Human Collagen Prolyl 4-Hydroxylase is Activated by Ligands for its Iron Center

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General

Biphenyl-4-carboxylic acid, biphenyl-3-carboxylic acid, 3-(pyridin-2-yl)benzoic acid, 4-(pyridin-2-yl)benzoic acid, 2-phenylisonicotinic acid, 6-phenylnicotinic acid, 5-(pyridin-2-yl)-1*H*-pyrazole-3-carboxylic acid, and 2-(pyridin-2-yl)thiazole-4-carboxylic acid were from Combi-Blocks (San Diego, CA). 2-(Pyridin-2-yl)thiazole-5-carboxylic acid was from Enamine (Monmouth Junction, NJ). 2,2′-Bipyridine-5,5′-dicarboxylate was from Sigma–Aldrich (St. Louis, MO). Phosphine ligands, phosphonium salts, and $Pd(OAc)_2$ were from either Sigma–Aldrich or Strem (Newberryport, MA), stored in a dessicator, and used without further purification. All other reagent chemicals were obtained from commercial sources (Sigma–Aldrich, Acros, Combi-Blocks, Oakwood Products, Enamine, Bachem, or Novabiochem) and used without further purification. HIF-1α peptide$_{556–575}$ was from AnaSpec (Fremont, CA) and was used without further purification.

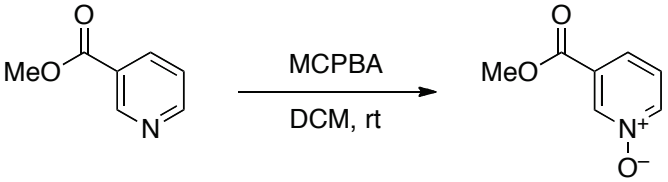
All glassware was flame- or oven-dried, and reactions were performed under N_2(g) unless indicated otherwise. DCM and toluene were dried over a column of alumina. Dimethylformamide was dried over alumina and purified further by passage through an isocyanate scrubbing column. Other anhydrous solvents were obtained in septum-sealed bottles. Flash chromatography was performed with columns of 40–63 Å silica gel, 230–400 mesh (Silicycle, Québec City, Canada). Thin-layer chromatography (TLC) was performed on plates of EMD 250-μm silica 60-F_{254} with visualization by UV light or staining with $KMnO_4$.

The phrase "concentrated under reduced pressure" refers to the removal of solvents and other volatile materials using a rotary evaporator at water aspirator pressure (<20 torr) while maintaining water-bath temperature below 40 °C. Residual solvent was removed from samples at high vacuum (<0.1 torr). The term "high vacuum" refers to vacuum achieved by a mechanical belt-drive oil pump. All reported yields are unoptimized.

To assess their purity, new final compounds were analyzed by HPLC using a system from Waters (Milford, MA) equipped with a Waters 996 photodiode array detector, Empower 2 software, and a Nucleodur® C18 Gravity reversed-phase column (4.6 × 250 mm, 5-μm particle size) from Macherey–Nagel (Bethlehem, PA). Samples (50 μL) dissolved in H_2O were injected into the column and eluted at 1 mL/min with a linear gradient (34 min) of aqueous acetonitrile (5–56% v/v) containing TFA (0.1% v/v). The maximal absorbance in the range of 210–400 nm was used as the detection wavelength.

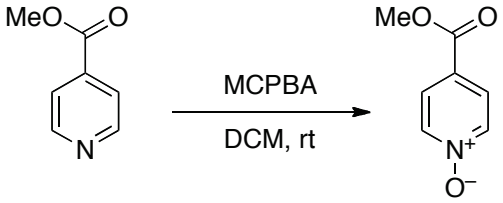
Synthetic Procedures

3-Methoxycarbonylpyridine N-oxide



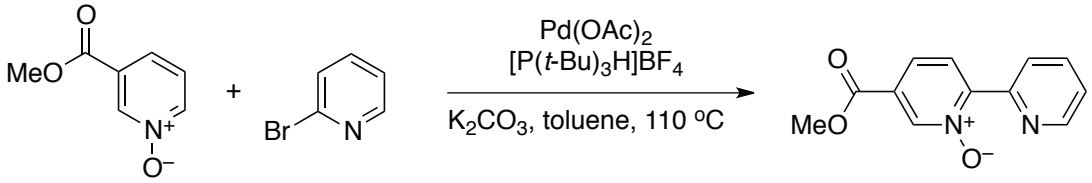
3-Methoxycarbonylpyridine *N*-oxide was prepared by oxidation of methyl nicotinate as described previously.[1] The spectral data and yields matched those reported previously.

4-Methoxycarbonylpyridine N-oxide



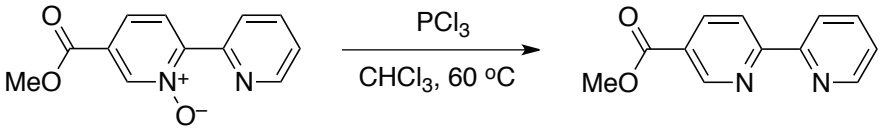
4-Methoxycarbonylpyridine *N*-oxide was prepared by oxidation of methyl isonicotinate as described previously [1]. The spectral data and yield matched those reported previously.

5-Methoxycarbonyl-2-(pyridin-2-yl)pyridine N-oxide



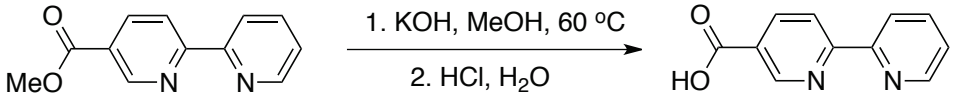
To a dried flask was added $Pd(OAc)_2$ (9 mg, 0.04 mmoles), $[P(t\text{-}Bu)_3H]BF_4$ (36 mg, 0.12 mmoles), K_2CO_3 (226 mg, 1.6 mmoles), and 3-methoxycarbonylpyridine *N*-oxide (500 mg, 3.3 mmoles). The flask was fitted with a reflux condenser that was capped with a septum, and the system was evacuated and purged with N_2(g) (~5 times). A degassed solution of 2-bromopyridine (129 mg, 0.82 mmoles) in dry toluene (5 mL) was added via syringe, and the reaction mixture was stirred at 110 °C for 18 h. The cooled reaction mixture was filtered through Celite®, and the filtrate was concentrated under reduced pressure. The crude product was then purified by chromatography on silica (40% v/v acetone in hexanes) to afford the title compound (100 mg, 53%) as a pale yellow solid. **^{1}H NMR** (400 MHz, $CDCl_3$, δ): 9.00 (dt, J = 1.0, 8.0 Hz, 1 H), 8.89 (dd, J = 0.4, 1.6 Hz, 1 H), 8.75 (ddd, J = 0.8, 1.6, 4.8 Hz, 1 H), 8.32 (d, J = 8.4 Hz, 1 H), 7.90 (dd, J = 1.6, 8.4 Hz, 1 H), 7.85 (td, J = 2.0, 8.0 Hz, 1 H), 7.39 (ddd, J = 0.8, 4.8, 7.6 Hz, 1 H), 3.98 (s, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$, δ): 163.5, 150.1 (2 signals), 149.6, 148.7, 141.9, 136.4, 128.5, 127.6, 125.7, 124.9, 53.0; **HRMS** (ESI) *m*/*z* 231.0766 [calculated for $C_{12}H_{11}N_2O_3$ $(M + H)^+$ 231.0765].

Methyl 2-(Pyridin-2-yl)pyridine-5-carboxylate (methyl bipy5C)



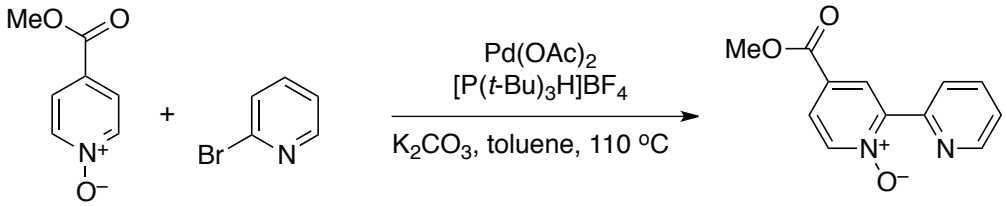
5-Methoxycarbonyl-2-(pyridin-2-yl)pyridine *N*-oxide (75 mg, 0.33 mmoles) was dissolved in dry $CHCl_3$ (3.3 mL), after which PCl_3 (34 μL, 0.39 mmoles) was added. The reaction mixture was stirred at 60 °C until the starting material was consumed completely, as judged by TLC. The reaction was quenched by the dropwise addition of saturated aqueous Na_2CO_3 (5 mL) while stirring on ice. The product was extracted with DCM (4 × 5 mL), and the combined organics were dried over Na_2SO_4(s) and concentrated under reduced pressure to afford the title compound (67 mg, 96%) as a tan solid. **^{1}H NMR** (400 MHz, $CDCl_3$, δ): 9.29 (d, J = 1.2 Hz, 1 H), 8.76 (bs, 1 H), 8.57 (d, J = 8.4 Hz, 1 H), 8.53 (d, J = 8.0 Hz, 1 H), 8.44 (dd, J = 2.0, 8.0 Hz, 1 H), 7.92 (t, J = 7.6 Hz, 1 H), 7.43 (dd, J = 4.8, 6.8 Hz, 1 H), 4.00 (s, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$, δ): 165.7, 158.6, 154.5, 150.5, 148.8, 138.2, 137.8, 125.9, 124.7, 122.3, 120.8, 52.5; **HRMS** (ESI) *m*/*z* 215.0814 [calculated for $C_{12}H_{11}N_2O_2$ $(M + H)^+$ 215.0816].

2-(Pyridin-2-yl)pyridine-5-carboxylic Acid (bipy5C)



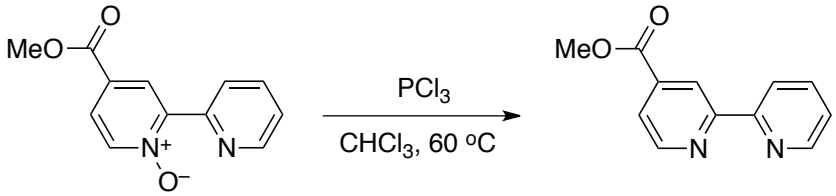
To a vial was added methyl bipy5C (50 mg, 0.23 mmoles) and KOH (60 mg, 0.83 mmoles). MeOH (2.3 mL) was added to the vial, and the reaction mixture was heated to 60 °C until complete the starting material was consumed completely, as judged by TLC. The reaction mixture was cooled and concentrated under reduced pressure, after which the crude product was dissolved in water (2 mL). The aqueous layer was washed with EtOAc (1 × 2 mL), and the product was precipitated from the aqueous layer by adjusting to pH 3–4 with 1 M HCl. After cooling to 4°C, the product was removed by filtration, washed with water (2 × 2 mL), and dried in vacuo to afford the title compound (28 mg, 60%) as a white solid. **^{1}H NMR** (400 MHz, DMSO-d_6, δ): 13.39 (bs, 1 H), 9.03 (dd, J = 0.5, 2.0 Hz, 1 H), 8.60 (dq, J = 1.0, 4.5 Hz, 1 H), 8.38 (dd, J = 0.5, 8.0 Hz, 1 H), 8.32 (d, J = 8.0 Hz, 1 H), 8.27 (dd, J = 2.0, 8.0 Hz, 1 H), 7.86 (dt, J = 2.0, 8.0 Hz, 1 H), 7.39 (ddd, J = 1.0, 5.0, 7.5 Hz, 1 H); **^{13}C NMR** (100 MHz, DMSO-d_6, δ): 166.5, 158.7, 154.5, 150.5, 149.9, 138.6, 137.9, 126.9, 125.3, 121.6, 120.6; **HRMS** (EI) m/z 200.0577 [calculated for $C_{11}H_8N_2O_2$ $(M)^+$ 200.0581].

4-Methoxycarbonyl-2-(pyridin-2-yl)pyridine N-oxide



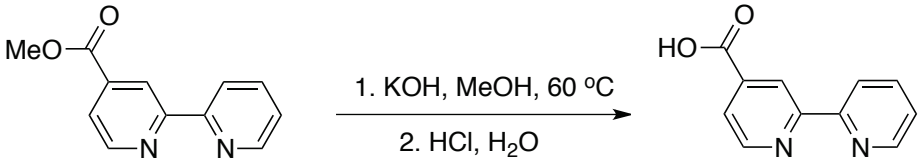
To a dried flask was added $Pd(OAc)_2$ (9 mg, 0.04 mmoles), $[P(t\text{-}Bu)_3H]BF_4$ (36 mg, 0.12 mmoles), K_2CO_3 (226 mg, 1.6 mmoles), and 3-methoxycarbonylpyridine *N*-oxide (500 mg, 3.3 mmoles). The flask was fitted with a reflux condenser that was capped with a septum, and the system was evacuated and purged with N_2(g) (~5 times). A degassed solution of 2-bromopyridine (129 mg, 0.82 mmoles) in dry toluene (5 mL) was added via syringe, and the reaction mixture was stirred at 110 °C for 18 h. The cooled reaction mixture was filtered through Celite®, and the filtrate concentrated under reduced pressure. The crude product was purified by chromatography on silica (40% v/v acetone in hexanes) to afford the title compound (128 mg, 68%) as a solid. **^{1}H NMR** (400 MHz, $CDCl_3$, δ): 8.94–9.76 (m, 3 H), 8.33 (d, J = 6.8 Hz, 1 H), 7.87–7.83 (m, 2 H), 7.38 (ddd, J = 1.2, 4.8, 7.6 Hz, 1 H), 3.97 (s, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$, δ): 164.1, 149.6, 148.9, 147.4, 141.0, 136.4, 128.4, 126.4, 125.2, 125.0, 124.6, 52.8; **HRMS** (ESI) m/z 231.0766 [calculated for $C_{12}H_{11}N_2O_3$ $(M + H)^+$ 231.0765].

Methyl 2-(Pyridin-2-yl)pyridine-4-carboxylate (methyl bipy4C)



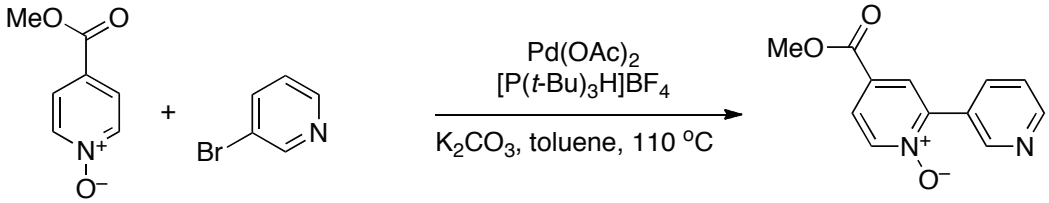
4-Methoxycarbonyl-2-(pyridin-2-yl)pyridine *N*-oxide (100 mg, 0.43 mmoles) was dissolved in dry $CHCl_3$ (4.0 mL), and PCl_3 (45 μL, 0.52 mmoles) was added. The reaction mixture was stirred at 60 °C until the starting material was consumed completely, as judged by TLC. The reaction was quenched by the dropwise addition of saturated aqueous Na_2CO_3 (10 mL) while stirring on ice. The product was extracted with DCM (5 × 10 mL), and the combined organics were dried over Na_2SO_4(s) and concentrated under reduced pressure. The crude product was purified by chromatography on silica (30% v/v acetone in hexanes) to afford the title compound (83 mg, 89%) as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$, δ): 8.95 (q, J = 0.8 Hz, 1 H), 8.83 (dd, J = 0.8, 4.8 Hz, 1 H), 8.73 (dq, J = 0.8, 4.8 Hz, 1 H), 8.43 (dt, J = 0.8, 8.0 Hz, 1 H), 7.88–7.82 (m, 2 H), 7.35 (ddd, J = 1.0, 4.8, 7.2 Hz, 1 H), 3.99 (s, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$, δ): 165.7, 157.3, 155.3, 149.9, 149.3, 138.4, 137.0, 124.1, 122.8, 121.2, 120.4, 52.7; **HRMS** (ESI) *m*/*z* 205.0818 [calculated for $C_{12}H_{11}N_2O_2$ $(M + H)^+$ 215.0816].

2-(Pyridin-2-yl)pyridine-4-carboxylic Acid (bipy4C)



To a vial was added methyl bipy4C (50 mg, 0.23 mmoles) and KOH (60 mg, 0.83 mmoles). MeOH (2.3 mL) was added to the vial, and the reaction mixture was heated to 60 °C until the starting material was consumed completely, as judged by TLC. The reaction mixture was cooled and concentrated under reduced pressure, and the crude product was dissolved in water (2 mL). The aqueous layer was washed with EtOAc (1 × 2 mL), and product was precipitated from the aqueous layer by adjusting the pH to 3–4 with 1 M HCl. After cooling to 4 °C, the product was removed by filtration, washed with water (2 × 2 mL), and dried in vacuo to afford the title compound (30 mg, 64%) as a white solid. **^{1}H NMR** (400 MHz, DMSO-d_6, δ): 13.81 (bs, 1 H), 8.89 (dd, J = 0.5, 5.0 Hz, 1 H), 8.84 (dd, J = 0.5, 1.0 Hz, 1 H), 8.74 (ddd, J = 0.5, 1.0, 4.5 Hz, 1 H), 8.43 (dt, J = 1.0, 8.0 Hz, 1 H), 8.00 (td, J = 1.5, 8.0 Hz, 1 H), 7.88 (dd, J = 1.5, 5.0 Hz, 1 H), 7.52 (ddd, J = 1.0, 4.5, 7.5 Hz, 1 H); **^{13}C NMR** (100 MHz, DMSO-d_6, δ): 166.6, 156.8, 154.8, 150.9, 150.0, 139.8, 138.0, 125.2, 123.5, 121.1, 119.9; **HRMS** (EI) *m*/*z* 200.0583 [calculated for $C_{11}H_8N_2O_2$ $(M)^+$ 200.0581].

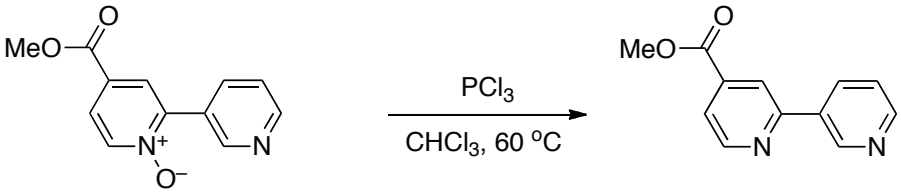
4-Methoxycarbonyl-2-(pyridin-3-yl)pyridine N-oxide



To a dried flask was added $Pd(OAc)_2$ (9 mg, 0.040 mmoles), $[P(t\text{-}Bu)_3H]BF_4$ (36 mg, 0.12 mmoles), K_2CO_3 (226 mg, 1.63 mmoles), and 4-methoxycarbonylpyridine *N*-oxide (500 mg, 3.26 mmoles). The flask was fitted with a reflux condenser that was capped with a septum, and the system was evacuated and purged with N_2(g) (~5 times). A degassed solution of 3-bromopyridine (129 mg, 0.82 mmoles) in dry toluene (5 mL) was added via syringe, and the reaction mixture was stirred at 110 °C for 18 h. The cooled reaction mixture was filtered through

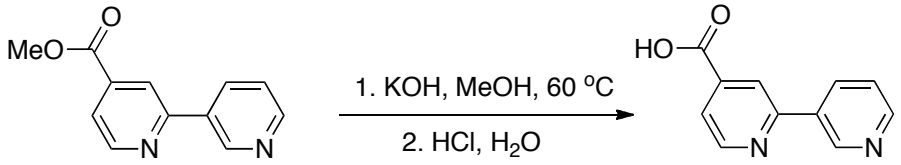
Celite®, and the filtrate was concentrated under reduced pressure. The crude product was further purified by chromatography on silica (4% v/v MeOH in EtOAc) to afford the title compound (100 mg) as a white solid. Due to the presence of minor contaminants that were difficult to remove by chromatography or recrystallization, the slightly crude product was used directly in the next reaction before further purification and characterization. **^{1}H NMR** (400 MHz, $CDCl_3$, δ): 8.95 (d, J = 1.6 Hz, 1 H), 8.71 (d, J = 0.8, 4.8 Hz, 1 H), 8.35 (d, J = 6.8 Hz, 1 H), 8.30 (dt, J = 1.6, 7.6 Hz, 1 H), 8.10 (d, J = 2.4 Hz, 1 H), 7.87 (dd, J = 2.4, 6.8 Hz, 1 H), 7.44 (dd, J = 5.2, 8.0 Hz, 1 H), 3.97 (s, 3 H); **HRMS** (ESI) m/z 231.0761 [calculated for $C_{12}H_{11}N_2O_3$ $(M + H)^+$ 231.0765].

Methyl 2-(Pyridin-3-yl)pyridine-4-carboxylate



4-Methoxycarbonyl-2-(pyridin-3-yl)pyridine *N*-oxide (75 mg, 0.33 mmoles) was dissolved in dry $CHCl_3$ (3.3 mL), and PCl_3 (68 μL, 0.78 mmoles) was added. The reaction mixture was stirred at 60 °C until the starting material was consumed completely, as judged by TLC. The reaction was quenched by the dropwise addition of saturated aqueous Na_2CO_3 (5 mL) while stirring on ice. The product was extracted with DCM (4 × 5 mL), and the combined organics were dried over Na_2SO_4(s) and concentrated under reduced pressure. The crude product was purified by chromatography on silica (60% v/v acetone in hexanes) to afford the title compound (40 mg, 31% over 2 steps) as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$, δ): 9.27 (d, J = 1.6 Hz, 1 H), 8.87 (dd, J = 0.8, 4.8 Hz, 1 H), 8.69 (dd, J = 1.2, 4.8 Hz, 1 H), 8.36 (ddd, J = 2.0, 2.4, 8.0 Hz, 1 H), 8.31 (dd, J = 0.8, 1.2 Hz, 1 H), 7.83 (dd, J = 1.6, 5.2 Hz, 1 H), 7.43 (ddd, J = 0.4, 4.8, 8.0 Hz, 1 H), 4.00 (s, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$, δ): 165.4, 155.9, 150.8, 150.4, 148.3, 138.4, 134.3, 134.0, 123.6, 121.9, 119.7, 52.8; **HRMS** (ESI) m/z 205.0815 [calculated for $C_{12}H_{11}N_2O_2$ $(M + H)^+$ 215.0816].

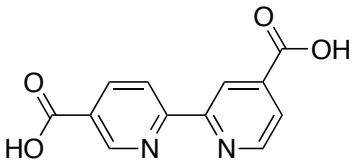
2-(Pyridin-3-yl)pyridine-4-carboxylic Acid



To a vial was added methyl 2-(pyridin-3-yl)pyridine-4-carboxylate (32 mg, 0.15 mmoles) and KOH (38 mg, 0.6 mmoles). MeOH (1.5 mL) was added to the vial and the reaction mixture was heated to 60 °C until the starting material was consumed completely, as judged by TLC. The reaction mixture was cooled and concentrated under reduced pressure, and the crude product was dissolved in water (2 mL). The aqueous layer was washed with EtOAc (1 × 1 mL), and the product was precipitated from the aqueous layer by adjusting to pH 3–4 with 1 M HCl. After cooling to 4°C, the product was removed by filtration, washed with water (2 × 1 mL), and dried in vacuo to afford the title compound (24 mg, 82%) as a white solid. **^{1}H NMR** (500 MHz, DMSO-d_6, δ): 13.71 (bs, 1 H), 9.17 (d, J = 2.5 Hz, 1 H), 8.77 (dd, J = 0.5, 5.0 Hz, 1 H), 8.54 (dd, J = 1.5, 5.0 Hz, 1 H), 8.36 (ddd, J = 1.5, 3.5, 8.0 Hz, 1 H), 8.24 (s, 1 H), 7.71 (dd, J = 1.5, 5.0

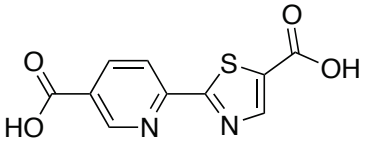
Hz, 1 H), 7.41 (ddd, J = 0.5, 4.5, 8.0 Hz, 1 H); **^{13}C NMR** (125 MHz, DMSO-d_6, δ): 166.5, 155.4, 151.4, 150.7, 148.3, 140.0, 134.7, 133.8, 124.3, 122.6, 119.9; **HRMS** (EI) *m*/*z* 200.0580 [calculated for $C_{11}H_8N_2O_2$ $(M)^+$ 200.0581].

Bipy45′DC



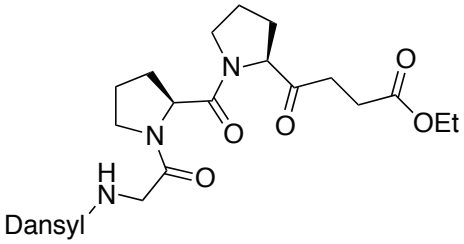
Bipy45′DC was synthesized in 4 steps as described previously,[1] with matching spectral data and yields for all synthetic transformations.

PythiDC



PythiDC was synthesized in 2 steps as described previously,[2] with matching spectral data and yields for all synthetic transformations.

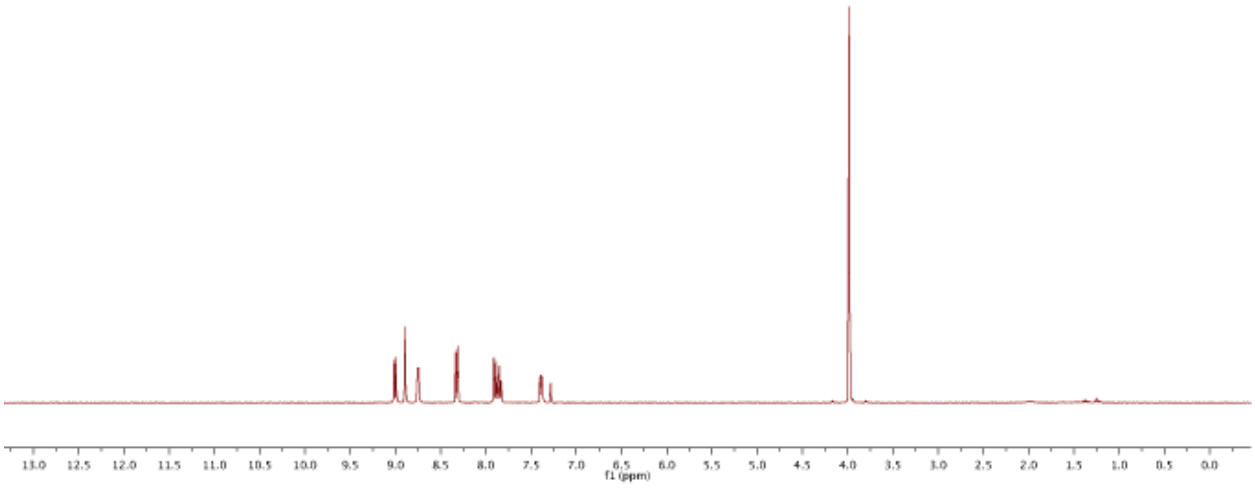
N-Dansylglycyl-(2S)-prolyl-(2S)-prolylglycine Ethyl Ester (DansylGlyProProGlyOEt)



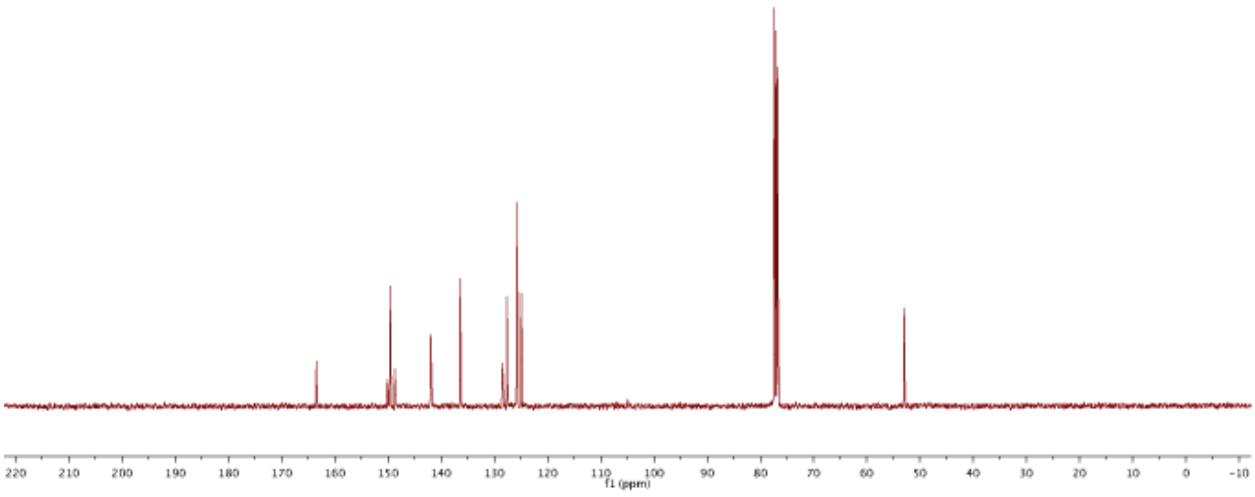
DansylGlyProProGlyOEt was synthesized as described previously.[1] The spectral data and yield matched those reported previously.

NMR Spectra

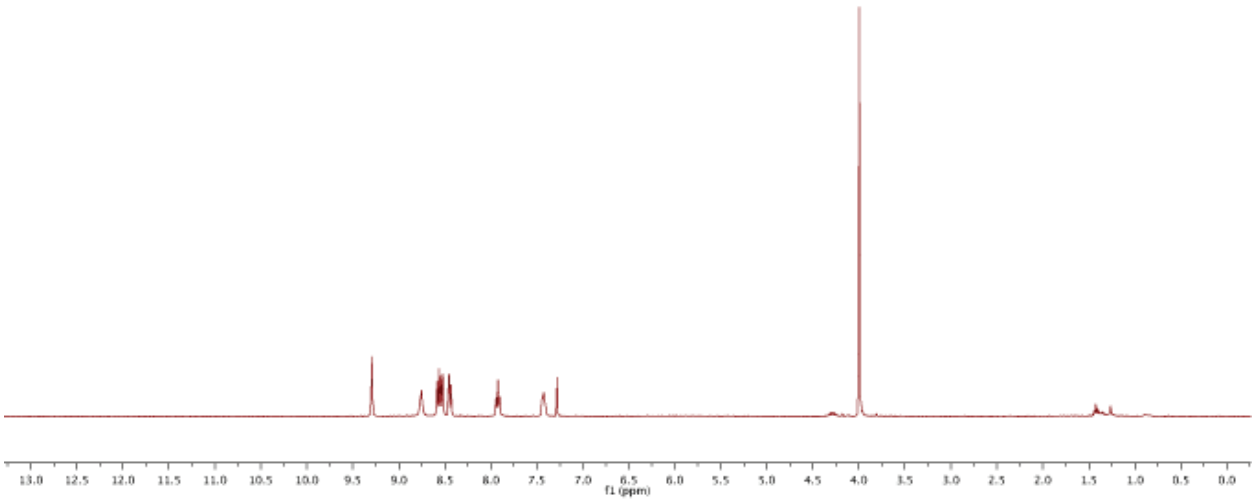
400 MHz ^{1}H NMR Spectrum of 5-Methoxycarbonyl-2-(pyridin-2-yl)pyridine N-oxide in $CDCl_3$



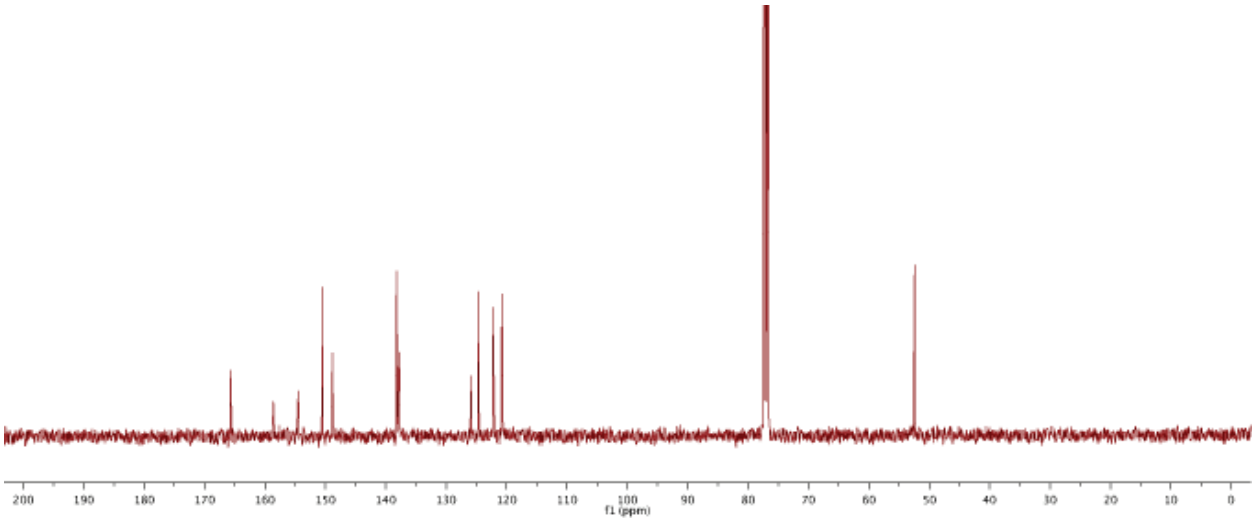
100 MHz ^{13}C NMR Spectrum of 5-Methoxycarbonyl-2-(pyridin-2-yl)pyridine N-oxide in $CDCl_3$



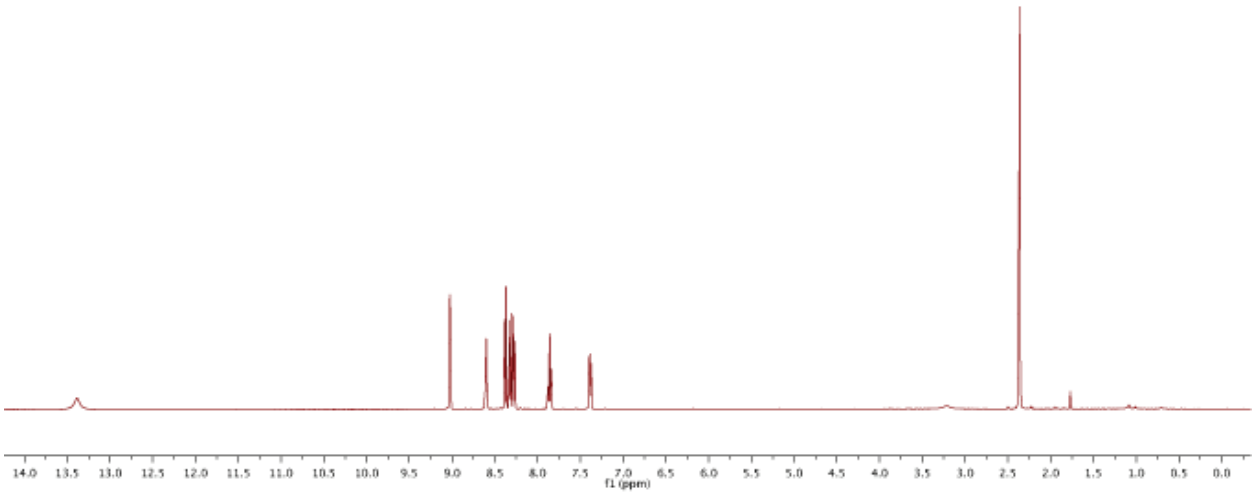
400 MHz ^{1}H NMR Spectrum of Methyl Bipy5C in $CDCl_3$



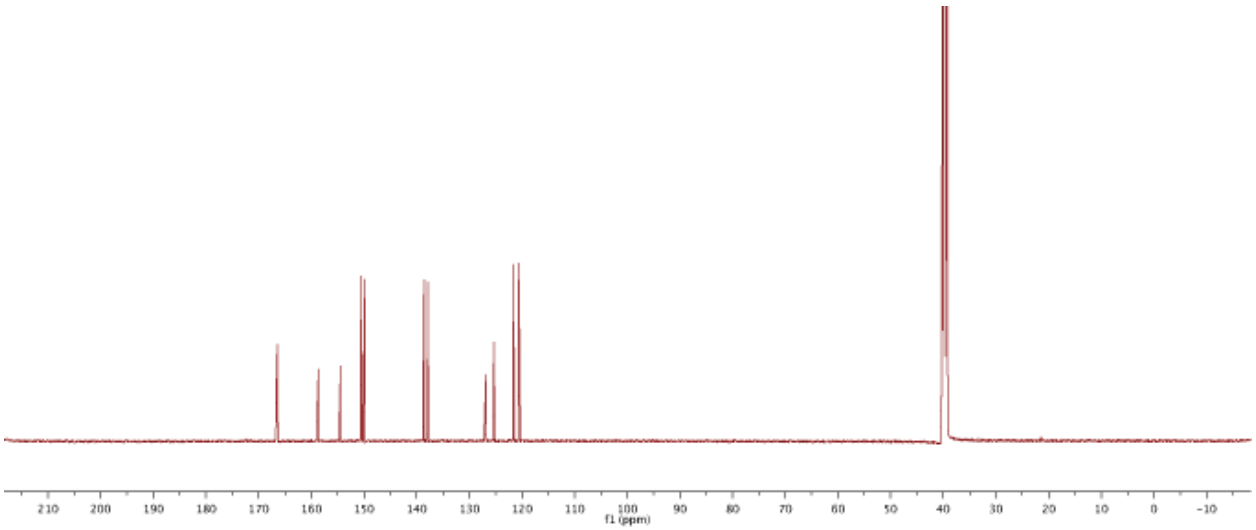
100 MHz ^{13}C NMR Spectrum of Methyl Bipy5C in $CDCl_3$



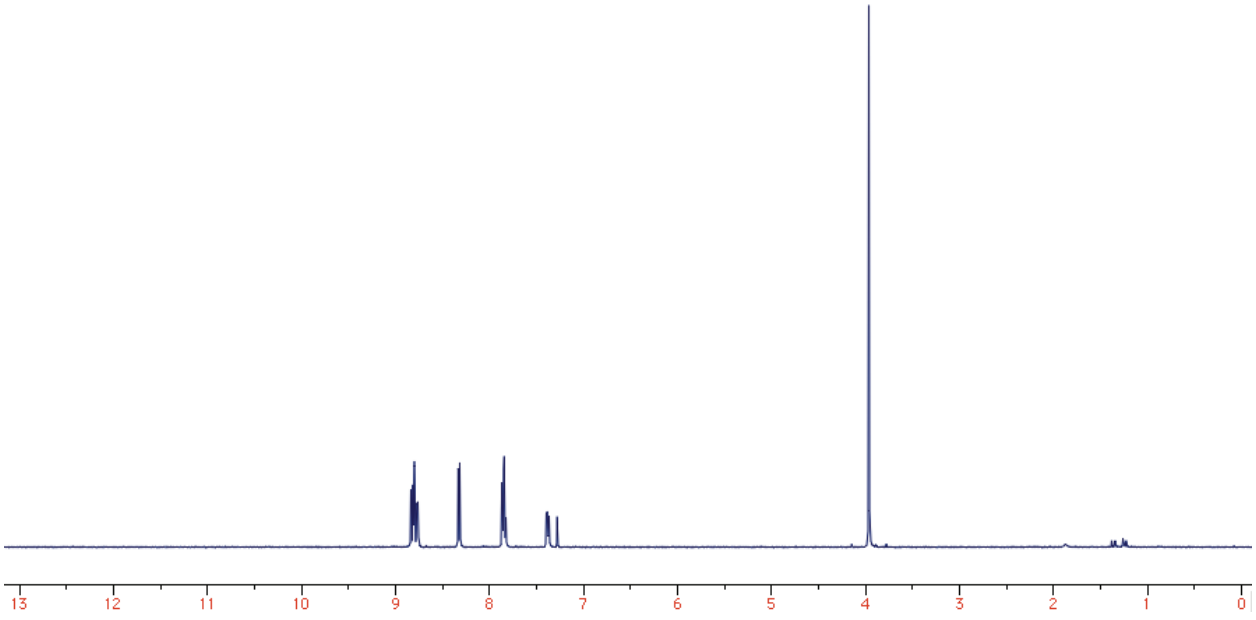
400 MHz ^{1}H NMR Spectrum of Bipy5C in DMSO-d_6



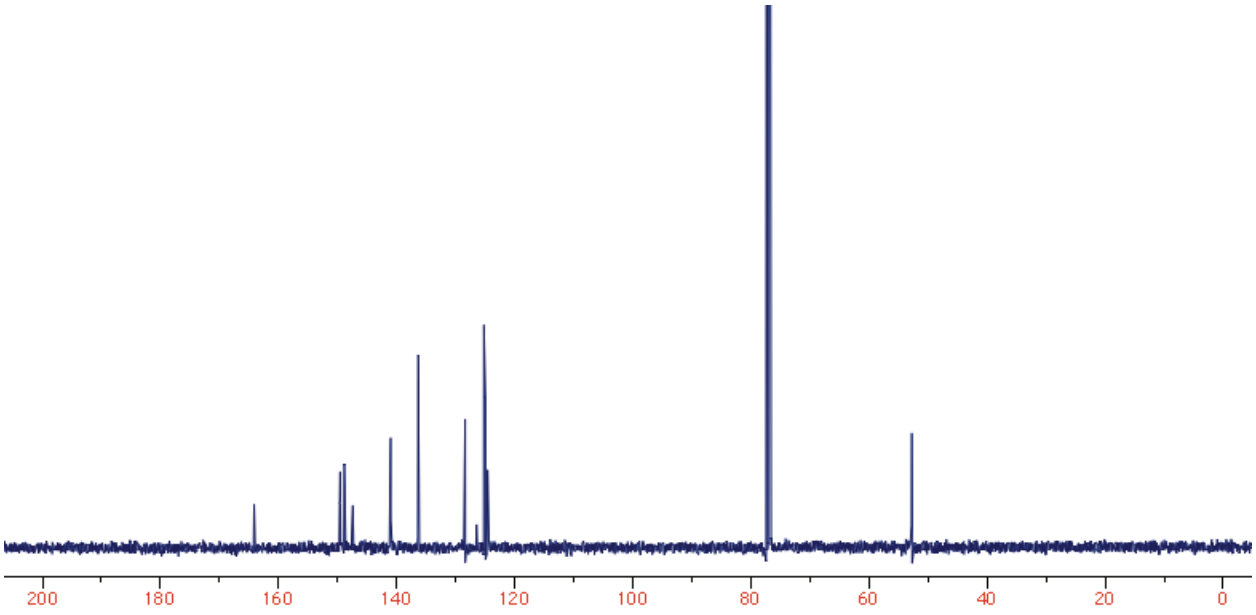
100 MHz ^{13}C NMR Spectrum of Bipy5C in DMSO-d_6



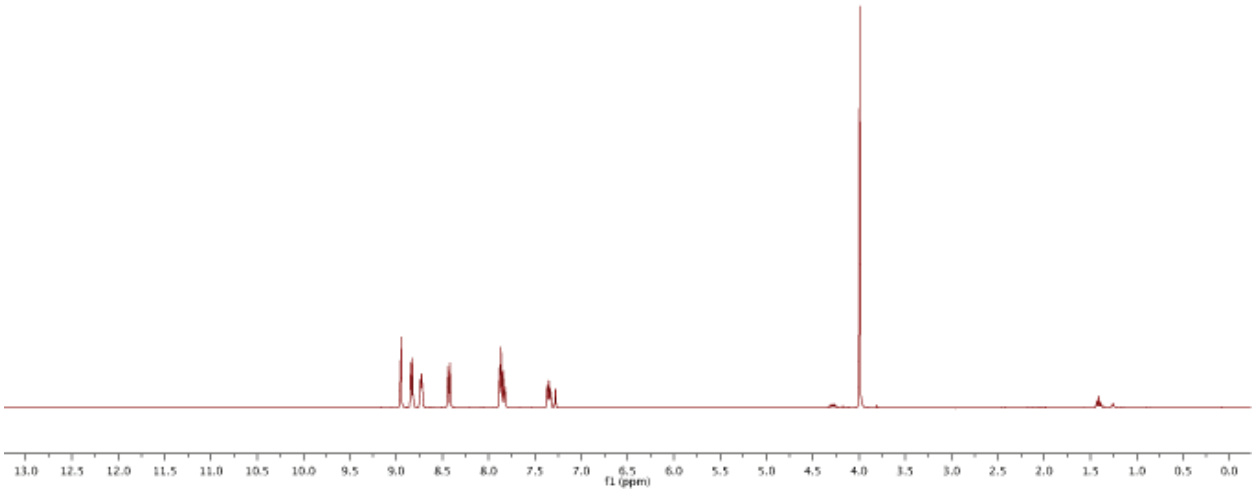
400 MHz ^{1}H NMR Spectrum of 4-Methoxycarbonyl-2-(pyridin-2-yl)pyridine N-Oxide in $CDCl_3$



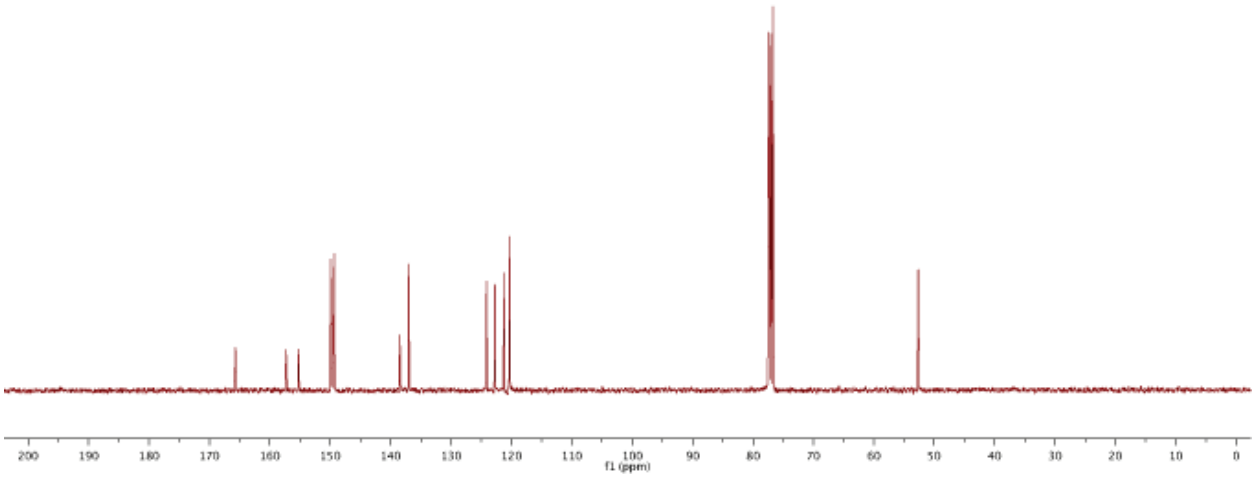
100 MHz ^{13}C NMR Spectrum of 4-Methoxycarbonyl-2-(pyridin-2-yl)pyridine N-Oxide in $CDCl_3$



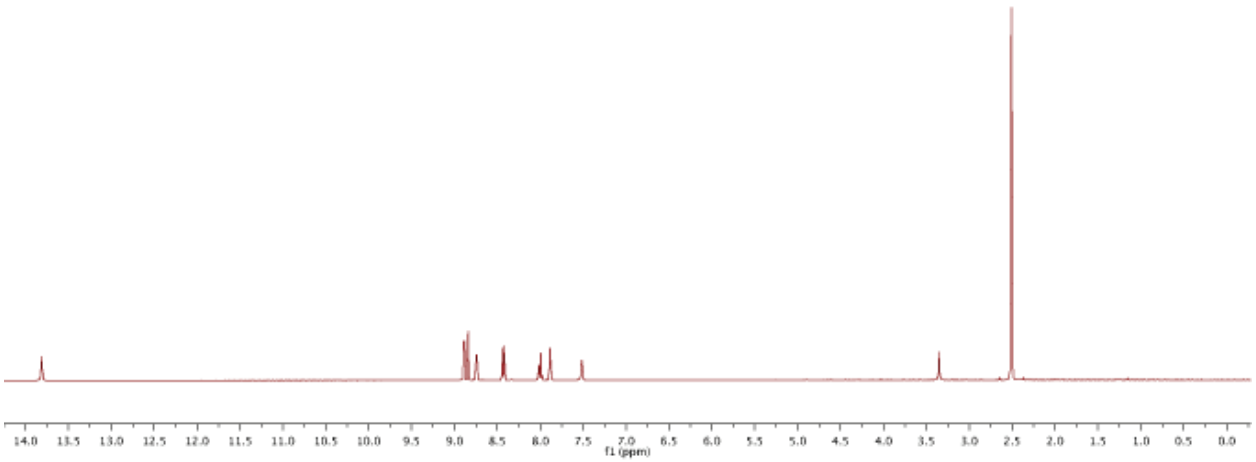
400 MHz ^{1}H NMR Spectrum of Methyl Bipy4C in $CDCl_3$



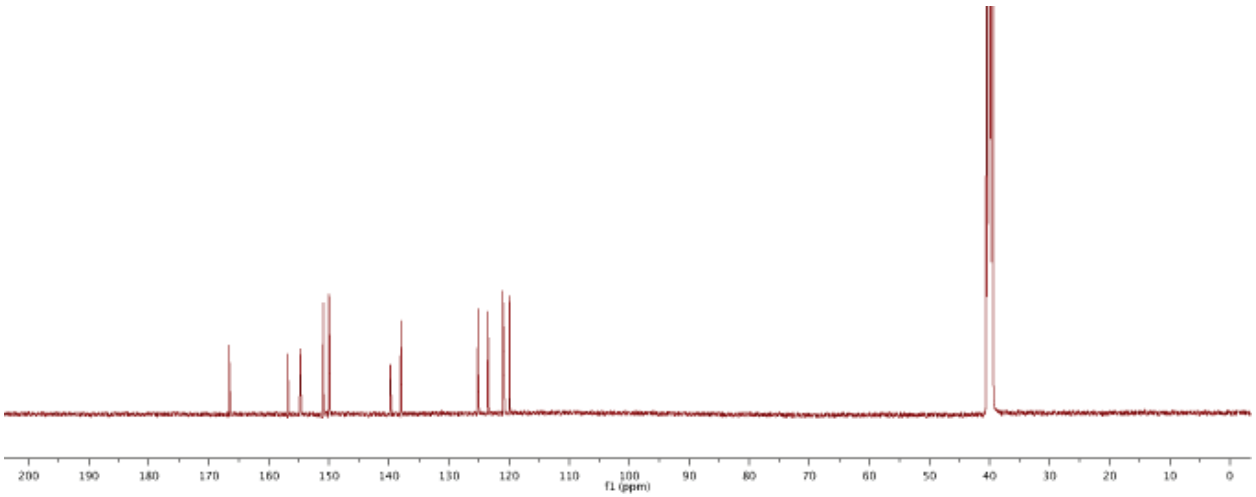
100 MHz ^{13}C NMR Spectrum of Methyl Bipy4C in $CDCl_3$



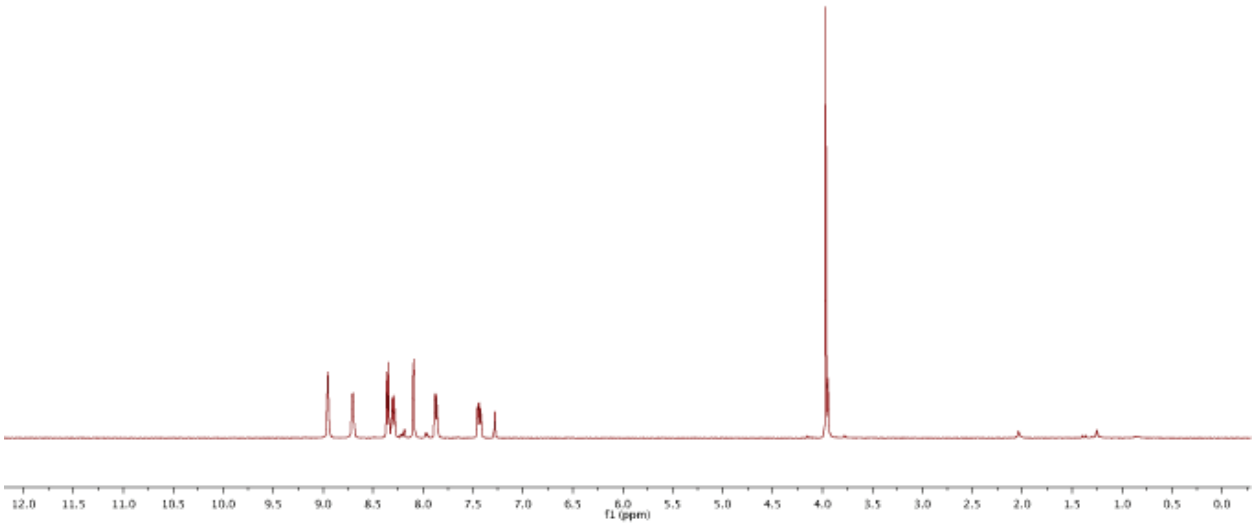
400 MHz ^{1}H NMR Spectrum of Bipy4C in DMSO-d_6



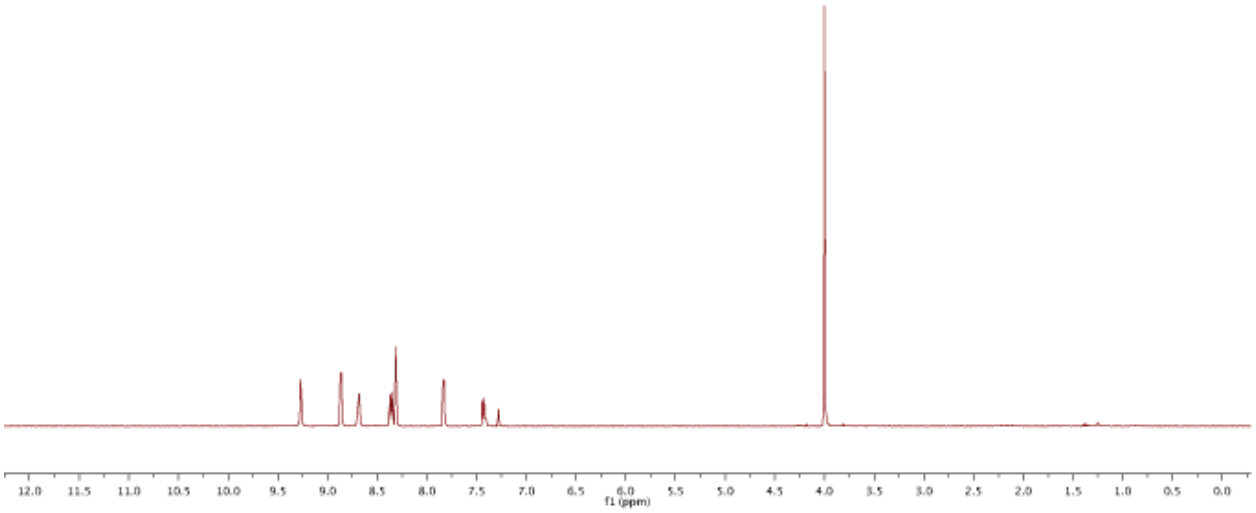
100 MHz ^{13}C NMR Spectrum of Bipy4C in DMSO-d_6



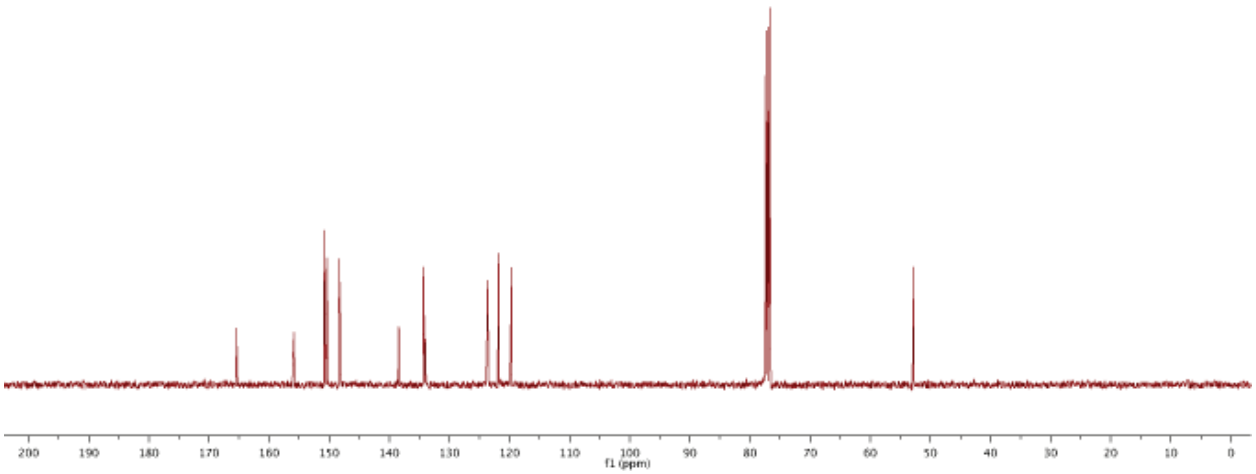
400 MHz ^{1}H NMR Spectrum of Methyl 2-(pyridin-3-yl)pyridine-4-carboxylate N-Oxide (Impure) in $CDCl_3$



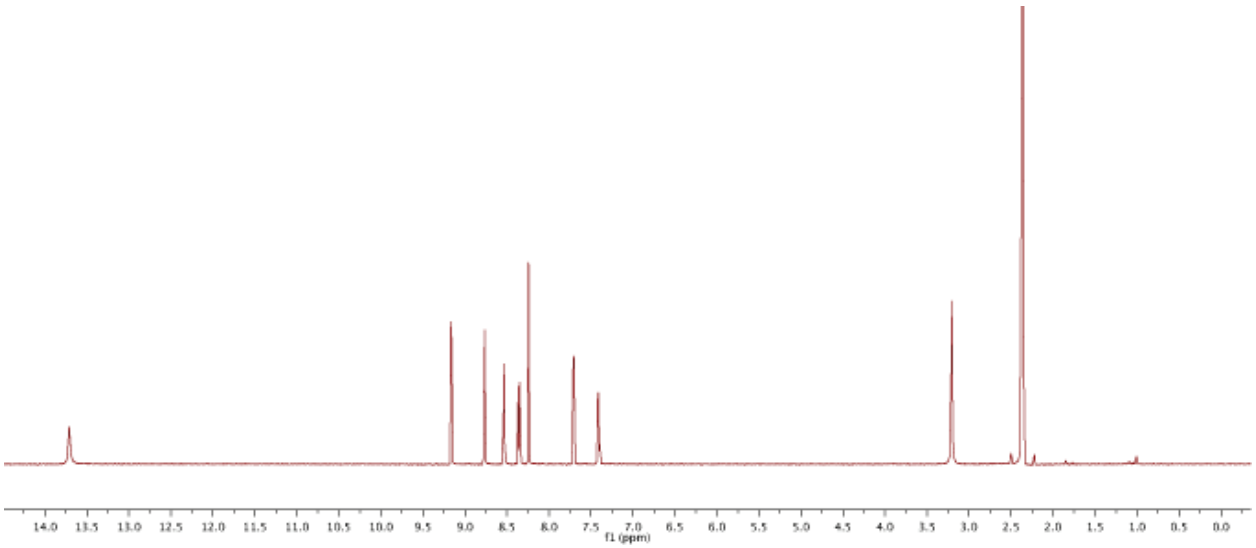
400 MHz ^{1}H NMR Spectrum of Methyl 2-(pyridin-3-yl)pyridine-4-carboxylate in $CDCl_3$



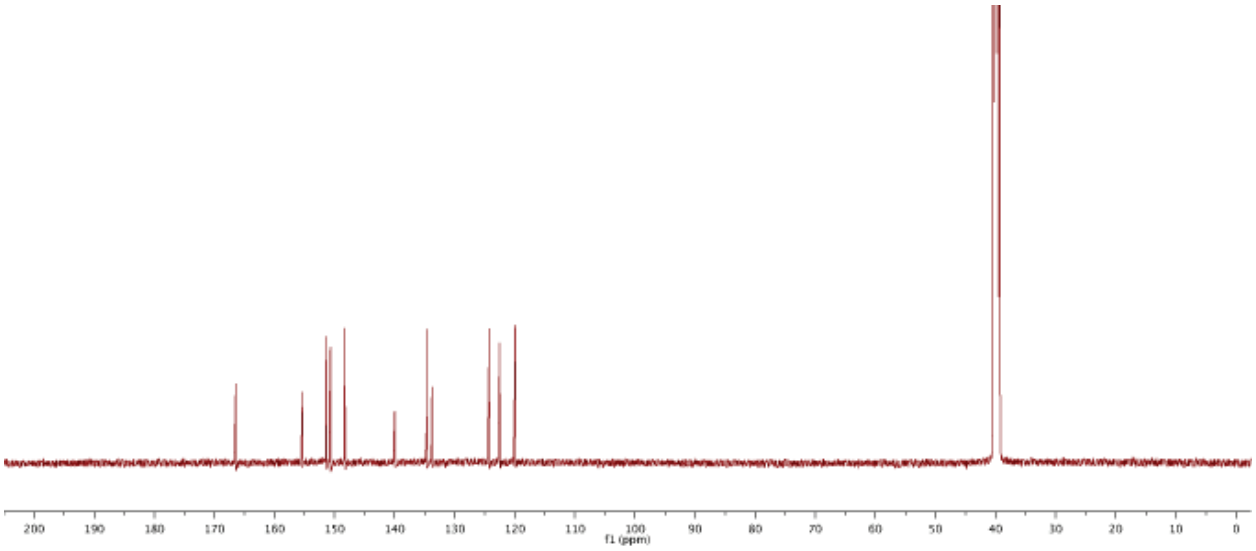
100 MHz ^{13}C NMR Spectrum of Methyl 2-(pyridin-3-yl)pyridine-4-carboxylate in $CDCl_3$



500 MHz ^{1}H NMR Spectrum of 2-(Pyridin-3-yl)pyridine-4-carboxylic Acid in DMSO-d_6

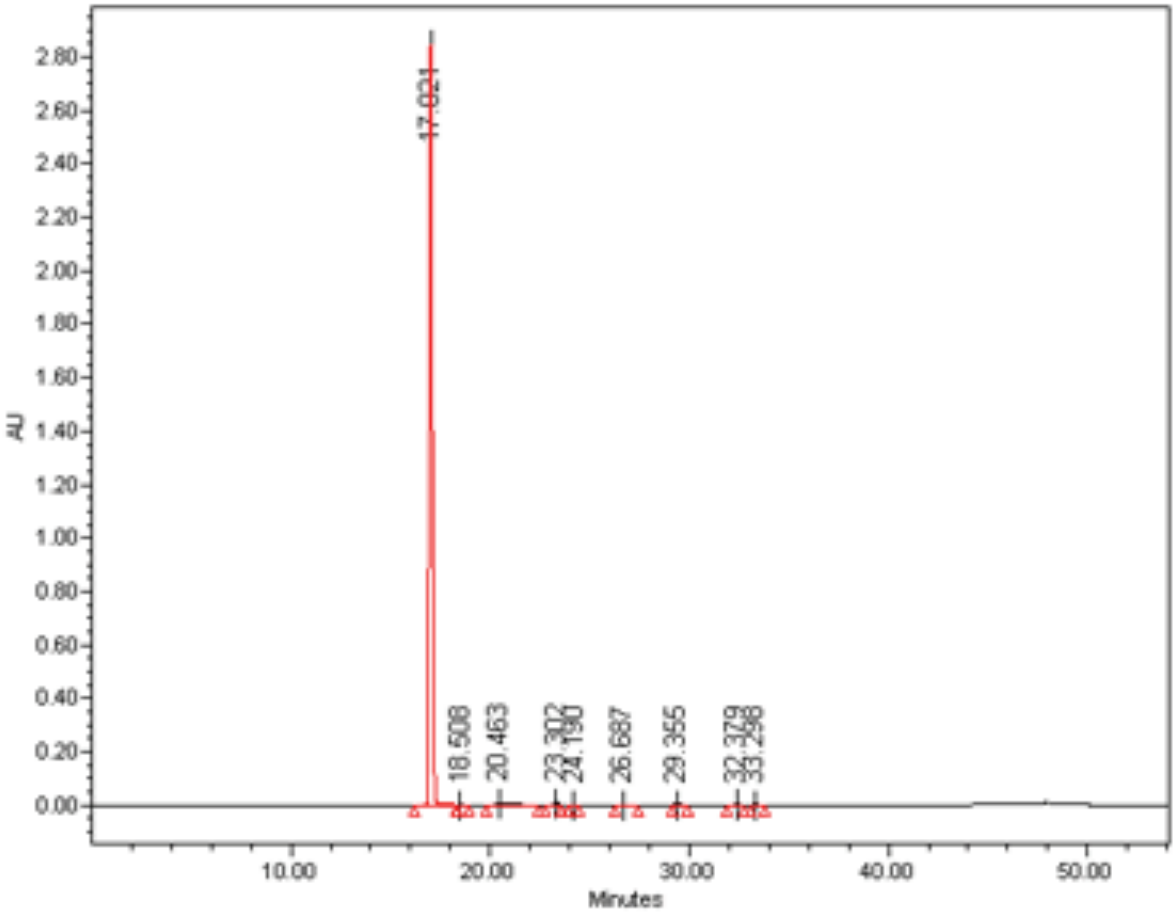


125 MHz ^{13}C NMR Spectrum of 2-(Pyridin-3-yl)pyridine-4-carboxylic Acid in DMSO-d_6



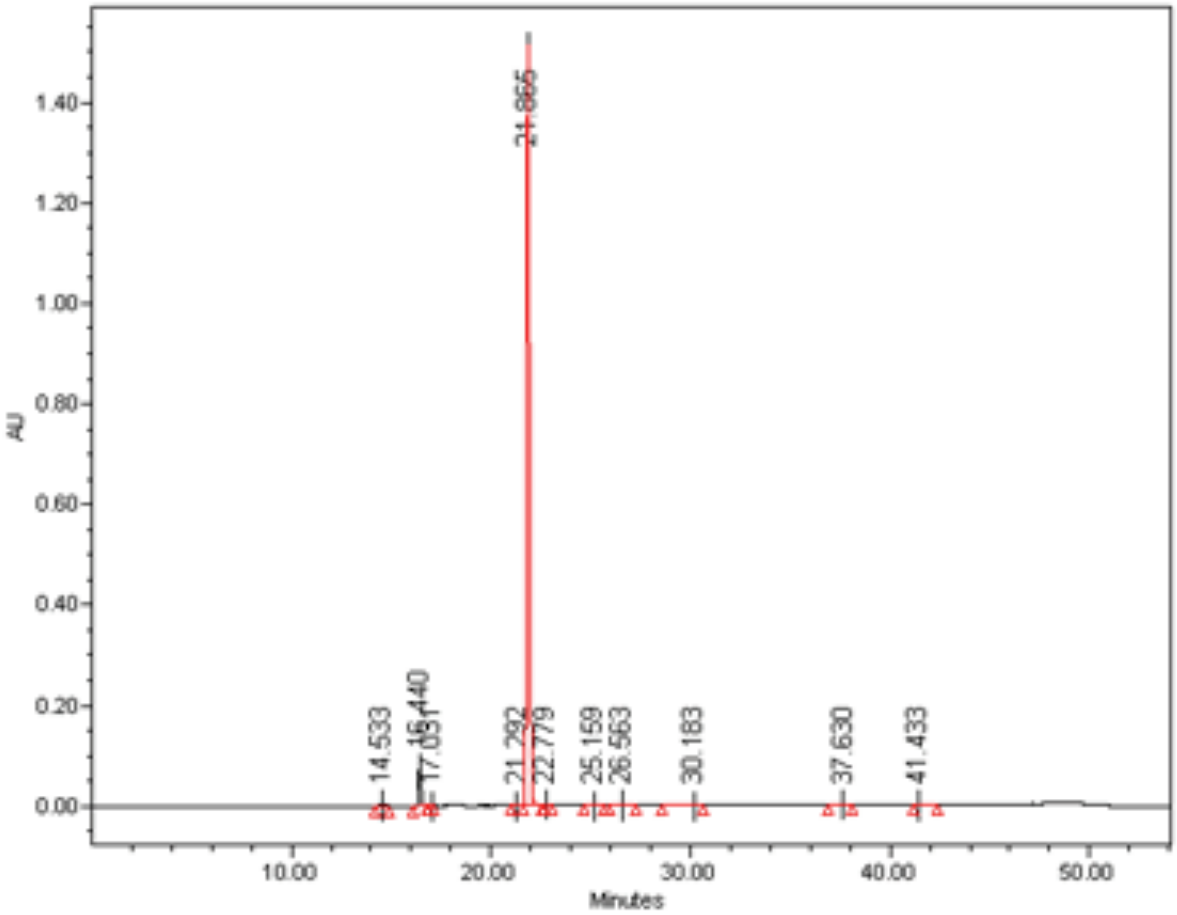
HPLC Chromatograms of Final Compounds

Bipy5C



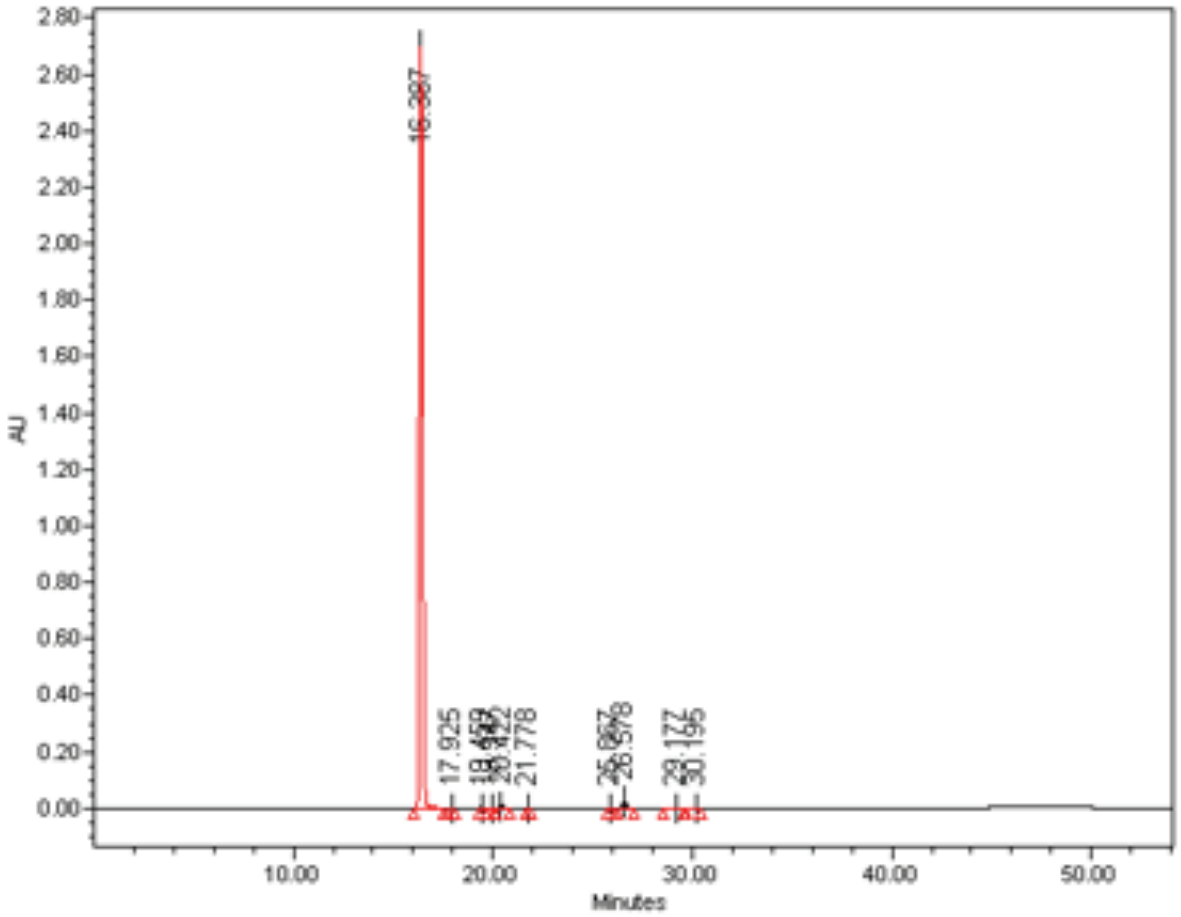
Peak	Retention Time (min)	Area (μV·s)	% Area	Height (μV)
1	17.021	32559287	98.87	2850687
2	18.508	9619	0.03	1072
3	20.463	151551	0.46	8172
4	23.302	93059	0.28	8529
5	24.190	3841	0.01	326
6	26.687	7768	0.02	411
7	29.355	36489	0.11	2674
8	32.379	36045	0.11	2964
9	33.298	32264	0.1	2651

Methyl Bipy4C



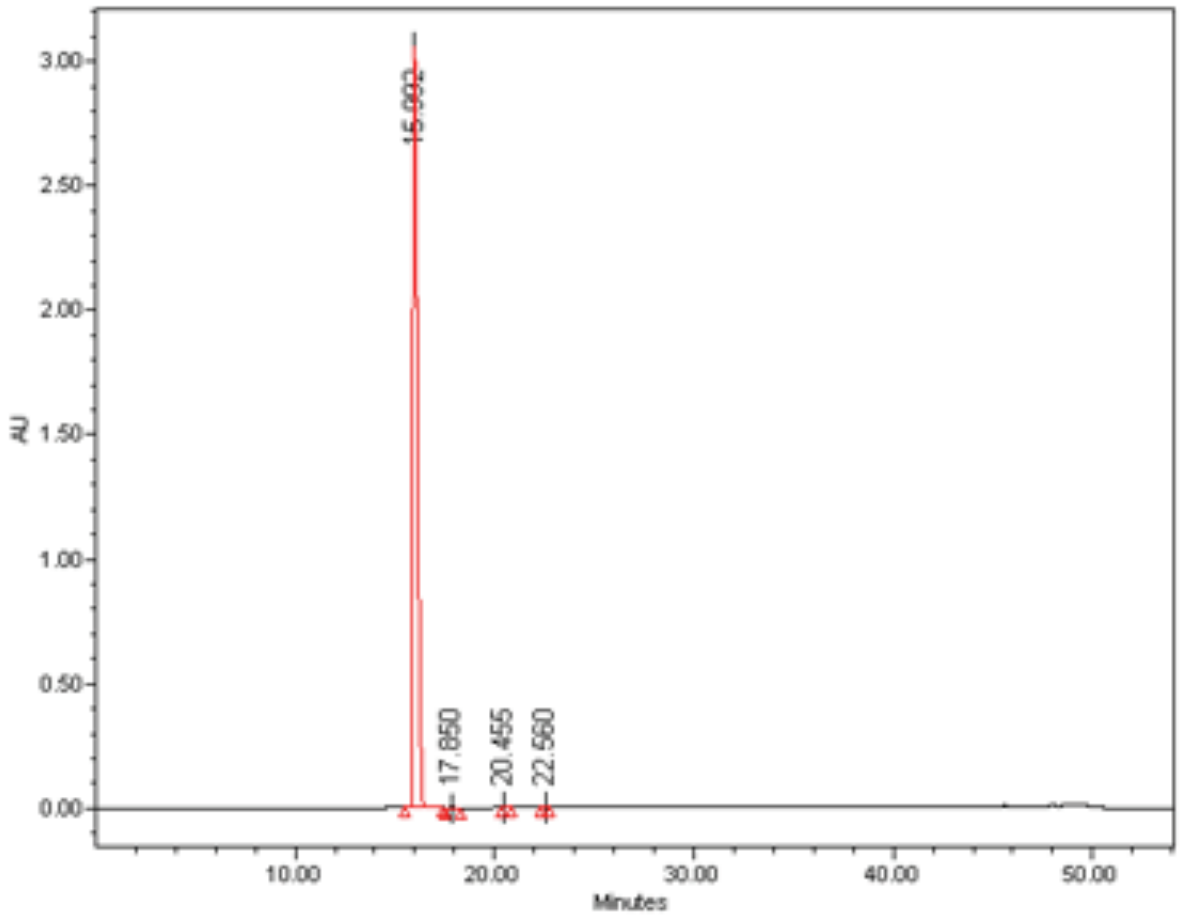
Peak	Retention Time (min)	Area (μV·s)	% Area	Height (μV)
1	14.533	20406	0.13	1513
2	16.440	669538	4.13	73884
3	17.031	3629	0.02	452
4	21.292	9134	0.06	756
5	21.865	15358256	94.83	1515017
6	22.779	19097	0.12	1990
7	25.159	7390	0.05	480
8	26.563	17757	0.11	1287
9	30.183	19086	0.12	645
10	37.630	43906	0.27	2643
11	41.433	28014	0.17	1711

Bipy4C



Peak	Retention Time (min)	Area (μV·s)	% Area	Height (μV)
1	16.387	31238247	98.64	2709775
2	17.925	2791	0.01	291
3	19.459	12298	0.04	1313
4	19.947	3913	0.01	370
5	20.422	88915	0.28	8275
6	21.778	5577	0.02	617
7	25.867	4108	0.01	475
8	26.578	290303	0.92	25471
9	29.177	10734	0.03	644
10	30.195	10885	0.03	838

*Bipy4C**



Peak	Retention Time (min)	Area (μV·s)	% Area	Height (μV)
1	15.992	48280156	99.87	3059525
2	17.850	5530	0.01	493
3	20.455	25817	0.05	2505
4	22.560	29168	0.06	2451

References

(1) Vasta, J. D., and Raines, R. T. (2015) Selective inhibition of prolyl 4-hydroxylases by bipyridinedicarboxylates, *Bioorg. Med. Chem. 23*, 3081–3090.

(2) Vasta, J. D., Andersen, K. A., Deck, K. M., Nizzi, C. P., Eisenstein, R. S., and Raines, R. T. (2016) Selective inhibition of collagen prolyl 4-hydroxylase in human cells, *ACS Chem. Biol. 11*, 193–199.