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Supporting Information

Photochemical C(sp^2)–H Pyridination via Arene–Pyridinium Electron Donor–Acceptor Complexes

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SUPPORTING INFORMATION

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1. General Information

NMR spectra were recorded at room temperature (23 °C) on Varian MR400 (400.53 MHz for ^{1}H), Varian Vnmrs 500 (500.09 MHz for ^{1}H, 470.56 MHz for ^{19}F), Bruker Avance Neo 500 (500.27 MHz for ^{1}H, 125.81 MHz for ^{13}C), Varian Vnmrs 600 (599.81 MHz for ^{1}H, 564.34 MHz for ^{19}F) or Varian Vnmrs 700 (699.76 MHz for ^{1}H; 175.95 MHz for ^{13}C) NMR spectrometers. Chemical shifts are reported in parts per million (ppm, δ) relative to the residual solvent peak (CD_3CN: ^{1}H: δ = 1.94 ppm, ^{13}C: δ = 118.26, 1.32 ppm) as the internal reference. Multiplicities are reported as follows: apparent (app), s (singlet), broad singlet (br s), d (doublet), t (triplet), q (quartet), p (pentet), dd (doublet of doublets), ddd (doublet of doublet of doublets), dt (doublet of triplets), td (triplet of doublets), and m (multiplet). Coupling constants (*J*) are reported in Hz. The yields reported in the manuscript were determined by isolation, and the ratios of products were determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixtures (with independently synthesized standards as references where necessary). Thin-layer chromatography was carried out on 0.25 mm E. Merck silica gel plates (60F-254) with visualization via ultraviolet light. High-resolution mass spectra were recorded on an Agilent Technologies 6230 TOF HPLC-MS or an Agilent Technologies 6520 Accurate Mass Q-TOF LC/MS using electrospray ionization (ESI+). Flash chromatography was conducted on a Biotage Isolera One chromatography system using preloaded high-performance silica gel columns (Biotage Sfär Silica HC D - 5 g). UV-Vis spectroscopic analysis was performed on a Varian Cary-50 spectrophotometer. Infared Spectra were recorded on a Bruker Alpha FTIR Spectrometer. Melting points were determined using a MelTemp 3.0 (Laboratory Devices, Inc) and are uncorrected. Pyridinium product standards were synthesized using literature procedures.[1]

2. Materials

All reagents were obtained from a commercial vendor at the highest commercial purity and used without further purification, unless otherwise stated (vendors include Sigma-Aldrich, Acros, Oakwood, TCI, Matrix Scientific, Alfa Aesar, eMolecules, Cambridge Isotope Laboratories, and Chem-Impex International). Acetonitrile (99.9%, Extra Dry, AcroSeal™) was purchased from Acros Organics and used as received. Pyridine (99+%, extra pure) was purchased from Acros Organics. Tetrafluoroboric acid diethyl ether complex (HBF_4•Et_2O) was purchased from Sigma-Aldrich. Oxygen (Ultra High Purity 4.4 Grad Size 300 Cylinder, CGA540) was purchased from Airgas. Latex balloons were purchased from Staples. 20 mL scintillation vials were purchased from Fisher Chemical. Open hole screw thread caps (GPI 22-400, Black, Open Hole, PP) were purchased from Chemglass. Septa for these caps (GPI 22-400 PTFE/SLN 22MMX0.060IN) were purchased from Chemglass. Septa stoppers, Suba-Seal septa 19/22 red (CG302403) were purchased from Fisher Chemical. Black phenolic 13-425 caps with TEF/SIL septa (C4015-66A) were purchased from Thermo Scientific. DCM, acetonitrile, and methanol utilized for purification were purchased from Fisher Chemical. 4 mL and 20 mL scintillation vials were purchased from Fisher Chemical. Stir bars for the 4 mL vials were purchased from Chemglass (CG-2003-16, Length x Dia. in mm: 10 x 3) and stir bars for the 20 mL vials were purchased from Fisher Chemical (Fisherbrand stir bar, octagon – Cat No: 14-513-62). Stir bars for the quartz test tubes were purchased from Fisher Chemical (Fisherbrand stir bar, octagon – Cat No: 14-513-58).

3. Photoreactor Instrumentation

Figure S1. The photochemical setup used in this study shown with the door closed (left) and the lights on/door open (right). These photographs were taken in the Sanford Laboratory by Matthew R. Lasky.

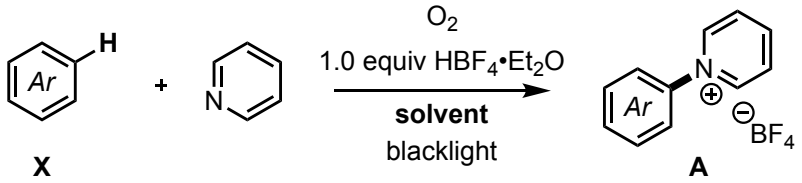
The photoreactor pictured in **Figure S1** was used for all photolysis reactions reported herein. The LZC-ORG photoreactor was purchased from Luzchem. Four stir plates were placed inside the photoreactor (Fisherbrand RT Basic Magnetic Stirrers). UVA compact fluorescent lamps (CFLs) (315-400 nm, 8W, F8T5BLB) were purchased from Luzchem (LZC-UVA) and are centered at ~350 nm (black light). UVB CFLs (280-315 nm, 8W, G8T5E) were also purchased from Luzchem (LZC-UVB) and are centered at ~300 nm, with a peak of 313 nm. For reactions performed with UVB CFLs, quartz test tubes were utilized as the reaction vessel (**Figure S2**). These quartz test tubes (max capacity 14 mL) were made in-house at the University of Michigan with the following dimensions: 18 mm x 4.25 in. All reaction vials were placed 5 mm away from the light source and were secured to the stir-plates using double-sided tape. The photoreactor is fan-cooled, and the temperature inside was consistently measured to be 31-33 °C during irradiation.

Figure S2. Quartz test tubes utilized when irradiating with UVB CFLs. The photochemical setup employed for the quartz tubes is depicted on the far right. These photographs were taken in the Sanford Laboratory by Matthew R. Lasky.

Reaction Vessel	Septum	Stir Bar (Cat. No.)	Light Source
4 mL vial	Thermo Scientific: C4015-66A	Chemglass: CG-2003-16	UVA
20 mL scintillation vial	Chemglass: GPI 22-400	Fisher: 14-513-62	UVA
Quartz test tube	Fisher: CG302403	Fisher: 14-513-58	UVB

Table S1. List of materials utilized under specific reaction conditions.

4. Reaction Optimization C(sp^2)–H Pyridination



X **A**

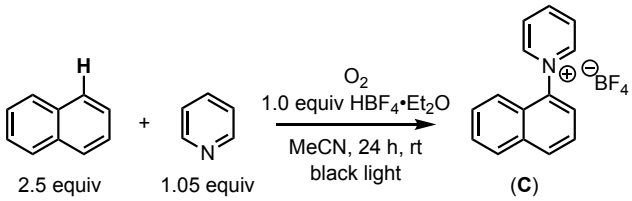
Optimization Procedure (**Table 1, entry 1**). Naphthalene (30.8 mg, 0.24 mmol, 1.0 equiv) was weighed into either a 4 or 20 mL scintillation vial equipped with the appropriate stir bar (see *Materials* section or Table S1). With a syringe, anhydrous acetonitrile (2.4 mL) was added, followed by pyridine (19.4 µL, 0.24 mmol, 1.0 equiv), and then HBF_4•Et_2O (32.9 µL, 0.24 mmol, 1.0 equiv). The vial was sealed using a septum cap, the cap was wrapped with electrical tape (Figure S1), and the solution was sparged with an O_2 balloon for 10 min. The resulting mixture was placed inside the photoreactor and allowed to stir under blacklight (UVA) irradiation (~350 nm) for 24 h. After 24 h, a needle was utilized to pierce the septum to release any build-up of pressure. Pentamethylbenzene (35.6 mg, 0.24 mmol, 1 equiv) was then added as an internal standard, and the crude reaction mixture was analyzed by ^{1}H NMR spectroscopy.

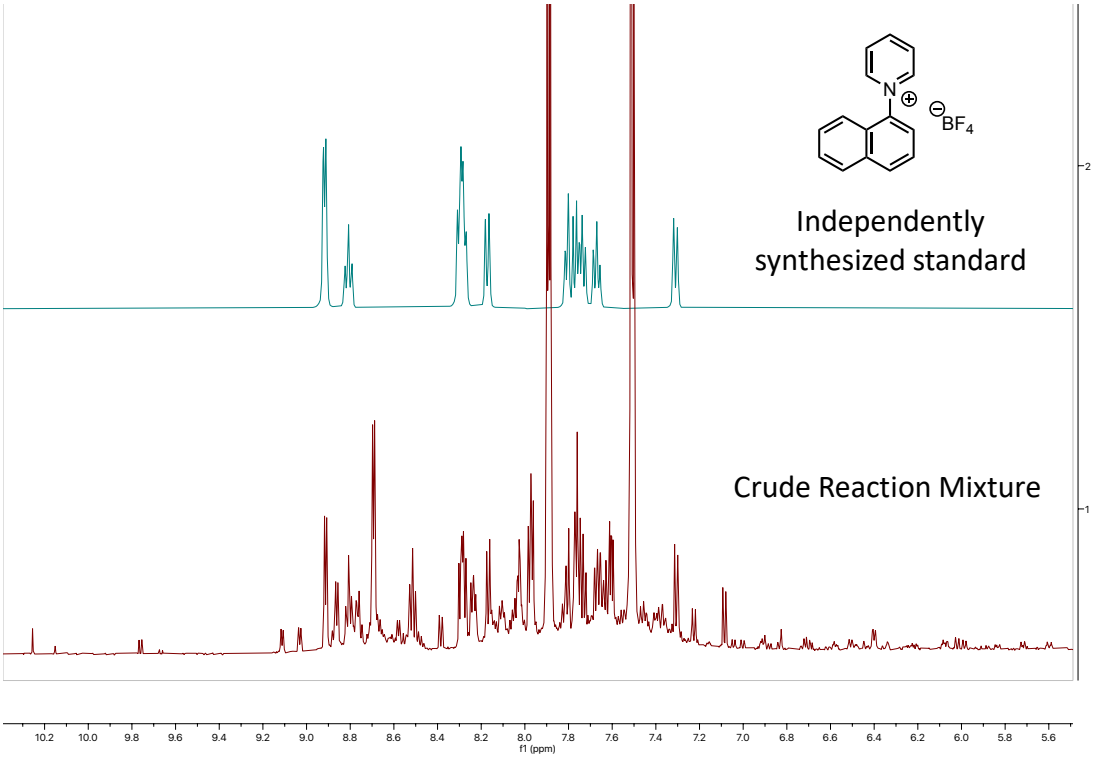
Entry	Pyridine (eq)	Arene X (eq)	Solvent	[HBF_4•Et_2O]	A
1	1.0	naphthalene, 1.0	MeCN	0.1 M	<1%
2	1.05	naphthalene, 1.0	MeCN	0.1 M	5%
3	1.05	naphthalene, 2.5	MeCN	0.1 M	6%
4[a]	1.05	naphthalene, 2.5	MeCN	0.1 M	<1%
5	2.0	naphthalene, 1.0	MeCN	0.1 M	8%
6	1.05	naphthalene, 2.5	MeCN	0.05 M	18%
7	2.0	naphthalene, 1.0	MeCN	0.05 M	18%
8	1.05	naphthalene, 2.5	MeCN	0.02 M	23%
9[a]	1.05	naphthalene, 2.5	MeCN	0.02 M	4%
10	1.5	naphthalene, 1.0	MeCN	0.02 M	22%
11	2.0	naphthalene, 1.0	MeCN	0.02 M	20%
12	5.0	naphthalene, 1.0	MeCN	0.02 M	25%
13[b]	1.05	naphthalene, 2.5	MeCN	0.02 M	NR, 0%
14[c]	1.05	naphthalene, 2.5	MeCN	0.02 M	22%
15[d]	1.05	naphthalene, 2.5	MeCN	0.02 M	16%
16	1.05	biphenyl, 1.0	MeCN	0.02 M	33%
17	1.05	biphenyl, 2.5	MeCN	0.02 M	72%

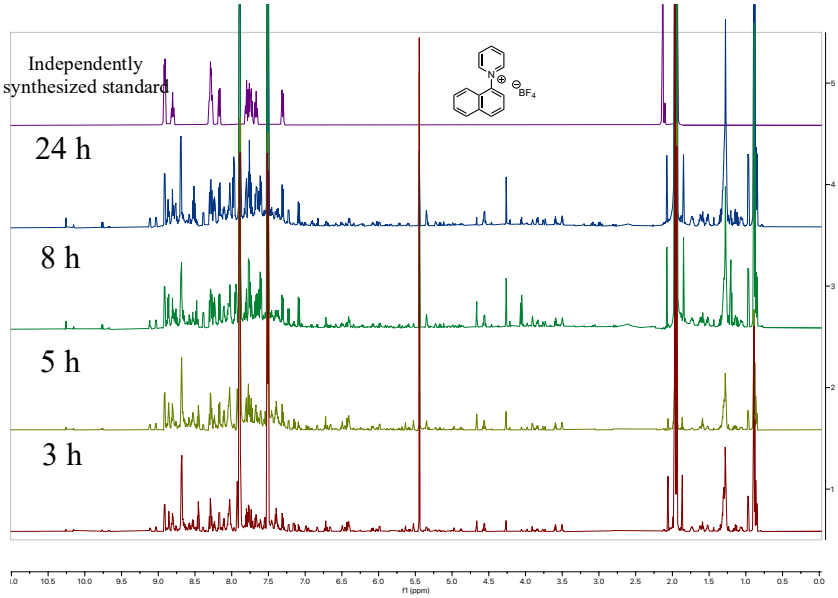
18	1.05	biphenyl, 5.0	MeCN	0.02 M	50%
19[e]	1.05	biphenyl, 2.5	MeCN	0.02 M	51%
20[f]	1.5	biphenyl, 1.0	MeCN	0.02 M	62%
21[f]	2.0	biphenyl, 1.0	MeCN	0.02 M	70%
22[g]	1.05	biphenyl, 2.5	MeCN	0.01 M	2%
23[h]	1.05	biphenyl, 2.5	DCM	0.02 M	NR, 0%
24[h]	1.05	biphenyl, 2.5	DCE	0.02 M	NR, 0%
25	1.05	biphenyl, 2.5	TFE	0.02 M	5%
26[b]	1.05	biphenyl, 2.5	MeCN	0.02 M	NR, 0%
27[c]	1.05	biphenyl, 2.5	MeCN	0.02 M	NR, 0%
28[d]	1.05	biphenyl, 2.5	MeCN	0.02 M	39%
29[a]	1.05	biphenyl, 2.5	MeCN	0.02 M	14%
30[i]	1.00	biphenyl, 2.5	MeCN	0.02 M	1%

Table S2. All reactions were conducted at a 0.24 mmol scale, unless otherwise noted. All yields of **A** are crude and were determined by ^{1}H NMR spectroscopy using pentamethylbenzene (0.24 mmol, 1 equiv) as a standard. [a] Reaction was not sparged with an O_2 balloon before light irradiation (ambient air). [b] Reaction performed in the dark (without a light source). [c] Reaction was conducted using two PR160L Kessil LEDs (440 nm, 45W). [d] Reaction conducted using two PR160L Kessil LEDs (390 nm, 52 W). [e] Reaction was conducted at 0.05 mmol scale. [f] The dipyridinated product was also observed in 19% and 18% respectively (entries 20 and 21). This product was also confirmed by HRMS (ESI+). [g] Reaction performed in a 50 mL round-bottom flask. [h] Upon addition of HBF_4•Et_2O to the reaction solution a precipitate immediately formed; we hypothesize that the pyridinium salt has poor solubility in DCM and DCE. [i] Reaction conducted without HBF_4•Et_2O. NR = no reaction.

Crude reaction mixture of naphthalene: NMR analysis







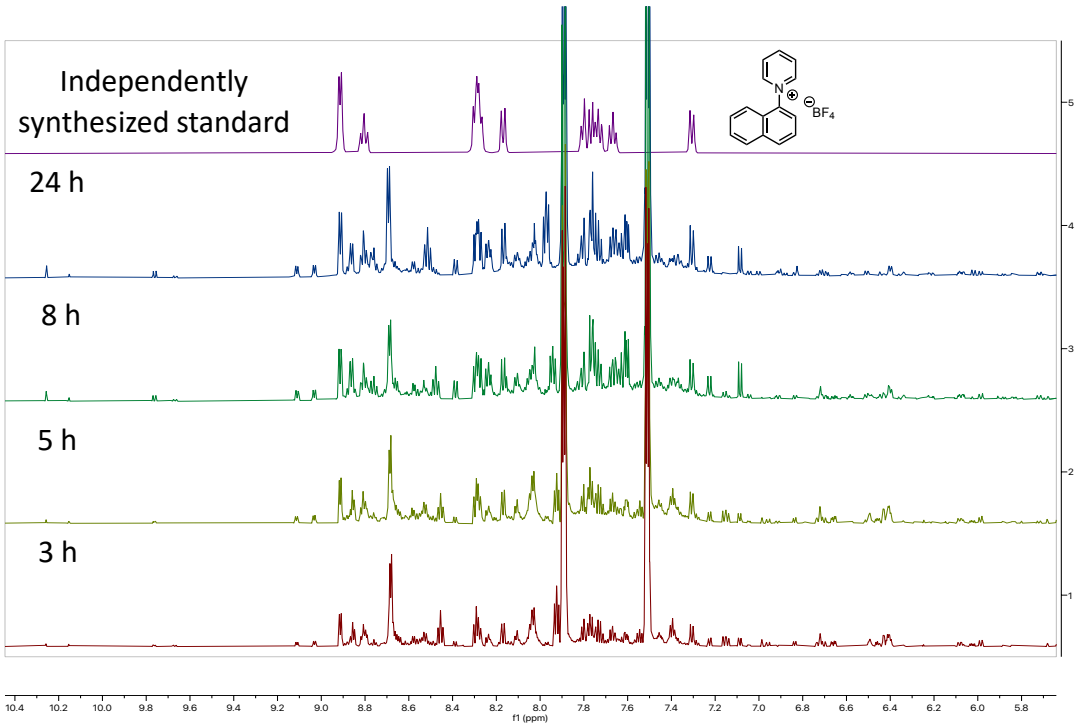
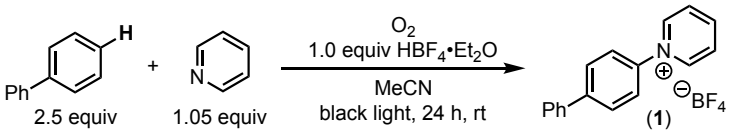
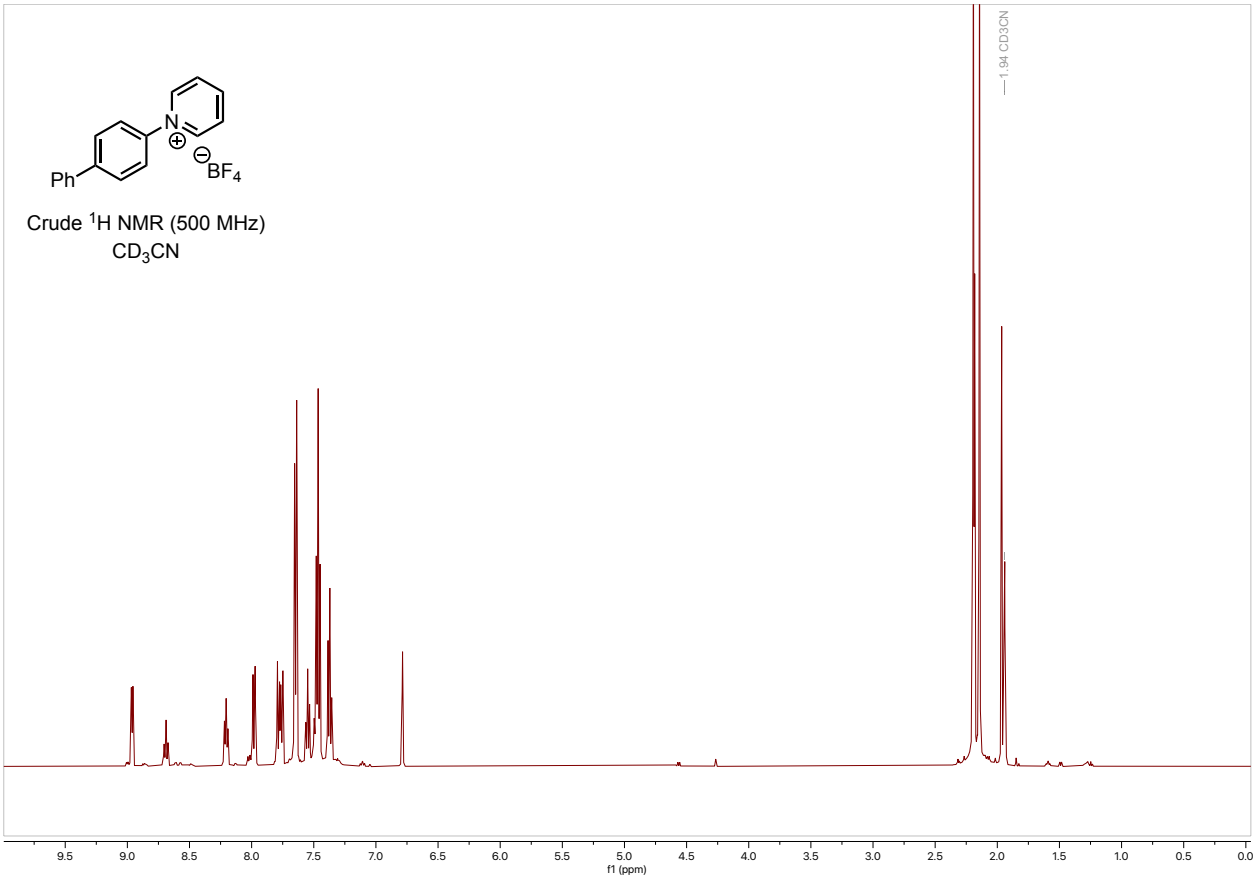


Figure S3. Overlayed ^{1}H NMR spectra of the crude reaction mixture for naphthalene. **Top**: Aromatic region of spectrum for authentic sample of product compared to crude reaction mixture after 24 h. **Middle:** Time course of photochemical reaction showing full ^{1}H NMR spectra (0 to 11 ppm). **Bottom:** Time course of photochemical reaction showing aromatic region of spectra (5.6-10.5 ppm).

Crude reaction mixture of biphenyl – NMR analysis





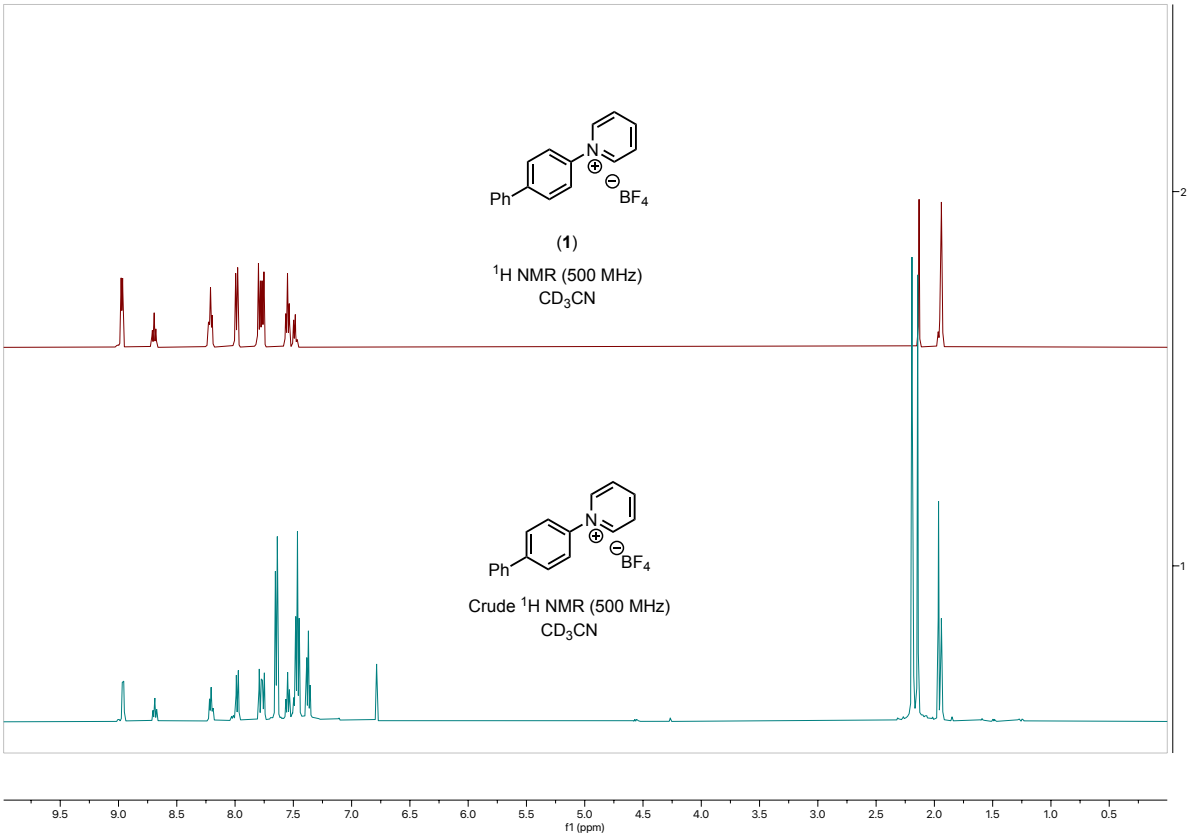
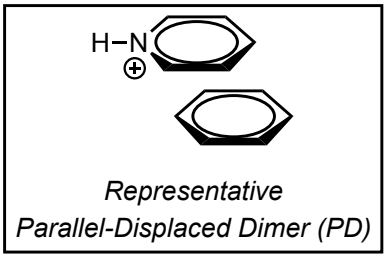


Figure S4. ^{1}H NMR spectrum of the crude reaction mixture for biphenyl after 24 h compared to the isolated product spectrum. Comparison to Figure S3 shows that the crude reaction mixture with biphenyl is much cleaner than that of naphthalene. **Top:** ^{1}H NMR spectrum of the crude reaction mixture for biphenyl after 24 h. **Bottom:** Comparison of the crude ^{1}H NMR spectrum of biphenyl to the isolated ^{1}H NMR spectrum of product **1**.

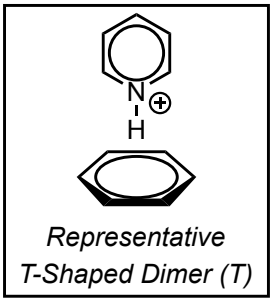
5. DFT Calculations

Ground state geometries of monomers and molecular dimers in different conformations were computed using density functional theory (DFT) at B3LYP level[2] and 6-311+G** basis set.[3] The effect of dispersion interactions is included using the D3 version of Grimme with Becke-Johnson damping.[4] In addition, the effect of the dielectric medium (ε = 35.69) is included, using the polarizable continuum model (cpcm) approach.[5] Ground state energies of a few conformations of dimers were explored and are reported below. The excited states of the parallel displaced conformer dimers were computed using time dependent density functional theory,[6] using the same basis set that is used for computing the ground state geometries. In addition, the effect of dielectric medium is also included in computing the excited states of the monomers and dimers. The excited states were fed into Gaussview[7] to compute the UV-Vis absorption spectra for monomers and dimers. In addition, the nature of the excited states was explored using the NTO analysis.[8] All calculations were performed using Gaussian16 suit of programs.[9]

Binding Energies in the Isolated Complexes[10]



Representative Parallel-Displaced Dimer (PD)



Representative T-Shaped Dimer (T)

Dimers	BE (kcal/mol) Current Study (DFT)		BE (kcal/mol) Literature	
	PD	T	PD	T
Bz-Bz	-3.6	-3.4	-2.7**	-2.7**
Py-Bz	-4.2	-3.8	-3.2**	-3.2**
Py-Py	-4.8	-4.0	-3.8**	-3.0**
PyH^+-Bz	-10.6	-15.8	-10.5*	-

Table S3. Binding energies (BE) of dimers; benzene is represented as Bz, pyridine as Py and pyridinium as PyH^+; the negative sign indicates that the two monomers interact favorably to form dimers/complexes. The trends in the binding energy with the current methodology are comparable to those found with higher level methodologies used in literature. The current approach is preferred because it is less time consuming to incorporate the effect of solvents and compute excited state energies. **CCSD(T)/CBS; *M062X-6-311++G(d, p). For comparing the binding energies with literature values, the effect of dielectric medium was excluded in this set of calculations.[10]

Effect of Solvation on Binding Energies

Dimer	Dielectric Medium	BE (kcal/mol) @ B3LYP/6-311+G**	
		PD	T
PyH^+-Bz	Isolated	-10.6	-15.8
	Benzene (ε =2.3)	-7.2	-9.9
	Pyridine (ε = 13.0)	-5.6	-6.5
	Acetonitrile (ε = 35.7)	-5.4	-6.0

Table S4. With increasing dielectric constant of the medium, binding energy drops more significantly compared to neutral complexes. The effect is more significant for the T dimer compared to the PD dimer. If the dielectric constant of the medium is high, the difference in energy between the PD and T dimers gets smaller, which is potentially due to screening of the cations by a medium with high dielectric constant.

Although the absolute binding energies, computed at the B3LYP level, are over-estimated by ~ 1.0 kcal/mol compared to the coupled cluster method, the trends are well captured by B3LYP. The relative difference between the T-shaped and parallel displaced (PD) dimers are also well captured by the B3LYP method. In addition, B3LYP provides low mean absolute error (~ 0.15 eV) for vertical excitation energies.[15] Thus, we choose B3LYP to explore the binding energies and the excited states of a wider range of electron donor-acceptor pairs.

Model System: Simulated Absorption Spectrum – PyH^+–Benzene

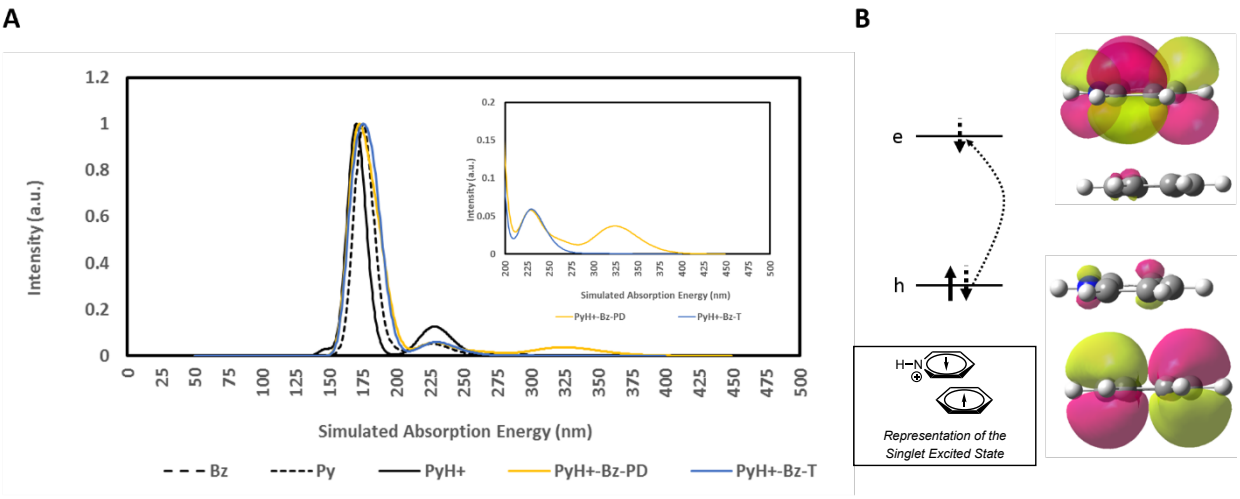
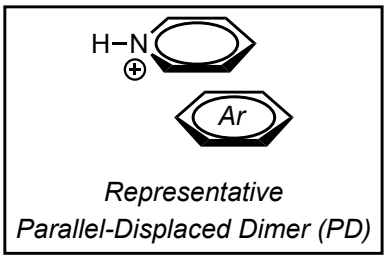


Figure S5. (A) Computed UV-Vis absorption spectra of monomers (Bz, Py and PyH^+) and dimer (PyH^+–Bz) in PD and T-shaped conformation in the presence of dielectric medium. The inset shows the low energy (high wavelength) bands of PD and T-shaped dimers; (B) Electron and hole wavefunctions, from NTO analysis, for the low energy absorption band of the PD dimer.

Figure S5 depicts the computed UV-Vis absorption spectra of monomers (Bz, Py and PyH^+) and dimer (PyH^+–Bz). The PD dimer shows an absorption band around 324 nm, whereas the absorption band for the T-shaped dimer is observed at lower wavelength. Based on NTO analysis, the low-energy singlet excited state of the PD dimer between pyridinium and benzene is charge-transfer (CT) in nature (benzene to pyridinium cation). The hole is primarily localized on the benzene, and the electron is localized on the pyridinium after excitation.

DFT Calculations to Determine Alternative Arene Donors



Representative Parallel-Displaced Dimer (PD)

Arene	Conformation	BE (kcal/mol)	Rel. |BE| w.r.t Benzene (PD)	Excitation Wavelength (λ_{max} PD)
benzene	PD	-5.4	-	324 nm
tert-butylbenzene	PD	-6.5	1.1	353 nm
anisole	PD	-7.2	1.8	399 nm
biphenyl	PD	-7.9	2.5	394 nm
naphthalene	PD	-9.1	3.7	395 nm

Table S5. Comparison of the energetics of the PyH^+–Benzene EDA complex with various arene substrates.

The calculations indicate that EDA complexation with the pyridinium cation (PyH^+) is energetically favorable for each of the arene donors. (Notably, in these calculations, the effect of entropy is neglected. For a comparison between different arenes the effect of entropy is expected to be negligible.) In all cases, DFT predicts that the charge transfer band of the EDA adduct will be in the UVA region (calculated λ_{max} ranging from 399 to 324 nm). Overall, biphenyl is predicted to have the most similar properties to naphthalene with a BE_{EDA} of -7.9 kcal/mol in the parallel displaced (PD) geometry (compared to -9.1 kcal/mol for naphthalene) and a λ_{max} of 394 nm (compared to 395 nm for naphthalene).

Simulated Absorption Spectrum – Benzene, Naphthalene, and Biphenyl

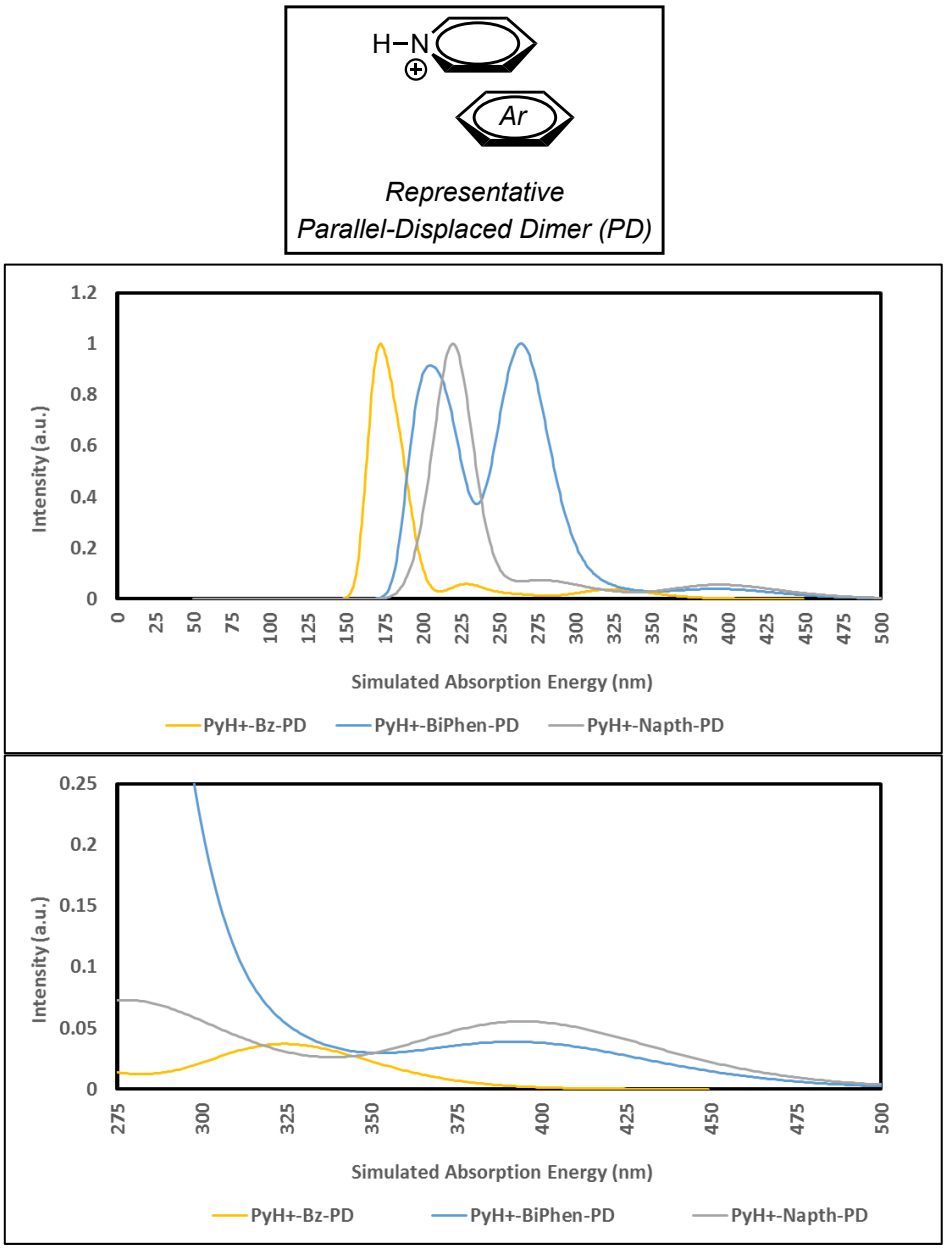


Figure S6. Simulated absorption spectrum for the PD PyH^+–Arene EDA complex: PyH^+–Benzene (Bz), PyH^+–BiPhen (biphenyl), and PyH^+–Naphth. See Table S5 for the specific excitation wavelength (nm) (λ_{maxCT}) of each EDA complex.

6. UV-Vis Spectroscopic Analysis

UV-Vis measurements were obtained on a Varian Cary-50 spectrophotometer using a 3 mL (1 cm path length) cuvette. Processing of UV-Vis data: the generated data was plotted in Microsoft Excel.

PyH$^+$–Naphthalene EDA complex:
To a flame-dried 5 mL volumetric flask, a 0.2 M stock solution was prepared for each of the following reagents in anhydrous MeCN:

1) Pyridine and HBF_4•Et_2O (0.2 M) = 80.6 µL (1.0 mmol) and 137.2 µL (1.0 mmol), respectively – **gray trace**
2) Naphthalene (0.2 M) = 128.2 mg (1.0 mmol) – **blue trace**
3) Pyridine + HBF_4•Et_2O : Naphthalene (1:1, 0.2 M) = 80.6 µL (1.0 mmol) and 137.2 µL (1.0 mmol) : 128.2 mg (1.0 mmol), respectively – **maize trace**

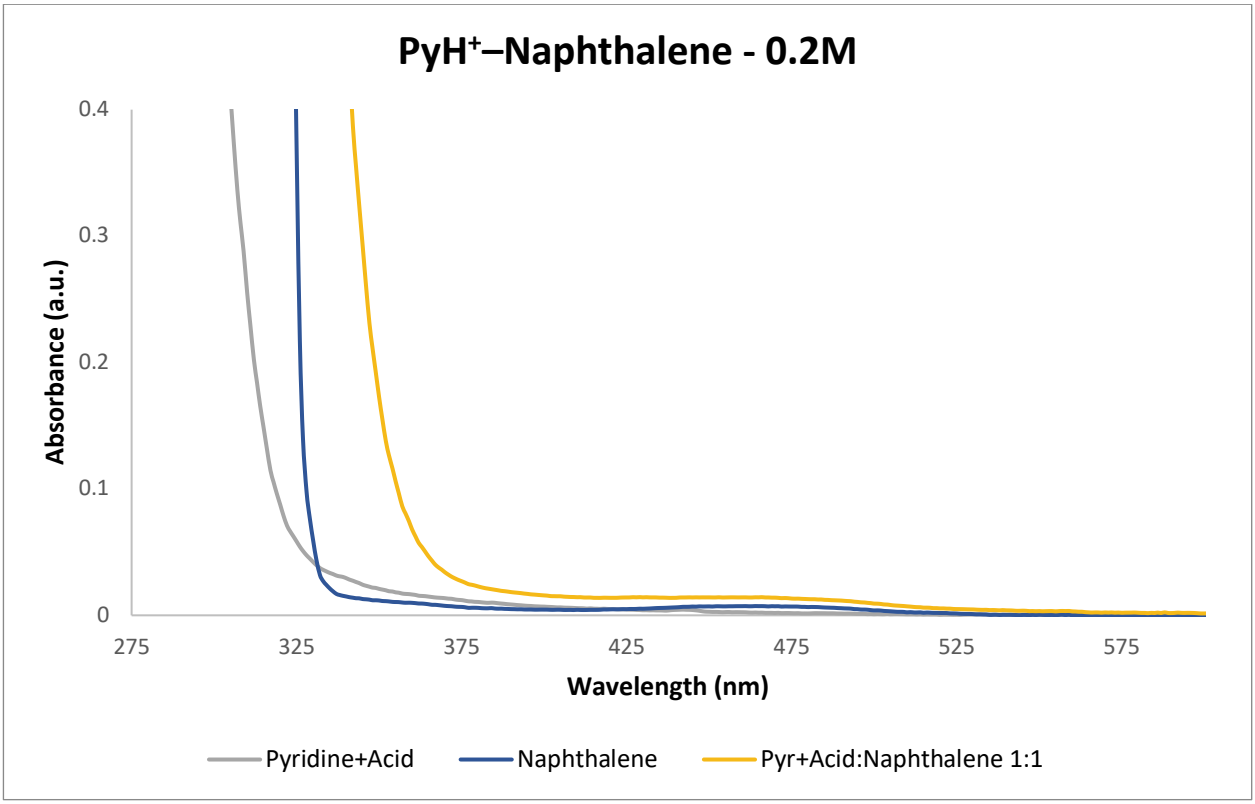


Figure S7. Experimental UV-Vis spectra for PyH$^+$–Naphthalene EDA Complex (0.2M) recorded on a Varian Cary-50 spectrophotometer. These results demonstrate a bathochromic shift diagnostic of EDA complex formation via aggregation of PyH$^+$ and naphthalene. AU = arbitrary units.

PyH⁺–Biphenyl EDA complex:

To a flame-dried 5 mL volumetric flask, a 0.2 M stock solution was prepared for each of the following reagents in anhydrous MeCN:

1) Pyridine and HBF_4•Et_2O (0.2 M) = 80.6 µL (1.0 mmol) and 137.2 µL (1.0 mmol), respectively – **gray trace**
2) Biphenyl (0.2 M) = 154.2 mg (1.0 mmol) – **blue trace**
3) Pyridine + HBF_4•Et_2O : Biphenyl (1:1, 0.2 M) = 80.6 µL (1.0 mmol) and 137.2 µL (1.0 mmol) : 154.2 mg (1.0 mmol), respectively – **maize trace**

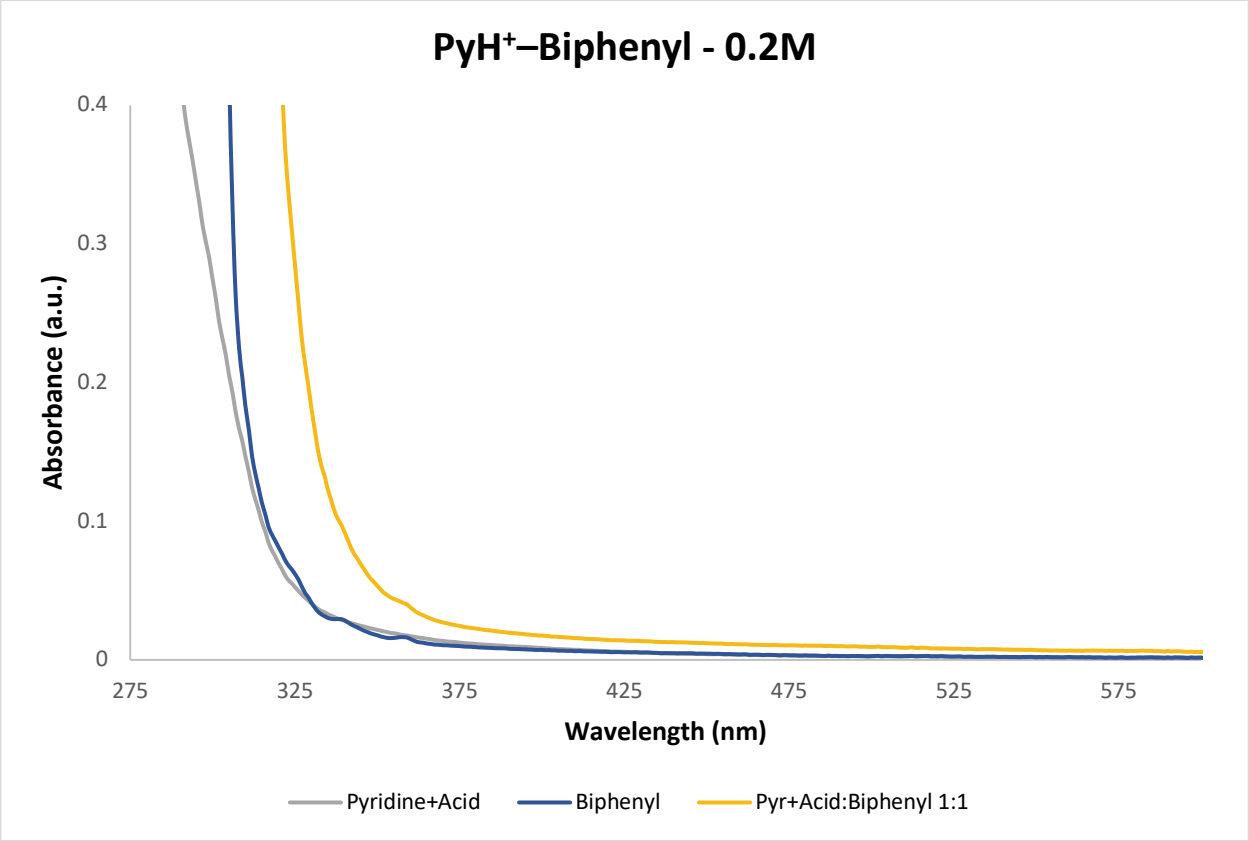


Figure S8. Experimental UV-Vis spectra for PyH⁺–Biphenyl EDA Complex (0.2M) recorded on a Varian Cary-50 spectrophotometer. These results demonstrate a bathochromic shift diagnostic of EDA complex formation via aggregation of PyH⁺ and biphenyl. AU = arbitrary units.

i. Job Plot Analysis:

Job plot of PyH⁺–Biphenyl EDA complex:

Two separate 0.50 M stock solutions of protonated pyridine and biphenyl were prepared in anhydrous acetonitrile.

Protonated Pyridine (PyH⁺) Stock Solution: To a flame-dried 25 mL volumetric flask, a 0.50 M stock solution was prepared for PyH⁺ in anhydrous MeCN.

- Pyridine and HBF_4•Et_2O (0.5 M): 1.01 mL (12.5 mmol) and 1.72 mL (12.5 mmol), respectively.

Biphenyl Stock Solution: To a flame-dried 10 mL volumetric flask, a 0.50 M stock solution was prepared for biphenyl in anhydrous MeCN.

- Biphenyl (0.5 M): 771.06 mg (5 mmol)

Preparation of samples: To a 4 mL vial was added PyH^+ stock solution, biphenyl stock solution and 1.8 mL of MeCN. The solutions were transferred via syringe to a 3 mL (1 cm path length cuvette). UV-Vis spectra were obtained on a Varian Cary-50 spectrophotometer.

Pyridine + Acid			Biphenyl			Void	Total
mmol	ratio	volume (µL)	mmol	ratio	volume (µL)	volume (µL)	volume (µL)
0	0	0	0.6	1	1200	1800	3000
0.06	0.1	120	0.54	0.9	1080	1800	3000
0.12	0.2	240	0.48	0.8	960	1800	3000
0.18	0.3	360	0.42	0.7	840	1800	3000
0.24	0.4	480	0.36	0.6	720	1800	3000
0.3	0.5	600	0.3	0.5	600	1800	3000
0.36	0.6	720	0.24	0.4	480	1800	3000
0.42	0.7	840	0.18	0.3	360	1800	3000
0.48	0.8	960	0.12	0.2	240	1800	3000
0.54	0.9	1080	0.06	0.1	120	1800	3000
0.6	1	1200	0	0	0	1800	3000

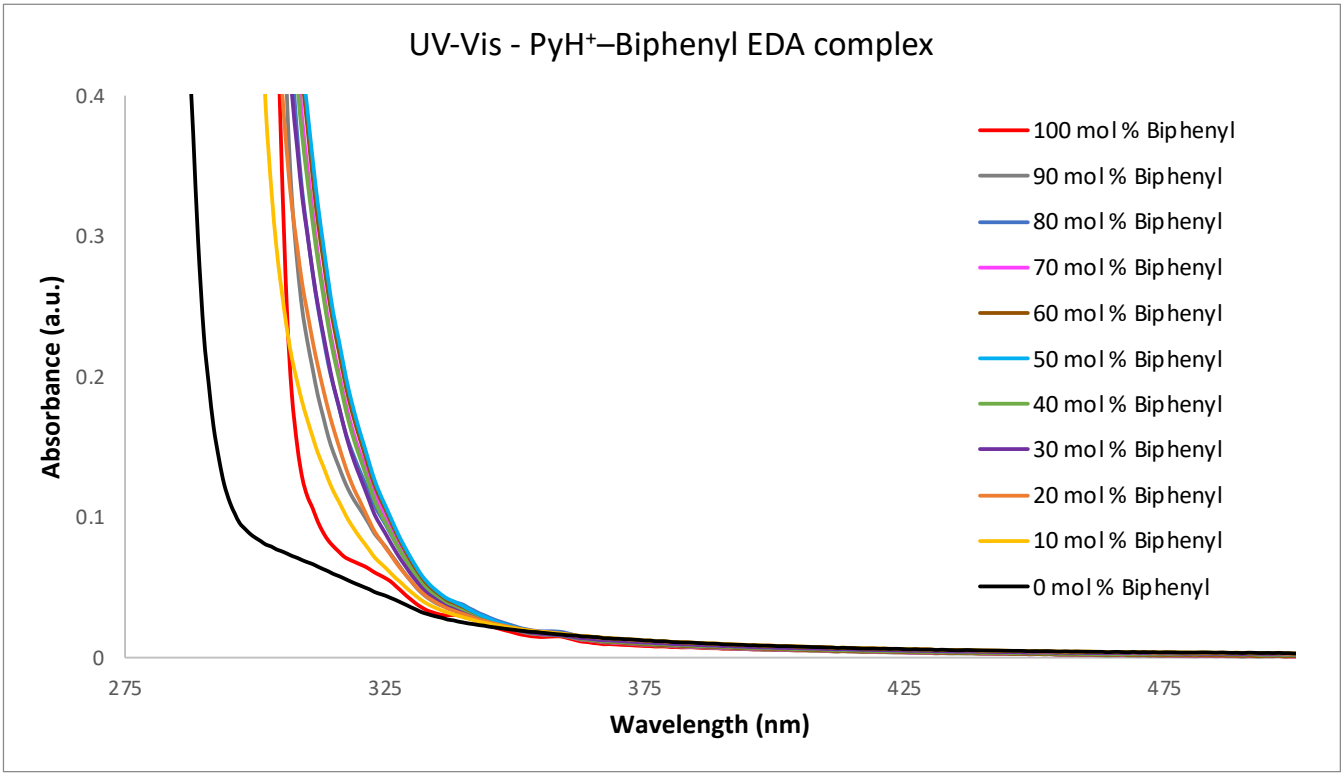


Figure S9. Experimental UV-Vis spectra for PyH^+–Biphenyl EDA Complex (0.20 M) with variation of biphenyl and PyH^+ components.

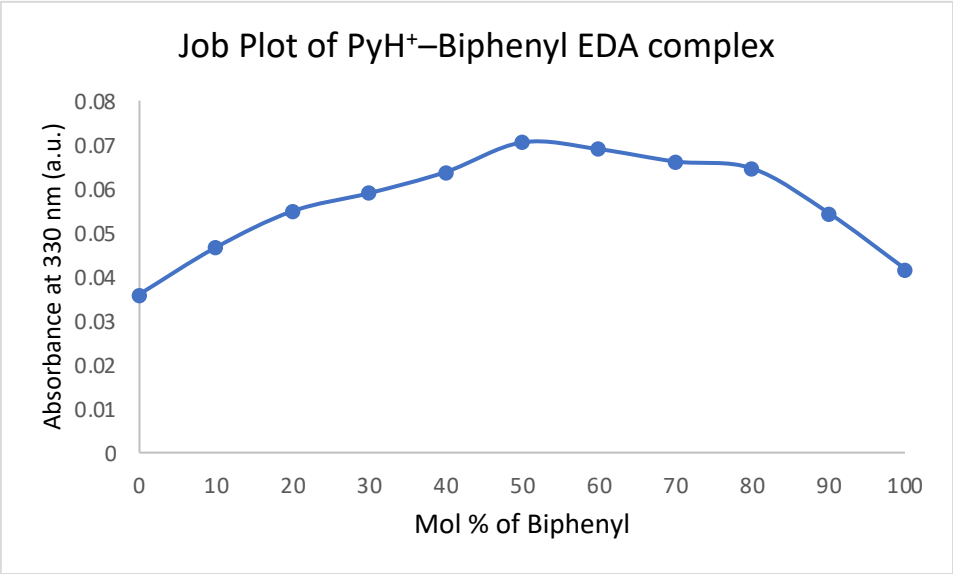
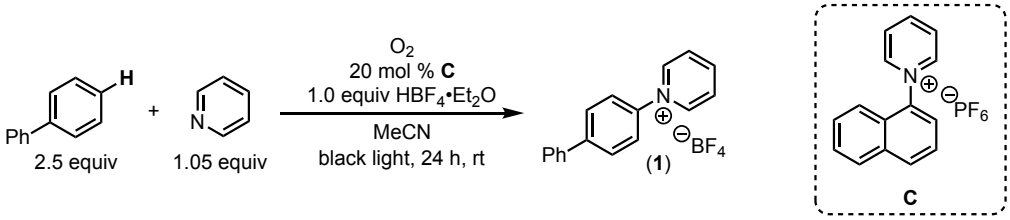


Figure S10. Job Plot of absorbance at 330 nm for PyH⁺–Biphenyl EDA Complex (0.20 M). These results suggest the EDA binding stoichiometry is a 1:1 complex between donor (biphenyl) and acceptor (PyH⁺).

7. Control Experiments

a) *Stability of N-Arylpyridinium Product **C**:*



The following control experiment was conducted to confirm that **C** is stable under photochemical conditions. A 20 mL scintillation vial equipped with a stir bar was charged with biphenyl (92.5 mg, 0.60 mmol, 2.5 equiv) and independently synthesized **C** (16.9 mg, 0.048 mmol, 0.20 equiv).[1] With a syringe, anhydrous acetonitrile (12 mL) was added, followed by pyridine (20.4 µL, 0.252 mmol, 1.05 equiv) and then HBF_4•Et_2O (32.9 µL, 0.24 mmol, 1.0 equiv). The vial was sealed using a septum-lined cap, the outside of the cap was wrapped with electrical tape, and the solution was sparged with an O_2 balloon for 10 min. The resulting mixture was placed inside the photoreactor and allowed to stir under black light (UVA) irradiation (~350 nm) for 24 h. After 24 h, a needle was utilized to pierce the septum to release any build-up of pressure. A crude ^{1}H NMR was taken of the reaction mixture using pentamethylbenzene (35.6 mg, 0.24 mmol, 1.0 equiv) as an internal standard. *Analysis of the crude reaction mixture demonstrates no decomposition to **C**, successfully retaining all 20 mol % of **C*** (see Figure S11).

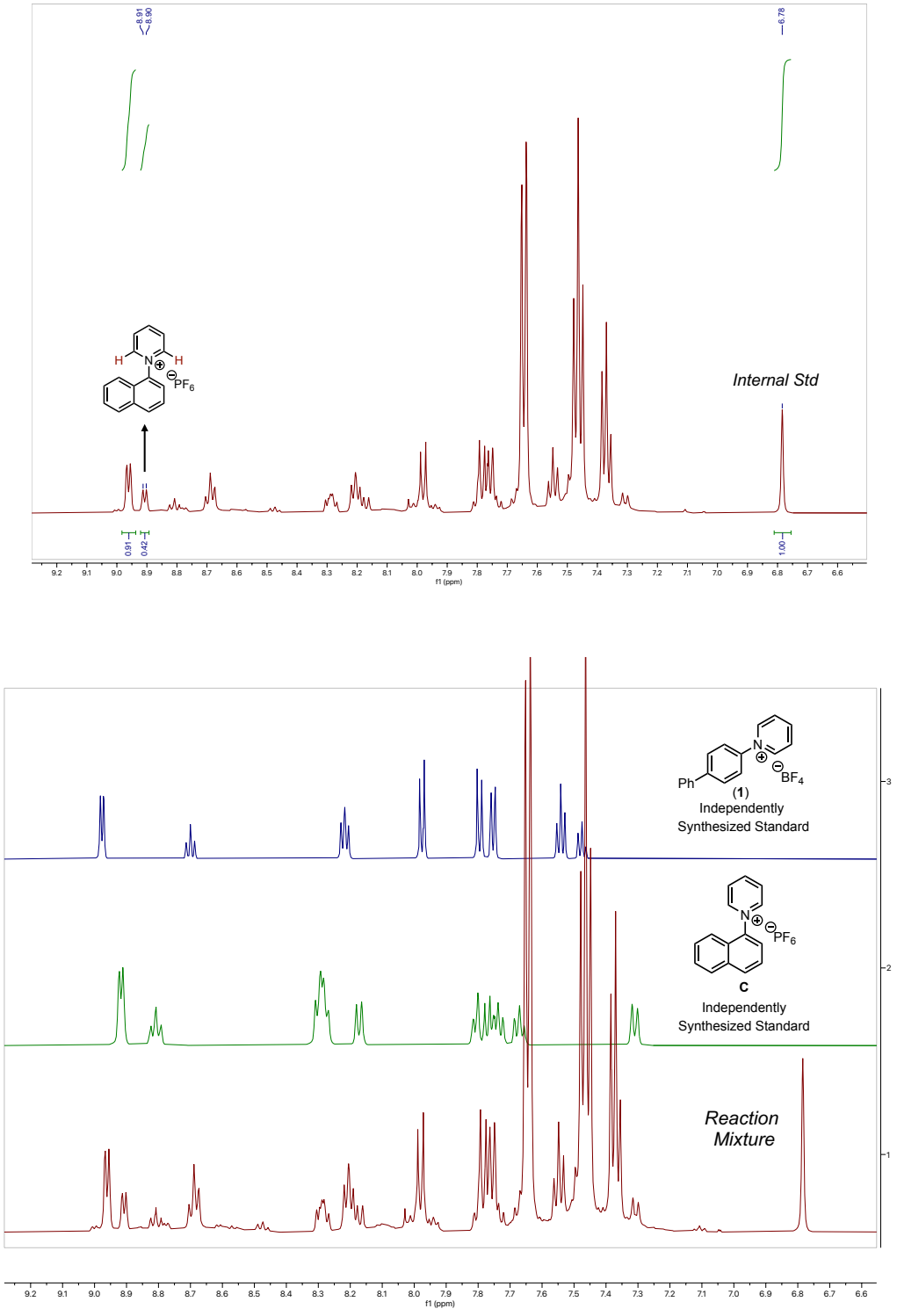


Figure S11. Crude ^{1}H NMR spectra investigating the decomposition of **C**. **Top**: Aromatic region analyzing the amount of **C** retained compared to an internal standard. We observe full retention of **C**, validating that it is stable under photochemical conditions. We also observe a 45% yield of **1**. **Bottom:** Overlayed reaction mixture with independently synthesized standards of **C** and **1**.

b) *NMR Study of PyH^+–Biphenyl EDA complex:*

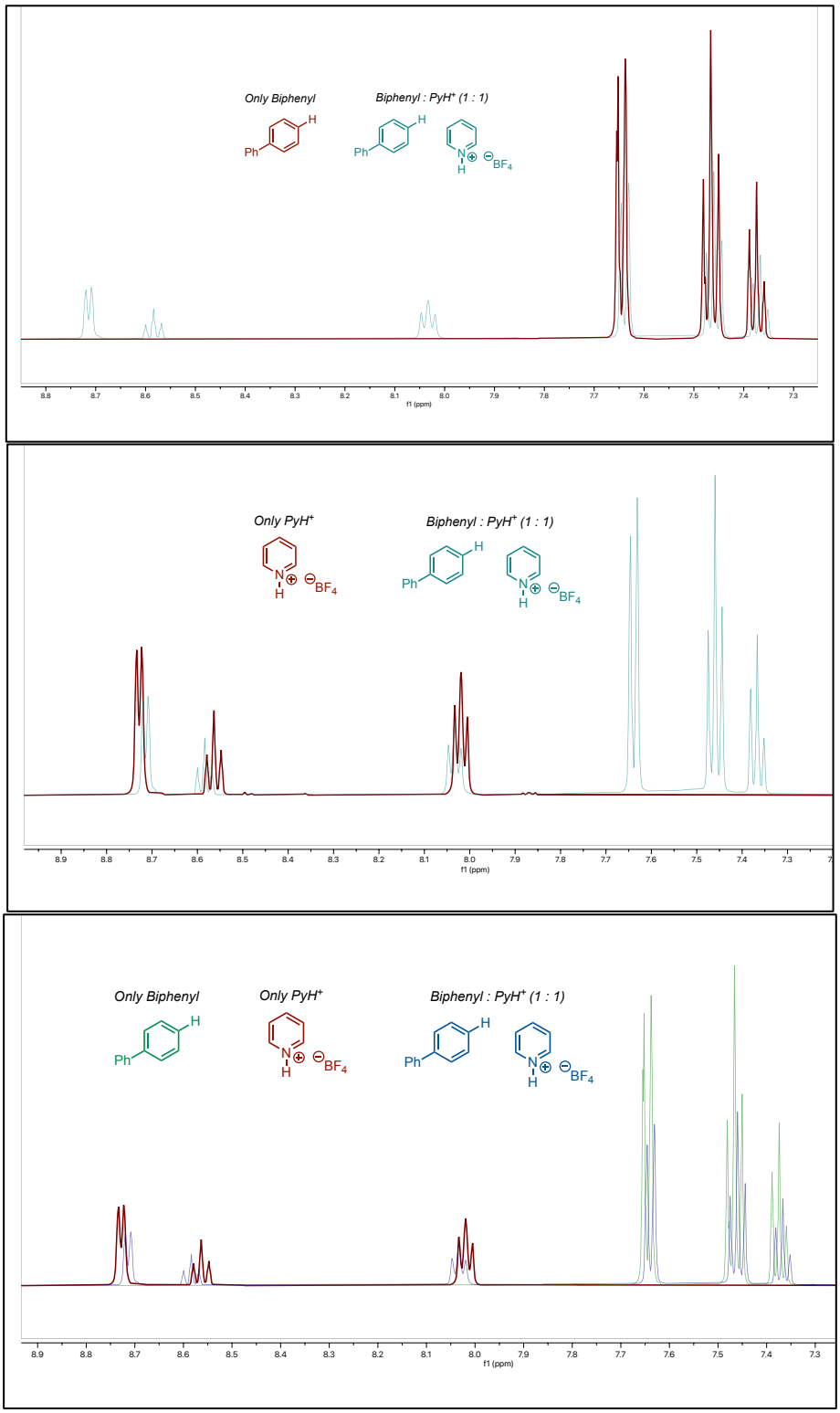
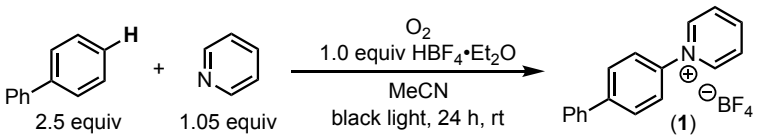


Figure S12. Top: ^{1}H NMR spectrum overlay of biphenyl (donor) and a 1 : 1 mixture of PyH^+ + biphenyl (in CD_3CN). **Middle**: ^{1}H NMR spectrum overlay of PyH^+ (acceptor) and a 1 : 1 mixture of PyH^+ + biphenyl (in CD_3CN). **Bottom**: ^{1}H NMR spectrum overlay of biphenyl (donor), PyH^+ (acceptor), and a 1 : 1 mixture of PyH^+ + biphenyl (in CD_3CN).[17]

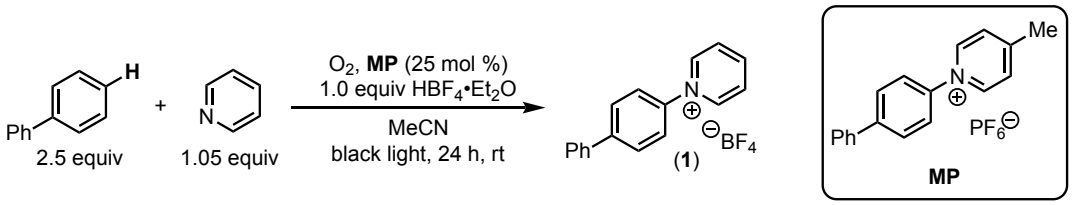
8. Initial Rate Investigation for C(sp^2)–H Pyridination

*Standard Reaction Conditions (**Maize Trace** – Figure S13):*



A flame dried 25 mL volumetric flask was charged with biphenyl (192.8 mg, 1.25 mmol, 2.5 equiv). With a syringe, anhydrous acetonitrile (20 mL) was added, followed by pyridine (42.5 µL, 0.525 mmol, 1.05 equiv) and then HBF_4•Et_2O (68.6 µL, 0.50 mmol, 1.0 equiv). The remaining anhydrous acetonitrile (5 mL) was added, and the stock solution was transferred to a 40 mL vial. Using a syringe, the stock solution was evenly distributed (2.5 mL each) to six 4 mL vials equipped with a stir. The vial was sealed using a septum-lined cap, the outside of the cap was wrapped with electrical tape, and the solution was sparged with an O_2 balloon for 10 min. The resulting mixture was placed inside the photoreactor and allowed to stir under black light (UVA) irradiation (~350 nm). Time points were taken every 10 minutes. Once removed from the photoreactor, a needle was utilized to pierce the septum to release any build-up of pressure. Utilizing a previously prepared stock solution (0.5 M in a 10 mL volumetric flask) of internal standard pentamethylbenzene, 100 µL of internal standard was added to each reaction mixture. The crude reaction mixture was then concentrated under reduced pressure and analyzed via ^{1}H NMR (CD_3CN). The generated data was plotted in Microsoft Excel.

*Standard Reaction Conditions with **MP** (**Blue Trace** – Figure S13):*



A flame dried 25 mL volumetric flask was charged with biphenyl (192.8 mg, 1.25 mmol, 2.5 equiv) and **MP** (48.9 mg, 0.125 mmol, 0.25 equiv). With a syringe, anhydrous acetonitrile (20 mL) was added, followed by pyridine (42.5 µL, 0.525 mmol, 1.05 equiv) and then HBF_4•Et_2O (68.6 µL, 0.50 mmol, 1.0 equiv). The remaining anhydrous acetonitrile (5 mL) was added, and the stock solution was transferred to a 40 mL vial. Using a syringe, the stock solution was evenly distributed (2.5 mL each) to six 4 mL vials equipped with a stir. The vial was sealed using a septum-lined cap, the outside of the cap was wrapped with electrical tape, and the solution was sparged with an O_2 balloon for 10 min. The resulting mixture was placed inside the photoreactor and allowed to stir under black light (UVA) irradiation (~350 nm). Time points were taken every 10 minutes. Once removed from the photoreactor, a needle was utilized to pierce the septum to release any build-up of pressure. Utilizing a previously prepared stock solution (0.5 M in a 10 mL volumetric flask) of internal standard pentamethylbenzene, 100 µL of internal standard was added to each reaction mixture. The crude reaction mixture was then concentrated under reduced pressure and analyzed via ^{1}H NMR (CD_3CN). The generated data was plotted in Microsoft Excel.

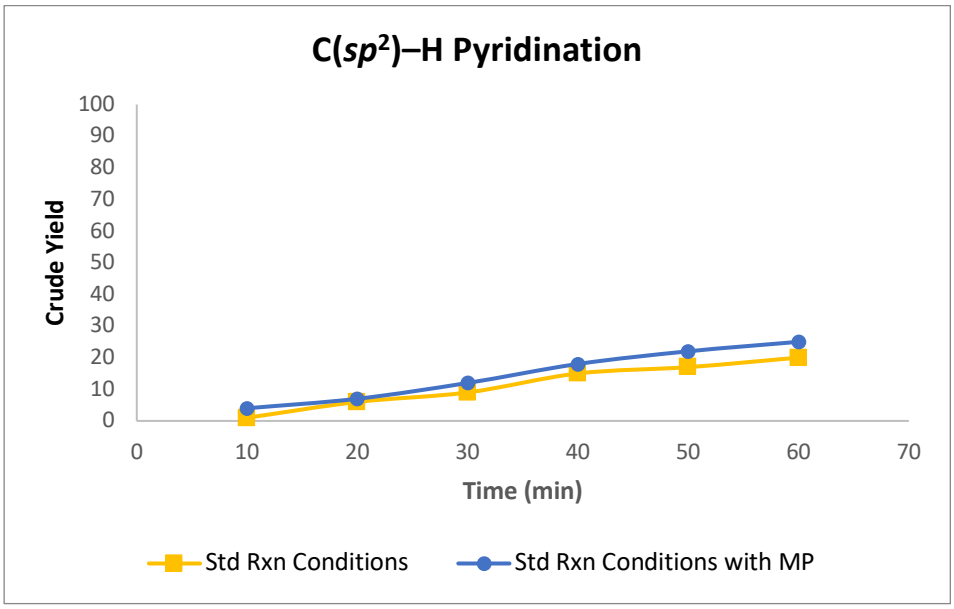
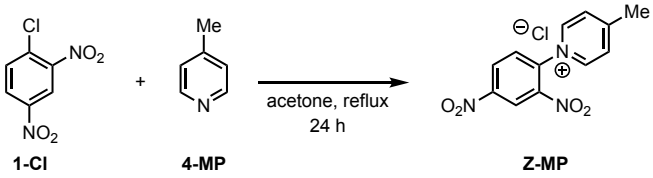


Figure S13. Reaction profile for the C–H pyridination of biphenyl, with and without **MP**. An increase in initial rate was not observed when pyridinium product **MP** was added to the reaction mixture, indicating no autocatalysis. Crude yields obtained by ^{1}H NMR spectroscopy are within error.

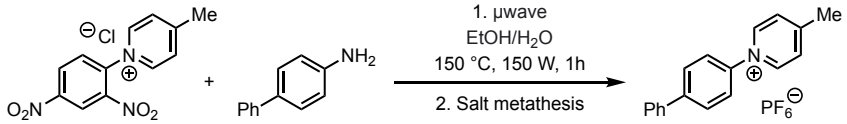
*Preparation of **MP**:*



*Synthesis of **Z-MP**:* Zincke Salt **Z-MP** was prepared from **1-Cl** and **4-MP** utilizing a literature procedure.[16]

^{1}H NMR (500 MHz, DMSO-d_6): δ 9.24 (d, J = 6.7 Hz, 2H), 9.11 (d, J = 2.6 Hz, 1H), 8.96 (dd, J = 8.7, 2.6 Hz, 1H), 8.40 (d, J = 8.7 Hz, 1H), 8.27 (d, J = 6.7 Hz, 2H), 2.78 (s, 3H).

^{13}C NMR (126 MHz, DMSO-d_6): δ 162.9, 149.0, 144.8, 143.2, 138.6, 132.0, 130.2, 128.3, 121.5, 22.1.



*Synthesis of **MP***: **MP** was prepared from **Z-MP** and **4-AB** following a literature procedure.[1] These data are consistent with that of **3**, see p. S29.

^{1}H NMR (500 MHz, CD_3CN): δ 8.78 (d, *J* = 6.5 Hz, 2H), 8.00 (d, *J* = 6.3 Hz, 2H), 7.97 (d, *J* = 8.6 Hz, 2H), 7.76 (overlapping peaks, 4H), 7.54 (t, *J* = 7.8 Hz, 2H), 7.48 (t, *J* = 7.5 Hz, 2H), 2.74 (s, 3H).

^{13}C NMR (126 MHz, CD_3CN): δ 162.5, 144.9, 144.3, 142.6, 139.6, 130.2, 129.8, 129.8, 129.7, 128.3, 125.8, 22.4.

^{19}F NMR (470 MHz, CD_3CN) δ –72.2, –73.7.

9. General Experimental Procedures for C(sp^2)–H Pyridination Reactions

For general procedure A or C, the yield is calculated with respect to HBF_4•Et_2O as the limiting reagent (1.0 equiv). For general procedure B or D is utilized, the yield is calculated with respect to the arene as the limiting reagent (1.0 equiv.) See Table S1 for a list of materials utilized under specific reaction conditions. Note that for the arene scope (Table 4, in the manuscript), comparable yields are observed when utilizing either excess arene or pyridine.

General Procedure A. *UVA Irradiation – Excess Arene*

A 20 mL scintillation vial equipped with a stir bar was charged with the corresponding arene substrate (0.60 mmol, 2.5 equiv).[11] With a syringe, anhydrous acetonitrile (12 mL) was added, followed by the appropriate pyridine (0.252 mmol, 1.05 equiv) and then HBF_4•Et_2O (32.9 µL, 0.24 mmol, 1.0 equiv). The vial was sealed using a septum-lined cap, the outside of the cap was wrapped with electrical tape, and the solution was sparged with an O_2 balloon for 10 min. The resulting mixture was placed inside the photoreactor and allowed to stir under black light (UVA) irradiation (~350 nm) for 24 h. After 24 h, a needle was utilized to pierce the septum to release any build-up of pressure. The reaction mixture was then concentrated under reduced pressure, and the product was purified by automated flash chromatography (DCM/MeCN) or preparative TLC (DCM/MeOH). The product was then dried *in vacuo* overnight.

General Procedure B. *UVA Irradiation – Excess Pyridine*

A 20 mL scintillation vial equipped with a stir bar was charged with the corresponding arene substrate (0.24 mmol, 1.0 equiv).[11] With a syringe, anhydrous acetonitrile (12 mL) was added, followed by the appropriate pyridine (0.48 mmol, 2.0 equiv) and then HBF_4•Et_2O (32.9 µL, 0.24 mmol, 1.0 equiv). The vial was sealed using a septum-lined cap, the outside of the cap was wrapped with electrical tape, and the solution was sparged with an O_2 balloon for 10 min. The resulting mixture was placed inside the photoreactor and allowed to stir under black light (UVA) irradiation (~350 nm) for 24 h. After 24 h, a needle was utilized to pierce the septum to release any build-up of pressure. The reaction mixture was then concentrated under reduced pressure, and the product was purified by automated flash chromatography (DCM/MeCN) or preparative TLC (DCM/MeOH). The product was then dried *in vacuo* overnight.

General Procedure C. *UVB Irradiation – Excess Arene*

A quartz test tube equipped with a stir bar was charged with the corresponding arene substrate (0.60 mmol, 2.5 equiv).[11] With a syringe, anhydrous acetonitrile (12 mL) was added, followed by the appropriate pyridine (0.252 mmol, 1.05 equiv) and then HBF_4•Et_2O (32.9 µL, 0.24 mmol, 1.0 equiv). The test tube was sealed using a septum cap, the outside of the septum was wrapped with parafilm and electrical tape, and the solution was sparged with an O_2 balloon for 10 min. The resulting mixture was placed inside the photoreactor and allowed to stir under UVB irradiation (~300 nm) for 24 h. After 24 h, a needle was utilized to pierce the septum to release any build-up of pressure. The reaction mixture was then concentrated under reduced pressure, and the product was purified by automated flash chromatography (DCM/MeCN) or preparative TLC (DCM/MeOH). The product was then dried *in vacuo* overnight.

General Procedure D. *UVB Irradiation – Excess Pyridine*

A quartz test tube equipped with a stir bar was charged with the corresponding arene substrate (0.24 mmol, 1.0 equiv).[11] With a syringe, anhydrous acetonitrile (12 mL) was added, followed by the appropriate pyridine (0.48 mmol, 2.0 equiv) and then HBF_4•Et_2O (32.9 µL, 0.24 mmol, 1.0 equiv). The test tube was sealed using a septum cap, the outside of the septum was wrapped with parafilm and electrical tape, and the solution was sparged with an O_2 balloon for 10 min. The resulting mixture was placed inside the photoreactor and allowed to stir under UVB irradiation (~300 nm) for 24 h. After 24 h, a needle was utilized to pierce the septum to release any build-up of pressure. The reaction mixture was then concentrated under reduced pressure, and the product was purified by automated flash chromatography (DCM/MeCN) or preparative TLC (DCM/MeOH). The product was then dried *in vacuo* overnight.

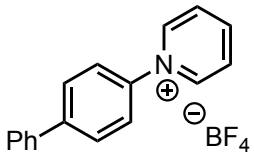
Converting HCl salt of drug substrate to HBF_4. *Fluoxetine Hydrochloride (Prozac) – Starting Material for* ***22***

Fluoxetine hydrochloride (Prozac) (504 mg, 1.63 mmol, 1.0 equiv) was dissolved in DCM (~10 mL) in a 250 mL Erlenmeyer flask. A saturated solution of $NaHCO_3$ (140 mL) was added, and the resulting mixture was allowed to stir at room temperature for 30 min. After that time, additional DCM (130 mL) was added to the reaction flask. The organic layer was separated, and the aqueous layer was extracted with DCM (2 x 50 mL). The organic extracts were combined, dried over Na_2SO_4, and concentrated via rotary evaporation to yield a colorless oil. The oil was dissolved in Et_2O (15 mL), and HBF_4•Et_2O (246 µL, 1.79 mmol, 1.1 equiv) was added at 0 °C. A white solid immediately precipitated from solution, and the mixture was allowed to stir for an additional 20 min. The solid was collected by filtration and dried *in vacuo* overnight to afford a white solid (**Prozac–HBF_4**). For NMR characterization see p. S132-133.

^{1}H NMR (700 MHz, DMSO-d_6) δ 8.31 (br s, 2H), 7.59 (d, J = 8.7 Hz, 2H), 7.41-7.38 (overlapping peaks, 4H), 7.31 (m, 1H), 7.06 (d, J = 8.7 Hz, 2H), 5.59 (dd, J = 8.5, 4.3 Hz, 1H), 3.04 (m, 1H), 2.60 (s, 3H), 2.24 (ddt, J = 14.2, 9.0, 4.5 Hz, 1H), 2.12 (ddt, J = 14.2, 10.0, 5.2 Hz, 1H).

^{19}F NMR (470 MHz, DMSO-d_6) δ –59.9, –148.3, –148.3.

10. Characterization of C(sp^2)–H Pyridination Products



(**1**)

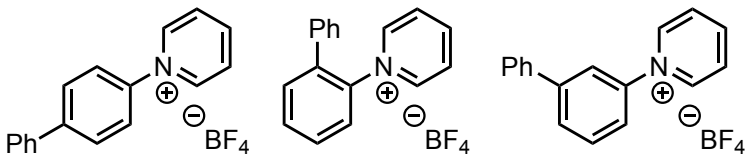
Prepared from biphenyl and pyridine using general procedure A. Purification by automated flash chromatography (DCM/MeCN gradient 0-50%) afforded the title compound (**1**) (53.7 mg, 70% yield, light yellow-orange solid). The characterization data for **1** match those reported in the literature.[12] An independently synthesized standard of **1** matched the ^{1}H and ^{13}C NMR spectra of the product (p. S53-55).[1]

^{1}H NMR (500 MHz, CD_3CN): δ 8.97 (d, *J* = 6.0 Hz, 2H), 8.69 (t, *J* = 7.7 Hz, 1H), 8.21 (t, *J* = 6.7 Hz, 2H), 7.98 (d, *J* = 8.7 Hz, 2H), 7.79 (d, *J* = 8.6 Hz, 2H), 7.76 (d, *J* = 8.0 Hz, 2H), 7.55 (t, *J* = 7.7 Hz, 2H), 7.48 (t, *J* = 7.0 Hz, 1H).

^{13}C NMR (176 MHz, CD_3CN): δ 147.8, 145.6, 145.1, 143.0, 139.5, 130.2, 129.8, 129.7, 129.5, 128.3, 125.9.

^{19}F NMR (470 MHz, CD_3CN): δ –151.86, –151.91.

HRMS (ESI+) calculated for $C_{17}H_{14}N^+$: 232.1121; found 232.1129



(**1B**) (**1Ba**) (**1Bb**)

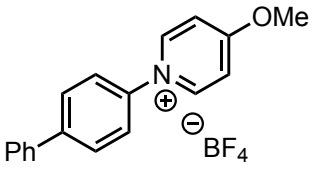
Prepared from biphenyl and pyridine using general procedure B. Purification by automated flash chromatography (DCM/MeCN gradient 0-50%) afforded the title compound (**1B**) as a mixture of isomers (35.7 mg, 47% yield, isolated product is a 22.0 : 2.0 : 1.0 ratio of **1B** : **1Bb : 1Ba**, light yellow-orange solid). Under these conditions, the crude yield was 70% of **1B**. Due to overlapping peaks and a messy baseline, a crude ratio of isomers was not attainable. The remaining mass balance for this transformation was primarily the dipyridinated product (18% yield, see Table S2, entry 21), along with traces of unreacted starting material. Purification of this substrate was not trivial due to the poor solubility of the dipyridinated product. The characterization data of **1B** match compound **1** and those reported in the literature.[12] Independently synthesized standards

of each isomer (*para*, *ortho*, *meta*) of **1B** matched the ^{1}H NMR spectra of the mixture of products (p. S57-58).[1]

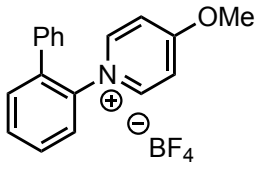
^{1}H NMR (500 MHz, CD_3CN): δ 9.01 (d, *J* = 6.4 Hz, 2H, **1Bb**), 8.97 (d, *J* = 6.4 Hz, 2H, **1B**), 8.73-8.68 (overlapping peaks, 4H, **1B**/**1Ba**/**1Bb**), 8.55 (t, *J* = 8.0 Hz, 1H, **1Ba**), 8.21 (overlapping peaks, 4H, **1B**/**1Bb**), 8.02-7.92 (overlapping peaks, 6H, **1B**/**1Ba**/**1Bb**), 7.82-7.68 (overlapping peaks, 12H, **1B**/**1Ba**/**1Bb**), 7.55-7.52 (overlapping peaks, 4H, **1B**/**1Bb**), 7.49-7.46 (overlapping peaks, 2H, **1B**/**1Bb**), 7.32 (m, 3H, **1Ba**), 7.11 (m, 2H, **1Ba**).

^{13}C NMR (126 MHz, CD_3CN): δ **1B**: 147.8, 145.6, 145.1, 143.0, 139.6, 130.2, 129.8, 129.7, 129.5, 128.3, 126.0.

^{13}C NMR spectral data could not be obtained for minor isomers **1Ba** and **1Bb** due to the ratio of the isolated product mixture **1B**/**1Ba**/**1Bb**.



(**2**)



(**2a**)

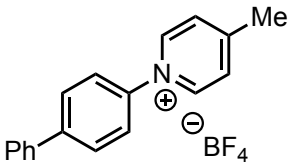
Prepared from biphenyl and 4-methoxypyridine using a modification of general procedure A as follows. A 20 mL scintillation vial equipped with a stir bar was charged with biphenyl (107.9 mg 0.70 mmol, 2.5 equiv). With a syringe, anhydrous acetonitrile (14 mL) was added, followed by 4-methoxypyridine (29.8 µL, 0.294 mmol, 1.05 equiv) and then HBF_4•Et_2O (38.4 µL, 0.28 mmol, 1.0 equiv). The vial was sealed using a septum-lined cap, the outside of the cap was wrapped with electrical tape, and the solution was sparged with an O_2 balloon for 10 min. The resulting mixture was placed inside the photoreactor and allowed to stir under black light (UVA) irradiation (~350 nm) for 24 h. After 24 h, a needle was utilized to pierce the septum to release any build-up of pressure. The reaction mixture was then concentrated under reduced pressure, and the resulting solids were washed with excess hexanes and ether. Purification by preparative TLC (DCM/MeOH 9:1) afforded the title compound (**2**) as a mixture of isomers that could not be separated (88.1 mg, 90% yield, isolated product is a 10 : 1 ratio of **2** : **2a**, off-white solid). The ratio of **2** : **2a** in the crude reaction mixture was 9.5 : 1 as determined by ^{1}H NMR spectroscopic analysis.

^{1}H NMR (700 MHz, CD_3CN): δ 8.74 (d, *J* = 6.9 Hz, 2H, **2**), 8.42 (d, *J* = 6.9 Hz, 2H, **2a**), 7.94 (d, *J* = 8.4 Hz, 2H), 7.78-7.72 (overlapping peaks, 5H, **2**/**2a**), 7.68 (t, *J* = 7.8 Hz, 1H, **2a**), 7.64 (m, 2H, **2a**), 7.57 (d, *J* = 7.0 Hz, 2H, **2**), 7.54 (t, *J* = 7.8 Hz, 2H, **2**), 7.47 (t, *J* = 7.4 Hz, 1H, **2**), 7.34 (m, 5H, **2a**), 7.14 (m, 2H, **2a**), 4.19 (s, 3H, **2**), 4.08 (s, 3H, **2a**).

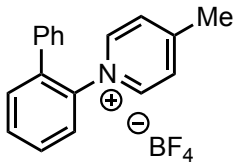
^{13}C NMR (126 MHz, CD_3CN): δ **2**: 173.4, 146.6, 144.4, 142.3, 139.7, 130.2, 129.7, 129.6, 128.2, 125.6, 114.6, 59.5.

^{13}C NMR (126 MHz, CD_3CN): δ **2a**: 173.2, 148.0, 140.8, 138.5, 136.8, 132.8, 132.6, 130.5, 129.7, 129.4, 130.0, 127.4 114.2, 59.4.

HRMS (ESI+) calculated for $C_{18}H_{16}NO^+$: 262.1226, found: 262.1230



(**3**)



(**3a**)

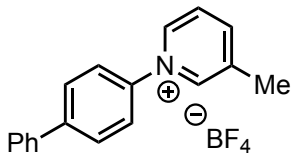
Prepared from biphenyl and 4-methylpyridine using a modification of general procedure A as follows. A 20 mL scintillation vial equipped with a stir bar was charged with biphenyl (107.9 mg 0.70 mmol, 2.5 equiv). With a syringe, anhydrous acetonitrile (14 mL) was added, followed by 4-methylpyridine (28.6 µL, 0.294 mmol, 1.05 equiv), and then HBF_4•Et_2O (38.4 µL, 0.28 mmol, 1.0 equiv). The vial was sealed using a septum-lined cap, the outside of the cap was wrapped with electrical tape, and the solution was sparged with an O_2 balloon for 10 min. The resulting mixture was placed inside the photoreactor and allowed to stir under black light (UVA) irradiation (~350 nm) for 24 h. After 24 h, a needle was utilized to pierce the septum to release any build-up of pressure. The reaction mixture was then concentrated under reduced pressure, and the resulting solids were washed with excess hexanes and ether. Purification by preparative TLC (DCM/MeOH 9:1) afforded the title compound (**3**) as a mixture of isomers that could not be separated (77.4 mg, 83% yield, isolated product is a 31 : 1 ratio of **3** : **3a,** white solid). Ratio of **3** : **3a** in the crude reaction mixture was 15 : 1 as determined by ^{1}H NMR spectroscopic analysis.

^{1}H NMR (700 MHz, CD_3CN): δ 8.83 (d, *J* = 6.6 Hz, 2H, **3a**), 8.79 (d, *J* = 6.8 Hz, 2H, **3**), 8.49 (d, *J* = 6.6 Hz, 2H, **3a**), 8.00 (d, *J* = 6.8 Hz, 2H, **3**), 7.96 (m, 2H, **3**), 7.80-7.64 (overlapping peaks, 8H, **3**/**3a**), 7.54 (t, *J* = 7.7 Hz, 2H, **3**), 7.48 (t, *J* = 7.6 Hz, 1H, **3**), 7.33 (m, 3H, **3a**), 7.12 (m, 2H, **3a**), 2.74 (s, 3H, **3**), 2.62 (s, 3H, **3a**).

^{13}C NMR (176 MHz, CD_3CN): δ **3**: 162.5, 144.9, 144.3, 142.7, 139.6, 130.2, 129.8, 129.8, 129.7, 128.3, 125.8, 22.4.

^{13}C NMR spectral data could not be obtained for minor isomer **3a** due to the ratio of the isolated product mixture **3**/**3a**.

HRMS (ESI+) calculated for $C_{18}H_{16}N^+$: 246.1277, found: 246.1281



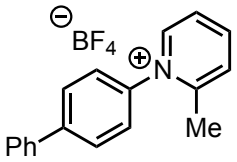
(**4**)

Prepared from biphenyl and 3-methylpyridine using a modified general procedure A as follows. A 20 mL scintillation vial equipped with a stir bar was charged with biphenyl (107.9 mg, 0.70 mmol, 2.5 equiv). With a syringe, anhydrous acetonitrile (14 mL) was added, followed by 3-methylpyridine (28.6 µL, 0.294 mmol, 1.05 equiv) and then HBF_4•Et_2O (38.4 µL, 0.28 mmol, 1.0 equiv). The vial was sealed using a septum-lined cap, the outside of the cap was wrapped with electrical tape, and the solution was sparged with an O_2 balloon for 10 min. The resulting mixture was placed inside the photoreactor and allowed to stir under black light (UVA) irradiation (~350 nm) for 24 h. After 24 h, a needle was utilized to pierce the septum to release any build-up of pressure. The reaction mixture was then concentrated under reduced pressure, and the resulting solids were washed with excess hexanes and ether. Purification by preparative TLC (DCM/MeOH 9:1) afforded the title compound (**4**) (84.9 mg, 91% yield, white solid).

^{1}H NMR (700 MHz, CD_3CN): δ 8.84 (s, 1H), 8.79 (d, *J* = 6.2 Hz, 1H), 8.50 (d, *J* = 8.0 Hz, 1H), 8.08 (d, *J* = 8.2, 6.3 Hz, 1H), 7.98 (d, *J* = 8.7 Hz, 2H), 7.78 (d, *J* = 8.7 Hz, 2H), 7.76 (d, *J* = 7.1 Hz, 2H), 7.55 (d, *J* = 7.5 Hz, 2H), 7.48 (tt, *J* = 7.3, 1.0 Hz, 1H), 2.63 (s, 3H).

^{13}C NMR (176 MHz, CD_3CN): δ 148.1, 145.1, 145.1, 143.0, 142.7, 141.2, 139.6, 130.2, 129.8, 129.7, 128.7, 128.3, 125.9, 18.6.

HRMS (ESI+) calculated for $C_{18}H_{16}N^+$: 246.1277, found: 246.1278



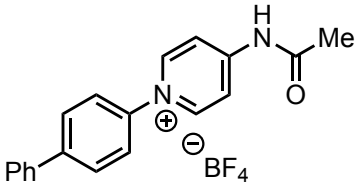
(**5**)

Prepared from biphenyl and 2-methylpyridine following general procedure A. Purification by preparative TLC (DCM/MeOH 9:1) afforded the title compound (**5**) (31.2 mg, 39% yield, light yellow oil).

^{1}H NMR (500 MHz, CD_3CN): δ 8.66 (d, *J* = 6.1 Hz, 1H), 8.56 (t, *J* = 8.0 Hz, 1H), 8.06 (t, *J* = 8.2 Hz, 1H), 7.99-7.95 (overlapping peaks, 3H), 7.75 (d, *J* = 8.2 Hz, 2H), 7.61 (d, *J* = 8.2 Hz, 2H), 7.55 (t, *J* = 7.7 Hz, 2H), 7.48 (t, *J* = 7.4 Hz, 1H), 2.57 (s, 3H).

^{13}C NMR (176 MHz, CD_3CN): δ 157.8, 147.8, 146.8, 145.0, 141.1, 139.7, 130.9, 130.2, 129.7, 129.7, 128.2, 126.9, 126.5, 21.9.

HRMS (ESI+) calculated for $C_{18}H_{16}N^+$: 246.1277, found: 246.1311



(**6**)

Prepared from biphenyl and 4-acetamidopyridine using a modification of general procedure B as follows. Upon conclusion of the reaction, the solvent was concentrated via rotary evaporation. The resulting crude solid was dissolved in ~500 µL of MeCN. Excess EtOAc was the added (12 mL, note: 4-acetamidopyridine is soluble in EtOAc), and a precipitate formed. The precipitate was collected by filtration and washed with excess EtOAc (40 mL). The resulting solid was collected and dried *in vacuo* overnight to afford title compound (**6**) (27.6 mg, 31% yield, off-white solid).

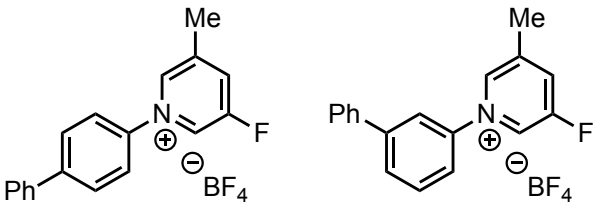
^{1}H NMR (700 MHz, CD_3CN): δ 9.78 (br s, 1H), 8.67 (d, *J* = 7.0 Hz, 2H), 8.19 (d, *J* = 7.0 Hz, 2H), 7.94 (d, *J* = 8.4 Hz, 2H), 7.74 (d, *J* = 7.7 Hz, 2H), 7.72 (d, *J* = 8.5 Hz, 2H), 7.53 (t, *J* = 7.6 Hz, 2H), 7.47 (t, *J* = 8.2 Hz, 1H), 2.27 (s, 3H).

^{13}C NMR (126 MHz, CD_3CN): δ 172.0, 154.1, 145.6, 144.4, 142.4, 139.7, 130.2, 129.7, 129.6, 128.2, 125.5, 116.0, 25.1.

HRMS (ESI+) calculated for $C_{15}H_{18}N^+$: 289.1335, found: 289.1343

IR (solid): 3324, 3132, 3079, 1714, 1639, 1511, 1485, 1460, 1195, 855, 767, 699, 536, 494 cm^{-1}

Melting Point: 244.6-245.5°C



(**7**) (**7a**)

Prepared from biphenyl and 3-fluoro-5-methylpyridine using a modification of general procedure B as follows. A 20 mL scintillation vial equipped with a stir bar was charged with biphenyl (37.0 mg, 0.24 mmol, 1.0 equiv). With a syringe, anhydrous acetonitrile (12 mL) was added, followed by 3-fluoro-5-methylpyridine (74.8 µL, 0.72 mmol, 3.0 equiv) and HBF_4•Et_2O (32.9 µL, 0.24 mmol, 1.0 equiv). The vial was sealed using a septum-lined cap, the outside of the cap was wrapped with electrical tape, and the solution was sparged with an O_2 balloon for 10 min. The

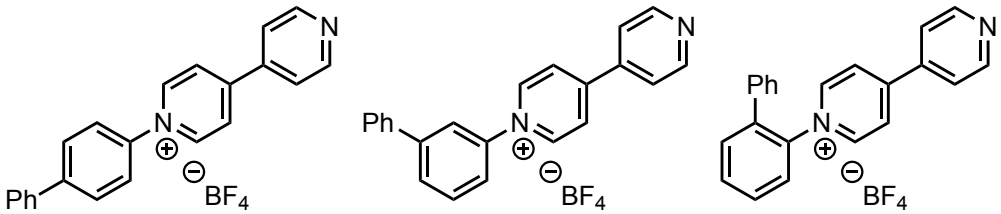
resulting mixture was placed inside the photoreactor and allowed to stir under black light (UVA) irradiation (~350 nm) for 24 h. After 24 h, a needle was utilized to pierce the septum to release any build-up of pressure. The reaction mixture was then concentrated under reduced pressure and purified by automated flash chromatography (DCM/MeCN gradient 0-40%). The resulting fractions were concentrated until ~1 mL DCM/MeCN remained, at which time diethyl ether (~8 mL) was added, and a precipitate formed. The precipitate was collected by filtration and washed with excess diethyl ether (20 mL). The solid was then redissolved in MeCN, concentrated under reduced pressure, and dried *in vacuo* overnight to afford title compound (**7**) as a mixture of isomers that could not be separated (19.6 mg, 23% yield, isolated product is a 34.2 : 1.0 ratio of **7** : **7a**, off-white solid). Spectral data could not be obtained for **7a** due to the ratio of the products. The ratio of **7** : **7a** in the crude reaction mixture was 8.3 : 1.0 as determined by ^{1}H NMR spectroscopic analysis. The isolated product was fully characterized using an HSQC NMR experiment (p. S71).

^{1}H NMR (700 MHz, CD_3CN): δ **7**: 8.91 (s, 1H), 8.77 (s, 1H), 8.38 (d, *J* = 8.3 Hz, 1H), 7.99 (d, *J* = 8.6 Hz, 2H), 7.80 (d, *J* = 8.6 Hz, 2H), 7.59 (d, *J* = 7.7 Hz, 2H), 7.55 (t, *J* = 7.8 Hz, 2H), 7.49 (t, *J* = 7.3 Hz, 1H), 2.65 (s, 3H).

^{13}C NMR (176 MHz, CD_3CN): δ **7**: 161.2 (d, *J* = 254.7 Hz), 145.5, 143.4 (d, *J* = 8.1 Hz), 142.7, 142.5, 139.5, 135.2 (d, *J* = 18.1 Hz), 132.8 (d, *J* = 39.2 Hz), 130.3, 129.9, 129.8, 128.3, 125.8, 18.8 (d, *J* = 1.6 Hz).

^{19}F NMR (470 MHz, CD_3CN): δ **7**: –118.75 (dd, *J* = 8.5, 3.6 Hz), –151.70, –151.76.

HRMS (ESI+) calculated for $C_{18}H_{15}FN^{+}$: 264.1183, found: 264.1188



(**8**) (**8a**) (**8b**)

Prepared from biphenyl and 4,4'–dipyridyl following general procedure A. Purification by automated flash chromatography (DCM/MeCN gradient 0-60%) afforded the title compound (**8**) as a mixture of isomers that could not be separated (61.9 mg, 65% yield, isolated product is a 42.1 : 5.8 : 1.0 ratio of **8** : **8a** : **8b**, yellow solid). Ratio of **8** : **8a** : **8b** in the crude reaction mixture was 23.1 : 3.0 : 1.0 as determined by ^{1}H NMR spectroscopic analysis. The isolated product mixture was fully characterized using a HSQC NMR experiment (p. S75).

^{1}H NMR (700 MHz, CD_3CN): δ 9.12 (d, *J* = 6.5 Hz, 2H, **8a**), 9.08 (d, *J* = 8.3 Hz, 2H, **8**), 8.89 (overlapping peaks, 4H, **8**/**8a**), 8.85 (d, *J* = 6.1 Hz, 2H, **8b**), 8.78 (d, *J* = 6.3 Hz, 2H, **8b**) 8.53-8.51 (overlapping peaks, 4H, **8**/**8a**), 8.29 (d, *J* = 6.3 Hz, 2H, **8b**) 8.03 (d, *J* = 8.1 Hz, 1H, **8a**), 8.01 (overlapping peaks, 3H, **8**/**8a**), 7.89 (overlapping peaks, 6H, **8**/**8a**/**8b**), 7.85-7.81 (overlap-

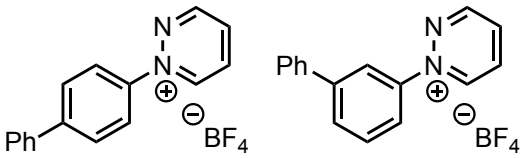
ping peaks, 4H, **8**/**8a**/**8b**) 7.78-7.77 (overlapping peaks, 4H, **8**/**8a**), 7.75-7.71 (overlapping peaks, 4H, **8a**/**8b**), 7.55 (overlapping peaks, 4H, **8**/**8a**), 7.49 (overlapping peaks, 2H, **8**/**8a**), 7.34 (m, 3H, **8b**), 7.17 (m, 2H, **8b**).

^{13}C NMR (176 MHz, CD_3CN): δ **8**: 155.9, 152.3, 145.8, 145.2, 142.5, 141.9, 139.5, 130.3, 129.9, 129.8, 128.3, 127.0, 125.9, 122.9.

^{13}C NMR (176 MHz, CD_3CN): δ **8a**: 156.0, 152.2, 147.4, 146.1, 144.3, 144.0, 141.7, 132.1, 131.0, 130.3, 129.7, 128.2, 127.0, 124.2, 124.0, 123.0.

^{13}C NMR spectral data could not be obtained for minor isomer **8b** due to the ratio of the isolated product mixture **8**/**8a**/**8b**.

HRMS (ESI+) calculated for $C_{22}H_{17}N_2^+$: 309.1386, found: 309.1384



(**9**) (**9a**)

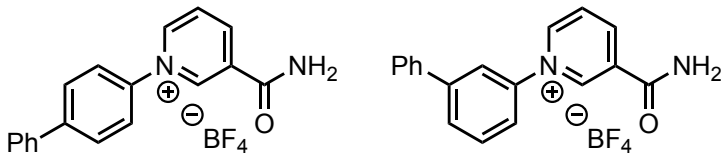
Prepared from biphenyl and pyridazine following general procedure B. Purification by automated flash chromatography (DCM/MeCN gradient 0-50%) afforded the title compound (**9**) as a mixture of isomers that could not be separated (15.3 mg, 20% yield, isolated product is an 18 : 1 ratio of **9** : **9a**, off-white solid). Ratio of **9** : **9a** in the crude reaction mixture was 5 : 1 as determined by ^{1}H NMR spectroscopic analysis. The isolated product mixture was fully characterized using a COSY NMR experiment (p. S77).

^{1}H NMR (700 MHz, CD_3CN): δ 9.89 (dt, *J* = 6.0, 1.3 Hz, 1H, **9a**), 9.84 (dt, *J* = 6.0, 1.3 Hz, 1H, **9**), 9.60-9.59 (overlapping peaks, 2H, **9**/**9a**), 8.70-8.66 (overlapping peaks, 2H, **9**/**9a**), 8.59 (m, 1H, **9a**), 8.56 (ddd, *J* = 8.4, 5.0, 1.2 Hz, 1H, **9**), 8.15 (app t, *J* = 2.0 Hz, 1H, **9a**), 8.06 (m, 1H, **9a**), 8.02 (s, 4H, **9**), 7.91 (m, 1H, **9a**), 7.83 (t, *J* = 8.1 Hz, 1H, **9a**), 7.78-7.75 (overlapping peaks, 4H, **9**/**9a**), 7.57-7.54 (overlapping peaks, 4H, **9**/**9a**), 7.51-7.48 (overlapping peaks, 4H, **9**/**9a**).

^{13}C NMR (126 MHz, CD_3CN): δ **9**: 155.7, 149.3, 146.2, 143.8, 139.5, 138.2, 137.3, 130.2, 129.9, 129.8, 128.3, 125.2.

^{13}C NMR spectral data could not be obtained for minor isomer **9a** due to the ratio of the isolated product mixture **9**/**9a**.

HRMS (ESI+) calculated for $C_{16}H_{13}N_2^+$: 233.1073, found: 233.1075



(**10**) (**10a**)

Prepared from biphenyl and 3-nicotinamide following a modification of general procedure B as follows. A 20 mL scintillation vial equipped with a stir bar was charged with biphenyl (46.3 mg, 0.30 mmol, 1.0 equiv) and 3-nicotinamide (73.3 mg, 0.6 mmol, 2.0 equiv). With a syringe, anhydrous acetonitrile (15 mL) was added followed by HBF_4•Et_2O (41.1 µL, 0.30 mmol, 1.0 equiv). The vial was sealed using a septum-lined cap, the outside of the cap was wrapped with electrical tape, and the solution was sparged with an O_2 balloon for 10 min. The resulting mixture was placed inside the photoreactor and allowed to stir under black light (UVA) irradiation (~350 nm) for 24 h. After 24 h, a needle was utilized to pierce the septum to release any build-up of pressure. The reaction mixture was then concentrated under reduced pressure and purified by automated flash chromatography (DCM/MeCN gradient 0-50%). The resulting fractions were concentrated until ~1 mL DCM/MeCN remained, at which time diethyl ether (~5 mL) and dichloromethane (~500 µL) were added and a precipitate formed. The precipitate was collected by filtration and washed with excess diethyl ether (20 mL). The solid was then dissolved in MeCN, and the resulting solution was filtered, concentrated under reduced pressure, and dried *in vacuo* overnight to afford title compound (**10**) as a mixture of isomers that could not be separated (18.3 mg, 17% yield, isolated product is a 14.5 : 1.0 ratio of **10** : **10a**, white solid). Ratio of **10** : **10a** in the crude reaction mixture was 9.2 : 1.0 as determined by ^{1}H NMR spectroscopic analysis.

^{1}H NMR (700 MHz, CD_3CN): δ **10**: 9.30 (s, 1H), 9.07 (d, *J* = 6.2 Hz, 1H), 8.98 (d, *J* = 8.4 Hz, 1H), 8.30 (dd, *J* = 8.5, 6.2 Hz, 1H), 8.00 (d, *J* = 8.6 Hz, 2H), 7.84 (d, *J* = 8.7 Hz, 2H), 7.76 (d, *J* = 6.8 Hz, 2H), 7.55 (t, *J* = 7.5 Hz, 2H), 7.49 (t, *J* = 7.5 Hz, 1H), 7.25 (br s, 1H), 6.66 (br s, 1H).

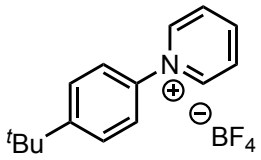
^{1}H NMR (700 MHz, CD_3CN): δ **10a**: 9.34 (s, 1H), 9.10 (d, *J* = 6.1 Hz, 1H), 9.01-8.98 (overlapping peaks with **10**, 1H), 8.32-8.29 (overlapping with **10**, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 8.01 (overlapping with **10**, 1H), 7.83-7.80 (overlapping with **10**, 1H), 7.77-7.70 (overlapping with **10**, 3H), 7.55-7.54 (overlapping with **10**, 2H), 7.50-7.47 (overlapping with **10**, 1H). Protons corresponding to amide hydrogens are not observed.

Note: A majority of the signals corresponding to **10a** overlap with the major *para*-isomer **10**, resulting in some signals not being observed.

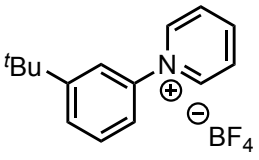
^{13}C NMR (176 MHz, CD_3CN): δ **10**: 163.6, 147.3, 146.0, 145.4, 145.2, 142.8, 139.5, 135.6, 130.3, 129.8, 129.8, 129.6, 128.3, 126.1.

^{13}C NMR spectral data could not be obtained for minor isomer **10a** due to the ratio of the isolated product mixture **10**/**10a**.

HRMS (ESI+) calculated for $C_{18}H_{15}N_2O^+$: 275.1179, found: 275.1181



(**11**)



(**11a**)

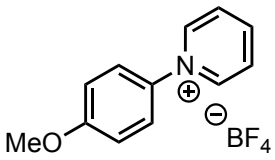
Prepared from *tert*-butylbenzene and pyridine following general procedure A. Purification by automated flash chromatography (DCM/MeCN gradient 0-50%) afforded the title compound (**11**) as a mixture of isomers that could not be separated (59.8 mg, 83% yield, isolated product is a 1.4 : 1.0 ratio of **11** : **11a**, yellow oil). Ratio of **11** : **11a** in the crude reaction mixture was 1.5 : 1.0 as determined by ^{1}H NMR spectroscopic analysis. The characterization data of **11** and **11a** match those reported in the literature.[13] Independently synthesized standards of **11** and **11a** matched the ^{1}H and ^{13}C NMR spectra of the product mixture (p. S81-82).[1]

^{1}H NMR (700 MHz, CD_3CN): δ 8.93-8.91 (overlapping peaks, 4H, **11**/**11a**), 8.67 (overlapping peaks, 2H, **11**/**11a**), 8.19-8.17 (overlapping peaks, 4H, **11**/**11a**), 7.80 (d, *J* = 8.2 Hz, 1H, **11a**), 7.76 (d, *J* = 8.3 Hz, 2H, **11**), 7.71 (m, 1H, **11a**), 7.66-7.63 (overlapping peaks, 3H, **11**/**11a**), 7.50 (d, *J* = 8.2 Hz, 1H, **11a**), 1.39 (s, 9H, **11**), 1.39 (s, 9H, **11a**).

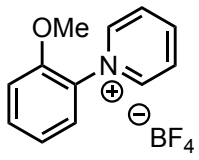
^{13}C NMR (126 MHz, CD_3CN): δ **11**: 156.2, 147.6, 145.5, 141.5, 129.4, 128.5, 124.9, 35.8, 31.3.

^{13}C NMR (126 MHz, CD_3CN): δ **11a**: 155.4, 147.6, 145.7, 143.9, 131.1, 129.6, 129.3, 122.8, 122.5, 36.0, 31.3.

HRMS (ESI+) calculated for $C_{15}H_{18}N^{+}$: 212.1434, found: 212.1437



(**12**)



(**12a**)

Prepared from anisole and pyridine following general procedure A. Purification by automated flash chromatography (DCM/MeCN gradient 0-50%) afforded the title compound (**12**) as a mixture of isomers that could not be separated (39.7 mg, 61% yield, isolated product is a 5 : 1 ratio of **12** : **12a**, yellow oil). Ratio of **12** : **12a** in the crude reaction mixture was 5 : 1 as determined by ^{1}H NMR spectroscopic analysis. The characterization data of **12** and **12a** match those reported in the literature (p. S83-84).[12]

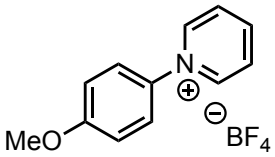
^{1}H NMR (700 MHz, CD_3CN): δ 8.88 (d, *J* = 6.2 Hz, 2H, **12**), 8.80 (d, *J* = 6.2 Hz, 2H, **12a**), 8.68 (t, *J* = 7.9 Hz, 1H, **12a**), 8.64 (t, *J* = 7.9 Hz, 1H, **12**), 8.18-8.15 (overlapping peaks, 4H, **12**/**12a**), 7.69 (t, *J* = 8.0 Hz, 1H, **12a**), 7.64 (d, *J* = 8.7 Hz, 2H, **12**), 7.56 (d, *J* = 7.9 Hz, 1H, **12a**), 7.34 (d,

J = 8.5 Hz, 1H, **12a**), 7.25-7.20 (overlapping peaks, 3H **12**/**12a**), 3.90 (s, 3H, **12**), 3.86 (s, 3H, **12a**).

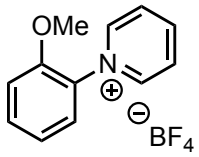
^{13}C NMR (126 MHz, CD_3CN): δ **12**: 162.9, 147.2, 145.6, 137.0, 129.4, 126.8, 116.4, 56.8.

^{13}C NMR (126 MHz, CD_3CN): δ **12a**: 153.1, 148.1, 147.3, 134.3, 132.2, 129.0, 127.5, 122.4, 114.4, 57.3.

HRMS (ESI+) calculated for $C_{12}H_{12}NO^+$: 186.0913, found: 186.0914

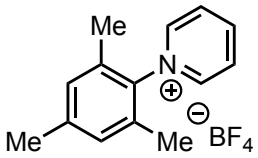


(**12B**)



(**12Ba**)

Prepared from anisole and pyridine following general procedure B. Purification by automated flash chromatography (DCM/MeCN gradient 0-50%) afforded the title compound (**12b**) as a mixture of isomers that could not be separated (36.9 mg, 56% yield, isolated product is a 5.3 : 1.0 ratio of **12B** : **12Ba**, yellow oil). Ratio of **12B** : **12Ba** in the crude reaction mixture was 5.4 : 1.0 as determined by ^{1}H NMR spectroscopic analysis. The characterization data of **12B** and **12Ba** match compound **12**/**12a** and those reported in the literature.[12]



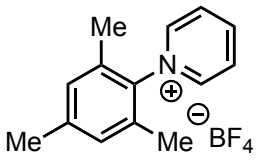
(**13**)

Prepared from mesitylene and pyridine following a modification of general procedure A. Two purifications by automated flash chromatography (DCM/MeCN gradient 0-50%) afforded the title compound (**13**) (36.5 mg, 53% yield, yellow-orange oil). The characterization data of **13** matched those reported in the literature.[12]

^{1}H NMR (700 MHz, CD_3CN): δ 8.76 (t, *J* = 7.8, 1.3 Hz, 1H), 8.70 (m, 2H), 8.26 (t, *J* = 7.4 Hz, 2H), 7.19 (s, 2H), 2.39 (s, 3H), 1.96 (s, 6H).

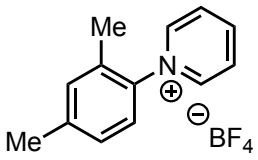
^{13}C NMR (176 MHz, CD_3CN): δ 148.5, 147.0, 142.8, 140.3, 133.8, 130.8, 130.3, 21.1, 17.2.

HRMS (ESI+) calculated for $C_{14}H_{16}N^+$: 198.1277, found: 198.1280



(**13B**)

Prepared from mesitylene and pyridine following a modification of general procedure B. Two purifications by automated flash chromatography (DCM/MeCN gradient 0-50%) afforded the title compound (**13B**) (33.4 mg, 49% yield, yellow oil). The characterization data of **13B** match compound **13** and those reported in the literature.[12]



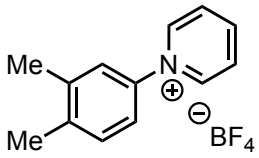
(**14**)

Prepared from *meta*-xylene and pyridine following a modification of general procedure A. A 20 mL scintillation vial equipped with a stir bar was charged with anhydrous acetonitrile (14 mL), followed by *meta*-xylene (86.4 µL, 0.70 mmol, 2.5 equiv), pyridine (23.8 µL, 0.294 mmol, 1.05 equiv), and then HBF_4•Et_2O (38.4 µL, 0.28 mmol, 1.0 equiv). The vial was sealed using a septum-lined cap, the outside of the cap was wrapped with electrical tape, and the solution was sparged with an O_2 balloon for 10 min. The resulting mixture was placed inside the photoreactor and allowed to stir under black light (UVA) irradiation (~350 nm) for 24 h. After 24 h, a needle was utilized to pierce the septum to release any build-up of pressure. The reaction mixture was then concentrated under reduced pressure, and the resulting solids were washed with excess hexanes and ether. Purification by preparative TLC (DCM/MeOH (9:1) afforded the title compound (**14**) (69.9 mg, 92% yield, yellow oil).

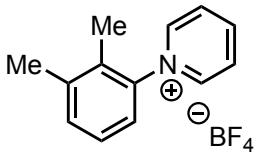
^{1}H NMR (700 MHz, CD_3CN): δ 8.74 (d, *J* = 6.0 Hz, 2H), 8.71 (d, *J* = 7.9 Hz, 1H), 8.19 (t, *J* = 7.0 Hz, 2H), 7.38-7.36 (overlapping peaks, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 2.44 (s, 3H), 2.20 (s, 3H).

^{13}C NMR (176 MHz, CD_3CN): δ 148.0, 146.8, 143.3, 140.9, 133.4, 133.3, 129.5, 129.2, 126.5, 21.2, 17.1.

HRMS (ESI+) calculated for $C_{13}H_{14}N^+$: 184.1121, found: 184.1124



(**15**)



(**15a**)

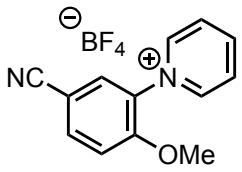
Prepared from *ortho*-xylene and pyridine following a modification of general procedure A. A 20 mL scintillation vial equipped with a stir bar was charged with anhydrous acetonitrile (14 mL), followed by *ortho*-xylene (86.4 µL, 0.70 mmol, 2.5 equiv), pyridine (23.8 µL, 0.294 mmol, 1.05 equiv), and then HBF_4•Et_2O (38.4 µL, 0.28 mmol, 1.0 equiv). The vial was sealed using a septum-lined cap, the outside of the cap was wrapped with electrical tape, and the solution was sparged with an O_2 balloon for 10 min. The resulting mixture was placed inside the photoreactor and allowed to stir under black light (UVA) irradiation (~350 nm) for 24 h. After 24 h, a needle was utilized to pierce the septum to release any build-up of pressure. The reaction mixture was then concentrated under reduced pressure, and the resulting solids were washed with excess hexanes and ether. Purification by automated flash chromatography (DCM/MeCN gradient 0-50%) afforded the title compound (**15**) as a mixture of isomers (60.7 mg, 80% yield, isolated product is a 2.5 : 1.0 ratio of **15** : **15a**, yellow oil). Ratio of **15** : **15a** in the crude reaction mixture was 3.2 : 1.0 as determined by ^{1}H NMR spectroscopic analysis. Independently synthesized standards of **15** and **15a** matched the ^{1}H and ^{13}C NMR spectra of the product mixture (p. S94-95).[1]

^{1}H NMR (700 MHz, CD_3CN): δ 8.90 (d, *J* = 6.6 Hz, 2H, **15**), 8.74-8.71 (overlapping peaks, 3H, **15a**), 8.66 (t, *J* = 7.9 Hz, 1H, **15**), 8.21 (t, *J* = 7.2 Hz, 2H, **15a**), 8.17 (t, *J* = 7.2 Hz, 2H, **15**), 7.52 (d, *J* = 7.5 Hz, 1H, **15a**), 7.49 (s, 1H, **15**), 7.47 (d, *J* = 8.2 Hz, 1H, **15**), 7.42 (dd, *J* = 8.3, 2.1 Hz, 1H, **15**), 7.39 (t, *J* = 7.8 Hz, 1H, **15a**), 7.33 (d, *J* = 8.0 Hz, 1H, **15a**), 2.41 (s, 3H, **15a**), 2.39 (s, 6H, **15**), 1.97 (s, 3H, **15a**).

^{13}C NMR (176 MHz, CD_3CN): δ **15**: 147.5, 145.5, 142.1, 141.8, 140.7, 132.2, 129.4, 126.0, 122.5, 19.9, 19.6.

^{13}C NMR (176 MHz, CD_3CN): δ **15a**: 148.1, 146.7, 143.3, 141.0, 133.8, 132.4, 129.5, 128.0, 124.3, 20.4, 14.3.

HRMS (ESI+) calculated for $C_{13}H_{14}N^+$: 184.1121, found: 184.1122



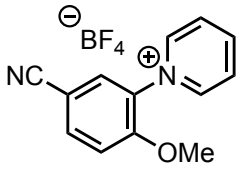
(**16**)

Prepared from anisonitrile and pyridine following general procedure A. Purification by automated flash chromatography (DCM/MeCN gradient 0-60%) afforded the title compound (**16**) (47.3 mg, 66% yield, light-orange solid). The characterization data of **16** match those reported in the literature.[13]

^{1}H NMR (600 MHz, CD_3CN): δ 8.77 (d, *J* = 6.0 Hz, 2H), 8.72 (t, *J* = 7.9 Hz, 1H), 8.20 (t, *J* = 7.3 Hz, 2H), 8.05 (dd, *J* = 8.9, 2.0 Hz, 1H), 7.96 (d, *J* = 2.0 Hz, 1H), 7.44 (d, *J* = 8.8 Hz, 1H), 3.92 (s, 3H).

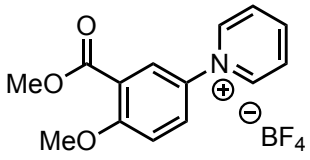
^{13}C NMR (126 MHz, CD_3CN): δ 157.0, 149.0, 147.3, 138.6, 132.2, 132.0, 129.3, 115.5, 105.3, 58.1. The carbon corresponding to the nitrile functional group is not observed, but the product is confirmed by high-resolution mass spectrometry (ESI+).

HRMS (ESI+) calculated for $C_{13}H_{11}N_2O^+$: 211.0866, found: 211.0869



(**16B**)

Prepared from anisonitrile and pyridine following general procedure B. Purification by automated flash chromatography (DCM/MeCN gradient 0-50%) afforded the title compound (**16B**) (37.4 mg, 52% yield, light-orange solid). The characterization data of **16B** match compound **16** and those reported in the literature.[13]



(**17**)

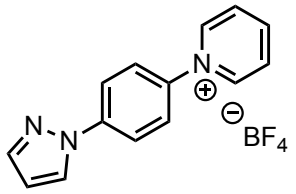
Prepared from methyl 2-methoxybenzoate and pyridine following a modification of general procedure A. Upon conclusion of the reaction, a crude ^{1}H NMR spectrum was acquired, and it showed the presence of protonated pyridinium. To remove this impurity, the reaction mixture was poured into a solution of saturated aqueous brine:$NaHCO_3$ (8:2, 20 mL) and extracted with MeCN (3 x 20 mL). The organic extracts were dried over sodium sulfate and concentrated under

reduced pressure. The resulting crude solid was redissolved in MeCN, and the solution was filtered to remove any remaining insoluble solids carried over from the extraction. This crude solution was then concentrated under reduced pressure. Purification by automated flash chromatography (DCM/MeCN gradient 0-50%) afforded the title compound (**17**) (38.1 mg, 48% yield, off-white solid). The characterization data of **17** match those reported in the literature.[12]

^{1}H NMR (700 MHz, CD_3CN): δ 8.89 (d, *J* = 6.0 Hz, 2H), 8.67 (t, *J* = 8.0 Hz, 1H), 8.18 (t, *J* = 6.9 Hz, 2H), 8.04 (d, *J* = 2.9 Hz, 1H), 7.85 (dd, *J* = 9.0, 2.9 Hz, 1H), 7.39 (d, *J* = 9.0 Hz, 1H), 3.97 (s, 3H), 3.87 (s, 3H).

^{13}C NMR (176 MHz, CD_3CN): δ 165.9, 161.5, 147.6, 145.7, 136.2, 130.3, 129.4, 128.3, 122.6, 115.1, 57.5, 53.2.

HRMS (ESI+) calculated for $C_{14}H_{14}NO_3^+$: 244.0968, found: 244.0969



(**18**)

Prepared from 1-phenylpyrazole and pyridine following a modification of general procedure B. A 20 mL scintillation vial equipped with a stir bar was charged with anhydrous acetonitrile (12 mL), followed by 1-phenylpyrazole (31.7 µL, 0.24 mmol, 1.0 equiv), pyridine (58.2 µL, 0.72 mmol, 3.0 equiv), and then HBF_4•Et_2O (32.9 µL, 0.24 mmol, 1.0 equiv). The vial was sealed using a septum-lined cap, the outside of the cap was wrapped with electrical tape, and the solution was sparged with an O_2 balloon for 10 min. The resulting mixture was placed inside the photoreactor and allowed to stir under black light (UVA) irradiation (~350 nm) for 24 h. After 24 h, a needle was utilized to pierce the septum to release any build-up of pressure. A crude ^{1}H NMR spectrum was acquired, and this showed the presence of protonated pyridinium. To remove this impurity, the reaction mixture was poured into a solution of saturated aqueous brine : $NaHCO_3$ (8 : 2, 20 mL) and extracted with MeCN (3 x 20 mL). The organic extracts were dried over sodium sulfate and then concentrated under reduced pressure. The resulting crude solid was redissolved in DCM/MeCN (1 mL), and this solution was passed through a silica plug (DCM/MeCN, 5:5). The resulting solution was concentrated until ~1 mL MeCN remained, at which time ethyl acetate (~5 mL) was added, and a precipitate formed. The precipitate was collected by filtration and washed with excess ethyl acetate and ether (2 x 10 mL). The solid was then redissolved in MeCN, and this solution was filtered, concentrated under reduced pressure, and dried *in vacuo* overnight to afford title compound (**18**) (14.2 mg, 19% yield, white solid).

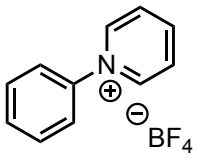
^{1}H NMR (700 MHz, CD_3CN): δ 8.94 (d, *J* = 5.4 Hz, 2H), 8.69 (t, *J* = 8.1 Hz, 1H), 8.29 (d, *J* = 2.6 Hz, 1H), 8.20 (t, *J* = 7.1 Hz, 2H), 8.11 (d, *J* = 9.0 Hz, 2H), 7.82-7.80 (overlapping peaks, 3H), 6.60 (t, *J* = 2.1 Hz, 1H).

^{13}C NMR (176 MHz, CD_3CN): δ 147.9, 145.6, 143.2, 143.2, 141.3, 129.5, 128.9, 126.9, 121.0, 109.8.

HRMS (ESI+) calculated for $C_{14}H_{12}N_3^+$: 222.1026, found: 222.1023

IR (solid): 3119, 3087, 1630, 1530, 1477, 1413, 1065, 937, 775, 685, 542 cm^{-1}

Melting Point: 223.5-224.3 °C



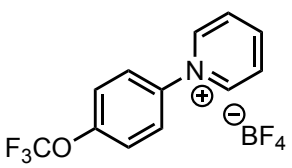
(**19**)

Prepared from benzene and pyridine following a modified general procedure C was followed. A quartz test tube equipped with a stir bar was charged with anhydrous acetonitrile (14 mL), followed by benzene (62.4 µL, 0.70 mmol, 2.5 eq), pyridine (23.8 µL, 0.294 mmol, 1.05 eq), and then HBF_4•Et_2O (38.4 µL, 0.28 mmol, 1.0 eq). The test tube was sealed using a septum cap, wrapped with parafilm/electrical tape, and sparged with an O_2 balloon for 10 minutes. The resulting mixture was placed inside the photoreactor and allowed to stir under UVB irradiation (~300 nm) for 24 h. After 24 h, a needle was utilized to pierce the septum to release any build-up of pressure. The reaction mixture was concentrated under reduced pressure and then washed with excess hexanes and ether. Purification by automated flash chromatography (DCM/MeCN gradient 0-40%) afforded the title compound (**19**) (61.2 mg, 90% yield, yellow oil). The characterization data of **19** match those reported in the literature.[13]

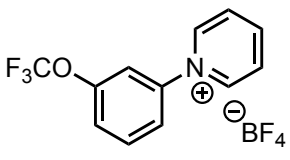
^{1}H NMR (700 MHz, CD_3CN): δ 8.92 (d, *J* = 6.2 Hz, 2H), 8.69 (t, *J* = 8.2 Hz, 1H), 8.20 (t, *J* = 6.9 Hz, 2H), 7.77-7.70 (overlapping peaks, 5H).

^{13}C NMR (176 MHz, CD_3CN): δ 147.8, 145.7, 143.9, 132.7, 131.5, 129.5, 125.5.

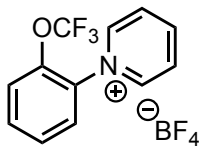
HRMS (ESI+) calculated for $C_{11}H_{10}N^+$: 156.0808, found: 156.0810



(**20**)



(**20a**)



(**20b**)

Prepared from trifluoromethoxybenzene and pyridine following general procedure C. Purification by automated flash chromatography (DCM/MeCN gradient 0-35%) afforded the title compound

(**20**) as a mixture of isomers that could not be separated (21.8 mg, 28% yield, isolated product is a 7.1 : 1.1 : 1.0 ratio of **20** : **20a** : **20b**, yellow oil). Ratio of **20** : **20b** : **20a** in the crude reaction mixture was 6.9 : 1.4 : 1.0 as determined by ^{1}H NMR spectroscopic analysis. Independently synthesized standards of **20**, **20a**, and **20b** matched the ^{1}H, ^{13}C, and ^{19}F NMR spectra of the product mixture (p. S106-108).[1]

^{1}H NMR (700 MHz, CD_3CN): δ 8.94-8.91 (overlapping peaks, 4H, **20**/**20a**), 8.86 (d, *J* = 6.1 Hz, 2H, **20b**), 8.78 (t, *J* = 8.3 Hz, 1H, **20b**), 8.74-8.69 (overlapping peaks, 2H, **20**/**20a**), 8.26 (t, *J* = 7.1 Hz, 2H, **20b**), 8.23-8.21 (overlapping peaks, 4H, **20**/**20a**), 7.87-7.80 (overlapping peaks, 5H, **20**/**20a**/**20b**), 7.74-7.65 (overlapping peaks, 5H, **20a**/**20b**), 7.64 (d, *J* = 8.6 Hz, 2H, **20**).

^{13}C NMR (126 MHz, CD_3CN): δ **20**: 151.8, 148.3, 145.8, 142.3, 129.5, 128.0, 123.7, 121.4 (q, *J* = 257.6 Hz).

^{13}C NMR (126 MHz, CD_3CN): δ **20a**: 150.4, 148.5, 145.8 (overlapping with **20**), 144.6, 133.3, 129.5 (overlapping with **20**), 125.1, 124.8, 121.4 (q, *J* = 257.5 Hz – signal not observed due overlapping peaks; confirmed by authenticate sample, see p. S106), 119.1.

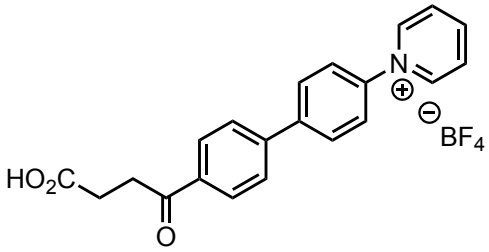
^{13}C NMR (126 MHz, CD_3CN): δ **20b**: 149.3, 147.1, 142.8, 135.2, 134.9, 129.8, 129.6, 129.0, 122.9, 121.0 (q, *J* = 259.3 Hz).

^{19}F NMR (470 MHz, CD_3CN): δ **20**: –58.69, –151.79, –151.84

^{19}F NMR (470 MHz, CD_3CN): δ **20a**: –58.78, –151.79, –151.84

^{19}F NMR (470 MHz, CD_3CN): δ **20b**: –58.84, –151.79, –151.84

HRMS (ESI+) calculated for $C_{12}H_{19}F_3NO^+$: 240.0631, found: 240.0634



(**21**)

Prepared from fenbufen (4-oxo-4-(4-phenylphenyl)butanoic acid) and pyridine following general procedure D. Purification by automated flash chromatography (DCM/MeCN gradient 0-50%) afforded the title compound (**21**) (19.1 mg, 19% yield, off-white solid). The isolated product was fully characterized using a COSY NMR experiment (p. S110).

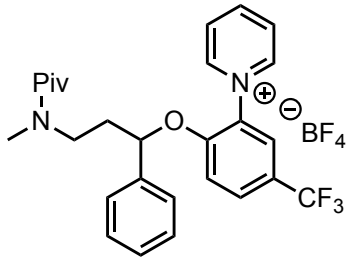
^{1}H NMR (700 MHz, DMSO-d_6): δ 12.17 (br s, 1H), 9.40 (d, *J* = 6.0 Hz, 2H), 8.81 (t, *J* = 7.9 Hz, 1H), 8.34 (t, *J* = 7.2 Hz, 2H), 8.15 (d, *J* = 8.5 Hz, 2H), 8.13 (d, *J* = 8.2 Hz, 2H), 8.03 (d, *J* = 8.5 Hz, 2H), 7.98 (d, *J* = 8.2 Hz, 2H), 3.33-3.31 (overlapping peaks, 2H), 2.62 (t, *J* = 6.2 Hz, 2H).

^{13}C NMR (126 MHz, DMSO-d_6): δ 198.1, 173.8, 146.7, 144.9, 142.6, 142.4, 141.6, 136.1, 128.7, 128.6, 128.1, 127.4, 125.5, 33.2, 27.9.

HRMS (ESI+) calculated for $C_{21}H_{18}NO_3^+$: 332.1281, found: 332.1280

IR (solid): 3339, 3125, 3075, 2932, 1744, 1681, 1602, 1474, 1398, 1162, 799, 774, 682, 559 cm^{-1}

Melting Point: 232.6-233.4 °C



(**22**)

Prepared from Prozac–HBF_4 (p. S26) and pyridine using a modification of general procedure D. A quartz test tube equipped with a stir bar was charged with Prozac–HBF_4 (79.4 mg, 0.20 mmol, 1 equiv). With a syringe, anhydrous acetonitrile (10 mL) was added, followed by pyridine (32.4 µL, 0.40 mmol, 2.0 equiv), and then HBF_4•Et_2O (27.4 µL, 0.20 mmol, 1.0 equiv). The test tube was sealed using a septum-lined cap, the outside of the cap was wrapped with electrical tape, and the solution was sparged with an O_2 balloon for 10 min. The resulting mixture was placed inside the photoreactor and allowed to stir under black light (UVB) irradiation (~300 nm) for 24 h. After 24 h, a needle was utilized to pierce the septum to release any build-up of pressure. NH_4OH (28% aqueous solution, 8 mL) was added to the crude reaction mixture, and the resulting mixture was transferred to an Erlenmeyer flask. Brine (10 mL) was added, and the product was extracted into MeCN (3 x 20 mL). The organic extracts were dried over Na_2SO_4 and concentrated by rotary evaporation. The crude product was then dissolved in MeCN (3 mL), and this solution was cooled to 0 °C in an ice bath. NEt_3 (139.4 µL, 1.00 mmol, 5 equiv) was added, and the mixture was allowed to stir for 5 min, at which time pivaloyl chloride (73.4 µL, 0.6 mmol, 3 equiv) was added dropwise at 0 °C. The reaction was left to stir for 4 h at room temperature. Note: the reaction turned to a red/brown color. After 4 h, MeCN (20 mL) was added. The organic layer was washed with NaOH (1 M, 3 x 15 mL), dried with Na_2SO_4, and concentrated by rotary evaporation.[14] Purification by automated flash chromatography (DCM/MeCN gradient 0-45%) afforded the title compound (**22**) (15.9 mg, 14% yield, orange/brown oil). The isolated product was fully characterized using COSY and HSQC NMR experiments (p. S112-113 and S115, respectively). Analysis of the crude ^{1}H NMR spectrum shows formation of other aromatic signals (presumably minor isomers), but when referenced to an internal standard these integrate to ≤ 5%.

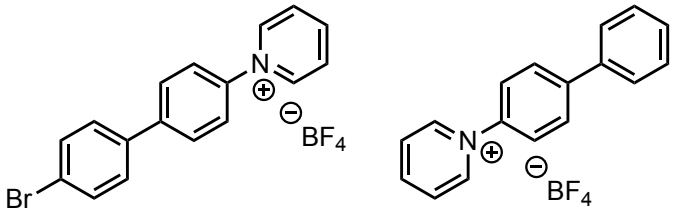
^{1}H NMR (700 MHz, CD_3CN): δ 9.01 (d, J = 6.1 Hz, 2H), 8.77 (t, J = 8.1 Hz, 1H), 8.27 (t, J = 7.1 Hz, 2H), 7.93 (d, J = 2.1 Hz, 1H), 7.79 (dd, J = 9.0, 2.1 Hz, 1H), 7.38 (t, J = 7.6 Hz, 2H), 7.34-7.31 (overlapping peaks, 3H), 7.18 (d, J = 9.0 Hz, 1H), 5.30 (m, 1H), 3.60 (m, 1H), 3.02-2.98 (overlapping peaks, 4H), 2.00 (m, 1H), 1.94-1.91 (overlapping peaks, 1H), 1.13 (s, 9H).

^{13}C NMR (126 MHz, CD_3CN): δ 177.9, 154.7, 148.7, 147.6, 140.2, 132.7, 131.0 (q, *J* = 3.7 Hz), 129.9, 129.5, 129.2, 126.9, 125.5 (q, *J* = 4.1 Hz), 124.6 (q, *J* = 270.8 Hz), 123.6 (q, *J* = 34.1 Hz), 116.9, 80.6, 46.3, 39.3, 36.8, 36.1, 28.4.

^{19}F NMR (470 MHz, CD_3CN): δ –62.44, –151.89, –151.94

HRMS (ESI+) calculated for $C_{27}H_{30}F_3N_2O_2^+$: 471.2254, found: 471.2257

IR (liquid): 3076, 2926, 1732, 1618, 1517, 1475, 1433, 1332, 1287, 1265, 1125, 732, 703 cm^{-1}



(**23**) (**24**)

Prepared from 4-bromobiphenyl and pyridine following general procedure A. Purification by automated flash chromatography (DCM/MeCN gradient 0-50%) afforded C–H functionalization product **23** (36%) and S_NAr product **24** (5%) as an inseparable mixture (38.9 mg, 41% yield, isolated product is a 8 : 1 ratio of **23** : **24** C–H : S_NAr, yellow-orange solid). The product mixture was compared to the ^{1}H and ^{13}C NMR spectra of **1** (p. S117-118).

^{1}H NMR (500 MHz, CD_3CN): δ 8.96-8.95 (overlapping peaks, 4H, **23**/**24**), 8.71-8.68 (overlapping peaks, 2H, **23**/**24**), 8.22-8.19 (overlapping peaks, 4H, **23**/**24**), 7.99-7.96 (overlapping peaks, 4H, **23**/**24**), 7.79-7.75 (overlapping peaks, 6H, **23**/**24**), 7.71 (d, *J* = 8.4 Hz, 2H, **23**), 7.67 (d, *J* = 8.4 Hz, 2H, **23**), 7.55 (t, *J* = 7.7 Hz, 2H, **24**), 7.48 (d, *J* = 872 Hz, 1H, **24**).

^{13}C NMR (176 MHz, CD_3CN): δ **23**: 147.9, 145.6, 143.9, 143.2, 138.7, 133.2, 130.2, 129.8, 129.5, 126.1, 123.6.

^{13}C NMR (176 MHz, CD_3CN): δ **24**: 147.8, 145. 6, 145.1, 143.0 (not observed, confirmed by comparison to **1**, see p. S112), 139.5, 130.2, 129.8, 129.7, 129.5, 128.3, 125.9.

HRMS (ESI+) calculated for $C_{17}H_{13}BrN^+$: 310.0226, found: 310.0227; $C_{17}H_{14}N^+$ 232.1121; found 232.1122

(**C**)

Prepared from naphthalene and pyridine following general procedure A. Purification by automated flash chromatography (DCM/MeCN gradient 0-40%) afforded the title compound (**C**) (12.1 mg, 17% yield, yellow/orange oil). The characterization data of **C** match those reported in the literature.[12]

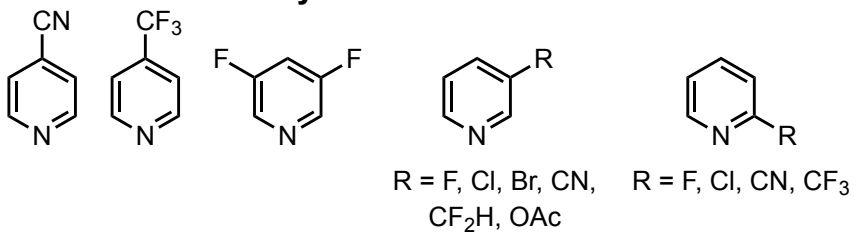
^{1}H NMR (700 MHz, CD_3CN): δ 8.92 (d, *J* = 5.2 Hz, 2H), 8.81 (t, *J* = 7.9 Hz, 1H), 8.31-8.28 (overlapping peaks, 3H), 8.17 (d, *J* = 8.2 Hz, 1H), 7.81 (d, *J* = 7.4 Hz, 1H), 7.78-7.73 (overlapping peaks, 2H), 7.67 (t, *J* = 7.8 Hz, 1H), 7.31 (d, *J* = 8.9 Hz, 1H).

^{13}C NMR (176 MHz, CD_3CN) δ 148.6, 147.3, 139.8, 135.1, 133.2, 130.1, 129.8, 129.7, 129.0, 128.1, 126.4, 125.5, 121.4,

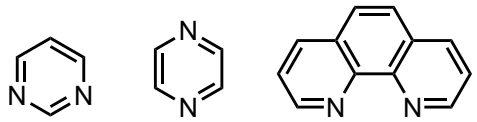
HRMS (ESI+) calculated for $C_{15}H_{12}N^+$: 206.0964, found: 206.0963

11. Substrate Limitations for C(sp^2)–H Pyridination

Pyridine Limitations



Other Nitrogen Nucleophile Limitations



Arene Limitations

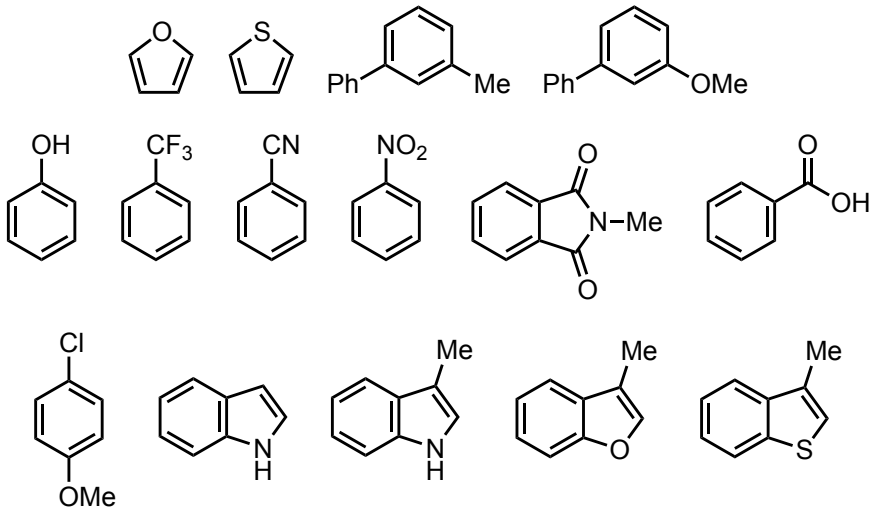
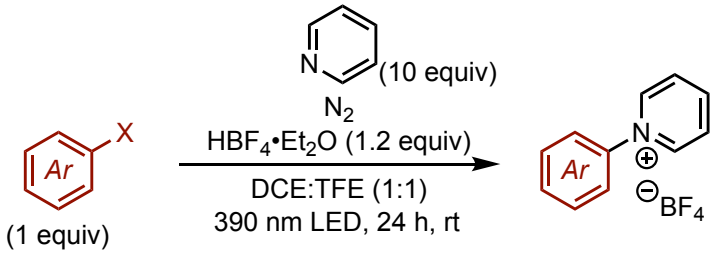


Table S6. Substrates that yielded <5% or no pyridinium product under the standard reaction conditions. In the case of 4-chloroanisole (under our standard reaction conditions, general procedure A), no C–H functionalization product is oberved, only the S_NAr pyridinated product is formed in 4% yield with unreacted starting material accounting for the mass balance.

12. General Experimental Procedure for S_NAr Pyridination Reactions



A 4 mL vial equipped with a stir bar was charged with the corresponding arene substrate (0.1 mmol, 1.0 equiv).[11] With a syringe, a 1 : 1 mixture of DCE : TFE (1 mL) was added, followed by pyridine (80.9 µL, 1.0 mmol, 10.0 equiv) and then HBF_4•Et_2O (16.5 µL, 0.12 mmol, 1.2 equiv). The vial was sealed with a septum cap, wrapped with electrical tape, and N_2 was bubbled through the reaction mixture for 2 minutes. The vial was then irradiated with two 390 nm Kessil LEDs (PR160L, 52W, 100%) inside a EvoluChem™ PhotoRedOx Duo (HCK1006-01-023) box for 24 h. After 24 h, a needle was utilized to pierce the septum to release any build-up of pressure. The reaction mixture was then concentrated under reduced pressure, and the product was purified by automated flash chromatography (DCM/MeCN). The product was then dried *in vacuo* overnight.

a) Photochemical Experimental Set-up:

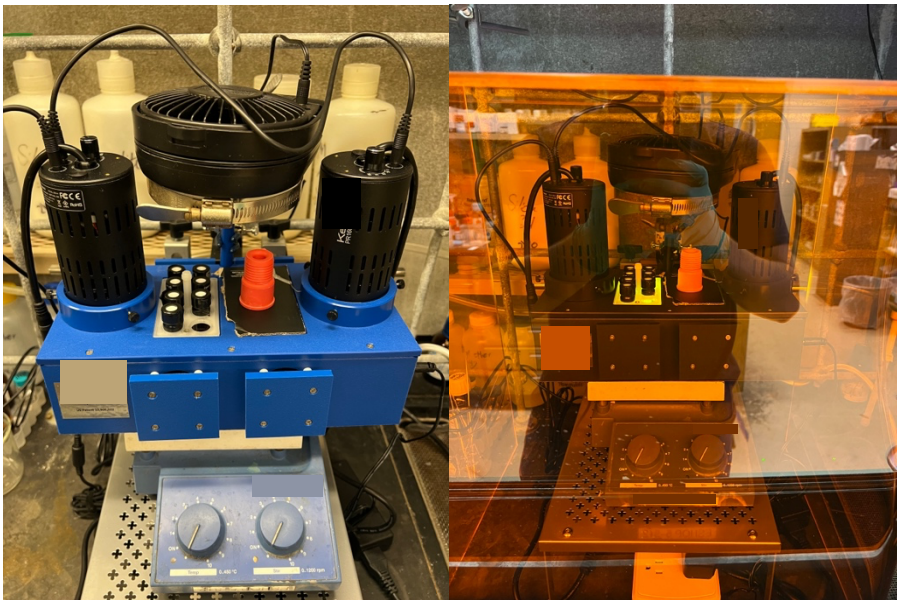
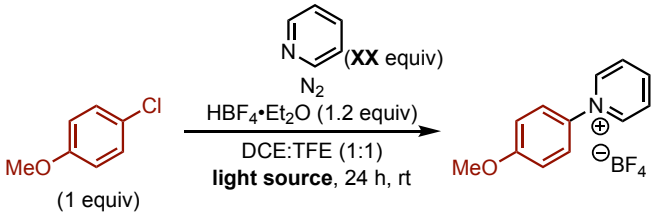


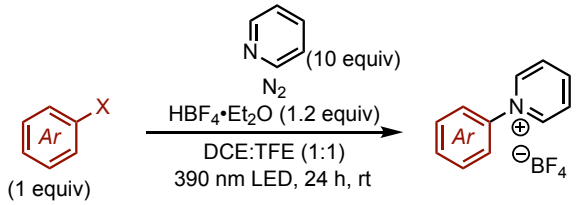
Figure S14 The photochemical experimental setup for S_NAr pyridination reactions using an EvoluChem™ PhotoRedOx Duo (HCK1006-01-023) box equipped with two 390 nm Kessil LEDs (PR160L) and air cooling. These photographs were taken in the Sanford Laboratory by Matthew R. Lasky.

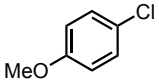
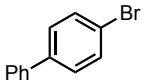
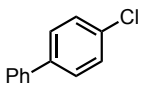
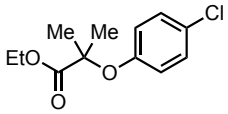
b) Reaction Optimization for S_NAr Pyridination:



Entry	Pyr (eq)	Light source	Crude Yield	Ar-Cl SM
1	10 eq	Black light (CFL)	61%	37%
2	5 eq	Black light (CFL)	71%	29%
3	2 eq	Black light (CFL)	50%	48%
4	10 eq	Kessil **390 nm LED**	84%	13%

Table S7. All reactions were conducted at a 0.1 mmol scale. All yields are crude and were determined by ^{1}H NMR spectroscopy using pentamethylbenzene (0.1 mmol, 1 equiv) as an internal standard. Ar-Cl SM indicates the mass balance of the transformation referring to the amount of 4-chloroanisole remaining. See Figure S1 (Section 3) for information on the photoreactor used for black light (CFL).



Ar-X	Light source	Crude Yield	SM Remaining
	Black light (CFL)	65%	37%
	Kessil **390 nm LED**	84%	13%
	Black light (CFL)	10%	90%
	Kessil **390 nm LED**	19%	75%
	Black light (CFL)	64%	32%
	Kessil **390 nm LED**	85%	6%
	Black light (CFL)	50%	48%
	Kessil **390 nm LED**	76%	25%

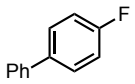
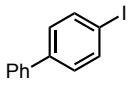
Ar-X	Light source	Crude Yield	SM Remaining
	Kessil **390 nm LED**	35%	54%
	Kessil **390 nm LED**	<1%	90%

Table S8. Small investigation into the substrate scope for S_NAr pyridination. All reactions were conducted at a 0.1 mmol scale. All yields are crude and were determined by ^1H NMR spectroscopy using pentamethylbenzene (0.1 mmol, 1 equiv) as an internal standard. SM remaining refers to the amount of unreacted aryl-halide starting material.

c) UV-Vis Spectroscopic Analysis

UV-Vis measurements were obtained on a Varian Cary-50 spectrophotometer using a 3 mL (1 cm path length) cuvette. Processing of UV-Vis data: the generated data was plotted in Microsoft Excel.

<u>PyH^+–4-chlorobiphenyl EDA complex:</u>
To a flame-dried 5 mL volumetric flask, a 0.2 M stock solution was prepared for each of the following reagents in DCE/TFE (1:1):

1) Pyridine and HBF_4•Et_2O (0.2 M) = 80.6 µL (1.0 mmol) and 137.2 µL (1.0 mmol), respectively – **gray trace**
2) 4-chlorobiphenyl (0.2 M) = 188.7 mg (1.0 mmol) – **blue trace**
3) Pyridine + HBF_4•Et_2O : 4-chlorobiphenyl (1:1, 0.2 M) = 80.6 µL (1.0 mmol) and 137.2 µL (1.0 mmol) : 188.7 mg (1.0 mmol), respectively – **maize trace**

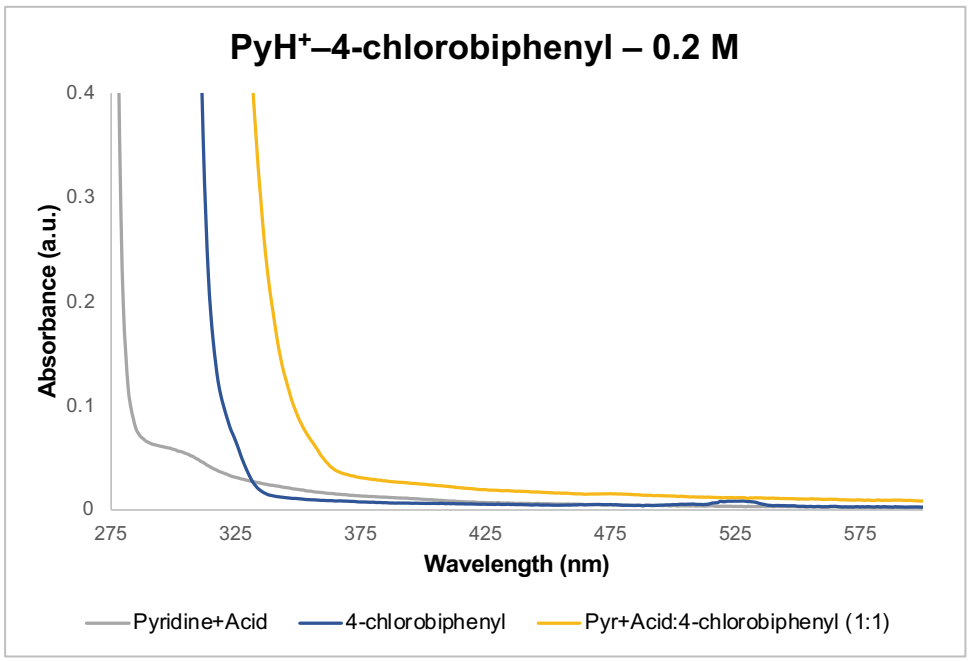
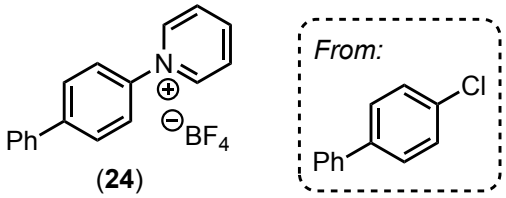


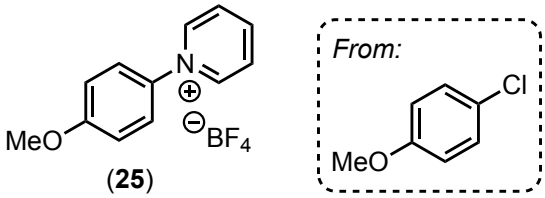
Figure S15. Experimental UV-Vis spectra for PyH^+–4-chlorobiphenyl EDA Complex (0.2M) recorded on a Varian Cary-50 spectrophotometer. These results demonstrate a bathochromic shift diagnostic of EDA complex formation via aggregation of PyH^+ and biphenyl. AU = arbitrary units.

13. Characterization of S_NAr Pyridination Products



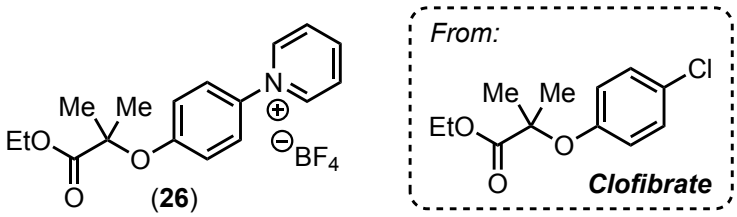
(**24**)

Prepared from 4-chlorobiphenyl and pyridine using the general procedure for S_NAr pyridination. Purification by automated flash chromatography (DCM/MeCN gradient 0-40%) afforded the title compound (**24**) (21.3 mg, 67% yield, light yellow-orange solid). The characterization data for **24** match compound **1** (p. S27) and those reported in the literature.[12]



(**25**)

Prepared from 4-chloroanisole and pyridine using the general procedure for S_NAr pyridination. Purification by automated flash chromatography (DCM/MeCN gradient 0-40%) afforded the title compound (**25**) (19.5 mg, 71% yield, white solid). The characterization data for **25** match those reported in the literature.[12]



(**26**)

Prepared from Clofibrate and pyridine using the general procedure for S_NAr pyridination. Two purifications by automated flash chromatography (DCM/MeCN gradient 0-40%) afforded the title compound (**26**) (20.1 mg, 54% yield, yellow oil). The characterization data for **26** match those reported in the literature.[12]

14. References

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[11] If the arene is not a solid and instead a liquid, add the arene after the solvent has been added to the reaction vessel.

[12] M. A. Mantell, M. R. Lasky, M. Lee, M. Remy, M. S. Sanford, *Org. Lett.* **2021**, *23*, 5213–5217.

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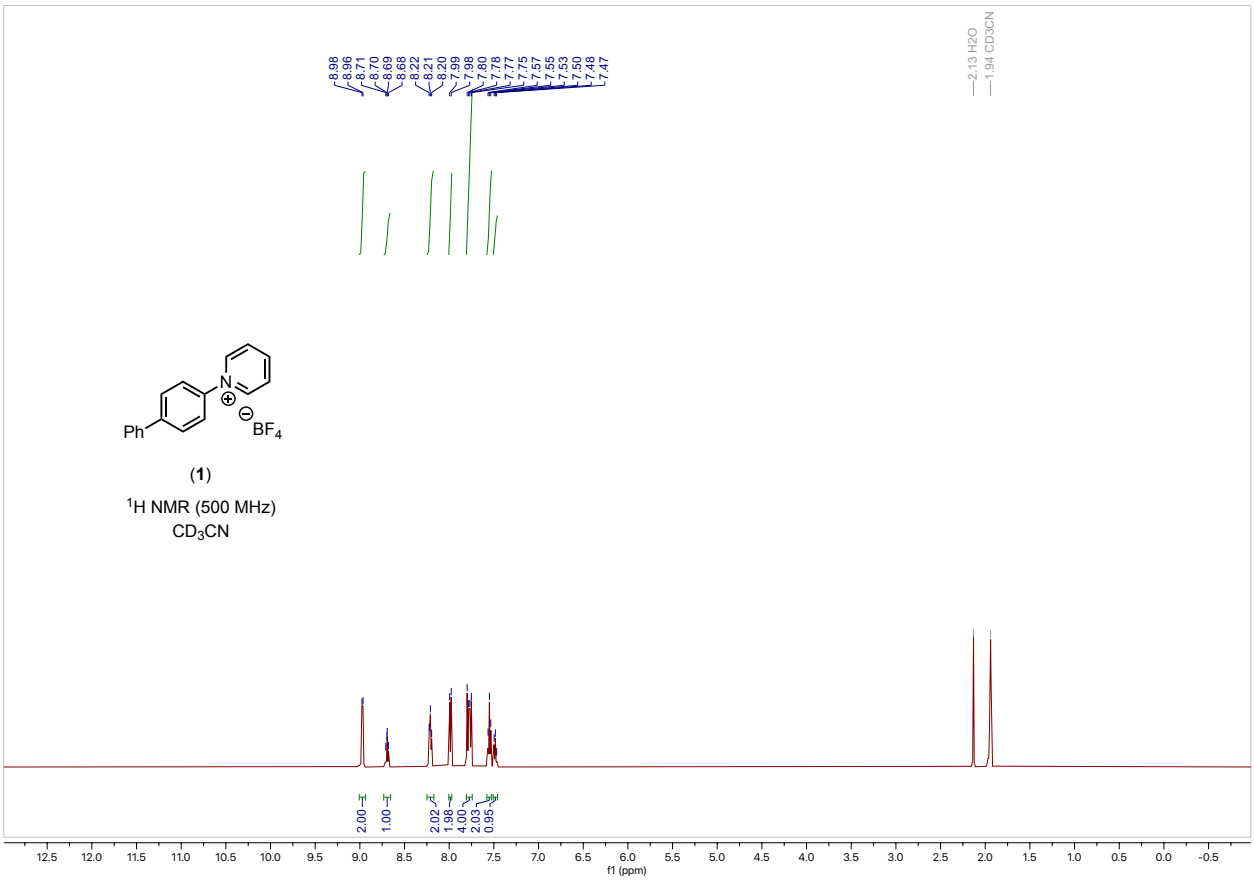
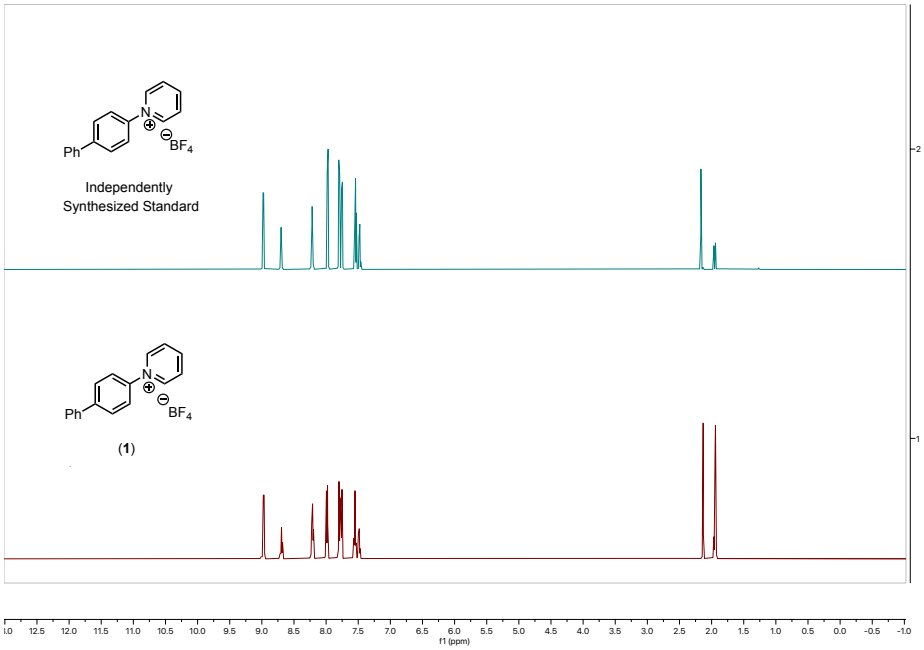
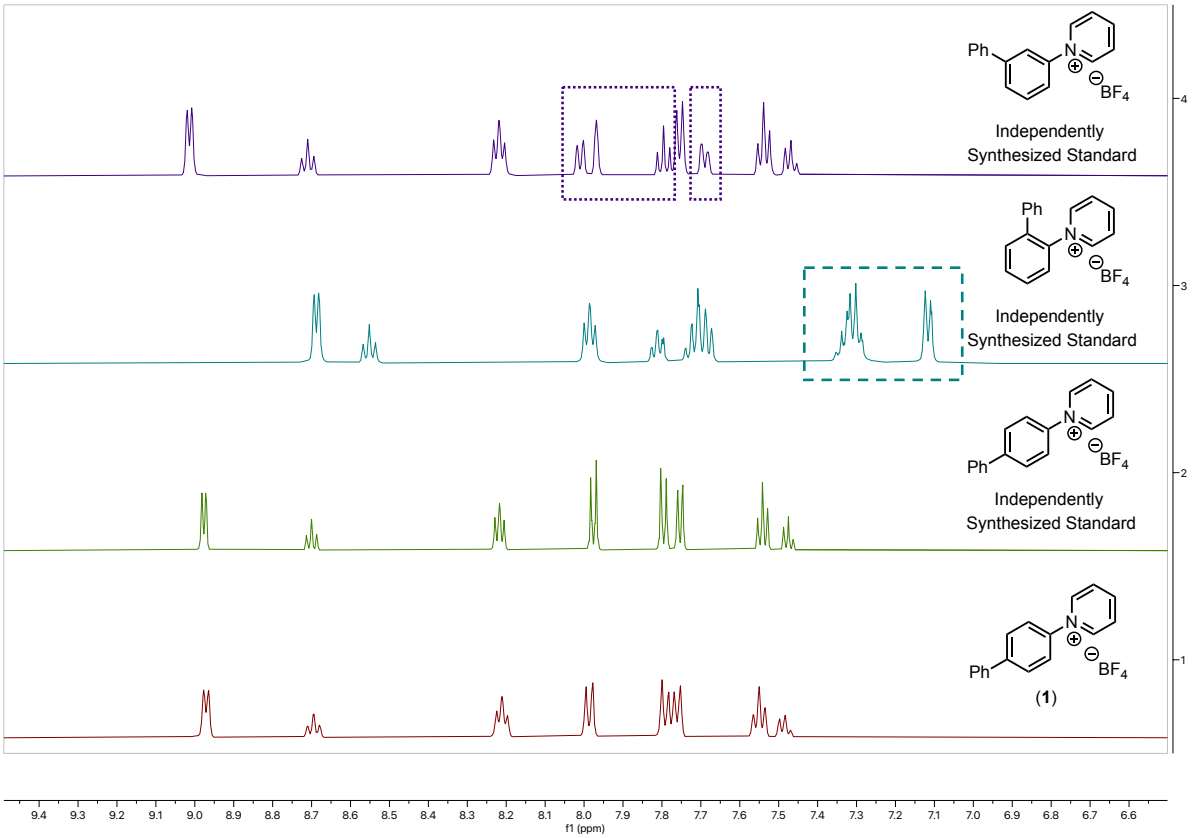
15. NMR Spectral Data




Ph
BF4
Independently
Synthesized Standard
Ph
BF4
(1)
f1 (ppm)

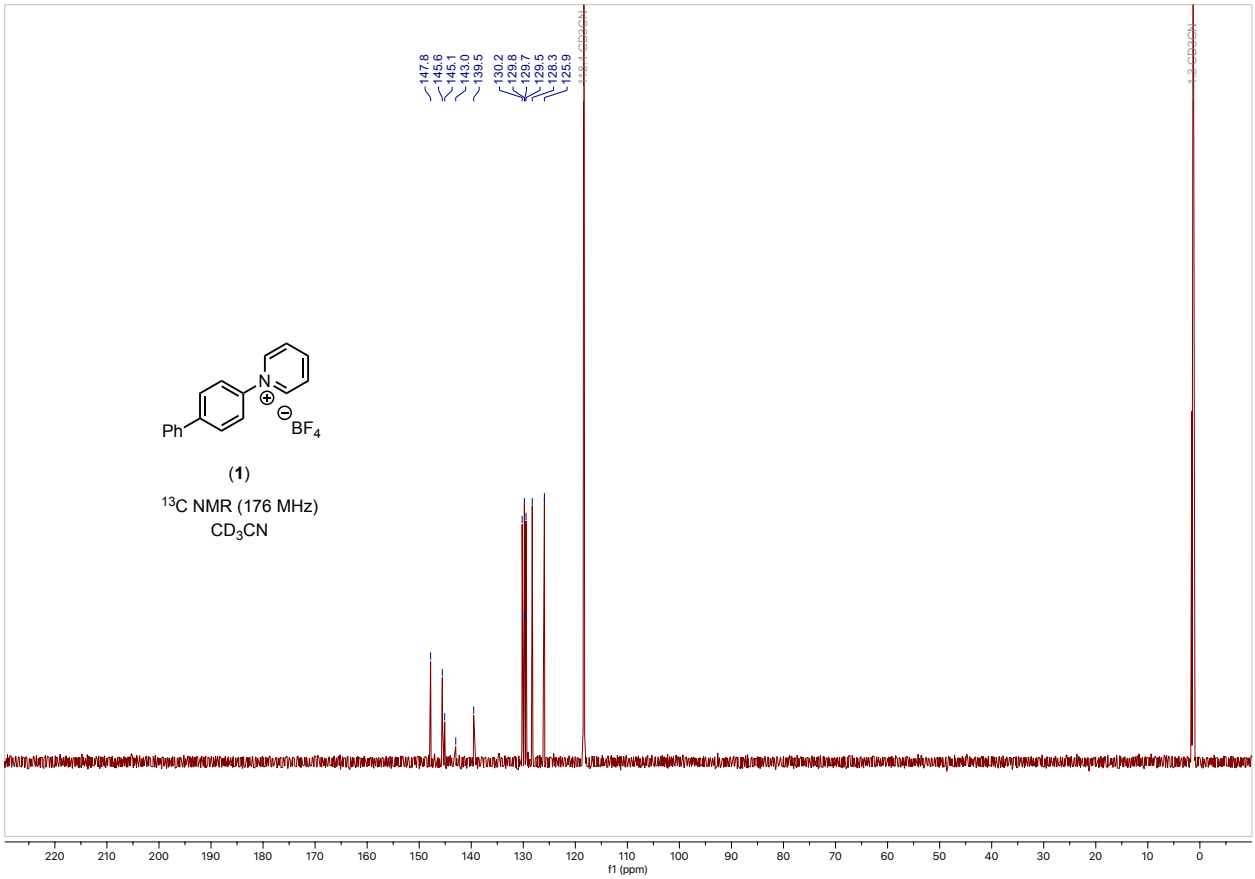

Ph
BF4
Independently
Synthesized Standard
Ph
BF4
Independently
Synthesized Standard
Ph
BF4
Independently
Synthesized Standard
Ph
BF4
(1)
f1 (ppm)

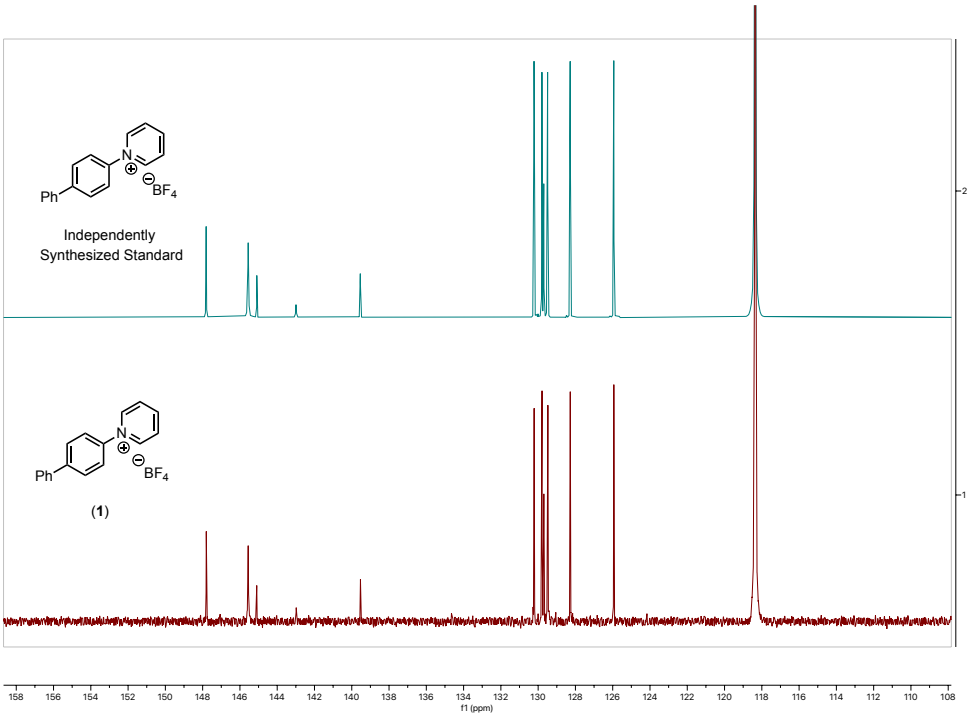
Three independently synthesized standards (*para*, *ortho*, *meta)* were made for model substrate **1** to confirm the regioselectivity of the reaction.[1] This overlay confirms that product **1** is formed solely as the *para* isomer. These standards of model substrate **1** were utilized as a benchmark comparison for the substituted pyridines that yielded mixtures of isomers. Each isomer exhibits characteristic aryl signals that are unique and easily identifiable across the range of substituted pyridines that resulted in mixtures of isomers as described below.

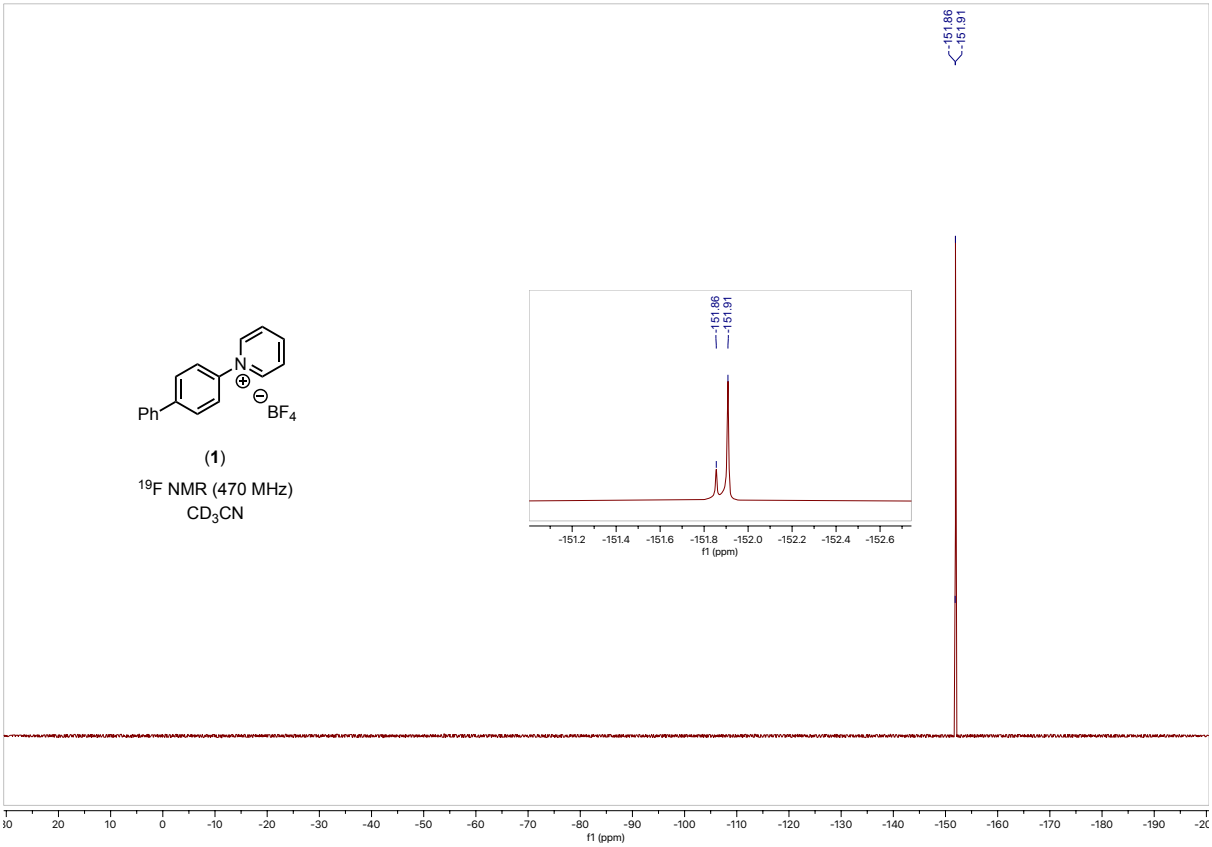
Para isomer: shows two distinct doublets exhibiting the "roofing effect," each integrating to two protons.

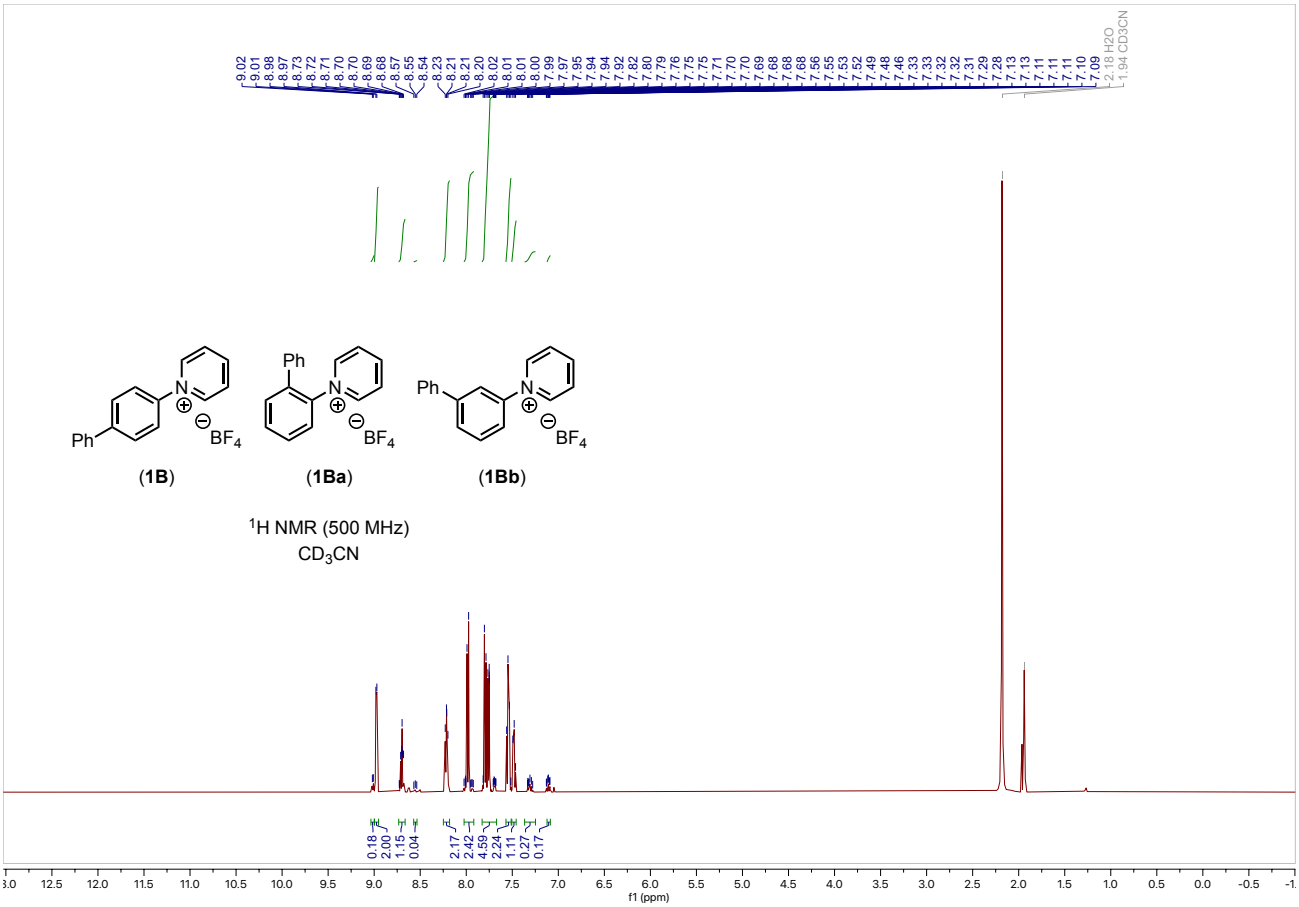
Ortho isomer: diagnostic upfield signals in the range of 7.0-7.4 ppm. The splitting pattern is a multiplet and doublet, with the doublet being furthest upfield. The multiplet integrates to three protons and the doublet integrates to two protons (see dashed box above*, ortho* isomer standard).

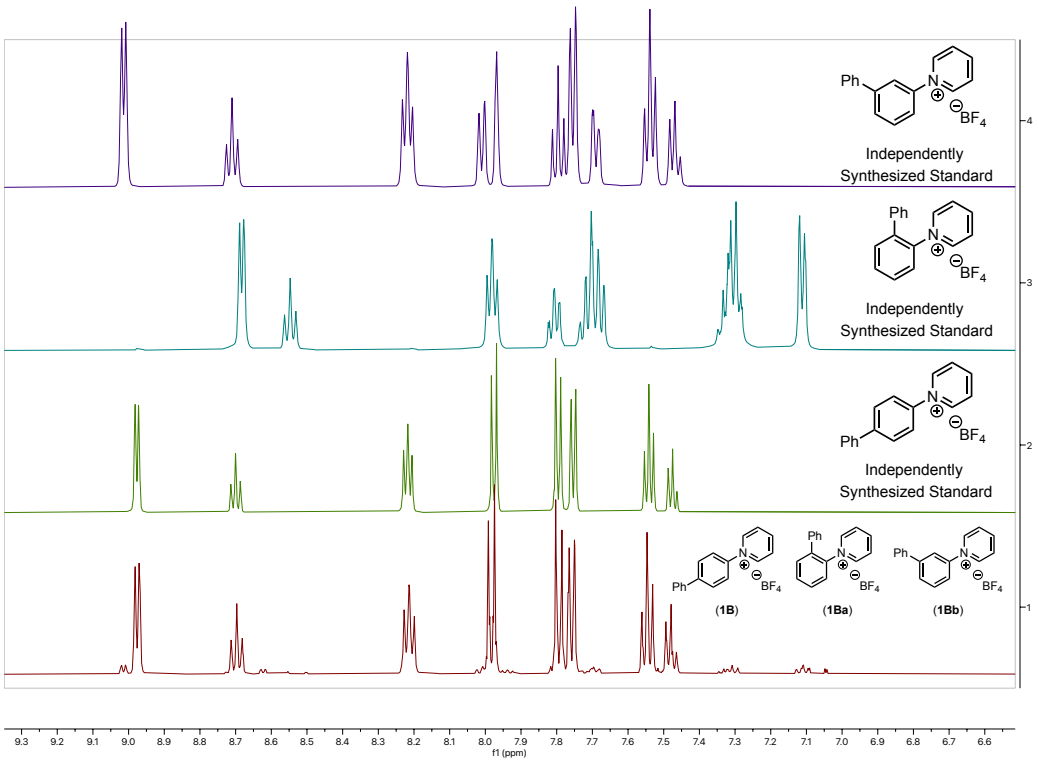
Meta isomer: a diagnostic splitting pattern is observed. Starting with the signal furthest downfield to upfield: doublet, singlet, triplet, doublet. Each signal integrates to one proton (see dotted boxes above, *meta isomer* standard).

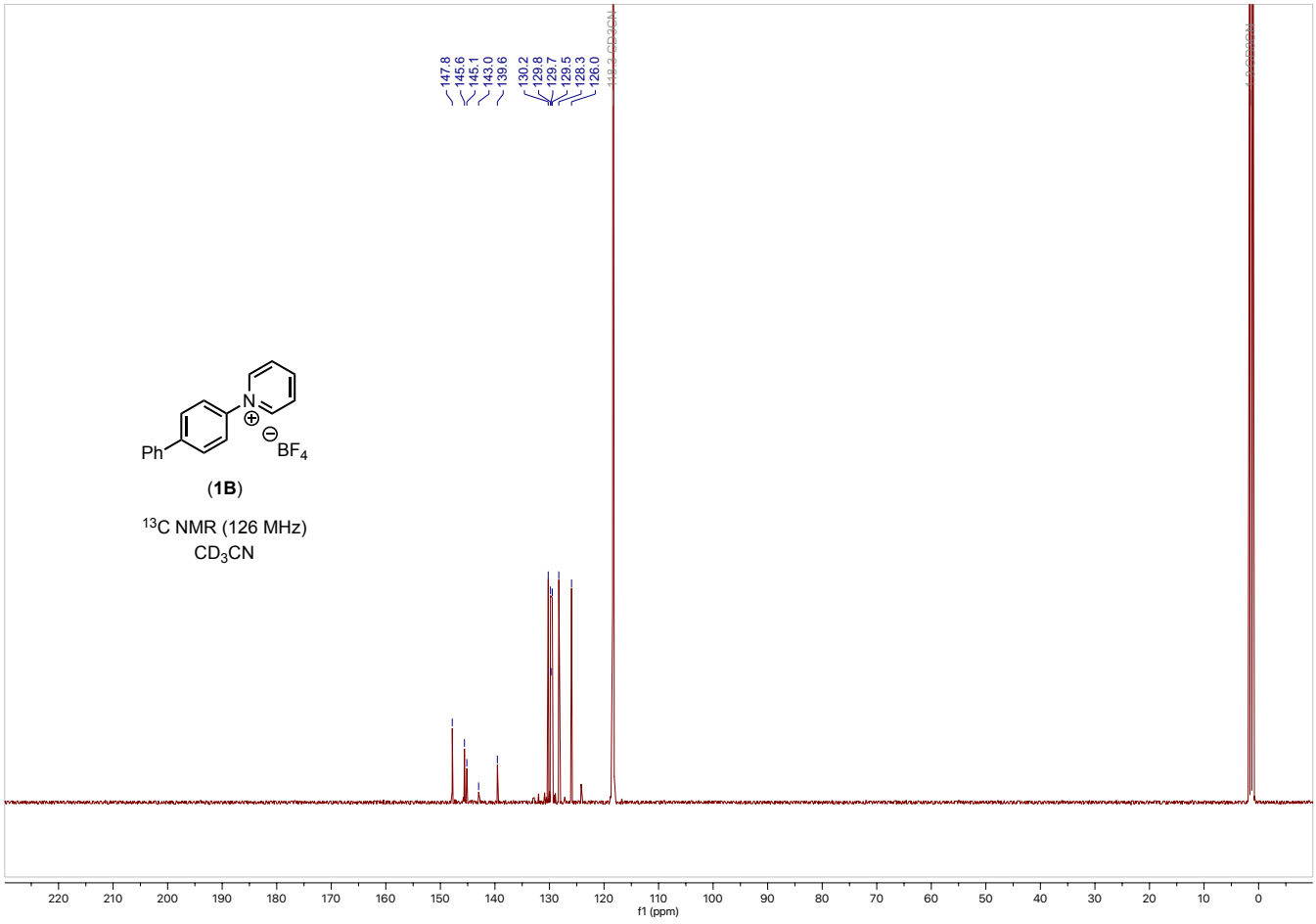

147.8
145.6
145.1
143.0
139.5
130.2
129.8
129.7
129.5
128.3
125.9
118.1 CD3CN
1.3 CD3CN
Ph
BF4
(1)
13C NMR (176 MHz)
CD3CN
f1 (ppm)

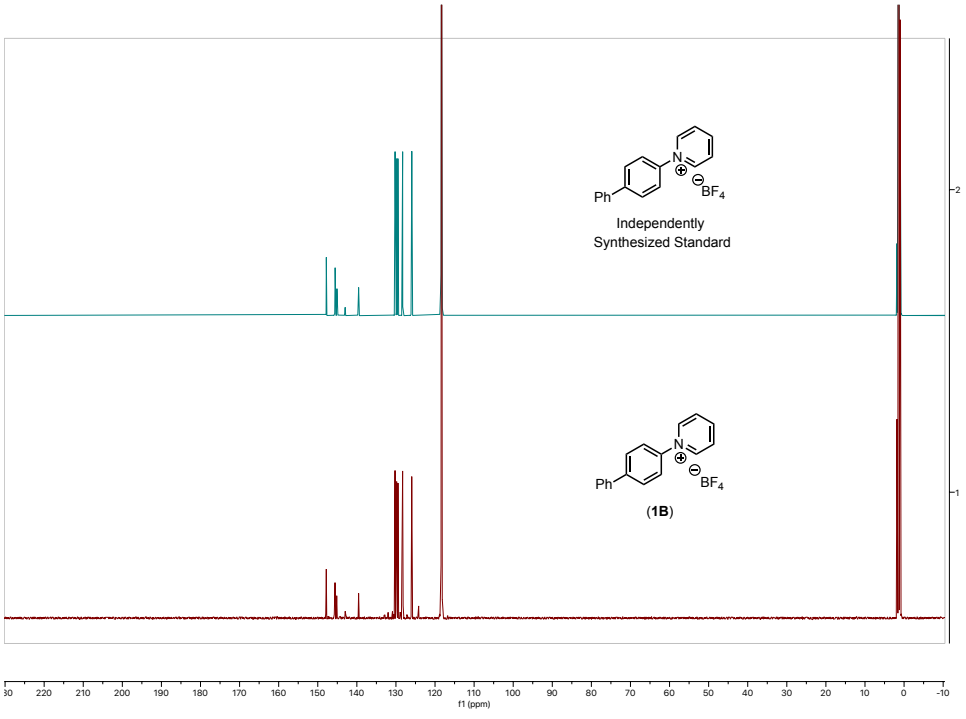

Ph
BF4
Independently
Synthesized Standard
Ph
BF4
(1)
f1 (ppm)

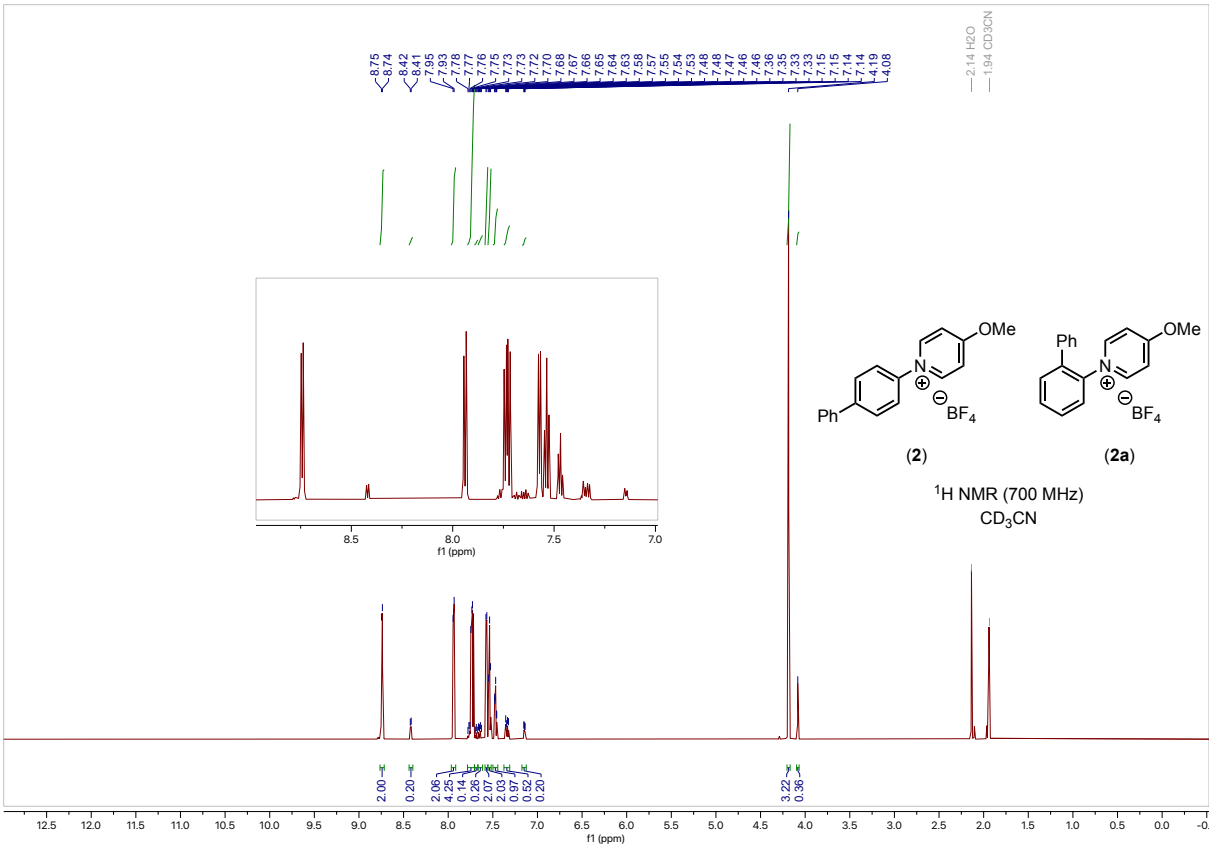

-151.86
-151.91
Ph
BF4
(1)
19F NMR (470 MHz)
CD3CN
f1 (ppm)

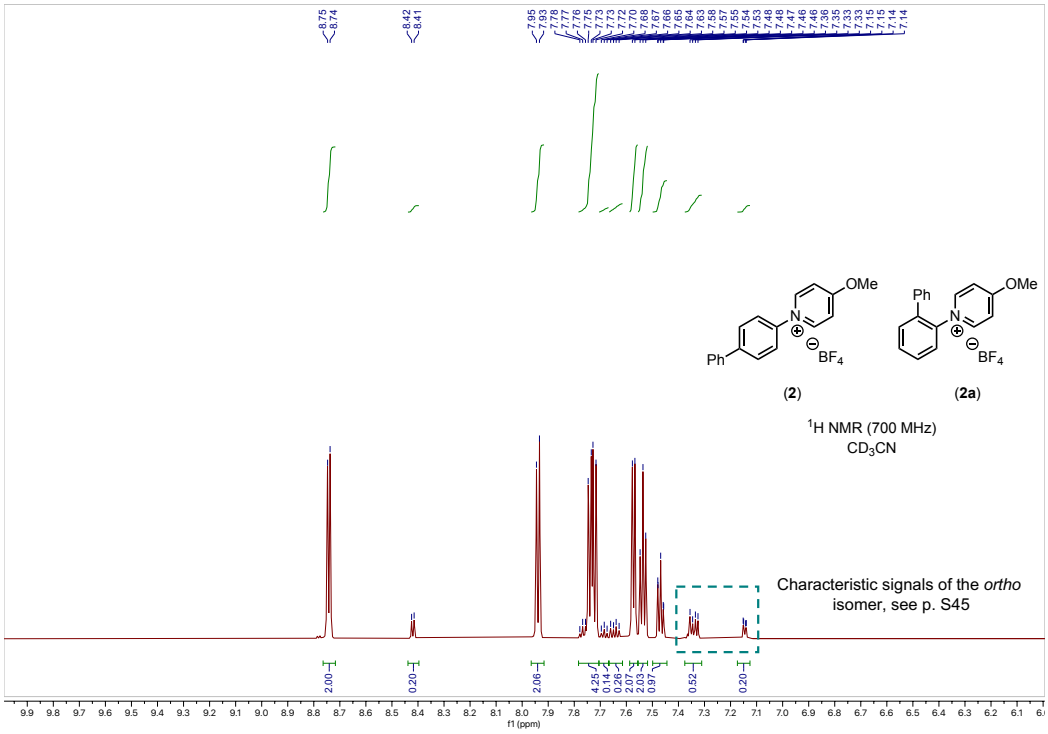

(1B)
(1Ba)
(1Bb)
1H NMR (500 MHz)
CD3CN
f1 (ppm)

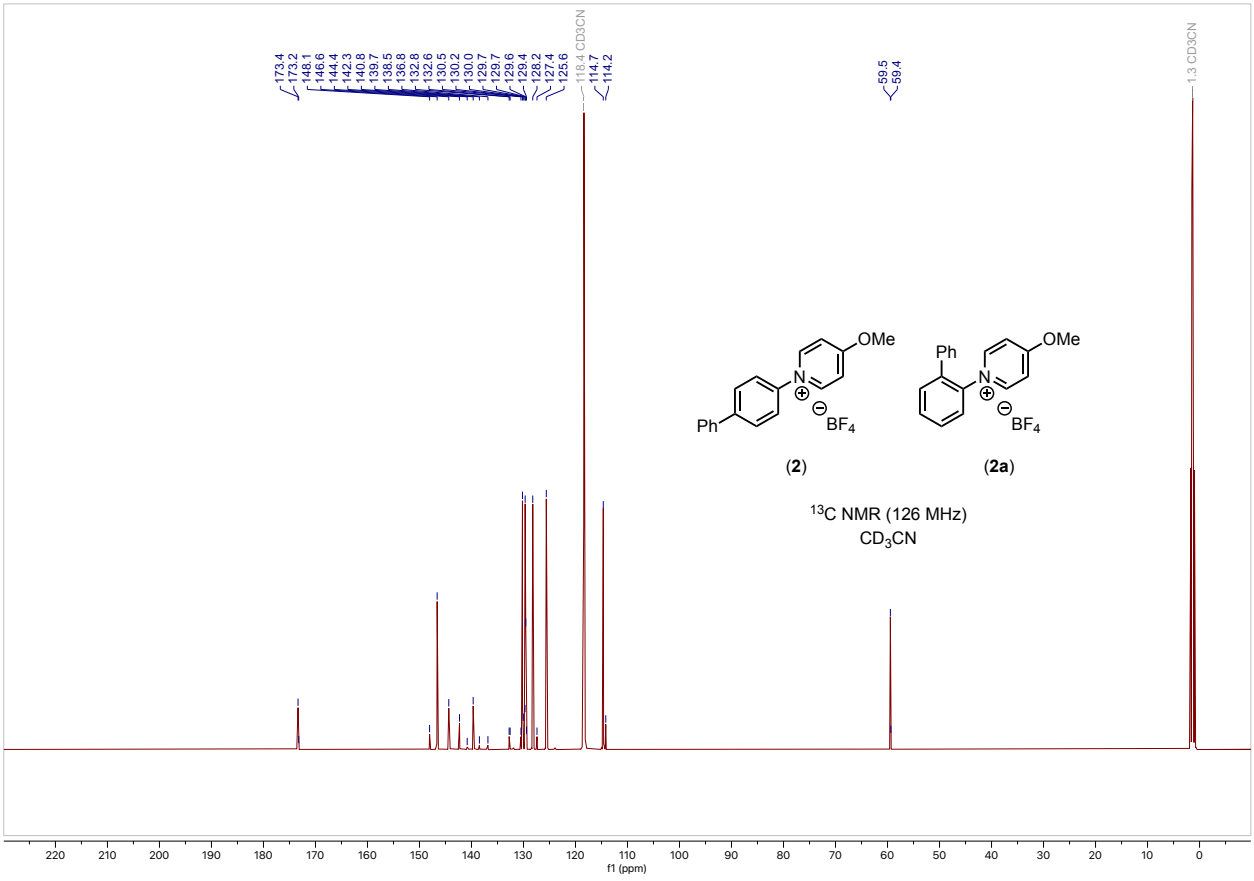

Independently Synthesized Standard
Independently Synthesized Standard
Independently Synthesized Standard
(1B)
(1Ba)
(1Bb)
f1 (ppm)

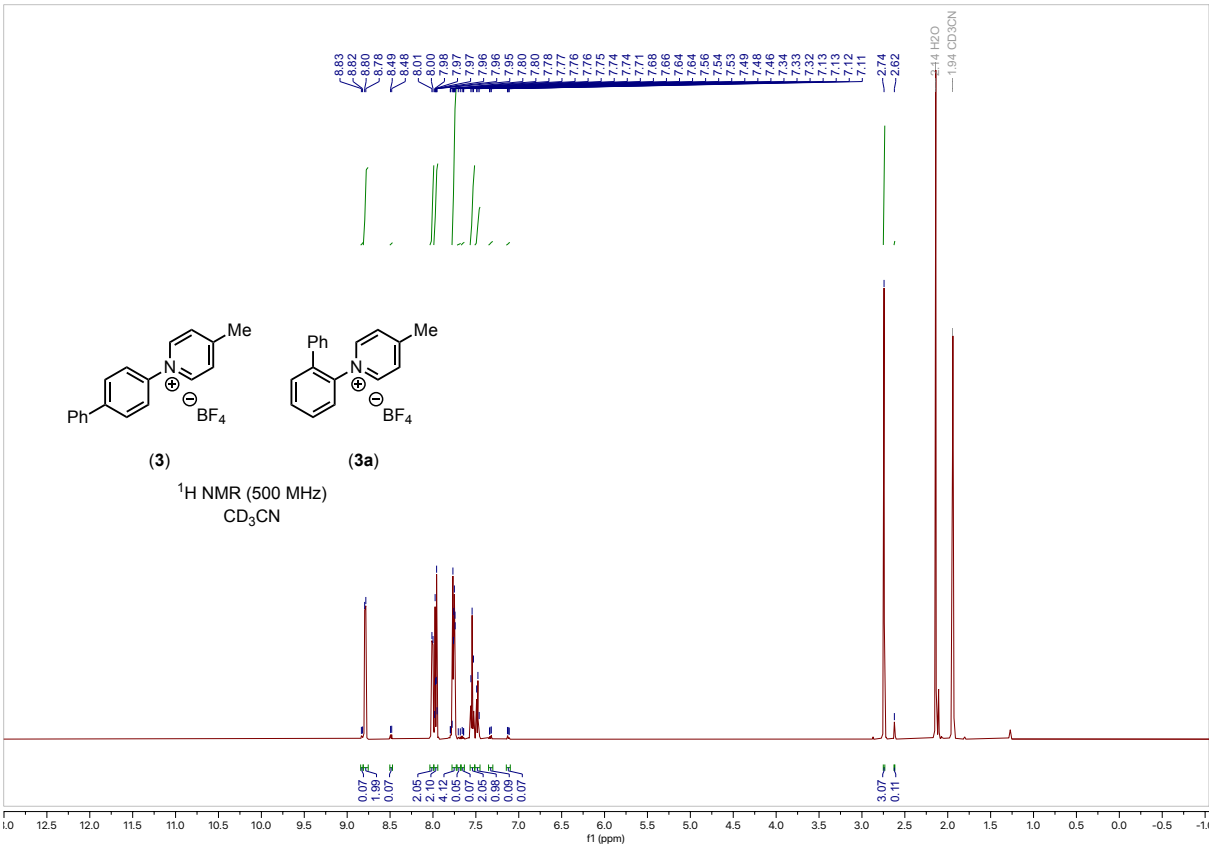

147.8
145.6
145.1
143.0
139.6
130.2
129.8
129.7
129.5
128.3
126.0
Ph
BF4
(1B)
13C NMR (126 MHz)
CD3CN
f1 (ppm)

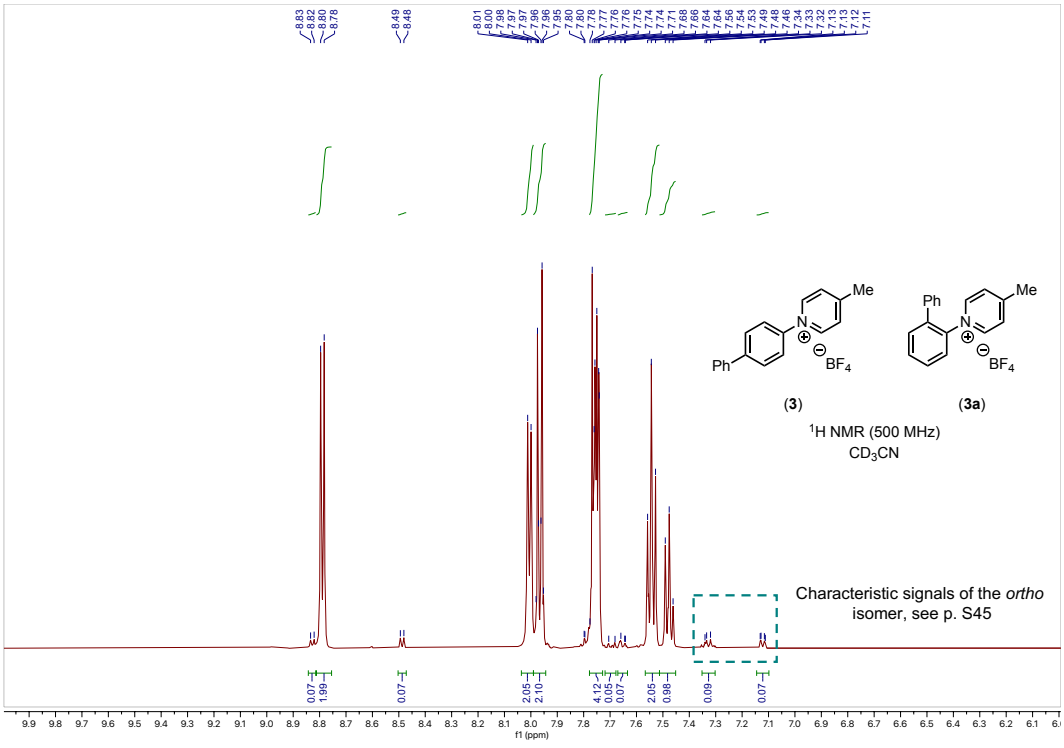

Ph
BF4
Independently
Synthesized Standard
Ph
BF4
(1B)
f1 (ppm)

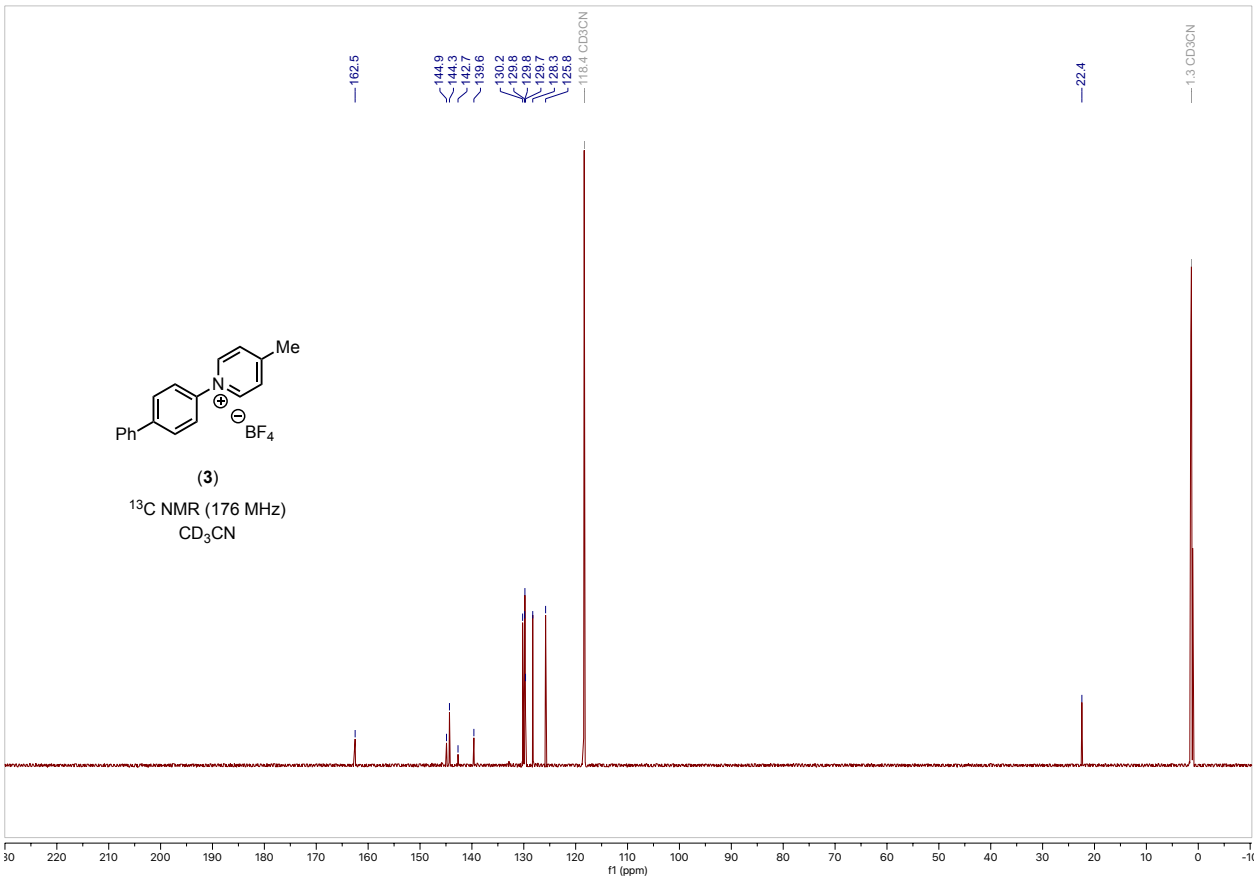

OMe
Ph
BF4
(2)
(2a)
1H NMR (700 MHz)
CD3CN
f1 (ppm)

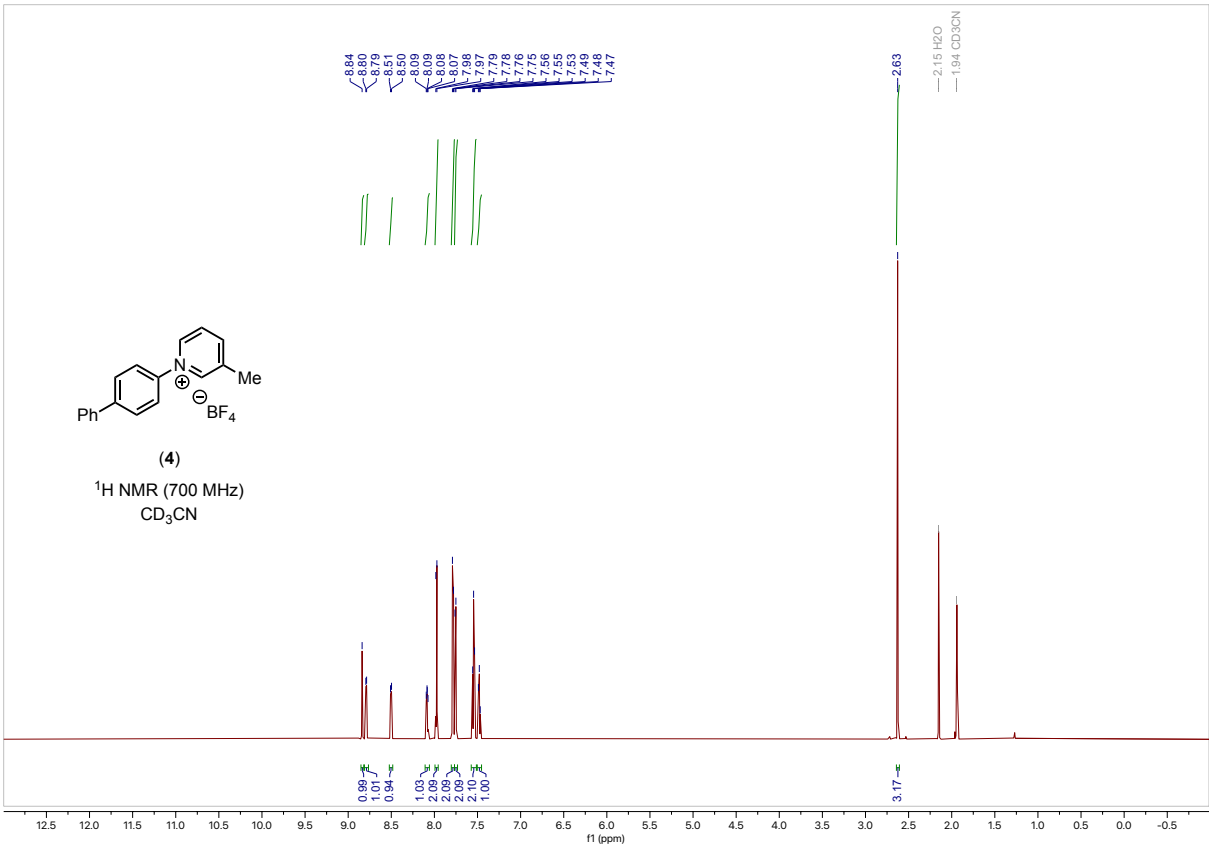

OMe
Ph
BF4
(2)
(2a)
1H NMR (700 MHz)
CD3CN
Characteristic signals of the ortho isomer, see p. S45
f1 (ppm)


173.4
173.2
148.1
146.6
144.4
142.3
140.8
139.7
138.5
136.8
132.8
132.6
130.5
130.2
130.0
129.7
129.7
129.6
129.4
128.2
127.4
125.6
118.4 CD3CN
114.7
114.2
59.5
59.4
1.3 CD3CN
OMe
Ph
BF4
(2)
OMe
Ph
BF4
(2a)
13C NMR (126 MHz)
CD3CN
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


Me
Ph
BF4
(3)
Ph
Me
BF4
(3a)
1H NMR (500 MHz)
CD3CN
f1 (ppm)


Me
Ph
BF4
(3)
Ph
Me
BF4
(3a)
1H NMR (500 MHz)
CD3CN
Characteristic signals of the ortho isomer, see p. S45
f1 (ppm)

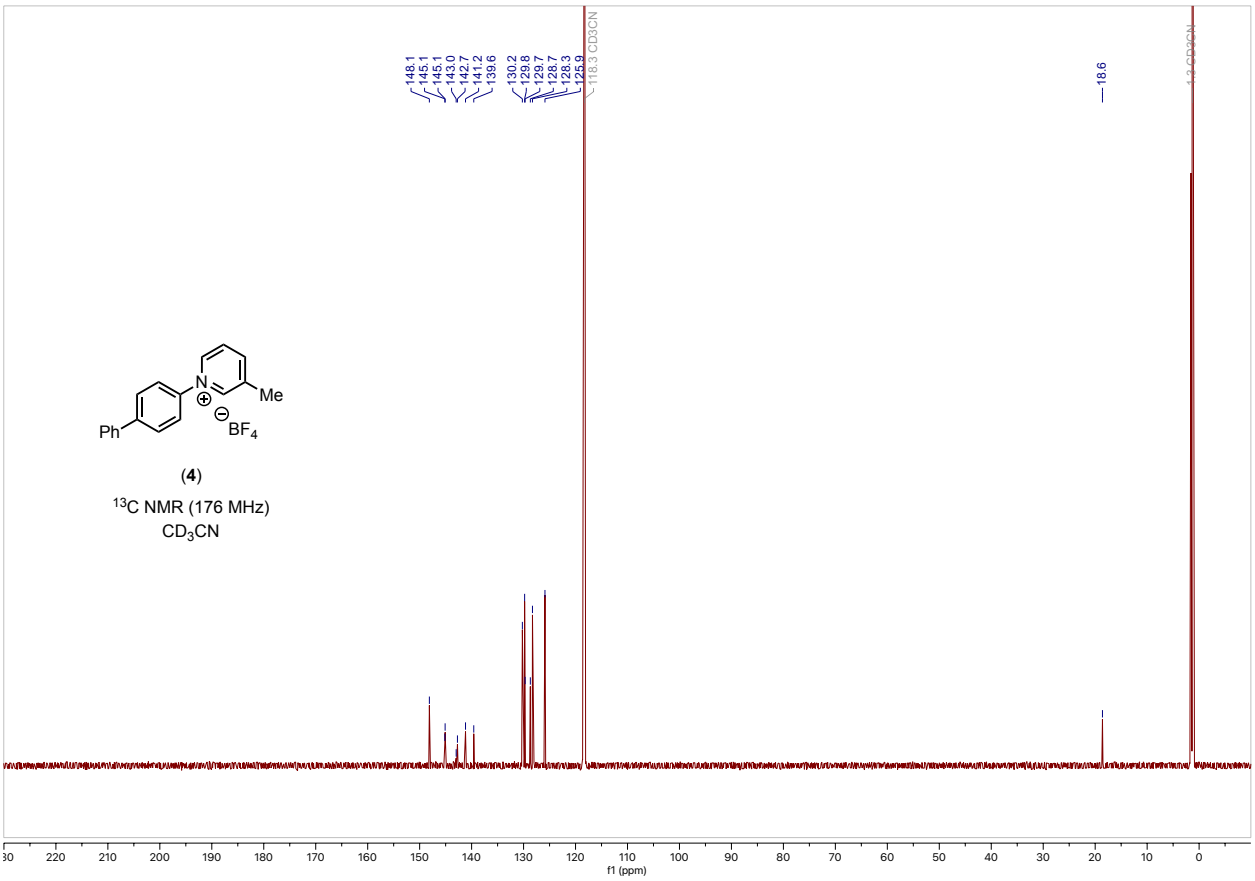

162.5
144.9
144.3
142.7
139.6
130.2
129.8
129.8
129.7
128.3
125.8
118.4 CD3CN
22.4
1.3 CD3CN
Me
N
Ph
BF4
(3)
13C NMR (176 MHz)
CD3CN
f1 (ppm)

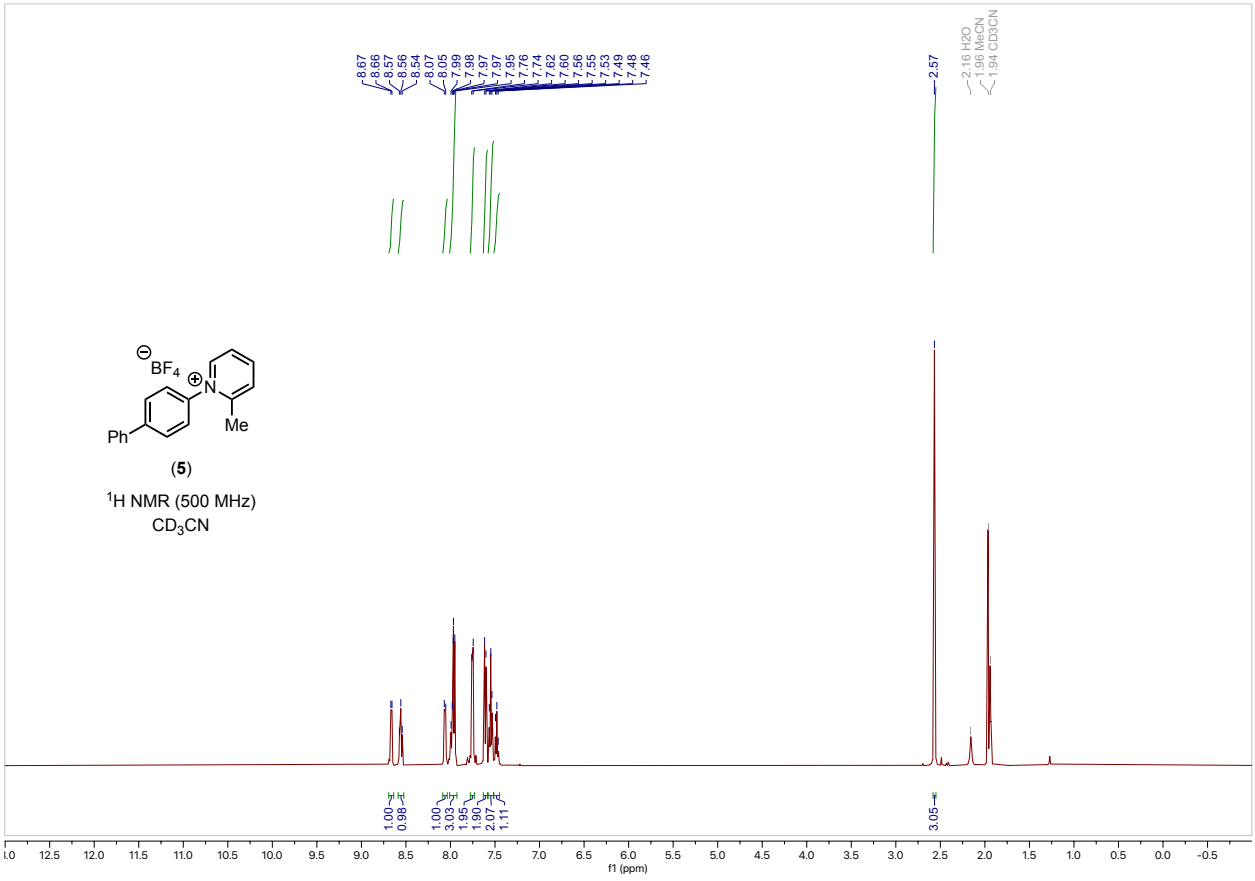


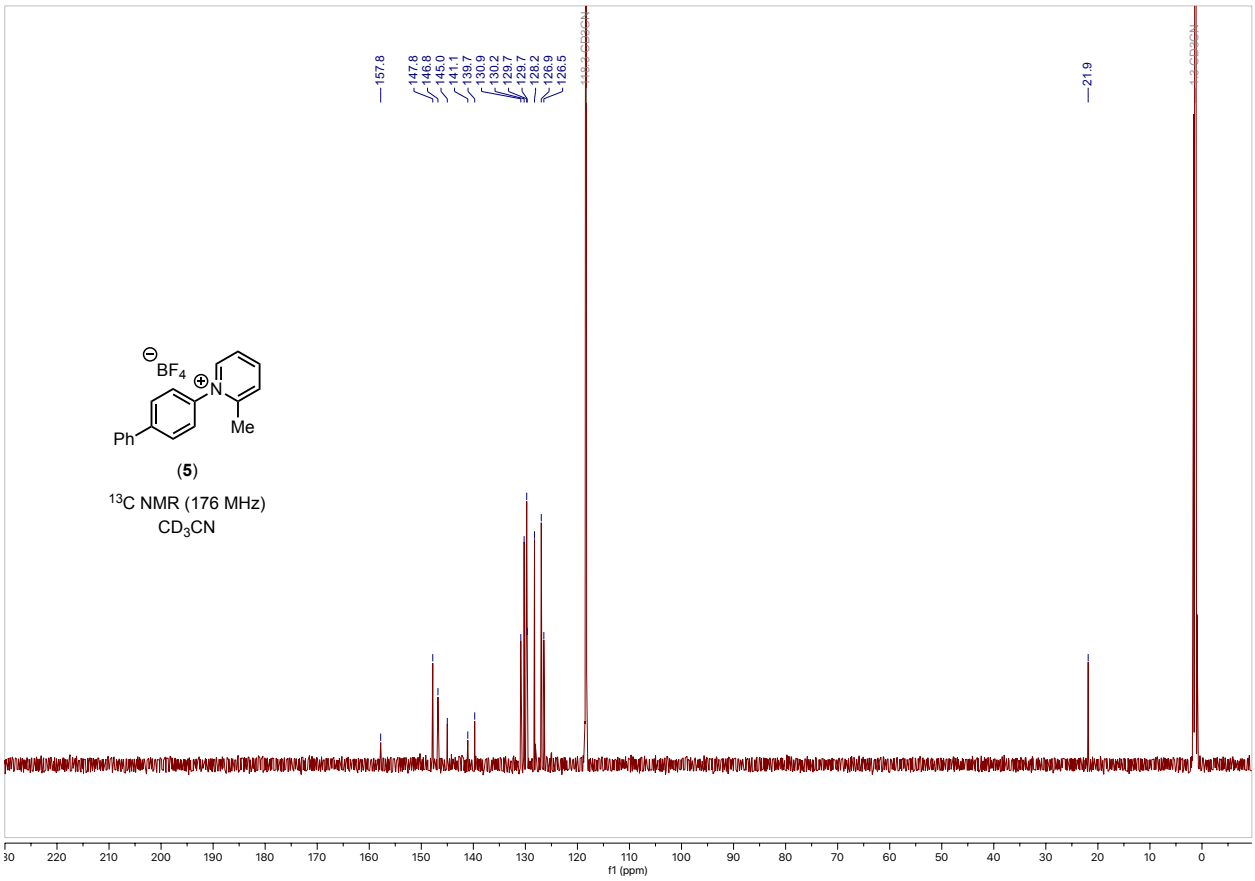
(**4**)

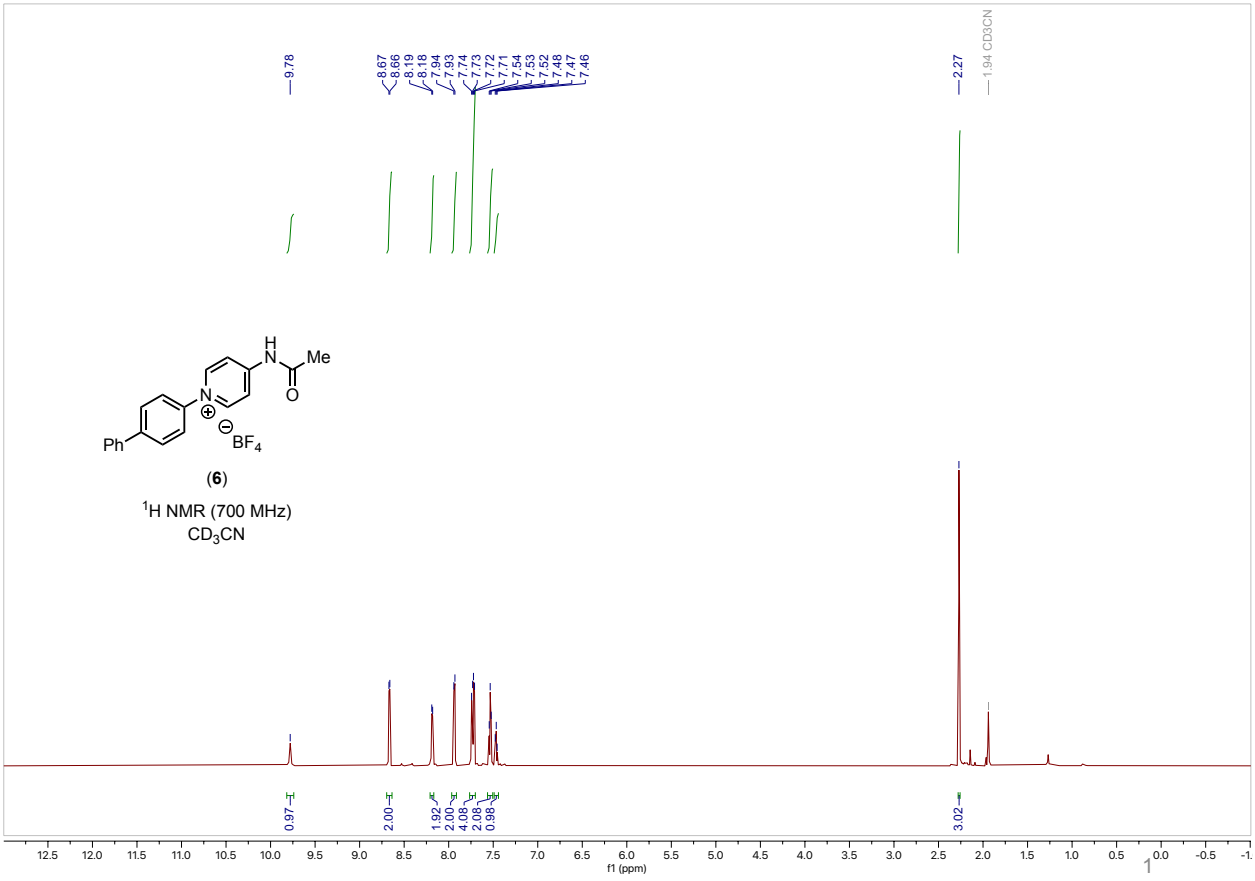
^{1}H NMR (700 MHz)

CD_3CN


148.1
145.1
145.1
143.0
142.7
141.2
139.6
130.2
129.8
129.7
128.7
128.3
125.9
118.3 CD3CN
18.6
1.3 CD3CN
Me
Ph
BF4
(4)
13C NMR (176 MHz)
CD3CN
f1 (ppm)

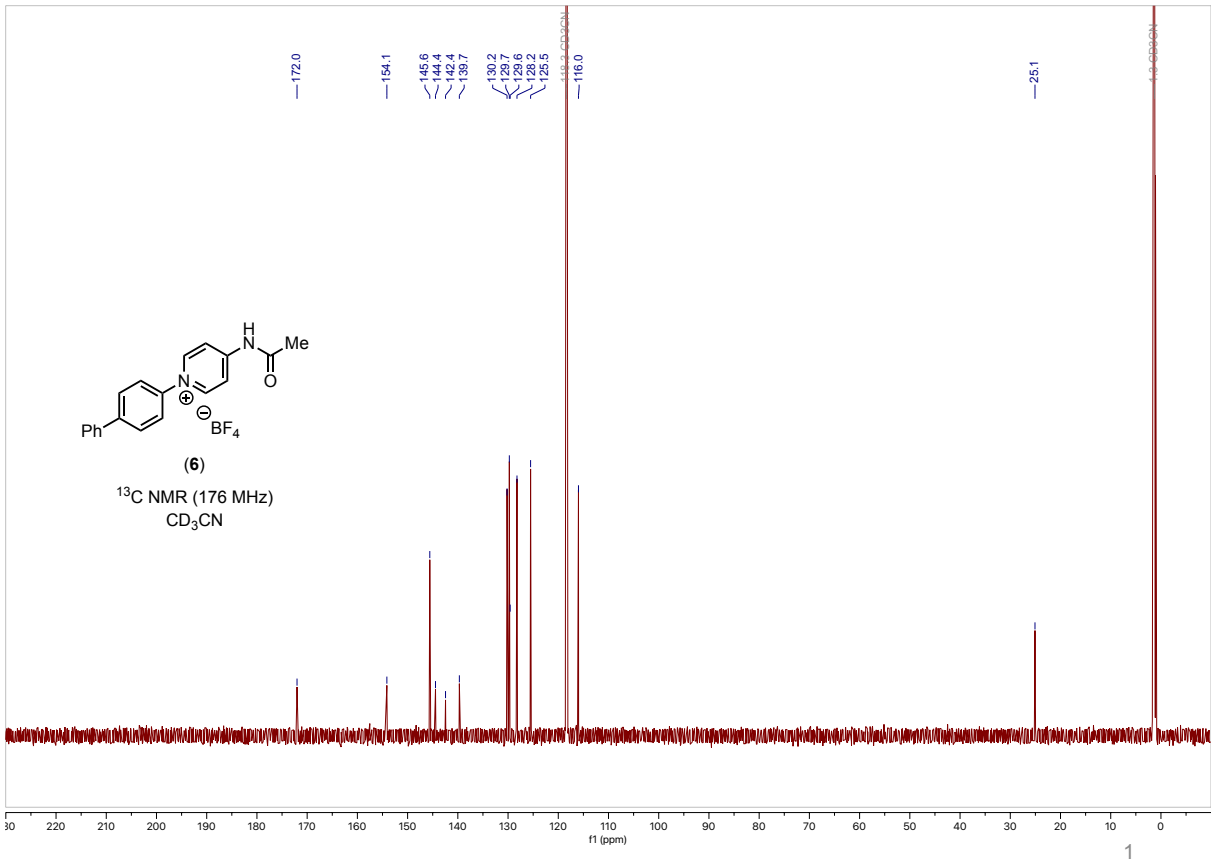

8.67
8.66
8.57
8.56
8.54
8.07
8.05
7.99
7.98
7.97
7.97
7.95
7.76
7.74
7.62
7.60
7.56
7.55
7.53
7.49
7.48
7.46
2.57
2.16 H2O
1.96 MeCN
1.94 CD3CN
BF4
N
Ph
Me
(5)
1H NMR (500 MHz)
CD3CN
1.00
0.98
1.00
3.03
1.95
1.90
2.07
1.11
3.05
f1 (ppm)

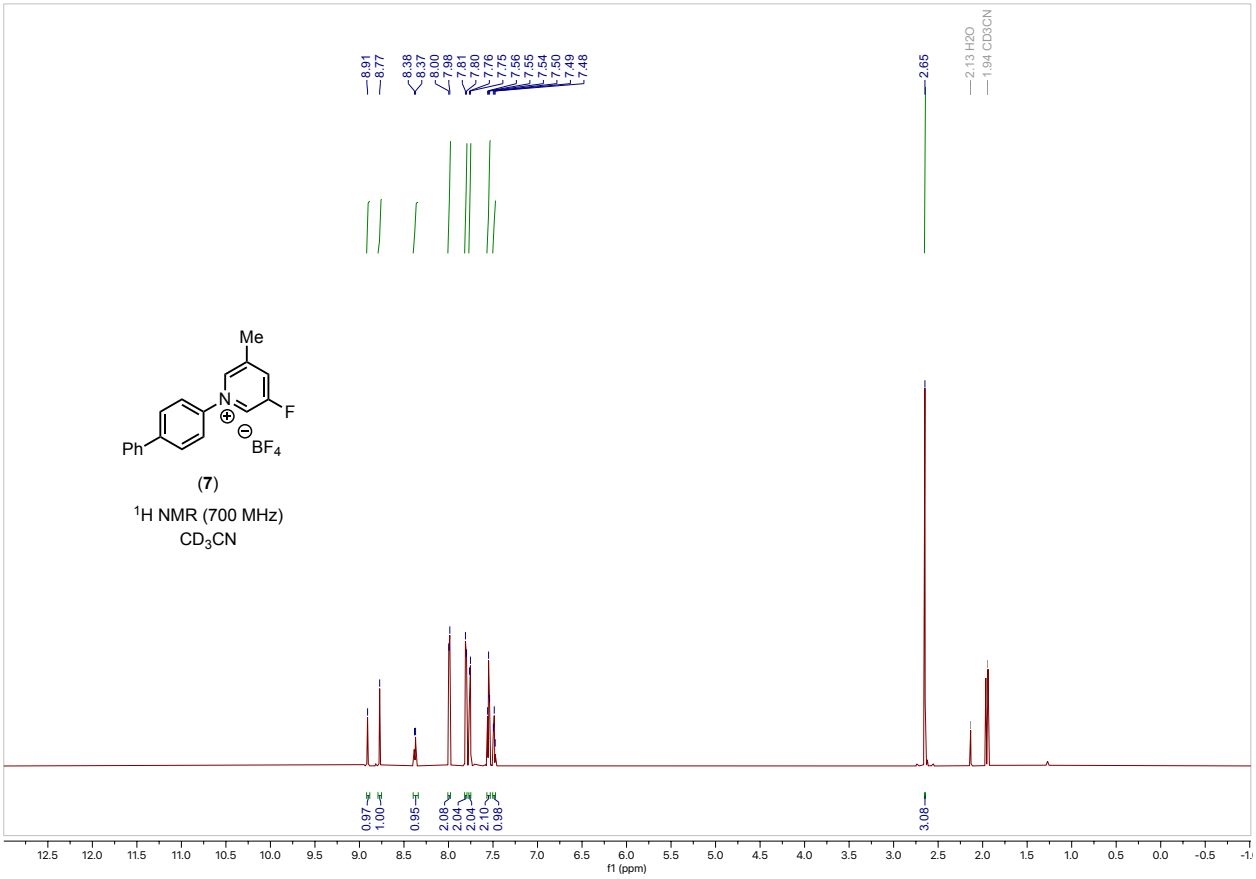

157.8
147.8
146.8
145.0
141.1
139.7
130.9
130.2
129.7
129.7
128.2
126.9
126.5
118.8 CD3CN
21.9
1.9 CD3CN
BF4
N
Ph
Me
(5)
13C NMR (176 MHz)
CD3CN
f1 (ppm)



(**6**)

^{1}H NMR (700 MHz)
CD_3CN

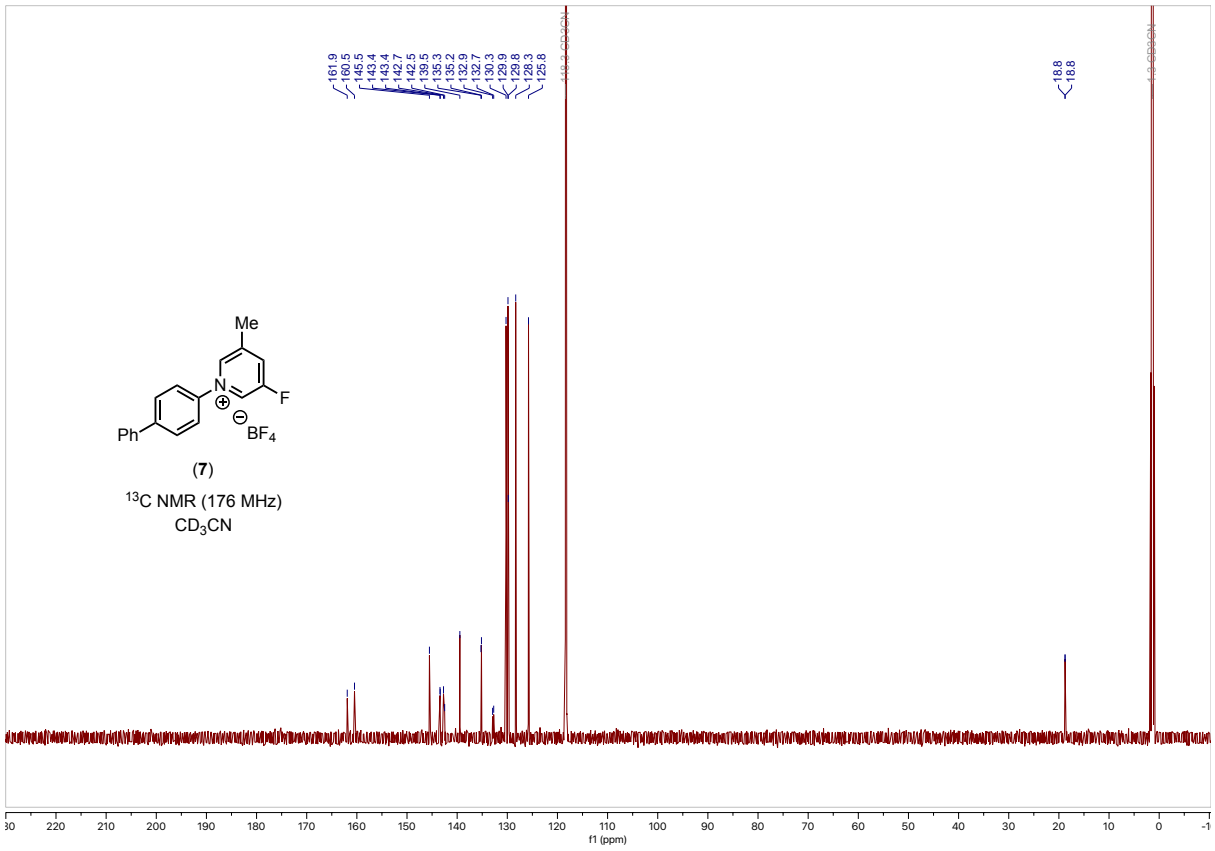

172.0
154.1
145.6
144.4
142.4
139.7
130.2
129.7
129.6
128.2
125.5
118.3 CD3CN
116.0
25.1
1.3 CD3CN
H
N
Me
O
N
Ph
BF4
(6)
13C NMR (176 MHz)
CD3CN
f1 (ppm)

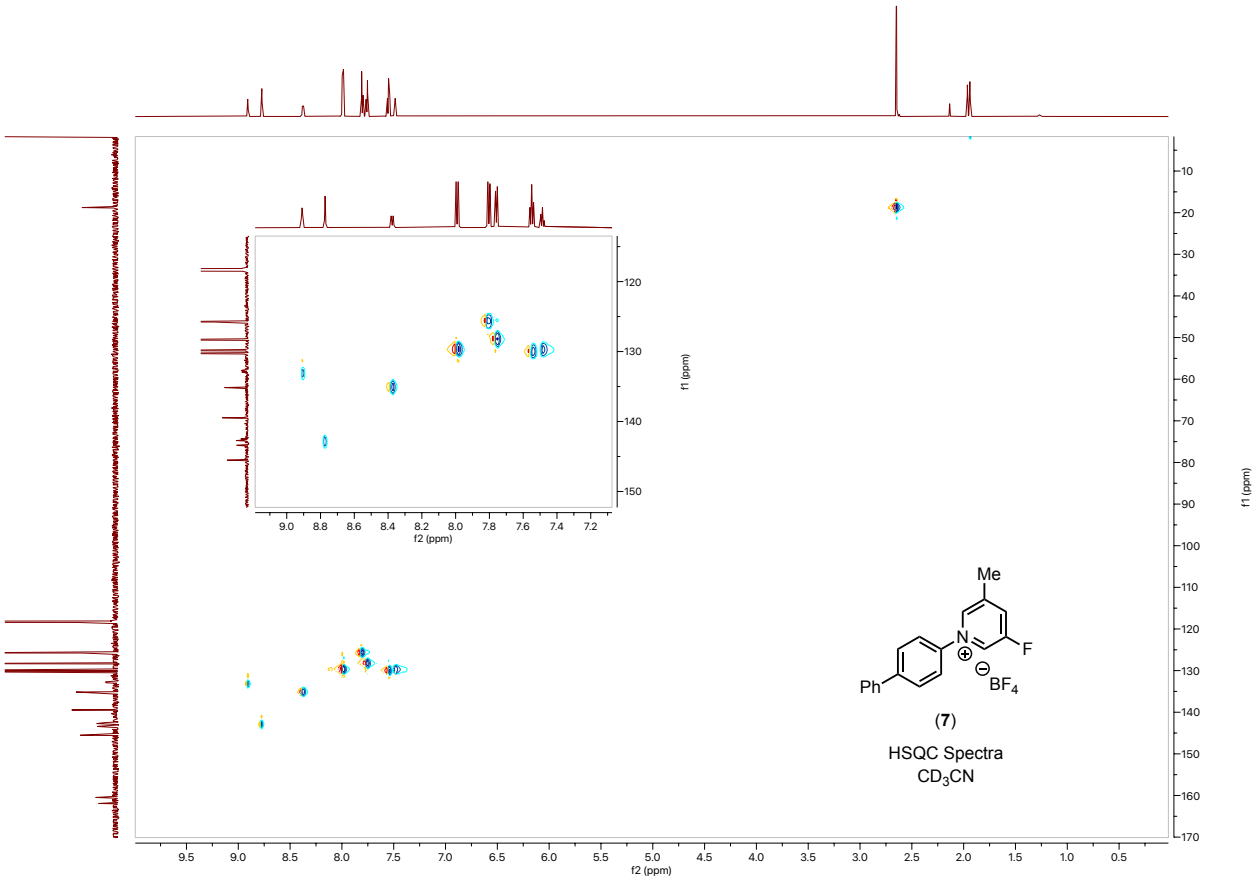


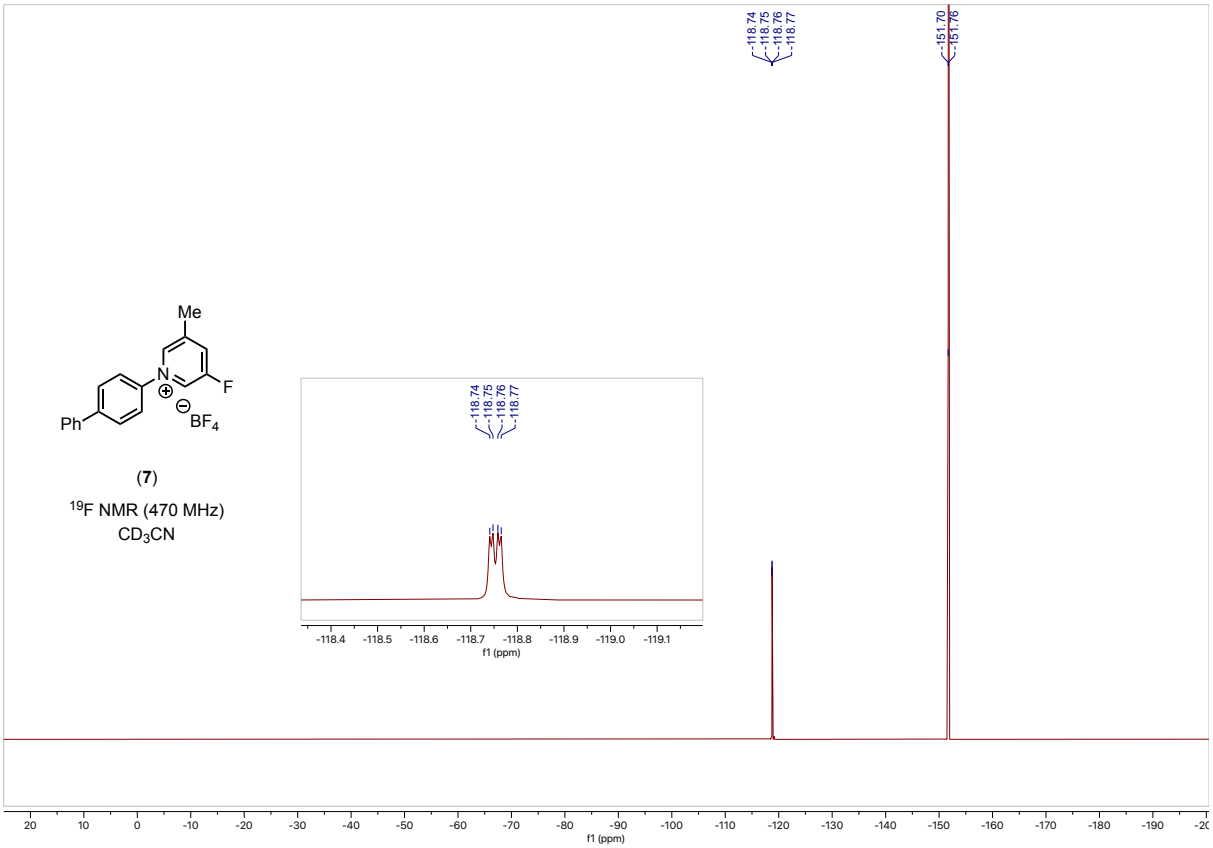
(**7**)

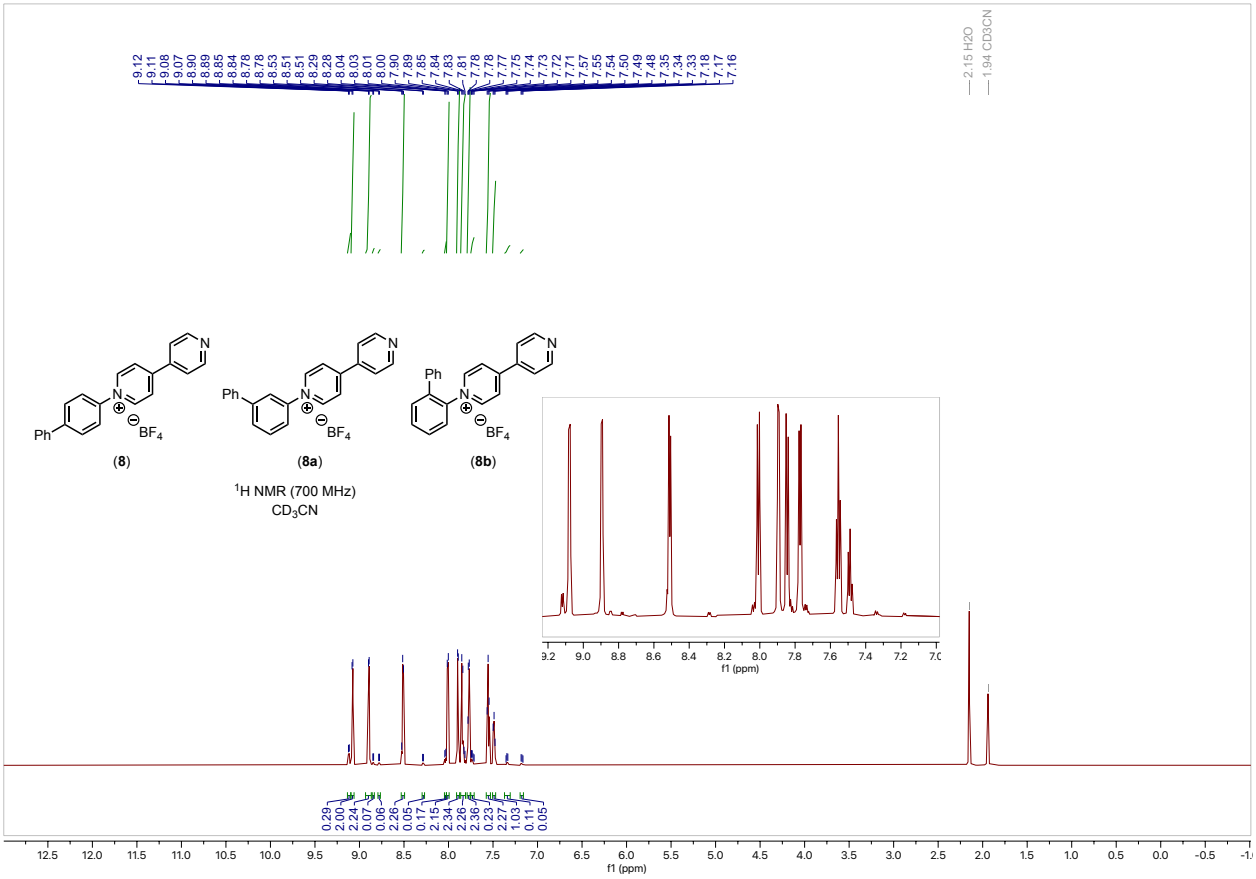
^{1}H NMR (700 MHz)

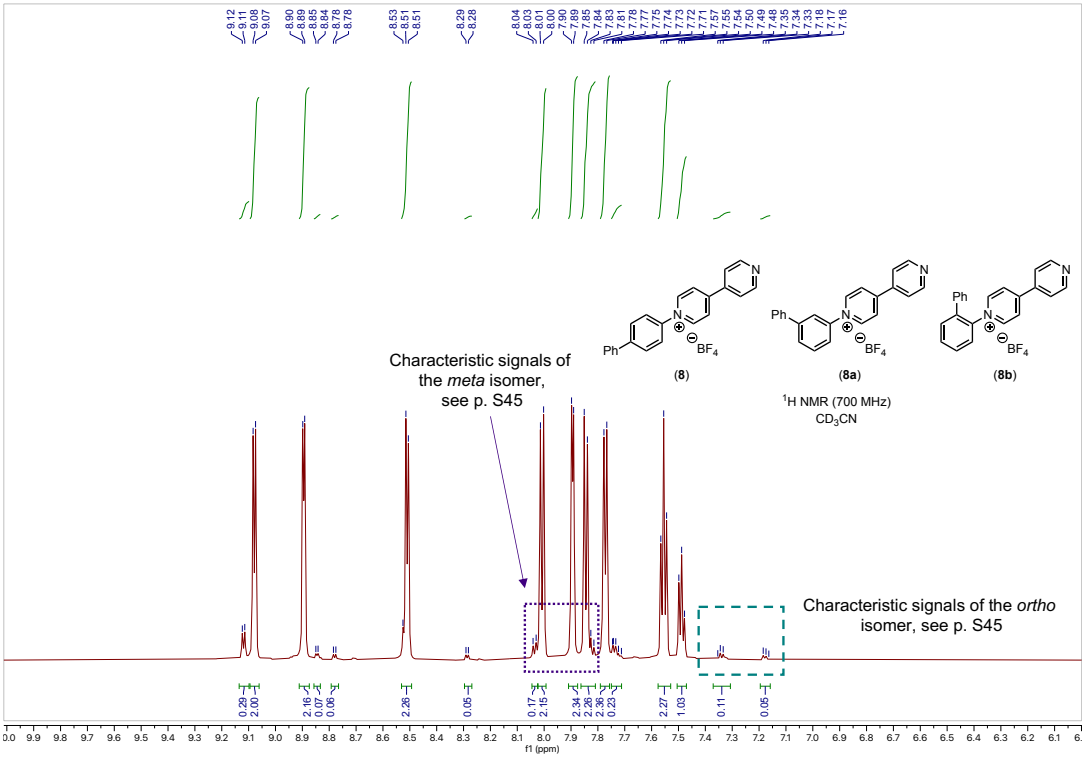
CD_3CN

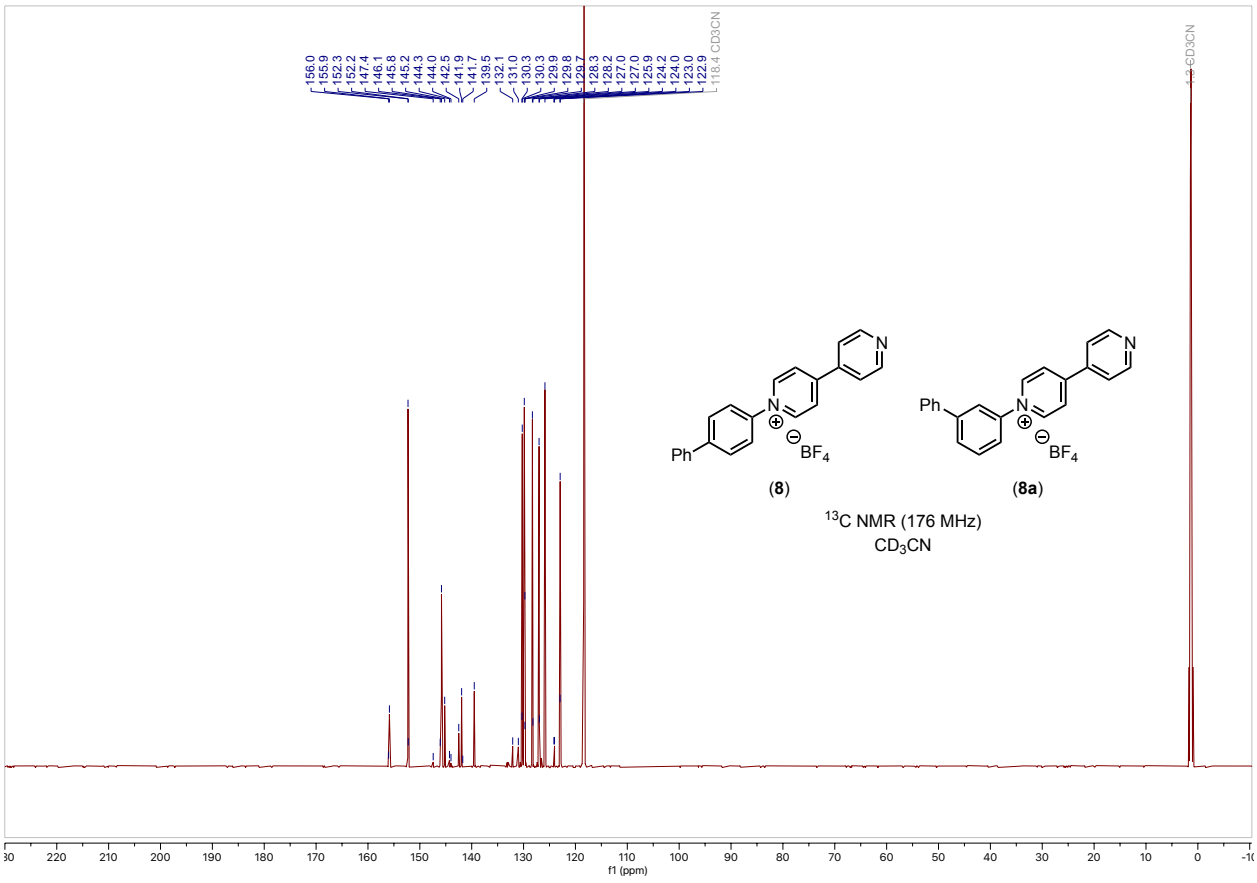

161.9
160.5
145.5
143.4
143.4
142.7
142.5
139.5
135.3
135.2
132.9
132.7
130.3
129.9
129.8
128.3
125.8
118.3 CD3CN
18.8
18.8
1.3 CD3CN
Me
N
F
Ph
BF4
(7)
13C NMR (176 MHz)
CD3CN
f1 (ppm)

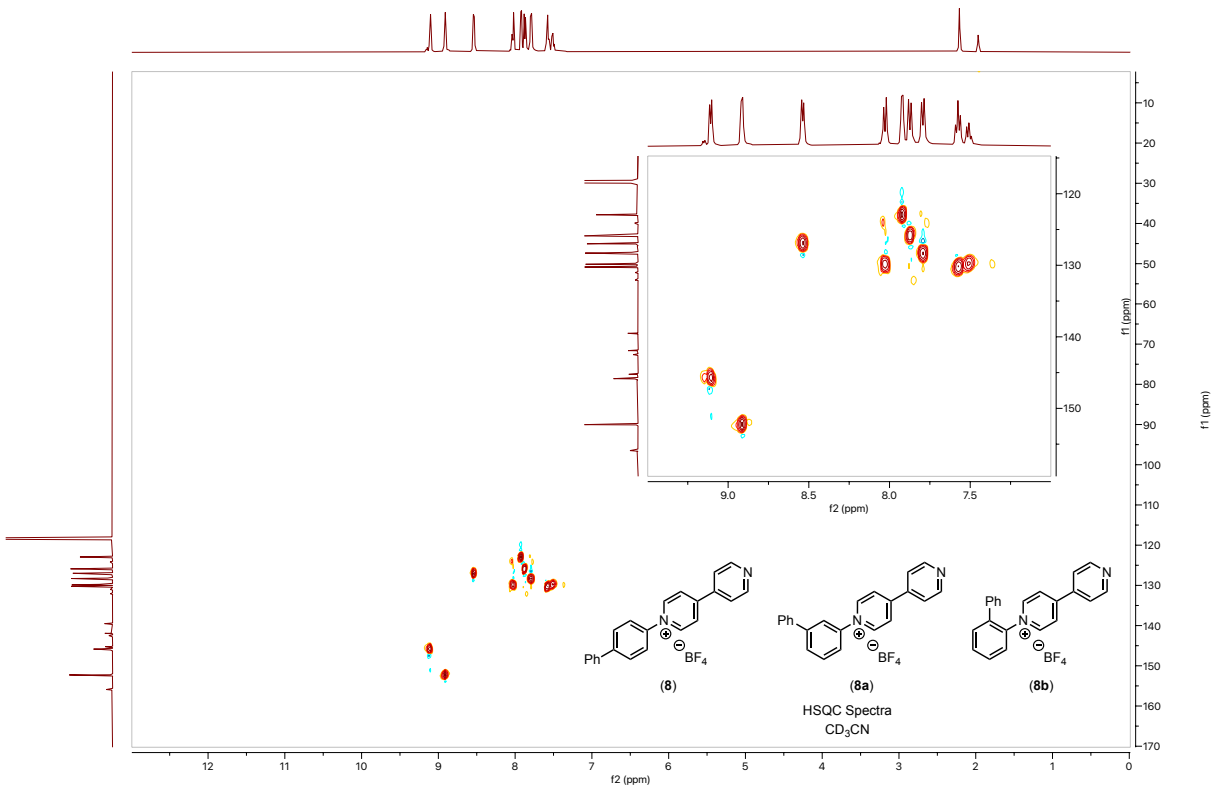

Me
F
Ph
BF4
(7)
HSQC Spectra
CD3CN
f2 (ppm)
f1 (ppm)

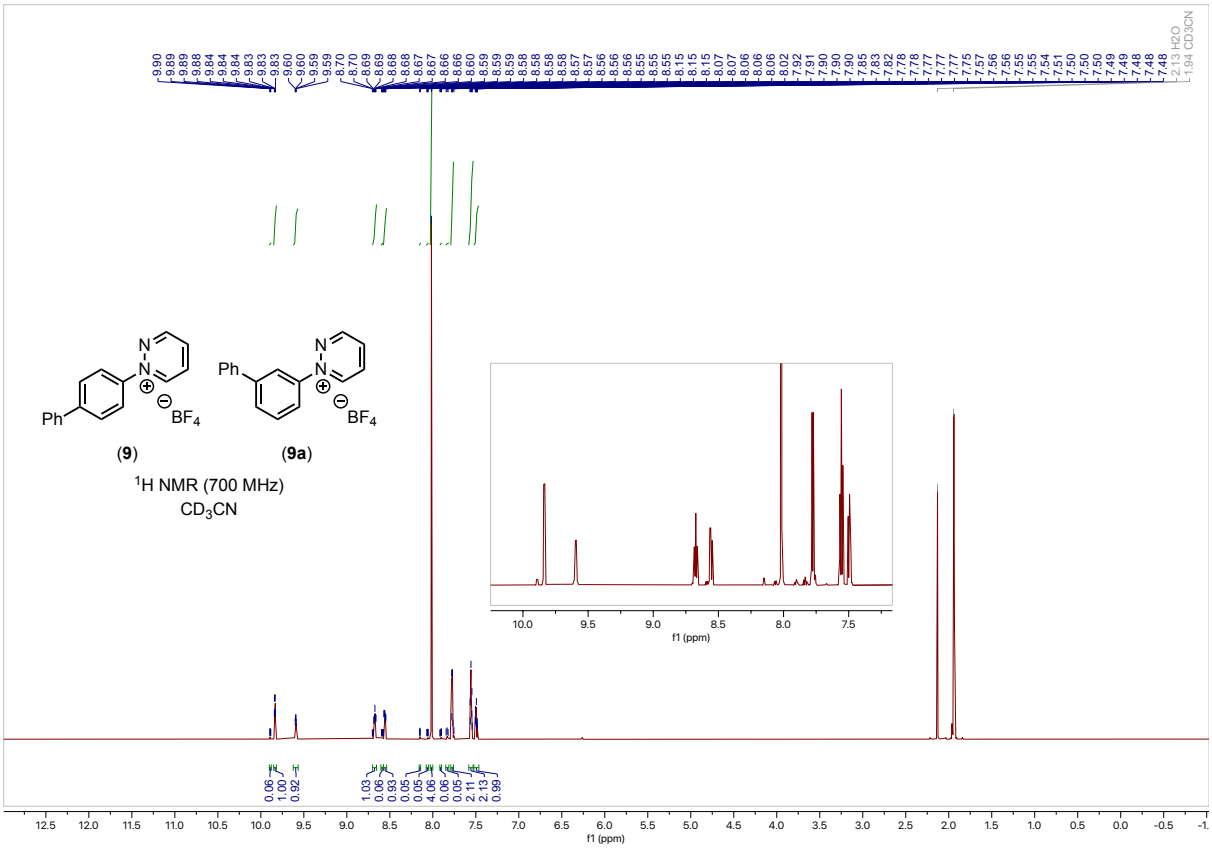

Me
N
F
Ph
BF4
(7)
19F NMR (470 MHz)
CD3CN
-118.74
-118.75
-118.76
-118.77
-151.70
-151.76
f1 (ppm)

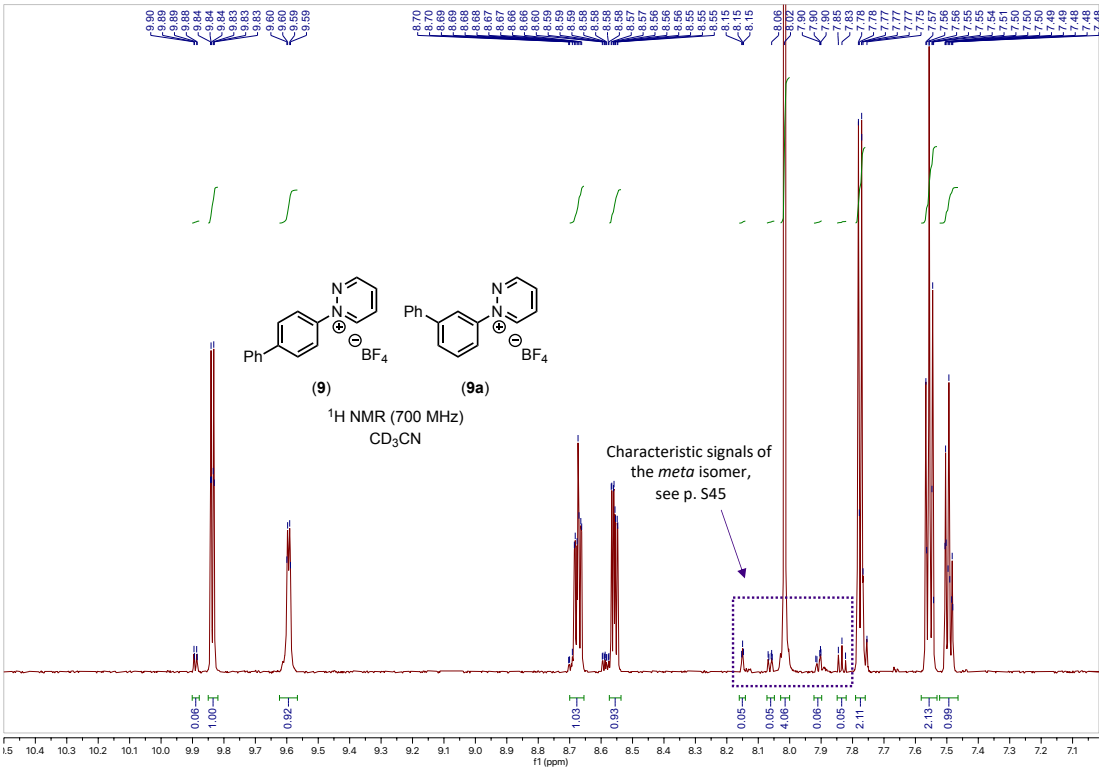

(8)
(8a)
(8b)
^{1}H NMR (700 MHz)
CD_3CN
f1 (ppm)

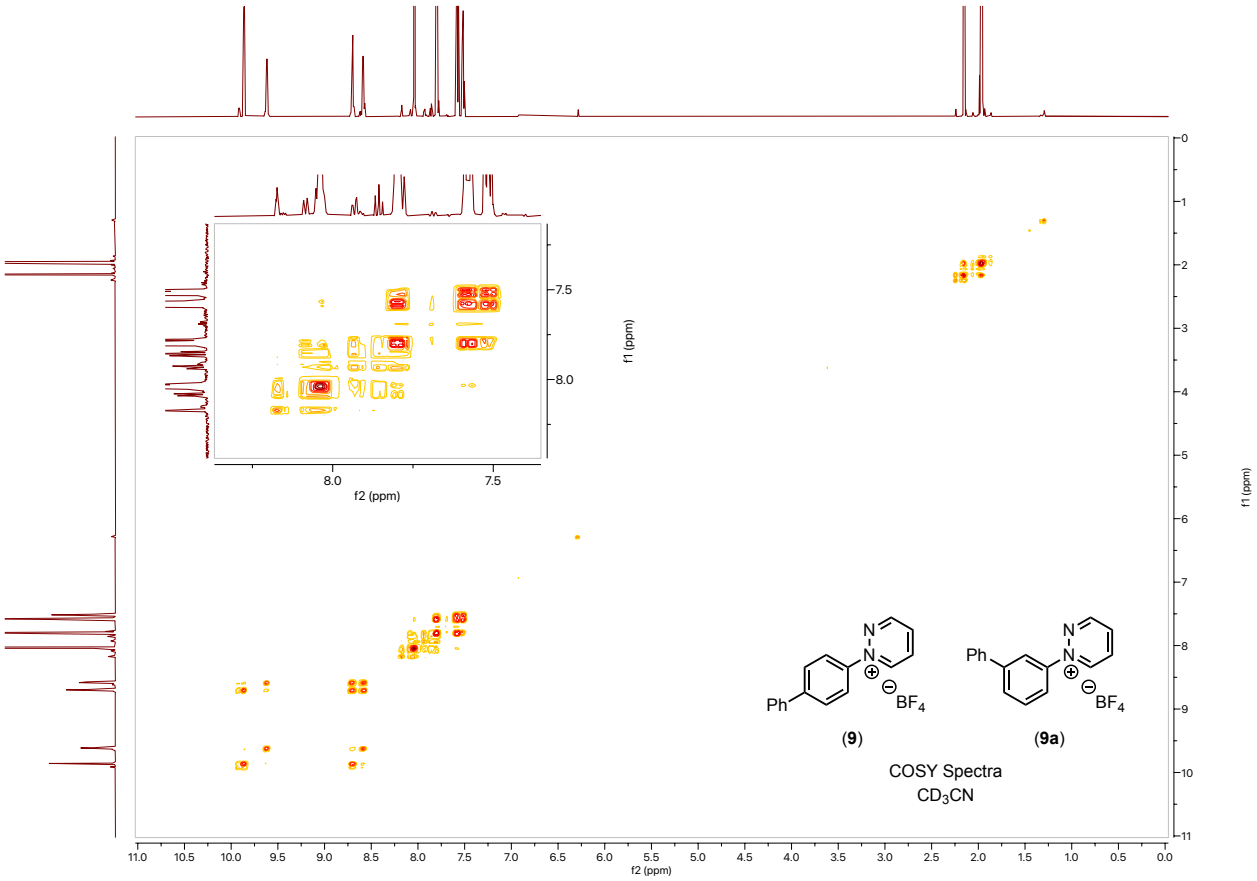

Characteristic signals of the *meta* isomer, see p. S45
Characteristic signals of the *ortho* isomer, see p. S45
(8)
(8a)
(8b)
^{1}H NMR (700 MHz)
CD_3CN
f1 (ppm)

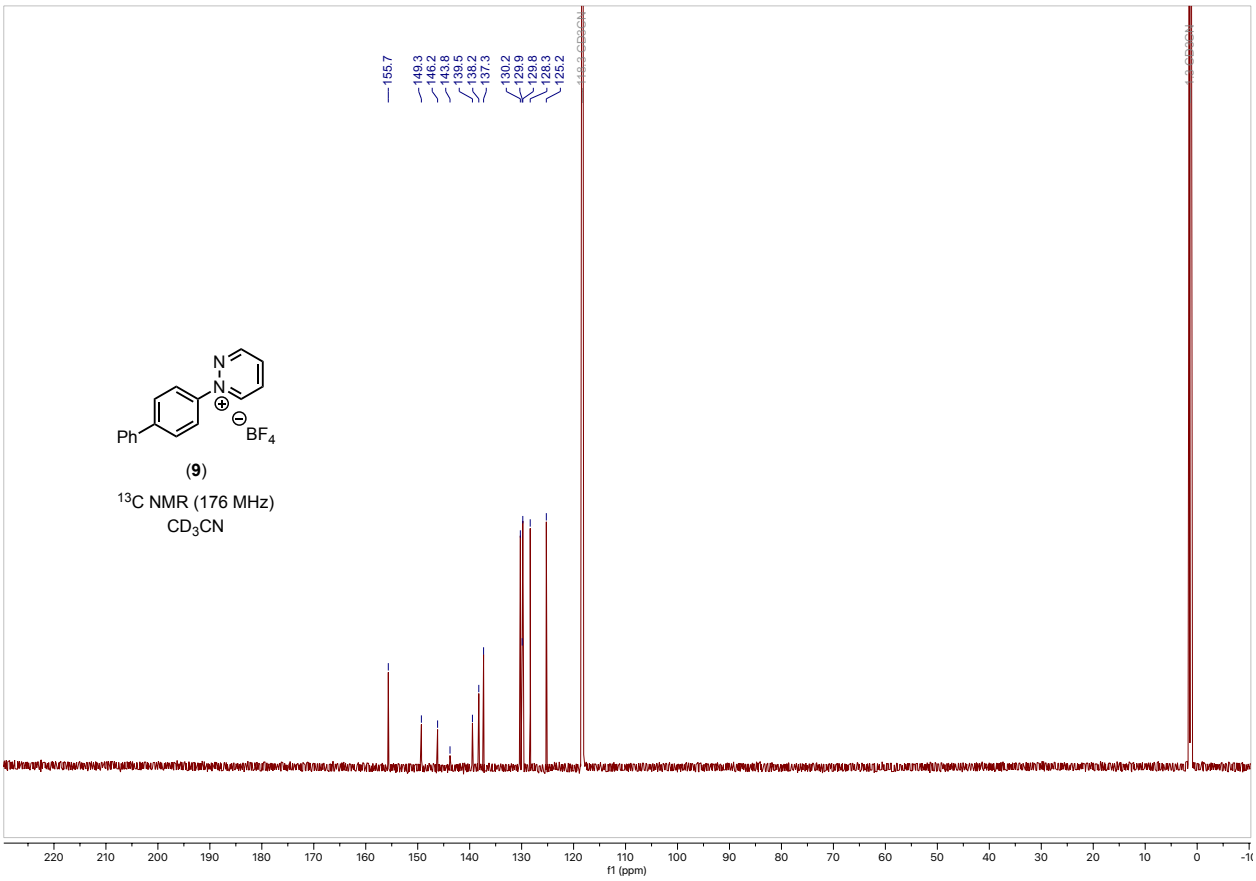

156.0
155.9
152.3
152.2
147.4
146.1
145.8
145.2
144.3
144.0
142.5
141.9
141.7
139.5
132.1
131.0
130.3
130.3
129.9
129.8
129.7
128.3
128.2
127.0
127.0
125.9
124.2
124.0
123.9
118.4 CD3CN
1.3 CD3CN
Ph
BF4
(8)
Ph
BF4
(8a)
13C NMR (176 MHz)
CD3CN
f1 (ppm)

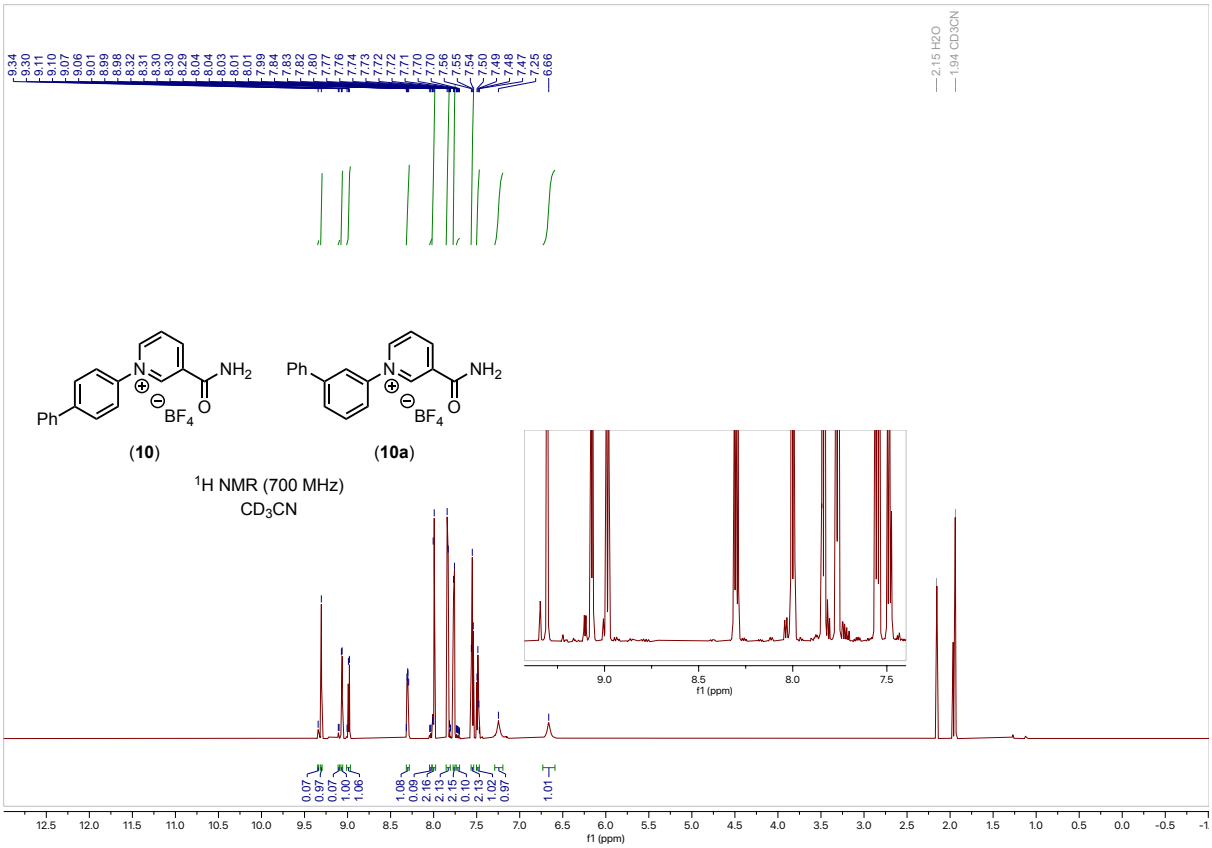

f2 (ppm)
f1 (ppm)
Ph
BF4
(8)
(8a)
(8b)
HSQC Spectra
CD3CN

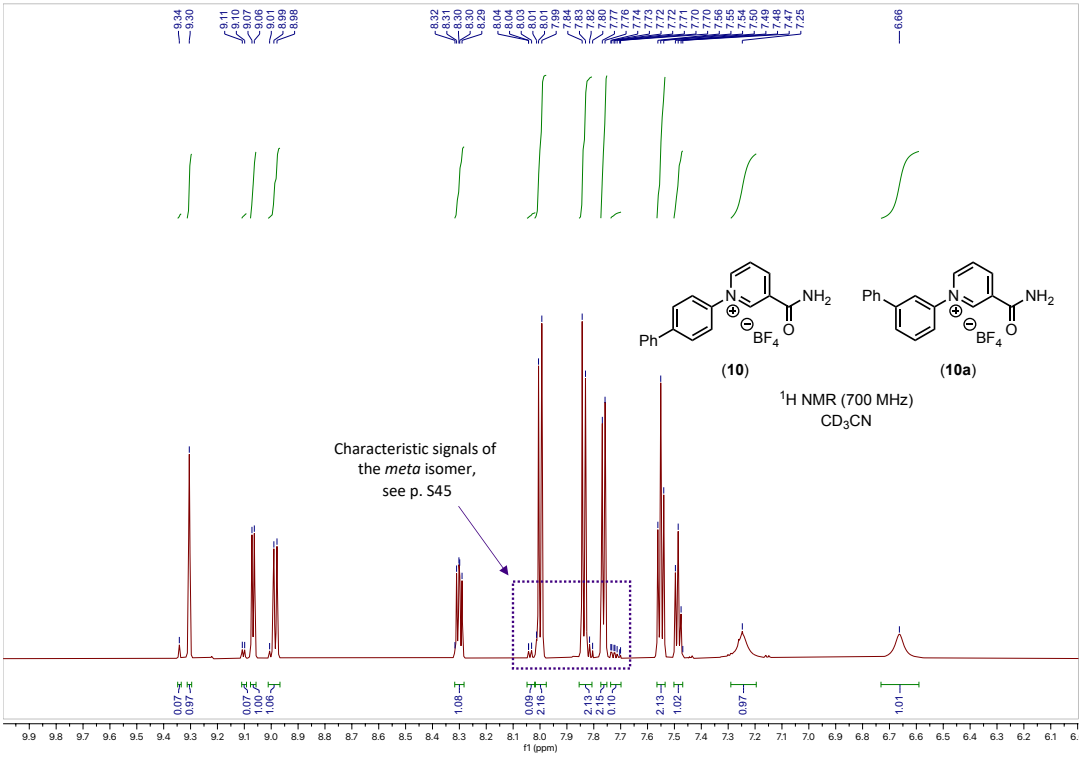

(9)
(9a)
^{1}H NMR (700 MHz)
CD_3CN
f1 (ppm)

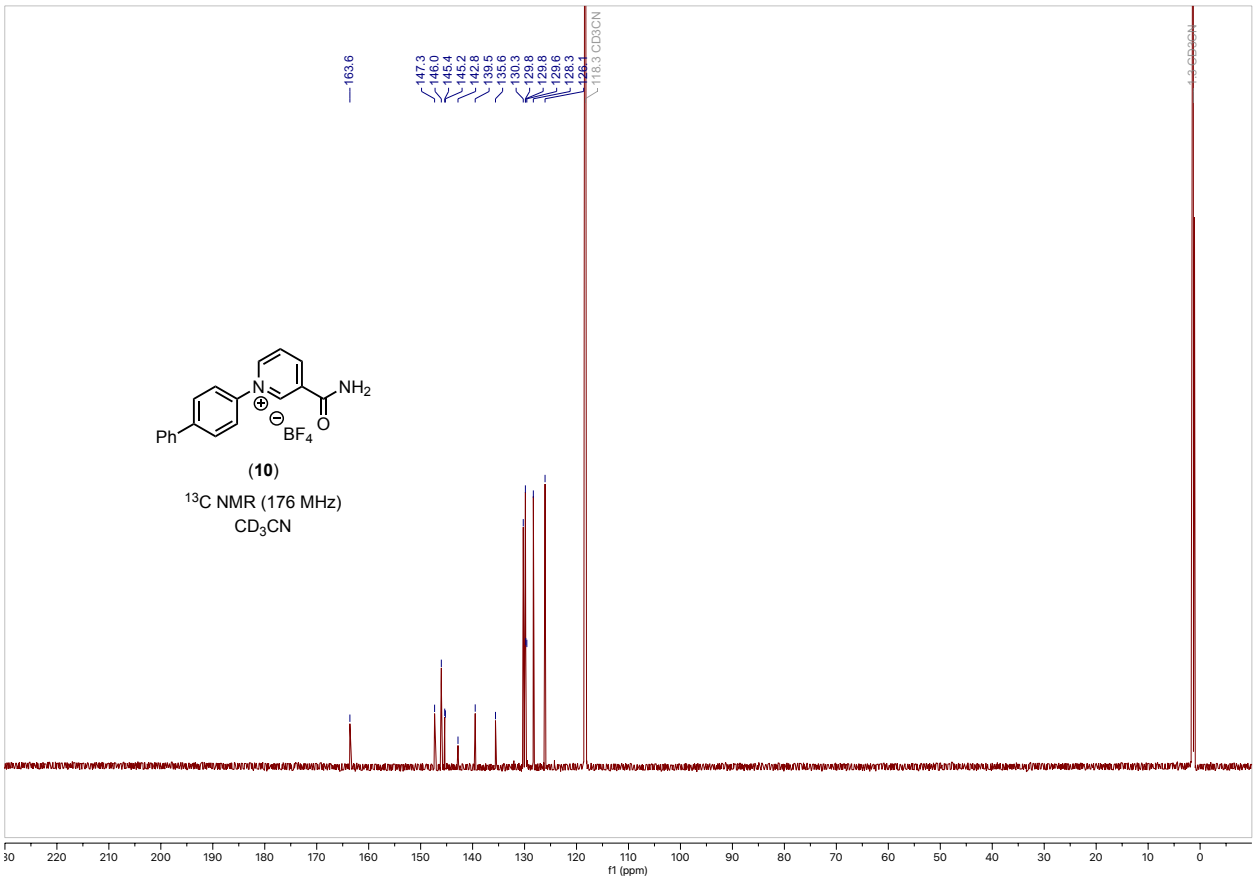

(9)
(9a)
^{1}H NMR (700 MHz)
CD_3CN
Characteristic signals of the *meta* isomer, see p. S45
f1 (ppm)

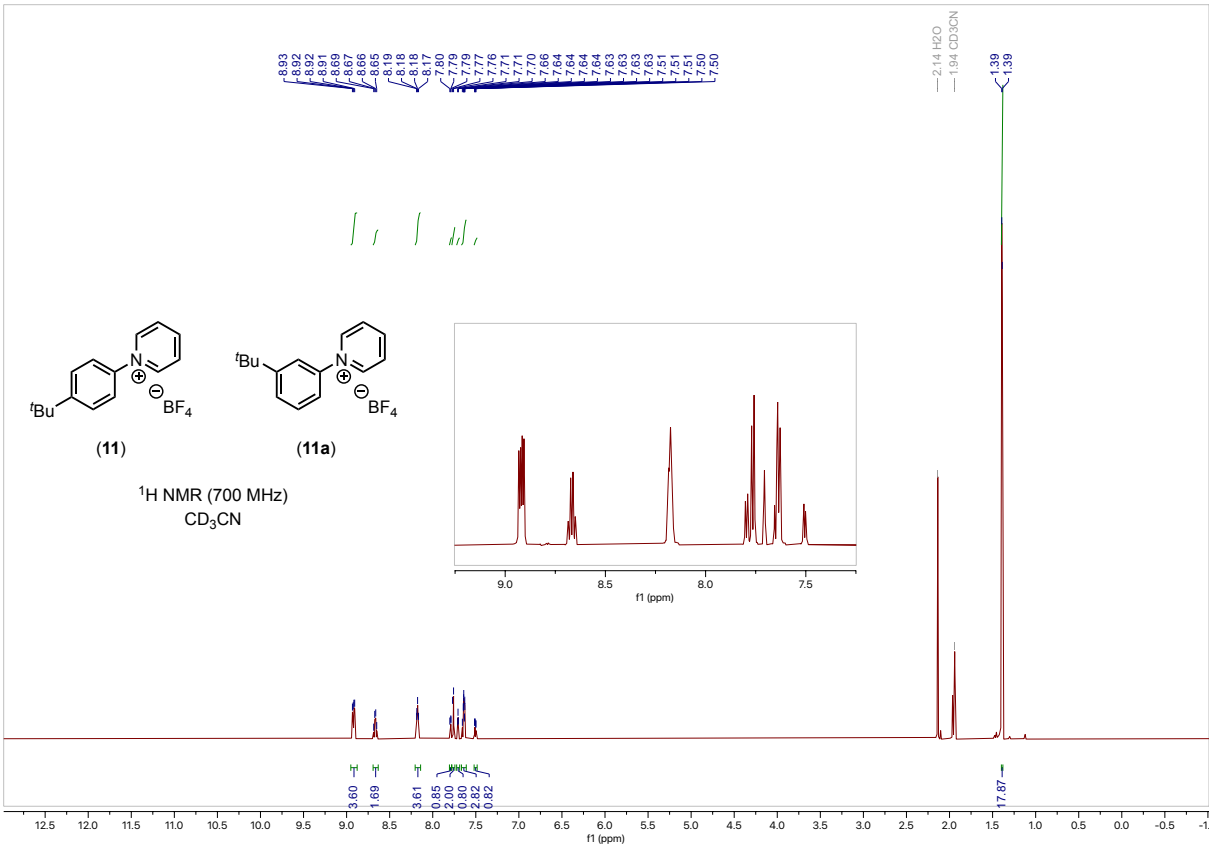

f2 (ppm)
f1 (ppm)
Ph
BF4
(9)
(9a)
COSY Spectra
CD3CN

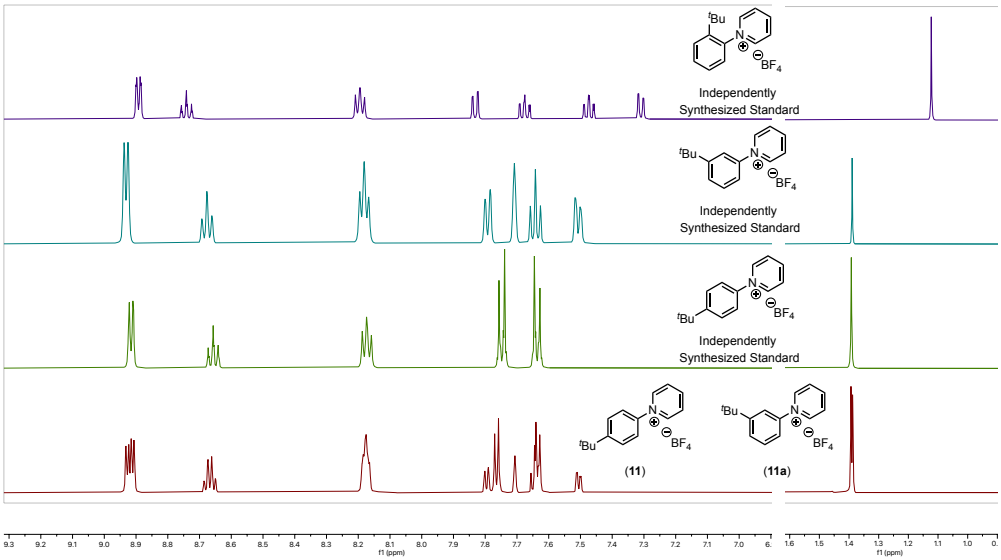

155.7
149.3
146.2
143.8
139.5
138.2
137.3
130.2
129.9
129.8
128.3
125.2
118.3 CD3CN
1.0 CD3CN
N
N
Ph
BF4
(9)
13C NMR (176 MHz)
CD3CN
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


(10)
(10a)
^{1}H NMR (700 MHz)
CD_3CN
f1 (ppm)

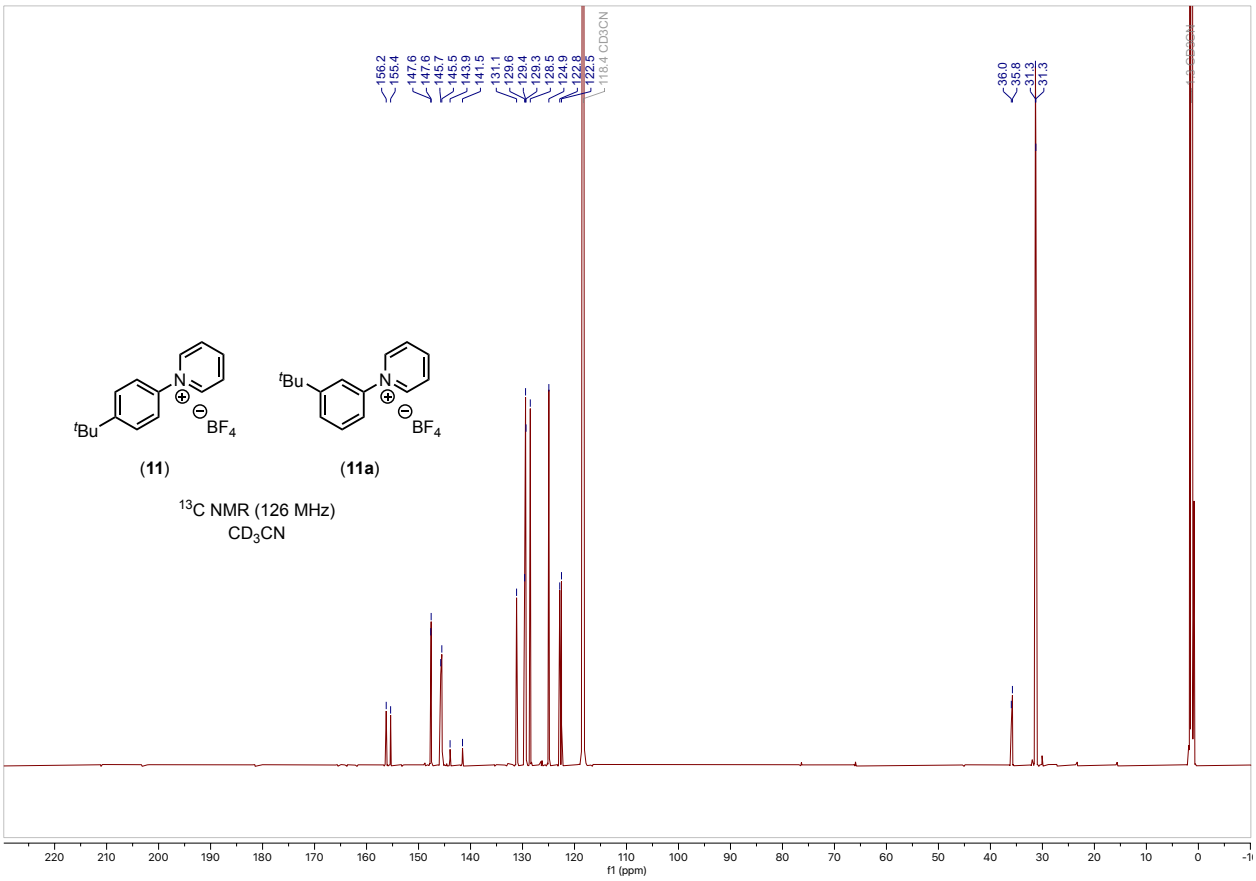

(10)
(10a)
^{1}H NMR (700 MHz)
CD_3CN
Characteristic signals of the *meta* isomer, see p. S45
f1 (ppm)

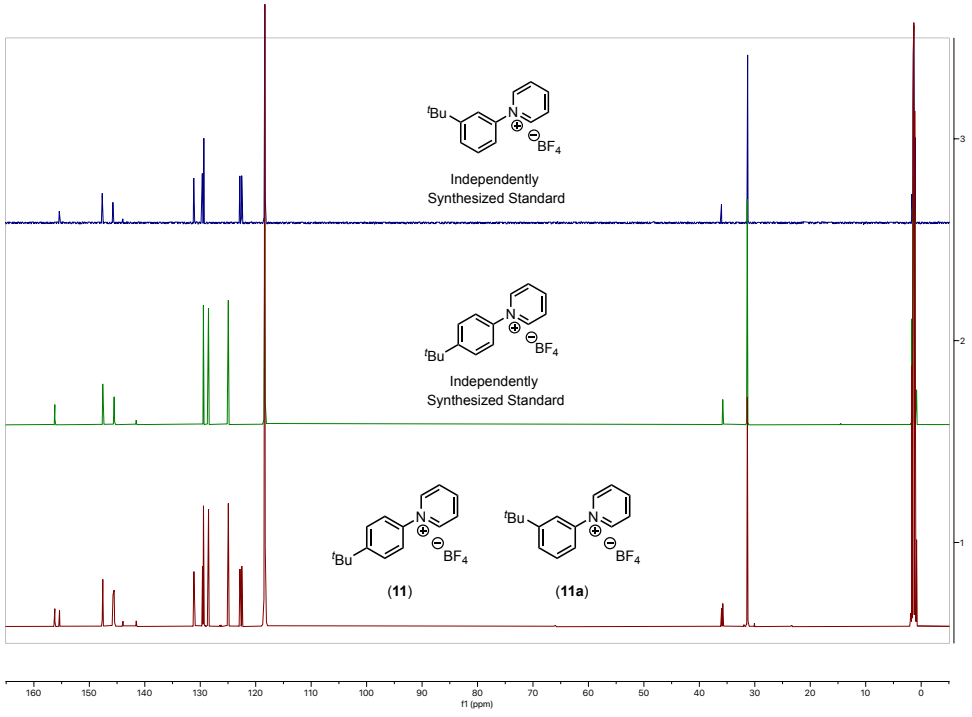

163.6
147.3
146.0
145.4
145.2
142.8
139.5
135.6
130.3
129.8
129.8
129.6
128.3
126.1
118.3 CD3CN
1.9 CD3CN
NH2
O
N
Ph
BF4
(10)
13C NMR (176 MHz)
CD3CN
f1 (ppm)

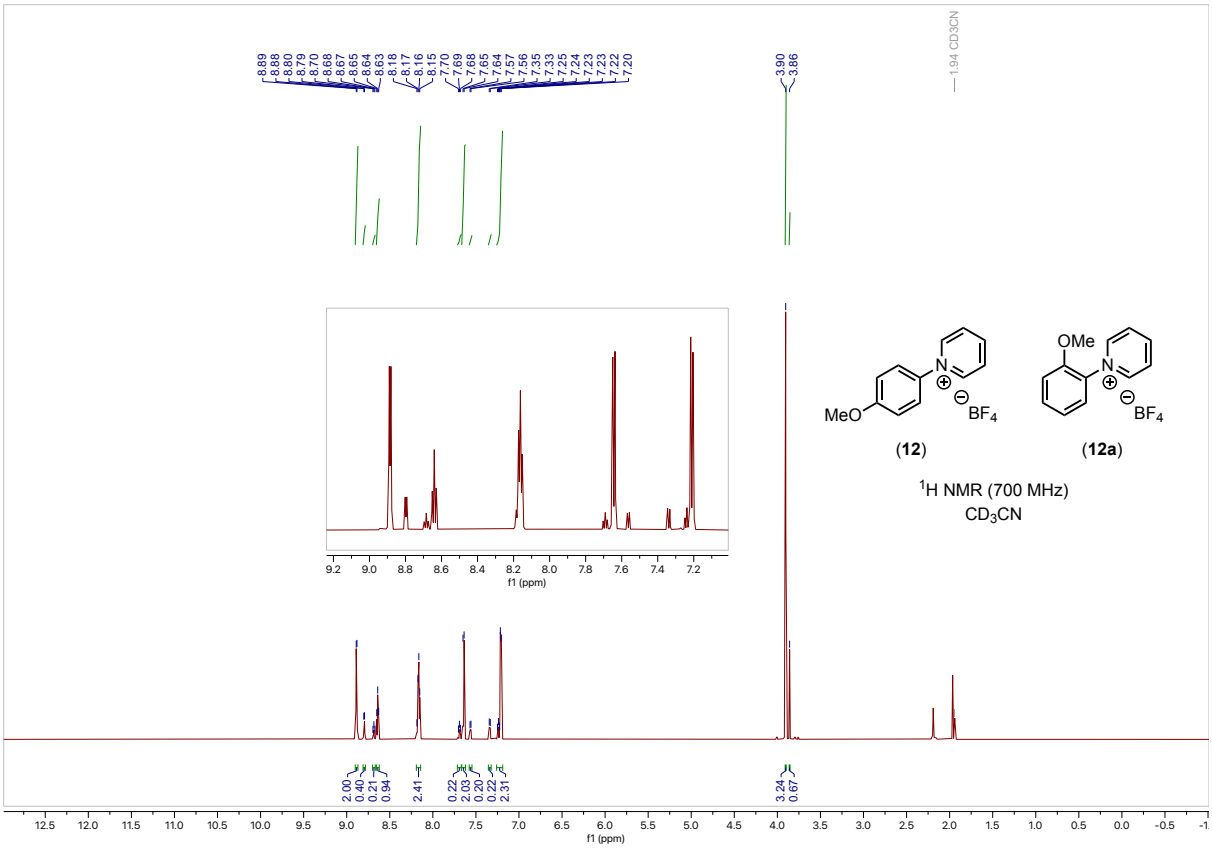

(11)
(11a)
^{1}H NMR (700 MHz)
CD_3CN
f1 (ppm)


Independently Synthesized Standard
Independently Synthesized Standard
Independently Synthesized Standard
(11)
(11a)
f1 (ppm)

SUPPORTING INFORMATION







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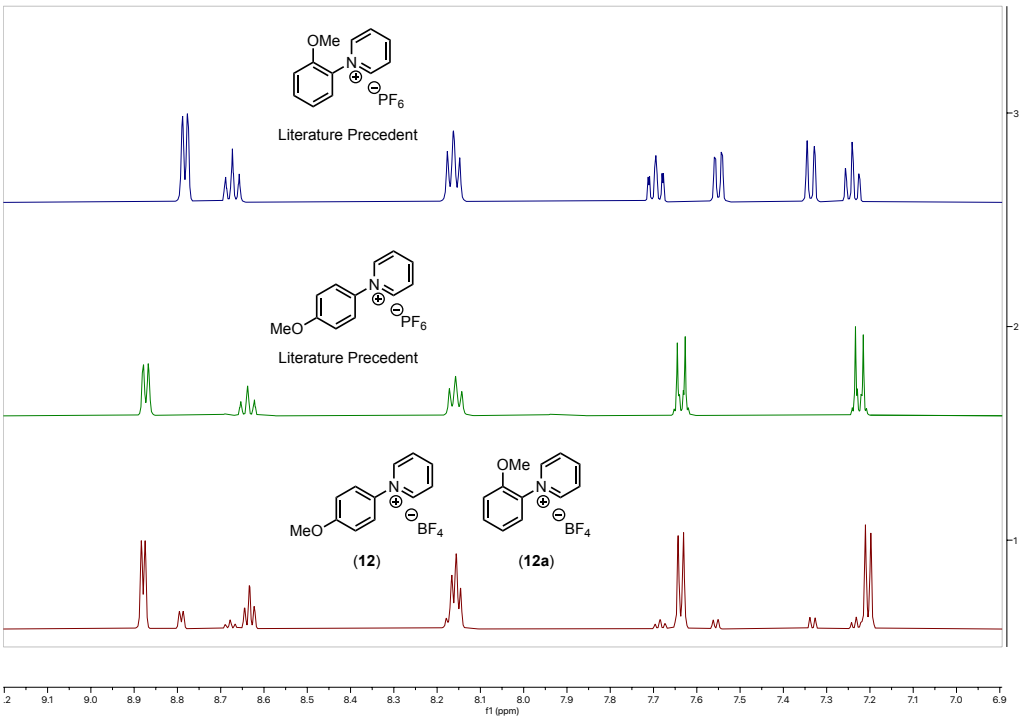

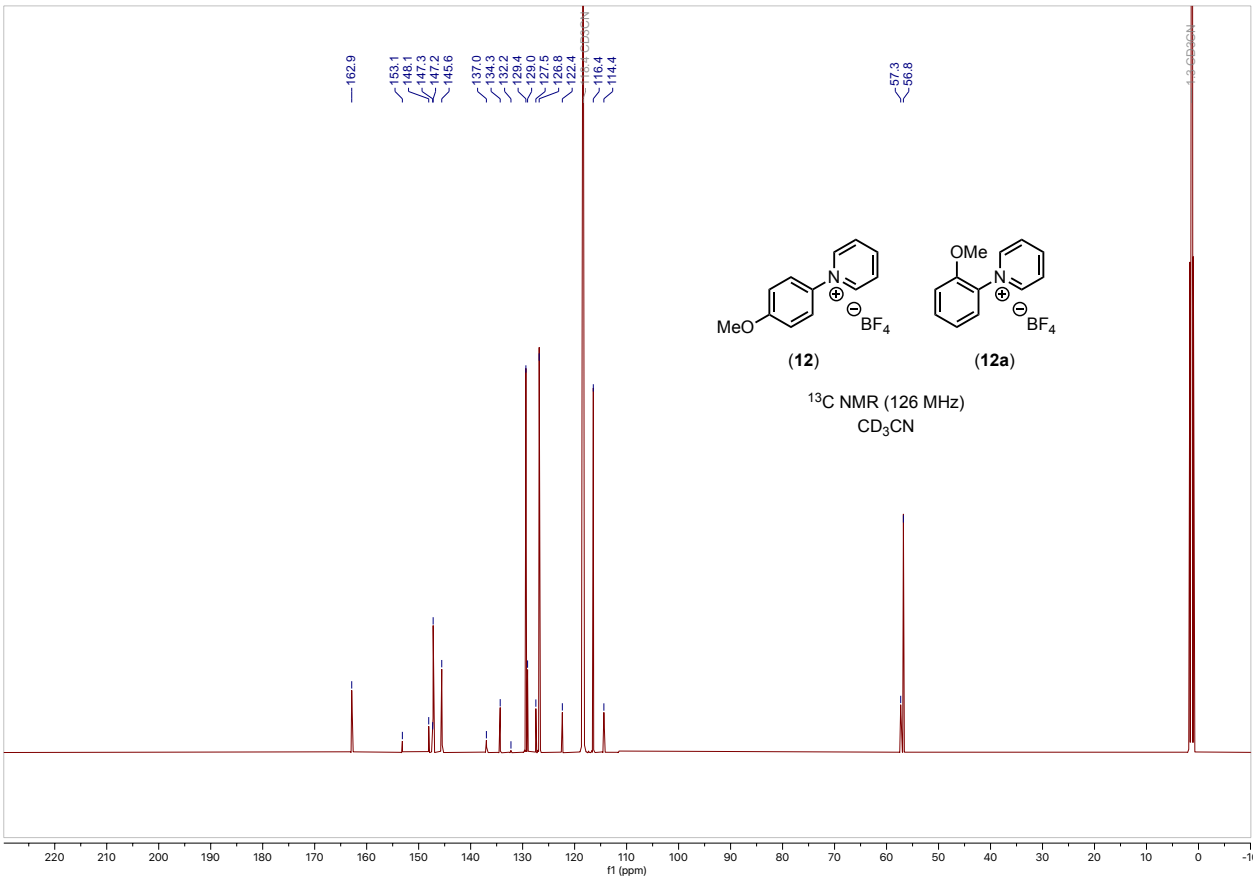

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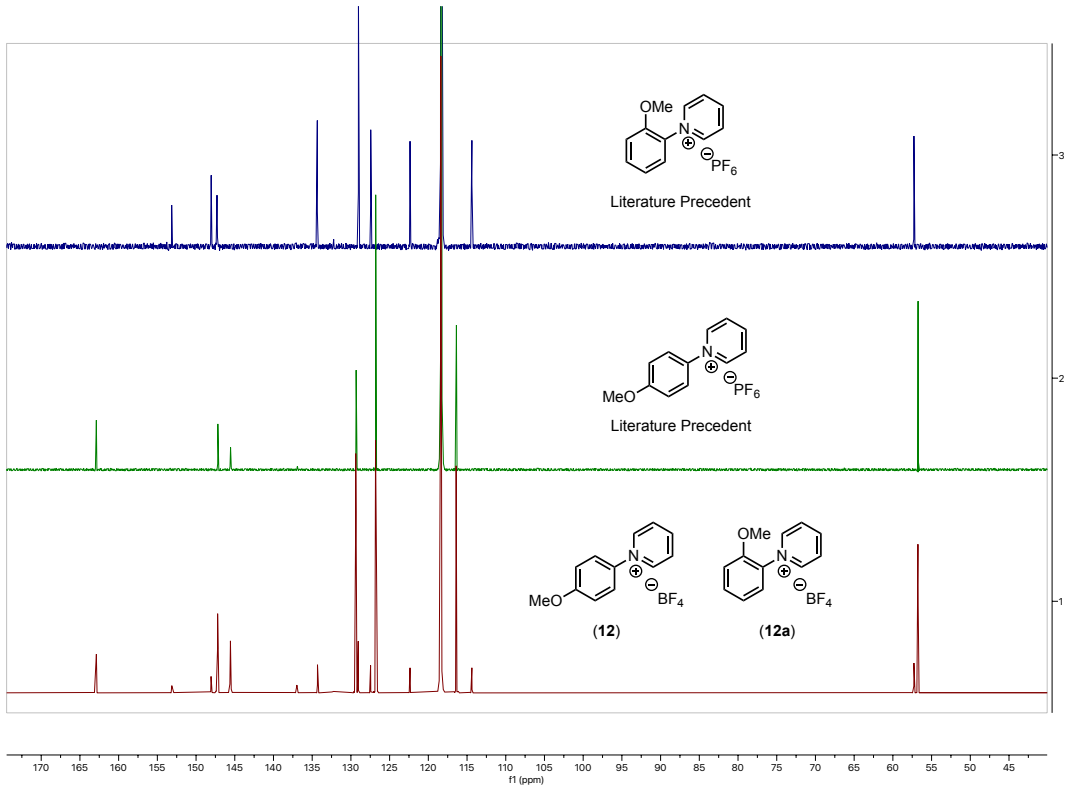
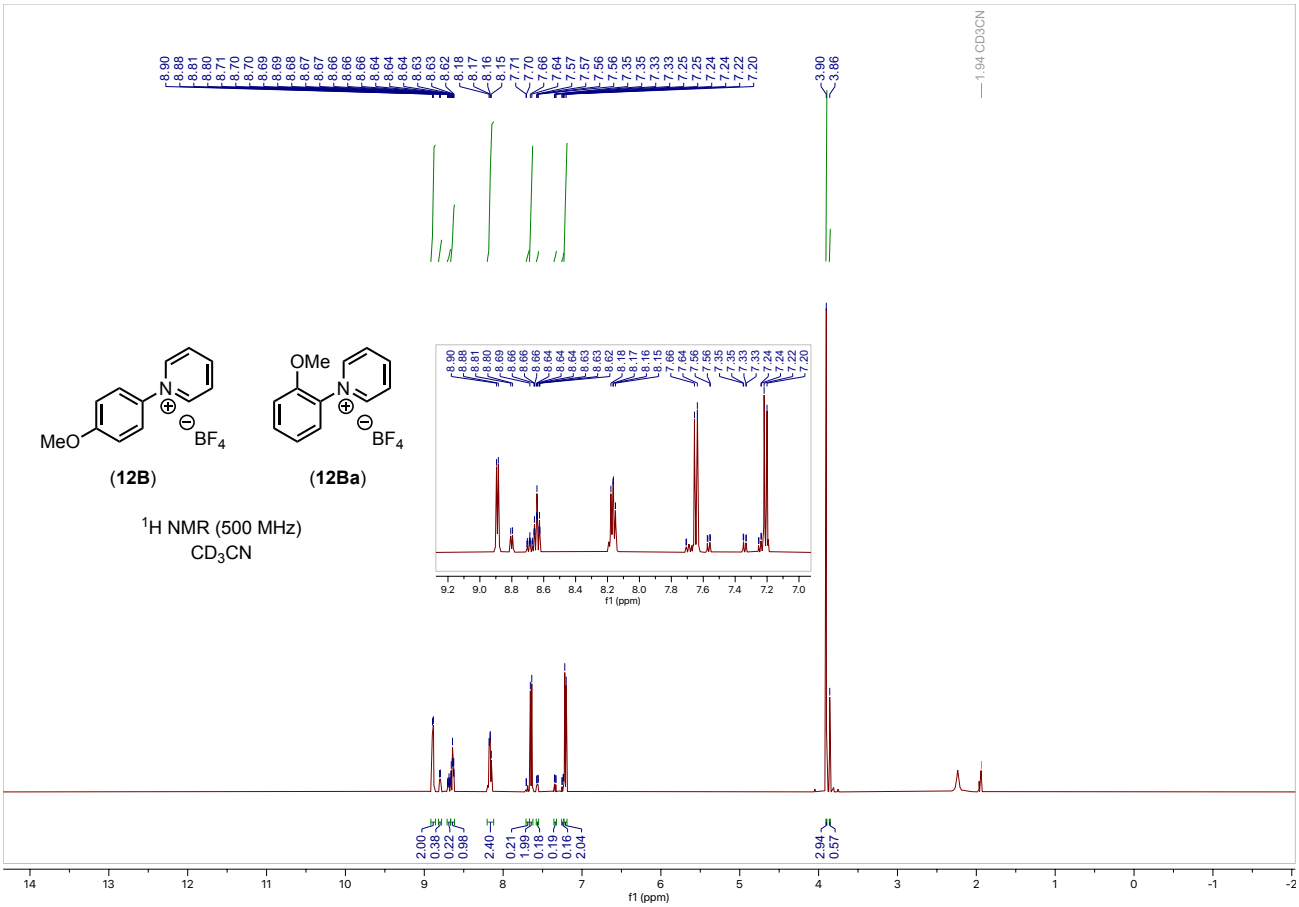
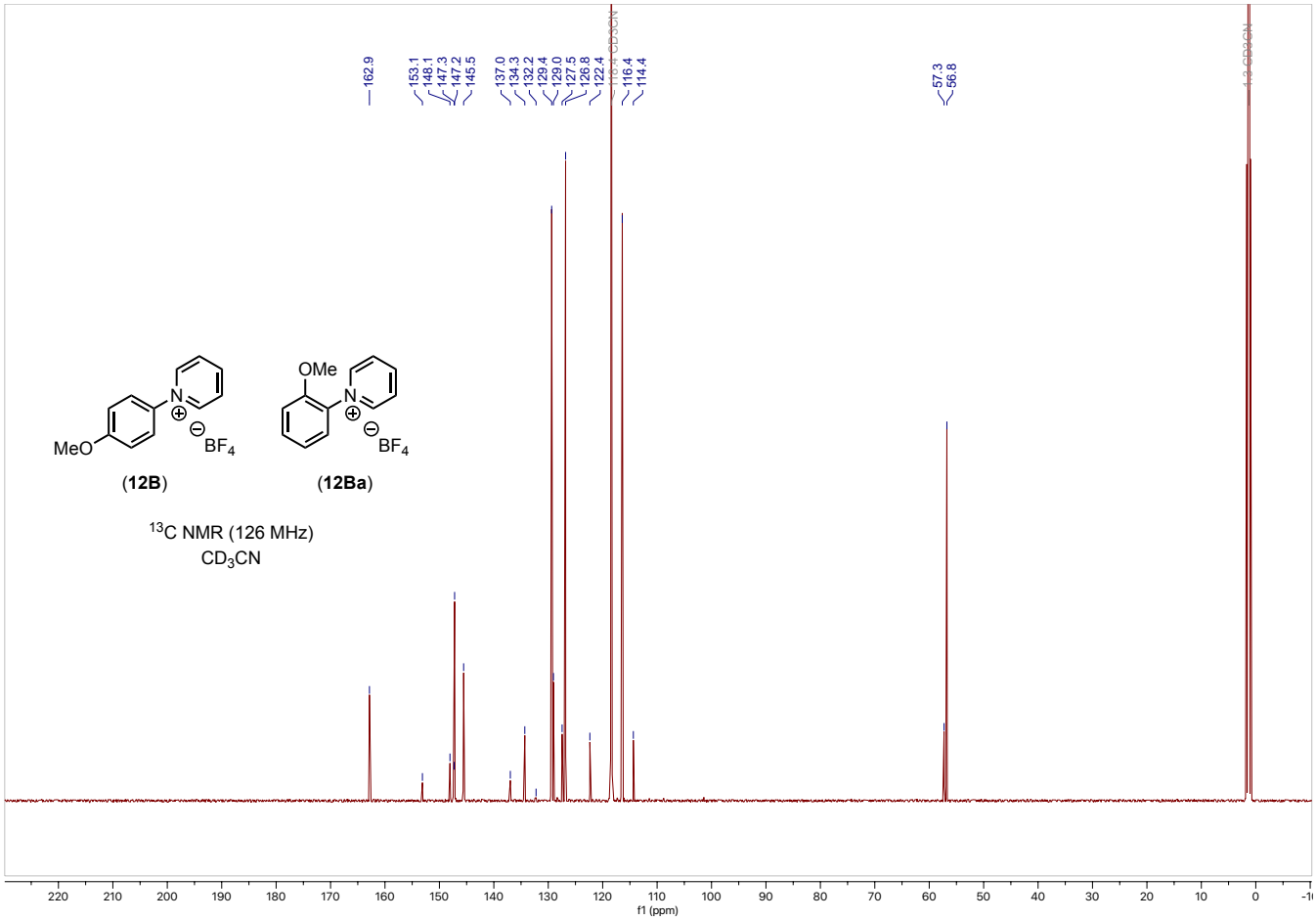
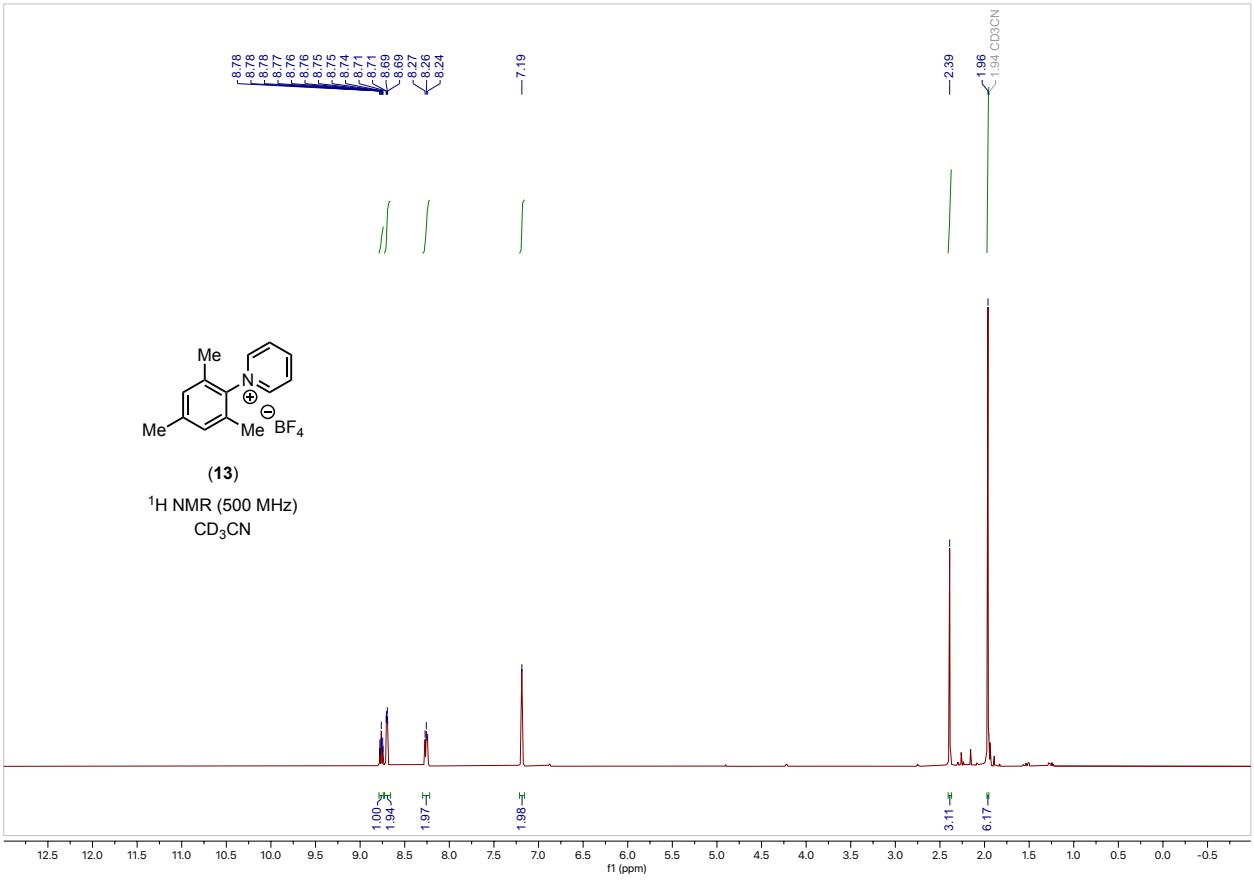
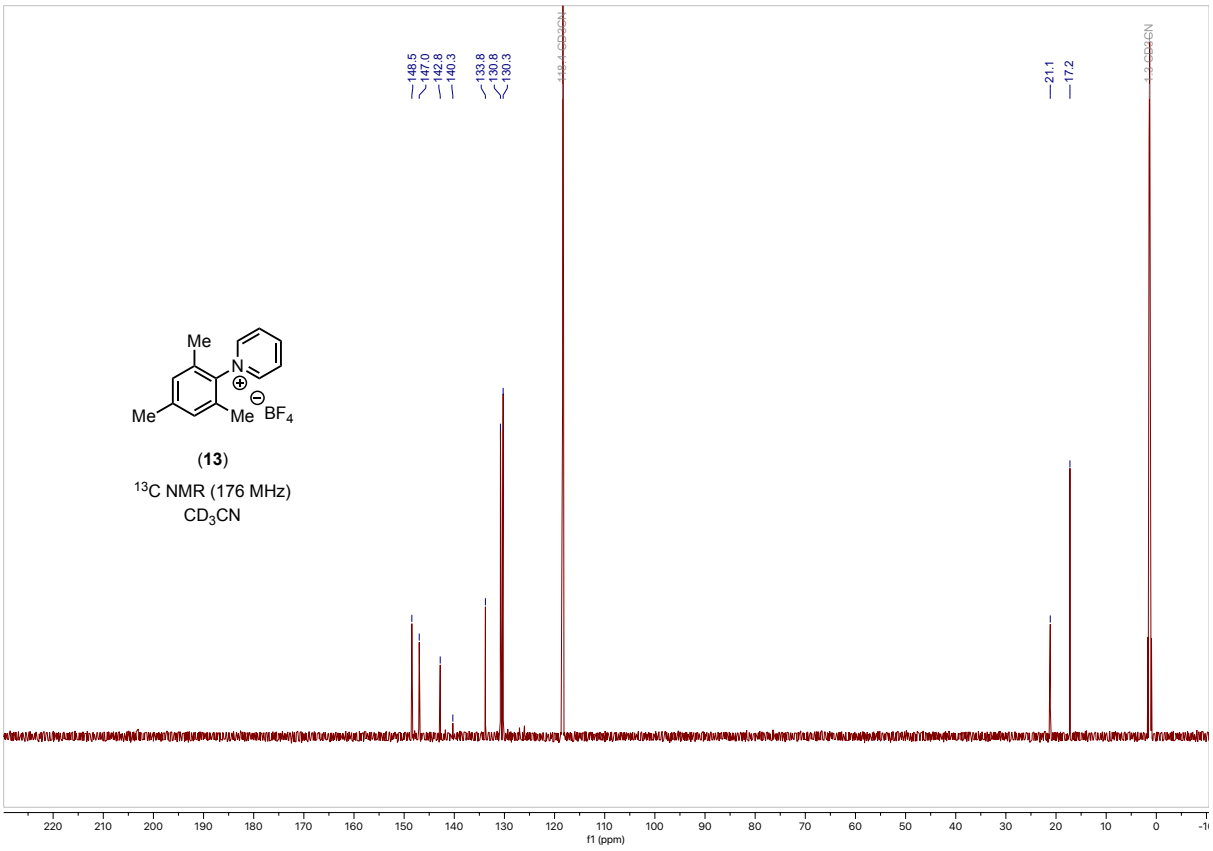


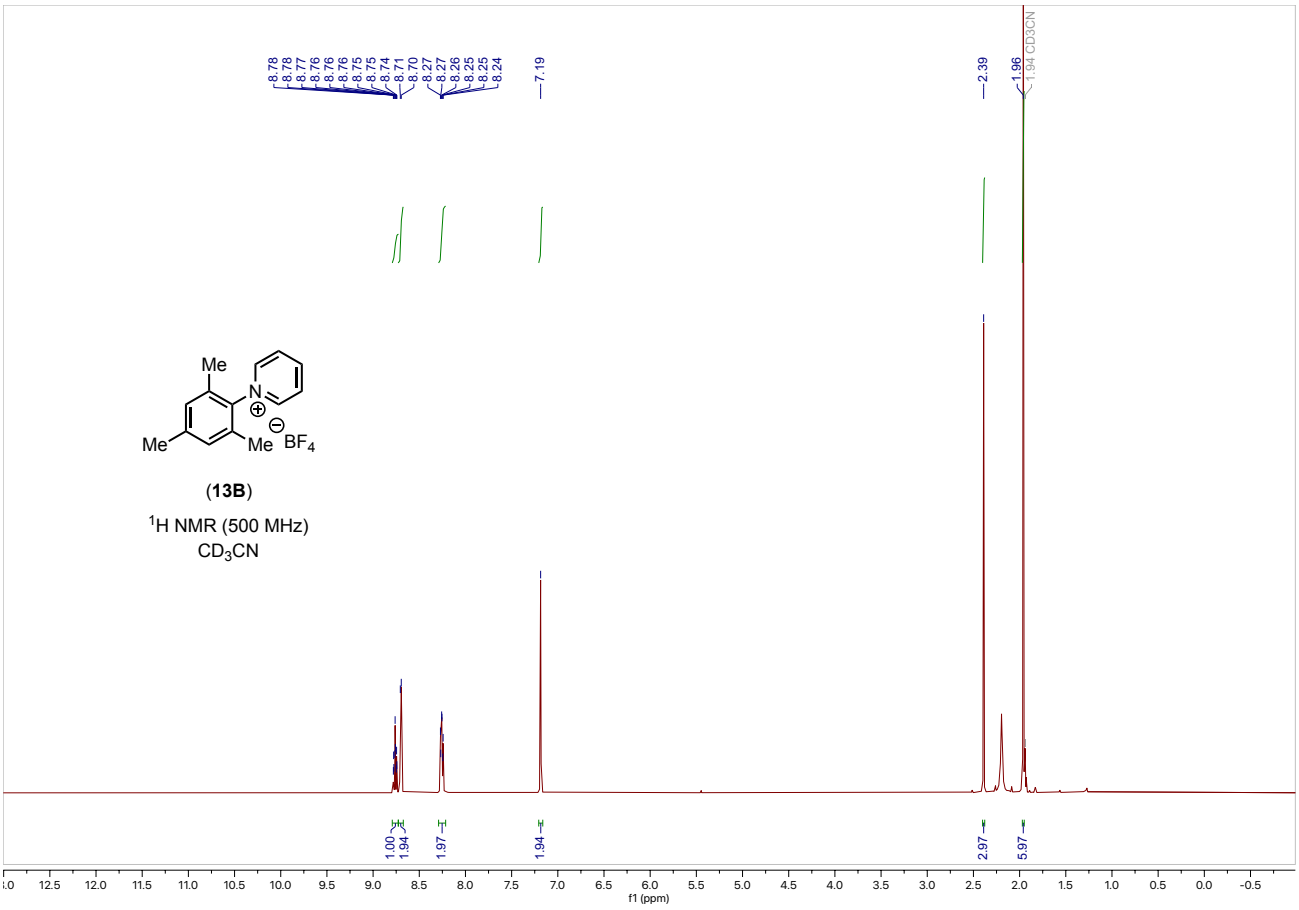

MeO
BF4
(12B)
OMe
BF4
(12Ba)
1H NMR (500 MHz)
CD3CN
f1 (ppm)

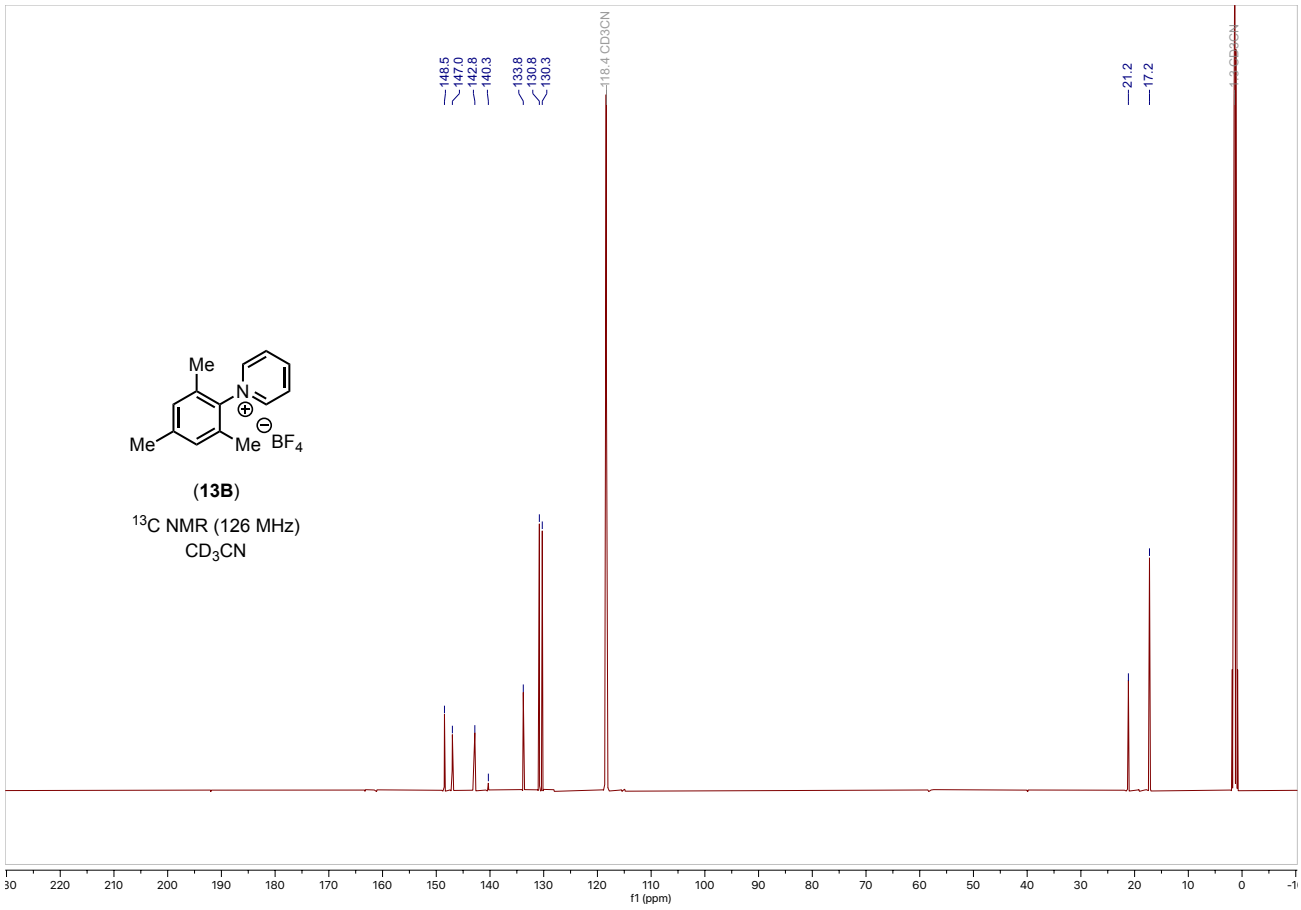
SUPPORTING INFORMATION

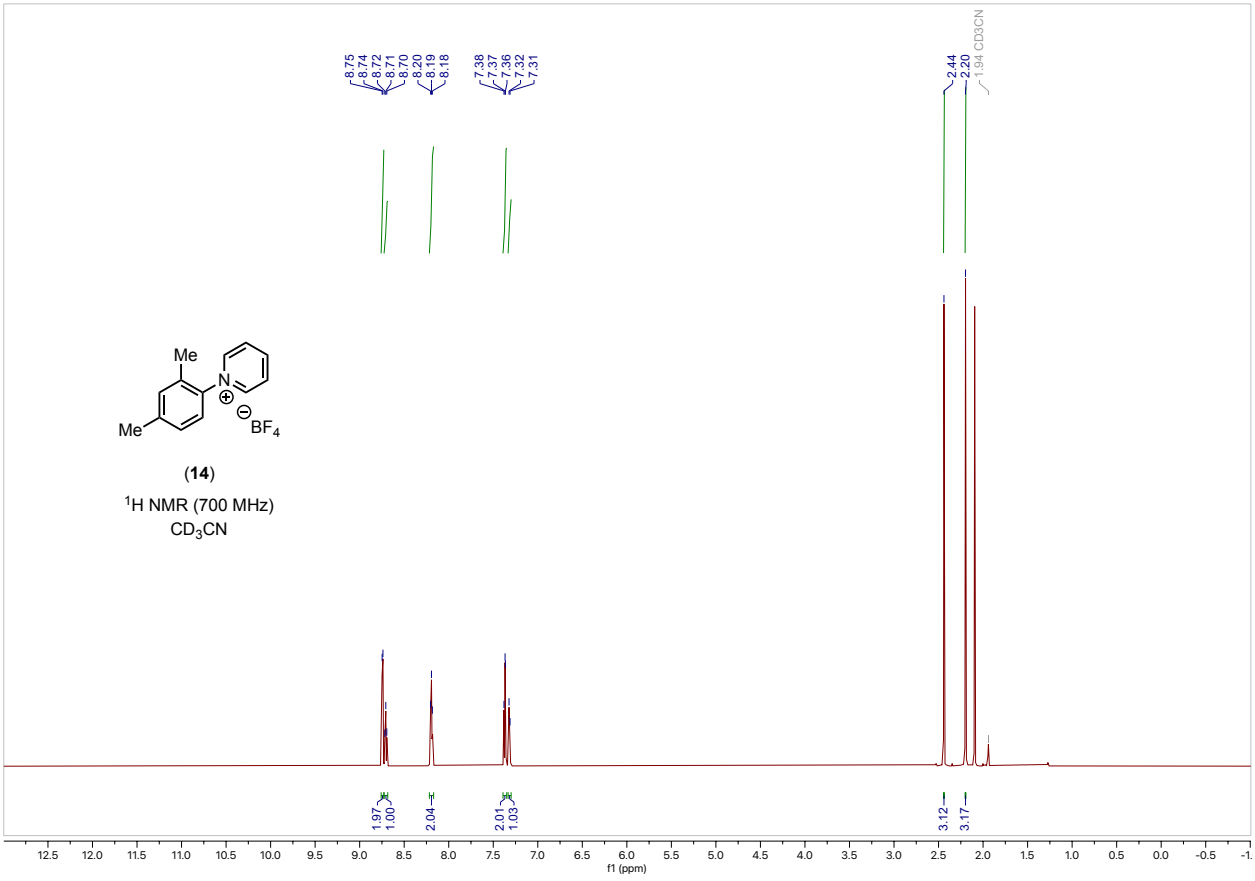


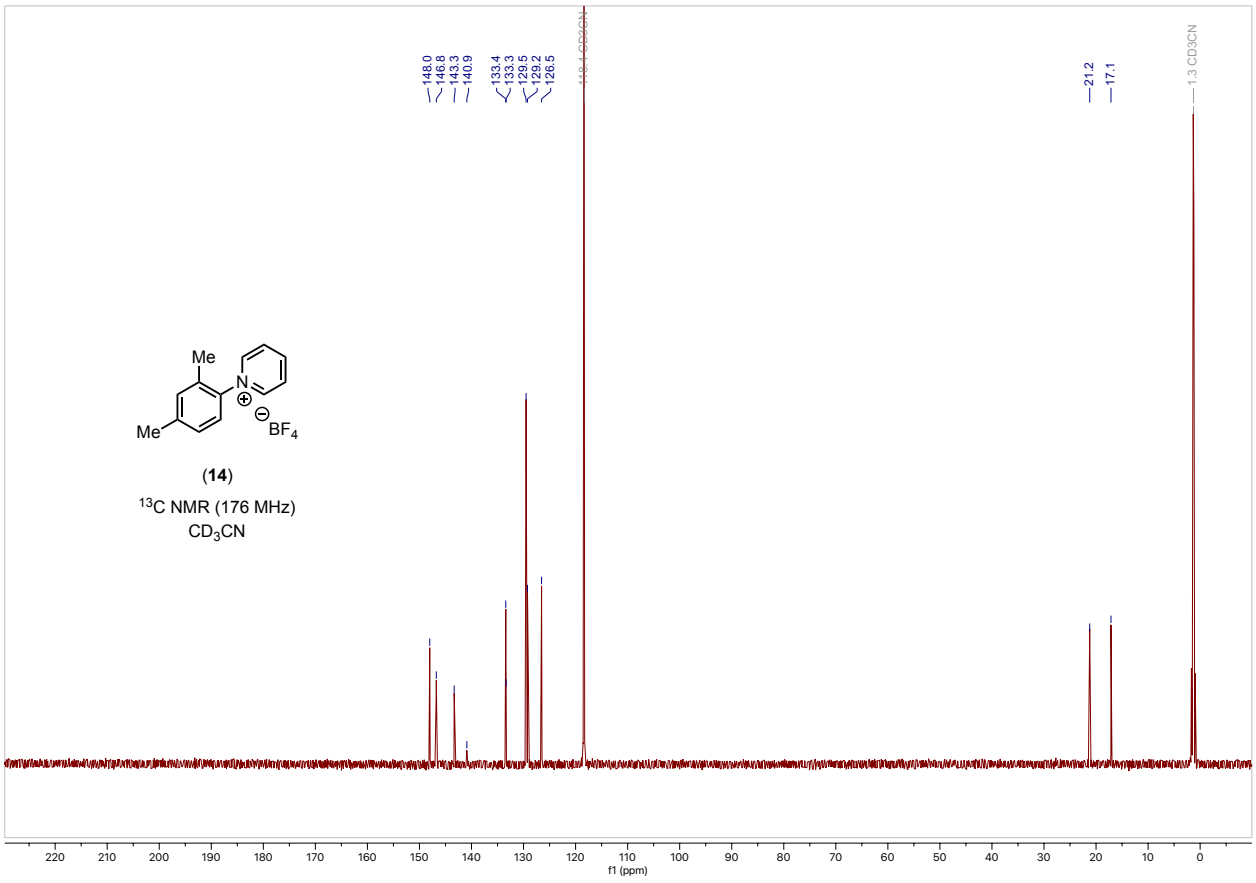

8.78
8.78
8.78
8.77
8.76
8.76
8.75
8.75
8.74
8.71
8.71
8.69
8.69
8.27
8.26
8.24
7.19
2.39
1.96
1.94 CD3CN
Me
Me
Me
BF4
(13)
1H NMR (500 MHz)
CD3CN
1.00
1.94
1.97
1.98
3.11
6.17
f1 (ppm)


148.5
147.0
142.8
140.3
133.8
130.8
130.3
118.4 CD3CN
21.1
17.2
1.3 CD3CN
Me
N
Me
Me
BF4
(13)
13C NMR (176 MHz)
CD3CN
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.78
8.78
8.77
8.76
8.76
8.76
8.75
8.75
8.74
8.71
8.70
8.27
8.27
8.26
8.25
8.25
8.24
7.19
2.39
1.96
1.94 CD3CN
Me
N
Me
Me
BF4
(13B)
1H NMR (500 MHz)
CD3CN
1.00
1.94
1.97
1.94
2.97
5.97
f1 (ppm)

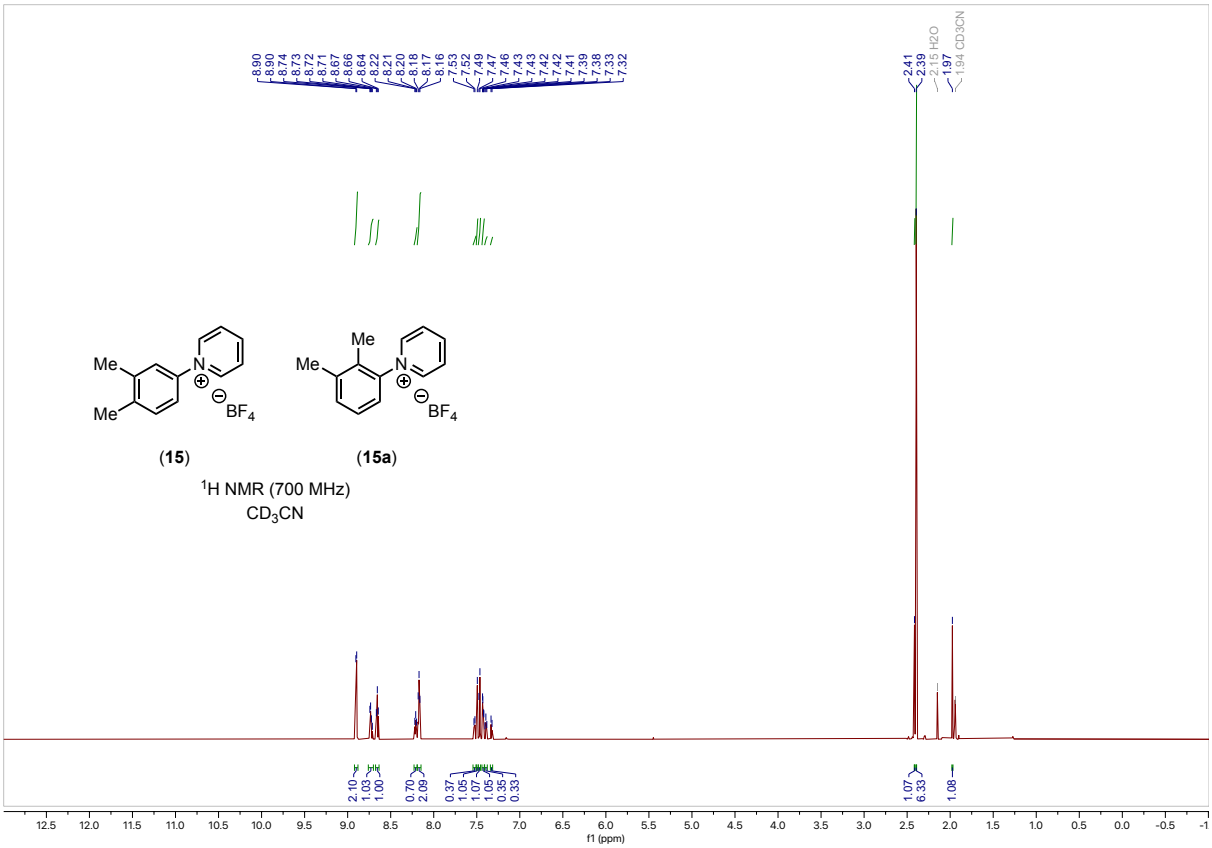

148.5
147.0
142.8
140.3
133.8
130.8
130.3
118.4 CD3CN
21.2
17.2
Me
Me
Me
BF4
(13B)
13C NMR (126 MHz)
CD3CN
f1 (ppm)

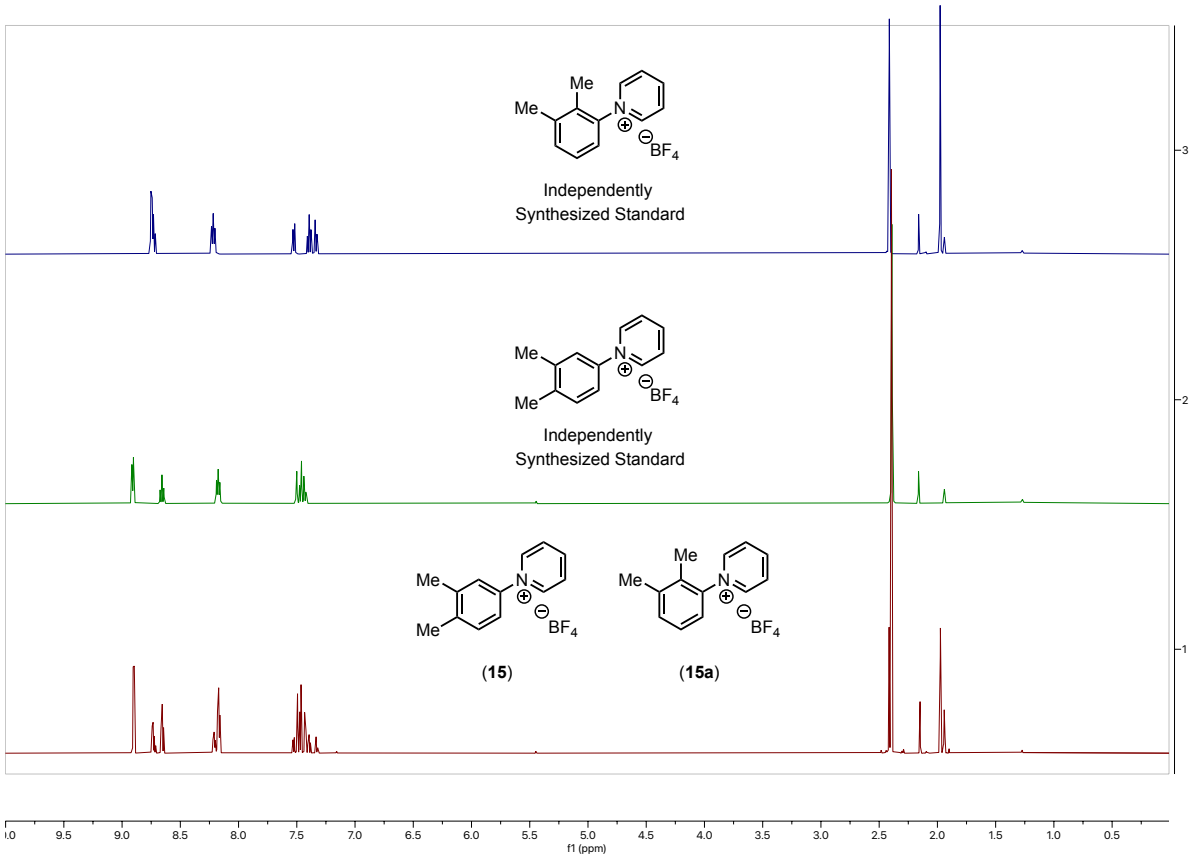

8.75
8.74
8.72
8.71
8.70
8.20
8.19
8.18
7.38
7.37
7.36
7.32
7.31
2.44
2.20
1.94 CD3CN
Me
Me
BF4
(14)
1H NMR (700 MHz)
CD3CN
1.97
1.00
2.04
2.01
1.03
3.12
3.17
f1 (ppm)

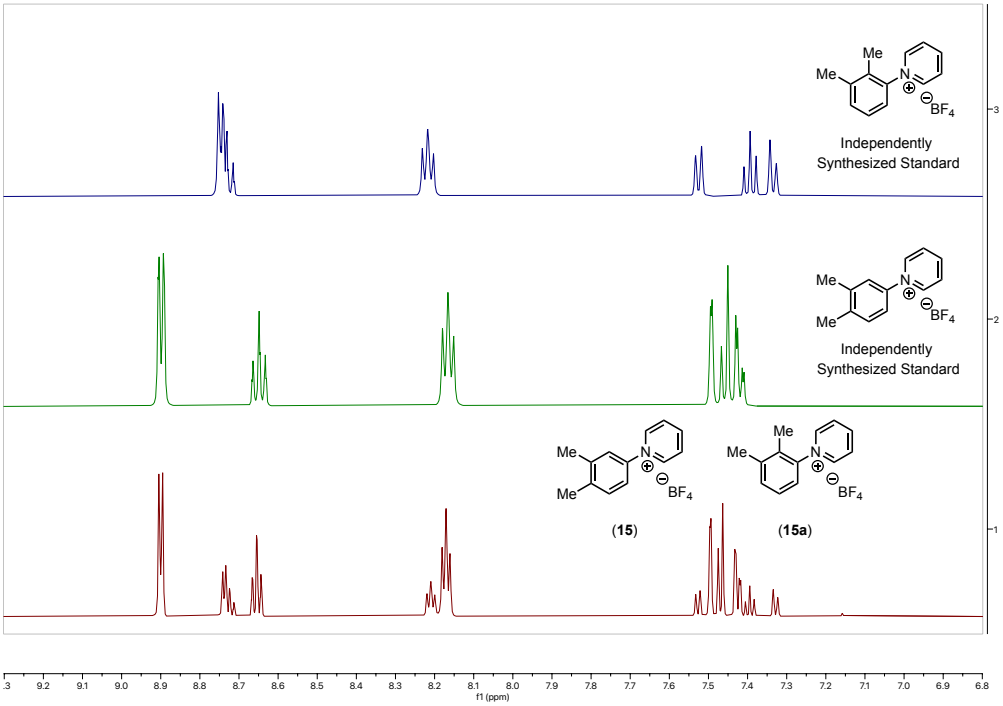


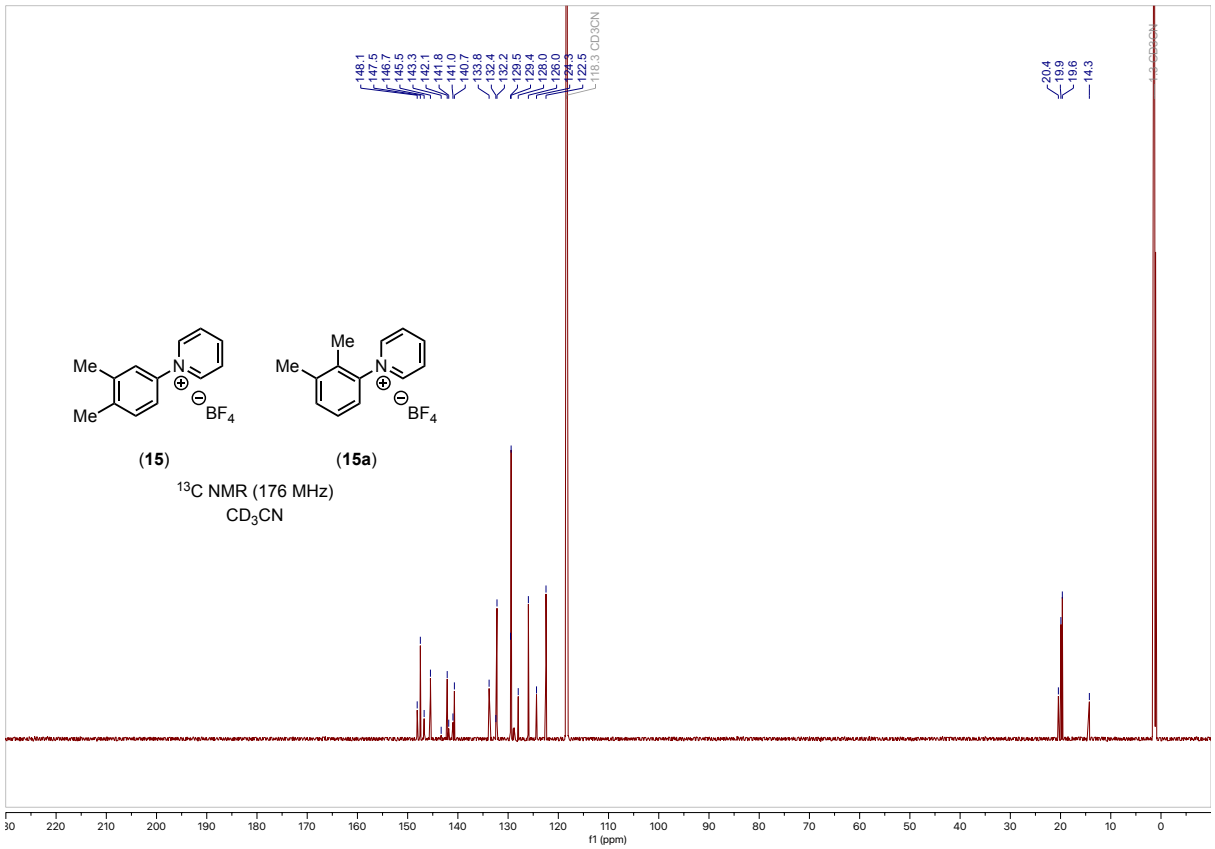
(**14**)

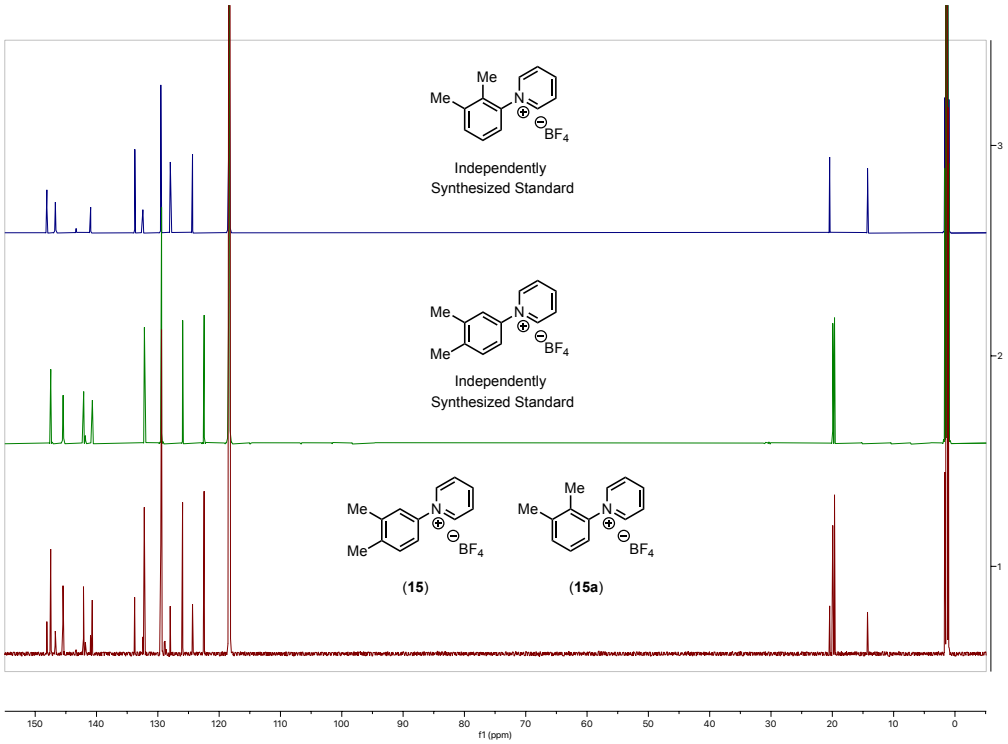
^{13}C NMR (176 MHz)
CD_3CN

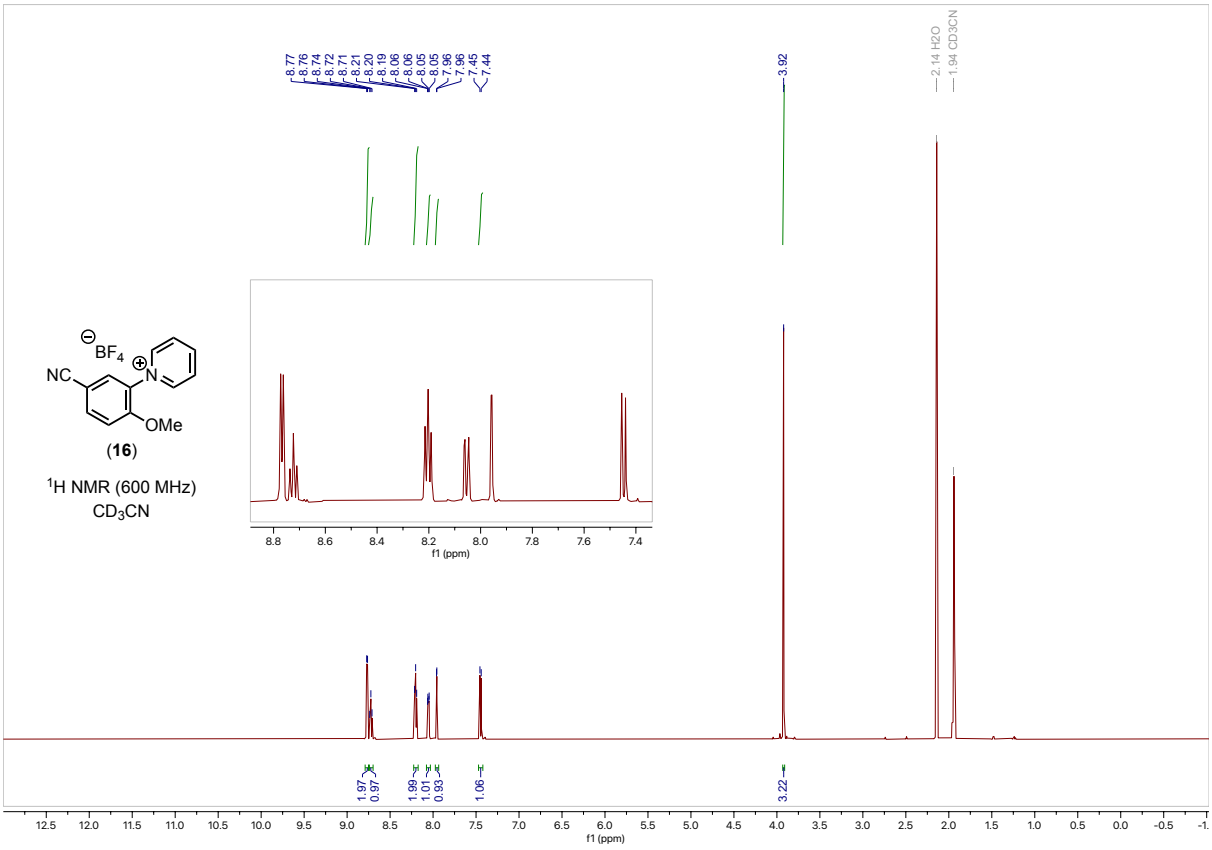

Me
Me
N
BF4
Me
Me
N
BF4
(15)
(15a)
1H NMR (700 MHz)
CD3CN
f1 (ppm)

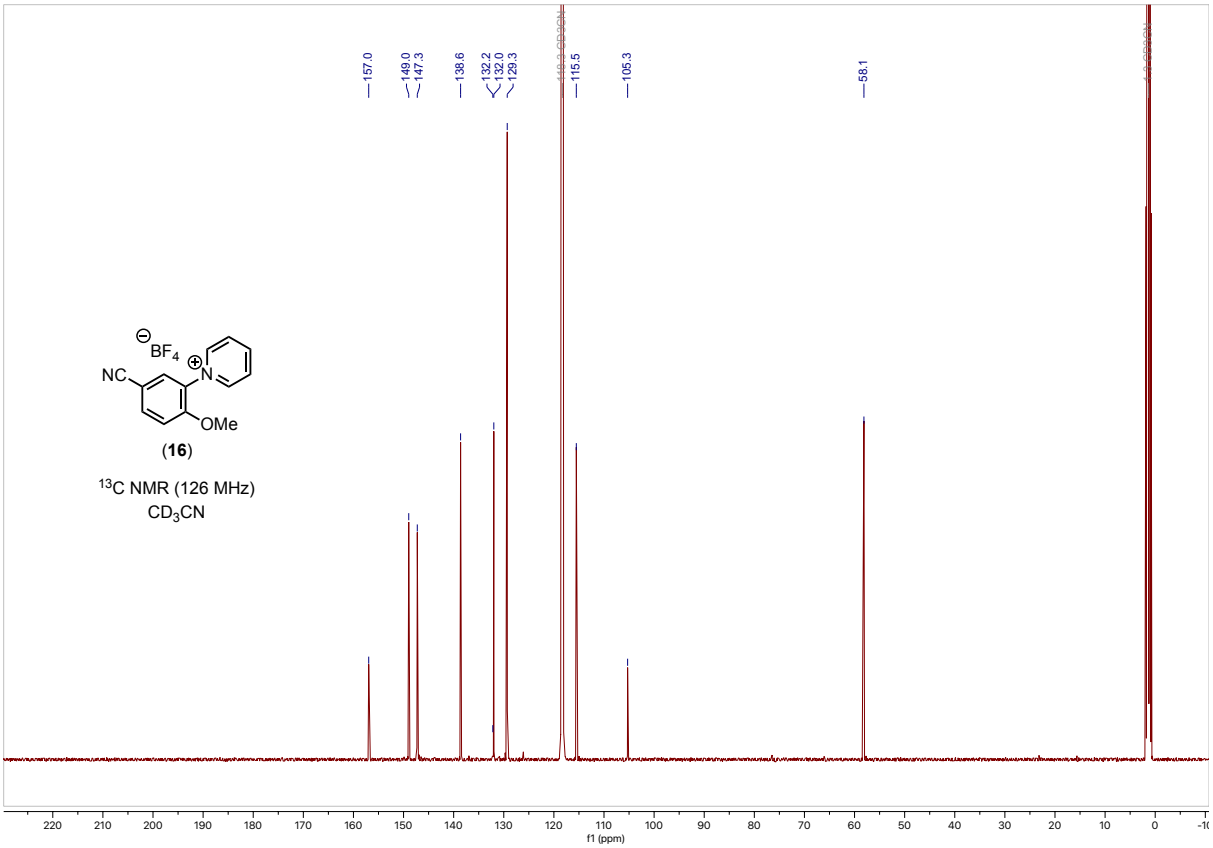

Me
Me
N
BF4
Independently
Synthesized Standard
Me
Me
N
BF4
Independently
Synthesized Standard
Me
Me
N
BF4
(15)
Me
Me
N
BF4
(15a)
3
2
1
f1 (ppm)


Me
Me
N
BF4
Independently
Synthesized Standard
Me
Me
N
BF4
Independently
Synthesized Standard
Me
Me
N
BF4
(15)
Me
Me
N
BF4
(15a)
3
2
1
f1 (ppm)

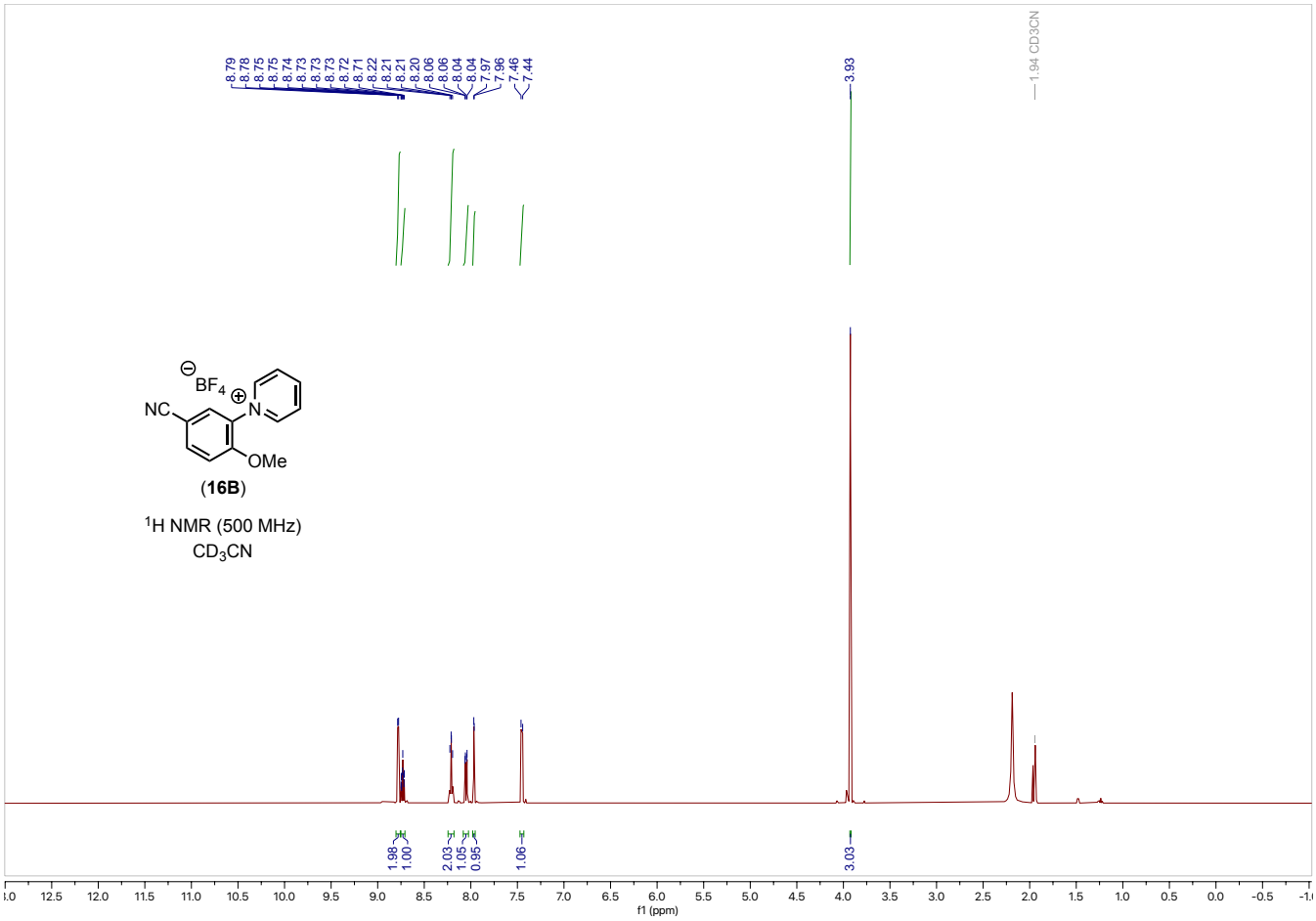

148.1
147.5
146.7
145.5
143.3
142.1
141.8
141.0
140.7
133.8
132.4
132.2
129.5
129.4
128.0
124.3
122.5
118.3 CD3CN
20.4
19.9
19.6
14.3
1.8 CD3CN
Me
Me
BF4
(15)
(15a)
13C NMR (176 MHz)
CD3CN
f1 (ppm)

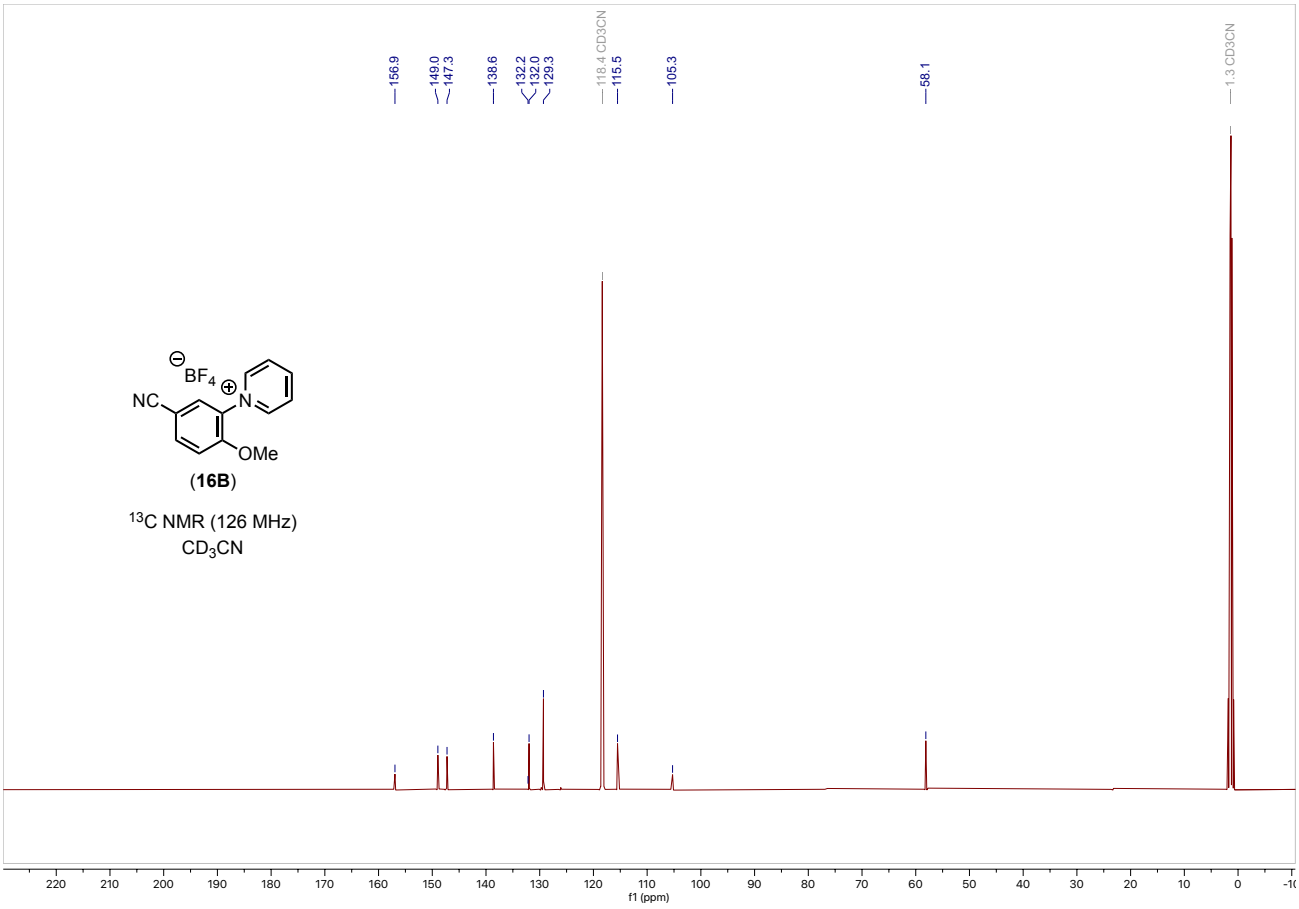

Independently
Synthesized Standard
Independently
Synthesized Standard
(15)
(15a)
f1 (ppm)

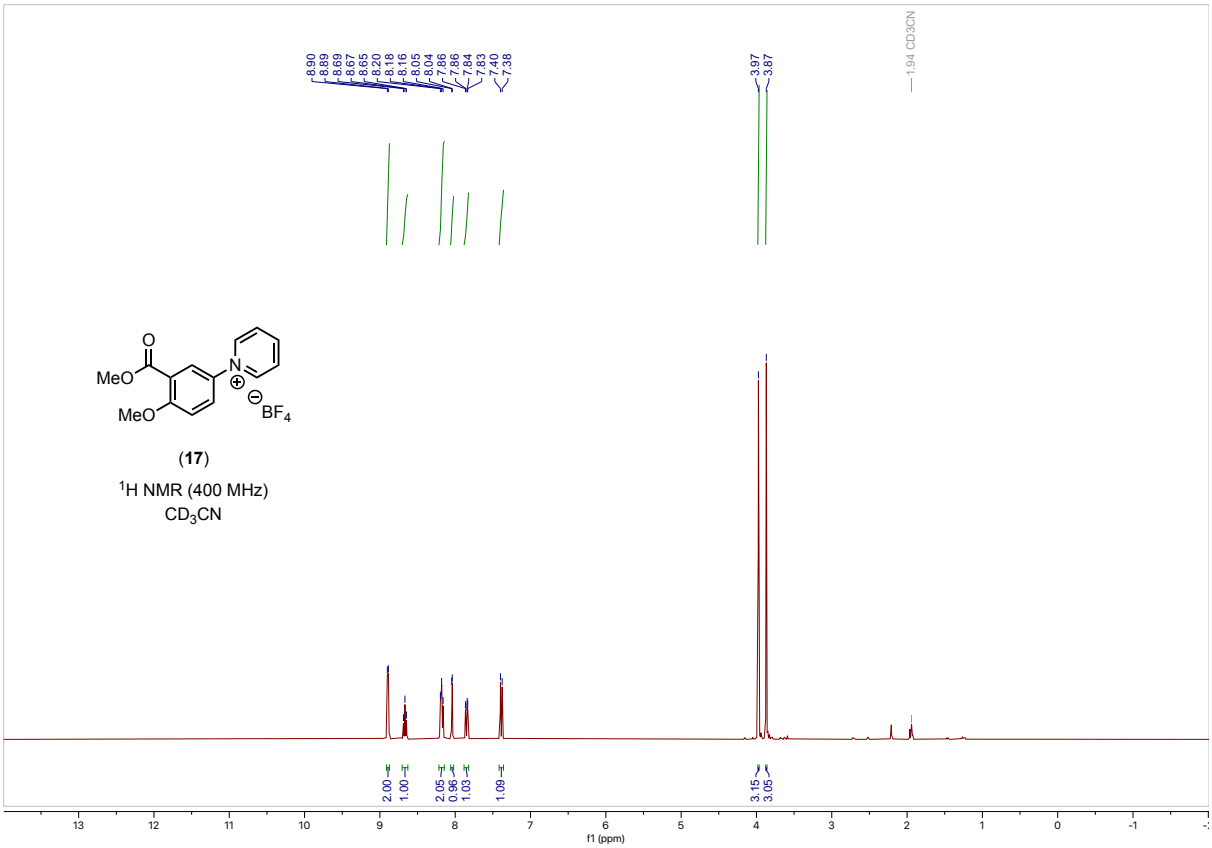

8.77
8.76
8.74
8.72
8.71
8.21
8.20
8.19
8.06
8.06
8.05
8.05
7.96
7.96
7.45
7.44
3.92
2.14 H2O
1.94 CD3CN
BF4
NC
N
OMe
(16)
1H NMR (600 MHz)
CD3CN
f1 (ppm)
1.97
0.97
1.99
1.01
0.93
1.06
3.22


157.0
149.0
147.3
138.6
132.2
132.0
129.3
118.3 CD3CN
115.5
105.3
58.1
1.3 CD2HCN
BF4
NC
N
OMe
(16)
13C NMR (126 MHz)
CD3CN
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

SUPPORTING INFORMATION



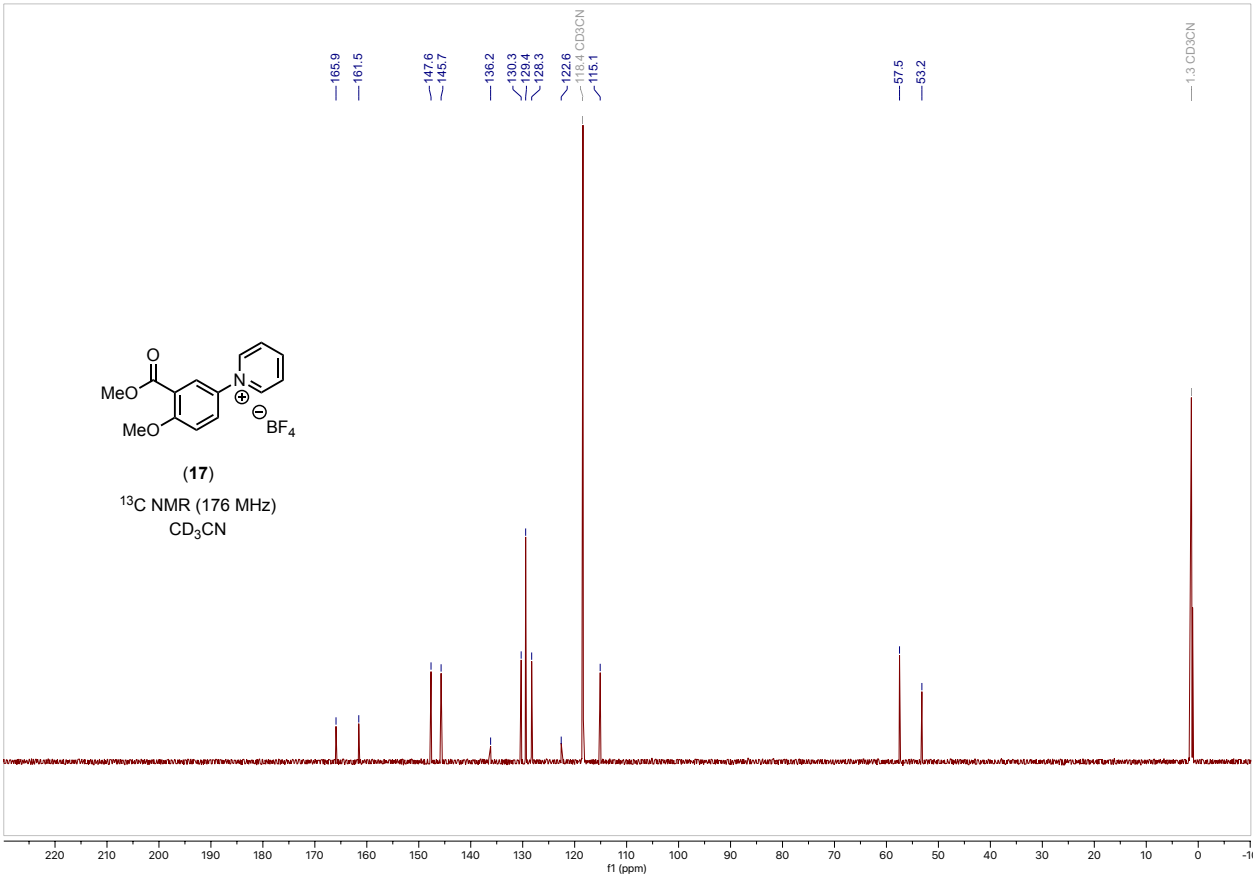

156.9
149.0
147.3
138.6
132.2
132.0
129.3
118.4 CD3CN
115.5
105.3
58.1
1.3 CD3CN
BF4
NC
N
OMe
(16B)
13C NMR (126 MHz)
CD3CN
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



(**17**)

^{1}H NMR (400 MHz)

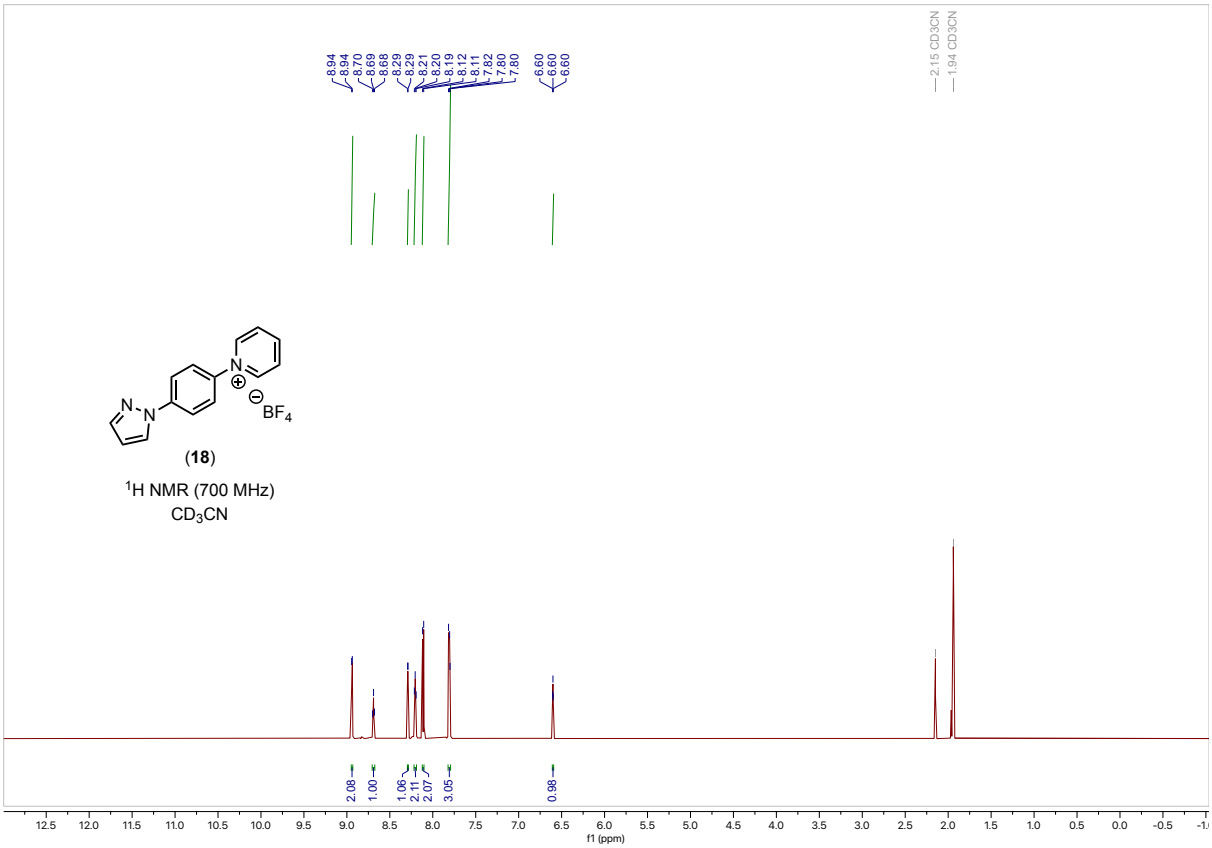
CD_3CN



(**17**)

^{13}C NMR (176 MHz)

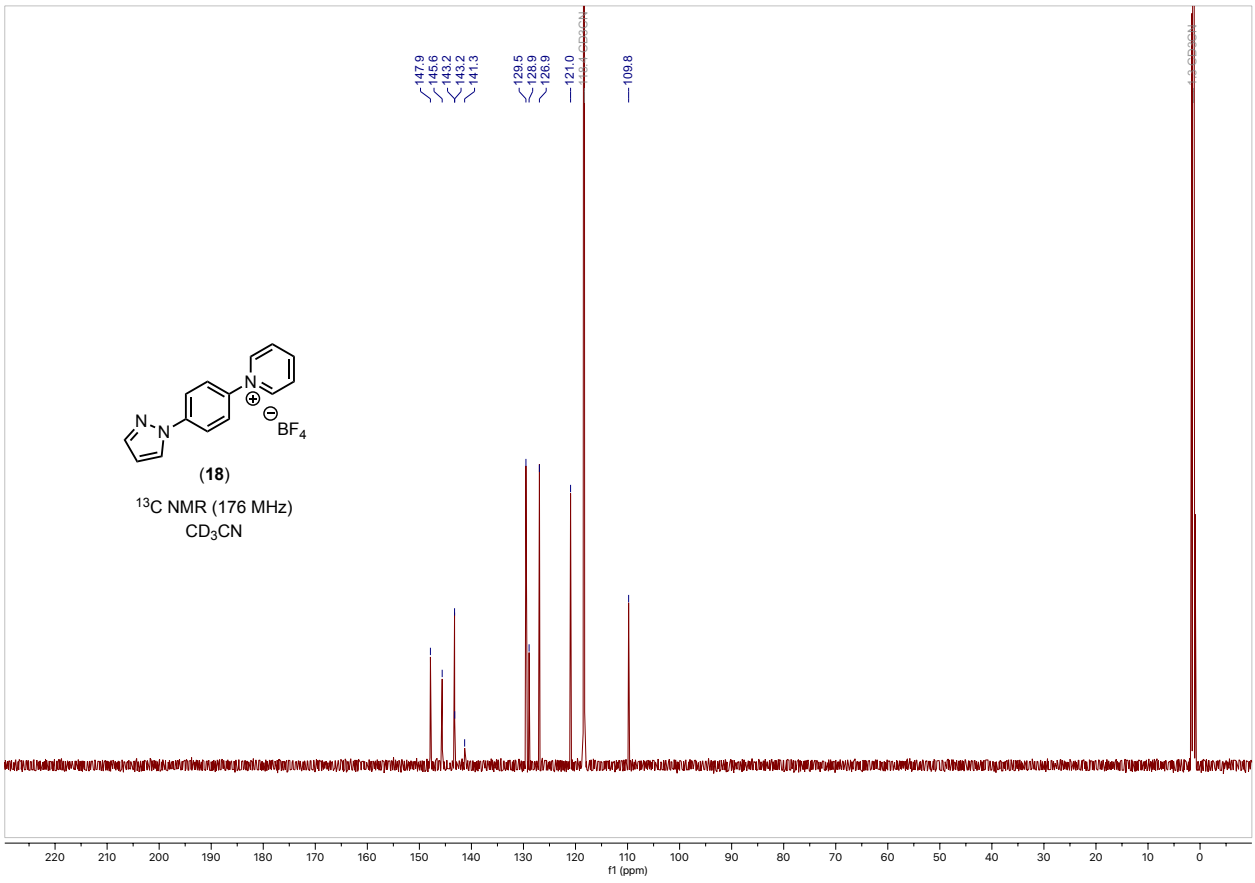
CD_3CN

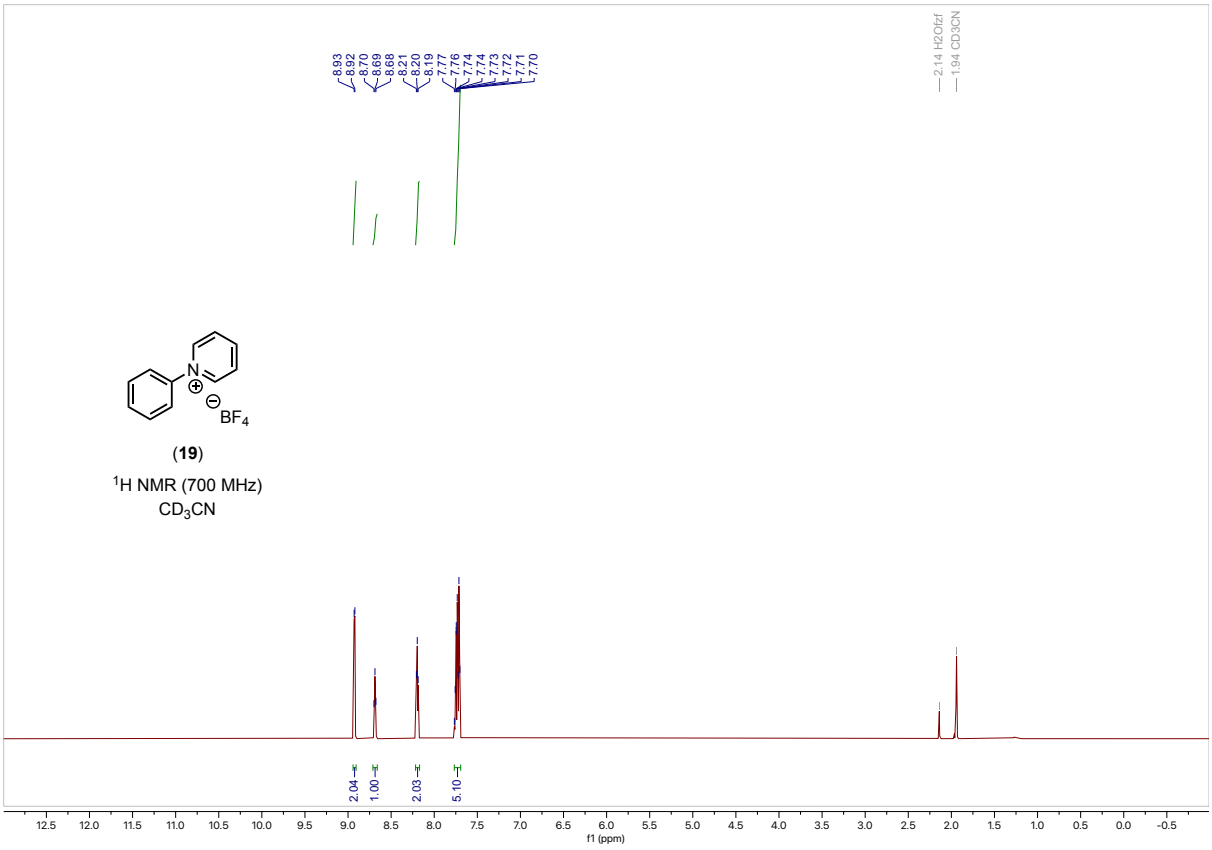


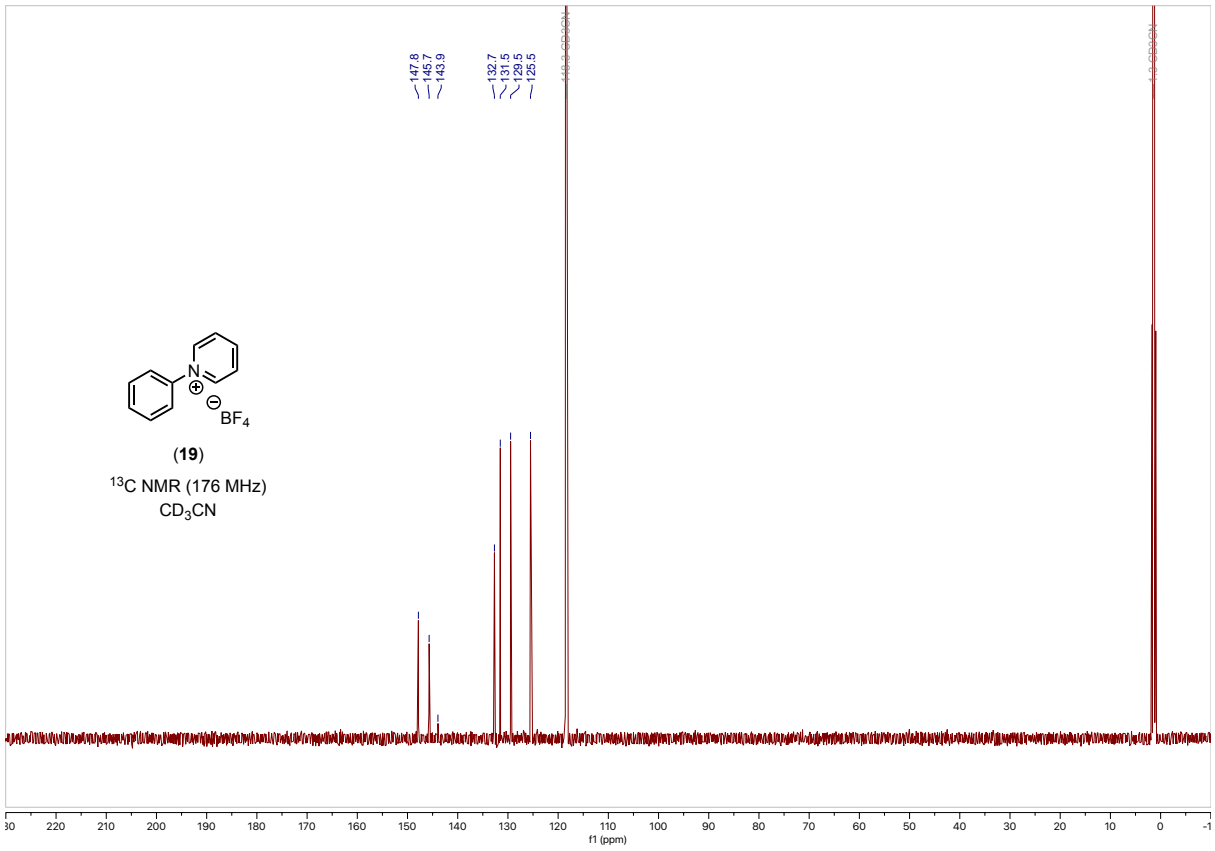
(**18**)

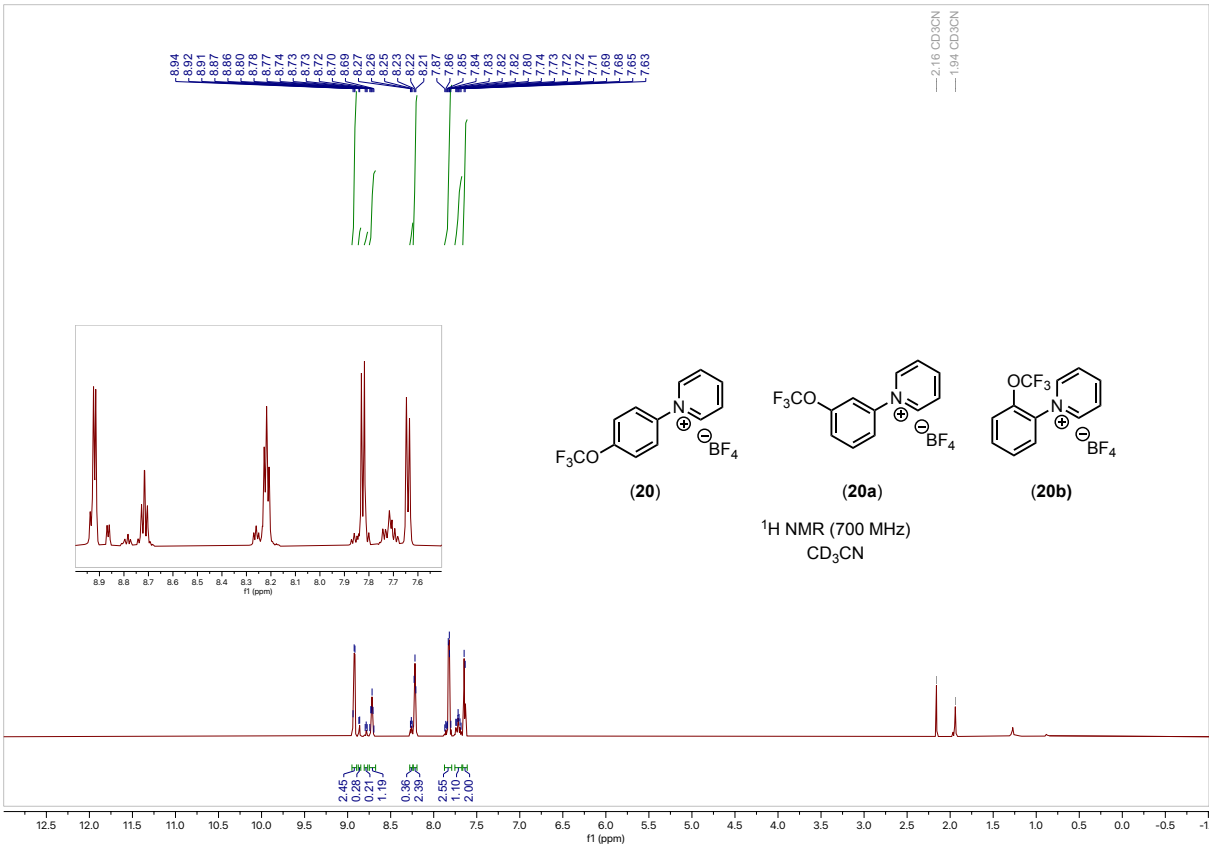
^{1}H NMR (700 MHz)

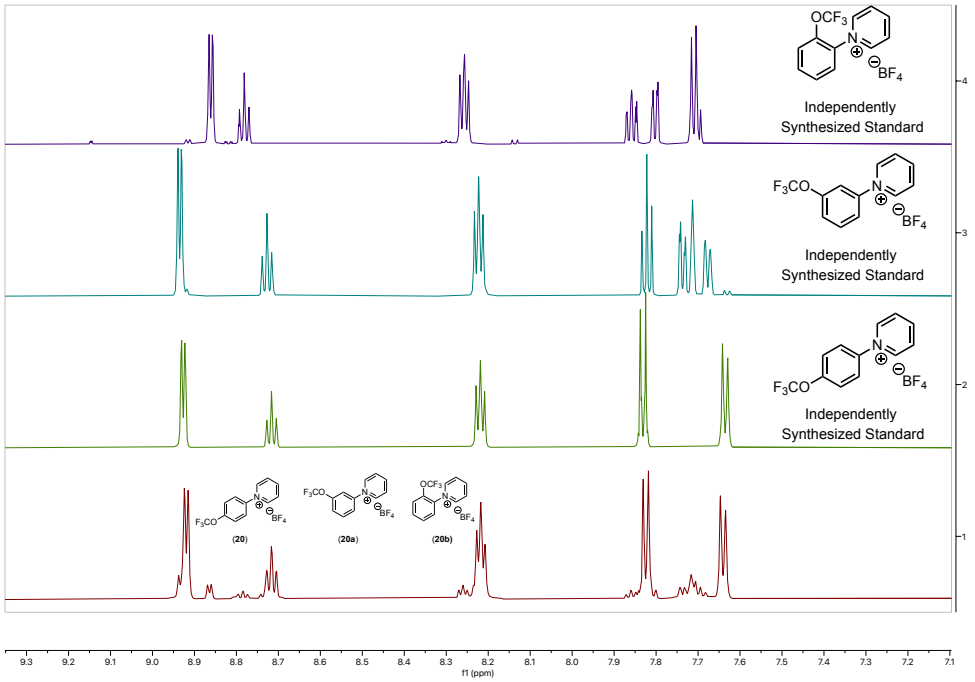
CD_3CN

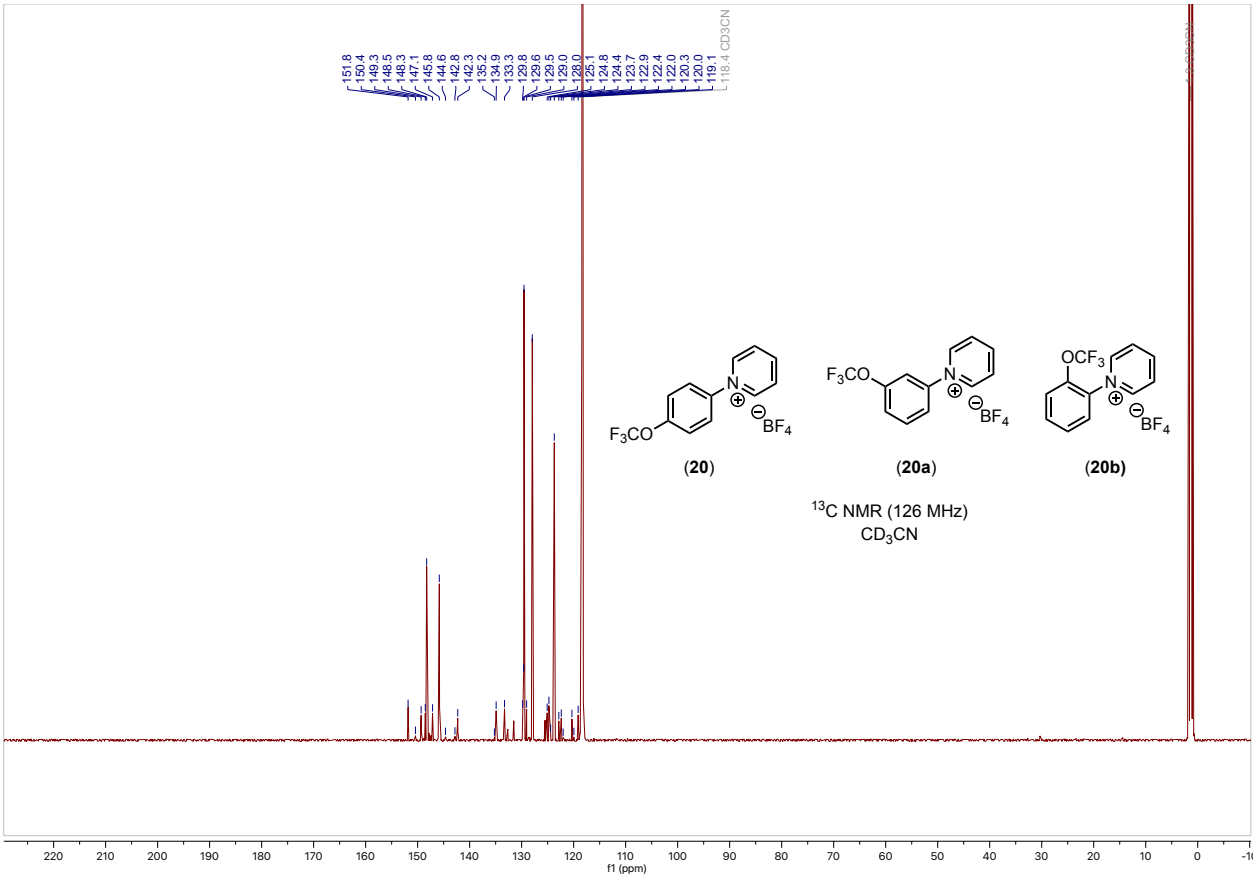

147.9
145.6
143.2
143.2
141.3
129.5
128.9
126.9
121.0
118.1 CD3CN
109.8
1.3 CD3CN
BF4
(18)
13C NMR (176 MHz)
CD3CN
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

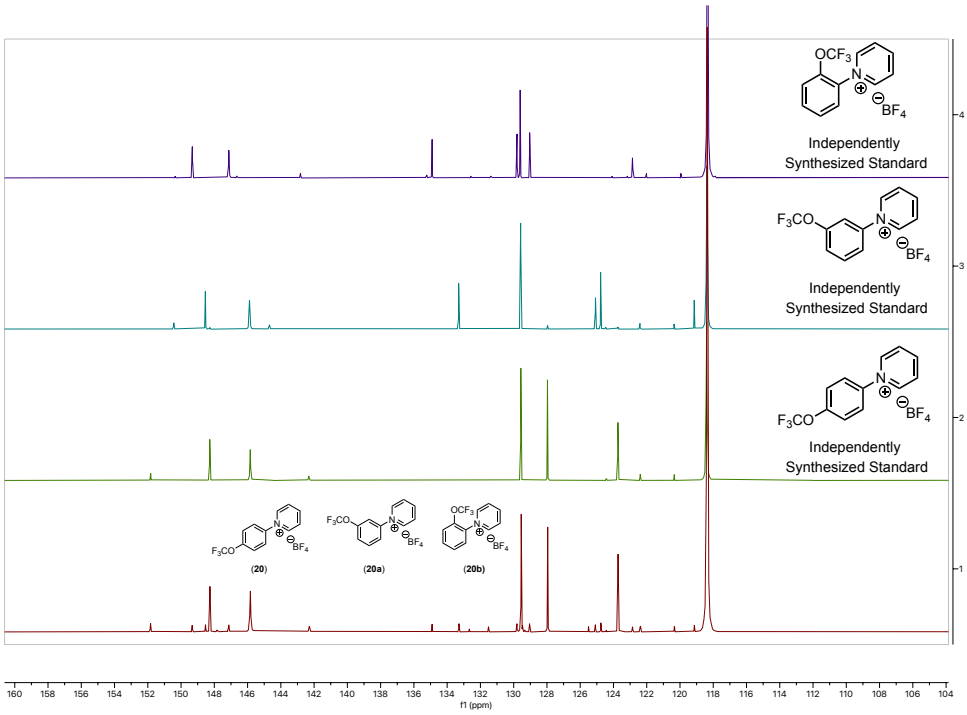

8.93
8.92
8.70
8.69
8.68
8.21
8.20
8.19
7.77
7.76
7.74
7.74
7.73
7.72
7.71
7.70
2.14 H2Ofzf
1.94 CD3CN
BF4
(19)
1H NMR (700 MHz)
CD3CN
2.04
1.00
2.03
5.10
f1 (ppm)

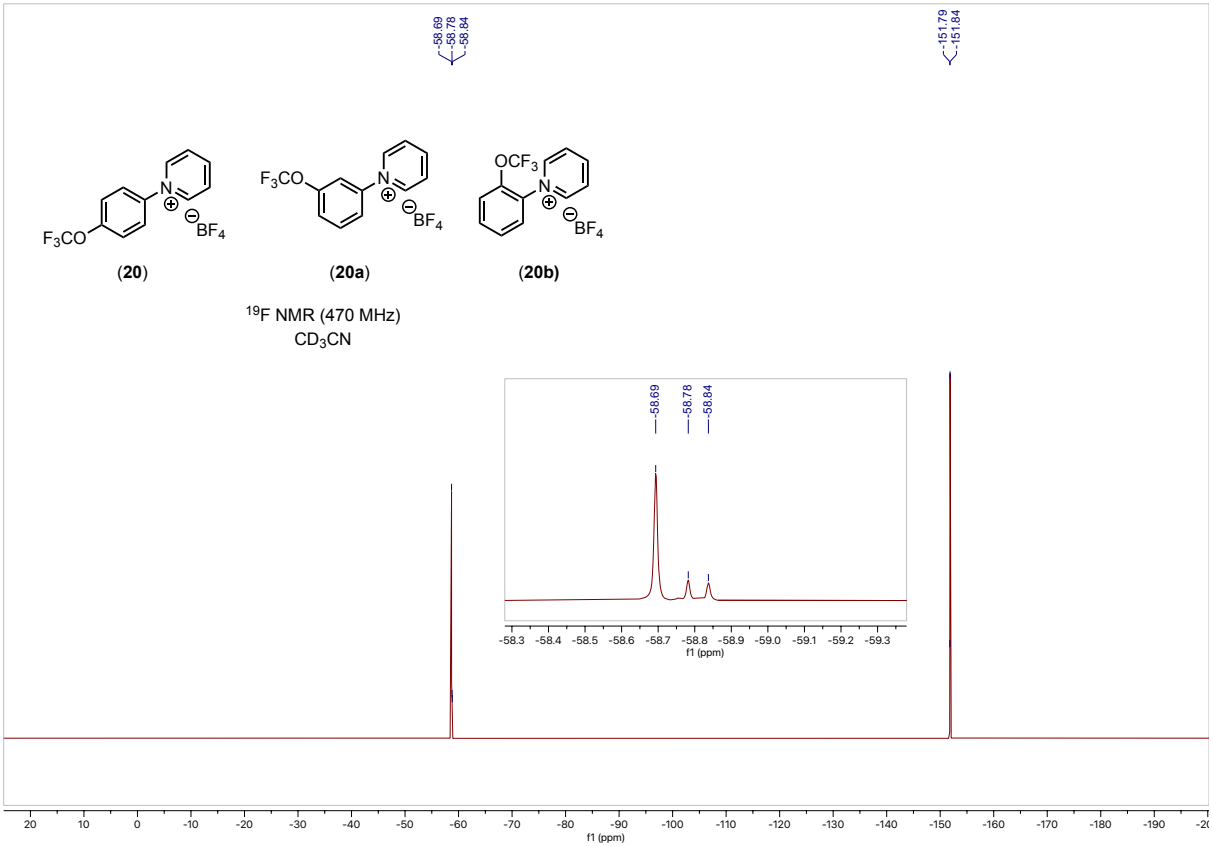

147.8
145.7
143.9
132.7
131.5
129.5
125.5
118.3 CD3CN
1.3 CD3CN
BF4
(19)
13C NMR (176 MHz)
CD3CN
f1 (ppm)

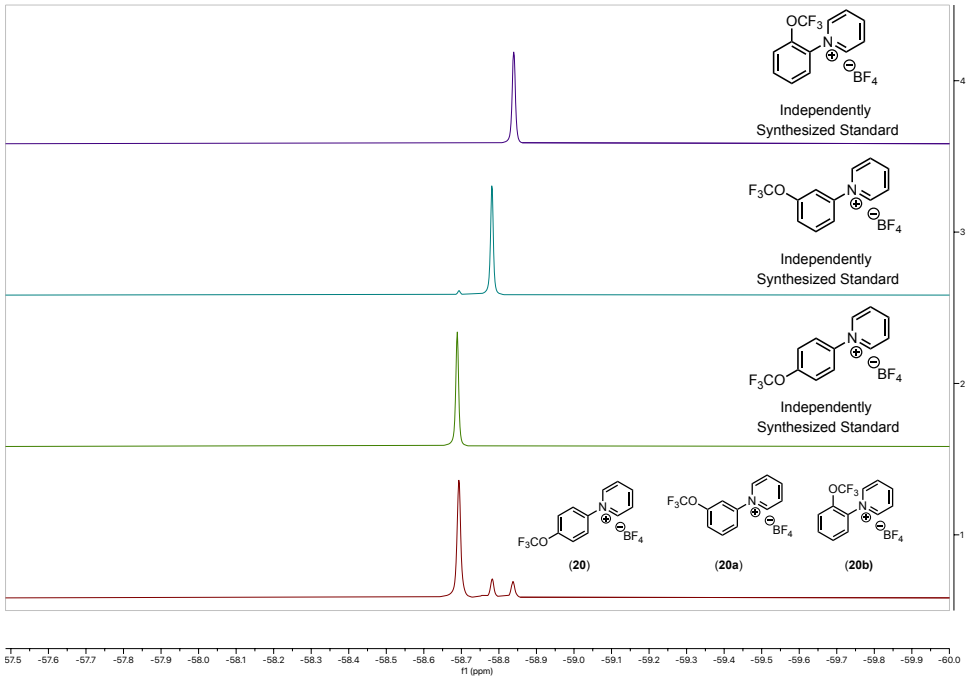

(20)
(20a)
(20b)
^{1}H NMR (700 MHz)
CD_3CN

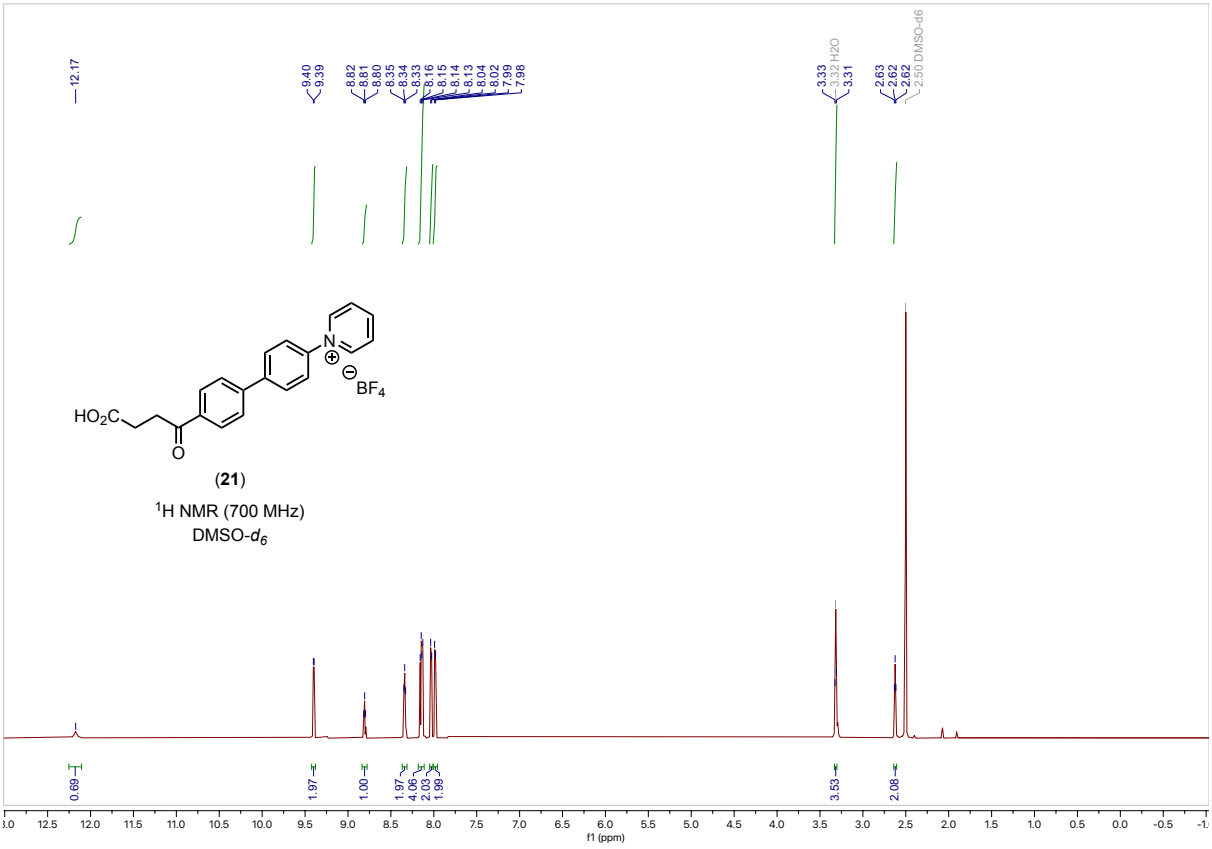

Independently
Synthesized Standard
Independently
Synthesized Standard
Independently
Synthesized Standard
(20)
(20a)
(20b)

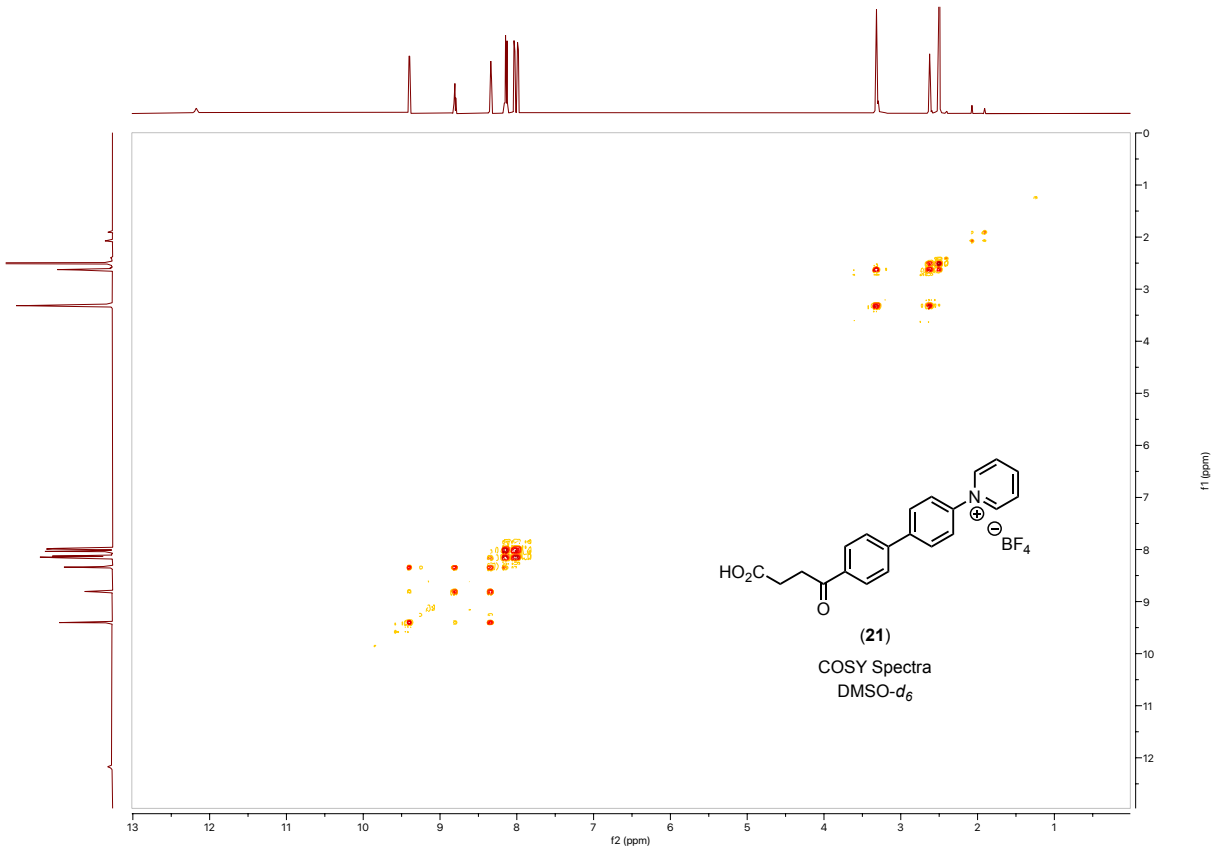

151.8
150.4
149.3
148.5
148.3
147.1
145.8
144.6
142.8
142.3
135.2
134.9
133.3
129.8
129.6
129.5
129.0
128.0
125.1
124.8
124.4
123.7
122.9
122.4
122.0
120.3
120.0
119.1
118.4 CD3CN
(20)
(20a)
(20b)
13C NMR (126 MHz)
CD3CN
f1 (ppm)


Independently
Synthesized Standard
Independently
Synthesized Standard
Independently
Synthesized Standard
(20)
(20a)
(20b)
f1 (ppm)


-58.69
-58.78
-58.84
-151.79
-151.84
F3CO
BF4
OCF3
(20)
(20a)
(20b)
19F NMR (470 MHz)
CD3CN
f1 (ppm)


OCF3
BF4
Independently
Synthesized Standard
F3CO
(20)
(20a)
(20b)
f1 (ppm)

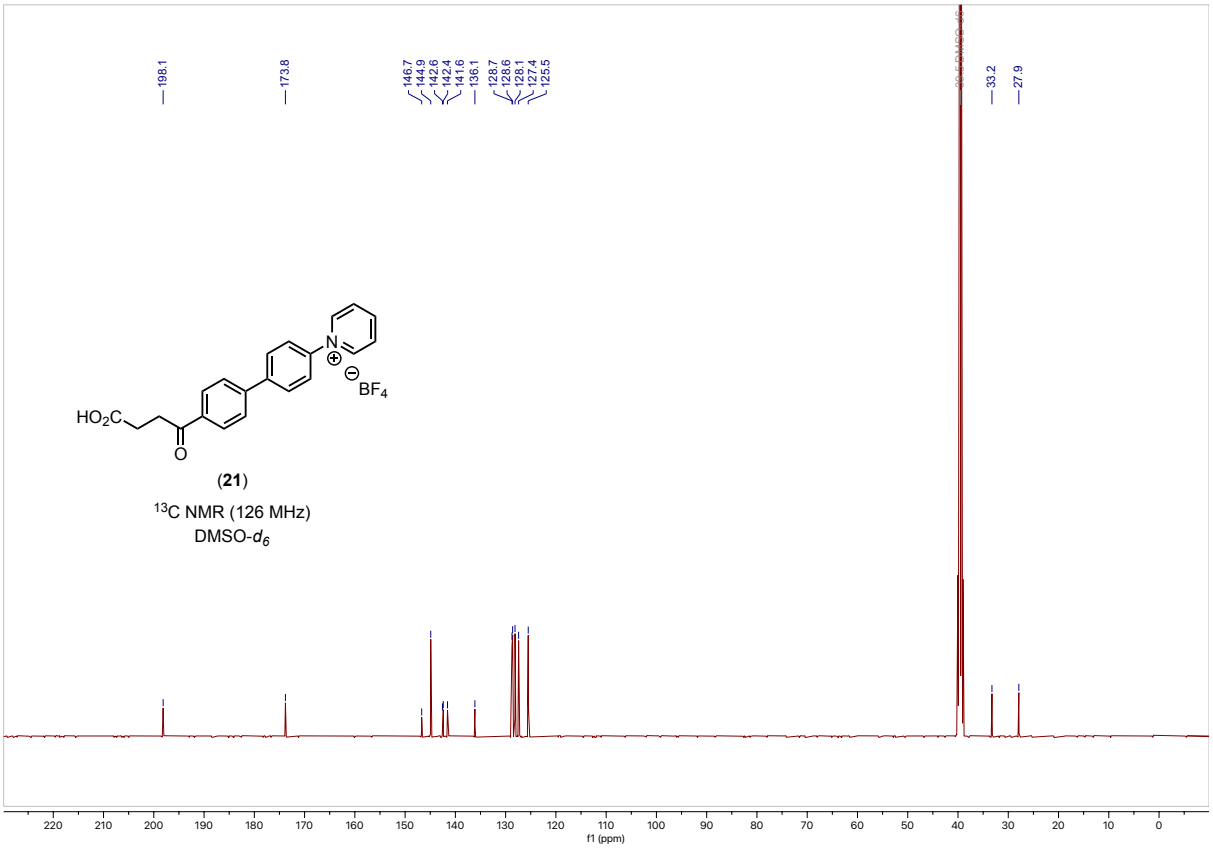

12.17
9.40
9.39
8.82
8.81
8.80
8.35
8.34
8.33
8.16
8.15
8.14
8.13
8.04
8.02
7.99
7.98
3.33
3.32 H2O
3.31
2.63
2.62
2.62
2.50 DMSO-d6
HO2C
O
N
BF4
(21)
1H NMR (700 MHz)
DMSO-d6
0.69
1.97
1.00
1.97
4.06
2.03
1.99
3.53
2.08
f1 (ppm)

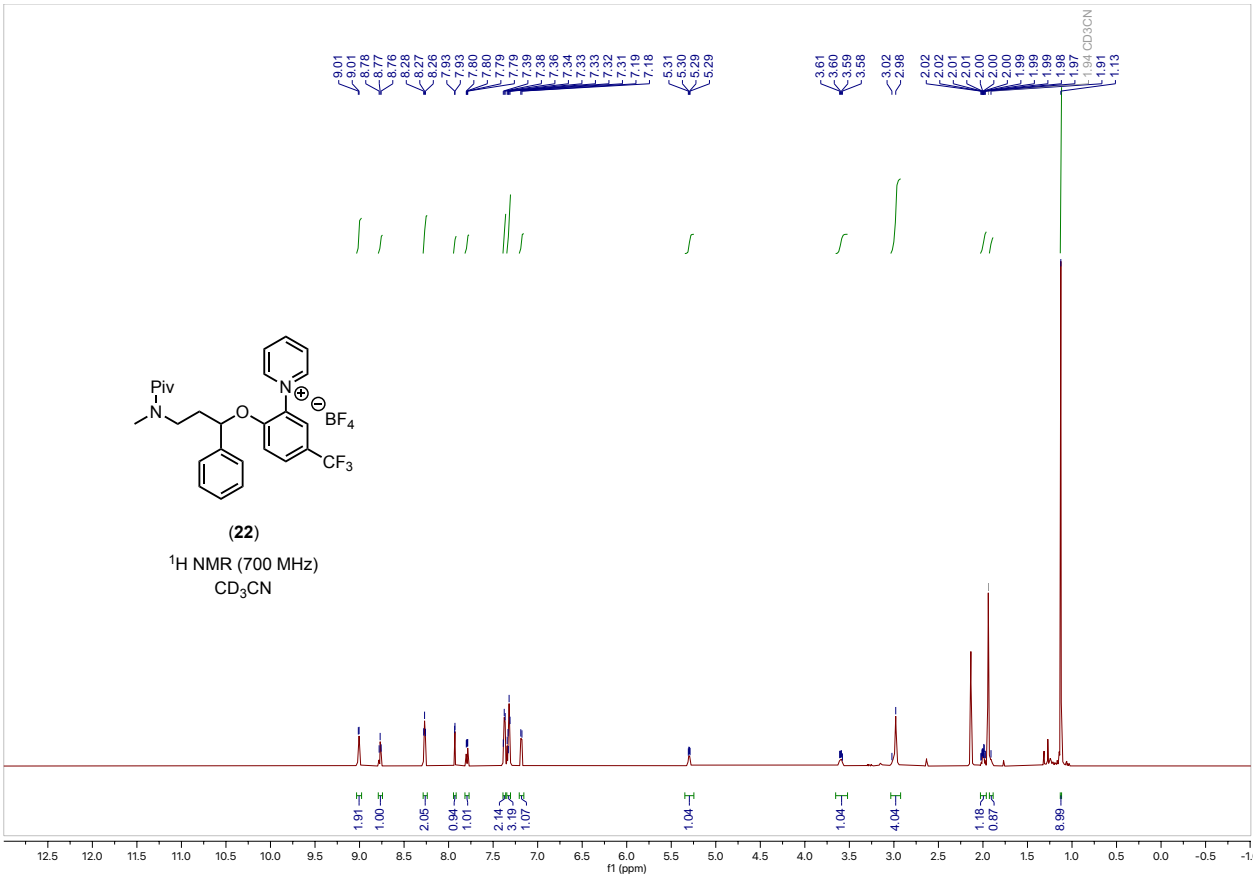


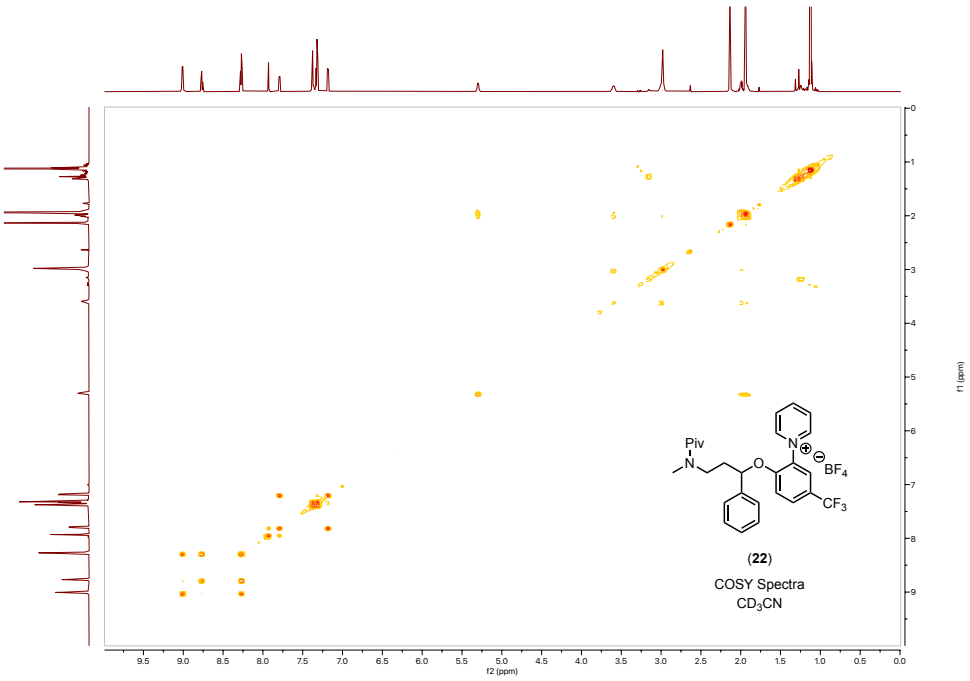
(**21**)

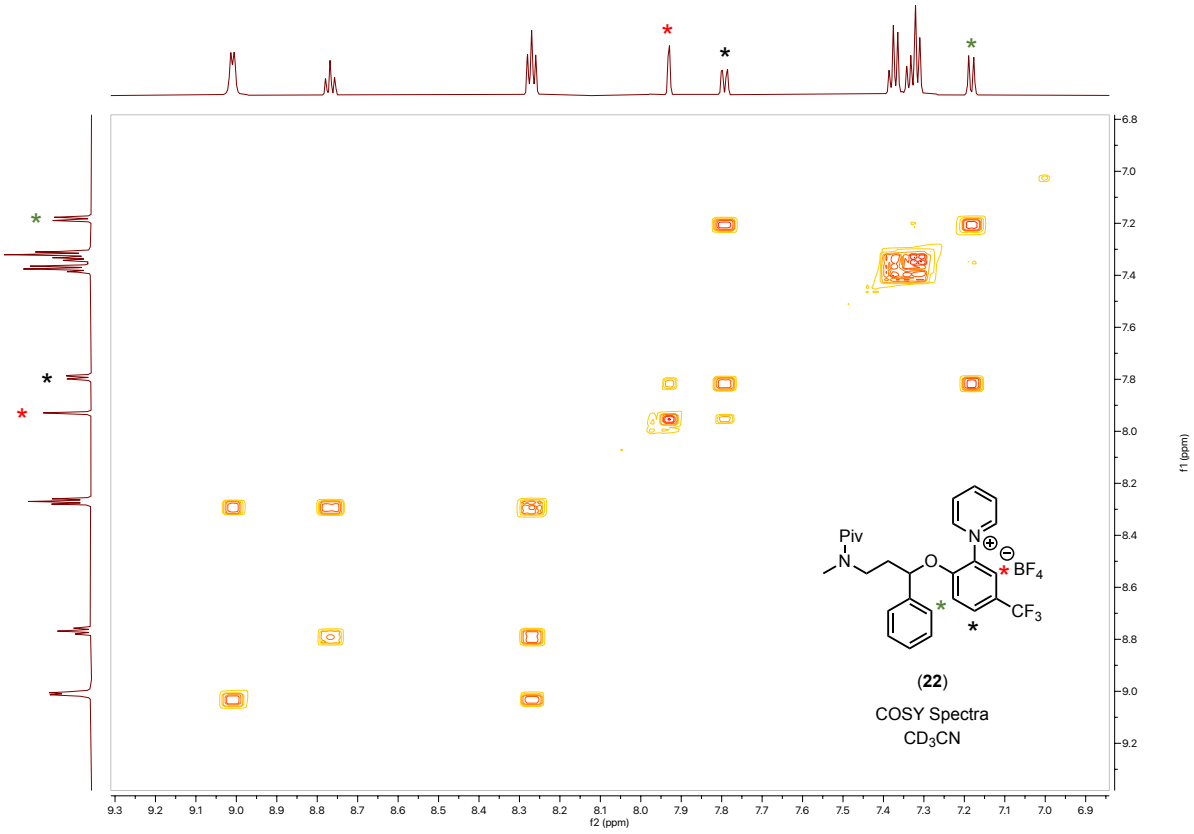
COSY Spectra

DMSO-d_6


198.1
173.8
146.7
144.9
142.6
142.4
141.6
136.1
128.7
128.6
128.1
127.4
125.5
39.5 DMSO-d6
33.2
27.9
HO2C
O
N
BF4
(21)
13C NMR (126 MHz)
DMSO-d6
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Piv
N
O
N
BF4
CF3
(22)
1H NMR (700 MHz)
CD3CN
f1 (ppm)

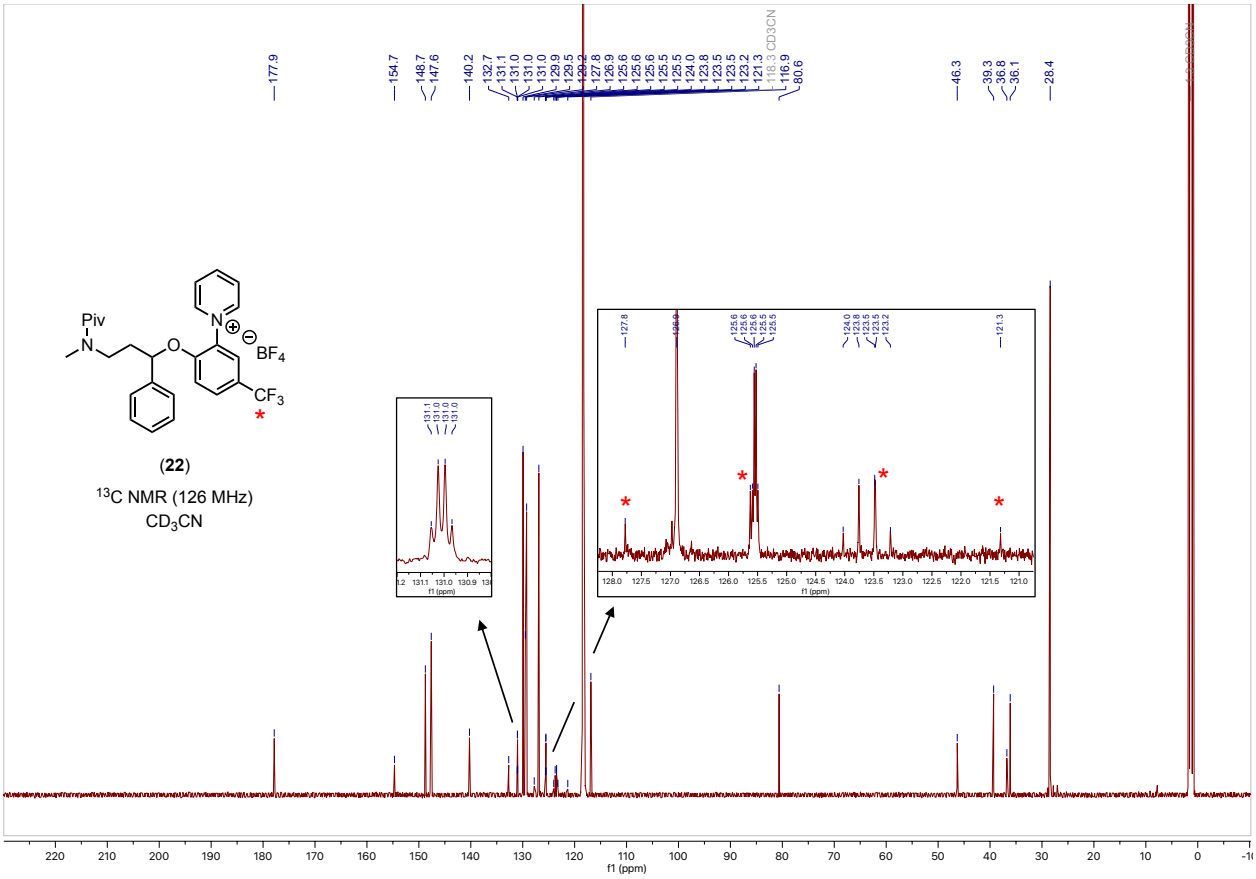

Piv
N
O
N
BF4
CF3
(22)
COSY Spectra
CD3CN
f2 (ppm)
f1 (ppm)

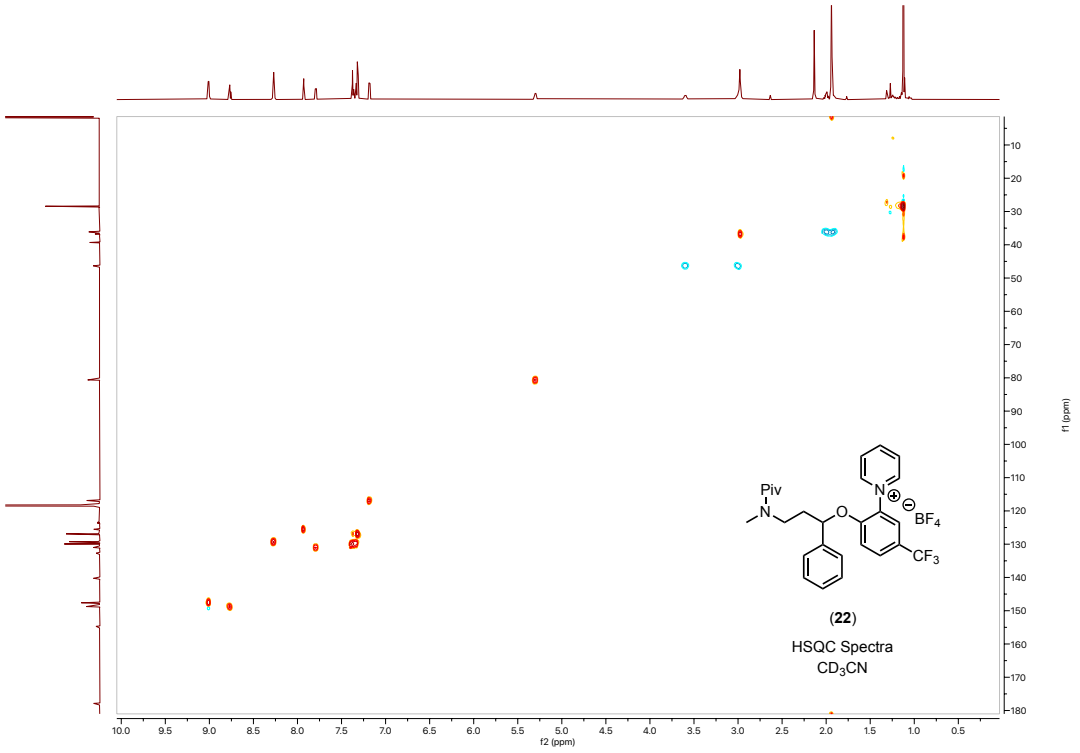


(**22**)

COSY Spectra

CD_3CN

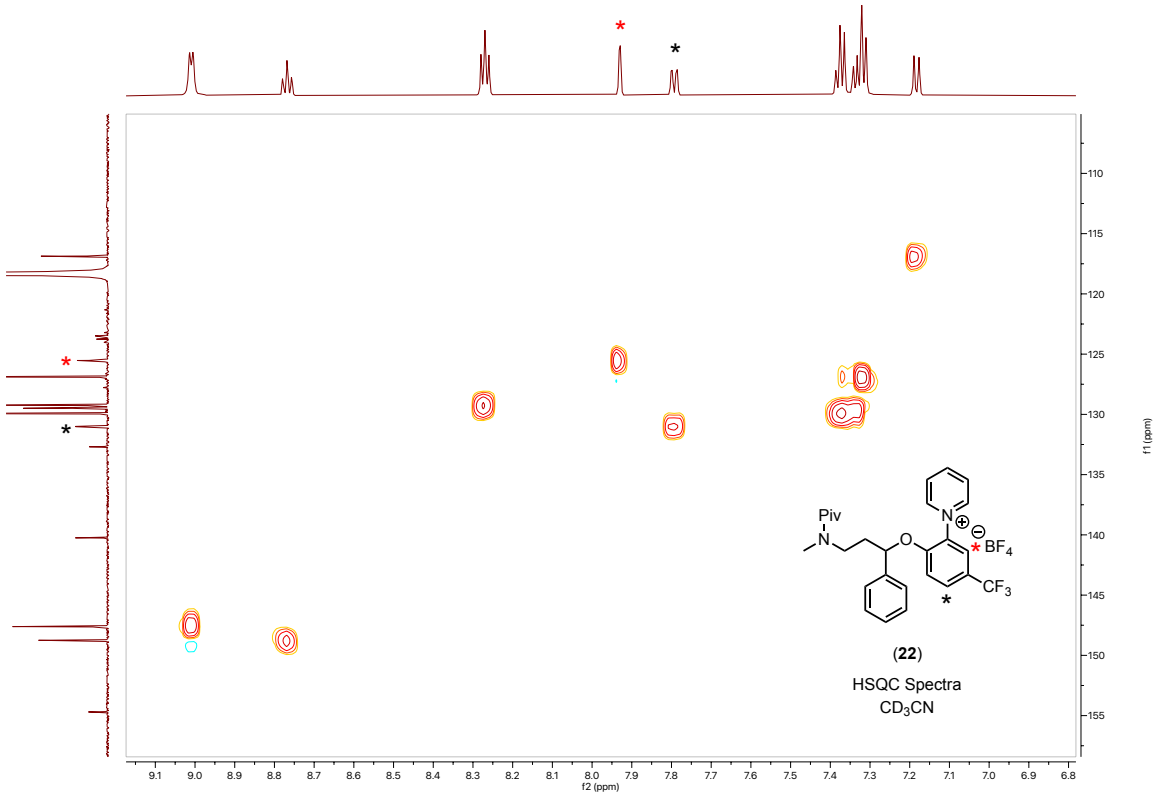

Piv
N
O
N
BF4
CF3
*
(22)
13C NMR (126 MHz)
CD3CN
177.9
154.7
148.7
147.6
140.2
132.7
131.1
131.0
131.0
129.9
129.5
127.8
126.9
125.6
125.6
125.5
125.5
124.0
123.8
123.5
123.2
121.3
CD3CN
116.9
80.6
46.3
39.3
36.8
36.1
28.4
f1 (ppm)



(**22**)

HSQC Spectra

CD_3CN



(**22**)

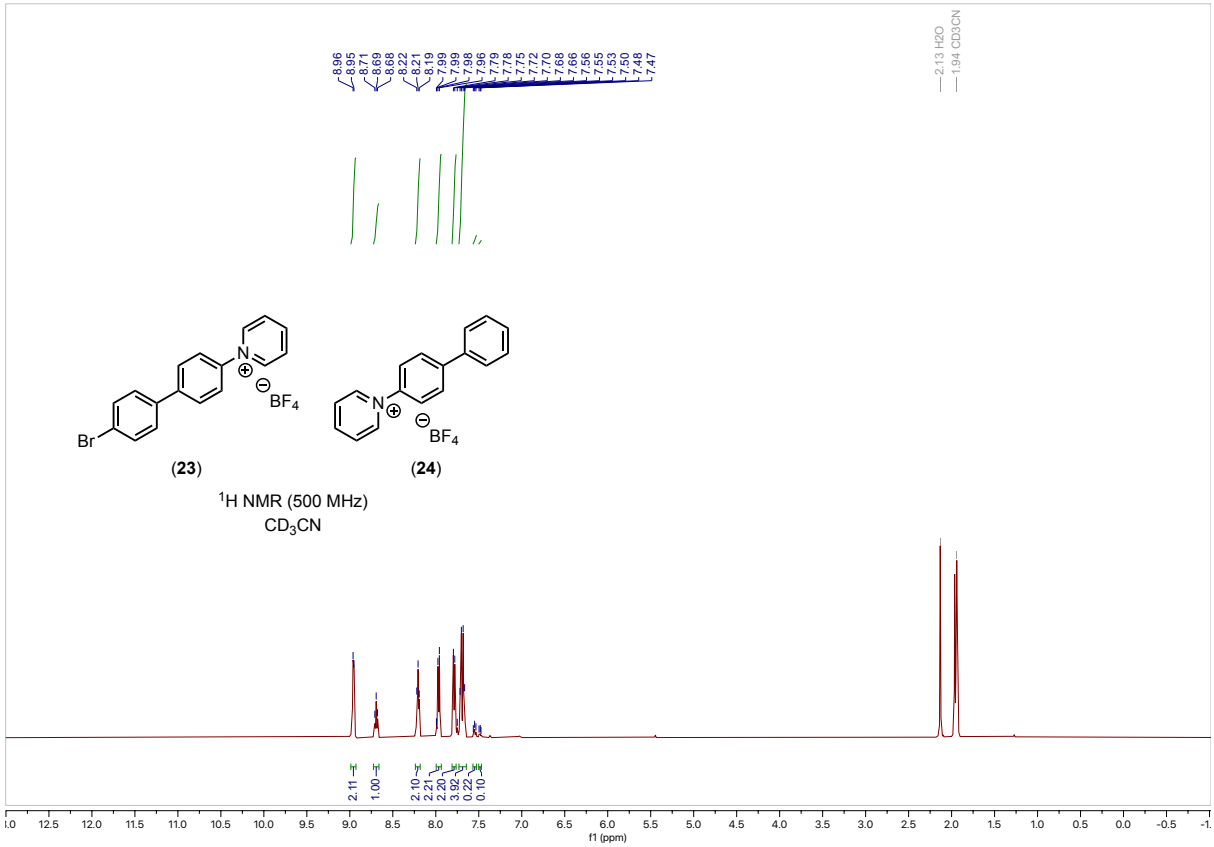
HSQC Spectra

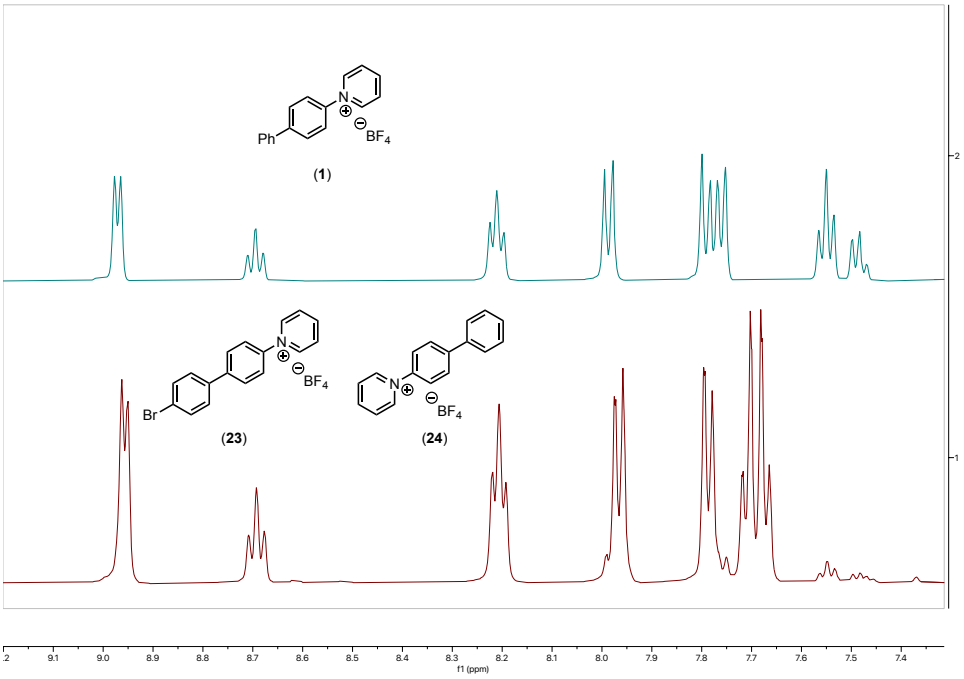
CD_3CN

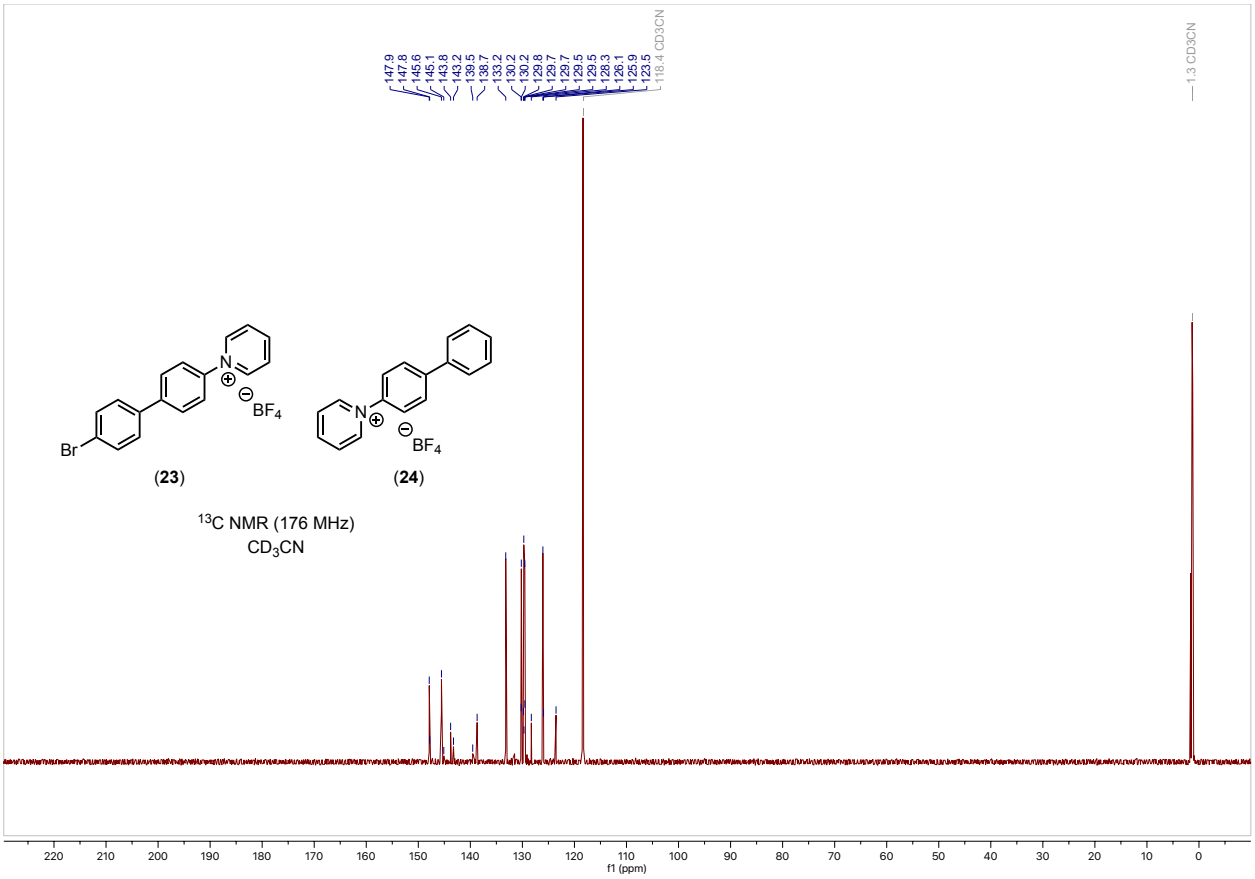
(**22**)

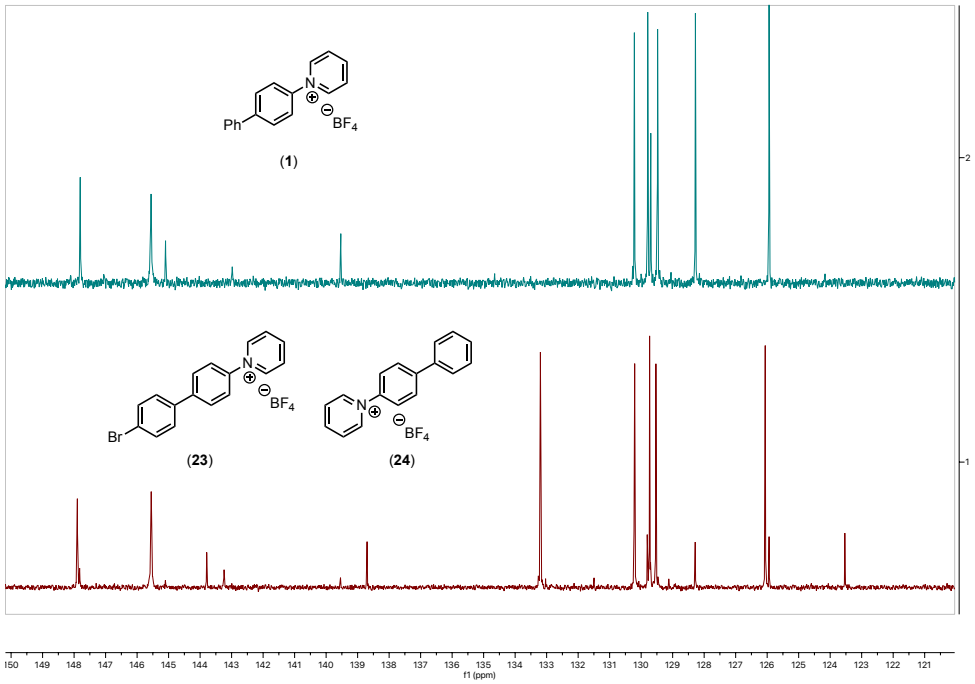
^{19}F NMR (470 MHz)

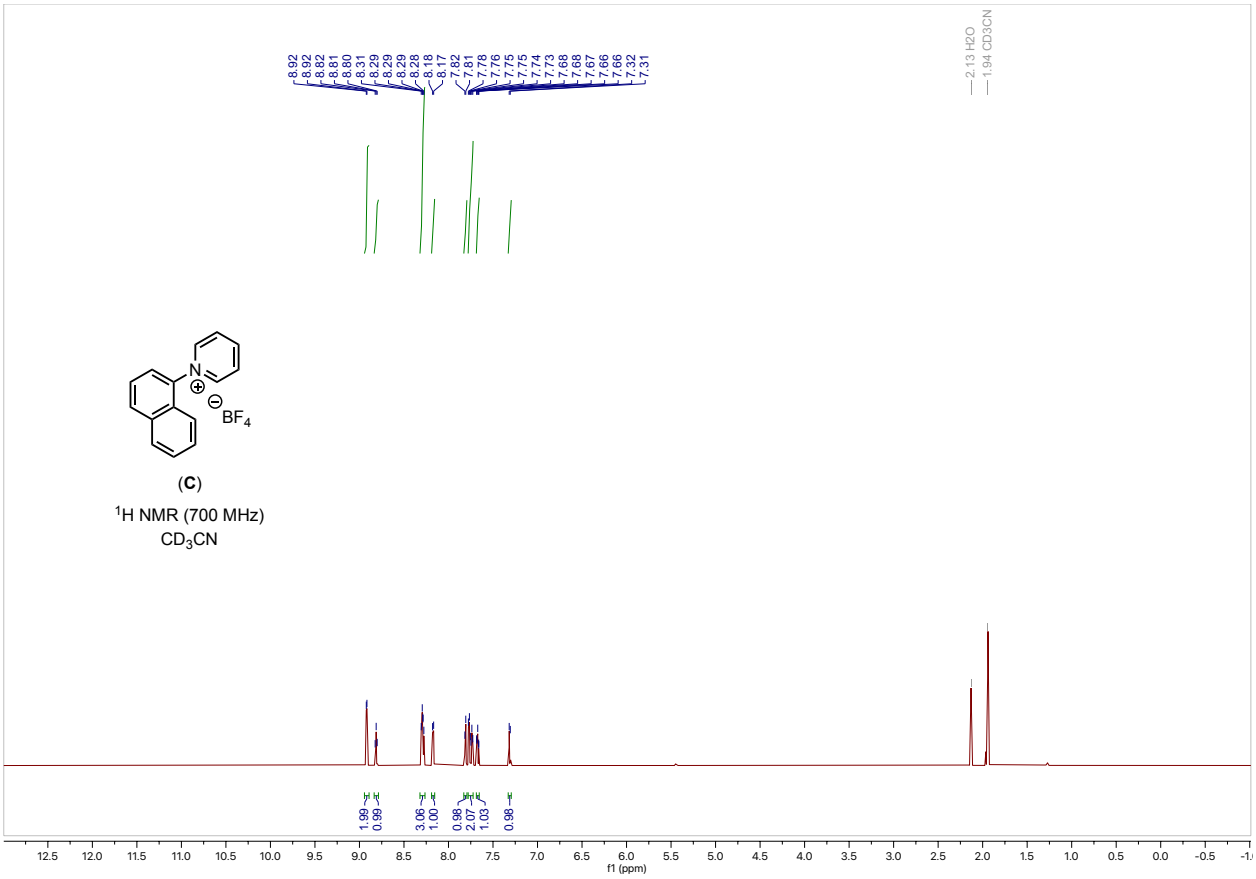
CD_3CN


8.96
8.95
8.71
8.69
8.68
8.22
8.21
8.19
7.99
7.99
7.98
7.96
7.79
7.78
7.75
7.72
7.70
7.68
7.66
7.56
7.55
7.53
7.50
7.48
7.47
2.13 H2O
1.94 CD3CN
Br
BF4
(23)
(24)
1H NMR (500 MHz)
CD3CN
2.11
1.00
2.10
2.21
2.20
3.92
0.22
0.10
f1 (ppm)


Ph
BF4
(1)
Br
(23)
(24)
f1 (ppm)


147.9
147.8
145.6
145.1
143.8
143.2
139.5
138.7
133.2
130.2
130.2
129.8
129.7
129.7
129.5
129.5
128.3
126.1
125.9
123.5
116.4 CD3CN
1.3 CD3CN
Br
BF4
(23)
(24)
13C NMR (176 MHz)
CD3CN
f1 (ppm)

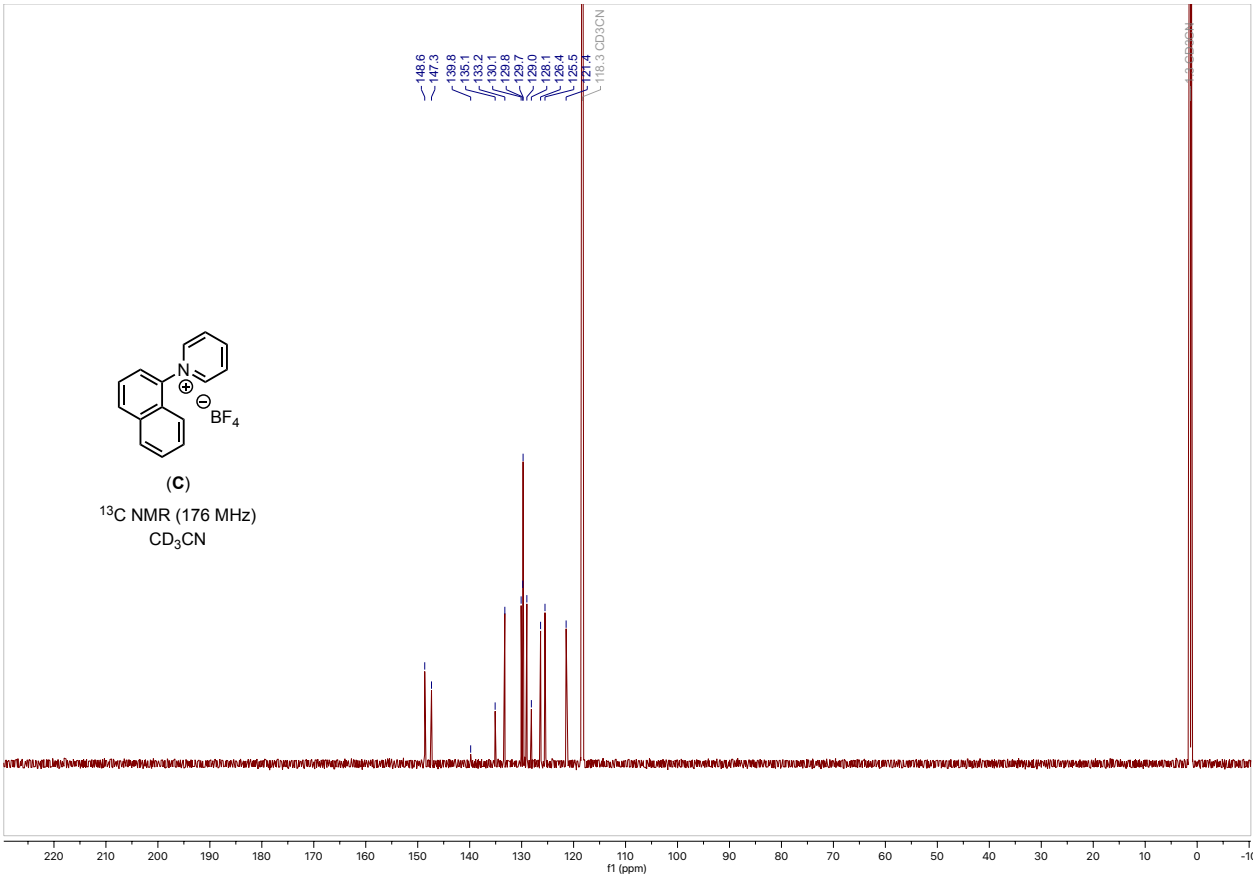

Ph
BF4
(1)
Br
(23)
(24)
f1 (ppm)

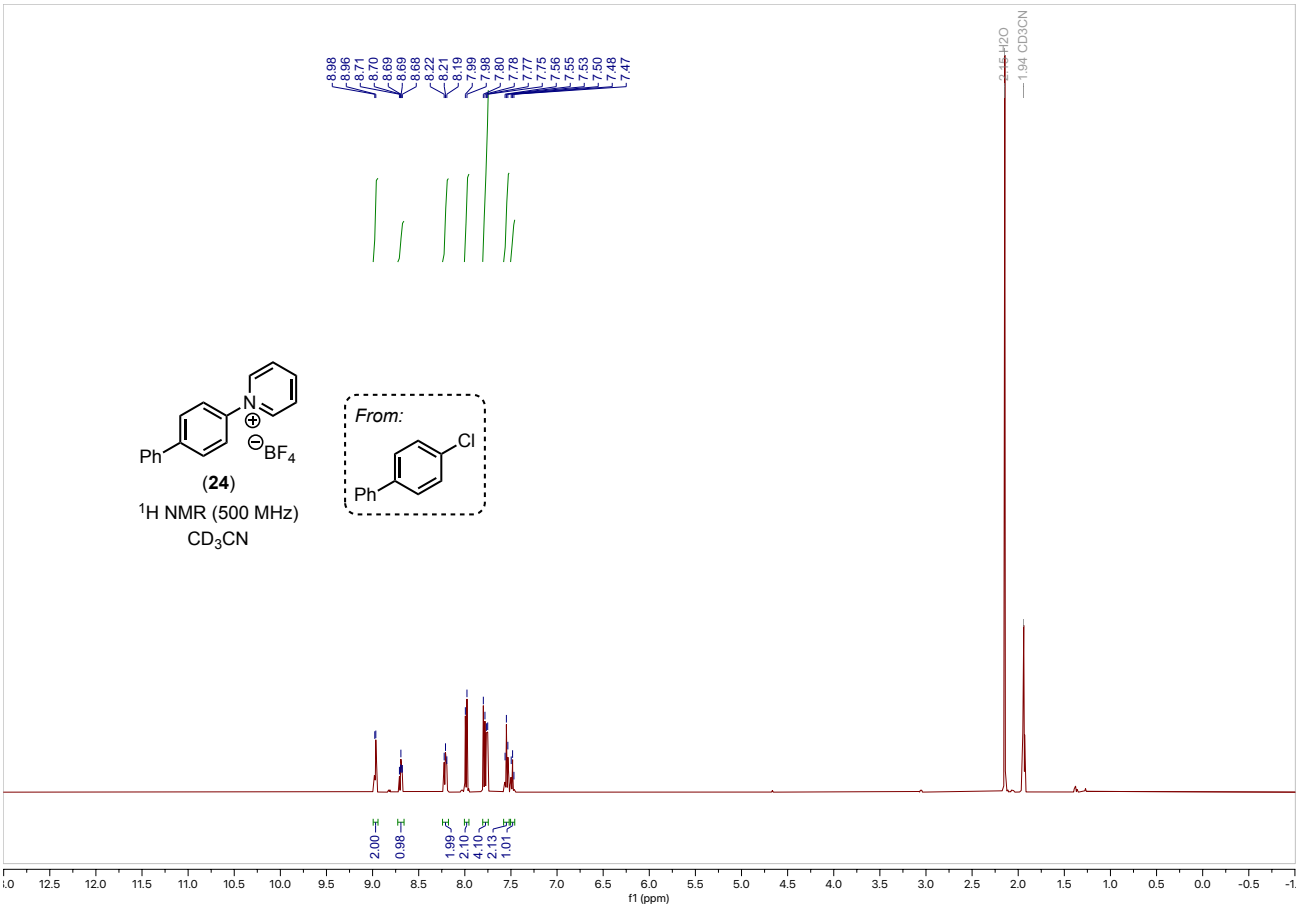


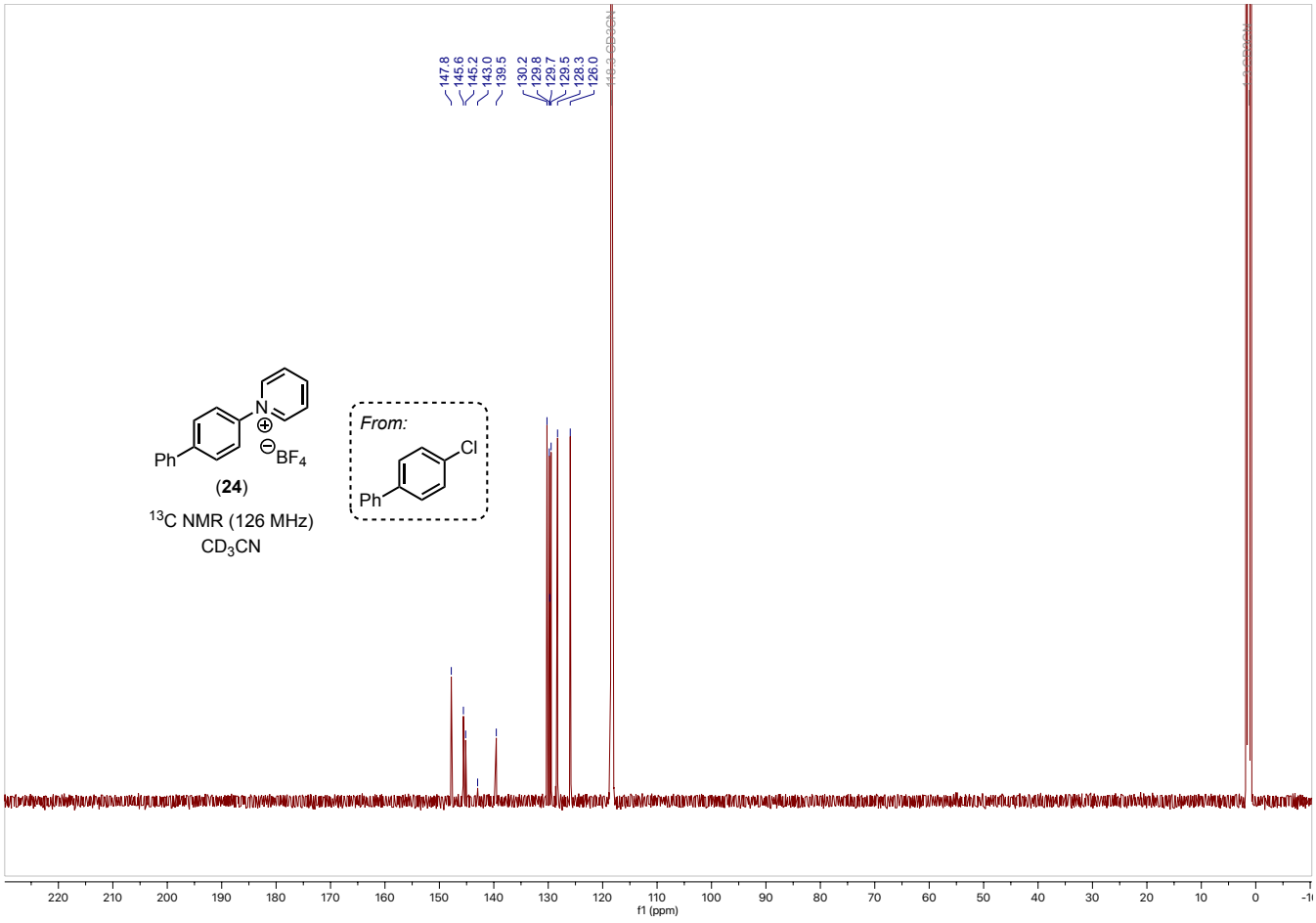
(**C**)

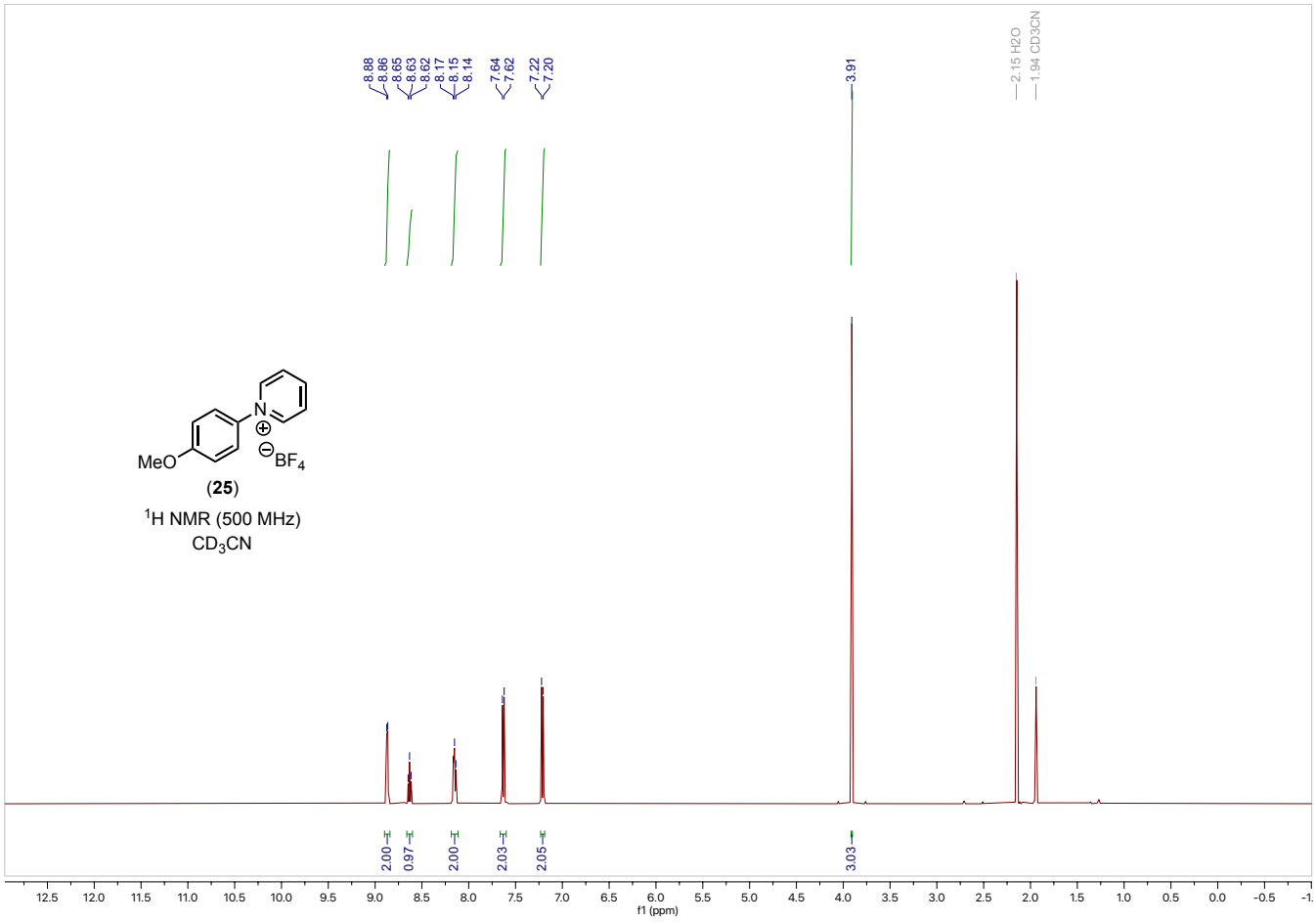
^{1}H NMR (700 MHz)

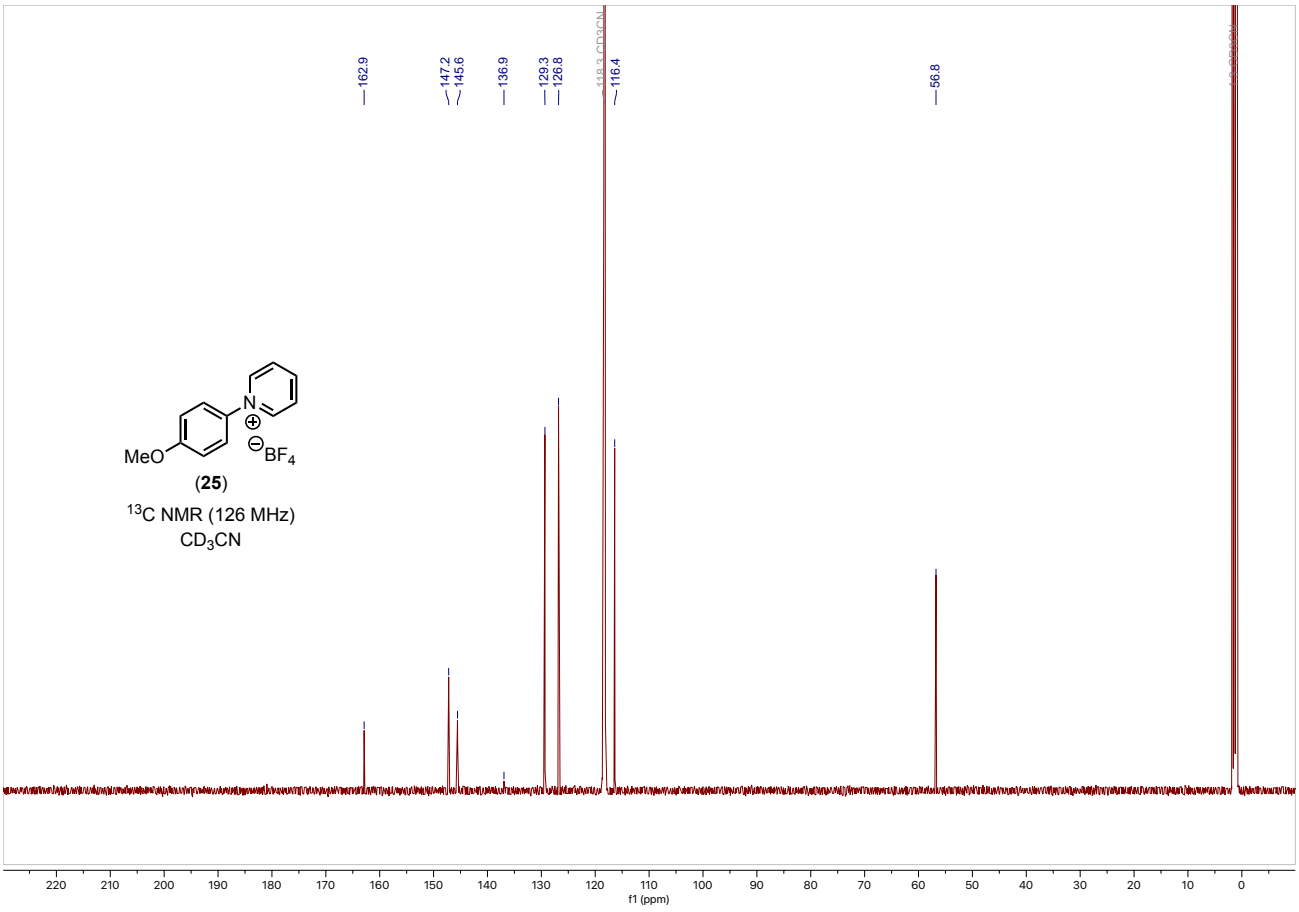
CD_3CN

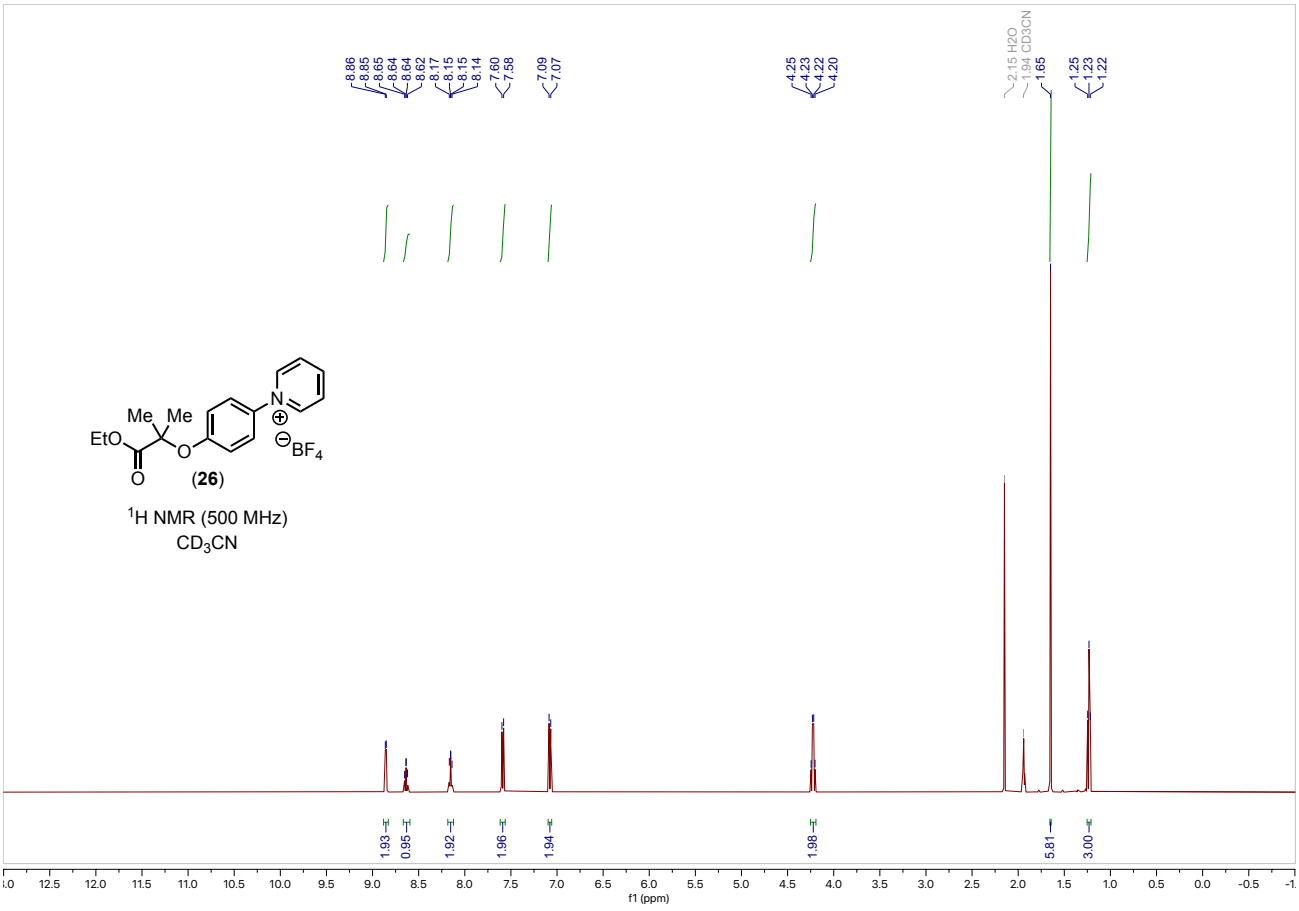

148.6
147.3
139.8
135.1
133.2
130.1
129.8
129.7
129.0
128.1
126.4
125.5
121.4
118.3 CD3CN
BF4
(C)
13C NMR (176 MHz)
CD3CN
f1 (ppm)

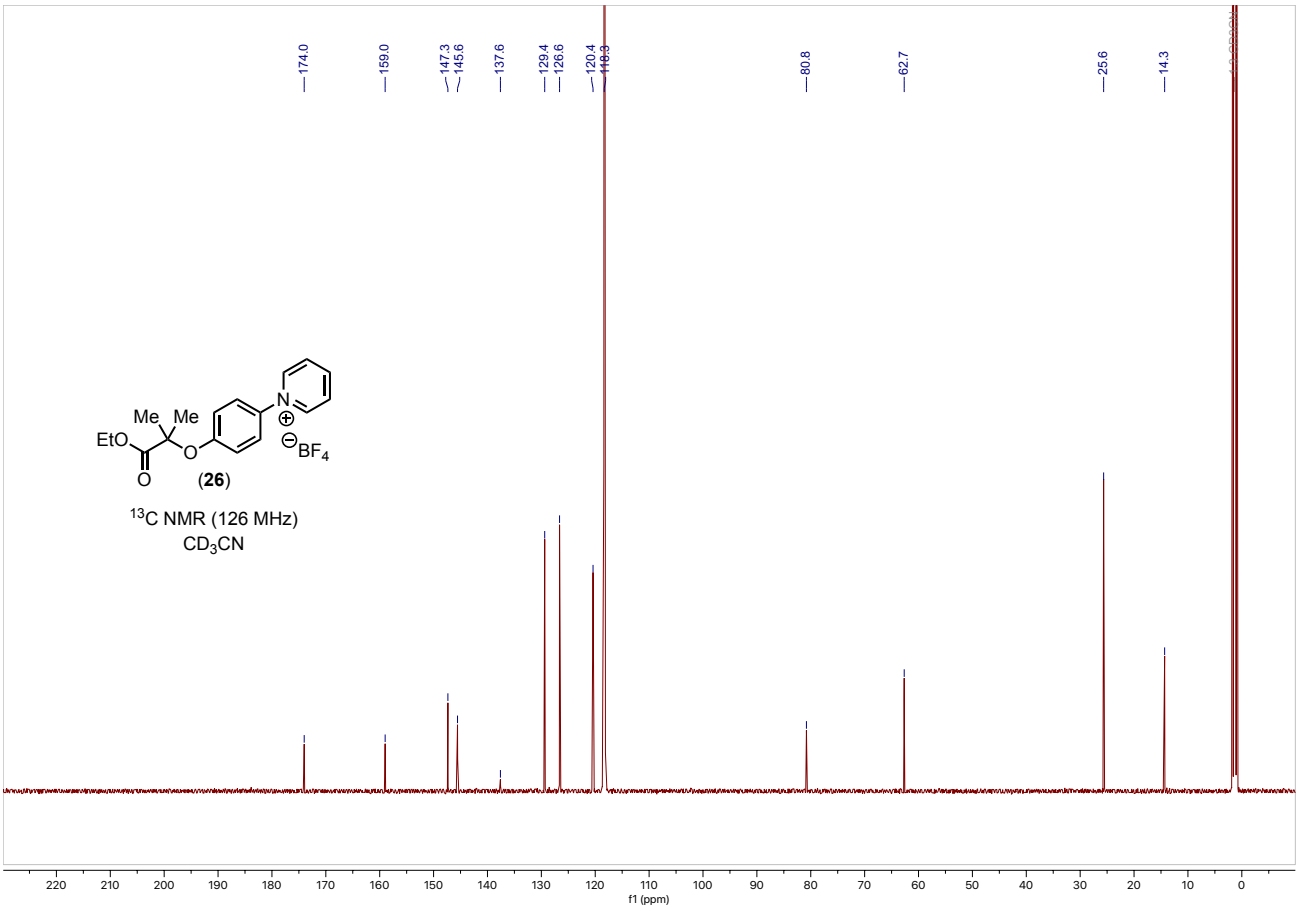

8.98
8.96
8.71
8.70
8.69
8.69
8.68
8.22
8.21
8.19
7.99
7.98
7.80
7.78
7.77
7.75
7.56
7.55
7.53
7.50
7.48
7.47
2.16 H2O
1.94 CD3CN
Ph
BF4
(24)
1H NMR (500 MHz)
CD3CN
From:
Cl
Ph
2.00
0.98
1.99
2.10
4.10
2.13
1.01
f1 (ppm)

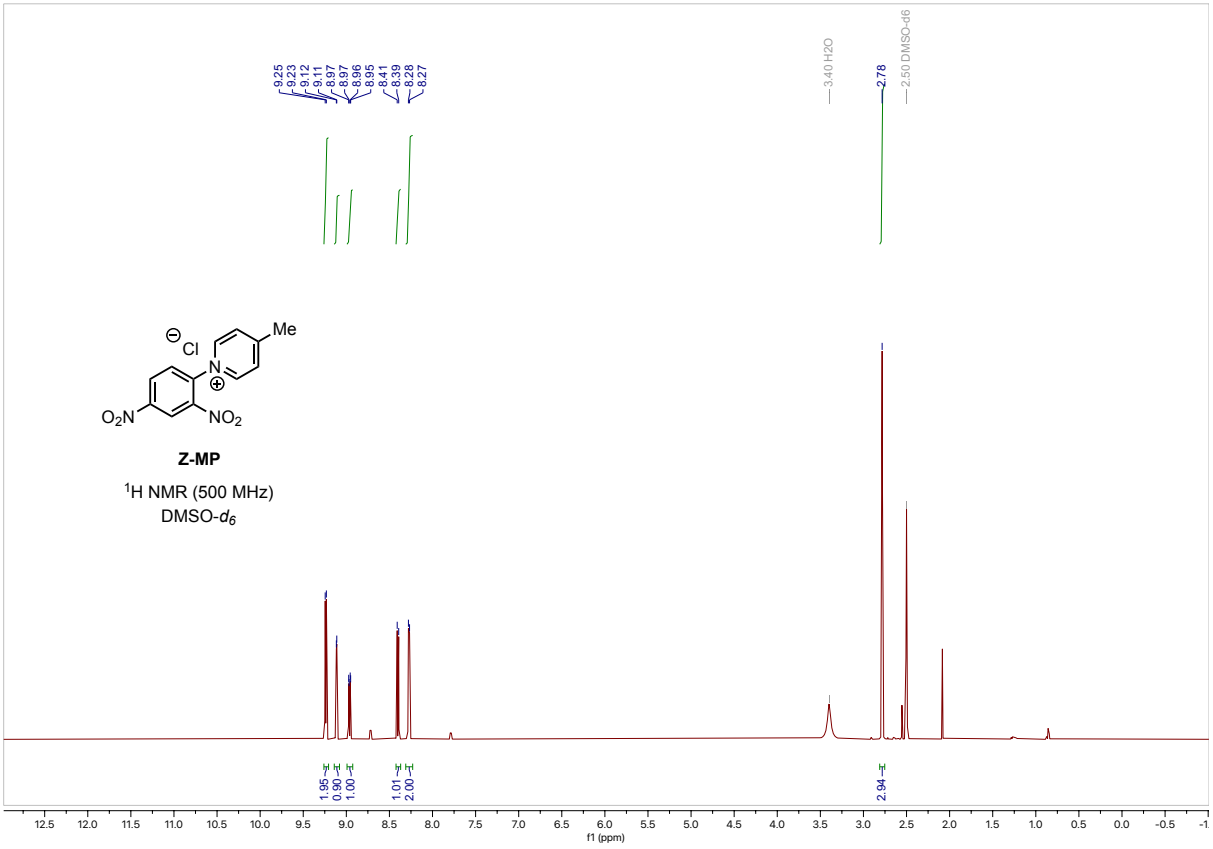

147.8
145.6
145.2
143.0
139.5
130.2
129.8
129.7
129.5
128.3
126.0
Ph
BF4
(24)
13C NMR (126 MHz)
CD3CN
From:
Cl
Ph
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

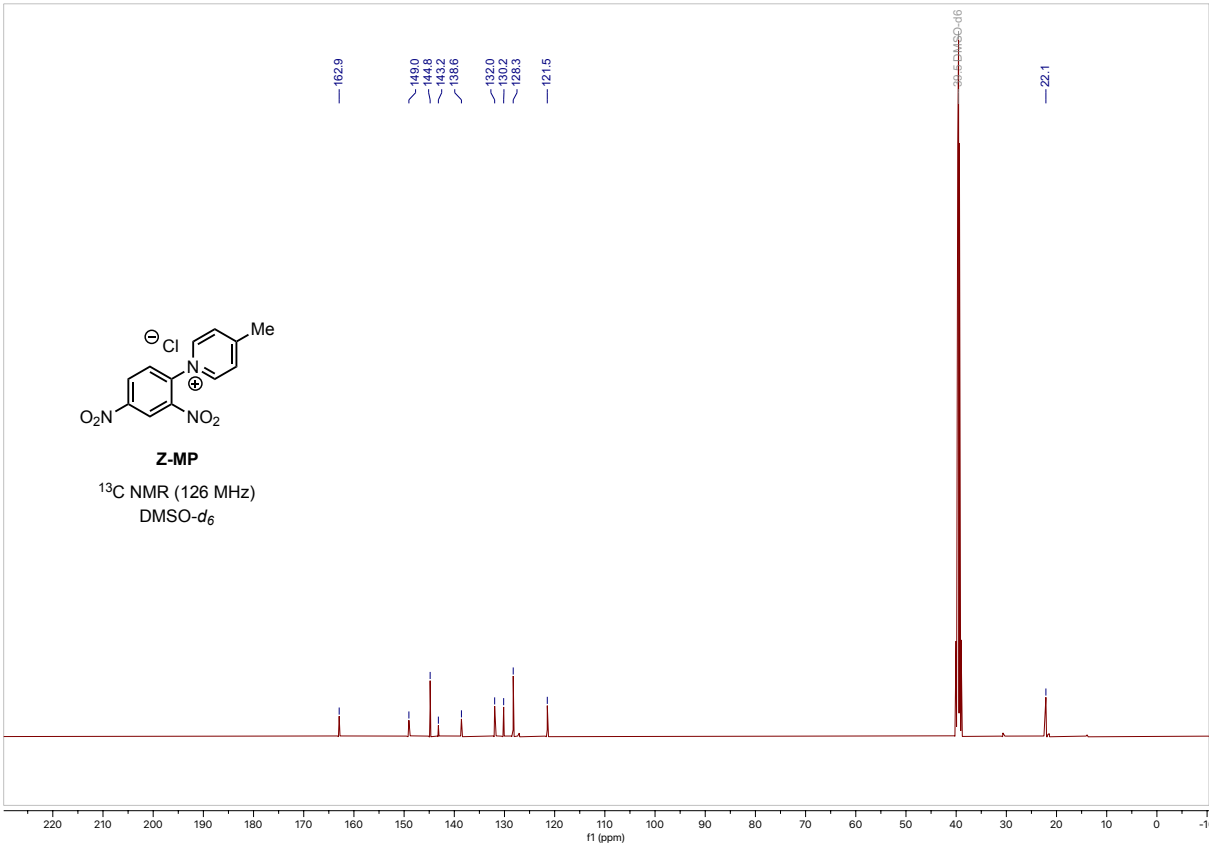

8.88
8.86
8.65
8.63
8.62
8.17
8.15
8.14
7.64
7.62
7.22
7.20
3.91
2.15 H2O
1.94 CD3CN
MeO
BF4
(25)
1H NMR (500 MHz)
CD3CN
2.00
0.97
2.00
2.03
2.05
3.03
f1 (ppm)

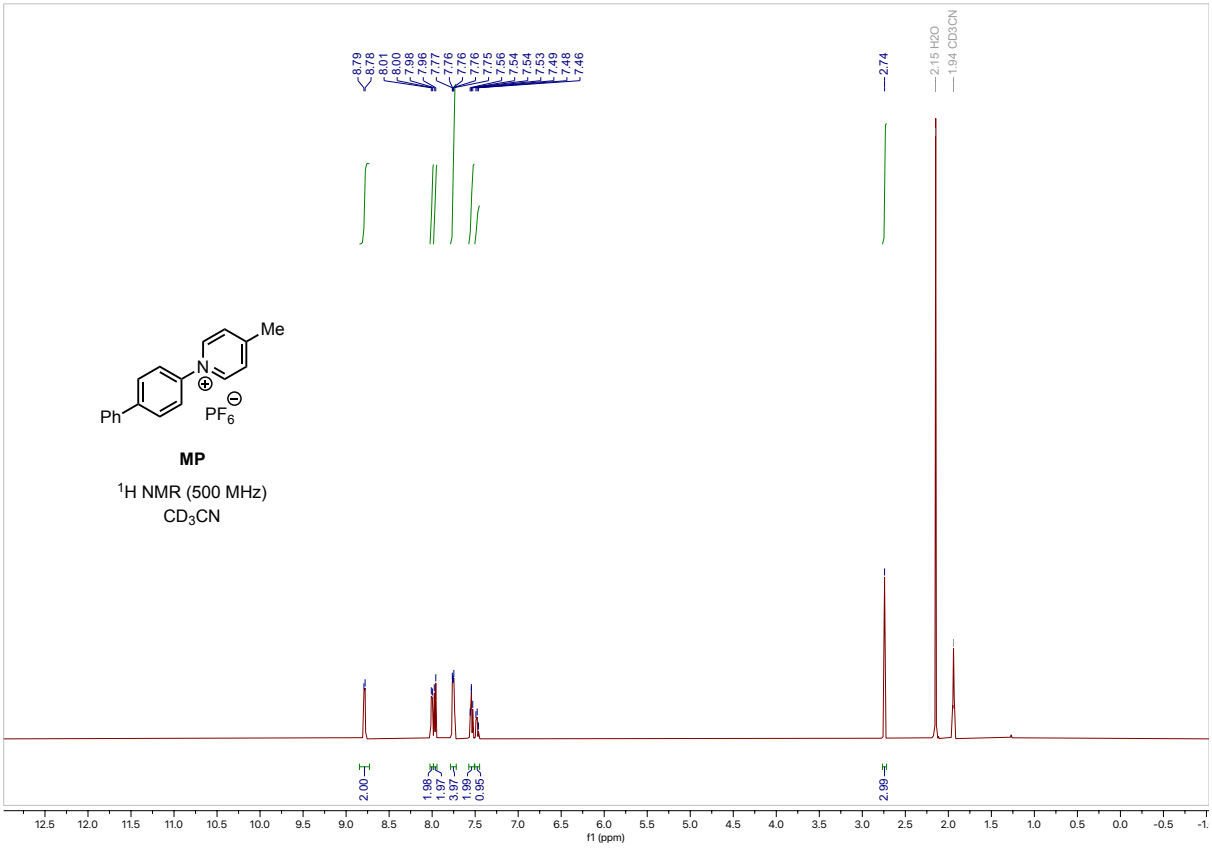

162.9
147.2
145.6
136.9
129.3
128.8
118.3 CD3CN
116.4
56.8
MeO
N
BF4
(25)
13C NMR (126 MHz)
CD3CN
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

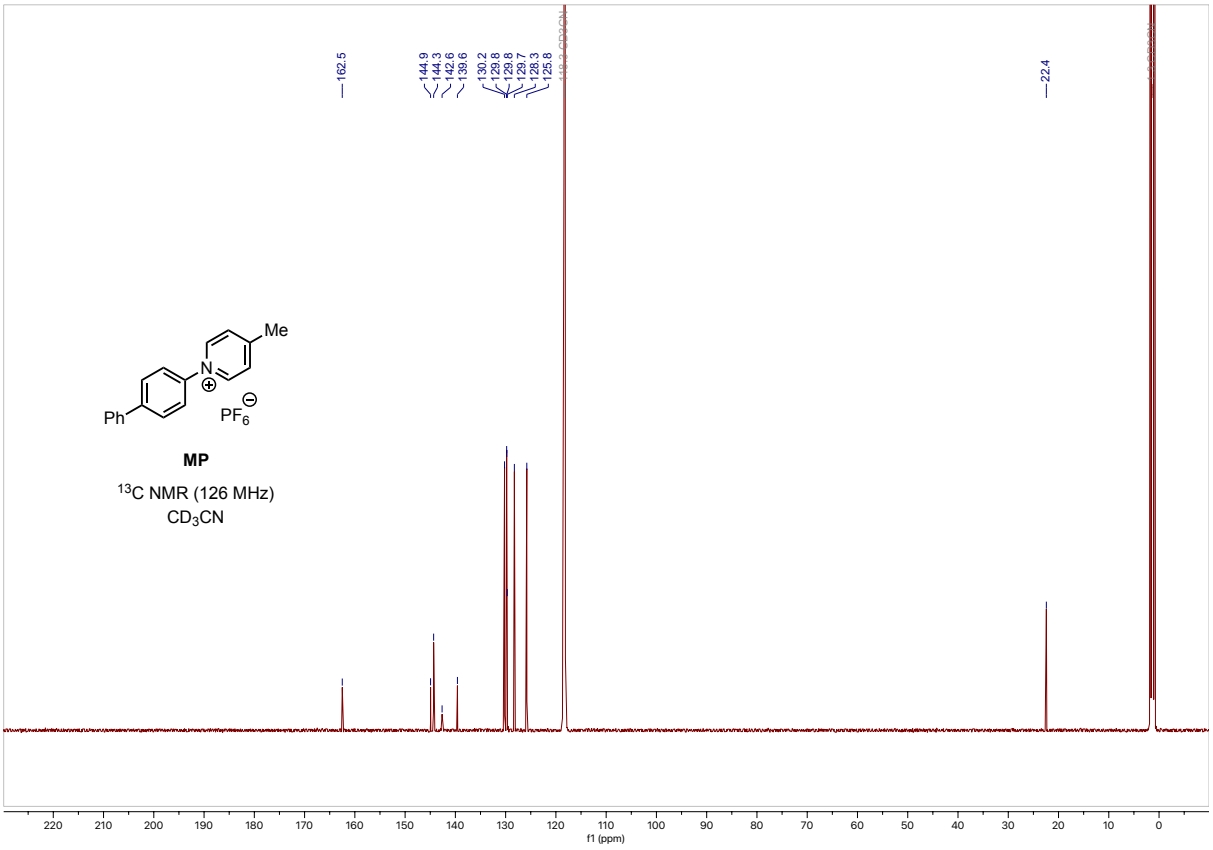

8.86
8.85
8.65
8.64
8.64
8.62
8.17
8.15
8.15
8.14
7.60
7.58
7.09
7.07
4.25
4.23
4.22
4.20
2.15 H2O
1.94 CD3CN
1.65
1.25
1.23
1.22
Me
Me
EtO
O
O
N
BF4
(26)
1H NMR (500 MHz)
CD3CN
1.93
0.95
1.92
1.96
1.94
1.98
5.81
3.00
f1 (ppm)

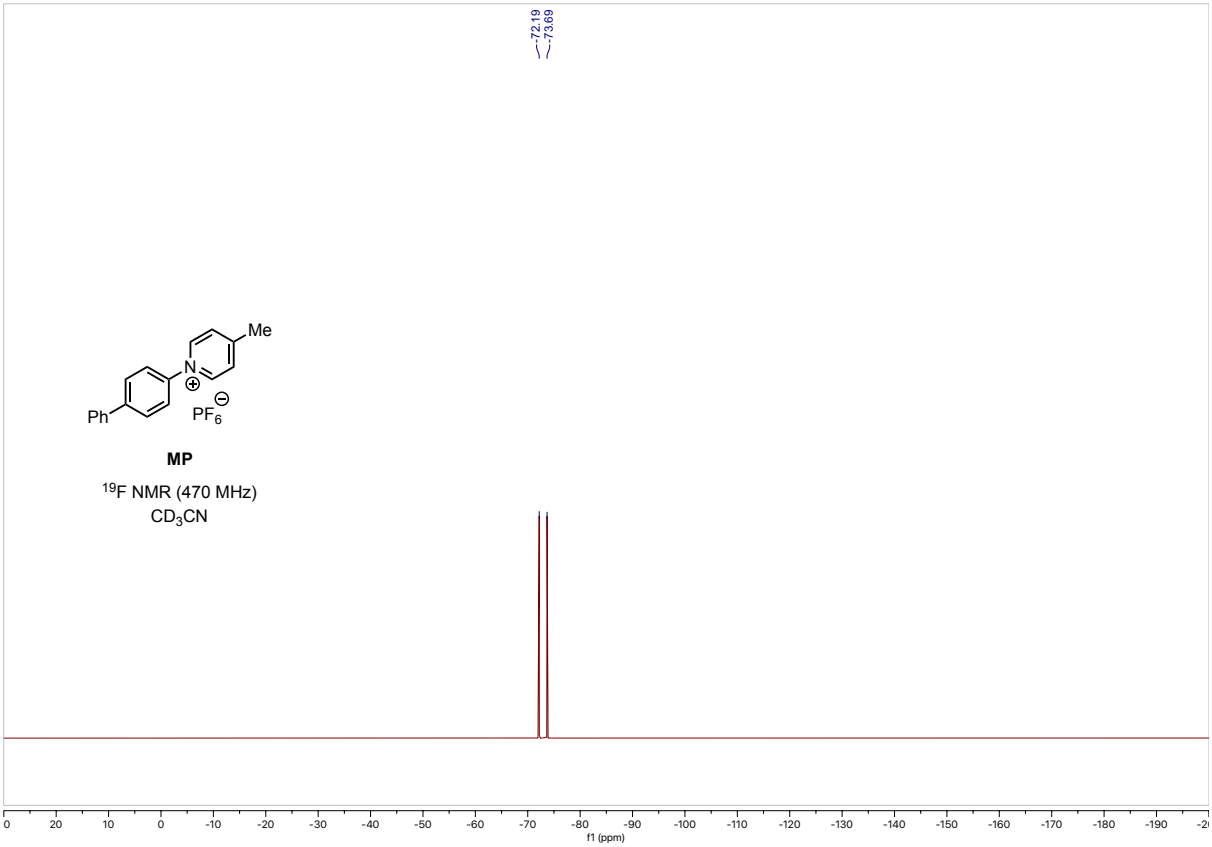

174.0
159.0
147.3
145.6
137.6
129.4
126.6
120.4
118.3
80.8
62.7
25.6
14.3
Me
Me
EtO
O
O
N
BF4
(26)
13C NMR (126 MHz)
CD3CN
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

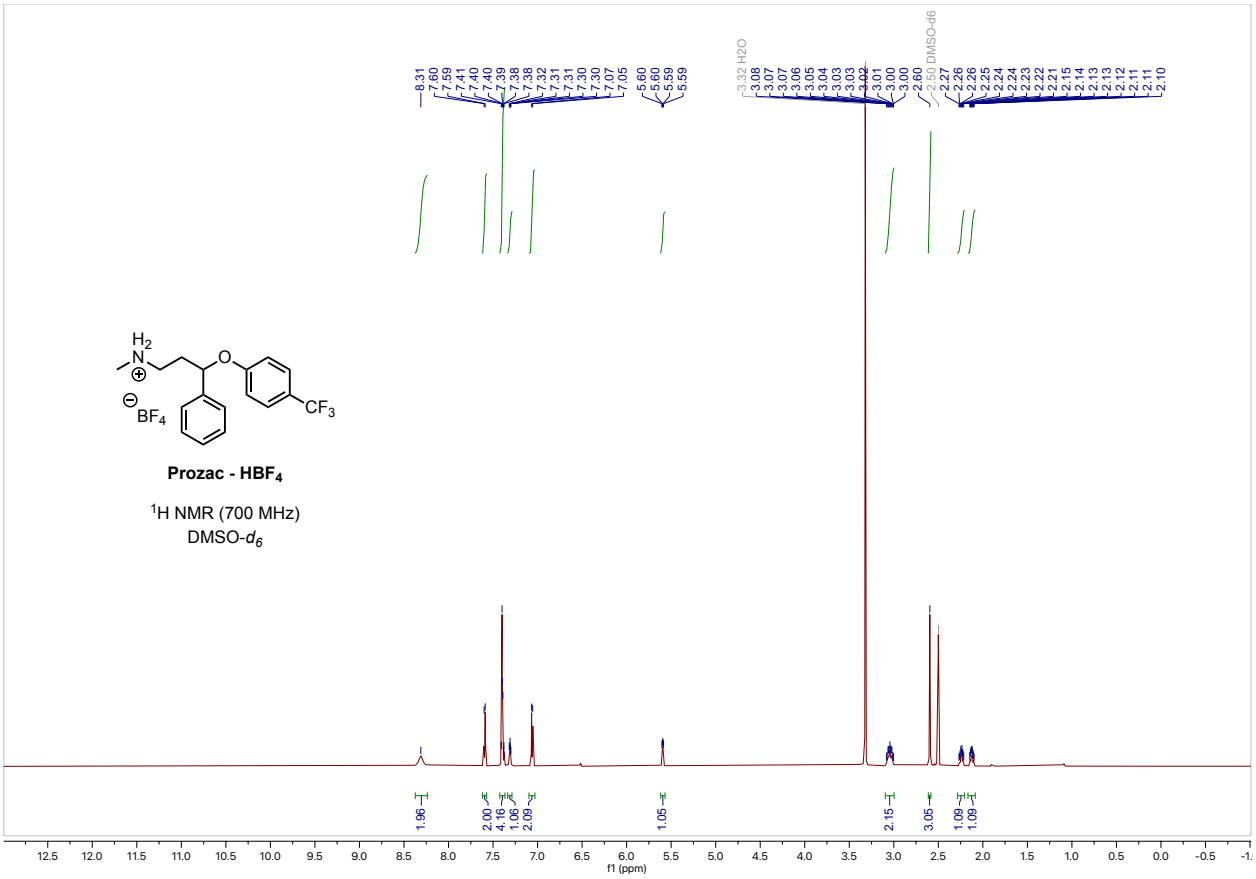

9.25
9.23
9.12
9.11
8.97
8.96
8.95
8.41
8.39
8.28
8.27
3.40 H2O
2.78
2.50 DMSO-d6
Cl
Me
N
O2N
NO2
Z-MP
1H NMR (500 MHz)
DMSO-d6
1.95
0.90
1.00
1.01
2.00
2.94
f1 (ppm)

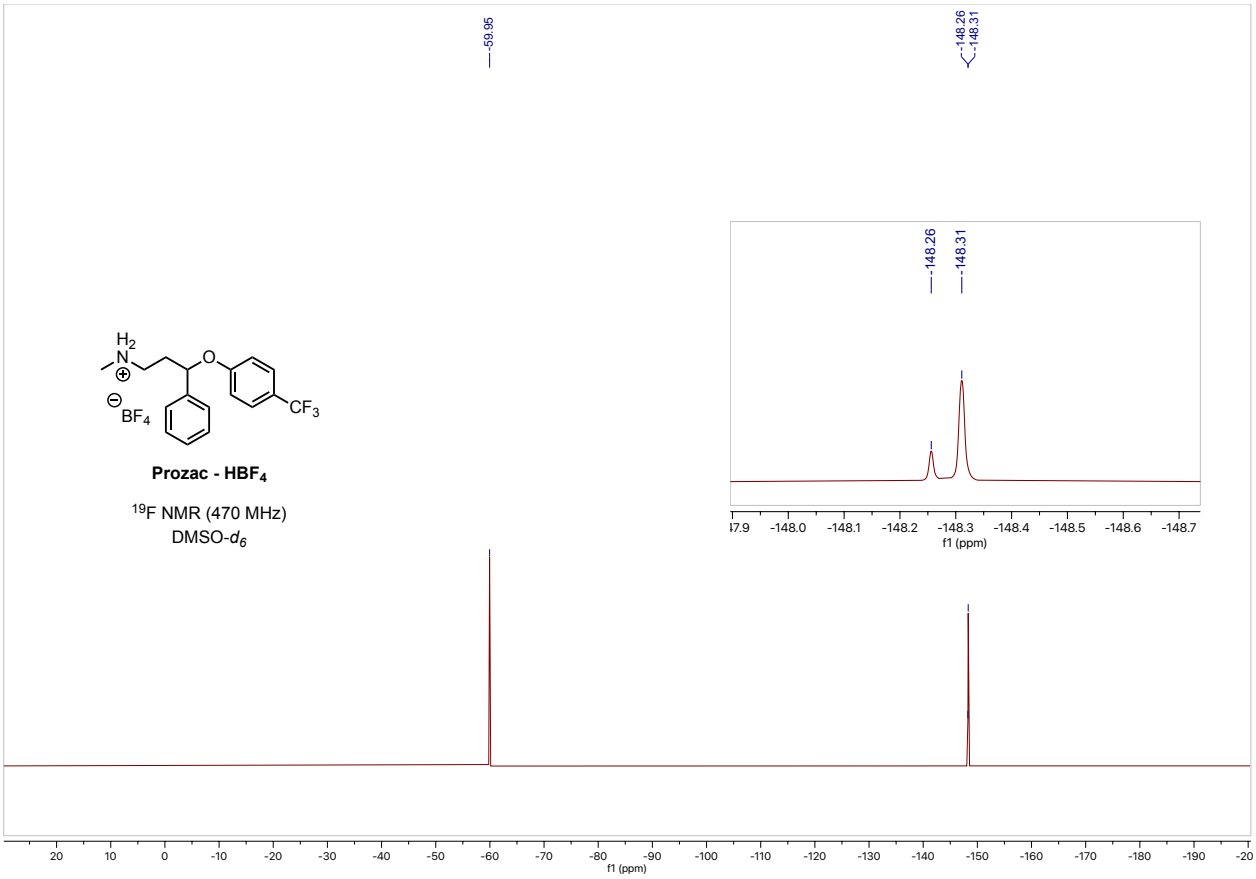

162.9
149.0
144.8
143.2
138.6
132.0
130.2
128.3
121.5
39.5 DMSO-d6
22.1
Cl
Me
N
O2N
NO2
Z-MP
13C NMR (126 MHz)
DMSO-d6
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.79
8.78
8.01
8.00
7.98
7.96
7.77
7.76
7.76
7.76
7.75
7.56
7.54
7.54
7.53
7.49
7.48
7.46
2.74
2.15 H2O
1.94 CD3CN
Me
N
Ph
PF6
MP
1H NMR (500 MHz)
CD3CN
2.00
1.98
1.97
3.97
1.99
0.95
2.99
f1 (ppm)


162.5
144.9
144.3
142.6
139.6
130.2
129.8
129.8
129.7
128.3
125.8
118.3
22.4
Me
N
Ph
PF6
MP
13C NMR (126 MHz)
CD3CN
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-72.19
-73.69
Me
N
Ph
PF6
MP
19F NMR (470 MHz)
CD3CN
0 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)


Prozac - HBF4
1H NMR (700 MHz)
DMSO-d6
f1 (ppm)


-59.95
-148.26
-148.31
H2
N
O
BF4
CF3
Prozac - HBF4
19F NMR (470 MHz)
DMSO-d6
-148.26
-148.31
-148.0
-148.1
-148.2
-148.3
-148.4
-148.5
-148.6
-148.7
f1 (ppm)
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-20
f1 (ppm)