 73%) as a white solid: R_T 10.2 min; ^{1}H NMR (600 MHz, DMSO-d_6) δ 5.82 (s, 2H), 7.19 (d, J = 6.0 Hz, 2H), 7.98 (d, J = 8.4 Hz, 2H), 8.19 (s, 1H), 8.38 (d, J = 8.4 Hz, 2H), 8.49 (d, J = 6.0 Hz, 2H), 8.53 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 49.0, 111.9, 113.6, 115.0, 118.7, 122.3, 128.0, 132.9, 134.3, 142.5, 146.2, 149.9, 151.3, 153.8, 156.5, 166.1; HRMS (ESI–) calcd for $C_{20}H_{12}N_5O_2$ $[M - H]^-$ 354.0991, found 354.0995 (error 1.1 ppm).

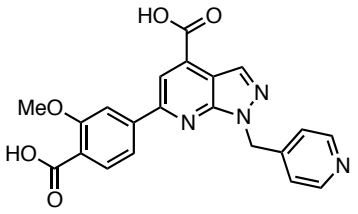


6-(4-Carbamoylphenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (57). Ethyl 6-(4-carbamoylphenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with benzamide-4-boronic acid pinacol ester (166 mg, 0.67 mmol, 2.0 equiv). After initial extraction with CH_2Cl_2 the aqueous phase was back extracted with EtOAc (15 mL) and the organic extracts were combined and concentrated. Purification by flash chromatography (0–10% MeOH/EtOAc) afforded the ethyl ester of the title compound (57.2 mg, 43%) as a brown solid: R_f 0.06 (EtOAc); ^{1}H NMR (600 MHz, DMSO-d_6) δ 1.45 (t, J = 7.2 Hz, 3H), 4.51 (q, J = 7.2 Hz, 2H), 5.90 (s, 2H), 7.22 (d, J = 6.0 Hz, 2H), 7.48 (s, 1H), 8.04 (d, J = 8.4 Hz, 2H), 8.11 (s, 1H), 8.32–8.33 (m, 3H), 8.50 (s, 1H), 8.51 (d, J = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 14.1, 49.1, 62.1, 111.8, 115.2, 122.4, 127.3, 128.2, 132.4, 133.4, 135.5, 139.9, 146.0, 149.9, 151.3, 155.4, 164.4, 167.4.

Ethyl 6-(4-carbamoylphenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (45.0 mg, 0.112 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 4 afforded the title compound (24.4 mg, 58%) as a pale brown solid: R_T 8.2 min; ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.88 (s, 2H), 7.22 (d, J = 6.0 Hz, 2H), 7.48 (s, 1H), 8.04 (d, J = 8.4 Hz, 2H), 8.11 (s, 1H), 8.31–8.33 (m, 3H), 8.48–8.52 (m, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 49.1, 112.2, 115.3, 122.4, 127.2, 128.2, 133.4, 133.9, 135.4, 140.1, 146.0, 149.9, 151.4, 155.3, 166.0, 167.4; HRMS (ESI–) calcd for $C_{20}H_{14}N_5O_3$ $[M - H]^-$ 372.1102, found 372.1079 (error 6.2 ppm).

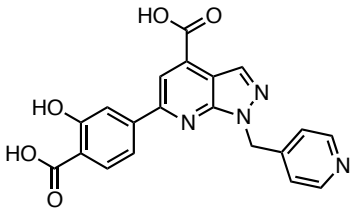


6-(4-carboxyphenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (58). Ethyl 6-(4-carboxyphenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with 4-boronobenzoic acid (111 mg, 0.67 mmol, 2 equiv). The crude residue containing the ester, was directly converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 3 afforded the title compound as a white solid (8.4 mg, 7%): R_T 6.9 min; ^{1}H NMR (600 MHz, CD_3OD) δ 5.89 (s, 2H), 7.32 (d, J = 6.0 Hz, 2H), 8.07 (d, J = 8.4 Hz, 2H), 8.19 (d, J = 8.4 Hz, 2H), 8.24 (s, 1H), 8.47 (d, J = 6.0 Hz, 2H), 8.53 (s, 1H); ^{13}C NMR (150 MHz, CD_3OD) δ 50.3, 114.8, 116.2, 124.1, 128.0, 130.7, 135.9, 140.2, 141.9, 143.1, 149.3, 150.3, 153.2, 158.5, 172.3, 174.9; HRMS (ESI–) calcd for $C_{20}H_{13}N_4O_4$ $[M - H]^-$ 373.0937, found 373.0942 (error 1.3 ppm).



6-(4-Carboxy-3-methoxyphenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (59). Ethyl 6-(3-methoxy-4-(methoxycarbonyl)phenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with 3-methoxy-4-(methoxycarbonyl)phenylboronic acid (141 mg, 0.67 mmol, 2.0 equiv). Purification by flash chromatography (EtOAc) afforded the ethyl ester of the title compound (112.0 mg, 75%) as a brown solid: R_f 0.29 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.51 (t, J = 7.2 Hz, 3H), 3.92 (s, 3H), 4.02 (s, 3H), 4.56 (q, J = 7.2 Hz, 2H), 5.81 (s, 2H), 7.20 (d, J = 6.0 Hz, 2H), 7.71 (d, J = 8.4 Hz, 1H), 7.77 (s, 1H), 7.93 (d, J = 8.4 Hz, 1H), 8.27 (s, 1H), 8.47 (s, 1H), 8.54 (d, J = 6.0 Hz, 2H); ^{13}C NMR (600 MHz, $CDCl_3$) δ 14.5, 50.1, 52.3, 56.3, 62.4, 111.1, 112.7, 116.1, 119.4, 121.3, 122.7, 132.4, 132.6, 134.1, 143.2, 145.7, 150.2, 151.8, 156.0, 159.7, 165.0, 166.4.

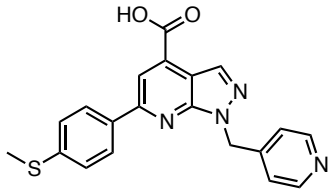
Ethyl 6-(3-methoxy-4-(methoxycarbonyl)phenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50.0 mg, 0.112 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 4 afforded the title compound (45 mg, quant) as an off-white solid: R_T 6.0 min: ^{1}H NMR (600 MHz, DMSO-d_6) δ 3.94 (s, 3H), 5.82 (s, 2H), 7.22 (d, J = 6.0 Hz, 2H), 7.74–7.79 (m, 2H), 7.83 (s, 1H), 8.14 (s, 1H), 8.49–8.50 (m, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 49.1, 55.8, 110.7, 113.6, 114.6, 118.9, 122.4, 131.12, 131.13, 134.4, 142.6, 146.3, 149.8, 151.3, 154.6, 158.30, 158.32, 166.9, 167.2; HRMS (ESI–) calcd for $C_{21}H_{15}N_4O_5$ $[M - H]^-$ 403.1048, found 403.1051 (error 0.7 ppm).



6-(4-Carboxy-3-hydroxyphenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (60). Boron trifluoride-methyl sulfide complex (0.12 mL, 1.1 mmol) was added dropwise to a stirred solution of ethyl 6-(3-methoxy-4-(methoxycarbonyl)phenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (see intermediate prepared for **59**) (50.0 mg, 0.112 mmol) in CH_2Cl_2 (2.0 mL) at 0°C. The reaction was warmed to rt and stirred for 3.5 h. The reaction was quenched by slow addition of the mixture to 0.5 M aqueous HCl (5.0 mL) at 0 °C. The aqueous layer was neutralized with 1 M aqueous NaOH and extracted with EtOAc (3 × 20 mL). The organic layer was washed consecutively with saturated aqueous $NaHCO_3$ (20 mL), saturated aqueous NaCl (20 mL), H_2O (20 mL), then dried ($MgSO_4$), filtered, and concentrated. Purification by flash chromatography afforded ethyl 6-[3-hydroxy-4-(methoxycarbonyl)phenyl]-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (18.1 mg, 37%) as a gray solid: R_f = 0.43 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.51 (t, J = 7.2 Hz, 3H), 3.99 (s, 3H), 4.55 (q, J = 7.2 Hz, 2H), 5.81 (s, 2H), 7.20 (d, J = 6.0 Hz, 2H), 7.67 (dd, J = 8.4, 1.8 Hz, 1H), 7.81 (d, J = 1.8 Hz, 1H), 7.96 (d, J = 8.4 Hz, 1H), 8.28 (s, 1H), 8.48 (s, 1H), 8.54 (d, J = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.5, 49.9, 52.7, 62.3, 112.8, 113.5, 116.1, 116.6, 118.3, 122.7, 130.6, 132.6, 134.1, 145.1, 145.7, 150.3, 151.8, 155.6, 161.9, 165.0, 170.4.

Ethyl 6-(3-hydroxy-4-(methoxycarbonyl)phenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (15.0 mg, 0.0347 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 4 afforded the title compound (13.4 mg, 99%) as a pale

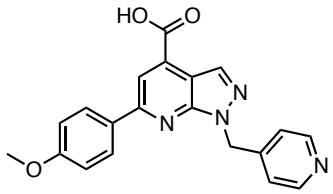
yellow solid: R_T 5.9 min; ^{1}H NMR (600 MHz, DMSO-d_6) δ 5.84 (s, 2H), 7.20 (d, J = 6.0 Hz, 2H), 7.55 (s, 1H), 7.85 (d, J = 7.8 Hz, 1H), 8.18 (s, 1H), 8.44 (s, 1H), 8.46–8.49 (m, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 49.0, 112.1, 114.8, 115.3, 122.2, 122.5, 130.7, 133.4, 146.1, 149.8, 150.0, 151.3, 155.3, 155.8, 159.3, 162.6, 166.0, 171.2; HRMS (ESI–) calcd for $C_{20}H_{13}N_4O_5$ $[M - H]^-$ 389.0891, found 389.0893 (error 0.5 ppm).



6-[4-(Methylthio)phenyl]-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (61). Ethyl 6-[4-(methylthio)phenyl]-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with 4-(methylthio)phenylboronic acid (113 mg, 0.67 mmol, 2.0 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (100.7 mg, 74%) as a yellow solid: R_f 0.40 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.50 (t, J = 7.2 Hz, 3H), 2.53 (s, 3H), 4.54 (q, J = 7.2 Hz, 2H), 5.78 (s, 2H), 7.20 (d, J = 6.0 Hz, 2H), 7.35 (d, J = 8.4 Hz, 2H), 8.08 (d, J = 8.4 Hz, 2H), 8.22 (s, 1H), 8.42 (s, 1H), 8.53 (d, J = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.5, 15.4, 49.8, 62.2, 112.0, 115.4, 122.7, 126.3, 127.9, 132.4, 134.0, 134.8, 141.7, 145.9, 150.2, 151.9, 156.8, 165.2.

Ethyl 6-[4-(methylthio)phenyl]-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50.0 mg, 0.124 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 4 afforded the title compound (46.6 mg, 100%) as a yellow solid: R_T 11.3 min; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.54 (s, 3H), 5.84 (s, 2H), 7.21 (d, J = 6.0 Hz, 2H),

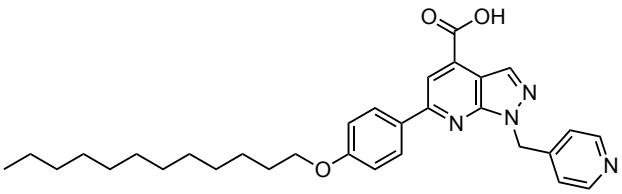
7.40 (d, J = 8.4 Hz, 2H), 8.18 (d, J = 8.4 Hz, 2H), 8.21 (s, 1H), 8.44 (s, 1H), 8.50 (d, J = 6.0 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 14.3, 49.0, 111.8, 114.6, 122.3, 125.8, 127.7, 133.4, 134.0, 134.2, 141.1, 146.1, 149.9, 151.4, 155.7, 166.1; HRMS (ESI–) calcd for $C_{20}H_{15}N_4O_2S$ [M – H]$^-$ 375.0921, found 375.0923 (error 0.5 ppm).



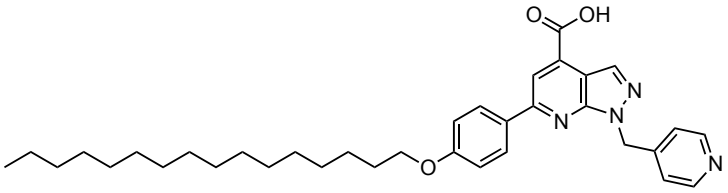
6-(4-Methoxyphenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (62). Ethyl 6-(4-methoxyphenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with 4-methoxyphenylboronic acid (102 mg, 0.67 mmol, 2 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (102 mg, 78%) as a white solid: R_f 0.33 (EtOAc); ^{1}H NMR (600 MHz, DMSO-d_6) δ 1.42 (t, J = 7.2 Hz, 3H), 3.82 (s, 3H), 4.46 (q, J = 7.2 Hz, 2H), 5.82 (s, 2H), 7.05 (d, J = 8.4 Hz, 2H), 7.20 (d, J = 6.0 Hz, 2H), 8.13 (ovlp s, 1H), 8.14 (ovlp d, J = 8.4 Hz, 2H), 8.38 (s, 1H), 8.50 (d, J = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.0, 49.0, 55.3, 61.8, 110.8, 114.2, 114.4, 122.3, 128.8, 129.8, 131.9, 133.1, 146.1, 149.8, 151.3, 156.0, 161.0, 164.4.

Ethyl 6-(4-methoxyphenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (100 mg, 0.257 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 2 afforded the title compound (51 mg, 55%) as a white solid: R_T 7.4 min; ^{1}H NMR (600 MHz, CD_3OD) δ 3.87 (s, 3H), 5.85 (s, 2H), 7.05 (d, J = 9.0 Hz, 2H), 7.30 (d, J = 5.4 Hz, 2H), 8.15 (d, J = 9.0 Hz, 2H), 8.17 (s, 1H), 8.46 (d, J = 5.4 Hz, 2H), 8.48 (s, 1H); ^{13}C

NMR (150 MHz, DMSO-d_6) δ 49.9, 55.3, 111.9, 114.2, 114.4, 122.3, 128.7, 130.4, 133.7, 146.3, 149.9, 151.4, 155.9, 156.5, 160.8, 166.5; HRMS (ESI–) calcd for $C_{20}H_{15}N_4O_3$ $[M - H]^-$ 359.1144, found 359.1154 (error 2.8 ppm).

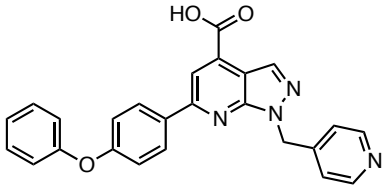


6-[4-(Dodecyloxy)phenyl]-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (64). The title compound was prepared using the general procedure for alkylation of **42-Ethyl ester** and hydrolysis employing dodecylbromide (290 μL, 1.2 mmol) to afford the title compound (38 mg, 24% over two steps) as a white solid: R_f 0.30 (1:4 MeOH/EtOAc); ^{1}H NMR (600 MHz, DMSO–d_6) δ 0.84 (t, J = 7.2 Hz, 3H), 1.23–1.32 (m, 16H), 1.42 (p, J = 7.2 Hz, 2H), 1.73 (p, J = 7.2 Hz, 2H), 4.03 (t, J = 7.2 Hz, 2H), 5.74 (s, 2H), 7.04 (d, J = 9.0 Hz, 2H), 7.16 (d, J = 5.4 Hz, 2H), 7.95 (s, 1H), 8.09 (d, J = 9.0 Hz, 2H), 8.44 (s, 1H), 8.48 (d, J = 5.4 Hz, 2H); Due to limited DMSO solubility, the ^{13}C NMR could not be obtained; HRMS (ESI–) calcd for $C_{31}H_{37}N_4O_3^-$ $[M - H]^-$ 513.2871, found 513.2837 (error 6.6 ppm).



6-[4-(Hexadecyloxy)phenyl]-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (65). The title compound was prepared using the general procedure for alkylation of **42-Ethyl ester** and hydrolysis employing hexadecylbromide (180 μL, 0.6 mmol) to afford the title compound (57 mg, 34% over two steps) as a white solid: R_f 0.40 (1:4 MeOH/EtOAc); ^{1}H NMR (600 MHz, DMSO–d_6) δ 0.84 (t, J = 7.2 Hz, 3H), 1.23–1.34 (m, 24H),

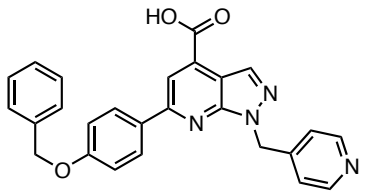
1.42 (p, *J* = 7.2 Hz, 2H), 1.73 (p, *J* = 7.2 Hz, 2H), 4.03 (t, *J* = 7.2 Hz, 2H), 5.75 (s, 2H), 7.05 (d, *J* = 8.7 Hz, 2H), 7.17 (d, *J* = 4.8 Hz, 2H), 7.98 (s, 1H), 8.10 (d, *J* = 8.7 Hz, 2H), 8.43 (s, 1H), 8.48 (d, *J* = 4.8 Hz, 2H); Due to limited DMSO solubility, the ^{13}C NMR could not be obtained; HRMS (ESI–) calcd for $C_{35}H_{45}N_4O_3$ $[M - H]^-$ 569.3497, found 569.3458 (error 6.9 ppm).



6-(4-Phenoxyphenyl)-1-(pyridin-4-ylmethyl)-1H-pyrazolo[3,4-b]pyridine-4-carboxylic acid (66). Ethyl 6-(4-phenoxyphenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109**, using 4-phenoxyphenylboronic acid (143 mg, 0.67 mmol, 2 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (105 mg, 70%) as a white solid: R_f 0.51 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.51 (t, *J* = 7.2 Hz, 3H), 4.54 (q, *J* = 7.2 Hz, 2H), 5.79 (s, 2H), 7.09 (d, *J* = 7.8 Hz, 2H), 7.12 (d, *J* = 7.8 Hz, 2H), 7.17 (t, *J* = 7.8 Hz, 1H), 7.20 (d, *J* = 4.2 Hz, 2H), 7.38 (t, *J* = 7.8 Hz, 2H), 8.14 (d, *J* = 7.8 Hz, 2H), 8.23 (s, 1H), 8.44 (s, 1H), 8.54 (d, *J* = 4.2 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.6, 49.9, 62.3, 112.0, 115.6, 118.8, 119.8, 122.7, 124.2, 129.4, 130.1, 132.5, 133.2, 134.1, 146.0, 150.3, 152.0, 156.6, 156.9, 159.6, 165.3.

Ethyl 6-(4-phenoxyphenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50 mg, 0.111 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 2 afforded the title compound (48 mg, 99%) as a white solid: R_T 15.2 min; ^{1}H NMR (600 MHz, CD_3OD) δ 5.85 (s, 2H), 7.07 (d, *J* = 7.8 Hz, 2H), 7.08 (d, *J* = 9.0 Hz, 2H), 7.16 (t, *J* = 7.8 Hz, 1H), 7.29 (d, *J* = 5.4 Hz, 2H), 7.40 (t, *J* = 7.8 Hz, 2H), 8.16 (s, 1H), 8.19 (d, *J* =

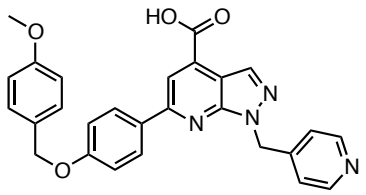
9.0 Hz, 2H), 8.46 (d, J = 5.4 Hz, 2H), 8.51 (s, 1H); ^{13}C NMR (150 MHz, CD_3OD) δ 50.3, 114.4, 115.7, 119.4, 120.5, 124.1, 125.0, 130.2, 131.0, 135.2, 135.9, 143.1, 149.3, 150.3, 153.2, 158.0, 158.2, 160.5, 172.4; HRMS (ESI–) calcd for $C_{25}H_{17}N_4O_3$ $[M - H]^-$ 421.1306, found 421.1307 (error 0.7 ppm).



6-[4-(Benzyloxy)phenyl]-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (67). Ethyl 6-[4-(benzyloxy)phenyl]-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with 4-(benzyloxy)phenylboronic acid (153 mg, 0.67 mmol, 2 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (129 mg, 83%) as a white solid: R_f 0.43 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.51 (t, J = 7.2 Hz, 3H), 4.54 (q, J = 7.2 Hz, 2H), 5.15 (s, 2H), 5.79 (s, 2H), 7.10 (d, J = 8.4 Hz, 2H), 7.20 (d, J = 5.4 Hz, 2H), 7.34 (t, J = 7.2 Hz, 1H), 7.40 (t, J = 7.2 Hz, 2H), 7.46 (d, J = 7.2 Hz, 2H), 8.13 (d, J = 8.4 Hz, 2H), 8.22 (s, 1H), 8.42 (s, 1H), 8.54 (d, J = 5.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.5, 49.7, 62.1, 70.2, 111.6, 115.4, 122.6, 127.6, 128.3, 128.5, 128.8, 129.1, 131.1, 132.3, 134.0, 136.7, 145.9, 150.3, 152.0, 157.1, 160.6, 165.3.

Ethyl 6-[4-(benzyloxy)phenyl]-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50 mg, 0.108 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 2 afforded the title compound (46 mg, 98%) as a white solid: R_T 15.5 min; ^{1}H NMR (600 MHz, CD_3OD) δ 5.16 (s, 2H), 5.83 (s, 2H), 7.11 (d, J = 8.4 Hz, 2H), 7.28–7.32 (m,

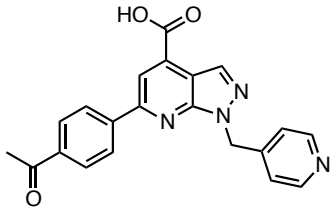
3H), 7.38 (t, J = 7.8 Hz, 2H), 7.46 (d, J = 7.8 Hz, 2H), 8.14–8.15 (m, 3H), 8.45 (d, J = 6.0 Hz, 2H), 8.49 (s, 1H); ^{13}C NMR (150 MHz, CD_3OD) δ 50.2, 71.1, 114.2, 115.6, 116.2, 124.1, 128.6, 128.9, 129.5, 130.0, 133.0, 135.9, 138.5, 142.9, 149.4, 150.3, 153.2, 158.7, 161.7, 172.5; HRMS (ESI–) calcd for $C_{26}H_{19}N_4O_3$ $[M - H]^-$ 435.1457, found 435.1471 (error 3.2 ppm).



6-[4-(4-Methoxybenzyloxy)phenyl]-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (68). Ethyl 6-[4-(4-methoxybenzyloxy)phenyl]-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with 4-(4-methoxybenzyloxy)phenylboronic acid (173 mg, 0.67 mmol, 2 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (143 mg, 86%) as a white solid: R_f 0.39 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.50 (t, J = 7.2 Hz, 3H), 3.80 (s, 3H), 4.53 (q, J = 7.2 Hz, 2H), 5.06 (s, 2H), 5.78 (s, 2H), 6.92 (d, J = 7.8 Hz, 2H), 7.09 (d, J = 8.4 Hz, 2H), 7.19 (d, J = 4.2 Hz, 2H), 7.37 (d, J = 7.8 Hz, 2H), 8.12 (d, J = 8.4 Hz, 2H), 8.21 (s, 1H), 8.41 (s, 1H), 8.54 (d, J = 4.2 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.4, 49.7, 55.4, 62.1, 70.0, 111.6, 114.2, 115.3 122.6, 128.7, 129.0, 129.3, 131.0, 132.2, 133.9, 145.9, 150.2, 151.9, 157.0, 159.7, 160.6, 165.3 (missing 1 aryl carbon).

Ethyl 6-[4-(4-methoxybenzyloxy)phenyl]-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50 mg, 0.101 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 2 afforded the title compound (45 mg, 95%) as a white solid: R_T 15.2 min; ^{1}H NMR (600 MHz, CD_3OD) δ 3.79 (s, 3H), 5.06 (s, 2H), 5.83 (s, 2H), 6.92 (d, J =

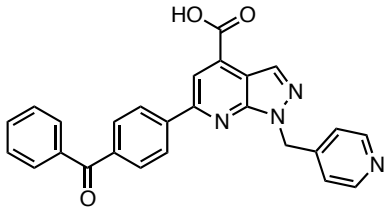
8.4 Hz, 2H), 7.09 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 5.4 Hz, 2H), 7.37 (d, *J* = 8.4 Hz, 2H), 8.13 (ovlp d, *J* = 8.4 Hz, 2H), 8.14 (ovlp s, 1H), 8.45 (d, *J* = 5.4 Hz, 2H), 8.49 (s, 1H); ^{13}C NMR (150 MHz, CD_3OD) δ 50.2, 50.7, 70.9, 114.2, 114.9, 115.6, 116.2, 124.1, 129.9, 130.3, 130.4, 132.9, 135.9, 142.9, 149.4, 150.3, 153.2, 158.7, 161.0, 161.8, 172.5; HRMS (ESI–) calcd for $C_{27}H_{21}N_4O_4$ $[M - H]^-$ 465.1563, found 465.1539 (error 5.2 ppm).



6-(4-Acetylphenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (69). Ethyl 6-(4-acetylphenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with 4-acetylphenylboronic acid (110 mg, 0.67 mmol, 2.0 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (83.4 mg, 62%) as a pale orange solid: R_f 0.38 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.51 (t, *J* = 7.2 Hz, 3H), 2.65 (s, 3H), 4.54 (q, *J* = 7.2 Hz, 2H), 5.81 (s, 2H), 7.20 (d, *J* = 6.0 Hz, 2H), 8.08 (d, *J* = 8.4 Hz, 2H), 8.23 (d, *J* = 8.4 Hz, 2H), 8.29 (s, 1H), 8.46 (s, 1H), 8.53 (d, *J* = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.4, 26.9, 49.9, 62.3, 112.6, 116.0, 122.6, 127.8, 129.0, 132.6, 134.0, 137.9, 142.4, 145.6, 150.3, 151.9, 155.9, 165.0, 197.7.

Ethyl 6-(4-acetylphenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50.0 mg, 0.125 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 4 afforded the title compound (37.6 mg, 81%) as a pale yellow solid: R_T 9.6 min; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.64 (s, 3H), 5.88 (s, 2H), 7.23 (d, *J* = 6.0 Hz, 2H), 8.10 (d, *J* = 8.4 Hz, 2H), 8.31 (s, 1H), 8.37 (d, *J* = 8.4 Hz, 2H), 8.49 (s, 1H), 8.51 (d, *J* = 6.0 Hz, 2H); ^{13}C

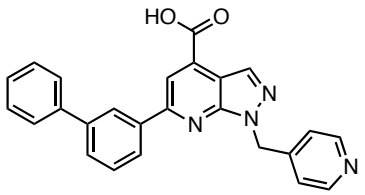
NMR (100 MHz, DMSO-d_6) δ 26.9, 49.1, 112.5, 115.3, 122.4, 127.6, 128.8, 133.5, 134.6, 137.5, 141.7, 146.0, 149.9, 151.3, 154.9, 165.9, 197.6; HRMS (ESI–) calcd for $C_{21}H_{15}N_4O_3$ [M H] 371.1150, found 371.1156 (error 1.6 ppm).



6-(4-Benzoylphenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (70). Ethyl 6-(4-benzoylphenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with 4-benzoylphenylboronic acid (151 mg, 0.67 mmol, 2.0 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (107.7 mg, 70%) as a pale brown solid: R_f 0.65 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.51 (t, J = 7.2 Hz, 3H), 4.55 (q, J = 7.2 Hz, 2H), 5.82 (s, 2H), 7.21 (d, J = 6.0 Hz, 2H), 7.48–7.51 (m, 2H), 7.59–7.61 (m, 1H), 7.82–7.84 (m, 2H), 7.94 (d, J = 8.4 Hz, 2H), 8.26 (d, J = 8.4 Hz, 2H), 8.32 (s, 1H), 8.48 (s, 1H), 8.54 (d, J = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.5, 49.9, 62.3, 112.6, 116.0, 122.7, 127.5, 128.5, 130.1, 130.7, 132.6, 132.8, 134.1, 137.5, 138.6, 141.8, 145.8, 150.2, 151.9, 156.0, 165.0, 196.2.

Ethyl 6-(4-benzoylphenyl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50.0 mg, 0.108 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 4 afforded the title compound (31.4 mg, 67%) as a white solid: R_T 12.1 min; ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.88 (s, 2H), 7.22 (d, J = 6.0 Hz, 2H), 7.57–7.61 (m, 2H), 7.69–7.73 (m, 1H), 7.78–7.81 (m, 2H), 7.90 (d, J = 8.4 Hz, 2H), 8.32 (s, 1H), 8.42 (d, J = 6.0 Hz, 2H), 8.51 (br s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 49.1, 112.6, 115.3, 122.3, 127.5, 128.6, 129.7, 130.3,

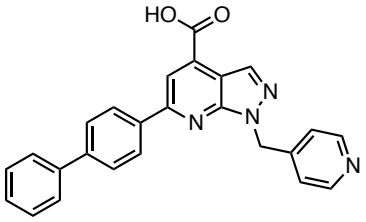
132.9, 133.6, 136.9, 137.8, 141.4, 146.0, 149.9, 151.4, 154.9, 166.0, 195.4 (missing one aryl carbon); HRMS (ESI–) calcd for $C_{26}H_{17}N_4O_3$ $[M - H]^-$ 433.1306, found 433.1308 (error 0.5 ppm).



6-(Biphenyl-3-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (71). Ethyl 6-(biphenyl-3-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with biphenyl-3-ylboronic acid (133 mg, 0.67 mmol, 2 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (97 mg, 73%) as a white solid: R_f 0.43 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.52 (t, J = 7.2 Hz, 3H), 4.56 (q, J = 7.2 Hz, 2H), 5.82 (s, 2H), 7.22 (d, J = 5.4 Hz, 2H), 7.41 (t, J = 7.8 Hz, 1H), 7.50 (t, J = 7.8 Hz, 2H), 7.59 (t, J = 7.8 Hz, 1H), 7.67–7.71 (m, 3H), 8.13 (d, J = 7.8 Hz, 1H), 8.32 (s, 1H), 8.36 (s, 1H), 8.47 (s, 1H), 8.55 (d, J = 5.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.5, 49.9, 62.2, 112.3, 116.0, 122.7, 126.58, 126.59, 127.4, 127.8, 128.9, 129.0, 129.5, 132.5, 134.0, 138.9, 141.0, 142.2, 145.8, 150.3, 152.0, 157.4, 165.2.

Ethyl 6-(biphenyl-3-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50 mg, 0.115 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 2 afforded the title compound (45 mg, 95%) as a white solid: R_T 15.4 min; ^{1}H NMR (600 MHz, CD_3OD) δ 5.87 (s, 2H), 7.32 (d, J = 6.0 Hz, 2H), 7.38 (t, J = 7.2 Hz, 1H), 7.48 (d, J = 7.8 Hz, 2H), 7.59 (d, J = 7.8 Hz, 1H), 7.70–7.72 (m, 3H), 8.17 (d, J = 7.2 Hz, 1H), 8.28 (s, 1H), 8.41 (s, 1H), 8.46 (d, J = 6.0 Hz, 2H), 8.54 (s, 1H); ^{13}C NMR (150 MHz, CD_3OD) δ 50.4, 114.8,

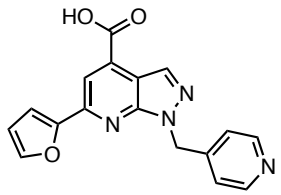
116.2, 124.1, 127.2, 127.5, 128.1, 128.6, 129.2, 129.9, 130.4, 135.9, 140.9, 142.1, 143.1, 149.3, 150.3, 153.2, 158.7, 172.3 (missing one aryl carbon); HRMS (ESI–) calcd for $C_{25}H_{17}N_4O_2$ [M – H]$^-$ 405.1360, found 405.1352 (error 2.0 ppm).



6-(Biphenyl-4-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (72). Ethyl 6-(biphenyl-4-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with 4-biphenylboronic acid (133 mg, 0.67 mmol, 2.0 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (96.8 mg, 67%) as a pale brown solid: R_f 0.41 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.53 (t, J = 7.2 Hz, 3H), 4.56 (q, J = 7.2 Hz, 2H), 5.83 (s, 2H), 7.23 (d, J = 6.0 Hz, 2H), 7.40 (t, J = 7.2 Hz, 1H), 7.48 (t, J = 7.2 Hz, 2H), 7.67 (d, J = 7.2 Hz, 2H), 7.76 (d, J = 8.7 Hz, 2H), 8.25 (d, J = 8.7 Hz, 2H), 8.33 (s, 1H), 8.47 (s, 1H), 8.56 (d, J = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.5, 49.9, 62.2, 112.2, 115.8, 122.7, 127.3, 127.8, 128.0, 128.1, 129.1, 132.4, 134.1, 137.2, 140.4, 142.9, 145.9, 150.3, 152.0, 157.1, 165.3.

Ethyl 6-(biphenyl-4-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50.0 mg, 0.115 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 4 afforded the title compound (45.1 mg, 96%) as a white solid: R_T 13.2 min; ^{1}H NMR (600 MHz, DMSO-d_6) δ 5.86 (s, 2H), 7.22 (d, J = 6.0 Hz, 2H), 7.41 (t, J = 7.2 Hz, 1H), 7.51 (t, J = 7.2 Hz, 2H), 7.76 (d, J = 7.2 Hz, 2H), 7.85 (d, J = 8.4 Hz, 2H), 8.27 (s, 1H), 8.32 (d, J = 8.4 Hz, 2H), 8.48 (s, 1H), 8.51 (d, J = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 49.0, 100.7, 112.4,

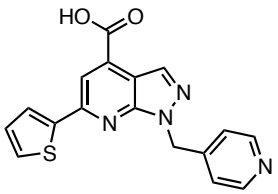
114.7, 122.3, 126.7, 127.2, 127.86, 127.91, 129.0, 133.7, 136.9, 139.3, 141.4, 146.2, 149.9, 151.4, 155.6, 166.2; HRMS (ESI–) calcd for $C_{25}H_{17}N_4O_2$ $[M - H]^-$ 405.1357, found 405.1361 (error 1.0 ppm).



6-(Furan-2-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (75). Ethyl 6-(furan-2-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with furan-2-ylboronic acid (75 mg, 0.67 mmol, 2.0 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (82.0 mg, 70%) as a brown solid: R_f 0.42 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.49 (t, J = 7.2 Hz, 3H), 4.52 (q, J = 7.2 Hz, 2H), 5.75 (s, 2H), 6.58 (dd, J = 3.0, 1.5 Hz, 1H), 7.18 (d, J = 4.8 Hz, 2H), 7.22 (d, J = 3.0 Hz, 1H), 7.61 (s, 1H), 8.20 (s, 1H), 8.42 (s, 1H), 8.54 (br s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.4, 49.7, 62.2, 111.0, 112.0, 112.6, 114.4, 122.7, 132.4, 134.1, 144.6, 145.8, 149.1, 150.2, 151.7, 153.2, 165.0.

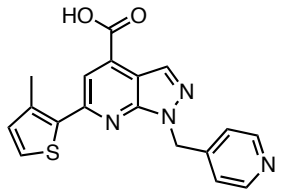
Ethyl 6-(furan-2-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50.0 mg, 0.144 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 4 afforded the title compound (45.2 mg, 98%) as a grey solid: R_T 8.5 min; ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.72 (s, 2H), 6.68 (dd, J = 3.6, 1.6 Hz, 1H), 7.15 (d, J = 6.0 Hz, 2H), 7.25 (dd, J = 3.6, 0.8 Hz, 1H), 7.89 (dd, J = 1.6, 0.8 Hz, 1H), 7.93 (s, 1H), 8.46 (s, 1H), 8.49 (d, J = 6.0 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 48.7, 110.1, 112.5, 112.8, 113.4, 122.2, 134.9, 143.5,

144.7, 146.5, 147.7, 149.8, 151.2, 153.2, 166.6; HRMS (ESI–) calcd for $C_{17}H_{11}N_4O_3$ $[M - H]^-$ 319.0837, found 319.0833 (error 1.3 ppm).



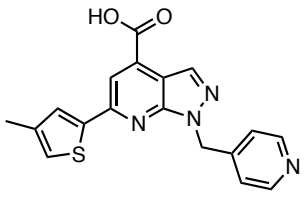
1-(Pyridin-4-ylmethyl)-6-(thiophen-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (76). Ethyl 1-(pyridin-4-ylmethyl)-6-(thiophen-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109**, using thiophen-2-ylboronic acid (86 mg, 0.67 mmol, 2 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (92 mg, 75%) as a white solid: R_f 0.39 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.51 (t, *J* = 7.2 Hz, 3H), 4.54 (q, *J* = 7.2 Hz, 2H), 5.75 (s, 2H), 7.16 (dd, *J* = 5.4, 4.2 Hz, 1H), 7.25 (d, *J* = 5.4 Hz, 2H), 7.49 (d, *J* = 5.4 Hz, 1H), 7.80 (d, *J* = 4.2 Hz, 1H), 8.15 (s, 1H), 8.39 (s, 1H), 8.54 (d, *J* = 5.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.5, 50.0, 62.3, 112.0, 114.7, 122.9, 127.1, 128.5, 129.4, 132.4, 134.2, 144.2, 145.6, 150.3, 151.5, 152.6, 165.1.

Ethyl 1-(pyridin-4-ylmethyl)-6-(thiophen-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50 mg, 0.137 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 2 afforded the title compound (37 mg, 80%) as a white solid: R_T 10.9 min; ^{1}H NMR (600 MHz, CD_3OD) δ 5.78 (s, 2H), 7.16 (dd, *J* = 4.8, 4.2 Hz, 1H), 7.32 (d, *J* = 6.0 Hz, 2H), 7.54 (d, *J* = 4.8 Hz, 1H), 7.85 (d, *J* = 4.2 Hz, 1H), 8.10 (s, 1H), 8.46–8.47 (m, 3H); ^{13}C NMR (150 MHz, CD_3OD) δ 50.3, 114.5, 114.8, 124.2, 127.7, 129.3, 129.8, 136.0, 143.1, 146.0, 149.1, 150.3, 152.8, 154.1, 172.1; HRMS (ESI–) calcd for $C_{17}H_{11}N_4O_2S$ $[M - H]^-$ 335.0603, found 335.0612 (error 2.7 ppm).



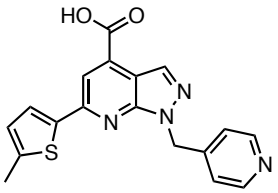
6-(3-Methylthiophen-2-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (77). Ethyl 6-(3-methylthiophen-2-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with 3-methylthiophene-2-boronic acid pinacol ester (150 mg, 0.67 mmol, 2.0 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (101.6 mg, 80%) as a pale yellow solid: R_f 0.41 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.48 (t, J = 7.2 Hz, 3H), 2.58 (s, 3H), 4.51 (q, J = 7.2 Hz, 2H), 5.71 (s, 2H), 6.94 (d, J = 5.1 Hz, 1H), 7.20 (d, J = 6.0 Hz, 2H), 7.32 (d, J = 5.1 Hz, 1H), 8.06 (s, 1H), 8.39 (s, 1H), 8.52 (d, J = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.4, 16.8, 50.0, 62.1, 111.2, 117.0, 122.7, 126.8, 132.1, 132.8, 133.9, 136.6, 138.2, 145.7, 150.2, 151.3, 153.6, 165.0.

Ethyl 6-(3-methylthiophen-2-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50.0 mg, 0.132 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 4 afforded the title compound (45.5 mg, 98%) as an off-white solid: R_T 10.2 min; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.55 (s, 3H), 5.77 (s, 2H), 7.07 (d, J = 5.2 Hz, 1H), 7.20 (d, J = 6.0 Hz, 2H), 7.64 (d, J = 5.2 Hz, 1H), 7.95 (s, 1H), 8.43 (s, 1H), 8.50 (d, J = 6.0 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 16.4, 49.2, 111.2, 115.9, 122.3, 127.5, 133.0, 133.5, 135.9, 137.9, 146.0, 149.9, 150.8, 152.6, 165.9 (missing one aryl carbon); HRMS (ESI–) calcd for $C_{18}H_{13}N_4O_2S$ $[M - H]^-$ 349.0765, found 349.0780 (error 4.3 ppm).



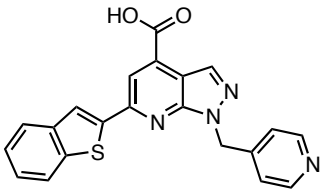
6-(4-Methylthiophen-2-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (78). Ethyl 6-(4-methylthiophen-2-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with 4-methylthiophen-2-ylboronic acid (95 mg, 0.67 mmol, 2.0 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (98.3 mg, 78%) as a pale yellow solid: R_f 0.45 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.50 (t, J = 7.2 Hz, 3H), 2.33 (s, 3H), 4.53 (q, J = 7.2 Hz, 2H), 5.73 (s, 2H), 7.06 (s, 1H), 7.24 (d, J = 6.6 Hz, 2H), 7.62 (s, 1H), 8.10 (s, 1H), 8.39 (s, 1H), 8.54 (d, 6.6 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.5, 16.0, 50.0, 62.2, 111.9, 114.7, 123.0, 125.0, 129.3, 132.3, 134.1, 139.2, 143.7, 145.7, 150.3, 151.5, 152.6, 165.1.

Ethyl 6-(4-methylthiophen-2-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50.0 mg, 0.132 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 2 afforded the title compound (45.6 mg, 99%) as an off-white solid: R_T 6.8 min; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.26 (s, 3H), 5.75 (s, 2H), 7.21 (d, J = 6.0 Hz, 2H), 7.34 (s, 1H), 7.88 (s, 1H), 8.11 (s, 1H), 8.39 (s, 1H), 8.51 (d, J = 6.0 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 15.5, 49.1, 111.7, 113.9, 122.4, 125.4, 130.0, 133.5, 134.0, 138.8, 142.8, 145.9, 149.9, 150.9, 151.8, 165.9; HRMS (ESI–) calcd for $C_{18}H_{13}N_4O_2S$ $[M - H]^-$ 349.0765, found 349.0755 (error 2.9 ppm).



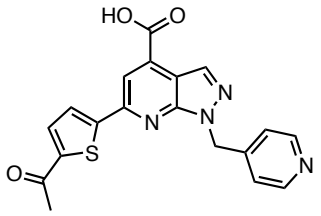
6-(5-Methylthiophen-2-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (79). Ethyl 6-(5-methylthiophen-2-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with 5-methylthiophen-2-ylboronic acid (95 mg, 0.67 mmol, 2 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (105 mg, 83%) as a white solid: R_f 0.41 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.51 (t, J = 7.2 Hz, 3H), 2.56 (s, 3H), 4.53 (q, J = 7.2 Hz, 2H), 5.72 (s, 2H), 6.81 (d, J = 3.6 Hz, 1H), 7.26 (d, J = 4.8 Hz, 2H), 7.59 (d, J = 3.6 Hz, 1H), 8.07 (s, 1H), 8.37 (s, 1H), 8.56 (d, J = 4.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.4, 15.9, 49.9, 62.1, 111.6, 114.4, 122.9, 126.9, 127.3, 132.1, 134.0, 141.7, 144.6, 145.6, 150.2, 151.5, 152,7, 165.1.

Ethyl 6-(5-methylthiophen-2-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50 mg, 0.132 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 2 afforded the title compound (45 mg, 97%) as a white solid: R_T 12.2 min; ^{1}H NMR (600 MHz, CD_3OD) δ 2.52 (s, 3H), 5.76 (s, 2H), 6.83 (d, J = 3.6 Hz, 1H), 7.31 (d, J = 6.0 Hz, 2H), 7.63 (d, J = 3.6 Hz, 1H), 8.02 (s, 1H), 8.45 (s, 1H), 8.46 (d, J = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, CD_3OD) δ 15.5, 50.3, 114.2, 114.5, 124.2, 127.8, 128.0, 136.0, 142.8, 143.6, 145.0, 149.2, 150.3, 152.8, 154.3, 172.2; HRMS (ESI–) calcd for $C_{18}H_{13}N_4O_2S$ $[M - H]^-$ 349.0759, found 349.0765 (error 1.7 ppm).



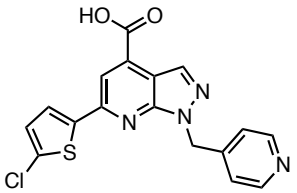
6-(Benzo[*b*]thiophen-2-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (80). Ethyl 6-(benzo[*b*]thiophen-2-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with benzo[*b*]thiophene-2-boronic acid (119 mg, 0.67 mmol, 2.0 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (87.4 mg, 63%) as a yellow solid: R_f 0.46 (EtOAc); ^{1}H NMR (600 MHz, DMSO-d_6) δ 1.46 (t, J = 7.2 Hz, 3H), 4.51 (q, J = 7.2 Hz, 2H), 5.81 (s, 2H), 7.25 (d, J = 6.0 Hz, 2H), 7.42–7.45 (m, 2H), 7.93–7.95 (m, 1H), 8.01–8.02 (m, 1H), 8.39 (s, 1H), 8.46 (s, 1H), 8.50 (s, 1H), 8.52 (d, J = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 14.1, 49.3, 62.1, 111.8, 114.4, 122.4, 122.8, 124.9, 125.00, 125.03, 126.1, 132.2, 133.6, 140.2, 140.4, 143.2, 145.8, 149.9, 150.8, 151.8, 164.2.

Ethyl 6-(benzo[*b*]thiophen-2-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50.0 mg, 0.121 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 4 afforded the title compound (30.7 mg, 66%) as a yellow solid: R_T 12.2 min; ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.78 (s, 2H), 7.24 (d, J = 6.0 Hz, 2H), 7.39–7.43 (m, 2H), 7.91–7.94 (m, 1H), 8.00–8.02 (m, 1H), 8.28 (s, 1H), 8.40 (s, 1H), 8.48 (s, 1H), 8.52 (d, J = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 49.0, 113.9, 122.3, 122.5, 123.7, 124.5, 124.7, 125.6, 127.4, 128.2, 134.4, 140.0, 140.2, 144.1, 146.0, 149.8, 150.8, 151.1, 165.9; HRMS (ESI–) calcd for $C_{21}H_{13}N_4O_2S$ $[M - H]^-$ 385.0765, found 385.0751 (error 3.6 ppm).



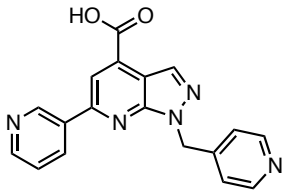
6-(5-Acetylthiophen-2-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (81). Ethyl 6-(5-acetylthiophen-2-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with 5-acetyl-2-thiopheneboronic acid (114 mg, 0.67 mmol, 2.0 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (92.2 mg, 68%) as a yellow solid: R_f 0.43 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.50 (t, J = 7.2 Hz, 3H), 2.60 (s, 3H), 4.54 (q, J = 7.2 Hz, 2H), 5.74 (s, 2H), 7.24 (d, J = 6.0 Hz, 2H), 7.69 (d, J = 4.2 Hz, 1H), 7.75 (d, J = 4.2 Hz, 1H), 8.16 (s, 1H), 8.42 (s, 1H), 8.54 (d, J = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.5, 26.9, 50.1, 62.4, 112.9, 114.7, 122.9, 127.0, 132.6, 133.1, 134.2, 145.3, 146.2, 150.3, 151.2, 151.30, 151.33, 164.7, 191.0.

Ethyl 6-(5-acetylthiophen-2-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50.0 mg, 0.123 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 4 afforded the title compound (39.3 mg, 84%) as a yellow solid: R_T 9.0 min; ^{1}H NMR (600 MHz, DMSO-d_6) δ 2.57 (s, 3H), 5.78 (s, 2H), 7.23 (d, J = 6.0 Hz, 2H), 7.98 (d, J = 4.2 Hz, 1H), 8.15 (d, J = 4.2 Hz, 1H), 8.25 (s, 1H), 8.46 (s, 1H), 8.51 (d, J = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 26.5, 49.2, 100.6, 113.0, 114.2, 122.4, 128.4, 133.9, 134.9, 145.5, 145.8, 149.9, 150.5, 150.67, 150.74, 165.8, 191.2; HRMS (ESI–) calcd for $C_{19}H_{13}N_4O_3S$ $[M - H]^-$ 377.0714, found 377.0717 (error 0.8 ppm).



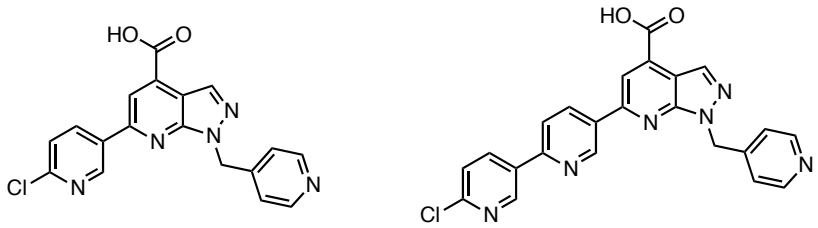
6-(5-Chlorothiophen-2-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (82). Ethyl 6-(5-chlorothiophen-2-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with 5-chlorothiophen-2-ylboronic acid (109 mg, 0.67 mmol, 2 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (77 mg, 58%) as a white solid: R_f 0.41 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.49 (t, J = 7.2 Hz, 3H), 4.52 (q, J = 7.2 Hz, 2H), 5.69 (s, 2H), 6.94 (d, J = 3.6 Hz, 1H), 7.22 (d, J = 6.0 Hz, 2H), 7.51 (d, J = 3.6 Hz, 1H), 8.02 (s, 1H), 8.37 (s, 1H), 8.54 (d, J = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.4, 50.0, 62.3, 112.1, 113.7, 122.9, 126.1, 127.7, 132.4, 134.1, 134.4, 142.7, 145.4, 150.3, 151.2, 151.5, 164.9.

Ethyl 6-(5-chlorothiophen-2-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (14 mg, 0.035 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 2 afforded the title compound (6.1 mg, 47%) as an off-white solid: R_T 13.7 min; ^{1}H NMR (600 MHz, CD_3OD) δ 5.76 (s, 2H), 7.04 (d, J = 4.2 Hz, 1H), 7.31 (d, J = 4.8 Hz, 2H), 7.66 (d, J = 4.2 Hz, 1H), 8.03 (s, 1H), 8.46–8.48 (m, 3H); ^{13}C NMR (150 MHz, CD_3OD) δ 50.4, 113.9, 114.8, 124.2, 127.1, 128.9, 134.1, 136.1, 143.3, 145.0, 149.0, 150.3, 152.5, 153.0, 171.8; HRMS (ESI–) calcd for $C_{17}H_{10}ClN_4O_2S$ $[M - H]^-$ 369.0213, found 369.0227 (error 3.8 ppm).



6-(Pyridin-3-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (83). Ethyl 6-(pyridin-3-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with pyridin-3-ylboronic acid (82 mg, 0.67 mmol, 2 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (65 mg, 54%) as a white solid: R_f 0.07 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.51 (t, *J* = 7.2 Hz, 3H), 4.55 (q, *J* = 7.2 Hz, 2H), 5.81 (s, 2H), 7.20 (d, *J* = 5.4 Hz, 2H), 7.45 (dd, *J* = 4.8, 7.8 Hz, 1H), 8.26 (s, 1H), 8.42 (d, *J* = 7.8 Hz, 1H), 8.48 (s, 1H), 8.54 (d, *J* = 5.4 Hz, 2H), 8.71 (d, *J* = 4.8 Hz, 1H), 9.39 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ14.5, 50.0, 62.4, 112.7, 115.5, 122.7, 123.8, 132.9, 133.9, 134.1, 134.9, 145.6, 149.0, 150.3, 150.9, 151.9, 154.8, 164.9.

Ethyl 6-(pyridin-3-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50 mg, 0.139 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 2 afforded the title compound (37 mg, 80%) as a white solid: R_T 8.8 min; ^{1}H NMR (600 MHz, CD_3OD) δ 5.88 (s, 2H), 7.30 (d, *J* = 5.4 Hz, 2H), 7.59 (dd, *J* = 7.2, 5.4 Hz, 1H), 8.23 (s, 1H), 8.46 (d, *J* = 5.4 Hz, 2H), 8.57 (s, 1H), 8.60–8.62 (m, 2H), 9.35 (s, 1H); ^{13}C NMR (150 MHz, CD_3OD) δ 50.4, 115.3, 115.8, 124.1, 125.4, 136.0, 136.6, 136.9, 143.5, 149.2, 149.2, 150.4, 150.6, 153.2, 155.5, 171.8; HRMS (ESI–) calcd for $C_{18}H_{12}N_5O_2$ $[M - H]^-$ 330.0991, found 330.0995 (error 1.2 ppm).



6-(6-Chloropyridin-3-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (84) and 6-(6'-Chloro-2,3'-bipyridin-5-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (85). The ethyl esters of the title compounds were prepared using the general procedure for Suzuki coupling of **109** with 6-chloropyridin-3-ylboronic acid (105 mg, 0.67 mmol, 2.0 equiv). After initial extraction with CH_2Cl_2 the aqueous phase was back extracted with EtOAc (3 × 10 mL) and the organic extracts were combined and concentrated. Purification by flash chromatography afforded ethyl 6-(6-chloropyridin-3-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (76.4 mg, 58%) and ethyl 6-(6'-chloro-2,3'-bipyridin-5-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (30.3 mg, 19%).

Data for ethyl 6-(6-chloropyridin-3-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate: R_f 0.52 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.52 (t, J = 7.2 Hz, 3H), 4.56 (q, J = 7.2 Hz, 2H), 5.80 (s, 2H), 7.19 (d, J = 5.4 Hz, 2H), 7.48 (d, J = 8.4 Hz, 1H), 8.23 (s, 1H), 8.40 (dd, J = 8.4, 2.4 Hz, 1H), 8.49 (s, 1H), 8.55 (d, J = 5.4 Hz, 2H), 9.15 (d, J = 2.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.5, 50.1, 62.5, 112.9, 115.3, 122.6, 124.6, 133.0, 133.1, 134.2, 137.6, 145.5, 148.9, 150.4, 151.9, 153.0, 153.5, 164.8.

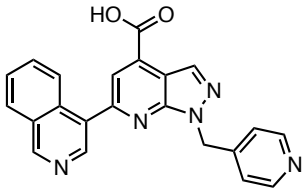
Data for ethyl 6-(6'-chloro-2,3'-bipyridin-5-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate: R_f 0.44 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.53 (t, J = 7.2 Hz, 3H), 4.57 (q, J = 7.2 Hz, 2H), 5.83 (s, 2H), 7.22 (d, J = 6.6 Hz, 2H), 7.47 (d, J = 8.4 Hz, 1H),

7.89 (d, J = 8.4 Hz, 1H), 8.32 (s, 1H), 8.40 (dd, J = 8.4, 2.4 Hz, 1H), 8.50 (s, 1H), 8.53–8.56 (m, 3H), 9.06 (d, J = 2.4 Hz, 1H), 9.49 (d, J = 2.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.5, 50.1, 62.5, 112.8, 115.4, 120.3, 122.7, 124.6, 132.9, 133.2, 133.3, 134.1, 135.9, 137.3, 145.5, 148.3, 149.4, 150.4, 151.9, 152.5, 154.1, 154.5, 164.9.

Ethyl 6-(6-chloropyridin-3-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50.0 mg, 0.127 mmol, 1.0 equiv) prepared above was converted to **84** using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 3 afforded the title compound **84** (16.4 mg, 35%) as a white solid: R_T 9.3 min; ^{1}H NMR (600 MHz, DMSO-d_6) δ 5.86 (s, 2H), 7.22 (d, J = 5.4 Hz, 2H), 7.68 (d, J = 8.4 Hz, 1H), 8.28 (s, 1H), 8.49–8.51 (m, 3H), 8.66 (dd, J = 8.4, 2.4 Hz, 1H), 9.24 (d, J = 2.4 Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 49.1, 100.5, 112.9, 114.9, 122.4, 124.5, 133.0, 133.8, 138.3, 146.0, 148.8, 149.9, 151.2, 151.3, 152.6, 165.9; HRMS (ESI–) calcd for $C_{18}H_{11}ClN_5O_2$ $[M - H]^-$ 364.0607, found 364.0610 (error 0.8 ppm).

Ethyl 6-(6'-chloro-2,3'-bipyridin-5-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (25.0 mg, 0.0531 mmol, 1.0 equiv) prepared above was converted to **85** using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 4 afforded the title compound **85** (18.0 mg, 77%) as a white solid: R_T 10.6 min; ^{1}H NMR (600 MHz, DMSO-d_6) δ 5.86 (s, 2H), 7.24 (d, J = 5.4 Hz, 3H), 7.69 (d, J = 9.0 Hz, 1H), 8.24–8.26 (m, 2H), 8.48–8.54 (m, 3H), 8.60 (dd, J = 2.4, 9.0 Hz, 1H), 8.70 (dd, J = 2.4, 9.0 Hz, 1H), 9.19 (d, J = 2.4 Hz,, 1H), 9.52 (d, J = 2.4 Hz,, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 49.1, 114.0, 114.5, 121.0, 122.5, 124.6, 133.2, 133.8, 134.1, 134.8, 136.0, 137.8, 146.6, 148.3, 148.7,

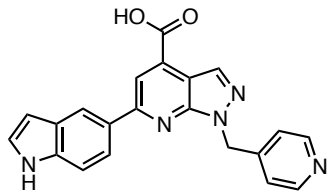
149.9, 151.0, 151.5, 152.9, 153.1, 166.4; HRMS (ESI–) calcd for $C_{23}H_{14}ClN_6O_2$ $[M - H]^-$ 441.0872, found 441.0881 (error 2.0 ppm).



6-(Isoquinolin-4-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (86). Ethyl 6-(isoquinolin-4-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with isoquinolin-4-ylboronic acid (116 mg, 0.67 mmol, 2.0 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (100 mg, 73%) as a grey solid: R_f 0.16 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.48 (t, J = 7.2 Hz, 3H), 4.53 (q, J = 7.2 Hz, 2H), 5.78 (s, 2H), 7.18 (d, J = 6.0 Hz, 2H), 7.61–7.65 (m, 2H), 8.02–8.05 (m, 2H), 8.11 (s, 1H), 8.54 (d, J = 6.0 Hz, 2H), 8.56 (s, 1H), 8.74 (s, 1H), 9.31 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.4, 50.2, 62.3, 112.5, 119.8, 122.6, 124.4, 127.7, 128.3, 128.6, 130.7, 131.3, 132.6, 133.6, 134.0, 144.3, 145.7, 150.3, 151.6, 153.9, 156.3, 164.8.

Ethyl 6-(isoquinolin-4-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50.0 mg, 0.122 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 4 afforded the title compound (45.4 mg, 98%) as a white solid: R_T 9.5 min; ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.84 (s, 2H), 7.15–7.25 (m, 2H), 7.69–7.77 (m, 2H), 8.03–8.08 (m, 2H), 8.25 (d, J = 8.0 Hz, 1H), 8.54–8.57 (m, 3H), 8.77 (s, 1H), 9.44 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 49.5, 112.2, 119.2, 122.1, 122.3, 124.0, 128.1, 130.0, 131.4, 132.7, 133.4, 143.7,

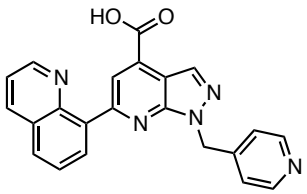
144.0, 146.0, 149.8, 150.0, 151.1, 153.8, 155.5, 165.8; HRMS (ESI–) calcd for $C_{22}H_{14}N_5O_2$ [M – H]$^-$ 380.1153, found 380.1158 (error 1.3 ppm).



6-(1*H*-Indol-5-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (87). Ethyl 6-(1*H*-indol-5-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109**, using 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indole (163 mg, 0.67 mmol, 2 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (125 mg, 94%) as a white solid: R_f 0.33 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.51 (t, J = 7.2 Hz, 3H), 4.55 (q, J = 7.2 Hz, 2H), 5.82 (s, 2H), 6.66 (s, 1H), 7.23 (d, J = 6.0 Hz, 2H), 7.26 (s, 1H), 7.48 (d, J = 8.4 Hz, 1H), 8.04 (dd, J = 8.4, 1.2 Hz, 2H), 8.35 (s, 1H), 8.43 (s, 1H), 8.46 (s, 1H), 8.54 (d, J = 6.0 Hz, 2H), 8.85 (br s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.5, 49.7, 62.1, 103.6, 111.4, 111.7, 116.1, 120.7, 121.8, 122.8, 125.6, 128.5, 130.3, 132.1, 134.0, 137.2, 146.4, 150.0, 152.1, 159.0, 165.5.

Ethyl 6-(1*H*-indol-5-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (63 mg, 0.159 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 2 afforded the title compound (48 mg, 82%) as a white solid: R_T 9.0 min; ^{1}H NMR (600 MHz, CD_3OD) δ 5.85 (s, 2H), 6.56 (d, J = 3.0 Hz, 1H), 7.28 (d, J = 3.0 Hz, 1H), 7.30 (d, J = 6.0 Hz, 2H), 7.48 (d, J = 7.8 Hz, 1H), 7.99 (dd, J = 7.8, 1.8 Hz, 1H), 8.27 (s, 1H), 8.40 (br s, 1H), 8.46 (d, J = 6.0 Hz, 2H), 8.49 (s, 1H); ^{13}C NMR (150 MHz, CD_3OD) δ 50.2, 103.5, 112.5, 113.7,

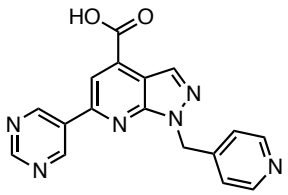
116.4, 121.2, 122.2, 124.1, 126.8, 129.9, 131.4, 135.7, 138.8, 141.3, 149.4, 150.3, 153.3, 161.0, 172.1; HRMS (ESI–) calcd for $C_{21}H_{14}N_5O_2$ $[M - H]^-$ 368.1147, found 368.1155 (error 2.2 ppm).



1-(Pyridin-4-ylmethyl)-6-(quinolin-8-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (88). Ethyl 1-(pyridin-4-ylmethyl)-6-(quinolin-8-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109**, using quinolin-8-ylboronic acid (116 mg, 0.67 mmol, 2.0 equiv). Purification by flash chromatography afforded the ester (88.5 mg, 65%) as a gray solid: R_f = 0.26 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.47 (t, J = 7.2 Hz, 3H), 4.52 (q, J = 7.2 Hz, 2H), 5.82 (s, 2H), 7.18 (d, J = 6.0 Hz, 2H), 7.46 (dd, J = 8.4, 4.2 Hz, 1H), 7.68 (t, J = 7.8 Hz, 1H), 7.94 (dd, J = 8.4, 1.2 Hz, 1H), 8.11 (dd, J = 7.2, 1.2 Hz, 1H), 8.24 (dd, J = 7.8, 1.8 Hz, 1H), 8.50–8.54 (m, 3H), 8.58 (s, 1H), 8.96 (dd, J = 4.2, 1.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.4, 49.8, 61.9, 112.1, 121.5, 122.4, 122.6, 126.5, 128.8, 129.8, 130.8, 131.7, 134.0, 136.6, 138.3, 145.96, 146.02, 150.2, 150.8, 152.0, 158.0, 165.4.

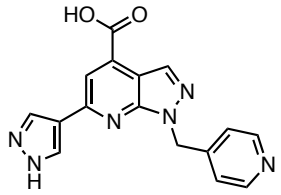
Ethyl 1-(pyridin-4-ylmethyl)-6-(quinolin-8-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50.0 mg, 0.122 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 4 afforded the title compound (31.9 mg, 69%) as a white solid: R_T 9.7 min; ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.85 (s, 2H), 7.21 (d, J = 6.0 Hz, 2H), 7.63 (dd, J = 8.2, 4.0 Hz, 1H), 7.78 (t, J = 7.6 Hz, 1H), 8.14–8.18 (m, 2H), 8.45 (s, 1H), 8.50–8.51 (m, 4H), 8.98 (dd, J = 4.0, 1.6 Hz, 1H); ^{13}C NMR (150 MHz, DMF-d_7) δ 50.5, 113.0, 122.9, 123.4, 123.6, 127.6, 129.9,

131.2, 132.4, 132.8, 134.5, 138.0, 138.9, 146.8, 147.6, 151.1, 152.0, 152.9, 158.6, 167.6; HRMS (ESI–) calcd for $C_{22}H_{14}N_5O_2$ $[M - H]^-$ 380.1153, found 380.1150 (error 0.8 ppm).



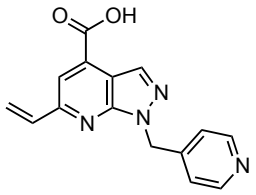
1-(Pyridin-4-ylmethyl)-6-(pyrimidin-5-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (89). Ethyl 1-(pyridin-4-ylmethyl)-6-(pyrimidin-5-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** with pyrimidin-5-ylboronic acid (83 mg, 0.67 mmol, 2 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (102 mg, 84%) as a white solid: R_f 0.09 (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.51 (t, J = 7.2 Hz, 3H), 4.56 (q, J = 7.2 Hz, 2H), 5.81 (s, 2H), 7.19 (d, J = 6.0 Hz, 2H), 8.25 (s, 1H), 8.51 (s, 1H), 8.54 (d, J = 6.0 Hz, 2H), 9.30 (s, 1H), 9.46 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.4, 50.1, 62.5, 113.2, 115.0, 122.6, 131.7, 133.3, 134.2, 145.3, 150.3, 151.78, 151.83, 155.7, 159.34, 164.6.

Ethyl 1-(pyridin-4-ylmethyl)-6-(pyrimidin-5-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (50 mg, 0.139 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 2 afforded the title compound (24 mg, 53%) as a white solid: R_T 5.1 min; ^{1}H NMR (600 MHz, CD_3OD) δ 5.89 (s, 2H), 7.31 (d, J = 6.0 Hz, 2H), 8.25 (s, 1H), 8.47 (d, J = 6.0 Hz, 2H), 8.59 (s, 1H), 9.22 (s, 1H), 9.55 (s, 2H); ^{13}C NMR (150 MHz, CD_3OD) δ 50.5, 115.6, 115.8, 124.1, 134.1, 136.1, 143.9, 149.1, 150.4, 152.7, 153.1, 156.8, 159.3, 171.5; HRMS (ESI–) calcd for $C_{17}H_{11}N_6O_2$ $[M - H]^-$ 331.0943, found 331.0949 (error 1.8 ppm).



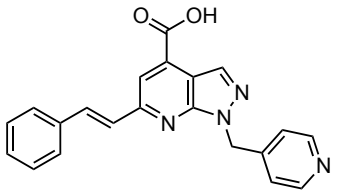
6-(1*H*-Pyrazol-4-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (90). Ethyl 6-(1*H*-pyrazol-4-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109**, using 1H-pyrazole-4-boronic acid pinacol ester (130 mg, 0.67 mmol, 2.0 equiv). After initial extraction with DCM the aqueous phase was back extracted with EtOAc (15 mL) and the organic extracts were combined and concentrated. Purification by flash chromatography afforded the ester (24.0 mg, 21%) as a brown oil: R_f = 0.50 (10% MeOH/EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.50 (t, J = 7.2 Hz, 3H), 4.53 (q, J = 7.2 Hz, 2H), 5.75 (s, 2H), 7.19 (d, J = 6.0 Hz, 2H), 7.97 (s, 1H), 8.24 (br s, 2H), 8.39 (s, 1H), 8.53 (d, J = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.5, 49.7, 62.2, 111.5, 115.6, 122.7, 122.8, 132.3, 133.5 (broad), 134.1, 146.2, 150.1, 151.9, 152.1, 165.2.

Ethyl 6-(1*H*-pyrazol-4-yl)-1-(pyridin-4-ylmethyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (20.0 mg, 0.0574 mmol, 1.0 equiv) prepared above was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 4 afforded the title compound (18.4 mg, 100%) as a brown solid: R_T 8.3 min; ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.78 (s, 2H), 7.22 (d, J = 6.0 Hz, 2H), 8.02 (s, 1H), 8.35 (s, 1H), 8.42 (br s, 2H), 8.51 (d, J = 6.0 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 48.8, 110.9, 115.1, 121.6, 122.4, 122.5, 133.3, 133.6, 146.2, 149.8, 151.3, 152.3, 166.2; HRMS (ESI–) calcd for $C_{16}H_{11}N_6O_2$ $[M - H]^-$ 319.0949, found 319.0944 (error 1.6 ppm).



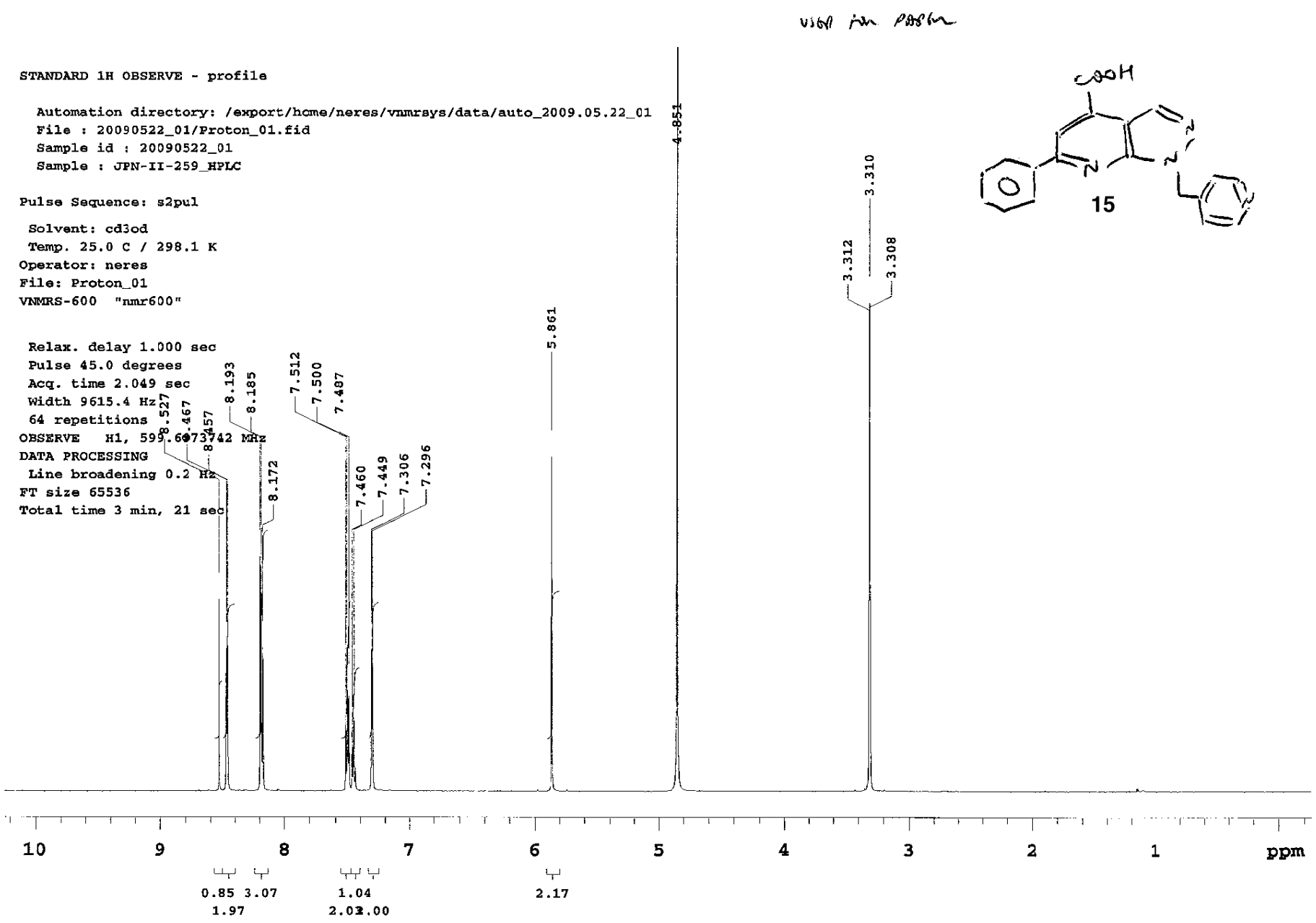
1-(Pyridin-4-ylmethyl)-6-vinyl-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (91). Ethyl 1-pyridin-4-ylmethyl-6-vinyl-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** (0.5 mmol, 1.0 equiv) with vinyl boronic acid pinacolate (154 mg, 1 mmol, 2.0 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (117 mg, 76%) as a white solid: R_f 0.28 (EtOAc); ^{1}H NMR (600 MHz, CD_3OD): δ 1.48 (t, *J* = 7.2 Hz, 3H), 4.51 (q, *J* = 7.2 Hz, 2H), 5.65 (d, *J* = 11.1 Hz, 1H), 5.74 (s, 2H), 6.40 (d, *J* = 17.4 Hz, 1H), 6.95 (dd, *J* = 17.4, 11.1 Hz, 1H), 7.16 (d, *J* = 6.0 Hz, 2H), 7.86 (s, 1H), 8.40 (s, 1H), 8.52 (d, *J* = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 14.4, 49.7, 62.1, 112.4, 116.6, 121.0, 122.7, 132.0, 134.0, 136.6, 146.0, 150.0, 151.7, 156.0, 165.1; HRMS (ESI+) calcd for $C_{17}H_{17}N_4O_2$ $[M + H]^+$ 309.1346, found 309.1364 (error 5.8 ppm).

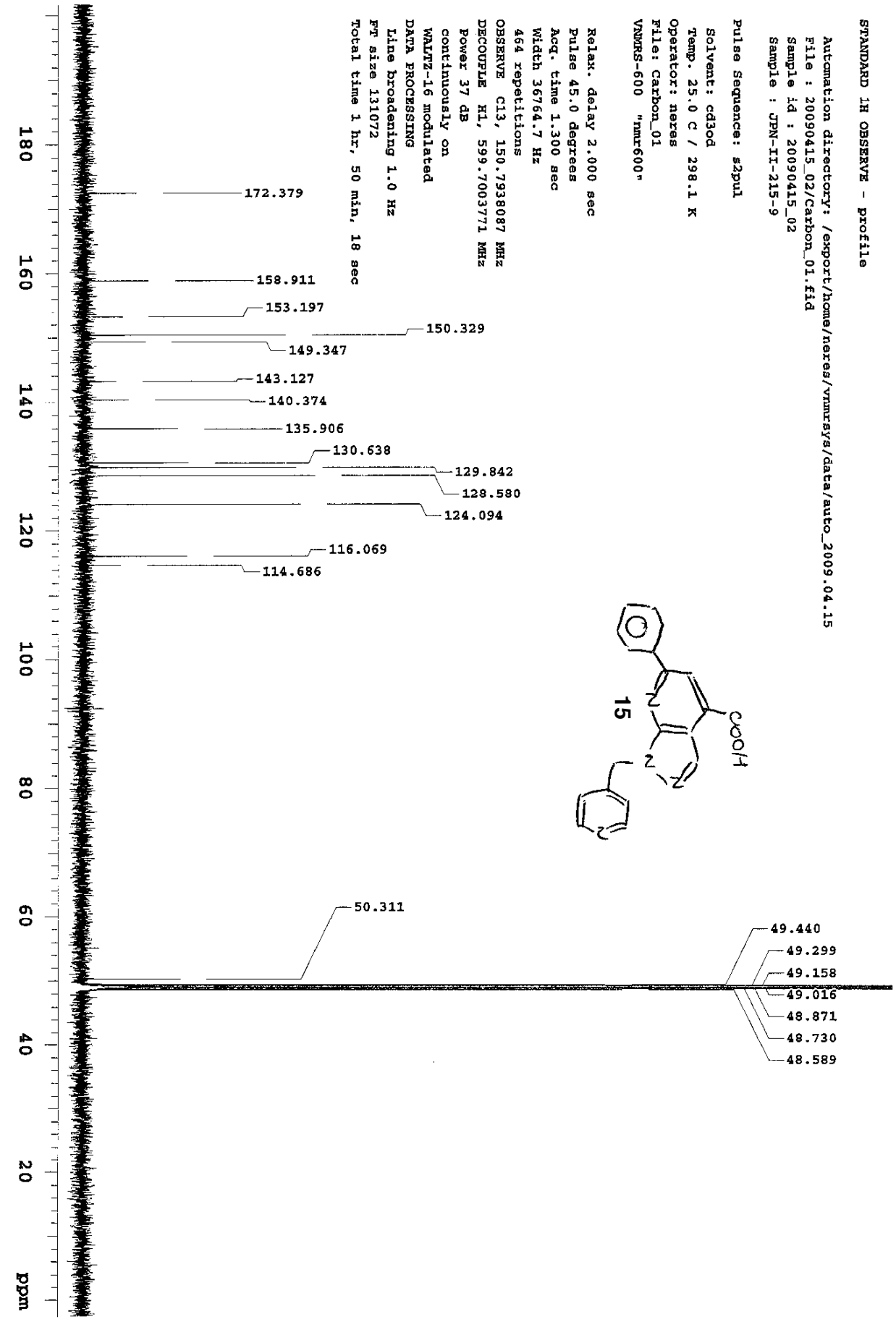
Ethyl 1-pyridin-4-ylmethyl-6-vinyl-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate prepared above (47 mg, 0.15 mmol) was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using method 8 followed by lyophilisation of the pooled product fractions afforded the title compound (15 mg, 36%) as a white solid: R_T = 12.5 min; ^{1}H NMR (600 MHz, CD_3OD) δ 5.65 (d, *J* = 10.8 Hz, 1H), 5.82 (s, 2H), 6.43 (d, *J* = 18.0 Hz, 1H), 6.96 (dd, *J* = 18.0, 10.8 Hz, 1H), 7.26 (d, *J* = 6.0 Hz, 2H), 7.92 (s, 1H), 8.45 (ovlp d, *J* = 6.0 Hz, 2H), 8.46 (ovlp s, 1H); ^{13}C NMR (150 MHz, D_2O, internal standard: MeOH) δ 49.8, 113.7, 115.6, 122.5, 123.3, 135.1, 136.6, 141.4, 148.7, 149.1, 151.6, 157.9, 173.0. HRMS (ESI–) calcd for $C_{15}H_{11}N_4O_2$ $[M - H]^-$ 279.0887, found: 279.0877 (error 3.6 ppm).

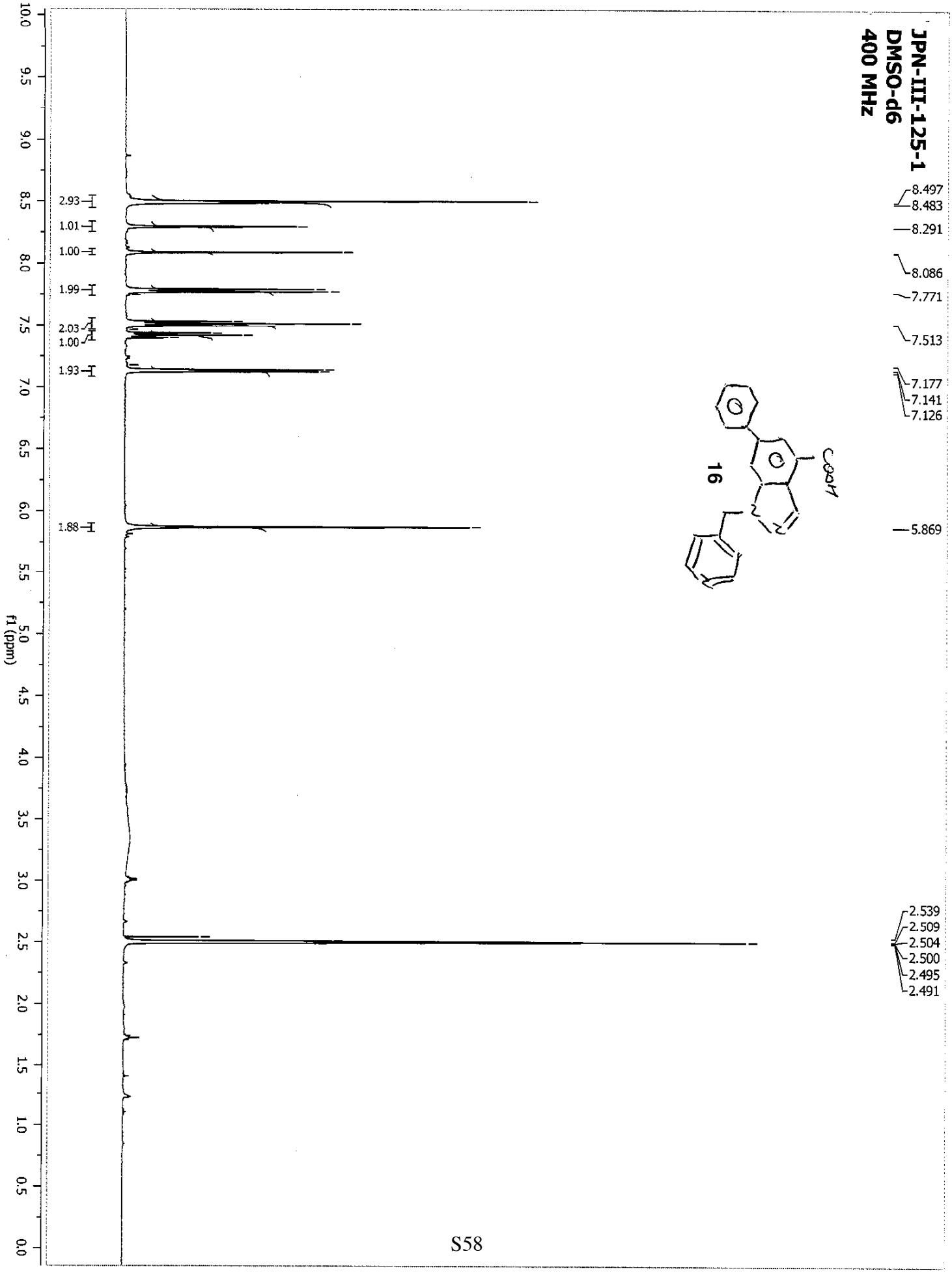


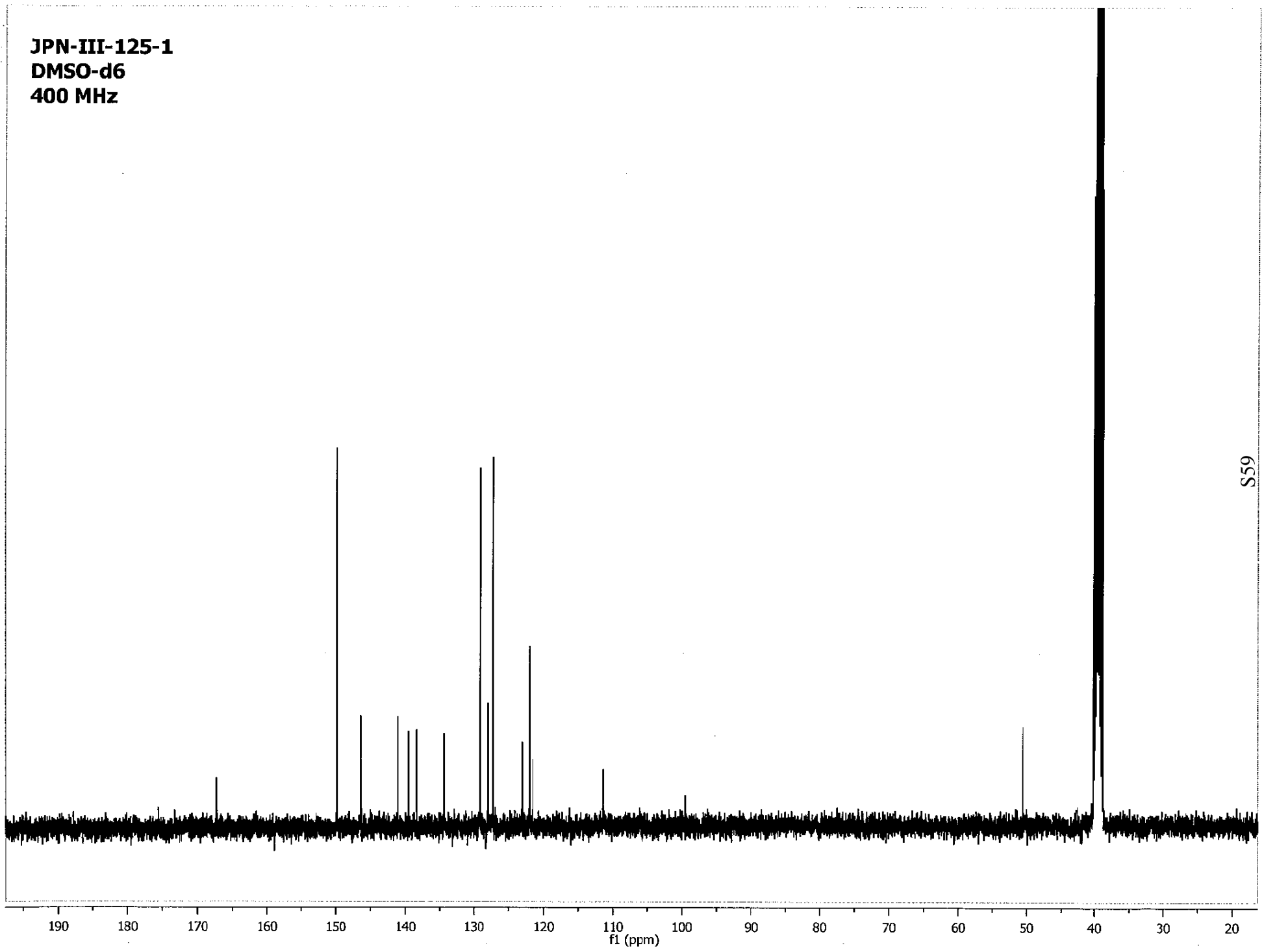
(*E*)-1-(Pyridin-4-ylmethyl)-6-styryl-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (92). (*E*)-ethyl 1-(pyridin-4-ylmethyl)-6-styryl-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate was prepared using the general procedure for Suzuki coupling of **109** (0.5 mmol, 1.0 equiv) with (*E*)-styrylboronic acid (148 mg, 1 mmol, 2.0 equiv). Purification by flash chromatography afforded the ethyl ester of the title compound (166 mg, 86%) as a yellow solid: R_f 0.39 (EtOAc); ^{1}H NMR (600 MHz, CD_3OD) δ 1.49 (t, J = 7.2 Hz, 3H), 4.51 (q, J = 7.2 Hz, 2H), 5.83 (s, 2H), 7.27–7.28 (m, 2H), 7.32–7.34 (m, 1H), 7.36–7.39 (m, 3H), 7.62–7.64 (m, 2H), 7.80–7.82 (m, 1H), 7.94 (s, 1H), 8.39 (s, 1H), 8.46–8.47 (m, 2H); ^{13}C NMR (150 MHz, CD_3OD) δ 14.7, 50.5, 63.3, 113.3, 118.7, 124.2, 128.4, 128.6, 130.0, 130.2, 133.5, 135.0, 136.9, 137.7, 149.1, 150.5, 153.2, 157.9, 166.3; HRMS calcd for $C_{23}H_{21}N_4O_2$ $[M + H]^+$ 385.1659, found 385.1678 (error 4.9 ppm).

(*E*)-ethyl 1-(pyridin-4-ylmethyl)-6-styryl-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate prepared above (77 mg, 0.20 mmol) was converted to the title compound using the general procedure for ester hydrolysis. Purification by preparative reverse-phase HPLC using followed by lyophilisation of the pooled product fractions afforded the title compound (26 mg, 36%) as a yellow solid: ^{1}H NMR (600 MHz, CD_3OD) δ 1.49 (t, J = 7.2 Hz, 3H), 4.51 (q, J = 7.2 Hz, 2H), 5.83 (s, 2H), 7.28–7.39 (m, 6H), 7.62–7.64 (m, 2H), 7.80–7.82 (m, 1H), 7.94 (s, 1H), 8.39 (s, 1H), 8.46–8.47 (m, 2H); HRMS calcd for $C_{21}H_{15}N_4O_2^-$ $[M - H]^-$ 355.1200, found 355.1184 (error 4.5 ppm).


STANDARD 1H OBSERVE - profile
Automation directory: /export/home/neres/vnmrsys/data/auto_2009.05.22_01
File : 20090522_01/Proton_01.fid
Sample id : 20090522_01
Sample : JPN-II-259_HPLC
Pulse Sequence: s2pul
Solvent: cd3od
Temp. 25.0 C / 298.1 K
Operator: neres
File: Proton_01
VNMRS-600 "nmr600"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 9615.4 Hz
64 repetitions
OBSERVE H1, 599.6073742 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 3 min, 21 sec
8.527
8.467
8.457
8.193
8.185
8.172
7.512
7.500
7.487
7.460
7.449
7.306
7.296
5.861
4.851
3.312
3.310
3.308
10
9
8
7
6
5
4
3
2
1
ppm
0.85
3.07
1.04
2.17
1.97
2.03
2.00
15


STANDARD 1H OBSERVE - profile
Automation directory: /export/home/neres/vnmrsys/data/auto_2009.04.15
File : 20090415_02/Carbon_01.fid
Sample id : 20090415_02
Sample : JPN-II-215-9
Pulse Sequence: s2pul
Solvent: cd3od
Temp. 25.0 C / 298.1 K
Operator: neres
File: Carbon_01
VNMRS-600 "nmr600"
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 36764.7 Hz
464 repetitions
OBSERVE C13, 150.7938087 MHz
DECOUPLE H1, 599.7003771 MHz
Power 37 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 1 hr, 50 min, 18 sec
172.379
158.911
153.197
150.329
149.347
143.127
140.374
135.906
130.638
129.842
128.580
124.094
116.069
114.686
50.311
49.440
49.299
49.158
49.016
48.871
48.730
48.589
15
COOH
180
160
140
120
100
80
60
40
20
ppm


JPN-III-125-1
DMSO-d6
400 MHz
8.497
8.483
8.291
8.086
7.771
7.513
7.177
7.141
7.126
5.869
2.539
2.509
2.504
2.500
2.495
2.491
2.93
1.01
1.00
1.99
2.03
1.00
1.93
1.88
16
COOH
f1 (ppm)


JPN-III-125-1
DMSO-d6
400 MHz
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

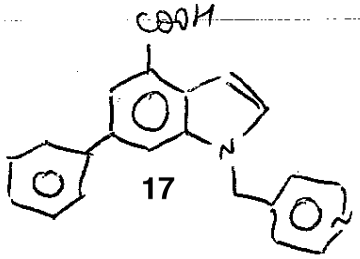
STANDARD 1H OBSERVE - profile

Automation directory: /export/home/neres/vnmrsys/data/auto_2009.07.01
File : 20090702_01/Proton_01.fid
Sample id : 20090702_01
Sample : JPN-II-261

Pulse Sequence: s2pul

Solvent: dmso
Temp. 25.0 C / 298.1 K
Operator: neres
File: Proton_01
VNMRS-600 "nmr600"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 9615.4 Hz
64 repetitions
OBSERVE H1, 599.6978530 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 3 min, 21 sec



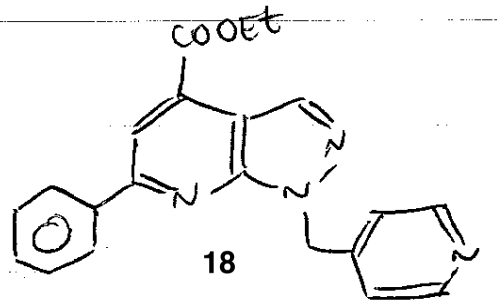
STANDARD 1H OBSERVE - profile

Automation directory: /export/home/neres/vnmrsys/data/auto_2009.07.14
File : 20090714_03/Proton_01.fid
Sample id : 20090714_03
Sample : JPN-II-275R

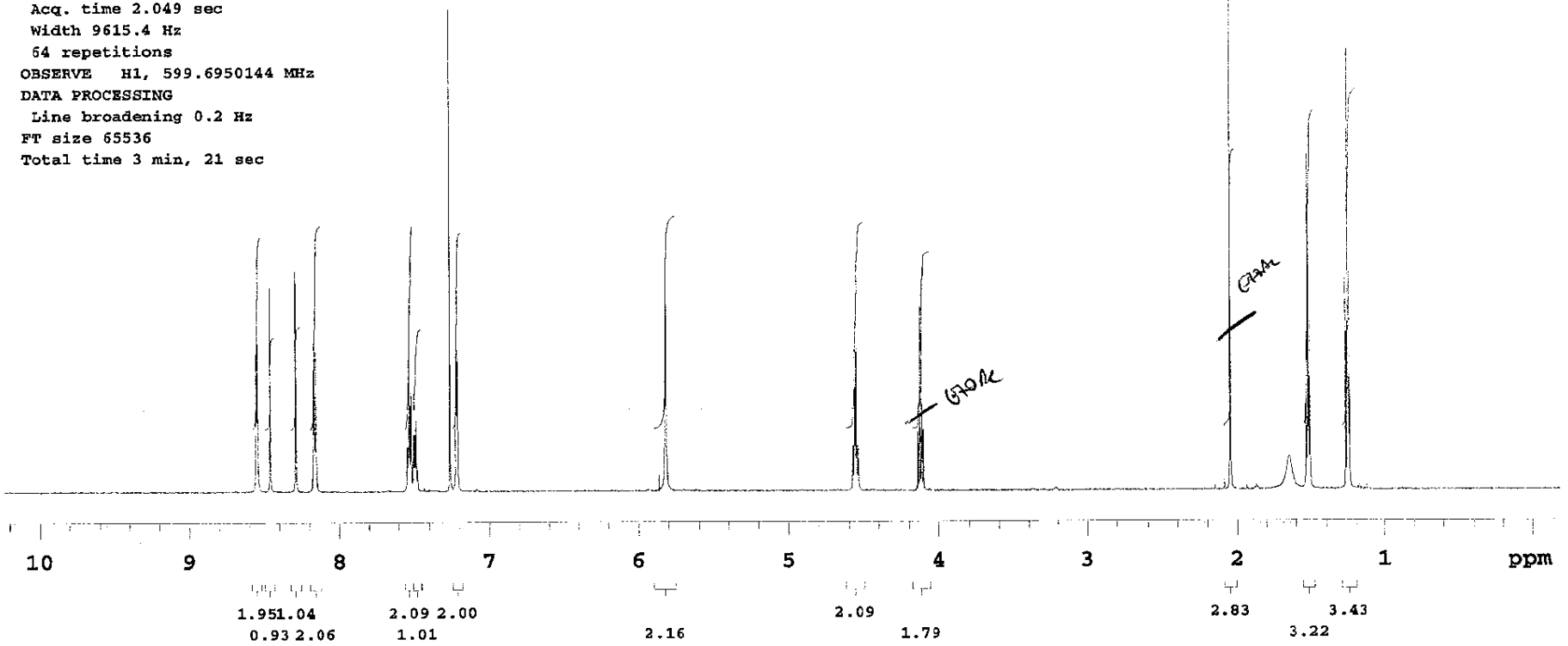
Pulse Sequence: s2pul

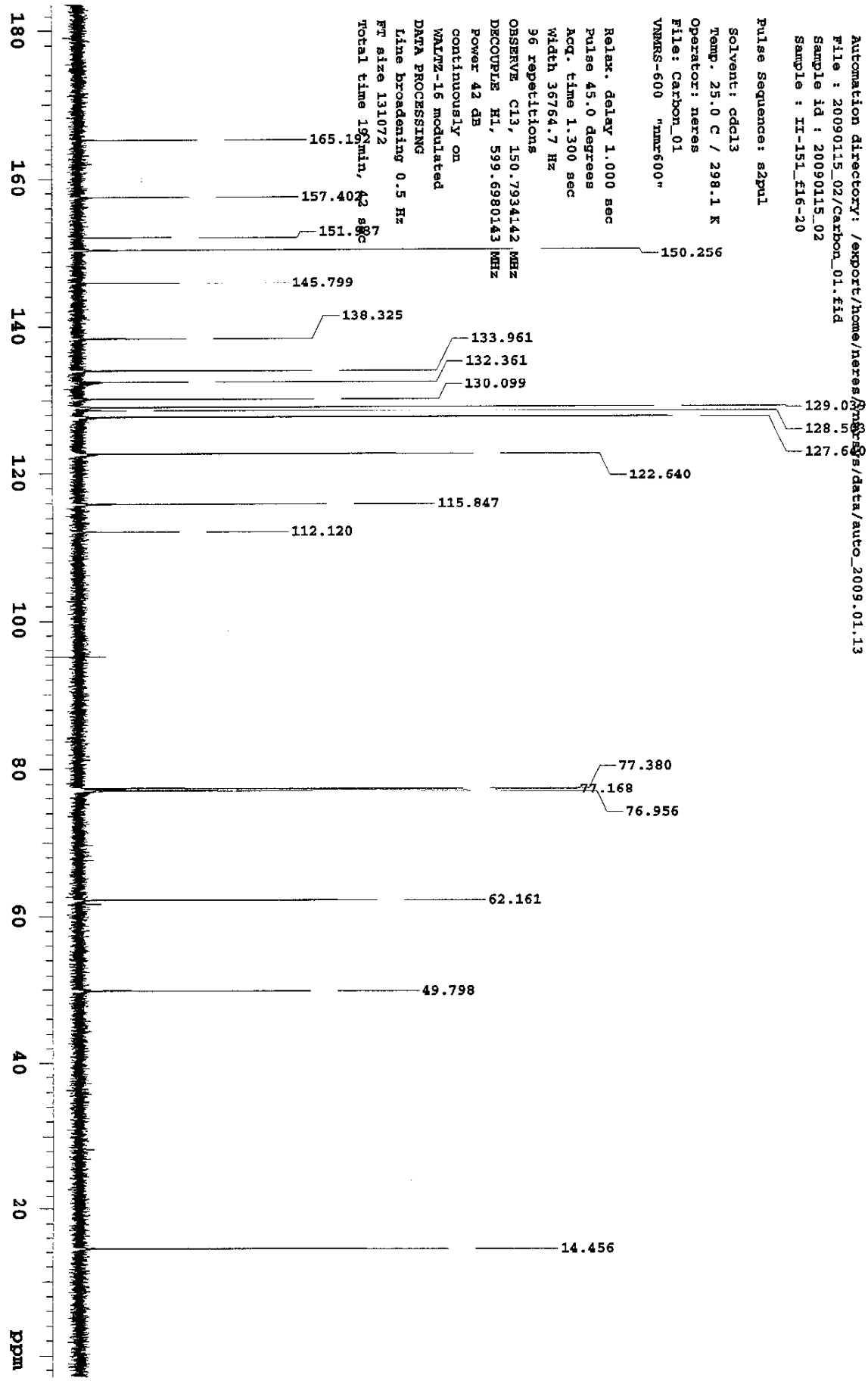
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: neres
File: Proton_01
VNMRS-600 "nmr600"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 9615.4 Hz
64 repetitions
OBSERVE H1, 599.6950144 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 3 min, 21 sec



18




Automation directory: /export/home/neres/vnmrsys/data/auto_2009.01.13
File : 20090115_02/Carbon_01.fid
Sample id : 20090115_02
Sample : II-151_f16-20
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: neres
File: Carbon_01
VNMRS-600 "nmr600"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 36764.7 Hz
96 repetitions
OBSERVE C13, 150.7934142 MHz
DECOUPLE H1, 599.6980143 MHz
Power 42 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 42 sec
165.197
157.402
151.987
150.256
145.799
138.325
133.961
132.361
130.099
129.039
128.583
127.640
122.640
115.847
112.120
77.380
77.168
76.956
62.161
49.798
14.456
180
160
140
120
100
80
60
40
20
ppm

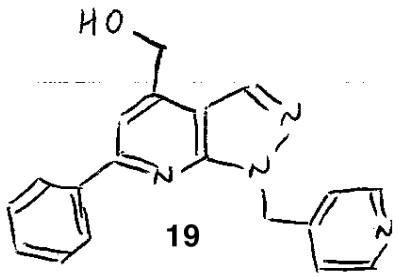
STANDARD 1H OBSERVE - profile

Automation directory: /export/home/neres/vnmrsys/data/auto_2009.07.16
File : 20090716_03/Proton_01.fid
Sample id : 20090716_03
Sample : JPN-III-103_f26-30

Pulse Sequence: s2pul

Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: neres
File: Proton_01
VNMRS-600 "nmr600"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 9615.4 Hz
64 repetitions
OBSERVE H1, 599.6950144 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 3 min, 21 sec



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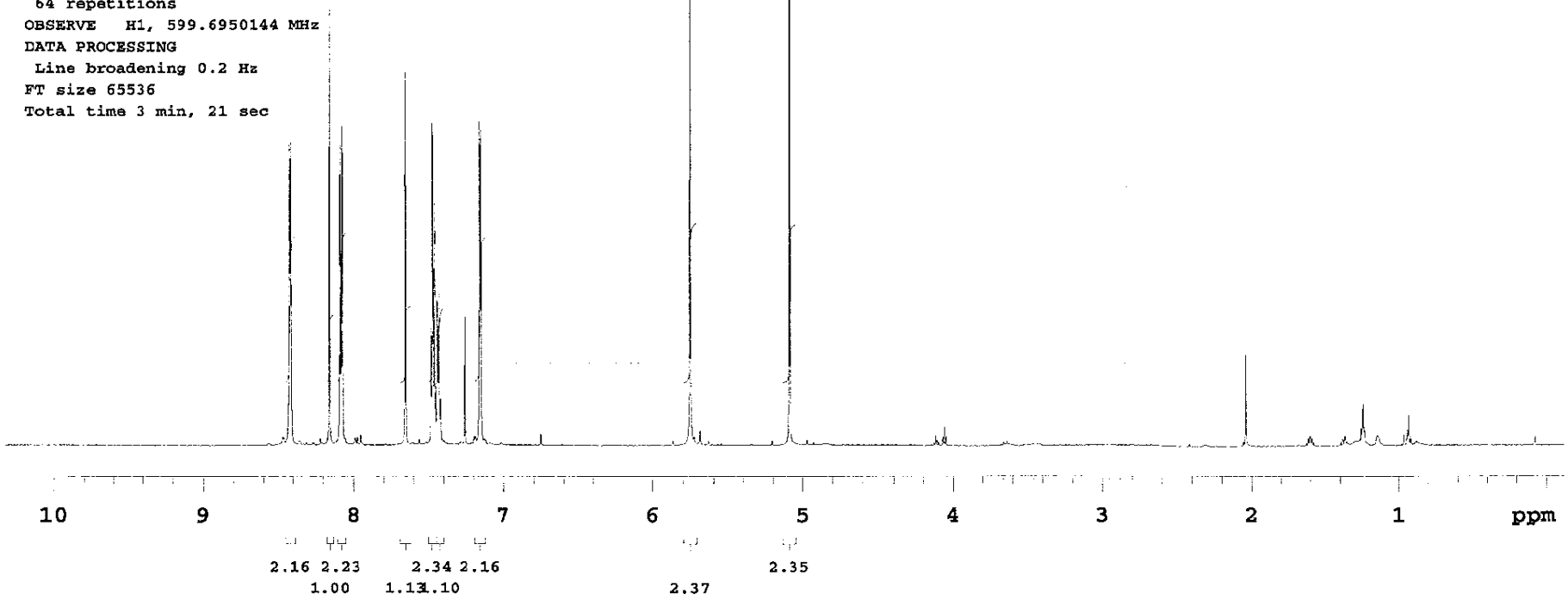

STANDARD 1H OBSERVE - profile
STANDARD 1H OBSERVE - profile

Automation directory: /export/home/neres/vnmrsys/data/auto_2009.07.16
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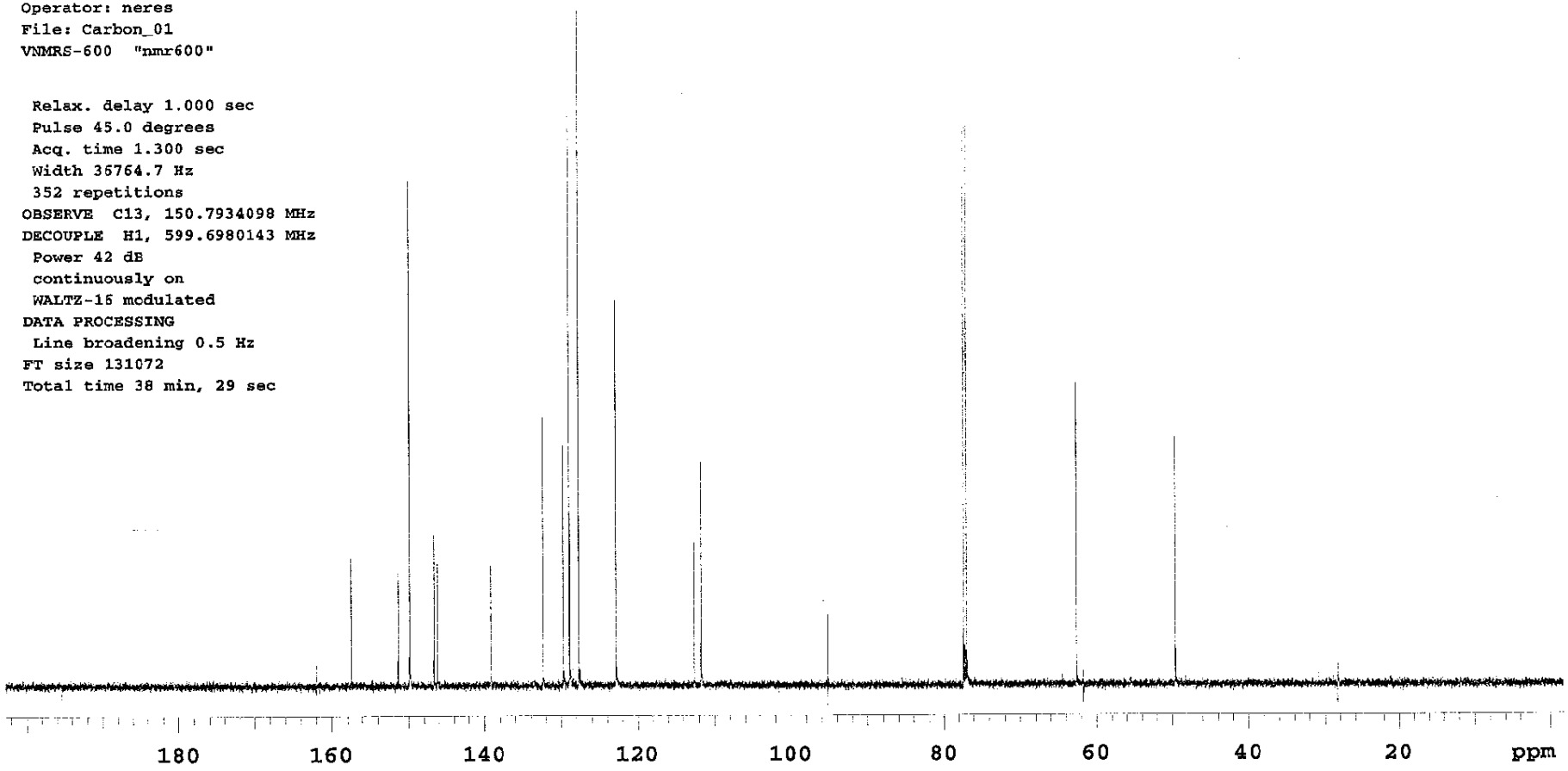
Sample id : 20090716_03
Sample : JPN-III-103_f26-30

Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: neres
File: Carbon_01
VNMRS-600 "nmr600"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 36764.7 Hz
352 repetitions
OBSERVE C13, 150.7934098 MHz
DECOUPLE H1, 599.6980143 MHz
Power 42 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 38 min, 29 sec



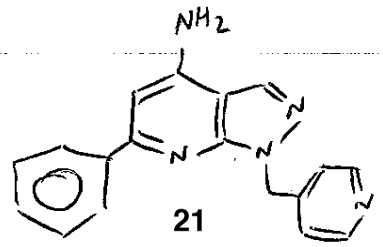
STANDARD 1H OBSERVE - profile

Automation directory: /export/home/neres/vnmrsys/data/auto_2009.07.16
File : 20090716_01/Proton_01.fid
Sample id : 20090716_01
Sample : JPN-II-299_f30-49

Pulse Sequence: s2pul

Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: neres
File: Proton_01
VNMRS-600 "nmr600"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 9615.4 Hz
64 repetitions
OBSERVE H1, 599.6950144 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 3 min, 21 sec



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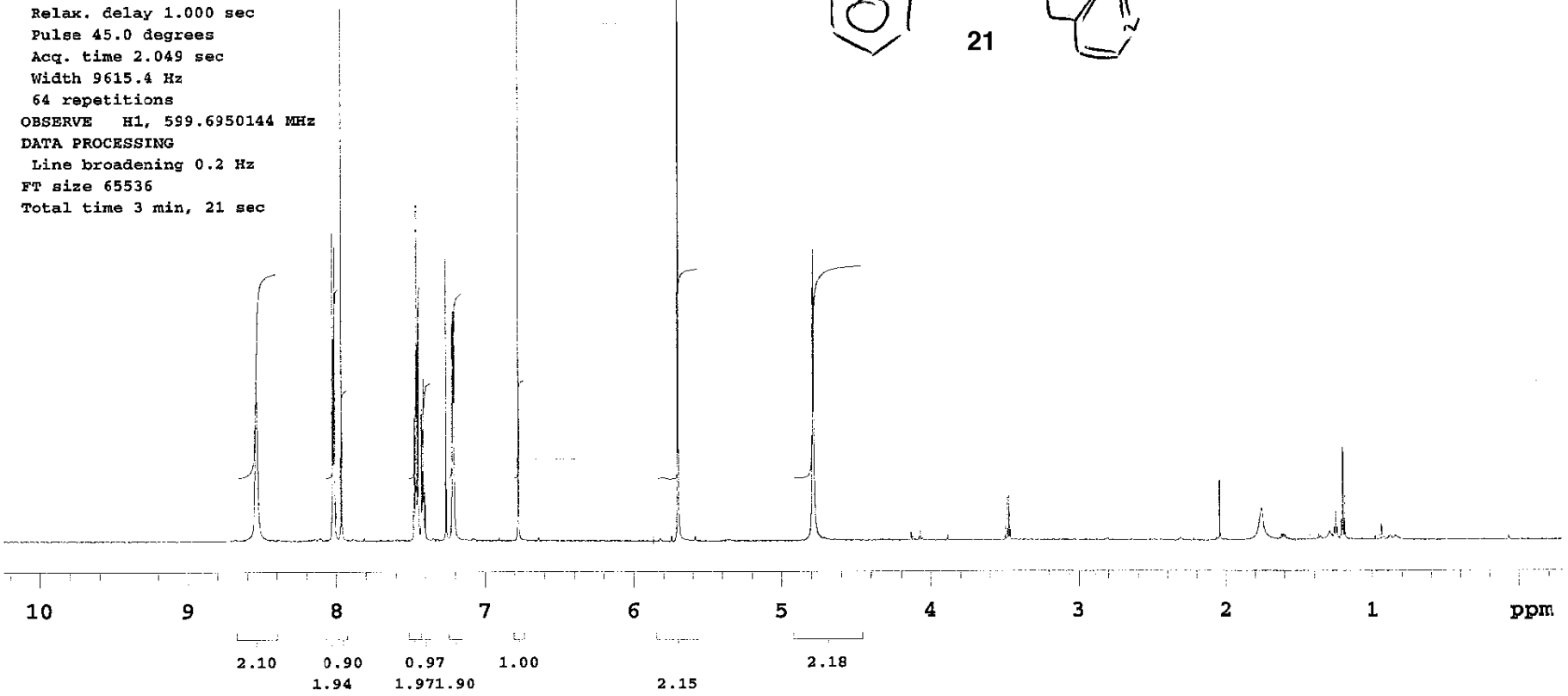


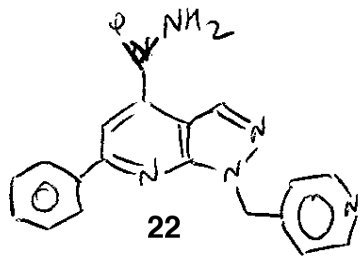
STANDARD 1H OBSERVE - profile

Automation directory: /export/home/neres/vnmrsys/data/auto_2009.08.01
File : 20090801_01/Proton_01.fid
Sample id : 20090801_01
Sample : JPN-III-113-1

Pulse Sequence: s2pul

Solvent: cd3od
Temp. 25.0 C / 298.1 K
Operator: neres
File: Proton_01
VNMRS-600 "nmr600"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 9615.4 Hz
64 repetitions
OBSERVE H1, 599.6908604 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 3 min, 21 sec



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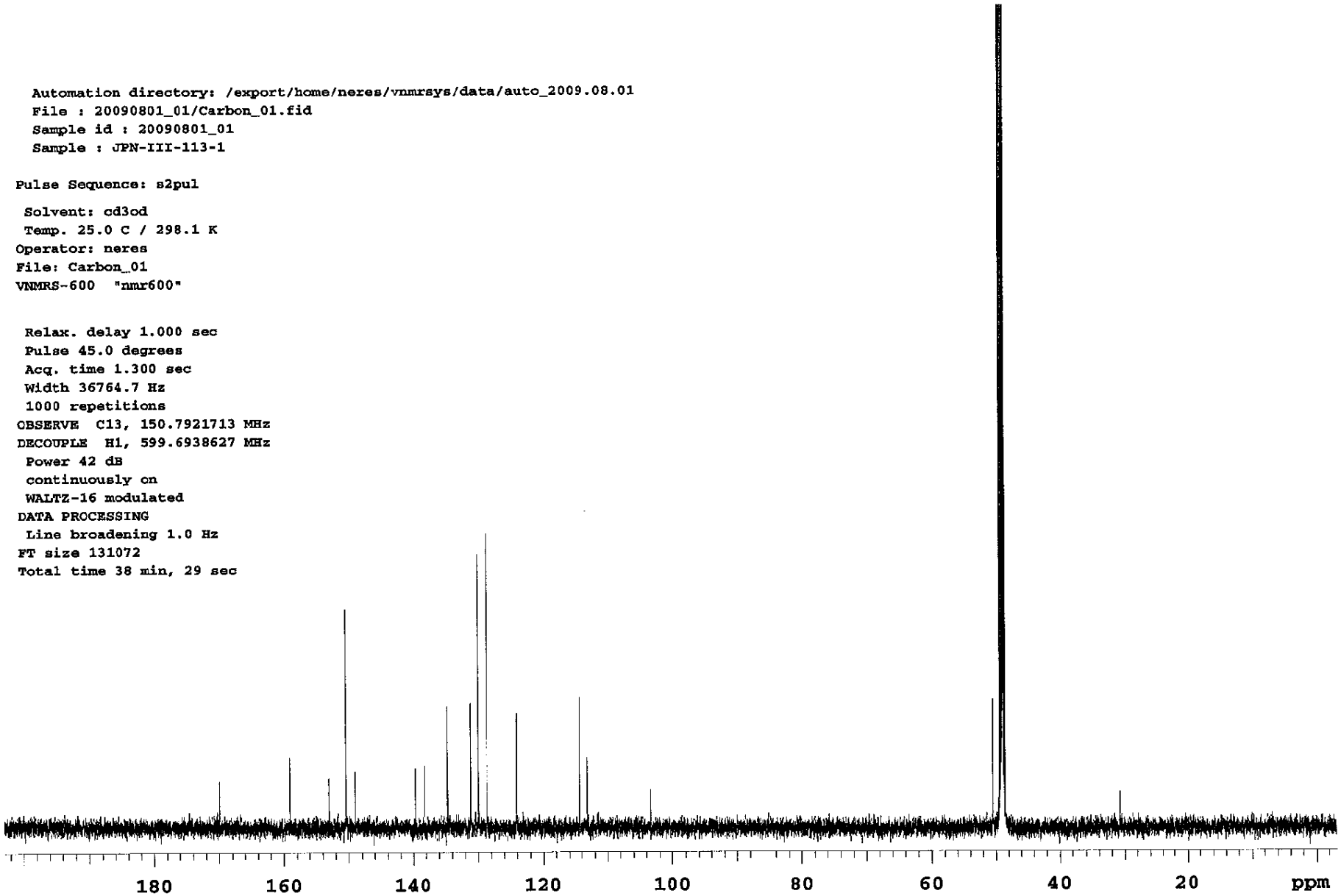
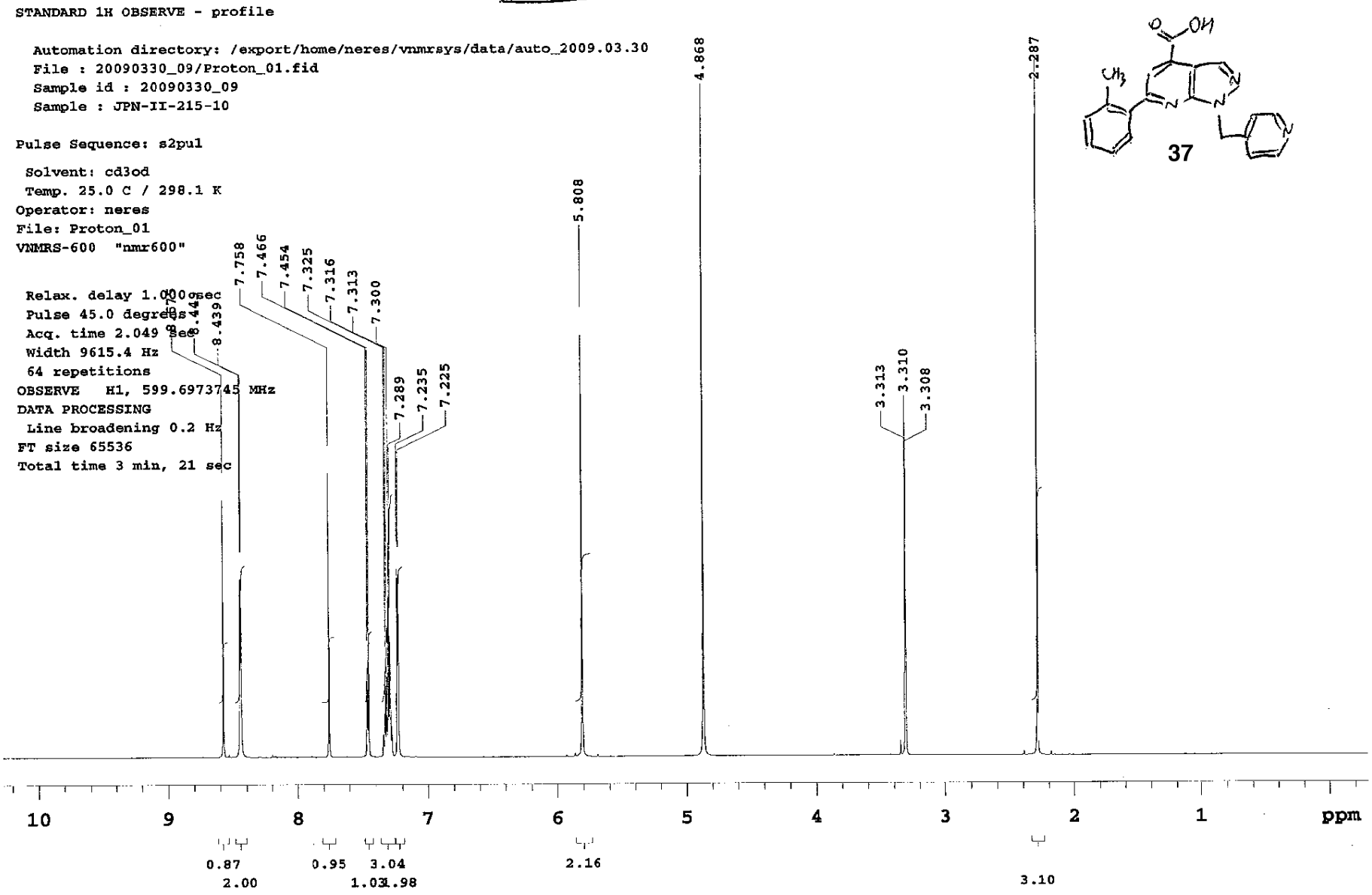

Automation directory: /export/home/neres/vnmrsys/data/auto_2009.08.01
File : 20090801_01/Carbon_01.fid
Sample id : 20090801_01
Sample : JPN-III-113-1
Pulse Sequence: s2pul
Solvent: cd3od
Temp. 25.0 C / 298.1 K
Operator: neres
File: Carbon_01
VNMRS-600 "nmr600"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 36764.7 Hz
1000 repetitions
OBSERVE C13, 150.7921713 MHz
DECOUPLE H1, 599.6938627 MHz
Power 42 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 38 min, 29 sec
180
160
140
120
100
80
60
40
20
ppm

JPN. II - 215 - 10


STANDARD 1H OBSERVE - profile
Automation directory: /export/home/neres/vnmrsys/data/auto_2009.03.30
File : 20090330_09/Proton_01.fid
Sample id : 20090330_09
Sample : JPN-II-215-10
Pulse Sequence: s2pul
Solvent: cd3od
Temp. 25.0 C / 298.1 K
Operator: neres
File: Proton_01
VNMRS-600 "nmr600"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 9615.4 Hz
64 repetitions
OBSERVE H1, 599.6973745 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 3 min, 21 sec
8.439
8.441
7.758
7.466
7.454
7.325
7.316
7.313
7.300
7.289
7.235
7.225
5.808
4.868
3.313
3.310
3.308
2.287
37
10
9
8
7
6
5
4
3
2
1
ppm
0.87
2.00
0.95
3.04
1.03
1.98
2.16
3.10

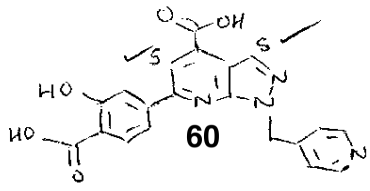
STANDARD 1H OBSERVE - profile

Automation directory: /export/home/engel313/vnmrsys/data/auto_2009.08.27
File : CAE-I-40_6b_200908270101.fid
Sample id : CAE-I-40_6b_2009082701
Sample : CAE-I-40_6b

Pulse Sequence: s2pul

Solvent: dmso + some D_2O
Temp. 25.0 C / 298.1 K
Operator: engel313
File: CAE-I-40_6b_200908270101
VNMRS-600 "nmr600"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 9615.4 Hz
64 repetitions
OBSERVE H1, 599.6913344 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 3 min, 21 sec



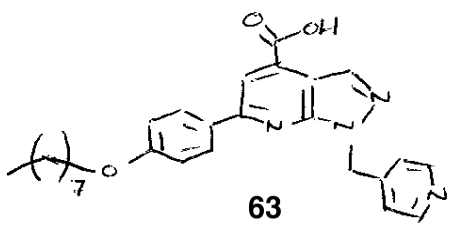
2 Bn
9 Ar
2 doublets
(4 H)

Automation directory: /export/home/pfu/vnmrsys/data/auto_2010.03.04_01
File : exp
Sample id : tmpstudy
Sample : pf-I-058-p

Pulse Sequence: s2pul

Solvent: dmso
Temp. 25.0 C / 298.1 K
Operator: pfu
VNMRS-600 "nmr600"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 9615.4 Hz
52 repetitions
OBSERVE H1, 599.6913391 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 3 min, 21 sec



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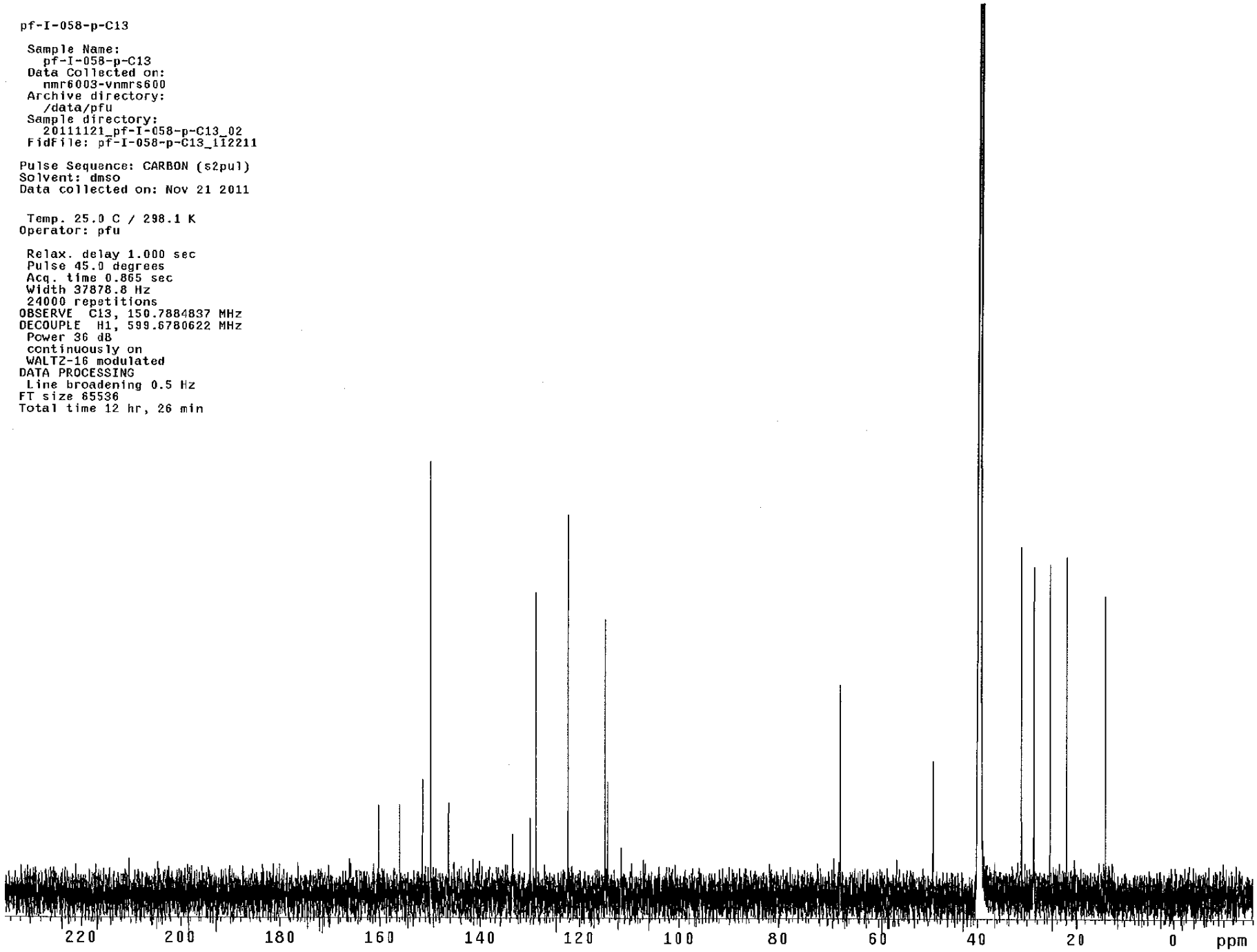
pf-I-058-p-C13

Sample Name:
pf-I-058-p-C13
Data Collected on:
nmr6003-vnmrs600
Archive directory:
/data/pfu
Sample directory:
20111121_pf-I-058-p-C13_02
FidFile: pf-I-058-p-C13_112211

Pulse Sequence: CARBON (s2pul)
Solvent: dmso
Data collected on: Nov 21 2011

Temp. 25.0 C / 298.1 K
Operator: pfu

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 0.865 sec
Width 37878.8 Hz
24000 repetitions
OBSERVE C13, 150.7884837 MHz
DECOUPLE H1, 599.6780622 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 12 hr, 26 min



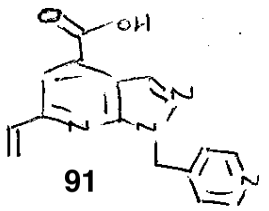
STANDARD 1H OBSERVE - profile

Automation directory: /export/home/pfu/vnmrsys/data/auto_2010.02.05
File : pf-I-042-p_201002050101.fid
Sample id : pf-I-042-p_2010020501
Sample : pf-I-042-p

Pulse Sequence: s2pul

Solvent: cd3od
Temp. 25.0 C / 298.1 K
Operator: pfu
File: pf-I-042-p_201002050101
VNMRS-600 "nmr600"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 9615.4 Hz
16 repetitions
OBSERVE H1, 599.6908586 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min, 55 sec



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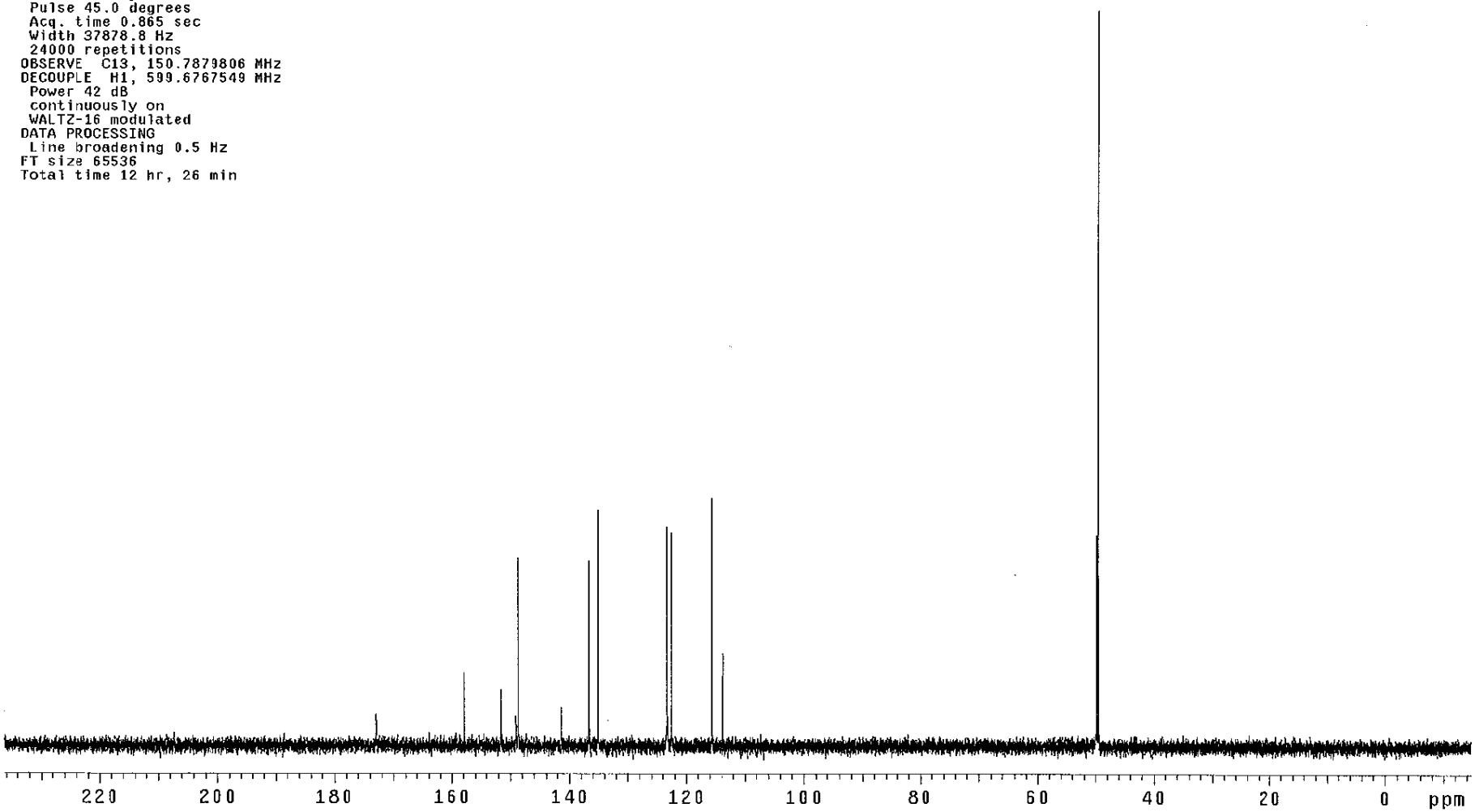
pf-I-036-p-C13

Sample Name:
pf-I-036-p-C13
Data Collected on:
nmr6003-vnmrs600
Archive directory:
/data/pfu
Sample directory:
20111114_pf-I-036-p-C13_01
FidFile: pf-I-036-p-C13_CARBON_01

Pulse Sequence: CARBON (s2pul)
Solvent: d2o
Data collected on: Nov 14 2011

Temp. 25.0 C / 298.1 K
Operator: pfu

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 0.865 sec
Width 37878.8 Hz
24000 repetitions
OBSERVE C13, 150.7879806 MHz
DECOUPLE H1, 599.6767549 MHz
Power 42 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 12 hr, 26 min



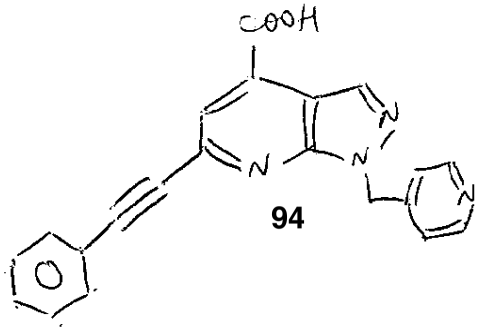
STANDARD 1H OBSERVE - profile

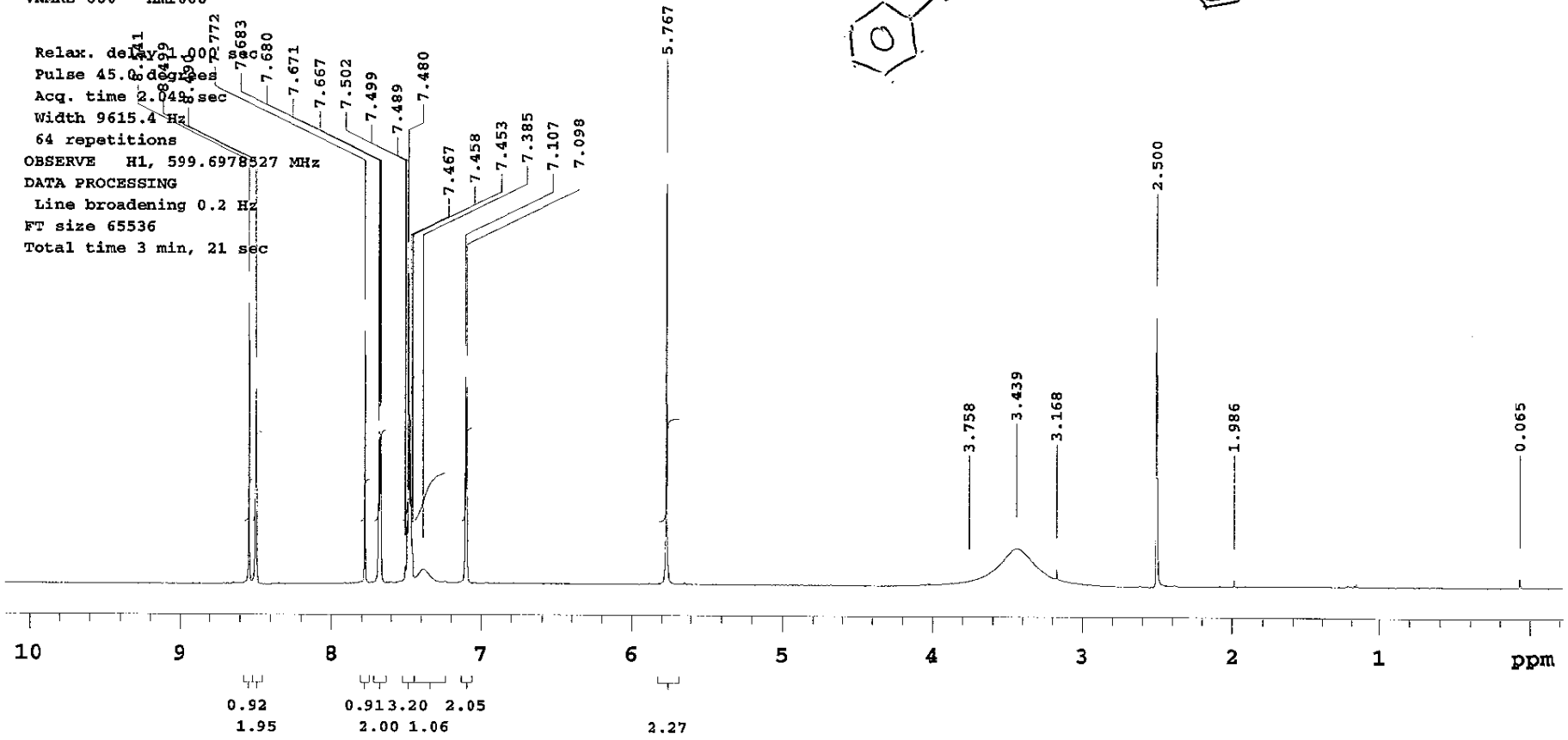
Automation directory: /export/home/neres/vnmrsys/data/auto_2009.05.02
File : 20090502_02/Proton_01.fid
Sample id : 20090502_02
Sample : JPN-II-241

Pulse Sequence: s2pul

Solvent: dmso
Temp. 25.0 C / 298.1 K
Operator: neres
File: Proton_01
VNMRS-600 "nmr600"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 9615.4 Hz
64 repetitions
OBSERVE H1, 599.6978527 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 3 min, 21 sec





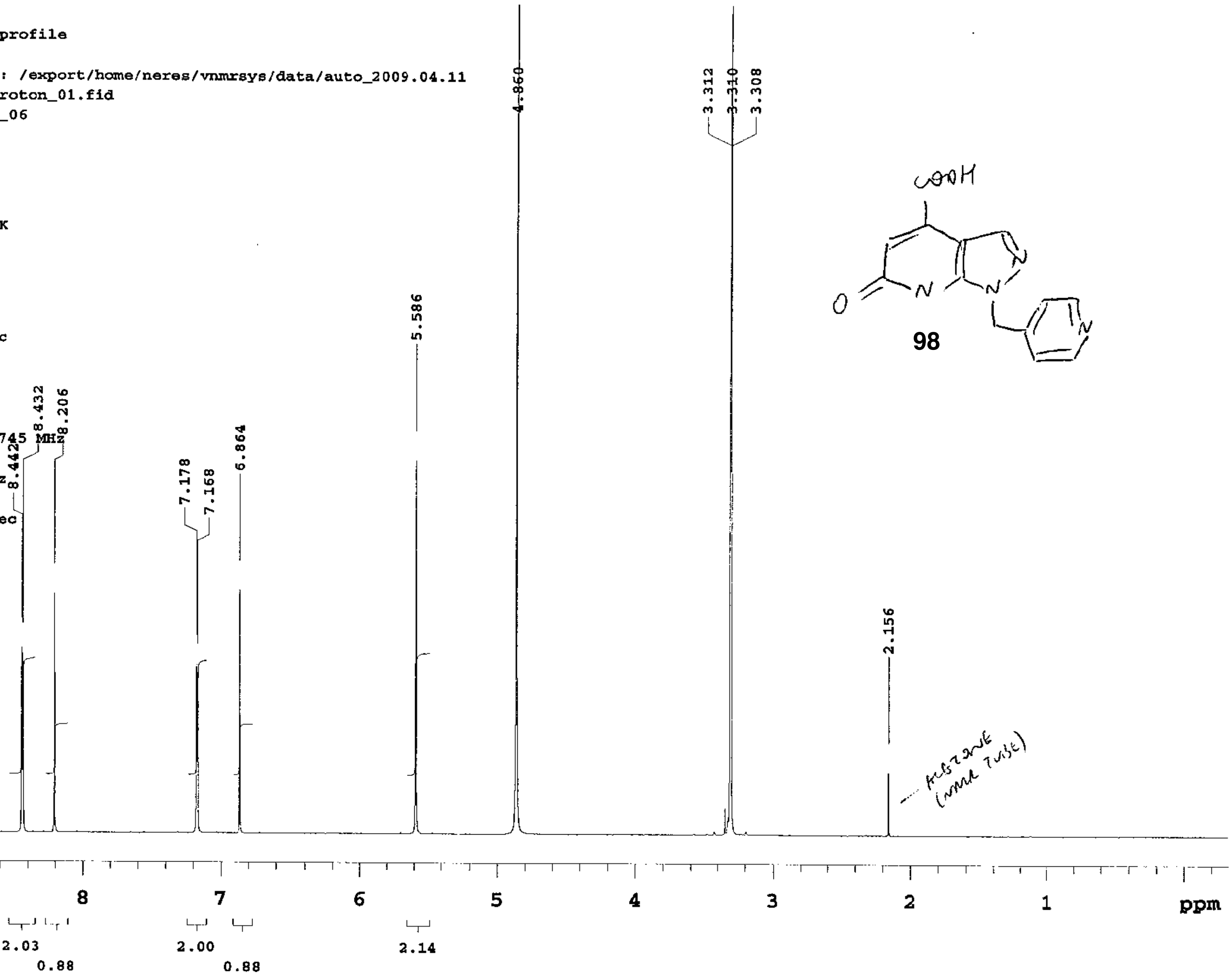
STANDARD 1H OBSERVE - profile

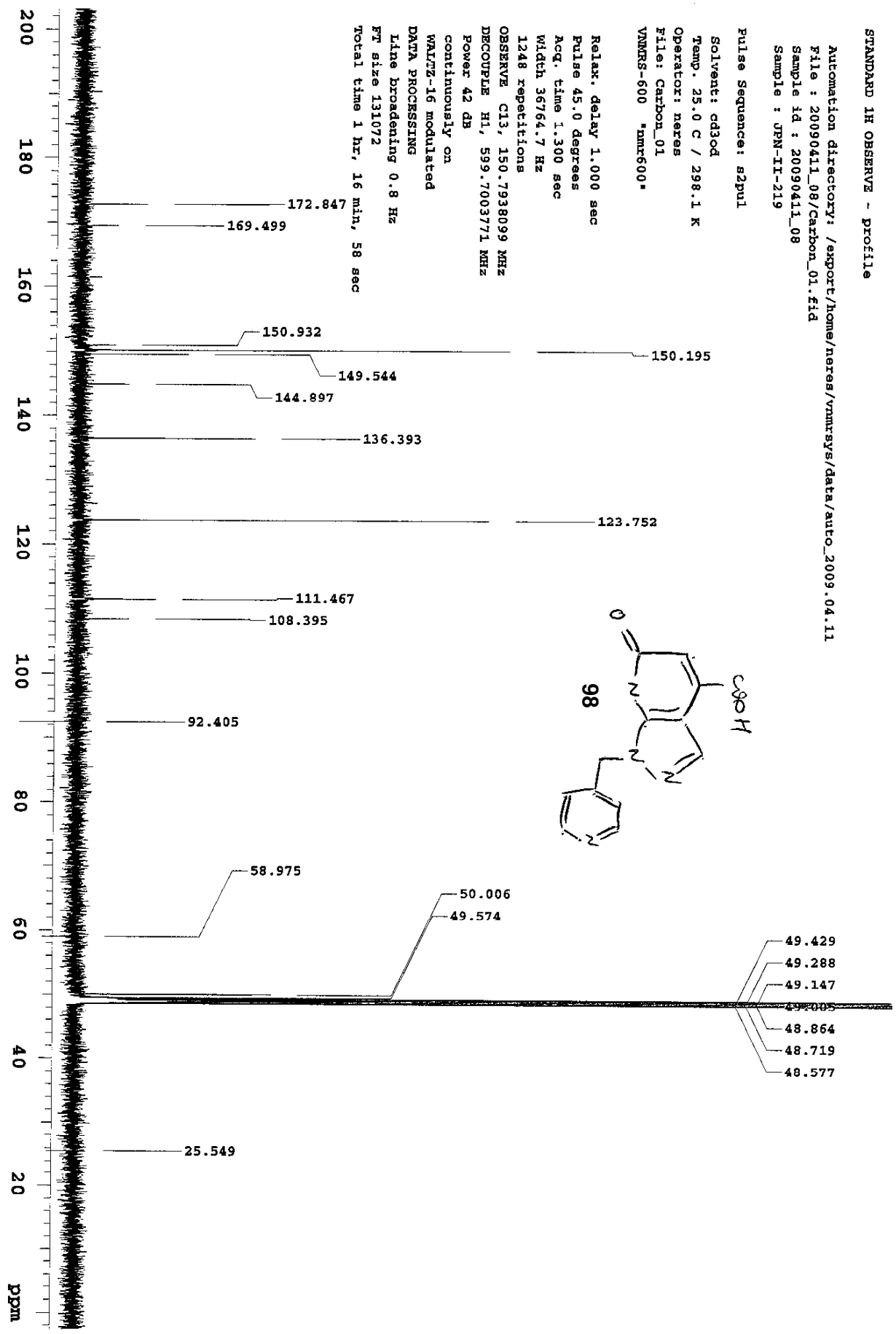
Automation directory: /export/home/neres/vnmrsys/data/auto_2009.04.11
File : 20090411_06/Proton_01.fid
Sample id : 20090411_06
Sample : JPN-II-219

Pulse Sequence: s2pul

Solvent: cd3od
Temp. 25.0 C / 298.1 K
Operator: neres
File: Proton_01
VNMRS-600 "nmr600"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 9615.4 Hz
64 repetitions
OBSERVE H1, 599.6973745 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 3 min, 21 sec




STANDARD 1H OBSERVE - profile
Automation directory: /export/home/neres/vnmrsys/data/auto_2009.04.11
File : 20090411_08/Carbon_01.fid
Sample id : 20090411_08
Sample : JPN-II-219
Pulse Sequence: s2pul
Solvent: cd3od
Temp. 25.0 C / 298.1 K
Operator: neres
File: Carbon_01
VNMRS-600 "nmr600"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 36764.7 Hz
1248 repetitions
OBSERVE C13, 150.7938099 MHz
DECOUPLE H1, 599.7003771 MHz
Power 42 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 131072
Total time 1 hr, 16 min, 58 sec
172.847
169.499
150.932
150.195
149.544
144.897
136.393
123.752
111.467
108.395
92.405
58.975
50.006
49.574
49.429
49.288
49.147
48.864
48.719
48.577
25.549
98
200
180
160
140
120
100
80
60
40
20
ppm