Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supplementary Information

Regioselective C2-Arylation of Imidazo[4,5-*b*]pyridines.

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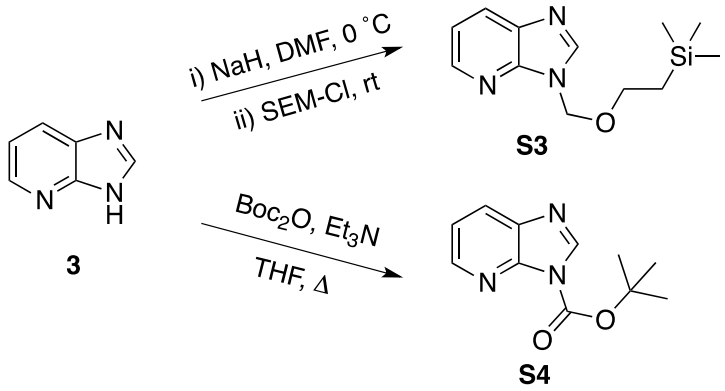
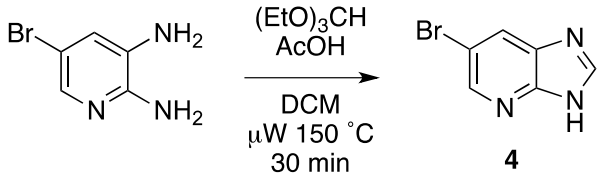
1. Synthetic Schemes to Intermediates

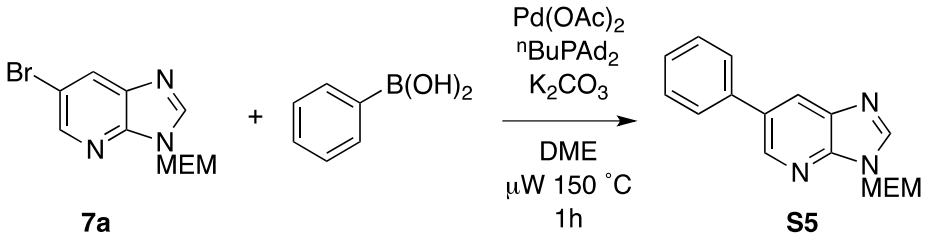
Scheme S1. Synthesis of *N3*-methylimidazo[4,5-*b*]pyridine, **S2**.



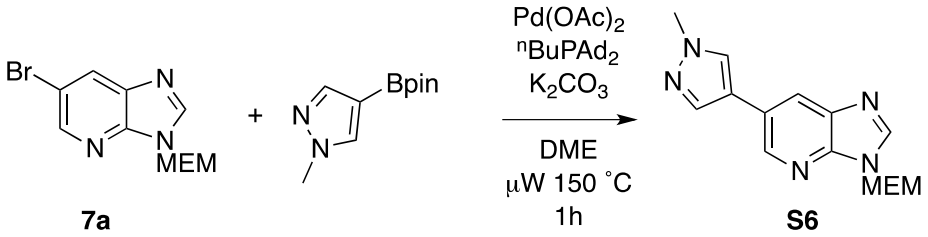
Scheme S2. Synthesis of *N3*-SEM and Boc protected imidazo[4,5-b]pyridines.



Scheme S3. Synthesis of 6-bromoimidazo[4,5-*b*]pyridine **4**.

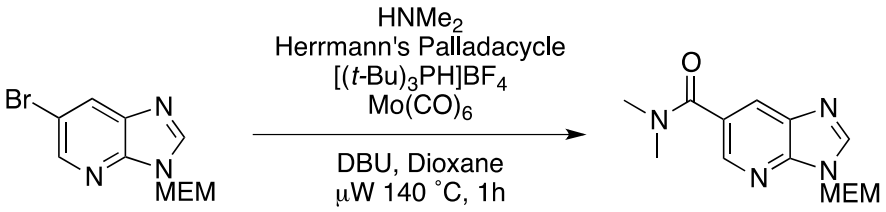


Scheme S4. Suzuki cross-coupling to 3-((2-methoxyethoxy)methyl)-6-phenyl-3H-imidazo[4,5-*b*]pyridine, **S5**.



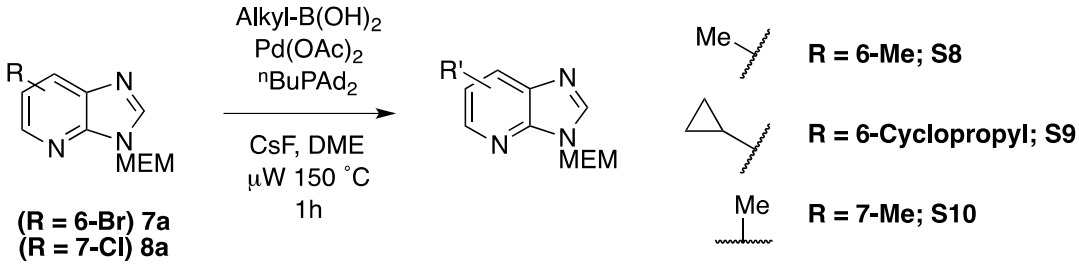
7a **S6**

Scheme S5. Suzuki cross-coupling to 3-((2-methoxyethoxy)methyl)-6-(1-methyl-1H-pyrazol-4-yl)-3H-imidazo[4,5-*b*]pyridine, **S6**.



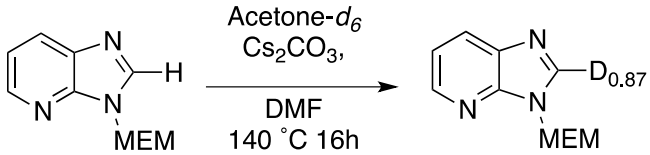
7a **S7**

Scheme S6. Aminocarbonylation protocol affording 3-((2-methoxyethoxy)methyl)-*N*,*N*-dimethyl-3*H*-imidazo[4,5-*b*]pyridine-6-carboxamide, **S7**.[1]



(R = 6-Br) 7a
(R = 7-Cl) 8a

Scheme S7. Preparation of alkyl-substituted *N3*-MEM-imidazo[4,5-*b*]pyridines, **S8-S10**.

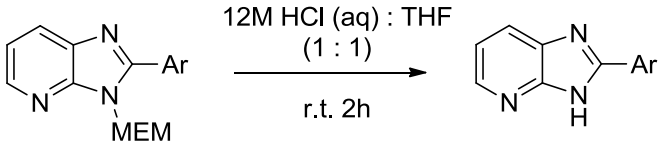


Scheme S8: Investigating the reaction mechanism; C2-deprotonation under C-H arylation conditions.

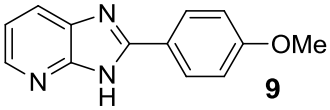
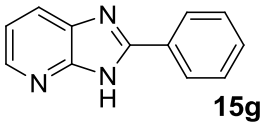
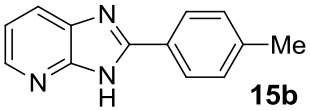
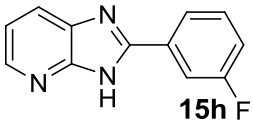
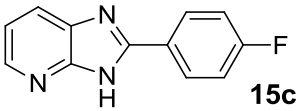
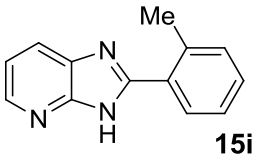
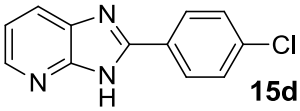
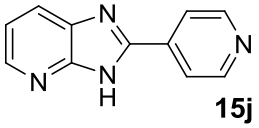
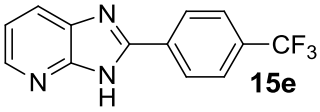
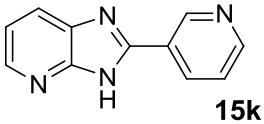
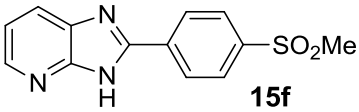
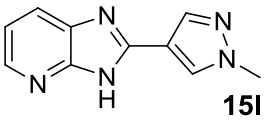
[1] (a) Appukkuttan, P.; Axelsson, L.; der Eycken, E. V.; Larhed, M. *Tet. Lett.* **2008**, *49*, 5625. (b) Lagerlund, O.; Larhed, M. *J. Comb. Chem.* **2006**, *8*,4.

2. Deprotection of C-H Arylation Products

Table S1. Acid-mediated deprotection of C-H arylation products.



13a-l **9 and 15b-l**

Entry	Product	Isolated Yield	Entry	Product	Isolated Yield
1	 **9**	98%	7	 **15g**	81%
2	 **15b**	86%	8	 **15h**	90%
3	 **15c**	98%	9	 **15i**	76%
4	 **15d**	50%	10	 **15j**	46%
5	 **15e**	53%	11	 **15k**	38%
6	 **15f**	67%	13	 **15l**	48%

3. Kinetic Isotope Experiment

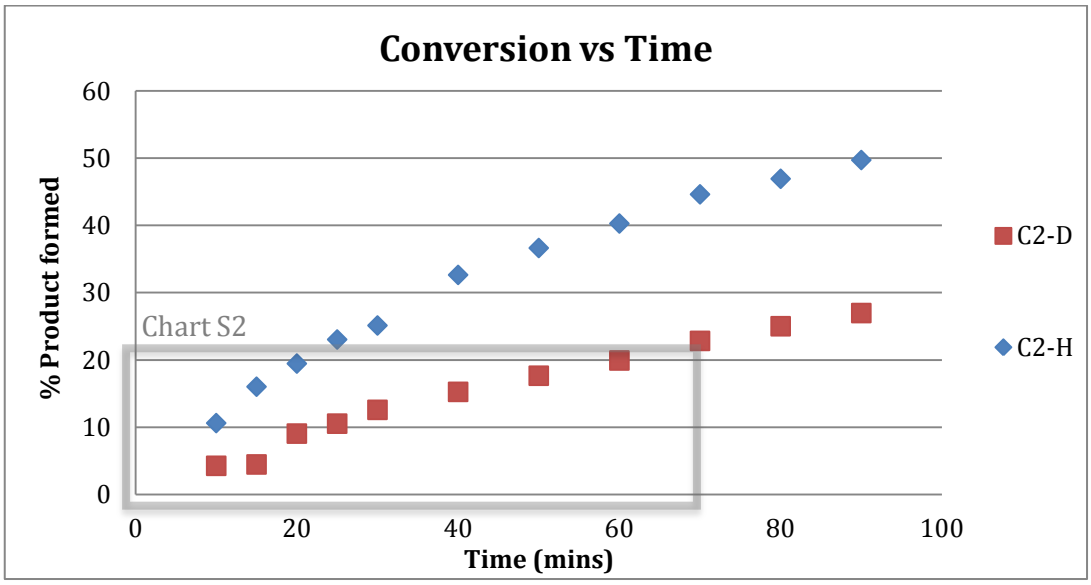


Chart S1. Chart showing conversion versus time for KIE experiments. The '% product formed' is defined as the ratio of product formed to remaining starting material, as measured by LCMS UV-Absorbance at λ254 nm.

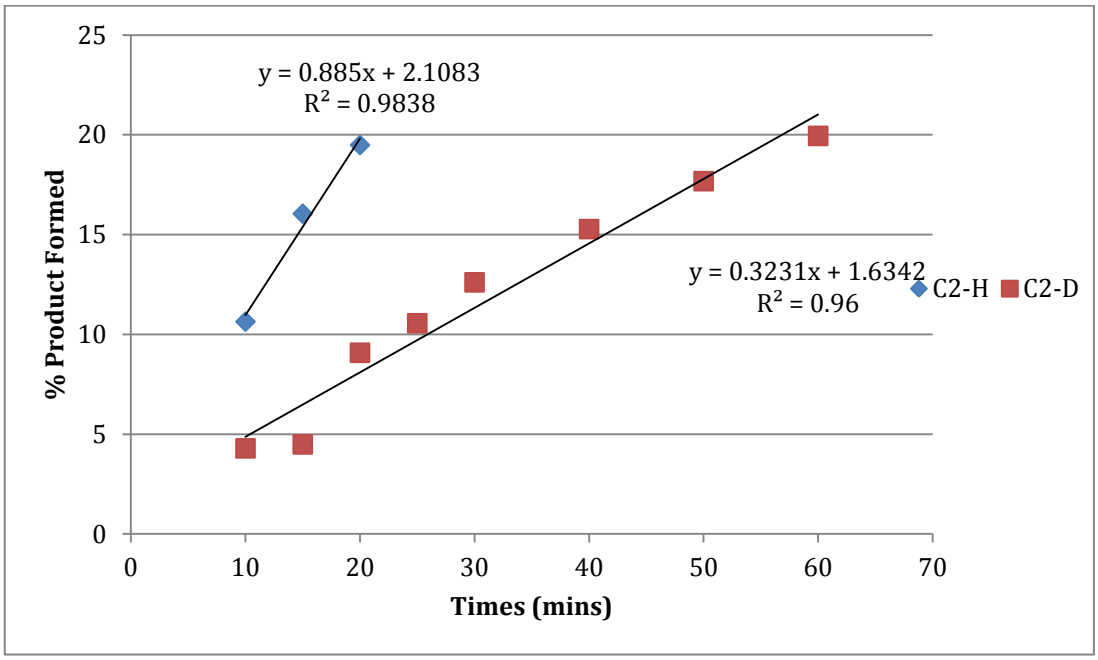


Chart S2. Initial rate corresponding to 20% conversion.

Kinetic Isotope Effect calculation: $KIE = \frac{k_H}{k_D} = \frac{0.885}{0.323} = \mathbf{2.74}$

4. Experimental for synthesis of intermediates

See main manuscript for general experimental.

***N*2-Methylpyridine-2,3-diamine, S1:** A flask containing *N*-methyl-3-nitropyridin-2-amine (2 g, 13.1 mmol) and Pd/C (10 %) (60 mg) was flushed with N_2 and DME (15 mL) added. The mixture was stirred at 40 °C and hydrazine monohydrate (1.8 mL, 40 mmol) was added drop-wise. Upon complete addition the mixture was heated to reflux for 90 minutes. Upon cooling, the mixture was filtered through a bed of celite (upper) and silica (lower). The filter bed was washed with EtOAc:Et_2O (1:1; 60 mL), the solvent mixture was removed under reduced pressure to yield the product as a purple solid (1.6 g, quant.) which was used without further purification. ^{1}H NMR: (500 MHz, $CDCl_3$) δ_H 7.81 (dd, *J* = 5.1, 1.5 Hz, 1H), 6.85 (dd, *J* = 7.4, 1.5 Hz, 1H), 6.54 (dd, *J* = 7.4, 5.1 Hz, 1H), 4.17 (s, 1H), 3.17 (s, 2H), 3.04 (d, *J* = 2.8 Hz, 3H); ^{13}C NMR: (126 MHz, $CDCl_3$) δ_C 151.2, 139.3, 128.4, 121.8, 113.2, 28.7; LCMS t_R 0.41 min, *m/z* 124 $(M+H)^+$; Purity (AUC) ≥ 95%; HRMS $(M+H)^+$ *calculated* for $C_6H_{10}N_3$ = 124.0869, *found* = 124.0959.

3-Methyl-3*H*-imidazo[4,5-*b*]pyridine, S2: To a suspension of *N*^{2}-methylpyridine-2,3-diamine, **S1** (1.16 g, 9.4 mmol) in CH_2Cl_2 (5 mL) was added triethylorthoformate (10 mL) and acetic acid (1.5 mL). The mixture was reacted under microwave irradiation at 150 °C for 30 min. The residue was purified by flash chromatography; conditions (CH_2Cl_2:EtOH:NH_3 (95:4:1) yielding the product as a brown solid (1.17g, 8.79 mmol, 93 %). Lit. m.p. 76-78;[2] Observed m.p. 74-77°C; ^{1}H NMR: (500 MHz, $CDCl_3$) δ_H 8.45 (dd, *J* = 4.8, 1.4 Hz, 1H), 8.10 (dd, *J* = 8.0, 1.4 Hz, 1H), 8.06 (s, 1H), 7.28-7.23 (m, 1H), 3.96 (s, 3H); ^{13}C NMR: (126 MHz, $CDCl_3$) δ_C 147.0, 144.0, 143.8, 134.9, 127.4, 117.6, 29.2; LCMS t_R = 0.81 mins, *m/z* = 134 $(M+H)^+$; Purity (AUC) ≥ 95%; HRMS $(M+H)^+$ *calculated* for $C_7H_8N_3$ = 134.0713, *found* = 134.0718, $(M+Na)^+$ *calculated* for $C_7H_7N_3Na$ = 156.0532, *found* = 156.0535.

[2] Y. Mizuno, M. Ikehara, T. Itoh and K. Saito, *J. Org. Chem.*, 1963, **28**, 1837-1841.

3-((2-(Trimethylsilyl)ethoxy)methyl)-3*H*-imidazo[4,5-*b*]pyridine, S3:

Imidazo[4,5-*b*]pyridine, **3** (1191 mg, 10 mmol) in DMF (100 mL) was cooled to 0 ˚C in an ice/water bath. To this was added portionwise NaH (480 mg, 12 mmol) and upon complete addition the mixture was stirred for 15 minutes. SEMCl (2.12 mL, 12 mmol) was added dropwise before stirring the mixture at room temperature for 24 h. The mixture was concentrated *in vacuo*, the residue was taken in 1:1 EtOAc:Cyclohexane (200 mL), washed with water (50 mL), sat. aq. NaCl (3 x 50 mL), dried ($MgSO_4$) and concentrated to give crude product which was purified by column chromatography (10 – 50 % EtOAc in cyclohexane) to afford a yellow oil (1.52g, 61%). ^{1}H NMR: (500 MHz, $CDCl_3$) δ_H 8.44 (dd, *J* = 1.4, 8.8 Hz, 1H), 8.21 (s, 1H), 8.10 (dd, *J* = 1.5, 8.0, 1H), 7.28 (dd, *J* = 4.8, 8.0 Hz, 1H), 5.70 (s, 2H), 3.65 – 3.61 (m, 2H), 0.95 – 0.92 (m, 2H), -0.05 (s, 9H); ^{13}C NMR: (126 MHz, $CDCl_3$) δ_C 147.1, 144.7, 144.2, 135.2, 128.1, 118.7, 72.0, 67.1, 17.7, -1.48; LCMS t_R = 2.95 mins, *m/z* = 250 $(M+H)^+$; Purity (AUC) ≥ 95%; HRMS $(M+H)^+$ *calculated* for $C_{12}H_{20}N_3OSi$ = 250.1376, *found* = 250.1367.

***tert*-Butyl 3*H*-imidazo[4,5-*b*]pyridine-3-carboxylate, S4:** To a stirred suspension of imidazo[4,5-*b*]pyridine, **3** (1191 mg, 10 mmol), Et_3N (334 µL, 2.4 mmol) and DMAP (24 mg, 0.2 mmol) in THF (10 mL) at r.t. under an N_2 atmosphere, was added Boc_2O (2M in THF) (1.1 mL, 2.2 mmol). The mixture was heated to 65 °C for 1 hour. Upon cooling the mixture was concentrated *in vacuo* and purified by flash column chromatography (20-40% EtOAc in cyclohexane) to yield a white solid (951 mg, 43%). Observed m.p. = 90 – 92 ˚C; ^{1}H NMR: (500 MHz, $CDCl_3$) δ_H 8.67 (s, 1H), 8.62 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.29 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.35 (dd, *J* = 8.1, 4.8 Hz, 1H), 1.72 (s, 9H); ^{13}C NMR: (126 MHz, $CDCl_3$) δ_C 156.5, 147.4, 146.5, 144.1, 124.2, 122.6, 120.2, 85.6, 28.0; LCMS t_R = 2.54 mins, *m/z* = 164 (loss of *t*-Bu, $M+H^+$); Purity (AUC) ≥ 95%; HRMS $(M+H)^+$ *calculated* for $C_{11}H_{14}N_3O_2$ = 220.1081, *found* = 220.1077, also 164.0626 (loss of *tert*-butyl).

6-Bromo-3*H*-imidazo[4,5-*b*]pyridine, 4: A solution of 5-bromopyridine-2,3-diamine (500 mg, 2.66 mmol), triethylorthoformate (5 mL), acetic acid (0.75 mL) and CH_2Cl_2 (2.5 mL) was irradiated in a μW at 150 °C for 30 mins. The solvents were removed under reduced pressure and the residue was purified by Biotage SP1 (50 g SNAP column, 40 mL/min, 3 CV Cyclohexane, 9 CV 0-10 % MeOH in CH_2Cl_2). The product was obtained as a cream solid (358 mg, 69 %). Lit. m.p.[3] 227-229; Observed m.p. 229-231˚C; ^{1}H NMR (CD_3OD, 500MHz) δ_H 8.48 (d, *J* = 2.1 Hz, 1H), 8.42 (s, 1H), 8.23 (d, *J* = 2.1 Hz, 1H); ^{13}C NMR (CD_3OD, 126 MHz) δ_C 149.6, 145.0, 144.9, 126.0, 113.5, one q C does not appear; LCMS t_R 1.74 min, *m/z* 197, 199 $(M+H)^+$ bromine isotopic pattern; Purity (AUC) ≥ 95%; HRMS $(M+H)^+$ *calculated* for $C_6H_5N_3Br$ = 197.9661, *found* = 197.9670; CHN Microanalysis *calculated* for $C_6H_4BrN_3$ = C, 36.39; H, 2.04; N, 21.22%, *observed* = C, 36.33; H, 2.06; N, 21.16%.

3-((2-Methoxyethoxy)methyl)-6-phenyl-3*H*-imidazo[4,5-*b*]pyridine, S5: 6-Bromo-3-((2-methoxyethoxy)methyl)-3*H*-imidazo[4,5-*b*]pyridine, **7a** (589 mg, 2.0 mmol), phenyl boronic acid (488mg, 4.0 mmol), K_2CO_3 (4.0 ml, 1 M, 4.0 mmol), $Pd(OAc)_2$ (18 mg, 4 mol%) and $nBuPAd_2$ (57 mg, 8 mol%) were dissolved in DME (5.0 ml) and heated in a microwave reactor at 150 °C for 1 h. The mixture was diluted with ethyl acetate (100 mL) and washed with H_2O. The crude mixture was concentrated *in vacuo* and purified on Biotage SP1 (12g SINGLE StEP column, 15 mL/min, 3 CV CH_2Cl_2 then 12 CV 0-100% (5% MeOH in CH_2Cl_2)) to afford product as an orange oil (521 mg, 92%). ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.66 (d, *J* = 1.9 Hz, 1H), 8.28 (s, 1H), 8.27 (d, *J* = 1.9 Hz, 1H), 7.65 - 7.61 (m, 2H), 7.53 – 7.47 (m, 2H), 7.44 – 7.38 (m, 1H), 5.80 (s, 2H), 3.78 – 3.73 (m, 2H), 3.56 – 3.51 (m, 2H), 3.36 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C 146.6, 144.9, 144.2, 138.6, 135.3, 133.0, 129.1, 127.6, 127.5 126.5, 73.0, 71.6, 68.9, 59.1; LCMS t_R = 2.74 min, *m/z* 284 $(M+H)^+$; Purity (AUC) ≥ 95%; HRMS $(M+H)^+$ *calculated* for $C_{16}H_{18}N_3O_2$ = 284.1394, *found* = 284.1388.

[3] H. Graboyes and A. R. Day, *J. Am. Chem. Soc.*, 1957, **79**, 6421-6426.

3-((2-Methoxyethoxy)methyl)-6-(1-methyl-1*H*-pyrazol-4-yl)-3*H*-imidazo[4,5-*b*]pyridine, S6: 6-Bromo-3-((2-methoxyethoxy)methyl)-3*H*-imidazo[4,5-*b*]pyridine, **7a** (1.0M in DMF, 0.25 mL, 0.25 mmol), 1-methylpyrazole-4-boronic acid pinacol ester (78 mg, 0.375 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol) and $nBuPAd_2$ (7 mg, 0.02 mmol) were taken in 1.0 M aq. K_2CO_3 (0.5 mL, 0.5 mmol) and DME (0.75 mL), the combined reagents were irradiated in μW at 150 ˚C for 1h. The mixture was filtered through a bed of celite (top layer) and silica (bottom layer), eluting with $CHCl_3$/MeOH affording crude product which was purified on Biotage SP1 (12g SINGLE StEP column, 15 mL/min, 0 – 5% MeOH in CH_2Cl_2) to afford the product as a brown oil (62 mg, 86%). ^{1}H NMR: (500 MHz, $CDCl_3$) δ_H 8.60 (d, *J* = 2.0 Hz, 1H), 8.30 (s, 1H), 8.16 (d, *J* = 2.0 Hz, 1H), 7.83 (d, *J* = 0.9 Hz, 1H), 7.70 (d, *J* = 0.9 Hz, 1H), 5.80 (s, 2H), 4.01 (s, 3H), 3.79 – 3.73 (m, 2H), 3.57 – 3.52 (m, 2H), 3.37 (s, 3H); ^{13}C NMR: (126 MHz, $CDCl_3$) δ_C 145.7, 144.5, 143.1, 136.9, 127.1, 124.9, 124.5, 120.3, 73.1, 71.6, 69.0, 59.1, 39.2; LCMS t_R = 2.06 mins, *m/z* = 288 $(M+H)^+$; Purity (AUC) ≥ 95%; HRMS $(M+H)^+$ *calculated* for $C_{14}H_{18}N_5O_2$ = 288.1455, *found* = 288.1459.

3-((2-Methoxyethoxy)methyl)-*N*,*N*-dimethyl-3*H*-imidazo[4,5-*b*]pyridine-6-carboxamide, S7: 6-Bromo-3-((2-methoxyethoxy)methyl)-3*H*-imidazo[4,5-*b*]pyridine, **7a** (1.0M in DMF, 0.25 mL, 0.25 mmol), dimethylamine (2.0M in THF, 625 μL, 1.25 mmol), Herrmann's Palladacycle (6 mg, 0.00625 mmol), [(*t*-Bu)$_3$PH]BF_4 (5 mg, 0.0175 mmol), $Mo(CO)_6$ (66mg, 0.25 mmol) and DBU (1.0M in THF, 0.75 mL, 0.75 mmol) were combined in 1,4-dioxane (2.5 mL) and irradiated in μW at 140 ˚C for 1 h. The reaction mixture was filtered through a bed of celite (top layer) and silica (bottom layer) with $CHCl_3$/MeOH to afford crude product. Purification using Biotage SP1 (10g SNAP, 15 mL/min, 0 – 5% MeOH in CH_2Cl_2) afforded the product as a brown oil (60mg, 86%). ^{1}H NMR: (500 MHz, $CDCl_3$) δ_H 8.57 (d, *J* = 1.9 Hz, 1H), 8.32 (s, 1H), 8.18 (d, *J* = 1.9 Hz, 1H), 5.80 (s, 2H), 3.78 – 3.70 (m, 2H), 3.56 – 3.51 (m, 2H), 3.36 (s, 3H), 3.19 (bs, 3H), 3.09 (bs, 3H); ^{13}C NMR: (126 MHz, $CDCl_3$) δ_C 169.6, 147.5, 145.6, 144.2, 134.3, 127.6, 127.2, 73.0, 71.5, 69.0, 59.1, 39.9, 35.7; LCMS t_R = 1.62 mins, *m/z* = 279

$(M+H)^+$; Purity (AUC) ≥ 95%; HRMS $(M+H)^+$ *calculated* for $C_{13}H_{19}N_4O_3$ = 279.1452, *found* = 279.1455.

3-((2-Methoxyethoxy)methyl)-6-methyl-3*H*-imidazo[4,5-*b*]pyridine, S8: 6-Bromo-3-((2-methoxyethoxy)methyl)-3*H*-imidazo[4,5-*b*]pyridine, **7a** (589 mg, 2.0 mmol), methylboronic acid (239 mg, 4.0 mmol), CsF (636 mg, 4.0 mmol), $Pd(OAc)_2$ (18 mg, 4 mol%) and $nBuPAd_2$ (57 mg, 8 mol%) were dissolved in DME (5.0 ml) and heated in a microwave reactor at 150 °C for 1 h. The crude mixture was concentrated *in vacuo* and purified by column chromatography (CH_2Cl_2 to EtOH:CH_2Cl_2 10:90) to afford the product as a yellow oil (354 mg, 80%); ^1H NMR (500 MHz, $CDCl_3$) δ_H 8.27 (d, *J* = 1.8 Hz, 1H), 8.19 (s, 1H), 7.90 (d, *J* = 1.8 Hz, 1H), 5.75 (s, 2H), 3.72 – 3.70 (m, 2H), 3.52 – 3.50 (m, 2H), 3.36 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C 145.6, 145.5, 144.2, 135.1, 128.4, 128.1, 72.9, 71.5, 68.8, 59.0, 18.6; LCMS t_R = 1.62 min, *m/z* = 222 $(M+H)^+$; Purity (AUC) ≥ 95%; HRMS $(M+H)^+$ *calculated* for $C_{11}H_{16}N_3O_2$ = 222.1237, *found* = 222.1232.

6-Cyclopropyl-3-((2-methoxyethoxy)methyl)-3*H*-imidazo[4,5-*b*]pyridine, S9: 6-Bromo-3-((2-methoxyethoxy)methyl)-3*H*-imidazo[4,5-*b*]pyridine, **7a** (589 mg, 2.0 mmol), cyclopropylboronic acid (344 mg, 4.0 mmol), CsF (636 mg, 4.0 mmol), $Pd(OAc)_2$ (18 mg, 4 mol%) and $nBuPAd_2$ (57 mg, 8 mol%) were dissolved in DME (5.0 ml) and heated in a microwave reactor at 150 °C for 1 h. The crude mixture was concentrated *in vacuo* and purified by column chromatography (CH_2Cl_2 to EtOH: CH_2Cl_2 10:90) to afford the product as a yellow oil (440 mg, 89%); ^1H NMR (500 MHz, $CDCl_3$) δ_H 8.36 (d, J = 2.0 Hz, 1H), 8.08 (s, 1H), 7.45 (d, J = 2.0 Hz, 1H), 5.57 (s, 2H), 3.54 – 3.48 (m, 2H), 3.47 – 3.42 (m, 2H), 3.28 (s, 3H), 2.00 (ddd, J = 8.5, 5.2, 3.4 Hz, 1H), 1.04 – 0.96 (m, 2H), 0.70 (dt, J = 6.4, 4.8 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C 155.1, 145.0, 144.6, 134.9, 125.9, 115.1, 75.4, 71.7, 67.7, 59.0, 13.4, 9.1; LCMS t_R = 1.95 min, *m/z* = 248 $(M+H)^+$; Purity (AUC) ≥ 95%; HRMS $(M+H)^+$ *calculated* for $C_{13}H_{18}N_3O_2$ = 248.1394, *found* = 248.1394.

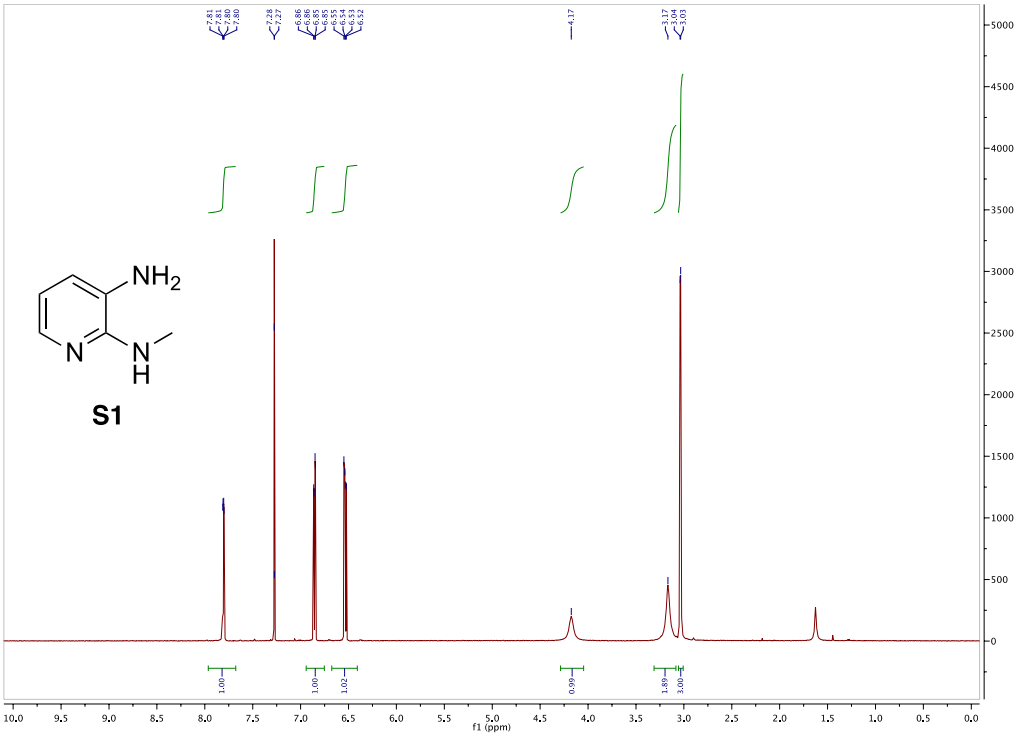
3-((2-Methoxyethoxy)methyl)-7-methyl-3*H*-imidazo[4,5-*b*]pyridine, S10:

7-Chloro-3-((2-methoxyethoxy)methyl)-3*H*-imidazo[4,5-*b*]pyridine, **8a** (1.0M in DMF, 0.2 mL, 0.2 mmol), methylboronic acid (18 mg, 0.3 mmol), CsF (60 mg, 0.4 mmol), $Pd(OAc)_2$ (2.2 mg, 5 mol%) and $nBuPAd_2$ (7.2 mg, 10 mol%) were dissolved in DME (1.0 ml) and heated in a microwave reactor at 150 °C for 2.5 h. The reaction mixture was filtered through a plug of silica (bottom layer) and celite (top layer), eluting with $CHCl_3$ & MeOH. The filtrate was concentrated *in vacuo* and purified by column chromatography (0 – 5% MeOH in CH_2Cl_2) to afford the product as a yellow oil (35 mg, 80%). ^1H NMR: (500 MHz, $CDCl_3$) δ_H 8.32 (d, *J* = 4.9 Hz, 1H), 8.29 (s, 1H), 7.12 (dd, *J* = 4.9 0.8 Hz, 1H), 5.78 (s, 2H), 3.75 – 3.71 (m, 2H), 3.54 – 3.50 (m, 2H), 3.35 (s, 3H), 2.73 (d, *J* = 0.8 Hz, 3H); ^{13}C NMR: (126 MHz, $CDCl_3$) δ_C 146.2, 144.8, 142.9, 139.9, 134.2, 120.1, 73.2, 71.5, 68.9, 59.1, 16.3; LCMS t_R = 1.96 mins, *m/z* = 222 $(M+H)^+$; Purity (AUC) ≥ 95%; HRMS $(M+H)^+$ *calculated* for $C_{11}H_{16}N_3O_2$ = 222.1237, *found* = 222.1240.

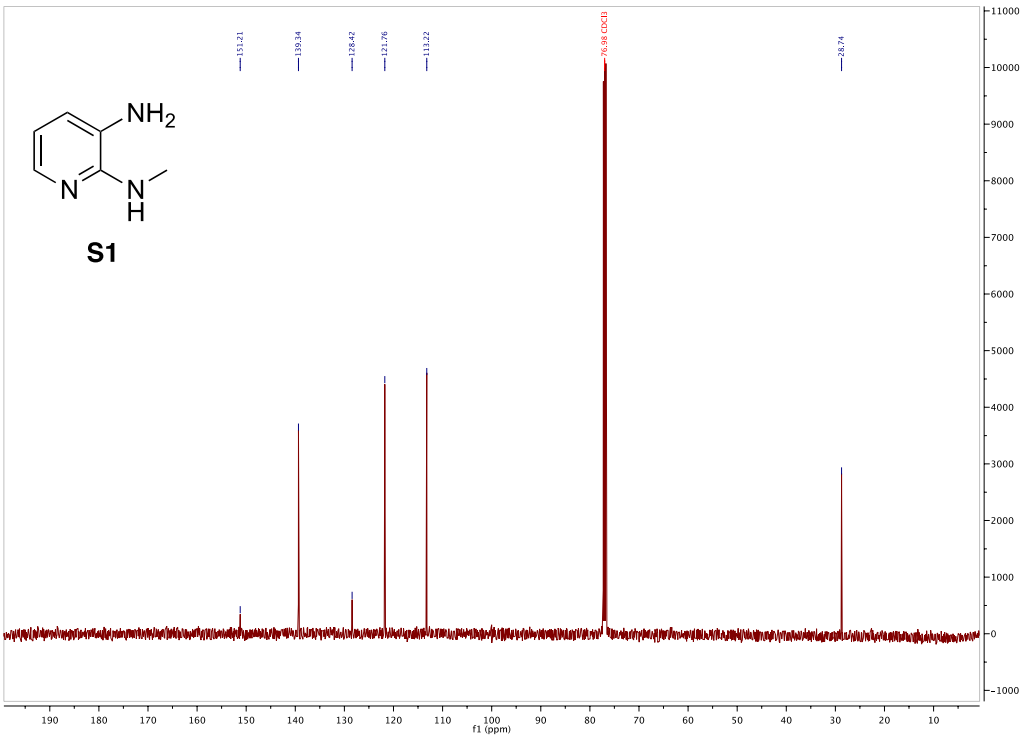
5. NMR Spectra

5.1 Spectra of intermediates

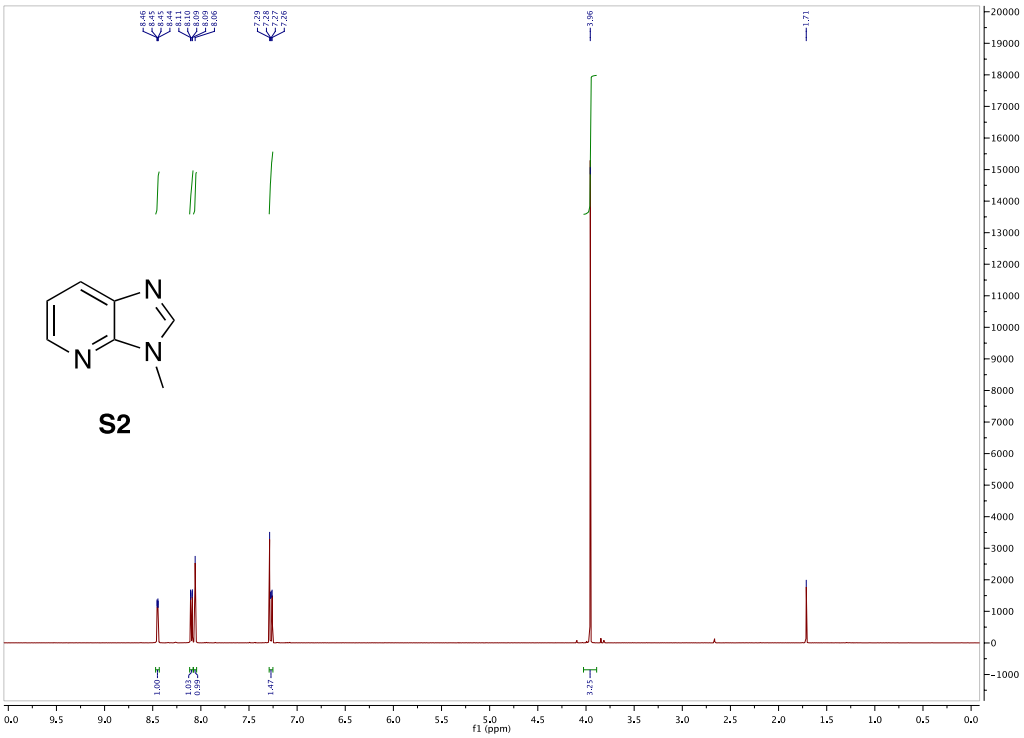
^{1}H NMR:



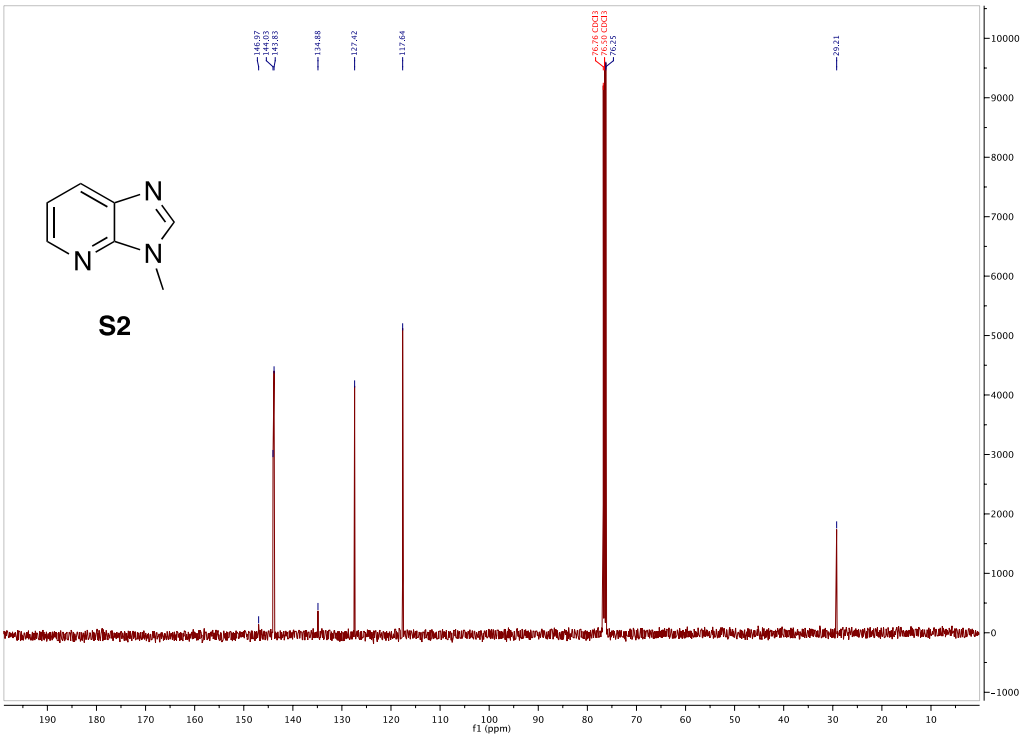
^{13}C NMR:



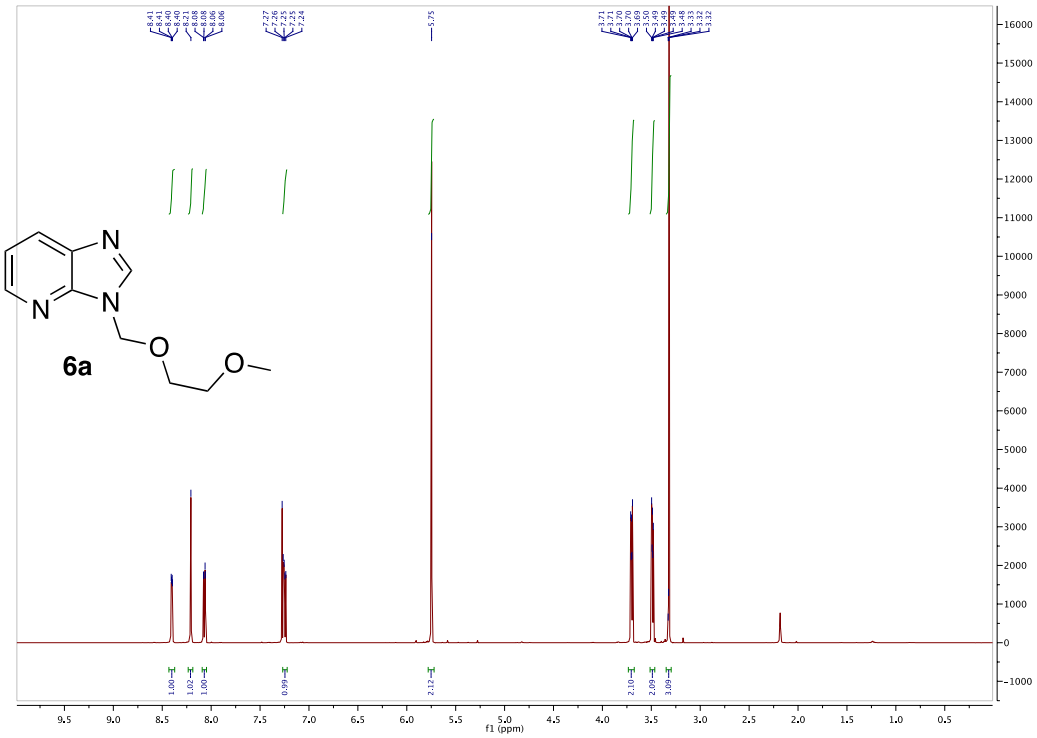
^{1}H NMR:



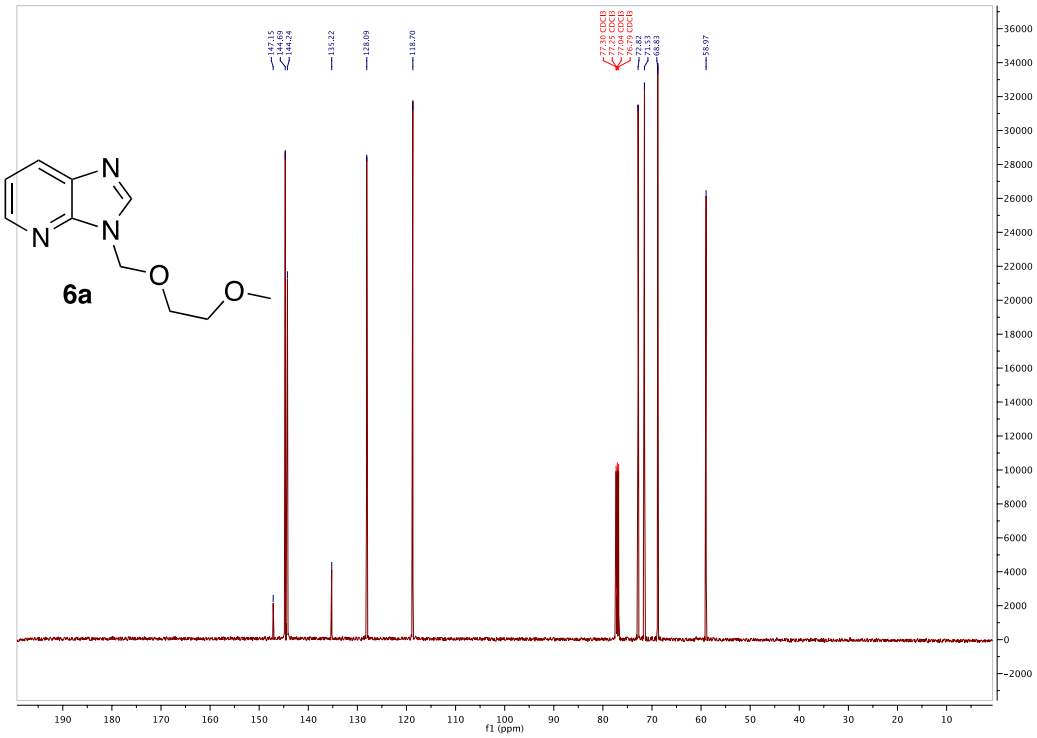
^{13}C NMR:



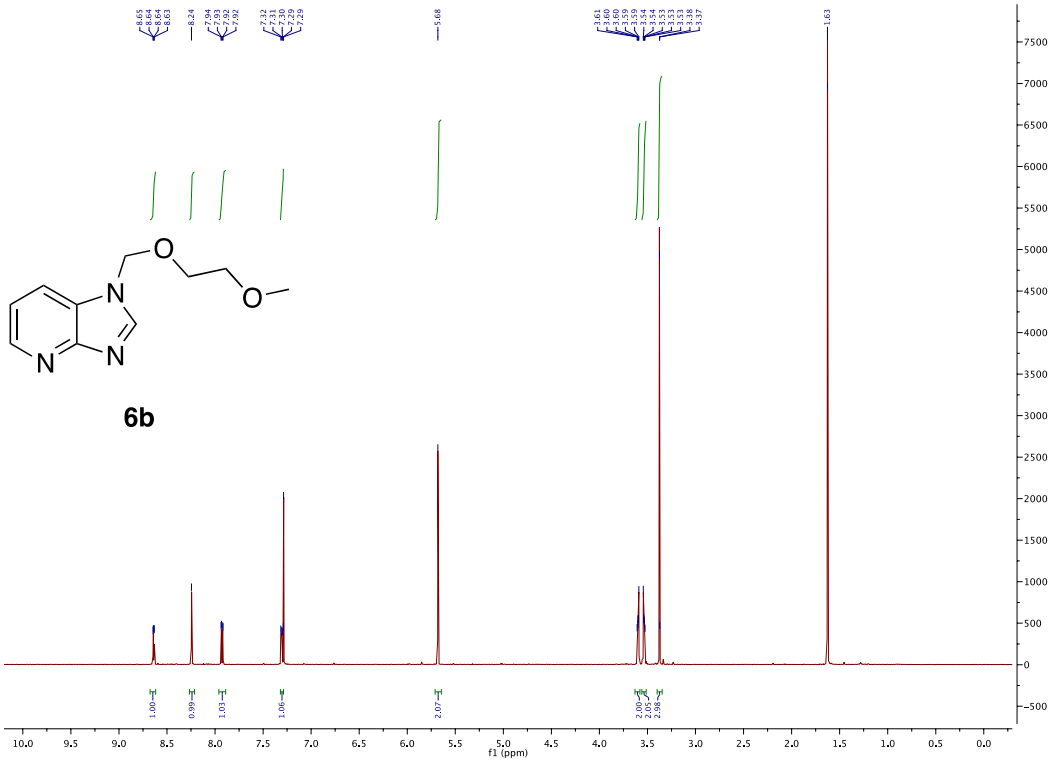
^{1}H NMR:



^{13}C NMR:

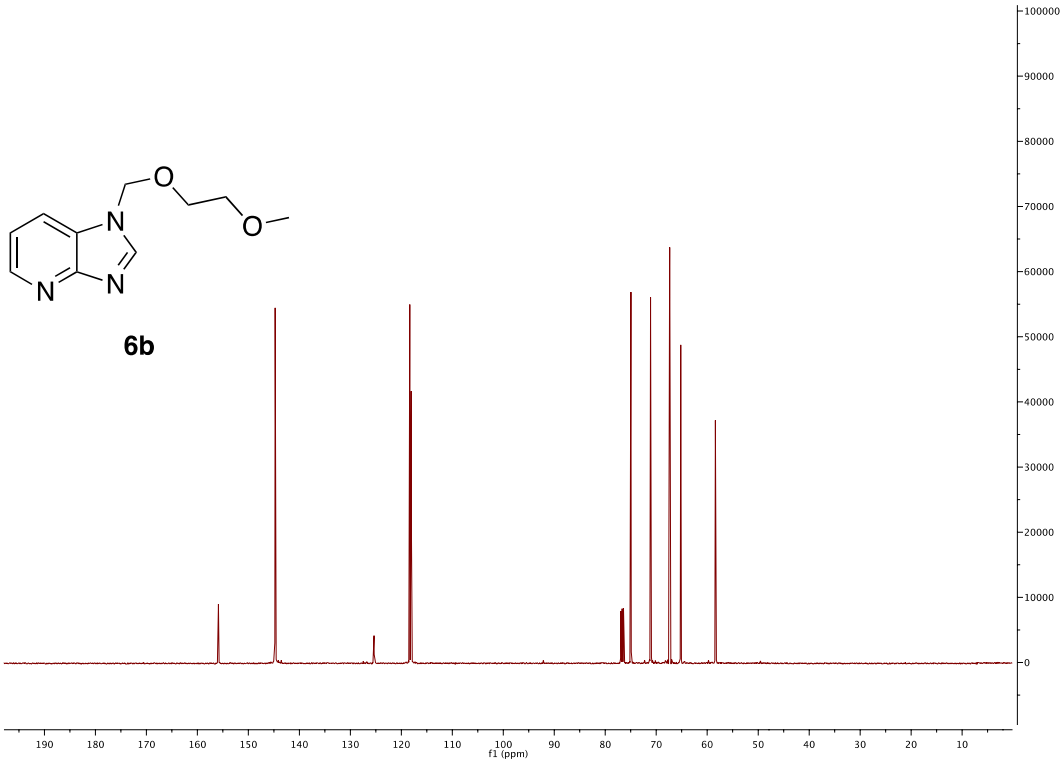


^{1}H NMR:



6b

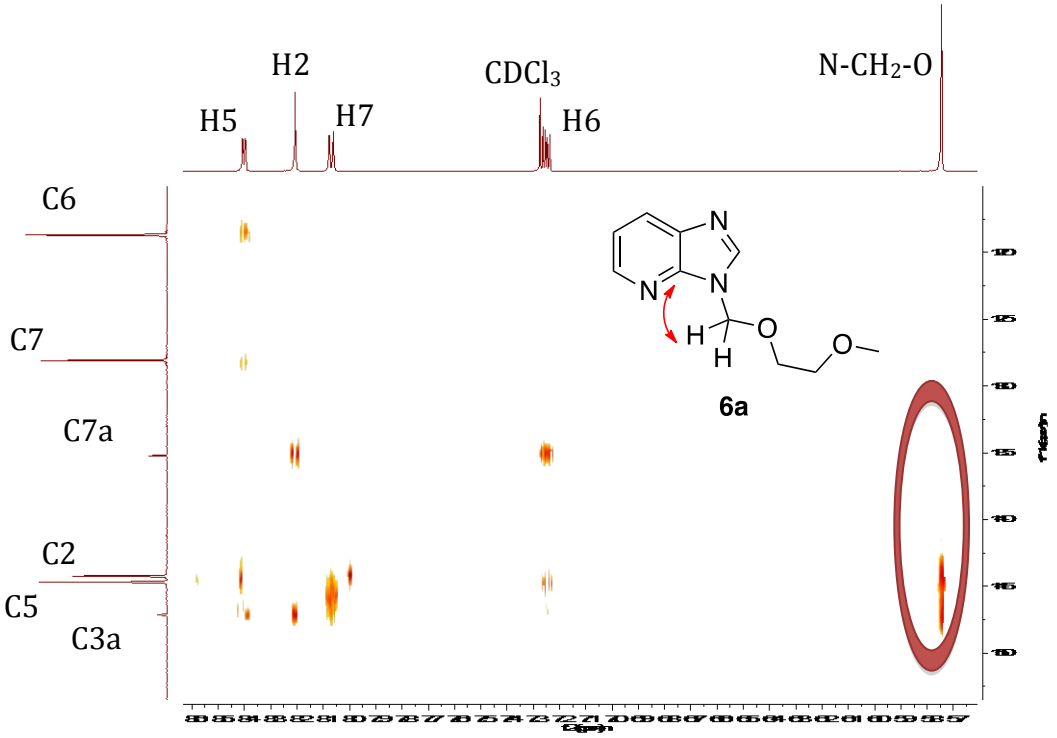
^{13}C NMR:



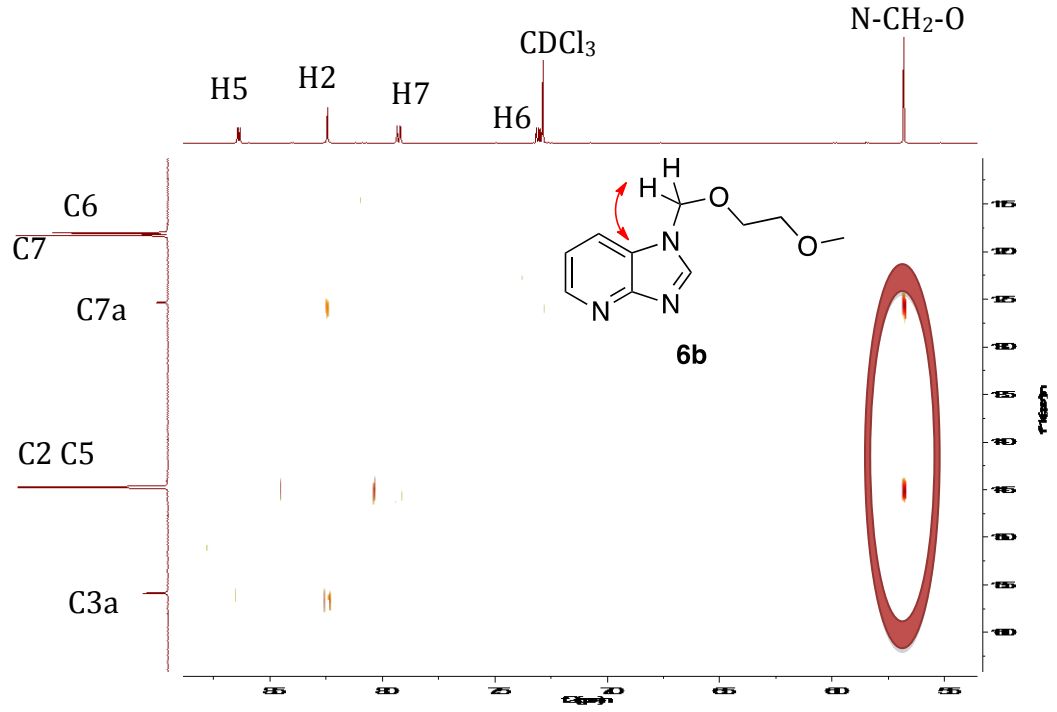
6b

2D NMR – HMBC Experiment

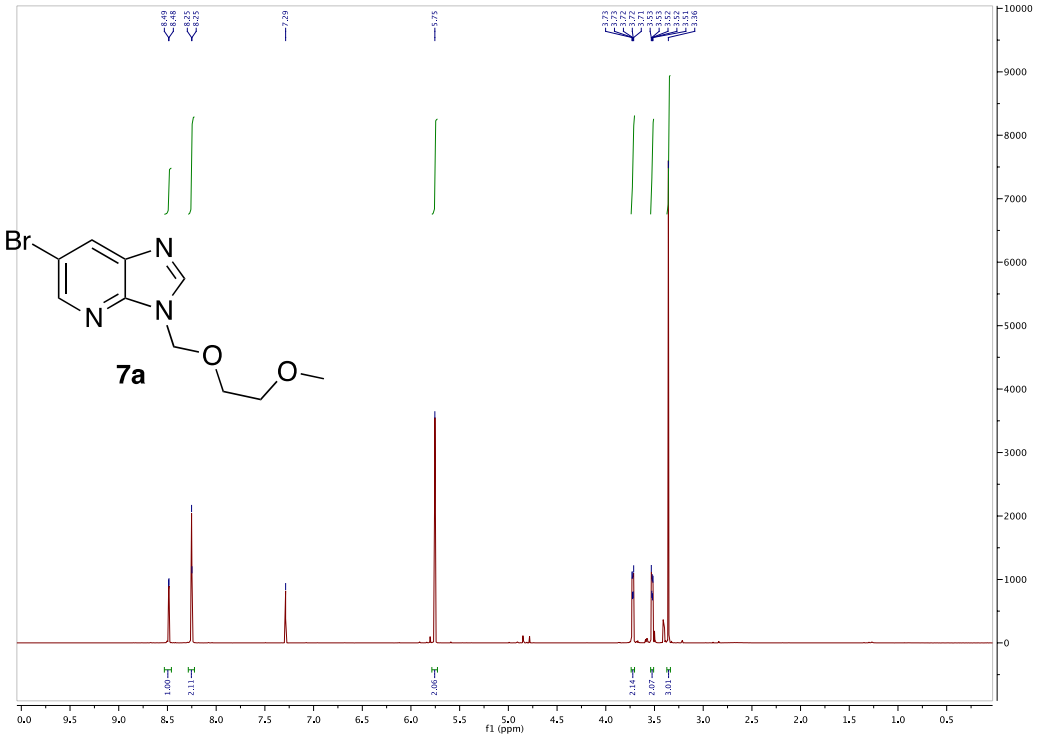
N3 MEM, 4a – N-CH_2-O correlates to C3a and C2 and not C7a.



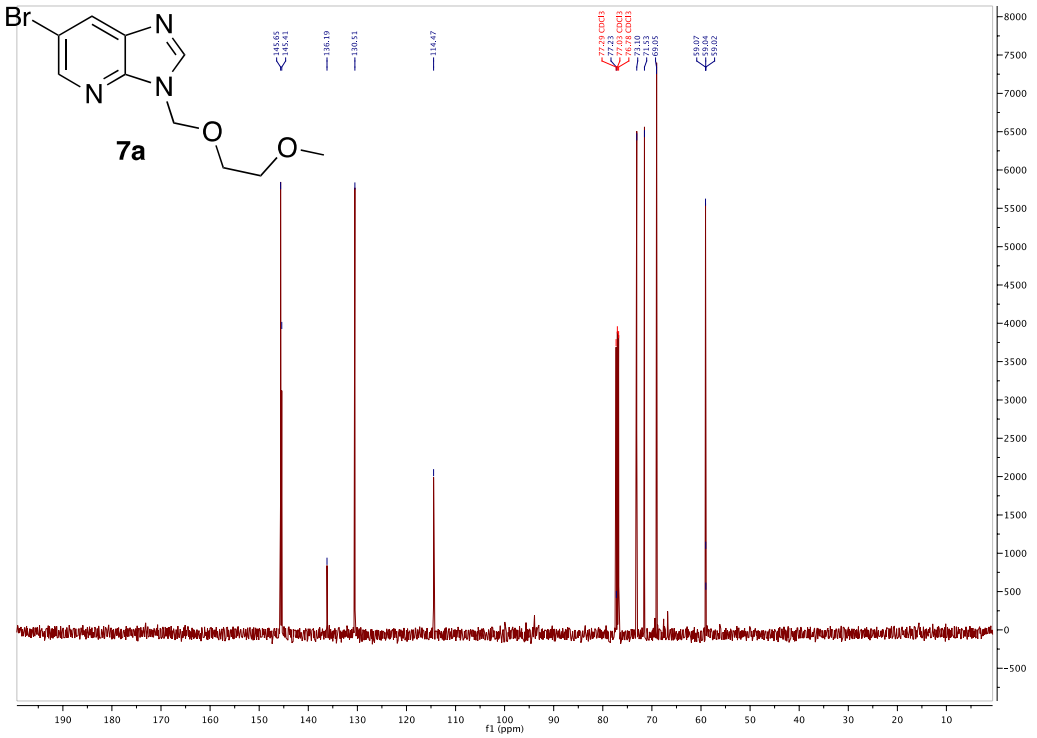
N1 MEM, 4b – N-CH_2-O correlates to C7a and C2 and not C3a.



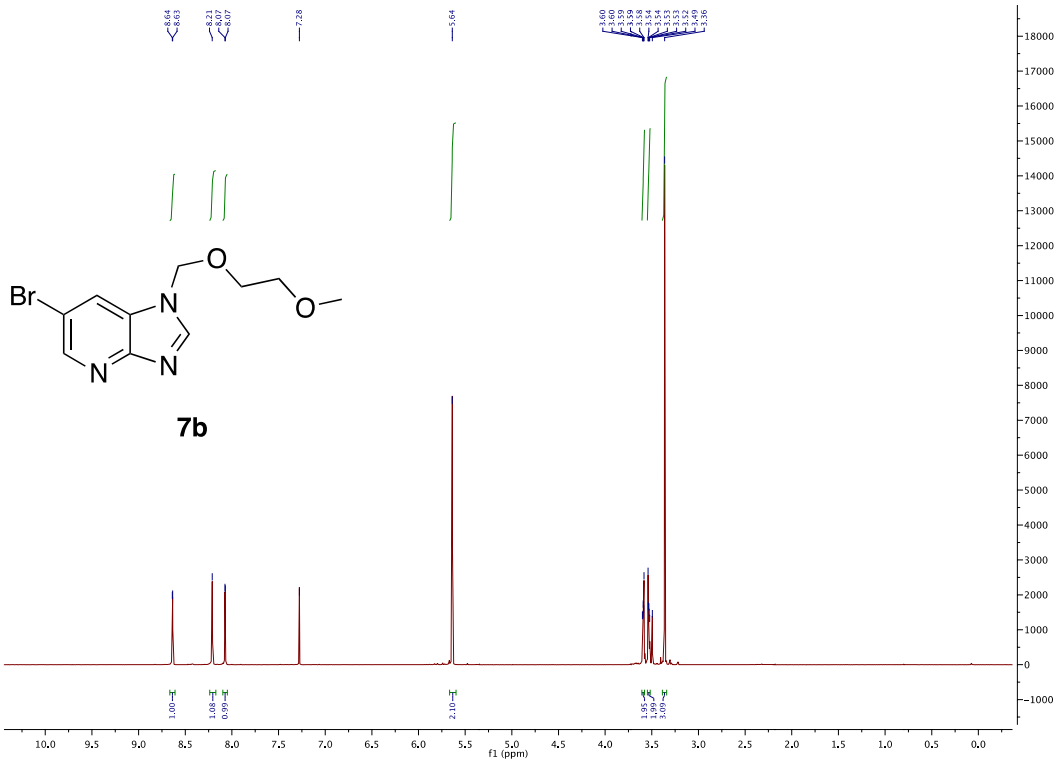
^{1}H NMR:



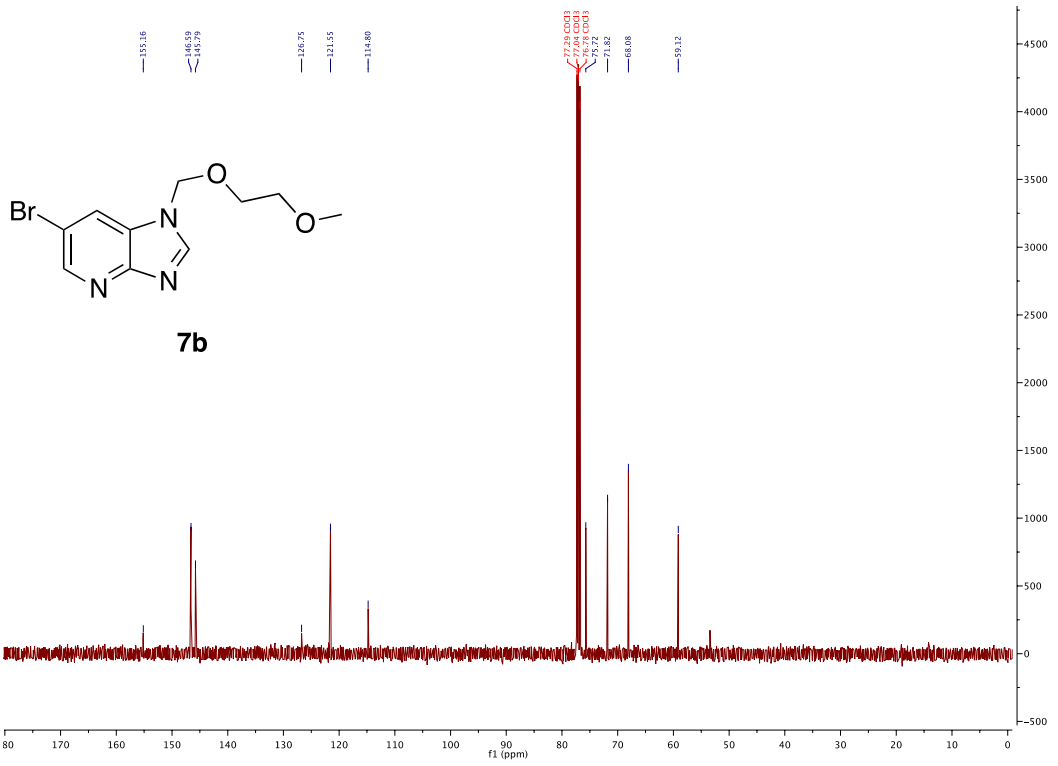
^{13}C NMR:



^{1}H NMR:

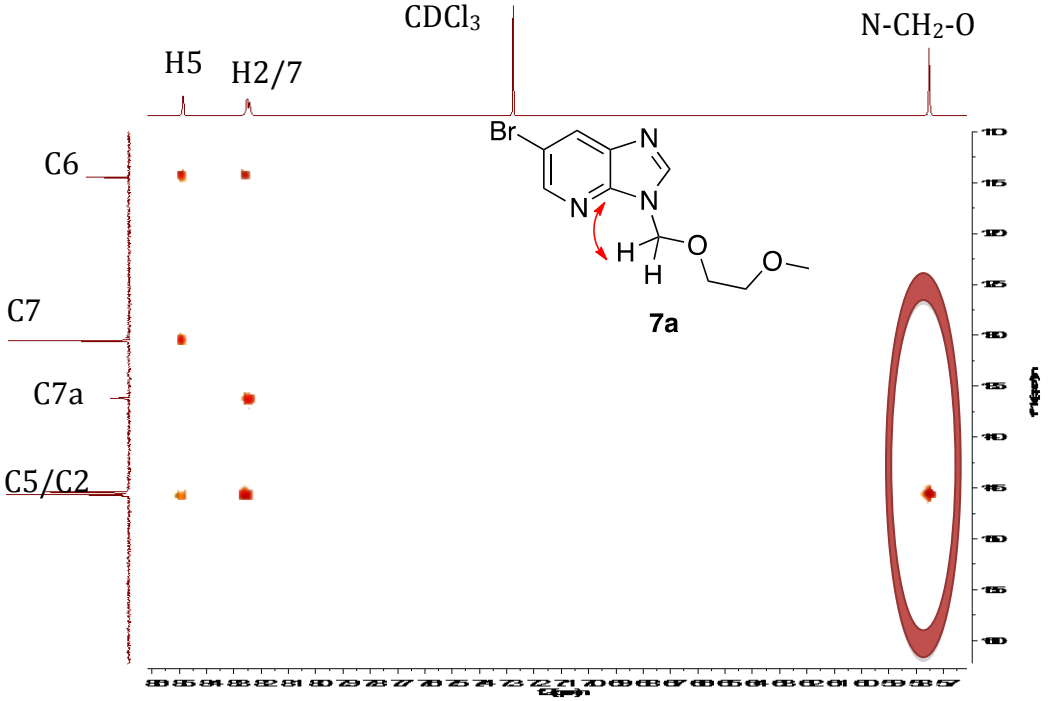


^{13}C NMR:

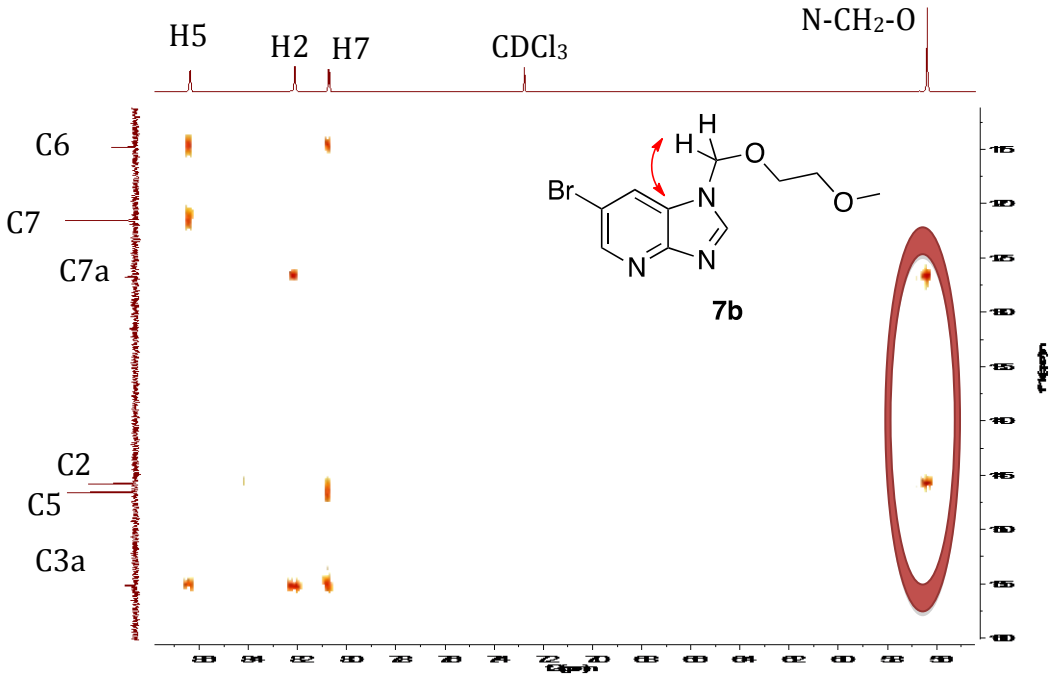


2D NMR – HMBC Experiment

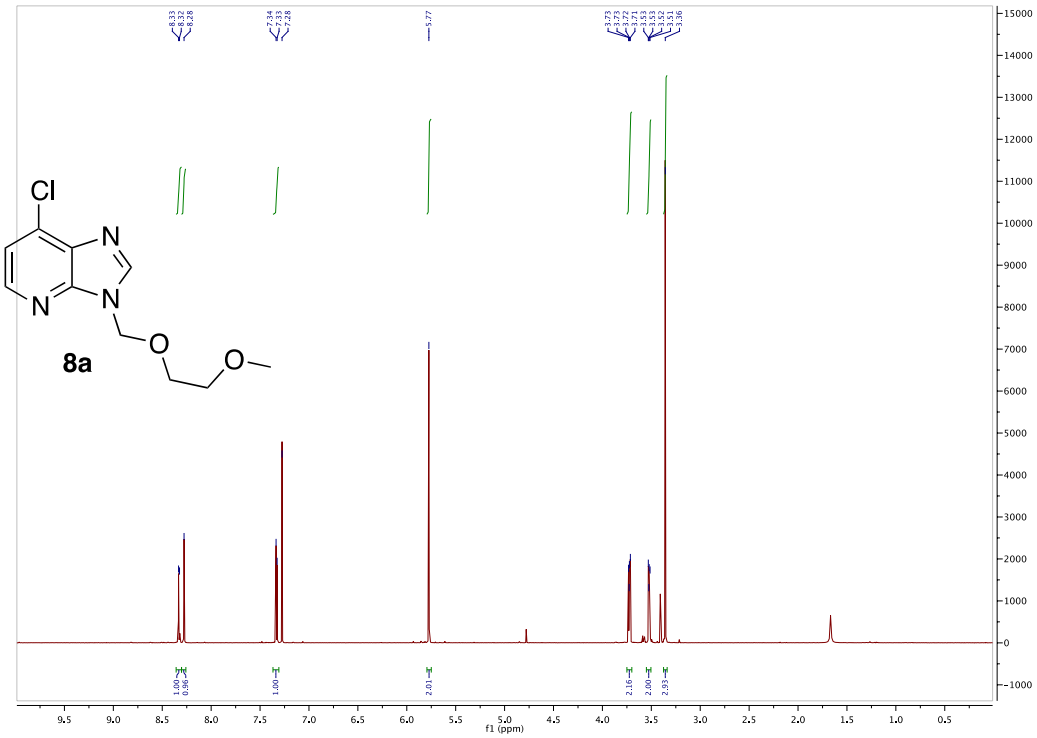
6-Br N3 MEM, 5a – N-CH_2-O does not show correlation to either quaternary C, but it does to C2 - inconclusive.



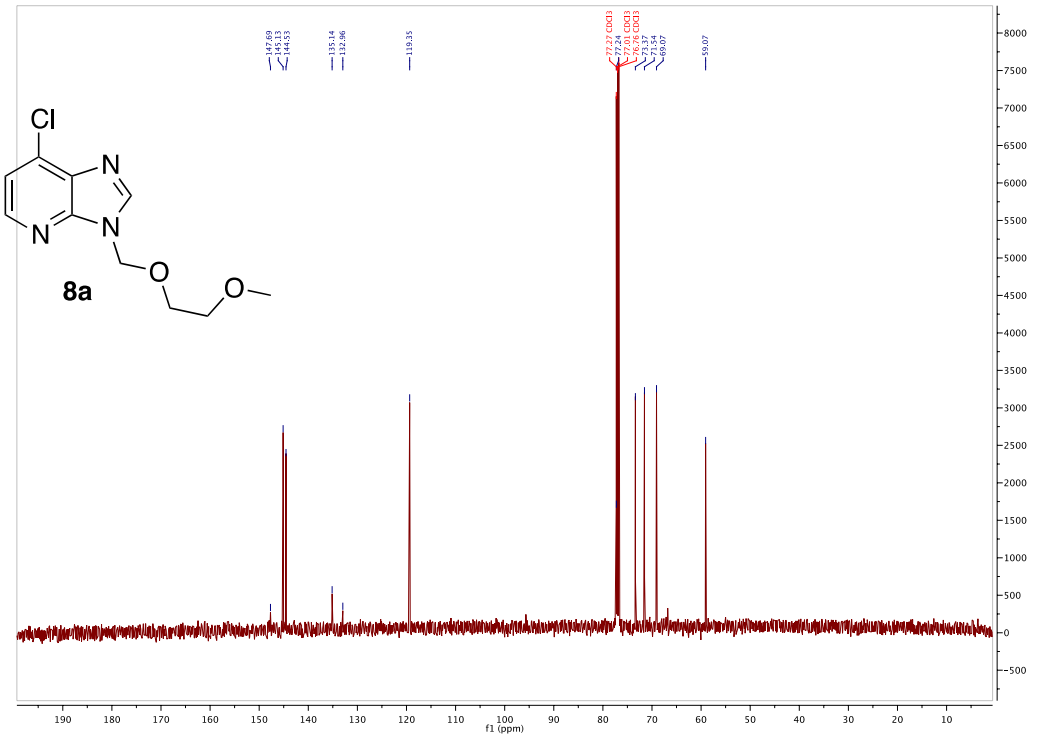
6-Br N1 MEM, 5b – However, the N1 regioisomer is easily distinguished as the N-CH_2-O correlates to C7a and C2 and not C3a.



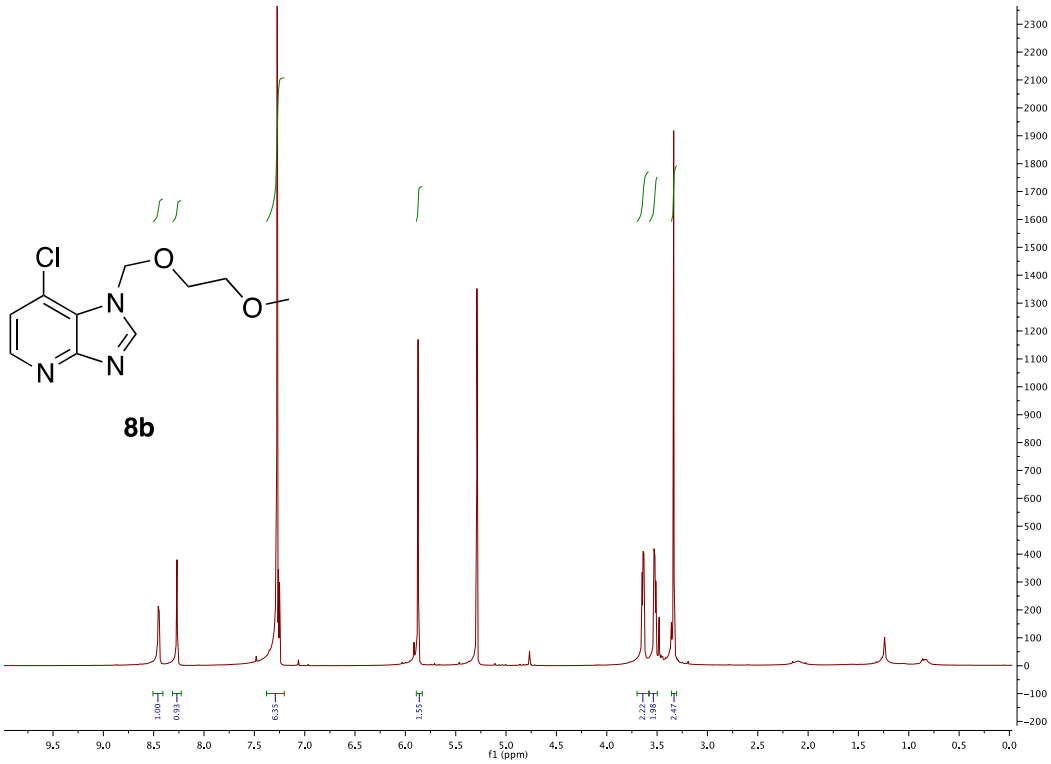
^{1}H NMR:



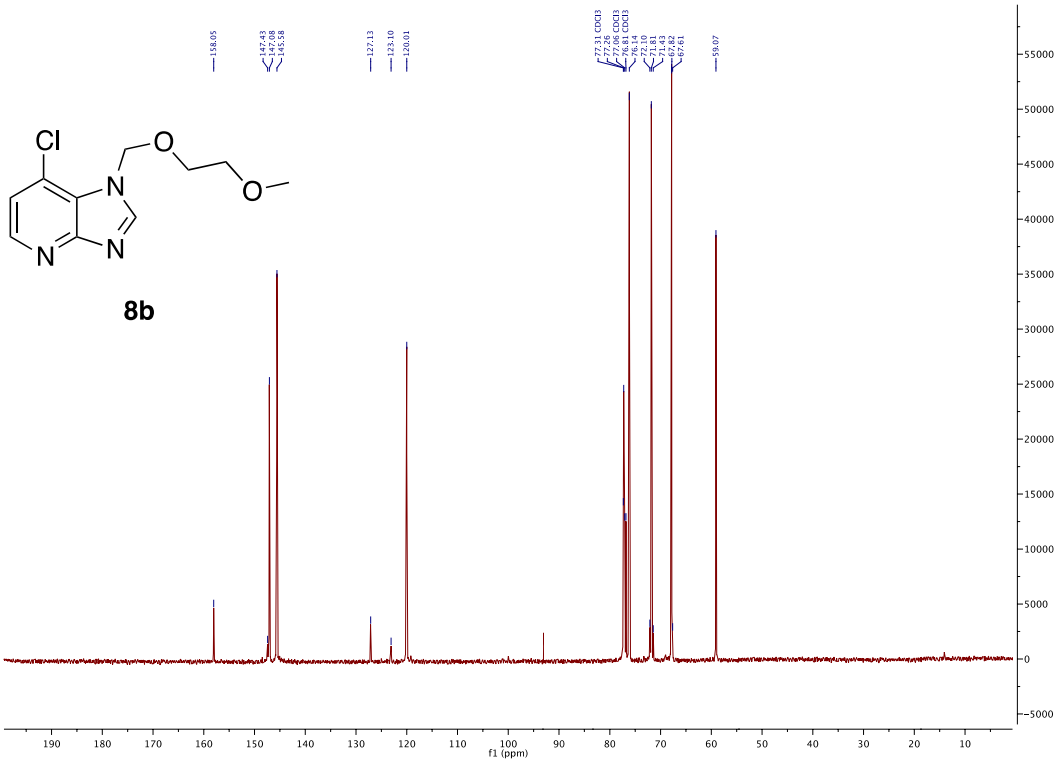
^{13}C NMR:



^{1}H NMR:

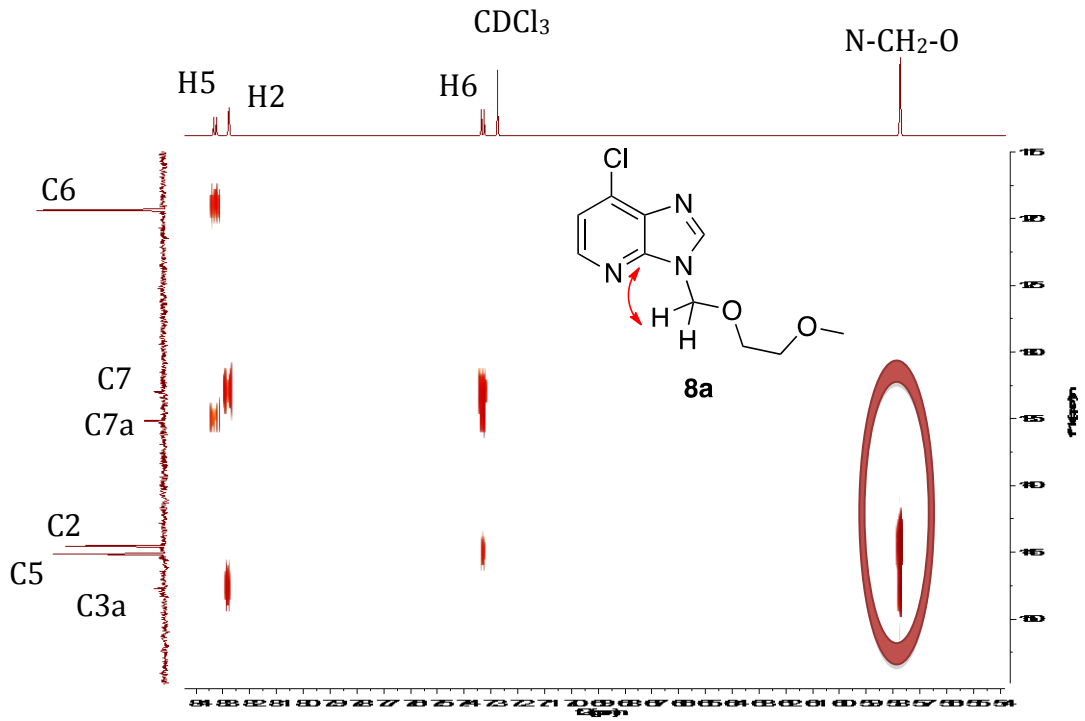


^{13}C NMR:

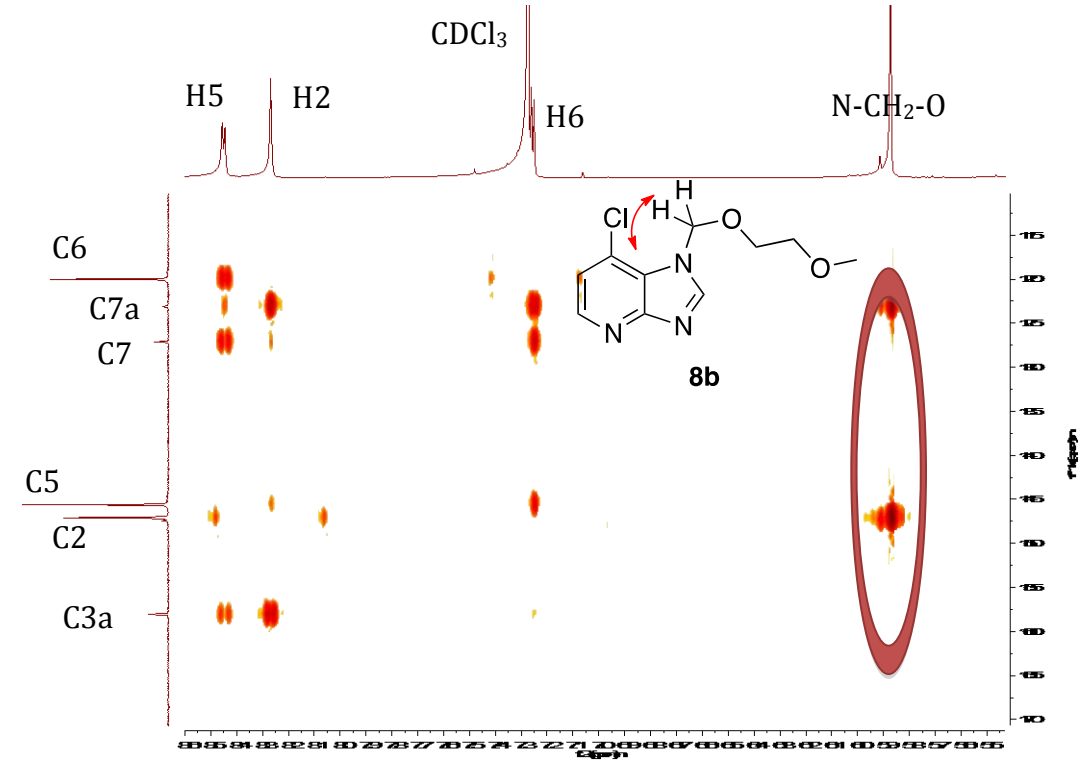


2D NMR – HMBC Experiment

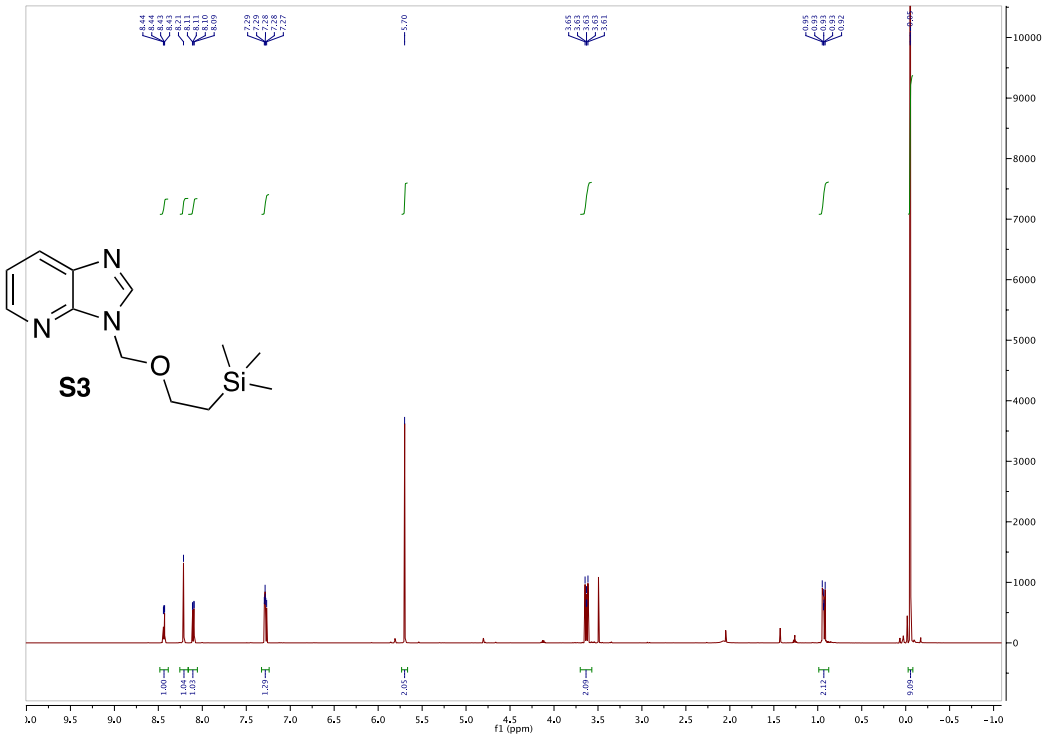
7-Cl N3 MEM, 6a – N-CH_2-O correlates to C3a and C2 and not C7a.



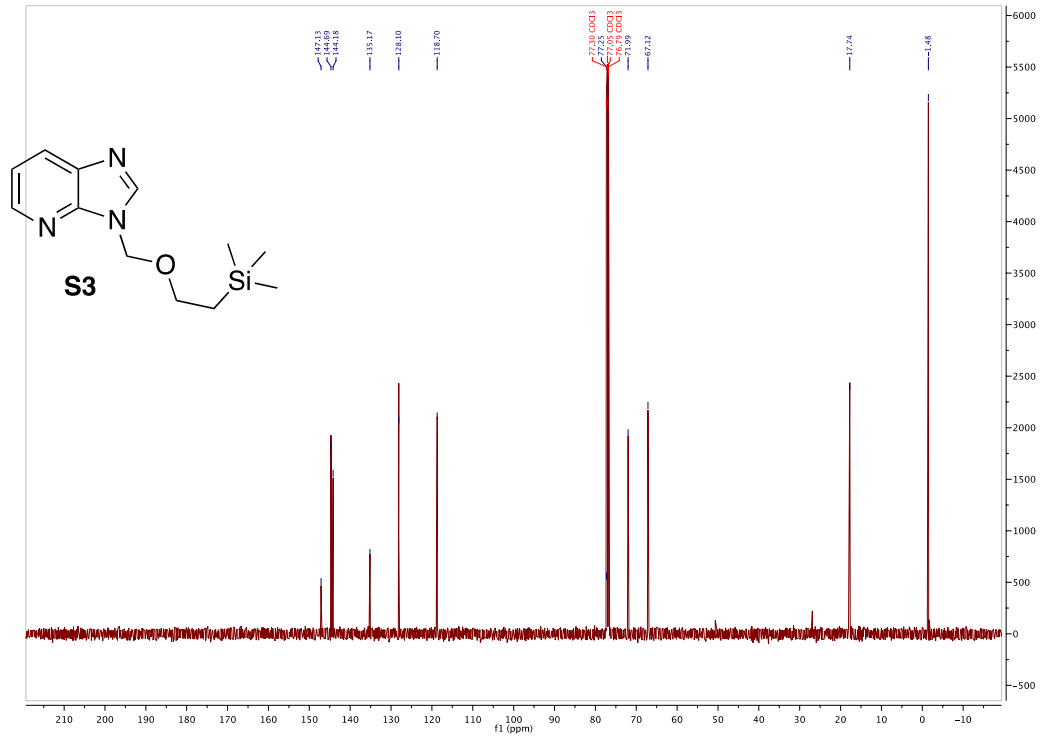
7-Cl N1 MEM, 6b – N-CH_2-O correlates to C7a and C2 and not C3a.



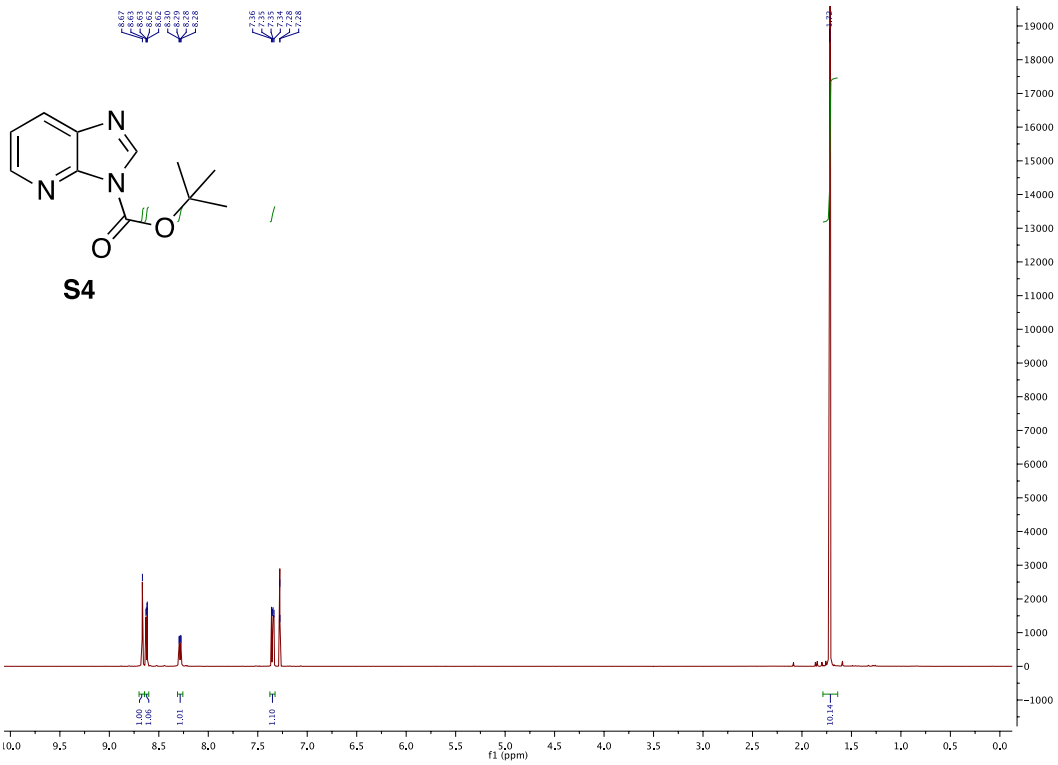
^{1}H NMR:



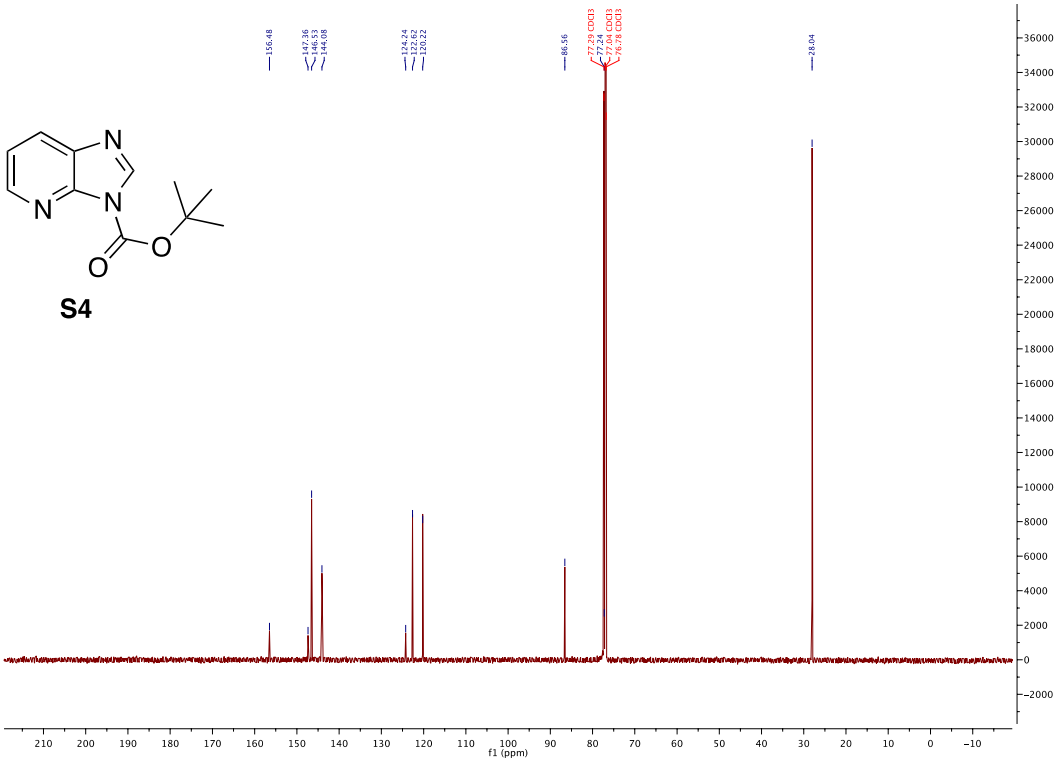
^{13}C NMR:



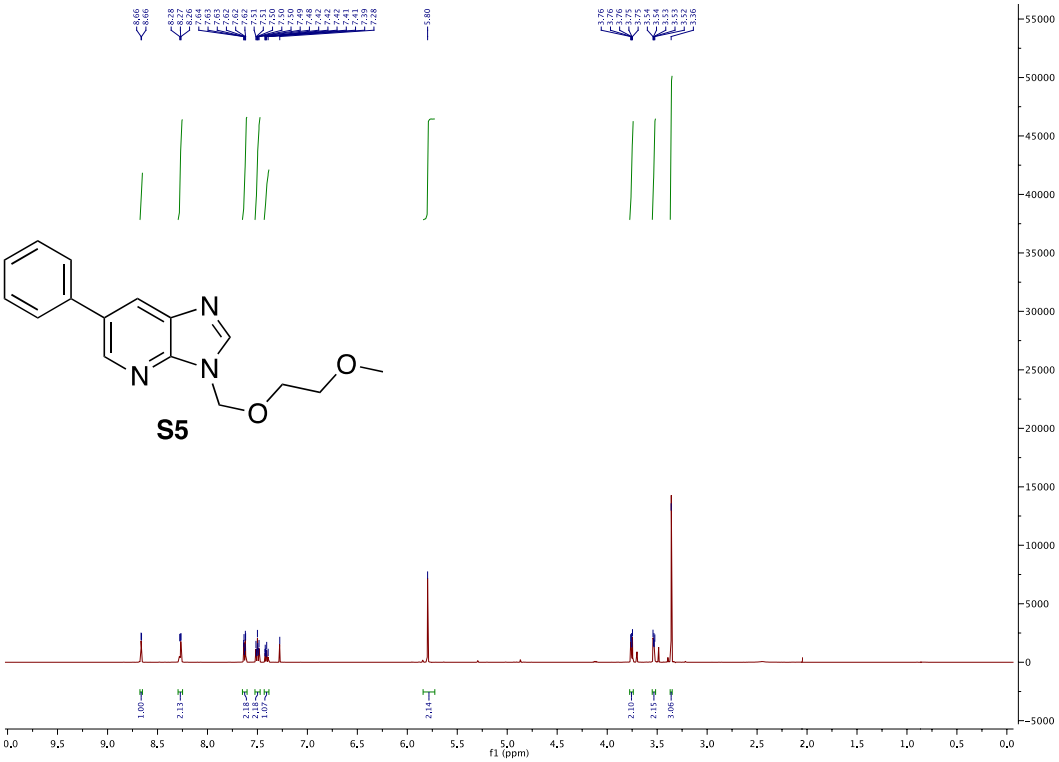
^{1}H NMR:



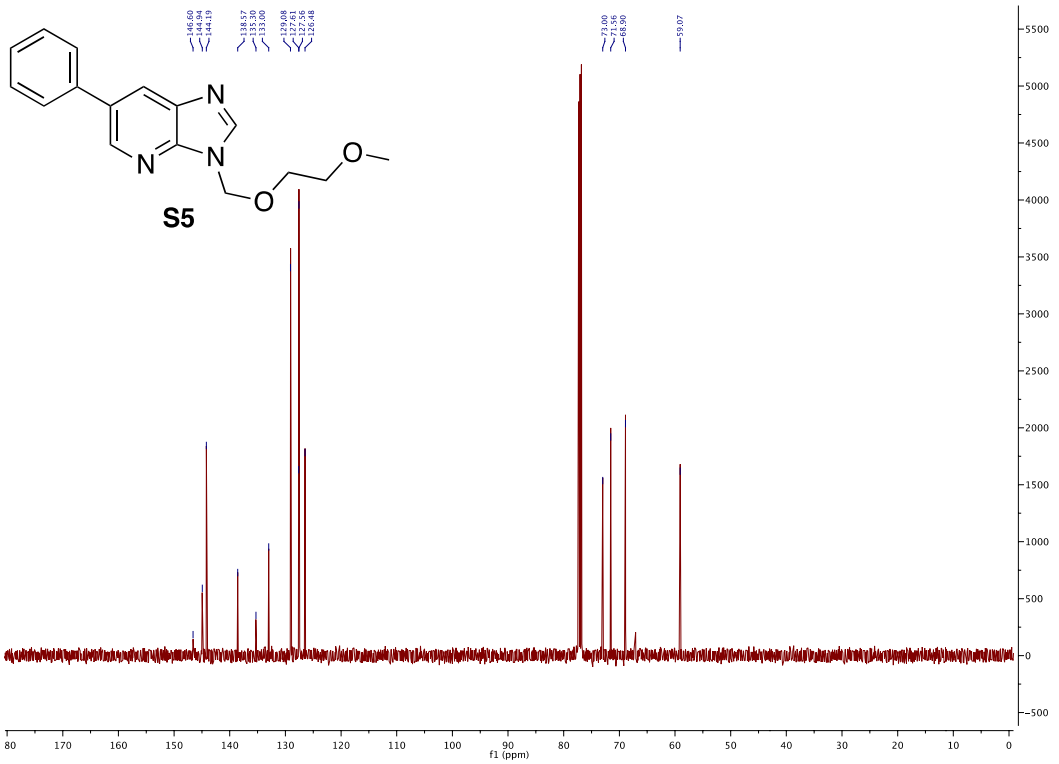
^{13}C NMR:



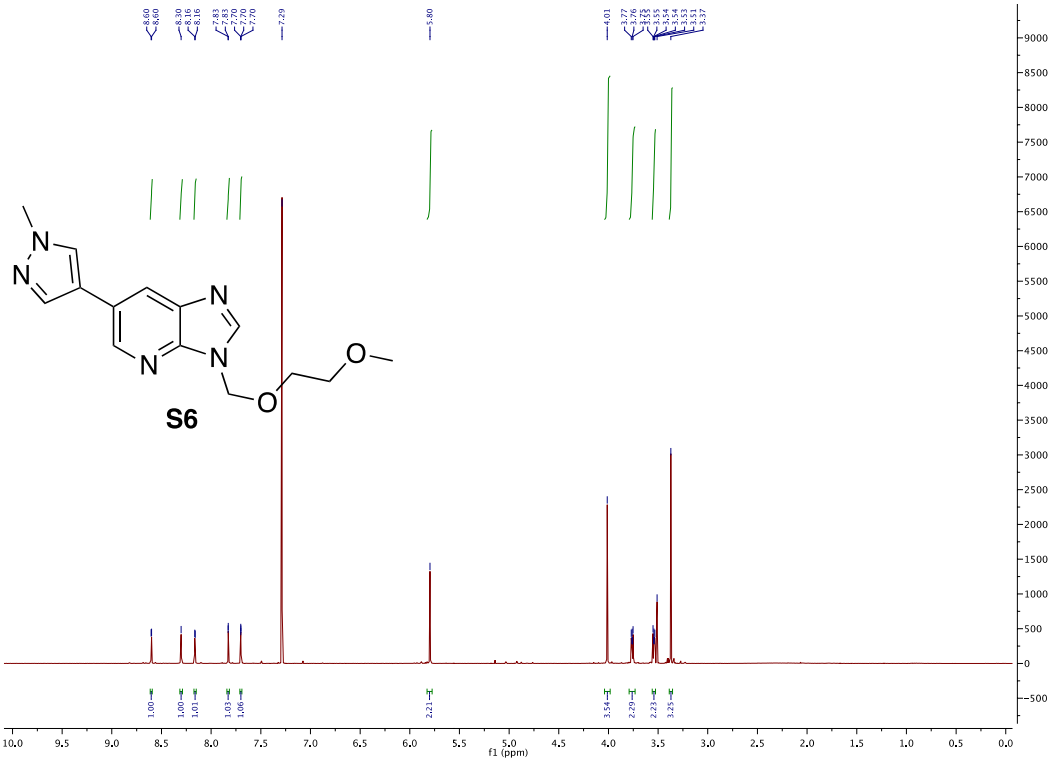
^{1}H NMR:



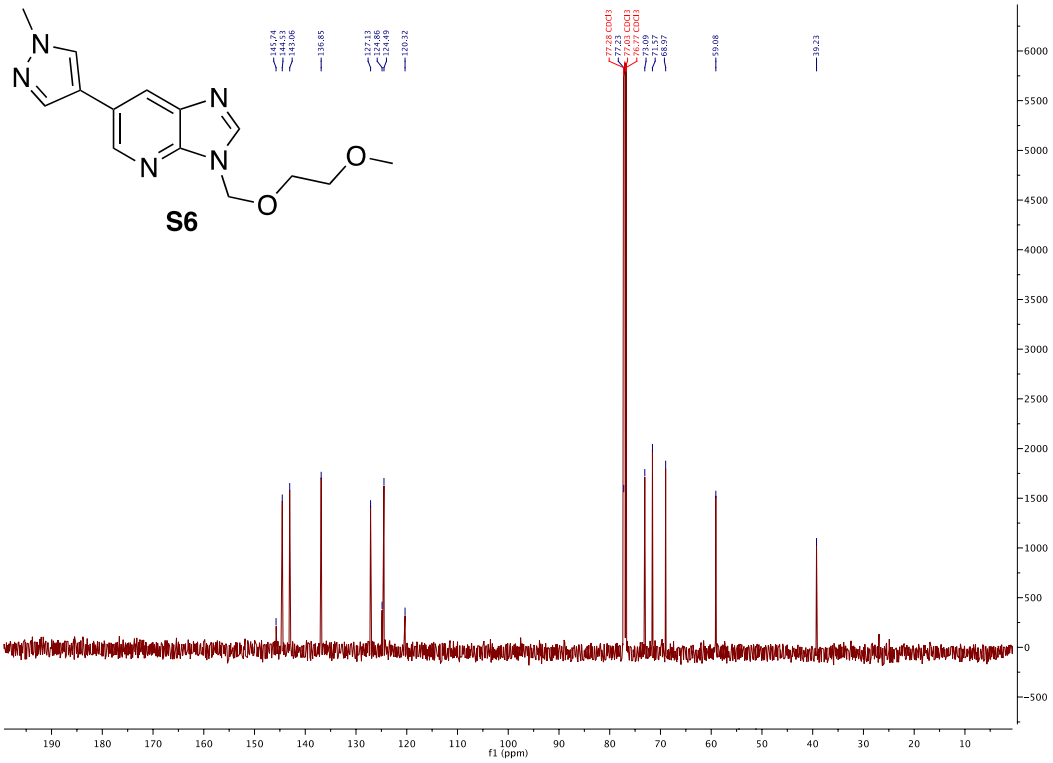
^{13}C NMR:



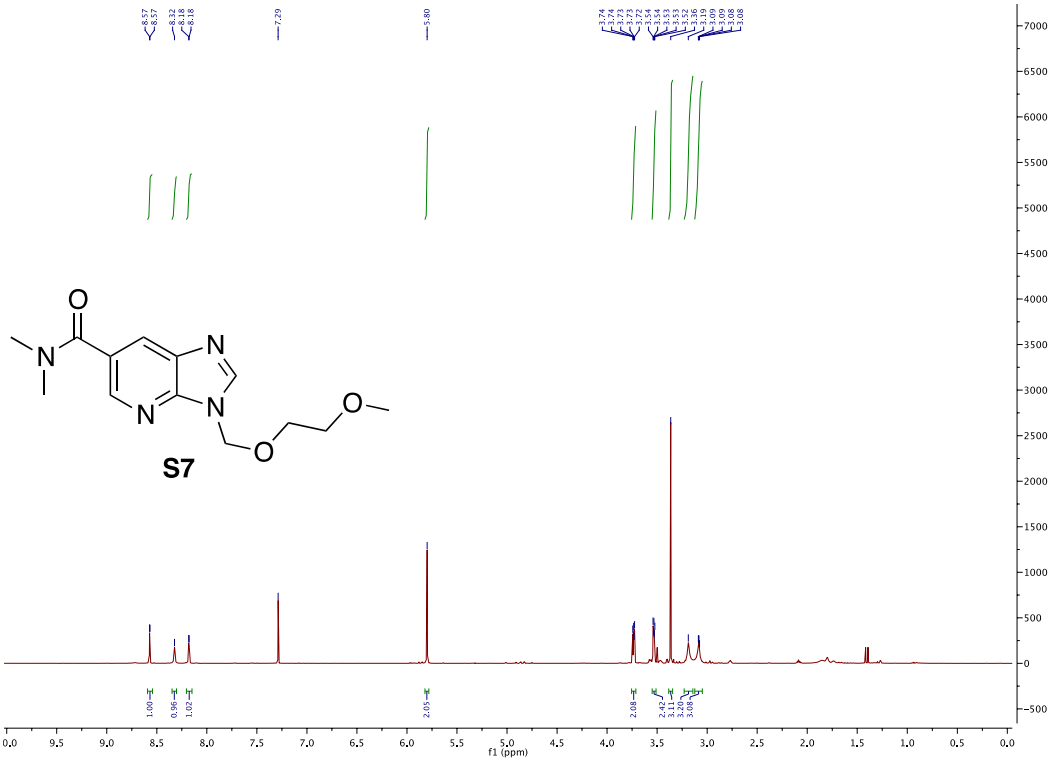
^{1}H NMR:



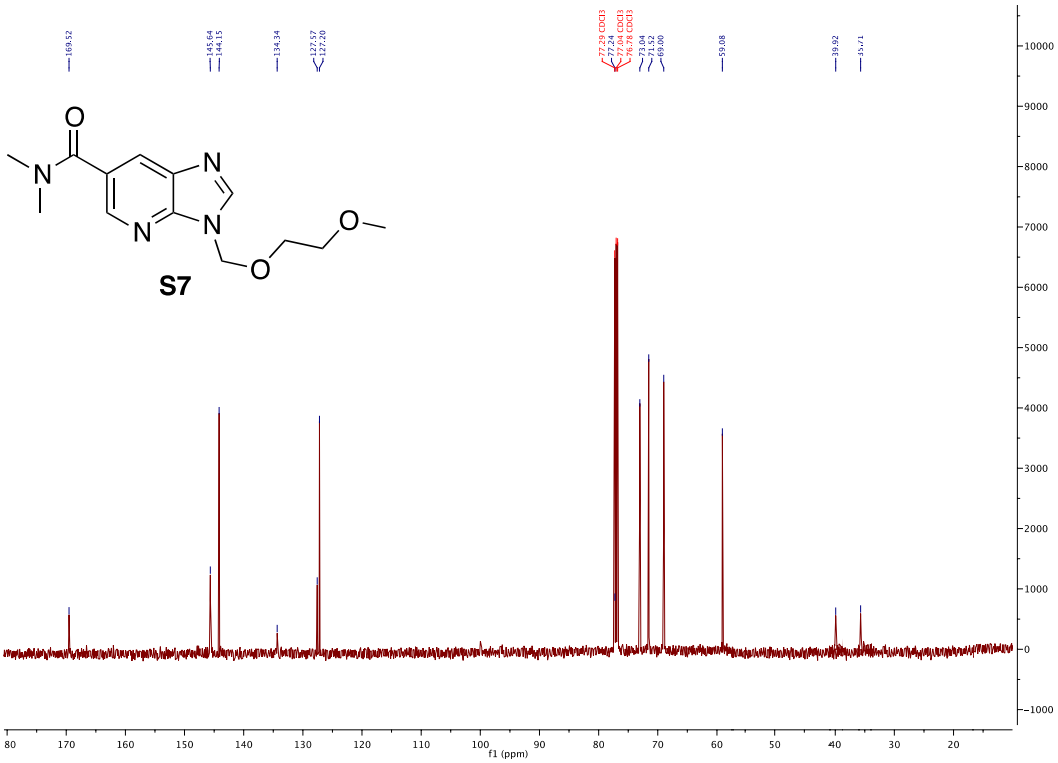
^{13}C NMR:



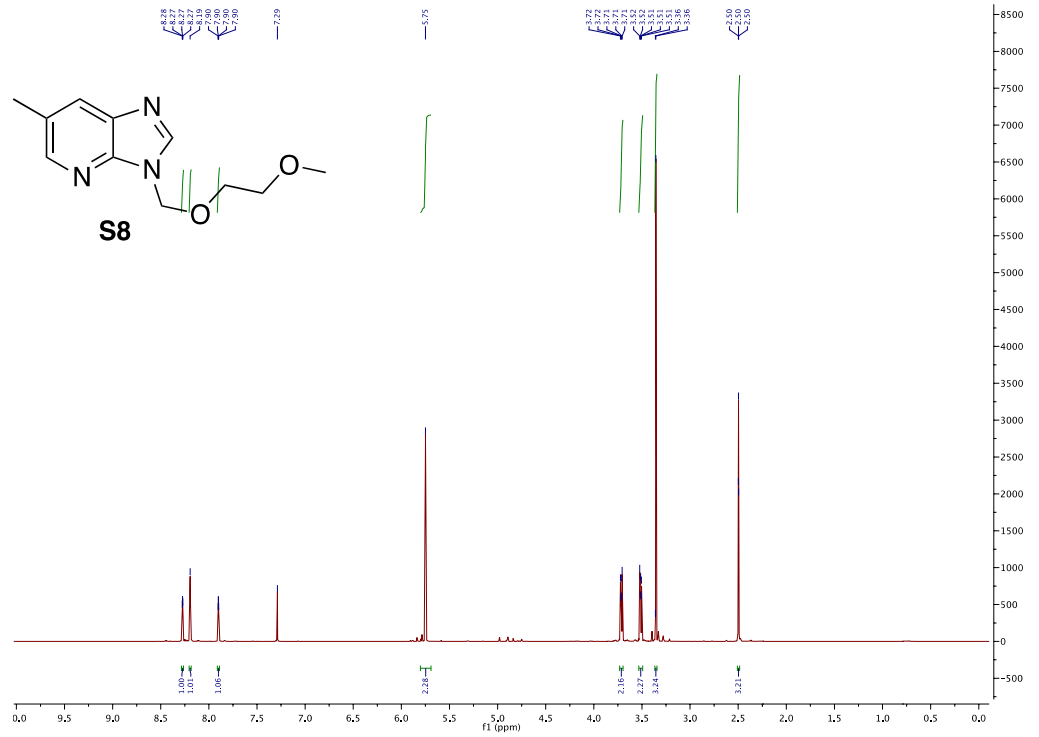
^{1}H NMR:



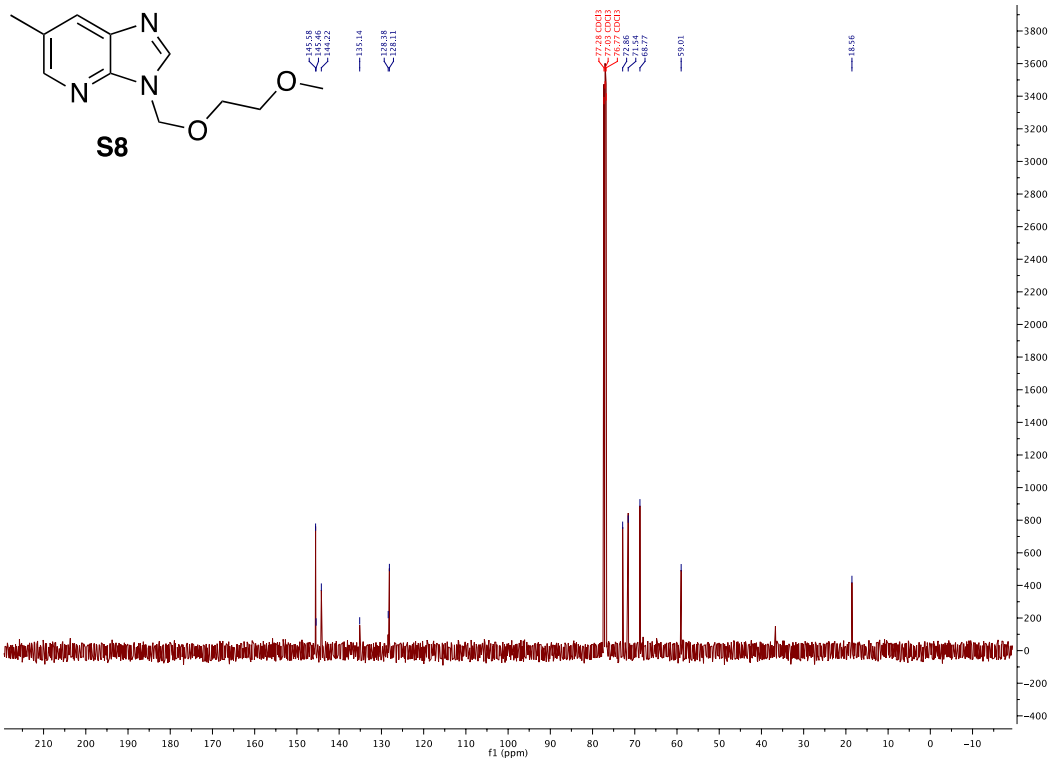
^{13}C NMR:



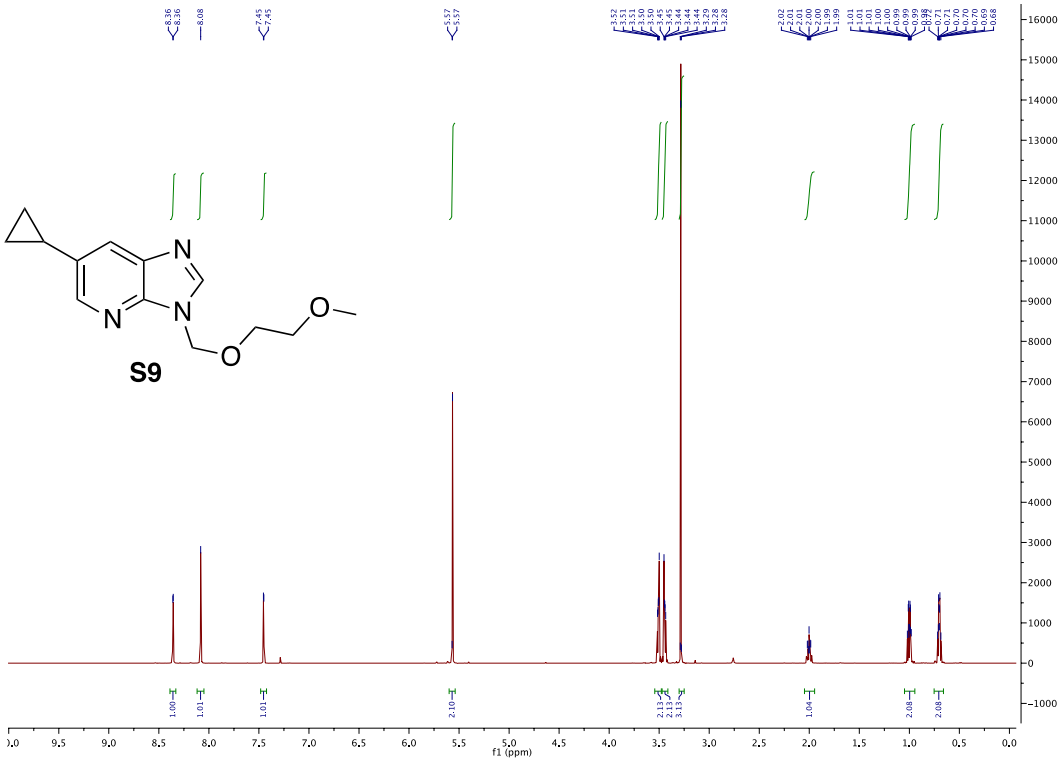
^{1}H NMR:



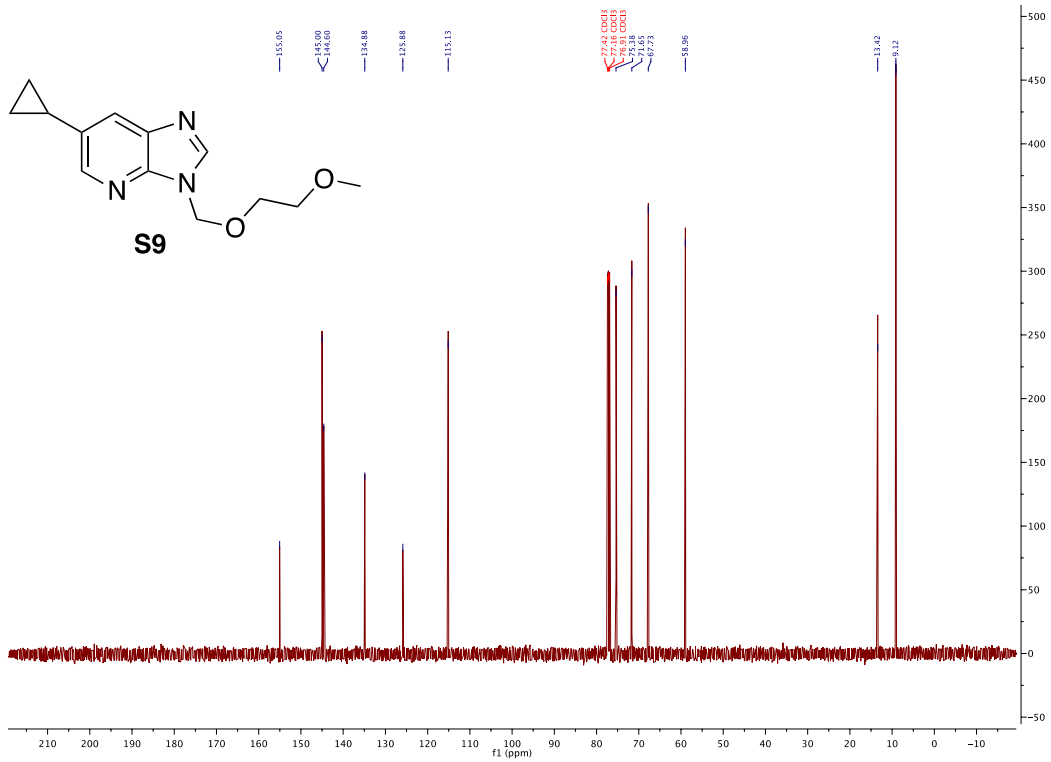
^{13}C NMR:



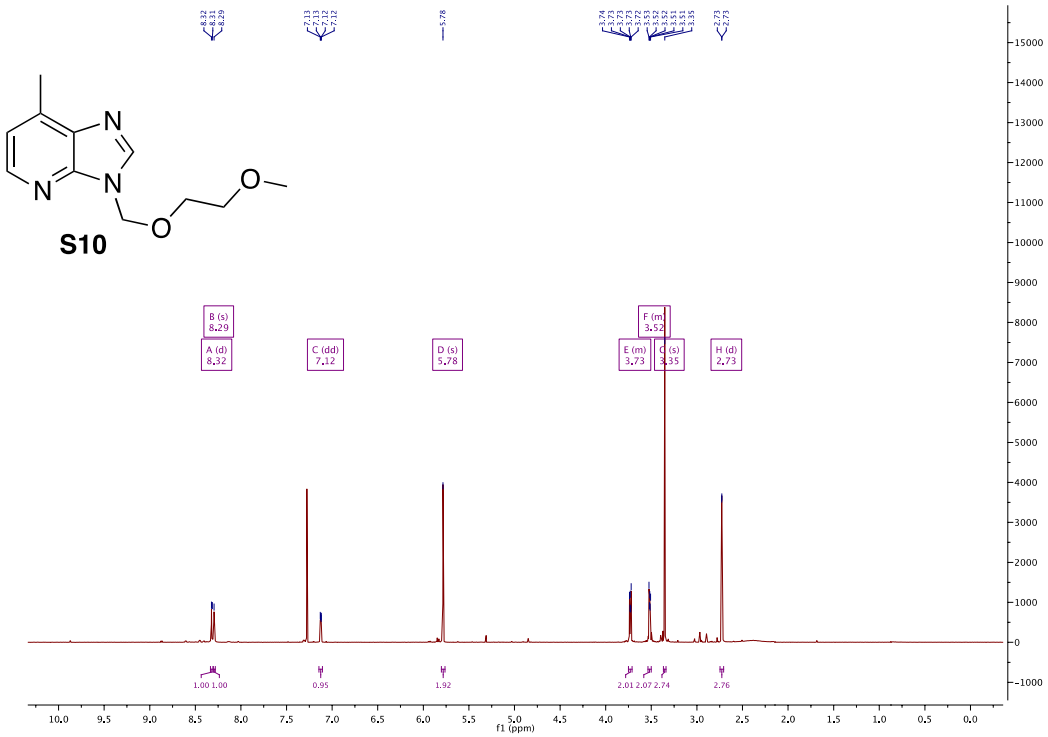
^{1}H NMR:



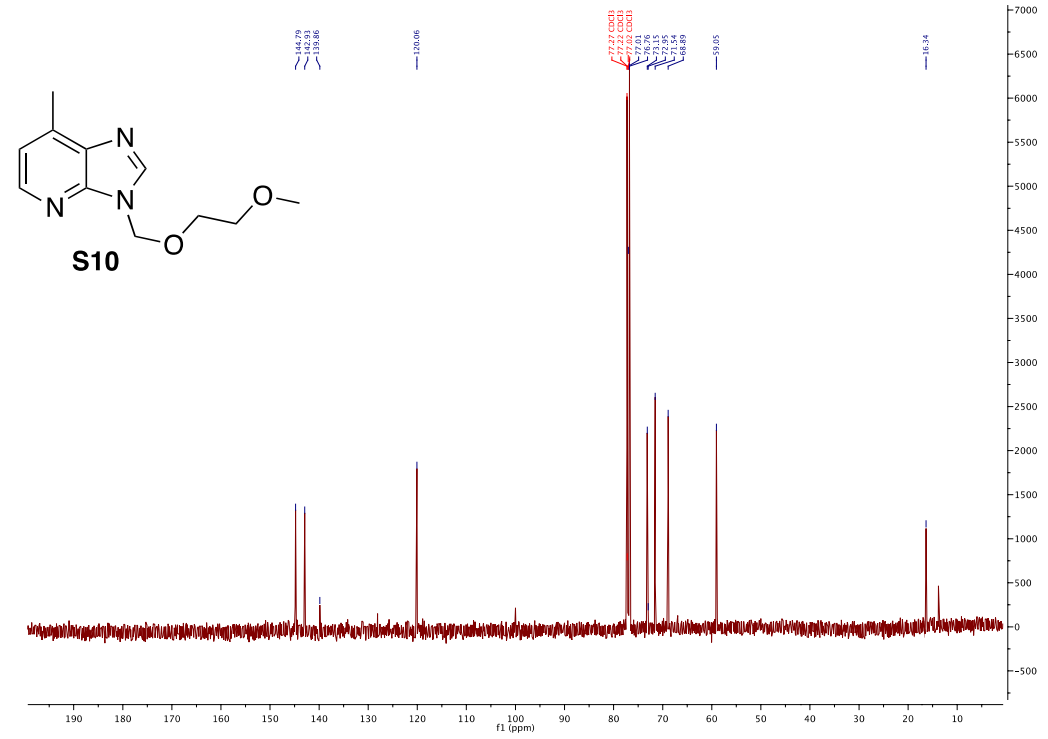
^{13}C NMR:



^{1}H NMR:

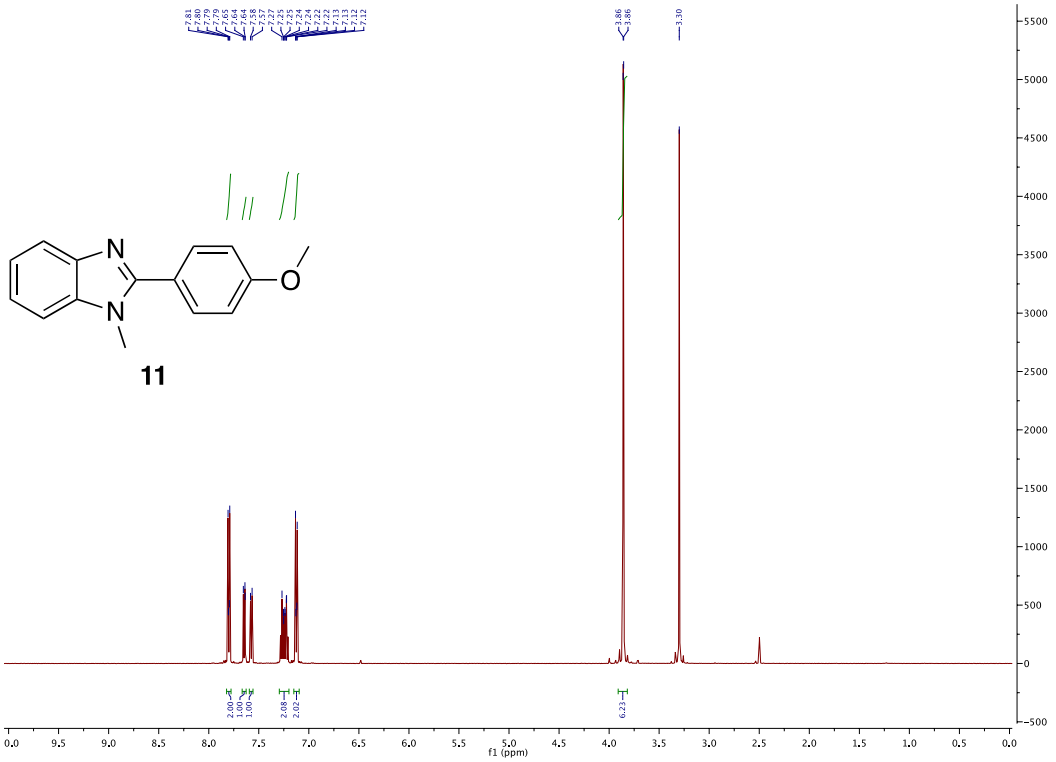


^{13}C NMR:

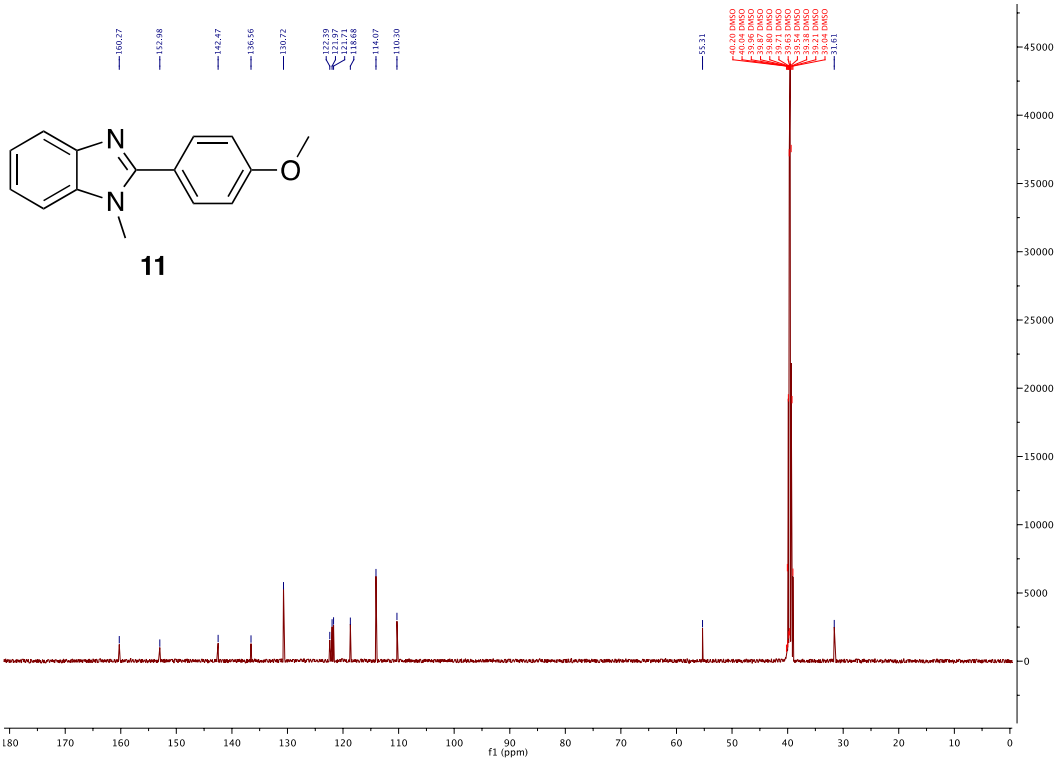


5.2 Spectra of C-H arylation products

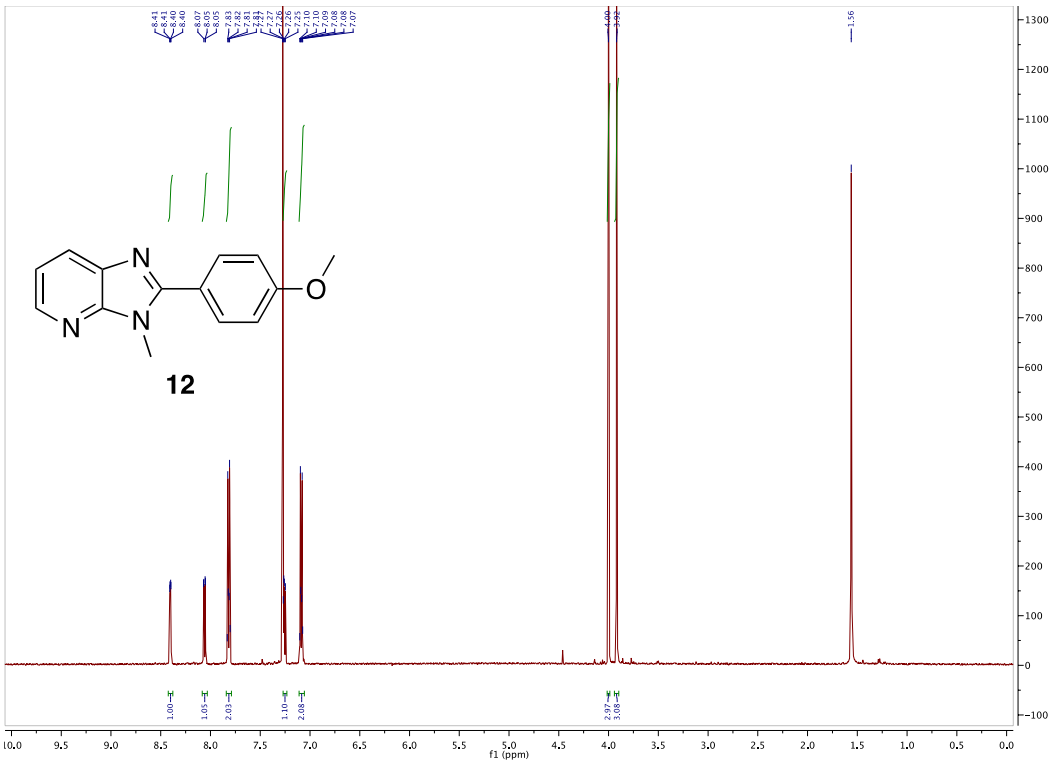
^{1}H NMR:



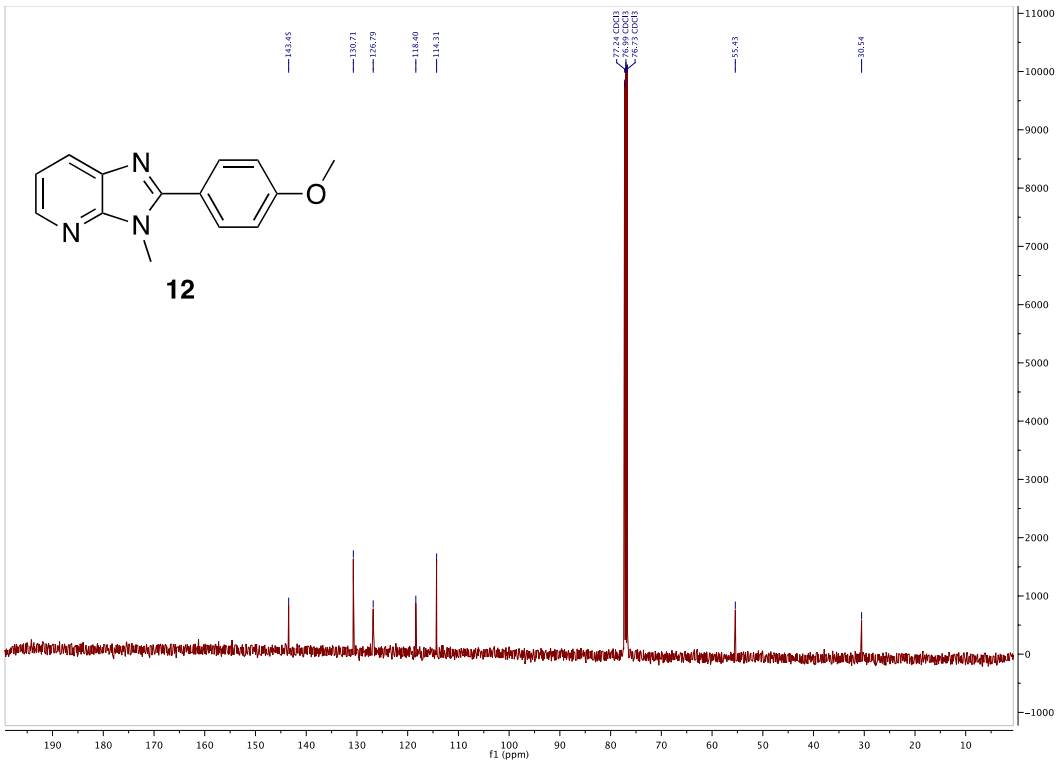
^{13}C NMR:



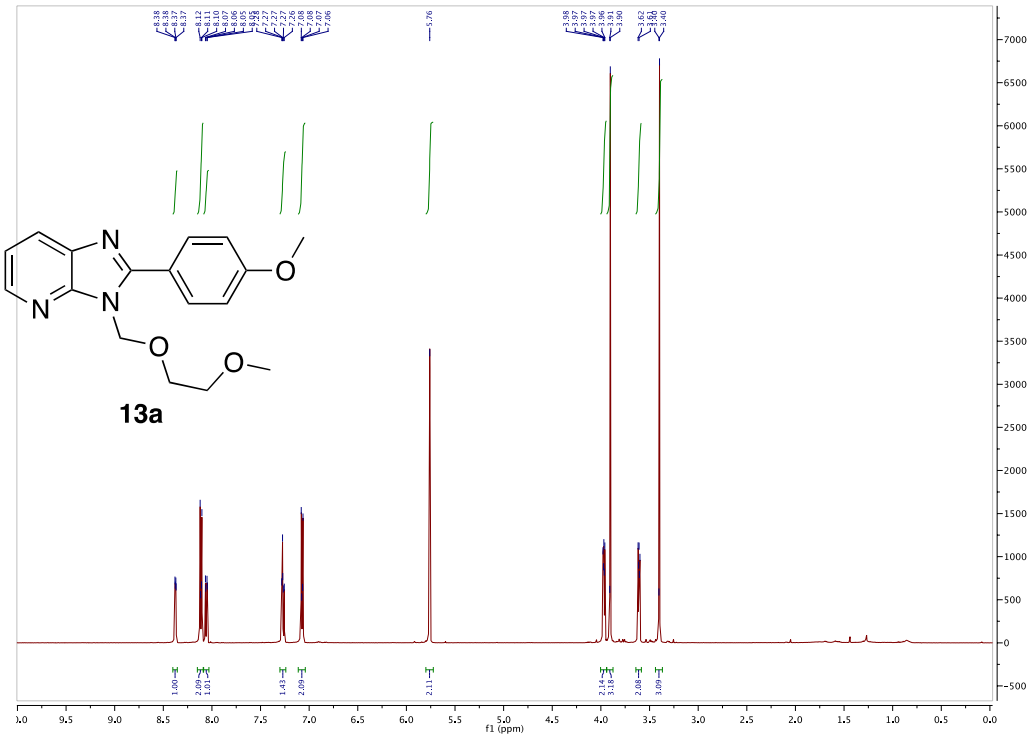
^{1}H NMR:



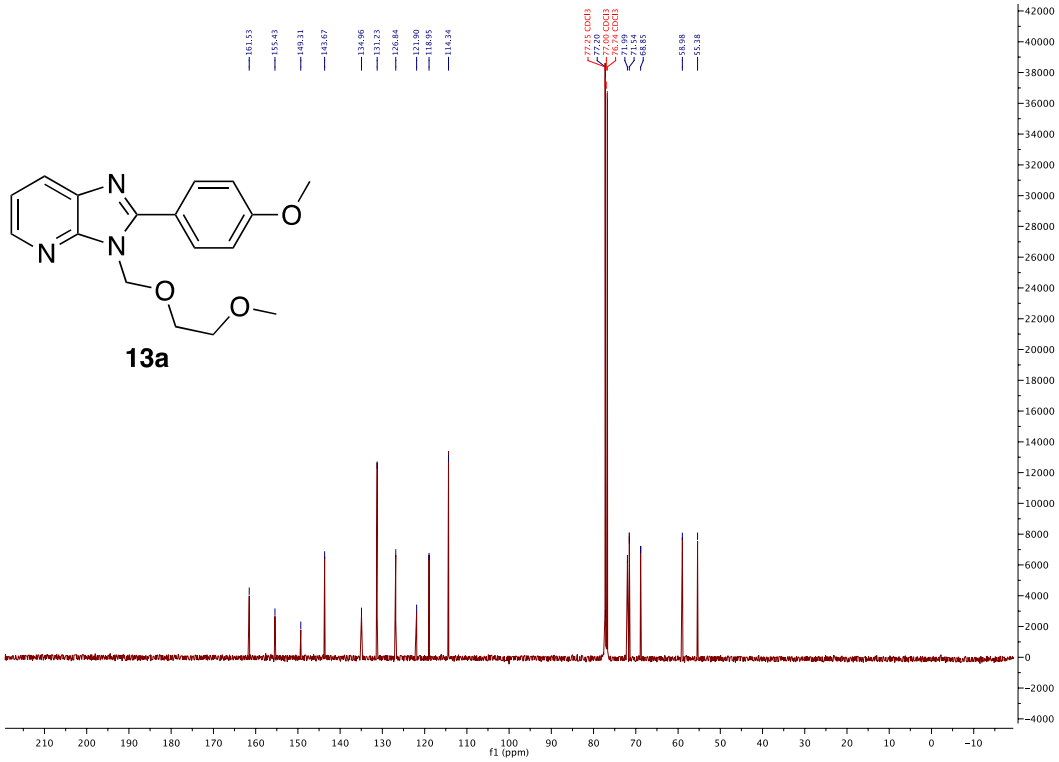
^{13}C NMR:



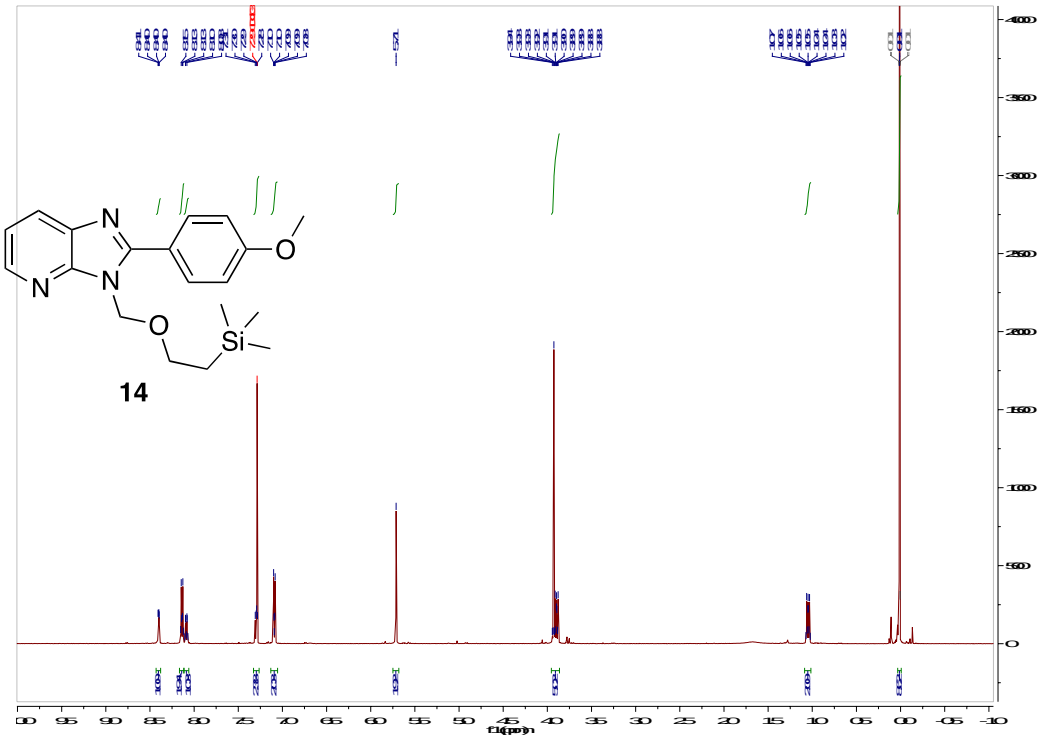
^{1}H NMR:



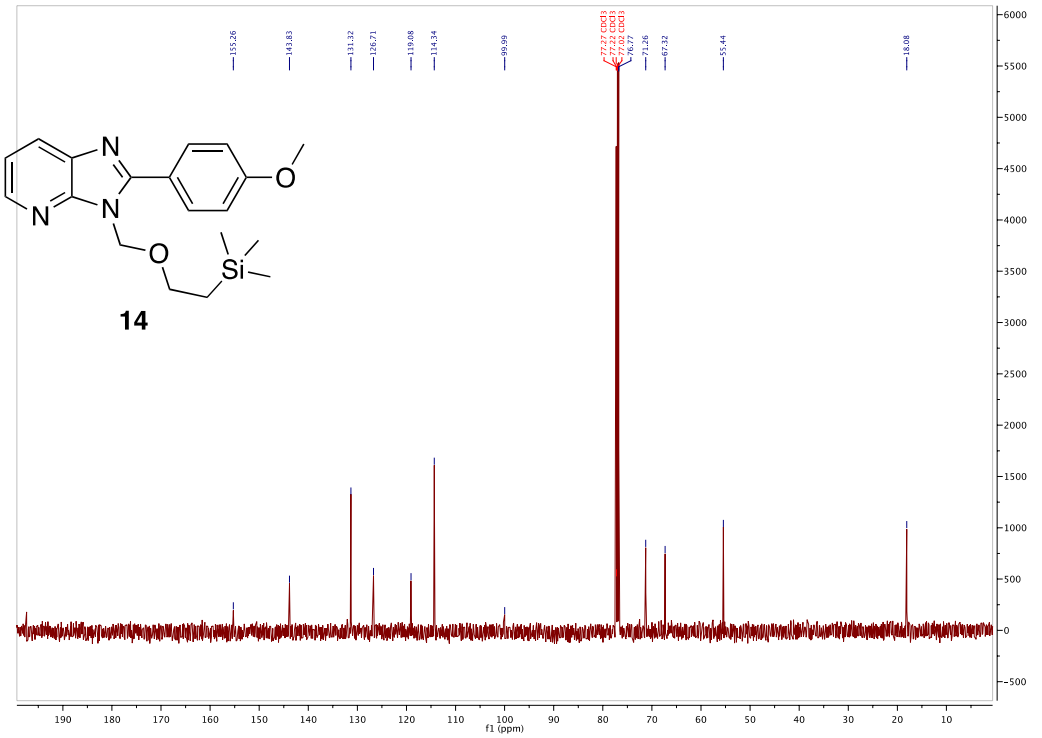
^{13}C NMR:



^{1}H NMR:

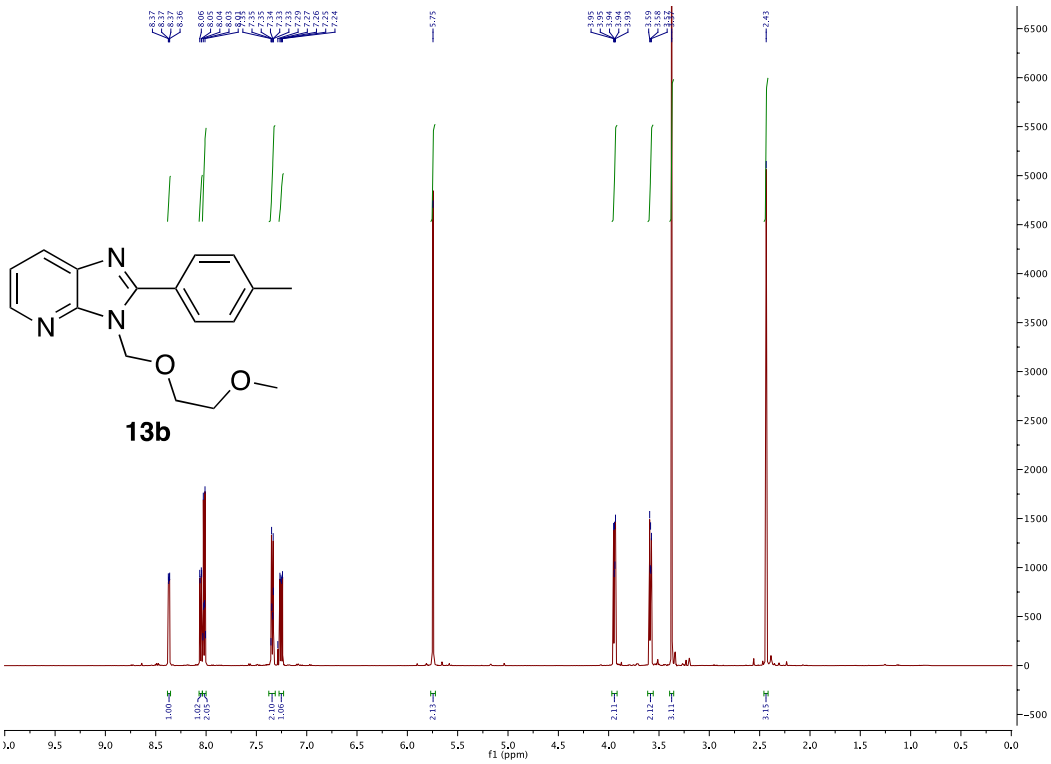


^{13}C NMR:

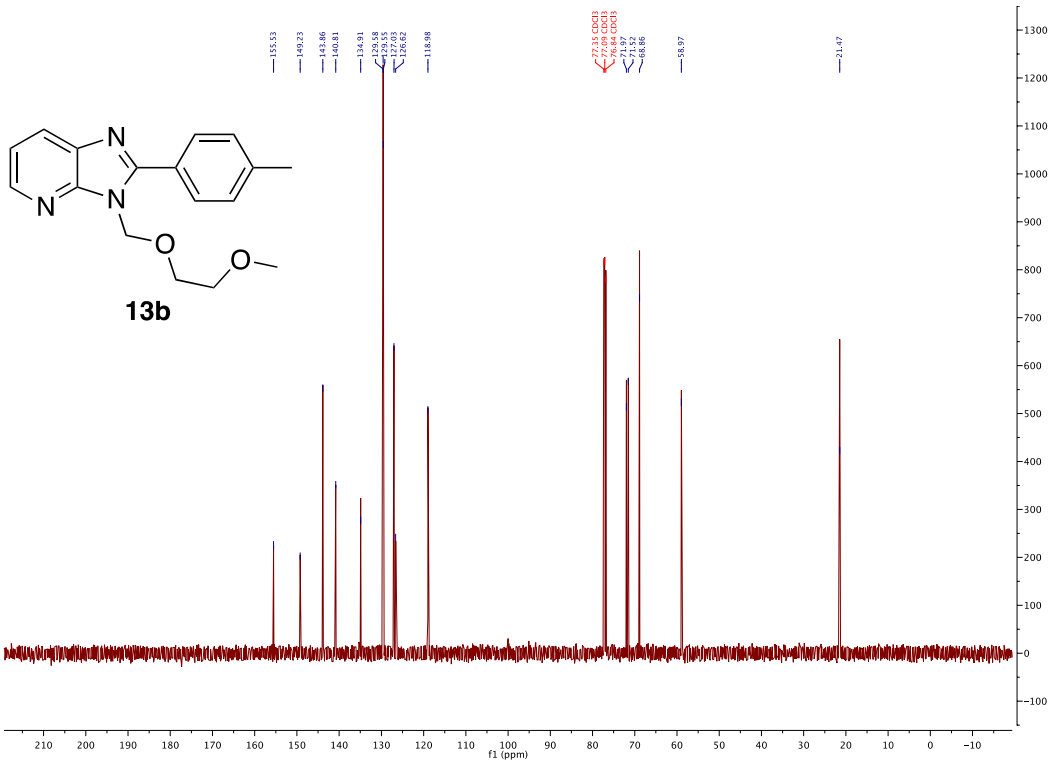


^{13}C peak for $Si(CH_3)_3$ assigned from HSQC experiment, δ_C = -1.2 ppm.

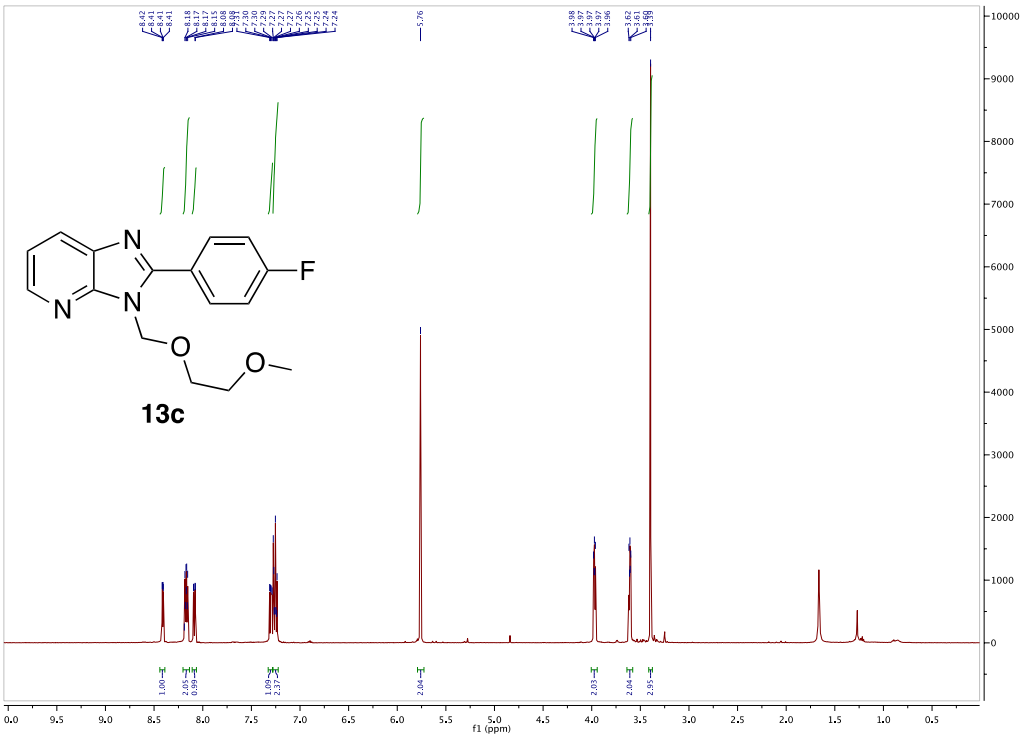
^{1}H NMR:



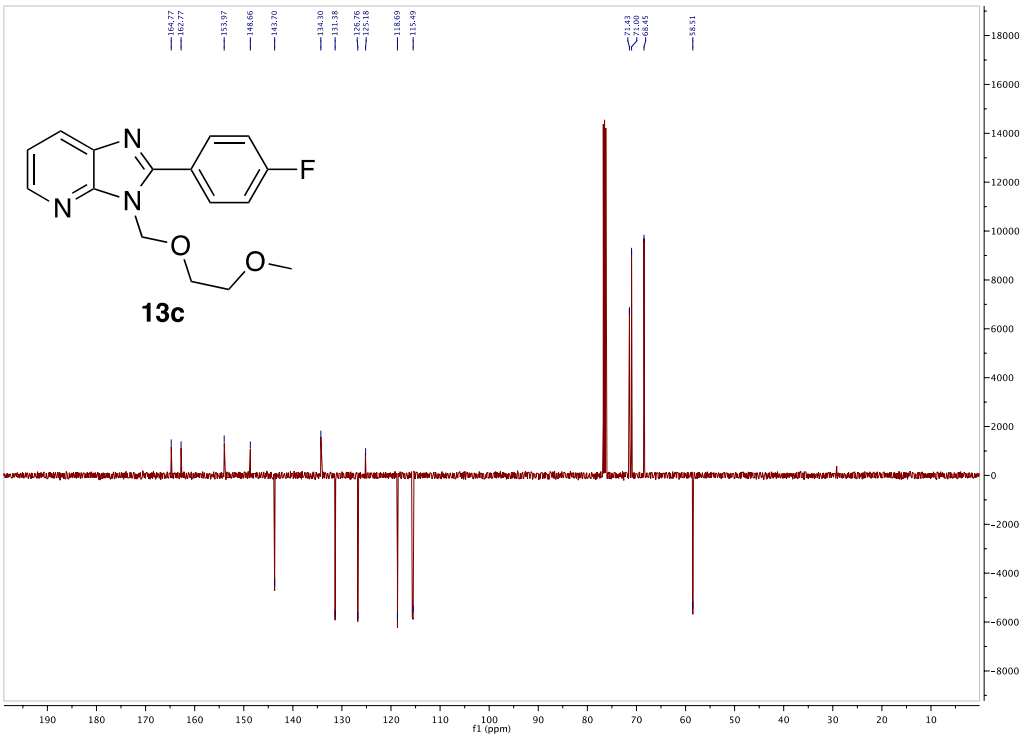
^{13}C NMR:



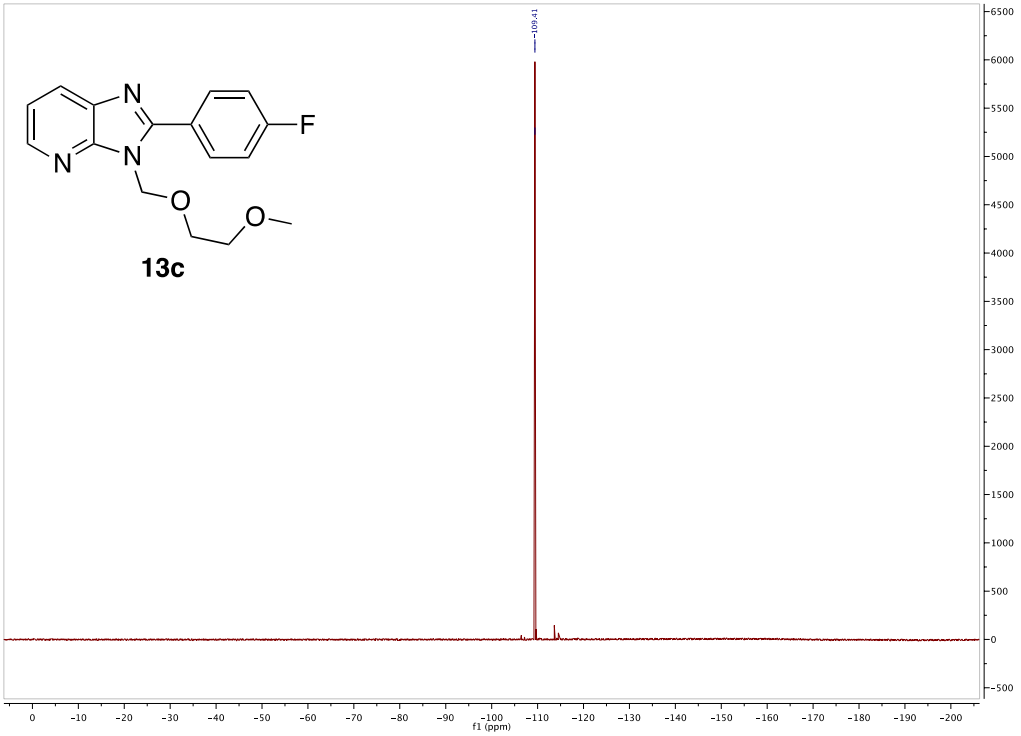
^{1}H NMR:



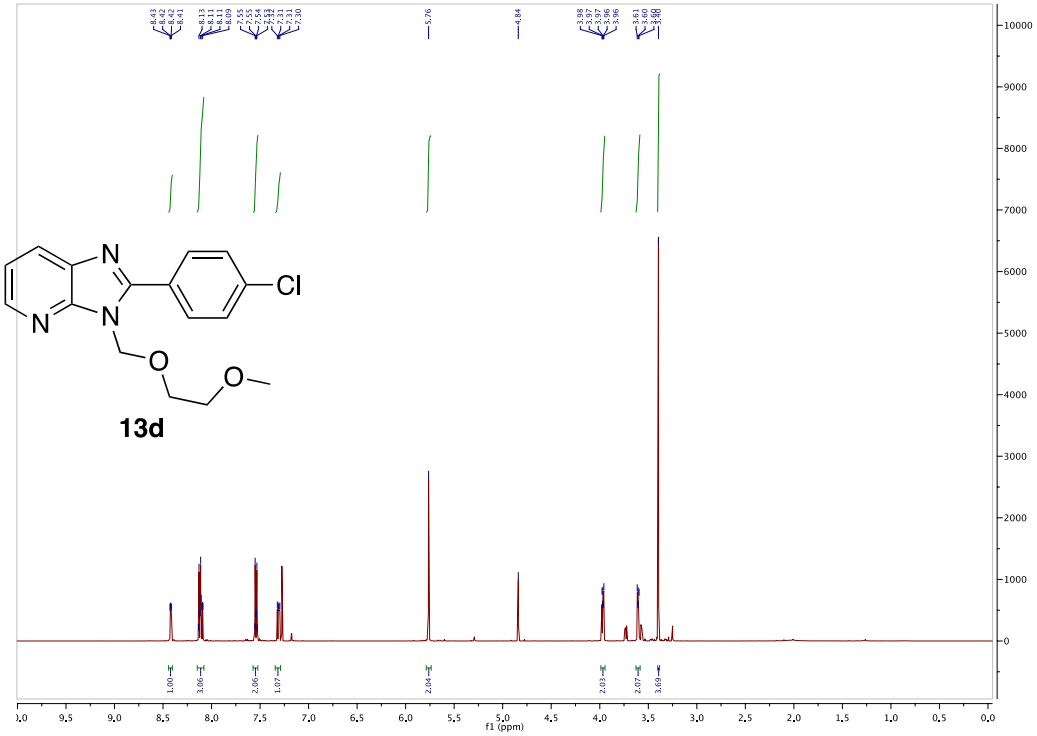
^{13}C NMR, DEPT135:



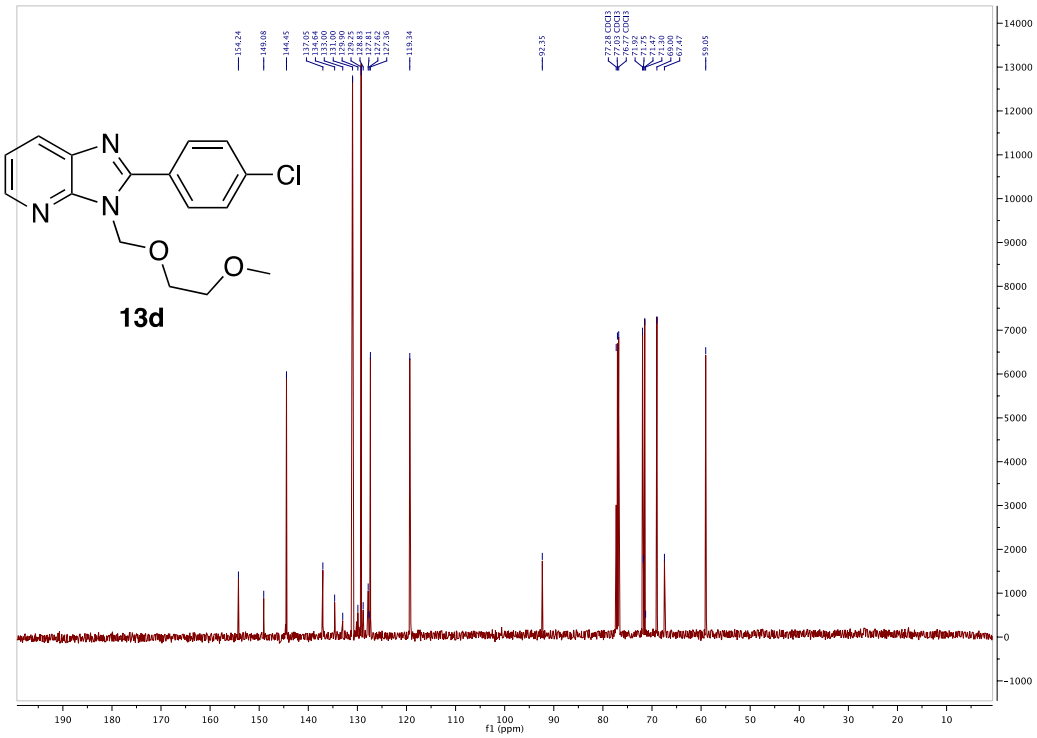
^{19}F NMR:



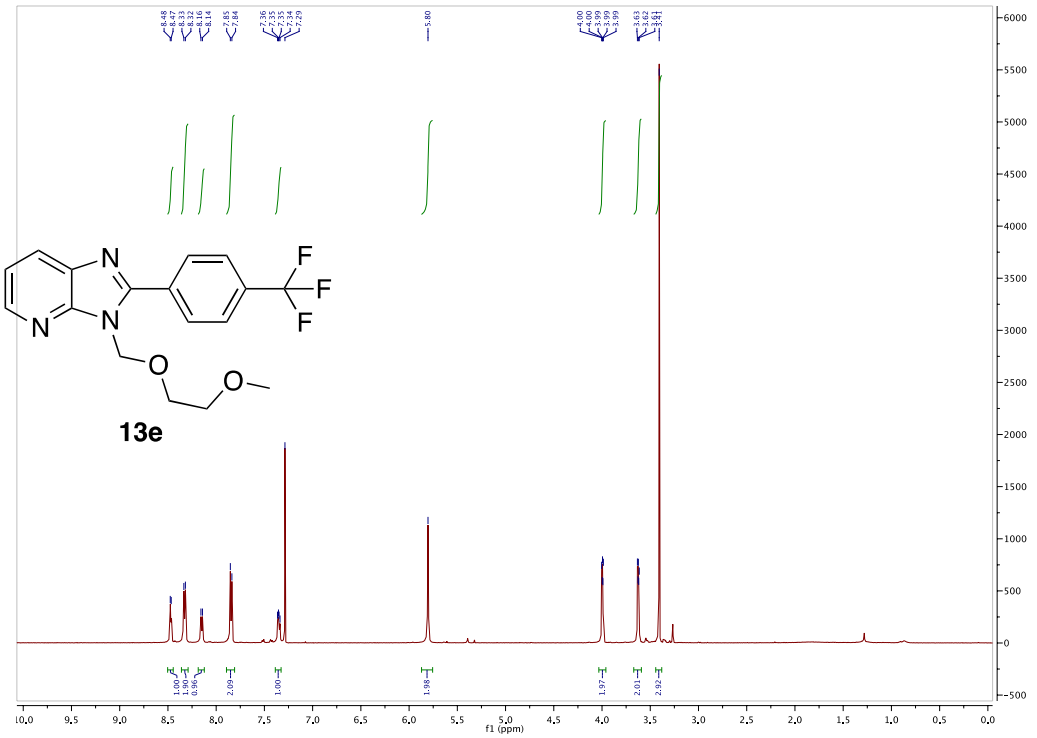
^{1}H NMR:



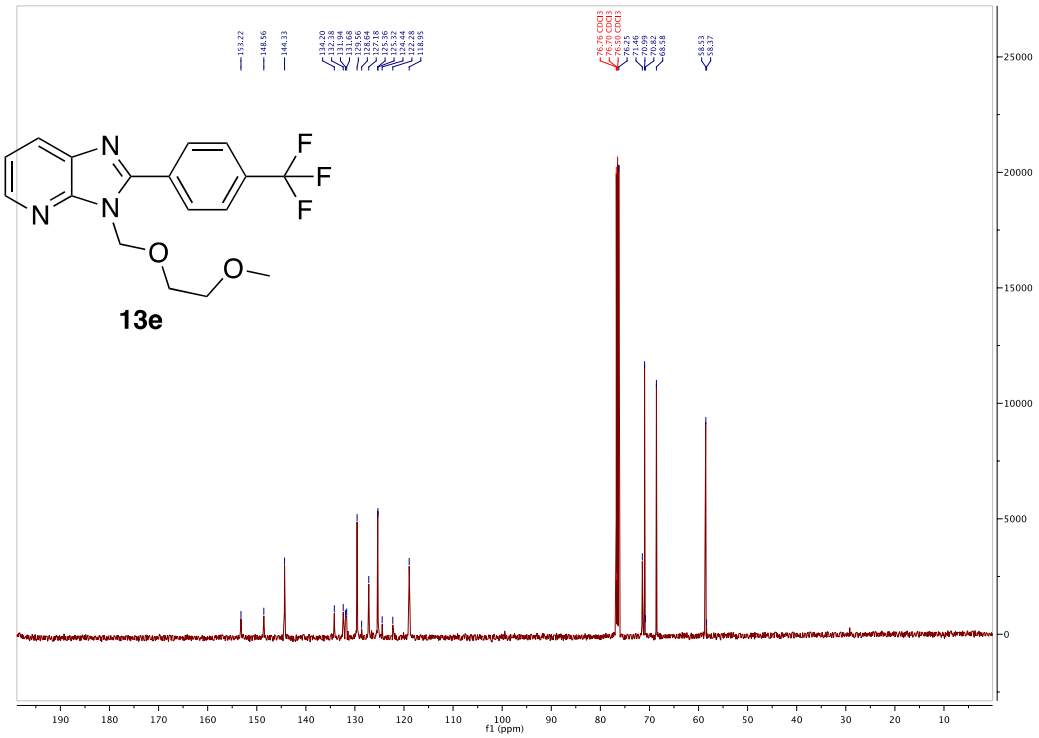
^{13}C NMR:



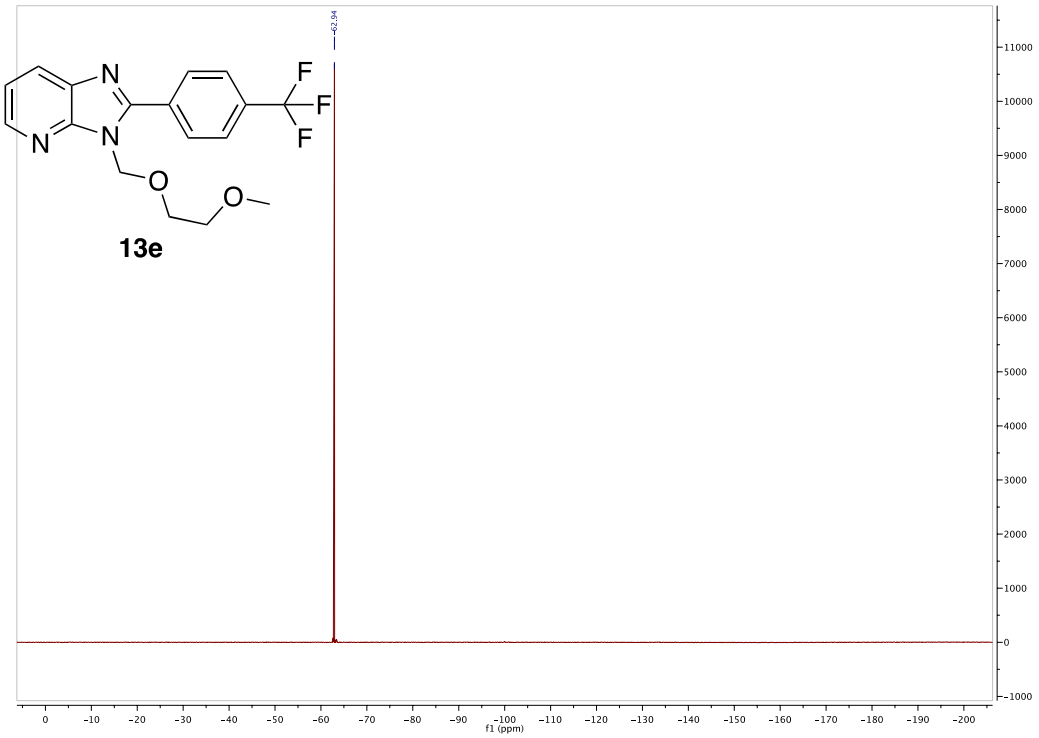
^{1}H NMR:



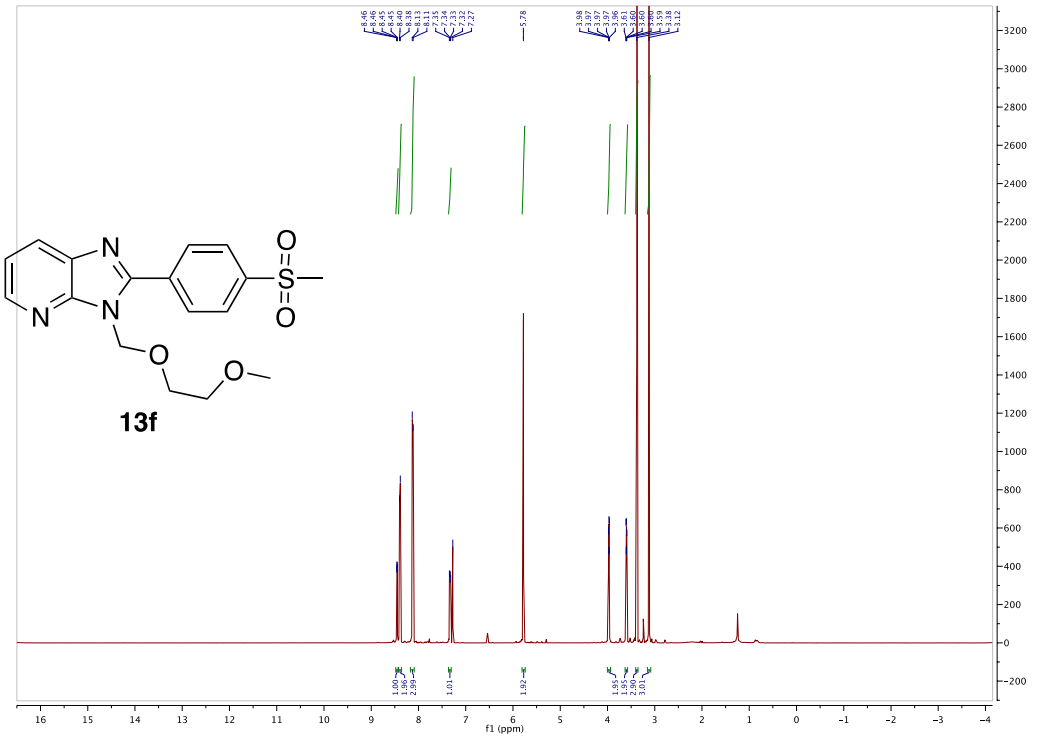
^{13}C NMR:



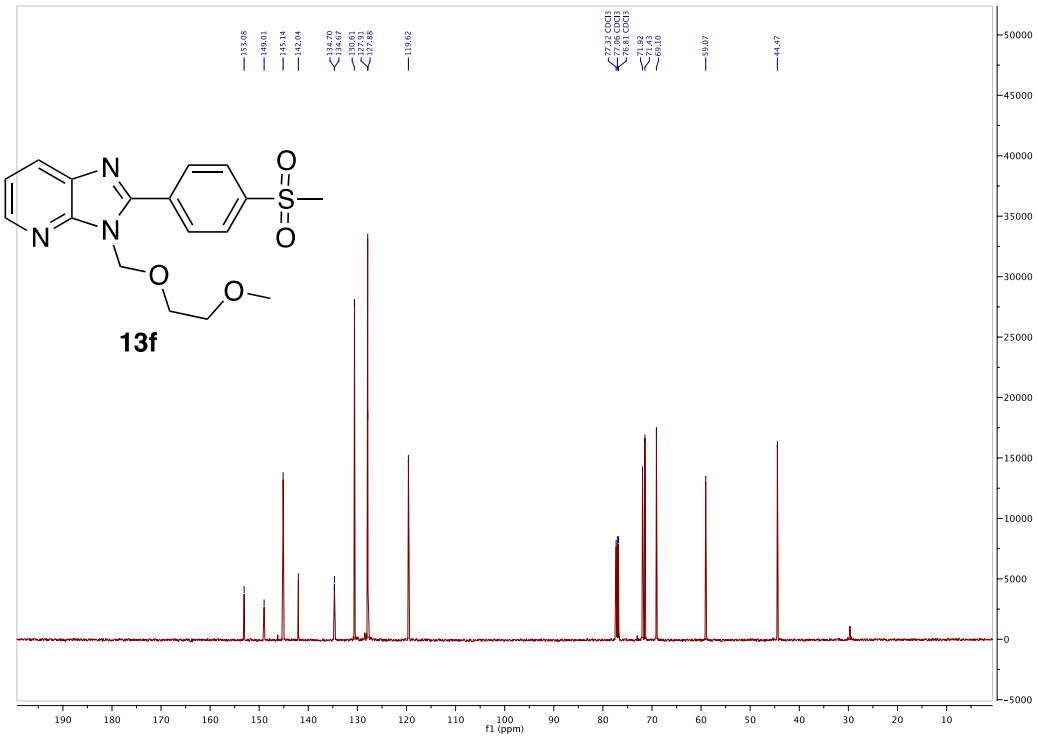
^{19}F NMR:



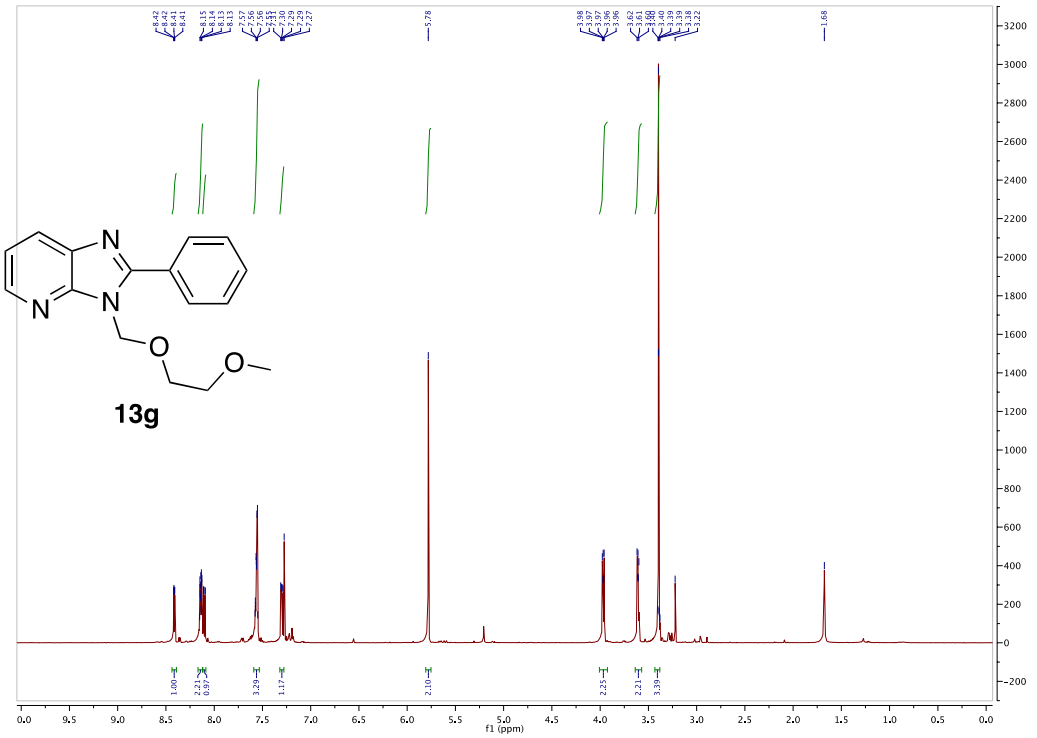
^{1}H NMR:



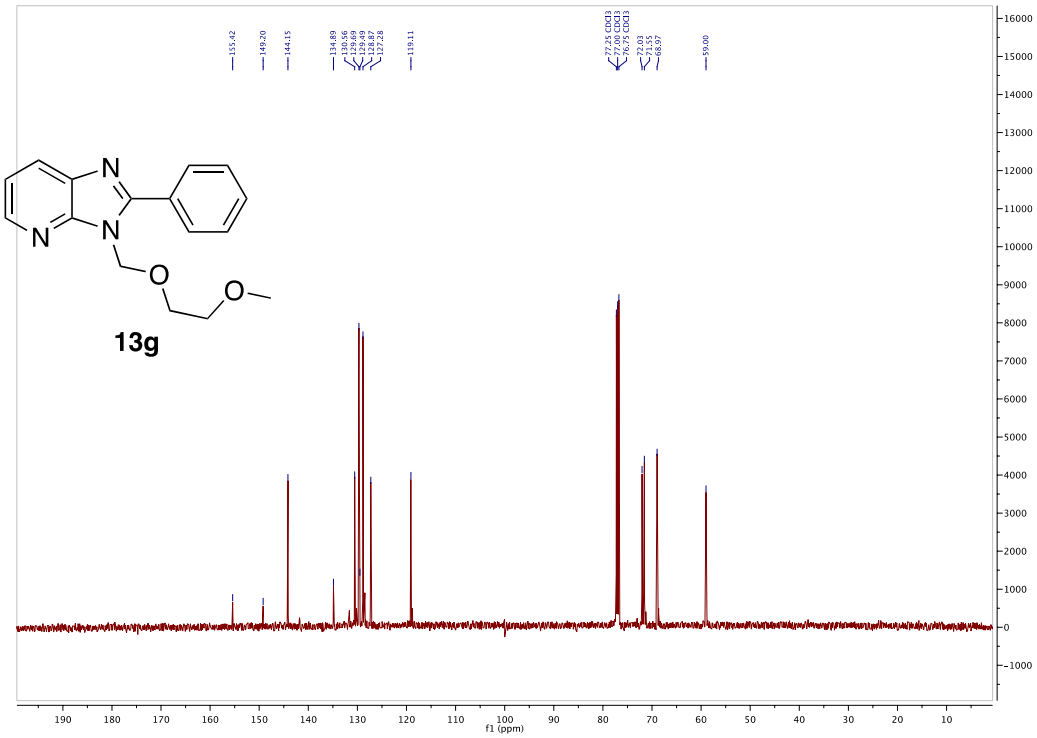
^{13}C NMR:



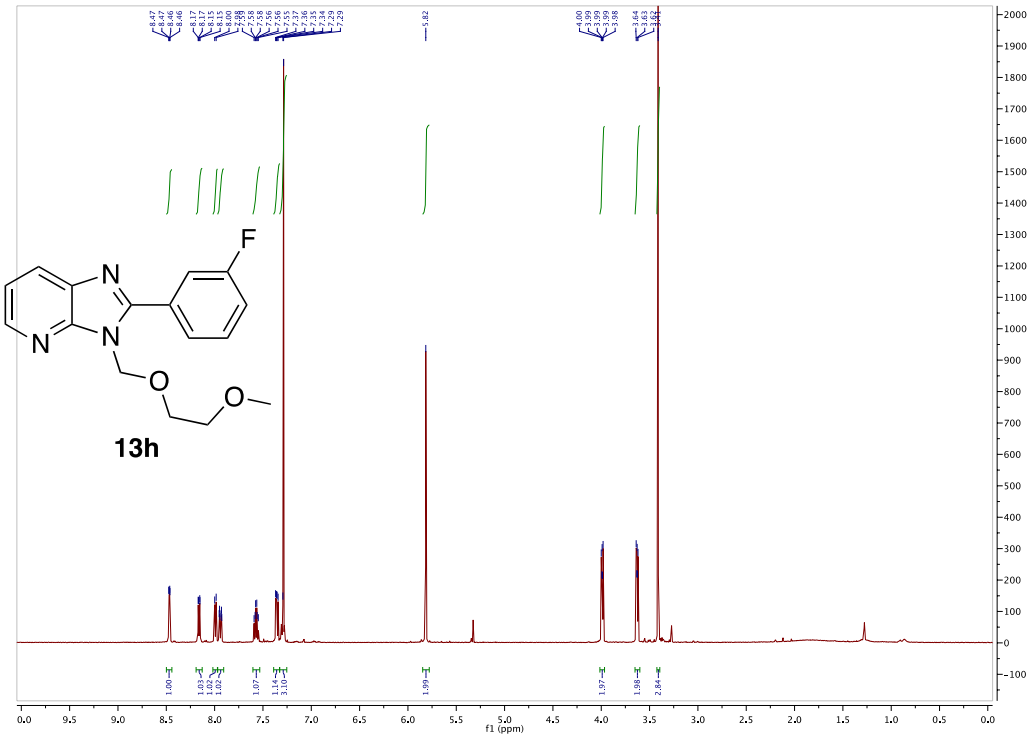
^{1}H NMR:



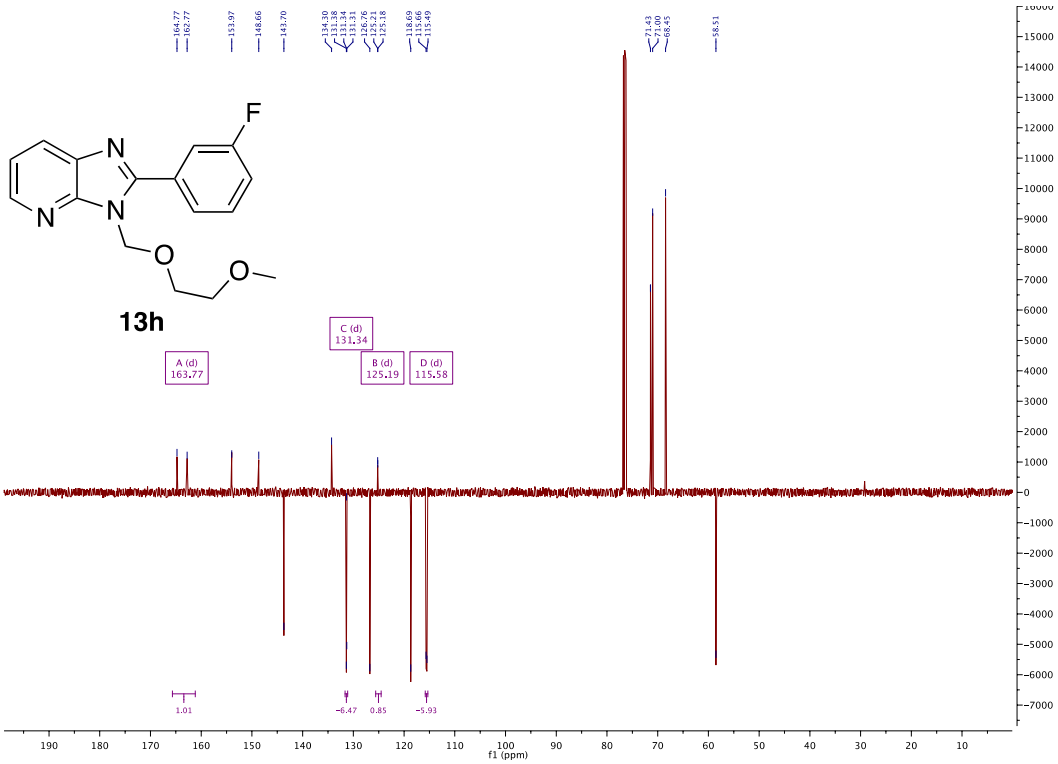
^{13}C NMR:



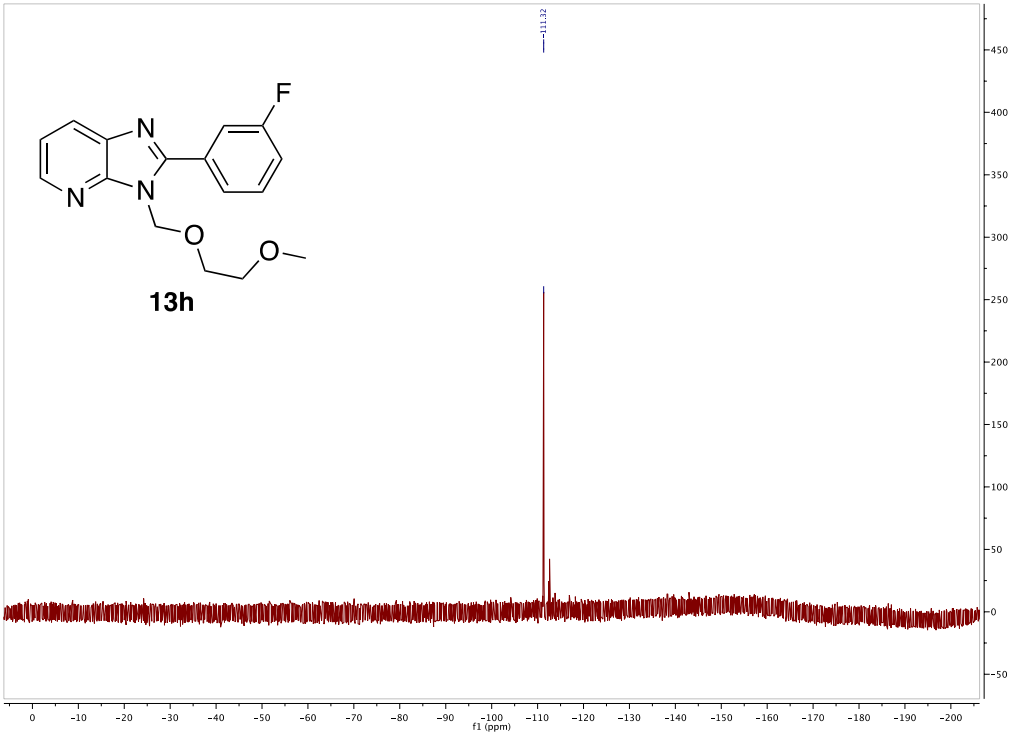
^{1}H NMR:



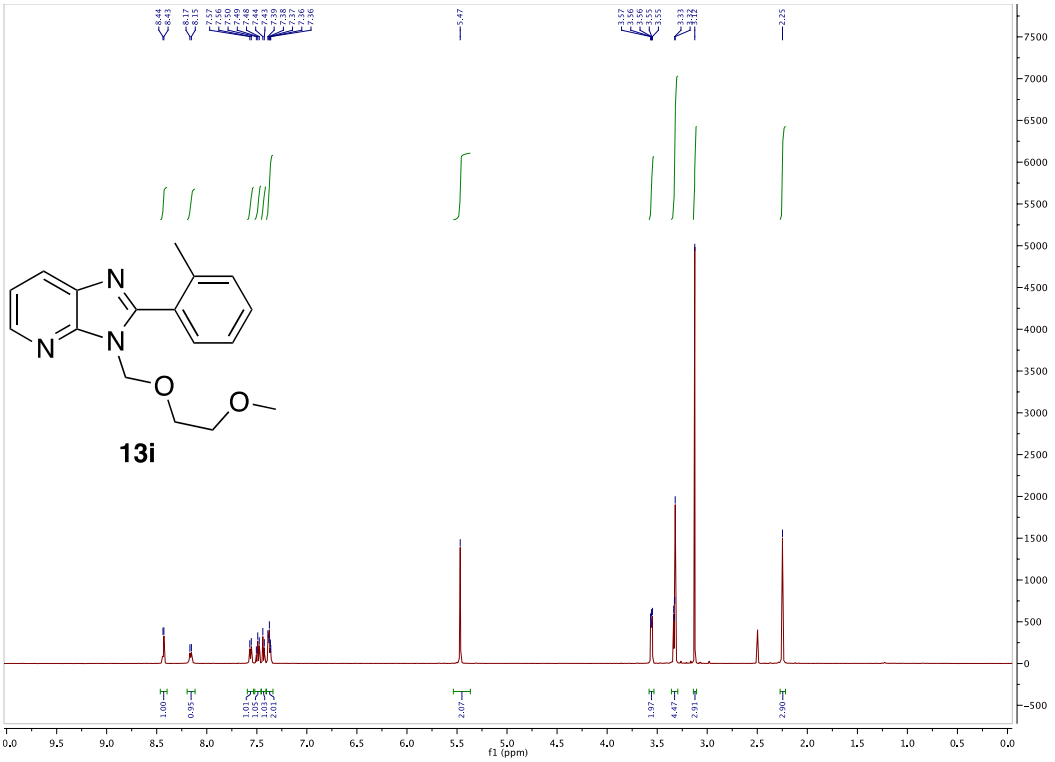
^{13}C NMR:



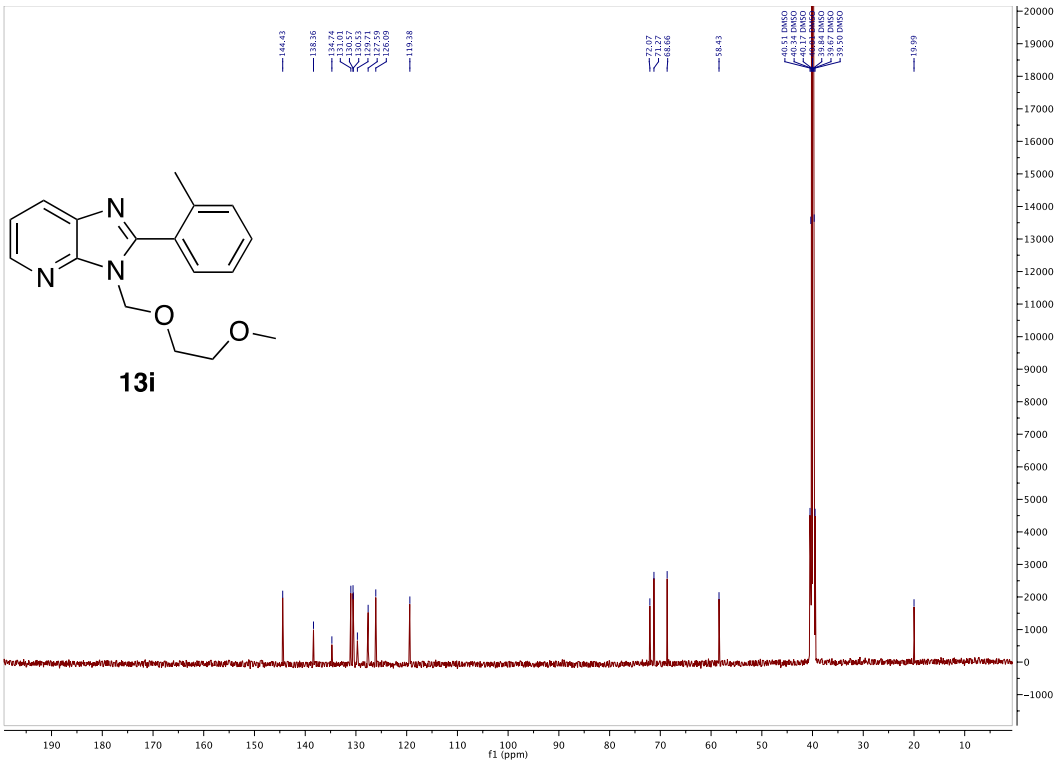
^{19}F NMR:


F
N
N
N
O
O
13h
-111.32
450
400
350
300
250
200
150
100
50
0
-50
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

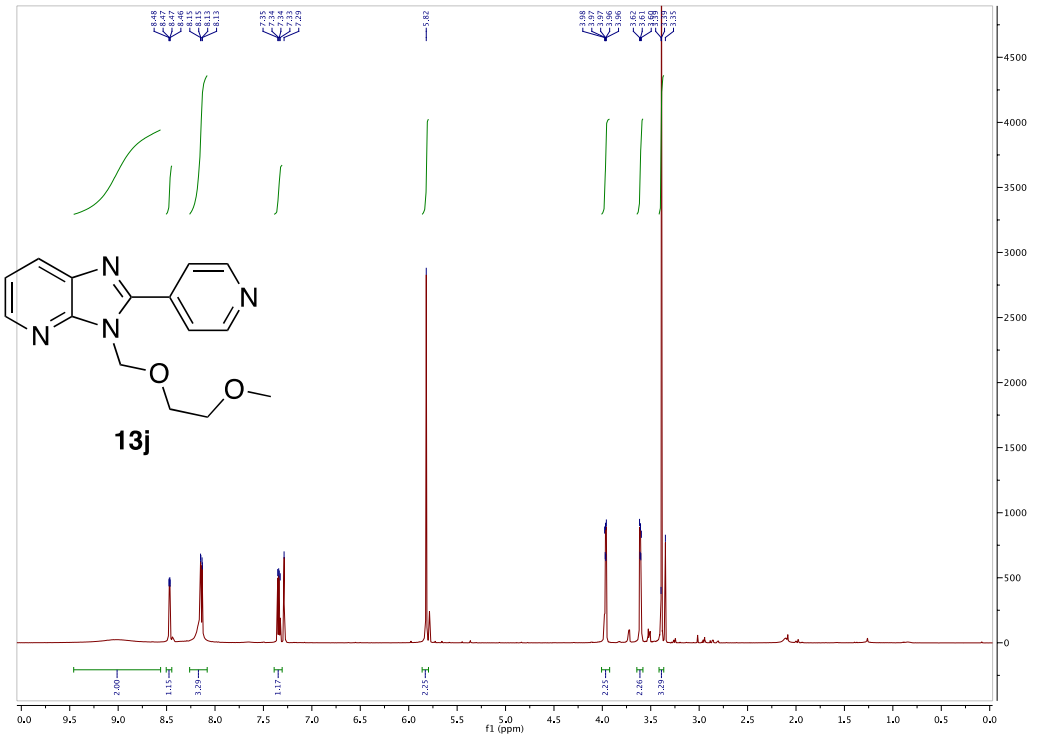
^{1}H NMR:



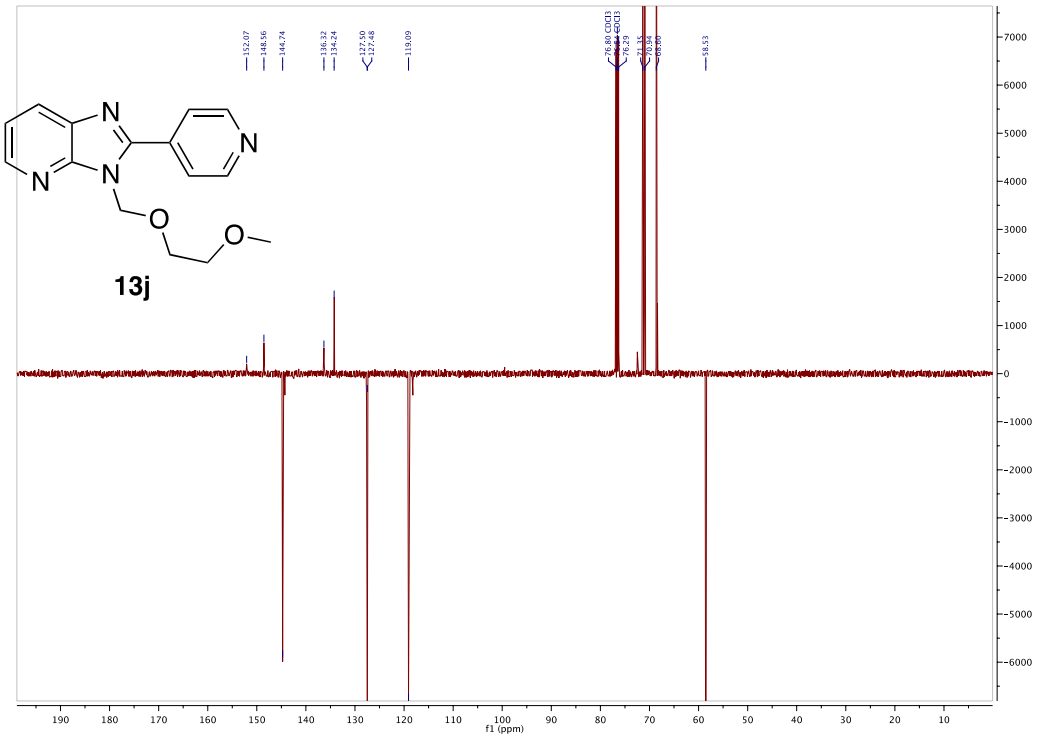
^{13}C NMR:



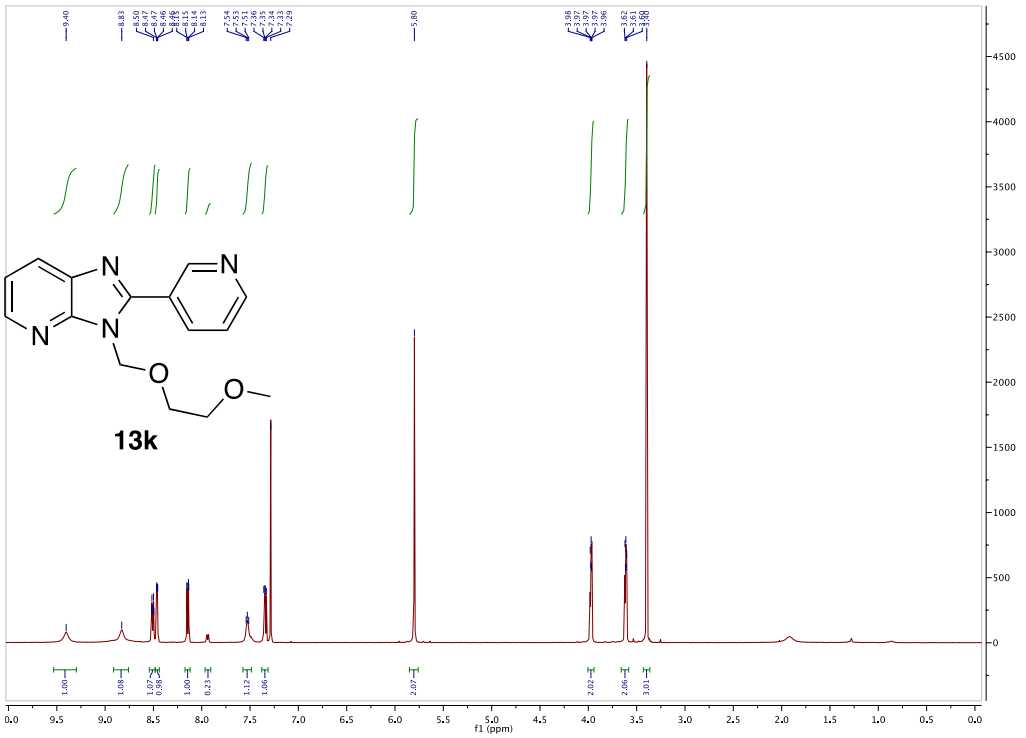
^{1}H NMR:



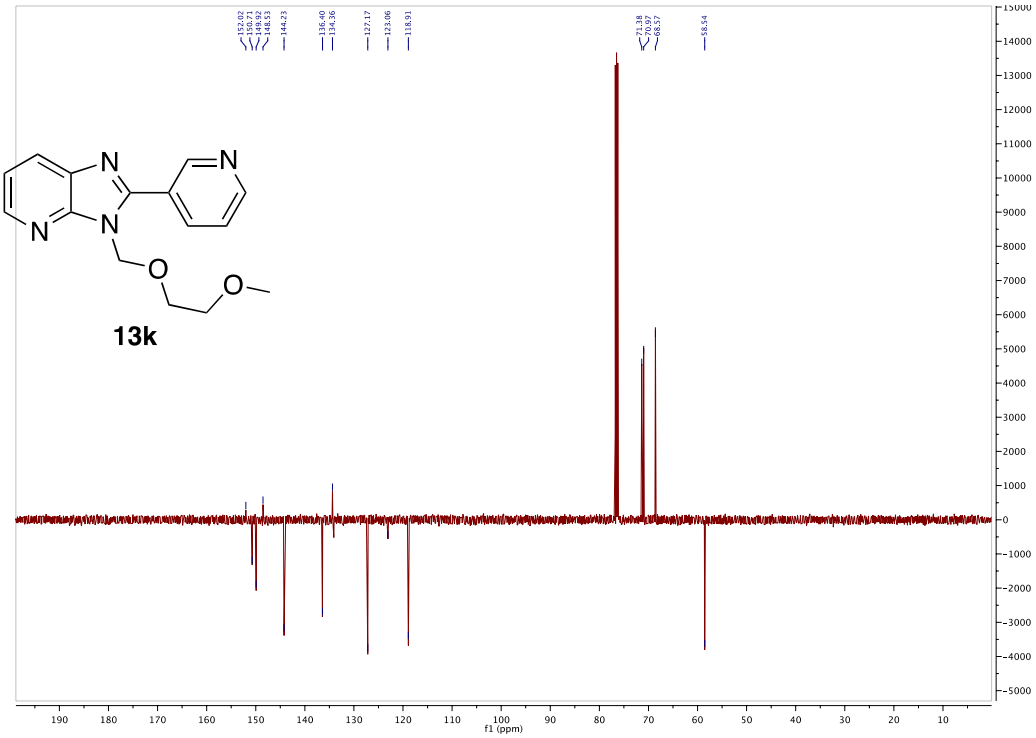
^{13}C NMR, DEPT135:



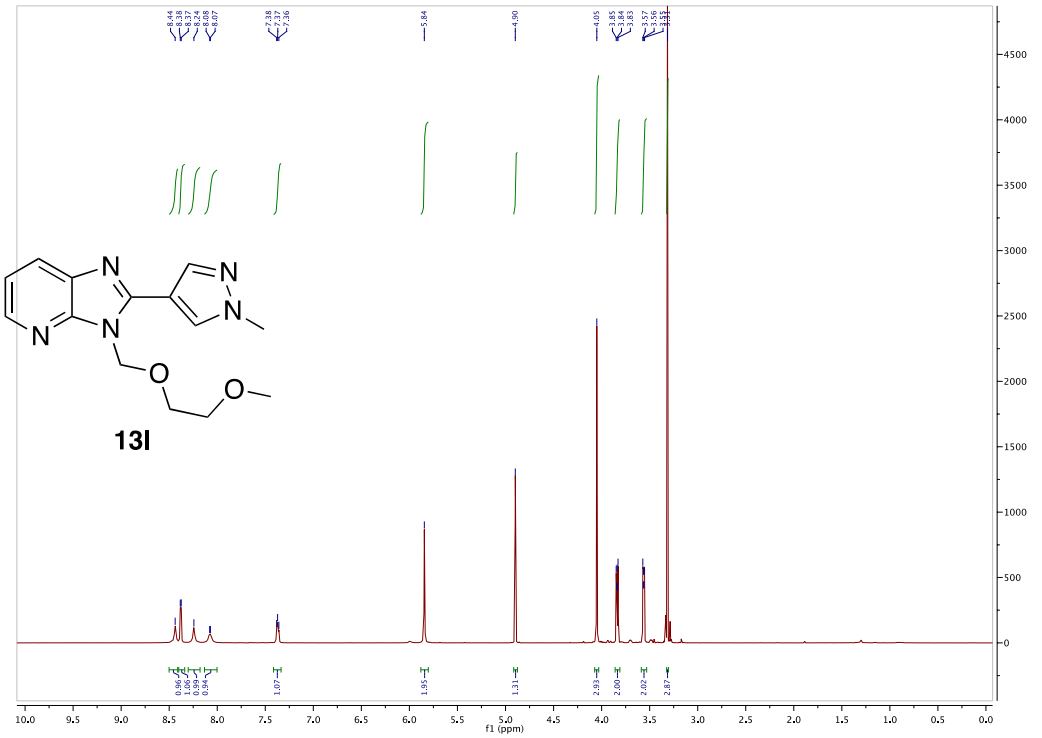
^{1}H NMR:



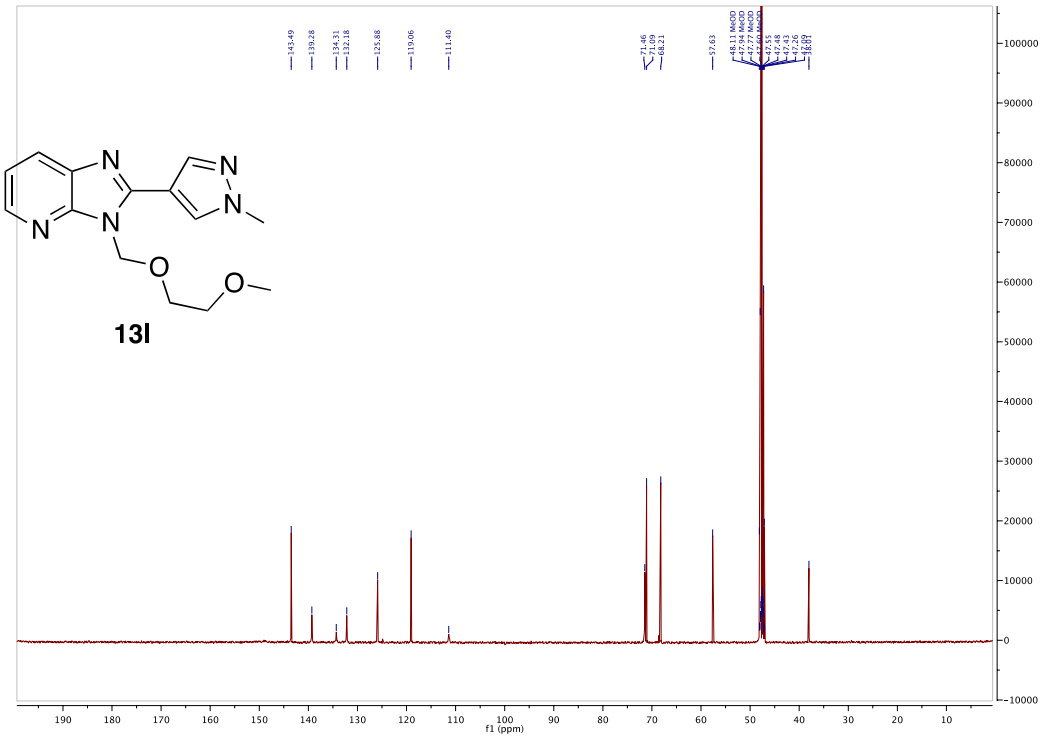
^{13}C NMR, DEPT135:



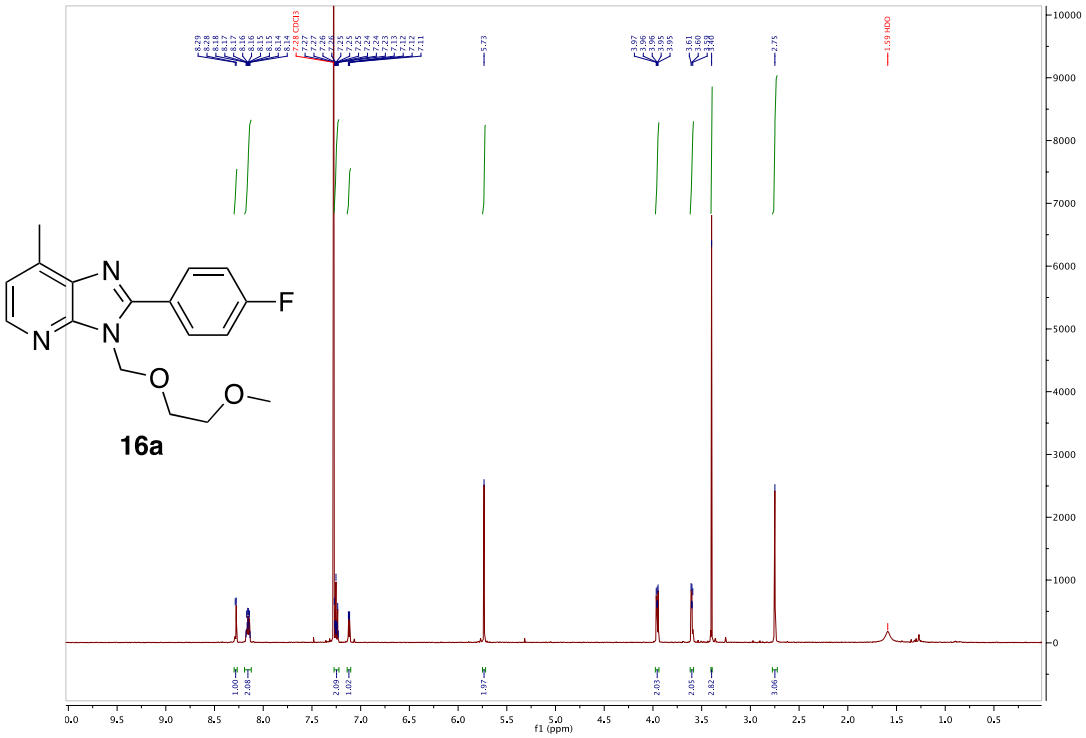
^{1}H NMR:



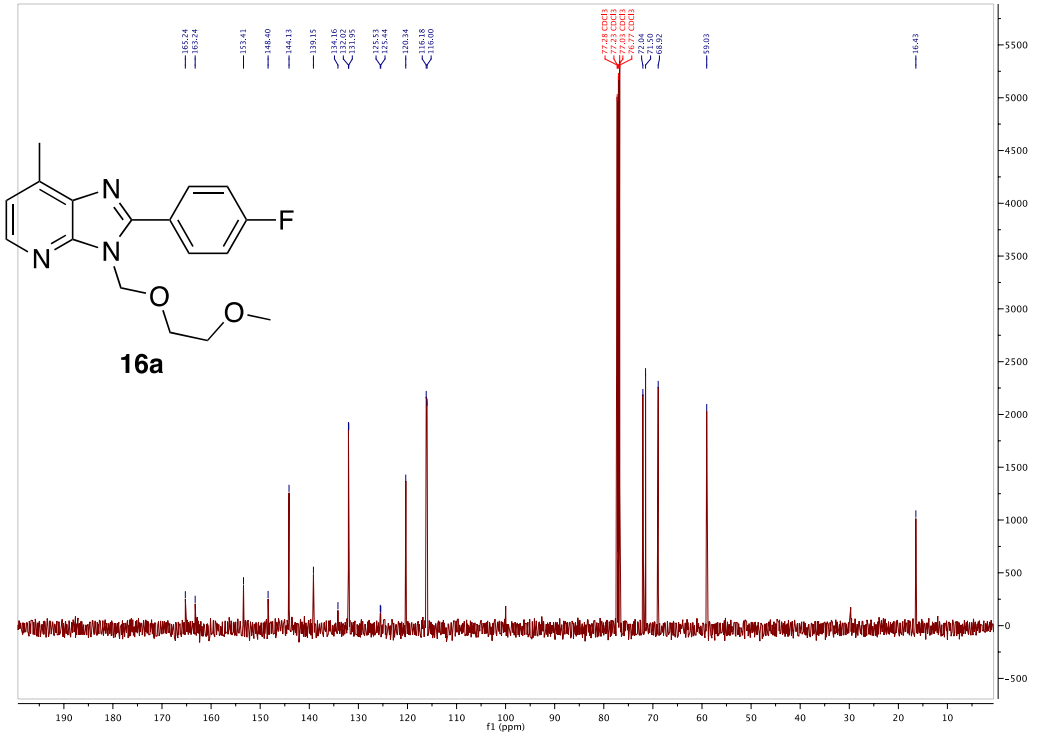
^{13}C NMR:



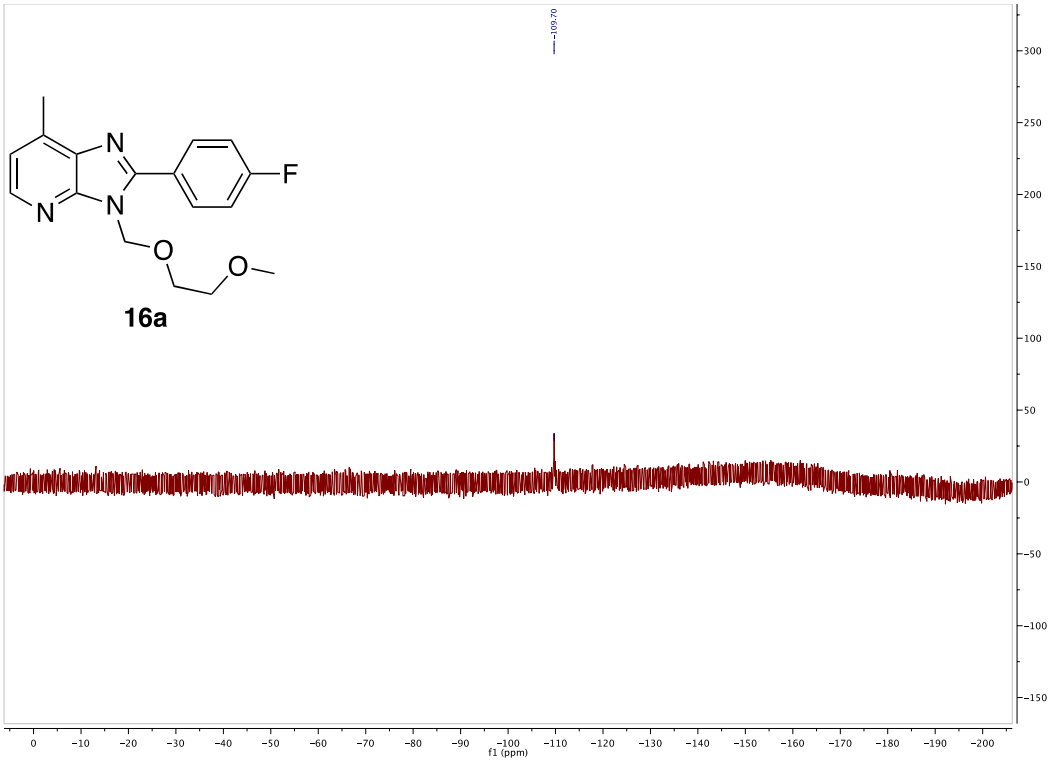
^{1}H NMR:



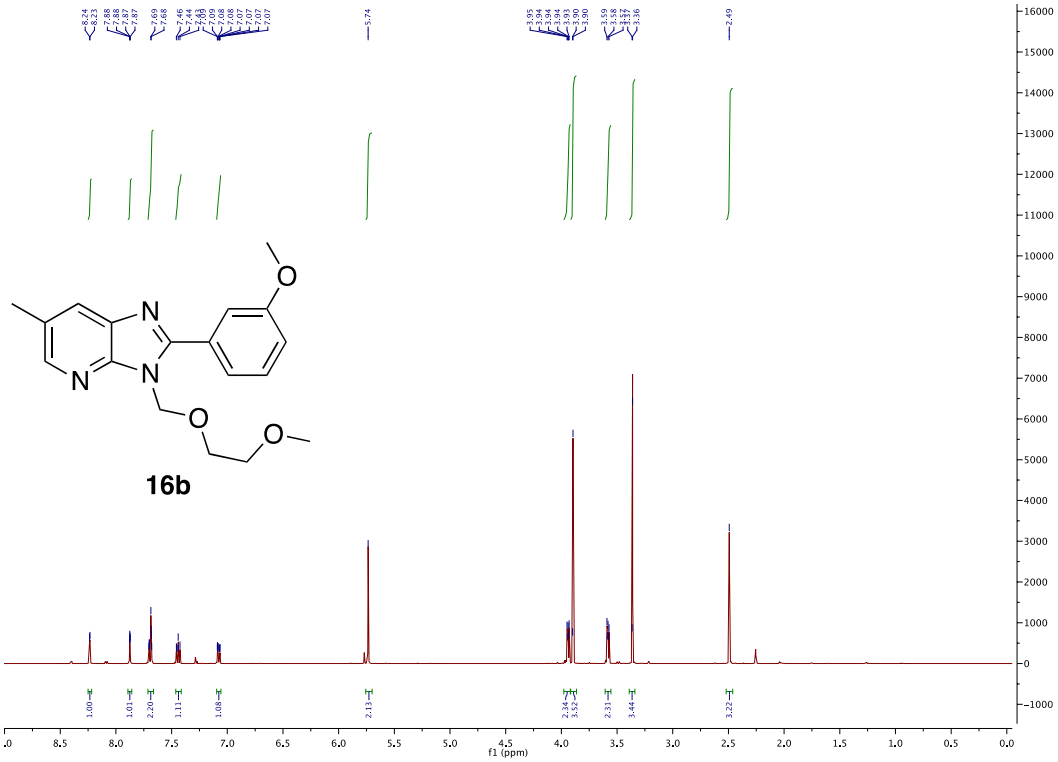
^{13}C NMR:



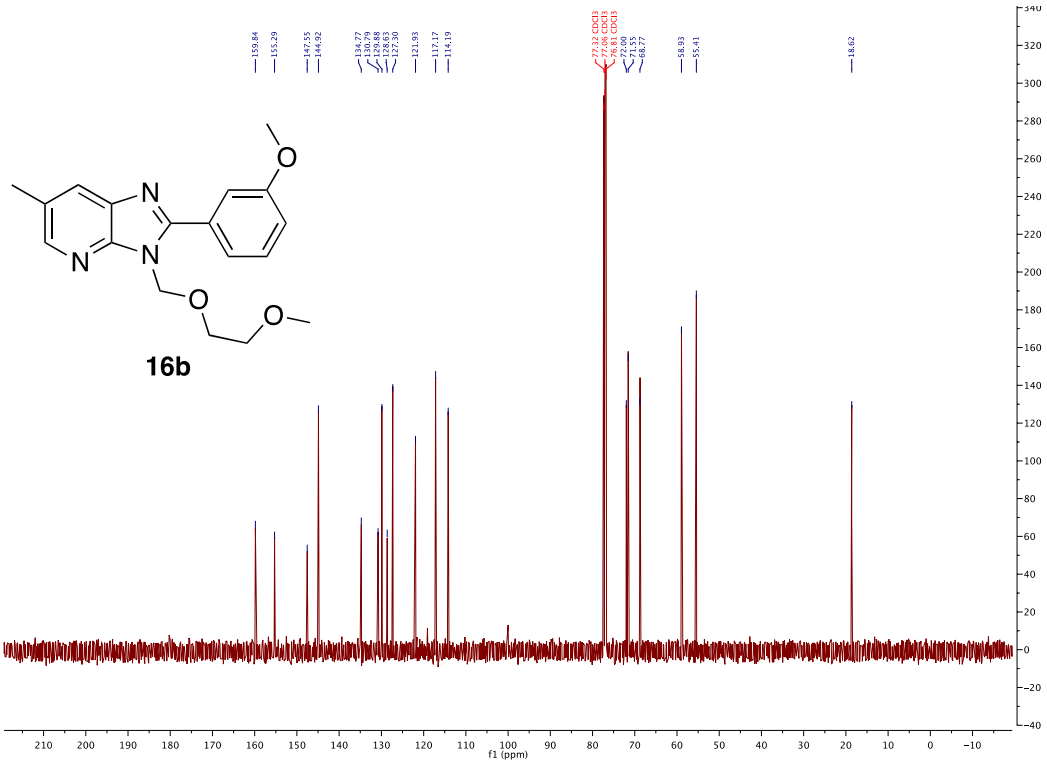
^{19}F NMR:


-109.70
N
N
F
O
O
16a
300
250
200
150
100
50
0
-50
-100
-150
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

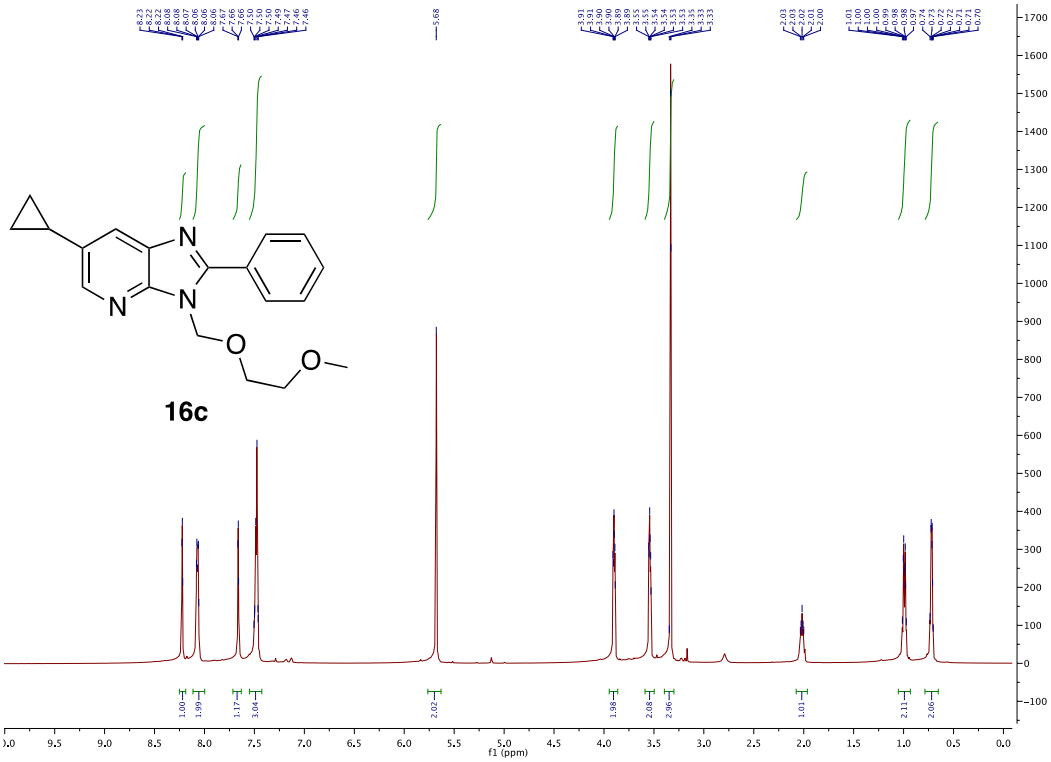
^{1}H NMR:



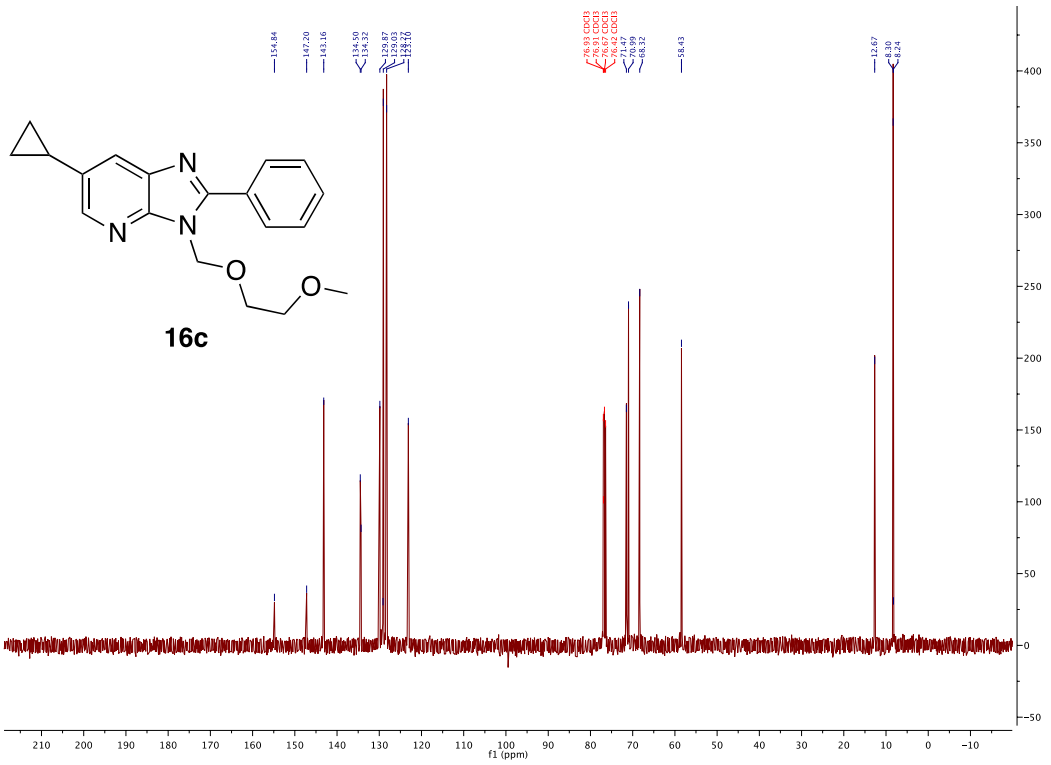
^{13}C NMR:



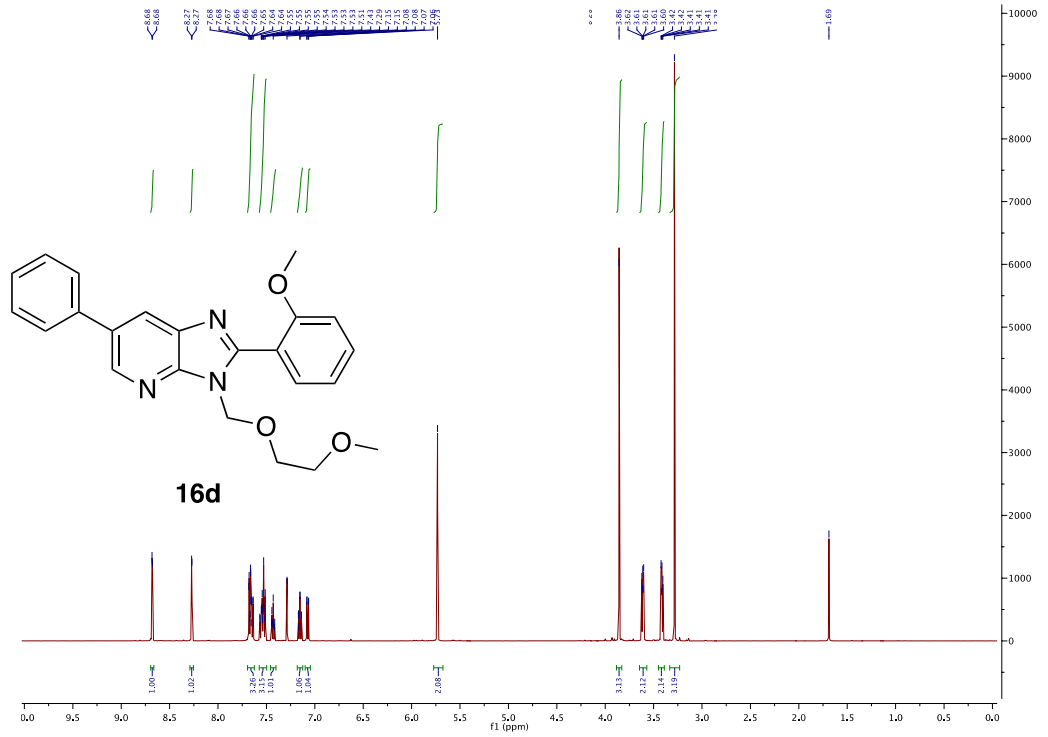
^{1}H NMR:



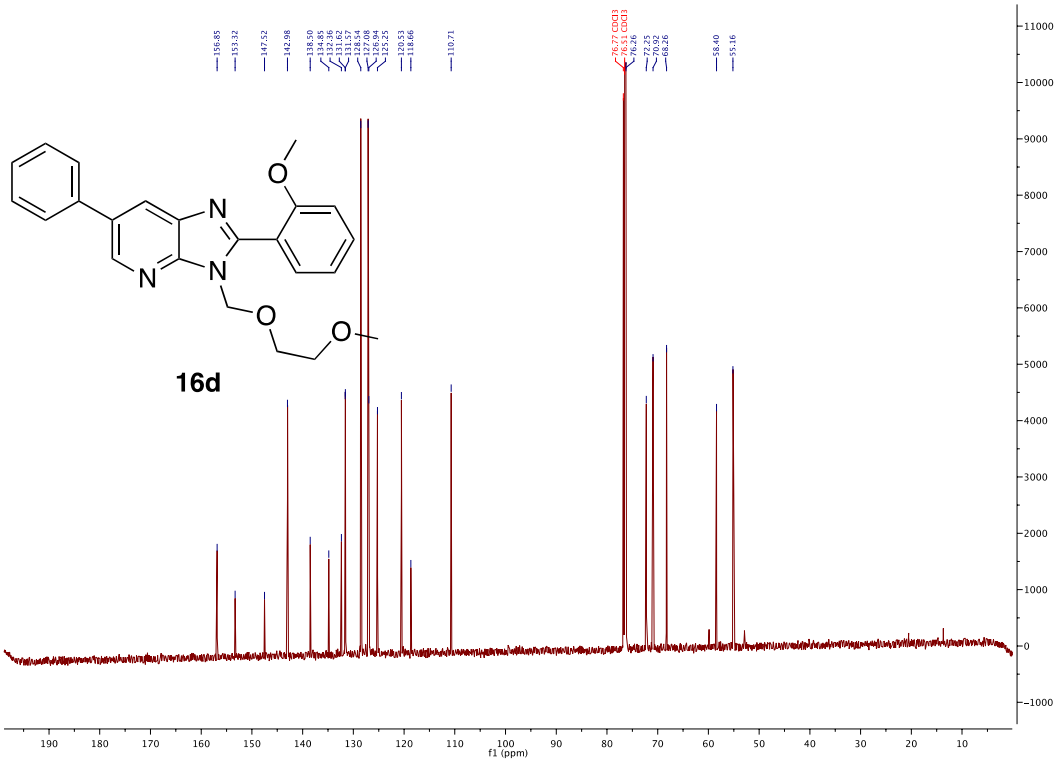
^{13}C NMR:



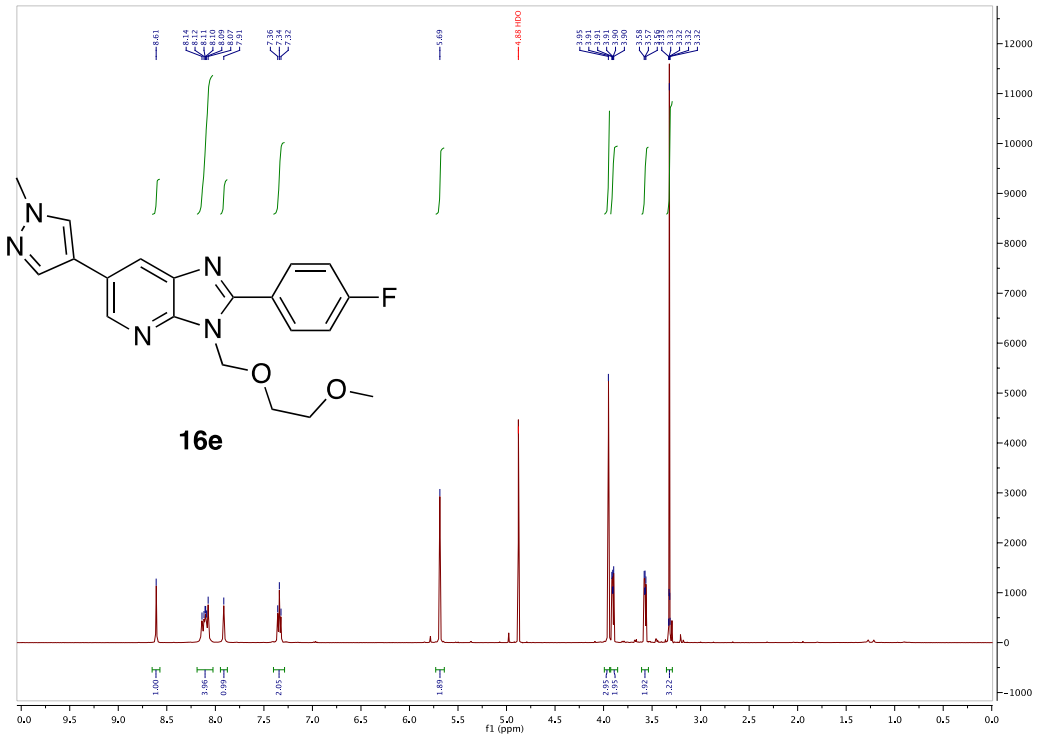
^{1}H NMR:



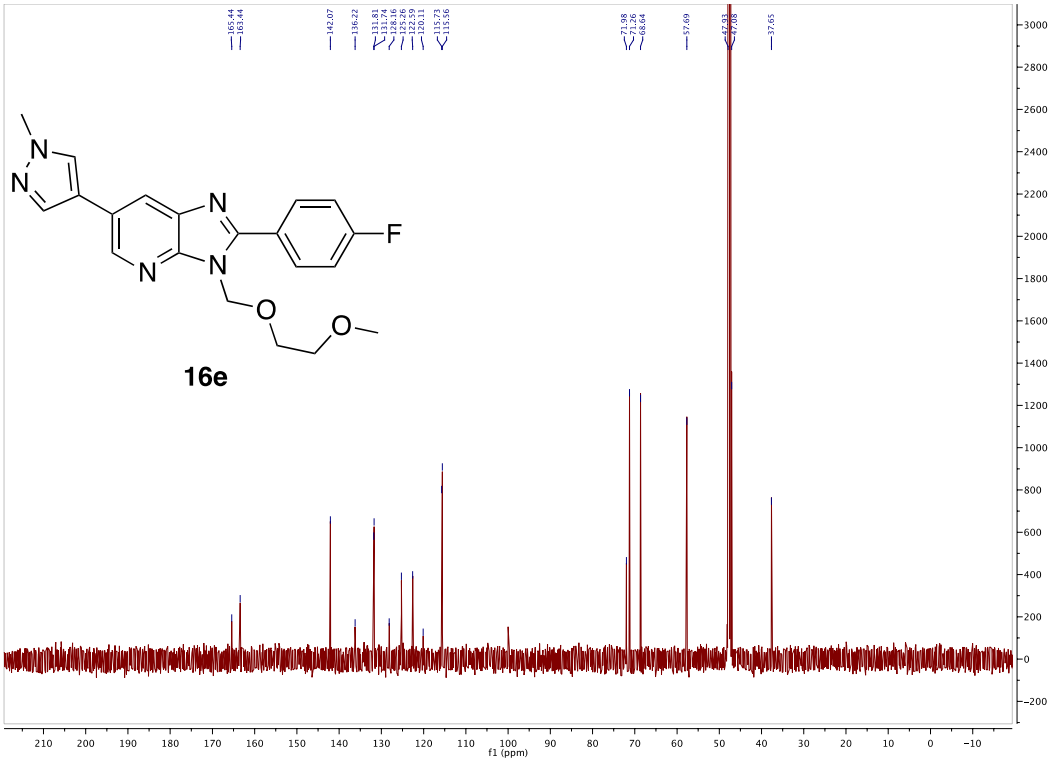
^{13}C NMR:



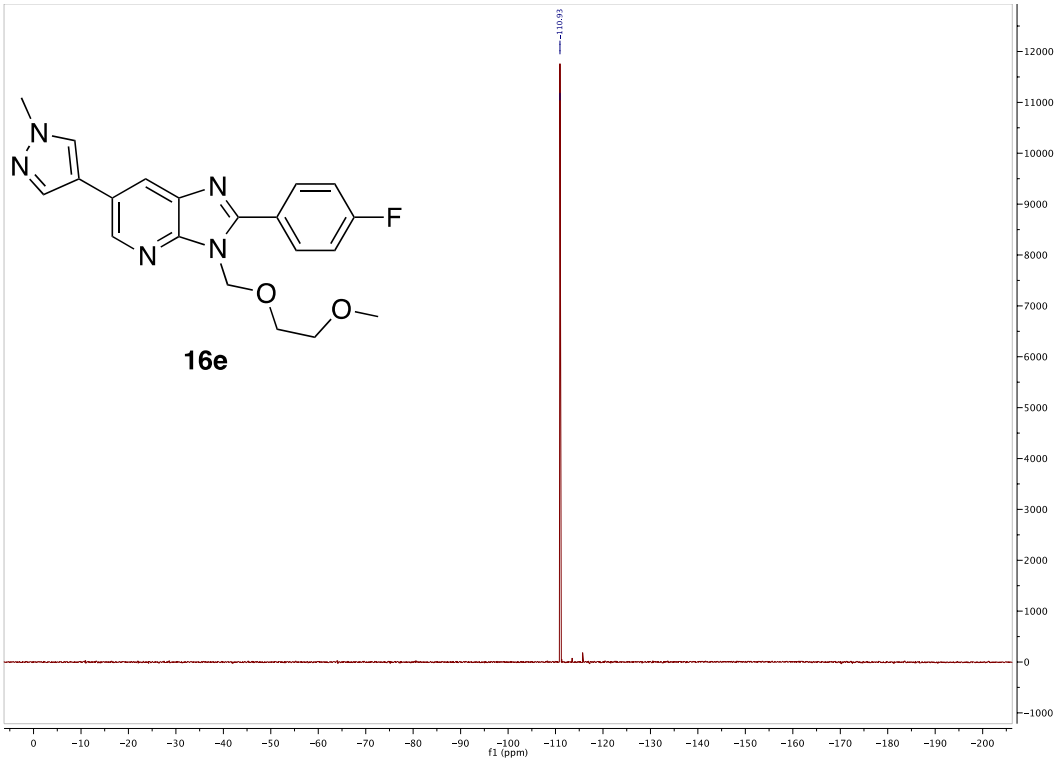
^{1}H NMR:



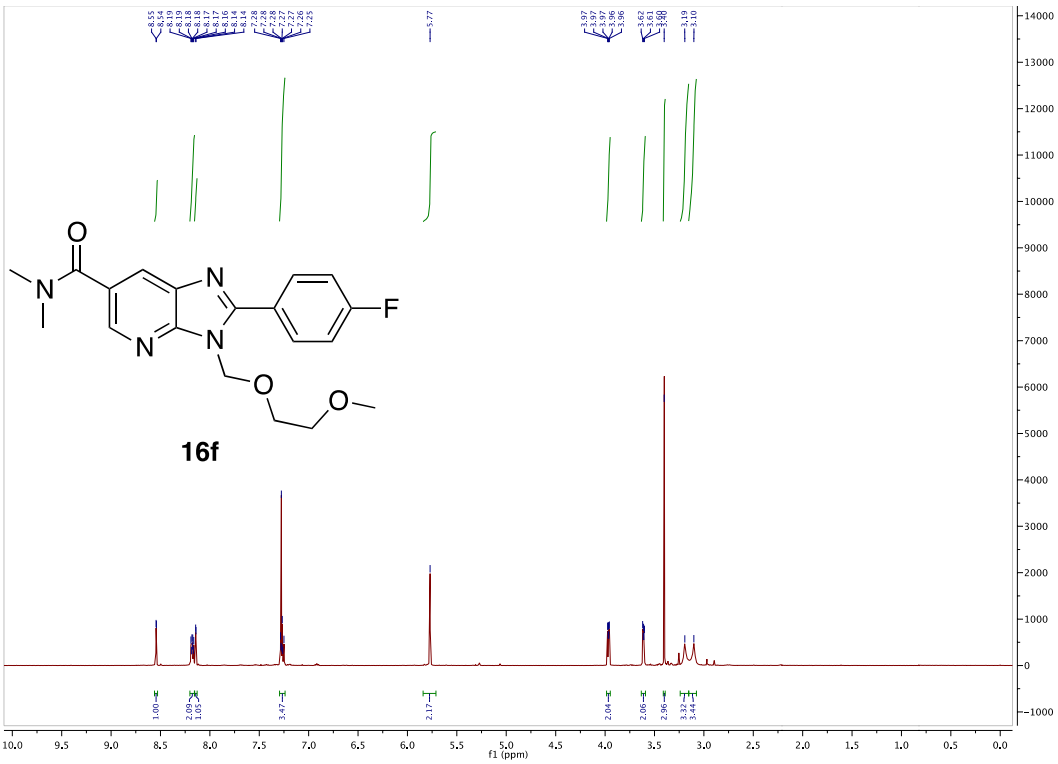
^{13}C NMR:



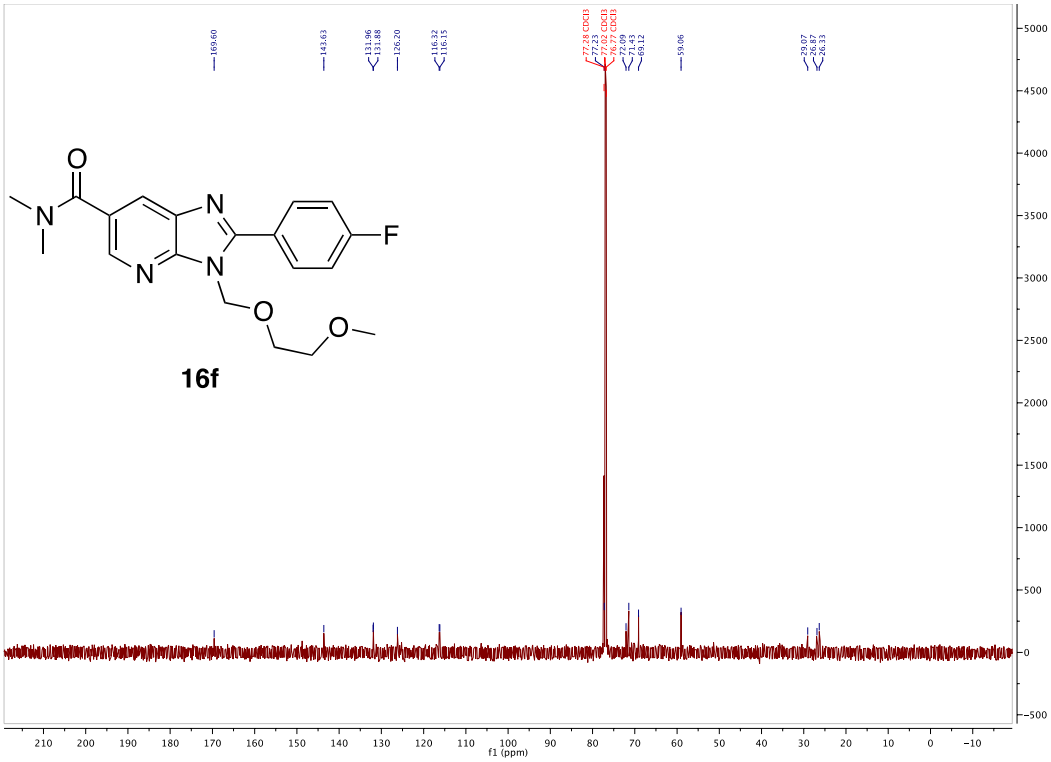
^{19}F NMR:



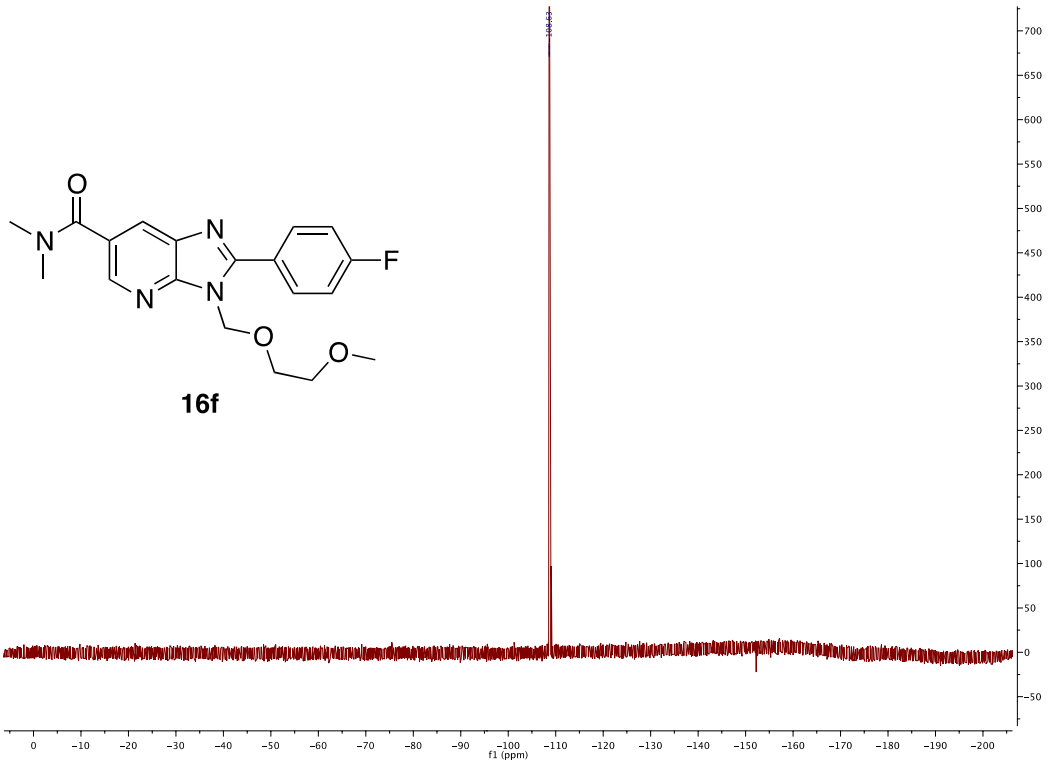
^{1}H NMR:



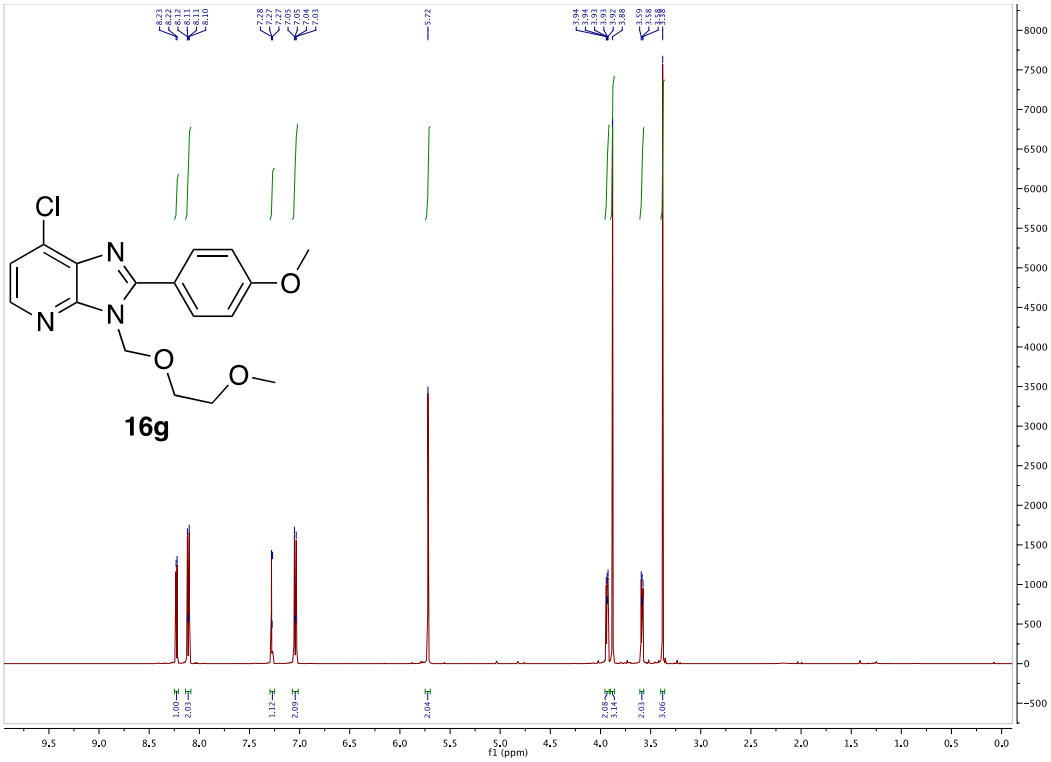
^{13}C NMR:



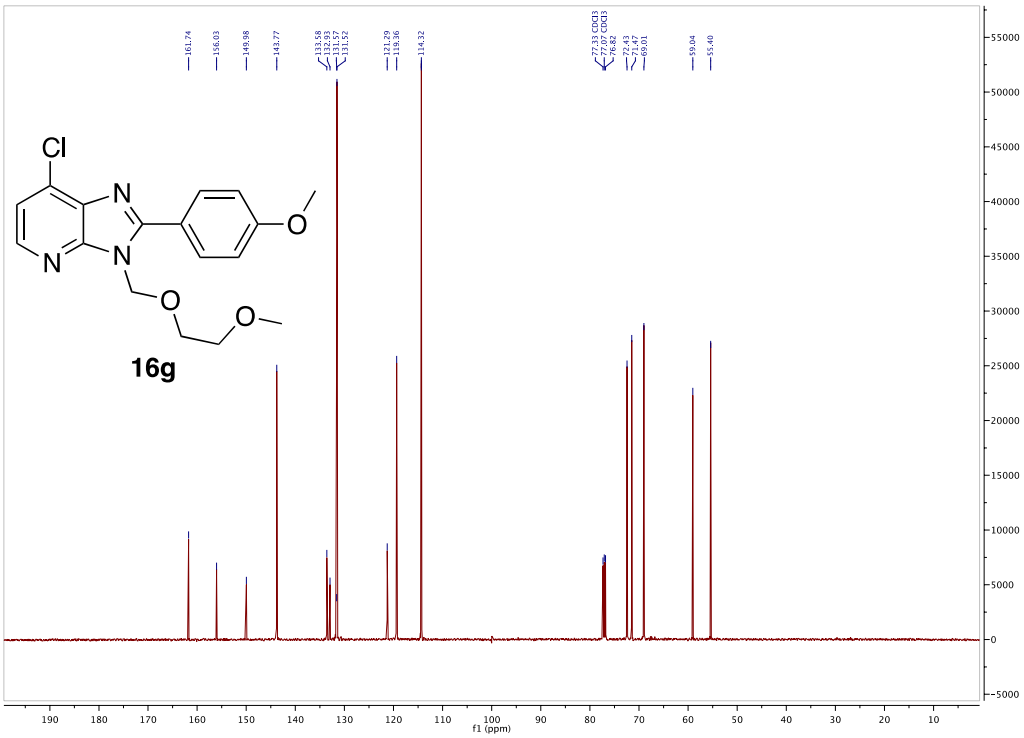
^{19}F NMR:



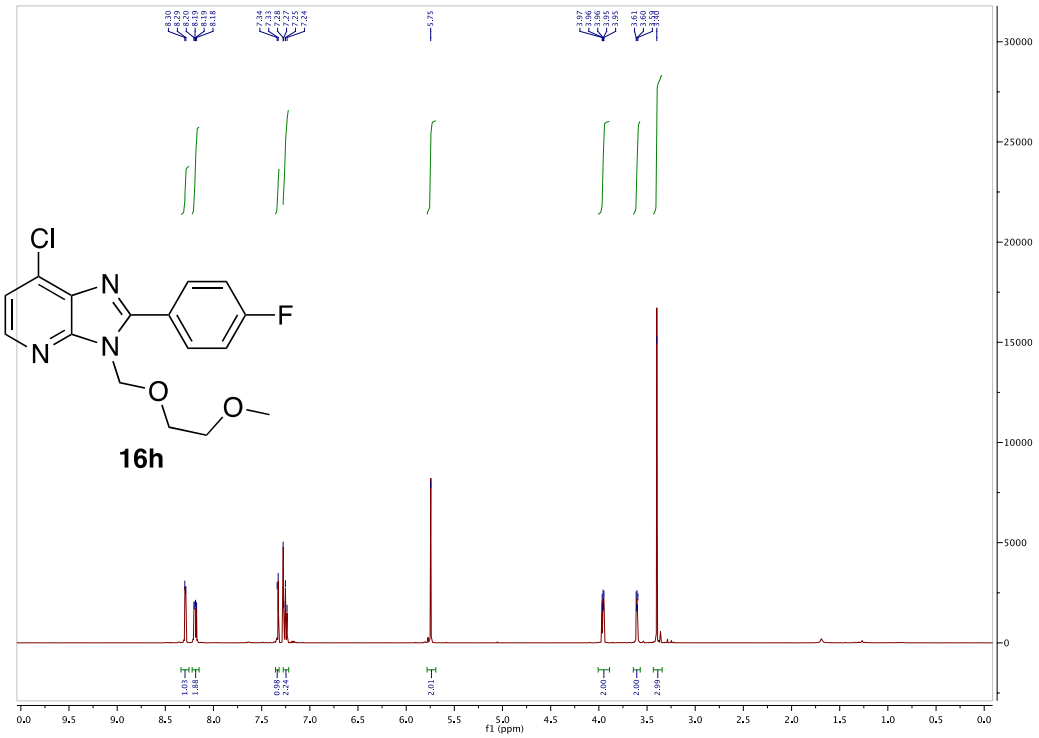
^{1}H NMR:



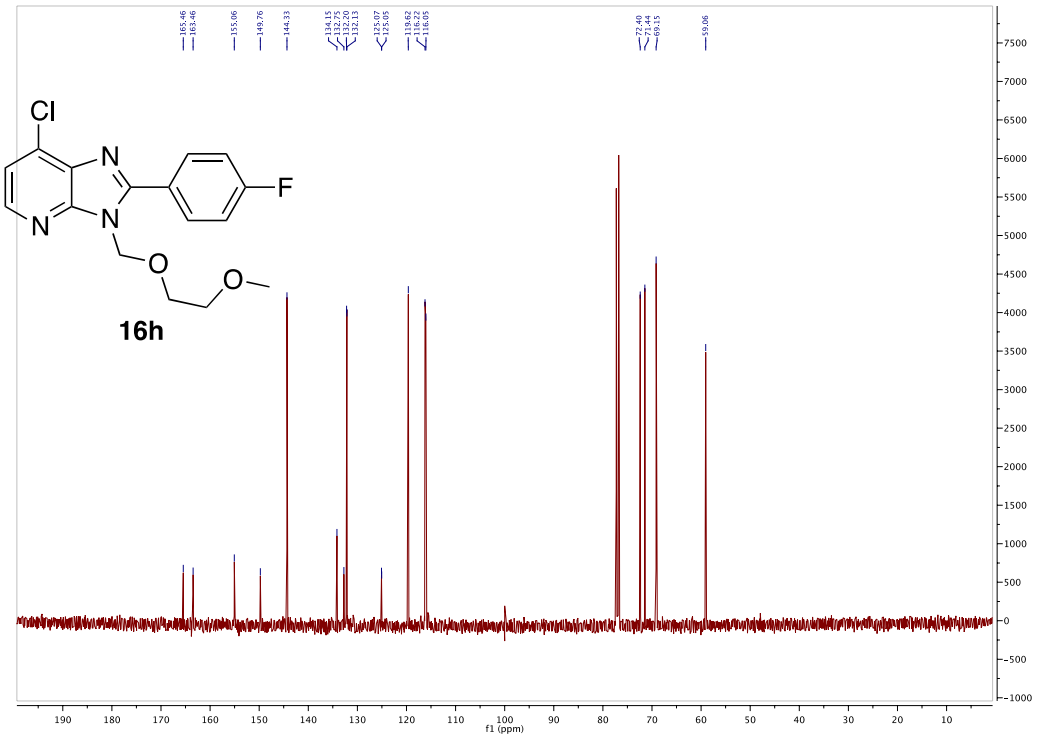
^{13}C NMR:



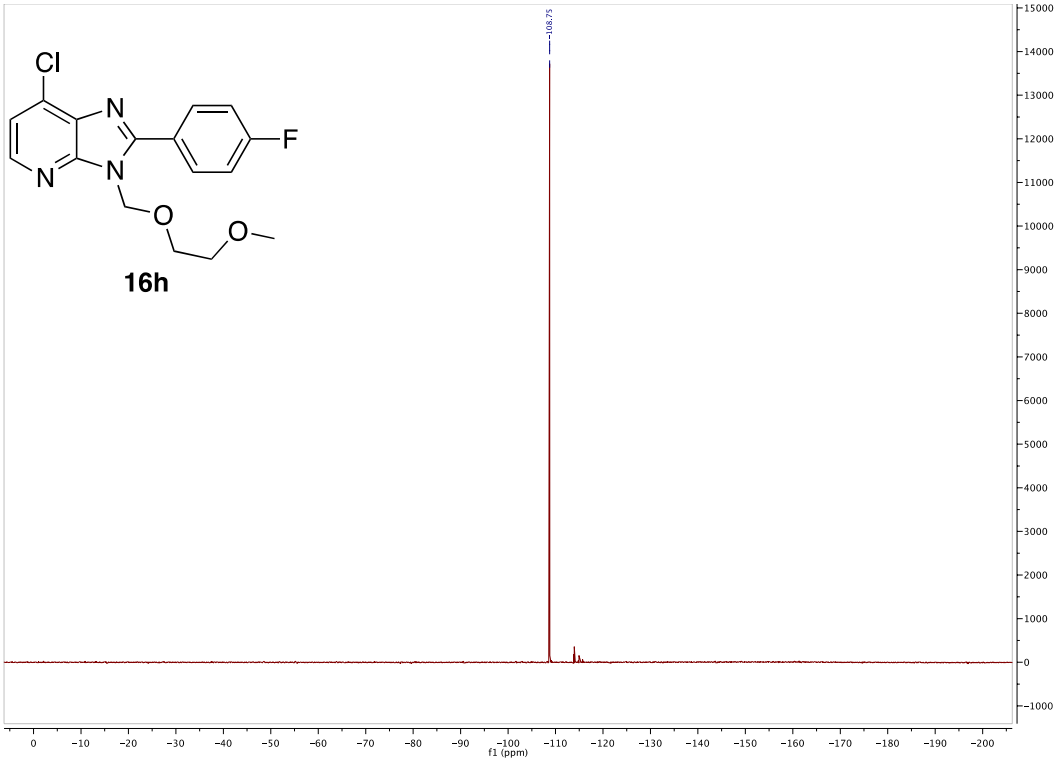
^{1}H NMR:



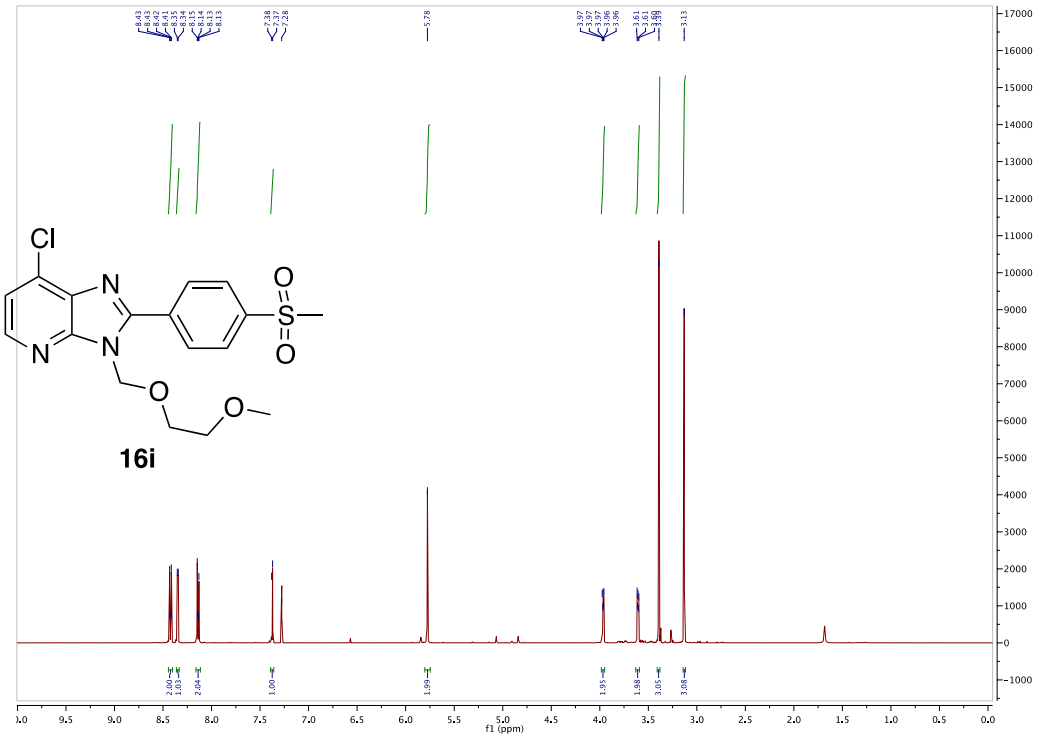
^{13}C NMR:



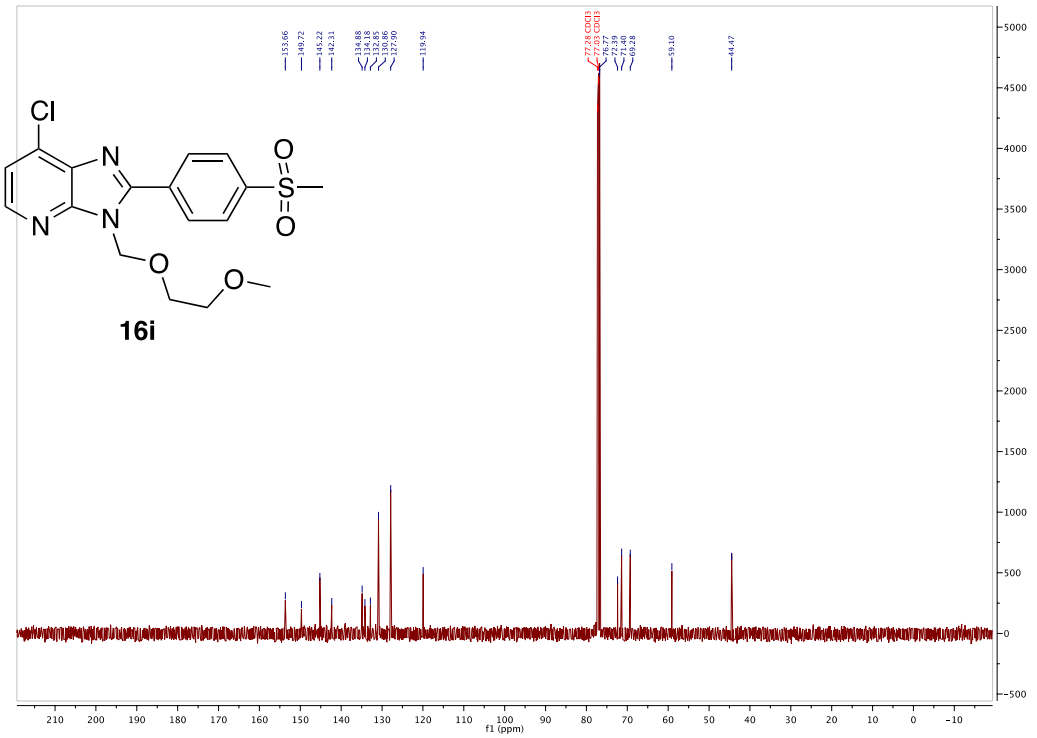
^{19}F NMR:


Cl
N
N
N
F
O
O
16h
-108.75
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

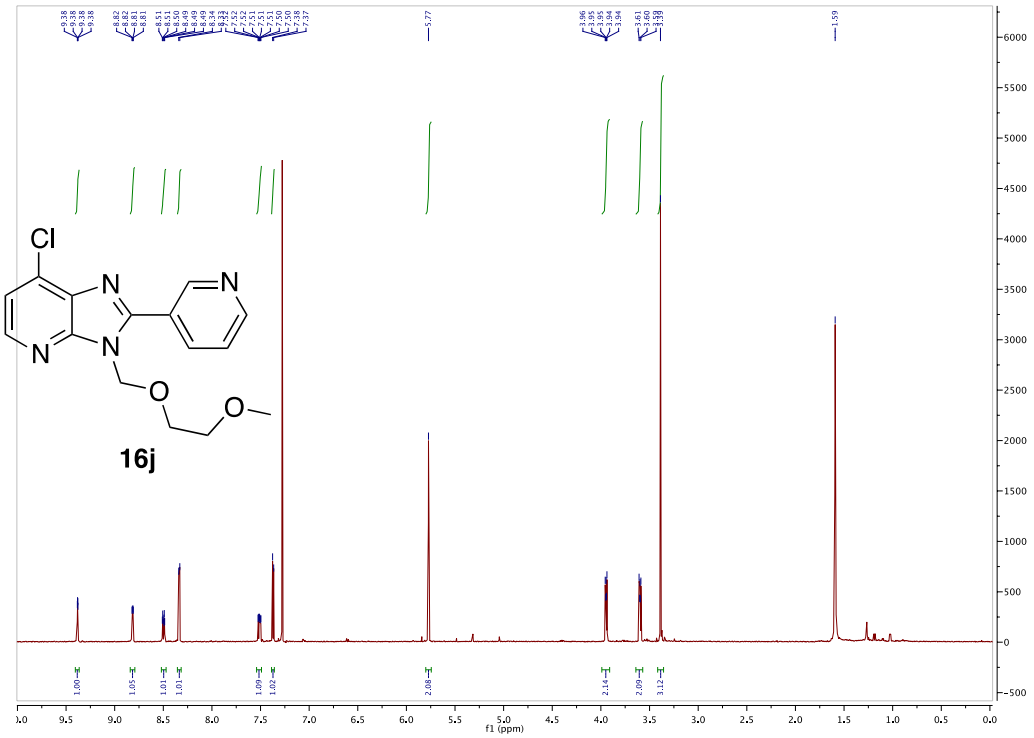
^{1}H NMR:



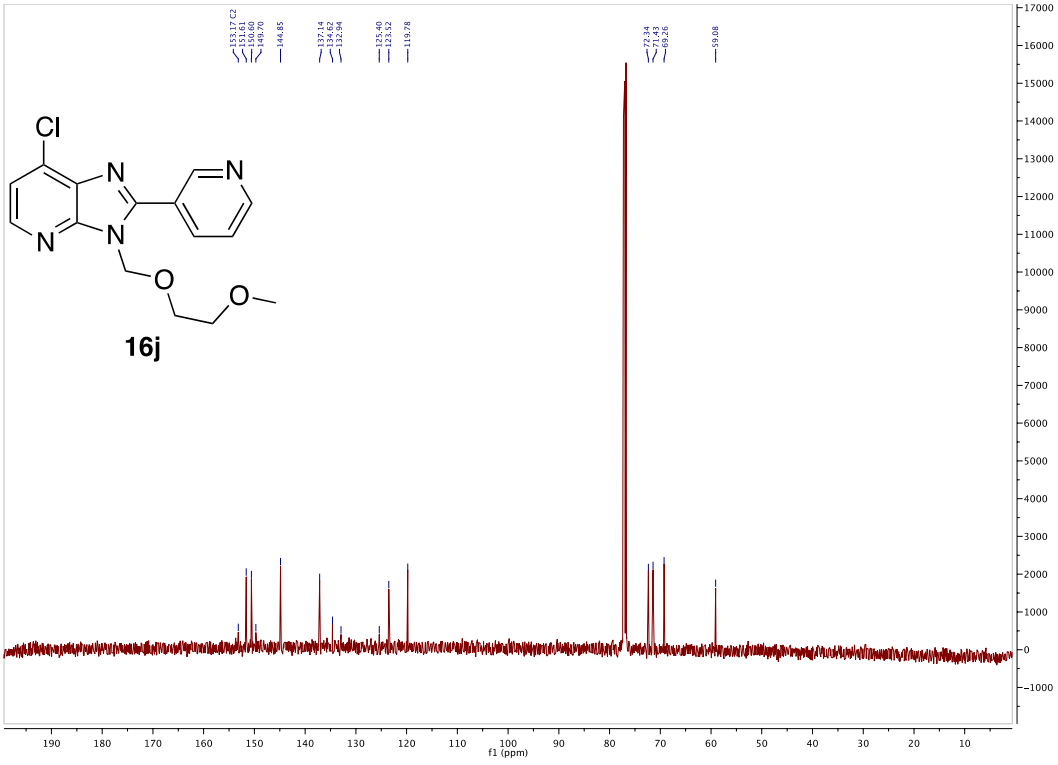
^{13}C NMR:



^{1}H NMR:

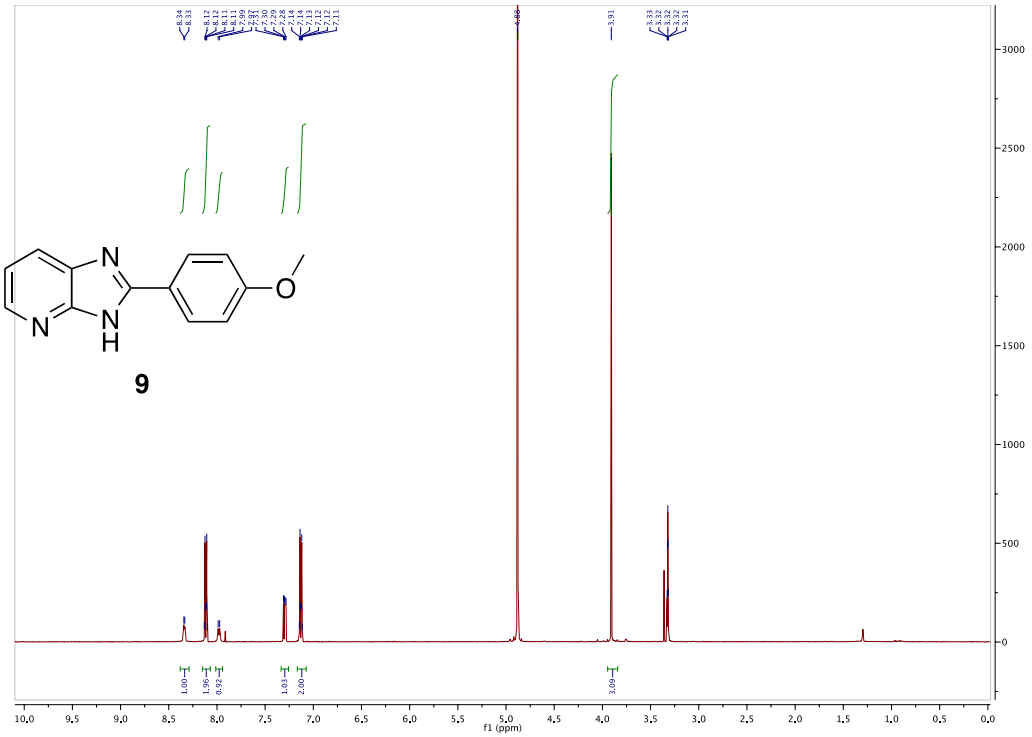


^{13}C NMR:



5.3 Spectra of deprotected C2-arylated products

^{1}H NMR:



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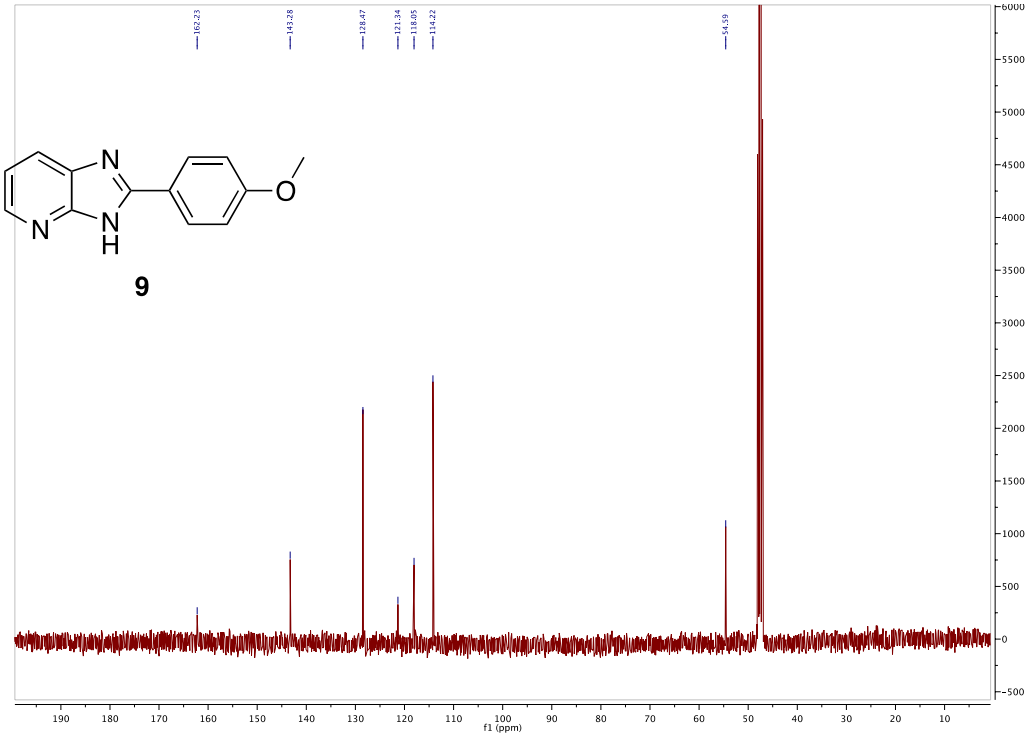
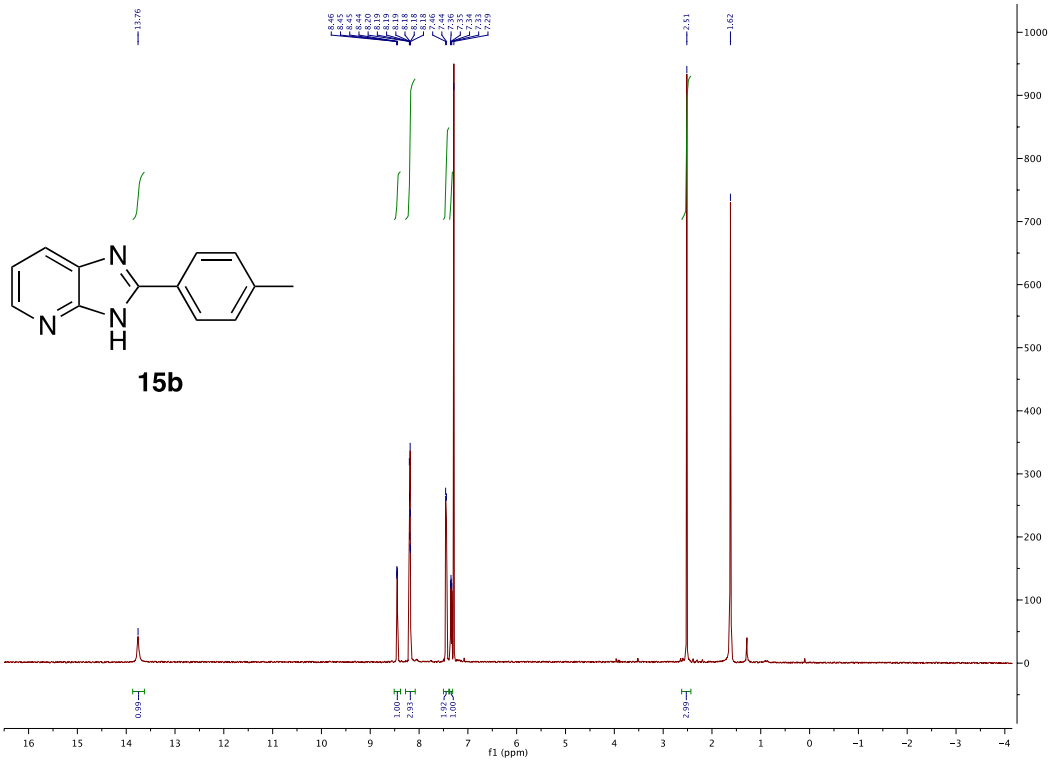


^{1}H NMR:



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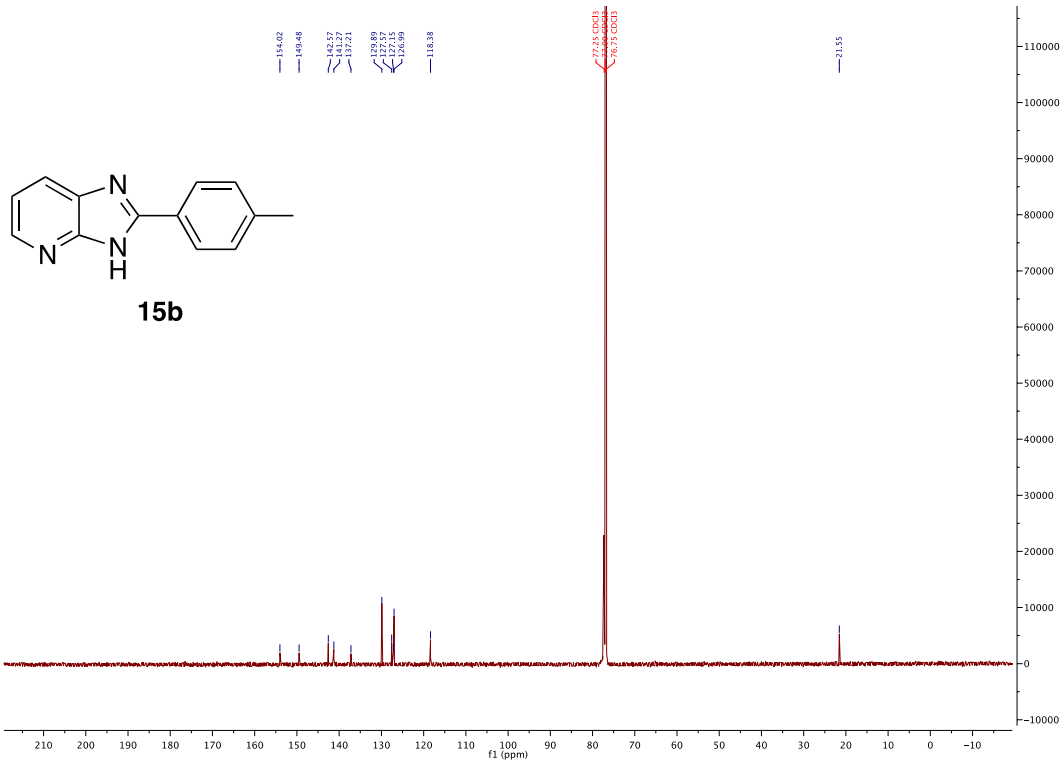

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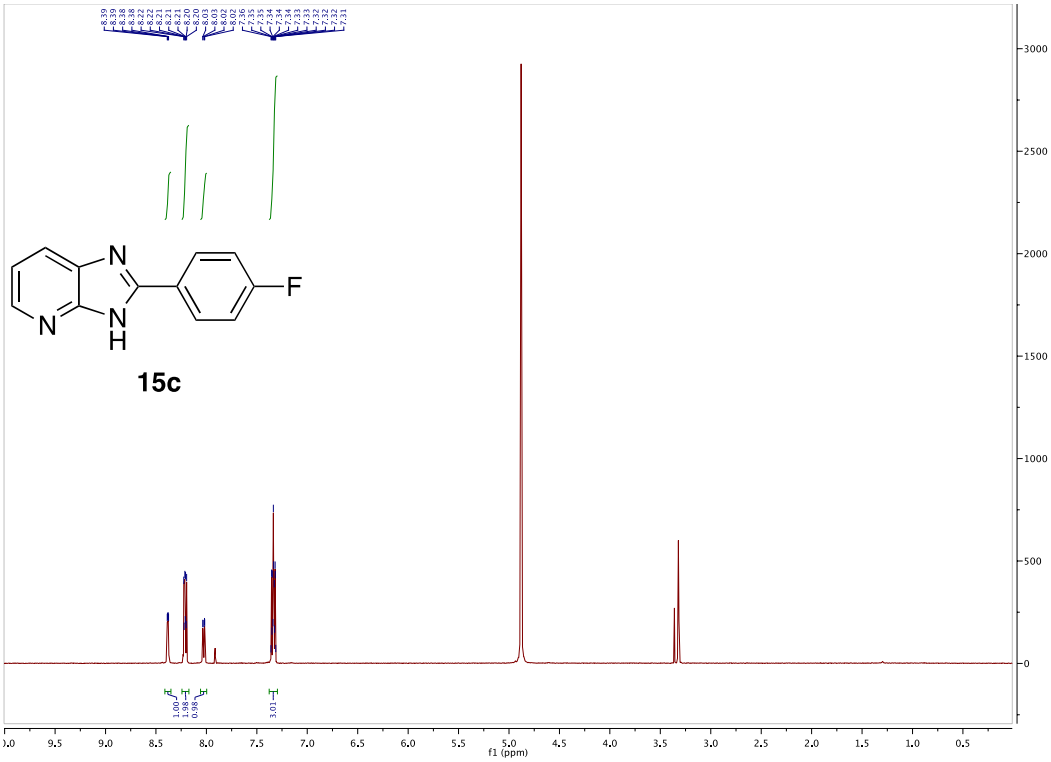
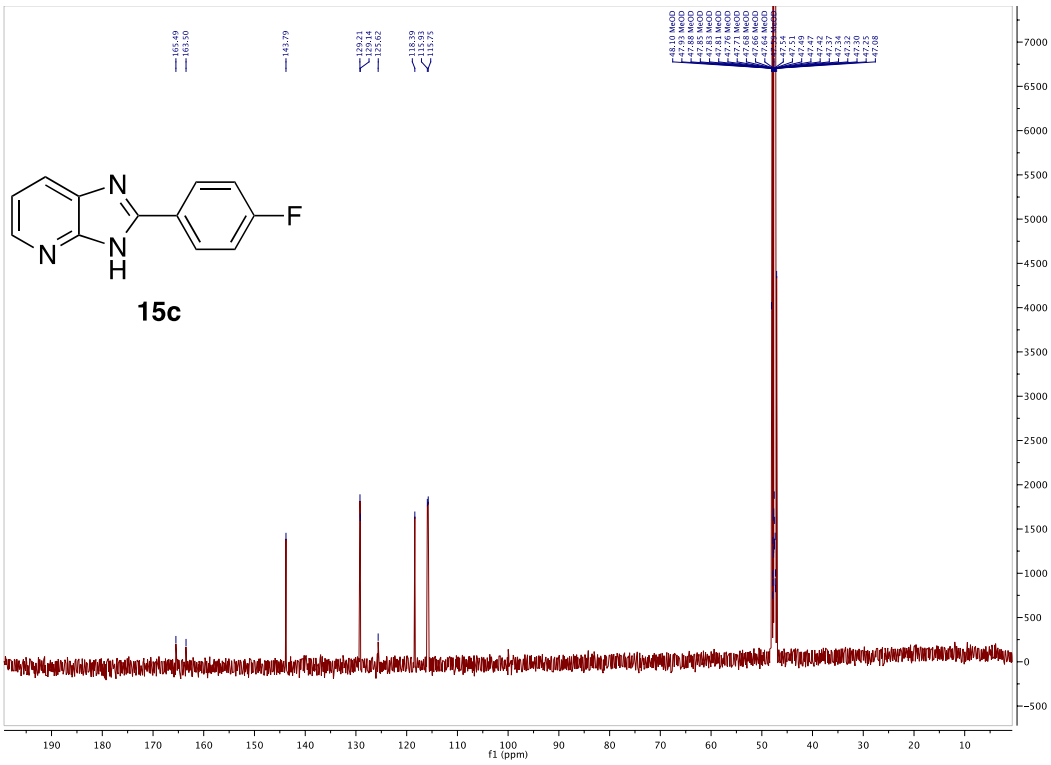
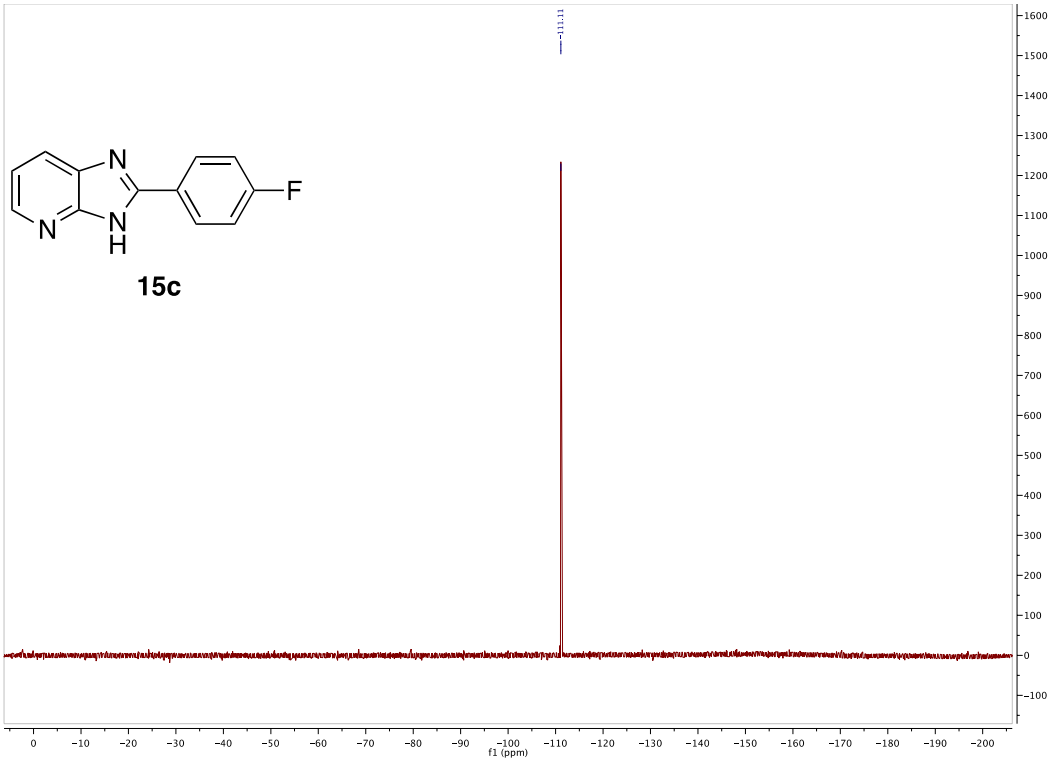


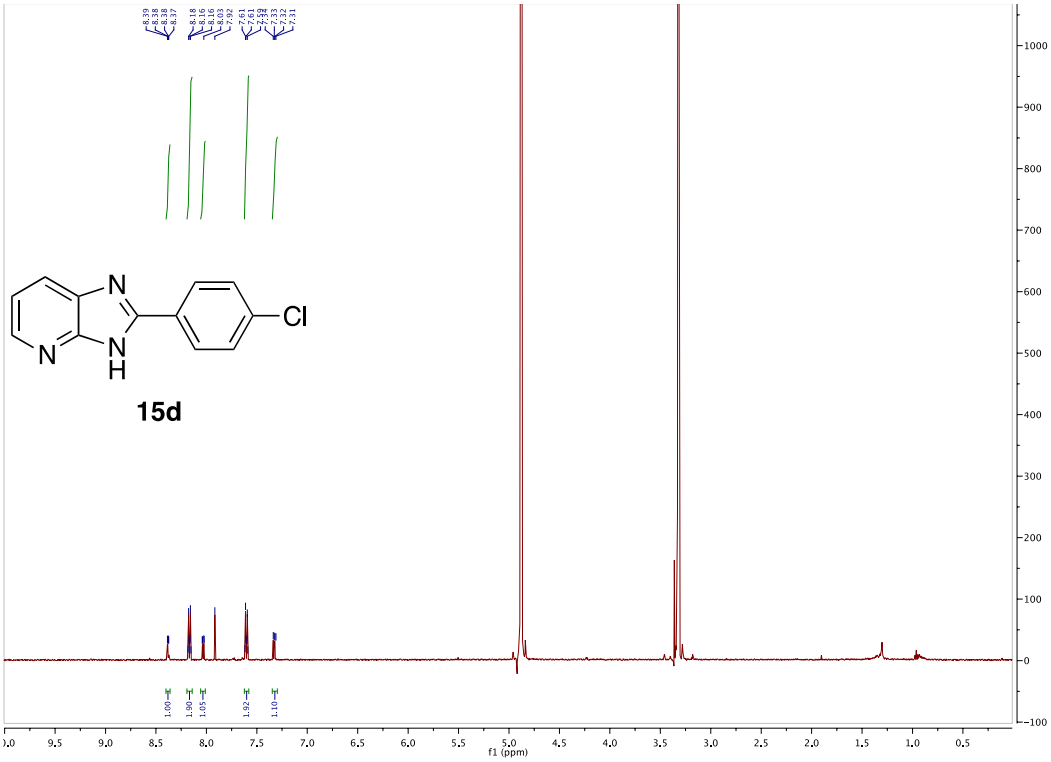
^{13}C NMR:



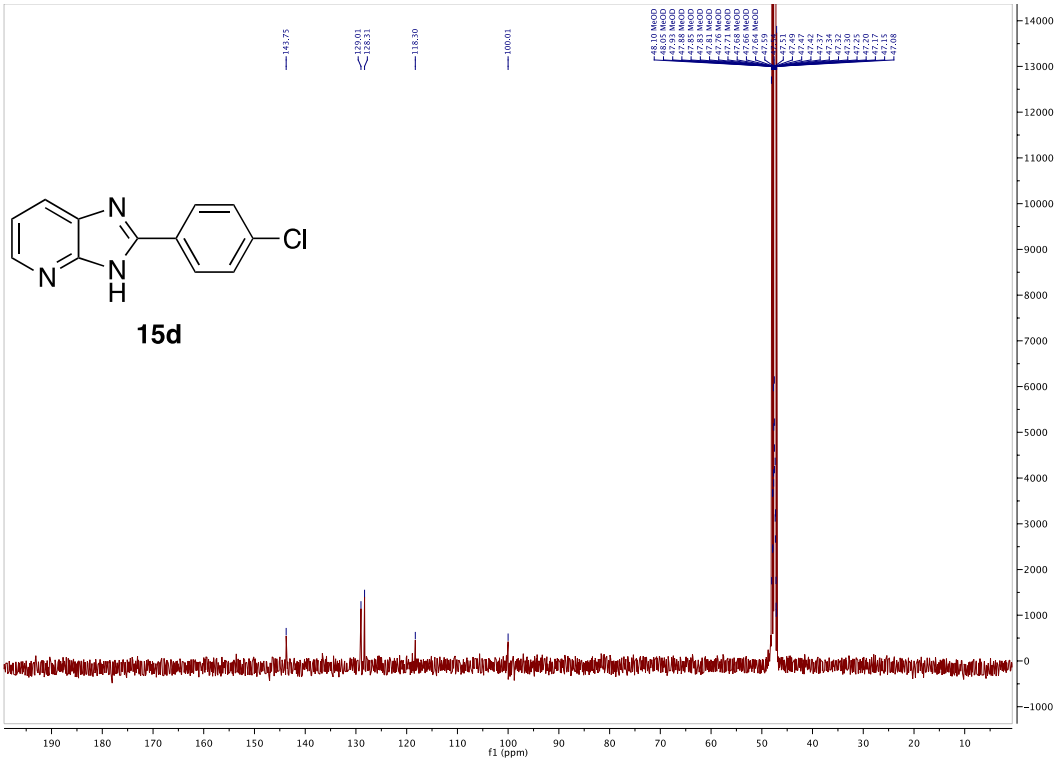
^{19}F NMR:



^{1}H NMR:



^{13}C NMR:



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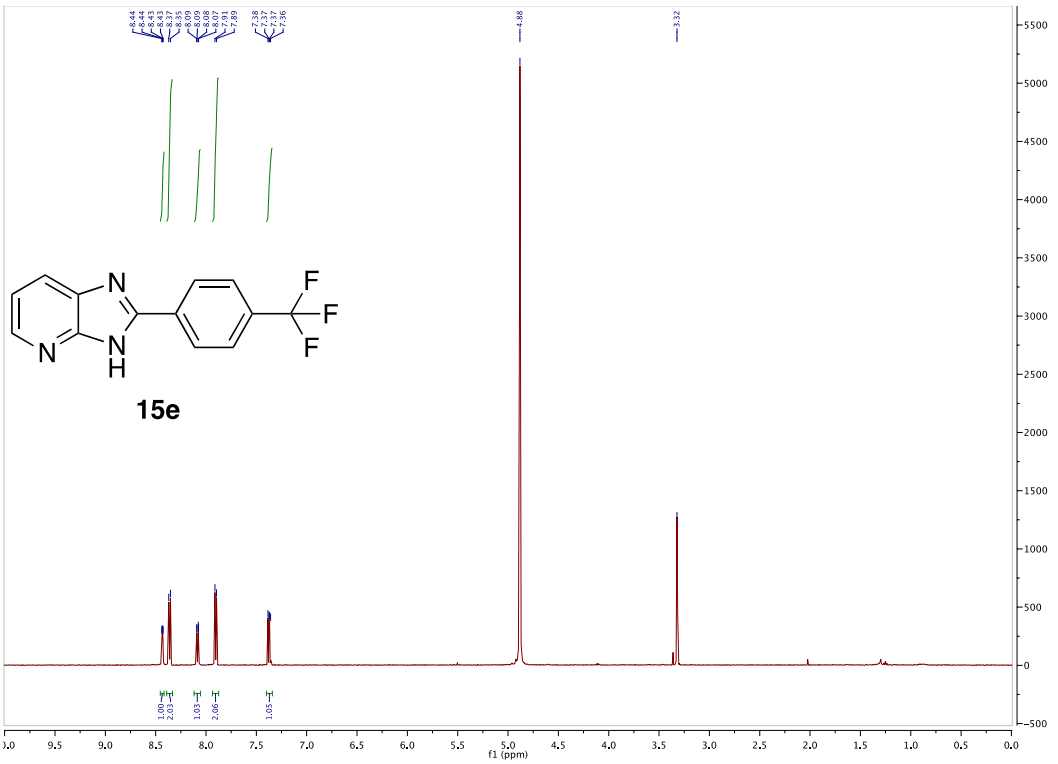

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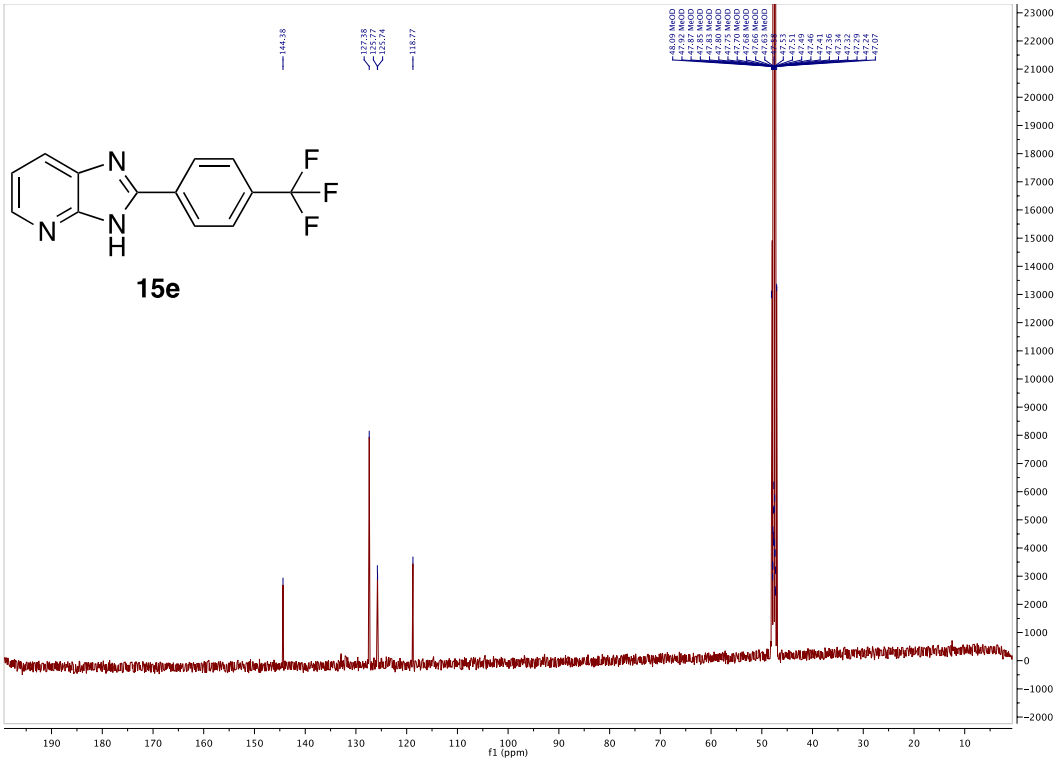
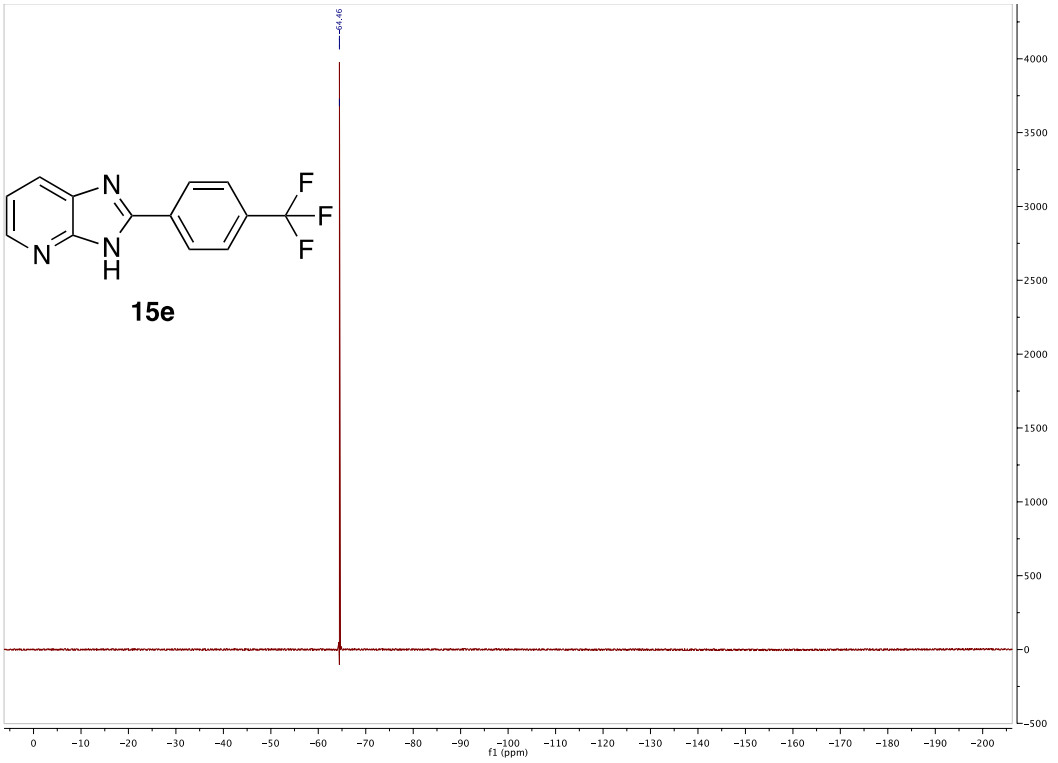
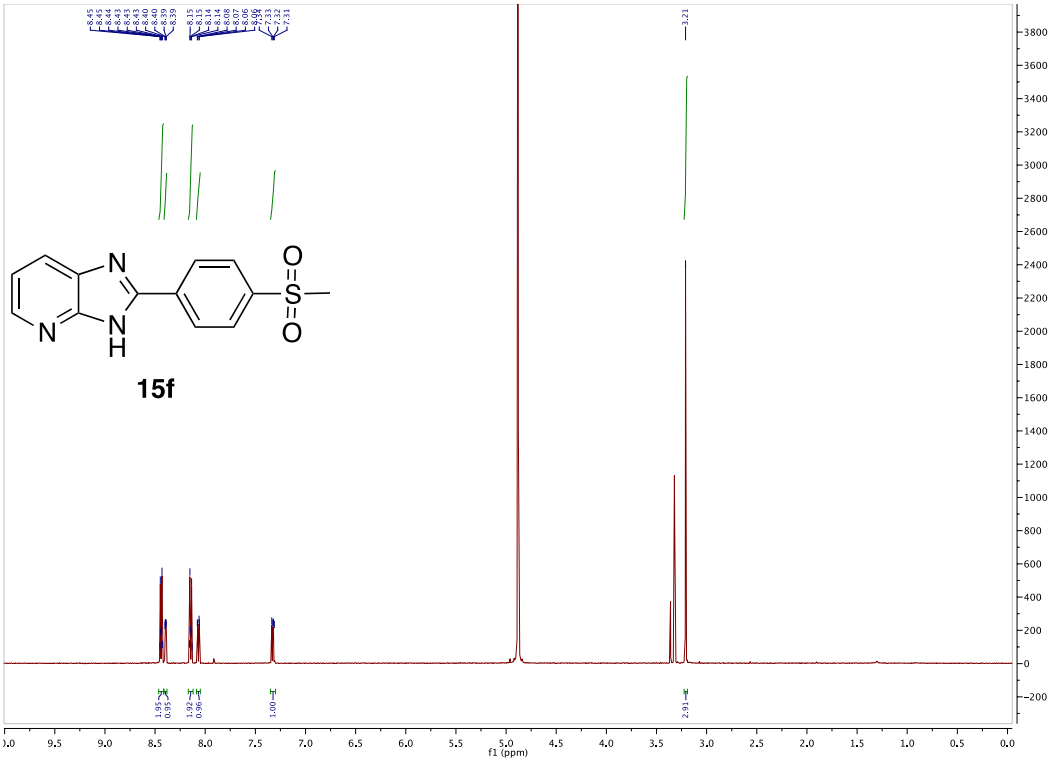


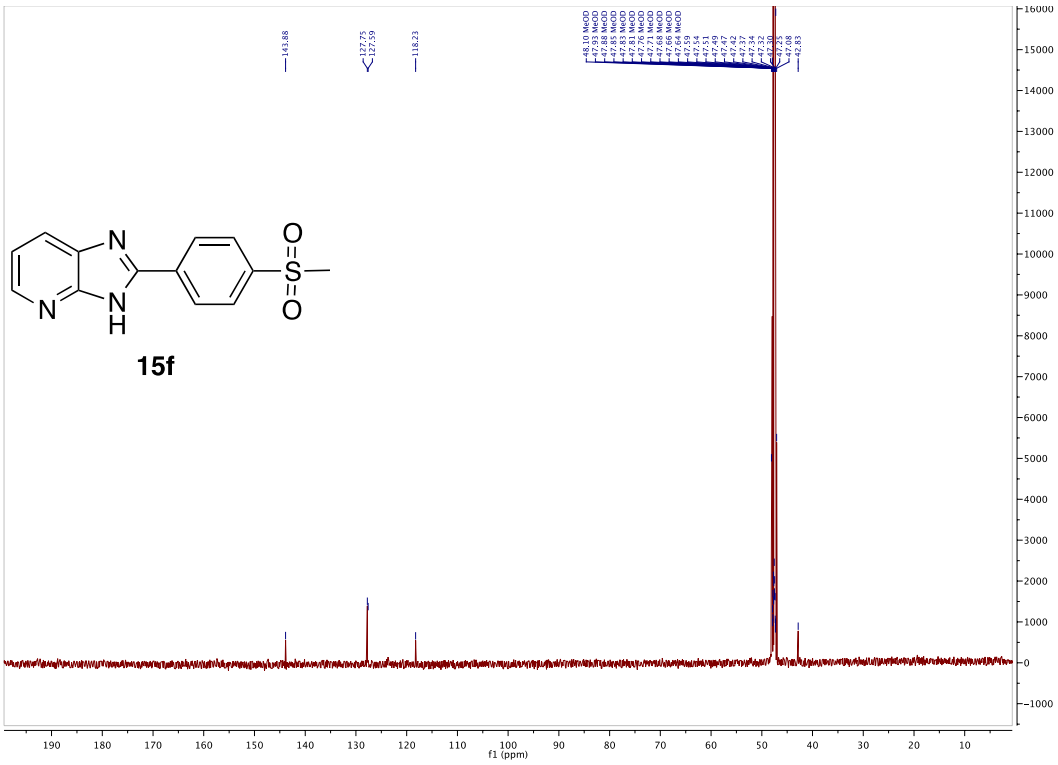
^{19}F NMR:



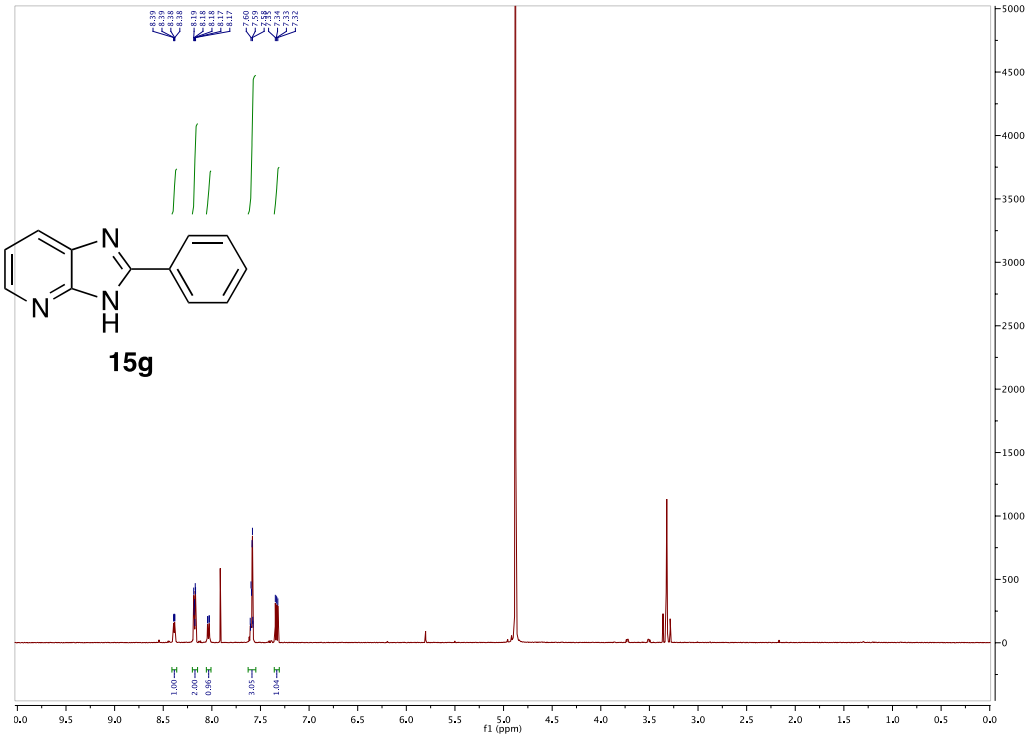
^{1}H NMR:



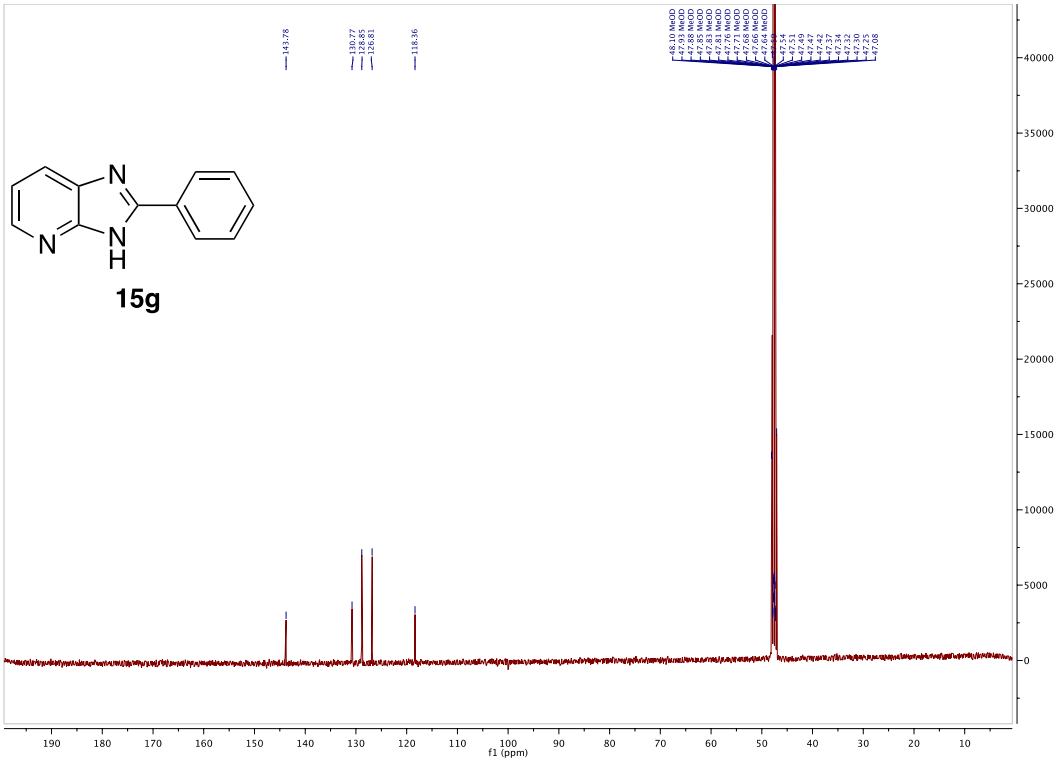
^{13}C NMR:



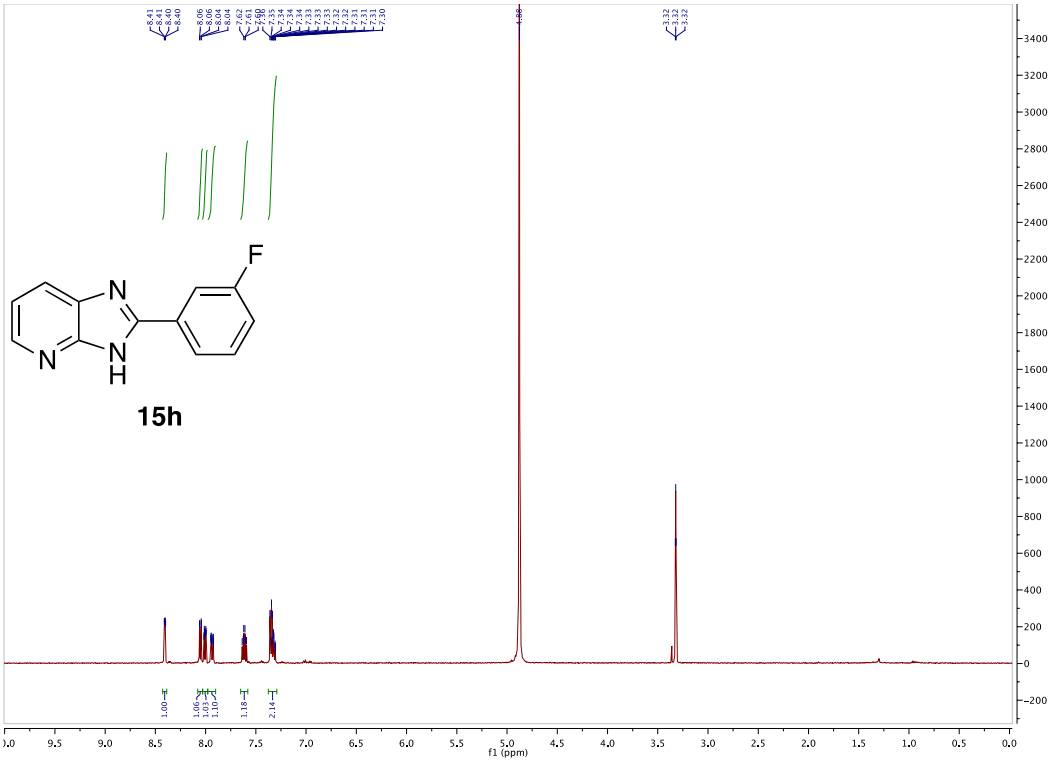
^{1}H NMR:



^{13}C NMR:



^{1}H NMR:



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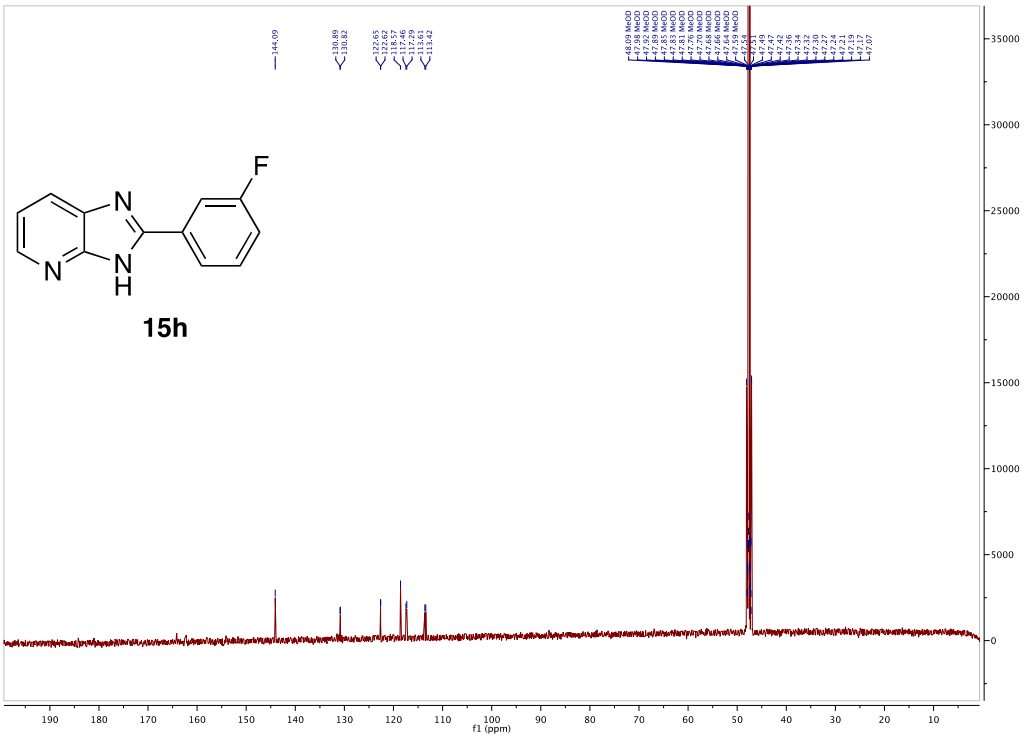
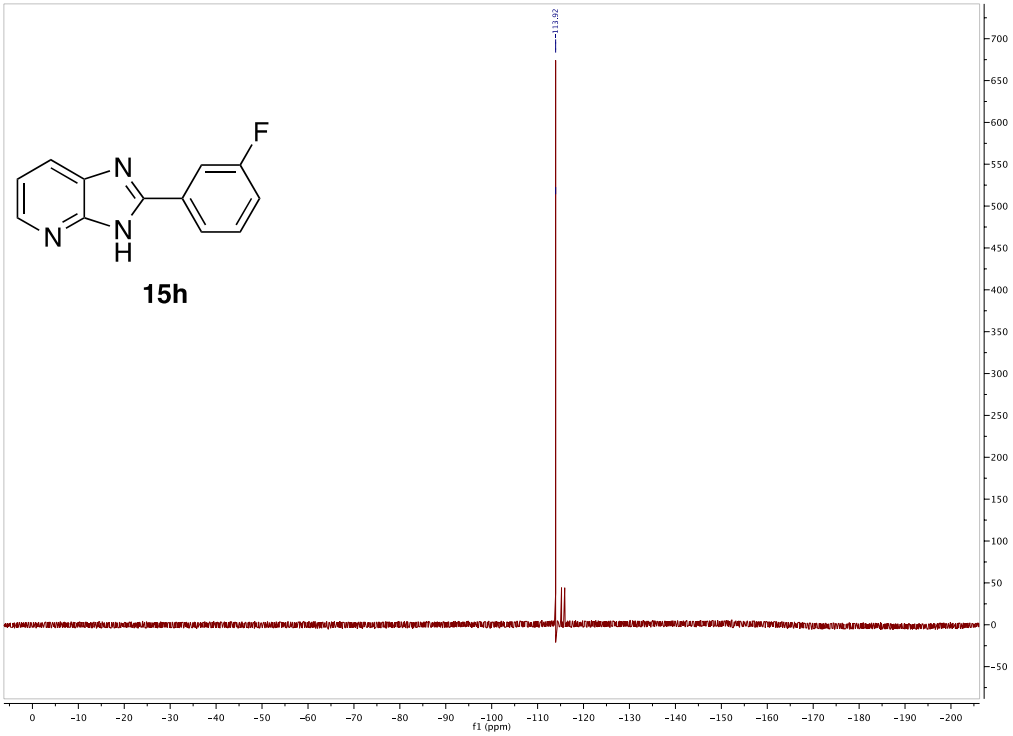
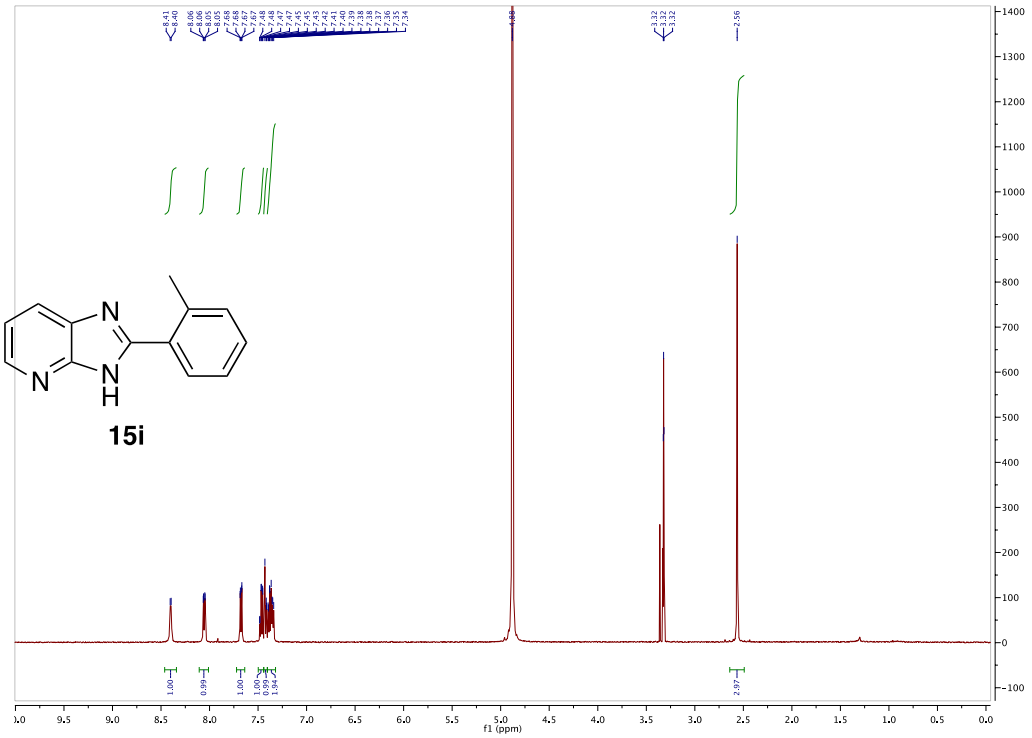


^{19}F NMR:



^{1}H NMR:



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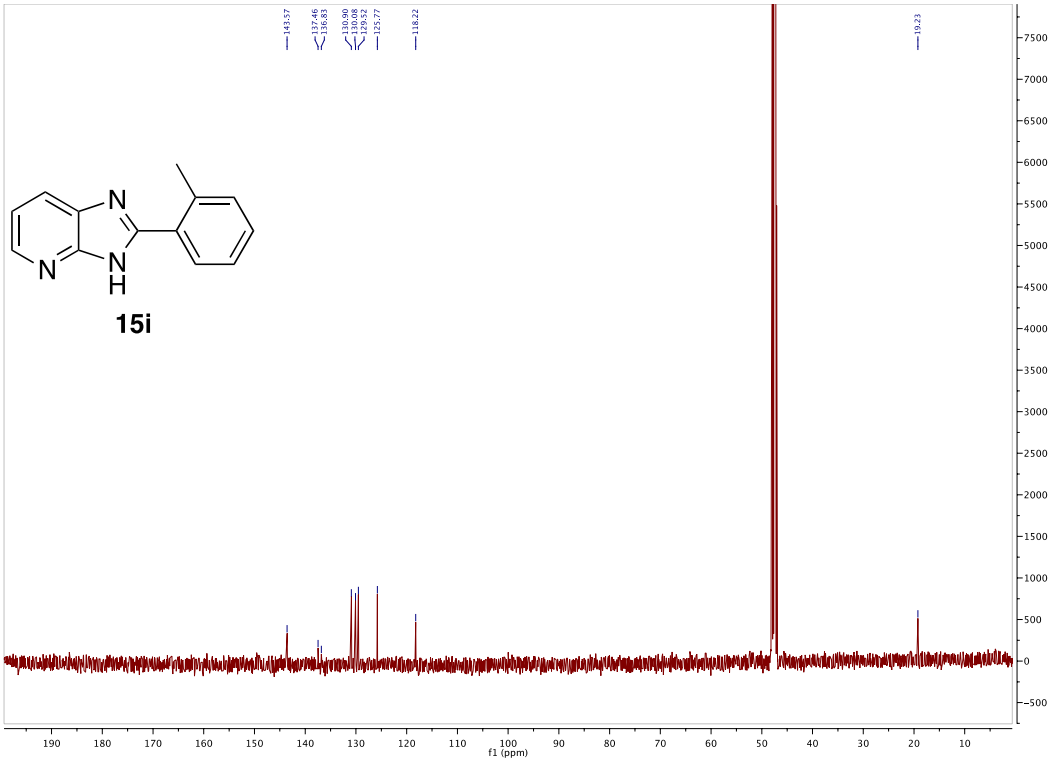
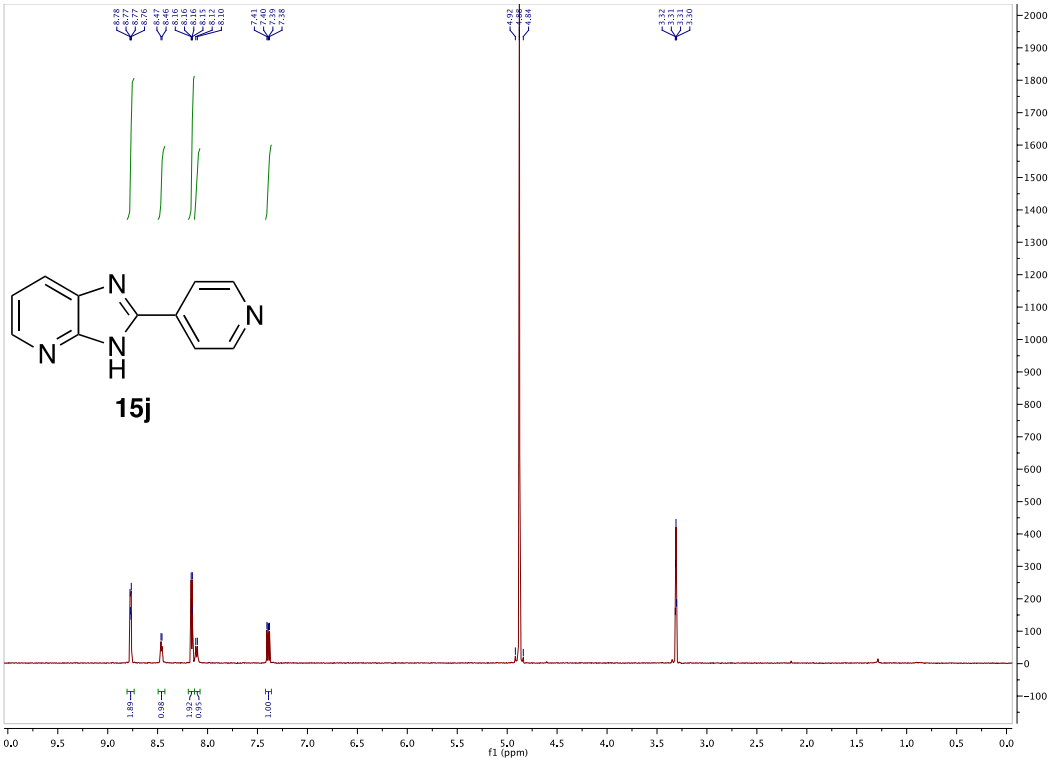


^{1}H NMR:



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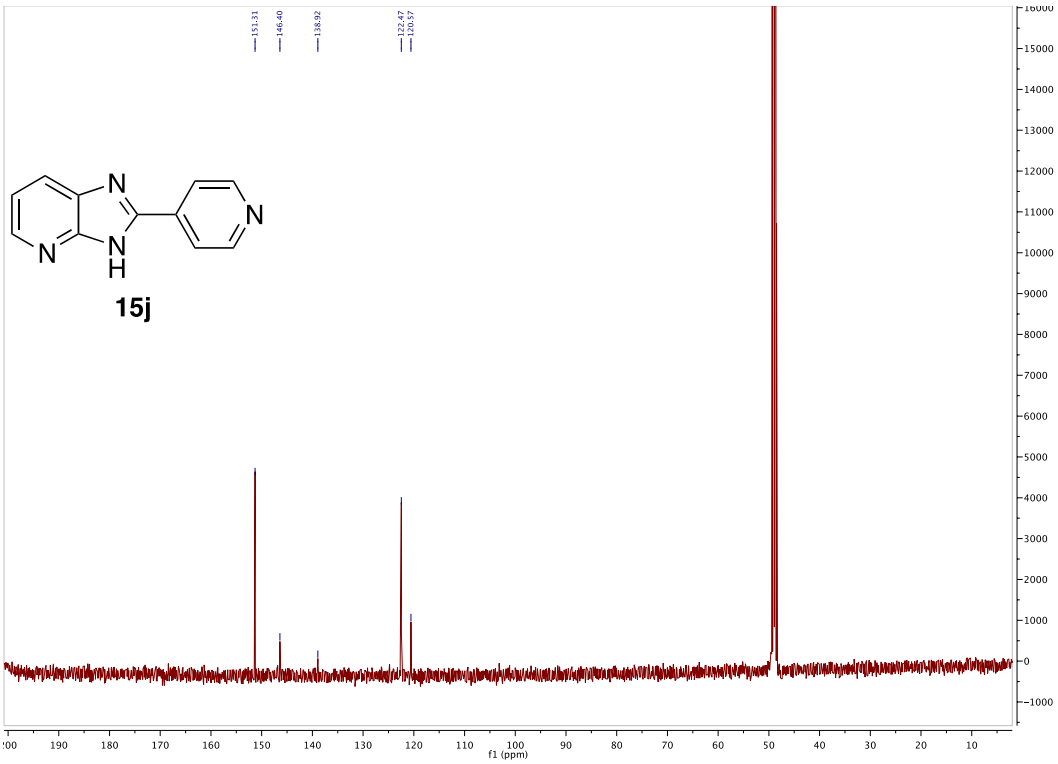
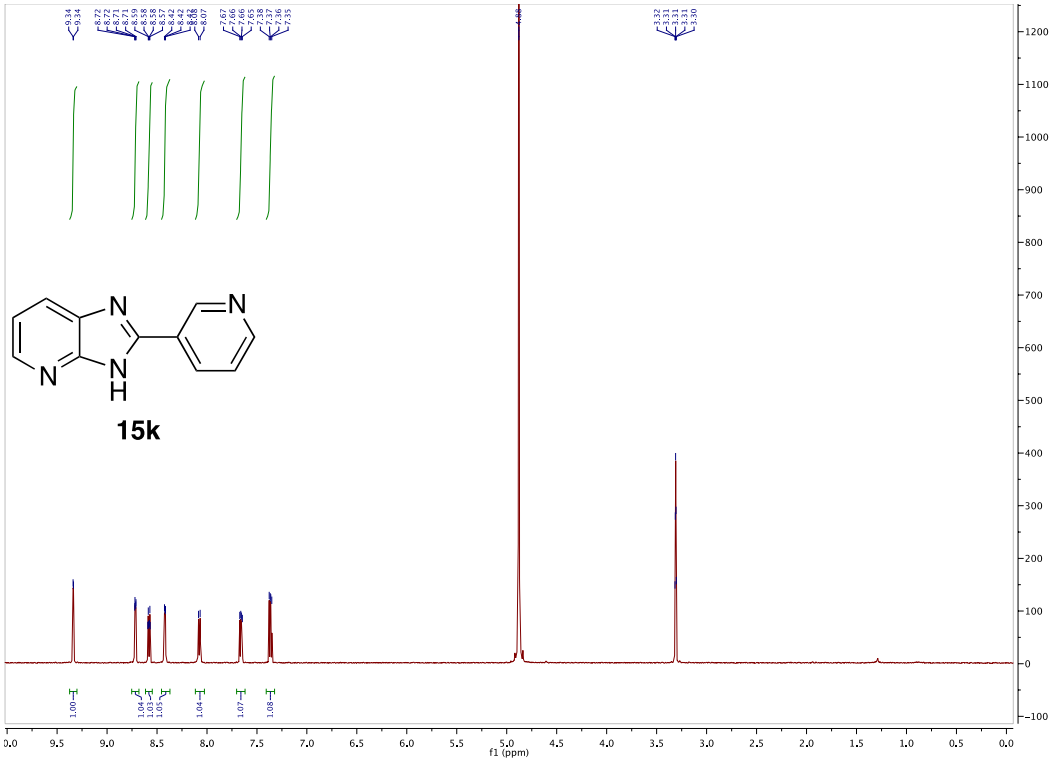
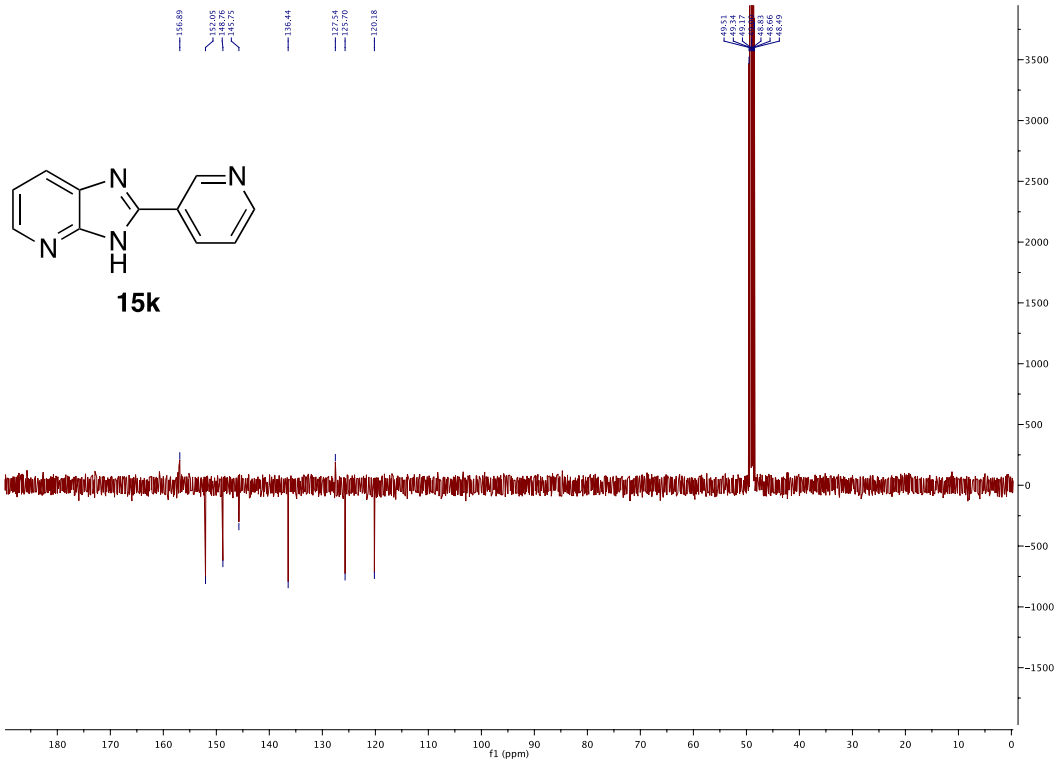


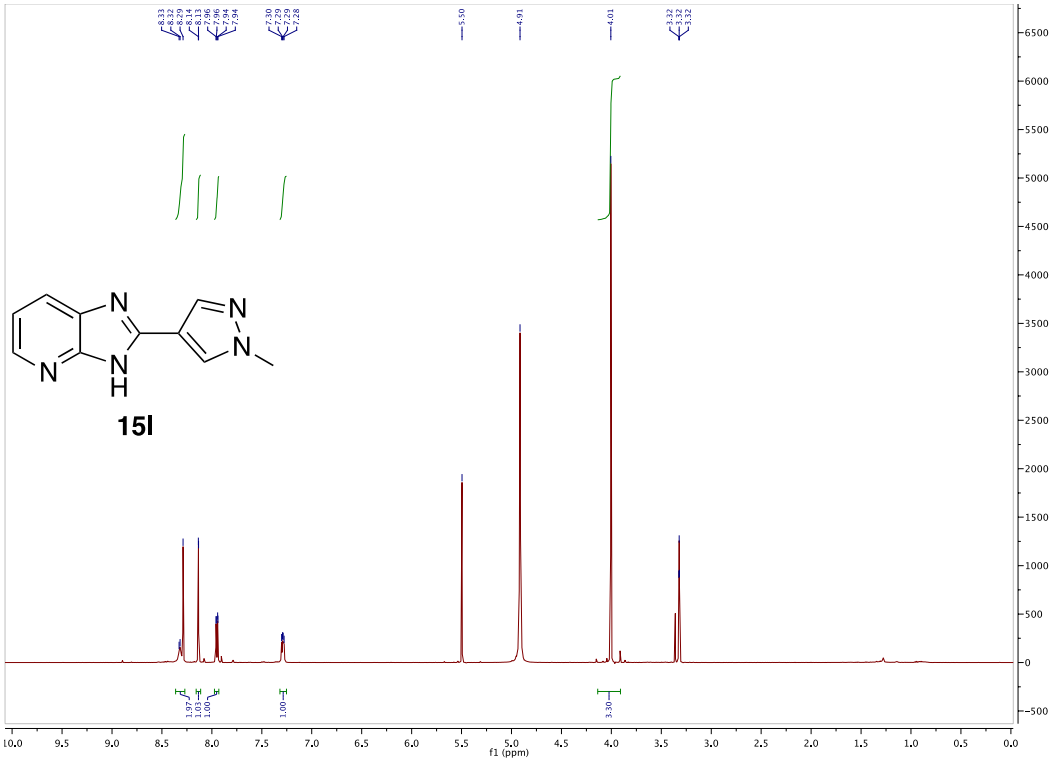
^{1}H NMR:



^{13}C NMR, DEPT:



^{1}H NMR:



^{13}C NMR: