Electronic Supplementary Material (ESI) for Chemical Science.

Supporting Information

Construction of vicinal 4°/3°-carbons *via* reductive Cope rearrangement.

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Contents

General Experimental

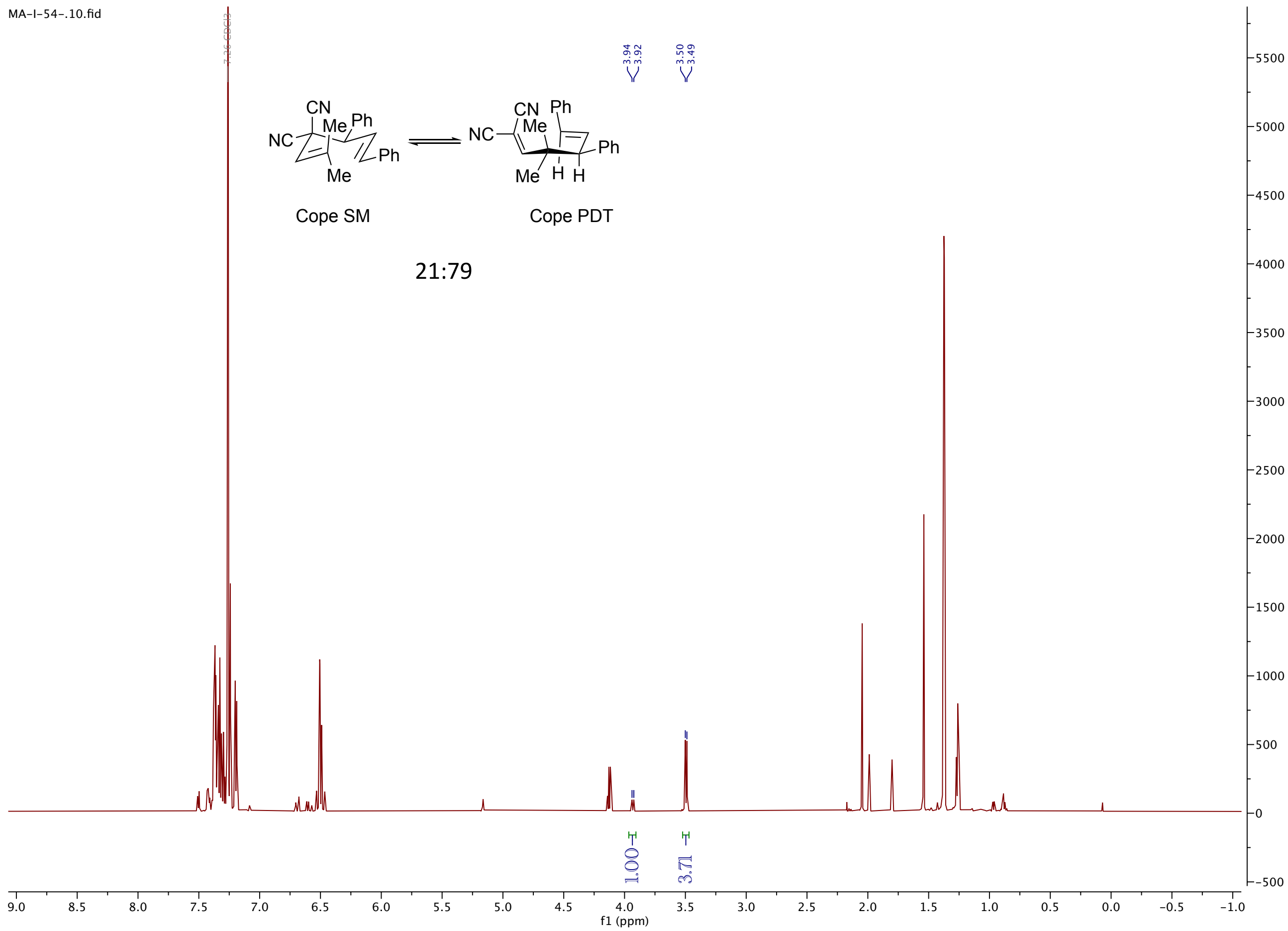
All commercial materials were used without further purification unless otherwise specified. ^{1}H NMR, ^{13}C NMR, ^{19}F NMR spectra were recorded in $CDCl_3$ (with $CHCl_3$ residual peak as an internal standard) or toluene-d_8 (with toluene-d_7 residual peak as an internal standard) using a Bruker 400 MHz or 600 MHz NMR spectrometer. Variable temperature NMR (80 °C) was used to record all samples run in toluene-d_8. All ^{13}C NMR spectra were recorded with complete proton decoupling. HRMS data were recorded on Agilent Time of Flight 6200 spectrometer. Reaction progress was monitored by thin-layer chromatography (TLC) and visualized by UV light, phosphomolybdic acid stain, anisaldehyde and $KMnO_4$ stain. All reactions were carried out using commercially available anhydrous solvents.

Noted abbreviations: m= multiplet, s= singlet, app.= apparent

General procedure for determining the Cope equilibrium with the diphenyl allyl electrophile

To a flame dried Schlenk flask purged with nitrogen gas, 1.0 eq of alkylidene malononitrile, 1.5 eq of diphenyl allyl acetate, and 1 mol % of $Pd(PPh_3)_4$ were added and dissolved in 0.1 M THF. Then 2.0 eq of NaH (60% dispersed in mineral oil) was added and the reaction mixture was heated to 50 °C overnight. Once the reaction was complete the reaction mixture was run through a silica plug with a 50:50 mixture of EtOAc:Hx. The crude material was purified *via* column chromatography with a 0-30% EtOAc gradient. The product mixture was isolated in a 73% yield and a 21:79 ratio of the Cope starting material:Cope product. The NMR spectrum can be seen below on page 4.

Determining the Cope equilibrium with the diphenyl allyl electrophile



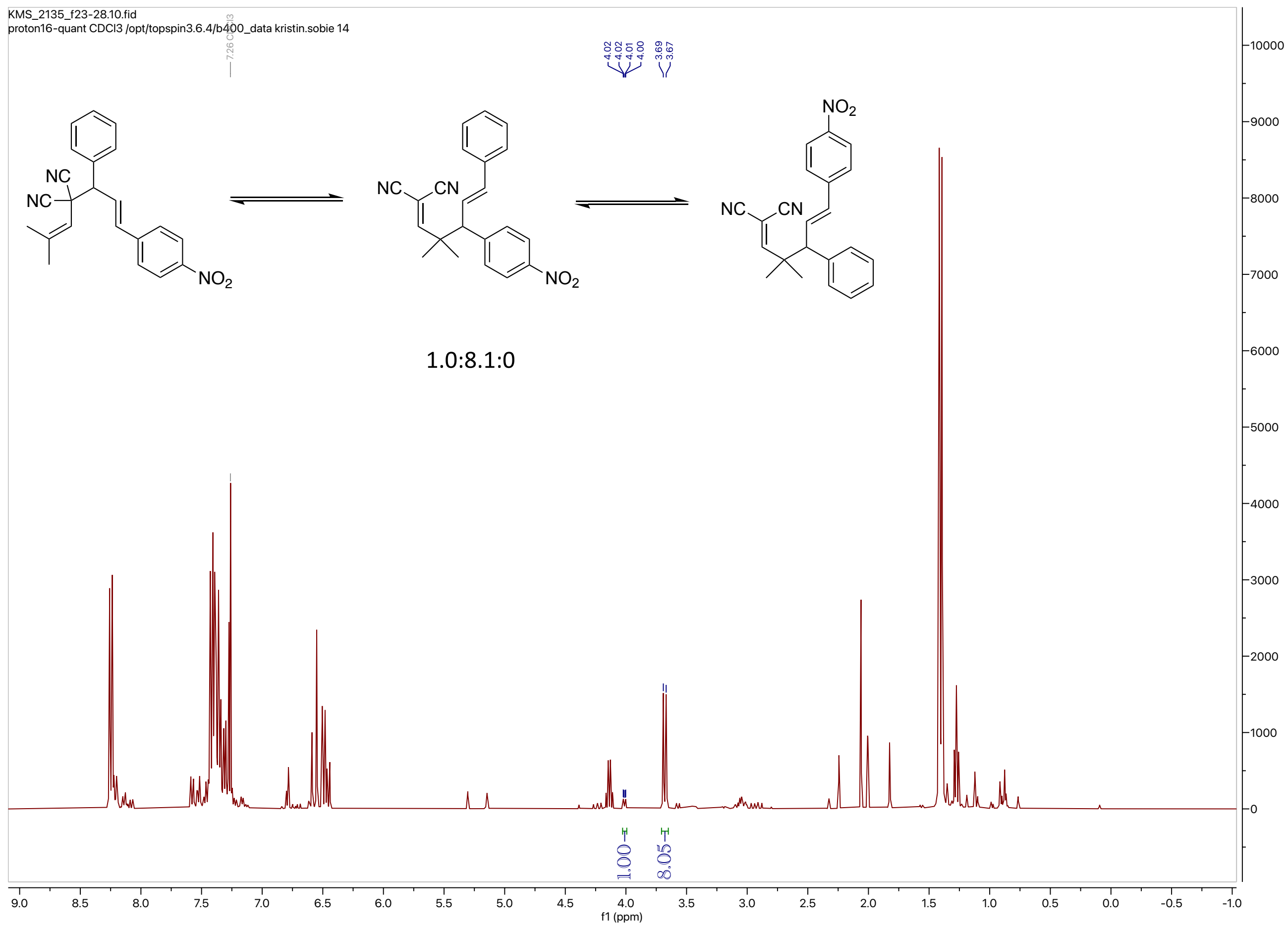
General procedure for determining the Cope equilibrium with the phenyl/p-nitrophenyl allyl electrophile

To a flame dried Schlenk flask purged with nitrogen gas, 1.0 eq of alkylidene malononitrile, 1.3 eq of phenyl/p-nitrophenyl allyl acetate, and 5 mol % of $Pd(PPh_3)_4$ were added and dissolved in 0.1 M DCM. Then 2.0 eq of DMAP was added and the reaction mixture was heated to 40 °C for two hours. Once the reaction was complete the reaction mixture was run through a silica plug with a 100% EtOAc. The crude material was purified *via* column chromatography with a 0-30% EtOAc gradient. The product mixture was isolated in a 45% yield and a 12:88 ratio of the Cope starting material:Cope product. The NMR spectrum can be seen below on page 6.

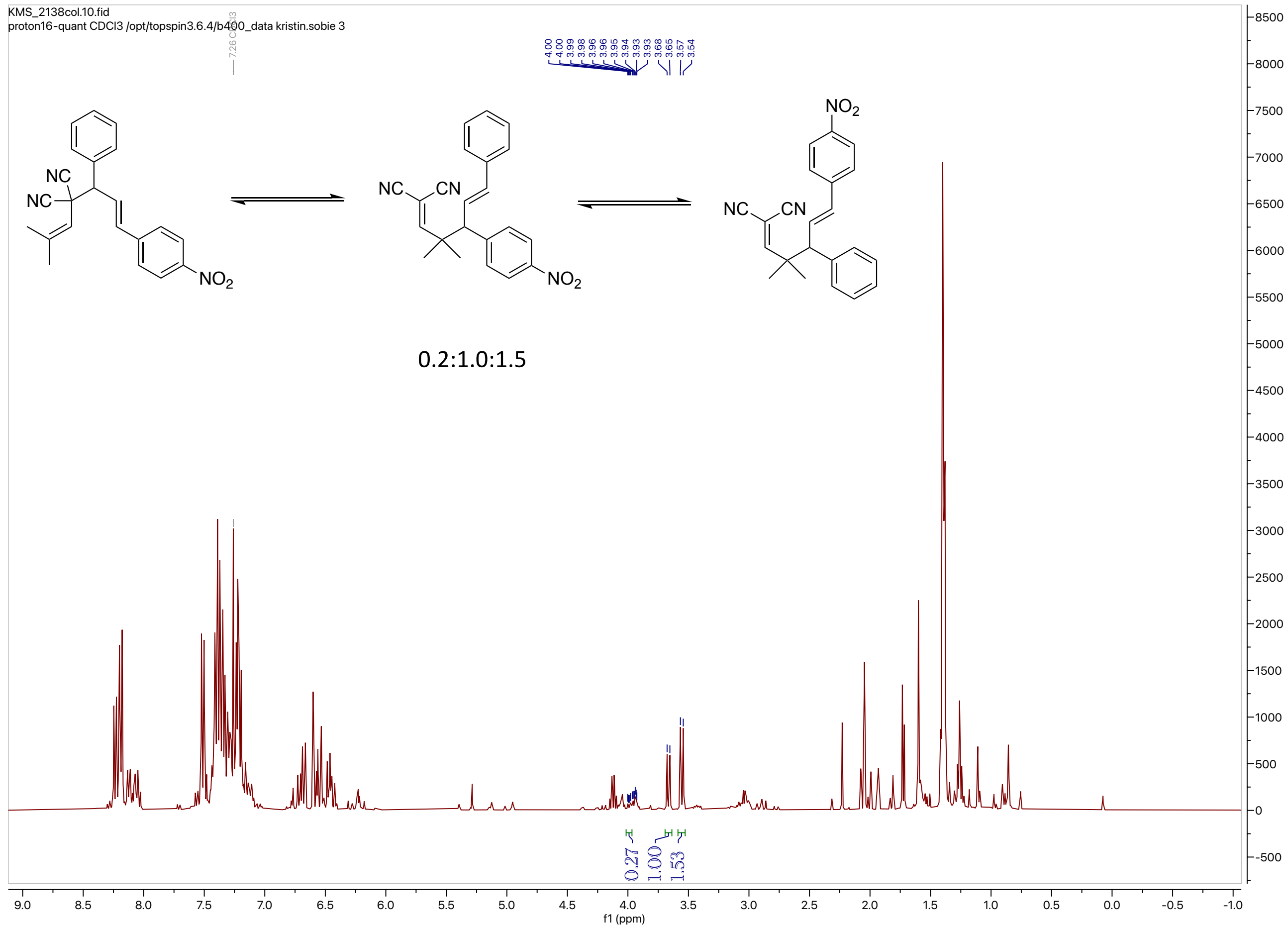
General procedure for the mechanistic investigation

The product mixture from above was heated to 100 °C for three hours in toluene. After three hours the solution was cooled to room temperature and concentrated under reduced pressure. The product was purified *via* column chromatography with a 0-30% EtOAc gradient. This showed us that the dissociative mechanistic pathway can be observed at high temperatures. The NMR spectrum can be seen below on page 7.

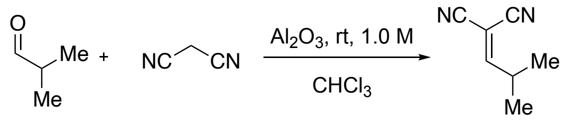
Determining the Cope equilibrium with the phenyl/p-nitrophenyl allyl electrophile



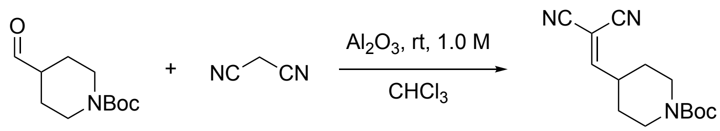
Mechanistic investigation with the phenyl/p-nitrophenyl allyl electrophile



General procedure for nucleophile synthesis:

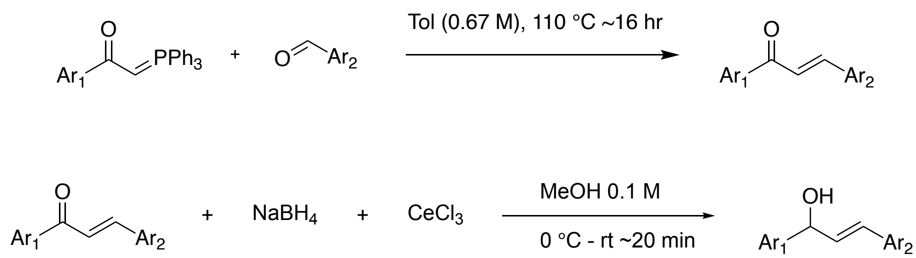


To a flame dried round bottom flask 1.1 eq of aldehyde was added with 1.0 M chloroform. Next, 2.0 eq of neutral alumina was added and let spin for about 5 minutes before the addition of 1.0 eq of malononitrile. The reaction was stirred for 1 hour or until completion by TLC analysis. The alumina was filtered off by gravity filtration and rinsed with dichloromethane due to the low boiling point of the product and concentrated under reduced pressure. The crude material was purified *via* vacuum distillation.



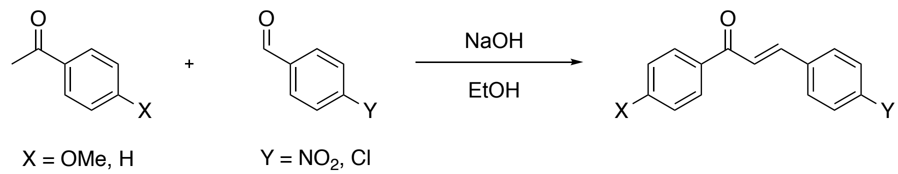
To a flame dried round bottom flask 1.1 eq of aldehyde was added with 1.0 M chloroform. Next, 2.0 eq of neutral alumina was added and let spin for about 5 minutes before the addition of 1.0 eq of malononitrile. The reaction was stirred overnight or until completion by TLC analysis. The alumina was filtered off by gravity filtration and rinsed with chloroform. The solution was concentrated under reduced pressure. The crude material was purified *via* recrystallization with hot ethanol.

General procedure for electrophile synthesis:



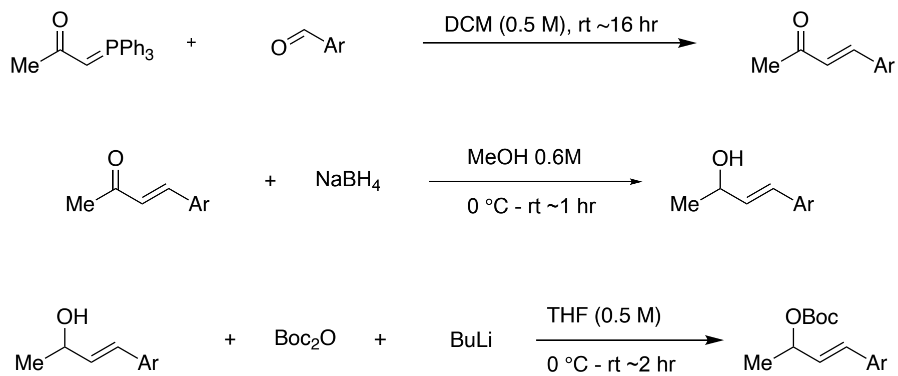
To a microwave vial the Wittig reagent (1.0 eq) was added and dissolved in toluene (0.67 M). The aldehyde (1.0 eq) was added, and the vial was sealed and heated to 110 °C overnight. After 16 hours the reaction mixture was allowed to cool to room temperature before transferring the reaction mixture to a round bottom flask with MeOH and cooled to 0 °C. Cerium chloride (1.2 eq) was added followed by 3.0 eq of sodium borohydride and allowed to spin for approximately 20 minutes or when complete by TLC. The crude reaction mixture was diluted with EtOAc, run through a silica plug, and washed with 100% EtOAc. The crude material was concentrated under reduced pressure and then purified *via* flash column chromatography on a 0-40% gradient EtOAc in hexanes.

Alternative method:



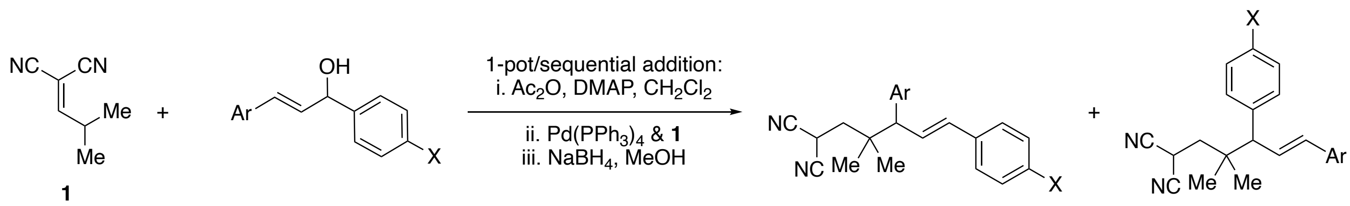
The ketone and benzaldehyde were added in a round bottom flask and dissolved in 0.4 M EtOH. NaOH (0.2 eq) was dissolved in MeOH (minimum amount to dissolve and added to the reaction flask. The reaction mixture was stirred for 16 hours at room temperature before being cooled in an ice bath. The precipitated product was filtered, washed with ice cold ethanol, and then dried over vacuum. The filtrate was concentrated to approximately 5 mL, cooled in an ice bath. The new precipitated product was filtered and dried over vacuum.

General procedure for the methyl/aryl allyl electrophile:



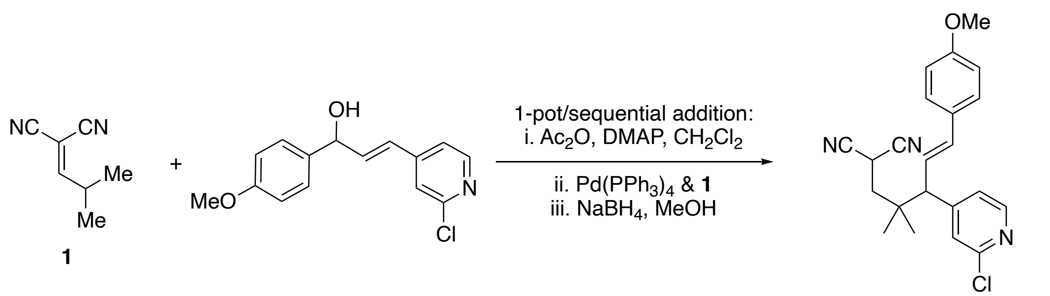
To a round bottom flask the Wittig reagent (1.1 eq) was dissolved in DCM (0.5 M). The aldehyde)1.0 eq) was added and the reaction mixture was stirred at room temperature for 16 hours. After 16 hours, MeOH (0.6 M) was added to the flask and the mixture cooled to 0 °C in an ice bath. Once cooled $NaBH_4$ (3.0 eq) was added, and the reaction stirred for about an hour and warmed to room temperature. Once the reaction was complete by TLC, the mixture was added to a separatory funnel and the organic layer was washed with water and brine (1:1x 3) and dried with anhydrous Na_2SO_4 and the crude material was then concentrated under reduced pressure. The crude material was purified *via* column chromatography on a 0-30% EtOAc gradient, and the allyl alcohol was isolated (on average) in an 80% yield. Once the allyl alcohol was obtained, 1.0 eq was dissolved in THF (0.5 M) and cooled to 0 °C in an ice bath. BuLi (1.1 eq) was added dropwise to the reaction and then Boc_2O (1.2 eq) was added. The reaction was allowed to spin for about 2 hours (or when complete by TLC). The reaction was quenched by the addition of water and extracted with diethyl ether. The organic layer was the washed with brine and dried with anhydrous Na_2SO_4 and the crude material was then concentrated under reduced pressure. The crude material was purified *via* column chromatography on a 0-10% EtOAc gradient. (ref. Org. Lett., 2012, 14, 1, 390).

General procedure for 1-pot sequential addition reductive Cope rearrangement:



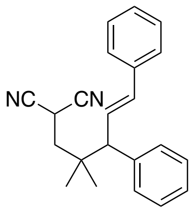
The alcohol reagent (1.3 eq) was dissolved in dichloromethane (0.2 M) in a flame dried Schlenk flask under inert atmosphere. To the solution DMAP (3.0 eq) and acetic anhydride (1.25 eq) were sequentially added. The reaction was stirred at room temperature until the alcohol was fully consumed by TLC analysis. Then dichloromethane (0.1 M) was added followed by 5 mol% palladium tetrakis and 1 eq. **1**. The resulting mixture was heated to 40 °C for 30 min – 1 hour. The reaction was then cooled to 0 °C and MeOH (0.1 M) was added followed by sodium borohydride (2.0 eq), the ice bath was removed, and the reaction was stirred for 10 – 15 min. The reaction was then diluted with EtOAc, run through a silica plug and washed with 100% EtOAc. The crude material was concentrated under reduced pressure and then purified *via* flash column chromatography.

2.8 mmol scale up procedure



3.6 mmol (1 g) of the alcohol reagent (1.3 eq) was dissolved in 14 mL of dichloromethane (0.2 M) in a flame dried Schlenk flask under inert atmosphere. To the solution, 8.4 mmol (1.02 g) of DMAP (3.0 eq) and 3.5 mmol (0.33 mL) of acetic anhydride (1.25 eq) were sequentially added. The reaction was stirred at room temperature until the alcohol was fully consumed by TLC analysis. Then 14 mL more of dichloromethane (0.1 M) was added followed by 0.14 mmol (161 mg) of palladium tetrakis (5 mol%) and 2.8 mmol (335 mg) (1 eq.) of **1**. The resulting mixture was heated to 40 °C for 30 min – 1 hour. The reaction was then cooled to 0 °C and 28 mL of MeOH (0.1 M) was added followed by 5.58 mmol (211 mg) of sodium borohydride (2.0 eq), the ice bath was removed, and the reaction was stirred for 10 – 15 min. The reaction was then diluted with EtOAc, run through a silica plug and washed with 100% EtOAc. The crude material was concentrated under reduced pressure and then purified *via* flash column chromatography on a 0-35% gradient of EtOAc in hexanes. The product was isolated in 2.18 mmol (827 mg) or 78% yield.

(*E*)-2-(2,2-dimethyl-3,5-diphenylpent-4-en-1-yl)malononitrile (10a)



Colorless oil, 76% yield

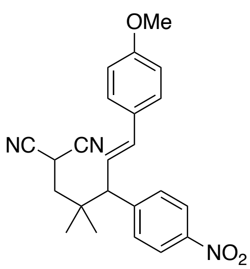
Purified using 0-30% gradient EtOAc in hexanes

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.41 – 7.31 (m, 6H), 7.29 (d, *J* = 7.4 Hz, 1H), 7.26 – 7.22 (m, 3H), 6.58 (dd, *J* = 15.6, 9.7 Hz, 1H), 6.50 (d, *J* = 15.6 Hz, 1H), 3.60 (t, *J* = 6.7 Hz, 1H), 3.30 (d, *J* = 9.7 Hz, 1H), 2.18 – 2.08 (m, 2H), 1.13 (s, 3H), 1.08 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 140.4, 136.9, 133.7, 129.2, 128.8, 128.7, 127.9, 127.8, 127.3, 126.5, 113.8, 113.7, 59.6, 41.9, 39.2, 37.5, 26.2, 24.7, 24.3, 21.6, 20.9, 18.4.

HRMS (DART) m/z: $[M + H]^+$ Calcd for $C_{22}H_{23}N_2$ 315.1861; Found 315.1869.

(*E*)-2-(5-(4-methoxyphenyl)-2,2-dimethyl-3-(4-nitrophenyl)pent-4-en-1-yl)malononitrile (10b)



White solid, 61% yield, >20:1 rr

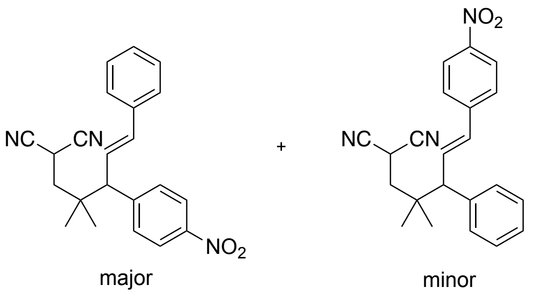
Purified using 0-30% gradient EtOAc in hexanes

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.21 (d, *J* = 8.7 Hz, 2H), 7.43 – 7.38 (m, 2H), 7.33 – 7.28 (m, 2H), 6.90 – 6.84 (m, 2H), 6.47 (d, *J* = 15.6 Hz, 1H), 6.38 (d, *J* = 9.8 Hz, 1H), 3.81 (s, 3H), 3.73 (t, *J* = 6.8 Hz, 1H), 3.43 (d, *J* = 9.8 Hz, 1H), 2.15 (dd, *J* = 8.0, 6.8 Hz, 2H), 1.14 (s, 3H), 1.07 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 159.5, 148.3, 148.2, 146.7, 134.27, 134.25, 129.9, 128.82, 128.81, 127.5, 123.55, 123.52, 123.4, 114.0, 113.38, 113.35, 113.32, 113.3, 59.0, 55.2, 41.4, 37.4, 24.5, 23.5, 18.2.

HRMS (neg-ESI) m/z: $[M - H]^-$ Calcd for $C_{23}H_{22}N_3O_3$ 388.1661; Found 388.1665.

(*E*)-2-(2,2-dimethyl-3-(4-nitrophenyl)-5-phenylpent-4-en-1-yl)malononitrile (10c)



Orange foam, 70% yield, 20:1 rr

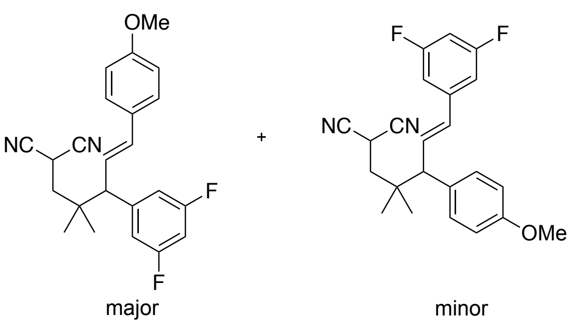
Purified using 0-30% gradient EtOAc in hexanes

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.25 – 8.17 (m, 2H), 7.43 – 7.40 (m, 2H), 7.40 – 7.37 (m, 2H), 7.34 (dd, *J* = 8.4, 6.8 Hz, 2H), 7.31 – 7.27 (m, 1H), 6.58 – 6.49 (m, 2H), 3.75 (t, *J* = 6.8 Hz, 1H), 3.47 (dd, *J* = 7.0, 2.2 Hz, 1H), 2.20 – 2.10 (m, 2H), 1.15 (s, 3H), 1.07 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 147.9, 146.9, 136.1, 135.0, 130.0, 129.9, 128.7, 128.1, 126.3, 125.8, 123.5, 113.3, 113.2, 59.0, 41.4, 37.4, 24.5, 23.6, 18.2.

HRMS (neg-ESI) m/z: $[M - H]^-$ Calcd for $C_{22}H_{20}N_3O_2$ 358.1556; Found 358.1560.

(*E*)-2-(3-(3,5-difluorophenyl)-5-(4-methoxyphenyl)-2,2-dimethylpent-4-en-1-yl)malononitrile (10d)



Pale yellow solid, 44% yield, 6:1 rr

Purified using 0-30% gradient EtOAc in hexanes

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.6 Hz, 2H), 6.90 – 6.85 (m, 2H), 6.78 – 6.75 (m, 2H), 6.73 (td, *J* = 8.8, 4.4 Hz, 1H), 6.45 (d, *J* = 15.5 Hz, 1H), 6.29 (dd, *J* = 15.5, 9.9 Hz, 1H), 3.82 (s, 3H), 3.70 (t, *J* = 6.7 Hz, 1H), 3.25 (d, *J* = 9.9 Hz, 1H), 2.12 (qd, *J* = 14.6, 7.0 Hz, 2H), 1.11 (s, 3H), 1.05 (s, 4H).

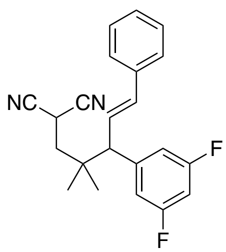
^{13}C NMR (151 MHz, $CDCl_3$) δ 163.5, 163.4, 161.9, 161.8, 159.5, 144.4, 133.8, 129.9, 128.9, 127.5, 123.85, 123.83, 114.02, 114.00, 113.40, 113.37, 113.35, 112.04, 112.00, 111.9, 111.87, 102.6, 102.4, 102.2, 59.0, 55.21, 55.17, 41.4, 37.3, 24.4, 23.6, 18.12, 18.10.

^{19}F NMR (565 MHz, $CDCl_3$) δ -109.2, -110.1.

HRMS (DART) m/z: $[M + H]^+$ Calcd for $C_{23}H_{23}F_2N_2O$ 381.1778; Found 381.1787.

$[M + NH_4]^+$ Calcd for $C_{23}H_{26}F_2N_3O$ 398.2044; Found 398.2051.

(*E*)-2-(3-(3,5-difluorophenyl)-2,2-dimethyl-5-phenylpent-4-en-1-yl)malononitrile (10e)



Clear oil, 77% yield, 3:1 rr

Purified using 0-30% gradient EtOAc in hexanes

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.41 – 7.38 (m, 2H), 7.38 – 7.32 (m, 3H), 7.24 – 7.21 (m, 1H), 6.77 (ddd, *J* = 10.1, 7.4, 2.2 Hz, 2H), 6.52 (d, *J* = 15.5 Hz, 1H), 6.48 – 6.42 (m, 1H), 3.70 (t, *J* = 6.8 Hz, 1H), 3.31 – 3.28 (m, 1H), 2.19 – 2.09 (m, 2H), 1.13 (app. s, 4H), 1.08 (s, 3H).

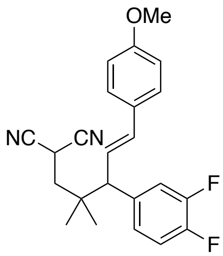
^{13}C NMR (151 MHz, $CDCl_3$) δ 163.6, 163.5, 161.9, 161.8, 144.1, 139.6, 136.2, 134.5, 131.5, 131.5, 130.7, 129.0, 128.6, 128.0, 127.3, 126.3, 126.1, 113.5, 113.4, 113.4, 113.3, 112.1, 112.0, 111.9, 111.9, 111.9, 109.0, 109.0, 108.8, 108.8, 102.8, 102.7, 102.5, 102.4, 59.3, 59.1, 59.1, 59.0, 41.6, 41.4, 37.3, 37.3, 24.5, 24.3, 23.8, 23.7, 18.2, 18.1.

^{19}F NMR (565 MHz, $CDCl_3$) δ -109.1, -110.0.

HRMS (DART) m/z: $[M + H]^+$ Calcd for $C_{22}H_{21}F_2N_2$ 351.1673; Found 351.1677.

$[M + NH_4]^+$ Calcd for $C_{22}H_{24}F_2N_3$ 368.1938; Found 368.1942.

(*E*)-2-(3-(3,4-difluorophenyl)-5-(4-methoxyphenyl)-2,2-dimethylpent-4-en-1-yl)malononitrile (10f)



Yellow oil, 58% yield, 3:1 rr

Purified using 0-30% gradient EtOAc in hexanes

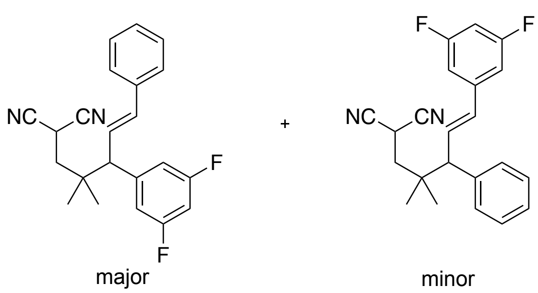
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.7 Hz, 2H), 7.14 – 7.11 (m, 1H), 7.07 – 7.03 (m, 1H), 6.93 (ddd, *J* = 8.5, 4.0, 1.8 Hz, 1H), 6.86 (d, *J* = 8.7 Hz, 2H), 6.43 (d, *J* = 15.5 Hz, 1H), 6.30 (dd, *J* = 15.5, 9.9 Hz, 1H), 3.81 (d, *J* = 1.4 Hz, 4H), 3.70 (t, *J* = 6.7 Hz, 1H), 3.25 (d, *J* = 10.1 Hz, 1H), 2.16 – 2.06 (m, 3H), 1.10 (s, 3H), 1.04 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 159.5, 137.5, 133.6, 129.9, 129.0, 127.5, 125.1, 125.02, 125.01, 124.98, 124.3, 117.9, 117.7, 117.2, 117.0, 114.1, 114.0, 113.4, 113.3, 58.5, 55.3, 41.5, 37.3, 24.4, 23.7, 18.2.

^{19}F NMR (565 MHz, $CDCl_3$) δ -136.9, -139.9. (major regioisomer)

HRMS (neg-ESI) m/z: $[M - H]^-$ Calcd for $C_{23}H_{21}F_2N_2O$ 379.1622; Found 379.1627.

(*E*)-2-(3-(3,4-difluorophenyl)-2,2-dimethyl-5-phenylpent-4-en-1-yl)malononitrile (10g)



Clear oil, 67% yield, 1:1 rr

Purified using 0-30% gradient EtOAc in hexanes

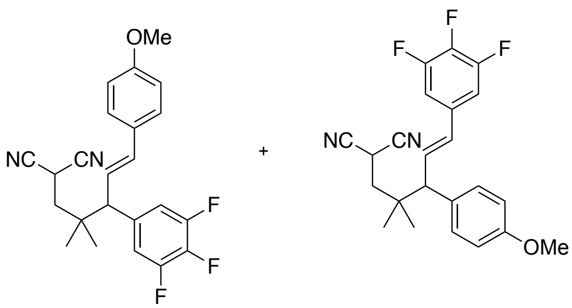
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42 – 7.33 (m, 6H), 7.08 – 7.01 (m, 2H), 6.97 – 6.92 (m, 1H), 6.53 – 6.46 (m, 2H), 3.69 (t, *J* = 6.8 Hz, 1H), 3.58 (t, *J* = 6.8 Hz, 1H), 3.29 (dd, *J* = 9.6, 5.5 Hz, 2H), 2.19 – 2.05 (m, 4H), 1.13 (s, 3H), 1.08 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 139.8, 136.3, 134.2, 131.4, 128.99, 128.98, 128.96, 128.63, 128.60, 128.0, 127.2, 126.6, 126.3, 125.06, 125.04, 125.02, 125.00, 122.54, 122.51, 122.50, 122.47, 117.9, 117.8, 117.3, 117.22, 117.20, 117.1, 114.6, 114.5, 113.5, 113.44, 113.37, 113.3, 59.3, 58.4, 41.6, 41.5, 37.3, 37.2, 29.6, 24.5, 24.3, 23.9, 23.7, 18.2, 18.1.

^{19}F NMR (565 MHz, $CDCl_3$) δ -136.8, -137.7, -138.8, -139.7.

HRMS (neg-ESI) m/z: $[M - H]^-$ Calcd for $C_{22}H_{19}F_2N_2$ 349.1517; Found 349.1530.

(*E*)-2-(5-(4-methoxyphenyl)-2,2-dimethyl-3-(3,4,5-trifluorophenyl)pent-4-en-1-yl)malononitrile (10h)



Rose oil, 79% yield, 15:1 rr

Purified using 0-30% gradient EtOAc in hexanes

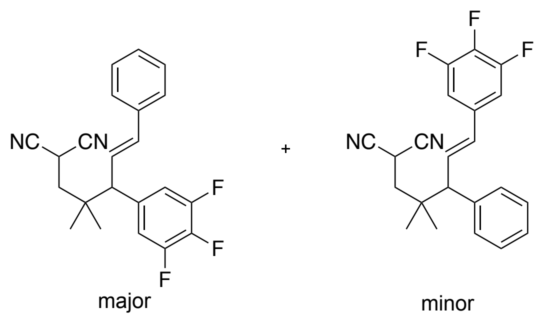
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.7 Hz, 2H), 6.89 – 6.81 (m, 4H), 6.44 (d, *J* = 15.5 Hz, 1H), 6.23 (dd, *J* = 15.5, 9.9 Hz, 1H), 3.81 (s, 3H), 3.76 – 3.68 (m, 1H), 3.22 (d, *J* = 9.9 Hz, 1H), 2.16 – 2.06 (m, 2H), 1.10 (s, 3H), 1.05 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 159.6, 135.0, 134.2, 128.8, 128.0, 127.6, 123.4, 114.1, 113.3, 113.2, 113.13, 113.10, 113.02, 112.99, 58.6, 55.3, 41.5, 37.3, 24.5, 23.5, 18.2.

^{19}F NMR (565 MHz, $CDCl_3$) δ -133.6, -133.7, -162.1.

HRMS (DART) m/z: $[M + H]^+$ Calcd for $C_{23}H_{22}F_3N_2O$ 399.1684; Found 399.1682.

(*E*)-2-(2,2-dimethyl-5-phenyl-3-(3,4,5-trifluorophenyl)pent-4-en-1-yl)malononitrile (10i)



Clear oil, 52% yield, 2:1 rr

Purified using 0-30% gradient EtOAc in hexanes

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 – 7.33 (m, 6H), 6.86 (dd, J = 8.3, 6.2 Hz, 2H), 6.51 (d, J = 15.6 Hz, 1H), 6.43 – 6.37 (m, 1H), 3.71 (t, J = 6.7 Hz, 1H), 3.57 (t, J = 6.7 Hz, 1H), 3.28 – 3.25 (m, 1H), 2.15 – 2.09 (m, 3H), 1.12 (s, 3H), 1.07 (s, 3H).

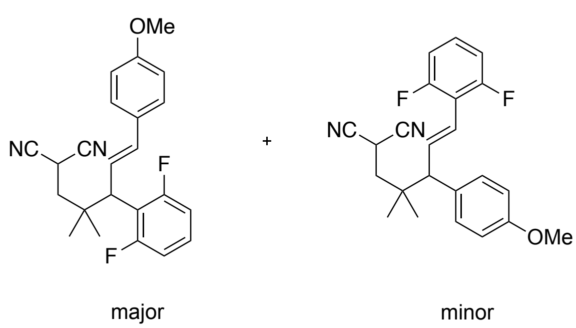
^{13}C NMR (151 MHz, $CDCl_3$) δ 140.0, 136.5, 135.2, 131.2, 130.9, 129.4, 129.13, 129.12, 128.6, 127.8, 126.8, 126.2, 113.84, 113.80, 113.7, 113.63, 113.60, 113.57, 113.49, 113.46, 110.54, 110.51, 110.43, 110.40, 59.7, 59.0, 42.1, 41.9, 37.77, 37.75, 25.1, 24.9, 24.3, 24.0, 18.62, 18.57.

^{19}F NMR (565 MHz, $CDCl_3$) δ -133.5, -133.5, -134.4, -161.3, -161.3, -161.9.

HRMS (DART) m/z: $[M + H]^+$ Calcd for $C_{22}H_{20}F_3N_2$ 369.1579; Found 369.1588.

$[M + NH_4]^+$ Calcd for $C_{22}H_{23}F_3N_3$ 386.1844; Found 386.1830.

(*E*)-2-(3-(2,6-difluorophenyl)-5-(4-methoxyphenyl)-2,2-dimethylpent-4-en-1-yl)malononitrile (10j)



Clear oil, 88% yield, 5:1 rr

Purified using 0-30% gradient EtOAc in hexanes

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32 (d, J = 8.7 Hz, 2H), 7.22 (tt, J = 8.3, 6.2 Hz, 1H), 6.93 – 6.85 (m, 4H), 6.63 (ddt, J = 15.5, 10.0, 3.4 Hz, 1H), 6.48 (dd, J = 15.8, 9.9 Hz, 1H), 3.81 (app. s, 4H), 3.76 (t, J = 6.6 Hz, 1H), 2.20 – 2.14 (m, 2H), 1.12 (app. d, J = 20.8 Hz, 7H).

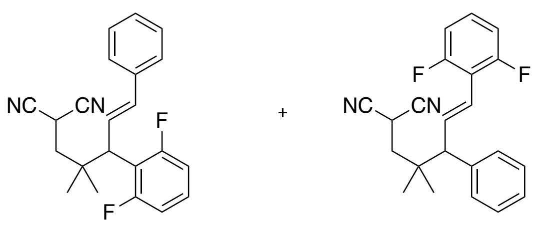
^{13}C NMR (151 MHz, $CDCl_3$) δ 159.4, 134.0, 130.0, 129.3, 128.8, 128.75, 128.68, 127.6, 123.2, 123.1, 114.0, 113.9, 113.5, 111.5, 55.3, 55.2, 49.5, 41.4, 38.5, 24.51, 24.49, 24.4, 18.24, 18.17.

^{19}F NMR (565 MHz, $CDCl_3$) δ -104.8, -104.8, -111.4, -111.4.

HRMS (DART) m/z: $[M + H]^+$ Calcd for $C_{23}H_{23}F_2N_2O$ 381.1778; Found 381.1780.

$[M + NH_4]^+$ Calcd for $C_{23}H_{26}F_2N_3O$ 398.2044; Found 398.2044.

(*E*)-2-(3-(2,6-difluorophenyl)-2,2-dimethyl-5-phenylpent-4-en-1-yl)malononitrile (10k)



Yellow oil, 86% yield, 1.5:1 rr

Purified using 0-30% gradient EtOAc in hexanes

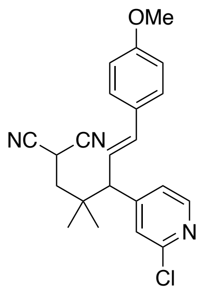
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 (d, J = 7.7 Hz, 2H), 7.34 (dt, J = 13.3, 7.6 Hz, 4H), 7.30 – 7.26 (m, 2H), 7.26 – 7.20 (m, 3H), 7.14 (tt, J = 8.4, 6.2 Hz, 1H), 6.97 – 6.84 (m, 4H), 6.56 (d, J = 15.6 Hz, 1H), 6.50 (d, J = 16.0 Hz, 1H), 3.84 (d, J = 10.1 Hz, 1H), 3.76 (t, J = 6.6 Hz, 1H), 3.61 (t, J = 6.7 Hz, 1H), 3.28 (d, J = 10.2 Hz, 1H), 2.22 – 2.15 (m, 2H), 2.15 – 2.04 (m, 1H), 1.16 (s, 3H), 1.13 (s, 2H), 1.12 (s, 3H), 1.09 (s, 2H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 161.6, 161.5, 159.90, 159.85, 139.8, 136.5, 135.4, 135.34, 135.29, 134.6, 129.1, 128.92, 128.85, 128.77, 128.62, 128.57, 128.52, 128.2, 128.1, 128.0, 127.8, 127.2, 126.4, 125.5, 125.44, 125.41, 119.6, 116.4, 116.3, 116.2, 114.0, 113.54, 113.49, 113.45, 112.6, 112.4, 111.52, 111.49, 111.41, 111.38, 111.35, 60.8, 49.4, 41.6, 41.3, 38.4, 37.2, 36.5, 24.6, 24.5, 24.40, 24.38, 24.37, 24.0, 23.2, 21.4, 18.2, 18.1.

^{19}F NMR (565 MHz, $CDCl_3$) δ -104.7, -111.4, -113.6, -113.6.

HRMS (neg-ESI) m/z: $[M - H]^-$ Calcd for $C_{22}H_{19}F_2N_2$ 349.1517; Found 349.1517.

(*E*)-2-(3-(2-chloropyridin-4-yl)-5-(4-methoxyphenyl)-2,2-dimethylpent-4-en-1-yl)malononitrile (10l)



Orange foam, 87% yield, >20:1 rr

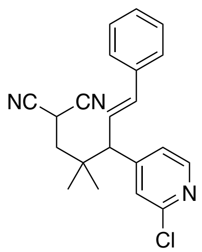
Purified using 0-30% gradient EtOAc in hexanes

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.34 (d, *J* = 5.1 Hz, 1H), 7.33 – 7.29 (m, 2H), 7.19 (d, *J* = 1.5 Hz, 1H), 7.08 (dd, *J* = 5.1, 1.5 Hz, 1H), 6.89 – 6.85 (m, 2H), 6.47 (d, *J* = 15.5 Hz, 1H), 6.28 (dd, *J* = 15.5, 10.0 Hz, 1H), 3.82 (s, 3H), 3.74 (t, *J* = 6.8 Hz, 1H), 3.28 (d, *J* = 10.0 Hz, 1H), 2.19 – 2.09 (m, 2H), 1.13 (s, 3H), 1.07 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 159.8, 152.8, 151.8, 149.5, 134.9, 128.6, 127.7, 124.7, 123.1, 122.5, 114.1, 113.2, 113.1, 58.6, 55.3, 41.4, 37.3, 24.7, 23.4, 18.2.

HRMS (DART) m/z: $[M + H]^+$ Calcd for $C_{22}H_{23}ClN_3O$ 380.1530; Found 380.1527.

(*E*)-2-(3-(2-chloropyridin-4-yl)-2,2-dimethyl-5-phenylpent-4-en-1-yl)malononitrile (10m)



Orange foam, 52% yield, >20:1 rr

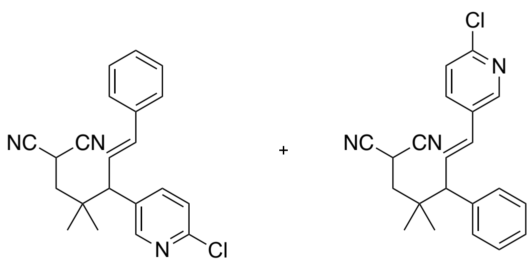
Purified using 0-30% gradient EtOAc in hexanes

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.35 (d, *J* = 5.1 Hz, 1H), 7.41 – 7.32 (m, 5H), 7.32 – 7.27 (m, 1H), 7.20 (d, *J* = 1.4 Hz, 1H), 7.09 (dd, *J* = 5.1, 1.6 Hz, 1H), 6.54 (d, *J* = 15.5 Hz, 1H), 6.43 (dd, *J* = 15.5, 9.9 Hz, 1H), 3.74 (t, *J* = 6.8 Hz, 1H), 3.32 (d, *J* = 9.9 Hz, 1H), 2.20 – 2.08 (m, 2H), 1.14 (s, 3H), 1.08 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 153.0, 152.3, 150.0, 136.3, 136.0, 129.2, 128.8, 126.8, 125.3, 125.1, 123.5, 113.6, 113.5, 59.0, 41.8, 37.7, 31.3, 25.0, 23.9, 18.6.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{21}ClN_3$ 350.1424; Found 350.1424.

(*E*)-2-(3-(6-chloropyridin-3-yl)-2,2-dimethyl-5-phenylpent-4-en-1-yl)malononitrile (10n)



White solid, 62% yield, 1.3:1 rr

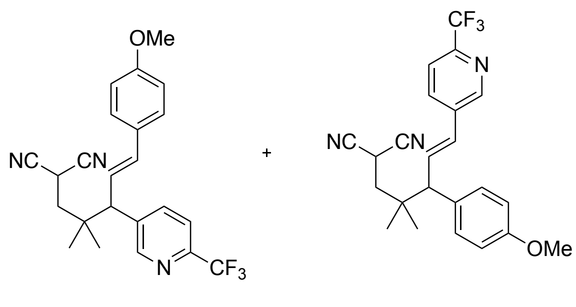
Purified using 0-30% gradient EtOAc in hexanes

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.33 (d, *J* = 2.5 Hz, 1H), 8.28 (d, *J* = 2.6 Hz, 1H), 7.67 (dd, *J* = 8.3, 2.5 Hz, 1H), 7.54 (dd, *J* = 8.3, 2.6 Hz, 1H), 7.39 – 7.30 (m, 7H), 7.30 (s, 2H), 7.24 – 7.19 (m, 2H), 6.62 (dd, *J* = 15.7, 9.9 Hz, 1H), 6.54 (d, *J* = 15.6 Hz, 1H), 6.50 – 6.42 (m, 2H), 3.74 (t, *J* = 6.8 Hz, 1H), 3.57 (t, *J* = 6.7 Hz, 1H), 3.36 (d, *J* = 9.7 Hz, 1H), 3.32 (d, *J* = 9.9 Hz, 1H), 2.21 – 2.10 (m, 3H), 1.12 (s, 3H), 1.06 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 150.14, 150.07, 149.9, 147.7, 139.5, 139.0, 1356.0, 135.4, 135.0, 134.9, 131.3, 131.1, 128.9, 128.68, 128.66, 128.61, 128.1, 127.4, 126.3, 125.6, 124.1, 123.9, 113.44, 113.40, 113.3, 113.2, 59.6, 56.0, 41.5, 41.3, 37.3, 37.2, 24.6, 24.4, 23.8, 23.2, 18.2, 18.1.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{21}ClN_3$ 350.1424; Found 350.1435.

(*E*)-2-(5-(4-methoxyphenyl)-2,2-dimethyl-3-(6-(trifluoromethyl)pyridin-3-yl)pent-4-en-1-yl)malononitrile (10o)



Pale yellow oil, 66% yield, 11:1 rr

Purified using 0-30% gradient EtOAc in hexanes

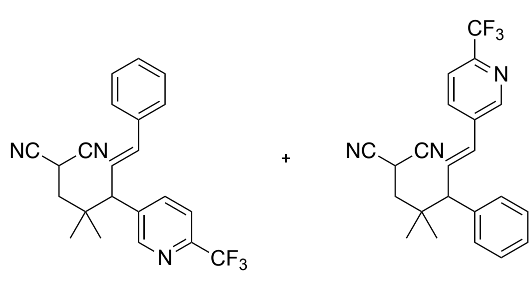
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.62 (d, *J* = 2.1 Hz, 1H), 7.74 (dd, *J* = 8.1, 2.1 Hz, 1H), 7.67 (d, *J* = 8.1 Hz, 1H), 7.33 – 7.28 (m, 2H), 6.89 – 6.85 (m, 2H), 6.50 (d, *J* = 15.5 Hz, 1H), 6.35 (dd, *J* = 15.5, 10.0 Hz, 1H), 3.81 (s, 3H), 3.76 (t, *J* = 6.8 Hz, 1H), 3.43 (d, *J* = 9.9 Hz, 1H), 2.17 (app. h, *J* = 7.3 Hz, 2H), 1.14 (s, 3H), 1.07 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 160.2, 150.9, 140.0, 138.0, 135.4, 129.0, 128.0, 123.2, 120.5, 114.6, 113.6, 113.5, 57.1, 55.7, 41.8, 37.8, 25.1, 23.6, 18.7.

^{19}F NMR (565 MHz, $CDCl_3$) δ -67.8.

HRMS (DART) m/z: $[M + H]^+$ Calcd for $C_{23}H_{23}F_3N_3O$ 414.1793; Found 414.1799.

(*E*)-2-(2,2-dimethyl-5-phenyl-3-(6-(trifluoromethyl)pyridin-3-yl)pent-4-en-1-yl)malononitrile (10p)



Orange foam, 77% yield, 2:1 rr

Purified using 0-30% gradient EtOAc in hexanes

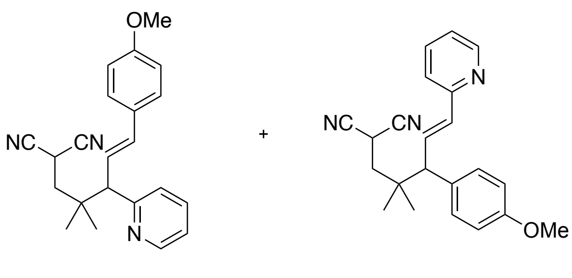
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.63 (d, *J* = 2.1 Hz, 1H), 7.75 (d, *J* = 2.1 Hz, 1H), 7.68 (d, *J* = 8.2 Hz, 1H), 7.40 – 7.33 (m, 5H), 7.25 – 7.21 (m, 1H), 6.61 – 6.51 (m, 2H), 3.77 (t, *J* = 6.8 Hz, 1H), 3.47 (d, *J* = 9.4 Hz, 1H), 2.21 – 2.11 (m, 3H), 1.14 (s, 3H), 1.07 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 161.6, 161.5, 159.9, 159.8, 139.8, 136.5, 135.4, 135.34, 135.29, 134.6, 129.1, 128.92, 128.85, 128.8, 128.62, 128.57, 128.5, 128.2, 128.1, 128.0, 127.8, 127.2, 126.4, 125.5, 125.44, 125.41, 119.6, 116.4, 116.3, 116.2, 114.0, 113.54, 113.49, 113.5, 112.6, 112.4, 111.52, 111.49, 111.41, 111.38, 111.35, 60.8, 49.4, 41.6, 41.3, 38.4, 37.2, 36.5, 24.6, 24.5, 24.40, 24.38, 24.37, 24.0, 23.2, 21.4, 18.2, 18.1.

^{19}F NMR (565 MHz, $CDCl_3$) δ -67.7.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{21}F_3N_3$ 384.1688; Found 384.1670.

(*E*)-2-(5-(4-methoxyphenyl)-2,2-dimethyl-3-(pyridin-2-yl)pent-4-en-1-yl)malononitrile (10q)



major minor

Orange solid, 50% yield, 17:1 rr

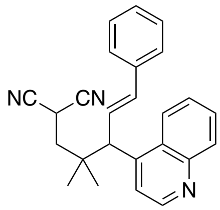
Purified using 0-40% gradient EtOAc in hexanes

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.57 (dd, *J* = 5.2, 2.0 Hz, 1H), 7.63 (td, *J* = 7.6, 1.8 Hz, 1H), 7.35 – 7.31 (m, 3H), 7.17 (ddt, *J* = 7.2, 3.8, 1.6 Hz, 2H), 6.87 – 6.84 (m, 2H), 6.46 (d, *J* = 7.6 Hz, 2H), 4.63 (dd, *J* = 8.1, 5.4 Hz, 1H), 3.80 (s, 4H), 3.47 (dd, *J* = 7.2, 1.8 Hz, 1H), 2.18 – 2.05 (m, 2H), 1.13 (d, *J* = 14.2 Hz, 7H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 160.9, 159.4, 149.2, 136.6, 133.4, 129.6, 127.7, 125.3, 124.1, 122.1, 114.3, 114.2, 114.1, 114.0, 60.2, 55.4, 41.3, 38.1, 25.9, 25.7, 18.6.

HRMS (DART) m/z: $[M + H]^+$ Calcd for $C_{22}H_{24}N_3O$ 346.1919; Found 346.1904.

(*E*)-2-(2,2-dimethyl-5-phenyl-3-(quinolin-4-yl)pent-4-en-1-yl)malononitrile (10s)



White solid, 33% yield, >20:1 rr

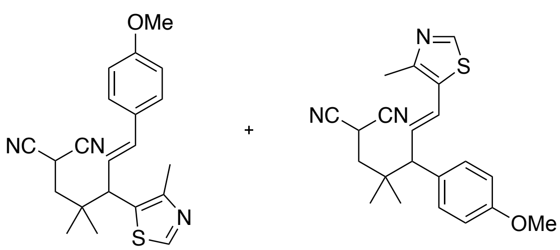
Purified using 0-30% gradient EtOAc in hexanes

^{1}H NMR (600 MHz, CDCl$_3$) δ 8.92 (d, *J* = 4.6 Hz, 1H), 8.23 (d, *J* = 8.4 Hz, 1H), 8.17 (dd, *J* = 8.4, 1.3 Hz, 1H), 7.77 (ddd, *J* = 8.4, 6.8, 1.3 Hz, 1H), 7.66 (ddd, *J* = 8.4, 6.8, 1.3 Hz, 1H), 7.43 – 7.36 (m, 3H), 7.36 – 7.31 (m, 2H), 6.65 – 6.56 (m, 2H), 4.41 – 4.35 (m, 1H), 3.74 (t, *J* = 6.8 Hz, 1H), 2.33 – 2.20 (m, 2H), 1.24 (s, 3H), 1.06 (s, 3H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 149.3, 148.7, 146.7, 136.1, 134.6, 130.8, 129.4, 128.7, 128.1, 127.5, 127.0, 126.7, 126.4, 122.8, 120.8, 113.31, 113.27, 50.9, 41.7, 38.3, 30.9, 29.6, 24.5, 23.8, 18.3.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{25}H_{24}N_3$ 366.1970; Found 366.1976.

(*E*)-2-(5-(4-methoxyphenyl)-2,2-dimethyl-3-(4-methylthiazol-5-yl)pent-4-en-1-yl)malononitrile (10t)



Pale yellow solid, 80% yield, 2.5:1 rr

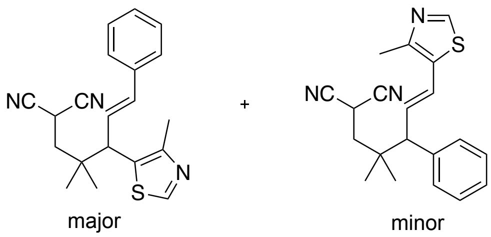
Purified using 0-40% gradient EtOAc in hexanes

^{1}H NMR (600 MHz, CDCl$_3$) δ 8.69 (s, 1H), 7.29 (s, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 6.42 (d, *J* = 15.5 Hz, 1H), 6.06 (dd, *J* = 15.5, 9.4 Hz, 1H), 3.81 (d, *J* = 1.0 Hz, 4H), 3.73 – 3.69 (m, 2H), 2.49 (s, 3H), 2.42 (s, 1H), 2.23 – 2.14 (m, 2H), 1.18 (s, 3H), 1.11 (s, 4H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 159.6, 158.7, 150.3, 150.0, 149.8, 149.3, 133.3, 131.7, 130.8, 130.3, 129.9, 129.6, 128.7, 127.6, 125.2, 122.9, 114.05, 114.03, 113.5, 113.4, 113.31, 113.26, 58.8, 55.3, 55.2, 51.9, 41.6, 41.3, 38.2, 37.4, 24.6, 23.89, 23.87, 23.84, 18.3, 18.2, 16.0, 15.2.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{24}N_3OS$ 366.1640; Found 366.1617.

(*E*)-2-(2,2-dimethyl-3-(4-methylthiazol-5-yl)-5-phenylpent-4-en-1-yl)malononitrile (10u)



White solid, 60% yield, 1.7:1 rr

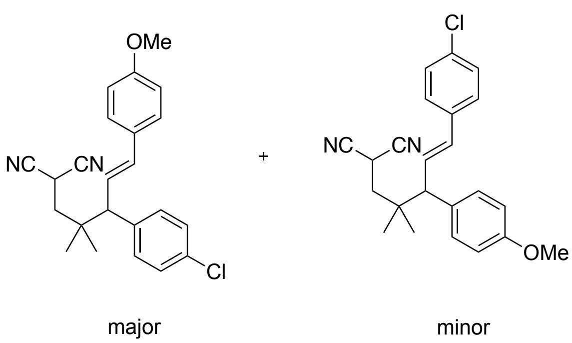
Purified using 0-40% gradient EtOAc in hexanes

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (s, 1H), 7.35 (tdd, *J* = 7.9, 5.0, 3.0 Hz, 5H), 7.23 – 7.17 (m, 2H), 6.58 (d, *J* = 15.3 Hz, 1H), 6.36 – 6.24 (m, 1H), 3.61 (s, 1H), 3.29 (d, *J* = 9.9 Hz, 1H), 2.42 (s, 3H), 2.09 (t, *J* = 6.4 Hz, 2H), 1.12 (s, 3H), 1.06 (s, 4H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 150.6, 150.2, 150.1, 149.5, 139.9, 136.2, 134.0, 130.7, 130.1, 129.7, 129.1, 128.78, 128.76, 128.2, 127.6, 127.4, 126.5, 123.3, 113.7, 113.6, 113.52, 113.47, 59.8, 52.1, 41.7, 41.3, 38.3, 37.5, 24.7, 24.1, 24.0, 23.9, 18.5, 18.3, 16.1, 15.3.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{22}N_3S$ 336.1534; Found 336.1524.

(*E*)-2-(3-(4-chlorophenyl)-5-(4-methoxyphenyl)-2,2-dimethylpent-4-en-1-yl)malononitrile (10v)



White solid, 95% yield, 2.6:1 rr

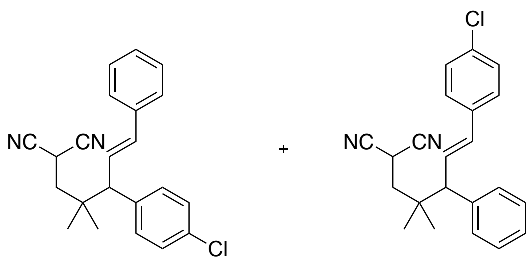
Purified using 0-10% gradient EtOAc in hexanes

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30 (dd, J = 16.8, 7.4 Hz, 5H), 7.15 (d, J = 8.4 Hz, 2H), 6.86 (d, J = 8.7 Hz, 2H), 6.42 (q, J = 7.4 Hz, 1H), 6.35 (dd, J = 15.5, 9.6 Hz, 1H), 3.81 (s, 3H), 3.67 (t, J = 6.8 Hz, 1H), 3.26 (d, J = 9.9 Hz, 1H), 2.17 – 2.08 (m, 2H), 1.10 (s, 3H), 1.04 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 159.5, 158.8, 139.1, 135.5, 133.5, 133.4, 133.0, 132.13, 132.11, 130.5, 130.1, 129.4, 129.0, 128.9, 128.70, 127.65, 127.62, 125.0, 114.2, 114.1, 113.71, 113.68, 113.63, 58.9, 58.7, 55.44, 55.39, 41.8, 41.7, 37.5, 37.4, 29.81, 29.77, 24.7, 24.5, 24.11, 24.07, 18.4, 18.3.

HRMS (neg-ESI) m/z: $[M - H]^-$ Calcd for $C_{23}H_{22}ClN_2O$ 377.1421; Found 377.1414.

(*E*)-2-(3-(4-chlorophenyl)-2,2-dimethyl-5-phenylpent-4-en-1-yl)malononitrile (10w)



White solid, 90% yield, 1.1:1 rr

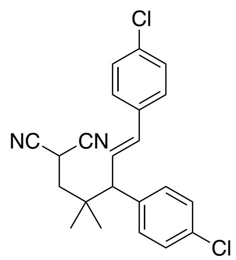
Purified using 0-10% gradient EtOAc in hexanes

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 – 7.35 (m, 4H), 7.35 – 7.30 (m, 6H), 7.24 – 7.21 (m, 2H), 7.18 – 7.15 (m, 2H), 6.58 – 6.51 (m, 1H), 6.44 (d, J = 15.6 Hz, 1H), 3.67 (t, J = 6.7 Hz, 1H), 3.58 (t, J = 6.7 Hz, 1H), 3.31 – 3.28 (m, 1H), 2.17 – 2.10 (m, 3H), 1.13 (s, 3H), 1.08 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 140.0, 138.7, 136.5, 135.2, 133.9, 133.2, 132.9, 132.3, 130.3, 129.0, 128.7, 128.58, 128.56, 128.55, 128.49, 127.8, 127.4, 127.2, 127.10, 127.08, 126.3, 113.4, 59.4, 58.7, 41.6, 41.5, 37.3, 37.2, 29.6, 24.5, 24.2, 24.0, 23.9, 18.2, 18.1.

HRMS (neg-ESI) m/z: $[M - H]^-$ Calcd for $C_{22}H_{20}ClN_2$ 347.1315; Found 347.1311.

(*E*)-2-(3,5-bis(4-chlorophenyl)-2,2-dimethylpent-4-en-1-yl)malononitrile (10x)



White foam, 71% yield

Purified using 0-30% gradient EtOAc in hexanes

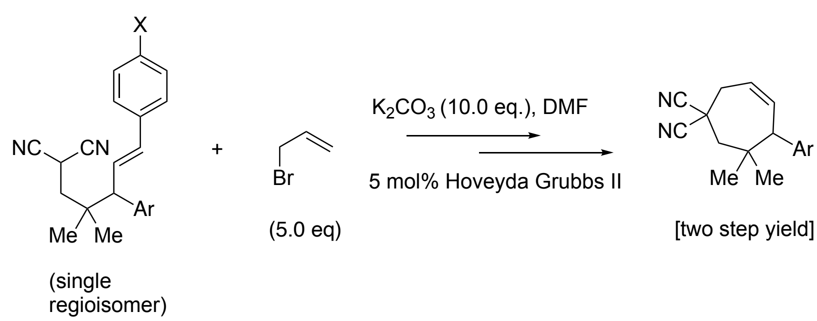
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32 (d, J = 8.5 Hz, 2H), 7.29 (app. s, 4H), 7.15 (d, J = 8.5 Hz, 2H), 6.52 – 6.41 (m, 2H), 3.67 (t, J = 6.8 Hz, 1H), 3.29 (d, J = 8.9 Hz, 1H), 2.17 – 2.06 (m, 2H), 1.11 (s, 3H), 1.05 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 138.5, 134.9, 133.5, 133.0, 132.7, 130.3, 128.7, 128.6, 127.8, 127.5, 113.4, 113.3, 58.7, 41.5, 37.3, 24.2, 24.0, 18.2.

HRMS (neg-ESI) m/z: $[M - H]^-$ Calcd for $C_{22}H_{19}Cl_2N_2$ 381.0926; Found 381.0920.

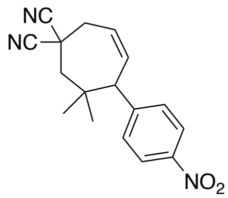
General procedure for ring closing metathesis:

A)



A single regioisomer of the reduced Cope product was dissolved in DMF (0.1 M) in a vial. Potassium carbonate (10.0 eq) followed by allyl bromide (5.0 eq) were added and the reaction was stirred for 1 hour at room temperature. Upon completion, EtOAc was added and the organic layer was washed with a solution of 2 M HCl and brine (1:1x 3) and dried with anhydrous Na_2SO and the crude material was then concentrated under reduced pressure. This crude material was then dissolved in toluene (0.01 M) and Hoveyda Grubbs II catalyst (5 mol %) was added and the reaction mixture was heated to 60 °C for 1 hour. After cooling to room temperature, the crude reaction mixture was filtered over a silica plug and washed with EtOAc and concentrated under reduced pressure. The crude product was purified *via* flash column chromatography.

6,6-dimethyl-5-(4-nitrophenyl)cyclohept-3-ene-1,1-dicarbonitrile (11a)



White solid, 36% yield, 20:1 rr

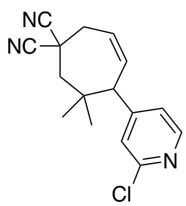
Purified using 0-20% gradient EtOAc in hexanes

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 8.7 Hz, 2H), 7.41 (d, *J* = 8.7 Hz, 2H), 6.26 – 6.17 (m, 1H), 6.03 (dtd, *J* = 10.7, 6.7, 2.2 Hz, 1H), 3.70 (dd, *J* = 5.9, 2.2 Hz, 1H), 3.04 – 2.96 (m, 2H), 2.52 (d, *J* = 14.5 Hz, 1H), 2.36 – 2.21 (m, 1H), 1.31 (s, 3H), 0.69 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 148.9, 147.0, 140.5, 129.8, 124.6, 123.6, 116.5, 115.1, 54.1, 53.7, 36.7, 34.6, 31.9, 21.4.

HRMS (neg-ESI) m/z $[M - H]^-$ Calcd for $C_{17}H_{16}N_3O_2$ 294.1243; Found 294.1249.

5-(2-chloropyridin-4-yl)-6,6-dimethylcyclohept-3-ene-1,1-dicarbonitrile (11e)



Green oil, 83% yield, 20:1 rr

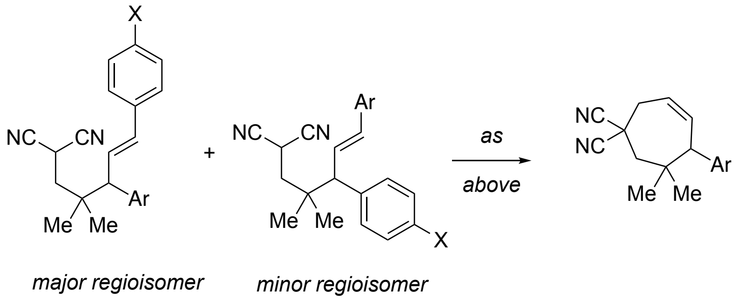
Purified using 0-20% gradient EtOAc in hexanes

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.37 (d, *J* = 5.1 Hz, 1H), 7.21 (d, *J* = 1.6 Hz, 1H), 7.10 (dd, *J* = 5.1, 1.6 Hz, 1H), 6.14 (ddd, *J* = 10.6, 5.9, 2.2 Hz, 1H), 6.08 – 6.01 (m, 1H), 3.55 (dd, *J* = 5.9, 2.2 Hz, 1H), 3.06 – 2.90 (m, 2H), 2.51 (dd, *J* = 14.5, 1.6 Hz, 1H), 2.26 (d, *J* = 14.5 Hz, 1H), 1.30 (s, 3H), 0.74 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 153.9, 152.3, 150.1, 140.0, 125.5, 125.1, 123.3, 116.8, 115.4, 54.1, 53.9, 36.9, 34.9, 32.2, 30.1, 21.8.

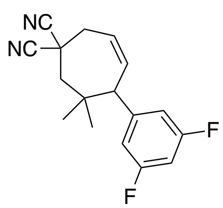
HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{16}H_{17}ClN_3$ 286.1111; Found 286.1106.

B)



A mixture of regioisomers of the reduced Cope product was dissolved in DMF (0.1 M) in a vial. Potassium carbonate (10.0 eq) followed by allyl bromide (5.0 eq) were added and the reaction was stirred for 1 hour at room temperature. Upon completion, EtOAc was added and the organic layer was washed with a solution of 2 M HCl and brine (1:1x 3) and dried with anhydrous Na_2SO and the crude material was then concentrated under reduced pressure. This crude material was then dissolved in toluene (0.01 M) and Hoveyda Grubbs II catalyst (5 mol %) was added and the reaction mixture was heated to 60 °C for 1 hour. After cooling to room temperature, the crude reaction mixture was filtered over a silica plug and washed with EtOAc and concentrated under reduced pressure. The crude product was purified *via* flash column chromatography.

5-(3,5-difluorophenyl)-6,6-dimethylcyclohept-3-ene-1,1-dicarbonitrile (11b)



White solid, 40% yield, 20:1 rr

Purified using 0-20% gradient EtOAc in hexanes

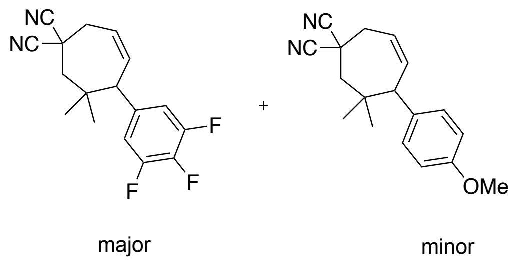
^{1}H NMR (600 MHz, $CDCl_3$) δ 6.75 (ddt, *J* = 10.8, 6.5, 2.2 Hz, 3H), 6.17 (ddd, *J* = 10.5, 6.0, 1.5 Hz, 1H), 6.02 – 5.95 (m, 1H), 3.53 (dd, *J* = 6.1, 2.2 Hz, 1H), 2.96 (dd, *J* = 7.5, 1.5 Hz, 2H), 2.49 (dd, *J* = 14.5, 1.5 Hz, 1H), 2.23 (d, *J* = 14.5 Hz, 1H), 1.29 (s, 3H), 0.72 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 163.6, 163.5, 162.0, 161.9, 145.32, 145.26, 141.1, 124.1, 116.6, 115.2, 112.0, 111.9, 111.82, 111.79, 102.8, 102.6, 102.4, 53.98, 53.97, 53.96, 53.7, 36.6, 34.5, 31.9, 31.8, 21.3.

^{19}F NMR (565 MHz, $CDCl_3$) δ -109.3.

HRMS (DART) m/z $[M + H]^+$ Calcd for $C_{17}H_{17}F_2N_2$ 287.1360; Found 287.1357.

6,6-dimethyl-5-(3,4,5-trifluorophenyl)cyclohept-3-ene-1,1-dicarbonitrile (11c)



White solid, 20% yield, 15:1 rr

Purified using 0-20% gradient EtOAc in hexanes

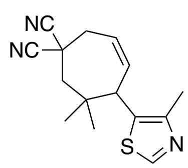
^{1}H NMR (600 MHz, $CDCl_3$) δ 6.86 (dd, *J* = 8.6, 6.4 Hz, 2H), 6.12 (ddd, *J* = 10.6, 5.9, 2.0 Hz, 1H), 5.99 (dtd, *J* = 11.0, 5.8, 2.9 Hz, 1H), 3.49 (dd, *J* = 6.0, 2.2 Hz, 1H), 2.95 (ddd, *J* = 8.0, 6.9, 1.9 Hz, 2H), 2.49 (dd, *J* = 14.5, 1.8 Hz, 1H), 2.22 (d, *J* = 14.5 Hz, 1H), 1.27 (s, 3H), 0.72 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 140.7, 124.3, 116.5, 115.1, 113.0, 112.89, 112.86, 53.6, 36.6, 34.5, 31.9, 31.8, 21.2.

^{19}F NMR (565 MHz, $CDCl_3$) δ -133.6, -133.7, -161.9.

HRMS (neg-ESI) m/z $[M - H]^-$ Calcd for $C_{17}H_{14}F_3N_2$ 303.1109; Found 303.1104.

6,6-dimethyl-5-(4-methylthiazol-5-yl)cyclohept-3-ene-1,1-dicarbonitrile (11d)



White solid, 47% yield, 20:1 rr

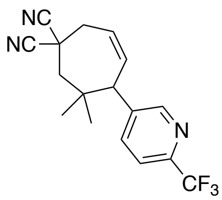
Purified using 0-20% gradient EtOAc in hexanes

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.71 (s, 1H), 6.09 – 6.03 (m, 1H), 6.01 – 5.92 (m, 1H), 4.02 – 3.97 (m, 1H), 3.04 – 2.99 (m, 2H), 2.56 (d, *J* = 14.5 Hz, 1H), 2.46 (s, 3H), 2.28 (d, *J* = 14.5 Hz, 1H), 1.34 (s, 3H), 0.83 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 150.1, 142.1, 123.7, 116.5, 115.1, 53.2, 45.9, 37.4, 34.6, 31.8, 30.6, 29.6, 21.4, 15.8.

HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{15}H_{18}N_3S$ 272.1221; Found 272.1222.

6,6-dimethyl-5-(6-(trifluoromethyl)pyridin-3-yl)cyclohept-3-ene-1,1-dicarbonitrile (11f)



White solid, 53% yield, 20:1 rr

Purified using 0-20% gradient EtOAc in hexanes

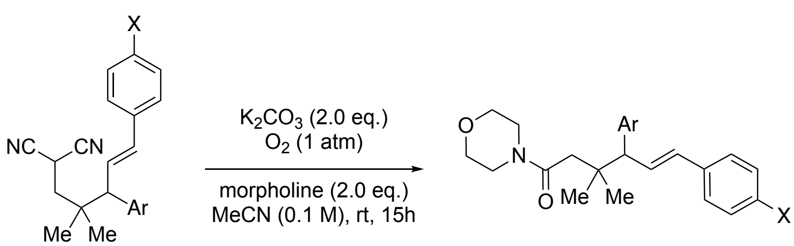
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.61 (d, *J* = 2.2 Hz, 1H), 7.78 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.70 (d, *J* = 8.1 Hz, 1H), 6.17 (ddd, *J* = 10.4, 5.9, 1.3 Hz, 1H), 6.06 (dtd, *J* = 9.9, 7.2, 6.7, 2.2 Hz, 1H), 3.70 (dd, *J* = 5.9, 2.2 Hz, 1H), 3.04 – 2.98 (m, 2H), 2.53 (dd, *J* = 14.5, 1.2 Hz, 1H), 2.31 (d, *J* = 14.5 Hz, 1H), 1.30 (s, 3H), 0.71 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 150.5, 140.3, 139.9, 137.1, 125.2, 120.21, 120.19, 120.17, 120.15, 116.4, 115.1, 53.5, 51.5, 36.7, 34.5, 31.9, 31.8, 21.3.

^{19}F NMR (565 MHz, $CDCl_3$) δ -67.8.

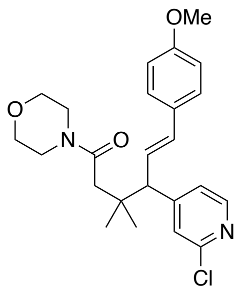
HRMS (neg-ESI) m/z $[M - H]^-$ Calcd for $C_{17}H_{15}F_3N_3$ 318.1218; Found 318.1218.

General procedure for oxidative amidation:



In a round bottom flask, the malononitrile was dissolved in acetonitrile (0.1 M). Morpholine (2.0 eq) and potassium carbonate (2.0 eq) were added. An oxygen balloon was bubbled through the reaction mixture and the reaction was stirred at room temperature overnight. Once complete, the reaction mixture was *vacuum* filtered through a silica plug and washed with EtOAc and concentrated under reduced pressure.

(*E*)-4-(2-chloropyridin-4-yl)-6-(4-methoxyphenyl)-3,3-dimethyl-1-morpholinohex-5-en-1-one (12a)



Yellow foam, 73% yield, 20:1 rr

Purified *via* silica plug with 100% EtOAc

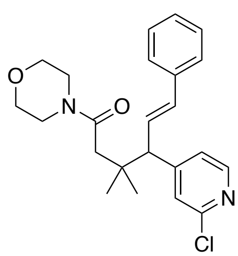
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.28 (d, *J* = 5.2 Hz, 1H), 7.32 – 7.28 (m, 2H), 7.26 (s, 1H), 7.17 (d, *J* = 5.1 Hz, 1H), 6.88 – 6.82 (m, 2H), 6.45 (d, *J* = 15.5 Hz, 1H), 6.35 (ddd, *J* = 15.6, 10.0, 1.4 Hz, 1H), 4.02 (d, *J* = 9.9 Hz, 1H), 3.80 (d, *J* = 1.4 Hz, 3H), 3.65 (d, *J* = 9.4 Hz, 4H), 3.55 (d, *J* = 5.2 Hz, 2H), 3.35 (t, *J* = 4.7 Hz, 2H), 2.28 (d, *J* = 15.5 Hz, 1H), 2.09 (d, *J* = 15.5 Hz, 1H), 1.12 (s, 3H), 1.05 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 169.7, 159.3, 154.8, 151.3, 149.0, 133.4, 129.5, 127.4, 125.0, 124.6, 123.5, 114.0, 66.9, 66.4, 55.4, 55.3, 55.2, 46.4, 41.7, 41.4, 37.5, 29.6, 25.5, 25.3.

HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{24}H_{30}ClN_2O_3$ 429.1945; Found 429.1934.

$[M + Na]^+$ Calcd for $C_{24}H_{29}ClN_2O_3Na$ 451.1765; Found 451.1750.

(*E*)-4-(2-chloropyridin-4-yl)-3,3-dimethyl-1-morpholino-6-phenylhex-5-en-1-one (12b)



Yellow oil, 95% yield, 20:1 rr

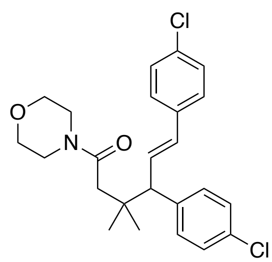
Purified *via* silica plug with 100% EtOAc

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, *J* = 5.2 Hz, 1H), 7.39 – 7.27 (m, 5H), 7.26 – 7.22 (m, 1H), 7.18 (dd, *J* = 5.2, 1.5 Hz, 1H), 6.54 – 6.49 (m, 2H), 4.09 (dd, *J* = 5.6, 3.8 Hz, 1H), 3.65 (dt, *J* = 10.6, 4.7 Hz, 4H), 3.56 (t, *J* = 4.7 Hz, 2H), 3.36 (t, *J* = 4.7 Hz, 2H), 2.28 (d, *J* = 15.5 Hz, 1H), 2.09 (d, *J* = 15.5 Hz, 1H), 1.14 (s, 3H), 1.06 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 169.7, 154.6, 151.4, 149.0, 136.8, 134.1, 128.6, 127.7, 127.0, 126.2, 125.0, 123.5, 66.9, 66.4, 55.3, 46.4, 41.7, 41.4, 37.6, 29.6, 25.5, 25.4.

HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{23}H_{28}ClN_2O_2$ 399.1839; Found 399.1851.

(*E*)-4,6-bis(4-chlorophenyl)-3,3-dimethyl-1-morpholinohex-5-en-1-one (12c)



Pale yellow oil, 95% yield, 20:1 rr

Purified *via* silica plug with 100% EtOAc

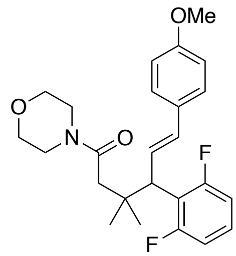
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (s, 6H), 7.21 (d, *J* = 8.6 Hz, 2H), 6.56 (dd, *J* = 15.6, 9.8 Hz, 1H), 6.42 (d, *J* = 15.6 Hz, 1H), 3.89 (d, *J* = 9.8 Hz, 1H), 3.63 (q, *J* = 6.4, 5.0 Hz, 4H), 3.55 (t, *J* = 4.8 Hz, 2H), 3.33 (t, *J* = 4.8 Hz, 2H), 2.29 – 2.09 (m, 2H), 1.12 (s, 3H), 1.03 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 170.1, 140.2, 135.8, 132.9, 132.2, 131.5, 130.7, 129.9, 128.6, 128.1, 127.3, 67.0, 66.5, 56.2, 46.5, 41.7, 41.4, 37.6, 29.6, 25.41, 25.40.

HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{24}H_{28}Cl_2NO_2$ 432.1492; Found 432.1486.

$[M + Na]^+$ Calcd for $C_{24}H_{27}Cl_2NO_2Na$ 454.1311; Found 454.1309.

(*E*)-4-(2,6-difluorophenyl)-6-(4-methoxyphenyl)-3,3-dimethyl-1-morpholinohex-5-en-1-one (12d)



Pale yellow oil, 95% yield, 6:1 rr

Purified *via* silica plug with 100% EtOAc

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.7 Hz, 2H), 7.21 – 7.12 (m, 1H), 6.97 – 6.81 (m, 4H), 6.75 – 6.67 (m, 1H), 6.46 (dd, *J* = 15.8, 5.2 Hz, 1H), 4.10 (d, *J* = 10.2 Hz, 1H), 3.79 (d, *J* = 5.2 Hz, 3H), 3.69 – 3.53 (m, 6H), 3.45 – 3.33 (m, 2H), 2.36 (d, *J* = 3.3 Hz, 2H), 1.13 (d, *J* = 8.6 Hz, 6H).

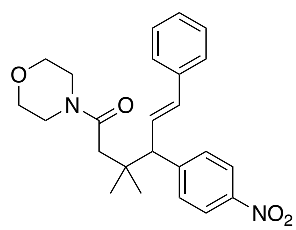
^{13}C NMR (151 MHz, $CDCl_3$) δ 170.2, 159.1, 132.9, 130.3, 130.0, 128.1, 128.0, 127.4, 125.1, 117.8, 113.9, 113.4, 111.3, 67.0, 66.5, 55.2, 49.6, 46.8, 41.7, 41.2, 38.9, 25.3, 25.2.

^{19}F NMR (565 MHz, $CDCl_3$) δ -104.7, -104.7, -110.6, -113.8.

HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{25}H_{30}F_2NO_3$ 430.2194; Found 430.2203.

$[M + Na]^+$ Calcd for $C_{24}H_{29}F_2NO_3Na$ 452.2014; Found 452.2013.

(*E*)-3,3-dimethyl-1-morpholino-4-(4-nitrophenyl)-6-phenylhex-5-en-1-one (12e)



Yellow oil, 68% yield, 20:1 rr

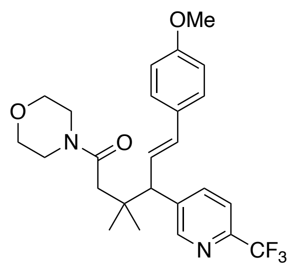
Purified *via* silica plug with 100% EtOAc

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 – 8.14 (m, 2H), 7.53 – 7.45 (m, 2H), 7.38 – 7.28 (m, 4H), 7.26 – 7.22 (m, 1H), 6.60 (dd, *J* = 15.6, 9.7 Hz, 1H), 6.51 (d, *J* = 15.6 Hz, 1H), 4.17 (d, *J* = 9.7 Hz, 1H), 3.74 – 3.49 (m, 6H), 3.37 (t, *J* = 4.9 Hz, 2H), 2.31 (d, *J* = 15.3 Hz, 1H), 2.13 (d, *J* = 15.3 Hz, 1H), 1.13 (s, 3H), 1.06 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 169.9, 150.0, 146.5, 136.9, 133.6, 130.2, 128.6, 127.9, 127.6, 126.2, 123.1, 66.9, 66.4, 56.2, 46.5, 41.7, 41.4, 37.8, 29.6, 25.6, 25.3.

HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{24}H_{29}N_2O_4$ 409.2127; Found 409.2133.

(*E*)-6-(4-methoxyphenyl)-3,3-dimethyl-1-morpholino-4-(6-(trifluoromethyl)pyridin-3-yl)hex-5-en-1-one (12f)



Pale yellow oil, 91% yield, 12:1 rr

Purified *via* silica plug with 100% EtOAc

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, J = 2.2 Hz, 1H), 7.82 (dd, J = 8.1, 2.2 Hz, 1H), 7.61 (d, J = 8.1 Hz, 1H), 7.31 – 7.26 (m, 2H), 6.87 – 6.81 (m, 2H), 6.47 – 6.36 (m, 2H), 4.17 – 4.12 (m, 1H), 3.79 (s, 3H), 3.69 – 3.59 (m, 4H), 3.59 – 3.51 (m, 2H), 3.36 (t, J = 4.8 Hz, 2H), 2.32 (d, J = 15.4 Hz, 1H), 2.11 (d, J = 15.4 Hz, 1H), 1.12 (s, 3H), 1.06 (s, 3H).

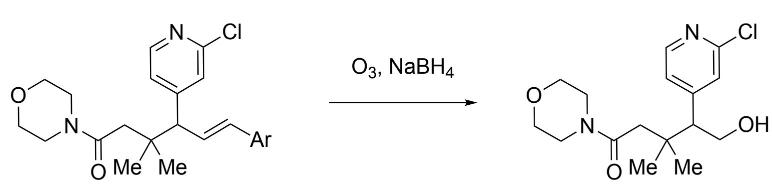
^{13}C NMR (151 MHz, $CDCl_3$) δ 169.8, 159.3, 150.8, 141.3, 137.9, 133.4, 129.5, 127.4, 125.0, 119.67, 119.65, 114.1, 114.0, 66.9, 66.4, 55.3, 53.8, 46.5, 41.7, 41.4, 37.7, 29.6, 25.5, 25.1.

^{19}F NMR (565 MHz, $CDCl_3$) δ -67.7.

HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{25}H_{30}F_3N_2O_3$ 463.2208; Found 463.2222.

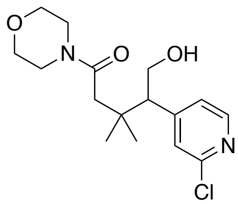
$[M + Na]^+$ Calcd for $C_{24}H_{29}F_2N_2O_3Na$ 485.2028; Found 485.2035.

General procedure for ozonolysis:



The amide was added to a flame dried Schlenk flask with a 5:1 mixture of DCM:MeOH (0.02 M: 0.1 M) and sodium bicarbonate (0.25 eq.). Next, the solution was cooled to -78 °C and ozone was bubbled through until the solution turned blue. Once the blue was observed, the ozone was turned off, sodium borohydride (2.0 eq) was added, and nitrogen was bubbled through the solution for 1 hour and the solution was warmed to room temperature. The crude reaction mixture was run through a celite plug with 100% EtOAc and concentrated under reduced pressure. The crude product was then purified *via* flash column chromatography.

4-(2-chloropyridin-4-yl)-5-hydroxy-3,3-dimethyl-1-morpholinopentan-1-one (13a)



Pale yellow oil, 77% yield

Purified *via* flash column chromatography 0-50% EtOAc gradient followed by MeOH flush

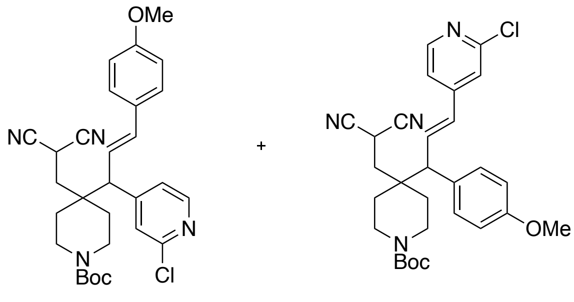
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 5.2 Hz, 1H), 7.20 (d, *J* = 1.5 Hz, 1H), 7.10 (dd, *J* = 5.2, 1.5 Hz, 1H), 4.10 (dd, *J* = 11.1, 6.0 Hz, 1H), 3.94 (dd, *J* = 11.1, 7.7 Hz, 1H), 3.73 – 3.58 (m, 6H), 3.41 (dt, *J* = 7.3, 3.3 Hz, 2H), 2.74 (s, 2H), 2.41 (d, *J* = 15.1 Hz, 1H), 2.18 (d, *J* = 15.1 Hz, 1H), 1.14 (s, 3H), 0.92 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.0, 153.7, 151.2, 148.9, 125.5, 123.7, 66.7, 66.3, 62.0, 53.6, 46.5, 41.8, 41.7, 36.0, 29.5, 26.5, 25.4, 0

HRMS (DART) m/z $[M + H]^+$ Calcd for $C_{31}H_{41}ClN_3O_5$ 327.1475; Found 327.1474.

Synthesized by general procedure for 1-pot sequential addition reductive Cope rearrangement:

***tert*-butyl-(*E*)-4-(1-(2-chloropyridin-4-yl)-3-(4-methoxyphenyl)allyl)-4-(2,2-dicyanoethyl)piperidine-1-carboxylate (14a)**



White solid, 37% yield, 10:1 rr

Purified using 0-30% gradient EtOAc in hexanes

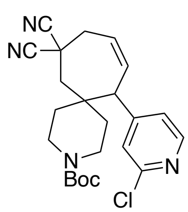
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.36 (d, *J* = 5.1 Hz, 1H), 7.30 (d, *J* = 8.7 Hz, 2H), 7.17 (d, *J* = 1.5 Hz, 1H), 7.06 (dd, *J* = 5.1, 1.5 Hz, 1H), 6.90 – 6.84 (m, 2H), 6.51 (d, *J* = 15.5 Hz, 1H), 6.27 (dd, *J* = 15.5, 10.1 Hz, 1H), 3.82 (d, *J* = 2.8 Hz, 5H), 3.62 (d, *J* = 10.1 Hz, 1H), 3.14 (q, *J* = 6.7 Hz, 2H), 2.39 (s, 2H), 1.68 (ddd, *J* = 14.6, 10.4, 4.5 Hz, 1H), 1.64 – 1.47 (m, 4H), 1.43 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 160.2, 154.8, 152.3, 152.0, 150.0, 135.8, 128.4, 127.9, 125.1, 123.4, 123.2, 121.5, 114.4, 113.1, 113.0, 80.4, 80.1, 61.1, 55.5, 54.5, 53.2, 46.6, 42.9, 38.7, 33.8, 31.0, 30.6, 28.48, 28.46, 17.6.

HRMS (neg-ESI) m/z: $[M - H]^-$ Calcd for $C_{29}H_{32}ClN_4O_3$ 519.2163; Found 519.2183.

Synthesized by general procedure for ring closing metathesis B:

***tert*-butyl 7-(2-chloropyridin-4-yl)-11,11-dicyano-3-azaspiro[5.6]dodec-8-ene-3-carboxylate (15)**



Brown solid, 85% yield, 20:1 rr

Purified using 0-20% gradient EtOAc in hexanes

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.38 (d, *J* = 5.1 Hz, 1H), 7.20 (s, 1H), 7.09 (d, *J* = 5.1 Hz, 1H), 6.19 – 6.13 (m, 1H), 6.10 – 6.03 (m, 1H), 3.81 (s, 1H), 3.68 (dd, *J* = 6.5, 2.0 Hz, 1H), 3.23 (d, *J* = 15.0 Hz, 1H), 3.08 –

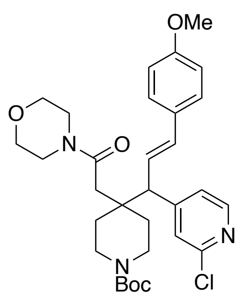
2.95 (m, 3H), 2.86 (qd, J = 13.9, 13.4, 6.5 Hz, 2H), 2.29 (dd, J = 14.1, 2.9 Hz, 1H), 2.00 (d, J = 15.0 Hz, 1H), 1.39 (d, J = 16.1 Hz, 10H), 1.25 (t, J = 7.1 Hz, 1H), 1.17 (dq, J = 14.0, 2.9 Hz, 1H), 1.00 – 0.90 (m, 1H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 159.5, 154.6, 152.1, 151.8, 149.9, 149.8, 149.1, 138.4, 125.1, 124.7, 123.2, 122.9, 116.2, 115.4, 114.9, 114.3, 114.0, 80.0, 60.8, 55.3, 54.3, 52.9, 46.3, 43.9, 42.7, 37.6, 37.3, 36.6, 35.7, 34.6, 31.1, 29.6, 28.2, 26.9.

HRMS (neg-ESI) m/z $[M - H]^-$ Calcd for $C_{23}H_{26}ClN_4O_2$ 425.1745; Found 425.1758.

Synthesized by general procedure for oxidative amidation:

***tert*-butyl (*E*)-4-(1-(2-chloropyridin-4-yl)-3-(4-methoxyphenyl)allyl)-4-(2-morpholino-2-oxoethyl)piperidine-1-carboxylate (16)**



Yellow oil, 78% yield, 20:1 rr

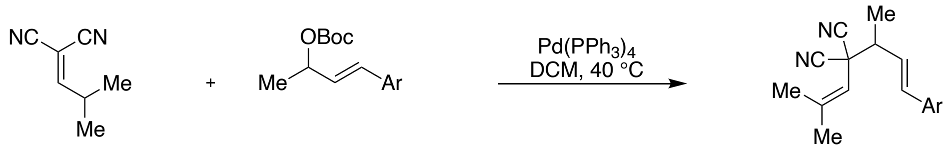
Purified *via* silica plug with 100% EtOAc

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, J = 5.1 Hz, 1H), 7.28 (s, 3H), 7.20 – 7.17 (m, 1H), 7.10 (dd, J = 5.1, 1.5 Hz, 1H), 6.87 – 6.81 (m, 2H), 6.43 (d, J = 15.5 Hz, 1H), 6.33 (dd, J = 15.5, 10.0 Hz, 1H), 4.28 (d, J = 10.0 Hz, 1H), 3.90 (d, J = 4.9 Hz, 2H), 3.80 (d, J = 5.7 Hz, 4H), 3.71 – 3.55 (m, 4H), 3.50 (d, J = 4.9 Hz, 2H), 3.29 (t, J = 4.9 Hz, 2H), 2.91 – 2.82 (m, 2H), 2.51 (d, J = 16.7 Hz, 1H), 1.41 (s, 9H), 1.37 (s, 2H), 1.31 – 1.18 (m, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 169.3, 159.4, 154.9, 153.9, 151.5, 149.8, 149.1, 134.1, 129.2, 127.4, 125.1, 124.7, 123.5, 122.9, 114.0, 79.6, 66.8, 66.3, 60.8, 55.3, 55.2, 53.9, 52.9, 46.3, 45.9, 42.7, 41.6, 38.8, 36.6, 35.7, 34.4, 32.5, 31.1, 30.9, 29.6, 28.4, 28.3, 28.2.

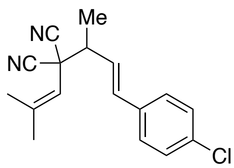
HRMS (DART) m/z $[M + H]^+$ Calcd for $C_{31}H_{41}ClN_3O_5$ 570.2734; Found 570.2739.

General procedure for alkylation utilizing methyl/aryl allyl electrophile:



To a flame dried Schlenk flask purged with nitrogen, the allyl electrophile (1.3 eq) was dissolved in DCM (0.1 M). Then $Pd(PPh_3)_4$ (5 mol %) was added followed by the alkylidene malononitrile (1.0 eq). The resulting mixture was heated to 40 °C and stirred for 2 hours and checked by NMR (Rf values of product and alkylidene malononitrile are the same). The reaction was then run through a celite plug and washed with 100% DCM. The crude material was concentrated under reduced pressure and then purified *via* flash column chromatography on a 0-10% EtOAc gradient.

(*E*)-2-(4-(4-chlorophenyl)but-3-en-2-yl)-2-(2-methylprop-1-en-1-yl)malononitrile (3a)



Colorless oil, 50% yield

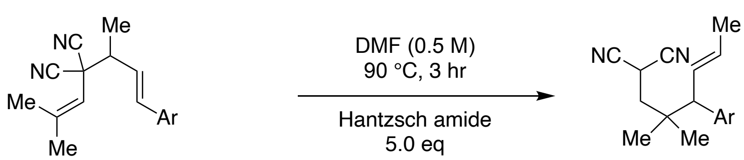
Purified using 0-10% gradient EtOAc in hexanes

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 – 7.29 (m, 4H), 6.60 (d, J = 15.7 Hz, 1H), 6.11 (dd, J = 15.7, 8.7 Hz, 1H), 5.10 (dt, J = 2.9, 1.5 Hz, 1H), 2.98 – 2.90 (m, 1H), 2.03 (d, J = 1.5 Hz, 3H), 1.84 (d, J = 1.5 Hz, 3H), 1.49 (d, J = 6.8 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 145.7, 134.2, 134.0, 133.8, 128.8, 127.8, 126.3, 114.5, 114.4, 114.2, 45.5, 39.3, 26.3, 19.6, 16.5.

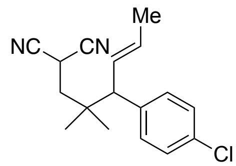
HRMS (DART) m/z: $[M + NH_4]^+$ Calcd for $C_{17}H_{21}ClN_3$ 302.1419; Found 302.1423.

General procedure for reductive Cope utilizing methyl/aryl allyl electrophile:



The starting material was added to a flame dried Schlenk flask purged with nitrogen with DMF (0.5 M). Hantzsch amide (5.0 eq) was added and the heat left on for 3 hours. The reaction mixture was cooled to room temperature, DCM was added and the organic layer was washed with a solution of 2 M HCl (x 3) and dried with anhydrous Na_2SO_4 and the crude material was then concentrated under reduced pressure. The crude material was purified *via* flash column chromatography on a 0-20% EtOAc gradient.

(*E*)-2-(3-(4-chlorophenyl)-2,2-dimethylhex-4-en-1-yl)malononitrile (17)



Pale yellow oil, 65% yield

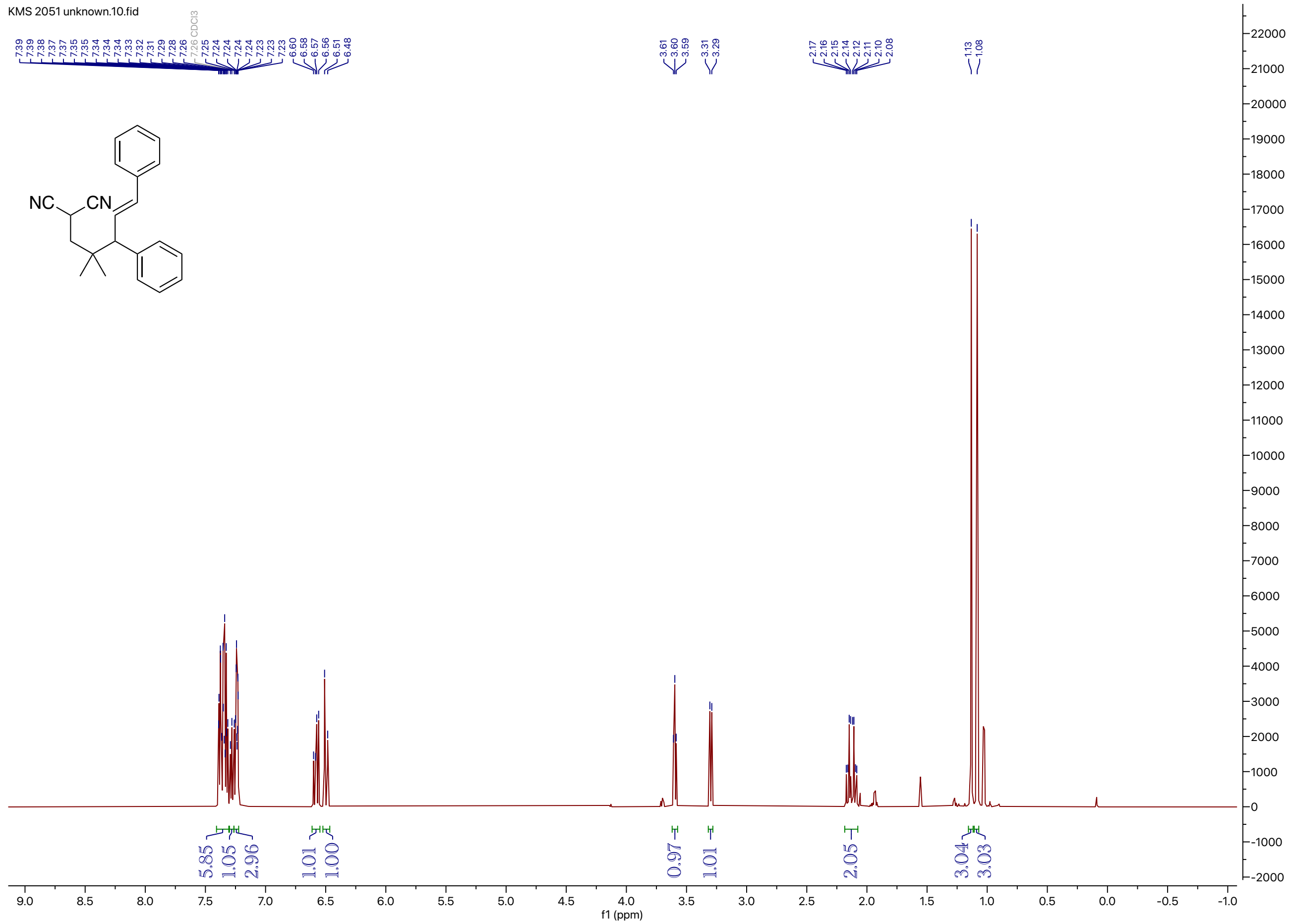
Purified using 0-20% gradient EtOAc in hexanes

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 2H), 7.12 – 7.04 (m, 2H), 5.78 (ddq, *J* = 15.0, 9.8, 1.7 Hz, 1H), 5.57 (dq, *J* = 15.0, 6.4 Hz, 1H), 3.66 (t, *J* = 6.7 Hz, 1H), 3.07 (d, *J* = 9.8 Hz, 1H), 2.17 – 1.98 (m, 2H), 1.72 (dd, *J* = 6.4, 1.7 Hz, 3H), 0.99 (d, *J* = 16.6 Hz, 6H).

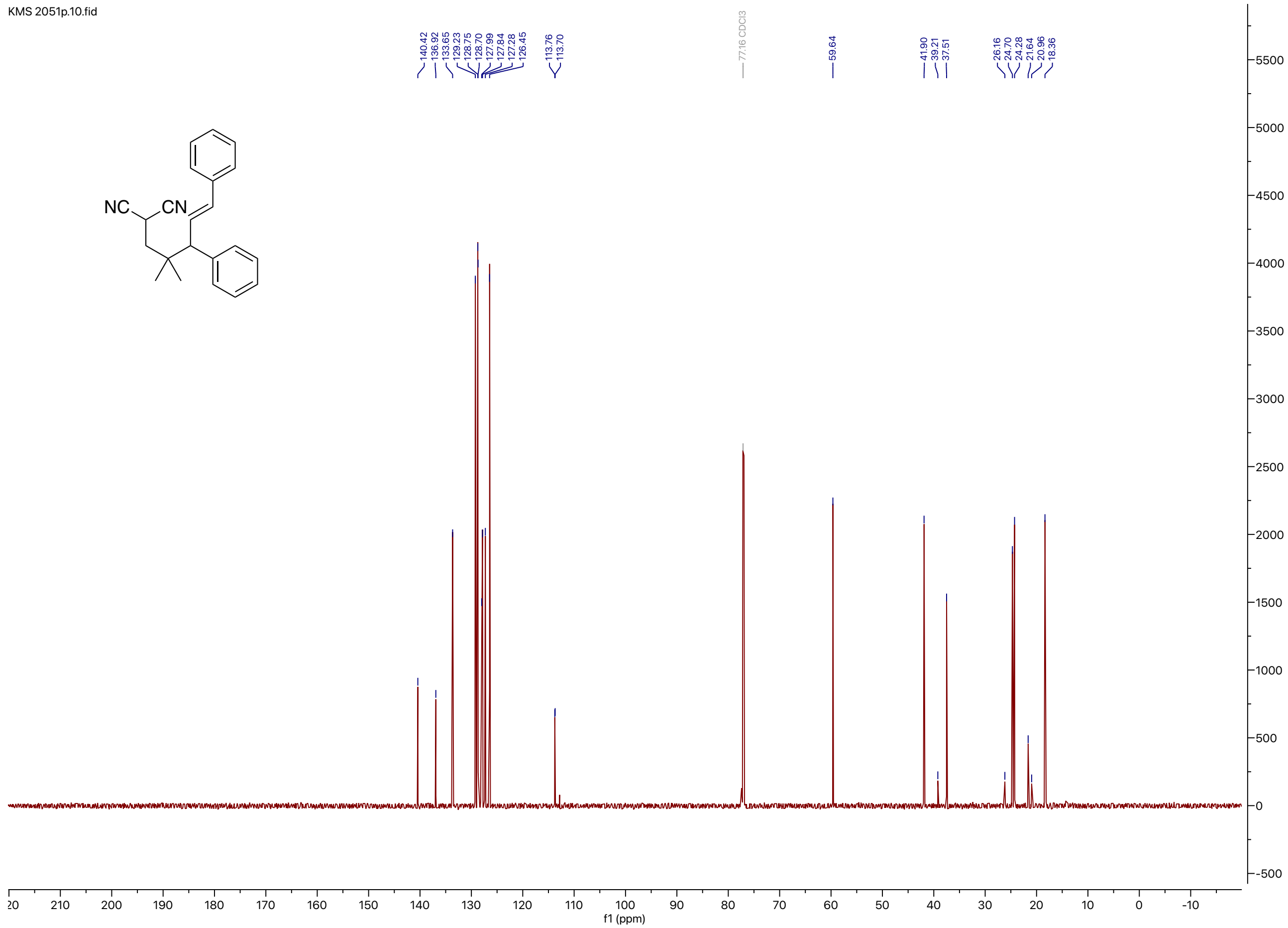
^{13}C NMR (101 MHz, $CDCl_3$) δ 139.5, 132.8, 130.5, 129.9, 128.7, 128.6, 128.5, 113.8, 113.7, 58.4, 51.5, 41.8, 36.9, 29.8, 24.6, 23.8, 18.3.

HRMS (DART) m/z: $[M + NH_4]^+$ Calcd for $C_{17}H_{23}ClN_3$ 304.1575; Found 304.1590.

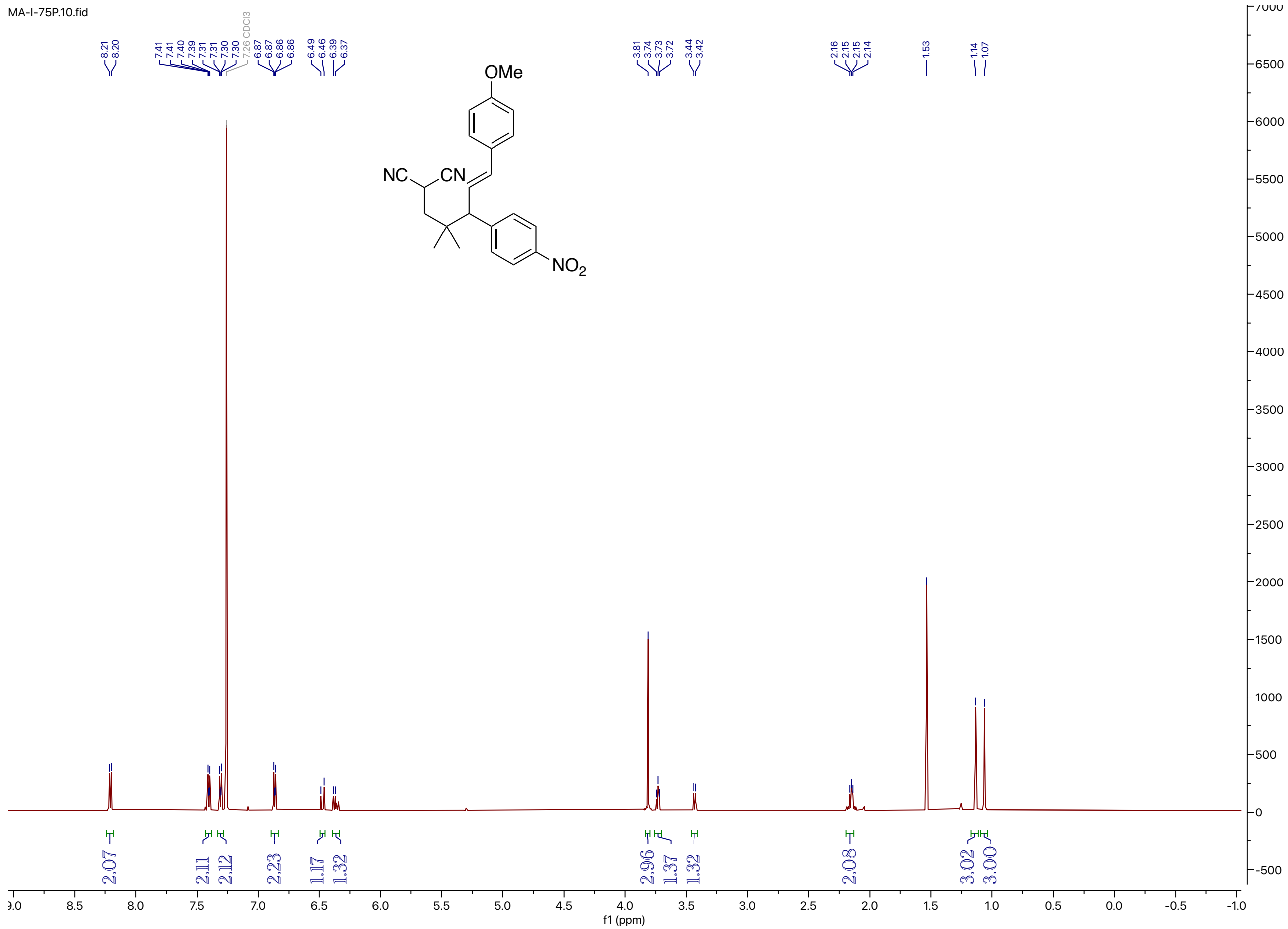
^{1}H NMR Spectrum of 10a ($CDCl_3$)



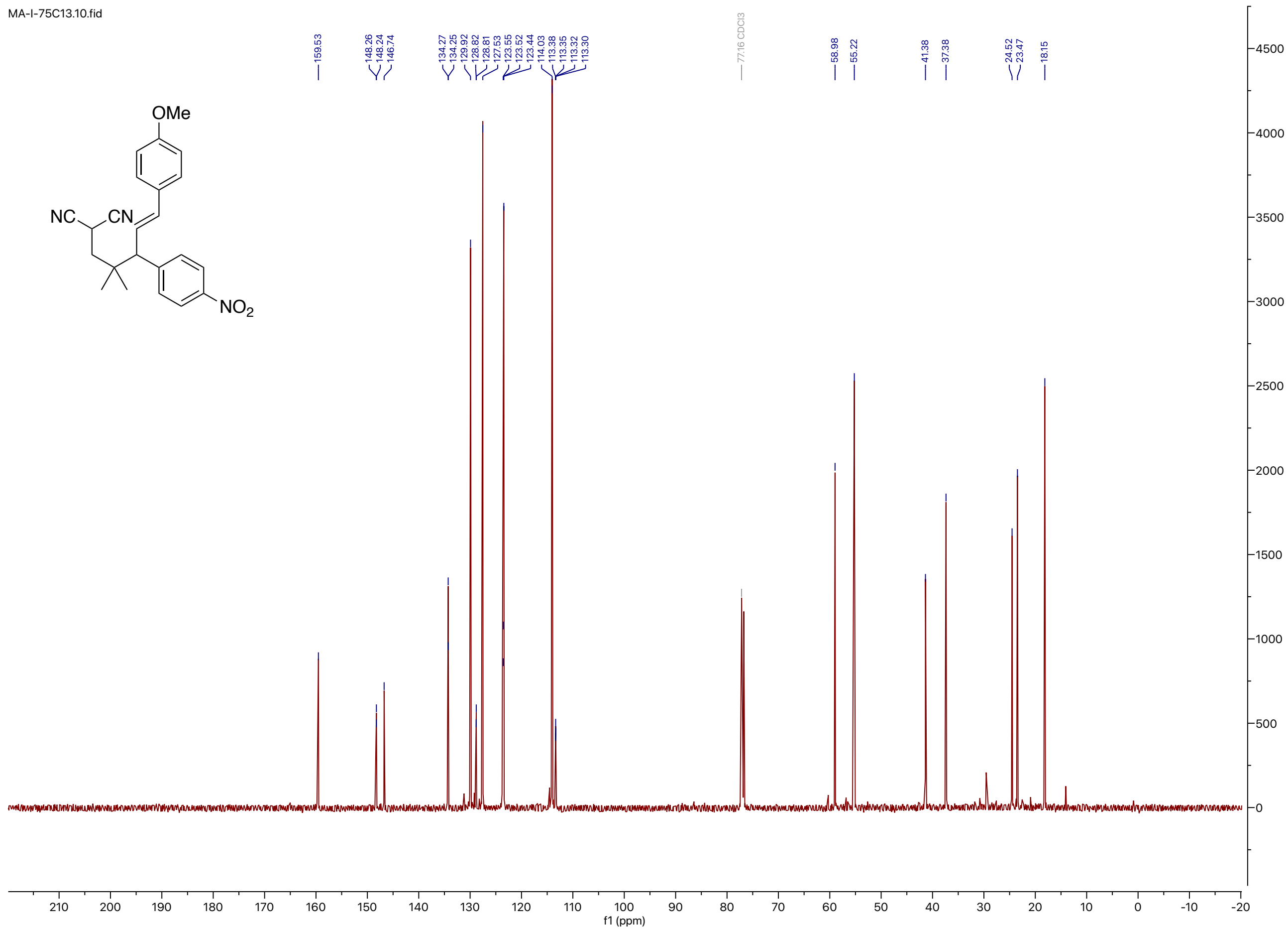
^{13}C NMR Spectrum of 10a ($CDCl_3$)



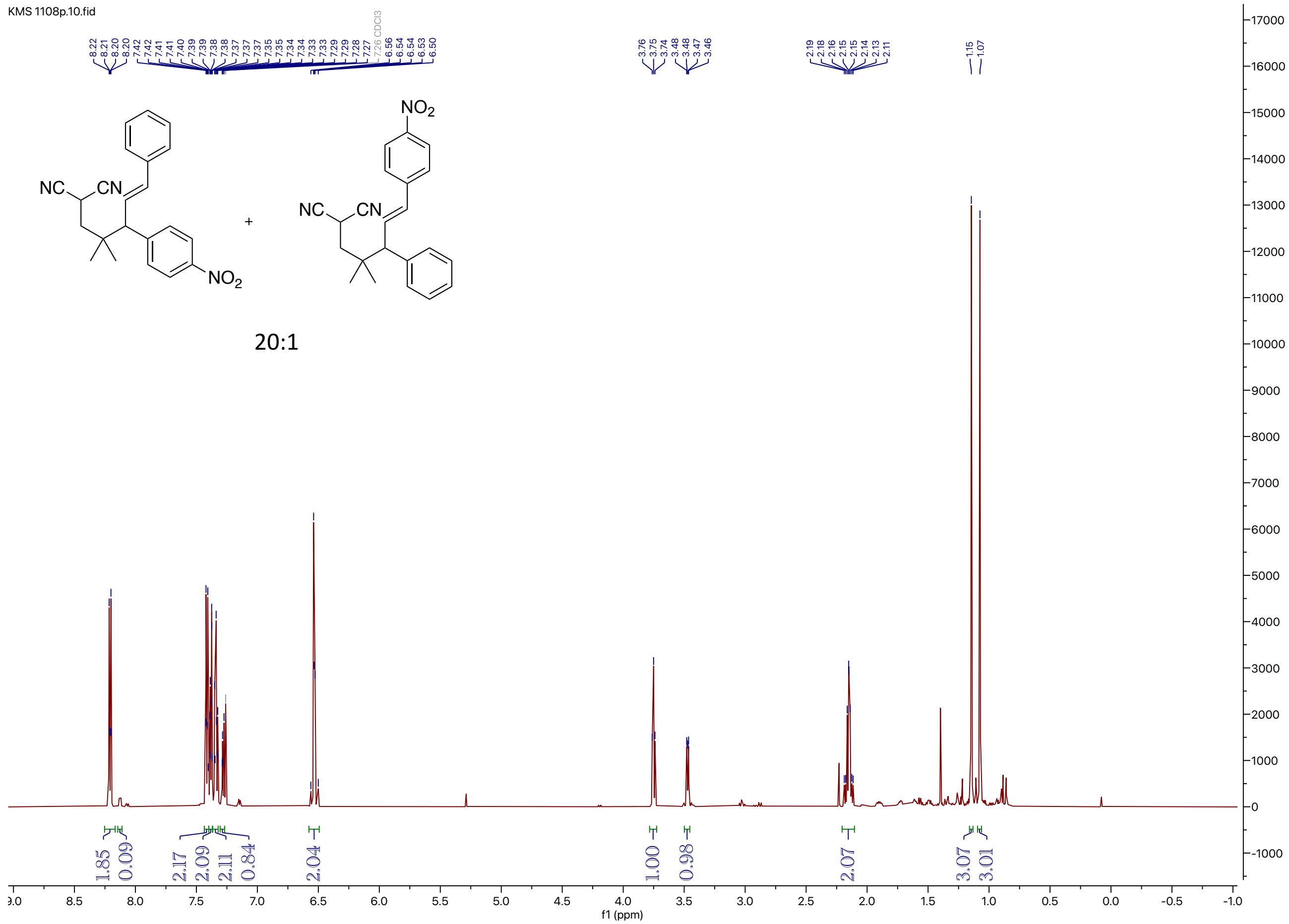
1H NMR Spectrum of 10b ($CDCl_3$)



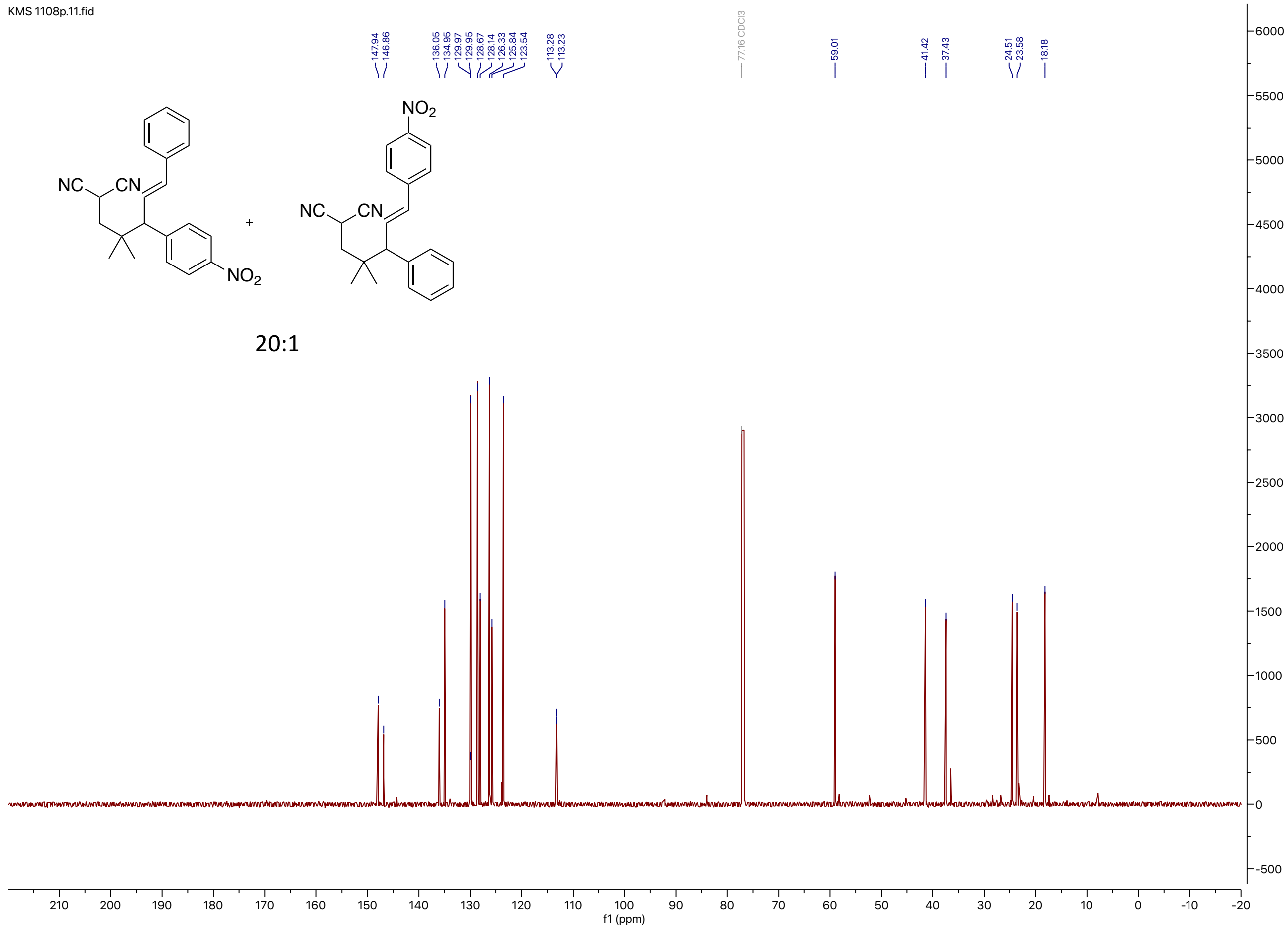
^{13}C NMR Spectrum of 10b ($CDCl_3$)



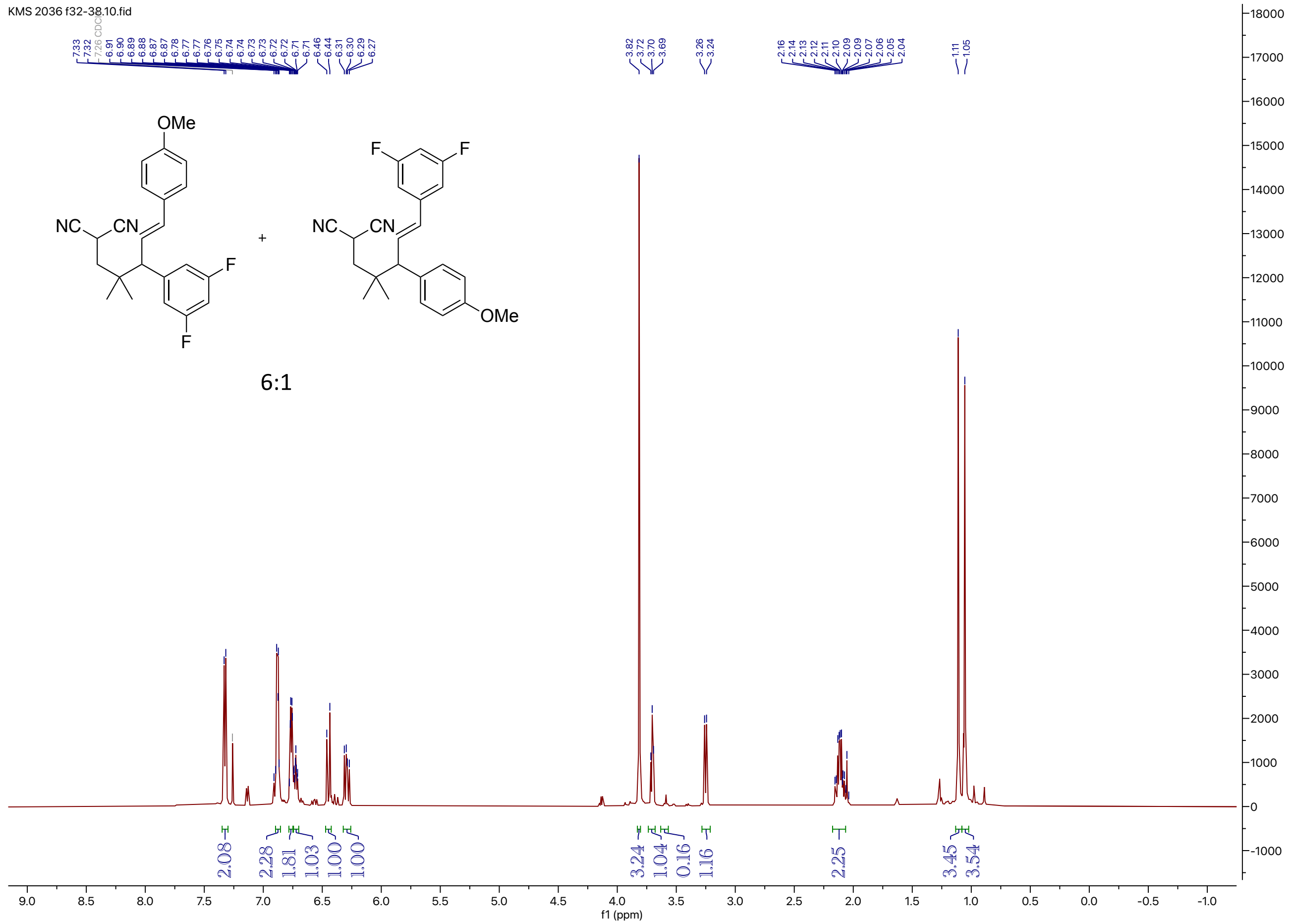
[1]H NMR Spectrum of 10c ($CDCl_3$)



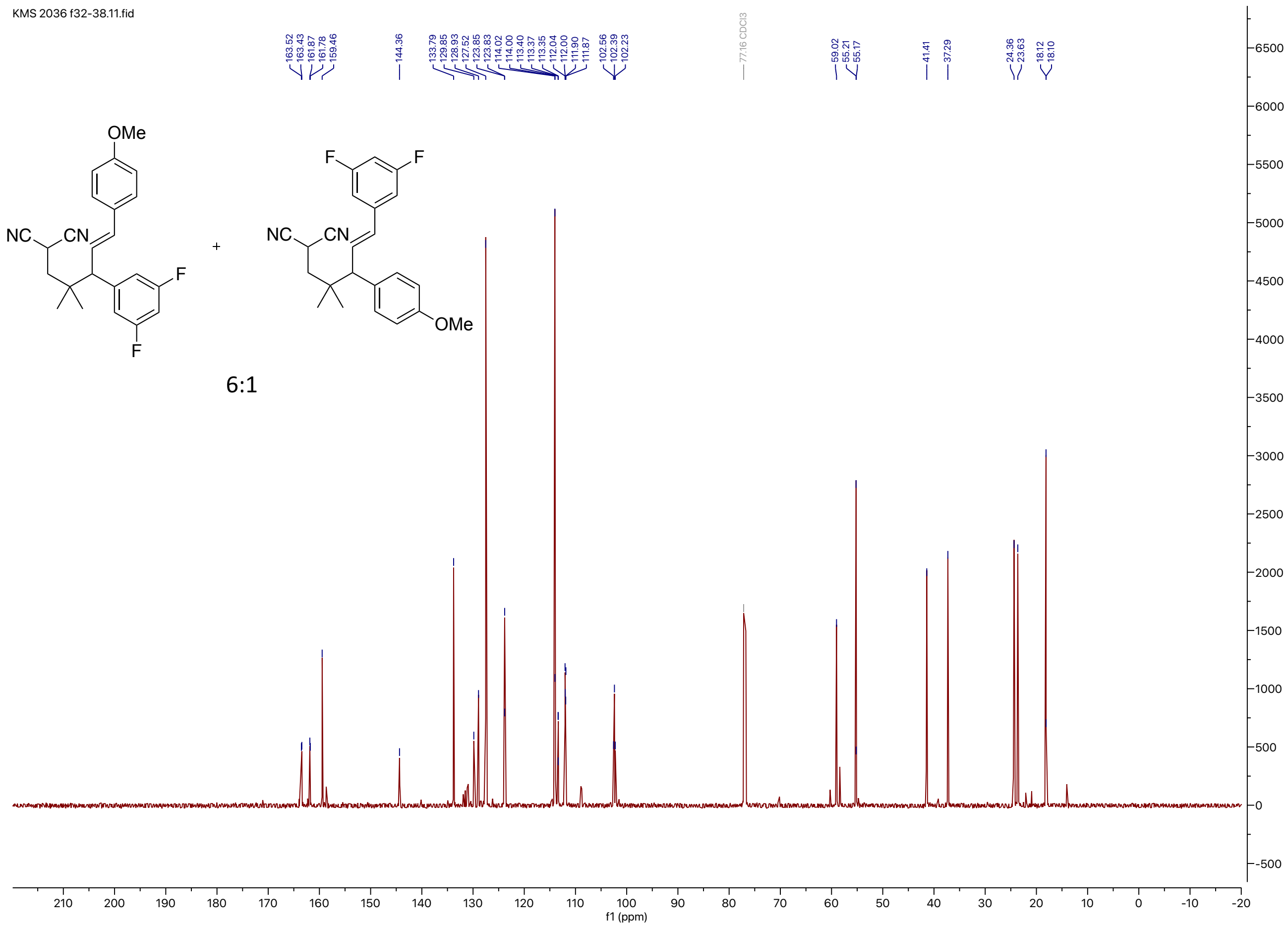
^{13}C NMR Spectrum of 10c ($CDCl_3$)



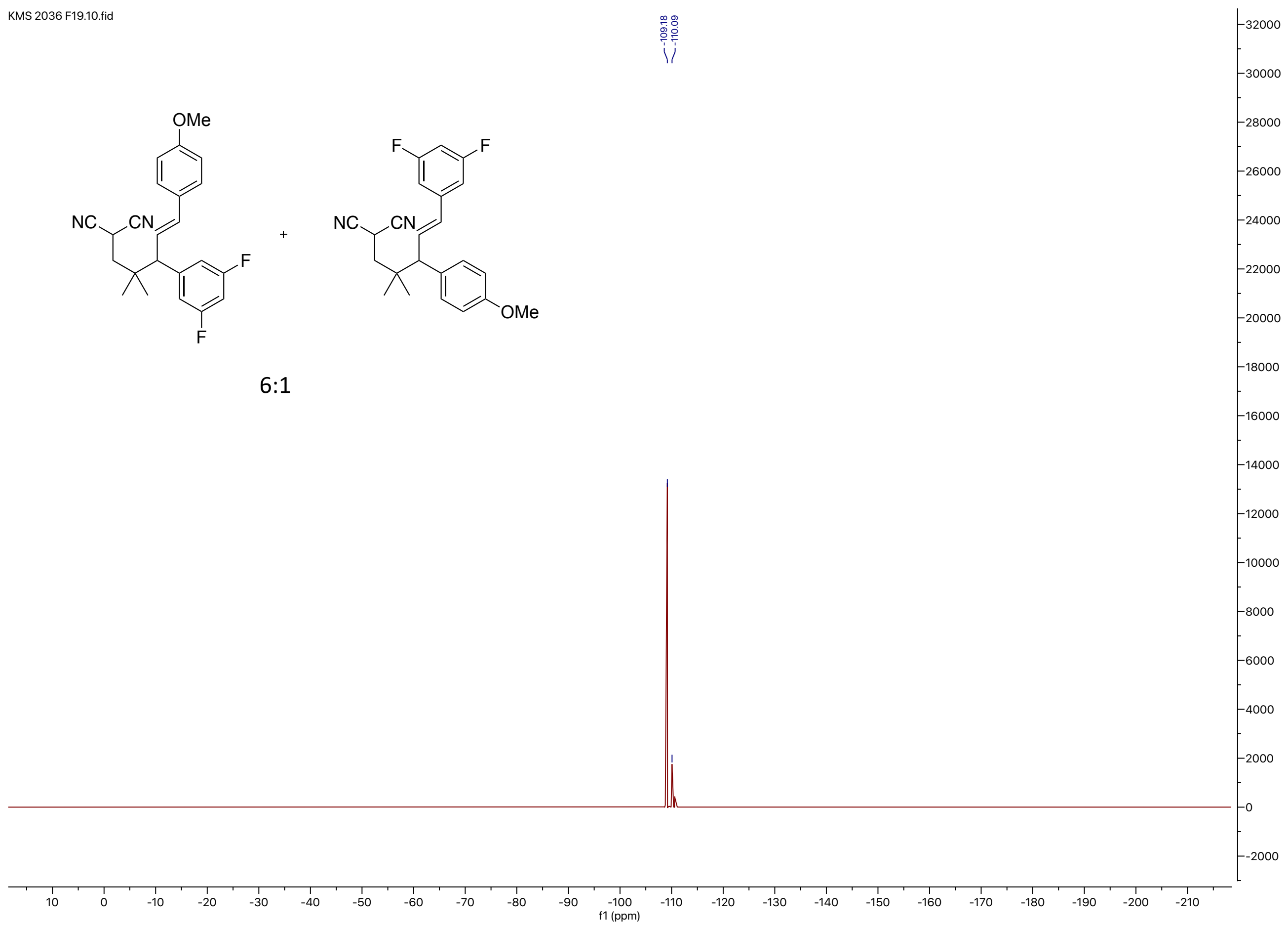
^{1}H NMR Spectrum of 10d ($CDCl_3$)



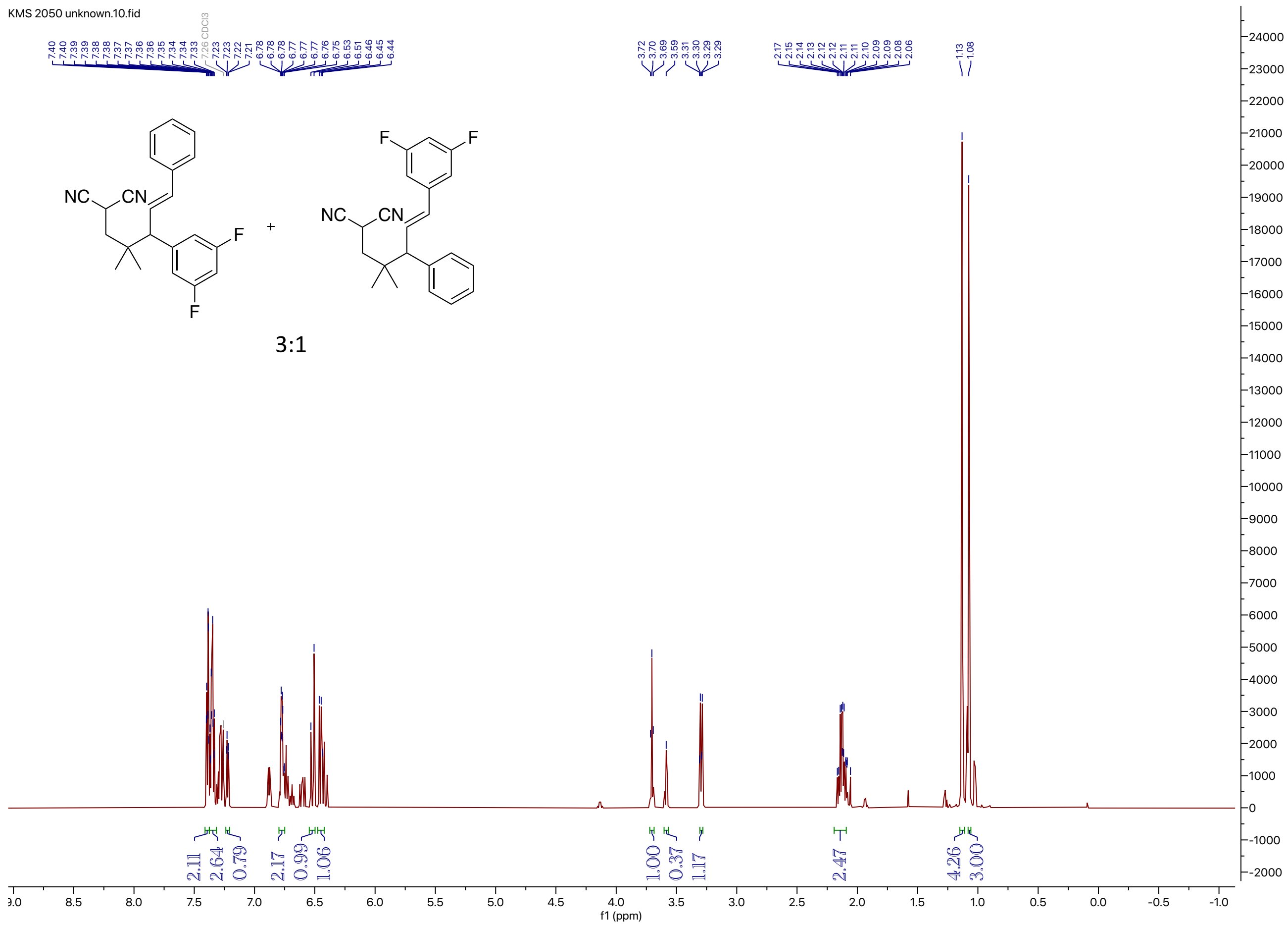
^{13}C NMR Spectrum of 10d ($CDCl_3$)



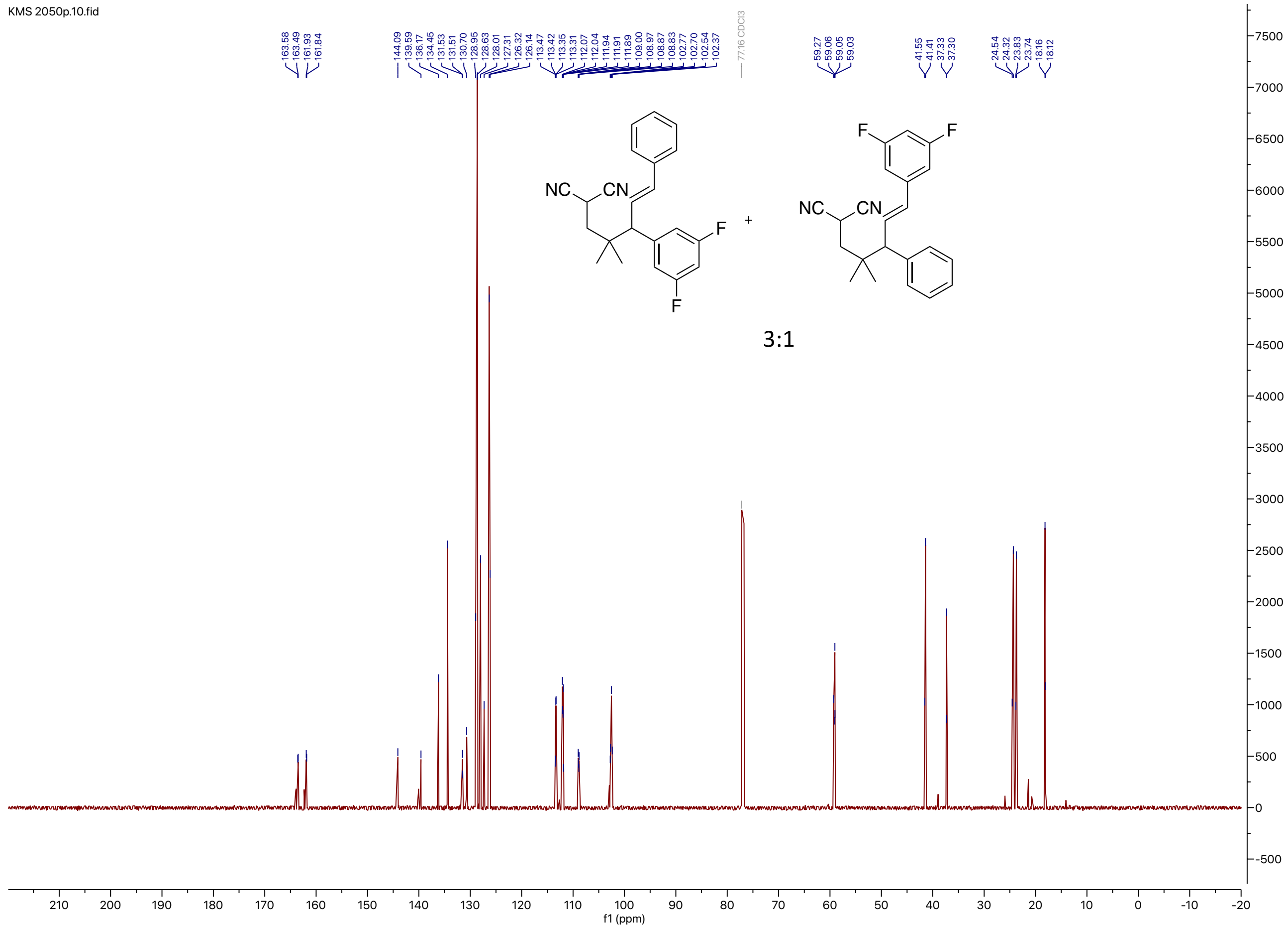
^{19}F NMR Spectrum of 10d ($CDCl_3$)



^{1}H NMR Spectrum of 10e ($CDCl_3$)

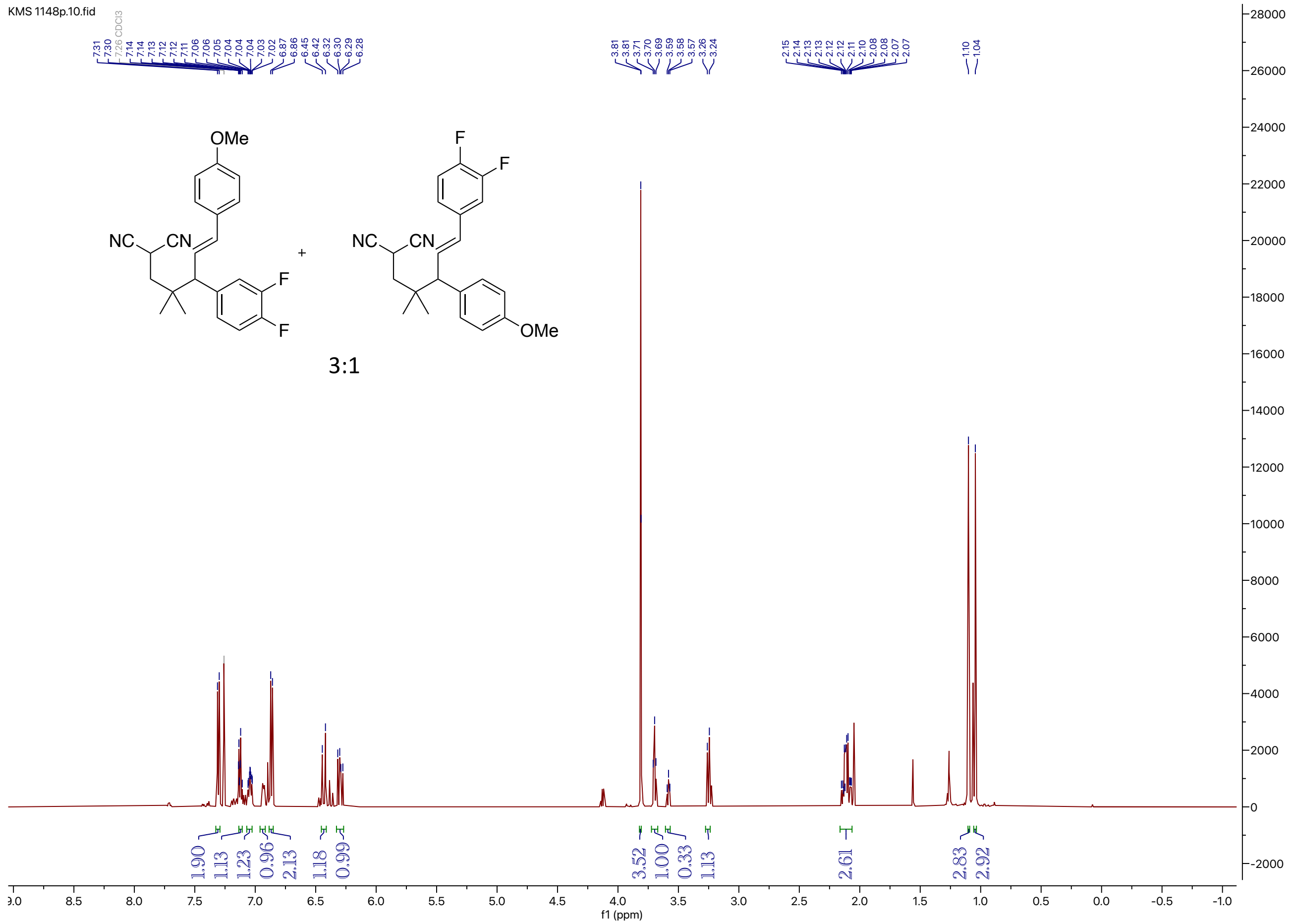


^{13}C NMR Spectrum of 10e ($CDCl_3$)

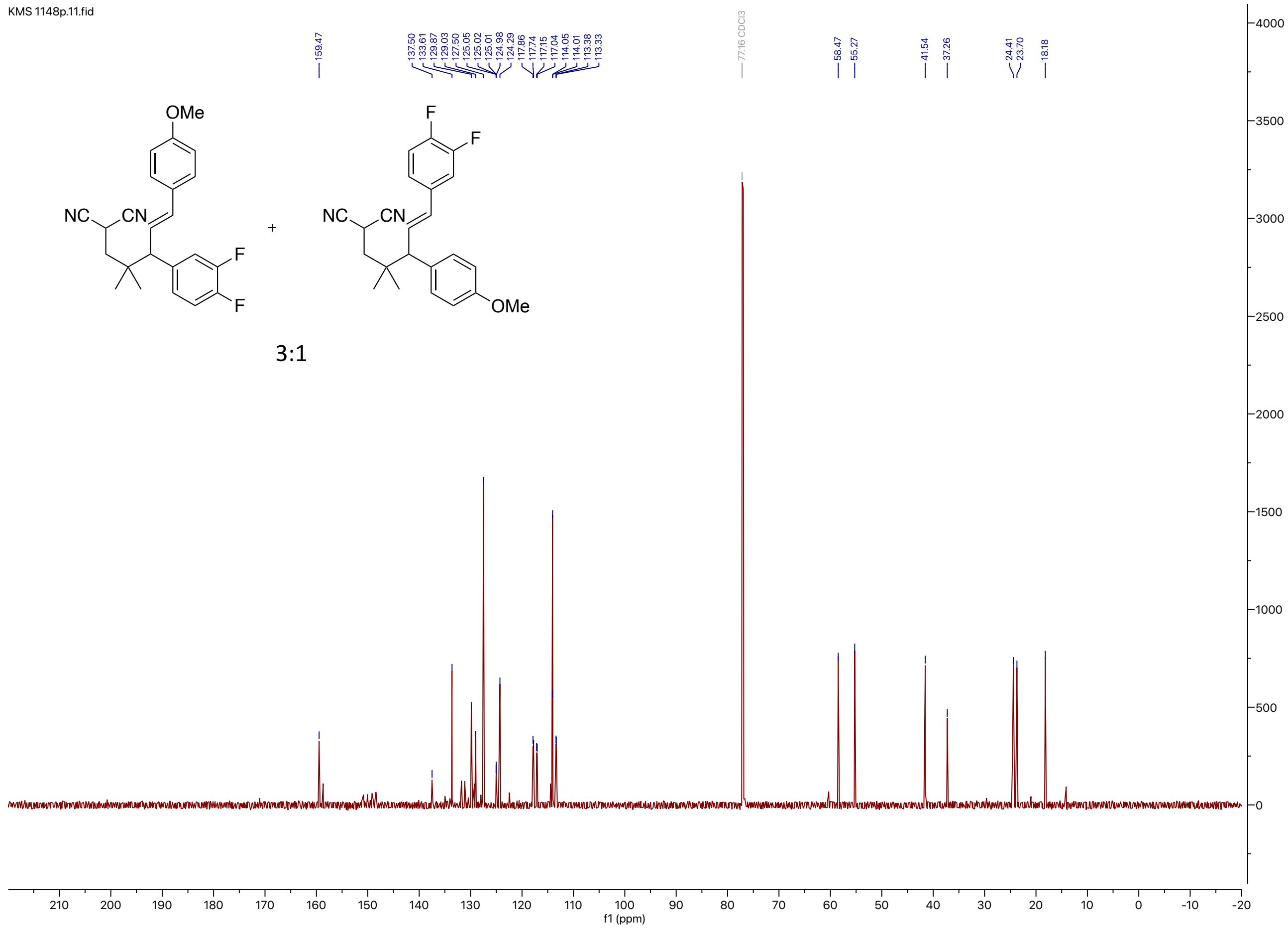


^{19}F NMR Spectrum of 10e ($CDCl_3$)

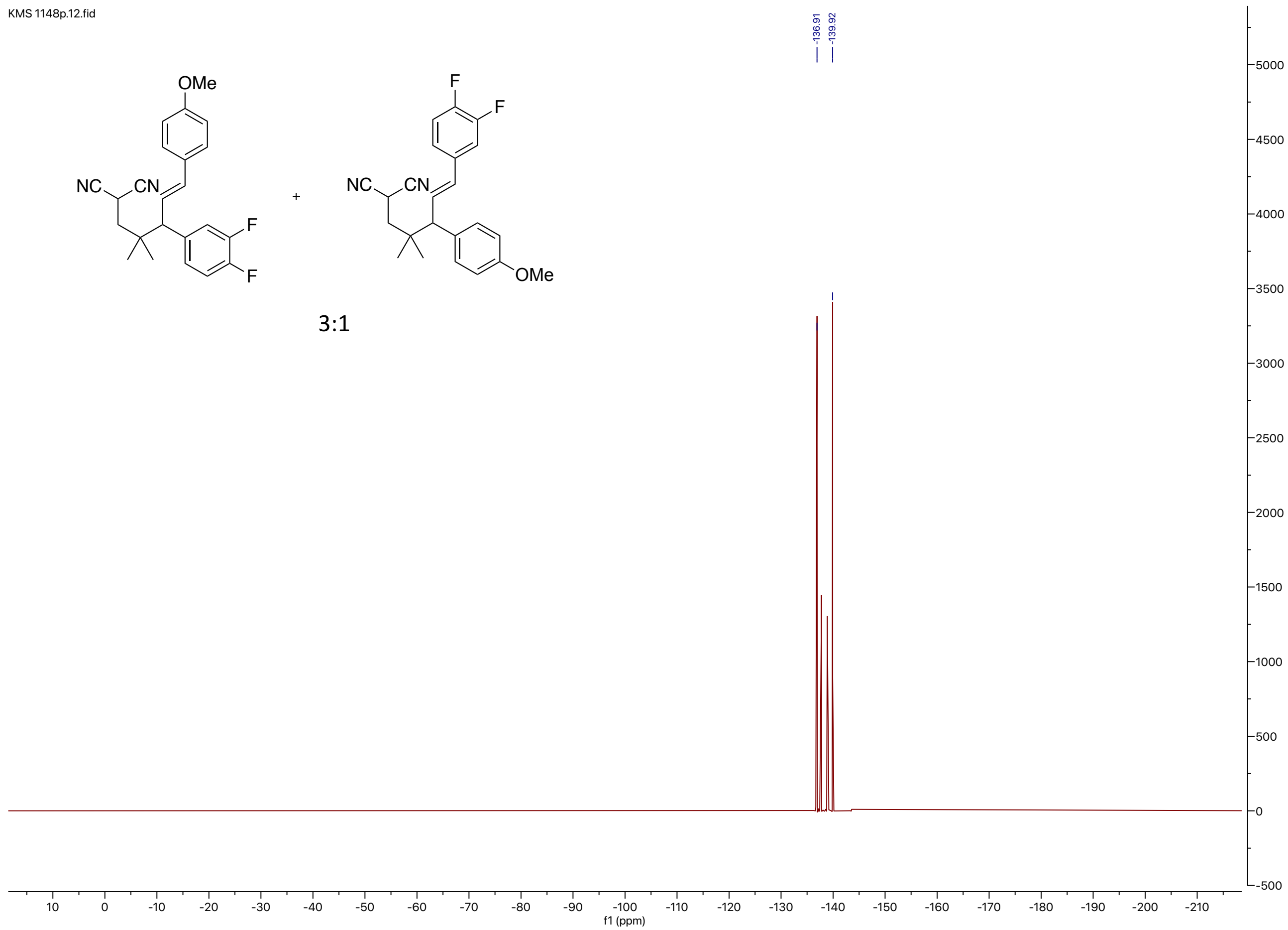
[1]H NMR Spectrum of 10f ($CDCl_3$)



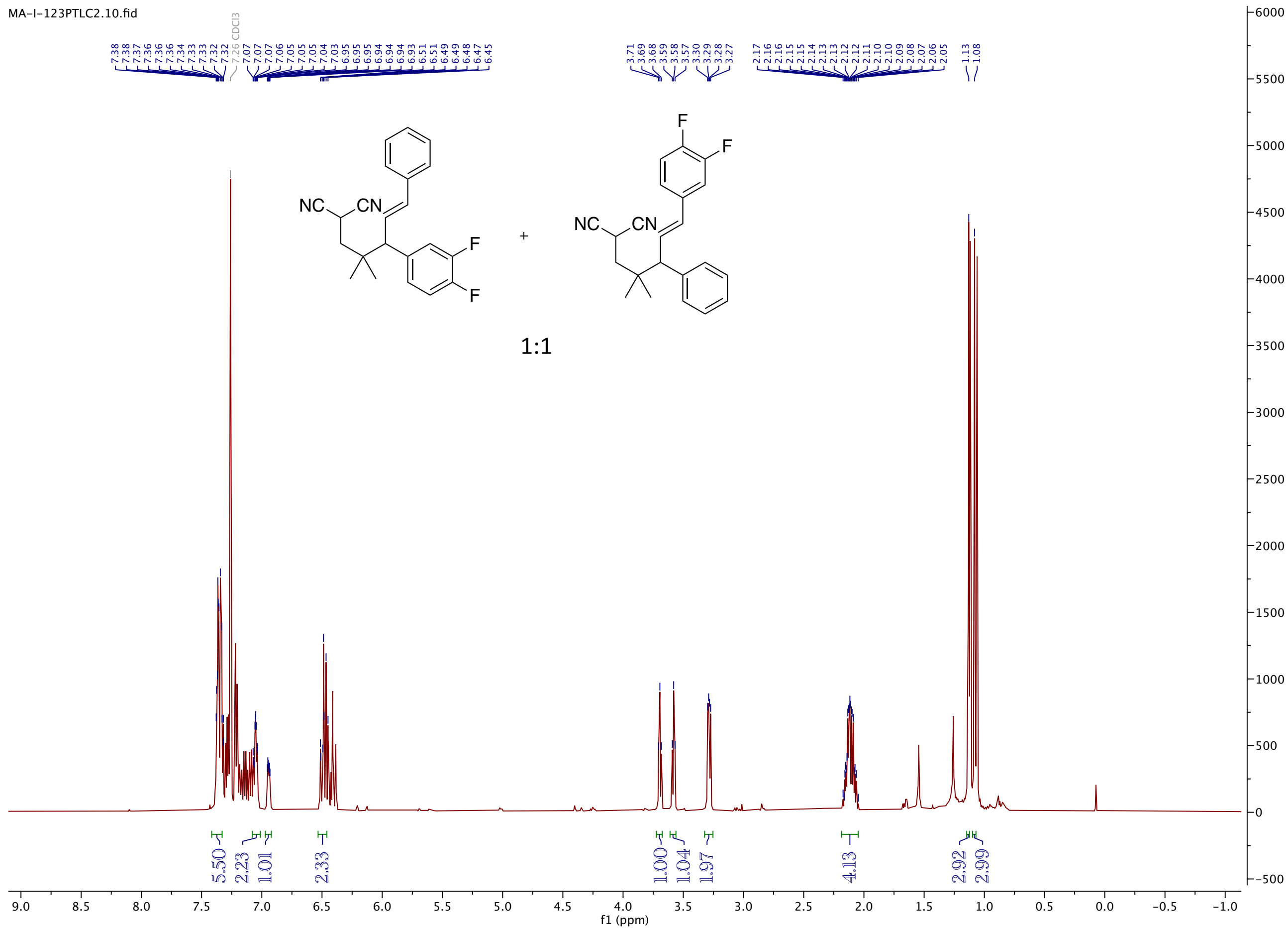
^{13}C NMR Spectrum of 10f ($CDCl_3$)



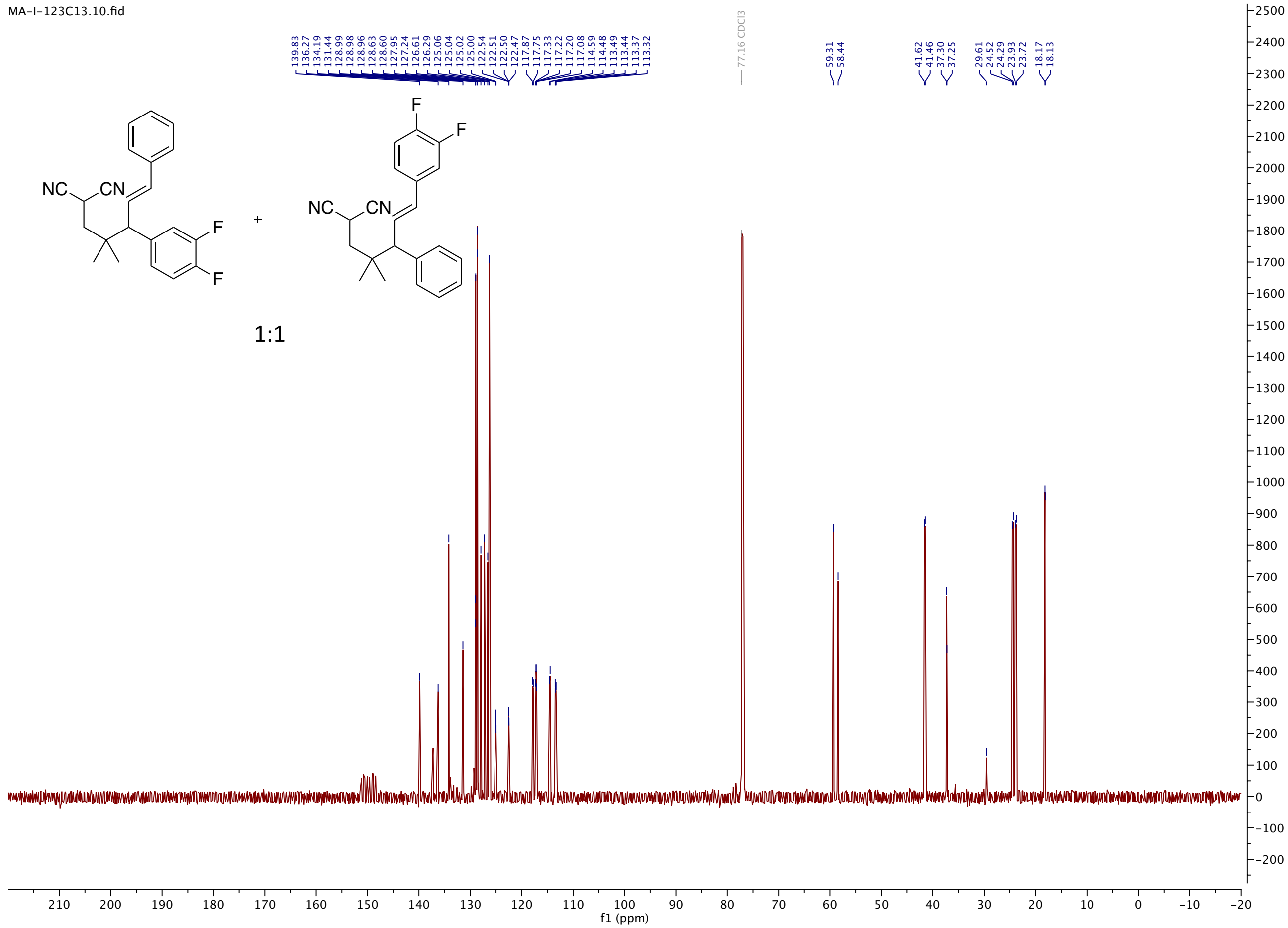
^{19}F NMR Spectrum of 10f ($CDCl_3$)



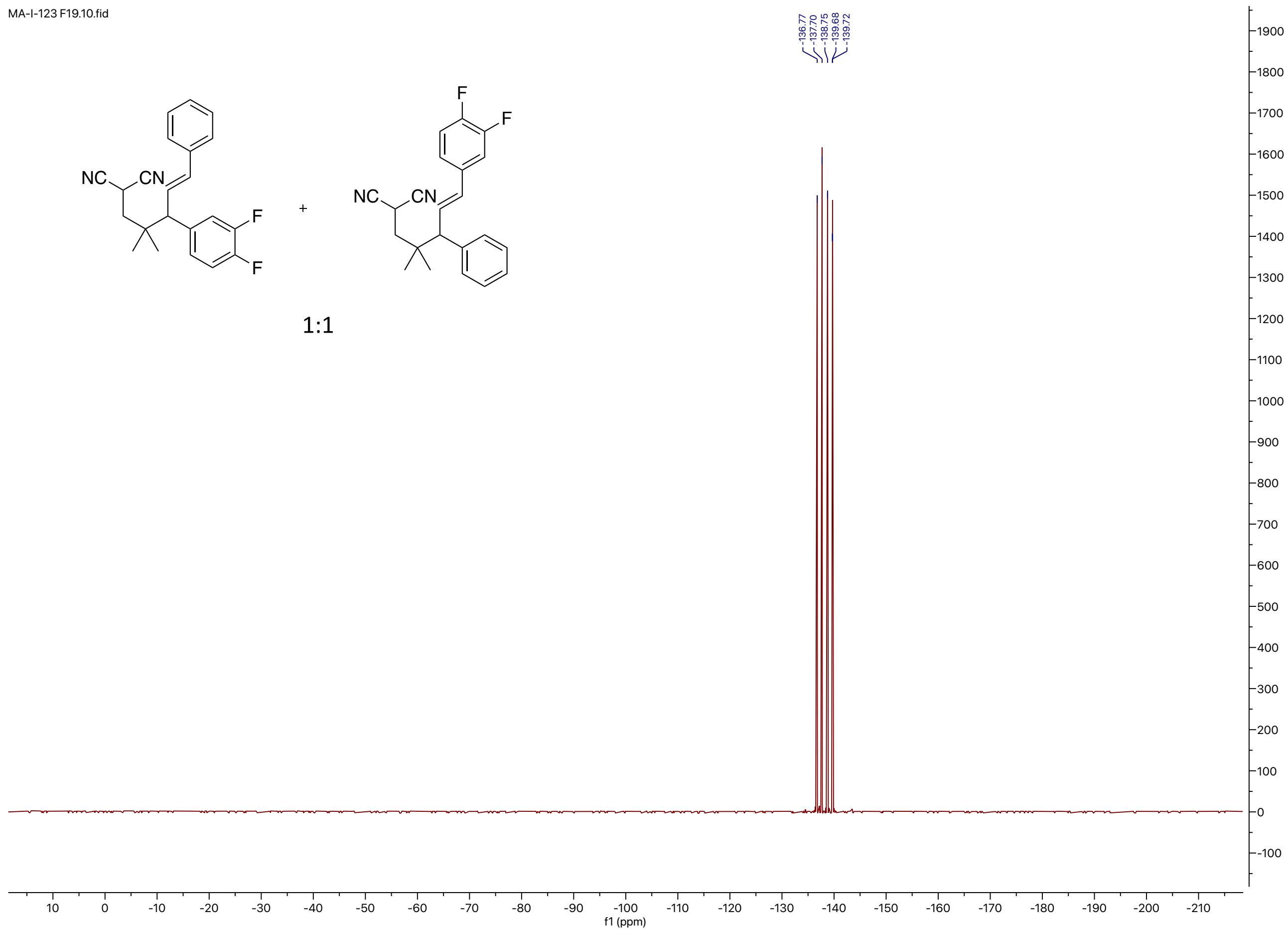
^{1}H NMR Spectrum of 10g ($CDCl_3$)



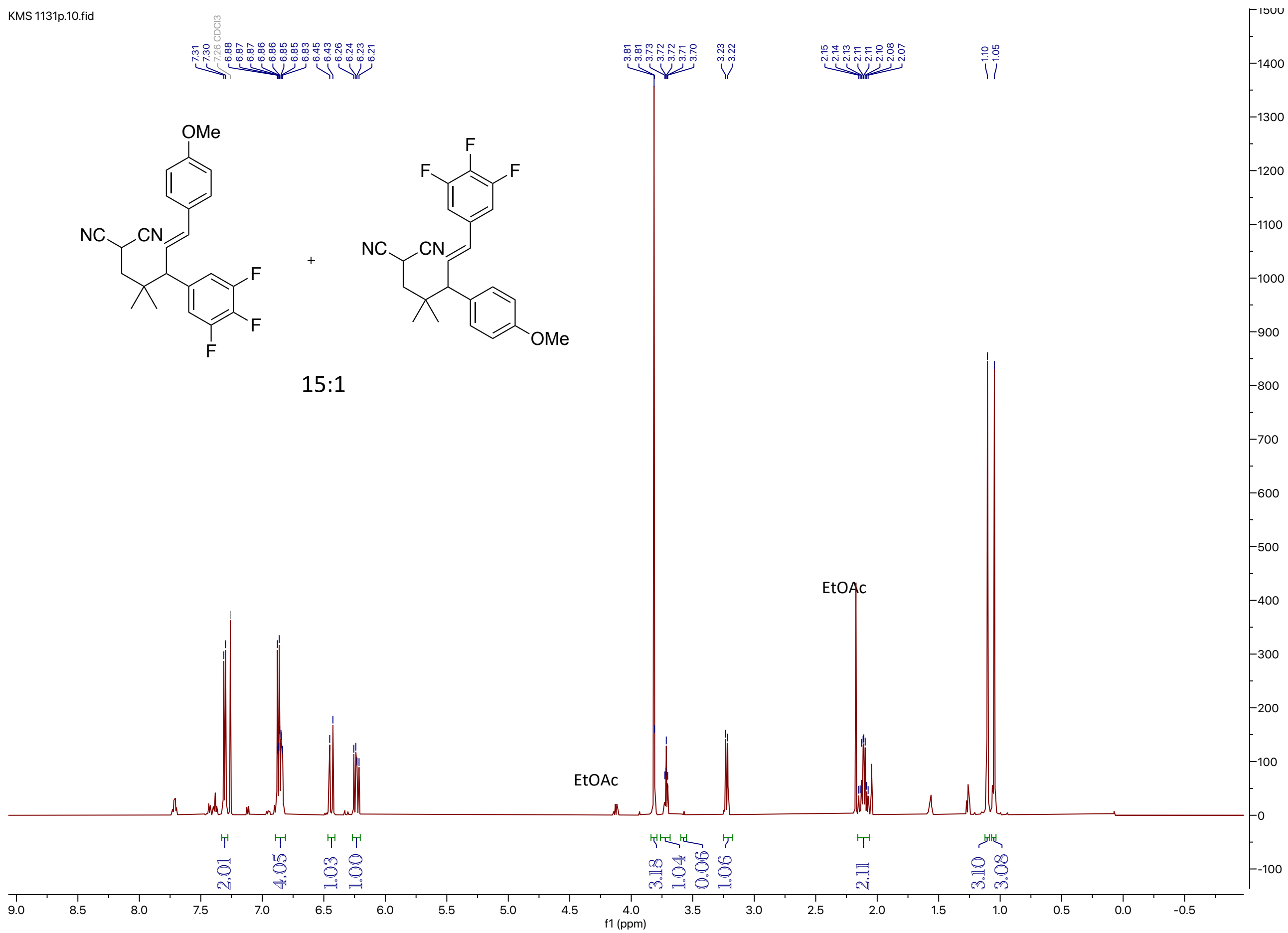
^{13}C NMR Spectrum of 10g ($CDCl_3$)



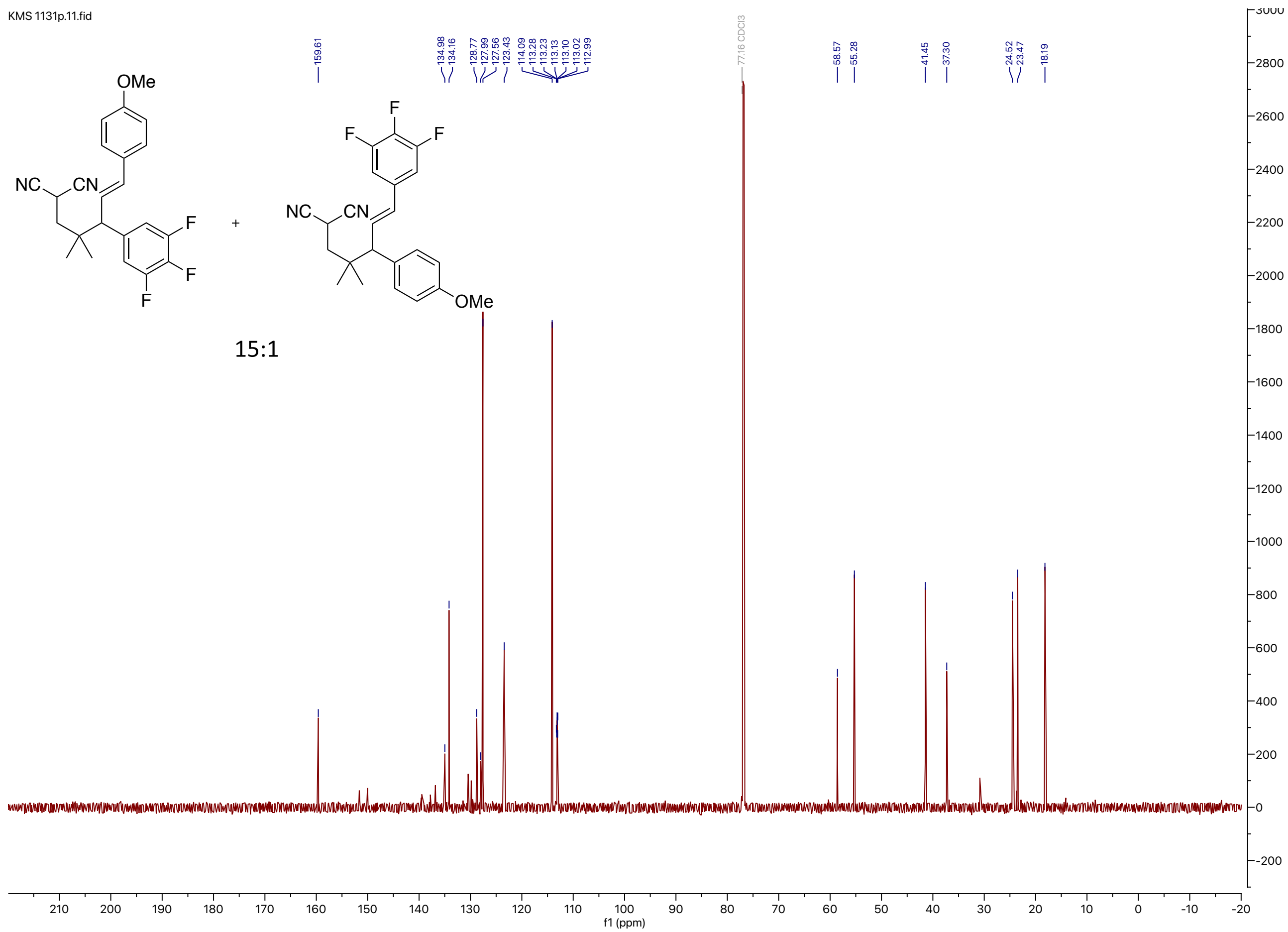
^{19}F NMR Spectrum of 10g ($CDCl_3$)



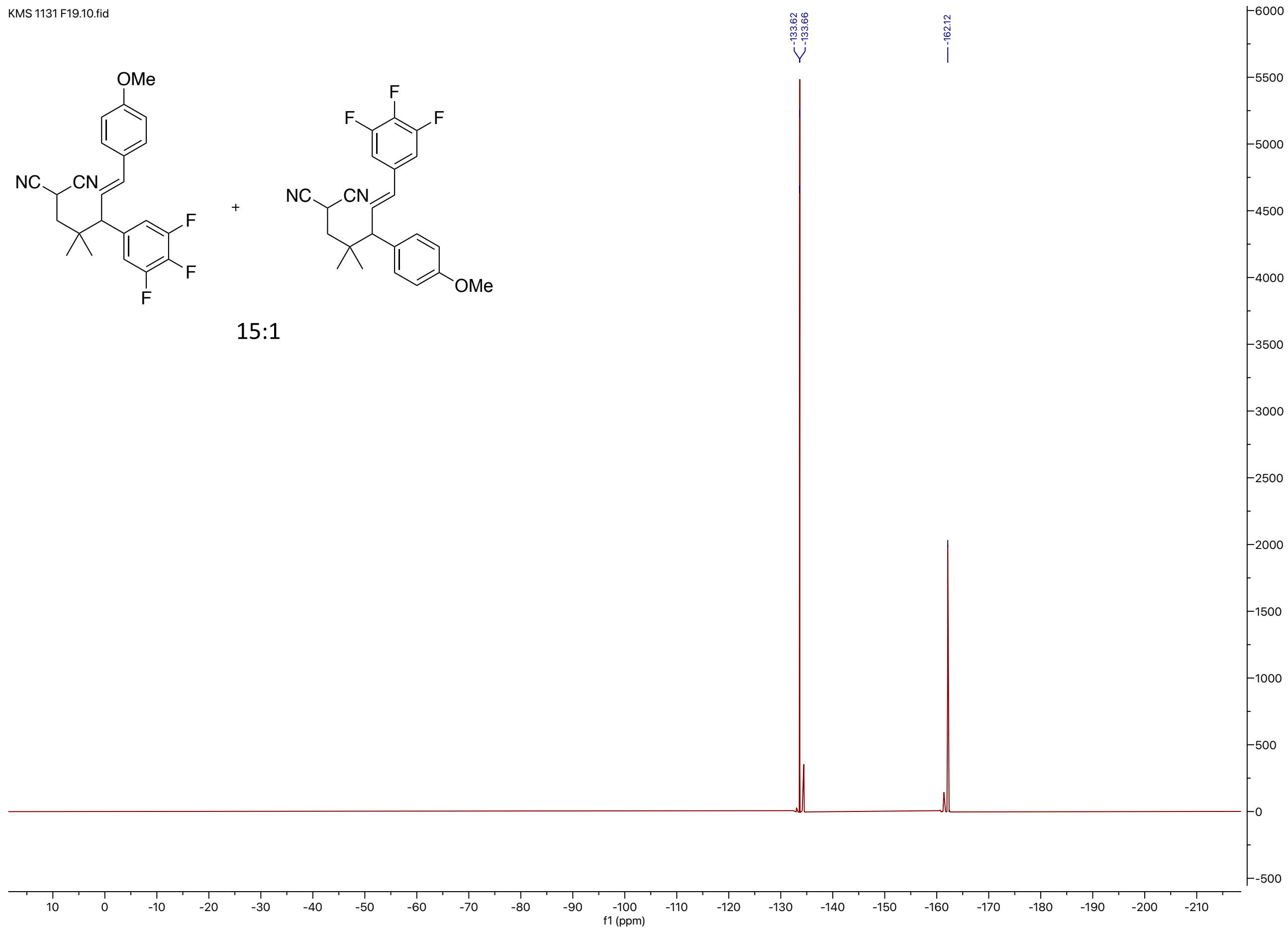
^{1}H NMR Spectrum of 10h ($CDCl_3$)



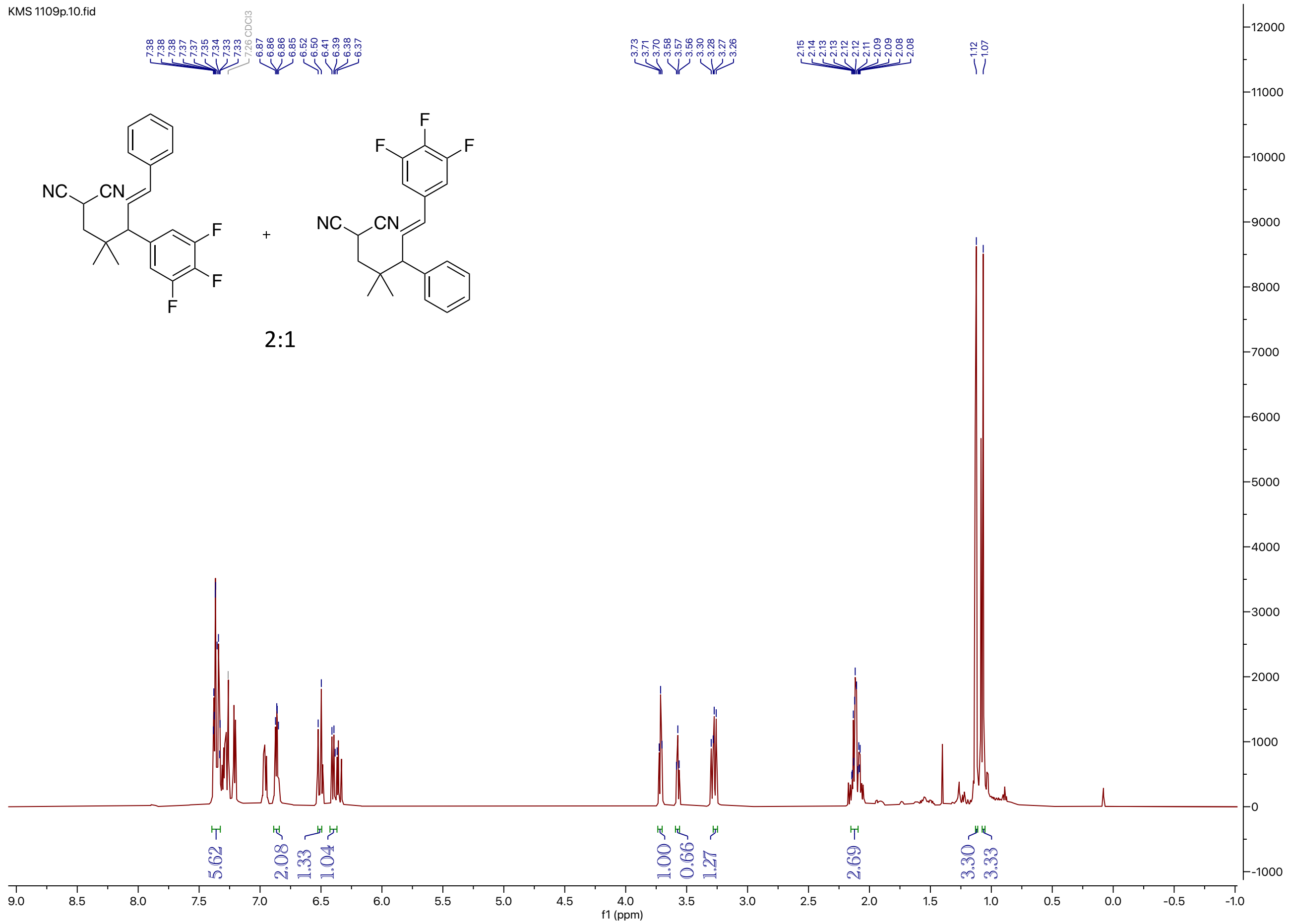
^{13}C NMR Spectrum of 10h ($CDCl_3$)



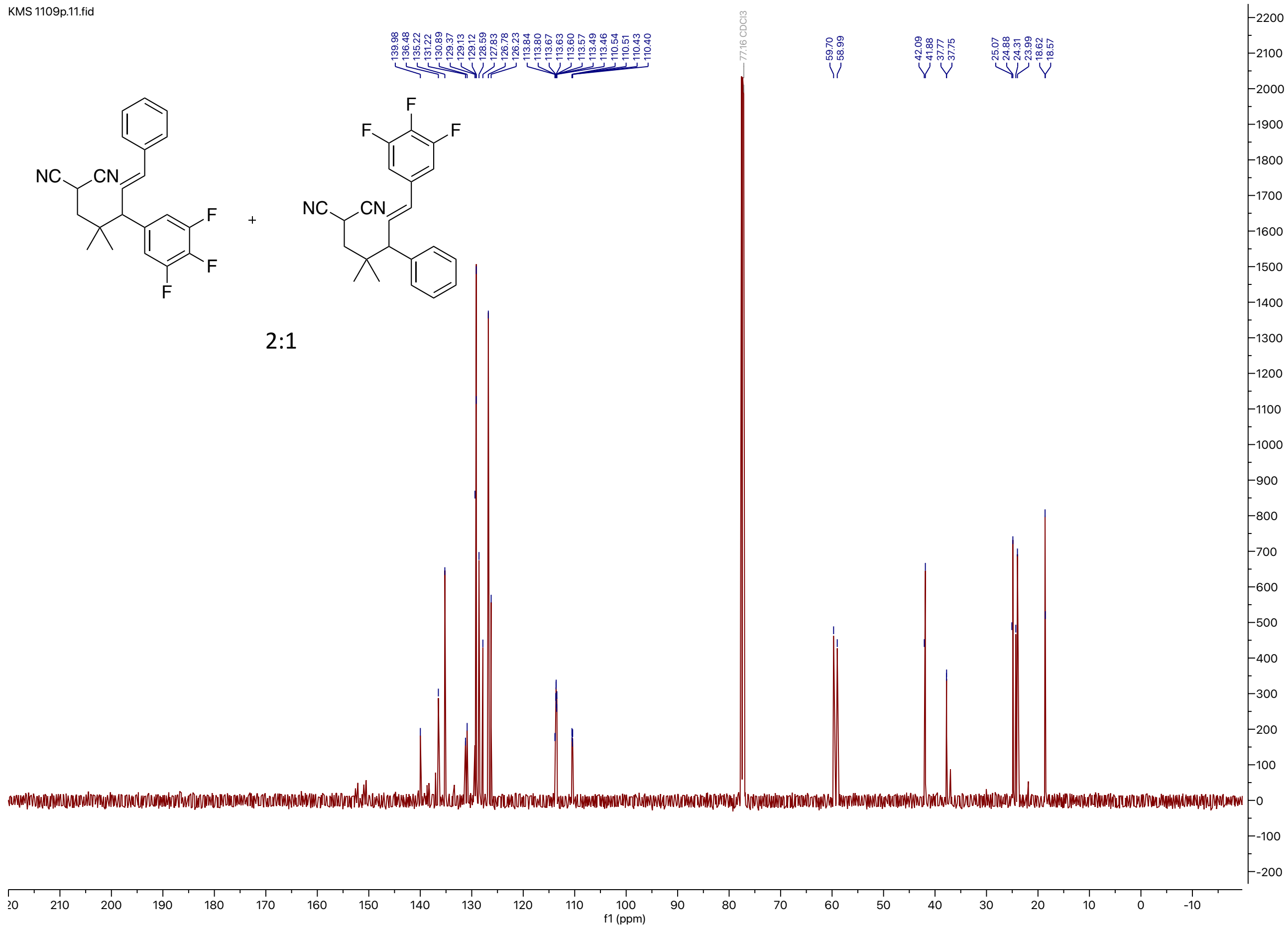
^{19}F NMR Spectrum of 10h ($CDCl_3$)



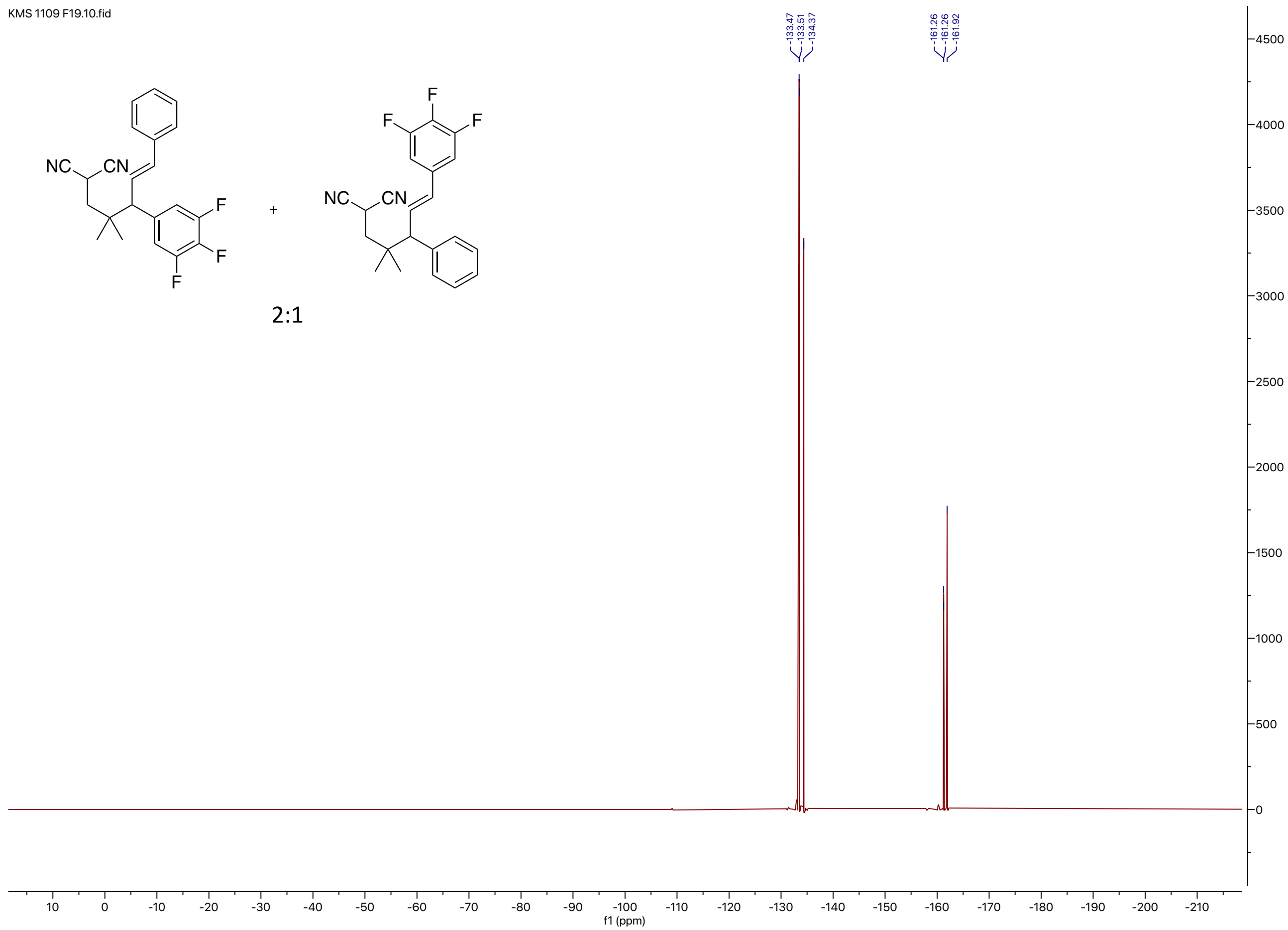
1H NMR Spectrum of 10i ($CDCl_3$)



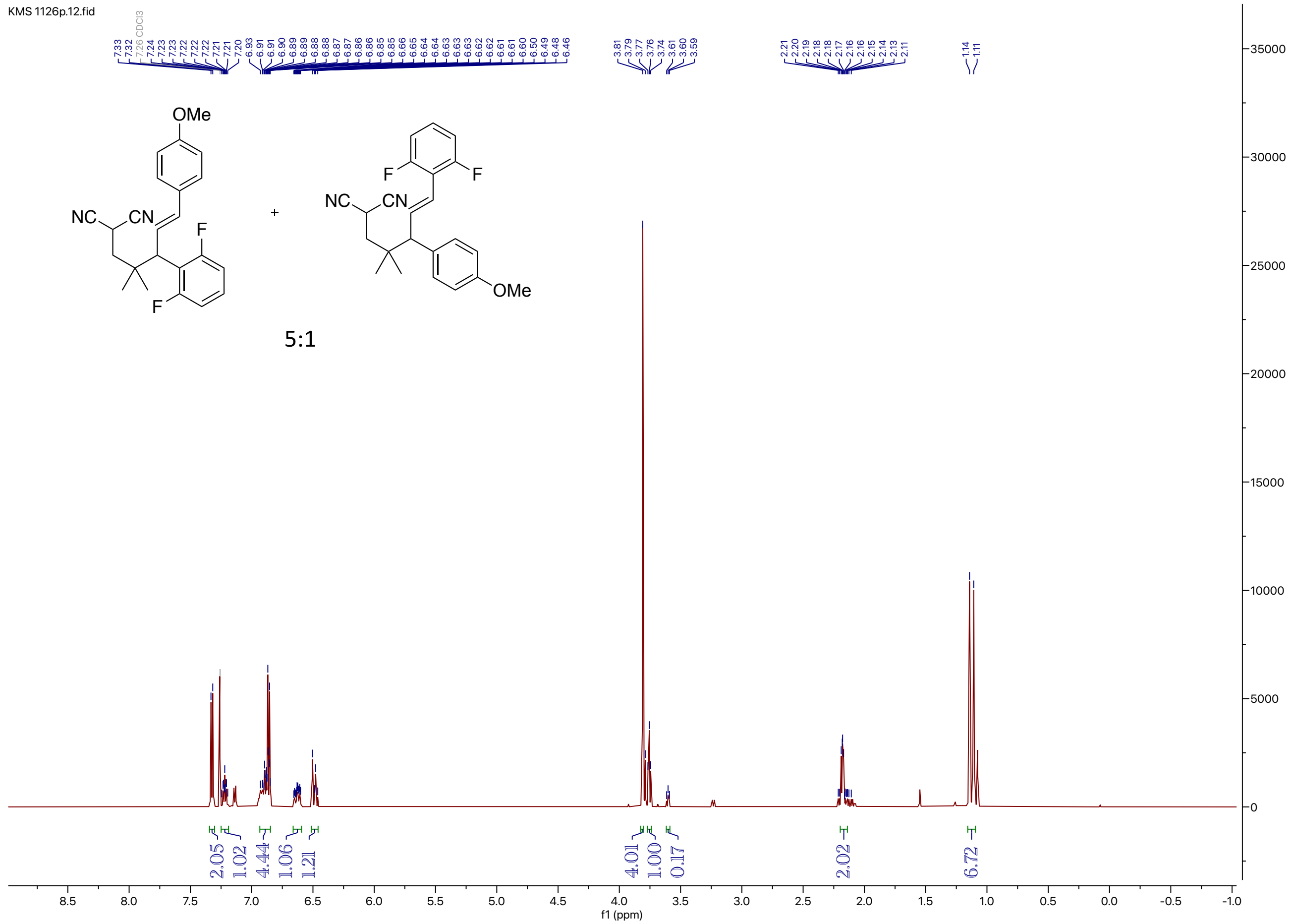
^{13}C NMR Spectrum of 10i ($CDCl_3$)



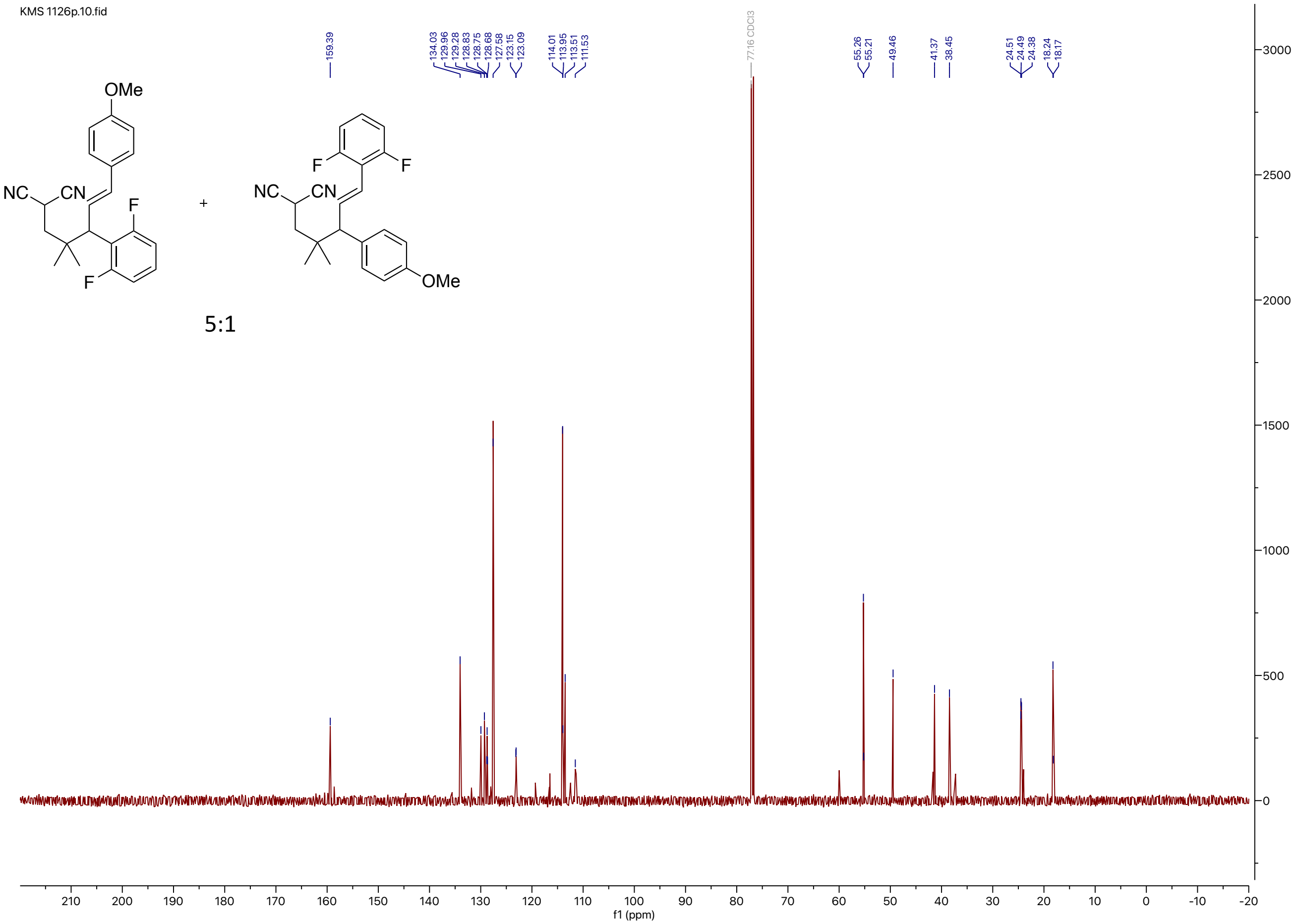
^{19}F NMR Spectrum of 10i ($CDCl_3$)



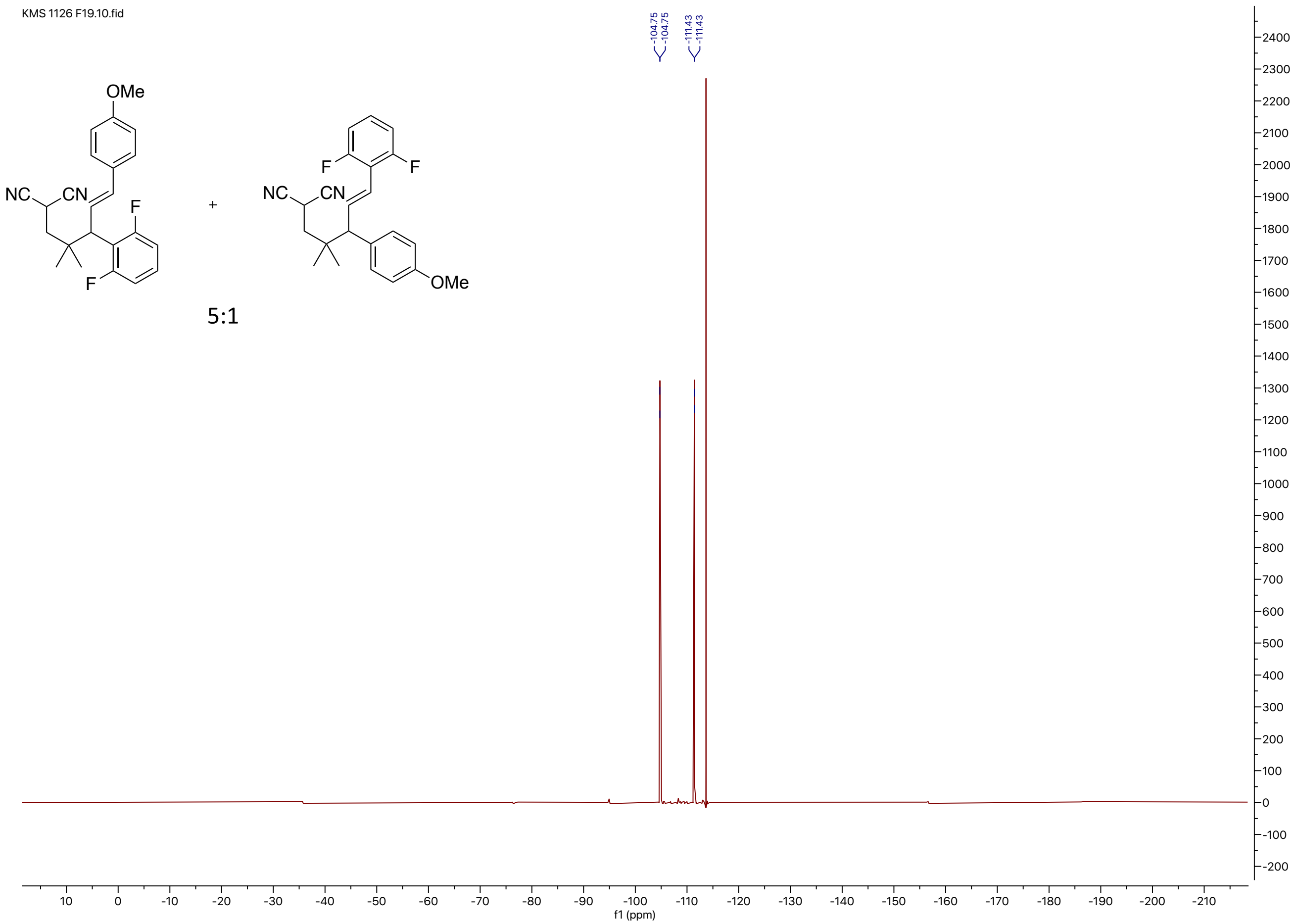
^{1}H NMR Spectrum of 10j ($CDCl_3$)



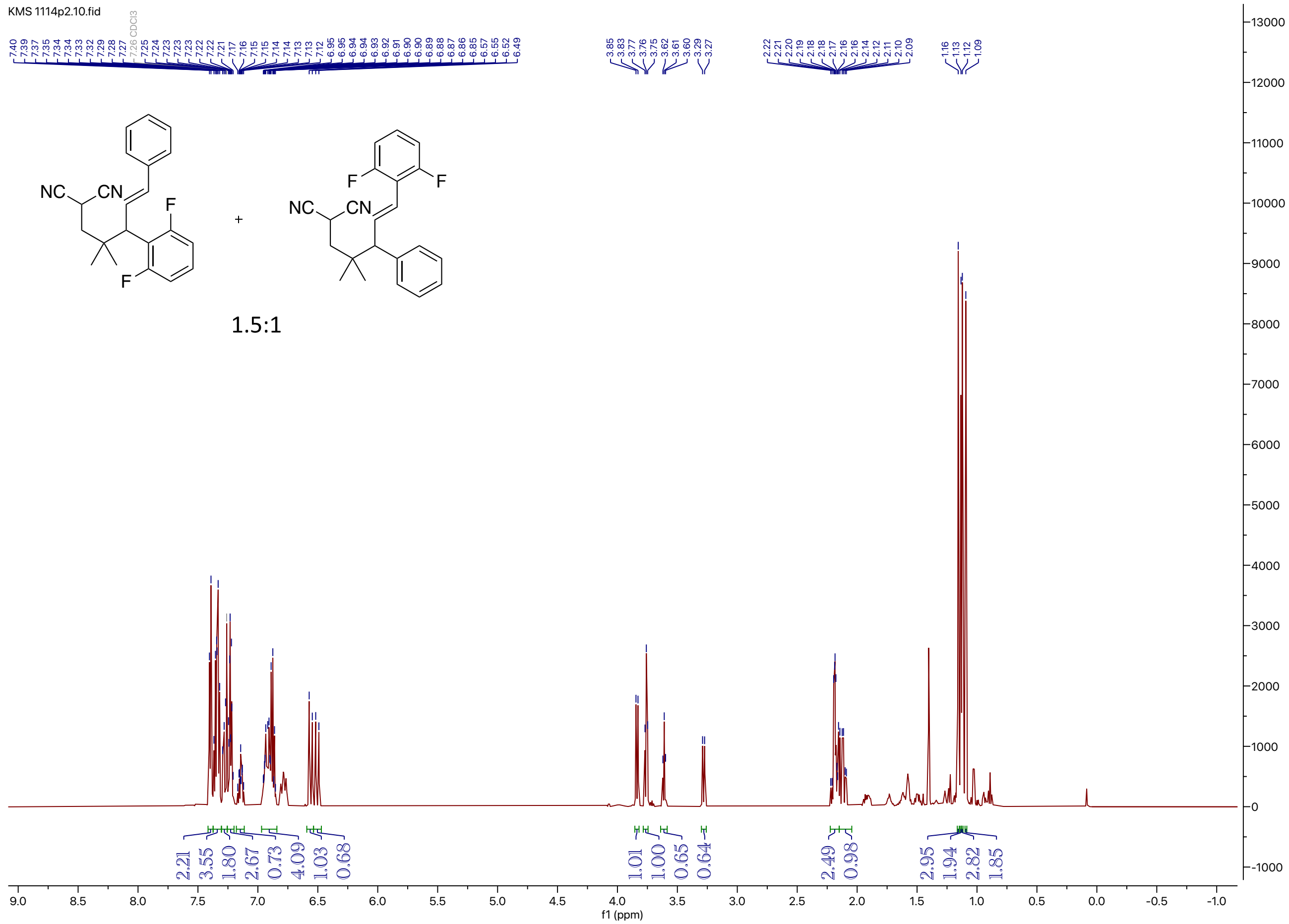
^{13}C NMR Spectrum of 10j ($CDCl_3$)



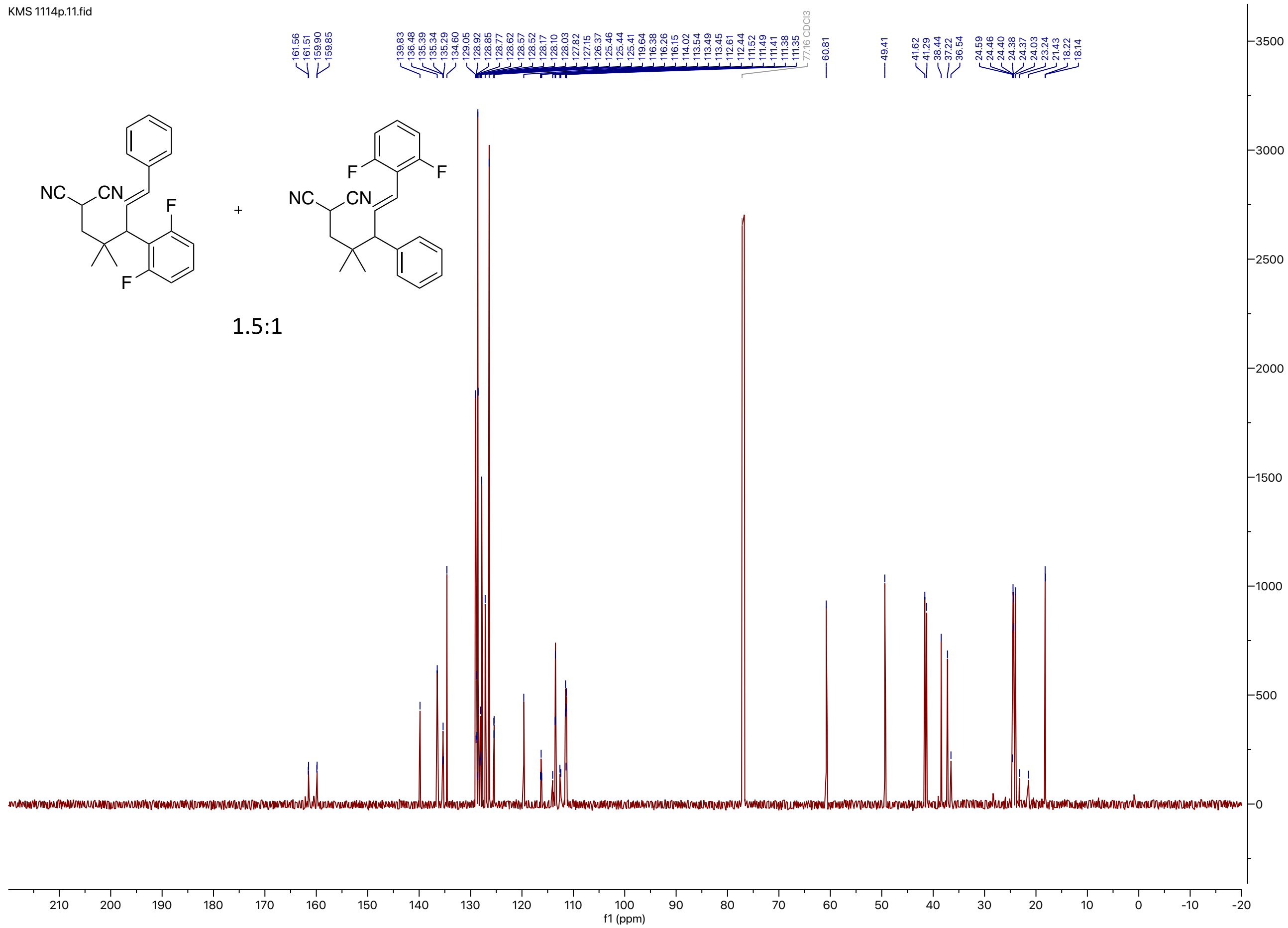
^{19}F NMR Spectrum of 10j ($CDCl_3$)



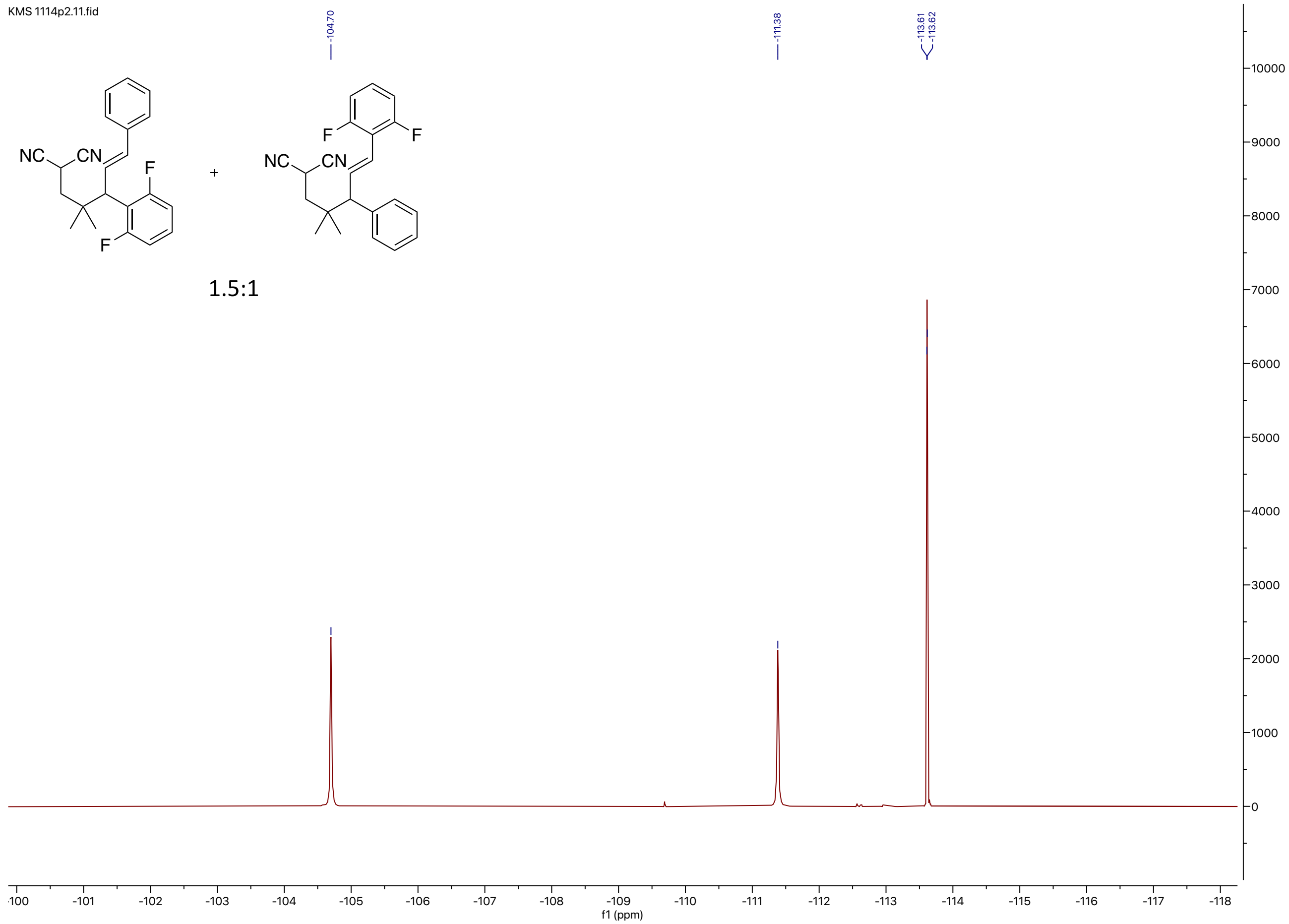
^{1}H NMR Spectrum of 10k ($CDCl_3$)



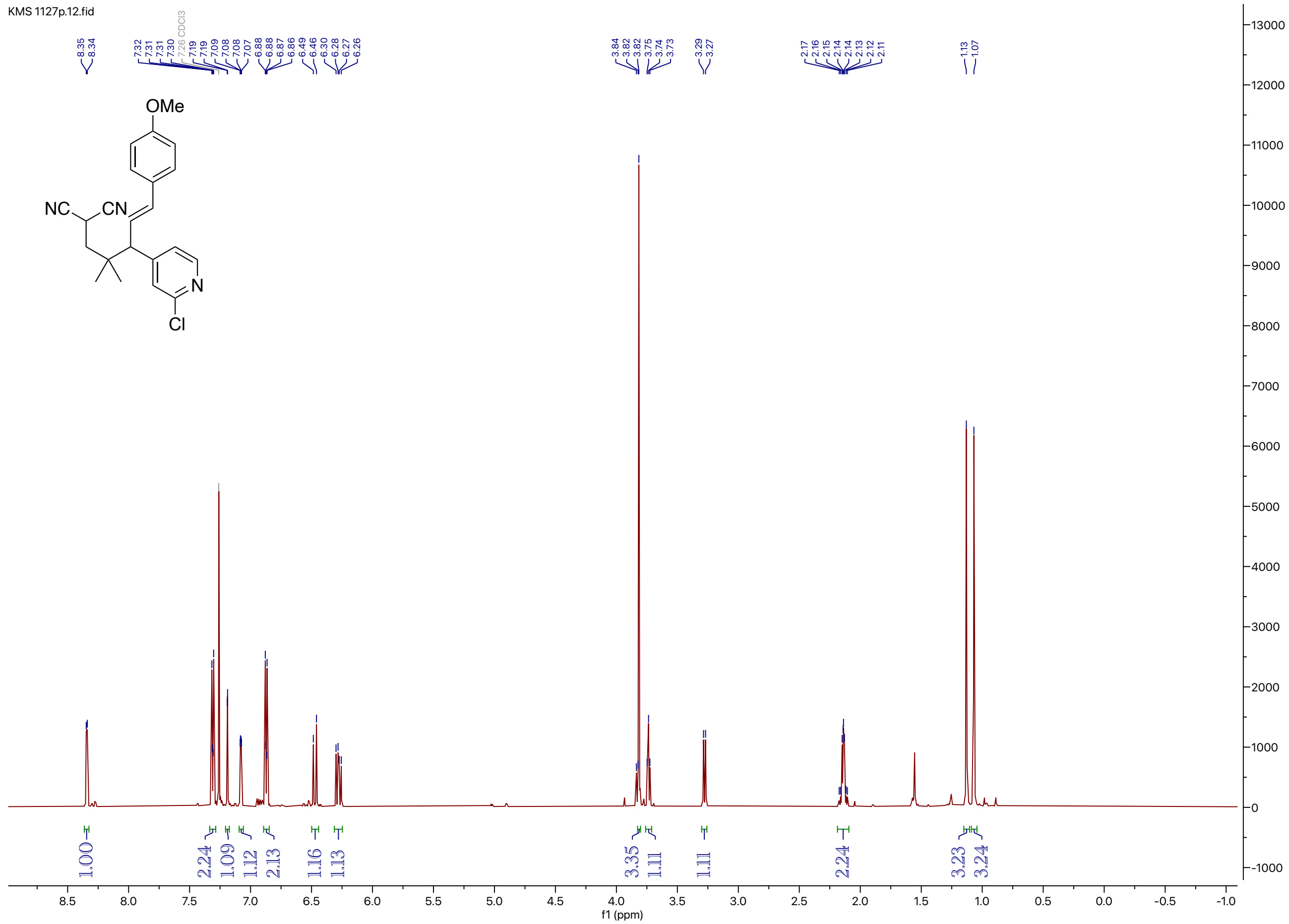
^{13}C NMR Spectrum of 10k ($CDCl_3$)



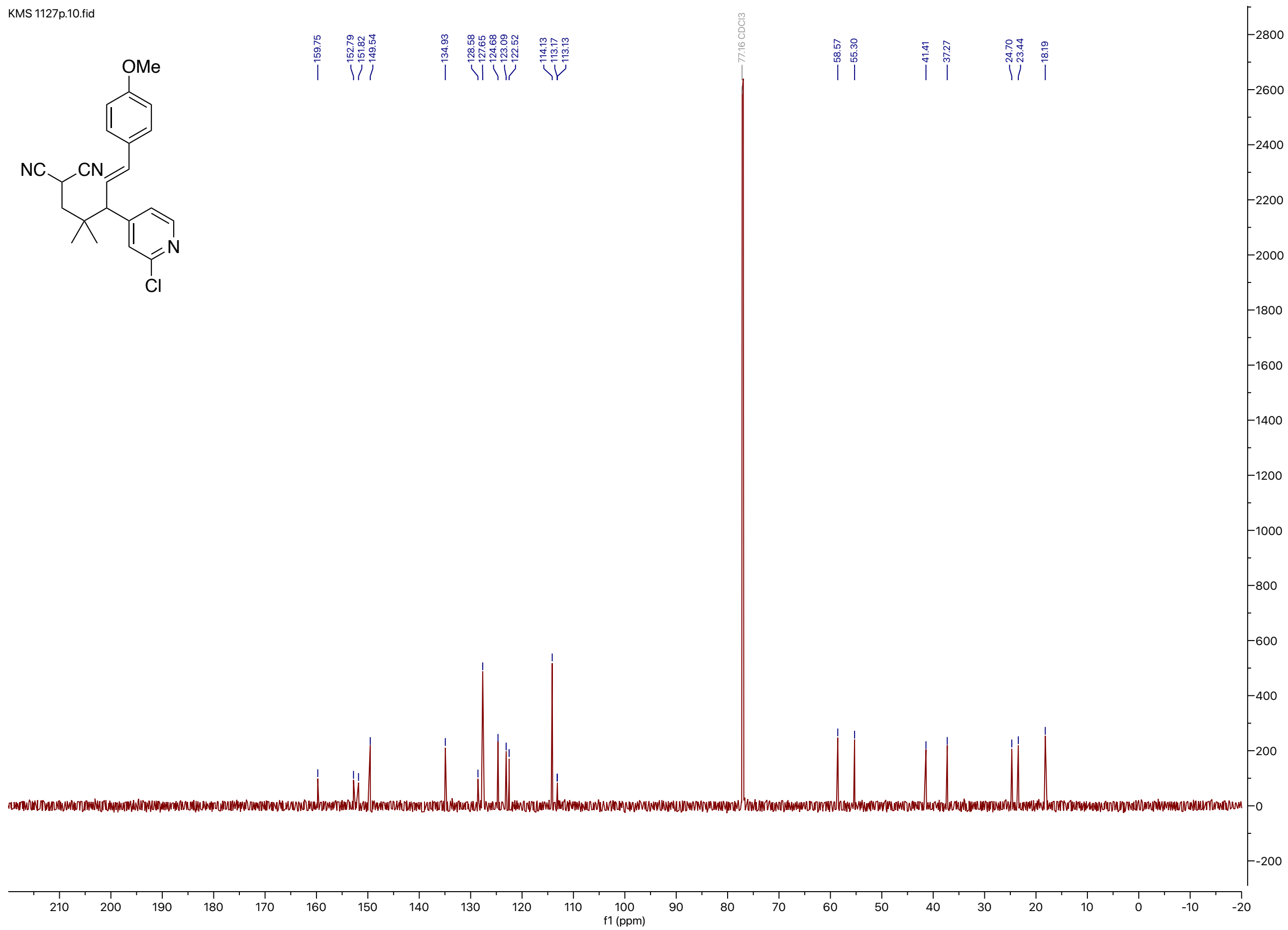
^{19}F NMR Spectrum of 10k ($CDCl_3$)



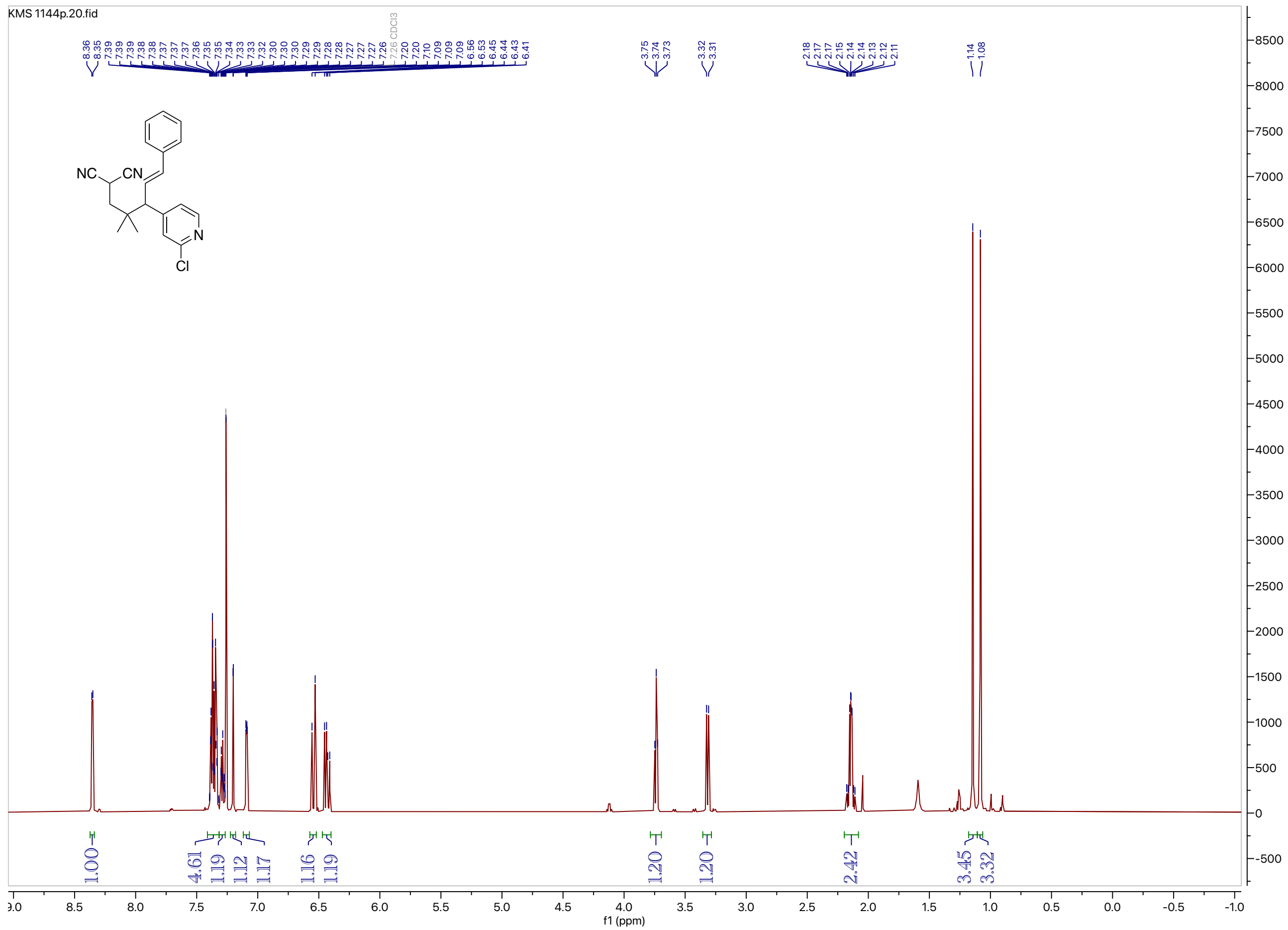
^{1}H NMR Spectrum of 10l ($CDCl_3$)



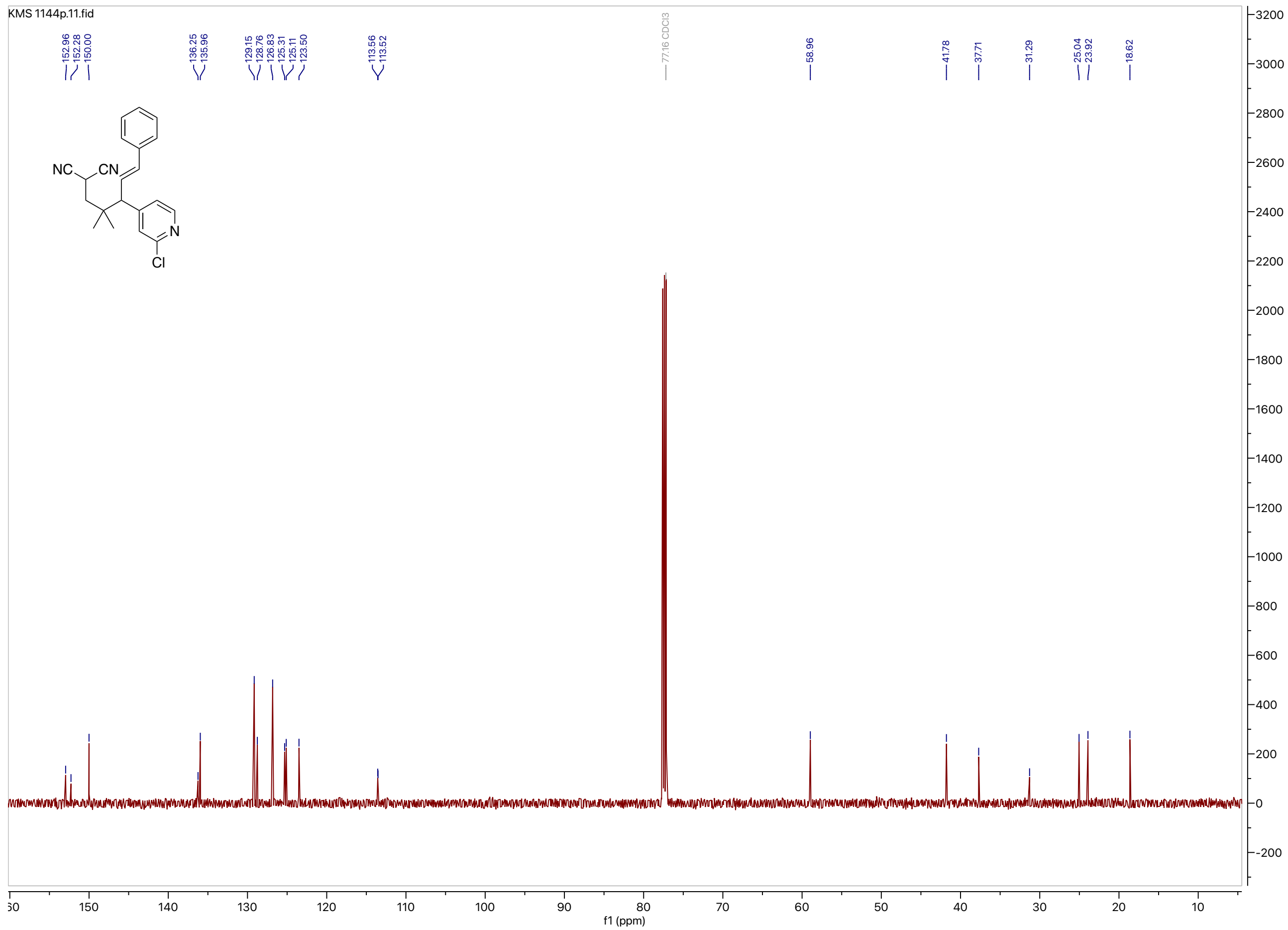
^{13}C NMR Spectrum of 10l ($CDCl_3$)



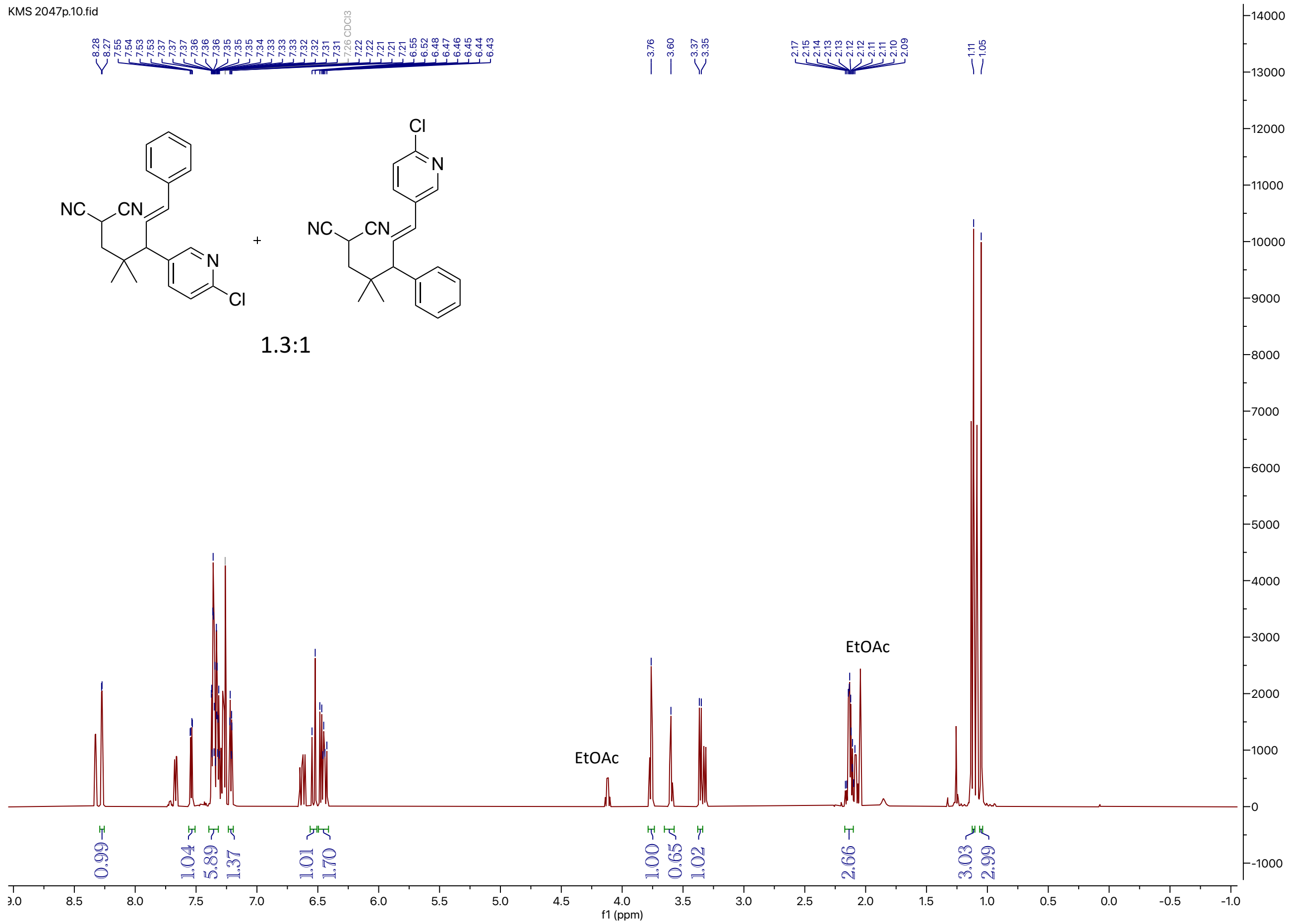
[1]H NMR Spectrum of 10m ($CDCl_3$)



^{13}C NMR Spectrum of 10m ($CDCl_3$)

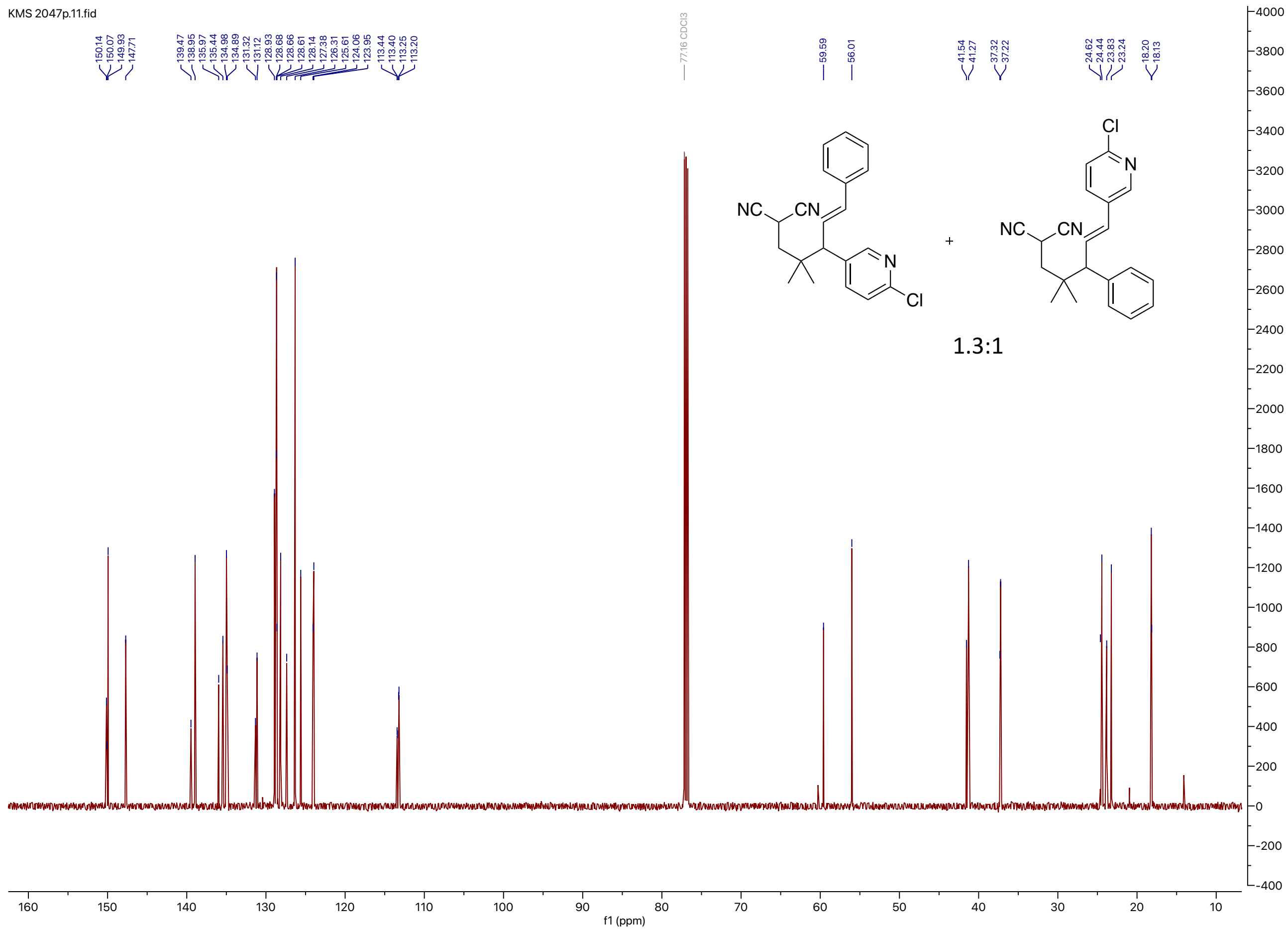


^{1}H NMR Spectrum of 10n ($CDCl_3$)

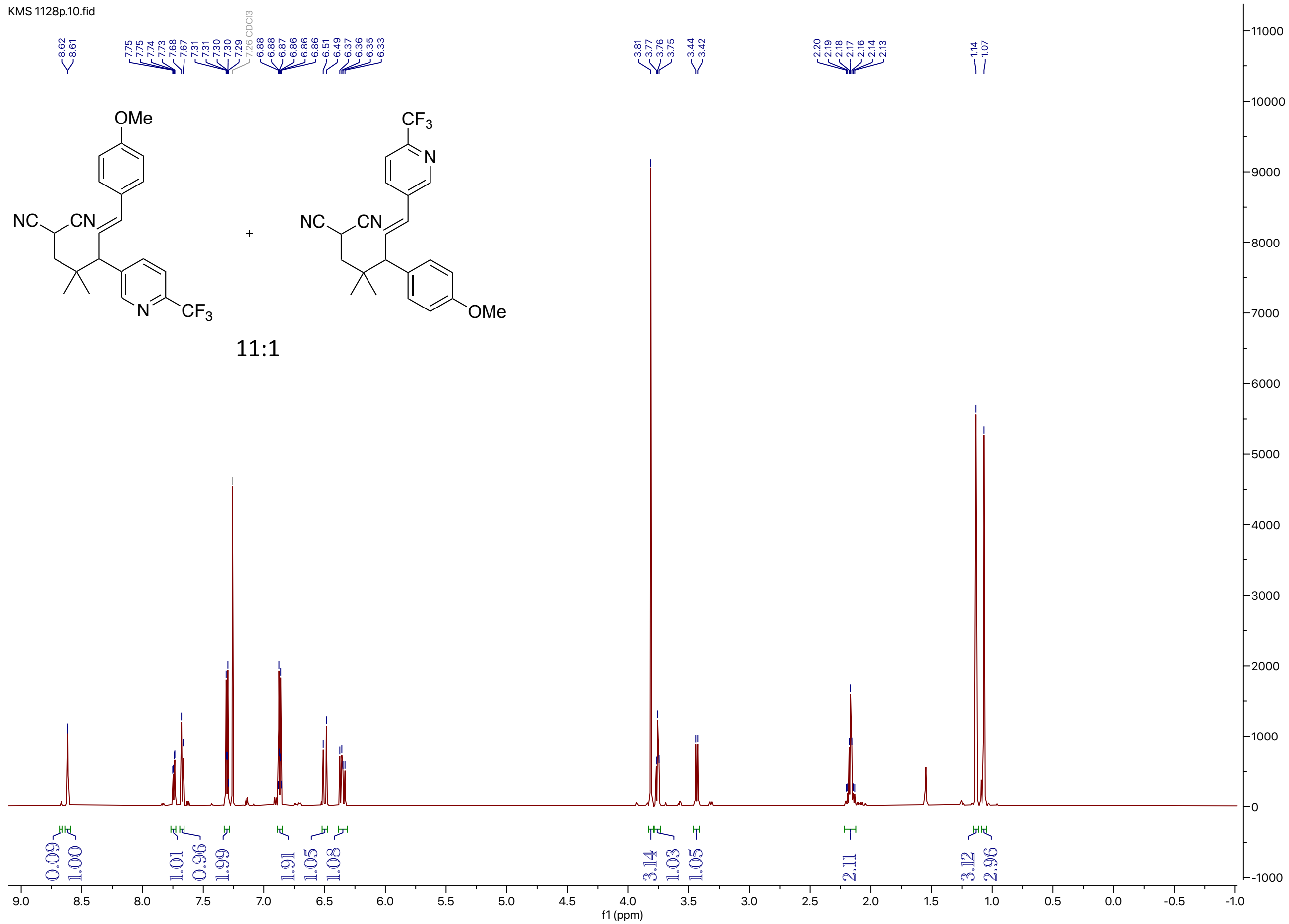


1.3:1

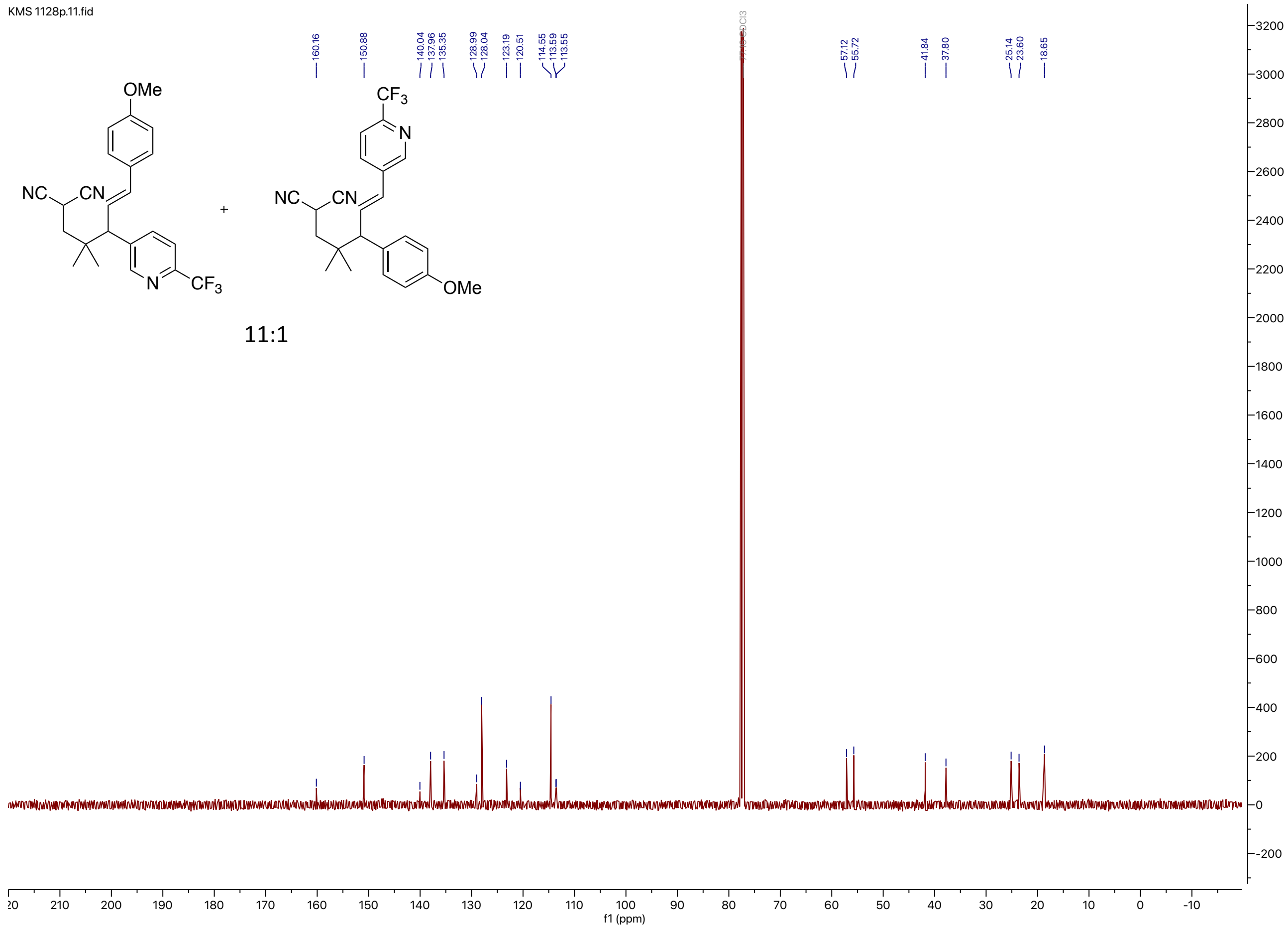
^{13}C NMR Spectrum of 10n ($CDCl_3$)



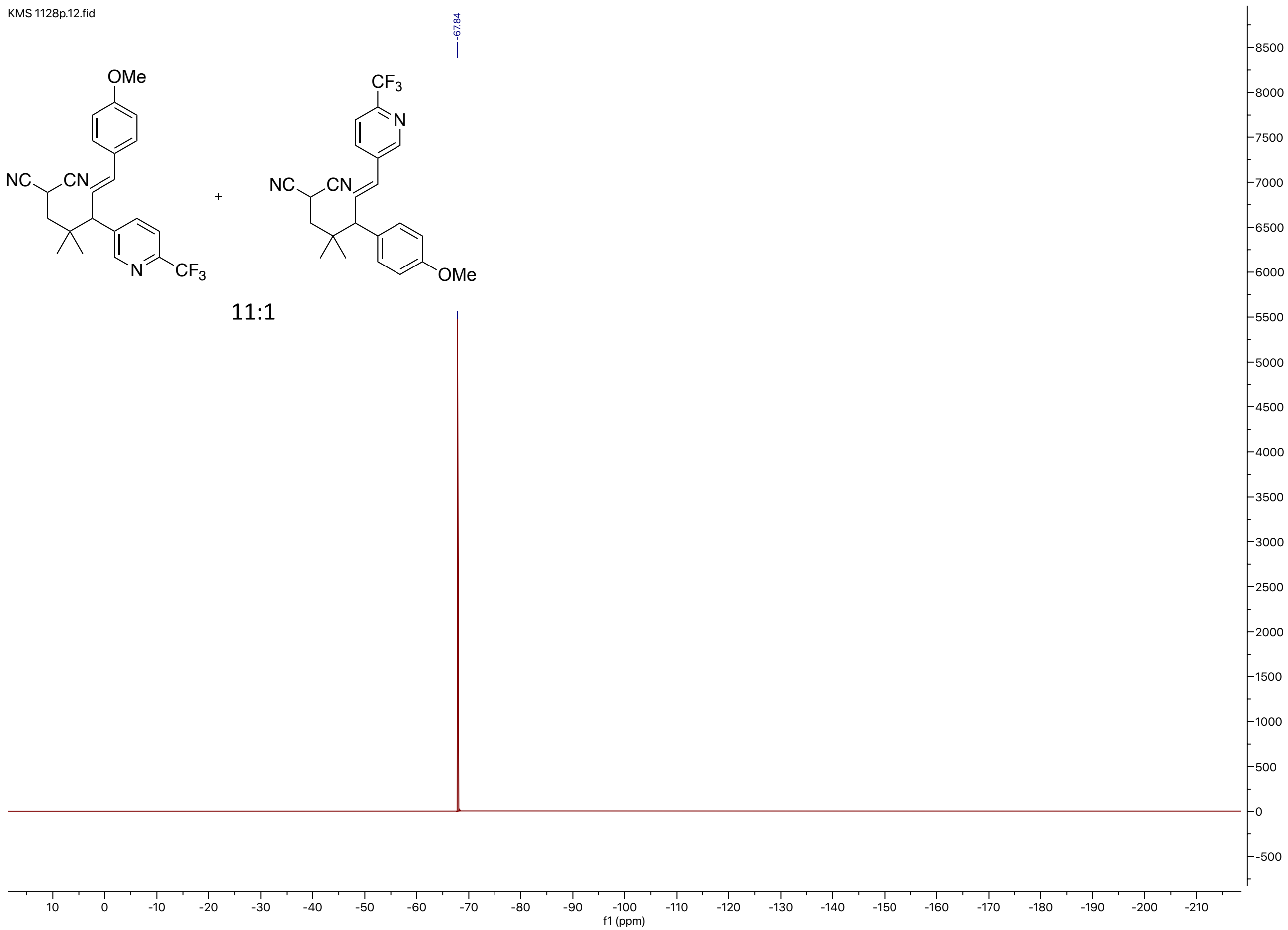
^{1}H NMR Spectrum of 10bo ($CDCl_3$)



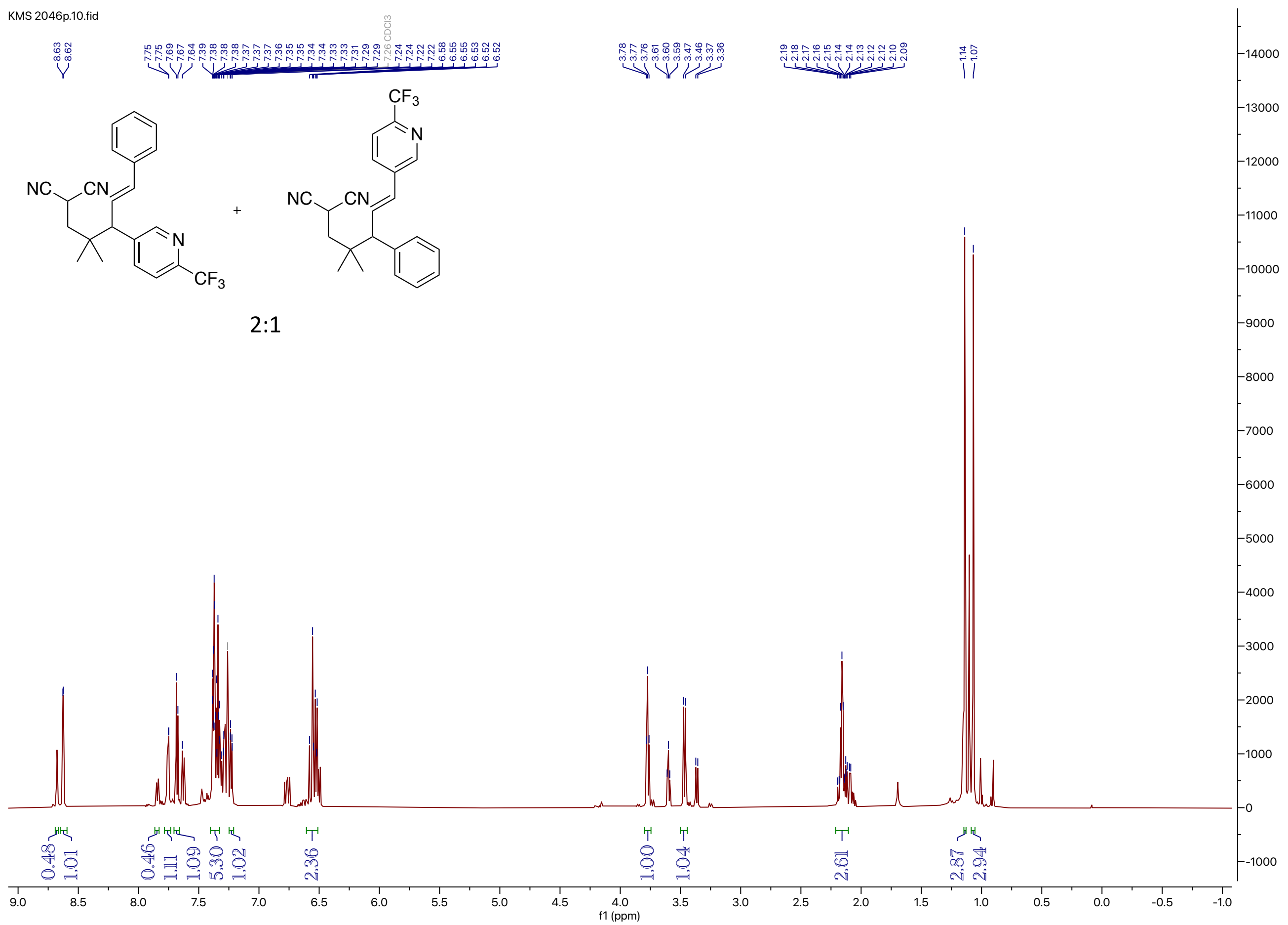
^{13}C NMR Spectrum of 10o ($CDCl_3$)



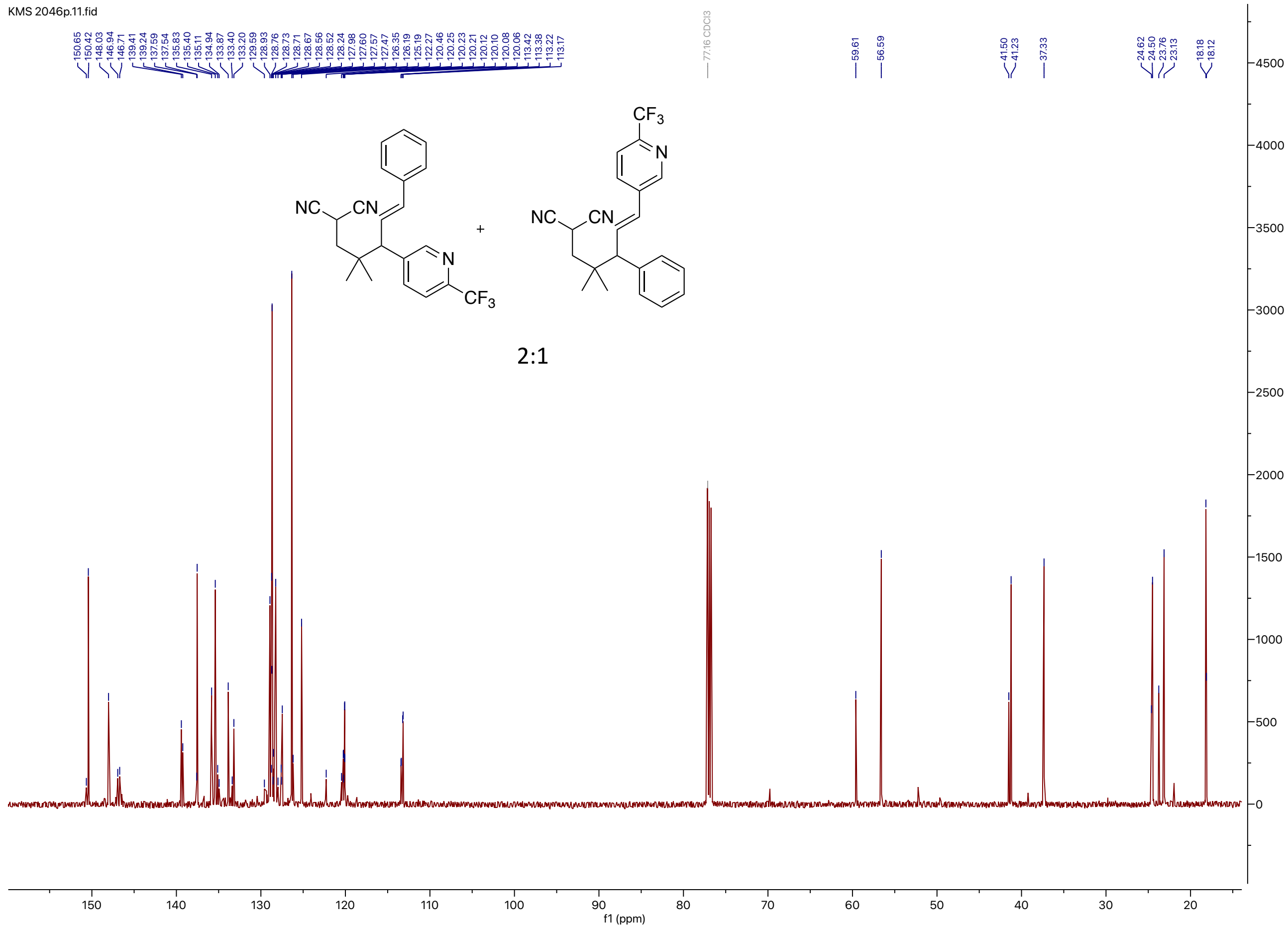
^{19}F NMR Spectrum of 10o ($CDCl_3$)



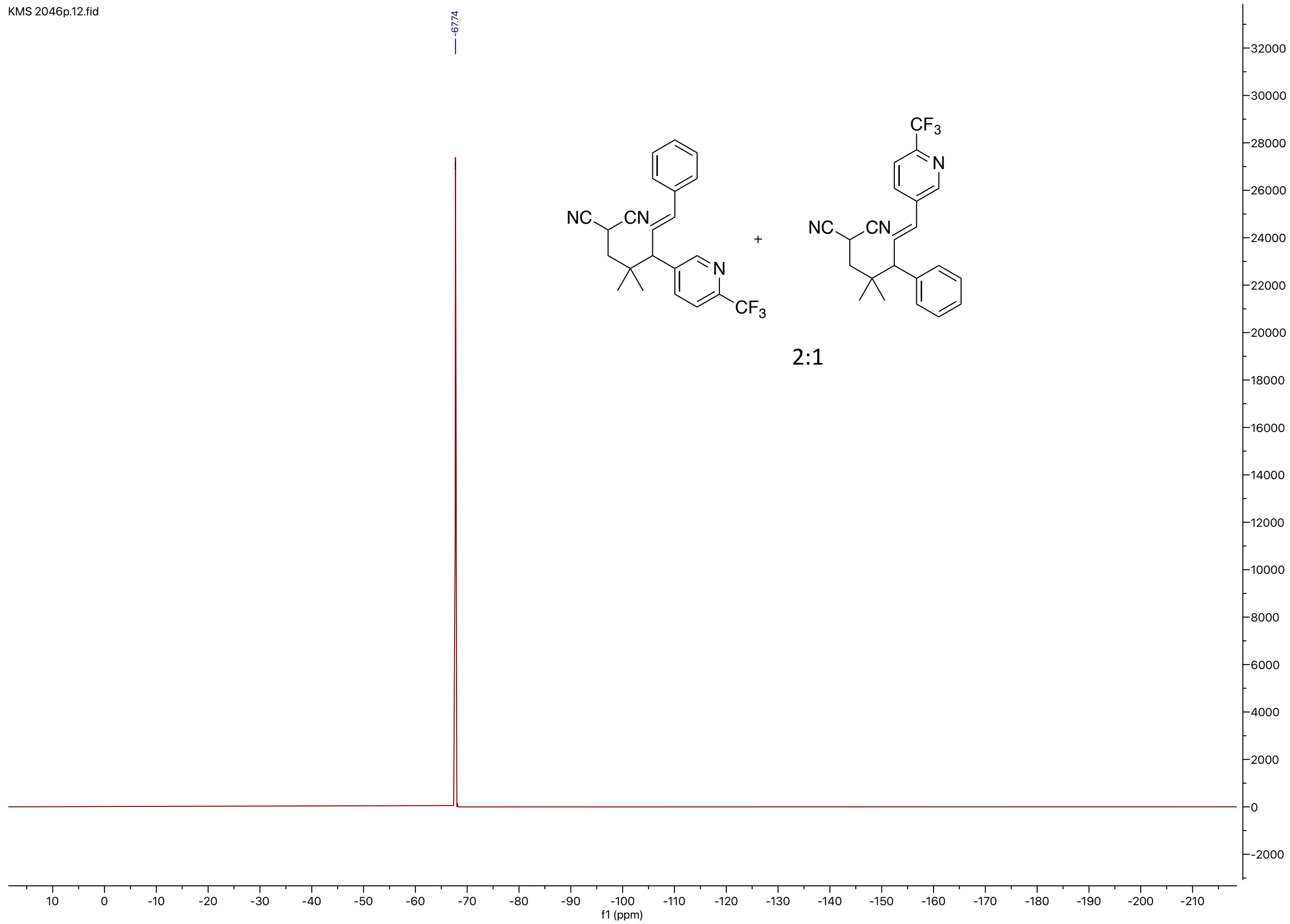
[1]H NMR Spectrum of 10p (CDCl$_3$)



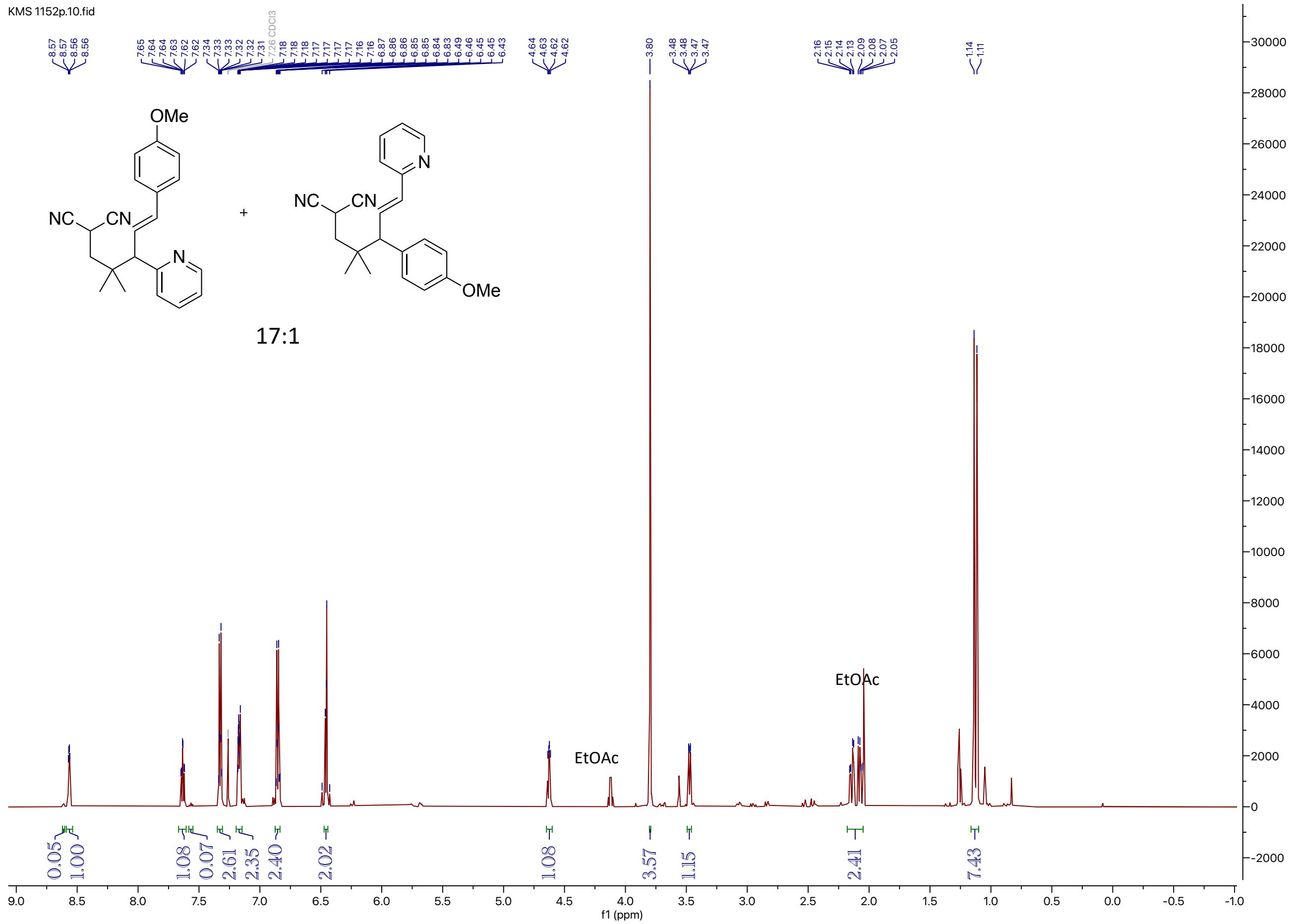
^{13}C NMR Spectrum of 10p ($CDCl_3$)



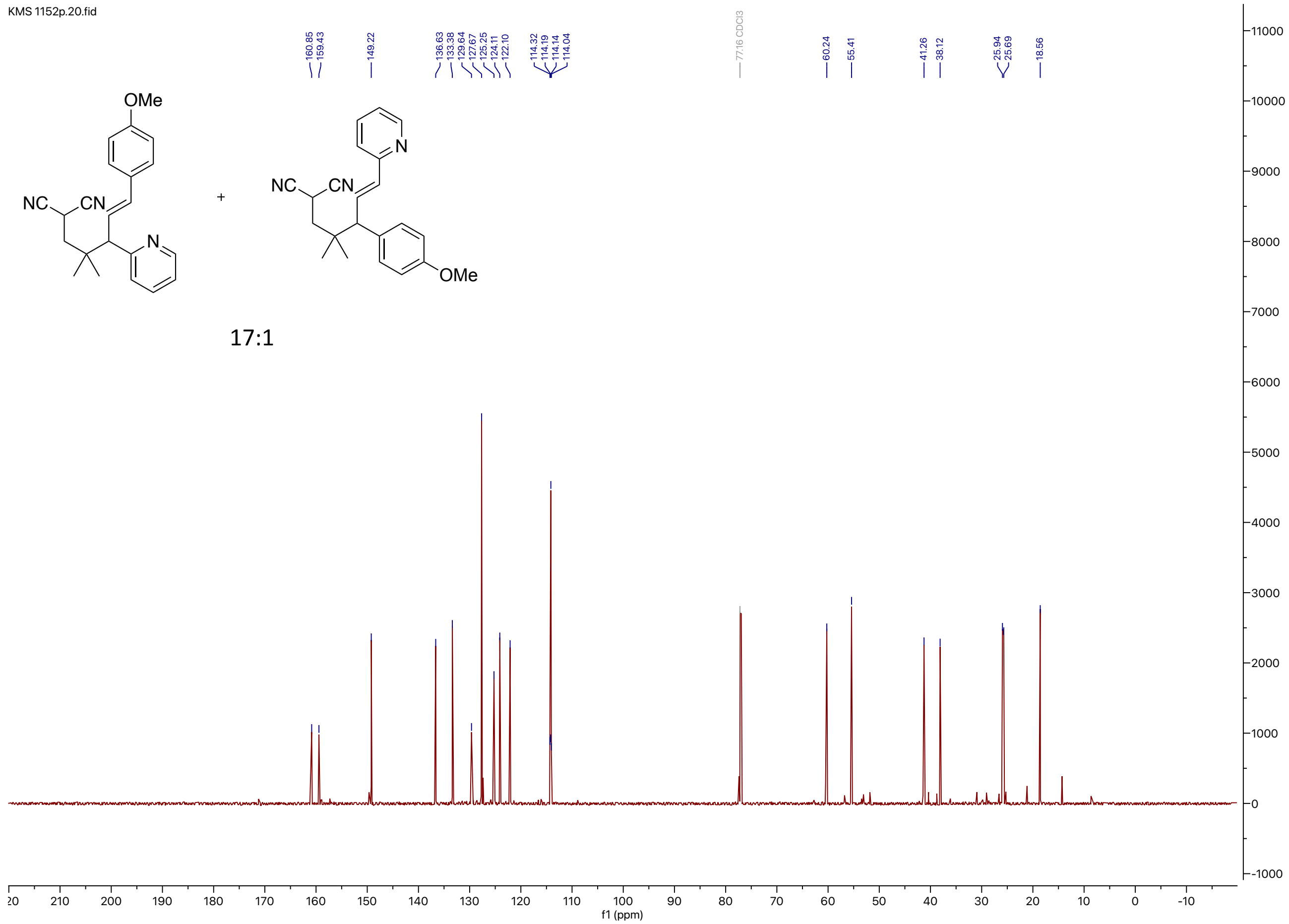
^{19}F NMR Spectrum of 10p ($CDCl_3$)



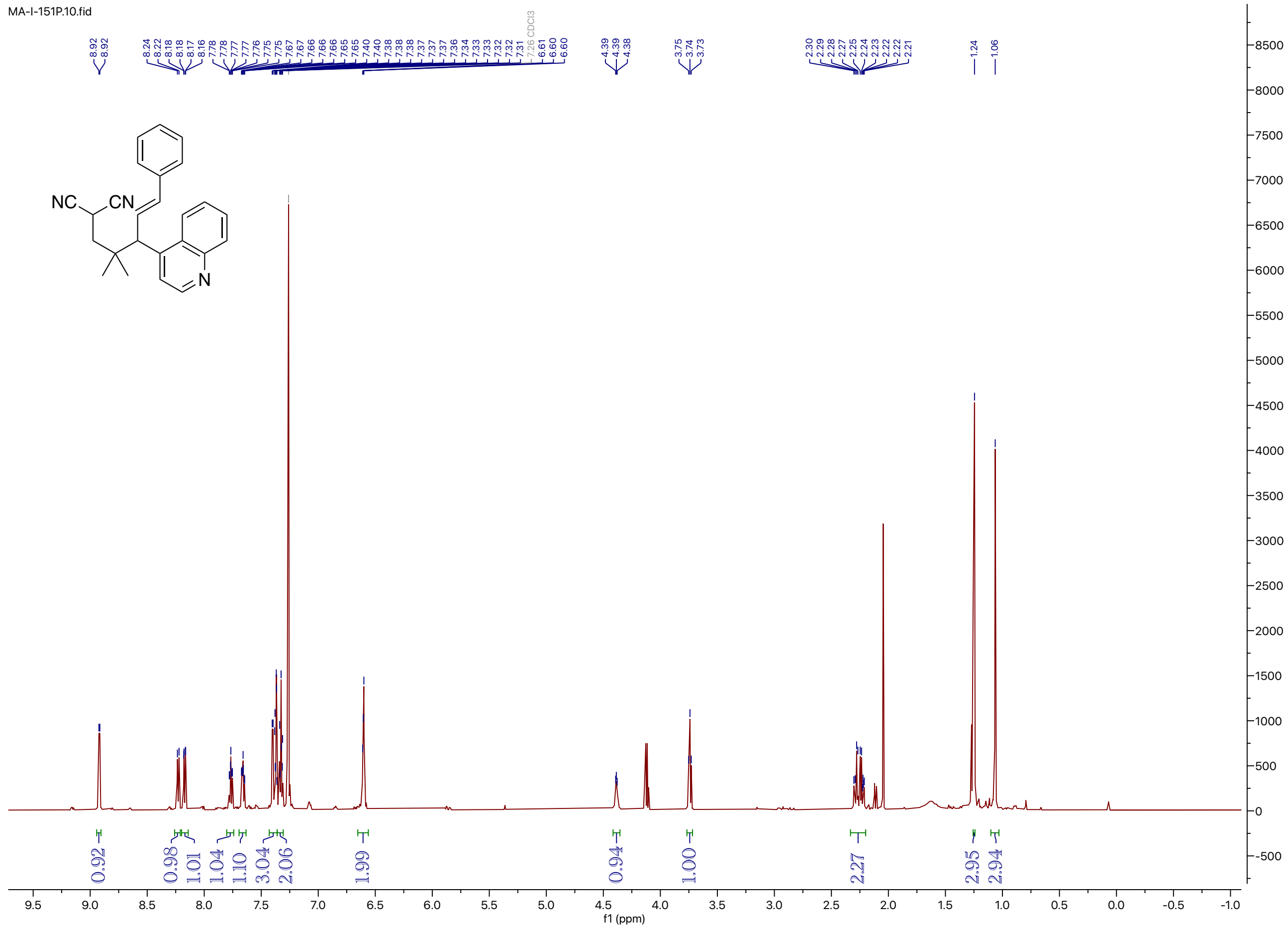
^{1}H NMR Spectrum of 10q ($CDCl_3$)



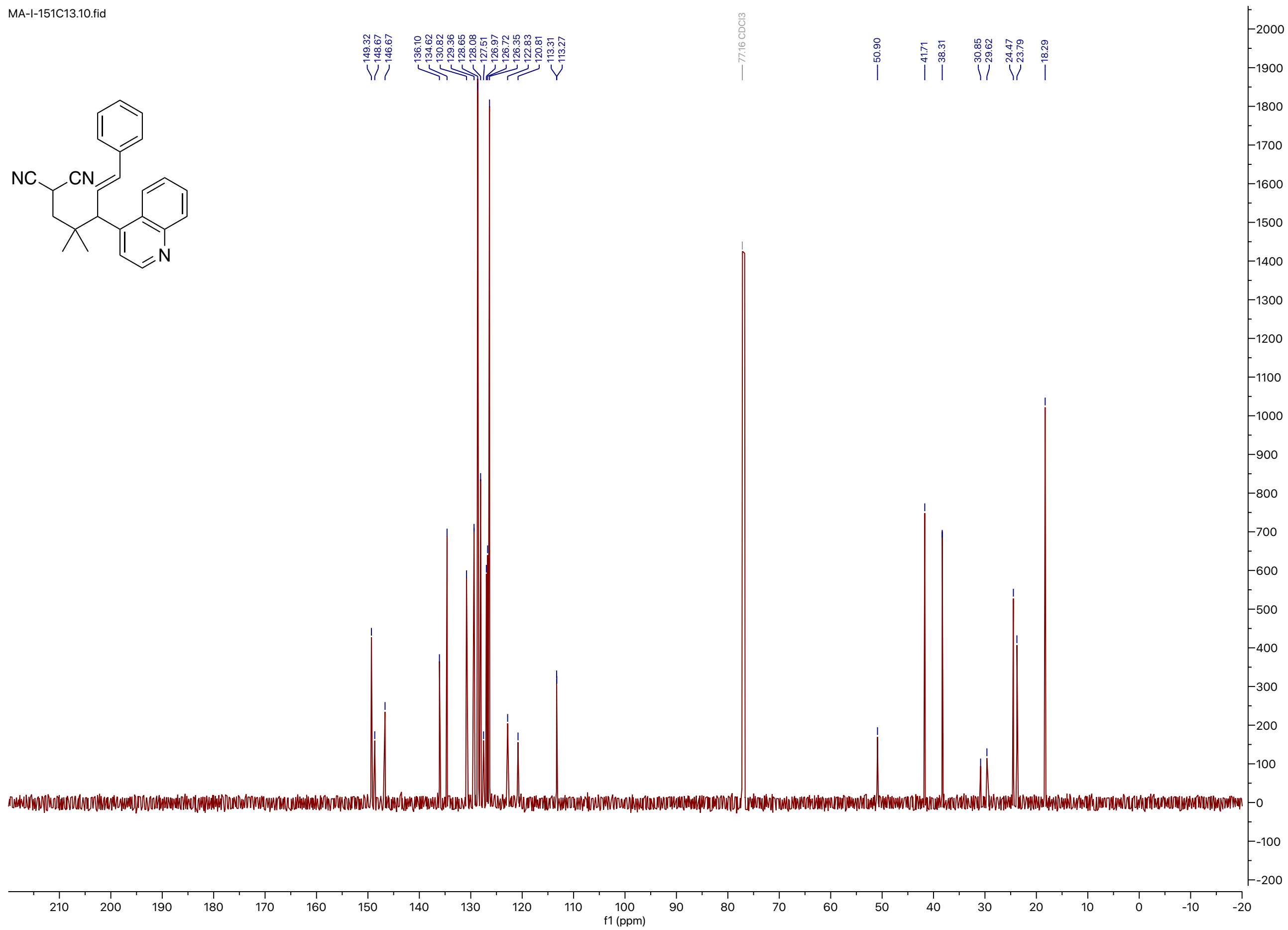
[13]C NMR Spectrum of 10q ($CDCl_3$)



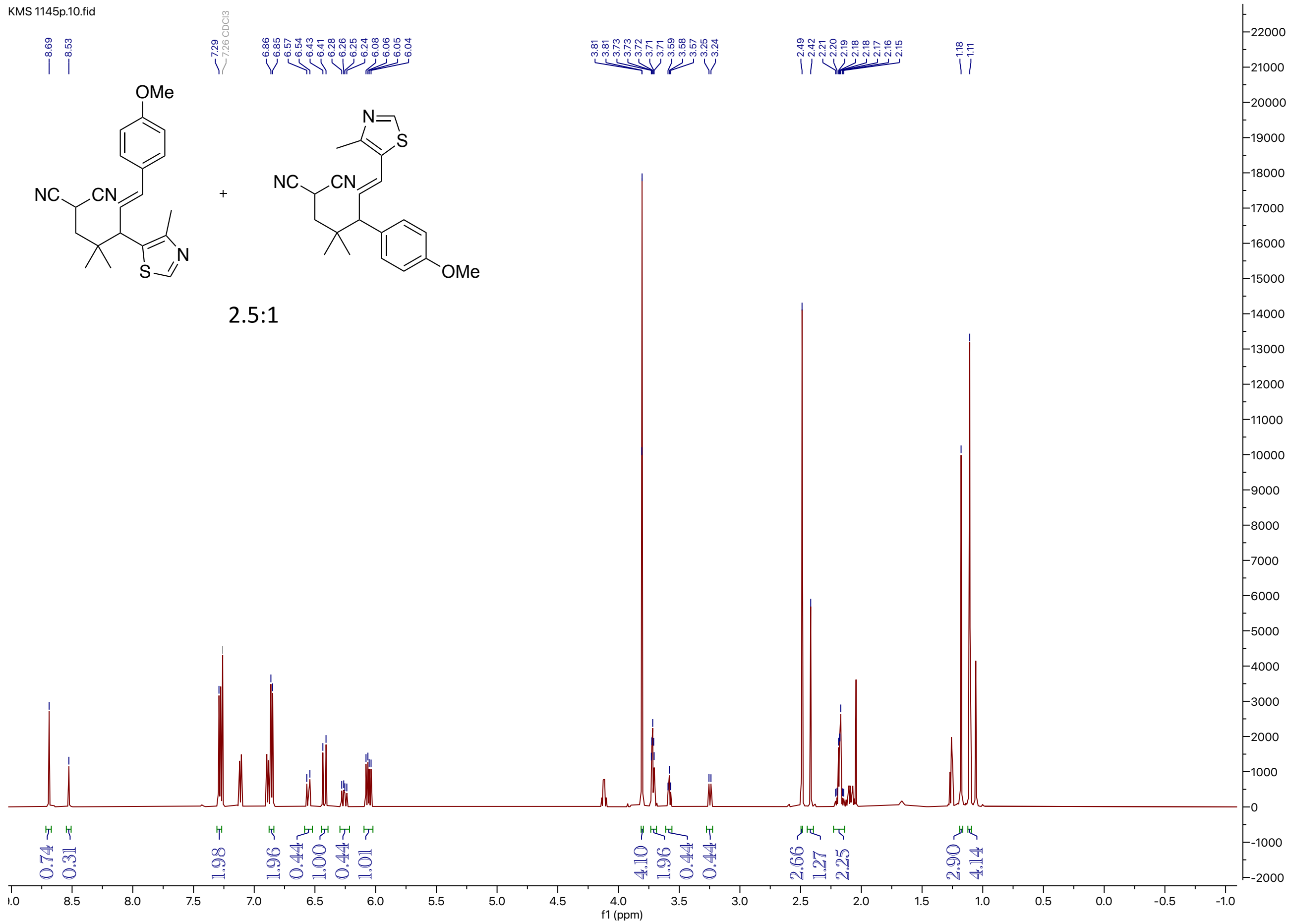
[1]H NMR Spectrum of 10s ($CDCl_3$)



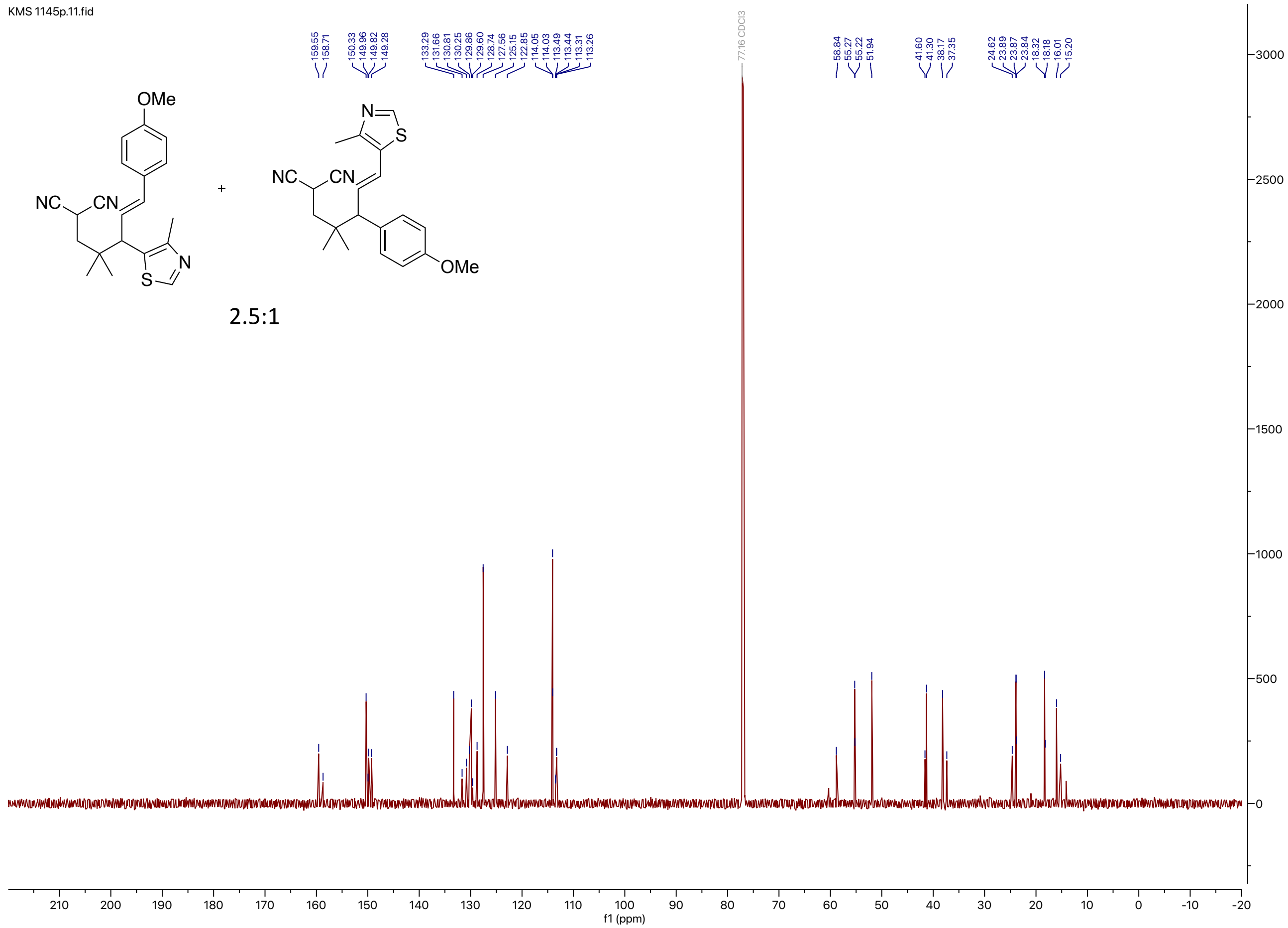
^{13}C NMR Spectrum of 10s ($CDCl_3$)



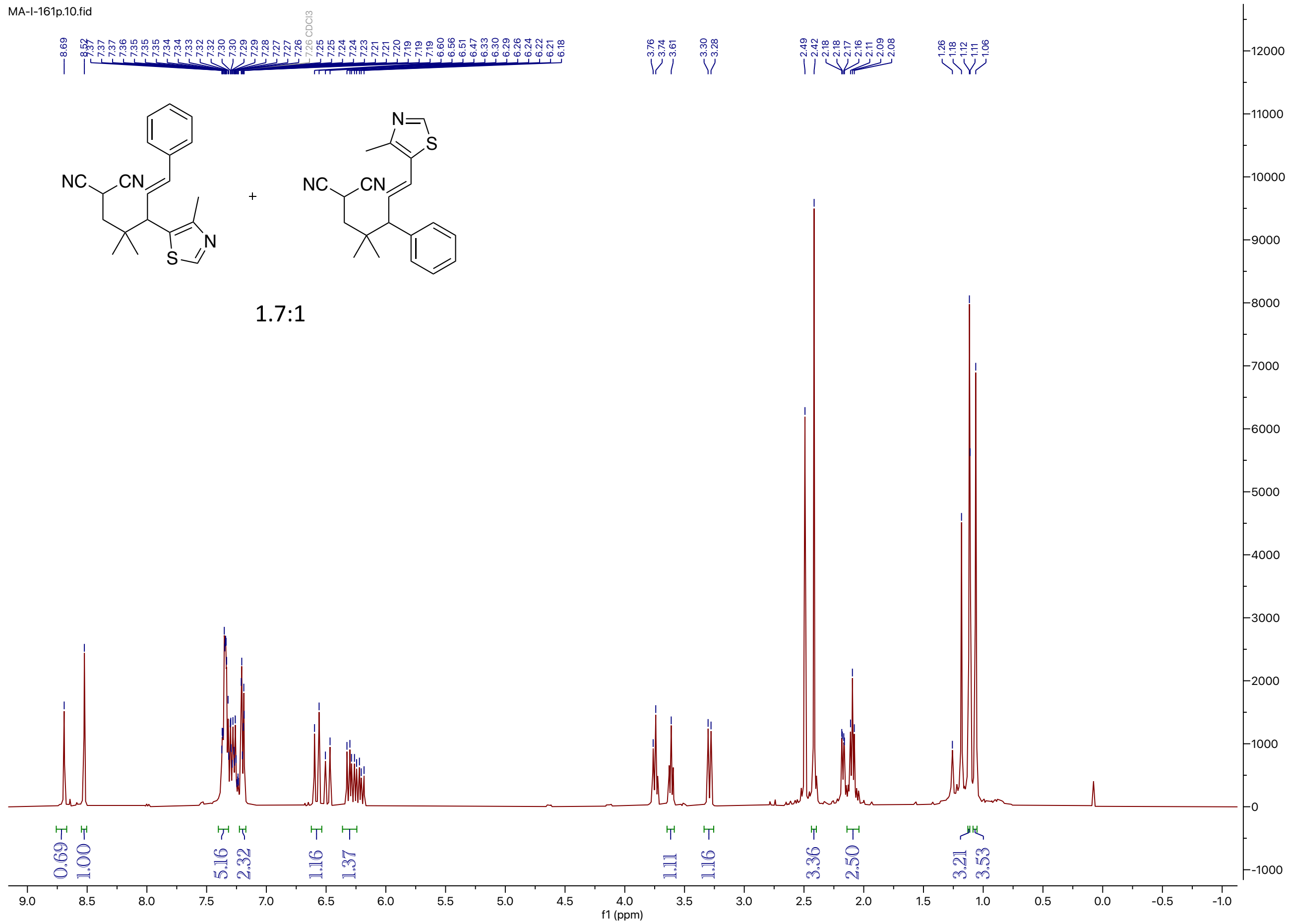
^{1}H NMR Spectrum of 10t ($CDCl_3$)



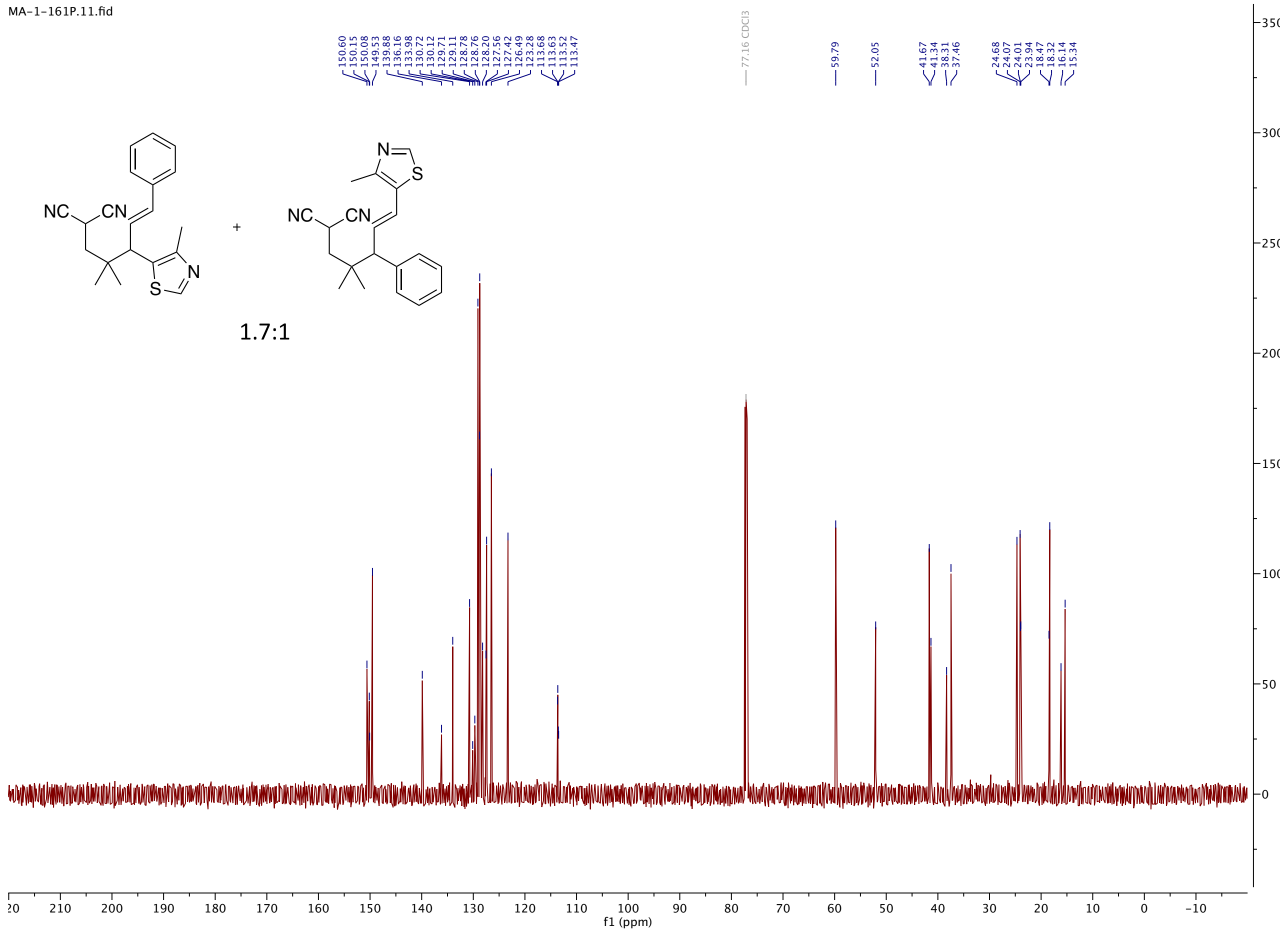
^{13}C NMR Spectrum of 10t ($CDCl_3$)



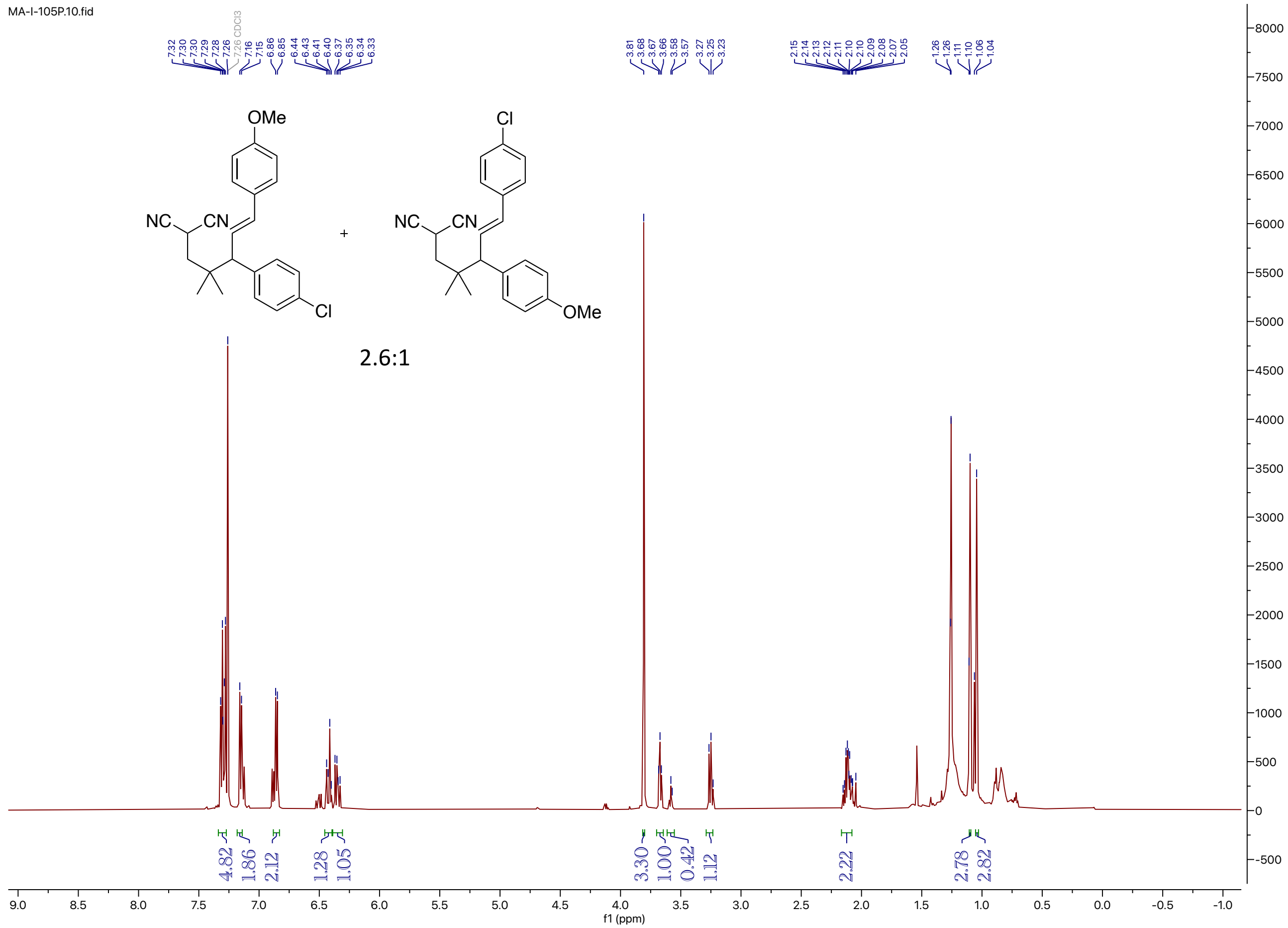
1H NMR Spectrum of 10u ($CDCl_3$)



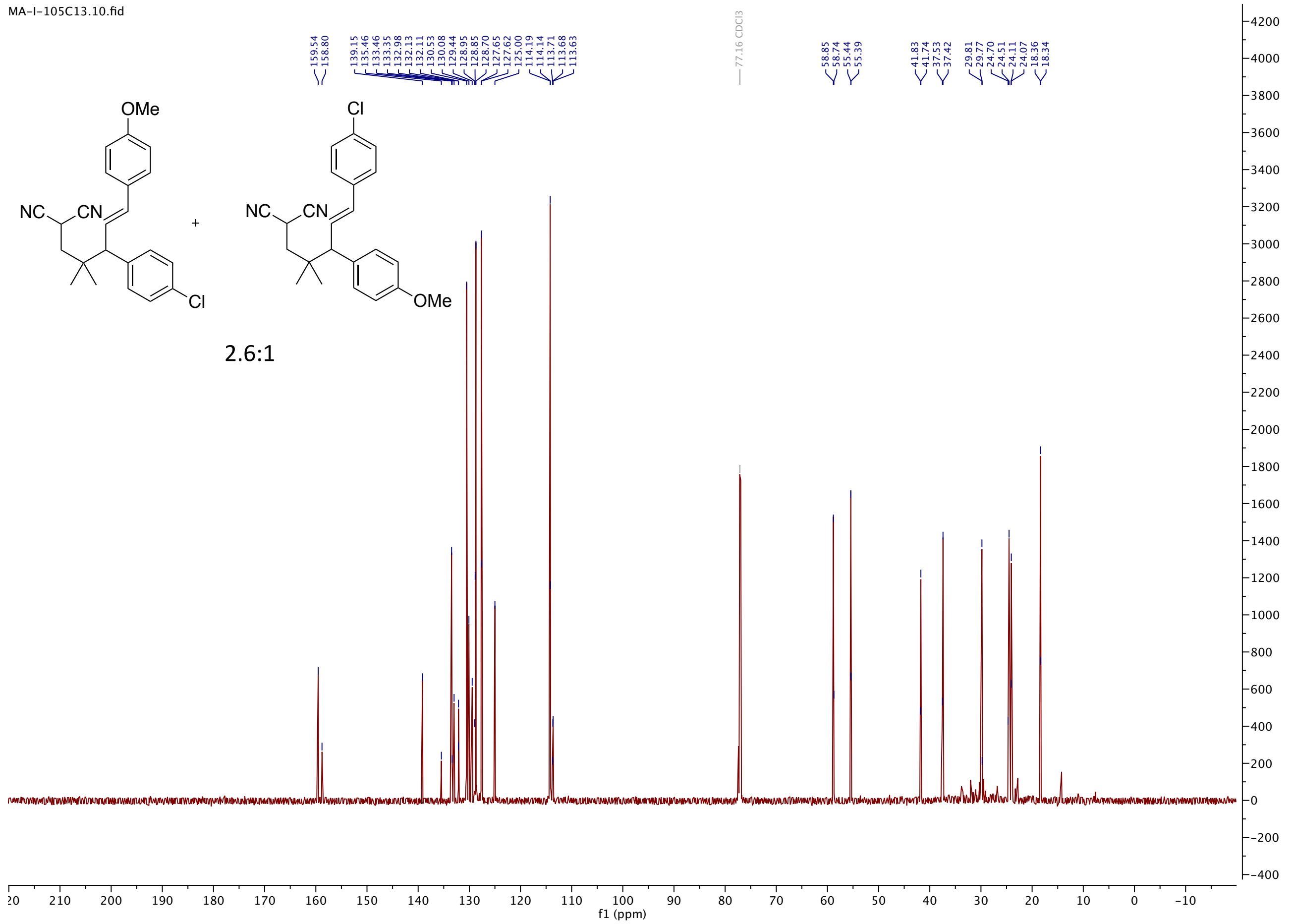
^{13}C NMR Spectrum of 10u ($CDCl_3$)



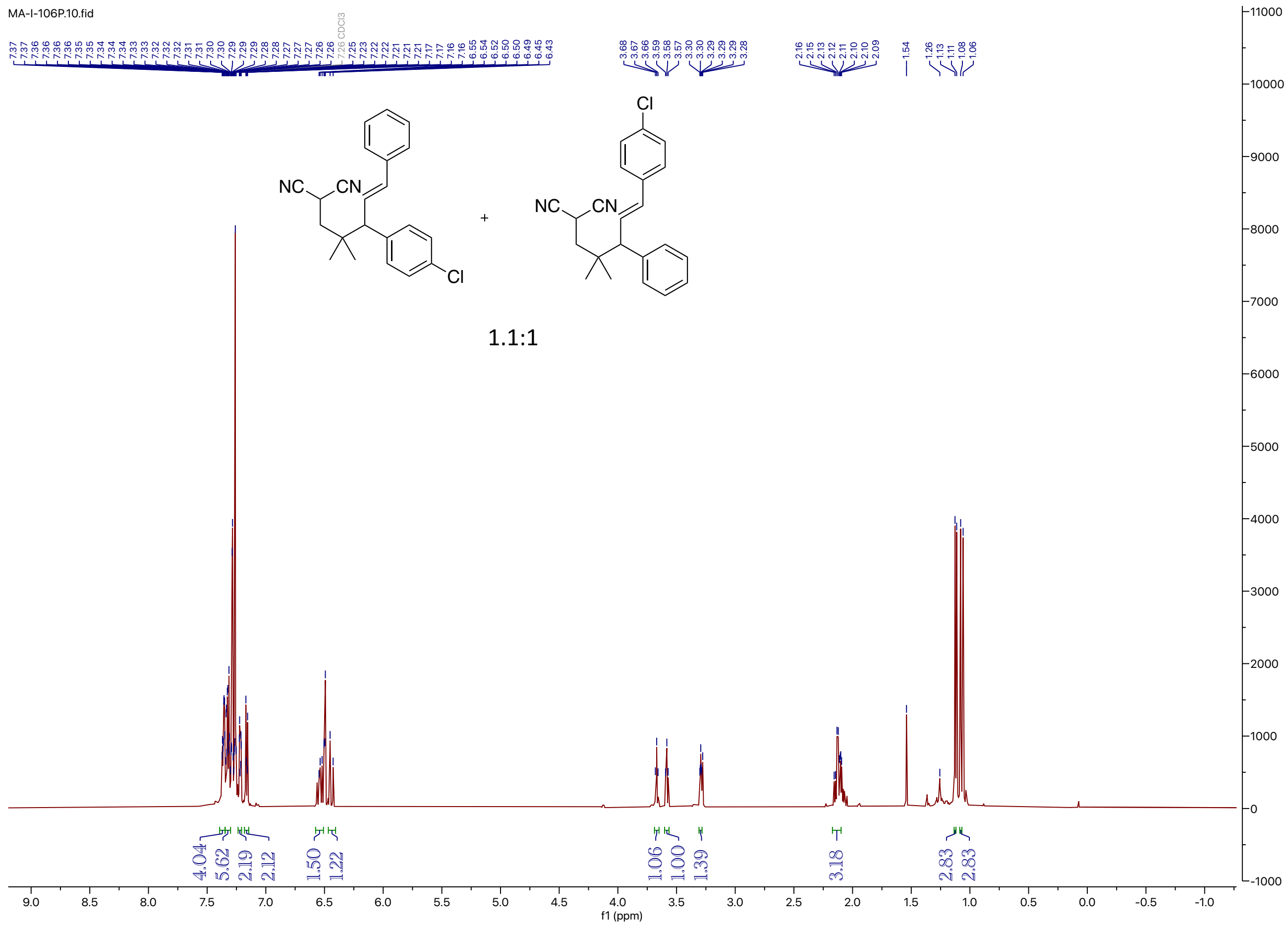
^{1}H NMR Spectrum of 10v ($CDCl_3$)



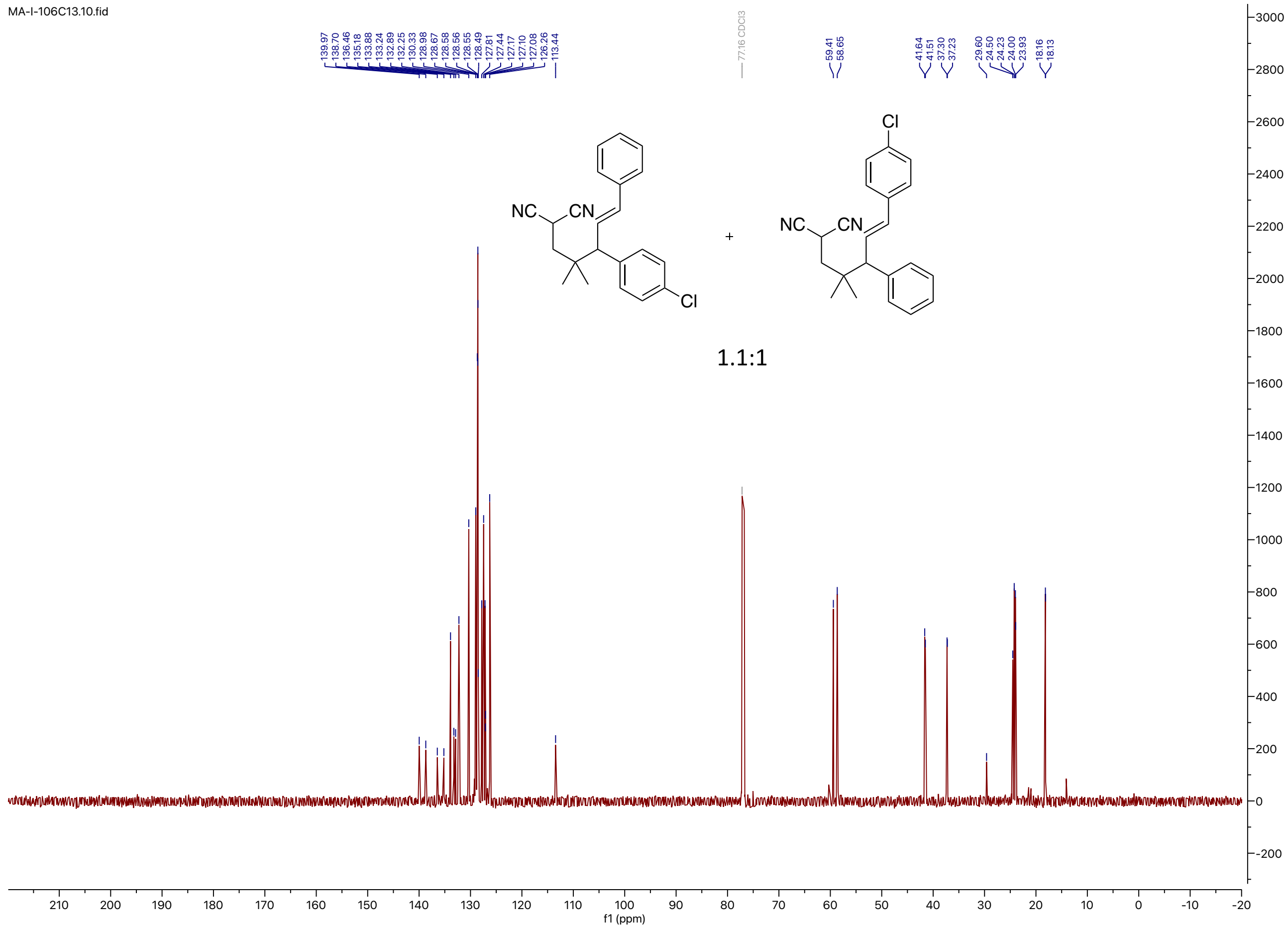
^{13}C NMR Spectrum of 10v ($CDCl_3$)



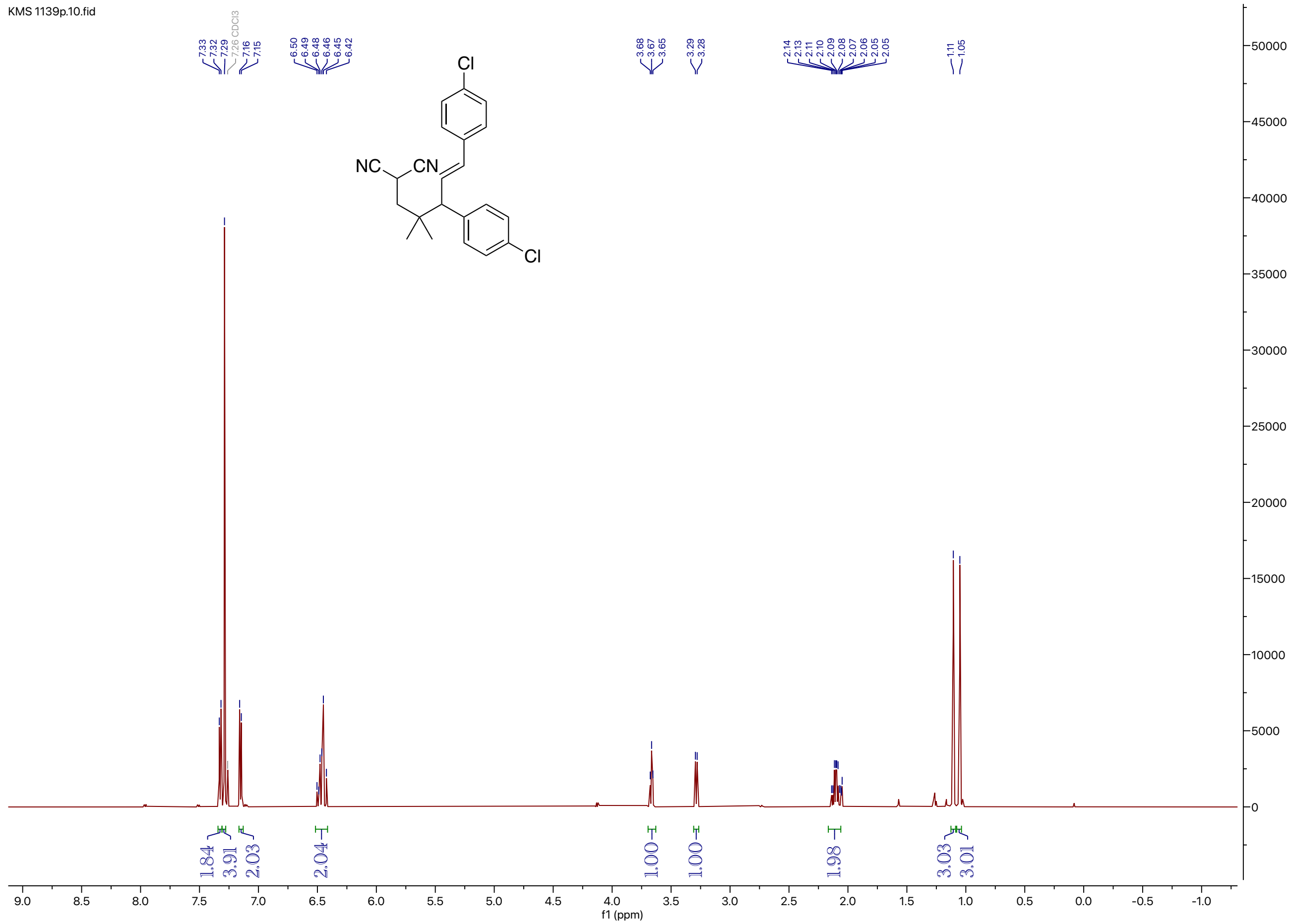
[1]H NMR Spectrum of 10w ($CDCl_3$)



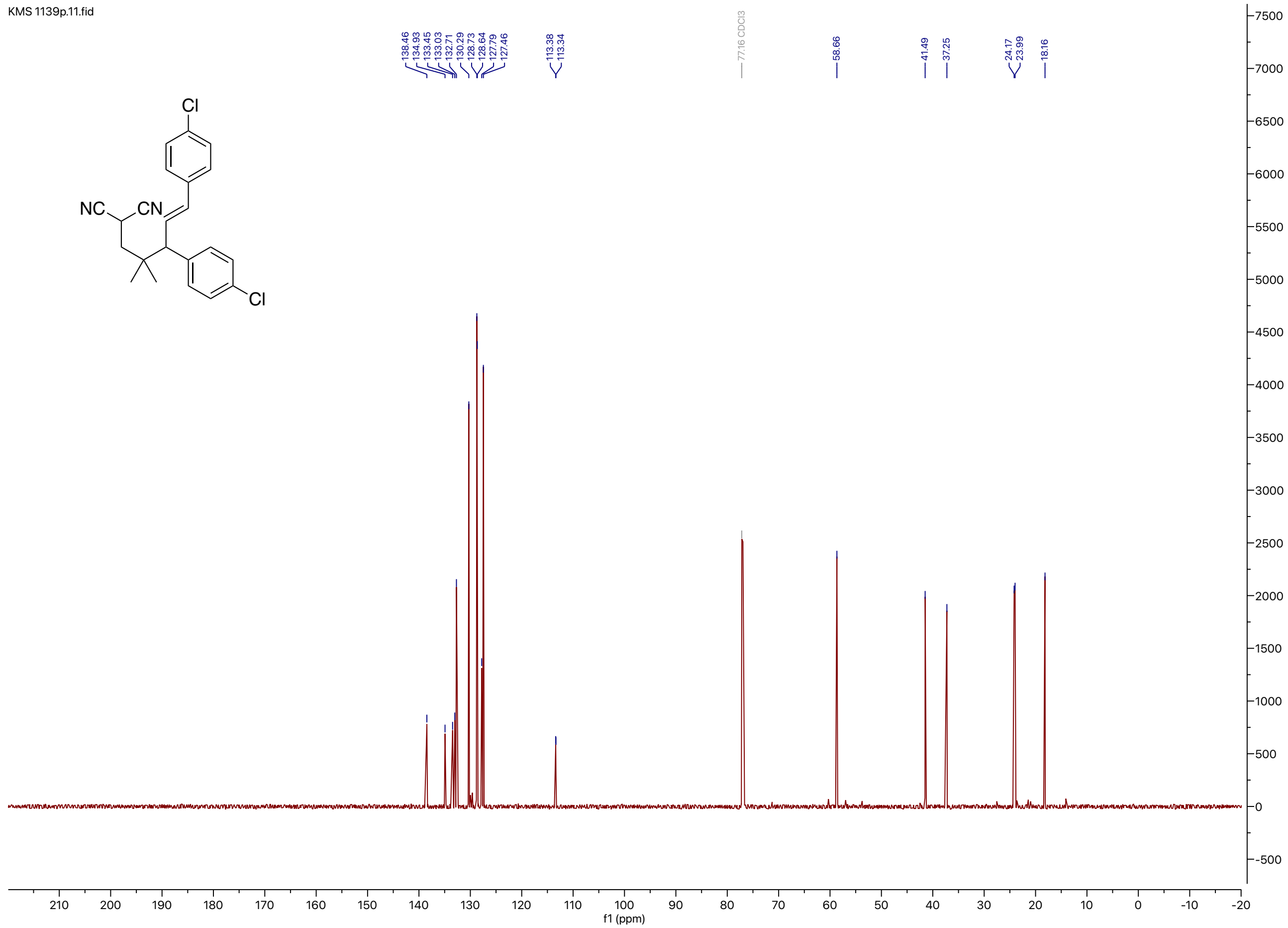
^{13}C NMR Spectrum of 10w ($CDCl_3$)



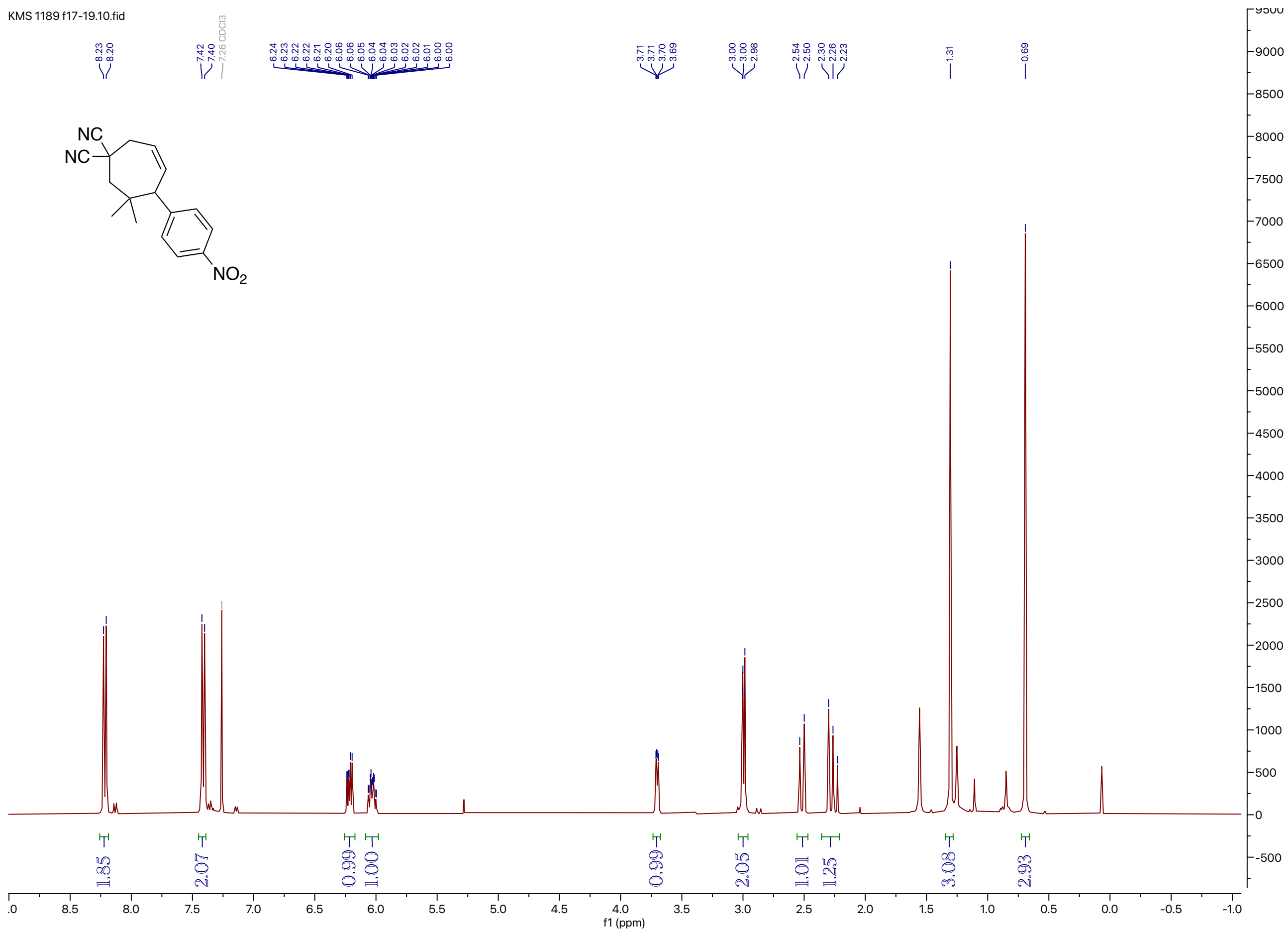
[1]H NMR Spectrum of 10x ($CDCl_3$)



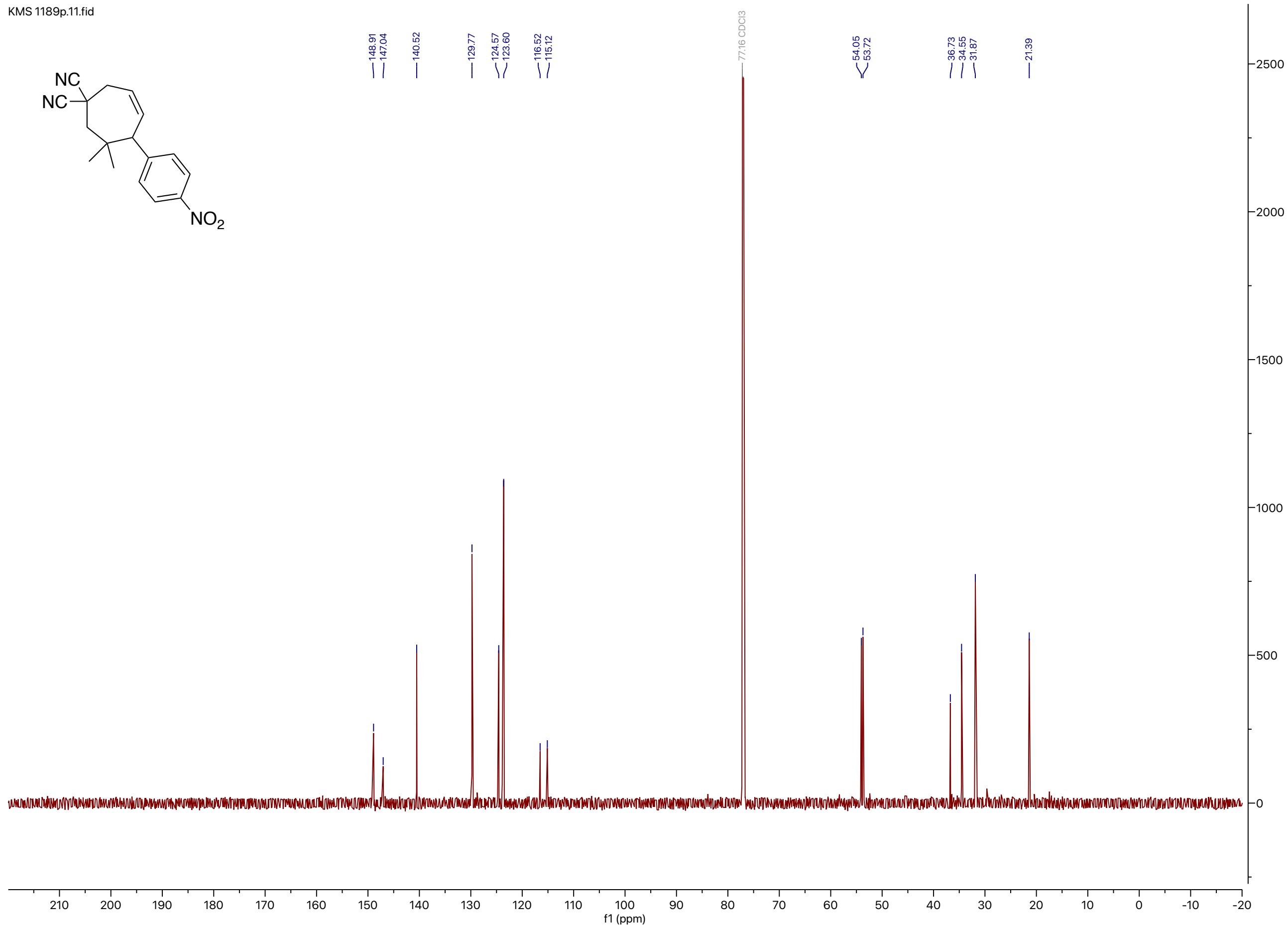
^{13}C NMR Spectrum of 10x ($CDCl_3$)



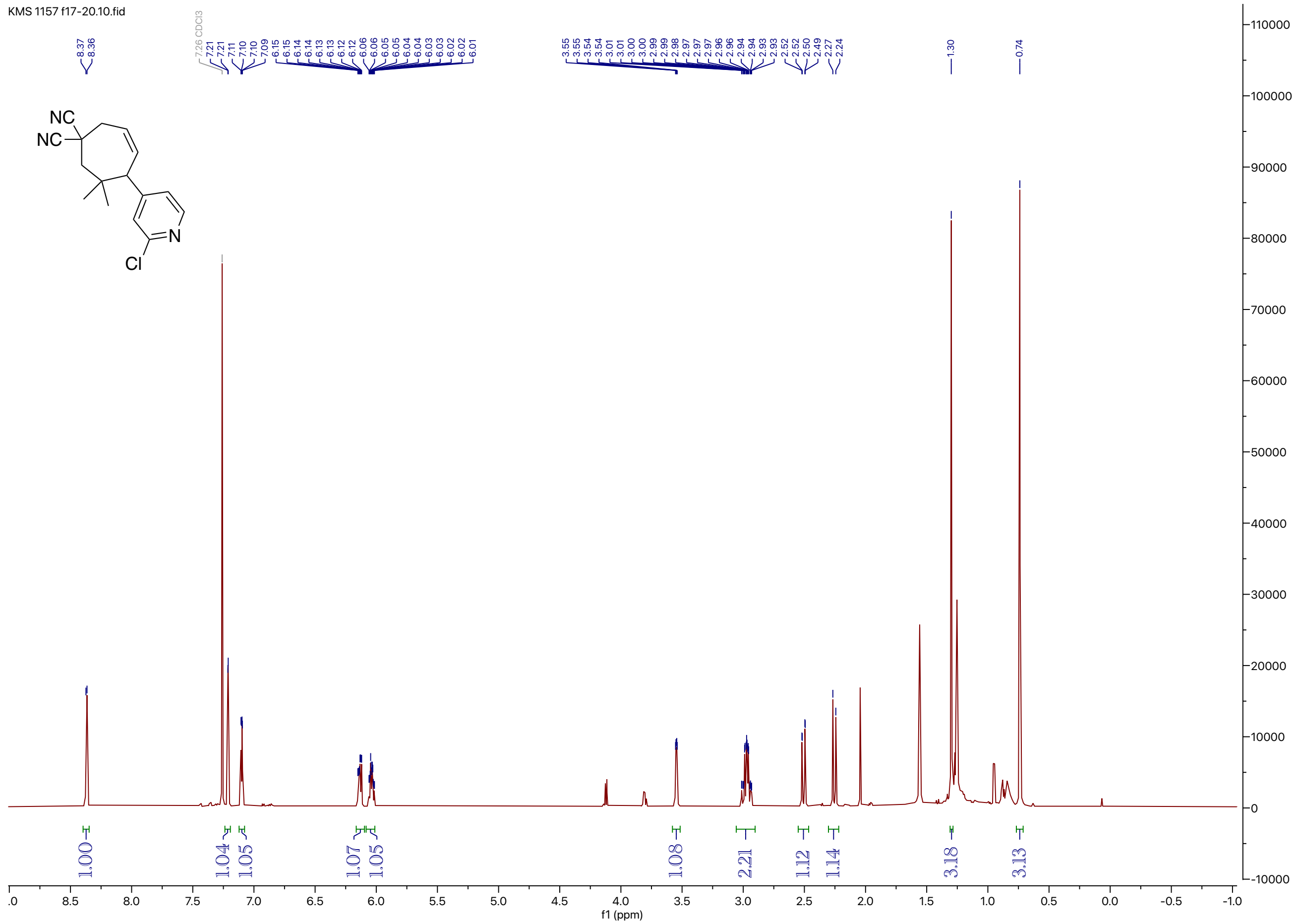
1H NMR Spectrum of 11a (CDCl3)



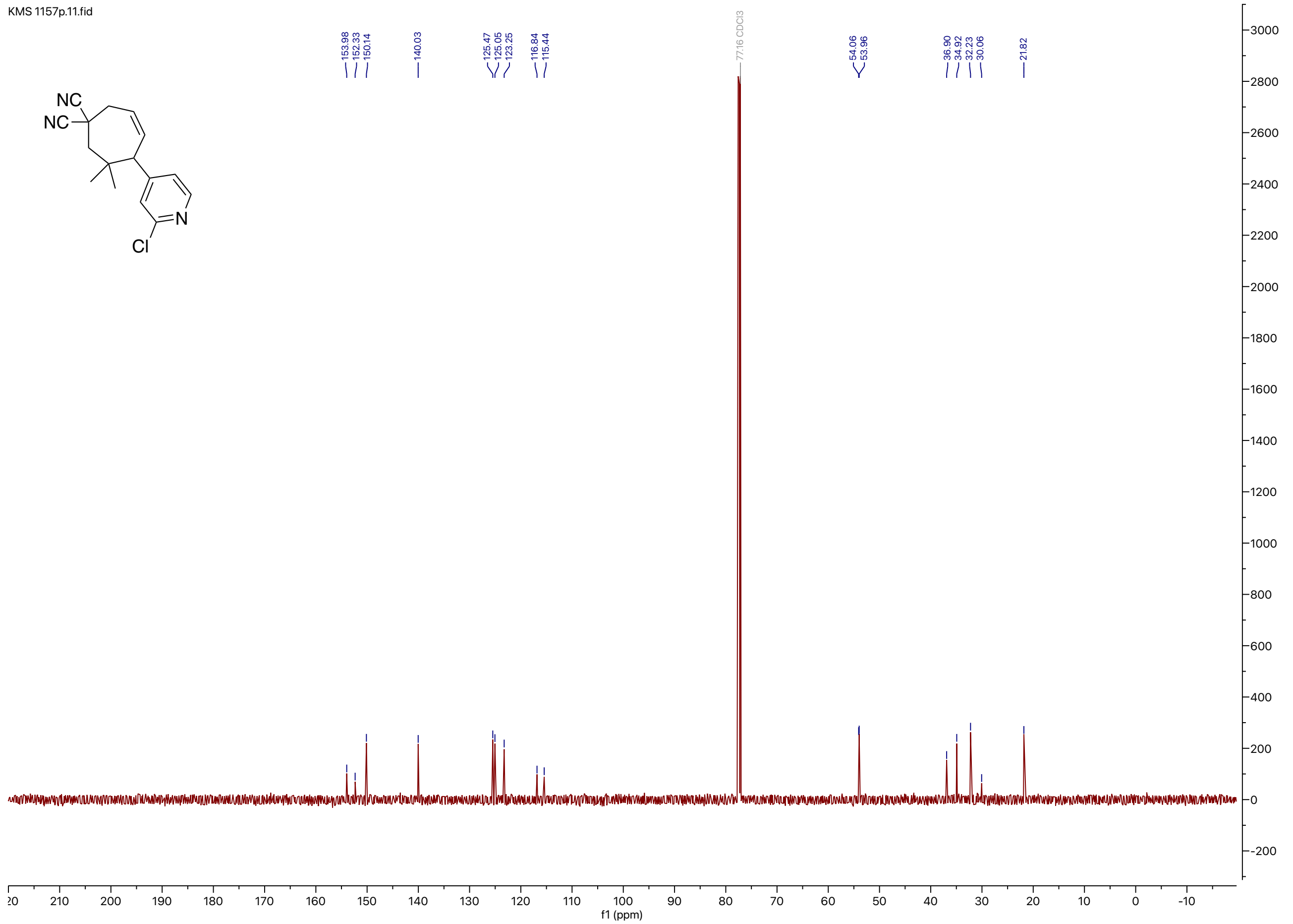
^{13}C NMR Spectrum of 11a ($CDCl_3$)



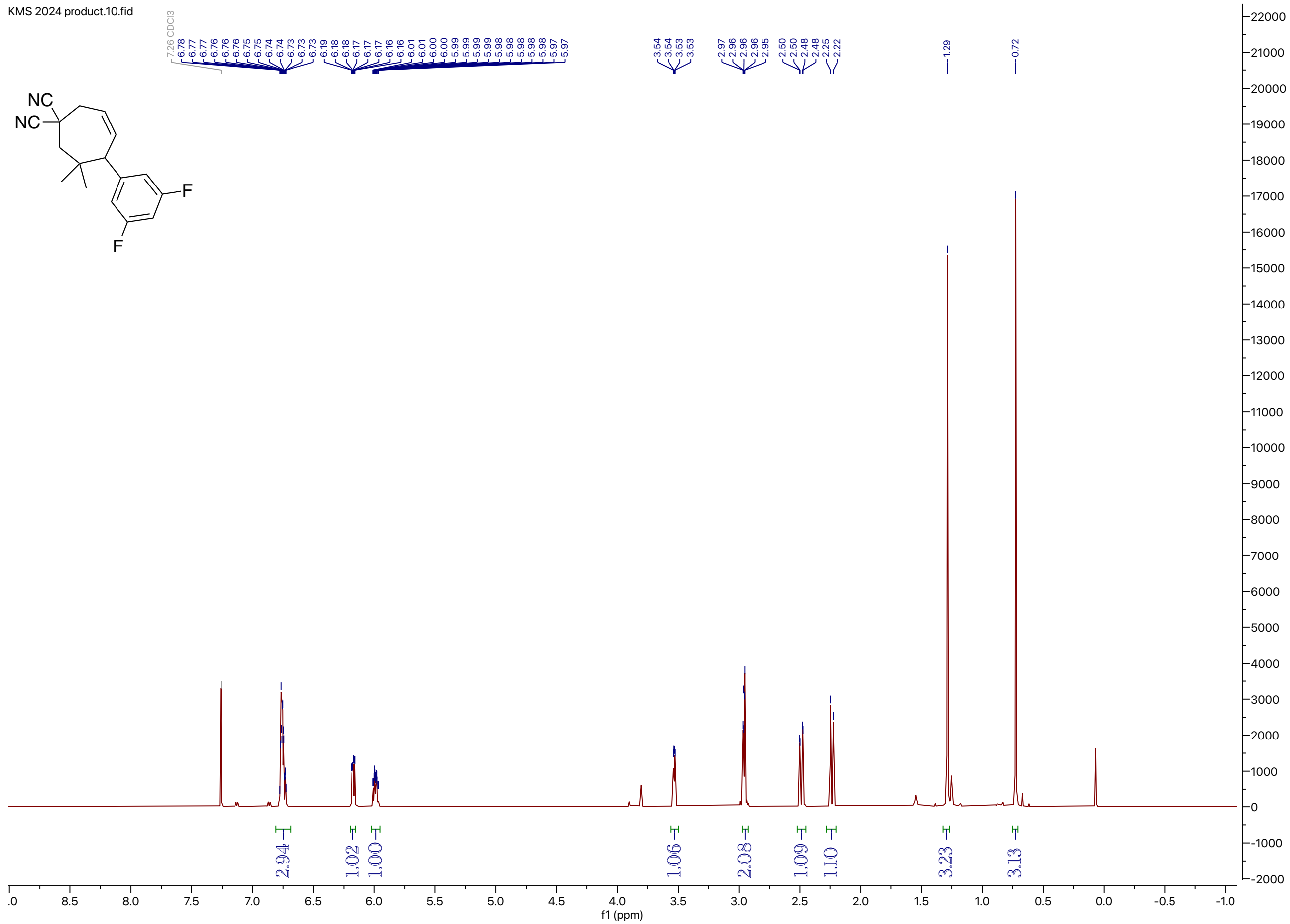
[1]H NMR Spectrum of 11e ($CDCl_3$)



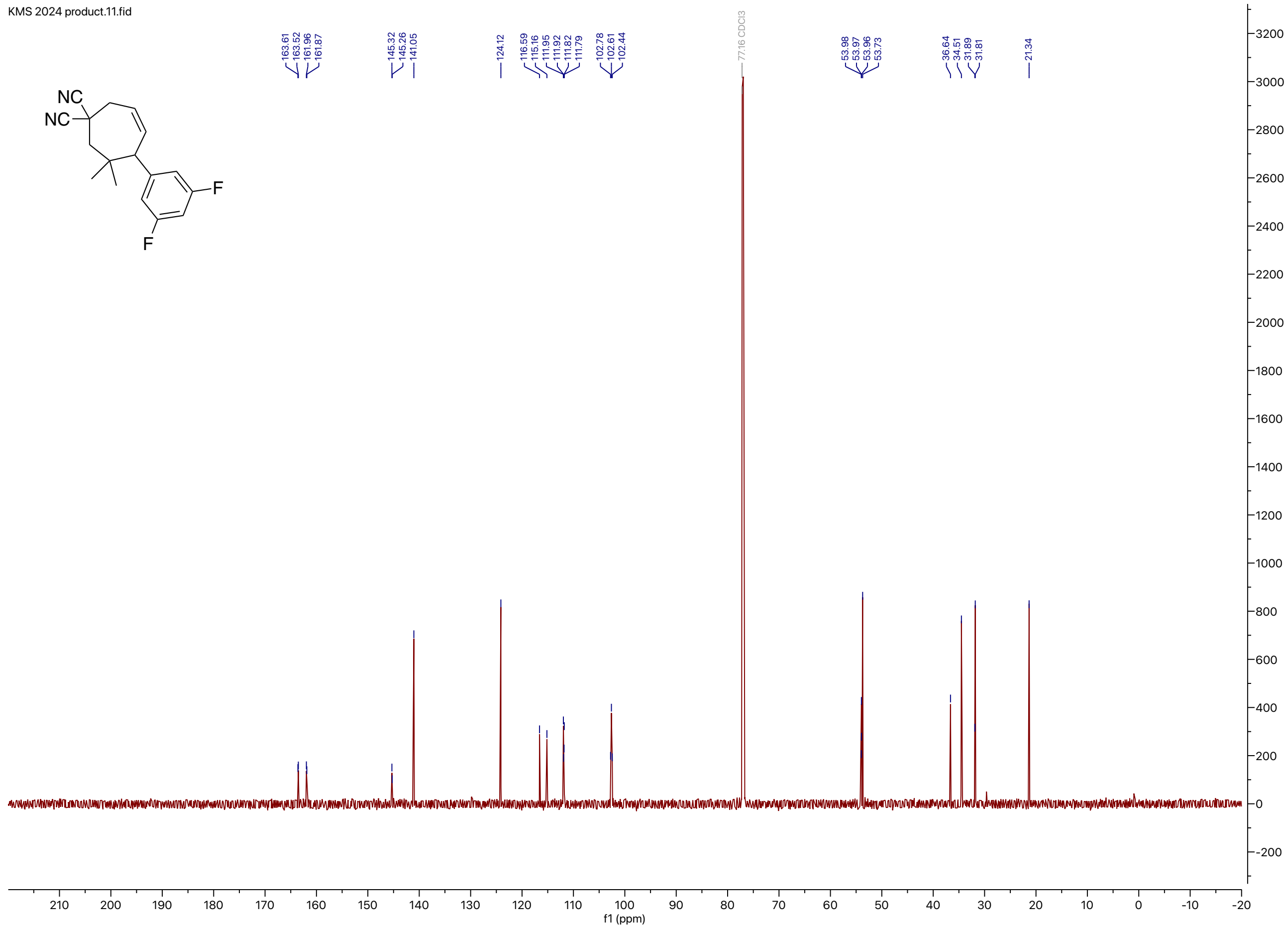
^{13}C NMR Spectrum of 11e ($CDCl_3$)



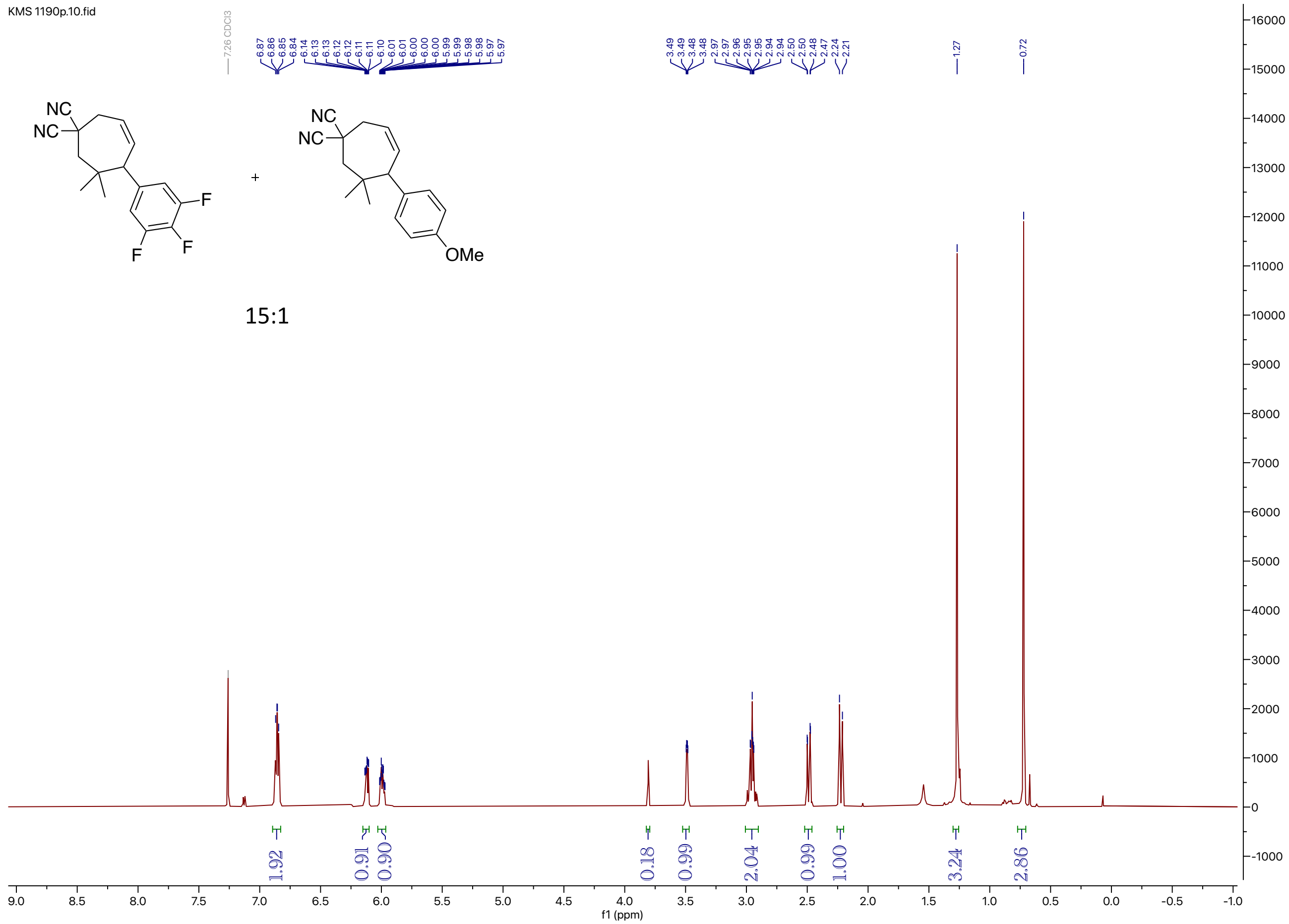
^{1}H NMR Spectrum of 11b ($CDCl_3$)



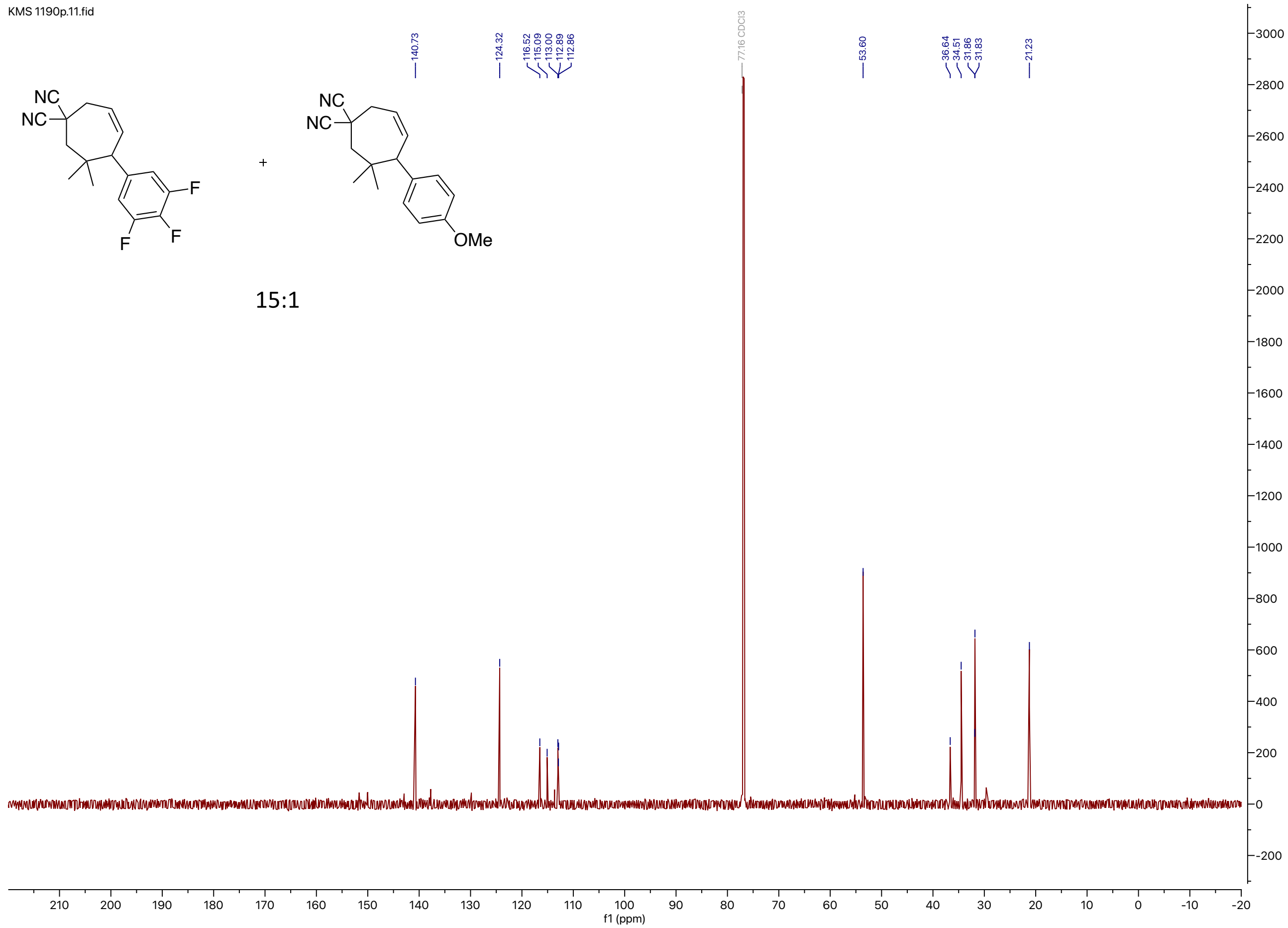
^{13}C NMR Spectrum of 11b ($CDCl_3$)



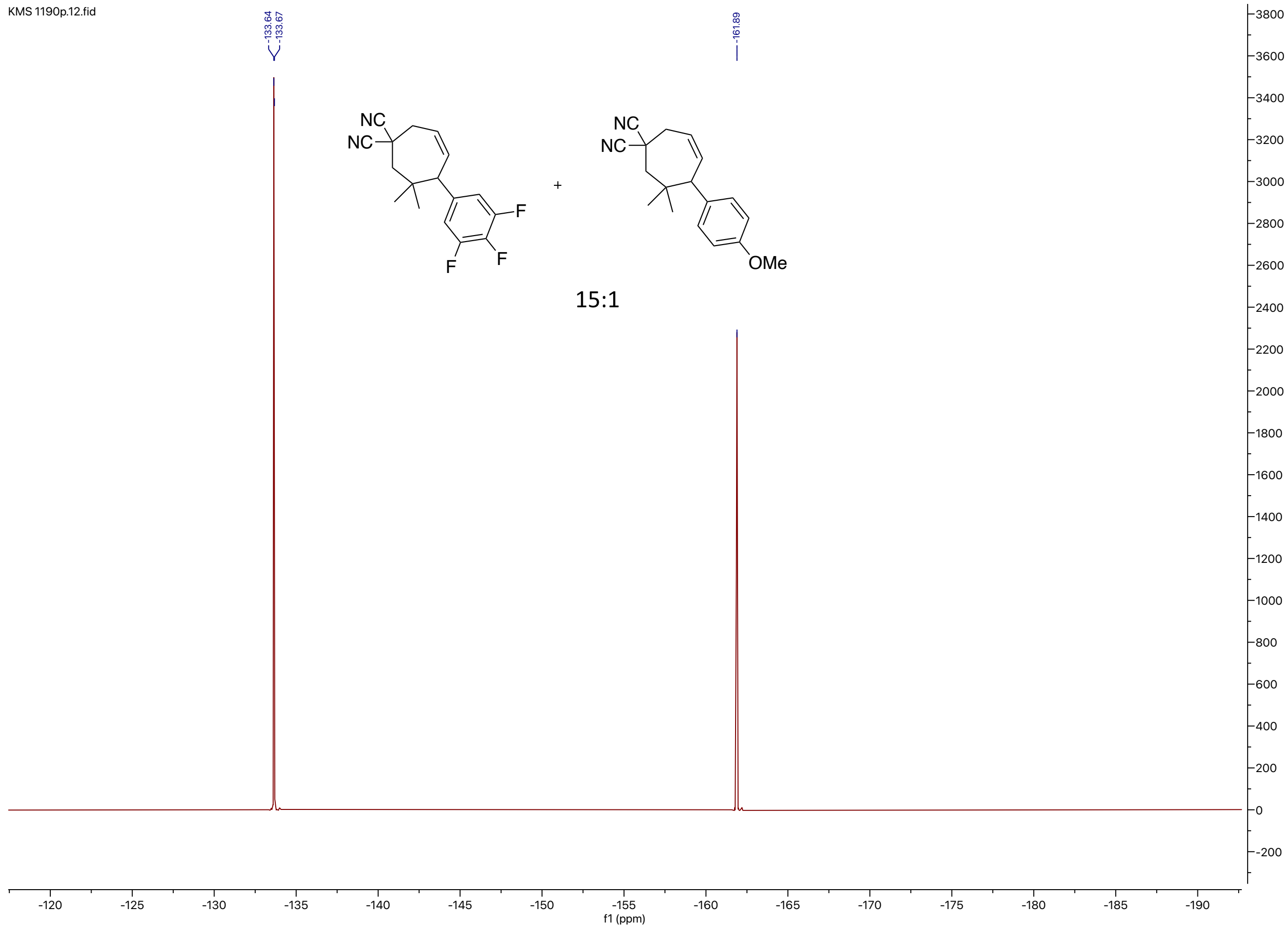
^{1}H NMR Spectrum of 11c ($CDCl_3$)



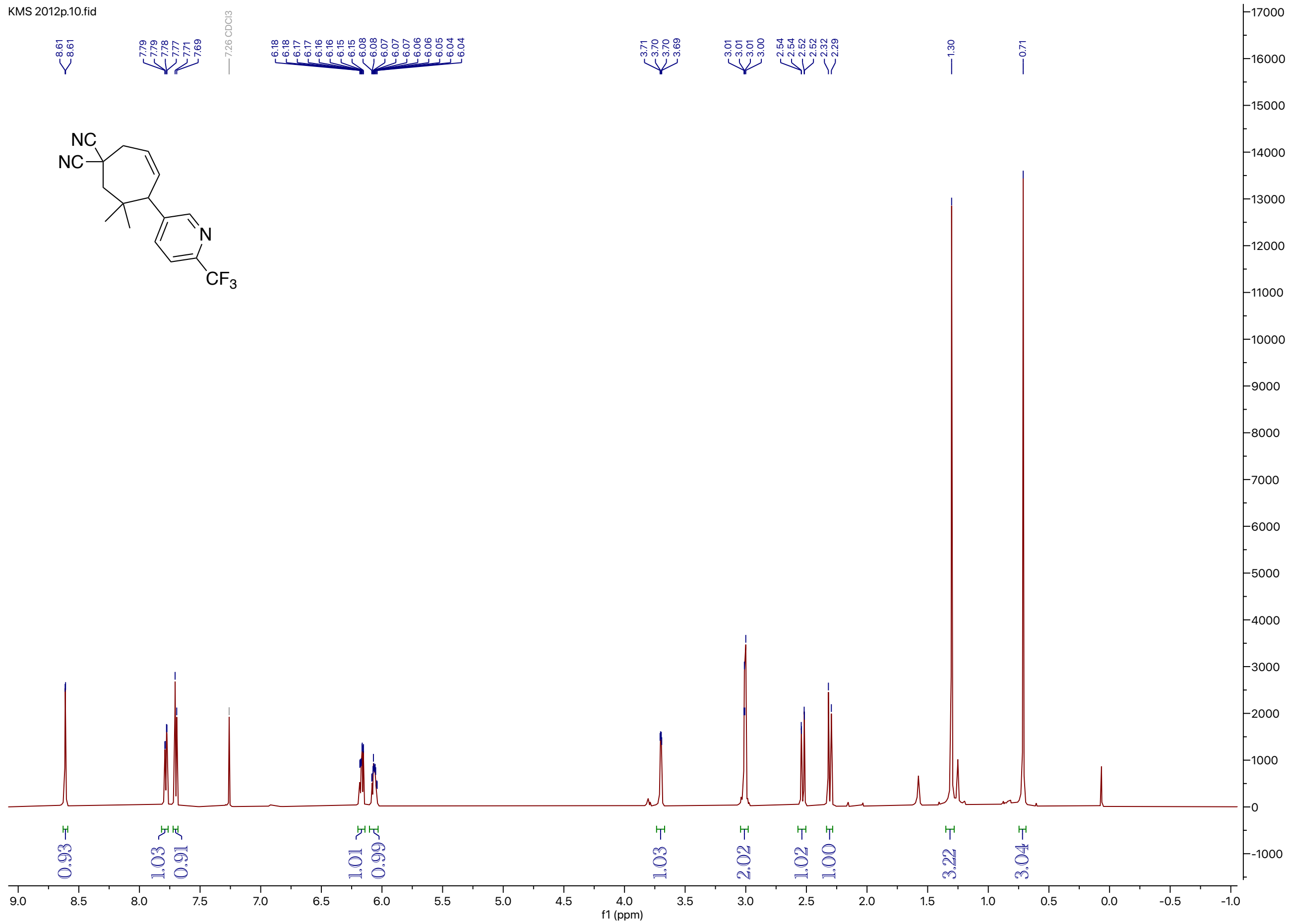
^{13}C NMR Spectrum of 11c ($CDCl_3$)



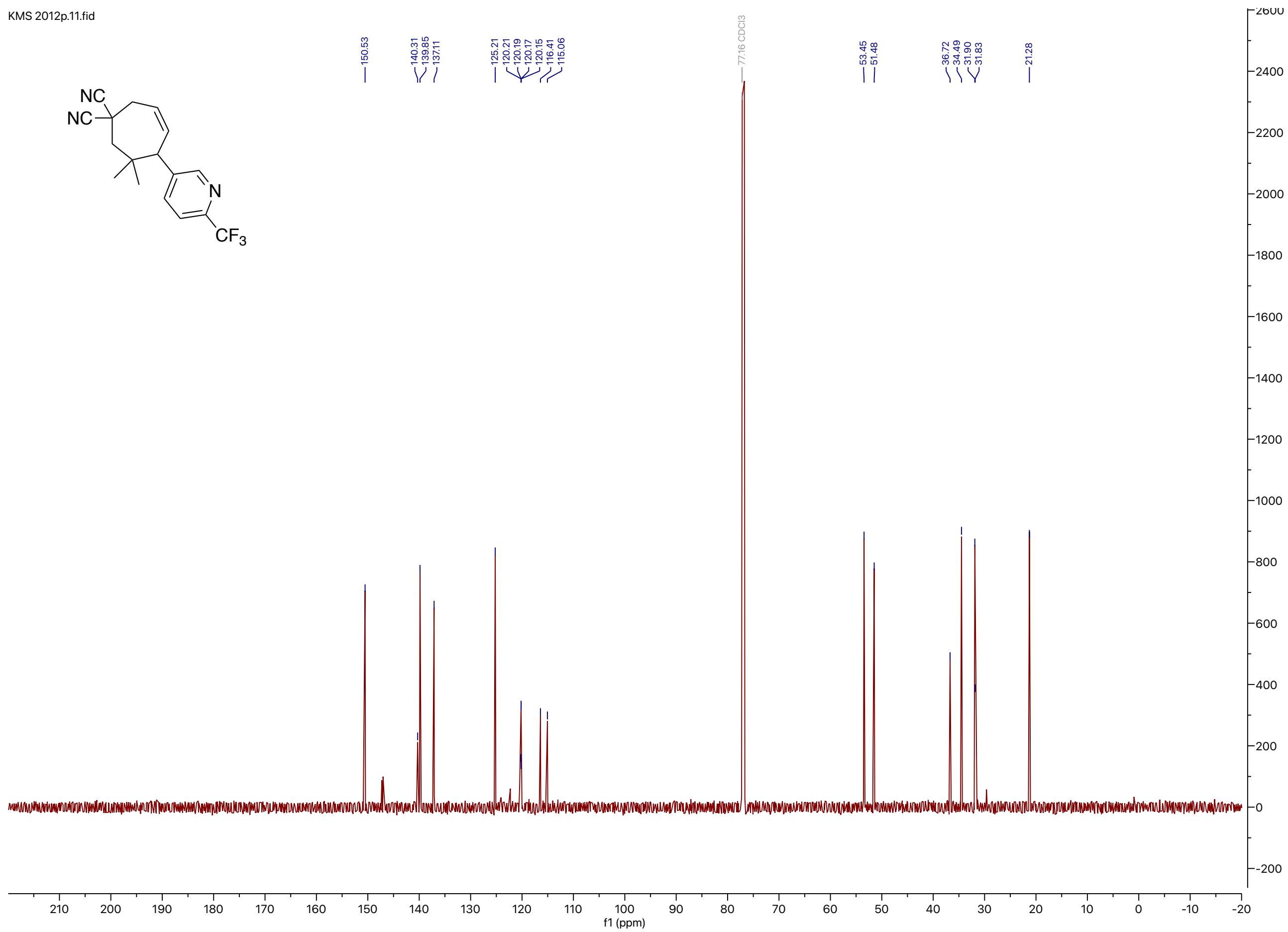
^{19}F NMR Spectrum of 11c ($CDCl_3$)



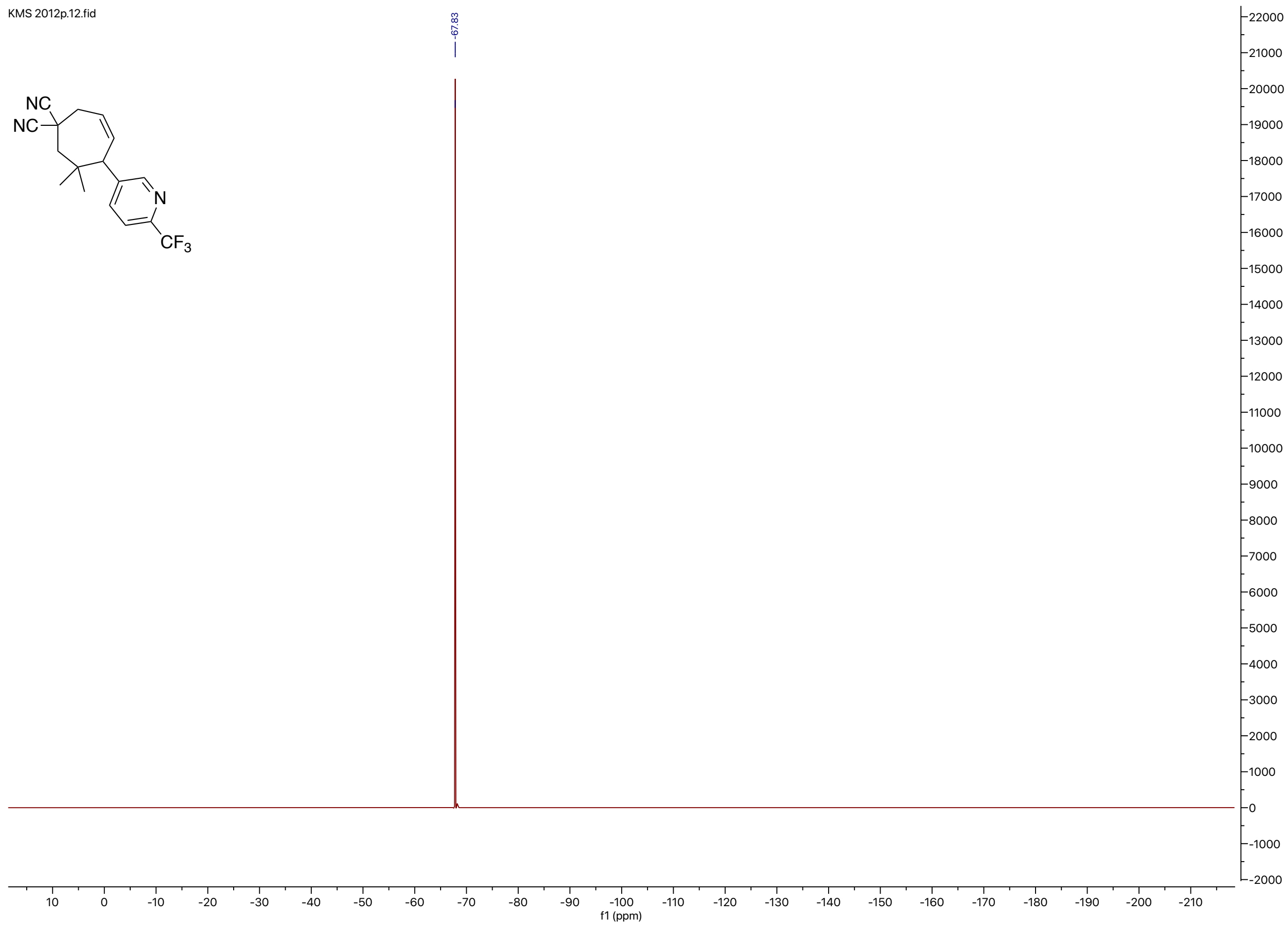
^{1}H NMR Spectrum of 11f ($CDCl_3$)



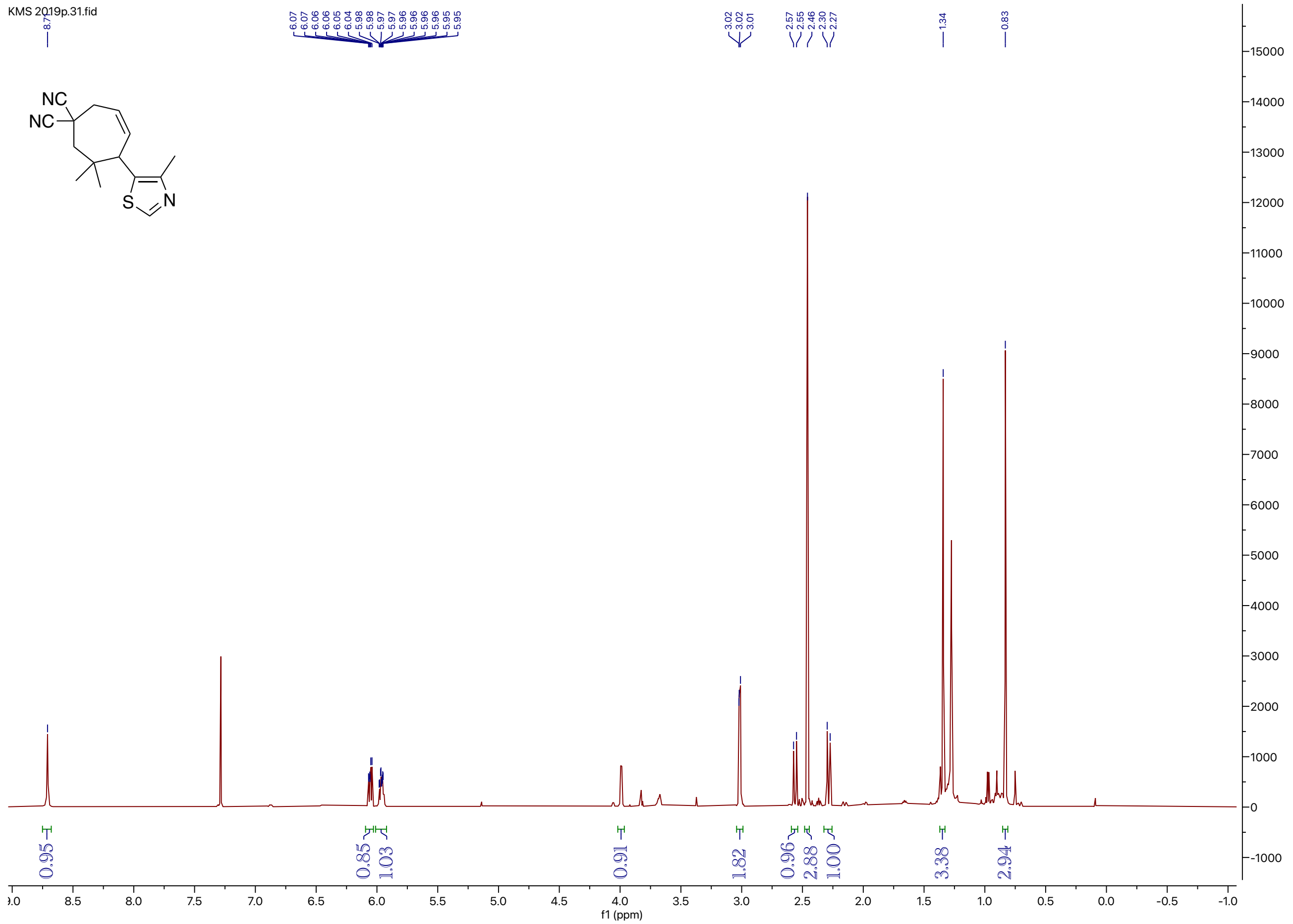
^{13}C NMR Spectrum of 11f ($CDCl_3$)



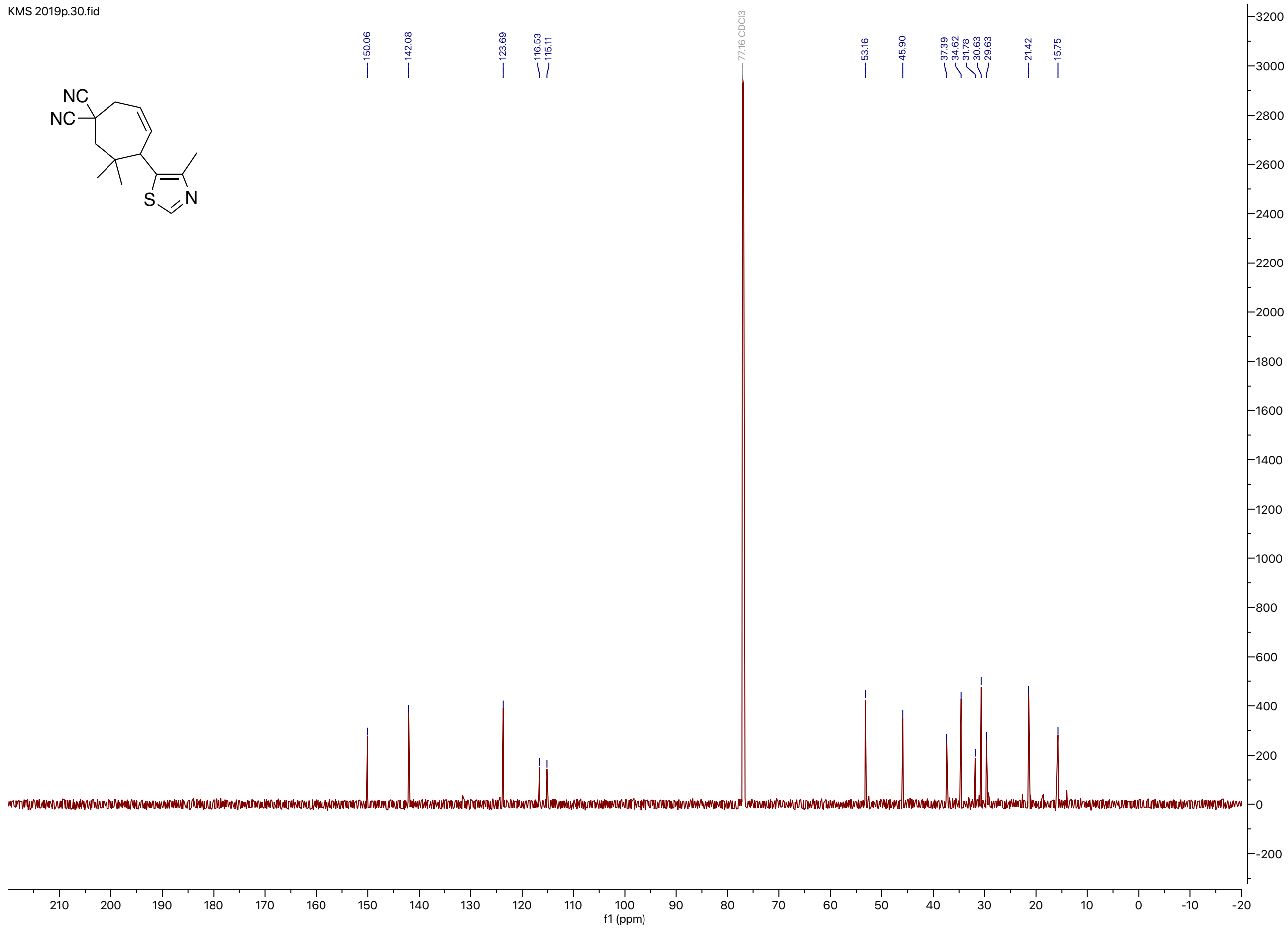
^{19}F NMR Spectrum of 11f ($CDCl_3$)



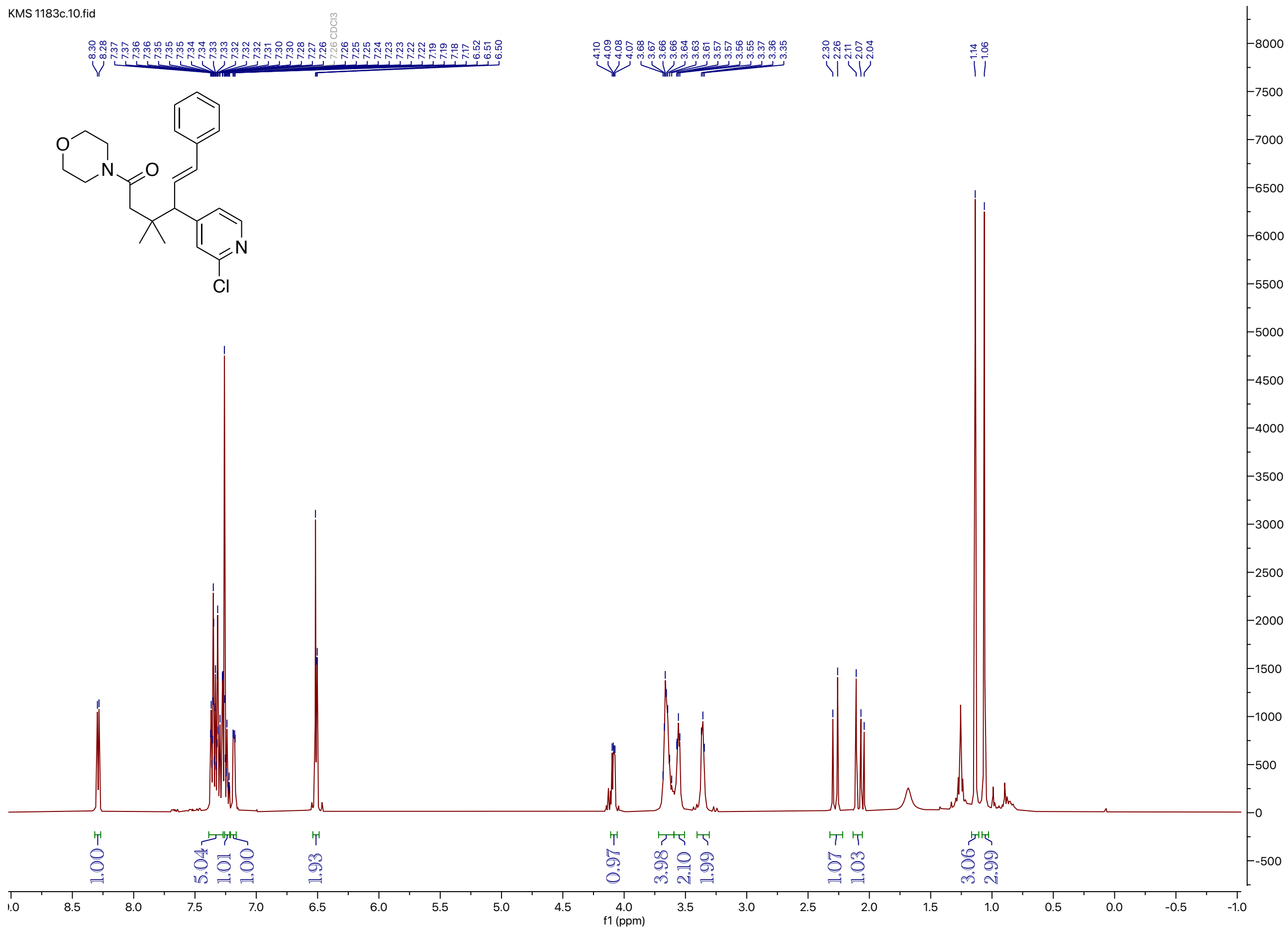
^{1}H NMR Spectrum of 11d ($CDCl_3$)



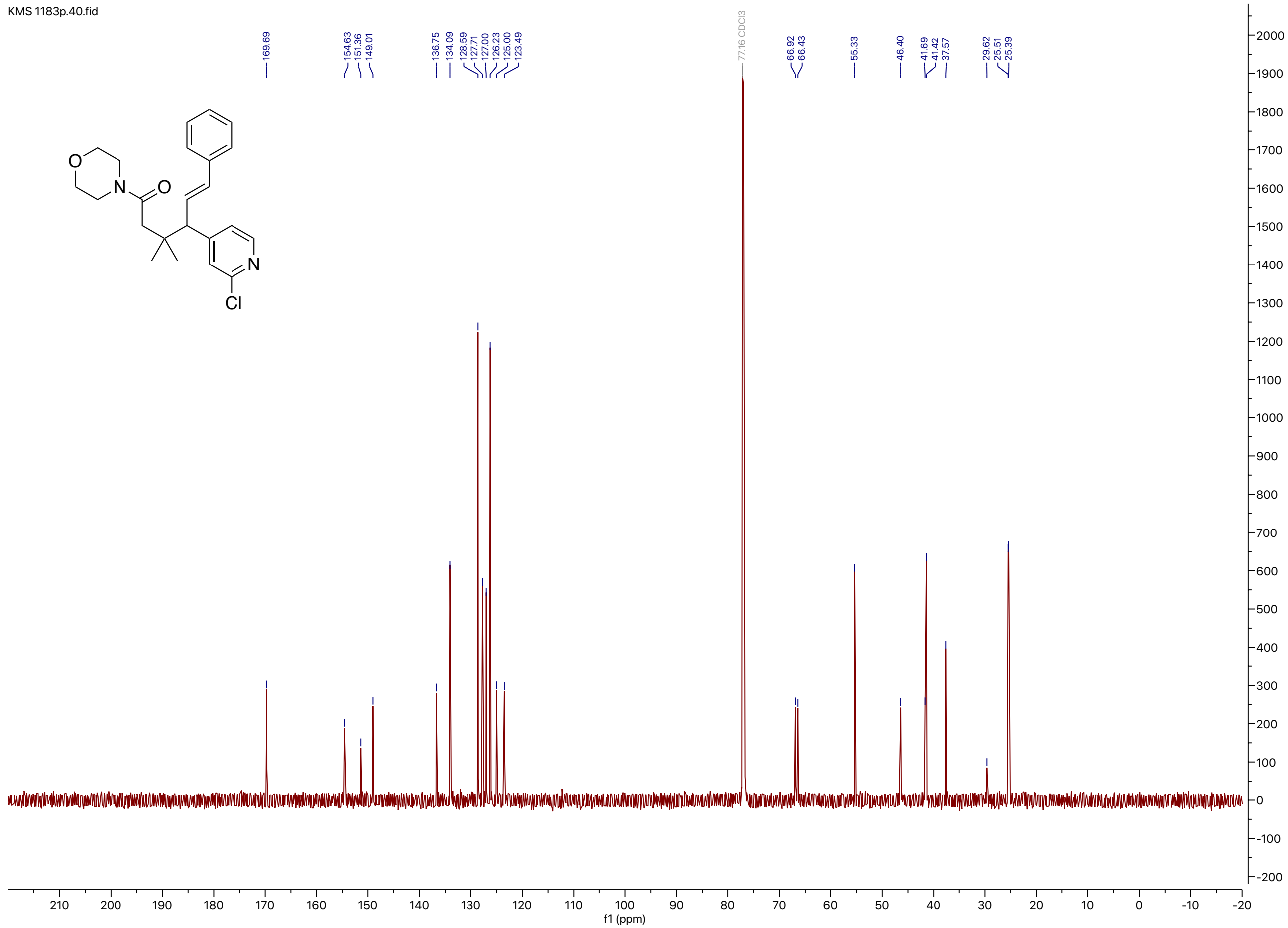
^{13}C NMR Spectrum of 11d ($CDCl_3$)



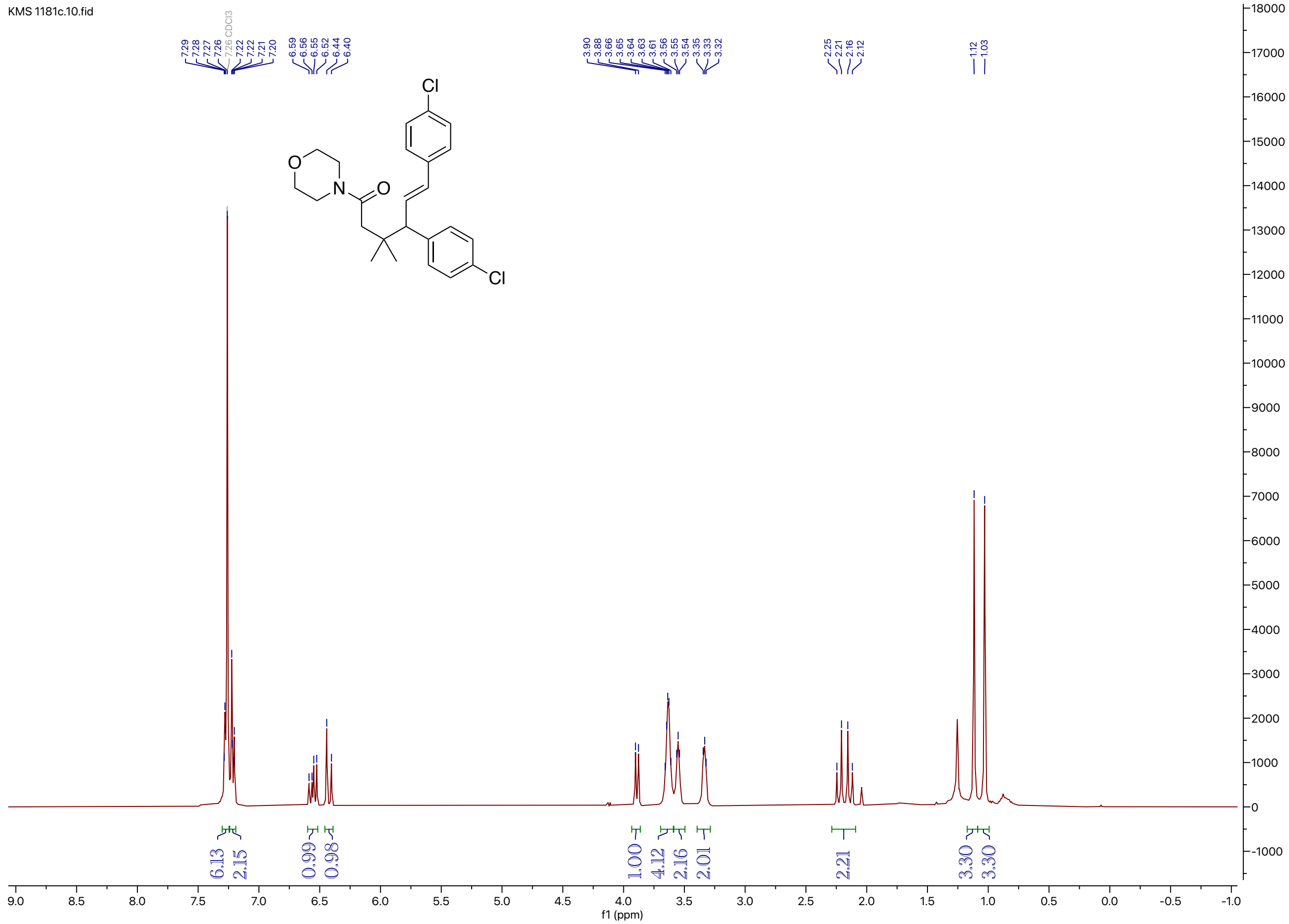
^{1}H NMR Spectrum of 12b ($CDCl_3$)



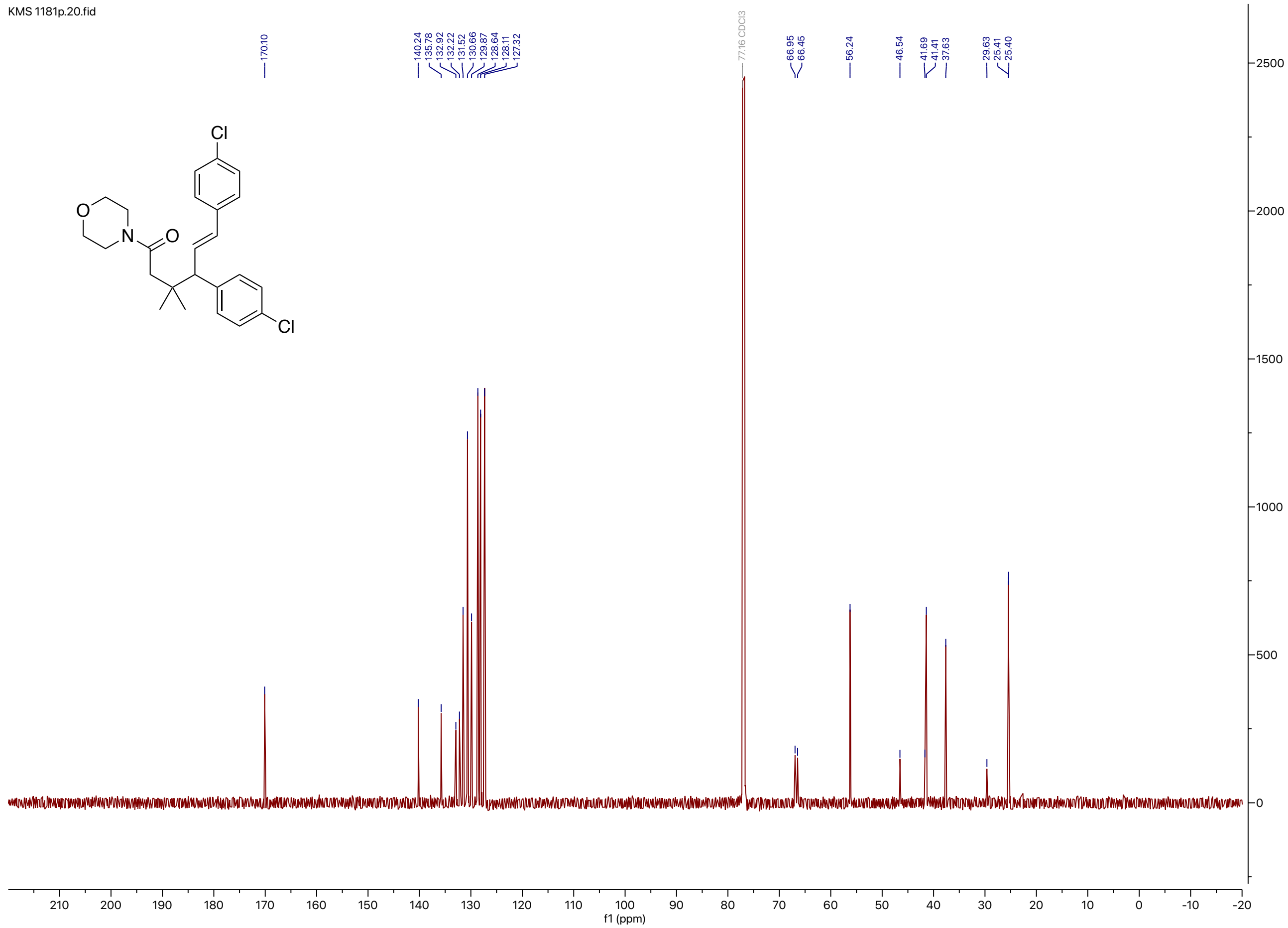
^{13}C NMR Spectrum of 12b ($CDCl_3$)



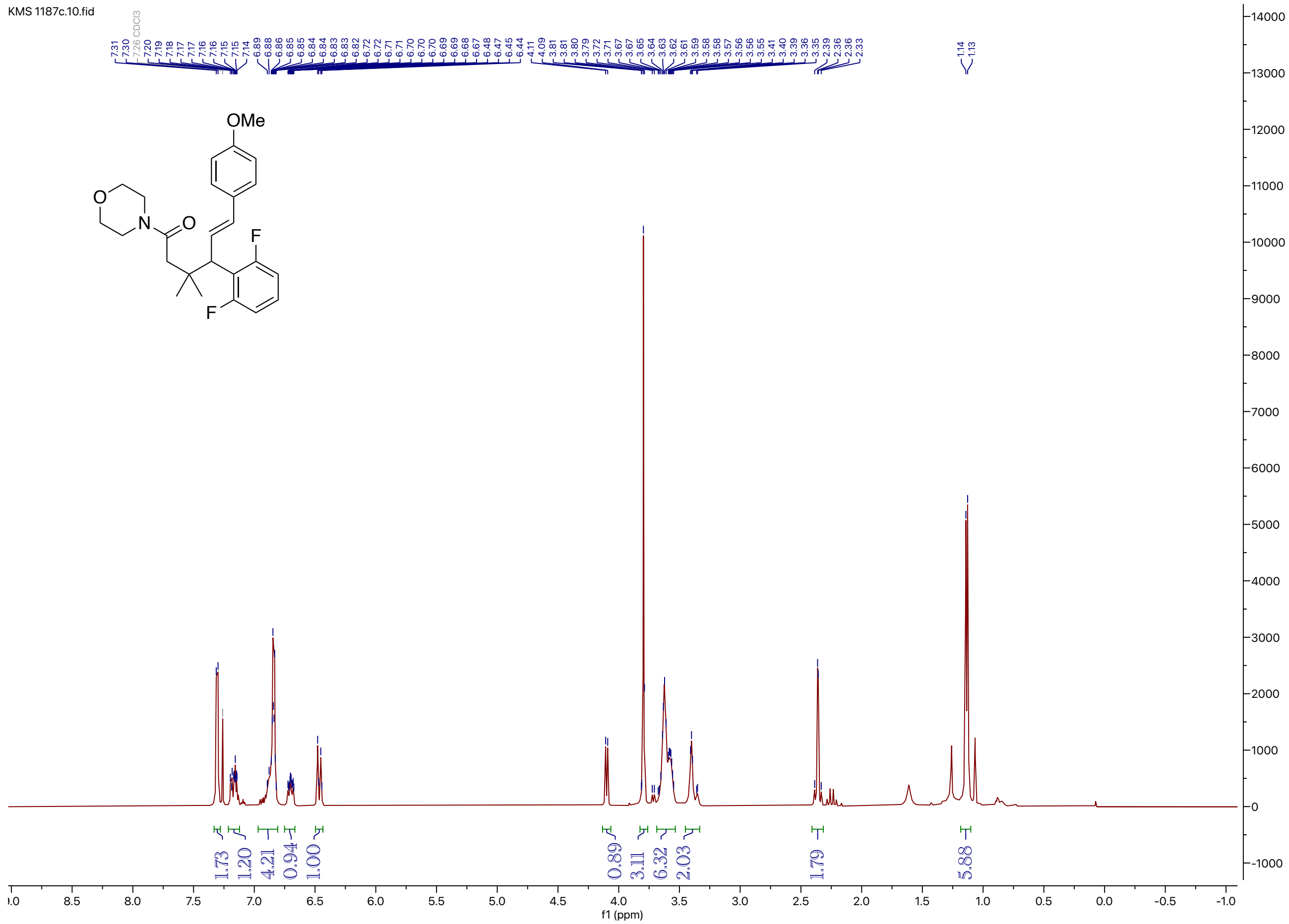
^{1}H NMR Spectrum of 12c ($CDCl_3$)



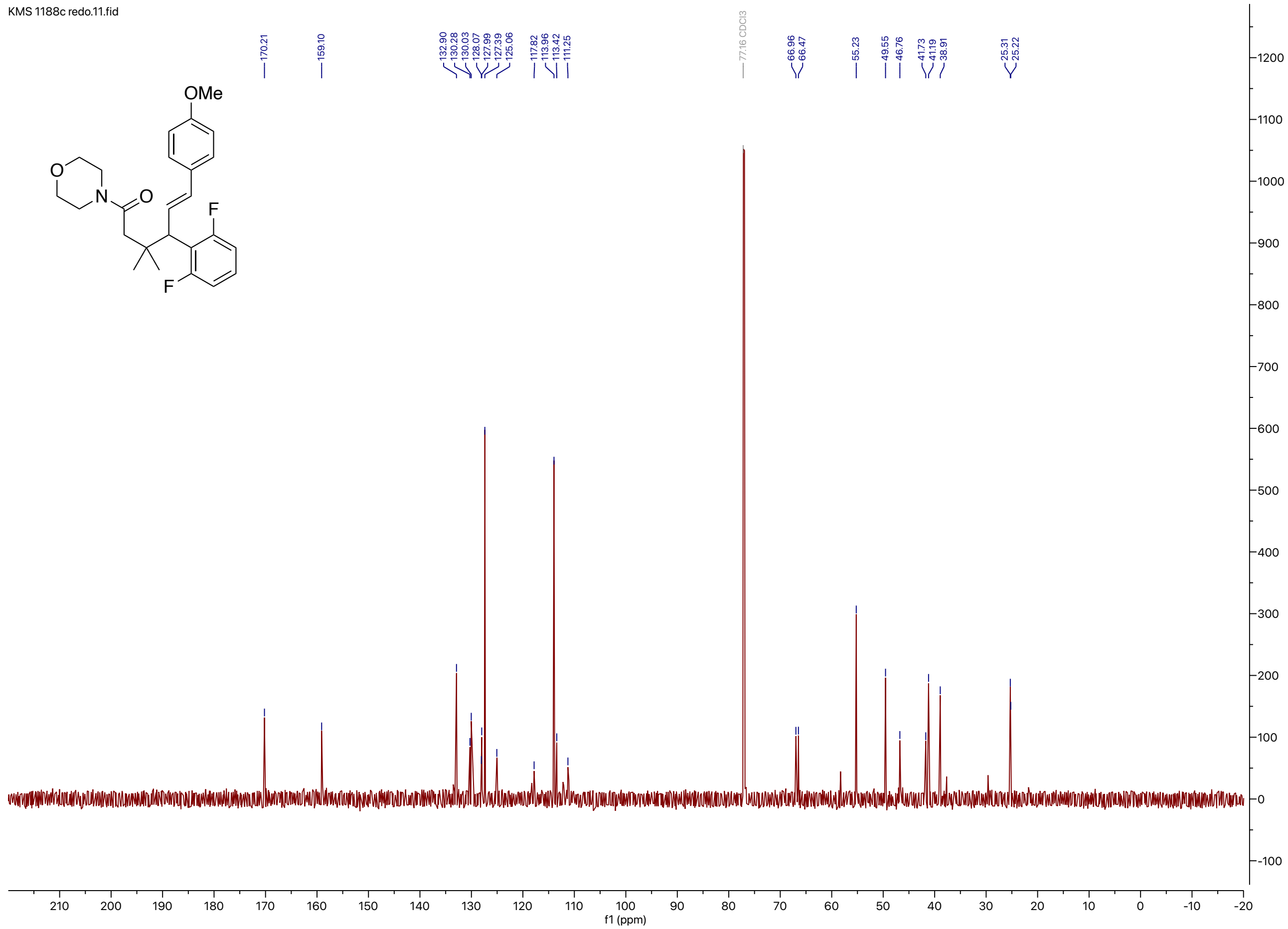
^{13}C NMR Spectrum of 12c ($CDCl_3$)



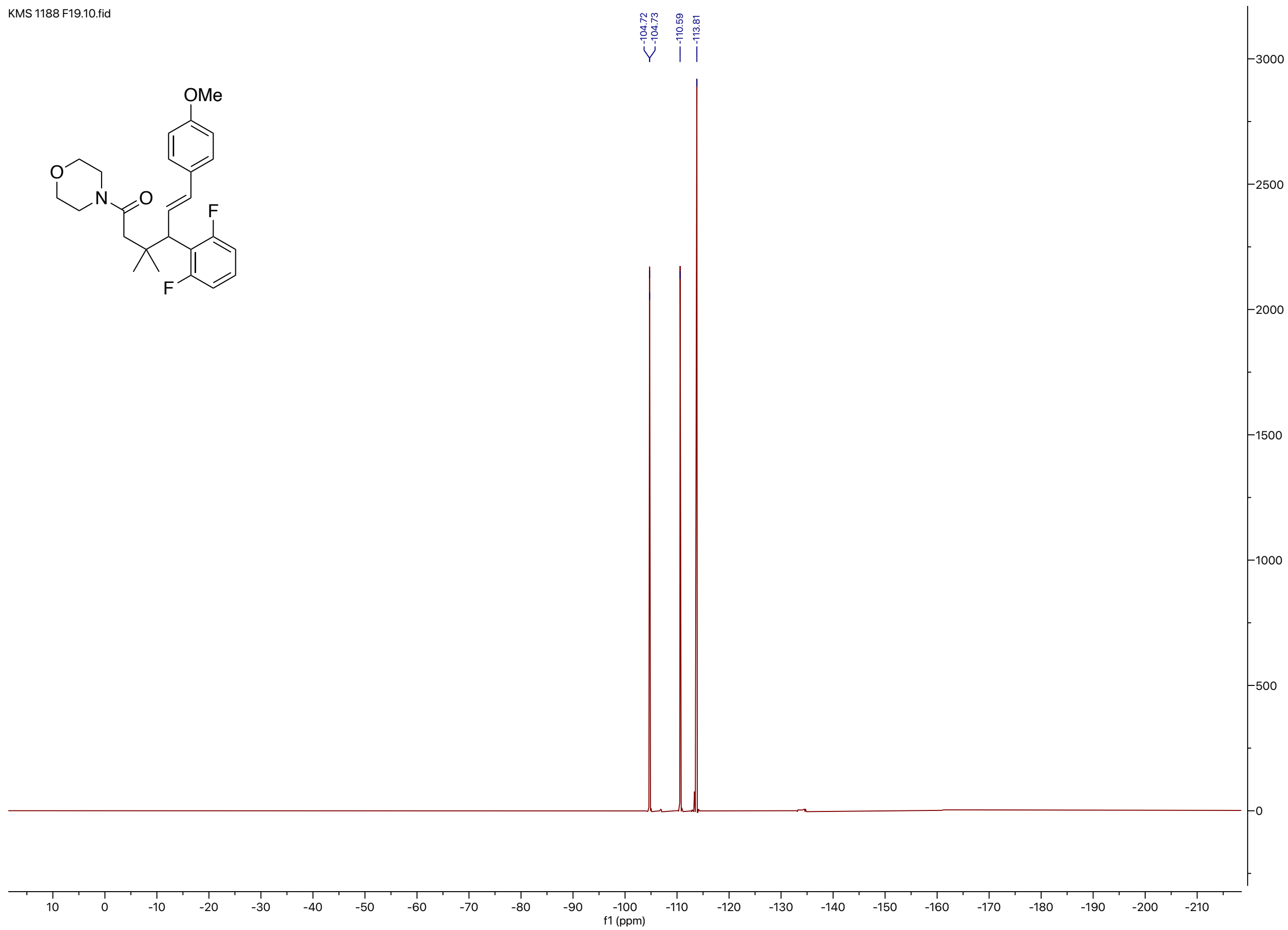
^{1}H NMR Spectrum of 12d ($CDCl_3$)



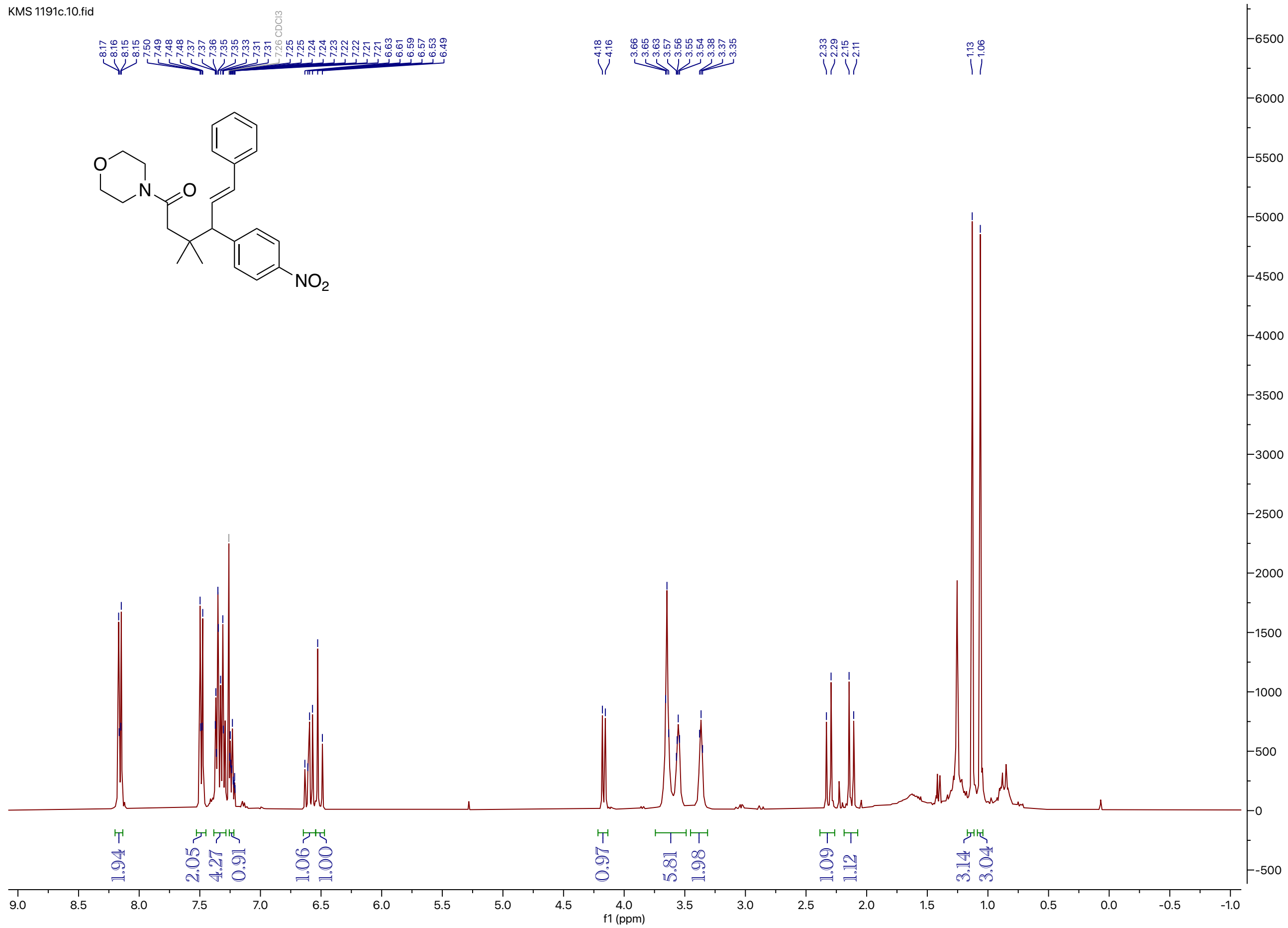
^{13}C NMR Spectrum of 12d ($CDCl_3$)



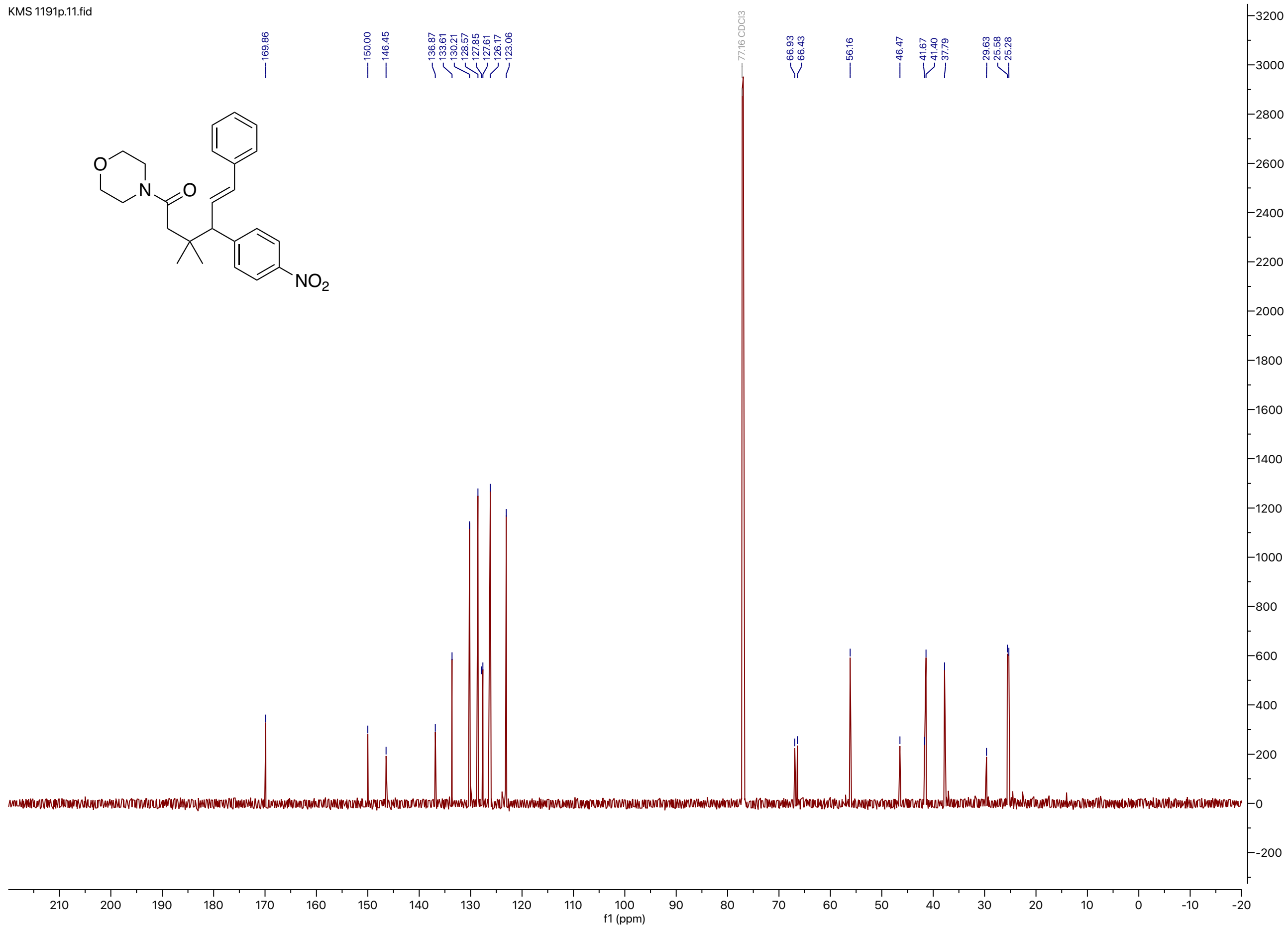
^{19}F NMR Spectrum of 12d ($CDCl_3$)



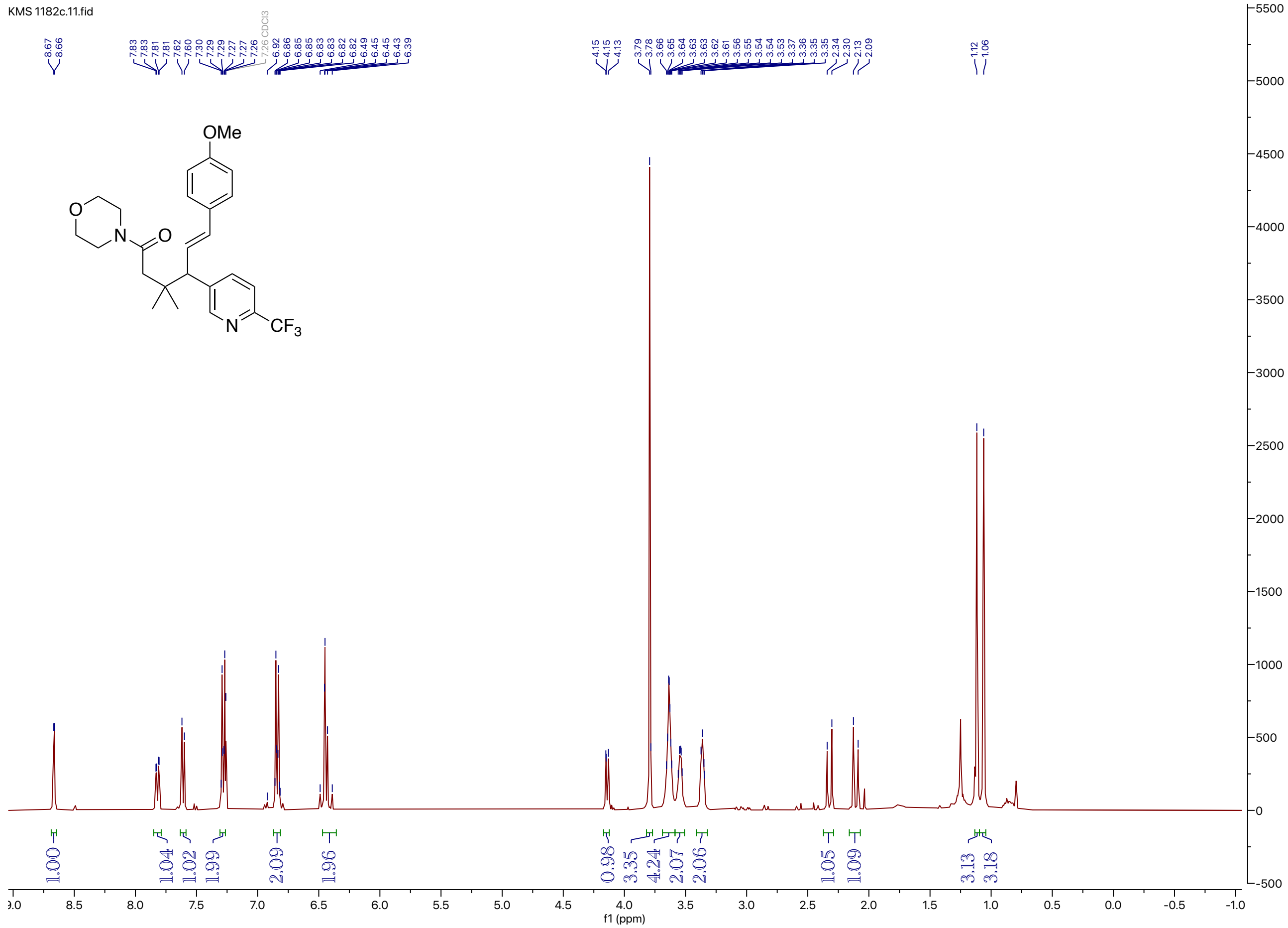
^{1}H NMR Spectrum of 12e ($CDCl_3$)



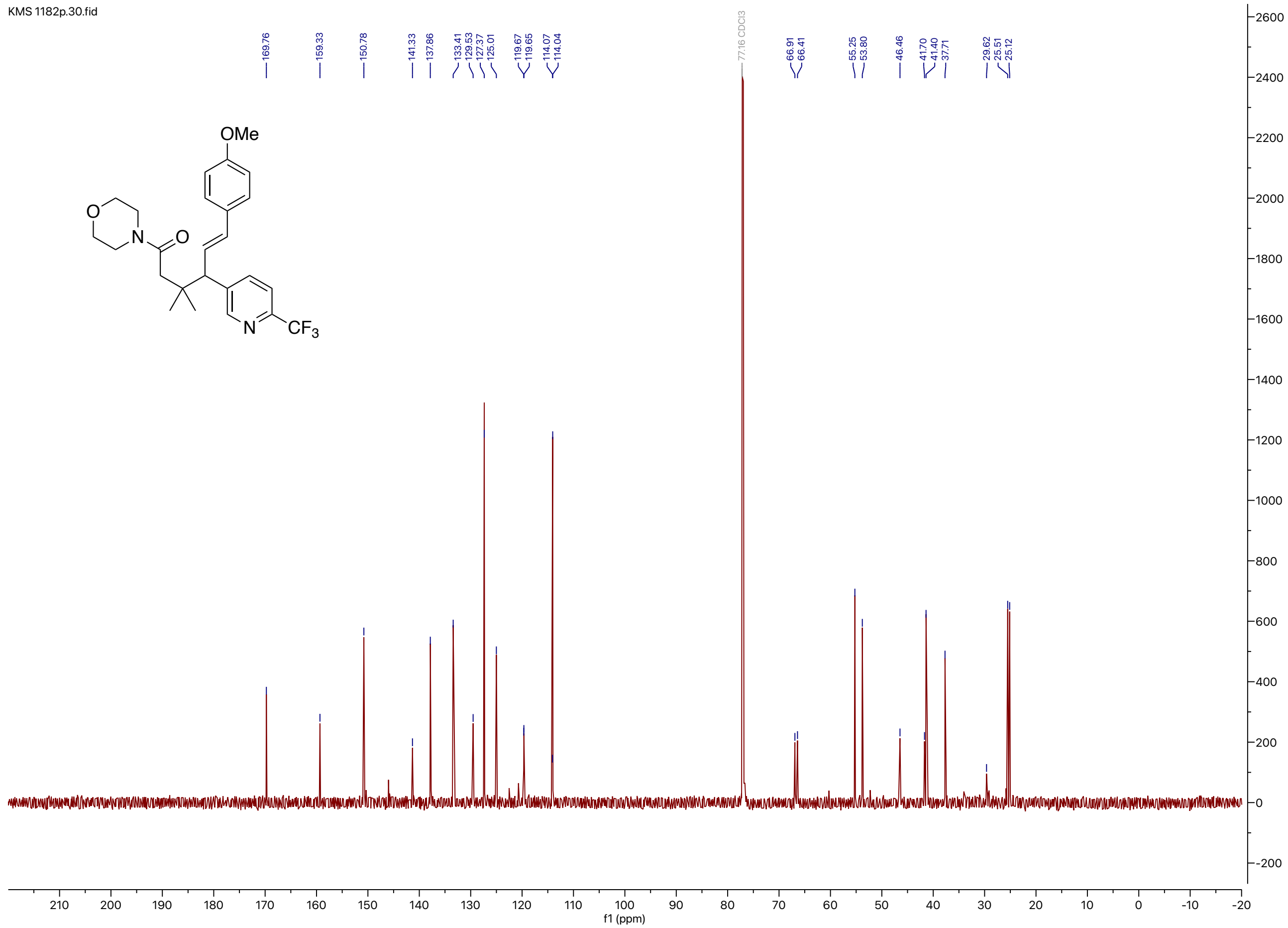
^{13}C NMR Spectrum of 12e ($CDCl_3$)



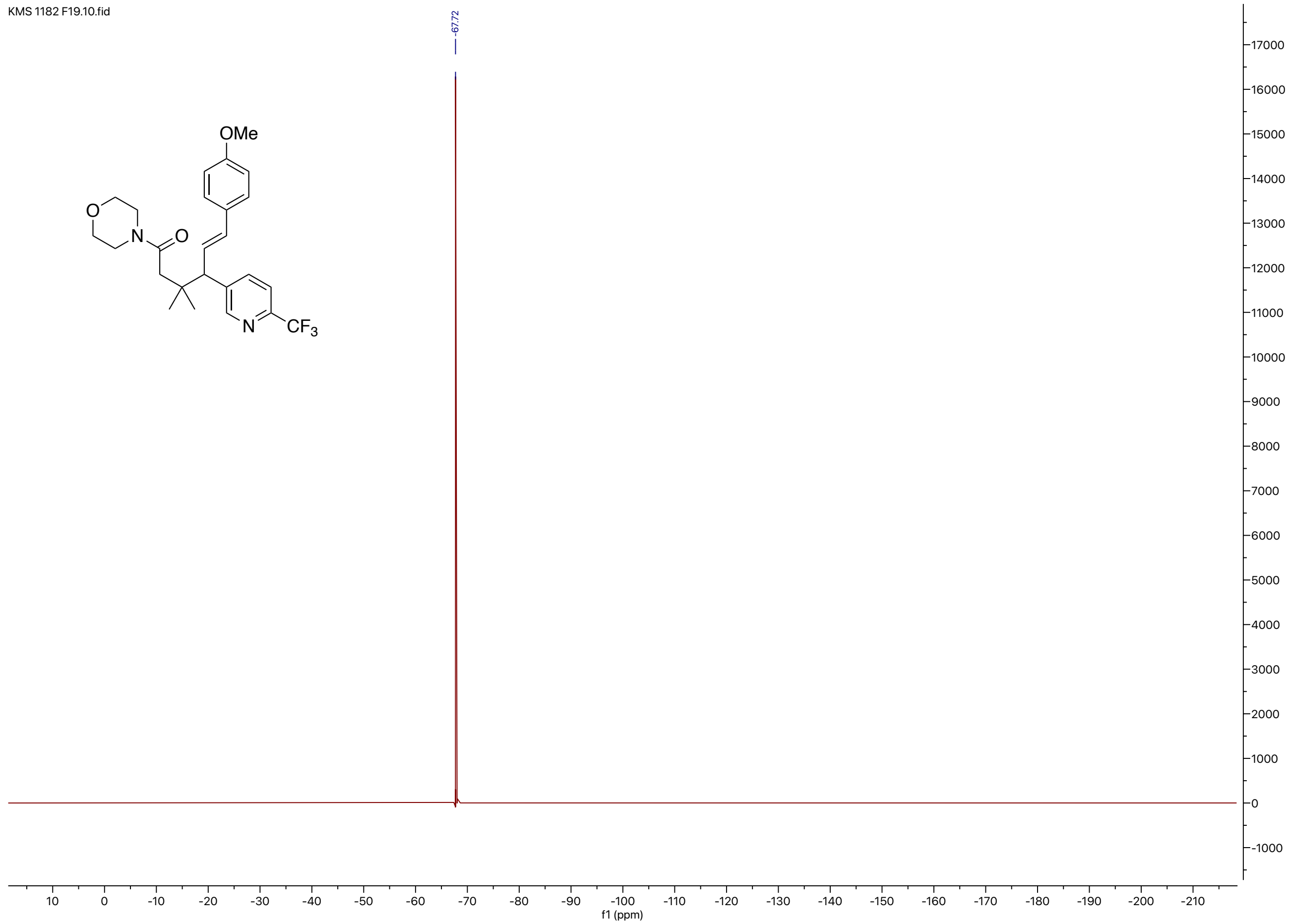
^{1}H NMR Spectrum of 12f ($CDCl_3$)



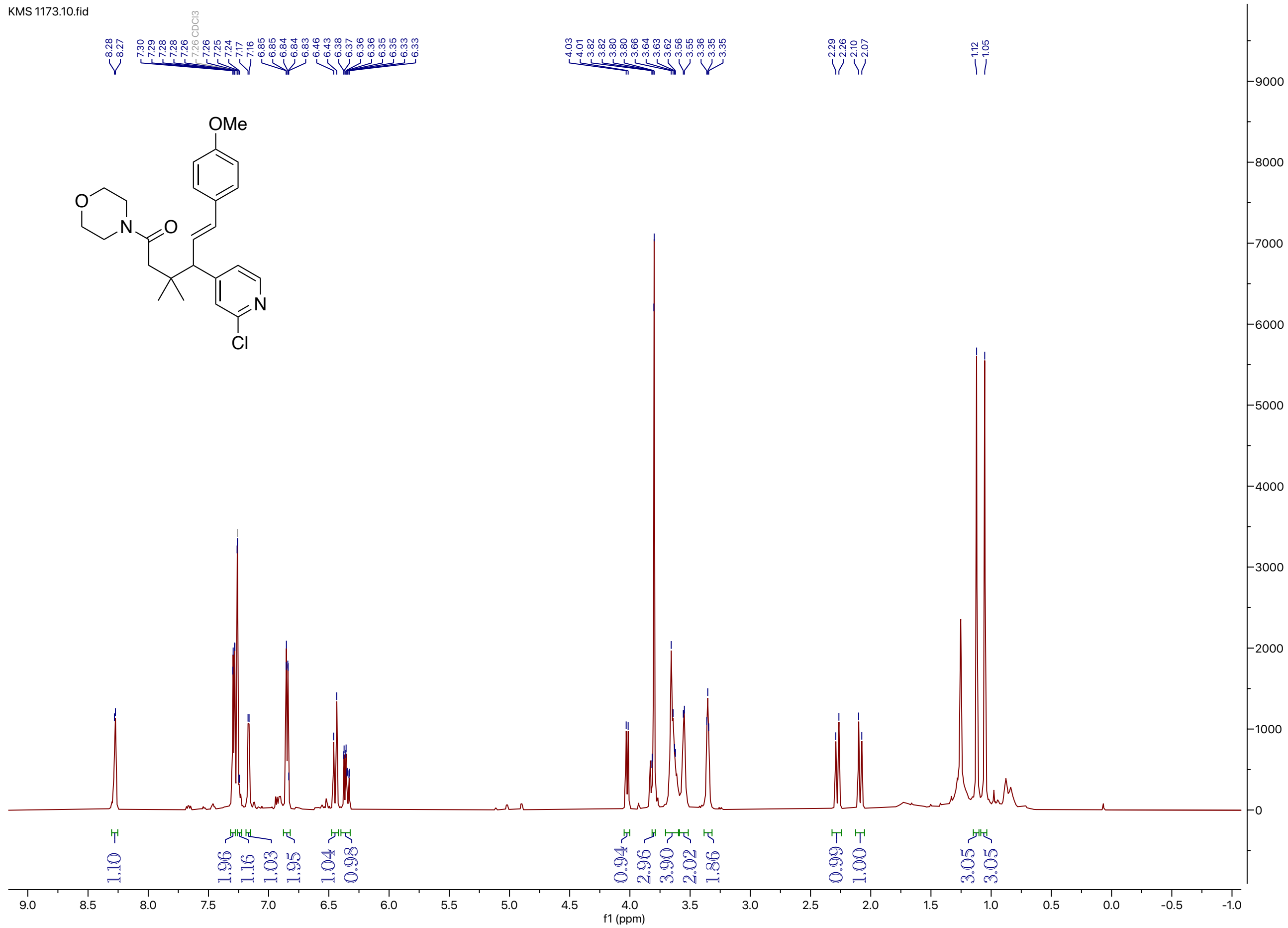
^{13}C NMR Spectrum of 12f ($CDCl_3$)



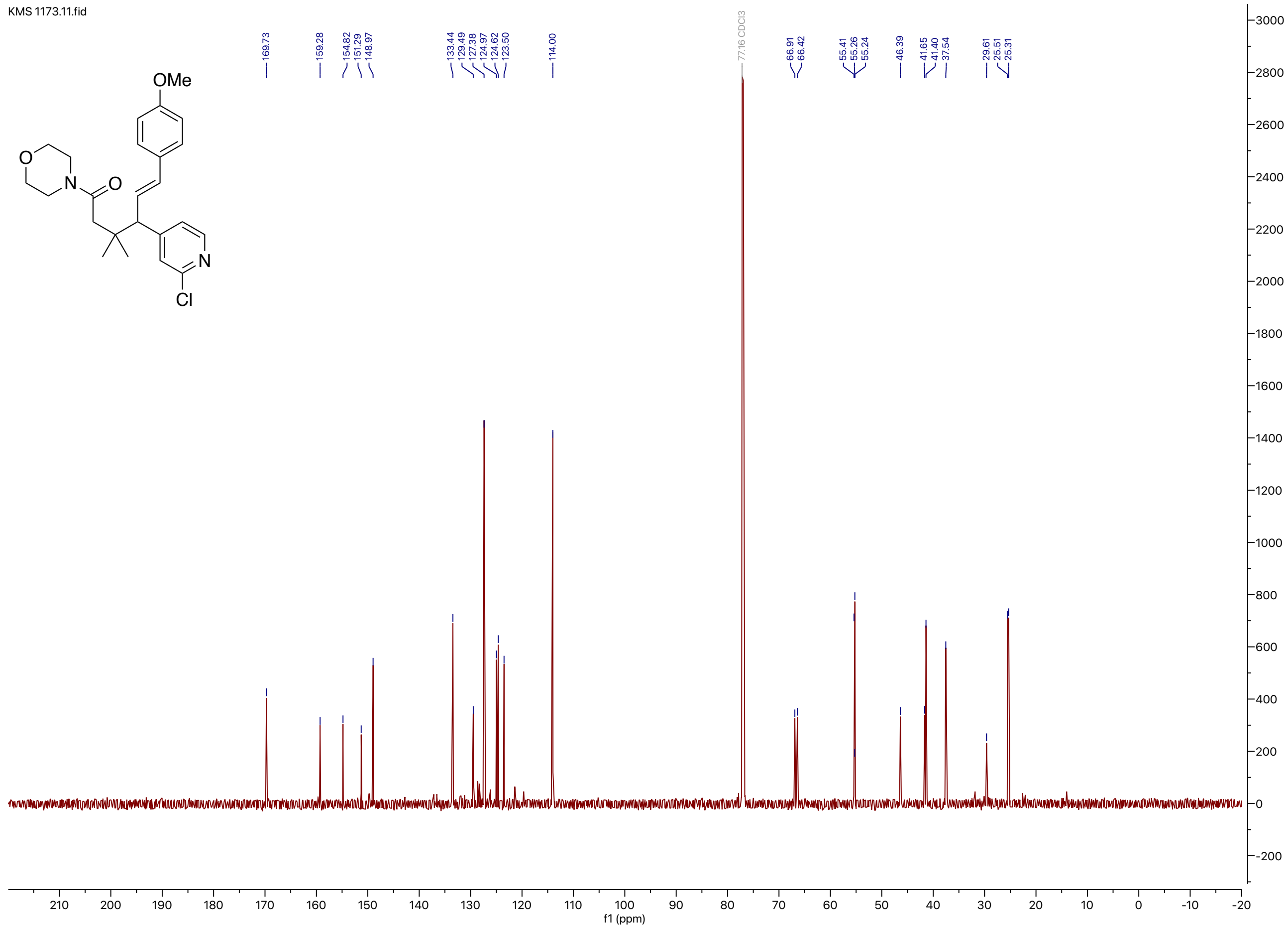
^{19}F NMR Spectrum of 12f ($CDCl_3$)



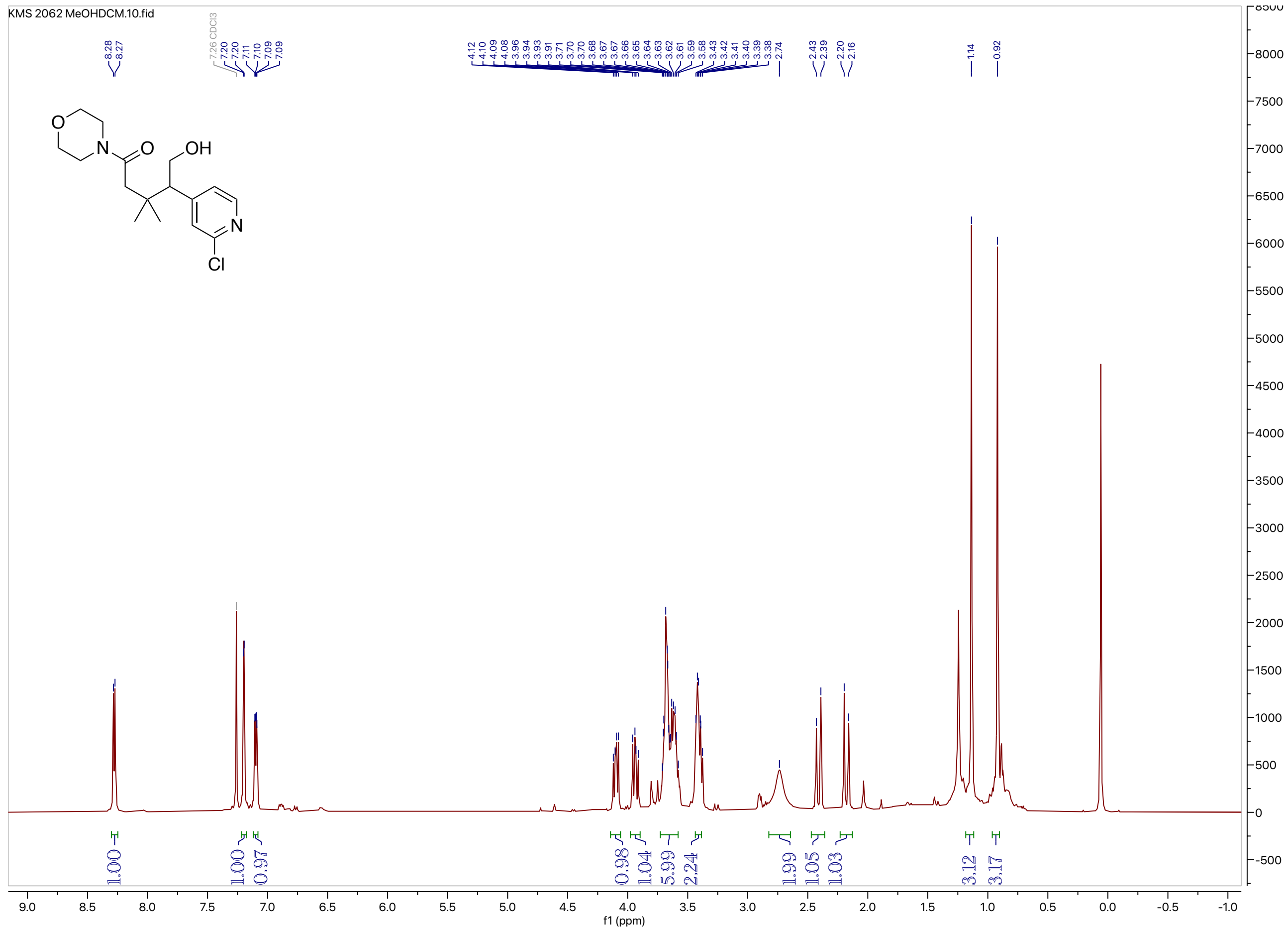
[1]H NMR Spectrum of 12a ($CDCl_3$)



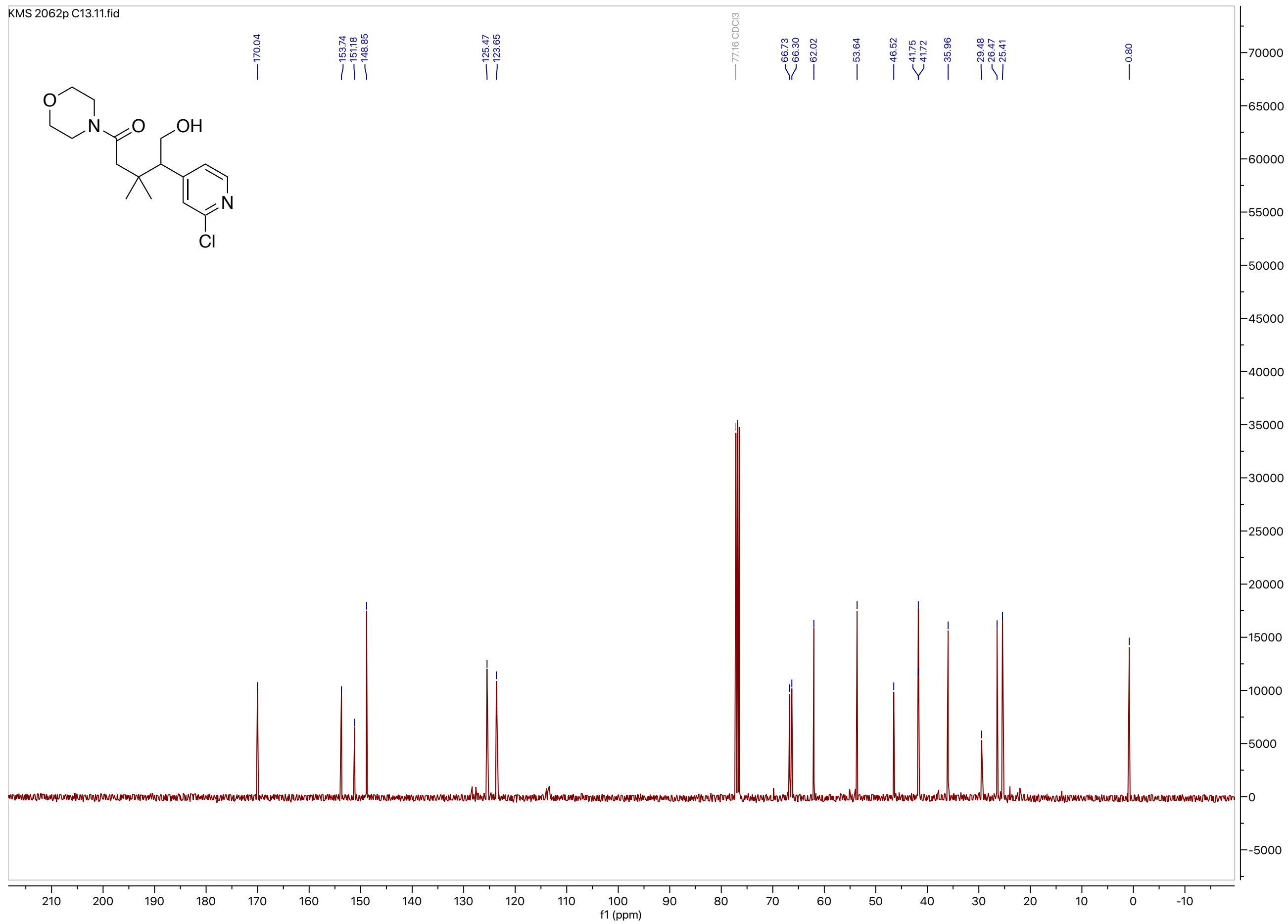
^{13}C NMR Spectrum of 12a ($CDCl_3$)



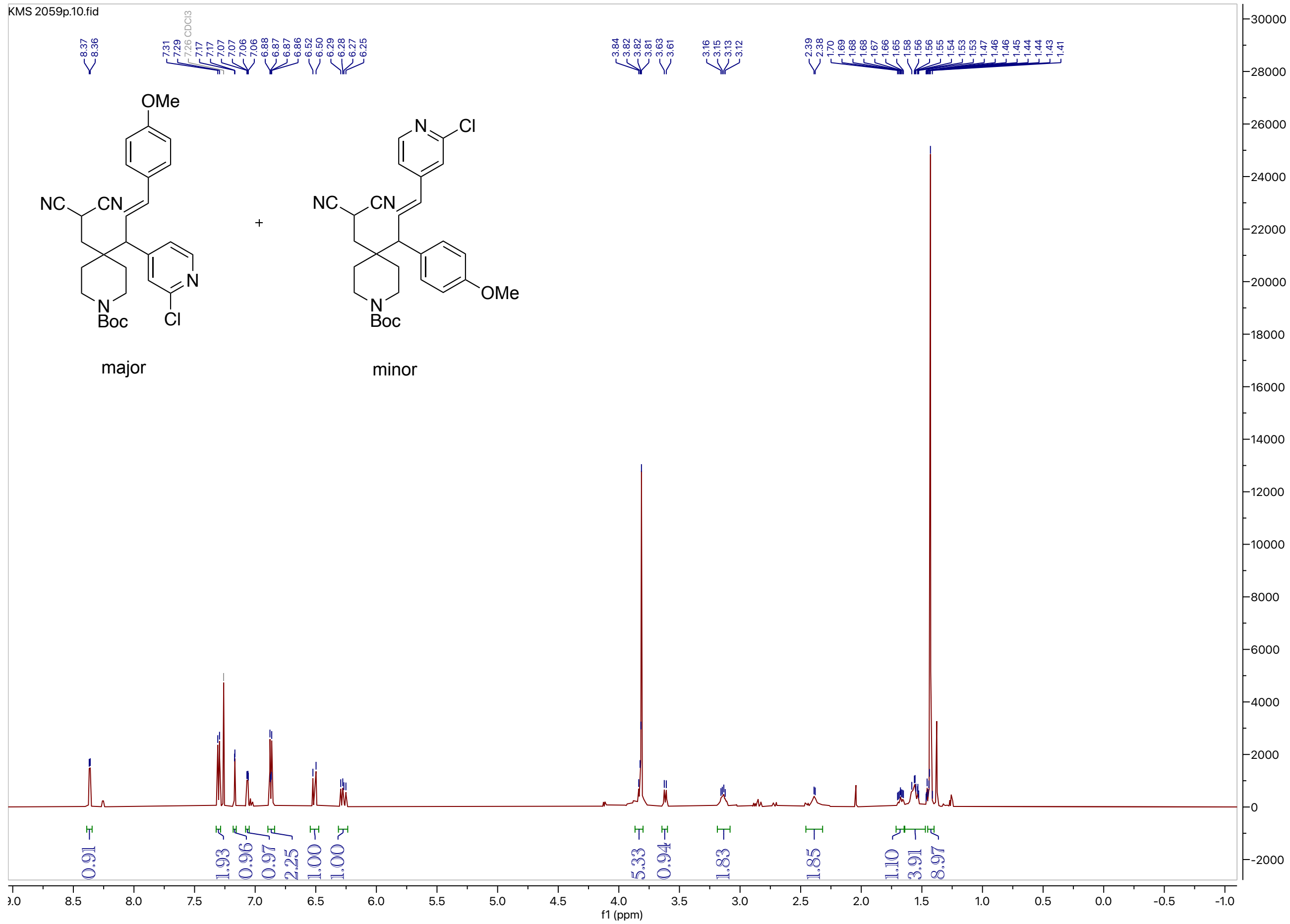
^{1}H NMR Spectrum of 13a ($CDCl_3$)



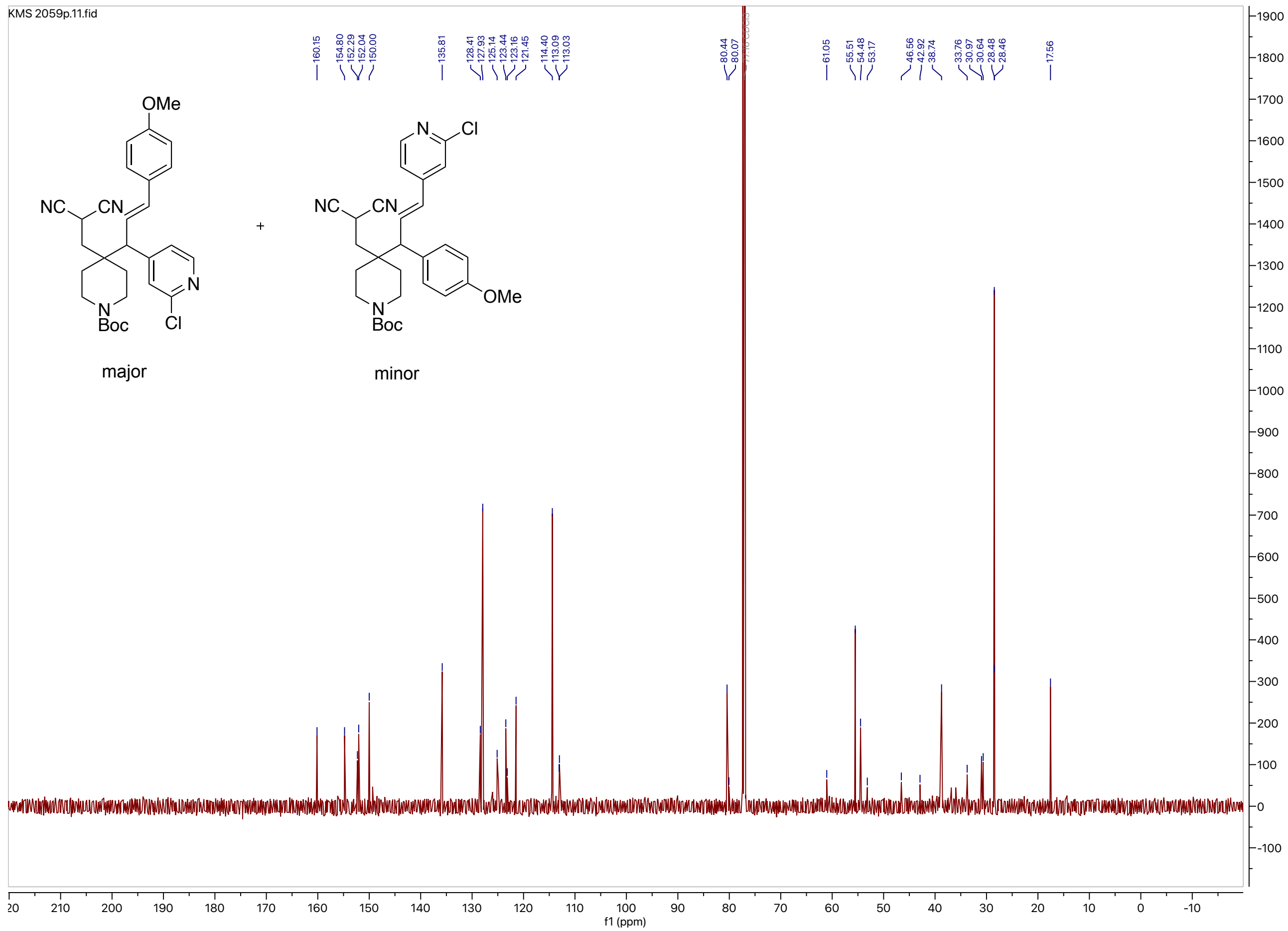
^{13}C NMR Spectrum of 13a ($CDCl_3$)



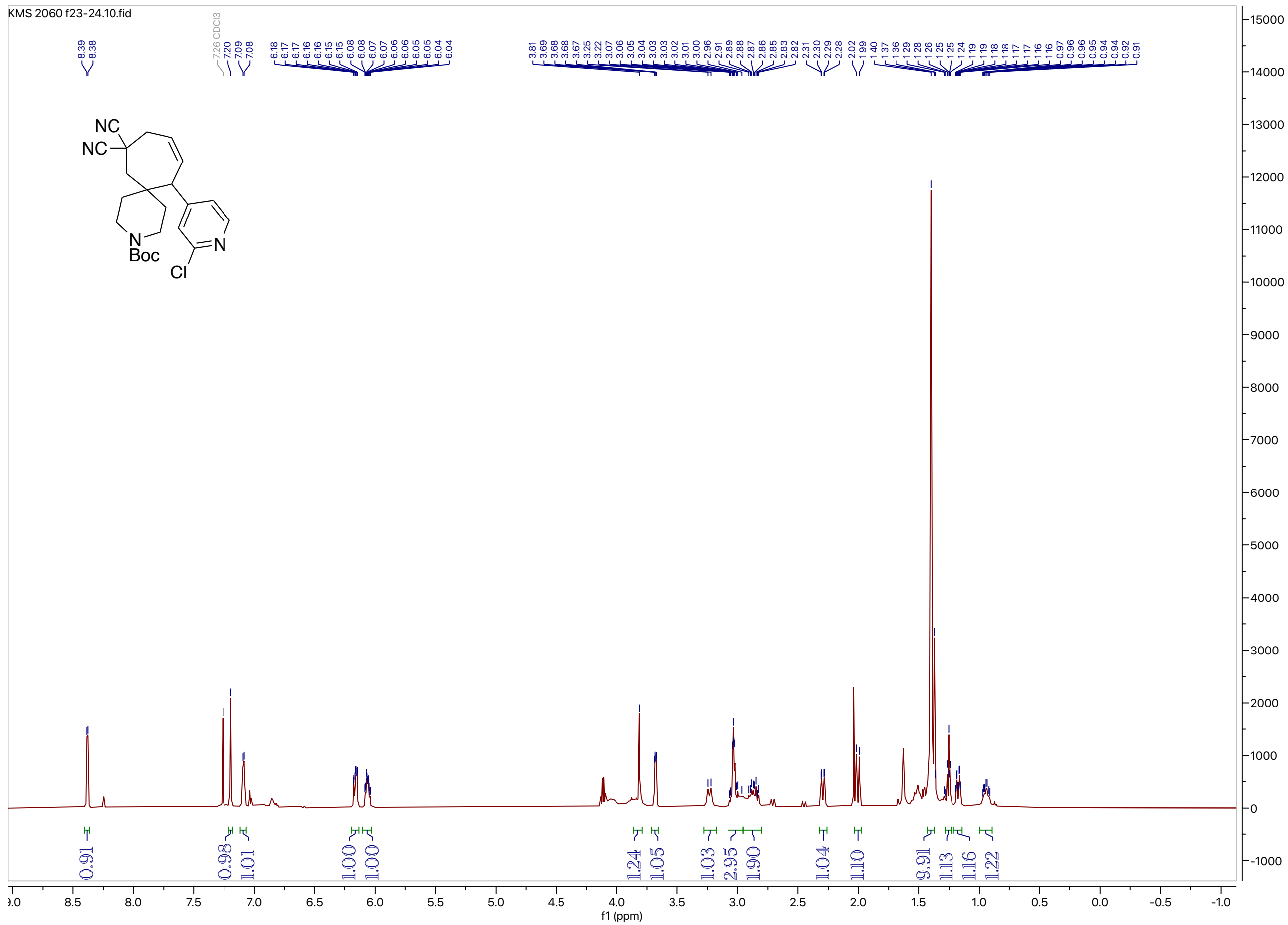
[1]H NMR Spectrum of 14a ($CDCl_3$)



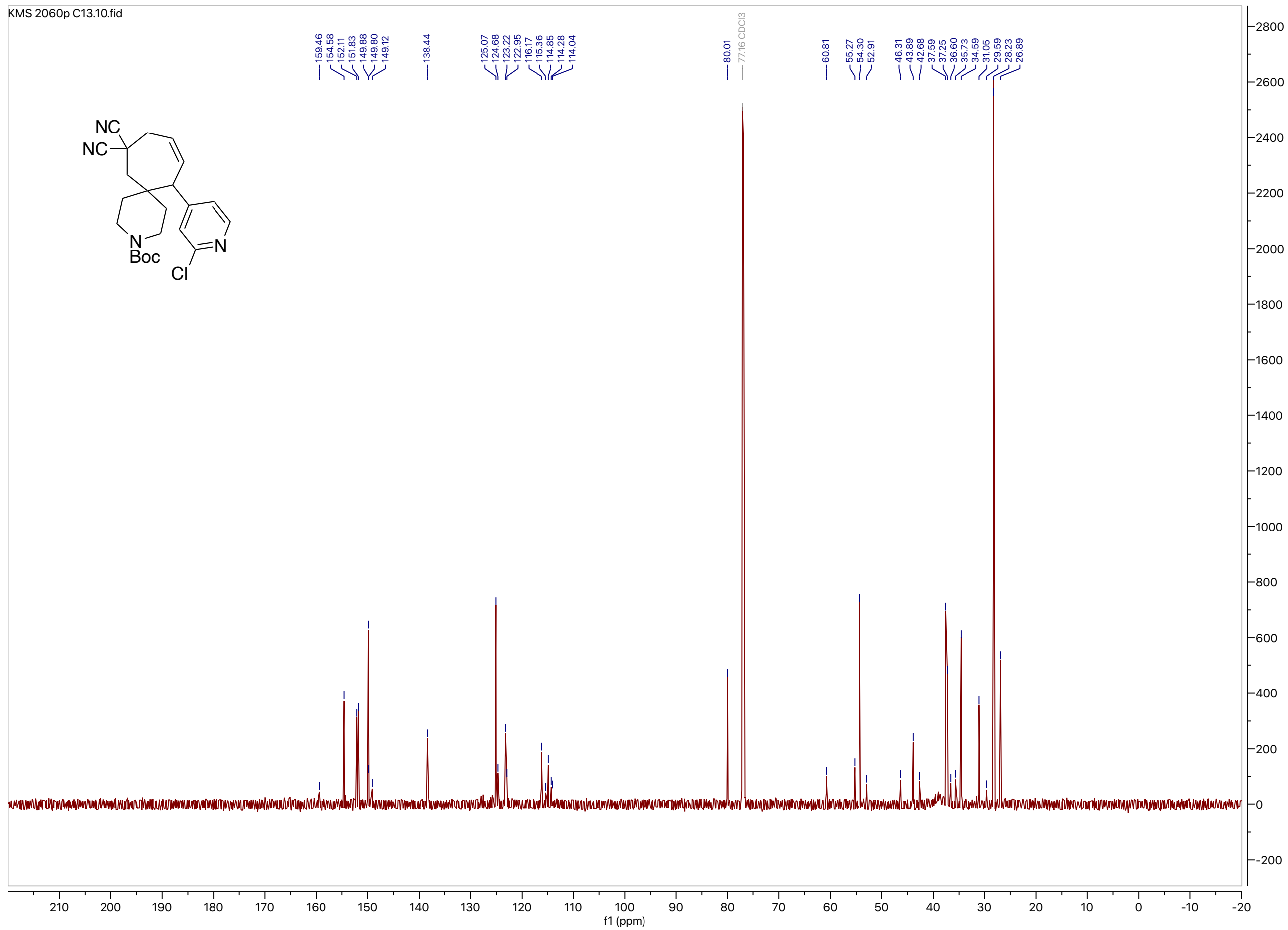
^{13}C NMR Spectrum of 14a ($CDCl_3$)



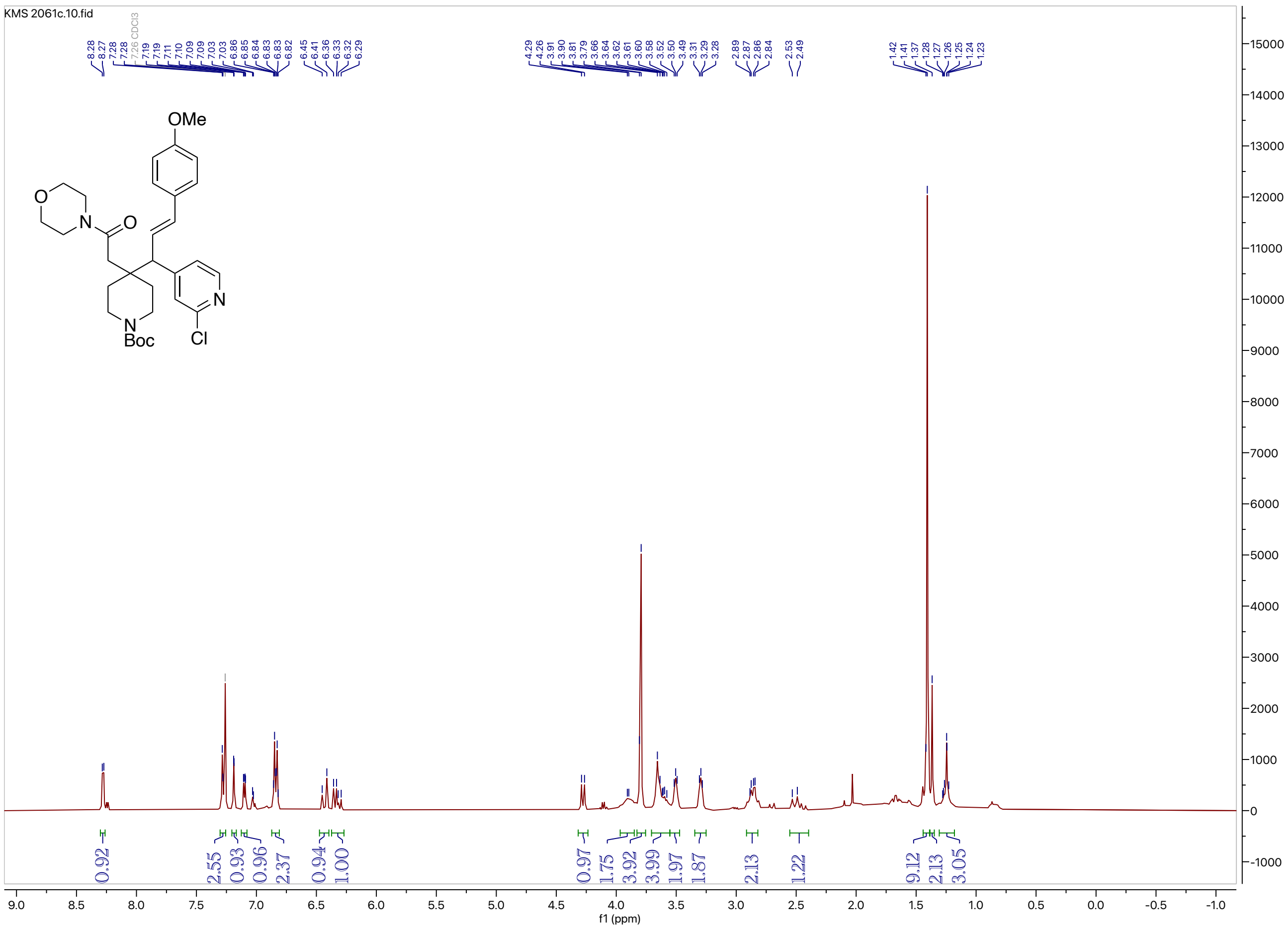
^{1}H NMR Spectrum of 15 ($CDCl_3$)



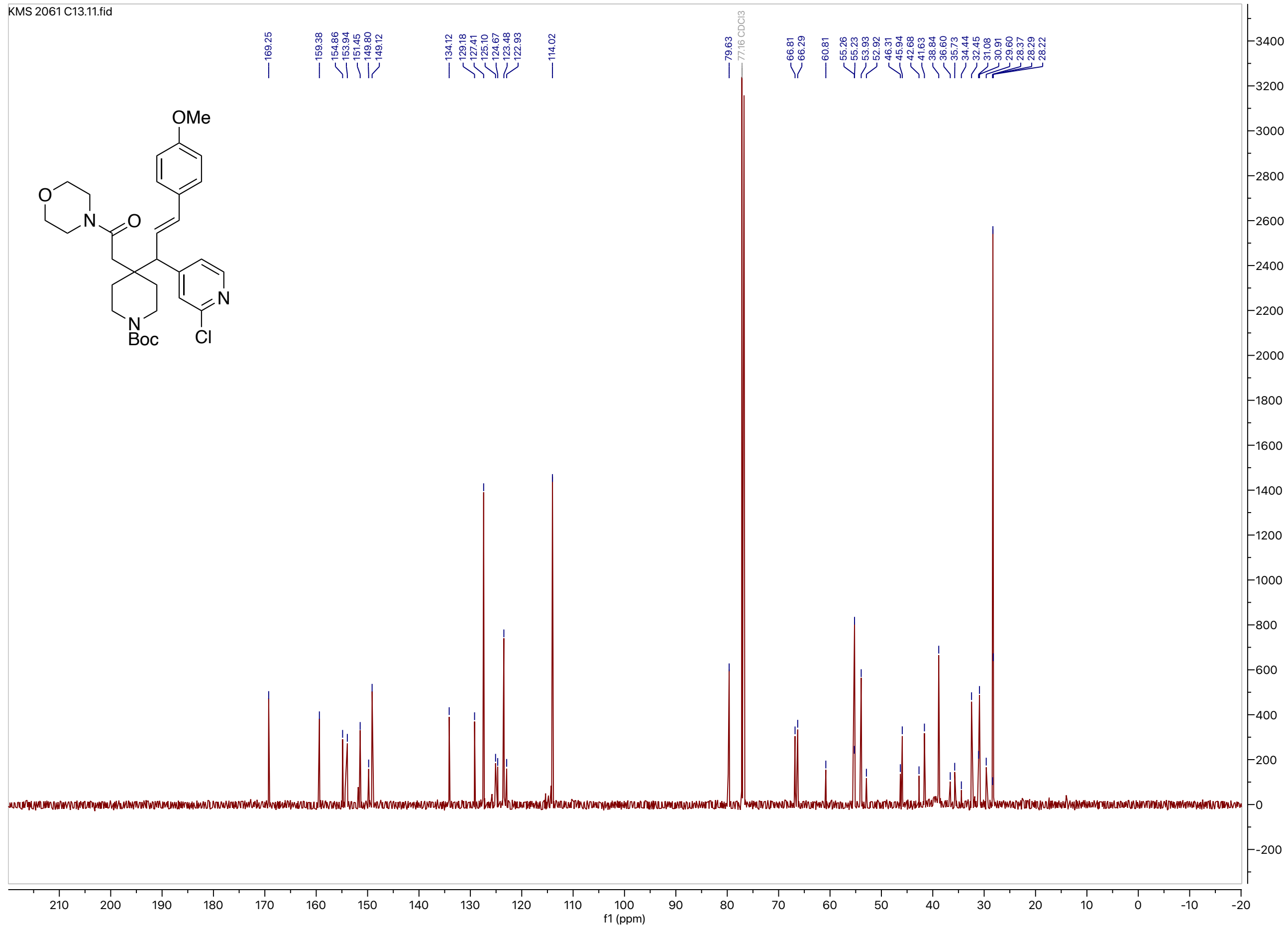
^{13}C NMR Spectrum of 15 ($CDCl_3$)



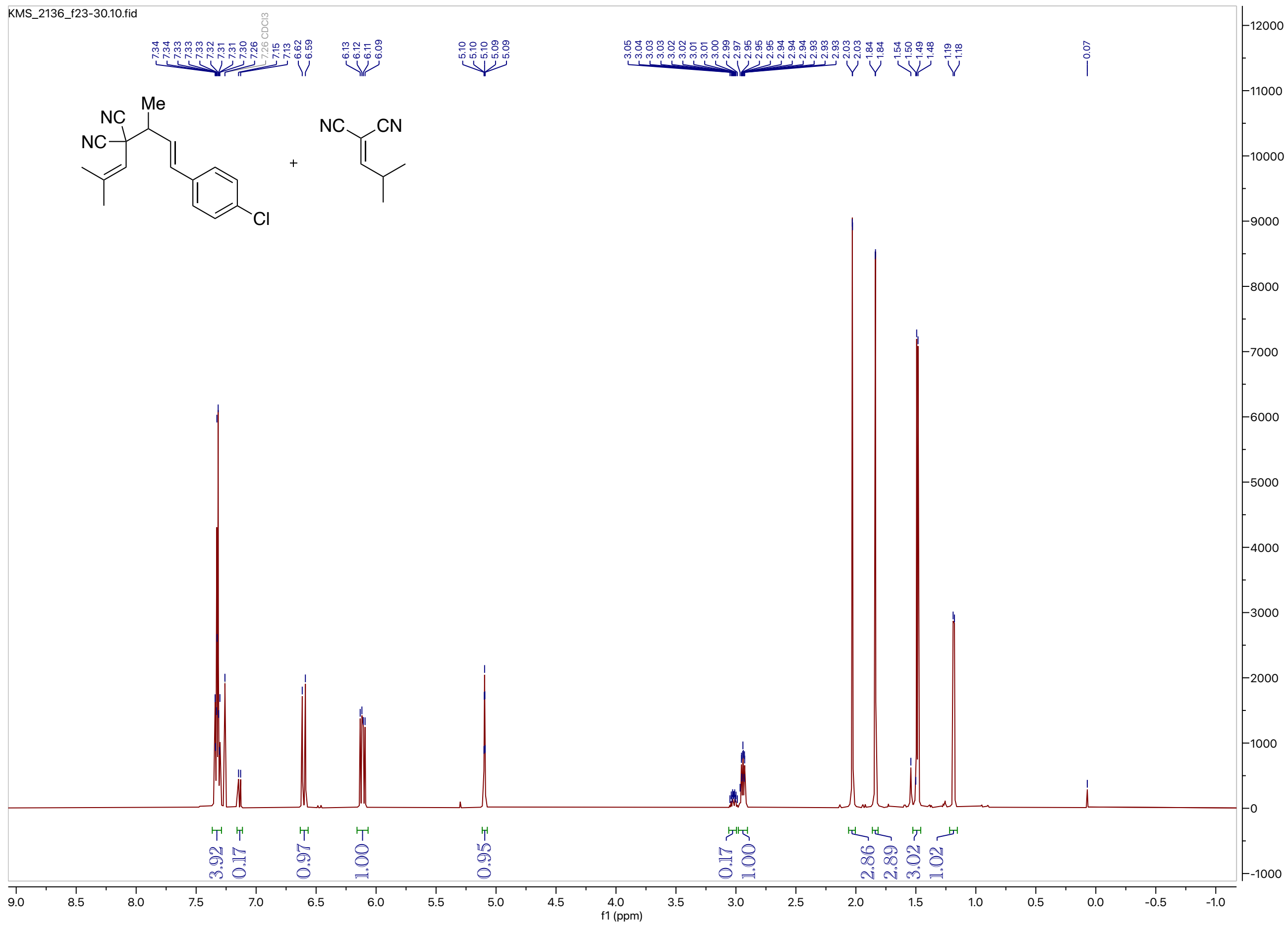
^{1}H NMR Spectrum of 16 ($CDCl_3$)



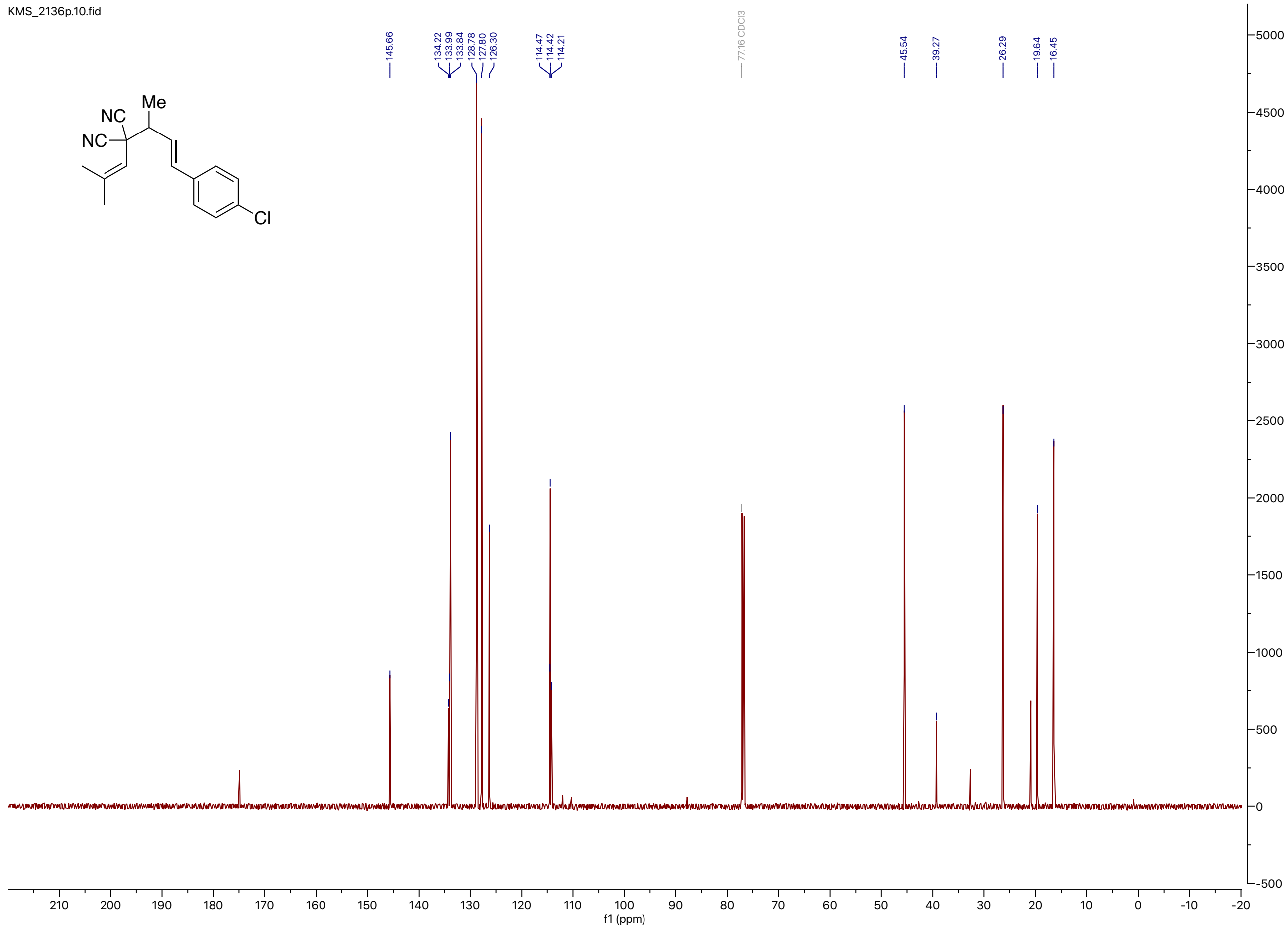
^{13}C NMR Spectrum of 16 ($CDCl_3$)



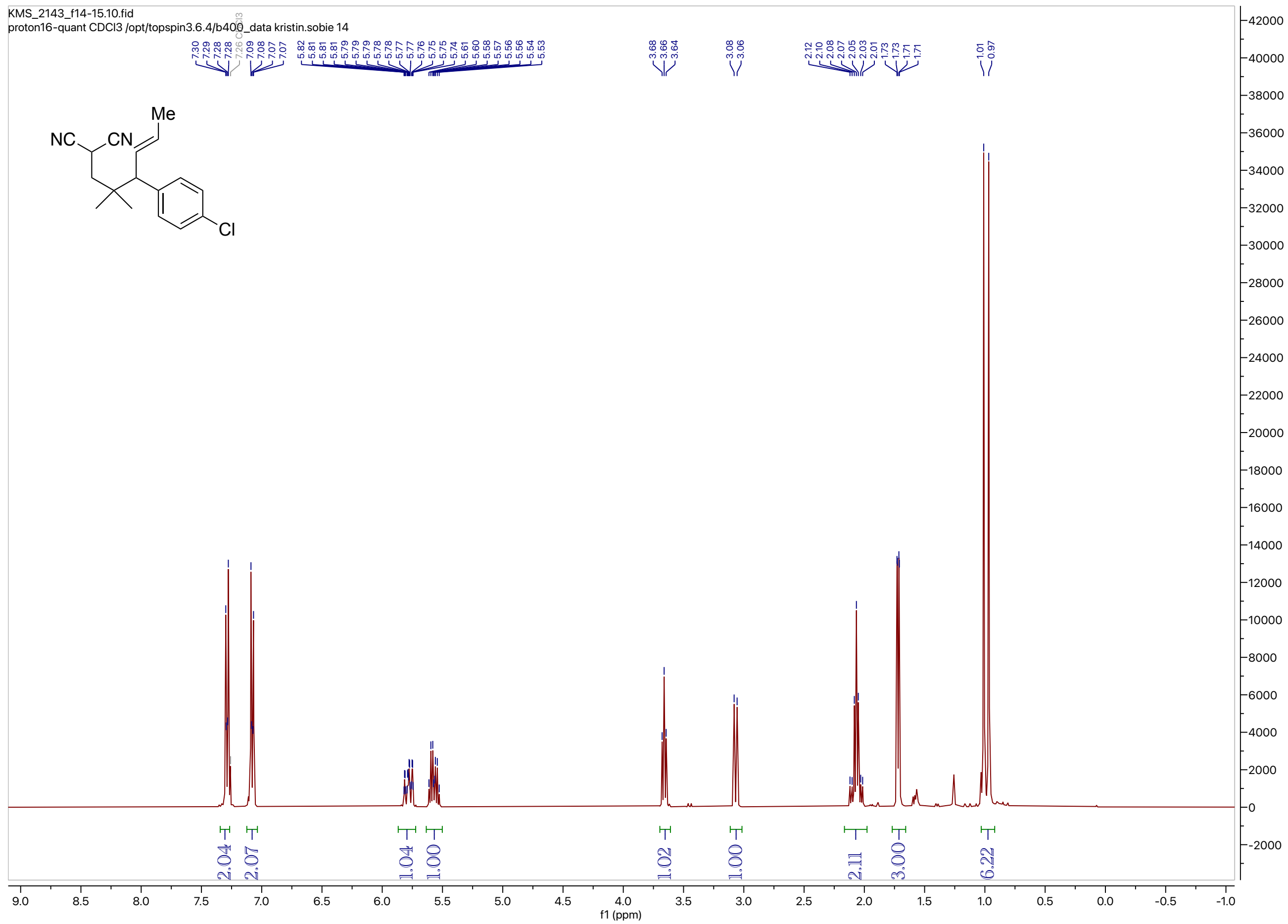
1H NMR Spectrum of 3a (CDCl3)



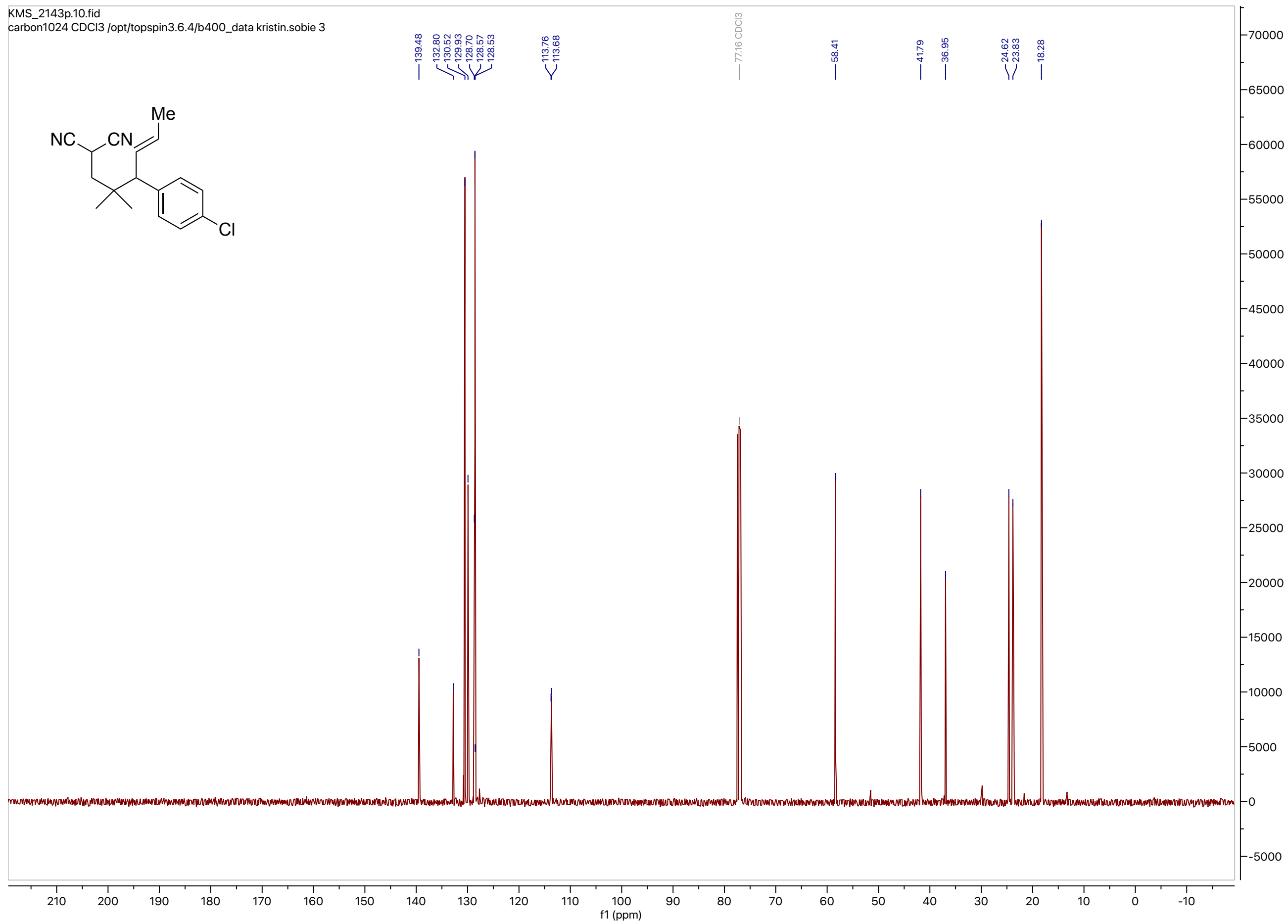
^{13}C NMR Spectrum of 3a ($CDCl_3$)



[1]H NMR Spectrum of 17 ($CDCl_3$)



^{13}C NMR Spectrum of 17 ($CDCl_3$)



S1. Computational method

Conformation generations on reactants and products were conducted with Confab algorithm in openbabel package[1]. All the following quantum calculations were performed with Gaussian 09 software package[2]. Semi-empirical method PM6[3] was used to find out low energy conformers in reactants and products. Structural optimizations on low energy conformers and transition states were carried out with M06-2x DFT method[4] and 6-31+G(d) basis set. At the same level of theory, frequencies were calculated to verify the nature of stationary points. Meanwhile, Intrinsic Reaction Coordinates (IRC) analysis[5-6] were conducted to make sure every transition state connects the correct reactant and product. To achieve more accurate energies, a larger basis set 6-311++G(2d,2p) and Grimme's D3 dispersion correction[7] were used for single-point energy calculation. In addition, a CPCM solvation model[8-10] (solvent=toluene) and an ultrafine integral grid were employed in all above DFT optimizations and single point calculations to increase accuracy. The Gibbs energies were calculated by the summation of high accuracy single-point energy and thermal correction to Gibbs energy in frequency calculation. The equilibrium constant K was estimated from equation $\Delta G = -RTlnK$, where $R = 8.314\, J/(mol \cdot K)$ and $T = 298.15K$, which gives the predicted reactant/product percentages.

S2. Gibbs energies and coordinates for optimized structures

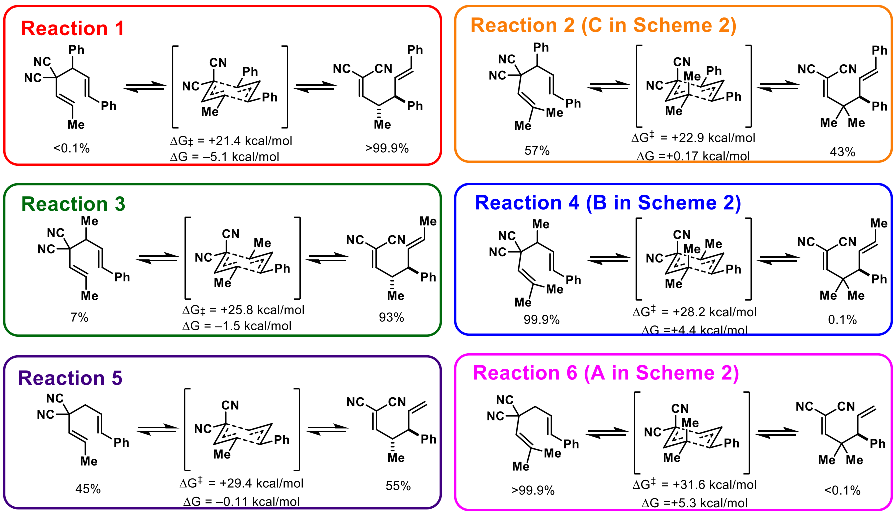
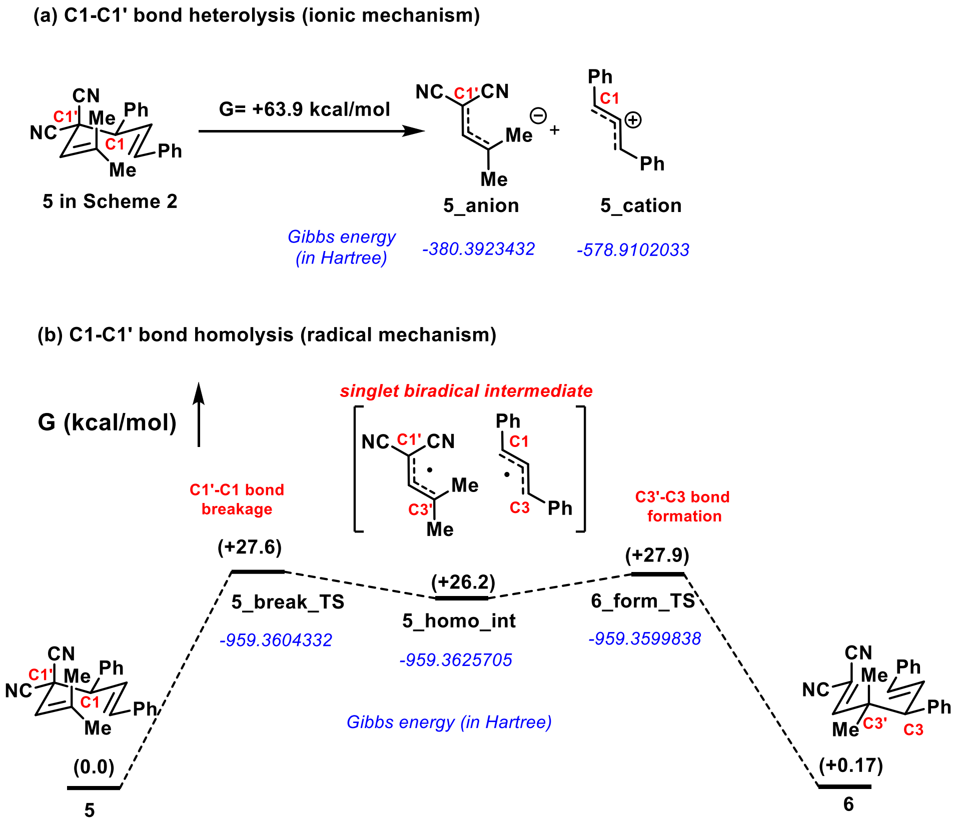


Table S1. Gibbs energies for all optimized structures (in Hartree)

	Gibbs energy (Hartree)		Gibbs energy (Hartree)		Gibbs energy (Hartree)
Reactant1	-920.1221448	**TS1**	-920.0880514	**Product1**	-920.1302051
Reactant2	-959.4043939	**TS2**	-959.3679133	**Product2**	-959.4041254
Reactant3	-728.4555666	**TS3**	-728.4144113	**Product3**	-728.4580014
Reactant4	-767.7384886	**TS4**	-767.6935549	**Product4**	-767.7314314
Reactant5	-689.1742425	**TS5**	-689.1273529	**Product5**	-689.1744173
Reactant6	-728.4561526	**TS6**	-728.4057471	**Product6**	-728.447721

S3. Details about the unfavorable ionic and radical mechanisms

Mechanistic study is based on **reaction C** in Scheme 2 (**substrate 5**). Scheme S1 shows the details of the two unfavorable mechanisms. The ionic mechanism is very unfavorable due to the unstability of dissociated cation and anion. In radical mechanism, to properly simulate the homolytic bond breakage and formation, a "broken-symmetry" guess was applied in an open-shell singlet system together with population calculation in every optimization step to verify the radical property (keyword: "guess=(mix,always) nosymm pop=always"). The radical pathway undergoes a very flat transition process. A biradical intermediate with gibbs energy of +26.2 kcal/mol can be produced through the C1-C1' bond homolytic cleavage with a barrier of +27.6 kcal/mol. The following C3-C3' bond formation process undergoes with a similar energy barrier of +27.9 kcal/mol. Overall, both ionic and radical mechanisms are unfavorable comparing to favorable cope mechanism with $\Delta G^{\ddagger}$ of +22.9 kcal/mol.



Scheme S1. Ionic and radical mechanisms

S4. Coordinates of minimums and transition states

Reactant1

C 1.17158 -1.40463 0.13747
C 0.54280 -0.10922 -0.54295
C 2.57841 -1.66102 -0.37991
C 3.68810 -1.61075 0.35324
C -0.85202 0.14565 -0.04161
H 0.49102 -0.36866 -1.60688
C -1.94004 -0.08220 -0.78597
H 2.61763 -1.86118 -1.45009
H -0.94635 0.51300 0.97956
C 5.06422 -1.81026 -0.20398
H 3.61746 -1.40334 1.42107
H 5.03643 -2.02384 -1.27570
H 5.56966 -2.63767 0.30513
H 5.67211 -0.91326 -0.04269
C 1.14882 -1.26368 1.60607
C 0.31700 -2.55728 -0.22506
N 1.13564 -1.12627 2.75289
N -0.33361 -3.44561 -0.57517
C -3.33975 0.13355 -0.37888
H -1.80583 -0.48491 -1.79112
C -3.69400 0.89475 0.74521
C -4.36110 -0.44164 -1.14658
C -5.69949 -0.28043 -0.79403
C -6.03808 0.46850 0.33141
C -5.02963 1.05765 1.09752
H -2.92352 1.37587 1.34099
H -4.09962 -1.02819 -2.02413
H -5.28662 1.65229 1.96922
H -6.47602 -0.73903 -1.39902
H -7.07995 0.59930 0.60810
C 1.47379 1.07901 -0.38844
C 2.26093 1.47466 -1.47407
C 1.58594 1.78048 0.81685
C 3.14781 2.54347 -1.36174
H 2.17892 0.93969 -2.41760
C 2.47724 2.84647 0.93334
H 0.98427 1.50030 1.67680
C 3.26099 3.23063 -0.15382
H 3.74856 2.83822 -2.21708
H 2.55473 3.37894 1.87657
H 3.95177 4.06337 -0.06156

TS1

C -2.67888 2.61830 -0.03875
C -1.42235 1.95001 0.43267
C -0.17655 2.35793 0.02807
C 1.02927 1.77860 0.49162
C 1.03209 1.03208 1.71378
C 2.28570 2.30119 0.05133
N 3.29693 2.70462 -0.34949
N 0.98028 0.39976 2.68513
C -1.38193 -0.09479 -0.86943
C -2.70843 -0.59039 -0.47957
C -0.19309 -0.66134 -0.43281
C 1.04385 -0.19371 -0.87340
C -2.94376 -1.18025 0.77288
C -4.21176 -1.64277 1.10745
C -5.26771 -1.52139 0.20052
C -5.04870 -0.92664 -1.04120
C -3.77976 -0.45843 -1.37475
H -1.50142 1.32848 1.32372
H -1.35330 0.51874 -1.76840
H -3.50311 1.90337 -0.12693
H -2.99241 3.38081 0.68444
H -0.22814 -1.41929 0.34630
H 1.04439 0.47979 -1.72968
H -2.13592 -1.25708 1.49699
H -4.38070 -2.09168 2.08163
H -6.25697 -1.88183 0.46588
H -5.86559 -0.82349 -1.74909
H -3.61018 0.00976 -2.34165
H -2.53215 3.10813 -1.00662
H -0.08718 3.06019 -0.79941
C 2.33668 -0.80448 -0.55987
C 3.45191 -0.46139 -1.34182
C 2.50938 -1.70793 0.50368
C 4.70239 -1.01252 -1.07971
H 3.33145 0.24595 -2.15830
C 3.76049 -2.25384 0.76592
H 1.67049 -1.97467 1.13886
C 4.85968 -1.91064 -0.02488
H 5.55338 -0.73663 -1.69480
H 3.88087 -2.94688 1.59301
H 5.83493 -2.34005 0.18424

Product1

C -1.43751 1.68260 -0.02590
C -1.33343 0.22463 -0.59642
C -0.28220 2.48382 -0.53192
H -1.37971 1.61761 1.06826
C -2.75006 2.36081 -0.43307
C -2.57270 -0.57563 -0.23549
H -2.86436 2.35454 -1.52358
H -2.77514 3.39903 -0.08942
H -3.60339 1.83402 0.00054
C 0.86701 2.70944 0.13500
H -0.36642 2.89986 -1.53588
C 1.09189 2.17080 1.45185
C 1.93732 3.47329 -0.45080
N 1.25374 1.72266 2.50651
N 2.78955 4.09125 -0.93067
C -3.42142 -1.05403 -1.23582
C -2.89121 -0.84104 1.10178
C -4.56685 -1.78263 -0.91226
H -3.18462 -0.85421 -2.27849
C -4.87669 -2.04055 0.42143
H -5.21515 -2.14737 -1.70371
C -4.03413 -1.56703 1.42860
H -2.24587 -0.47718 1.89902
H -4.26713 -1.76410 2.47097
H -5.76731 -2.60698 0.67649
C -0.08142 -0.45383 -0.10551
H -1.28423 0.30502 -1.69132
C 0.97268 -0.72554 -0.88272
H -0.05961 -0.70789 0.95507
H 0.91065 -0.48725 -1.94627
C 2.24008 -1.33961 -0.44521
C 3.09479 -1.89603 -1.40650
C 2.63253 -1.37689 0.90160
C 4.29606 -2.49674 -1.03569
H 2.80862 -1.86116 -2.45524
C 3.83273 -1.97527 1.27273
H 2.00878 -0.91546 1.66241
C 4.66771 -2.54137 0.30712
H 4.94196 -2.92663 -1.79570
H 4.12341 -1.99015 2.31911
H 5.60535 -3.00428 0.60003

Reactant2

C -1.47847 0.93400 -0.02200
C -0.71161 -0.34627 -0.55031
C -0.75845 2.20499 -0.48262
C -1.11761 3.45846 -0.18540
C 0.69082 -0.37233 -0.00479
H -0.66331 -0.20145 -1.63633
C 1.77401 -0.34966 -0.78951
H 0.11669 2.01769 -1.09912
H 0.79232 -0.42919 1.07844
C -0.31279 4.61764 -0.70897
C -2.29586 3.84104 0.66776
H 0.55033 4.28724 -1.29173
H 0.04300 5.23700 0.12257
H -0.93847 5.25809 -1.34128
C -2.85533 0.91355 -0.56207
C -1.54354 0.88797 1.45529
N -3.91151 0.91136 -1.03132
N -1.54127 0.85967 2.61075
C 3.18101 -0.39176 -0.35258
H 1.62867 -0.30769 -1.87031
C 4.18175 -0.52873 -1.32386
C 3.56510 -0.29476 0.99385
C 4.90770 -0.34469 1.35260
C 5.89525 -0.48924 0.37499
C 5.52768 -0.57965 -0.96594
H 3.89866 -0.60001 -2.37150
H 2.81400 -0.16995 1.76851
H 6.28698 -0.68904 -1.73465
H 5.18678 -0.26632 2.39925
H 6.94264 -0.52658 0.65904
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C -2.25996 -2.18436 -1.29827
C -1.45620 -2.25660 0.97187
C -2.99619 -3.34699 -1.07955
H -2.29089 -1.70181 -2.27258
C -2.19422 -3.41817 1.19268
H -0.85900 -1.84816 1.78205
C -2.96592 -3.96629 0.16889
H -3.59268 -3.76631 -1.88420
H -2.16276 -3.89557 2.16747
H -3.53859 -4.87234 0.34287
H -2.93750 3.00461 0.94933
H -2.91246 4.57486 0.13652
H -1.94337 4.32150 1.58855

TS2

C -2.67736 2.46089 0.07628
C -1.38686 1.83385 0.52649
C -0.21745 2.22275 -0.09720
C 1.10932 1.85395 0.21068
C 1.54398 1.34142 1.47277
C 2.16075 2.34937 -0.62462
N 3.00053 2.71963 -1.33540
N 1.93376 0.91669 2.48038
C -1.32221 -0.23952 -0.88253
C -2.66271 -0.72123 -0.55091
C -0.13770 -0.79968 -0.41159
C 1.09449 -0.39552 -0.90535
C -2.92814 -1.52103 0.57478
C -4.21965 -1.96249 0.84061
C -5.27270 -1.61730 -0.00970
C -5.02508 -0.82370 -1.12960
C -3.73348 -0.37746 -1.39332
C -1.44258 1.16863 1.87510
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H -2.94271 3.28066 0.75760
H -0.17379 -1.51903 0.40294
H 1.09477 0.20738 -1.81256
H -2.12454 -1.79599 1.25187
H -4.40703 -2.57832 1.71513
H -6.27921 -1.96604 0.20064
H -5.83735 -0.55136 -1.79671
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H -0.31938 2.79605 -1.01756
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C 3.50377 -0.68642 -1.33990
C 2.57343 -1.70925 0.64526
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H 3.37525 -0.08590 -2.23670
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H 1.73780 -1.89696 1.31265
C 4.92470 -1.95080 0.14364
H 5.60897 -0.97660 -1.65431
H 3.95689 -2.79190 1.87713
H 5.90463 -2.34005 0.40342
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H -1.27084 1.91029 2.66649
H -0.69804 0.37982 1.99848

Product2

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C -0.46712 1.27320 -2.54063
C -1.96196 -1.31487 -0.02443
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N 1.68019 3.03039 -0.45168
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C -3.88201 -2.59849 1.58336
H -4.26928 -3.82339 -0.14701
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H 5.89608 -2.52324 -0.49361
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H -3.59133 0.26072 -1.43271
H -2.75698 -0.18963 -2.93020
H -3.15293 1.51000 -2.61725

Reactant3

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C 2.76318 0.00077 0.99167
C 4.78845 -0.17418 -0.91602
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C 5.09849 0.19321 0.39201
H 5.57205 -0.24114 -1.66500
C 4.07933 0.28209 1.34318
H 1.98113 0.09318 1.74006
H 6.12451 0.41581 0.66926
H 4.31125 0.57928 2.36175
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C 0.02011 -0.93441 0.06591
H 0.90954 -0.76553 -1.81721
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H 0.13768 -0.91218 1.15071
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C -1.26614 3.59888 -0.58154
H -1.83515 2.31442 1.12873
H -1.17171 3.50456 -1.66647
H -0.29854 3.90918 -0.17274
H -1.98036 4.39935 -0.36108
H -1.11420 -3.41470 -0.26390
H -2.81082 -2.90021 -0.27695
H -1.81670 -2.66653 1.17847

TS3

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C 0.15243 1.50117 0.54483
C 1.44518 1.55542 0.07445
C 2.41103 0.55925 0.33987
C 2.27440 -0.27452 1.50107
C 3.73923 0.70677 -0.18046
N 4.79726 0.80116 -0.64540
N 2.11252 -0.95969 2.42238
C -0.55296 -0.16952 -0.90054
C -1.95257 -0.26217 -0.45261
C 0.39205 -1.16413 -0.64762
C 1.69018 -1.08959 -1.13078
C -2.30656 -0.89523 0.74913
C -3.63854 -0.96720 1.14321
C -4.63976 -0.40575 0.34699
C -4.29874 0.23462 -0.84348
C -2.96399 0.31099 -1.23586
H -0.06049 0.84548 1.38827
H -0.38157 0.48186 -1.75606
H -1.85613 2.24799 0.29177
H -0.75183 3.36027 1.09833
H 0.15828 -1.94677 0.07343
H 1.89348 -0.38779 -1.93904
H -1.53442 -1.31633 1.38894
H -3.89703 -1.45584 2.07787
H -5.67843 -0.46192 0.65838
H -5.07050 0.67795 -1.46554
H -2.69844 0.81566 -2.16198
H -0.62529 3.11713 -0.65336
H 1.70654 2.29262 -0.68316
C 2.67969 -2.20039 -0.94396
H 2.49626 -2.74033 -0.01010
H 3.70961 -1.83134 -0.94937
H 2.58845 -2.91279 -1.77314

Product3

C -0.24821 -1.19681 0.02151
C 0.47323 0.05539 -0.58812
C -1.65146 -1.23603 -0.48820
H -0.26296 -1.07645 1.11240
C 0.46429 -2.50364 -0.34422
C 1.95112 0.03603 -0.24083
H 0.56362 -2.59589 -1.43235
H -0.09309 -3.36906 0.02603
H 1.46626 -2.52764 0.09082
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H -1.80450 -1.64021 -1.48898
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C 2.37533 0.11951 1.09095
C 4.27429 -0.10205 -0.93221
H 2.59807 -0.14060 -2.28432
C 4.68646 -0.02047 0.39623
H 5.00926 -0.18774 -1.72738
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H 1.64314 0.20481 1.89154
H 4.04305 0.15530 2.44662
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H 0.37836 -0.01298 -1.68102
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H -0.05125 1.58933 0.92709
H -1.06608 1.85055 -1.94982
C -1.62477 3.36463 -0.43088
H -1.43393 3.54644 0.63070
H -2.70810 3.28258 -0.57629
H -1.29081 4.24008 -0.99900

Reactant4

C 3.85564 0.02525 -1.27324
C 2.83896 -0.15030 -0.32500
C 3.13353 0.09773 1.02452
C 5.13545 0.42099 -0.88879
H 3.63922 -0.15617 -2.32351
C 5.41762 0.65455 0.45562
H 5.90981 0.54739 -1.63969
C 4.41001 0.49347 1.40975
H 2.35920 -0.00654 1.77924
H 6.41247 0.96550 0.76011
H 4.61946 0.68357 2.45834
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C 0.49405 -1.00207 -0.01888
H 1.36268 -0.56115 -1.86751
C -0.82502 -1.46861 -0.56855
H 0.60571 -1.06779 1.06445
C -1.98926 -0.54294 -0.04943
C -1.07117 -2.93910 -0.22009
H -0.82860 -1.34202 -1.65828
C -3.26682 -1.03951 -0.60690
C -2.04863 -0.64096 1.42674
N -4.24776 -1.42006 -1.08534
N -2.04723 -0.71329 2.58028
C -1.76503 0.90691 -0.48701
C -2.56667 1.94098 -0.21024
H -0.86193 1.05516 -1.07305
C -2.22574 3.31677 -0.71695
C -3.83551 1.86075 0.59343
H -1.29723 3.32237 -1.29277
H -2.12085 4.01419 0.12217
H -3.03403 3.69788 -1.35178
H -0.26911 -3.54932 -0.64256
H -2.02401 -3.29521 -0.62310
H -1.07367 -3.08869 0.86527
H -4.07463 0.86074 0.95864
H -4.67870 2.20740 -0.01565
H -3.76723 2.52936 1.45955

TS4

C -0.83930 2.56080 -0.06325
C 0.13275 1.50952 0.40367
C 1.36514 1.44570 -0.22394
C 2.45991 0.61317 0.08100
C 2.70043 0.01028 1.35936
C 3.62036 0.68770 -0.75871
N 4.53868 0.71209 -1.46737
N 2.92997 -0.50774 2.37177
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C -1.99000 -0.42285 -0.47799
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C 1.63515 -1.43086 -0.92994
C -2.47112 -1.06155 0.67818
C -3.82645 -1.03691 0.98895
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C -4.26803 0.26047 -0.99766
C -2.91093 0.23957 -1.30653
C -0.12785 0.99031 1.79437
H -0.35117 0.07410 -1.79553
H -1.87296 2.21153 0.03026
H -0.74446 3.45257 0.57049
H 0.12789 -1.99255 0.45724
H 1.82548 -0.91222 -1.86884
H -1.78449 -1.57666 1.34360
H -4.18006 -1.53468 1.88692
H -5.78791 -0.36176 0.39884
H -4.96349 0.77388 -1.65478
H -2.55181 0.73866 -2.20380
H -0.65989 2.85969 -1.10066
H 1.46753 1.99170 -1.16072
C 2.64487 -2.45549 -0.51543
H 2.47820 -2.78696 0.51340
H 3.66603 -2.07109 -0.60446
H 2.57311 -3.32892 -1.17575
H -1.20482 0.95614 1.98405
H 0.31675 1.66984 2.53315
H 0.28544 -0.00405 1.97135

Product4

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C -0.83663 -0.27915 -0.07441
C 1.40663 -0.62656 0.99118
C -0.28303 -2.48072 1.08216
C -0.53145 -0.43701 2.49131
C -0.56625 1.21568 -0.17514
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H -0.00760 -0.97270 3.29068
H -1.60346 -0.60906 2.62529
C 2.27190 -1.03929 0.04106
H 1.82950 0.03689 1.74522
C 1.91470 -1.87152 -1.07918
C 3.64541 -0.60454 0.07528
N 1.64103 -2.51946 -1.99823
N 4.74711 -0.25248 0.10771
C 0.37944 1.68504 -1.09444
C -1.23365 2.15252 0.62381
C 0.66753 3.04490 -1.20232
H 0.89144 0.97654 -1.74276
C 0.00547 3.96475 -0.39098
H 1.40500 3.38351 -1.92418
C -0.94942 3.51347 0.51963
H -1.98859 1.82532 1.33374
H -1.47942 4.22234 1.14927
H 0.22531 5.02499 -0.47292
C -2.31078 -0.59431 -0.04051
H -0.43491 -0.74098 -0.98537
C -2.91480 -1.38437 -0.93059
H -2.90909 -0.13922 0.74992
H -2.31394 -1.83678 -1.72224
C -4.37976 -1.70634 -0.93444
H -4.89788 -1.21025 -0.10854
H -4.54196 -2.78651 -0.84559
H -4.84607 -1.39025 -1.87427
H -0.11046 -2.89947 0.08729
H -1.31660 -2.70389 1.36075
H 0.38179 -2.98165 1.79320

Reactant5

C -3.68924 -1.28959 -0.29099
C -2.69061 -0.30678 -0.29855
C -3.06294 1.02741 -0.07417
C -5.02553 -0.95255 -0.08453
H -3.41252 -2.32888 -0.45211
C -5.38376 0.37768 0.12524
H -5.78455 -1.72927 -0.08507
C -4.39611 1.36546 0.13231
H -2.30603 1.80598 -0.04465
H -6.42330 0.64464 0.29030
H -4.66606 2.40259 0.30833
C -1.29444 -0.71536 -0.53511
C -0.26575 0.09167 -0.82036
H -1.11037 -1.78968 -0.48222
C 1.13037 -0.41177 -1.02936
H -0.40952 1.16812 -0.90539
C 2.10451 -0.04937 0.14433
H 1.57895 0.01408 -1.93341
H 1.14241 -1.50248 -1.12321
C 2.12395 1.41695 0.31542
C 1.59075 -0.66050 1.39119
N 2.13643 2.56868 0.40164
N 1.19648 -1.19526 2.33634
C 3.49640 -0.59869 -0.13729
C 4.59851 0.13318 -0.28674
H 3.52169 -1.68326 -0.23328
C 5.94607 -0.44276 -0.59933
H 4.54338 1.21636 -0.17818
H 5.90713 -1.53149 -0.68837
H 6.66343 -0.18191 0.18603
H 6.33187 -0.02863 -1.53693

TS5

C -0.43245 -1.96033 -1.52675
C 0.45363 -0.83828 -1.06026
C 1.74825 -1.07901 -0.63855
C 2.63607 -0.05093 -0.26346
C 2.46434 1.26601 -0.81958
C 3.96576 -0.38624 0.16972
N 5.01882 -0.67178 0.55930
N 2.26766 2.31779 -1.26388
C -0.41539 -0.27877 0.93827
C -1.80962 -0.01690 0.53487
C 0.45983 0.73991 1.33621
C 1.74607 0.45604 1.75346
C -2.17289 1.14717 -0.15941
C -3.49692 1.36655 -0.52565
C -4.47984 0.42620 -0.20843
C -4.12843 -0.73858 0.47237
C -2.80149 -0.96015 0.83498
H 0.22106 0.15162 -1.45078
H -0.23059 -1.27579 1.33617
H -1.49017 -1.70020 -1.43469
H -0.23856 -2.17026 -2.58482
H 0.19455 1.77469 1.12934
H 1.99851 -0.53840 2.11194
H -1.41398 1.87765 -0.43061
H -3.76279 2.27005 -1.06615
H -5.51214 0.59921 -0.49715
H -4.88576 -1.47674 0.71882
H -2.52736 -1.87153 1.36145
H -0.24536 -2.87789 -0.95932
H 2.04486 -2.09445 -0.38096
H 2.42076 1.25384 2.05215

Product5

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C 0.42017 -0.75020 -0.08264
C -1.86062 -0.36852 0.83397
H -0.45436 1.16983 0.42366
C 0.06839 0.18233 2.27447
C 1.86577 -0.28427 -0.06264
H 0.12348 -0.83177 2.68708
H -0.58112 0.78294 2.91747
H 1.07224 0.61441 2.29696
C -2.92492 0.23920 0.27418
H -2.03253 -1.32670 1.32491
C -2.80084 1.49147 -0.42738
C -4.23752 -0.35009 0.32633
N -2.68285 2.49286 -0.99494
N -5.28865 -0.83086 0.37510
C 2.87209 -1.12389 0.42006
C 2.21619 0.99041 -0.52371
C 4.20232 -0.70329 0.44452
H 2.61247 -2.11668 0.78074
C 4.54131 0.56781 -0.01489
H 4.97165 -1.36991 0.82330
C 3.54304 1.41415 -0.49973
H 1.45026 1.66270 -0.90513
H 3.79799 2.40620 -0.86092
H 5.57557 0.89807 0.00324
C -0.12090 -0.78155 -1.49136
H 0.38416 -1.77065 0.32406
C -0.56807 -1.88051 -2.09702
H -0.13758 0.17239 -2.02157
H -0.56490 -2.84599 -1.59482
H -0.94894 -1.85289 -3.11341

Reactant6

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C 0.72324 -0.51707 1.26478
C 3.18103 -0.52029 0.65608
C 4.32492 -0.28721 0.00393
C -0.65721 -0.00723 0.98384
H 1.06105 -0.21196 2.26198
C -1.64045 -0.78600 0.51785
H 3.17645 -1.14005 1.54979
H -0.83092 1.05077 1.17728
C 5.61463 -0.88288 0.50069
C 4.45014 0.54634 -1.24161
H 5.46667 -1.49401 1.39423
H 6.33276 -0.08863 0.73469
H 6.06813 -1.50609 -0.27868
C 1.43619 -0.44704 -1.09669
C 1.78439 1.49073 0.28992
N 1.15560 -0.85397 -2.14128
N 1.77115 2.64429 0.35934
C -3.01760 -0.36302 0.20611
H -1.43273 -1.84576 0.36151
C -3.38428 0.98495 0.07392
C -4.00223 -1.34410 0.02925
C -5.32151 -0.99340 -0.25088
C -5.67566 0.34948 -0.36666
C -4.70050 1.33666 -0.20625
H -2.63455 1.76469 0.17391
H -3.72855 -2.39295 0.11689
H -4.96610 2.38471 -0.30908
H -6.07045 -1.76906 -0.38084
H -6.70169 0.62727 -0.58869
H 0.75599 -1.61041 1.21370
H 3.52325 1.03089 -1.55276
H 4.79720 -0.08181 -2.07077
H 5.20502 1.32622 -1.08978

TS6

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C 0.42604 -0.55474 -1.20050
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C 2.67467 -0.12669 -0.15976
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C 3.84124 -0.77306 0.37891
N 4.75661 -1.30899 0.84638
N 3.07317 2.36180 -0.78572
C -0.46713 -0.32765 0.95889
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C 0.39669 0.65414 1.46980
C 1.65552 0.32509 1.91736
C -2.38995 1.18767 0.35113
C -3.73767 1.36230 0.05458
C -4.60194 0.26570 0.02700
C -4.10787 -1.00977 0.29872
C -2.75840 -1.18467 0.59219
C 0.14296 0.82456 -1.74238
H -0.22783 -1.36105 1.20510
H -1.50688 -1.38488 -1.68693
H -0.23578 -1.73121 -2.85805
H 0.13635 1.70574 1.37111
H 1.89164 -0.70062 2.18702
H -1.73460 2.05372 0.36368
H -4.11614 2.35818 -0.15553
H -5.65369 0.40650 -0.20304
H -4.77260 -1.86823 0.28280
H -2.37504 -2.18042 0.80365
H -0.26933 -2.61012 -1.31632
H 1.79643 -2.00557 -0.49755
H 2.33624 1.08712 2.28641
H -0.93163 0.94606 -1.90689
H 0.64199 0.94624 -2.71237
H 0.48612 1.62992 -1.09162

Product6

C -0.51564 -0.82907 1.03747
C 0.48001 -1.20741 -0.13149
C -1.06466 0.54976 0.78812
C -1.58826 -1.91931 1.15391
C 1.69964 -0.30022 -0.19818
H -2.08400 -2.13430 0.20703
H -2.34684 -1.63944 1.89270
H -1.11013 -2.84388 1.49554
C -2.22356 0.93781 0.21498
H -0.41896 1.36745 1.10749
C -3.23536 0.06920 -0.33248
C -2.50551 2.34677 0.07935
N -4.07439 -0.57394 -0.80221
N -2.72135 3.47836 -0.02824
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C 1.64325 0.97794 -0.76796
C 4.05150 0.07399 0.29300
H 2.98487 -1.73472 0.76070
C 3.97934 1.34882 -0.26601
H 4.98872 -0.28978 0.70410
C 2.77093 1.79724 -0.79852
H 0.71597 1.34549 -1.20192
H 2.70458 2.78535 -1.24436
H 4.85827 1.98587 -0.29241
C -0.21227 -1.30438 -1.46823
H 0.83102 -2.21365 0.13539
C -0.36421 -2.44192 -2.14473
H -0.59873 -0.37895 -1.89693
H 0.00644 -3.38781 -1.75443
H -0.86384 -2.46562 -3.10843
C 0.25767 -0.76620 2.36704
H 1.01178 0.02628 2.36572
H 0.76561 -1.72000 2.54588
H -0.43272 -0.58748 3.19801

5_cation

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C 2.51824 -0.31607 -0.00013
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C -1.19322 -0.84833 -0.00075
C 2.78512 1.07391 -0.00031
C 4.09188 1.52654 -0.00014
C 5.15069 0.60818 0.00043
C 4.90605 -0.76725 0.00072
C 3.59872 -1.22783 0.00037
H 1.11888 -1.93620 -0.00037
H -0.00005 0.94431 -0.00147
H -1.11891 -1.93621 -0.00045
H 1.97051 1.79058 -0.00071
H 4.29859 2.59136 -0.00040
H 6.17373 0.97184 0.00065
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H 3.39429 -2.29515 0.00053
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C -4.90606 -0.76723 0.00040
H -3.39433 -2.29516 -0.00012
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C -5.15068 0.60821 0.00050
H -5.73286 -1.46918 0.00058
H -4.29854 2.59137 0.00043
H -6.17371 0.97189 0.00073

5_anion

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C 0.94219 -0.10345 -0.01325
C 1.11066 1.28290 -0.18009
C 2.11012 -0.87757 0.11533
N 3.06474 -1.54799 0.22035
N 1.25196 2.43424 -0.34203
C -1.87487 1.11043 0.51313
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H -3.41121 -0.69636 -1.06899
H -2.52127 -2.14691 -0.57577
H -0.26126 -1.83222 -0.42267
H -2.79592 1.12370 1.11041
H -2.01778 1.81984 -0.31433
H -1.06091 1.49849 1.13188

5_break_TS

C -0.78455 1.22978 0.89606
C -0.62536 -1.83763 -1.24042
C -2.09758 0.76827 1.09564
C -3.10561 0.61453 0.15987
C 0.53944 -1.42046 -0.61058
H -0.66220 -1.75450 -2.32691
C 1.60763 -0.86893 -1.30512
H -2.32486 0.48207 2.12012
H 0.61025 -1.51184 0.47206
C -4.44305 0.11615 0.59982
C -2.93563 0.90766 -1.29821
H -4.49501 -0.04908 1.67834
H -4.66960 -0.83000 0.08962
H -5.22512 0.82905 0.30833
C 0.11796 1.21304 2.00106
C -0.25138 1.73124 -0.32482
N 0.83388 1.17382 2.91467
N 0.21760 2.15081 -1.30105
C 2.83126 -0.35021 -0.73343
H 1.51087 -0.78217 -2.38676
C 3.80132 0.20472 -1.59326
C 3.09928 -0.35143 0.65147
C 4.28157 0.18301 1.14708
C 5.23238 0.72718 0.27931
C 4.98549 0.73421 -1.09504
H 3.60833 0.22051 -2.66327
H 2.37730 -0.76299 1.35002
H 5.71607 1.15786 -1.77793
H 4.46094 0.18013 2.21828
H 6.15444 1.14491 0.67203
C -1.80304 -2.39022 -0.60967
C -2.87920 -2.80987 -1.42090
C -1.94159 -2.53268 0.78874
C -4.02371 -3.37289 -0.86855
H -2.79721 -2.69939 -2.49994
C -3.08783 -3.09352 1.33862
H -1.14287 -2.20765 1.44975
C -4.13381 -3.52196 0.51623
H -4.83189 -3.69776 -1.51753
H -3.16796 -3.19811 2.41697
H -5.02555 -3.96341 0.95090
H -2.06629 0.38019 -1.70961
H -2.77000 1.97766 -1.47383
H -3.82381 0.60086 -1.85584

5_homo_int

C 0.39004 -1.05488 1.53959
C 0.08847 0.62777 -1.46877
C 1.59210 -0.37385 1.55881
C -0.72913 -0.58606 2.41302
C 1.24640 1.47121 -1.28810
H -0.49530 0.34593 2.93332
H -0.97375 -1.35626 3.15672
H -1.63512 -0.44304 1.80916
C 2.73696 -0.60584 0.77339
H 1.68414 0.45812 2.25359
C 2.80289 -1.52527 -0.31207
C 3.91409 0.16029 1.01283
N 2.86459 -2.25668 -1.21227
N 4.87002 0.78132 1.23512
C 2.38483 1.24167 -2.08883
C 1.31652 2.49858 -0.32197
C 3.53554 2.00798 -1.94264
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C 3.58383 3.02178 -0.98573
H 4.40056 1.80588 -2.56728
C 2.46780 3.26021 -0.17669
H 0.46718 2.69557 0.32632
H 2.50335 4.04115 0.57741
H 4.48641 3.61096 -0.85719
C -1.12673 0.72225 -0.79741
H 0.18693 -0.15857 -2.21809
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H -2.02108 -0.94363 -1.75961

C -3.46714 -0.15022 -0.36541
C -3.86157 0.83750 0.56261
C -4.38310 -1.18186 -0.65641
C -5.10929 0.78515 1.17085
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C -5.63096 -1.23200 -0.04551
H -4.09968 -1.95033 -1.37185
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H -5.39198 1.55777 1.88007
H -6.31682 -2.03876 -0.28697
H -6.97598 -0.28456 1.35121
C 0.12192 -2.28050 0.71739
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H 0.90503 -3.03468 0.84605

6_form_TS

C 0.75632 -1.40479 1.01495
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C -0.54855 -1.57172 1.72492
C 1.08004 1.22575 -1.06666
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H -0.52333 -2.48783 2.33170
H -1.37753 -1.69063 1.01458
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H 1.23263 0.32285 2.12981
C 3.77336 -1.10068 0.30944
C 3.65459 0.94649 1.56272
N 4.45689 -1.81353 -0.30258
N 4.21225 1.88844 1.95331
C 2.21273 0.79318 -1.78475
C 1.13951 2.48727 -0.43165
C 3.34860 1.59234 -1.88930
H 2.19269 -0.18001 -2.27124
C 3.38170 2.83821 -1.26786
H 4.20974 1.23276 -2.44440
C 2.27103 3.27904 -0.53701
H 0.29609 2.84615 0.15039
H 2.30290 4.24100 -0.03455
H 4.26922 3.45958 -1.33482
C -1.32202 0.69116 -0.44875
H 0.00141 -0.57745 -1.54071
C -2.41325 -0.12456 -0.59991
H -1.42568 1.62625 0.09614
H -2.28348 -1.03611 -1.18503
C -3.75289 0.10148 -0.07941
C -4.08083 1.18912 0.75323
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C -5.37767 1.35575 1.22208
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H -4.53211 -1.65595 -1.05578
C -6.37822 0.44331 0.87527
H -5.61198 2.19979 1.86388
H -6.83913 -1.35630 -0.21868
H -7.39014 0.57789 1.24502
C 1.12283 -2.49494 0.04825
H 1.75750 -2.14457 -0.76884
H 0.21686 -2.93647 -0.37980
H 1.67011 -3.29905 0.55910

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