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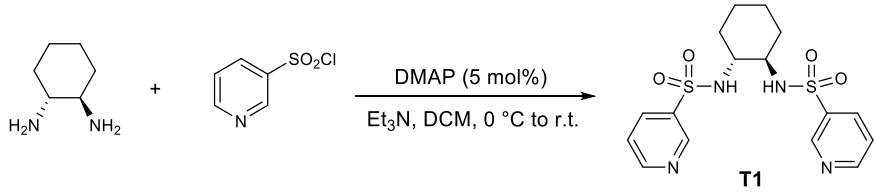
1. General Information

Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. Anhydrous solvents were obtained from the solvent purification system produced by JC Meyer Solvent Systems. Analytical thin layer chromatography (TLC) was performed on Merck Millipore precoated (0.25 mm thickness) silica gel plates with F254 indicator. Visualization was accomplished by irradiation with UV light at 254 nm or PMA or $KMnO_4$ stain solution. Flash column chromatography was performed on silica gel (32-63 μm) supplied by Dynamic Adsorbents. ^{1}H NMR spectra were recorded on a Bruker DRX-600 spectrometer (600 MHz) in deuterated solvent and chemical shifts were reported in ppm (δ) relative to tetramethylsilane with the solvent resonance employed as the internal standard ($CDCl_3$, δ 7.26 ppm; DMSO-d_6, δ 2.50 ppm; acetonitrile-d_3, δ 1.94 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constants (Hz) and integration. ^{13}C NMR spectra were recorded on a Bruker DRX-600 spectrometer (151 MHz) in deuterated solvent with complete proton decoupling and chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$, δ 77.0 ppm; DMSO-d_6, δ 39.5 ppm; acetonitrile-d_3, δ 1.32 ppm). High-resolution mass spectra (HRMS) were recorded on an Agilent LC/MSD TOF mass spectrometer. The single crystal X-ray diffraction studies were carried out on a Bruker Kappa APEX-II CCD diffractometer equipped with Mo K_α radiation (λ = 0.71073 Å). The substrates **1b-v** were synthesized according to the literature known procedures[1,2].

2. General Procedure for Synthesis of Bisdentate Templates T1-10

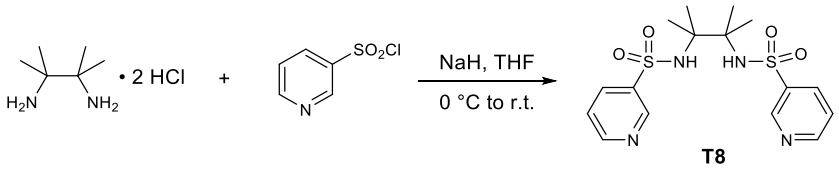
2.1 Procedure for Synthesis of T1, T3-7, T9-10



(1*R*, 2*R*)-cyclohexane-1,2-diamine (343 mg, 3.0 mmol) and DMAP (18mg, 0.15 mmol) were placed in a pre-dried 100 mL three-necked flask and flushed with nitrogen. DCM (25 mL) and Et_3N (1.25 mL, 9.0 mmol) were added into the flask under nitrogen. The reaction solution was

cooled to 0 °C and pyridine-3-sulfonyl chloride (0.75 mL, 6.3 mmol) was added dropwise. The reaction mixture was stirred at 0 °C for 2 hours and warmed to room temperature slowly then stirred overnight. The solvent and volatile compounds were evaporated under reduced pressure at 45 °C. The residue was purified by column chromatography on silica gel using DCM/MeOH (20:1) as the eluent giving the template **T1** in its pure form.

2.2 Procedure for Synthesis of T8

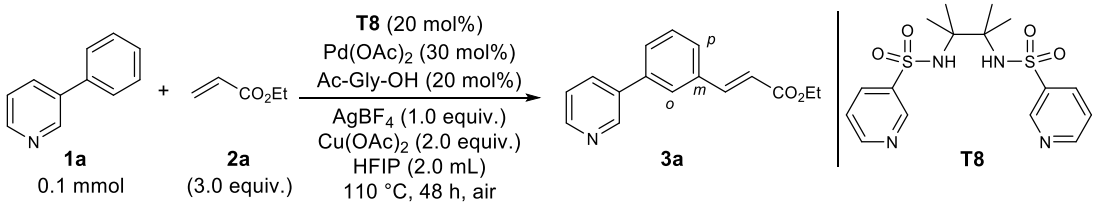


T8

Sodium hydride (1.476g, 36.9 mmol, 60 % dispersion in mineral oil) was placed in a pre-dried 50 mL Schlenk flask under nitrogen. THF (10 mL) was added and the mixture was cooled to 0 °C. 2,3-Dimethyl-2,3-butanediamine dihydrochloride (698 mg, 3.69 mmol) was added into the flask in portions under nitrogen, the mixture was stirred at 0 °C for 0.5 hour then warmed to room temperature and stirred for 0.5 hour. The mixture was cooled to 0 °C and pyridine-3-sulfonyl chloride (1.32 mL, 11.07 mmol) was added dropwise. The reaction mixture was stirred at 0 °C for 2 hours and warmed to room temperature slowly then stirred overnight. 2 N aquesous solution of HCl (11 mL) was added at 0 °C slowly and the mixture was extracted with ethyl acetate (50 mL) and DCM (50 mL) three times respectively. The organic layers were then combined and dried with Na_2SO_4. After removal of the solvents, the residue was purified by column chromatography on silica gel using DCM/MeOH (20:1) as the eluent giving the template **T8** in its pure form.

Template **T2**[3], **T4**[4], **T5**[5], **T9**[6] and **T10**[7] have been synthesized and characterized before.

3. General Procedure for Remote Site-selective C–H Olefination of Substrates 1



1a 0.1 mmol

2a (3.0 equiv.)

3a

T8

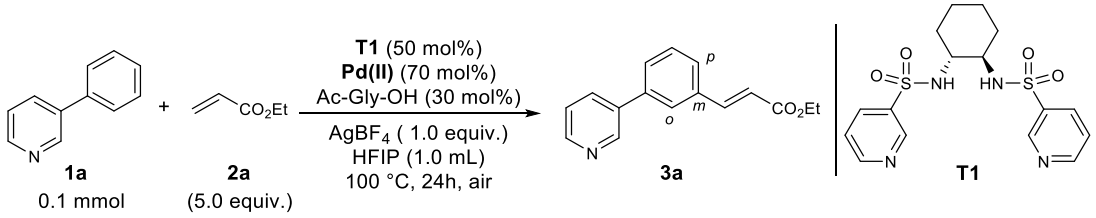
A reaction tube (15 mL) with magnetic stir bar was charged with **1a** (14.3 μL, 0.1 mmol), **T8** (8.0 mg, 0.02 mmol), $Pd(OAc)_2$ (6.7 mg, 0.03 mmol), Ac-Gly-OH (2.3mg, 0.02 mmol), $AgBF_4$ (19.5 mg, 0.1 mmol), $Cu(OAc)_2$ (36.3 mg, 0.2 mmol), HFIP (2.0 ml) and **2a** (31.8 μl, 0.3 mmol) in air. The reaction tube was sealed and allowed to stir at ambient temperature for 10 minutes, then heated to 110 °C for 48 hours. Upon completion, the reaction mixture was cooled to 0 °C and saturated aquesous solution of sodium sulfide (1.0 mL) was added followed by water (3.0 mL). The mixture was extracted with DCM (10 mL) for three times and the organic layers were combined and filtered through a silica gel plug then dried with Na_2SO_4. The solvent and volatile compounds were evaporated under reduced pressure at 45 °C. The crude reaction mixture was purified on preparative TLC using hexanes/ethyl acetate (2:1) as the eluent to afford the desired product **3a**.

Caution: The operator should have appropriate protection all the time when the reaction is running due to the high pressure generated in the sealed reaction flask under high temperature.

4. Optimization of Reaction Conditions

4.1 Screening of the Palladium Salts

Table S1 Screening of the Palladium Salts



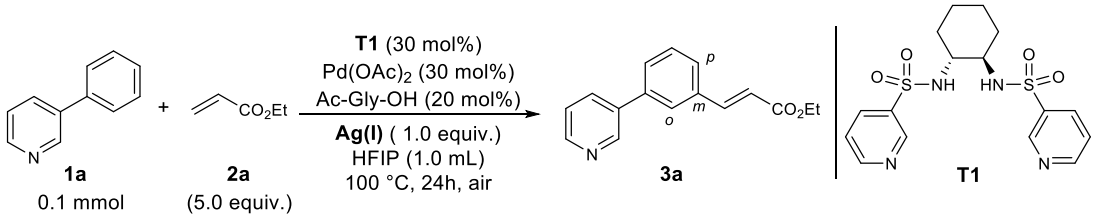
Entry	Pd(II)	Yield (%)[a]	*m*:(*o*+*p*)[a]
1	$Pd(CH_3CN)_2(BF_4)_2$	2	79:21
2	$Pd(TFA)_2$	7	73:27
3	$Pd(acac)_2$	1	60:40
4	$PdSO_4$	1	70:30

5	$PdCl_2$	<1	N.D.
6	**$Pd(OAc)_2$**	**49**	**73:27**

[a] The yield of the olefinated products, the *meta*:(*ortho* + *para*) ratio of mono-olefinated products were determined by ^1H NMR analysis of the unpurified reaction mixture using CH_2Br_2 as the internal standard (assisted with GC-MS analysis), the variance is estimated to be within 5%. Ac-Gly-OH: *N*-acetyl-glycine.

4.2 Screening of the Silver Salts

Table S2 Screening of the Silver Salts

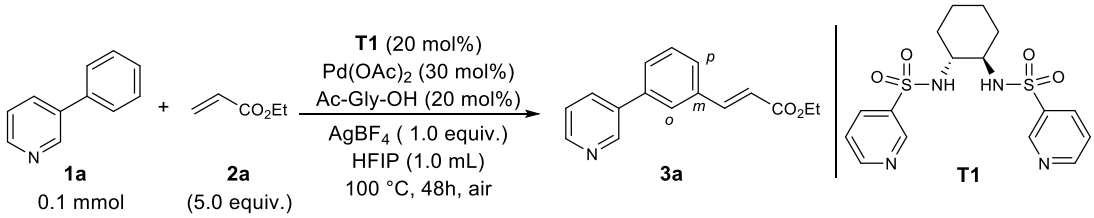


Entry	Ag(I)	Yield (%)[a]	*m*:(*o*+*p*)[a]
1	AgTFA	21	63:37
2	AgOTf	29	63:37
3	AgF	4	63:37
4	$AgPF_6$	14	71:29
5	$AgSbF_6$	23	66:34
6	**$AgBF_4$**	**32**	**72:28**

[a] The yield of the olefinated products, the *meta*:(*ortho* + *para*) ratio of mono-olefinated products were determined by ^1H NMR analysis of the unpurified reaction mixture using CH_2Br_2 as the internal standard (assisted with GC-MS analysis), the variance is estimated to be within 5%. Ac-Gly-OH: *N*-acetyl-glycine.

4.3 Screening of the Oxidants/Additives

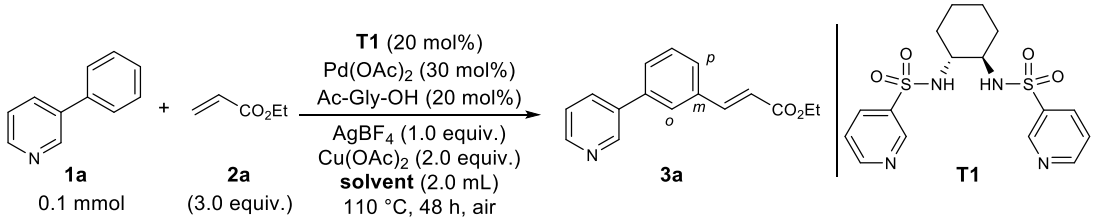
Table S3 Screening of the Oxidants/Additives



Entry	Additive (2.0 equiv. of Cu)	Yield (%)[a]	*m*:(*o*+*p*)[a]
1	$Cu(OTf)_2$	0	N.D.
2	$Cu(TFA)_2 \cdot xH_2O$	0	N.D.
3	$Cu_3(PO_4)_2$	33	84:16
4	$CuCl_2$	0	N.D.
5	CuF_2	45	85:15
6	CuO	34	81:19
7	$Cu(NO_3)_2 \cdot 3H_2O$	0	N.D.
8	$Cu(ClO_4) \cdot 6H_2O$	0	N.D.
9	$Cu(TCA)_2$	0	N.D.
10	**$Cu(OAc)_2$**	**53**	**85:15**

[a] The yield of the olefinated products, the *meta*:(*ortho* + *para*) ratio of mono-olefinated products were determined by ^1H NMR analysis of the unpurified reaction mixture using CH_2Br_2 as the internal standard (assisted with GC-MS analysis), the variance is estimated to be within 5%.

4.4 Screening of the Solvents



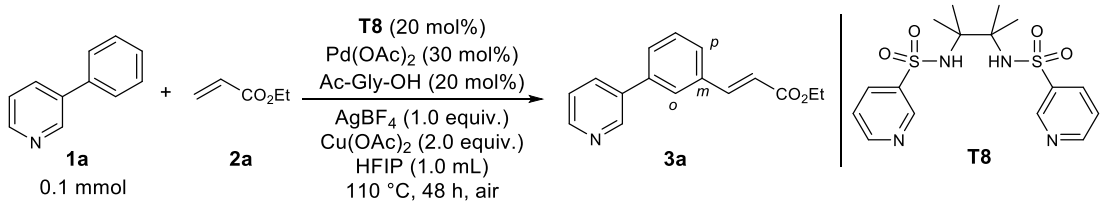
HFIP: 75%, *m*:(*o*+*p*) = 89:11, mono:di = 87:13.

When *t*-Amyl-OH, Dioxane, DMSO, MeOH, DMF, EtOAc, MeCN, THF, TBME or DME was used as solvent, no desired product was observed.

When DCE or Toluene was used as solvent, only trace amount of desired product was observed.

4.5 Screening of the Loading of 2a

Table S4 Screening of the loading of 2a

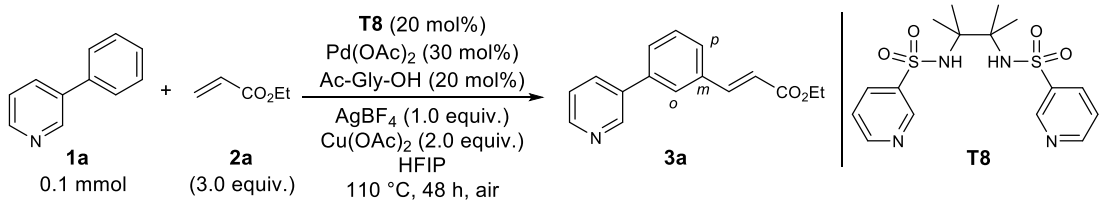


Entry	**2a** (equiv.)	Yield (%)[a]	*m*:(*o*+*p*)[a]
1	5.0	60	94.4:5.6
2	4.0	66	94.0:6.0
3	**3.0**	**75**	**94.3:5.7**
4	2.0	70	93.8:6.2

[a] The yield of the olefinated products, the *meta*:(*ortho* + *para*) ratio of mono-olefinated products were determined by ^{1}H NMR analysis of the unpurified reaction mixture using CH_2Br_2 as the internal standard (assisted with GC-MS analysis), the variance is estimated to be within 5%.

4.6 Screening of the Concentrations

Table S5 Screening of the Concentrations

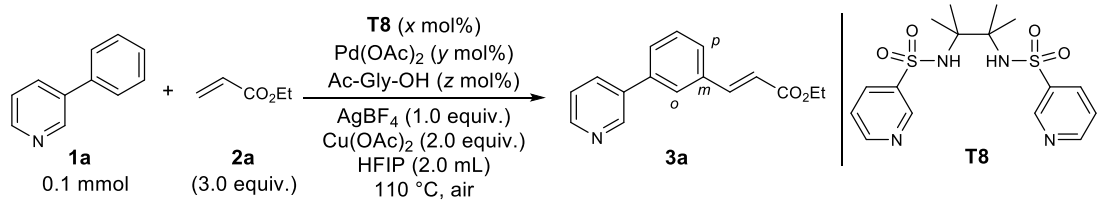


Entry	HFIP (mL)	Concentration (M)	Yield (%)[a]	*m*:(*o*+*p*)[a]
1	1.0	0.100	75	94:6
2	**2.0**	**0.050**	**77**	**95:5**
3	3.0	0.033	69	95:5
4	4.0	0.025	57	94:6
5	5.0	0.020	51	93:7

[a] The yield of the olefinated products, the *meta*:(*ortho* + *para*) ratio of mono-olefinated products were determined by ^{1}H NMR analysis of the unpurified reaction mixture using CH_2Br_2 as the internal standard (assisted with GC-MS analysis), the variance is estimated to be within 5%.

4.7 Screening of the Loading of Template, $Pd(OAc)_2$ and Ligand

Table S6 Screening of the Loading of Template, $Pd(OAc)_2$ and Ligand

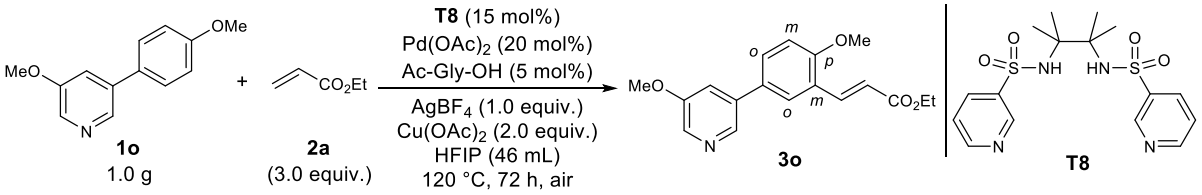


Entry	**T8** (mol%)	$Pd(OAc)_2$ (mol%)	Ac-Gly-OH (mol%)	Yield (%)[a]	*m*:(*o*+*p*)[a]
1	10	15	10	14	89:11
2	10	15	15	25	90:10
3	10	20	5	62	94:6

4	10	20	10	60	94:6
5	10	20	15	40	92:8
6	**15**	**20**	**5**	**64**	**95:5**
7	15	30	15	65	95:5
8	20	30	10	76	95:5
9	**20**	**30**	**20**	**77**	**95:5**

[a] The yield of the olefinated products, the *meta*:(*ortho* + *para*) ratio of mono-olefinated products were determined by ^{1}H NMR analysis of the unpurified reaction mixture using CH_2Br_2 as the internal standard (assisted with GC-MS analysis), the variance is estimated to be within 5%.

5. Gram-scale Reaction



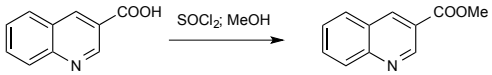
A reaction tube (250 mL) with magnetic stir bar was charged with **1o** (1.0 g, 4.646 mmol), **T8** (277 mg, 0.697 mmol), $Pd(OAc)_2$ (209 mg, 0.929 mmol), Ac-Gly-OH (27 mg, 0.232 mmol), $AgBF_4$ (0.904 g, 4.646 mmol), $Cu(OAc)_2$ (1.688 g, 9.292 mmol), HFIP (46 ml) and **2a** (1.48 mL, 13.937 mmol) in air. The reaction tube was sealed and allowed to stir at ambient temperature for 10 minutes, then heated to 120 °C for 72 hours. Upon completion, the reaction mixture was cooled to 0 °C and saturated aquesous solution of sodium sulfide (10 mL) was added followed by water (30 mL) and DCM (30 mL). The mixture was filtered through a pad of celite and washed with DCM. The solvents were evaporated under reduced pressure at 45 °C and then the mixture was extracted with DCM (100 mL) for three times. After dried with Na_2SO_4, the solvent and volatile compounds were evaporated under reduced pressure at 45 °C. A sample (10 mg) was taken from the unpurified reaction mixture and the *m*:*o* ratio of mono-olefinated products was determined to be 99:1 and the mono:di ratio was determined to be 98:2 by ^{1}H NMR analysis. The rest crude reaction mixture and the sample for ^{1}H NMR analysis were combined and purified by

column chromatography on silica gel using hexane/ethyl acetate (5:1 to 2:1) then DCM/MeOH (10:1) as the eluents giving **3o** (1.03 g, 70% yield) and **T8 (**266 mg, 96% recovered).

Caution: The operator should have appropriate protection all the time when the reaction is running due to the high pressure generated in the sealed reaction flask under high temperature.

6. General Procedure for Synthesis of Tridentate Templates T11-19

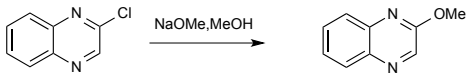
Scheme S1 Synthesis of **4k**



4k

Quinoline-3-carboxylic acid (0.245 g, 1.41 mmol) was charged in the flask with stir bar and thionyl chloride was added. The resulting mixture was allowed to stir at 80 ^{o}C overnight. Upon completion, the reaction mixture was cooled to room temperature and concentrated *in vacuo*. MeOH was added to this crude mixture and was heated under reflux for 8 h. Upon completion, the reaction mixture was cooled to room temperature, diluted with DCM, and was washed with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with DCM twice, and the combined organic layers were dried with anhydrous Na_2SO_4. After removal of the solvents, the residue was purified by column chromatography on silica gel using EtOAc/ hexanes (1: 6) as the eluent to give **4k** (0.161 g, 61%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.46 (d, J = 2.1 Hz, 1H), 8.86 (d, J = 2.2 Hz, 1H), 8.17 (d, J = 8.5 Hz, 1H), 7.95 (d, J = 8.2 Hz, 1H), 7.84 (ddd, J = 8.5, 6.9, 1.4 Hz, 1H), 7.63 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H), 4.03 (s, 3H). ^{1}H NMR matches previously reported data[8].

Scheme S2 Synthesis of **4l**

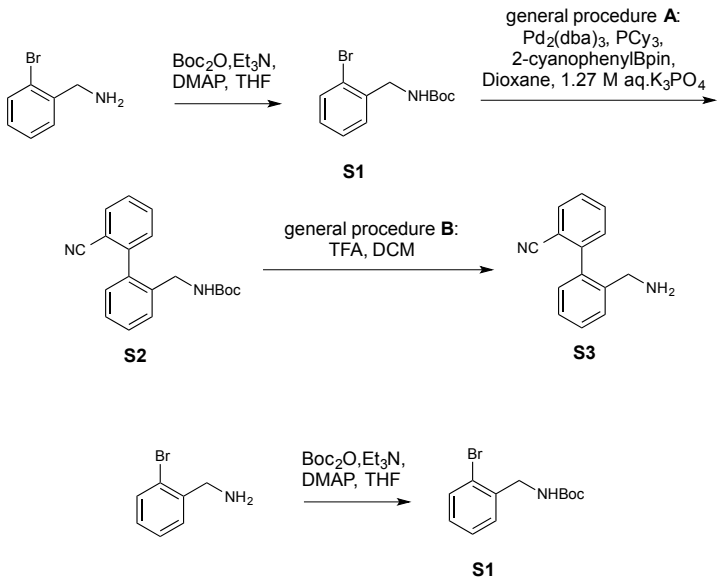


4l

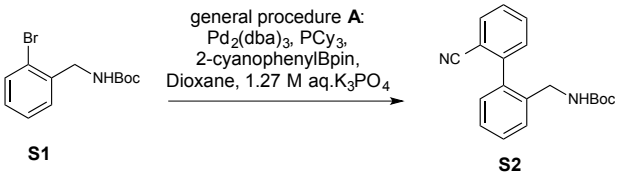
2-Chloroquinoxaline (0.823g, 5 mmol) and NaOMe (1.89g, 35 mmol) were charged in the flask with stir bar and MeOH (10 mL) was added to this mixture. The resulting solution was heated at 80 ^{o}C for 4 h. Upon completion, the reaction mixture was cooled to room temperature and filtered through celite (the celite pad was washed with EtOAc). The filtrate was concentrated *in*

vacuo. Water was added to this crude mixture and extracted with EtOAc three times. The combined organic layers were dried with anhydrous Na_2SO_4. After removal of the solvents, the residue was purified by column chromatography on silica gel using EtOAc/hexanes as the eluent giving pure product. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.47 (s, 1H), 8.02 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.85 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.67 (ddd, *J* = 8.4, 7.0, 1.5 Hz, 1H), 7.56 (ddd, *J* = 8.3, 7.0, 1.4 Hz, 1H), 4.10 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 157.67, 140.38, 139.59, 138.87, 130.09, 128.98, 127.18, 126.51, 53.69. ^{1}H NMR , ^{13}C NMR matches previously reported data[9].

Scheme S3 Synthesis of **S3**



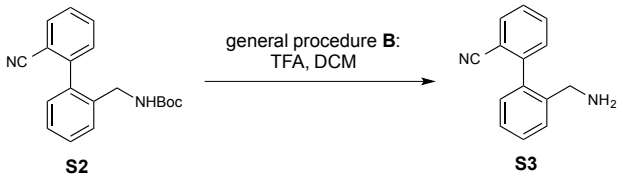
To a solution of the 2-bromobenzylamine (0.63 mL, 5.0 mmol) in THF (25 mL) at 0 ^{o}C was added Et_3N (4.18 mL, 30 mmol), followed by DMAP (0.01 g, 0.08 mmol). To the reaction mixture was added di-*tert*-butyl dicarbonate (1.31 g, 6.0 mmol) and the solution was warmed to room temperature and stirred for 5 h. Upon completion, the reaction was quenched with cold water and extracted with EtOAc three times. The combined organic layers were washed with water and brine, dried with anhydrous Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel using EtOAc/hexanes (1: 10) as the eluent giving the pure product. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.38 (d, *J* = 7.7 Hz, 1H), 7.29 (d, *J* = 7.4, 1.2 Hz, 1H), 7.14 (dd, *J* = 7.8, 1.8 Hz, 1H), 5.01 (br, 1H), 4.39 (d, *J* = 6.3 Hz, 2H), 1.45 (s, 9H). ^{1}H NMR matches previously reported data[10].



S1 **S2**

(General procedure **A**: Suzuki–Miyaura cross coupling)

2-cyanophenylboronic acid pinacol ester (0.504 g, 2.2 mmol), $Pd_2(dba)_3$ (0.0366g, 0.04 mmol), PCy_3 (0.0269 g, 0.096 mmol), and **S1** (0.572 g, 2 mmol) were added to a Schlenk flask equipped with a stir bar. After dioxane (5.4 mL) and 1.27 M K_3PO_4 aqueous solution (2.7 mL) were added, the flask was evacuated and refilled with nitrogen three times. The Schlenk flask was sealed and the resulting reaction mixture was stirred at 100 ^oC overnight. Upon completion, the reaction mixture was cooled to room temperature and filtered through celite (the celite pad was washed thoroughly with EtOAc). Water was added to this mixture and extracted three times with EtOAc. The combined organic layers were dried with anhydrous Na_2SO_4. After removal of the solvents, the residue was purified by column chromatography on silica gel using EtOAc/hexanes (1:6) as the eluent giving pure product.

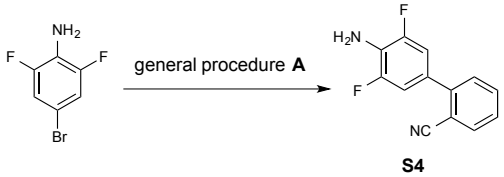


S2 **S3**

(General Procedure **B**: Deprotection of Boc protecting group)

To a solution of the **S2** (0.64 g, 2 mmol) in DCM (32 mL) at 0 ^oC was added TFA (3 mL) slowly. The solution was warmed to room temperature and stirred for 2 hours. Upon completion, the reaction was quenched with saturated aqueous $NaHCO_3$ and the organic layer was separated. Water layer was extracted with DCM three times and the combined organic layers were dried with anhydrous Na_2SO_4, and concentrated to give the crude amine **S3**, which was used in the next step without further purification.

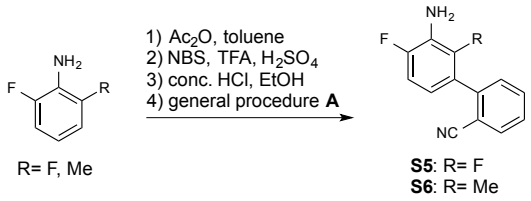
Scheme S4 Synthesis of **S4**



S4

S4 was synthesized using general procedure **A** and was purified by column chromatography on silica gel using EtOAc/hexanes (1:10) as the eluent.

Scheme S5 Synthesis of **S5** and **S6**



R= F, Me

S5: R= F
S6: R= Me

For **S5** (R= F)

To a solution of 2,6-difluoroaniline (1.0 mL, 10 mmol) in toluene (20 mL) was added acetic anhydride (1.13 mL, 12 mmol) in one portion. The reaction mixture was allowed to stir overnight at 110 ^{o}C. Upon completion, the solvent was removed under reduced pressure. Water was added to this crude mixture and extracted with EtOAc three times. The combined organic layers were washed with brine and dried with anhydrous Na_2SO_4. The solvent was removed to afford *N*-(2,6-difluorophenyl)acetamide, which was used in the next step without further purification.

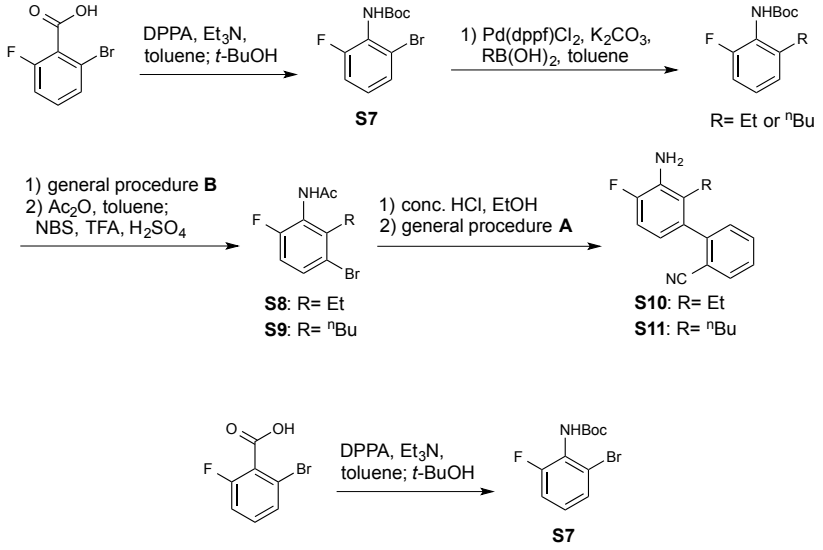
To a solution of *N*-(2,6-difluorophenyl)acetamide in TFA (8.2 mL) and H_2SO_4 (11 mL) at 0 ^{o}C was added NBS (1.72 g, 9.7 mmol) in portions. The reaction mixture was stirred at 0 ^{o}C for 10 min and warmed to room temperature slowly then stirred overnight. Upon completion, ice was added to the reaction mixture and the white precipitate was collected by filtration. The crude product was washed with water and hexane extensively to give *N*-(3-bromo-2,6-difluorophenyl)acetamide, which was used in the next step without further purification.

To a solution of *N*-(3-bromo-2,6-difluorophenyl)acetamide in EtOH (5.7 mL) was added concentrated HCl (5.7 mL) at room temperature. The reaction mixture was allowed to stir overnight at 75 ^{o}C. Upon completion, the reaction mixture was cooled to room temperature. The reaction mixture was cooled to 0 ^{o}C and basified with aqueous NaOH solution. The reaction mixture was extracted three times with EtOAc. The combined organic layers were dried with anhydrous Na_2SO_4 and concentrated *in vacuo* to give 3-bromo- 2,6-difluoroaniline, which was used in the next step without further purification.

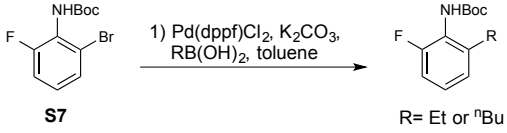
3-bromo-2,6-difluoroaniline was converted to **S5** using general procedure **A** and was purified by column chromatography on silica gel using EtOAc/hexanes as the eluent.

S6 was synthesized using the same procedure as **S5**.

Scheme S6 Synthesis of **S10** and **S11**

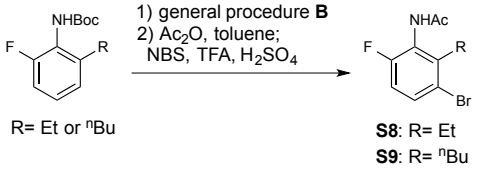


To a solution of the 2-bromo-6-fluorobenzoic acid (2.19 g, 10 mmol) in toluene (40 mL) at room temperature was added Et_3N (1.46 mL, 10.5 mmol), followed by DPPA (2.26 mL, 10.5 mL). The reaction mixture was gradually heated to 70 ^oC and stirred at the same temperature until bubling stops. The solution was heated to 110 ^oC. After 1 h, to the reaction mixture was added ^{t}BuOH (7.4 g) and the solution was allowed to stir overnight at the same temperature. Upon completion, the reaction was cooled down to room temperature. Water was added and extracted with EtOAc three times. The combined organic layers were washed with 0.1 M HCl, water, saturated aqueous $NaHCO_3$, and brine, dried with anhydrous Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel using EtOAc/hexanes (1:20 to 1:10) as the eluent to give **S7** (1.69 g, 58%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.39–7.35 (m, 1H), 7.10–7.06 (m, 2H), 6.07 (br, 1H), 1.50 (s, 9H). ^{1}H NMR matches previously reported data[11].



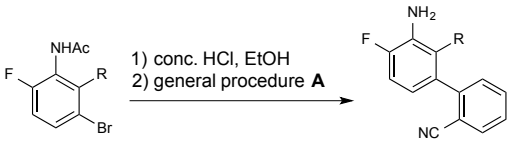
For **S8** (R= Et)

In the air, ethylboronic acid (3.69 g, 49.8 mmol), $Pd(dppf)Cl_2$ (0.91 g, 1.25 mmol), K_2CO_3 (10.3 g, 74.7 mmol), and **S7** (7.23 g, 24.9 mmol) were added to a Schlenk flask equipped with a stir bar. After toluene was added, the flask was evacuated and refilled with nitrogen three times. The schlenk flask was sealed and the resulting reaction mixture was stirred at 110 ^oC overnight. Upon completion, the reaction mixture was cooled to room temperature and filtered through celite (the celite pad was washed thoroughly with EtOAc). The filtrate was concentrated under reduced pressure, and the crude mixture was diluted with DCM, washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The mixture was passed through a pad of silica gel using EtOAc/hexanes (1:10) as the eluent to give *tert*-butyl (2-ethyl-6-fluorophenyl)carbamate, which was used in the next step without further purification.



Tert-butyl (2-ethyl-6-fluorophenyl)carbamate was converted to 2-ethyl-6-fluoroaniline using general procedure **B**.

To a solution of 2-ethyl-6-fluoroaniline in toluene was added acetic anhydride (1.3 mL, 13.7 mmol) in one portion. The reaction mixture was allowed to stir overnight at 110 ^oC. Upon completion, the solvent was removed under reduced pressure. To this crude residue was added TFA (12.1 mL) and H_2SO_4 (16.3 mL). The reaction mixture was cooled to 0 ^oC and NBS (2.44 g, 13.7 mmol) was added in portions. The reaction mixture was stirred at 0 ^oC for 10 min and warmed to room temperature slowly then stirred overnight. Upon completion, ice was added to the reaction mixture and the white precipitate was collected by filtration. The crude product was washed with water and hexane extensively, followed by recrystallization from hot MeOH to give **S8** (1.55 g, 44%).



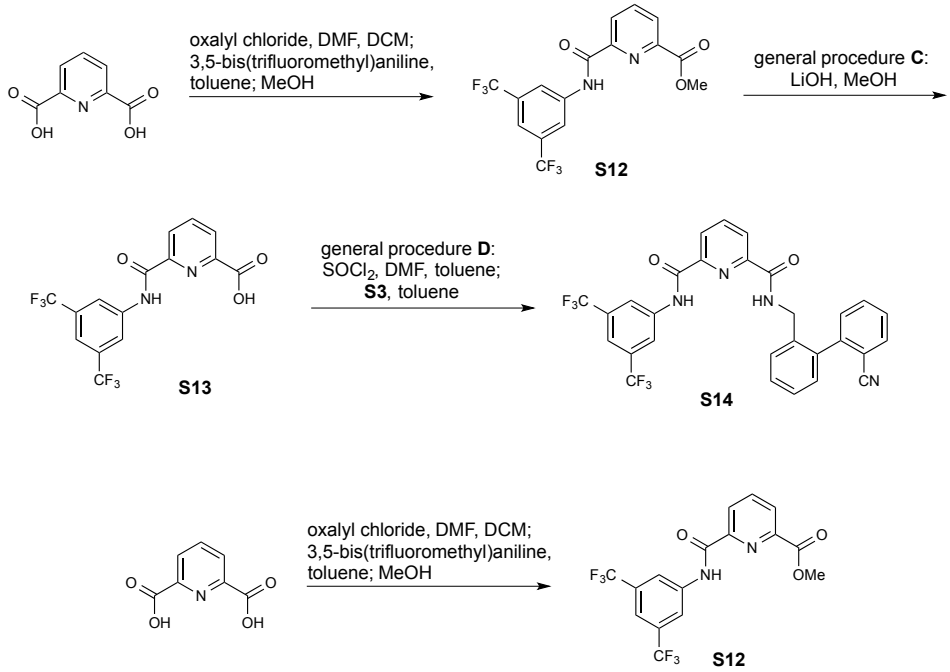
S8: R= Et
S9: R= ^{n}Bu

S10: R= Et
S11: R= ^{n}Bu

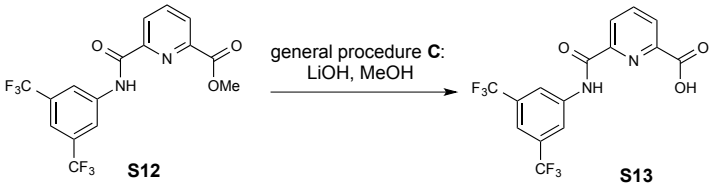
To a solution of **S8** (1.43 g, 5.48 mmol) in EtOH (3.7 mL) was added concentrated HCl (3.7 mL) at room temperature. The reaction mixture was allowed to stir overnight at 75 ^{o}C. Upon completion, the reaction mixture was cooled to room temperature. The reaction mixture was cooled to 0 ^{o}C and basified with aqueous NaOH solution. The reaction mixture was extracted three times with EtOAc. The combined organic layers were dried with anhydrous Na_2SO_4 and concentrated *in vacuo* to give the crude product. This product was used in the next step without further purification.

3-bromo-2-ethyl-6-fluoroaniline was converted to **S10** using general procedure **A** and was purified by column chromatography on silica gel using EtOAc/hexanes (1:10) as the eluent.
S11 was synthesized from **S9** in the same manner as **S10**.

Scheme S7 Synthesis of **S14**

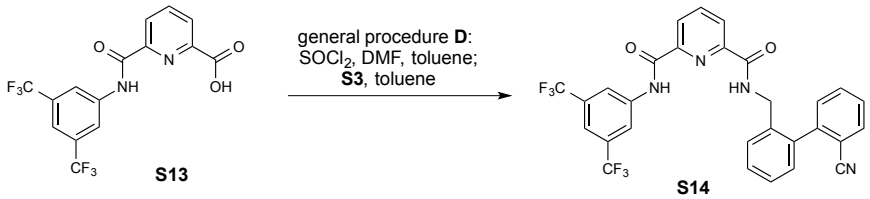


To a solution of 2,6-pyridinedicarboxylic acid (3.34 g, 20 mmol) in DCM (60 mL) was added oxalyl chloride (4 mL, 47.3 mmol) dropwise at room temperature. DMF (3 drops) was added and the reaction mixture was stirred for 10 h. Upon completion, the reaction mixture was concentrated under reduced pressure. Next, toluene (300 mL) and 3,5-bis(trifluoromethyl) aniline (2.5 mL, 16 mmol) were added to the reaction flask and submerged into an oil bath pre-heated to 70 ^{o}C. Then, the oil bath was heated to 120 ^{o}C and the reaction mixture was allowed to stir overnight. Upon completion, the reaction mixture was cooled to room temperature and concentrated under reduced pressure. MeOH (60 mL) was added to the reaction flask and heated under reflux for 9 h. Upon completion, the reaction mixture was cooled to room temperature. The white precipitate was collected by filtration and recrystallized from hot MeOH to give **S12** (1.93 g, 25%).



(General Procedure **C**: Deprotection of methyl ester)

To a solution of **S12** (1.84 g, 4.69 mmol) in MeOH (55 mL) was added LiOH monohydrate (0.39 g, 9.4 mmol) in portions. Upon completion, the solvent was removed *in vacuo*. The crude residue was dissolved in water and acidified by 6 M HCl, extracted with EtOAc three times, dried with anhydrous Na_2SO_4, and concentrated. The crude product was used in the next step without further purification.

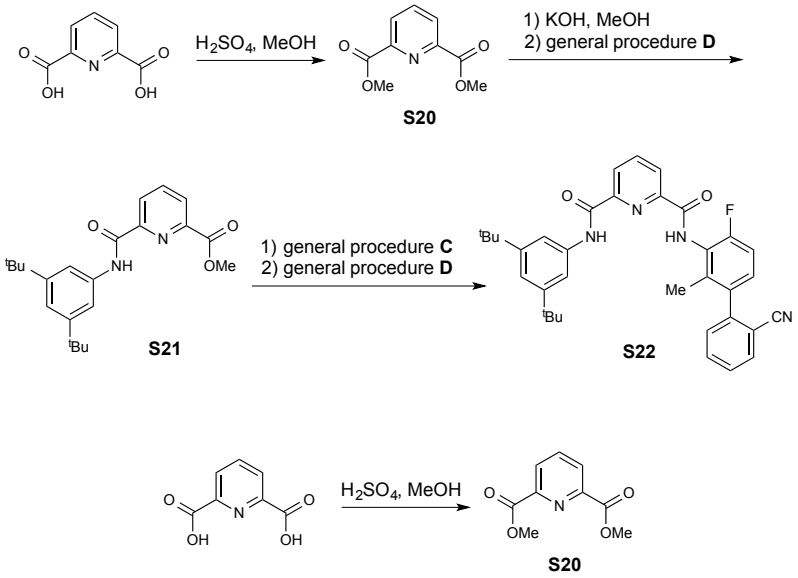


(General Procedure **D**: Amide formation)

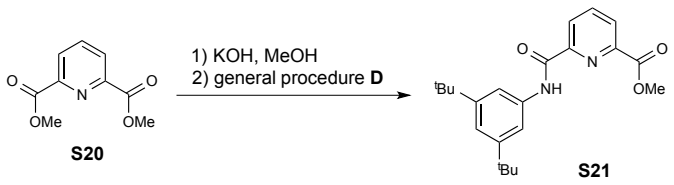
To a solution of **S13** (1.0 equiv.) in toluene was added thionyl chloride (2.5 equiv.) dropwise at room temperature. DMF (3 drops) was added and the reaction mixture was stirred at 80 ^{o}C. Upon

completion, the reaction mixture was concentrated under reduced pressure. Next, toluene and **S3** were added to the reaction flask and submerged into an oil bath pre-heated to 80 ^{o}C. Then, the oil bath was heated to 120 ^{o}C and the reaction mixture was allowed to stir overnight. Upon completion, the reaction mixture was cooled to room temperature and concentrated under reduced pressure. Pure product was isolated by recrystallization from hot MeOH. **S15-S19** were synthesized following the same procedure as **S14**. **S18** and **S19** were recrystallized from hot MeOH. **S16** was purified by column chromatography on silica gel using EtOAc/hexanes as the eluent. **S15** and **S17** were purified by trituration with DCM, MeOH, and Acetone.

Scheme S8 Synthesis of **S22**

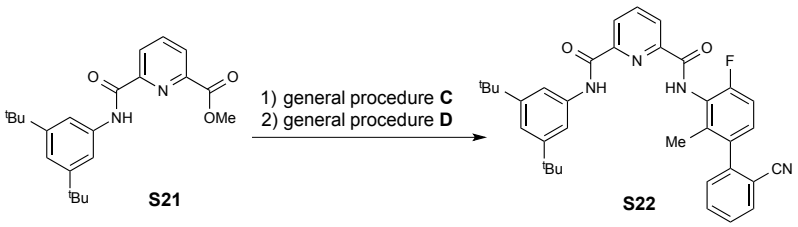


To a solution of 2,6-pyridinecarboxylic acid (1.67g, 10 mmol) in MeOH (57 mL) was added H_2SO_4 (0.19 mL) slowly at room temperature. The resulting mixture was allowed to stir at 90 ^{o}C overnight. Upon completion, solvent was removed *in vacuo*. To this residue was added DCM and saturated aqueous $NaHCO_3$. Water layer was extracted with DCM three times. The combined organic layers were dried with anhydrous Na_2SO_4, and concentrated. Recrystallization from hot MeOH gave **S20** (1.49 g, 76%) as colorless crystals. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.33 (d, J = 9.7 Hz, 2H), 8.04 (t, J = 7.8 Hz, 1H), 4.04 (s, 6H). ^{1}H NMR matches previously reported data[12].



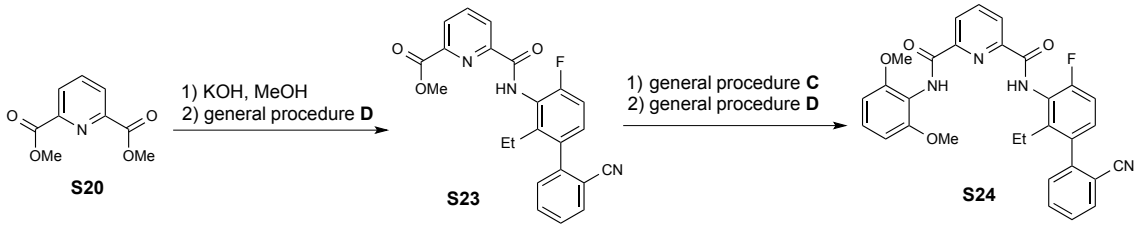
To a solution of **S20** in MeOH (265 mL) was added KOH (3.15 g, 56.1 mmol) in portions. The resulting mixture was stirred overnight at room temperature. Upon completion, the solvent was removed in vacuo, and the crude residue was washed with EtOAc extensively. This residue was dried under vacuum and used in the next step without further purification.

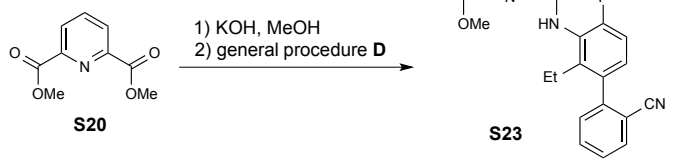
Potassium 6-(methoxycarbonyl)picolinate was converted to **S21** using general procedure **D** and was purified by column chromatography on silica gel using EtOAc/ hexanes (1:4) as the eluent.



S21 was converted to **S22** using general procedure **C** and **D**, then recrystallized from hot MeOH.

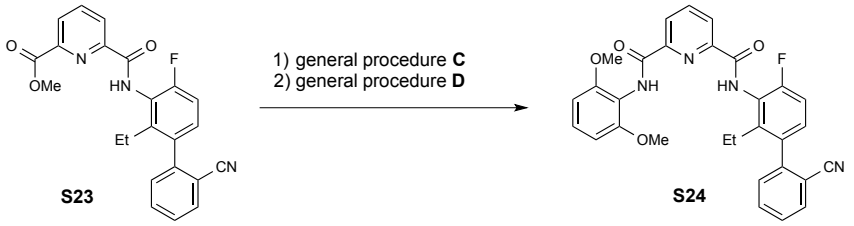
Scheme S9 Synthesis of **S24**





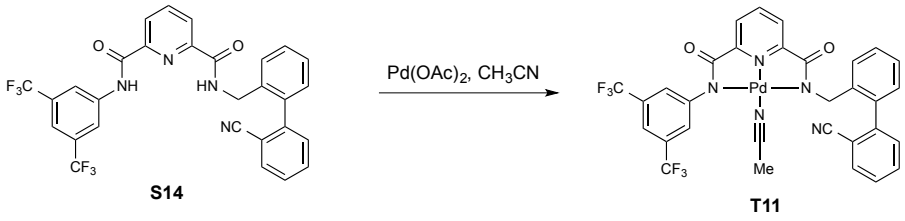
To a solution of **S20** in MeOH was added KOH in portions. The resulting mixture was stirred overnight at room temperature. Upon completion, the solvent was removed *in vacuo*, and the crude residue was washed with EtOAc extensively. This residue was dried under vacuum and used in the next step without further purification.

Potassium 6-(methoxycarbonyl)picolinate was converted to **S23** using general procedure **D** and was purified by column chromatography on silica gel using EtOAc/hexanes (1:2 to 1:1) as the eluent.



S23 was converted to **S24** using general procedure **C** and **D** and was purified by column chromatography on silica gel using EtOAc/hexanes (1:1) as the eluent.

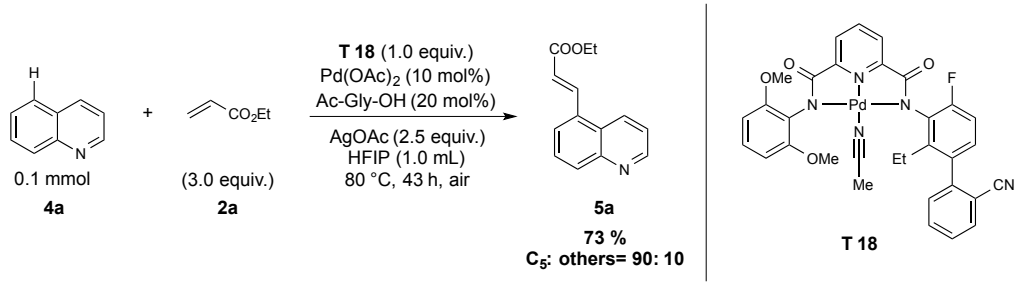
Scheme S10 Synthesis of **T11**



In the air, **S14** (0.188 g, 0.33 mmol) and $Pd(OAc)_2$ (67.4 mg, 0.3 mmol) were added to a flask equipped with a stir bar. Acetonitrile (10 mL) was added to this flask and the resulting mixture was stirred at 60 ^{o}C. Upon completion, solvent was removed *in vacuo*. The residue was purified by column chromatography on silica gel using DCM/MeOH (100:1 to 20:1) as the eluent giving the pure **T11**. (**T12**~**T19** were synthesized following the same procedure.)

7. Procedure for Remote Site–selective C–H Olefination of Substrate 4

7.1 General Procedure



A reaction tube (15 mL) was charged with **4a** (12.9 mg, 0.1 mmol), **T18** (67.0 mg, 0.1 mmol) and minimal amount of DCM to dissolve the substrate and template. After 5 min, the mixture was concentrated *in vacuo*. Magnetic stir bar, $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), Ac-Gly-OH (2.3 mg, 0.02 mmol), AgOAc (41.7 mg, 0.25 mmol), HFIP (1.0 ml) and **2a** (33.0 µl, 0.3 mmol) was added in the reaction tube in air. The reaction tube was sealed and allowed to stir at 80 °C for 43 h. Upon completion, the reaction mixture was cooled to room temperature. The crude reaction mixture was diluted with EtOAc and filtered through a short pad of celite. The sealed tube and celite pad were washed with additional EtOAc. The filtrate was concentrated *in vacuo*. To this residue toluene (2.0~2.5 mL) and DMAP (1.5~10 equiv.) was added. The solution was then stirred at 80 ^{o}C for 15 min. Upon completion, the reaction was cooled to room temperature. The mixture was passed through a short pad of silica (in the column) using EtOAc/hexanes=1:1 as the eluent to give the product mixture. (The silica pad was washed with DCM/MeOH=10:1 to give the crude template solution for the template regeneration. See **7.2 Template Recovery**.) The filtrate was concentrated *in vacuo* and the crude reaction mixture was purified on preparative TLC using DCM as the eluent to afford the desired product **5a**.

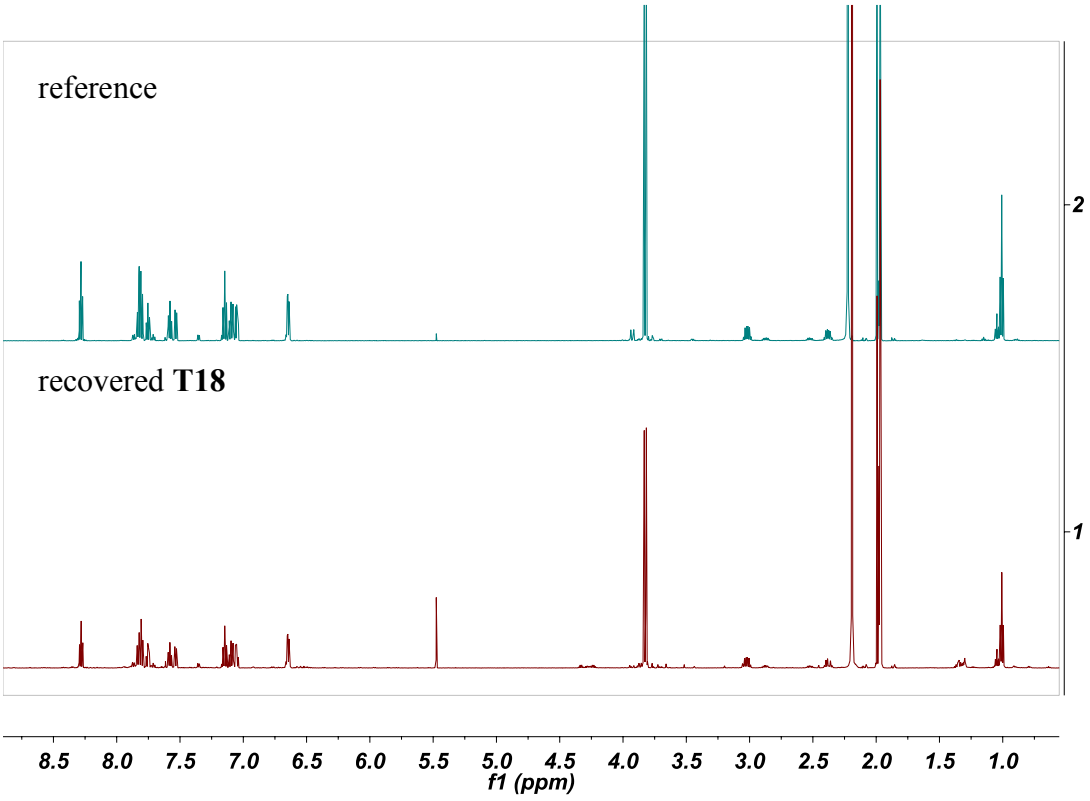
Caution: The operator should have appropriate protection all the time when the reaction is running due to the high pressure generated in the sealed reaction flask under high temperature.

7.2 Template Recovery

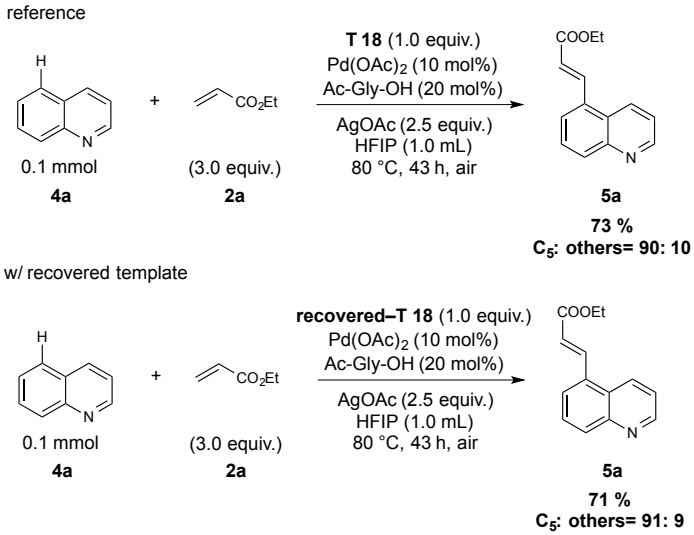
The crude template solution was concentrated *in vacuo* and dissolved in acetonitrile (3 mL). To this residue was added methanesulfonic acid (6.5 µl, 0.1 mmol) and the resulting mixture was heated at 60 ^{o}C for 2 h. Upon completion, the reaction mixture was cooled to room temperature.

The solvent was removed *in vacuo*. Water was added to the reaction mixture and extracted with DCM three times. The organic layer was dried with Na_2SO_4 and concentrated *in vacuo*. This crude mixture was dissolved in acetonitrile (3 mL). To this reaction methanesulfonic acid (3.0 µl, 0.046 mmol) was added and the resulting mixture was heated at 60 ^oC for 30 min. Upon completion, the reaction mixture was cooled to room temperature. The solvent was removed *in vacuo*. Water was added to the reaction mixture and extracted with DCM three times. The organic layer was dried with Na_2SO_4 and concentrated *in vacuo* to give template in 96 % yield (64.1 mg).

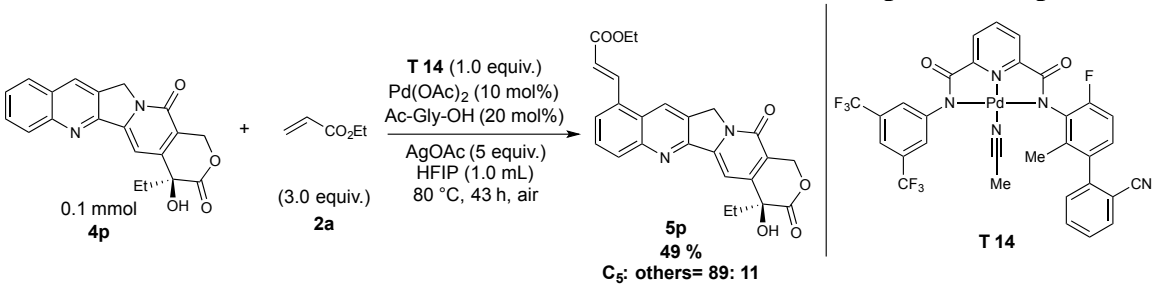
The ^{1}H NMR chart for the recovered T18



The Efficiency Test of Recovered T18

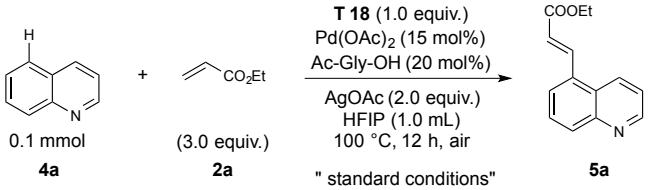


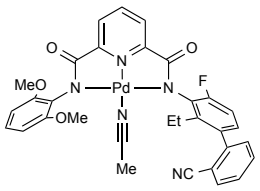
7.3 Procedure for Remote Site–selective C–H Olefination of Camptothecin 4p



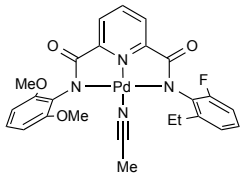
A reaction tube (15 mL) with magnetic stir bar was charged with **4p** (34.8 mg, 0.1 mmol), **T14** (73.2 mg, 0.1 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), Ac-Gly-OH (2.3 mg, 0.02 mmol), AgOAc (41.7 mg, 0.25 mmol), HFIP (1.0 ml) and **2a** (33.0 µl, 0.3 mmol) in air. The reaction tube was sealed and allowed to stir at 80 °C. After 24 h, additional AgOAc (41.7 mg, 0.25 mmol) was added to the reaction mixture and allowed to stir another 24 h at the same temperature. Upon completion, the reaction mixture was cooled to room temperature. The crude reaction mixture was diluted with EtOAc and filtered through a short pad of celite. The sealed tube and celite pad were washed with additional EtOAc. The filtrate was concentrated *in vacuo*. To this residue toluene (2.5 mL) and DMAP (1.5 equiv.) was added. The solution was then stirred at 80 ^{o}C for 15 min. Upon completion, the reaction was cooled to room temperature. The mixture was concentrated *in vacuo* and the crude reaction mixture was purified on preparative TLC using acetone/toluene (1:5) as the eluent to afford the desired product **5p**.

7.4 Control Experiments





T18

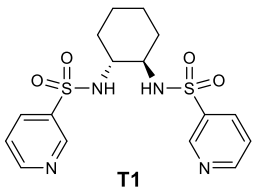


T19

entry	change from the " standard conditions"	yield (%) (C_5)	C_5 :others
1	none	69	92: 8
2	**T19**, instead of **T18**	0	
3	no $Pd(OAc)_2$	0	
4	no **T18**. 115 mol% $Pd(OAc)_2$, insteaed of 15 mol% $Pd(OAc)_2$	< 5	No selectivity
5	no Ac–Gly–OH	24	96: 4

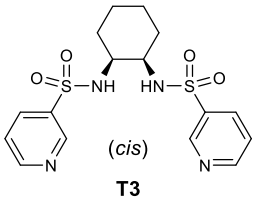
[a] The yield of the olefinated products, the C_5: others ratio of olefinated products were determined by ^1H NMR analysis of the unpurified reaction mixture using 1,3,5-trimethoxybenzene as the internal standard, the variance is estimated to be within 5%. Ac-Gly-OH: *N*-acetyl-glycine.

8. Characterization of Templates, Substrates and Products



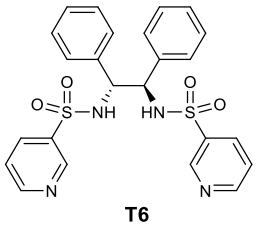
T1

N,*N*′-((1*R*,2*R*)-cyclohexane-1,2-diyl)bis(pyridine-3-sulfonamide) **T1**. Colorless solid, 0.974 g. Yield: 82%. TLC (CH_2Cl_2:MeOH, 90:10 v/v): RF = 0.49; ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.90 (dd, J = 2.4, 0.8 Hz, 2H), 8.79 (dd, J = 4.8, 1.6 Hz, 2H), 8.11 (ddd, J = 8.0, 2.4, 1.6 Hz, 2H), 7.80 (br, 1H), 7.79 (br, 1H), 7.59 (ddd, J = 8.0, 4.8, 0.8 Hz, 2H), 2.97–2.95 (m, 2H), 1.50–1.48 (m, 2H), 1.44–1.42 (m, 2H), 1.20–1.15 (m, 2H), 1.10–1.04 (m, 2H); ^{13}C NMR (151 MHz, DMSO-d_6): δ 152.79, 146.84, 138.12, 134.28, 124.15, 55.00, 30.54, 22.50; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{16}H_{21}N_4O_4S_2^+$, 397.0999; found 397.1001.



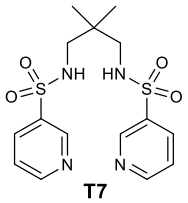
T3

N,*N*′-((1*R*,2*S*)-cyclohexane-1,2-diyl)bis(pyridine-3-sulfonamide) **T3**. Colorless solid, 0.927 g. Yield: 78%. TLC (CH_2Cl_2:MeOH, 90:10 v/v): RF = 0.46; ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.95 (dd, J = 2.4, 0.6 Hz, 2H), 8.78 (dd, J = 4.8, 1.6 Hz, 2H), 8.17 (ddd, J = 8.0, 2.4, 1.6 Hz, 2H), 7.73 (br, 1H), 7.72 (br, 1H), 7.60 (ddd, J = 8.0, 4.8, 0.7 Hz, 2H), 2.30–2.27 (m, 2H), 1.43–1.38 (m, 2H), 1.34–1.31 (m, 2H), 1.19–1.15 (m, 2H), 1.10–1.05 (m, 2H); ^{13}C NMR (151 MHz, DMSO-d_6): δ 152.82, 152.78, 146.97, 146.93, 138.07, 134.36, 124.16, 124.12, 53.82, 28.10, 20.92; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{16}H_{21}N_4O_4S_2^+$, 397.0999; found 397.1001.



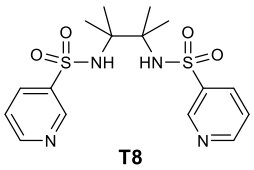
T6

N,*N*′-((1*R*,2*R*)-1,2-diphenylethane-1,2-diyl)bis(pyridine-3-sulfonamide) **T6**. White solid, 1.05 g. Yield: 71%. TLC (CH_2Cl_2:MeOH, 90:10 v/v): RF = 0.49; ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.90–8.86 (m, 2H), 8.48 (d, *J* = 1.8 Hz, 2H), 8.45 (dd, *J* = 4.8, 1.8 Hz, 2H), 7.63 (ddd, *J* = 7.8, 2.4, 1.8 Hz, 2H), 7.16 (ddd, *J* = 8.4, 4.8, 0.6 Hz, 2H), 6.83–6.75 (m, 10H), 4.58–4.54 (m, 2H); ^{13}C NMR (151 MHz, DMSO-d_6): δ 151.87, 151.83, 146.61, 146.57, 137.54, 136.68, 133.72, 133.67, 127.57, 127.38, 126.97, 123.31, 123.25, 62.24; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{24}H_{23}N_4O_4S_2^+$, 495.1155; found 495.1156.



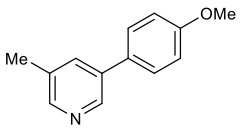
T7

N,*N*′-(2,2-dimethylpropane-1,3-diyl)bis(pyridine-3-sulfonamide) **T7**. White solid, 0.761 g. Yield: 66%. TLC (CH_2Cl_2:MeOH, 90:10 v/v): RF = 0.44; ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.93 (dd, *J* = 2.4, 0.6 Hz, 2H), 8.81 (dd, *J* = 4.8, 1.8 Hz, 2H), 8.15 (ddd, *J* = 8.0, 2.4, 1.8 Hz, 2H), 7.76 (br, 2H), 7.64 (ddd, *J* = 8.0, 4.8, 0.6 Hz, 2H), 2.60 (s, 4H), 0.78 (s, 6H); ^{13}C NMR (151 MHz, DMSO-d_6): δ 152.95, 152.91, 146.97, 146.93, 137.04, 134.41, 124.29, 124.24, 50.52, 35.05, 22.51, 22.50; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{15}H_{21}N_4O_4S_2^+$, 385.0999; found 385.0999.



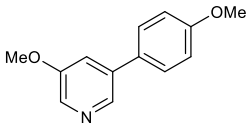
T8

N,*N*′-(2,3-dimethylbutane-2,3-diyl)bis(pyridine-3-sulfonamide) **T8**. Pale yellow solid, 388 mg. Yield: 53%. TLC (CH_2Cl_2:MeOH, 90:10 v/v): RF = 0.46; ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.99 (d, *J* = 2.4, Hz, 2H), 8.81 (dd, *J* = 4.8, 1.6 Hz, 2H), 8.22 (ddd, *J* = 8.0, 2.4, 1.6 Hz, 2H), 7.65 (ddd, *J* = 8.0, 4.8, 0.7 Hz, 2H), 7.58 (br, 2H), 1.07 (s, 12H); ^{13}C NMR (151 MHz, DMSO-d_6): δ 152.83, 146.93, 140.26, 134.29, 124.36, 62.14, 22.14; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{16}H_{23}N_4O_4S_2^+$, 399.1155; found 399.1155.



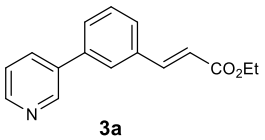
1m

3-(4-methoxyphenyl)-5-methylpyridine **1m**. TLC (Hexane:EtOAc, 50:50 v/v): RF = 0.41; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.62 (d, *J* = 2.4 Hz, 1H), 8.38 (d, *J* = 1.8 Hz, 1H), 7.64–7.62 (m, 1H), 7.51 (d, *J* = 9.0 Hz, 2H), 7.00 (d, *J* = 9.0 Hz, 2H), 3.86 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 159.63, 148.39, 145.20, 135.71, 134.46, 132.87, 130.35, 128.18, 114.45, 55.35, 18.46; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{13}H_{14}NO^+$, 200.1070; found 200.1064.



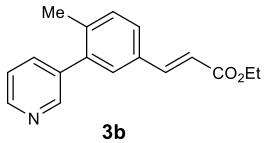
1o

3-methoxy-5-(4-methoxyphenyl)pyridine **1o**. TLC (Hexane:EtOAc, 50:50 v/v): RF = 0.39; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.42 (d, *J* = 1.8 Hz, 1H), 8.25 (d, *J* = 3.0 Hz, 1H), 7.51 (d, *J* = 9.0 Hz, 2H), 7.32 (dd, *J* = 3.0, 1.8 Hz, 1H), 7.00 (d, *J* = 9.0 Hz, 2H), 3.91 (s, 3H), 3.86 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 159.78, 155.71, 140.43, 136.93, 135.37, 130.04, 128.29, 118.63, 114.47, 55.58, 55.35; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{13}H_{14}NO_2^+$, 216.1019; found 216.1019.



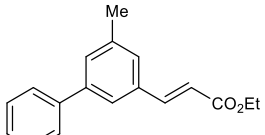
3a

ethyl (*E*)-3-(3-(pyridin-3-yl)phenyl)acrylate **3a**. Pale yellow solid, 16.3 mg. Yield: 64%. TLC (Hexane:EtOAc, 50:50 v/v): RF = 0.34; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.85 (s, 1H), 8.62 (d, *J* = 3.6 Hz, 1H), 7.87 (ddd, *J* = 7.8, 2.4, 1.8 Hz, 1H), 7.74 (d, *J* = 16.2 Hz, 1H), 7.70 (s, 1H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.50 (t, *J* = 7.8 Hz, 1H), 7.38 (dd, *J* = 7.8, 4.8 Hz, 1H), 6.51 (d, *J* = 16.2 Hz, 1H), 4.28 (q, *J* = 7.2 Hz, 2H), 1.34 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.74, 148.86, 148.24, 143.93, 138.59, 135.91, 135.31, 134.33, 129.62, 128.85, 127.48, 126.78, 123.58, 119.12, 60.60, 14.29; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{16}H_{16}NO_2^+$, 254.1176; found 254.1177.



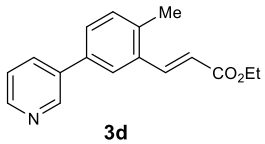
3b

ethyl (*E*)-3-(4-methyl-3-(pyridin-3-yl)phenyl)acrylate **3b**. Pale yellow solid, 16.0 mg. Yield: 60%. TLC (Hexane:EtOAc, 50:50 v/v): RF = 0.41; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.62 (dd, *J* = 4.8, 1.8 Hz, 1H), 8.59 (dd, *J* = 2.4, 1.2 Hz, 1H), 7.68 (d, *J* = 16.2 Hz, 1H), 7.65 (ddd, *J* = 7.8, 1.8, 1.2 Hz, 1H), 7.47 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.38–7.36 (m, 2H), 7.32 (d, *J* = 8.4 Hz, 1H), 6.43 (d, *J* = 16.2 Hz, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 2.28 (s, 3H), 1.33 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.94, 149.80, 148.51, 143.88, 138.72, 138.18, 136.67, 136.34, 132.49, 131.17, 129.49, 127.52, 123.10, 118.05, 60.48, 20.39, 14.30; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{17}H_{18}NO_2^+$, 268.1332; found 268.1337.



3c

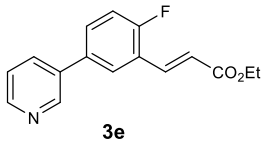
ethyl (*E*)-3-(3-methyl-5-(pyridin-3-yl)phenyl)acrylate **3c**. White solid, 16.0 mg. Yield: 60%. TLC (Hexane:EtOAc, 50:50 v/v): RF = 0.39; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.84 (d, *J* = 1.4 Hz, 1H), 8.62 (d, *J* = 4.0 Hz, 1H), 7.87 (dt, *J* = 7.9, 1.8 Hz, 1H), 7.72 (d, *J* = 16.0 Hz, 1H), 7.52 (s, 1H), 7.40 (s, 1H), 7.39 (s, 1H), 7.38 (dd, *J* = 7.9, 4.8 Hz, 1H), 6.50 (d, *J* = 16.0 Hz, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 2.45 (s, 3H), 1.35 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.85, 148.78, 148.27, 144.14, 141.74, 139.43, 138.56, 135.27, 134.37, 129.76, 128.24, 124.11, 123.56, 118.89, 60.57, 21.41, 14.31; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{17}H_{18}NO_2^+$, 268.1332; found 268.1328.



3d

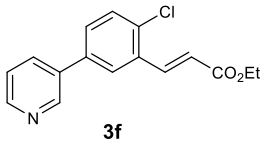
ethyl (*E*)-3-(2-methyl-5-(pyridin-3-yl)phenyl)acrylate **3d**. Pale yellow solid, 16.3 mg. Yield: 61%. TLC (Hexane:EtOAc, 50:50 v/v): RF = 0.39; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.83 (d, *J* = 2.4 Hz, 1H), 8.59 (dd, *J* = 4.8, 1.2 Hz, 1H), 8.00 (d, *J* = 16.2 Hz, 1H), 7.86 (dt, *J* = 7.8, 1.8 Hz, 1H), 7.74 (d, *J* = 1.2 Hz, 1H), 7.49 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.36 (dd, *J* = 7.8, 4.8 Hz, 1H), 7.32

(d, J = 7.8 Hz, 1H), 6.44 (d, J = 16.2 Hz, 1H), 4.28 (q, J = 7.2 Hz, 2H), 2.48 (s, 3H), 1.35 (t, J = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.82, 148.57, 148.10, 141.84, 137.51, 135.99, 135.94, 134.20, 134.14, 131.55, 128.44, 125.05, 123.54, 120.10, 60.59, 19.52, 14.30; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{17}H_{18}NO_2^+$, 268.1332; found 268.1335.



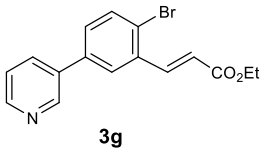
3e

ethyl (*E*)-3-(2-fluoro-5-(pyridin-3-yl)phenyl)acrylate **3e**. Pale yellow solid, 17.9 mg. Yield: 66%. TLC (Hexane:EtOAc, 50:50 v/v): RF = 0.32; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.80 (d, J = 1.8 Hz, 1H), 8.61 (dd, J = 4.8, 1.8 Hz, 1H), 7.84 (d, J = 16.2 Hz, 1H), 7.83 (dt, J = 7.8, 1.8 Hz, 1H), 7.71 (dd, J = 6.6, 2.4 Hz, 1H), 7.56–7.53 (m, 1H), 7.38 (dd, J = 7.8, 4.8 Hz, 1H), 7.22 (dd, J = 10.2, 8.4 Hz, 1H), 6.61 (d, J = 16.2 Hz, 1H), 4.28 (q, J = 7.2 Hz, 2H), 1.34 (t, J = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.56, 161.25 (d, $J_{C\text{-}F}$ = 256.7 Hz), 148.87, 148.07, 136.70 (d, $J_{C\text{-}F}$ = 2.4 Hz), 135.11, 134.47 (d, $J_{C\text{-}F}$ = 3.8 Hz), 134.21, 130.20 (d, $J_{C\text{-}F}$ = 8.9 Hz), 127.77 (d, $J_{C\text{-}F}$ = 3.3 Hz), 123.60, 123.14 (d, $J_{C\text{-}F}$ = 12.5 Hz), 121.68 (d, $J_{C\text{-}F}$ = 6.8 Hz), 116.97 (d, $J_{C\text{-}F}$ = 22.7 Hz), 60.72, 14.27; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{16}H_{15}FNO_2^+$, 272.1081; found 272.1081.



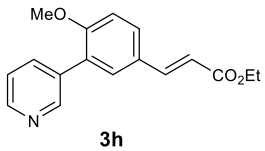
3f

ethyl (*E*)-3-(2-chloro-5-(pyridin-3-yl)phenyl)acrylate **3f**. White solid, 14.4 mg. Yield: 50%. TLC (Hexane:EtOAc, 50:50 v/v): RF = 0.38; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.82 (dd, J = 2.4, 0.8 Hz, 1H), 8.63 (dd, J = 4.8, 2.4 Hz, 1H), 8.11 (d, J = 16.0 Hz, 1H), 7.85 (ddd, J = 7.8, 2.4, 1.6 Hz, 1H), 7.79 (d, J = 2.0 Hz, 1H), 7.52 (d, J = 0.5 Hz, 1H), 7.51 (d, J = 2.0 Hz, 1H), 7.39 (ddd, J = 7.8, 4.8, 0.8 Hz, 1H), 6.52 (d, J = 16.0 Hz, 1H), 4.29 (q, J = 7.1 Hz, 2H), 1.35 (t, J = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.26, 149.14, 148.07, 139.96, 136.99, 135.01, 134.82, 134.22, 133.43, 130.83, 129.46, 126.21, 123.64, 121.66, 60.80, 14.28; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{16}H_{15}ClNO_2^+$, 288.0786; found 288.0788.



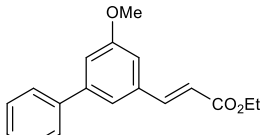
3g

ethyl (*E*)-3-(2-bromo-5-(pyridin-3-yl)phenyl)acrylate **3g**. White solid, 20.0 mg. Yield: 60%. TLC (Hexane:EtOAc, 50:50 v/v): RF = 0.38; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.83 (d, *J* = 2.4 Hz, 1H), 8.64 (dd, *J* = 4.2, 1.2 Hz, 1H), 8.08 (d, *J* = 16.2 Hz, 1H), 7.86 (dt, *J* = 7.8, 1.8 Hz, 1H), 7.77 (d, *J* = 2.4 Hz, 1H), 7.72 (d, *J* = 8.4 Hz, 1H), 7.43 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.39 (dd, *J* = 7.8, 4.8 Hz, 1H), 6.48 (d, *J* = 16.2 Hz, 1H), 4.30 (q, *J* = 7.2 Hz, 2H), 1.36 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.18, 149.21, 148.05, 142.51, 137.65, 135.30, 135.03, 134.18, 134.10, 129.63, 126.34, 125.07, 123.67, 121.84, 60.81, 14.29; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{16}H_{15}BrNO_2^+$, 332.0281; found 332.0280.



3h

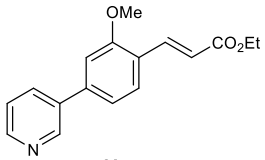
ethyl (*E*)-3-(4-methoxy-3-(pyridin-3-yl)phenyl)acrylate **3h**. White solid, 17.3 mg. Yield: 61%. TLC (Hexane:EtOAc, 50:50 v/v): RF = 0.31; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.75 (d, *J* = 1.8 Hz, 1H), 8.58 (dd, *J* = 4.8, 1.2 Hz, 1H), 7.83 (dt, *J* = 7.8, 1.8 Hz, 1H), 7.68 (d, *J* = 16.2 Hz, 1H), 7.54 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.49 (d, *J* = 2.4 Hz, 1H), 7.34 (dd, *J* = 7.8, 4.8 Hz, 1H), 7.01 (d, *J* = 8.4 Hz, 1H), 6.35 (d, *J* = 16.2 Hz, 1H), 4.25 (q, *J* = 7.2 Hz, 2H), 3.86 (s, 3H), 1.33 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 167.11, 158.19, 150.15, 148.32, 143.68, 136.68, 133.41, 130.24, 129.75, 127.63, 127.51, 122.94, 116.50, 111.43, 60.39, 55.73, 14.32; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{17}H_{18}NO_3^+$, 284.1281; found 284.1280.



3i

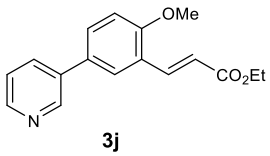
ethyl (*E*)-3-(3-methoxy-5-(pyridin-3-yl)phenyl)acrylate **3i**. Colorless liquid, 2.8 mg. Yield: 10%. TLC (Hexane:EtOAc, 50:50 v/v): RF = 0.36; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.84 (d, *J* = 4.8 Hz, 1H), 8.62 (dd, *J* = 4.8, 1.8 Hz, 1H), 7.87 (dt, *J* = 7.8, 1.8 Hz, 1H), 7.71 (d, *J* = 15.6 Hz, 1H), 7.37 (dd, *J* = 7.8, 4.8 Hz, 1H), 7.31 (s, 1H), 7.12 (s, 1H), 7.09 (s, 1H), 6.50 (d, *J* = 15.6 Hz, 1H), 4.28

(q, J = 7.2 Hz, 2H), 3.90 (s, 3H), 1.35 (t, J = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.74, 160.45, 148.95, 148.23, 143.98, 139.87, 136.58, 135.92, 134.45, 123.60, 119.68, 119.35, 114.99, 112.20, 60.65, 55.52, 14.31; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{17}H_{18}NO_3^+$, 284.1281; found 284.1274.



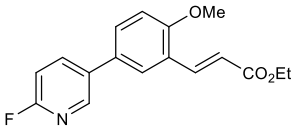
3i-*para*

ethyl (*E*)-3-(2-methoxy-4-(pyridin-3-yl)phenyl)acrylate **3i-*para***. Colorless liquid, 8.0 mg. Yield: 28%. TLC (Hexane:EtOAc, 50:50 v/v): RF = 0.26; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.86 (d, J = 2.4 Hz, 1H), 8.62 (dd, J = 4.8, 1.2 Hz, 1H), 8.00 (d, J = 16.2 Hz, 1H), 7.89 (ddd, J = 7.8, 2.4, 1.8 Hz, 1H), 7.61 (d, J = 8.4 Hz, 1H), 7.38 (dd, J = 7.8, 4.8 Hz, 1H), 7.18 (dd, J = 7.8, 1.8 Hz, 1H), 7.09 (d, J = 1.2 Hz, 1H), 6.58 (d, J = 16.2 Hz, 1H), 4.28 (q, J = 7.2 Hz, 2H), 3.97 (s, 3H), 1.35 (t, J = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 167.39, 158.71, 149.00, 148.18, 140.90, 139.23, 136.01, 134.30, 129.58, 123.59, 123.29, 119.55, 119.26, 109.79, 60.42, 55.63, 14.36; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{17}H_{18}NO_3^+$, 284.1281; found 284.1273.



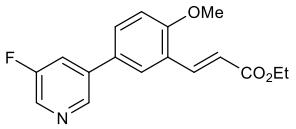
3j

ethyl (*E*)-3-(2-methoxy-5-(pyridin-3-yl)phenyl)acrylate **3j**. White solid, 23.8 mg. Yield: 84%. TLC (Hexane:EtOAc, 50:50 v/v): RF = 0.29; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.81 (d, J = 2.4 Hz, 1H), 8.57 (dd, J = 4.8, 1.2 Hz, 1H), 8.01 (d, J = 16.2 Hz, 1H), 7.83 (ddd, J = 7.8, 2.4, 1.8 Hz, 1H), 7.70 (d, J = 2.4 Hz, 1H), 7.56 (dd, J = 9.0, 2.4 Hz, 1H), 7.35 (ddd, J = 7.8, 4.8, 1.2 Hz, 1H), 7.02 (d, J = 8.4 Hz, 1H), 6.60 (d, J = 16.2 Hz, 1H), 4.27 (q, J = 7.2 Hz, 2H), 3.94 (s, 3H), 1.34 (t, J = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 167.26, 158.32, 148.23, 147.92, 139.51, 135.67, 133.87, 130.36, 129.86, 127.55, 124.08, 123.52, 119.62, 111.77, 60.44, 55.70, 14.34; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{17}H_{18}NO_3^+$, 284.1281; found 284.1286.



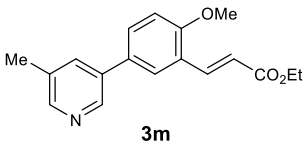
3k

ethyl (*E*)-3-(5-(6-fluoropyridin-3-yl)-2-methoxyphenyl)acrylate **3k**. White solid, 19.6 mg. Yield: 65%. TLC (Hexane:EtOAc, 50:50 v/v): RF = 0.70; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.37 (s, 1H), 8.00 (d, *J* = 16.2 Hz, 1H), 7.92 (td, *J* = 8.4, 2.4 Hz, 1H), 7.64 (d, *J* = 1.8 Hz, 1H), 7.50 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.02 (d, *J* = 8.4 Hz, 1H), 6.99 (dd, *J* = 9.0, 2.4 Hz, 1H), 6.59 (d, *J* = 16.2 Hz, 1H), 4.27 (q, *J* = 7.2 Hz, 2H), 3.94 (s, 3H), 1.34 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 167.24, 162.94 (d, J_{C-F} = 239.2 Hz), 158.35, 145.41 (d, J_{C-F} = 14.6 Hz), 139.41, 139.32 (d, J_{C-F} = 7.9 Hz), 133.94 (d, J_{C-F} = 4.5 Hz), 129.79, 129.27, 127.48, 124.15, 119.78, 111.84, 109.47 (d, J_{C-F} = 37.6 Hz), 60.50, 55.75, 14.36; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{17}H_{17}FNO_3^+$, 302.1187; found 302.1188.



3l

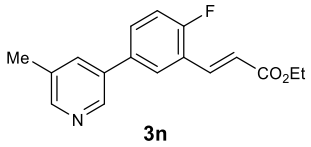
ethyl (*E*)-3-(5-(5-fluoropyridin-3-yl)-2-methoxyphenyl)acrylate **3l**. Pale yellow solid, 21.2 mg. Yield: 70%. TLC (Hexane:EtOAc, 50:50 v/v): RF = 0.56; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.63 (t, *J* = 1.7 Hz, 1H), 8.43 (d, *J* = 2.7 Hz, 1H), 8.00 (d, *J* = 16.2 Hz, 1H), 7.69 (d, *J* = 2.4 Hz, 1H), 7.56–7.53 (m, 2H), 7.03 (d, *J* = 8.6 Hz, 1H), 6.60 (d, *J* = 16.2 Hz, 1H), 4.27 (q, *J* = 7.2 Hz, 2H), 3.94 (s, 3H), 1.34 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 167.15, 159.66 (d, J_{C-F} = 256.7 Hz), 158.68, 143.67 (d, J_{C-F} = 4.5 Hz),139.25, 137.30 (d, J_{C-F} = 4.5 Hz), 136.37 (d, J_{C-F} = 22.7 Hz), 129.90, 128.87, 127.60, 124.25, 120.5 (d, J_{C-F} = 18.1 Hz), 119.89, 111.86, 60.47, 55.73, 14.32; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{17}H_{17}FNO_3^+$, 302.1187; found 302.1190.



3m

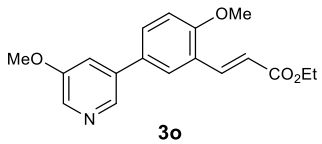
ethyl (*E*)-3-(2-methoxy-5-(5-methylpyridin-3-yl)phenyl)acrylate **3m**. White solid, 21.6 mg. Yield: 72%. TLC (Hexane:EtOAc, 50:50 v/v): RF = 0.28; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.60 (d, *J* = 1.8 Hz, 1H), 8.40 (d, *J* = 2.4 Hz, 1H), 8.01 (d, *J* = 16.2 Hz, 1H), 7.69 (d, *J* = 2.4 Hz, 1H),

7.63-7.62 (m, 1H), 7.55 (dd, J = 8.4, 2.4 Hz, 1H), 7.00 (d, J = 8.4 Hz, 1H), 6.60 (d, J = 16.2 Hz, 1H), 4.27 (q, J = 7.2 Hz, 2H), 3.93 (s, 3H), 2.40 (s, 3H), 1.34 (t, J = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 167.25, 158.21, 148.72, 145.07, 139.54, 135.13, 134.47, 133.00, 130.43, 129.85, 127.47, 123.98, 119.49, 111.69, 60.41, 55.67, 18.43, 14.33; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{18}H_{20}NO_3^+$, 298.1438; found 298.1434.



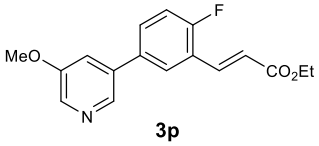
3n

ethyl (*E*)-3-(2-fluoro-5-(5-methylpyridin-3-yl)phenyl)acrylate **3n**. Pale yellow solid, 20.1 mg. Yield: 70%. TLC (Hexane:EtOAc, 50:50 v/v): RF = 0.40; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.60 (s, 1H), 8.45 (d, 1H), 7.84 (d, J = 16.2 Hz, 1H), 7.70 (dd, J = 6.8, 2.3 Hz, 1H), 7.63 (s, 1H), 7.55–7.52 (m, 1H), 7.20 (dd, J = 10.1, 8.5 Hz, 1H), 6.61 (d, J = 16.2 Hz, 1H), 4.28 (q, J = 7.1 Hz, 2H), 2.41 (s, 3H), 1.34 (t, J = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.58, 161.18 (d, $J_{C\text{-}F}$ = 255.6 Hz), 149.36, 145.23, 136.75 (d, $J_{C\text{-}F}$ = 2.4 Hz), 134.81, 134.63, 134.57 (d, $J_{C\text{-}F}$ = 3.5 Hz), 133.18, 130.20 (d, $J_{C\text{-}F}$ = 8.9 Hz), 127.70 (d, $J_{C\text{-}F}$ = 3.2 Hz), 123.06 (d, $J_{C\text{-}F}$ = 12.2 Hz), 121.57 (d, $J_{C\text{-}F}$ = 6.6 Hz), 116.88 (d, $J_{C\text{-}F}$ = 22.5 Hz), 60.71, 18.43, 14.27; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{17}H_{17}FNO_2^+$, 286.1238; found 286.1237.



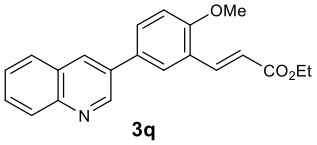
3o

ethyl (*E*)-3-(2-methoxy-5-(5-methoxypyridin-3-yl)phenyl)acrylate **3o**. Pale yellow solid, 26.6 mg. Yield: 85%. TLC (Hexane:EtOAc, 50:50 v/v): RF = 0.30; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.41 (d, J = 1.8 Hz, 1H), 8.27 (d, J = 3.0 Hz, 1H), 8.00 (d, J = 16.2 Hz, 1H), 7.69 (d, J = 2.4 Hz, 1H), 7.55 (dd, J = 9.0, 2.4 Hz, 1H), 7.31 (dd, J = 3.0, 1.8 Hz, 1H), 7.01 (d, J = 9.0 Hz, 1H), 6.60 (d, J = 16.2 Hz, 1H), 4.27 (q, J = 7.2 Hz, 2H), 3.93 (s, 3H), 3.92 (s, 3H), 1.34 (t, J = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 167.24, 158.36, 155.73, 140.29, 139.49, 136.33, 135.83, 130.17, 129.97, 127.62, 124.00, 119.60, 118.55, 111.70, 60.42, 55.69, 55.62, 14.32; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{18}H_{20}NO_4^+$, 314.1387; found 314.1387.



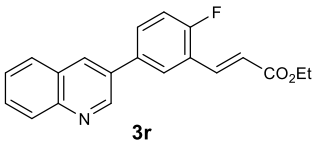
3p

ethyl (*E*)-3-(2-fluoro-5-(5-methoxypyridin-3-yl)phenyl)acrylate **3p**. Pale yellow solid, 19.0 mg. Yield: 63%. TLC (Hexane:EtOAc, 50:50 v/v): RF = 0.40; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.41 (s, 1H), 8.33 (s, 1H), 7.84 (d, J = 16.2 Hz, 1H), 7.70 (dd, J = 6.8, 2.3 Hz, 1H), 7.56–7.53 (m, 1H), 7.31 (dd, J = 2.5, 2.0 Hz, 1H), 7.21 (dd, J = 10.1, 8.6 Hz, 1H), 6.61 (d, J = 16.2 Hz, 1H), 4.29 (q, J = 7.1 Hz, 2H), 3.93 (s, 3H), 1.35 (t, J = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.58, 161.29 (d, $J_{C\text{-}F}$ = 255.8 Hz), 155.78, 140.40, 136.71 (d, $J_{C\text{-}F}$ = 1.5 Hz), 136.49, 135.82, 134.34 (d, $J_{C\text{-}F}$ = 3.5 Hz), 130.33 (d, $J_{C\text{-}F}$ = 8.9 Hz), 127.88 (d, $J_{C\text{-}F}$ = 3.0 Hz), 123.12 (d, $J_{C\text{-}F}$ = 12.2 Hz), 121.71 (d, $J_{C\text{-}F}$ = 6.6 Hz), 118.94, 116.94 (d, $J_{C\text{-}F}$ = 22.5 Hz), 60.74, 55.70, 14.29; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{17}H_{17}FNO_3^+$, 302.1187; found 302.1187.



3q

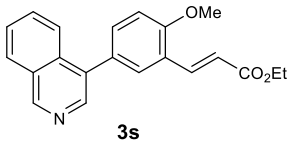
ethyl (*E*)-3-(2-methoxy-5-(quinolin-3-yl)phenyl)acrylate **3q**. Pale yellow solid, 24.7 mg. Yield: 74%. TLC (Hexane:EtOAc, 50:50 v/v): RF = 0.44; ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.14 (d, J = 2.4 Hz, 1H), 8.24 (d, J = 2.4 Hz, 1H), 8.13 (d, J = 8.4 Hz, 1H), 8.05 (d, J = 16.2 Hz, 1H), 7.86 (d, J = 8.4 Hz, 1H), 7.83 (d, J = 2.4 Hz, 1H), 7.72–7.69 (m, 1H), 7.68 (dd, J = 8.4, 2.4 Hz, 1H), 7.57 (ddd, J = 7.8, 7.2, 0.6 Hz, 1H), 7.06 (d, J = 8.4 Hz, 1H), 6.64 (d, J = 16.2 Hz, 1H), 4.28 (q, J = 7.2 Hz, 2H), 3.95 (s, 3H), 1.35 (t, J = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 167.26, 158.33, 149.52, 147.14, 139.53, 132.80, 132.53, 130.36, 130.11, 129.26, 129.18, 127.96, 127.85, 127.77, 127.04, 124.18, 119.66, 111.84, 60.45, 55.72, 14.34; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{21}H_{20}NO_3^+$, 334.1438; found 334.1436.



3r

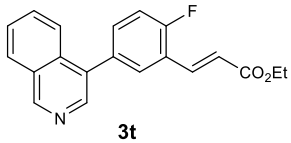
ethyl (*E*)-3-(2-fluoro-5-(quinolin-3-yl)phenyl)acrylate **3r**. Pale yellow solid, 17.7 mg. Yield: 55%. TLC (Hexane:EtOAc, 50:50 v/v): RF = 0.65; ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.13 (d, J =

2.2 Hz, 1H), 8.27 (d, J = 2.2 Hz, 1H), 8.15 (d, J = 8.5 Hz, 1H), 7.89 (d, J = 7.3 Hz, 1H), 7.88 (d, J = 16.2 Hz, 1H), 7.84 (dd, J = 6.8, 2.3 Hz, 1H), 7.75 (ddd, J = 8.3, 6.9, 1.4 Hz, 1H), 7.70–7.67 (m, 1H), 7.61 (ddd, J = 8.0, 6.9, 1.0 Hz, 1H), 7.27 (dd, J = 10.1, 8.5 Hz, 1H), 6.66 (d, J = 16.2 Hz, 1H), 4.30 (q, J = 7.1 Hz, 2H), 1.36 (t, J = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.60, 161.29 (d, $J_{C\text{-}F}$ = 256.1 Hz), 149.36, 147.43, 136.76 (d, $J_{C\text{-}F}$ = 2.4 Hz), 134.55 (d, $J_{C\text{-}F}$ = 3.5 Hz), 133.28, 132.27, 130.47 (d, $J_{C\text{-}F}$ = 8.9 Hz), 129.72, 129.27, 128.04 (d, $J_{C\text{-}F}$ = 3.5 Hz), 127.96, 127.82, 127.28, 123.28 (d, $J_{C\text{-}F}$ = 12.4 Hz), 121.76 (d, $J_{C\text{-}F}$ = 6.6 Hz), 117.08 (d, $J_{C\text{-}F}$ = 22.5 Hz), 60.76, 14.30; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{20}H_{17}FNO_2^+$, 322.1238; found 322.1239.



3s

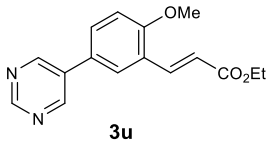
ethyl (*E*)-3-(5-(isoquinolin-4-yl)-2-methoxyphenyl)acrylate **3s**. Colorless liquid, 27.7 mg. Yield: 83%. TLC (Hexane:EtOAc, 50:50 v/v): RF = 0.35; ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.24 (s, 1H), 8.46 (s, 1H), 8.05 (d, J = 16.2 Hz, 1H), 8.04 (d, J = 7.8 Hz, 1H), 7.88 (d, J = 8.5 Hz, 1H), 7.68 (t, J = 6.9 Hz, 1H), 7.65 (d, J = 2.2 Hz, 1H), 7.63 (t, J = 7.5 Hz, 1H), 7.49 (dd, J = 8.5, 2.2 Hz, 1H), 7.08 (d, J = 8.5 Hz, 1H), 6.57 (d, J = 16.2 Hz, 1H), 4.25 (q, J = 7.1 Hz, 2H), 3.98 (s, 3H), 1.32 (t, J = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 167.30, 158.09, 151.93, 142.75, 139.52, 134.22, 132.83, 132.26, 130.65, 130.45, 129.32, 128.40, 127.93, 127.20, 124.52, 123.63, 119.52, 111.39, 60.39, 55.70, 14.31; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{21}H_{20}NO_3^+$, 334.1438; found 334.1440.



3t

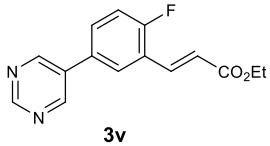
ethyl (*E*)-3-(2-fluoro-5-(isoquinolin-4-yl)phenyl)acrylate **3t**. Colorless oil, 16.7 mg. Yield: 52%. TLC (Hexane:EtOAc, 50:50 v/v): RF = 0.44; ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.29 (s, 1H), 8.47 (s, 1H), 8.06 (d, J = 8.2 Hz, 1H), 7.87 (d, J = 16.2 Hz, 1H), 7.82 (d, J = 8.4 Hz, 1H), 7.70 (ddd, J = 8.3, 6.8, 1.4 Hz, 1H), 7.68–7.65 (m, 2H), 7.50–7.48 (m, 1H), 7.27 (dd, J = 10.3, 8.4 Hz, 1H), 6.59 (d, J = 16.2 Hz, 1H), 4.27 (q, J = 7.1 Hz, 2H), 1.33 (t, J = 7.1 Hz, 3H); ^{13}C NMR (151 MHz,

$CDCl_3$): δ 166.61, 161.06 (d, J_{C-F} = 256.8 Hz), 152.48, 142.81, 136.72 (d, J_{C-F} = 1.7 Hz), 134.02, 133.47 (d, J_{C-F} = 3.6 Hz), 133.09 (d, J_{C-F} = 8.9 Hz), 131.61, 130.92, 130.55 (d, J_{C-F} = 2.7 Hz), 128.41, 128.05, 127.40, 124.24, 122.81 (d, J_{C-F} = 12.2 Hz), 121.62 (d, J_{C-F} = 6.6 Hz), 116.56 (d, J_{C-F} = 22.3 Hz), 60.70, 14.27; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{20}H_{17}FNO_2^+$, 322.1238; found 322.1239.



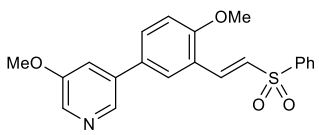
3u

ethyl (*E*)-3-(2-methoxy-5-(pyrimidin-5-yl)phenyl)acrylate **3u**. White solid, 20.2 mg. Yield: 71%. TLC (Hexane:EtOAc, 50:50 v/v): RF = 0.26; ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.17 (s, 1H), 8.91 (s, 2H), 7.99 (d, *J* = 16.2 Hz, 1H), 7.69 (d, *J* = 2.4 Hz, 1H), 7.55 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.06 (d, *J* = 8.4 Hz, 1H), 6.60 (d, *J* = 16.2 Hz, 1H), 4.27 (q, *J* = 7.2 Hz, 2H), 3.95 (s, 3H), 1.34 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 167.08, 158.88, 157.19, 154.44, 139.07, 133.44, 129.65, 127.34, 126.70, 124.51, 120.10, 112.07, 60.50, 55.75, 14.31; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{16}H_{17}N_2O_3^+$, 285.1234; found 285.1235.



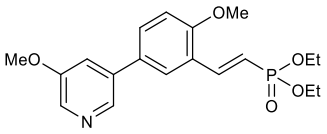
3v

ethyl (*E*)-3-(2-fluoro-5-(pyrimidin-5-yl)phenyl)acrylate **3v**. Pale yellow solid, 10.9 mg. Yield: 40%. TLC (Hexane:EtOAc, 50:50 v/v): RF = 0.37; ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.23 (s, 1H), 8.93 (s, 2H), 7.84 (d, *J* = 16.2 Hz, 1H), 7.71 (dd, *J* = 6.6, 2.4 Hz, 1H), 7.57–7.54 (m, 1H), 7.29–7.27 (m, 1H), 6.63 (d, *J* = 16.2 Hz, 1H), 4.29 (q, *J* = 7.2 Hz, 2H), 1.34 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.41, 161.71 (d, J_{C-F} = 256.7 Hz), 157.82, 154.76, 136.25 (d, J_{C-F} = 1.5 Hz), 132.98, 130.98 (d, J_{C-F} = 3.5 Hz), 130.02 (d, J_{C-F} = 9.2 Hz), 127.74 (d, J_{C-F} = 3.3 Hz), 123.70 (d, J_{C-F} = 12.7 Hz), 122.26 (d, J_{C-F} = 6.6 Hz), 117.48 (d, J_{C-F} = 22.8 Hz), 60.82, 14.27; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{15}H_{14}FN_2O_2^+$, 273.1034; found 273.1036.



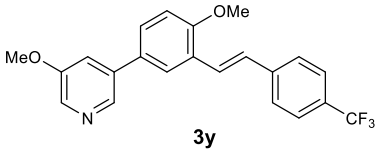
3w

(*E*)-3-methoxy-5-(4-methoxy-3-(2-(phenylsulfonyl)vinyl)phenyl)pyridine **3w**. Pale yellow solid, 31.6 mg. Yield: 83%. TLC (EtOAc): RF = 0.58; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.38 (d, *J* = 1.8 Hz, 1H), 8.28 (d, *J* = 3.0 Hz, 1H), 7.98–7.96 (m, 2H), 7.94 (d, *J* = 15.6 Hz, 1H), 7.62–7.58 (m, 3H), 7.56–7.53 (m, 2H), 7.29 (dd, *J* = 2.7, 2.0 Hz, 1H), 7.15 (d, *J* = 15.6 Hz, 1H), 7.03 (d, *J* = 8.6 Hz, 1H), 3.94 (s, 3H), 3.92 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 158.81, 155.75, 140.92, 140.20, 137.94, 136.09, 135.91, 133.21, 131.03, 130.38, 129.43, 129.26, 128.73, 127.64, 121.77, 118.50, 111.89, 55.79, 55.67; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{21}H_{20}NO_4S^+$, 382.1108; found 382.1105.



3x

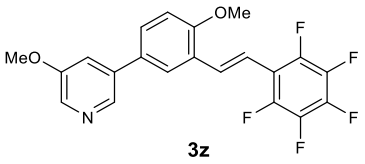
diethyl (*E*)-(2-methoxy-5-(5-methoxypyridin-3-yl)styryl)phosphonate **3x**. Colorless liquid, 36.3 mg. Yield: 96%. TLC (EtOAc): RF = 0.21; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.42 (s, 1H), 8.28 (d, *J* = 2.4 Hz, 1H), 7.83 (dd, *J* = 23.6, 17.8 Hz, 1H), 7.68 (d, *J* = 2.4 Hz, 1H), 7.56 (dd, *J* = 8.5, 2.4 Hz, 1H), 7.32 (dd, *J* = 2.6, 2.4 Hz, 1H), 7.01 (d, *J* = 8.5 Hz, 1H), 6.43 (dd, *J* = 19.1, 17.8 Hz, 1H), 4.18–4.12 (m, 4H), 3.93 (s, 3H), 3.92 (s, 3H), 1.36 (t, *J* = 6.9 Hz, 6H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 158.17, 155.77, 143.50 (d, J_{C-P} = 7.9 Hz), 140.28, 136.39, 135.83, 130.13, 129.99, 127.30, 124.35 (d, J_{C-P} = 23.3 Hz), 118.62, 115.32 (d, J_{C-P} = 190.1 Hz), 111.76, 61.83 (d, J_{C-P} = 5.6 Hz), 55.68, 55.67, 16.41 (d, J_{C-P} = 6.5 Hz); HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{19}H_{25}NO_5P^+$, 378.1465; found 378.1467.



3y

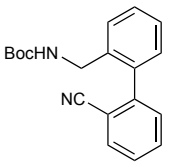
(*E*)-3-methoxy-5-(4-methoxy-3-(4-(trifluoromethyl)styryl)phenyl)pyridine **3y**. Pale yellow solid, 19.3 mg. Yield: 50%. TLC (Hexane:EtOAc, 50:50 v/v): RF = 0.41; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.47 (d, *J* = 1.8 Hz, 1H), 8.29 (d, *J* = 2.4 Hz, 1H), 7.78 (d, *J* = 1.8 Hz, 1H), 7.65–7.57 (m, 5H), 7.49 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.37 (dd, *J* = 2.4, 1.8 Hz, 1H), 7.21 (d, *J* = 16.2 Hz, 1H), 7.02 (d, *J* = 8.4 Hz, 1H), 3.96 (s, 3H), 3.94 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 157.28, 155.76, 141.14, 140.50, 136.89, 135.49, 130.27, 129.18 (q, J_{C-F} = 32.3 Hz), 128.26, 128.06, 126.67, 126.32,

125.66, 125.57 (q, J_{C-F} = 3.5 Hz), 125.53, 124.22 (q, J_{C-F} = 271.7 Hz), 118.91, 111.51, 55.74, 55.68; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{22}H_{19}F_3NO_2^+$, 386.1362; found 386.1365.



3z

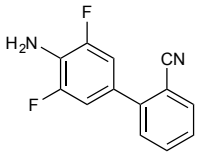
(*E*)-3-methoxy-5-(4-methoxy-3-(2-(perfluorophenyl)vinyl)phenyl)pyridine **3z**. Pale yellow solid, 35.1 mg. Yield: 86%. TLC (Hexane:EtOAc, 50:50 v/v): RF = 0.37; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.45 (d, *J* = 1.8 Hz, 1H), 8.28 (d, *J* = 2.7 Hz, 1H), 7.76 (d, *J* = 16.8 Hz, 1H), 7.72 (d, *J* = 2.3 Hz, 1H), 7.51 (dd, *J* = 8.5, 2.3 Hz, 1H), 7.35 (dd, *J* = 2.7, 1.8 Hz, 1H), 7.06 (d, *J* = 16.8 Hz, 1H), 7.01 (d, *J* = 8.5 Hz, 1H), 3.96 (s, 3H), 3.94 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 157.45, 155.74, 140.44, 136.68, 135.56, 132.07 (m), 130.32, 128.74, 126.14, 125.81, 118.85, 113.89, 111.55, 55.75, 55.65; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{21}H_{15}F_5NO_2^+$, 408.1017; found 408.1009. The carbon resonances corresponding to the pentafluorobenzene (C_6F_5) in this compound appear as a complex series of multiplets between 146 ppm to 112 ppm as a result of ^{13}C/^{19}F coupling. Due to the complexities of the system, the peaks are not listed. HRMS were used to confirm the presence of this ring system.



S2

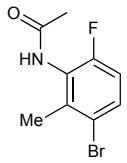
tert-butyl ((2'-cyano-[1,1'-biphenyl]-2-yl)methyl)carbamate **S2**. White solid. TLC (Hexanes:EtOAc, 80:20 v/v): RF = 0.23; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.75 (d, *J* = 7.8 Hz, 1H), 7.64 (td, *J* = 7.6, 1.3 Hz, 1H), 7.49–7.46 (m, 2H), 7.44 (td, *J* = 7.4, 1.4 Hz, 1H), 7.40 (d, *J* = 7.8 Hz, 1H), 7.37 (td, *J* = 7.5, 1.4 Hz, 1H), 7.22 (dd, *J* = 7.6, 1.3 Hz, 1H), 4.78–4.43 (m, 1H), 4.26–4.07 (m, 2H), 1.40 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 155.57, 144.60, 137.50, 136.50,

132.85, 132.63, 130.49, 129.93, 129.21, 128.59, 127.93, 127.52, 118.09, 112.74, 79.44, 42.18, 28.37; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{19}H_{21}N_2O_2^+$, 309.1598; found 309.1593.

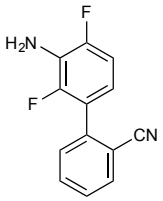


S4

4'-amino-3',5'-difluoro-[1,1'-biphenyl]-2-carbonitrile **S4**. White solid, 0.21 g. Yield: 46 %. TLC (Hexanes:EtOAc, 80:20 v/v): RF = 0.28; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.74 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.62 (td, *J* = 7.8, 1.2 Hz, 1H), 7.44 (d, *J* = 7.8 Hz, 1H), 7.42 (td, *J* = 7.8, 1.2 Hz, 1H), 7.11–7.05 (m, 2H), 3.91 (br, 2H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 151.63 (dd, $J_{C\text{-}F}$ = 241.4, 8.6 Hz), 143.56 (t, $J_{C\text{-}F}$ = 2.3 Hz), 133.89, 132.91, 129.76, 127.56, 126.63 (t, $J_{C\text{-}F}$ = 8.8 Hz), 124.66 (t, $J_{C\text{-}F}$ = 16.3 Hz), 118.50, 111.63 (dd, $J_{C\text{-}F}$ = 16.9, 6.5 Hz), 110.98; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{13}H_9F_2N_2^+$, 231.0728; found 231.0738.

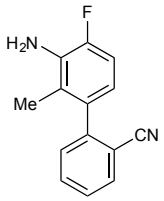


N-(3-bromo-6-fluoro-2-methylphenyl)acetamide. White solid. TLC (Hexanes:EtOAc, 50:50 v/v): RF = 0.39; ^{1}H NMR (600 MHz, DMSO-d_6): δ 9.66 (br, 1H), 7.56 (dd, *J* = 8.4, 4.8 Hz, 1H), 7.12 (dd, *J* = 9.6, 8.4 Hz, 1H), 2.33 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (151 MHz, DMSO-d_6): δ 161.38, 156.97 (d, $J_{C\text{-}F}$ = 246.4 Hz), 137.18, 131.00 (d, $J_{C\text{-}F}$ = 8.3 Hz), 125.76 (d, $J_{C\text{-}F}$ = 14.6 Hz), 118.65 (d, $J_{C\text{-}F}$ = 3.0 Hz), 114.74 (d, $J_{C\text{-}F}$ = 22.5 Hz), 22.48, 18.57 (dd, $J_{C\text{-}F}$ = 2.1 Hz); HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_9H_{10}BrFNO^+$, 245.9924; found 245.9932.



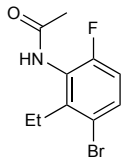
S5

3'-amino-2',4'-difluoro-[1,1'-biphenyl]-2-carbonitrile **S5**. Pale yellow solid, 0.093 g. Yield: 20 %. TLC (Hexanes:EtOAc, 80:20 v/v): RF = 0.28; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.77-7.76 (m, 1H), 7.64 (td, *J* = 7.8, 1.2 Hz, 1H), 7.48 (td, *J* = 7.8, 1.2 Hz, 1H), 7.47 (d, *J* = 7.8 Hz, 1H), 6.93 (ddd, *J* = 10.0, 8.5, 1.8 Hz, 1H), 6.70 (td, *J* = 7.8, 6.0 Hz, 1H), 3.87 (br, 2H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 152.27 (dd, $J_{C\text{-}F}$ = 242.5, 6.8 Hz), 148.76 (dd, $J_{C\text{-}F}$ = 242.2, 7.2 Hz), 139.29, 133.23, 132.55, 130.92 (d, $J_{C\text{-}F}$ = 1.7 Hz), 128.16, 124.54 (dd, $J_{C\text{-}F}$ = 16.5, 16.5 Hz), 121.89 (dd, $J_{C\text{-}F}$ = 13.3, 3.5 Hz), 118.07 (dd, $J_{C\text{-}F}$ = 8.6, 3.0 Hz), 118.05, 112.86, 111.02 (dd, $J_{C\text{-}F}$ = 19.0, 3.3 Hz); HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{13}H_9F_2N_2^+$, 231.0728; found 231.0734.



S6

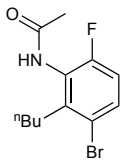
3'-amino-4'-fluoro-2'-methyl-[1,1'-biphenyl]-2-carbonitrile **S6**. Pale yellow solid, 1.79 g. Yield: 39 %. TLC (Hexanes:EtOAc, 80:20 v/v): RF = 0.25; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.73 (ddd, *J* = 7.8, 1.2, 0.6 Hz, 1H), 7.61 (td, *J* = 7.8, 1.2 Hz, 1H), 7.44 (td, *J* = 7.8, 1.2 Hz, 1H), 7.34 (ddd, *J* = 7.8, 1.2, 0.6 Hz, 1H), 6.95 (dd, *J* = 10.8, 8.4 Hz, 1H), 6.59 (dd, *J* = 8.4, 5.4 Hz, 1H), 3.79 (br, 2H), 2.00 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 151.53 (d, $J_{C\text{-}F}$ = 239.6 Hz), 145.60, 134.36 (d, $J_{C\text{-}F}$ = 3.2 Hz), 133.23 (d, $J_{C\text{-}F}$ = 12.2 Hz), 133.72, 132.41, 130.77, 127.51, 122.76 (d, $J_{C\text{-}F}$ = 3.8 Hz), 119.21 (d, $J_{C\text{-}F}$ = 7.7 Hz), 118.12, 113.18, 112.34 (d, $J_{C\text{-}F}$ = 19.5 Hz), 14.38 (d, $J_{C\text{-}F}$ = 2.7 Hz); HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{14}H_{12}FN_2^+$, 227.0979; found 227.0983.



S8

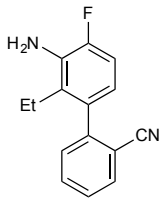
N-(3-bromo-2-ethyl-6-fluorophenyl)acetamide **S8**. White solid, 1.55 g. Yield: 44 %. TLC (Hexanes:EtOAc, 50:50 v/v): RF= 0.43; rotameric mixture. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.53–7.44 (m, 1H), 6.98-6.94 (m, 1H), 6.86 (t, *J* = 8.8 Hz, 1H), 2.84–2.68 (m, 2H), 2.20–1.87 (m, 3H),

1.12–1.07 (m, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 169.49, 157.70 (d, $J_{C\text{-}F}$ = 249.3 Hz), 143.30, 132.70 (d, $J_{C\text{-}F}$ = 8.0 Hz), 123.82 (d, $J_{C\text{-}F}$ = 14.1 Hz), 118.68 (d, $J_{C\text{-}F}$ = 3.1 Hz), 114.73 (d, $J_{C\text{-}F}$ = 22.1 Hz), 25.71, 23.08, 13.14; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{10}H_{12}BrFNO^+$, 260.0081; found 260.0088.



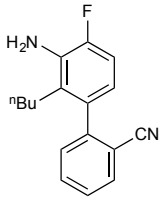
S9

N-(3-bromo-2-butyl-6-fluorophenyl)acetamide **S9**. White solid, 0.36 g. Yield: 31 %. TLC (Hexanes:EtOAc, 50:50 v/v): RF = 0.54; rotameric mixture. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.52–7.50 (m, 1H), 6.93–6.89 (m, 1H), 6.77–6.68 (m, 1H), 2.79–2.71 (m, 2H), 2.22–1.87 (m, 3H), 1.51–1.37 (m, 4H), 0.95 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 169.17, 157.67 (d, $J_{C\text{-}F}$ = 249.9 Hz), 142.19, 132.70 (d, $J_{C\text{-}F}$ = 8.0 Hz) , 123.92 (d, $J_{C\text{-}F}$ = 13.9 Hz), 119.00 (d, $J_{C\text{-}F}$ = 2.9 Hz), 114.74 (d, $J_{C\text{-}F}$ = 22.2 Hz), 32.01 (d, $J_{C\text{-}F}$ = 1.4 Hz), 30.94, 23.14, 22.80, 13.81; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{12}H_{16}BrFNO^+$, 288.0394; found 288.0404.



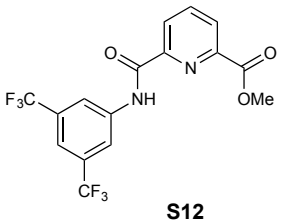
S10

3'-amino-2'-ethyl-4'-fluoro-[1,1'-biphenyl]-2-carbonitrile **S10**. Pale yellow solid, 0.78 g. Yield: 65 %. TLC (Hexanes:EtOAc, 80:20 v/v): RF = 0.27; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.73 (ddd, *J* = 7.8, 1.2, 0.6 Hz, 1H), 7.61 (td, *J* = 7.8, 1.2 Hz, 1H), 7.45 (td, *J* = 7.8, 1.2 Hz, 1H), 7.35 (ddd, *J* = 7.8, 1.2, 0.6 Hz, 1H), 6.94 (dd, *J* = 10.8, 8.4 Hz, 1H), 6.55 (dd, *J* = 8.4, 5.4 Hz, 1H), 3.82 (br, 2H), 2.46–2.40 (m, 1H), 2.36–2.30 (m, 1H), 1.03 (t, *J* = 7.8 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 151.91 (d, $J_{C\text{-}F}$ = 239.8 Hz), 145.65, 134.05 (d, $J_{C\text{-}F}$ = 3.2 Hz), 132.77 (d, $J_{C\text{-}F}$ = 12.2 Hz), 132.69, 132.13, 130.63, 128.49 (d, $J_{C\text{-}F}$ = 3.3 Hz), 127.58, 119.30 (d, $J_{C\text{-}F}$ = 7.9 Hz), 118.02, 113.32, 112.42 (d, $J_{C\text{-}F}$ = 19.3 Hz), 21.70 (d, $J_{C\text{-}F}$ = 2.7 Hz), 12.73; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{15}H_{14}FN_2^+$, 241.1136; found 241.1143.



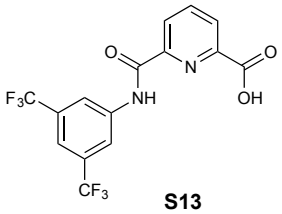
S11

3'-amino-2'-butyl-4'-fluoro-[1,1'-biphenyl]-2-carbonitrile **S11**. Pale yellow oil, 0.18 g. Yield: 57 %. TLC (Hexanes:EtOAc, 80:20 v/v): RF = 0.35; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.73 (ddd, *J* = 7.8, 1.2, 0.6 Hz, 1H), 7.61 (td, *J* = 7.8, 1.2 Hz, 1H), 7.45 (td, *J* = 7.8, 1.2 Hz, 1H), 7.35 (ddd, *J* = 7.8, 1.2, 0.6 Hz, 1H), 6.94 (dd, *J* = 10.8, 8.4 Hz, 1H), 6.55 (dd, *J* = 8.4, 5.4 Hz, 1H), 3.80 (br, 2H), 2.44–2.39 (m, 1H), 2.33–2.27 (m, 1H), 1.49–1.41 (m, 1H), 1.37–1.30 (m, 1H), 1.17 (sextet, *J* = 7.2 Hz, 2H), 0.74 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 151.91 (d, $J_{C\text{-}F}$ = 239.8 Hz), 145.70, 134.29 (d, $J_{C\text{-}F}$ = 3.2 Hz), 132.90 (d, $J_{C\text{-}F}$ = 12.2 Hz), 132.67, 132.08, 130.78, 127.53, 127.40 (d, $J_{C\text{-}F}$ = 3.3 Hz), 119.37 (d, $J_{C\text{-}F}$ = 7.7 Hz), 118.03, 113.39, 112.40 (d, $J_{C\text{-}F}$ = 19.5 Hz), 30.25, 28.14 (d, $J_{C\text{-}F}$ = 2.6 Hz), 22.70, 13.59; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{17}H_{18}FN_2^+$, 269.1449; found 269.1459.



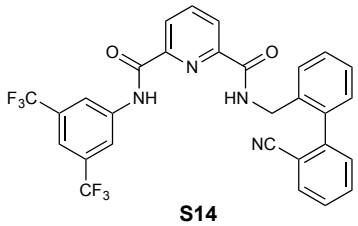
S12

methyl 6-((3,5-bis(trifluoromethyl)phenyl)carbamoyl)picolinate **S12**. White solid, 1.93 g. Yield: 25 %. TLC (Hexanes:EtOAc, 80:20 v/v): RF = 0.13; ^{1}H NMR (600 MHz, $CDCl_3$): δ 10.38 (br, 1H), 8.49 (dd, *J* = 7.8, 1.1 Hz, 1H), 8.34 (s, 2H), 8.32 (dd, *J* = 7.8, 1.1 Hz, 1H), 8.12 (t, *J* = 7.8 Hz, 1H), 7.66 (s, 1H), 4.08 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 164.62, 161.74, 149.13, 146.64, 139.22, 138.97, 132.44 (q, $J_{C\text{-}F}$ = 33.5 Hz), 128.11, 125.79, 123.14 (q, $J_{C\text{-}F}$ = 272.9 Hz), 119.79–119.71 (m), 117.84–117.74 (m), 53.17; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{16}H_{11}F_6N_2O_3^+$, 393.0668; found 393.0667.



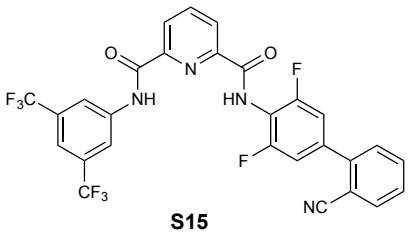
S13

6-((3,5-bis(trifluoromethyl)phenyl)carbamoyl)picolinic acid **S13**. White solid. ^{1}H NMR (600 MHz, CD_3CN): δ 10.41 (br, 1H), 8.47 (s, 2H), 8.47 (dd, J = 7.7, 1.1 Hz, 1H), 8.36 (dd, J = 7.7, 1.1 Hz, 1H), 8.23 (t, J = 7.8 Hz, 1H), 7.78 (s, 1H); ^{13}C NMR (151 MHz, CD_3CN): δ 164.99, 162.97, 149.57, 146.80, 141.39, 140.71, 132.58 (q, $J_{C\text{-}F}$ = 33.2 Hz), 128.42, 127.59, 124.44 (q, $J_{C\text{-}F}$ = 272.1 Hz), 121.73–121.36 (m), 118.57–118.32 (m); HRMS (ESI-TOF) m/z: $[M\text{-}H]^-$ calcd. for $C_{15}H_7F_6N_2O_3^-$, 377.0366; found 377.0372.



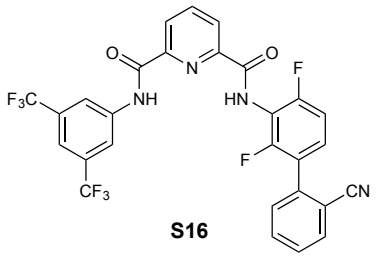
S14

N_2-(3,5-bis(trifluoromethyl)phenyl)-N_6-((2'-cyano-[1,1'-biphenyl]-2-yl)methyl)pyridine-2,6-dicarboxamide **S14**. White solid. TLC (Hexanes:EtOAc, 33:67 v/v): RF = 0.45; ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.18 (br, 1H), 9.68 (t, J = 6.2 Hz, 1H), 8.57 (s, 2H), 8.38-8.35 (m, 1H), 8.28-8.25 (m, 2H), 7.91 (s, 1H), 7.89 (ddd, J = 7.7, 1.3, 0.5 Hz, 1H), 7.74 (td, J = 7.7, 1.4 Hz, 1H), 7.61-7.58 (m, 2H), 7.53 (td, J = 7.6, 1.1 Hz, 1H), 7.49 (td, J = 7.6, 1.4 Hz, 1H), 7.42 (td, J = 7.5, 1.3 Hz, 1H), 7.29 (dd, J = 7.6, 1.3 Hz, 1H), 4.60-4.49 (m, 2H); ^{13}C NMR (151 MHz, DMSO-d_6): δ 162.88, 162.51, 148.70, 147.61, 143.87, 139.95, 139.93, 137.19, 136.66, 133.00, 132.95, 130.75 (q, $J_{C\text{-}F}$ = 32.9 Hz), 130.53, 129.89, 128.84, 128.25, 128.14, 127.11, 125.41, 125.15, 123.26 (q, $J_{C\text{-}F}$ = 272.8 Hz), 120.86–120.80 (m), 118.03, 117.26–117.21 (m), 111.90, 40.60; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{29}H_{19}F_6N_4O_2^+$, 569.1407; found 569.1407.



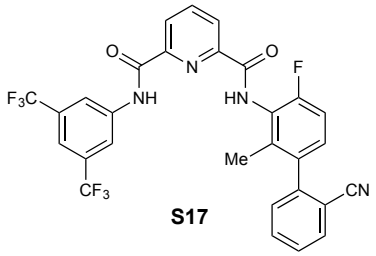
S15

N_2-(3,5-bis(trifluoromethyl)phenyl)-N_6-(2'-cyano-3,5-difluoro-[1,1'-biphenyl]-4-yl)pyridine-2,6-dicarboxamide **S15**. White solid, 0.99 g. Yield: 84 %. TLC (Hexanes:EtOAc, 33:67 v/v): RF = 0.60; ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.27 (br, 1H), 10.95 (br, 1H), 8.56 (s, 2H), 8.48 (dd, J = 7.7, 1.2 Hz, 1H), 8.44 (dd, J = 7.8, 1.2 Hz, 1H), 8.37 (t, J = 7.7 Hz, 1H), 8.02 (dd, J = 7.9, 1.2 Hz, 1H), 7.91 (s, 1H), 7.86 (td, J = 7.7, 1.4 Hz, 1H), 7.77 (d, J = 7.9 Hz, 1H), 7.67 (td, J = 7.7, 1.2 Hz, 1H), 7.63-7.61 (m, 2H); ^{13}C NMR (151 MHz, DMSO-d_6): δ 162.31, 157.91 (dd, $J_{C\text{-}F}$ = 250.1, 5.7 Hz), 148.05, 147.56, 141.70 (t, $J_{C\text{-}F}$ = 1.8 Hz), 140.48, 139.83, 138.70 (t, $J_{C\text{-}F}$ = 10.0 Hz), 133.86, 133.65, 130.78 (q, $J_{C\text{-}F}$ = 33.1 Hz), 130.19, 129.23, 126.07, 126.04, 123.22 (q, $J_{C\text{-}F}$ = 272.9 Hz), 121.20–121.12 (m), 118.08, 117.48–117.40 (m), 114.28 (t, $J_{C\text{-}F}$ = 17.1 Hz), 112.93 (dd, $J_{C\text{-}F}$ = 20.7, 4.4 Hz), 110.48; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{28}H_{15}F_8N_4O_2^+$, 591.1062; found 591.1062.



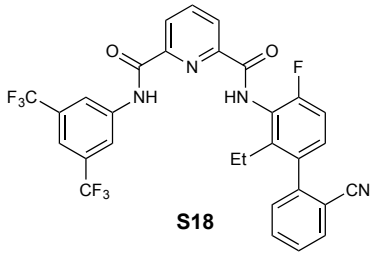
S16

N_2-(3,5-bis(trifluoromethyl)phenyl)-N_6-(2'-cyano-2,4-difluoro-[1,1'-biphenyl]-3-yl)pyridine-2,6-dicarboxamide **S16**. Pale yellow solid, 0.52 g. Yield: 87 %. TLC (Hexanes:EtOAc, 33:67 v/v): RF = 0.55; ^{1}H NMR (600 MHz, $CDCl_3$): δ 10.43 (br, 1H), 9.76 (br, 1H), 8.54 (dd, J = 7.8, 1.1 Hz, 1H), 8.50 (dd, J = 7.7, 1.1 Hz, 1H), 8.36 (s, 2H), 8.16 (t, J = 7.8 Hz, 1H), 7.69 (ddd, J = 7.8, 1.4, 0.6 Hz, 1H), 7.62 (td, J = 7.7, 1.4 Hz, 1H), 7.55 (s, 1H), 7.46 (td, J = 7.7, 1.2 Hz, 1H), 7.38 (d, J = 7.8 Hz, 1H), 7.22 (td, J = 8.2, 5.6 Hz, 1H), 6.79 (td, J = 8.8, 1.4 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 162.29, 162.15, 158.18 (dd, $J_{C\text{-}F}$ = 254.5, 4.0 Hz), 154.95 (dd, $J_{C\text{-}F}$ = 254.4, 4.7 Hz), 148.12, 147.97, 139.66, 138.76, 138.08, 133.11, 132.99, 132.18 (q, $J_{C\text{-}F}$ = 33.5 Hz), 130.90, 129.67 (dd, $J_{C\text{-}F}$ = 9.6, 3.7 Hz), 128.72, 126.45, 126.16, 122.97 (q, $J_{C\text{-}F}$ = 272.9 Hz), 122.66 (dd, $J_{C\text{-}F}$ = 14.6, 3.7 Hz), 120.42–120.37 (m), 118.39, 118.00–117.90 (m), 113.91 (t, $J_{C\text{-}F}$ = 16.8 Hz), 112.36, 111.74 (dd, $J_{C\text{-}F}$ = 20.4, 3.7 Hz); HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{28}H_{15}F_8N_4O_2^+$, 591.1062; found 591.1062.



S17

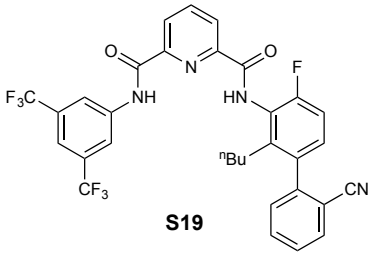
N_2-(3,5-bis(trifluoromethyl)phenyl)-N_6-(2'-cyano-4-fluoro-2-methyl-[1,1'-biphenyl]-3-yl)pyridine-2,6-dicarboxamide **S17**. White solid, 0.88 g. Yield: 51 %. TLC (Hexanes:EtOAc, 33:67 v/v): RF = 0.58; ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.32 (br, 1H), 10.93 (br, 1H), 8.54 (s, 2H), 8.47 (dd, J = 7.7, 1.3 Hz, 1H), 8.43 (dd, J = 7.7, 1.2 Hz, 1H), 8.36 (t, J = 7.7 Hz, 1H), 8.00 (d, J = 7.7 Hz, 1H), 7.91 (s, 1H), 7.83 (td, J = 7.7, 1.4 Hz, 1H), 7.65 (td, J = 7.7, 1.2 Hz, 1H), 7.53 (d, J = 7.7 Hz, 1H), 7.43–7.37 (m, 2H), 2.10 (s, 3H); ^{13}C NMR (151 MHz, DMSO-d_6): δ 162.37, 161.99, 158.01 (d, $J_{C\text{-}F}$ = 248.7 Hz), 148.15, 147.92, 143.64, 140.37, 139.85, 136.48 (d, $J_{C\text{-}F}$ = 0.8 Hz), 134.94 (d, $J_{C\text{-}F}$ = 3.3 Hz), 133.37, 133.13, 130.77 (q, $J_{C\text{-}F}$ = 32.9 Hz), 130.75, 129.89 (d, $J_{C\text{-}F}$ = 8.8 Hz), 128.60, 125.87, 125.80, 123.93 (d, $J_{C\text{-}F}$ = 13.3 Hz), 123.21 (q, $J_{C\text{-}F}$ = 273.0 Hz), 121.26–121.18 (m), 117.86, 117.46-117.41 (m), 113.46 (d, $J_{C\text{-}F}$ = 20.8 Hz), 111.98, 15.56 (d, $J_{C\text{-}F}$ = 2.1 Hz); HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{29}H_{18}F_7N_4O_2^+$, 587.1312; found 587.1313.



S18

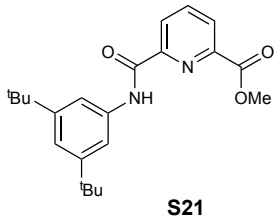
N_2-(3,5-bis(trifluoromethyl)phenyl)-N_6-(2'-cyano-2-ethyl-4-fluoro-[1,1'-biphenyl]-3-yl)pyridine-2,6-dicarboxamide **S18**. White solid, 0.20 g. Yield: 27 %. TLC (Hexanes:EtOAc, 33:67 v/v): RF = 0.61; ^{1}H NMR (600 MHz, $CDCl_3$): δ 10.39 (br, 1H), 9.54 (br, 1H), 8.58 (dd, J = 7.8, 1.1 Hz, 1H), 8.55 (dd, J = 7.8, 1.2 Hz, 1H), 8.36 (s, 2H), 8.20 (t, J = 7.8 Hz, 1H), 7.73 (dd, J = 7.8, 1.4 Hz, 1H), 7.65 (dd, J = 7.7, 1.4 Hz, 1H), 7.60 (s, 1H), 7.49 (td, J = 7.7, 1.3 Hz, 1H), 7.38 (d, J = 7.8 Hz, 1H), 7.09 (dd, J = 8.5, 5.3 Hz, 1H), 6.85 (t, J = 8.8 Hz, 1H), 2.57–2.51 (m, 1H), 2.33–2.27 (m, 1H), 0.87 (t, J = 7.6 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 162.64, 162.48, 158.28 (d, $J_{C\text{-}F}$ = 251.4 Hz), 148.61, 147.99, 144.40, 142.32, 139.80, 138.75, 134.58 (d, $J_{C\text{-}F}$ = 3.6 Hz), 132.88, 132.77, 132.35 (q, $J_{C\text{-}F}$ = 33.6 Hz), 130.75, 130.48 (d, $J_{C\text{-}F}$ = 8.6 Hz), 128.21, 126.58,

126.03, 122.96 (q, $J_{C\text{-}F}$ = 273.0 Hz), 122.74 (d, $J_{C\text{-}F}$ = 13.3 Hz), 120.31–120.23 (m), 118.41, 118.08–118.00 (m), 113.52 (d, $J_{C\text{-}F}$ = 21.0 Hz), 112.72, 22.77 (d, $J_{C\text{-}F}$ = 1.9 Hz), 14.26; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{30}H_{20}F_7N_4O_2^+$, 601.1469; found 601.1469.



S19

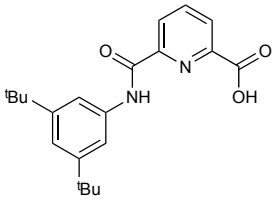
N_2-(3,5-bis(trifluoromethyl)phenyl)-N_6-(2-butyl-2'-cyano-4-fluoro-[1,1'-biphenyl]-3-yl)pyridine-2,6-dicarboxamide **S19**. White solid. TLC (Hexanes:EtOAc, 33:67 v/v): RF = 0.65; ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.39 (br, 1H), 10.88 (br, 1H), 8.55 (s, 2H), 8.47 (dd, *J* = 7.7, 1.1 Hz, 1H), 8.44 (dd, *J* = 7.8, 1.2 Hz, 1H), 8.37 (t, *J* = 7.7 Hz, 1H), 8.00 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.91 (s, 1H), 7.82 (td, *J* = 7.7, 1.3 Hz, 1H), 7.65 (td, *J* = 7.7, 1.2 Hz, 1H), 7.55 (d, *J* = 7.9 Hz, 1H), 7.40 (t, *J* = 8.7 Hz, 1H), 7.36 (dd, *J* = 8.6, 5.5 Hz, 1H), 2.63-2.59 (m, 1H), 2.40-2.35 (m, 1H), 1.40-1.33 (m, 1H), 1.32-1.24 (m, 1H), 1.00-0.93 (m, 2H), 0.47 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (151 MHz, DMSO-d_6): δ 162.45, 162.41, 158.33 (d, $J_{C\text{-}F}$ = 249.0 Hz), 148.16, 147.86, 143.55, 141.05, 140.47, 139.90, 134.91 (d, $J_{C\text{-}F}$ = 3.5 Hz), 133.09, 133.01, 130.84 (q, $J_{C\text{-}F}$ = 32.9 Hz), 130.80, 130.34 (d, $J_{C\text{-}F}$ = 8.8 Hz), 128.63, 125.85, 125.76, 123.65 (d, $J_{C\text{-}F}$ = 13.5 Hz), 123.19 (q, $J_{C\text{-}F}$ = 272.9 Hz), 120.79–120.74 (m), 117.88, 117.41–117.34 (m), 113.60 (d, $J_{C\text{-}F}$ = 21.0 Hz), 111.29, 30.98, 28.21, 21.83, 12.92; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{32}H_{24}F_7N_4O_2^+$, 629.1782; found 629.1783.



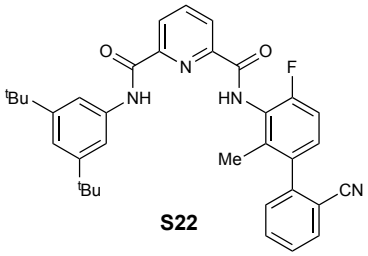
S21

methyl 6-((3,5-di-*tert*-butylphenyl)carbamoyl)picolinate **S21**. Pale yellow solid, 0.202 g. Yield: 71 %. TLC (Hexanes:EtOAc, 67:33 v/v): RF = 0.48; ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.91 (br, 1H), 8.50 (dd, *J* = 7.8, 1.1 Hz, 1H), 8.27 (dd, *J* = 7.8, 1.1 Hz, 1H), 8.07 (t, *J* = 7.7 Hz, 1H), 7.65 (d, *J* = 1.7 Hz, 2H), 7.25 (t, *J* =1.7 Hz, 1H), 4.07 (s, 3H), 1.37 (s, 18H); ^{13}C NMR (151 MHz,

$CDCl_3$): δ 164.90, 161.13, 151.70, 150.46, 146.50, 138.83, 136.75, 127.37, 125.48, 118.92, 114.84, 53.02, 35.02, 31.46; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{22}H_{29}FN_2O_3^+$, 369.2173; found 369.2172.

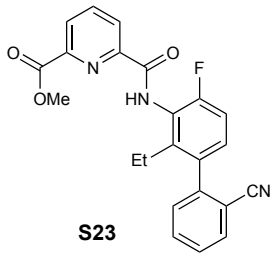


6-((3,5-di-*tert*-butylphenyl)carbamoyl)picolinic acid. White solid. ^{1}H NMR (600 MHz, DMSO-d_6): δ 10.79 (br, 1H), 8.41 (dd, *J* = 7.4, 1.5 Hz, 1H), 8.33 (dd, *J* = 7.7, 1.5 Hz, 1H), 8.30 (dd, *J* = 7.7, 7.4 Hz, 1H), 7.70 (d, *J* = 1.7 Hz, 2H), 7.24 (t, *J* =1.7 Hz, 1H), 1.33 (s, 18H); ^{13}C NMR (151 MHz, DMSO-d_6): δ 164.78, 161.37, 150.86, 149.42, 146.08, 140.16, 137.39, 126.92, 125.82, 118.18, 115.21, 34.67, 31.27; HRMS (ESI-TOF) *m*/*z*: $[M-H]^-$ calcd. for $C_{21}H_{25}N_2O_3^-$, 353.1871; found 353.1877.



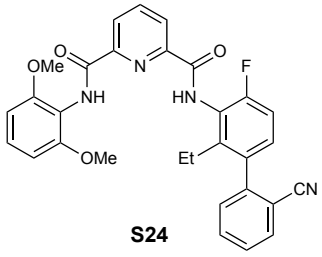
S22

N_2-(2'-cyano-4-fluoro-2-methyl-[1,1'-biphenyl]-3-yl)-N_6-(3,5-di-*tert*-butylphenyl)pyridine-2,6-dicarboxamide **S22**. White solid. TLC (Hexanes:EtOAc, 33:67 v/v): RF = 0.58; ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.04 (br, 1H), 10.91 (br, 1H), 8.43 (dd, *J* = 7.7, 1.3 Hz, 1H), 8.37 (dd, *J* = 7.7, 1.3 Hz, 1H), 8.32 (t, *J* = 7.7 Hz, 1H), 8.00 (ddd, *J* = 7.8, 1.4, 0.5 Hz, 1H), 7.83 (td, *J* = 7.7, 1.4 Hz, 1H), 7.65 (td, *J* = 7.7, 1.2 Hz, 1H), 7.60 (d, *J* = 1.7 Hz, 2H), 7.52 (ddd, *J* = 7.8, 1.3, 0.6 Hz, 1H), 7.40 (t, *J* = 8.8 Hz, 1H), 7.37 (dd, *J* = 8.6, 5.6 Hz, 1H), 7.26 (t, *J* = 1.7 Hz, 1H), 2.11 (s, 3H), 1.32 (s, 18H); ^{13}C NMR (151 MHz, DMSO-d_6): δ 162.18, 161.55, 158.00 (d, J_{C-F} = 248.6 Hz), 150.78, 149.07, 148.12, 143.68, 140.05, 137.08, 136.37 (d, J_{C-F} = 0.9 Hz), 134.89 (d, J_{C-F} = 3.3 Hz), 133.37, 133.11, 130.74, 129.71 (d, J_{C-F} = 8.7 Hz), 128.60, 125.37, 125.15, 124.04 (d, J_{C-F} = 13.4 Hz), 118.59, 117.83, 116.60, 113.44 (d, J_{C-F} = 20.9 Hz), 111.99, 34.64, 31.24, 15.52 (d, J_{C-F} = 2.2 Hz); HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{35}H_{36}FN_4O_2^+$, 563.2817; found 563.2818.



S23

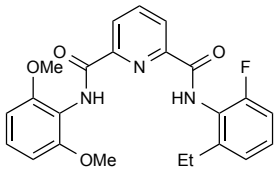
methyl 6-((2'-cyano-2-ethyl-4-fluoro-[1,1'-biphenyl]-3-yl)carbamoyl)picolinate **S23**. White solid, 3.54 g. Yield: 89 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.66 (br, 1H), 8.49 (d, J = 7.6 Hz, 1H), 8.32 (d, J = 7.7 Hz, 1H), 8.08 (t, J = 7.8 Hz, 1H), 7.78 (d, J = 7.9 Hz, 1H), 7.66 (td, J = 7.6, 1.4 Hz, 1H), 7.50 (td, J = 7.7, 1.2 Hz, 1H), 7.43 (d, J = 7.7 Hz, 1H), 7.19–7.14 (m, 2H), 4.03 (s, 3H), 2.67–2.61 (m, 1H), 2.53–2.47 (m, 1H), 0.98 (t, J = 7.6 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 164.88, 162.39, 158.40 (d, $J_{C\text{-}F}$ = 252.1 Hz), 149.33, 146.74, 144.54, 141.72, 138.79, 134.36 (d, $J_{C\text{-}F}$ = 3.7 Hz), 132.84, 132.46, 130.83, 130.08 (d, $J_{C\text{-}F}$ = 8.5 Hz), 128.02, 127.70, 125.72, 122.98 (d, $J_{C\text{-}F}$ = 13.3 Hz), 117.88, 113.95 (d, $J_{C\text{-}F}$ = 21.0 Hz), 113.30, 52.94, 22.88, 14.33; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{16}H_{11}F_6N_2O_3^+$, 404.1405; found 404.1406.



S24

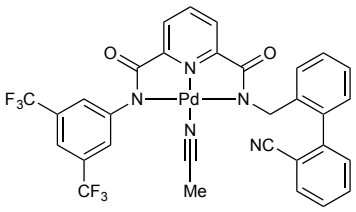
N_2-(2'-cyano-2-ethyl-4-fluoro-[1,1'-biphenyl]-3-yl)-N_6-(2,6-dimethoxyphenyl)pyridine-2,6-dicarboxamide **S24**. Pale yellow solid, 1.20 g. Yield: 64 %. TLC (Hexanes:EtOAc, 33:67 v/v): RF = 0.13; ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.25 (br, 1H), 8.98 (br, 1H), 8.54 (dd, J = 7.6, 1.1 Hz, 1H), 8.50 (dd, J = 7.7, 1.2 Hz, 1H), 8.14 (t, J = 7.7 Hz, 1H), 7.76 (ddd, J = 7.8, 1.3, 0.5 Hz, 1H), 7.66 (td, J = 7.7, 1.4 Hz, 1H), 7.50 (td, J = 7.7, 1.3 Hz, 1H), 7.44 (d, J = 7.7 Hz, 1H), 7.24 (t, J = 8.5 Hz, 1H), 7.19 (dd, J = 8.6, 5.7 Hz, 1H), 7.17 (t, J = 8.5 Hz, 1H), 6.65 (d, J = 8.5 Hz, 2H), 3.86 (s, 6H), 2.68–2.61 (m, 1H), 2.55–2.49 (m, 1H), 0.99 (t, J = 7.6 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 162.47, 161.29, 158.45 (d, $J_{C\text{-}F}$ = 251.8 Hz), 155.48, 149.34, 148.09, 144.49, 141.77, 139.26, 134.45 (d, $J_{C\text{-}F}$ = 3.7 Hz), 132.79, 132.56, 130.82, 130.25 (d, $J_{C\text{-}F}$ = 8.6 Hz), 128.08, 128.01, 126.07, 125.50, 122.87 (d, $J_{C\text{-}F}$ = 13.3 Hz), 117.90, 114.00 (d, $J_{C\text{-}F}$ = 20.9 Hz),

113.43, 113.26, 104.40, 56.11, 22.94 (d, $J_{C\text{-}F}$ = 2.2 Hz), 14.41; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{30}H_{26}FN_4O_4^+$, 525.1933; found 525.1932.



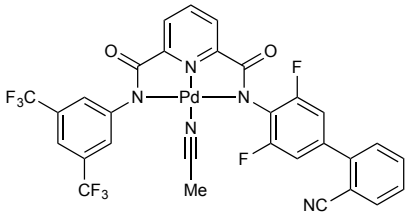
S25

N_2-(2,6-dimethoxyphenyl)-N_6-(2-ethyl-6-fluorophenyl)pyridine-2,6-dicarboxamide **S25**. White solid. TLC (Hexanes:EtOAc, 50:50 v/v): RF = 0.20; ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.16 (br, 1H), 8.98 (br, 1H), 8.52 (dd, *J* = 7.7, 1.1 Hz, 1H), 8.48 (dd, *J* = 7.9, 1.3 Hz, 1H), 8.12 (t, *J* = 7.8 Hz, 1H), 7.29–7.23 (m, 2H), 7.12 (d, *J* = 7.5 Hz, 1H), 7.04 (ddd, *J* = 9.6, 8.2, 1.3 Hz, 1H), 6.66 (d, *J* = 8.5 Hz, 2H), 3.86 (s, 6H), 2.73 (q, *J* = 7.6 Hz, 2H), 1.25 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 162.17, 161.31, 157.93 (d, $J_{C\text{-}F}$ = 248.5 Hz), 155.42, 149.20, 148.27, 143.32, 139.22, 128.46 (d, $J_{C\text{-}F}$ = 8.6 Hz), 128.00, 125.93, 125.49, 124.11 (d, $J_{C\text{-}F}$ = 3.2 Hz), 122.10 (d, $J_{C\text{-}F}$ = 12.9 Hz), 113.55 (d, $J_{C\text{-}F}$ = 20.5 Hz), 113.53, 104.43, 56.11, 24.74 (d, $J_{C\text{-}F}$ = 2.0 Hz), 14.25; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{23}H_{23}FN_3O_4^+$, 424.1667; found 424.1663.



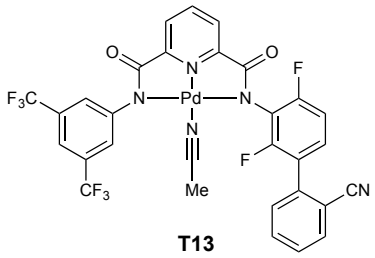
T11

T11. Yellow solid, 0.195 g. Yield: 86 %. ^{1}H NMR (600 MHz, CD_3CN): δ 8.15 (t, *J* = 7.8 Hz, 1H), 7.81 (s, 2H), 7.75 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.71 (ddd, *J* = 7.8, 1.4, 0.6 Hz, 1H), 7.68–7.65 (m, 2H), 7.59–7.56 (m, 2H), 7.50 (ddd, *J* = 8.3, 1.3, 0.6 Hz, 1H), 7.44 (td, *J* = 7.6, 1.4 Hz, 1H), 7.35 (td, *J* = 7.6, 1.3 Hz, 1H), 7.34 (td, *J* = 7.7, 1.3 Hz, 1H), 7.23 (dd, *J* = 7.5, 1.4 Hz, 1H), 4.48–4.38 (m, 2H); ^{13}C NMR (151 MHz, CD_3CN): δ 169.45, 168.56, 151.73, 150.75, 148.22, 144.95, 141.56, 138.85, 136.98, 132.21, 132.07, 130.15 (q, $J_{C\text{-}F}$ = 32.9 Hz), 129.98, 129.60, 128.04, 127.97, 127.26, 126.37–126.35 (m), 125.97, 124.96, 124.95, 123.21 (q, $J_{C\text{-}F}$ = 272.8 Hz), 118.17, 112.12, 48.68; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{31}H_{20}F_6N_5O_2Pd^+$, 714.0551; found 714.0551. The signals of CH_3CN for ^{1}H NMR and ^{13}C NMR were omitted because the bound CH_3CN was replaced by CD_3CN.



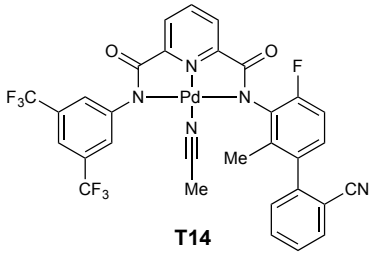
T12

T12. Yellow solid, 0.102 g. Yield: 46 %. ^{1}H NMR (600 MHz, CD_3CN): δ 8.33 (t, J = 7.8 Hz, 1H), 7.92 (dd, J = 7.9, 1.3 Hz, 1H), 7.89 (s, 2H), 7.88 (dd, J = 7.8, 1.3 Hz, 1H), 7.85 (ddd, J = 7.7, 1.3, 0.5 Hz, 1H), 7.75 (td, J = 7.7, 1.4 Hz, 1H), 7.68 (s, 1H), 7.62 (ddd, J = 7.9, 1.3, 0.5 Hz, 1H), 7.57 (td, J = 7.7, 1.2 Hz, 1H), 7.27–7.24 (m, 2H); ^{13}C NMR (151 MHz, CD_3CN): δ 170.07, 169.57, 158.64 (dd, $J_{C\text{-}F}$ = 247.9, 6.4 Hz), 152.90, 151.11, 149.64, 143.78, 143.75 (t, $J_{C\text{-}F}$ = 2.1 Hz), 137.57 (t, $J_{C\text{-}F}$ = 10.0 Hz), 134.72, 134.36, 131.70 (q, $J_{C\text{-}F}$ = 32.9 Hz), 131.04, 129.72, 127.82, 127.77–127.70 (m), 127.40, 124.96 (t, $J_{C\text{-}F}$ = 16.9 Hz), 124.63 (q, $J_{C\text{-}F}$ = 272.0 Hz), 119.33, 113.24 (dd, $J_{C\text{-}F}$ = 20.9, 5.5 Hz), 111.88; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{30}H_{16}F_8N_5O_2Pd^+$, 736.0206; found 736.0207. The signals of CH_3CN for ^{1}H NMR and ^{13}C NMR were omitted because the bound CH_3CN was replaced by CD_3CN.



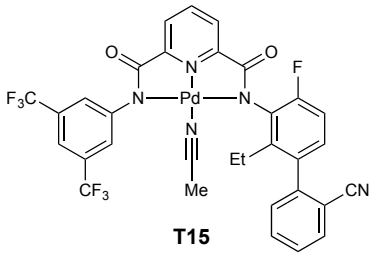
T13

T13. Yellow solid, 0.133 g. Yield: 91 %. ^{1}H NMR (600 MHz, CD_3CN): δ 8.31 (t, J = 7.8 Hz, 1H), 7.91 (dd, J = 7.8, 1.3 Hz, 1H), 7.87–7.86 (m, 4H), 7.76 (td, J = 7.8, 1.4 Hz, 1H), 7.67 (s, 1H), 7.60–7.56 (m, 2H), 7.33 (td, J = 8.1, 6.0 Hz, 1H), 7.16 (td, J = 9.0, 1.5 Hz, 1H); ^{13}C NMR (151 MHz, CD_3CN): δ 170.06, 169.74, 159.39 (dd, $J_{C\text{-}F}$ = 249.2, 4.8 Hz), 155.82 (dd, $J_{C\text{-}F}$ = 235.7, 5.5 Hz), 152.91, 151.12, 149.64, 143.74, 139.58, 134.21, 134.17, 132.05, 131.70 (q, $J_{C\text{-}F}$ = 32.9 Hz), 129.82, 128.92 (dd, $J_{C\text{-}F}$ = 9.8, 3.9 Hz), 127.77, 127.74–127.66 (m), 127.36, 125.13 (t, $J_{C\text{-}F}$ = 17.2 Hz), 124.62 (q, $J_{C\text{-}F}$ = 272.0 Hz), 123.58 (dd, $J_{C\text{-}F}$ = 15.4, 3.7 Hz), 118.96, 113.60, 112.52 (dd, $J_{C\text{-}F}$ = 21.4, 3.8 Hz); HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{30}H_{16}F_8N_5O_2Pd^+$, 736.0206; found 736.0203. The signals of CH_3CN for ^{1}H NMR and ^{13}C NMR were omitted because the bound CH_3CN was replaced by CD_3CN.



T14

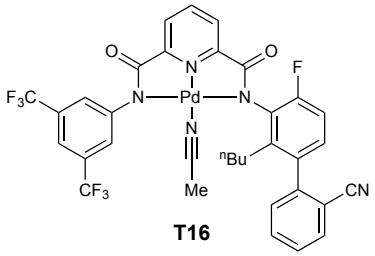
T14. Yellow solid, 0.77 g. Yield: 79 %. rotameric mixture. ^{1}H NMR (600 MHz, CD_3CN): δ 8.32–8.26 (m, 1H), 7.90 (dd, J = 7.8, 1.3 Hz, 1H), 7.87–7.82 (m, 4H), 7.76–7.71 (m, 1H), 7.70–7.66 (m, 1H), 7.55 (td, J = 7.6, 1.1 Hz, 1H), 7.48–7.37 (m, 1H), 7.15–7.10 (m, 2H), 2.19–2.17 (m, 3H); ^{13}C NMR (151 MHz, CD_3CN) rotameric mixture, resonances for the minor rotamer are enclosed in parenthesis [ ]: δ 170.05 [172.45], 169.23 [169.14], 158.51 (d, $J_{C\text{-}F}$ = 245.2 Hz) [158.48], 152.89 [152.84], 151.87 [151.92], 149.77 [149.84], 145.81 [145.53], 143.59, 136.61 [136.49], 135.85 (d, $J_{C\text{-}F}$ = 3.5 Hz), 134.98 (d, $J_{C\text{-}F}$ = 13.3 Hz) [134.86], 134.02 [134.32], 133.77 [133.82], 131.76 [131.97], 131.68 (q, $J_{C\text{-}F}$ = 32.9 Hz), 129.11 [129.08], 128.75 (d, $J_{C\text{-}F}$ = 8.6 Hz), 127.60–127.55 (m), 127.46, 127.14 [127.24], 124.63 (q, $J_{C\text{-}F}$ = 272.0 Hz), 119.19 [119.04], 113.70 (d, $J_{C\text{-}F}$ = 21.5 Hz), 16.02 (d, $J_{C\text{-}F}$ = 2.5 Hz) [16.20]; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{31}H_{18}F_7N_5O_2Pd^+$, 732.0456; found 732.0456. The signals of CH_3CN for ^{1}H NMR and ^{13}C NMR were omitted because the bound CH_3CN was replaced by CD_3CN.



T15

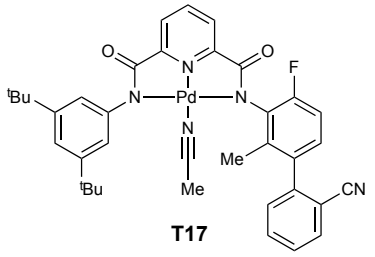
T15. Yellow solid, 0.128 g. Yield: 86 %. rotameric mixture. ^{1}H NMR (600 MHz, CD_3CN): δ 8.33–8.26 (m, 1H), 7.91–7.89 (m, 1H), 7.87–7.82 (m, 4H), 7.75–7.69 (m, 1H), 7.67(s, 1H), 7.58–7.55 (m, 1H), 7.51–7.37 (m, 1H), 7.13–7.09 (m, 2H), 2.95–2.83 (m, 1H), 2.55–2.39 (m, 1H), 1.02–0.98 (m, 3H); ^{13}C NMR (151 MHz, CD_3CN) rotameric mixture, resonances for the minor rotamer are enclosed in parenthesis [ ]: δ 170.07, 169.81 [169.57], 158.71 (d, $J_{C\text{-}F}$ = 245.3 Hz) [158.65], 152.86, 151.90 [151.96], 149.75 [149.84], 145.70 [145.43], 143.63 [143.65], 142.34 [142.31], 135.73 (d, $J_{C\text{-}F}$ = 3.6 Hz) [135.65], 134.75 (d, $J_{C\text{-}F}$ = 13.4 Hz) [134.61], 133.82 [134.03], 133.74 [133.57], 131.91 [132.06], 131.70 (q, $J_{C\text{-}F}$ = 32.9 Hz) [131.69], 129.21, 129.16–129.13

(m), 127.66–127.54 (m), 127.46 [127.48], 127.17 [127.25], 124.63 (q, J_{C-F} = 272.1 Hz) [124.64], 119.22 [119.05], 113.84 (d, J_{C-F} = 21.6 Hz) [113.86], 23.64 (d, J_{C-F} = 2.3 Hz), 14.65 [14.73]; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{32}H_{21}F_7N_5O_2Pd^+$, 746.0613; found 746.0613. The signals of CH_3CN for ^1H NMR and ^{13}C NMR were omitted because the bound CH_3CN was replaced by CD_3CN.



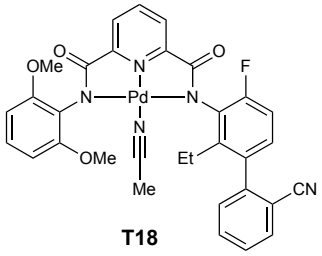
T16

T16. Yellow solid. rotameric mixture. ^1H NMR (600 MHz, CD_3CN): δ 8.33–8.27 (m, 1H), 7.91–7.67 (m, 7H), 7.59–7.34 (m, 2H), 7.25–6.95 (m, 2H), 3.28–2.79 (m, 1H), 2.55–2.36 (m, 1H), 1.55–1.27 (m, 2H), 1.22–1.06 (m, 2H), 0.65–0.59 (m, 3H); ^{13}C NMR (151 MHz, CD_3CN) rotameric mixture, resonances for the minor rotamer are enclosed in parenthesis [ ]: δ 170.05 [170.76, 170.34], 169.68 [169.47], 158.68 (d, J_{C-F} = 245.3 Hz) [158.8, 158.63], 152.88 [152.86, 152.45], 151.91 [151.96, 151.72], 149.72 [150.26, 149.82], 145.76 [145.80, 145.49], 143.67 [143.69, 142.85], 141.25, 135.90 (d, J_{C-F} = 3.6 Hz) [136.10, 135.86], 134.82 (d, J_{C-F} = 13.3 Hz) [134.71], 133.77 [134.14, 134.01], 133.71 [133.52, 133.15], 132.02 [132.17, 131.78], 131.71 (q, J_{C-F} = 32.9 Hz) [132.40, 131.70], 129.19–129.04 (m), 127.66–127.54 (m), 127.47 [127.24], 127.16 [126.96, 126.68], 124.63 (q, J_{C-F} = 272.0 Hz) [124.64, 124.61], 119.27 [119.52, 119.08], 113.79 (d, J_{C-F} = 21.7 Hz) [114.46, 113.96], 32.43 [33.11, 32.54], 29.85 (d, J_{C-F} = 2.2 Hz) [29.96, 29.80], 23.48 [23.36, 23.22], 13.82 [13.84, 13.74]; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{34}H_{24}F_7N_5O_2Pd^+$, 774.0926; found 774.0934. The signals of CH_3CN for ^1H NMR and ^{13}C NMR were omitted because the bound CH_3CN was replaced by CD_3CN.



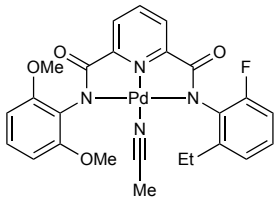
T17

T17. Orange solid, 0.202 g. Yield: 95 %. rotameric mixture. ^{1}H NMR (600 MHz, CD_3CN): δ 8.27–8.22 (m, 1H), 7.85–7.77 (m, 3H), 7.75–7.68 (m, 1H), 7.57–7.51 (m, 1H), 7.49–7.35 (m, 1H), 7.23–7.21 (m, 1H), 7.13–6.98 (m, 4H), 2.16 (s, 3H), 1.29 (s, 18H); ^{13}C NMR (151 MHz, CD_3CN) rotameric mixture, resonances for the minor rotamer are enclosed in parenthesis [ ]: δ 169.62 [172.51], 169.20 [169.11], 158.41 (d, $J_{C\text{-}F}$ = 245.0 Hz), 154.05 [154.01], 151.95 [151.99], 151.67 [151.62], 147.55 [147.61], 145.88 [145.60], 143.21, 136.41 (d, $J_{C\text{-}F}$ = 1.4 Hz), 135.82 (d, $J_{C\text{-}F}$ = 3.5 Hz), 135.28 (d, $J_{C\text{-}F}$ = 13.4 Hz), 134.05, 133.74 [133.77], 131.75 [131.97], 129.07 [129.04], 128.37 (d, $J_{C\text{-}F}$ = 8.5 Hz), 126.90, 126.40 [126.50], 121.55, 119.58 [119.49], 119.17, 113.62, 113.64 (d, $J_{C\text{-}F}$ = 21.7 Hz) [113.67], 35.42, 31.76, 20.65, 16.06 (d, $J_{C\text{-}F}$ = 2.5 Hz) [16.22]; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{37}H_{37}FN_5O_2Pd^+$, 708.1961; found 708.1961. The signals of CH_3CN for ^{1}H NMR and ^{13}C NMR were omitted because the bound CH_3CN was replaced by CD_3CN.



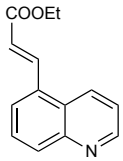
T18

T18. Yellow solid, 0.836 g. Yield: 83 %. rotameric mixture. ^{1}H NMR (600 MHz, CD_3CN): δ 8.28–8.24 (m, 1H), 7.85–7.76 (m, 3H), 7.74–7.67 (m, 1H), 7.57–7.53 (m, 1H), 7.52–7.32 (m, 1H), 7.14–7.10 (m, 1H), 7.08–7.01 (m, 2H), 6.63–6.60 (m, 2H), 3.81–3.80 (m, 3H), 3.79–3.79 (m, 3H), 3.02–2.81 (m, 1H), 2.52–2.32 (m, 1H), 1.03–0.97 (m, 3H); ^{13}C NMR (151 MHz, CD_3CN) rotameric mixture, resonances for the minor rotamer are enclosed in parenthesis [ ]: δ 169.61 [169.34], 168.78, 158.51 (d, $J_{C\text{-}F}$ = 245.1 Hz) [158.47], 156.11, 156.09, 152.88 [152.83], 152.31 [152.37], 145.87 [145.63], 143.23, 141.88 (d, $J_{C\text{-}F}$ = 1.4 Hz), 135.61 (d, $J_{C\text{-}F}$ = 3.6 Hz) [135.52], 135.37 (d, $J_{C\text{-}F}$ = 13.6 Hz) [135.27], 133.82 [134.00], 133.61 [133.52], 131.84 [132.07], 129.10 [129.05], 128.45 (d, $J_{C\text{-}F}$ = 8.7 Hz), 126.99 [126.97], 126.62, 126.57, 125.38 [125.53], 119.01 [119.10], 113.82 [113.89], 113.71 (d, $J_{C\text{-}F}$ = 21.9 Hz), 105.29, 105.28, 56.57, 56.55, 23.63 (d, $J_{C\text{-}F}$ = 2.3 Hz), 14.7 [14.78]; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{32}H_{27}FN_5O_4Pd^+$, 670.1076; found 670.1079. The signals of CH_3CN for ^{1}H NMR and ^{13}C NMR were omitted because the bound CH_3CN was replaced by CD_3CN.



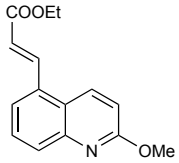
T19

T19. Yellow solid, 0.138 g. Yield: 81 %. ^{1}H NMR (600 MHz, CD_3CN): δ 8.24 (t, J = 7.8 Hz, 1H), 7.78–7.75 (m, 2H), 7.13–7.10 (m, 2H), 7.04 (d, J = 7.7 Hz, 1H), 6.94 (ddd, J = 9.9, 8.2, 1.4 Hz, 1H), 6.61 (d, J = 8.4 Hz, 2H), 3.80 (s, 3H), 3.79 (s, 3H), 2.89–2.83 (m, 1H), 2.76–2.69 (m, 1H), 1.26 (t, J = 7.5 Hz, 3H); ^{13}C NMR (151 MHz, CD_3CN): δ 169.83, 169.36, 158.91 (d, $J_{C\text{-}F}$ = 243.2 Hz), 150.67, 153.48, 153.90, 144.34, 143.78, 135.03 (d, $J_{C\text{-}F}$ = 13.1 Hz), 127.59 (d, $J_{C\text{-}F}$ = 8.6 Hz), 127.49, 127.12, 127.10, 126.25, 125.39 (d, $J_{C\text{-}F}$ = 3.1 Hz), 114.30 (d, $J_{C\text{-}F}$ = 21.4 Hz), 105.92, 105.89, 57.16, 57.15, 26.18 (d, $J_{C\text{-}F}$ = 2.5 Hz), 15.60; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{25}H_{24}FN_4O_4Pd^+$, 569.0811; found 569.0808. The signals of CH_3CN for ^{1}H NMR and ^{13}C NMR were omitted because the bound CH_3CN was replaced by CD_3CN.



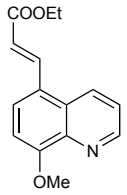
5a

ethyl (*E*)-3-(quinolin-5-yl)acrylate **5a**. Pale yellow solid, 16.7 mg. Yield: 73%. TLC (Hexanes:EtOAc, 67:33 v/v): RF = 0.17; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.97 (dd, J = 4.1, 1.6 Hz, 1H), 8.54 (d, J = 8.6 Hz, 1H), 8.42 (d, J = 15.8 Hz, 1H), 8.16 (d, J = 8.4 Hz, 1H), 7.82 (d, J = 7.3 Hz, 1H), 7.50 (dd, J = 8.3,7.3 Hz, 1H), 7.49 (dd, J = 8.6, 4.1 Hz, 1H), 6.56 (d, J = 15.7 Hz, 1H), 4.33 (q, J = 7.1 Hz, 2H), 1.38 (t, J = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.58, 150.68, 148.40, 139.89, 132.11, 131.75, 131.74, 129.03, 126.60, 125.28, 121.94, 121.59, 60.78, 14.36; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{14}H_{14}NO_2^+$, 228.1019; found 228.1027.



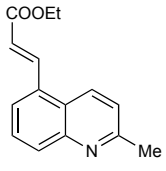
5b

ethyl (*E*)-3-(2-methoxyquinolin-5-yl)acrylate **5b**. White solid, 17.2 mg. Yield: 67%. TLC (Hexanes:EtOAc, 67:33 v/v): RF = 0.60; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.38–8.35 (m, 2H), 7.89 (d, *J* = 7.8 Hz, 1H), 7.64 (ddd, *J* = 7.2, 1.8, 0.6 Hz, 1H), 7.61 (t, *J* = 7.8 Hz, 1H), 6.98 (d, *J* = 9.0 Hz, 1H), 6.52 (d, *J* = 15.6 Hz, 1H), 4.31 (q, *J* = 7.2 Hz, 2H), 4.08 (s, 3H), 1.37 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.70, 162.39, 147.02, 140.49, 134.25, 131.83, 129.52, 129.12, 123.39, 122.71, 121.42, 113.67, 60.70, 53.44, 14.36; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{15}H_{16}NO_3^+$, 258.1125; found 258.1135.



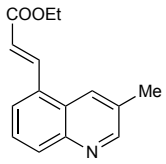
5c

ethyl (*E*)-3-(8-methoxyquinolin-5-yl)acrylate **5c**. Yellow solid, 23.4 mg. Yield: 91%. TLC (CH_2Cl_2:MeOH, 90:10 v/v): RF = 0.47; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.98 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.53 (dd, *J* = 8.4, 1.2 Hz, 1H), 8.35 (d, *J* = 15.6 Hz, 1H), 7.82 (d, *J* = 7.8 Hz, 1H), 7.53 (dd, *J* = 8.4, 4.2 Hz, 1H), 7.08 (d, *J* = 7.8 Hz, 1H), 6.48 (d, *J* = 15.6 Hz, 1H), 4.31 (q, *J* = 7.2 Hz, 2H), 4.13 (s, 3H), 1.37 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.95, 157.09, 149.44, 140.06, 139.70, 131.71, 127.67, 126.13, 123.72, 122.25, 119.25, 107.43, 60.59, 56.22, 14.39; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{15}H_{16}NO_3^+$, 258.1125; found 258.1136.



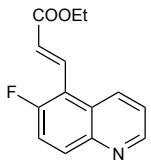
5d

ethyl (*E*)-3-(2-methylquinolin-5-yl)acrylate **5d**. White solid, 16.6 mg. Yield: 69%. TLC (Hexanes:EtOAc, 67:33 v/v): RF = 0.23; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.43–8.39 (m, 2H), 8.40 (d, *J* = 16.2 Hz, 1H), 8.06 (d, *J* = 8.4 Hz, 1H), 7.76 (d, *J* = 7.2 Hz, 1H), 7.69 (dd, *J* = 8.4, 7.2 Hz, 1H), 7.37 (d, *J* = 9.0 Hz, 1H), 6.54 (d, *J* = 15.6 Hz, 1H), 4.32 (q, *J* = 7.2 Hz, 2H), 2.76 (s, 3H), 1.38 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.68, 159.35, 148.04, 140.12, 131.80, 131.77, 130.96, 128.98, 124.85, 124.39, 122.55, 121.59, 60.74, 25.24, 14.36; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{15}H_{16}NO_2^+$, 242.1176; found 242.1182.



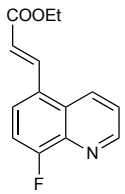
5e

ethyl (*E*)-3-(3-methylquinolin-5-yl)acrylate **5e**. Pale yellow solid, 19.8 mg. Yield: 82%. TLC (Hexanes:EtOAc, 67:33 v/v): RF = 0.20; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.81 (d, *J* = 2.4 Hz, 1H), 8.42 (d, *J* = 16.2 Hz, 1H), 8.28 (s, 1H), 8.11 (d, *J* = 8.4 Hz, 1H), 7.79 (d, *J* = 7.2 Hz, 1H), 7.64 (dd, *J* = 8.4, 7.8 Hz, 1H), 6.54 (d, *J* = 15.6 Hz, 1H), 4.33 (q, *J* = 7.2 Hz, 2H), 2.57 (s, 3H), 1.38 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.75, 152.62, 146.61, 140.14, 131.50, 131.50, 131.35, 130.42, 127.98, 126.45, 125.26, 121.45, 60.75, 19.05, 14.37; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{15}H_{16}NO_2^+$, 242.1176; found 242.1183.



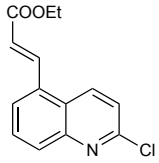
5f

ethyl (*E*)-3-(6-fluoroquinolin-5-yl)acrylate **5f**. Pale yellow solid, 10.5 mg. Yield: 43 %. TLC (Hexanes:EtOAc, 67:33 v/v): RF = 0.19; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.93 (dd, *J* = 4.2, 1.2 Hz, 1H), 8.54 (d, *J* = 9.0 Hz, 1H), 8.17–8.12 (m, 2H), 7.56–7.50 (m, 2H), 6.73 (dd, *J* = 16.2, 0.6 Hz, 1H), 4.33 (q, *J* = 7.2 Hz, 2H), 1.38 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.79, 159.19 (d, $J_{C\text{-}F}$ = 256.6 Hz), 149.78 (d, $J_{C\text{-}F}$ = 2.3 Hz), 145.49, 133.47, 133.31 (d, $J_{C\text{-}F}$ = 10.8 Hz), 131.92 (d, $J_{C\text{-}F}$ = 6.6 Hz), 127.45 (d, $J_{C\text{-}F}$ = 5.4 Hz), 125.97 (d, $J_{C\text{-}F}$ = 12.2 Hz), 122.14, 119.81 (d, $J_{C\text{-}F}$ = 27.6 Hz), 116.45 (d, $J_{C\text{-}F}$ = 12.0 Hz), 60.89, 14.33; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{14}H_{13}FNO_2^+$, 246.0925; found 246.0936.



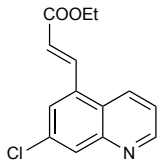
5g

ethyl (*E*)-3-(8-fluoroquinolin-5-yl)acrylate **5g**. White solid. Yield: 51% (calculated based on crude ^{1}H NMR). TLC (Hexanes:EtOAc, 67:33 v/v): RF = 0.20; ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.03 (dd, *J* = 4.2, 1.2 Hz, 1H), 8.56 (dt, *J* = 9.0, 1.8 Hz, 1H), 8.35 (d, *J* = 15.6 Hz, 1H), 7.79 (dd, *J* = 7.8, 4.8 Hz, 1H), 7.58 (dd, *J* = 9.0, 4.2 Hz, 1H), 7.44 (dd, *J* = 10.2, 8.4 Hz, 1H), 6.52 (dd, *J* = 16.2, 0.6 Hz, 1H), 4.32 (q, *J* = 7.2 Hz, 2H), 1.38 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.49, 159.09 (d, $J_{C\text{-}F}$ = 261.5 Hz), 150.77 (d, $J_{C\text{-}F}$ = 1.6 Hz), 139.01 (d, $J_{C\text{-}F}$ = 1.8 Hz), 138.53 (d, $J_{C\text{-}F}$ = 11.6 Hz), 131.86 (d, $J_{C\text{-}F}$ = 2.9 Hz), 128.13, 128.10 (d, $J_{C\text{-}F}$ = 3.9 Hz), 125.41 (d, $J_{C\text{-}F}$ = 8.3 Hz), 122.55, 121.67 (d, $J_{C\text{-}F}$ = 2.1 Hz), 113.49 (d, $J_{C\text{-}F}$ = 19.8 Hz), 60.83, 14.35; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{14}H_{13}FNO_2^+$, 246.0925; found 246.0933.



5h

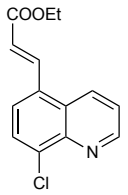
ethyl (*E*)-3-(2-chloroquinolin-5-yl)acrylate **5h**. White solid, 14.9 mg. Yield: 57%. TLC (Hexanes:EtOAc, 67:33 v/v): RF = 0.51; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.47 (dd, *J* = 9.0, 1.2 Hz, 1H), 8.34 (d, *J* = 15.6 Hz, 1H), 8.06 (d, *J* = 8.4 Hz, 1H), 7.82 (d, *J* = 7.2 Hz, 1H), 7.75 (dd, *J* = 7.8, 7.2 Hz, 1H), 7.47 (d, *J* = 9.0 Hz, 1H), 6.55 (d, *J* = 15.6 Hz, 1H), 4.32 (q, *J* = 7.2 Hz, 2H), 1.38 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.38, 151.16, 148.16, 139.39, 134.73, 132.26, 130.65, 130.64, 125.54, 125.20, 122.87, 122.59, 60.89, 14.34; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{14}H_{13}ClNO_2^+$, 262.0629; found 262.0631.



5i

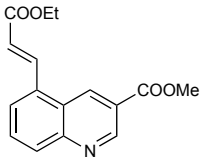
ethyl (*E*)-3-(7-chloroquinolin-5-yl)acrylate **5i**. Pale yellow solid, 13.2 mg. Yield: 50%. TLC (Hexanes:EtOAc, 67:33 v/v): RF = 0.32; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.96 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.48 (d, *J* = 9.0 Hz, 1H), 8.33 (d, *J* = 16.2 Hz, 1H), 8.14 (d, *J* = 2.4 Hz, 1H), 7.76 (d, *J* = 1.8 Hz, 1H), 7.49 (dd, *J* = 8.4, 4.2 Hz, 1H), 6.56 (d, *J* = 15.6 Hz, 1H), 4.33 (q, *J* = 7.2 Hz, 2H), 1.38 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.17, 151.67, 148.89, 138.55, 135.01,

133.76, 131.83, 130.26, 125.96, 125.05, 123.33, 121.69, 60.97, 14.32; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{14}H_{13}ClNO_2^+$, 262.0629; found 262.0640.



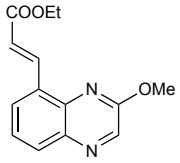
5j

ethyl (*E*)-3-(8-chloroquinolin-5-yl)acrylate **5j**. White solid. Yield: 27% (calculated based on crude ^{1}H NMR). TLC (Hexanes:EtOAc, 67:33 v/v): RF = 0.35; ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.11 (dd, *J* = 4.1, 1.6 Hz, 1H), 8.57 (dd, *J* = 8.6, 1.6 Hz, 1H), 8.37 (d, *J* = 15.7 Hz, 1H), 7.87 (d, *J* = 7.9 Hz, 1H), 7.75 (d, *J* = 7.9 Hz, 1H), 7.58 (dd, *J* = 8.6, 4.1 Hz, 1H), 6.55 (d, *J* = 15.7 Hz, 1H), 4.33 (q, *J* = 7.1 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.37, 151.15, 144.50, 139.03, 135.75, 132.41, 131.39, 129.33, 127.78, 125.10, 122.44, 122.37, 60.90, 14.34; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{14}H_{13}ClNO_2^+$, 262.0629; found 262.0640.



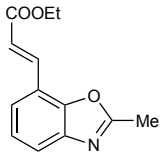
5k

methyl (*E*)-5-(3-ethoxy-3-oxoprop-1-en-1-yl)quinoline-3-carboxylate **5k**. White solid, 21.2 mg. Yield: 74%. TLC (Hexanes:EtOAc, 67:33 v/v): RF = 0.26; ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.49 (d, *J* = 2.4 Hz, 1H), 9.18 (dd, *J* = 1.8, 0.6 Hz, 1H), 8.46 (d, *J* = 15.6 Hz, 1H), 8.20 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 7.2 Hz, 1H), 7.84 (dd, *J* = 8.4, 7.2 Hz, 1H), 6.59 (d, *J* = 15.6 Hz, 1H), 4.35 (q, *J* = 7.2 Hz, 2H), 4.05 (s, 3H), 1.40 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.36, 165.65, 150.31, 149.96, 139.18, 134.38, 133.55, 131.51, 131.33, 126.01, 125.25, 123.30, 122.92, 60.94, 52.65, 14.35; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{16}H_{16}NO_4^+$, 286.1074; found 286.1084.



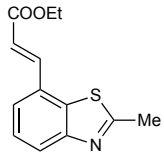
5l

ethyl (*E*)-3-(3-methoxyquinoxalin-5-yl)acrylate **5l**. White solid, 21.2 mg. Yield: 82%. TLC (Hexanes:EtOAc, 80:20 v/v): RF = 0.37; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.67 (d, *J* = 16.2 Hz, 1H), 8.52 (s, 1H), 8.05 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.96 (d, *J* = 7.2 Hz, 1H), 7.57 (ddd, *J* = 8.2, 7.5, 0.5 Hz, 1H), 6.84 (d, *J* = 16.2 Hz, 1H), 4.31 (q, *J* = 7.2 Hz, 2H), 4.16 (s, 3H), 1.37 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 167.24, 157.25, 139.93, 139.84, 138.95, 138.71, 131.16, 130.97, 128.71, 126.14, 120.25, 60.52, 54.02, 14.37; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{14}H_{15}N_2O_3^+$, 259.1077; found 259.1085.



5m

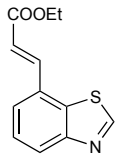
ethyl (*E*)-3-(2-methylbenzo[*d*]oxazol-7-yl)acrylate **5m**. White solid, 18.7 mg. Yield: 81%. TLC (Hexanes:EtOAc, 80:20 v/v): RF = 0.27; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.80 (d, *J* = 16.2 Hz, 1H), 7.67 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.38 (d, *J* = 7.8 Hz, 1H), 7.32 (t, *J* = 7.8 Hz, 1H), 6.89 (d, *J* = 16.2 Hz, 1H), 4.31 (q, *J* = 7.2 Hz, 2H), 2.71 (s, 3H), 1.38 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 167.00, 164.16, 149.14, 142.17, 138.84, 126.24, 124.47, 122.02, 121.19, 119.01, 60.69, 14.63, 14.37; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{13}H_{14}NO_3^+$, 232.0968; found 232.0975.



5n

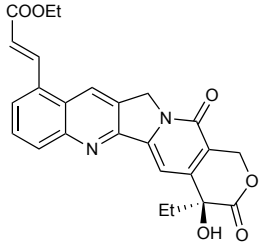
ethyl (*E*)-3-(2-methylbenzo[*d*]thiazol-7-yl)acrylate **5n**. White solid, 16.7 mg. Yield: 68%. TLC (Hexanes:EtOAc, 80:20 v/v): RF = 0.27; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.99 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.86 (d, *J* = 16.2 Hz 1H), 7.54 (d, *J* = 7.8 Hz, 1H), 7.49 (t, *J* = 7.8 Hz, 1H), 6.55 (d, *J* =

16.2 Hz, 1H), 4.31 (q, *J* = 7.2 Hz, 2H), 2.88 (s, 3H), 1.37 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 167.17, 166.70, 154.43, 142.57, 134.53, 128.92, 126.28, 126.23, 124.17, 120.56, 60.79, 20.09, 14.34; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{13}H_{14}NO_2S^+$, 248.0740; found 248.0749.



5o

ethyl (*E*)-3-(benzo[*d*]thiazol-7-yl)acrylate **5o**. White solid, 11.3 mg. Yield: 51%. TLC (Hexanes:EtOAc, 80:20 v/v): RF = 0.27; ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.08 (s, 1H), 8.19 (dd, *J* = 7.8, 0.6 Hz, 1H), 7.93 (d, *J* = 16.2 Hz, 1H), 7.65 (d, *J* = 7.2 Hz, 1H), 7.58 (dd, *J* = 7.8,7.2 Hz, 1H), 6.61 (d, *J* = 16.2 Hz, 1H), 4.32 (q, *J* = 7.2 Hz, 2H), 1.38 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.61, 154.30, 154.04, 142.32, 132.66, 129.40, 126.95, 126.57, 125.44, 120.86, 60.87, 14.34; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{12}H_{12}NO_2S^+$, 234.0583; found 234.0594.

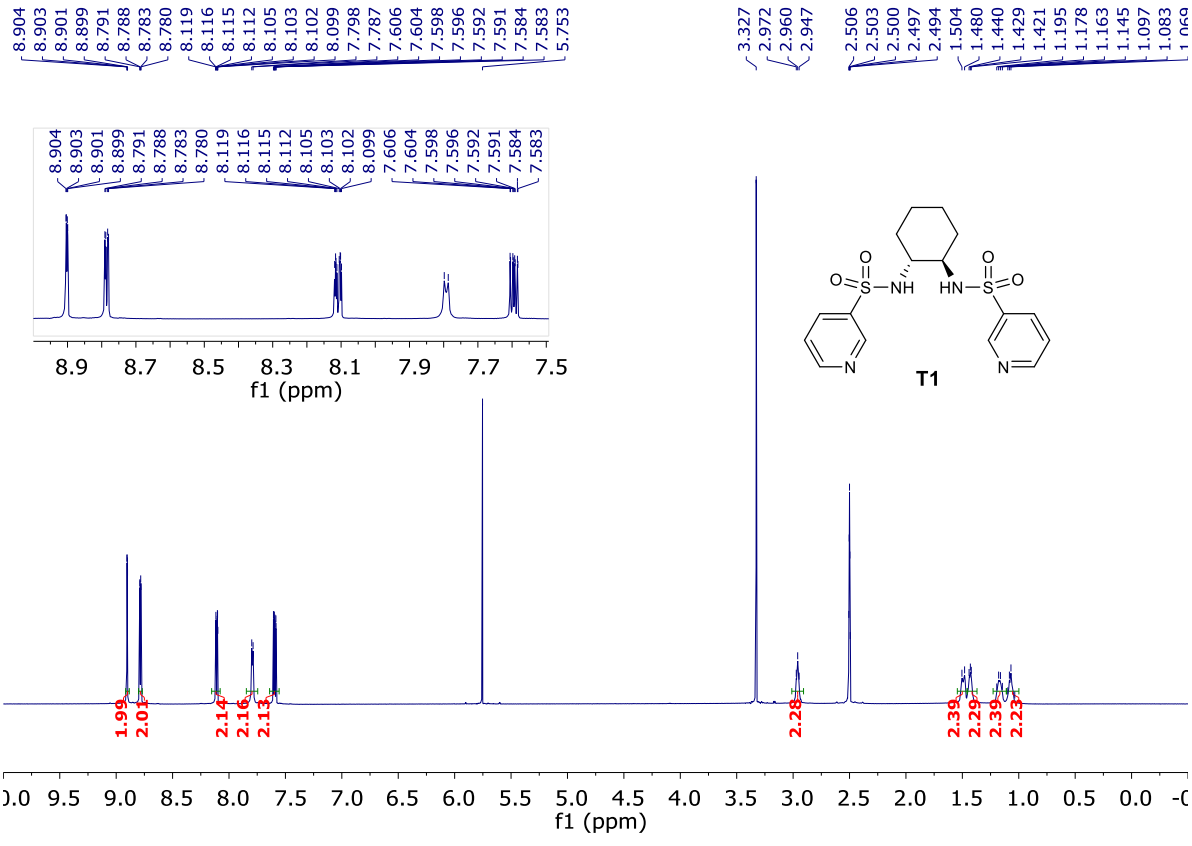


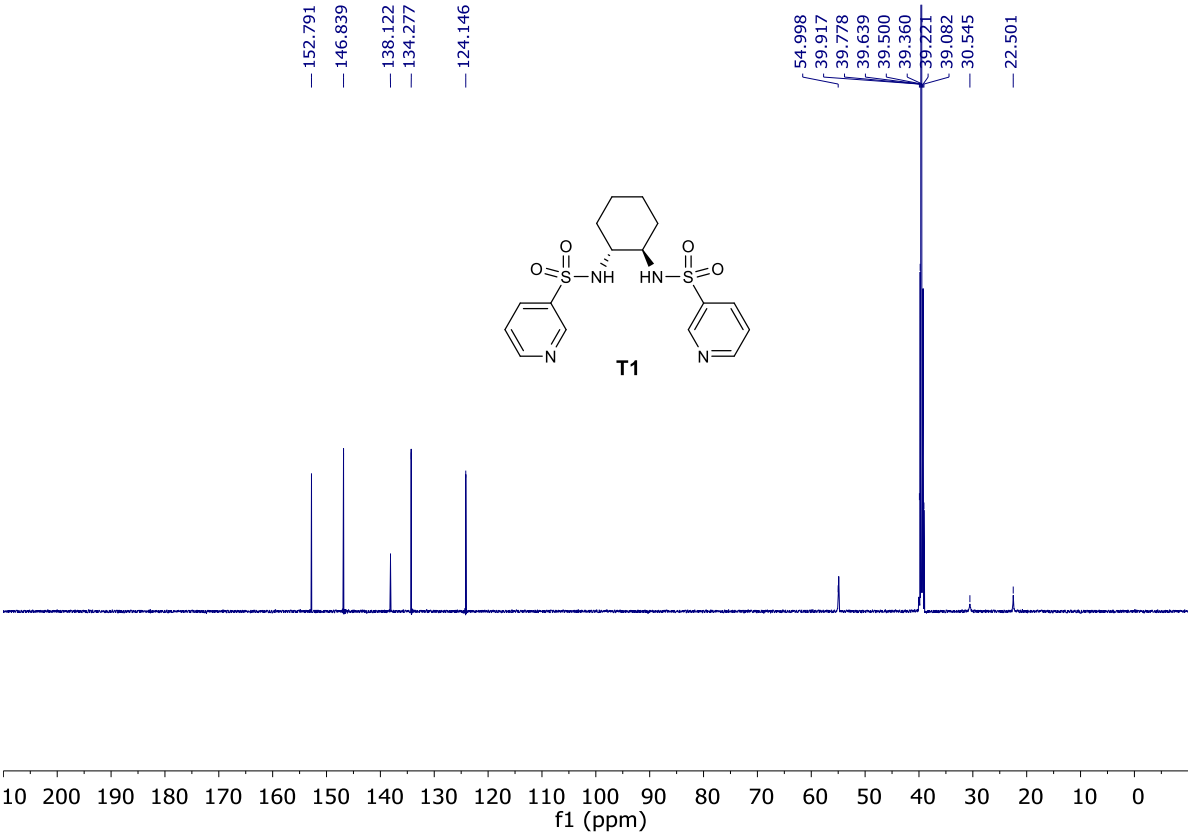
5p

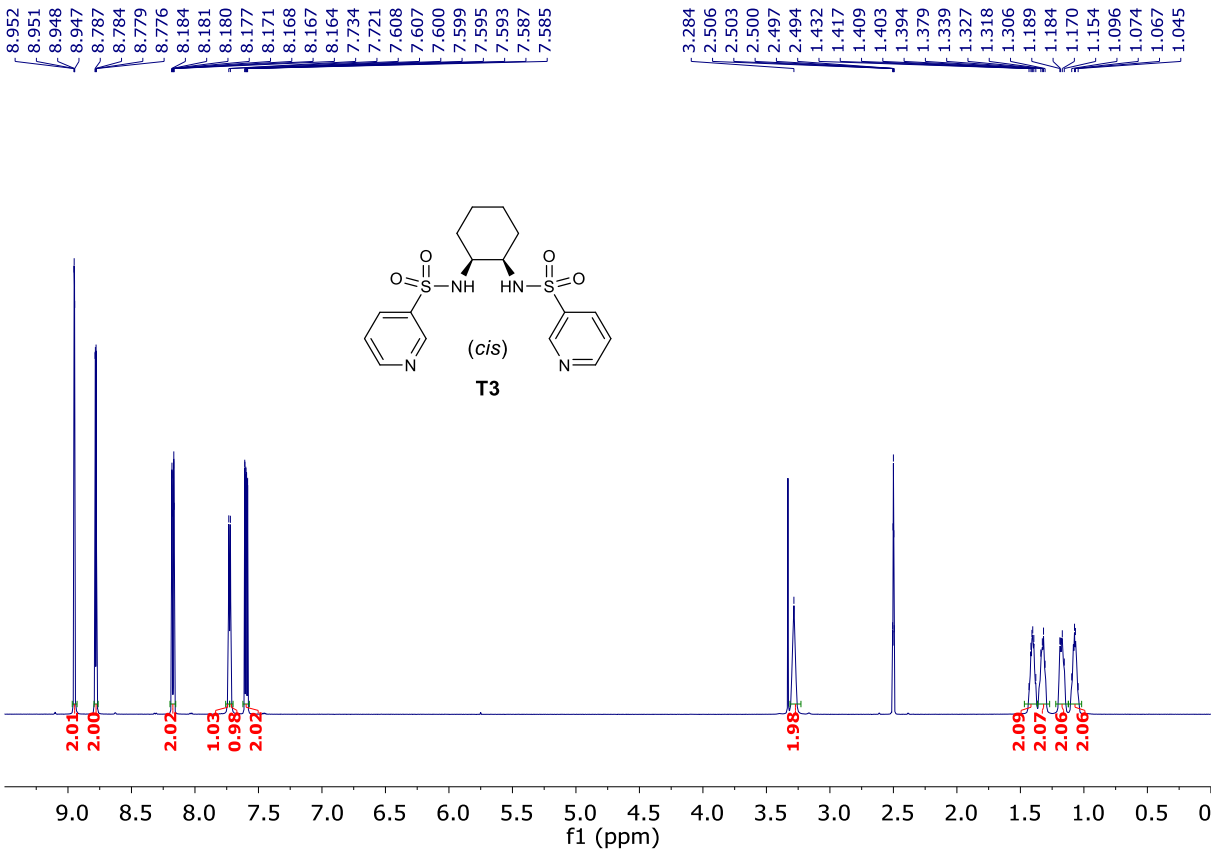
ethyl (*S*,*E*)-3-(4-ethyl-4-hydroxy-3,14-dioxo-3,4,12,14-tetrahydro-1*H*-pyrano[3',4':6,7] indolizino[1,2-*b*]quinolin-10-yl)acrylate **5p**. Pale yellow solid, 21.9 mg. Yield: 49%. TLC (CH_2Cl_2:MeOH, 90:10 v/v): RF = 0.41; ^{1}H NMR (600 MHz, DMSO-d_6): δ 9.10 (s, 1H), 8.47 (d, *J* = 15.7 Hz, 1H), 8.26 (d, *J* = 8.4 Hz, 1H), 8.18 (d, *J* = 7.3 Hz, 1H), 7.91 (dd, *J* = 8.5, 7.4 Hz, 1H), 7.37 (s, 1H), 6.82 (d, *J* = 15.7 Hz, 1H), 6.55 (s, 1H), 5.44 (s, 2H), 5.31 (s, 2H), 4.28 (q, *J* = 7.1 Hz, 2H), 1.94–1.83 (m, 2H), 1.33 (t, *J* = 7.1 Hz, 3H), 0.89 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (151 MHz, DMSO-d_6): δ 172.44, 165.88, 156.83, 152.83, 149.95, 148.11, 145.20, 139.36, 131.91, 131.38, 130.67, 130.03, 127.72, 126.62, 126.09, 122.20, 119.37, 96.94, 72.36, 65.26, 60.39,

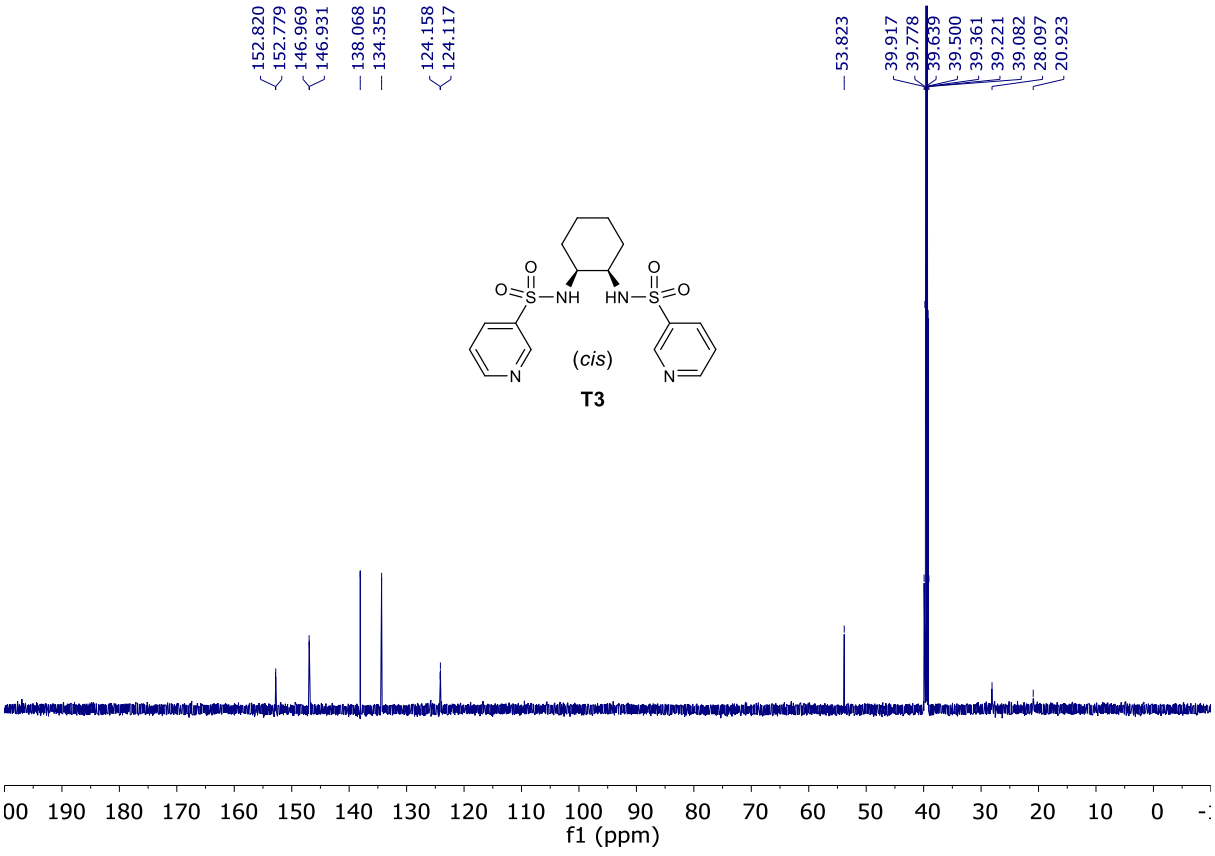
50.56, 30.30, 14.25, 7.77; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd. for $C_{25}H_{23}N_2O_6^+$, 447.1551; found 447.1552.

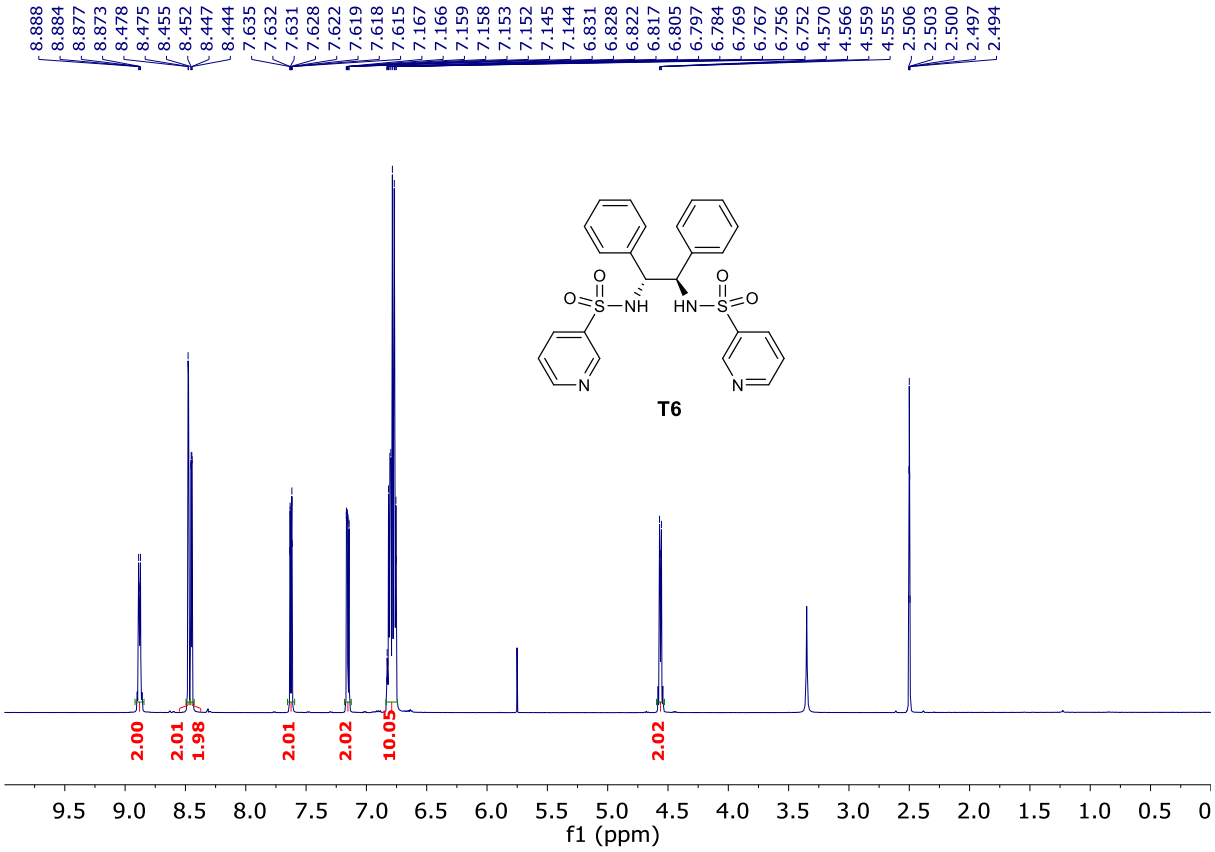
9. NMR Spectra

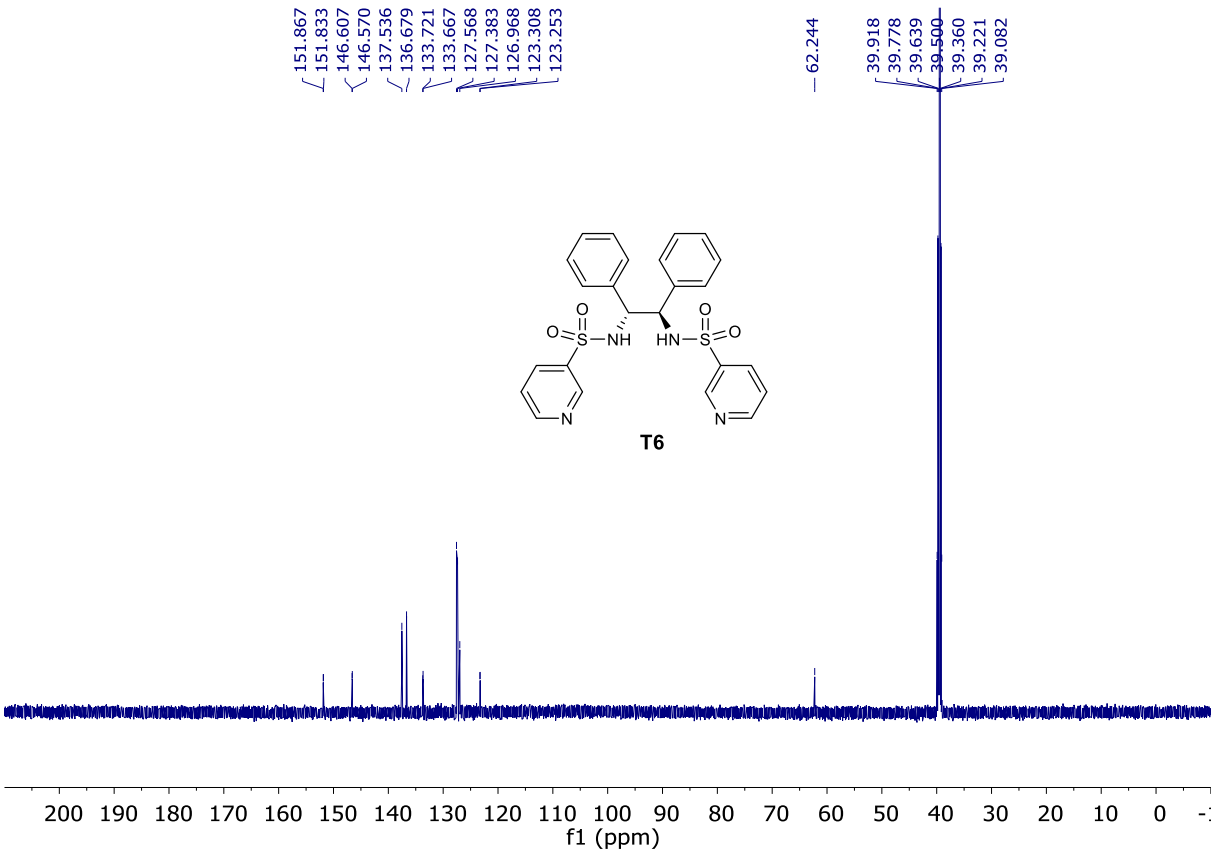

8.904
8.903
8.901
8.899
8.791
8.788
8.783
8.780
8.119
8.116
8.115
8.112
8.105
8.103
8.102
8.099
7.798
7.787
7.606
7.604
7.598
7.596
7.592
7.591
7.584
7.583
5.753
3.327
2.972
2.960
2.947
2.506
2.503
2.500
2.497
2.494
1.504
1.480
1.440
1.429
1.421
1.195
1.178
1.163
1.145
1.097
1.083
8.9 8.7 8.5 8.3 8.1 7.9 7.7 7.5
f1 (ppm)
T1
1.99
2.01
2.14
2.16
2.13
2.28
2.39
2.29
2.39
2.23
f1 (ppm)

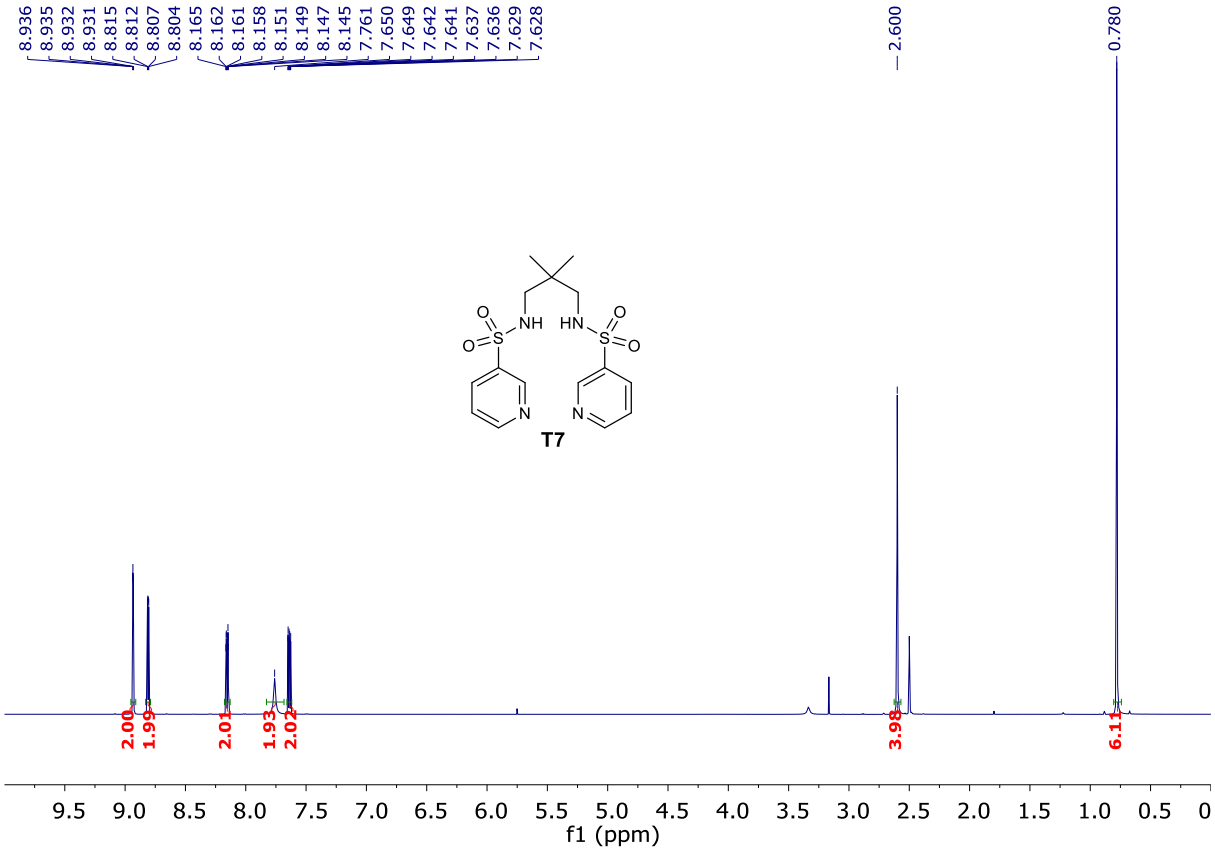

152.791
146.839
138.122
134.277
124.146
54.998
39.917
39.778
39.639
39.500
39.360
39.221
39.082
30.545
22.501
T1
f1 (ppm)


8.952
8.951
8.948
8.947
8.787
8.784
8.779
8.776
8.184
8.181
8.180
8.177
8.171
8.168
8.167
8.164
7.734
7.721
7.608
7.607
7.600
7.599
7.595
7.593
7.587
7.585
3.284
2.506
2.503
2.500
2.497
2.494
1.432
1.417
1.409
1.403
1.394
1.379
1.339
1.327
1.318
1.306
1.189
1.184
1.170
1.154
1.096
1.074
1.067
1.045
(cis)
T3
2.01
2.00
2.02
1.03
0.98
2.02
1.98
2.09
2.07
2.06
2.06
f1 (ppm)


152.820
152.779
146.969
146.931
138.068
134.355
124.158
124.117
53.823
39.917
39.778
39.639
39.500
39.361
39.221
39.082
28.097
20.923
(cis)
T3
f1 (ppm)


8.888
8.884
8.877
8.873
8.478
8.475
8.455
8.452
8.447
8.444
7.635
7.632
7.631
7.628
7.622
7.619
7.618
7.615
7.167
7.166
7.159
7.158
7.153
7.152
7.145
7.144
6.831
6.828
6.822
6.817
6.805
6.797
6.784
6.769
6.767
6.756
6.752
4.570
4.566
4.559
4.555
2.506
2.503
2.500
2.497
2.494
T6
2.00
2.01
1.98
2.01
2.02
10.05
2.02
f1 (ppm)


151.867
151.833
146.607
146.570
137.536
136.679
133.721
133.667
127.568
127.383
126.968
123.308
123.253
62.244
39.918
39.778
39.639
39.500
39.360
39.221
39.082
T6
f1 (ppm)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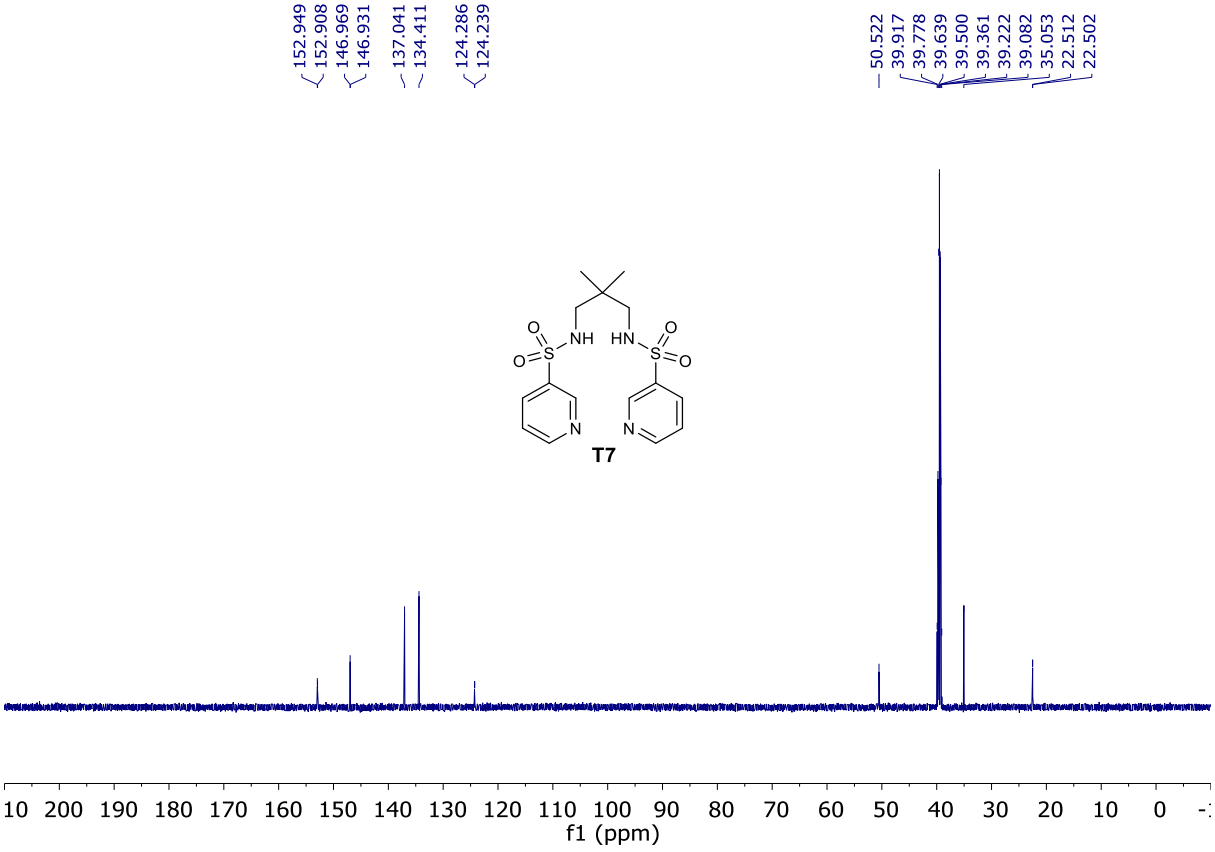
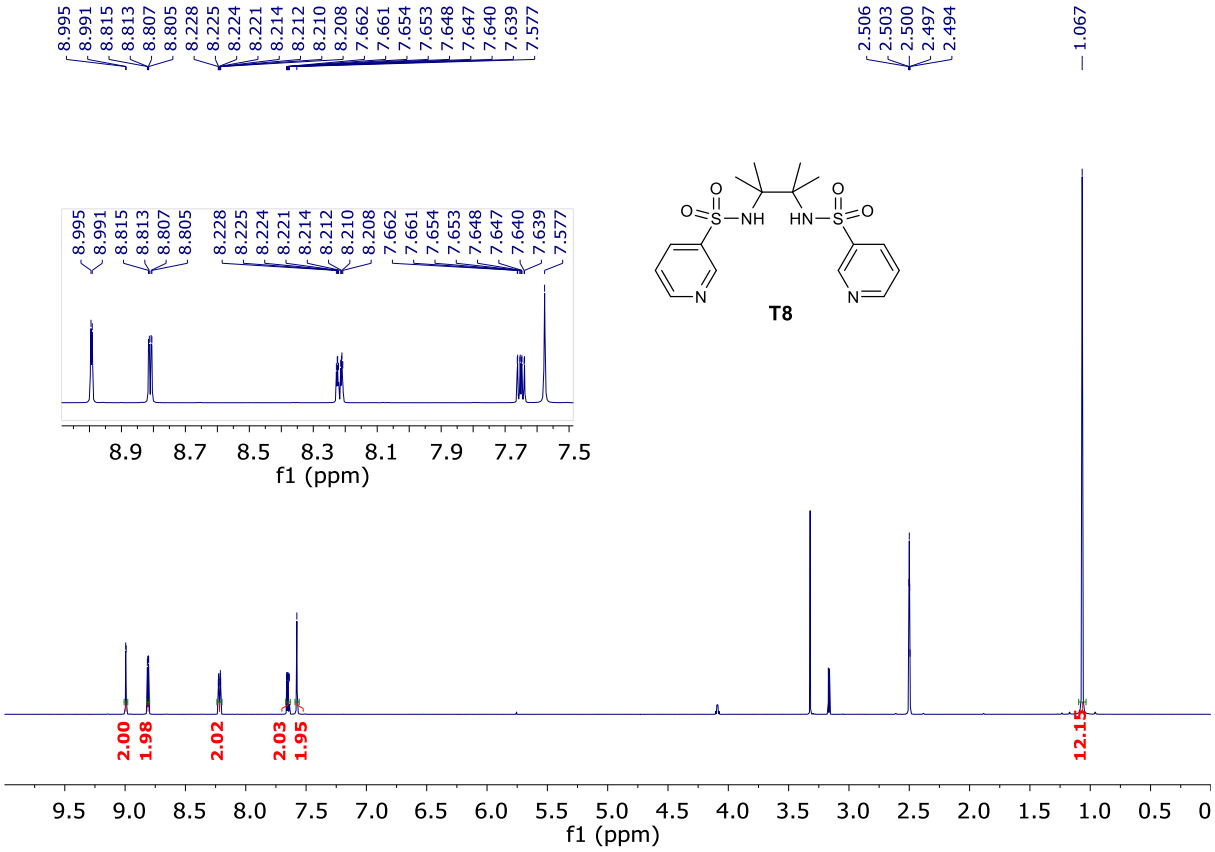
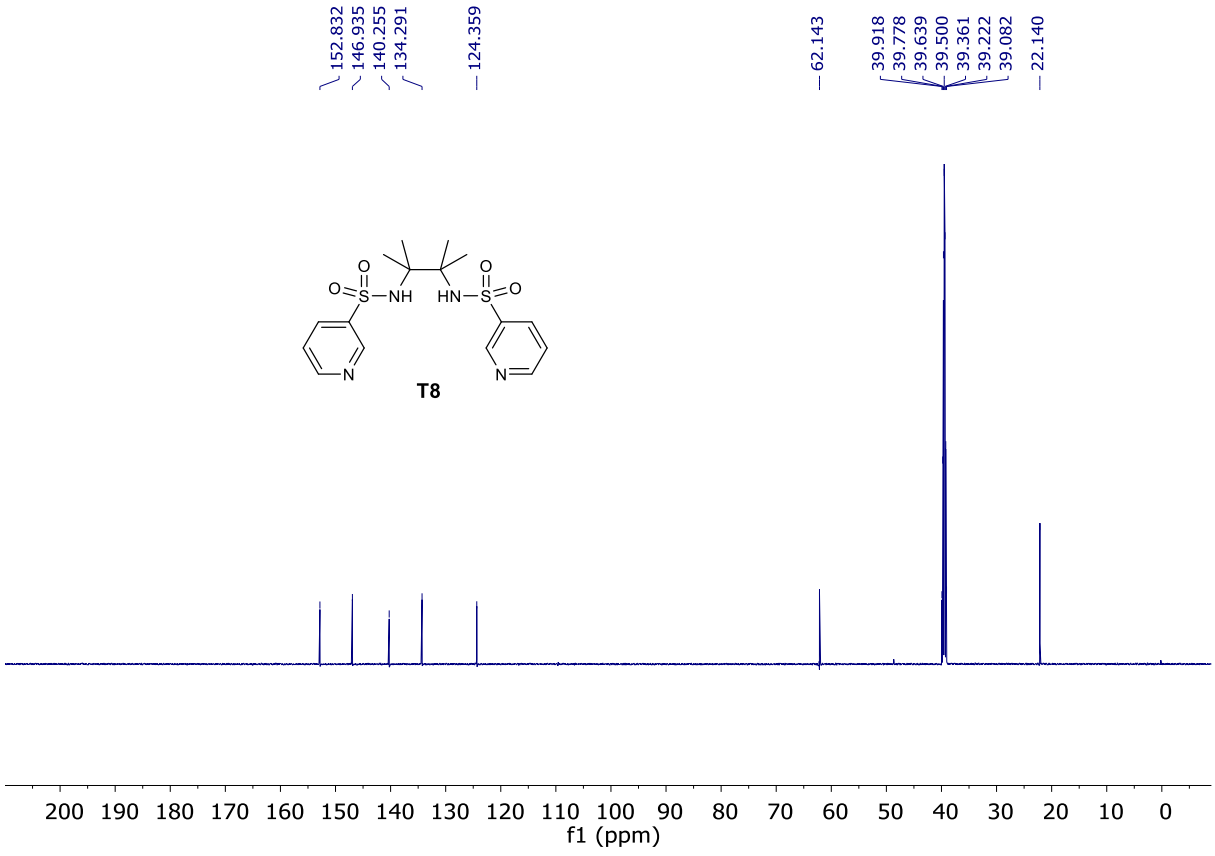
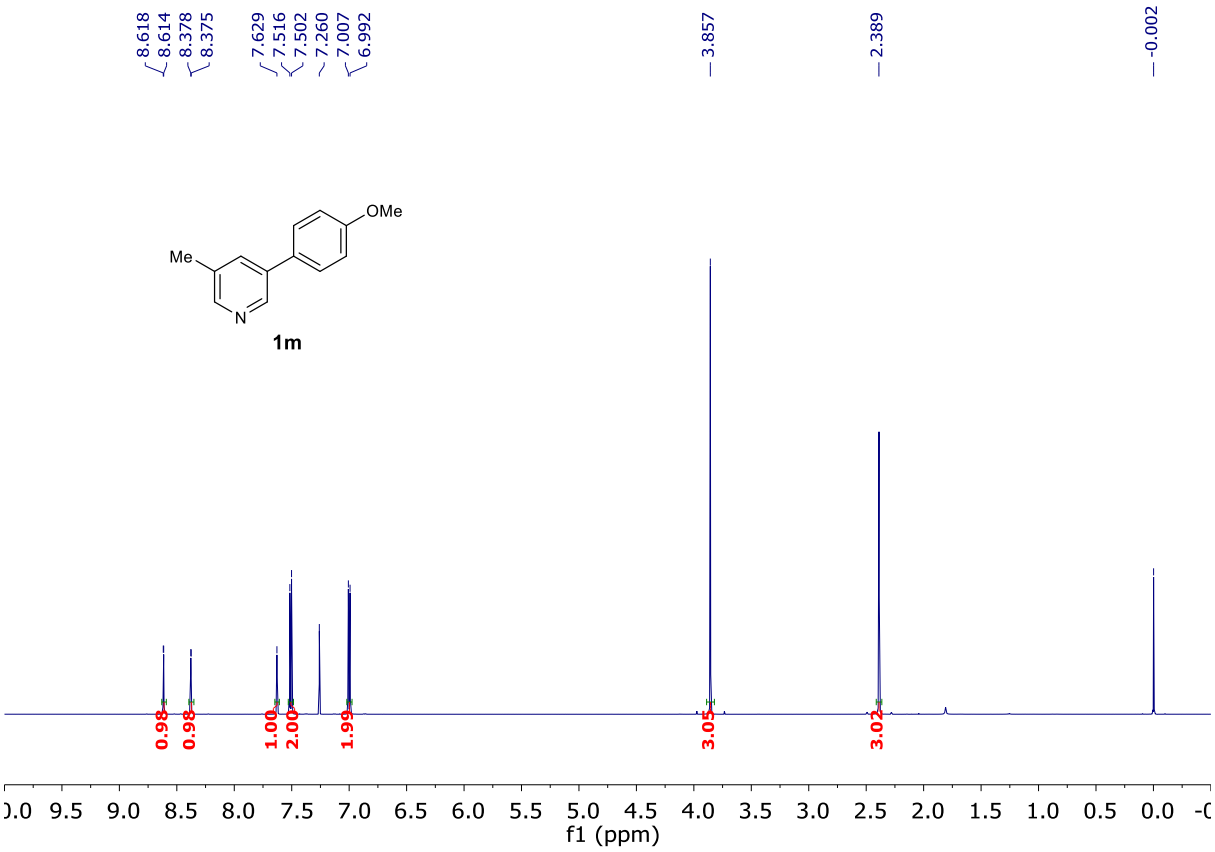
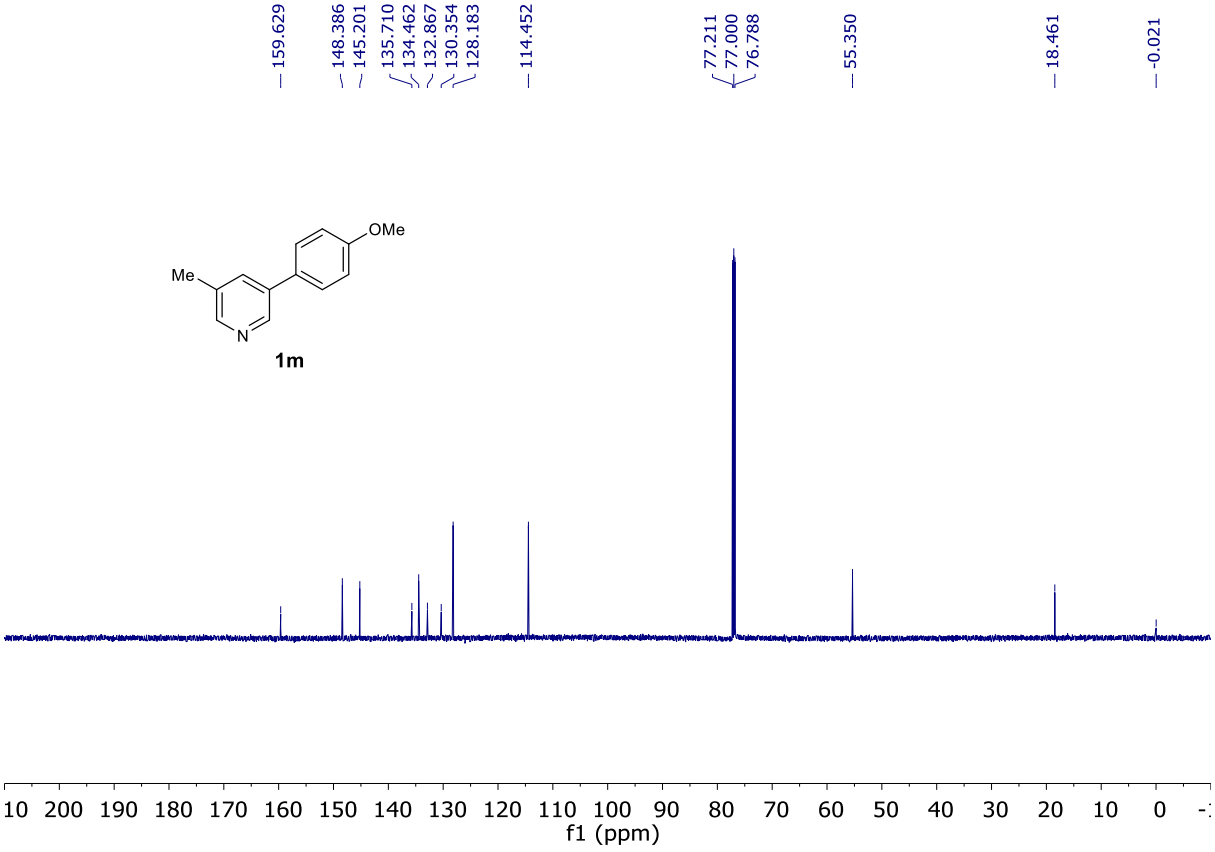
8.935
8.932
8.931
8.815
8.812
8.807
8.804
8.165
8.162
8.161
8.158
8.151
8.149
8.147
8.145
7.761
7.650
7.649
7.642
7.641
7.637
7.636
7.629
7.628
2.600
0.780
NH
HN
T7
2.00
1.99
2.01
1.93
2.02
3.98
6.11
f1 (ppm)

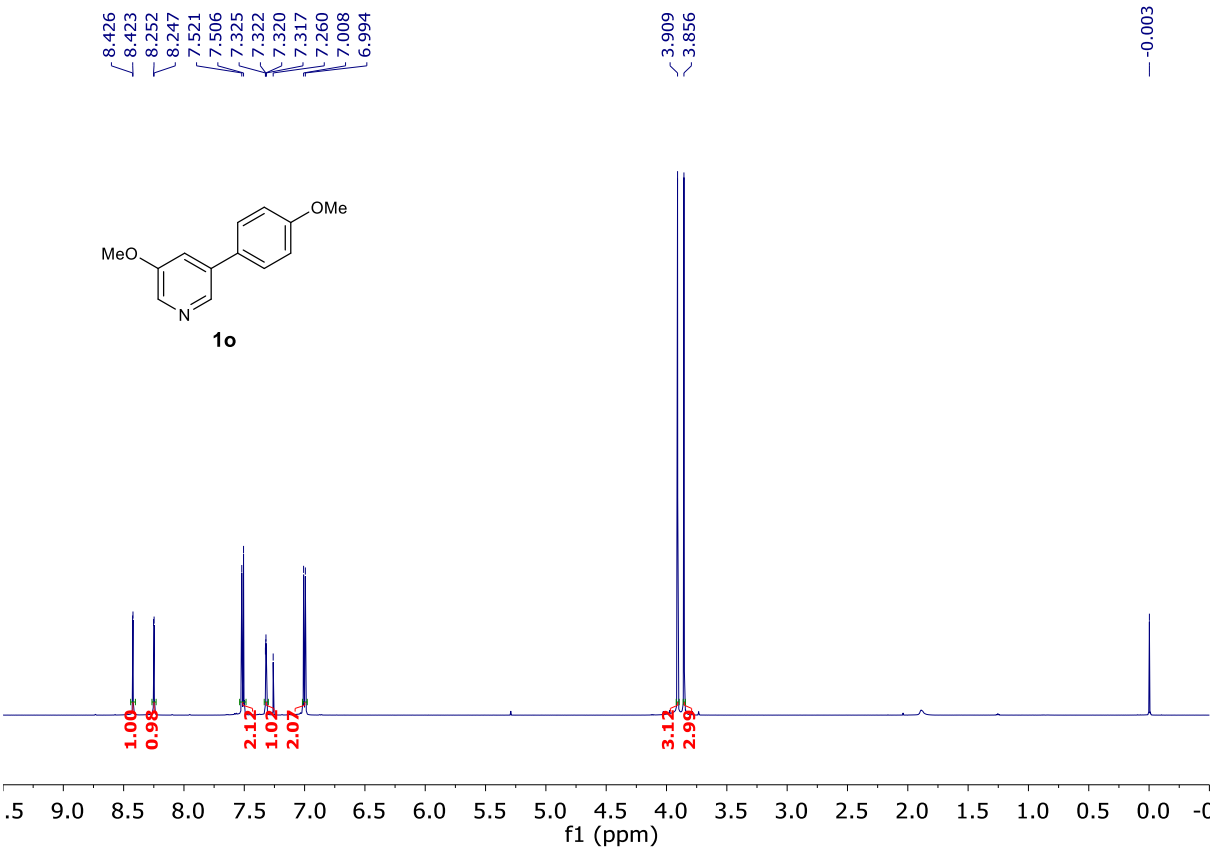

152.949
152.908
146.969
146.931
137.041
134.411
124.286
124.239
50.522
39.917
39.778
39.639
39.500
39.361
39.222
39.082
35.053
22.512
22.502
NH
HN
T7
f1 (ppm)

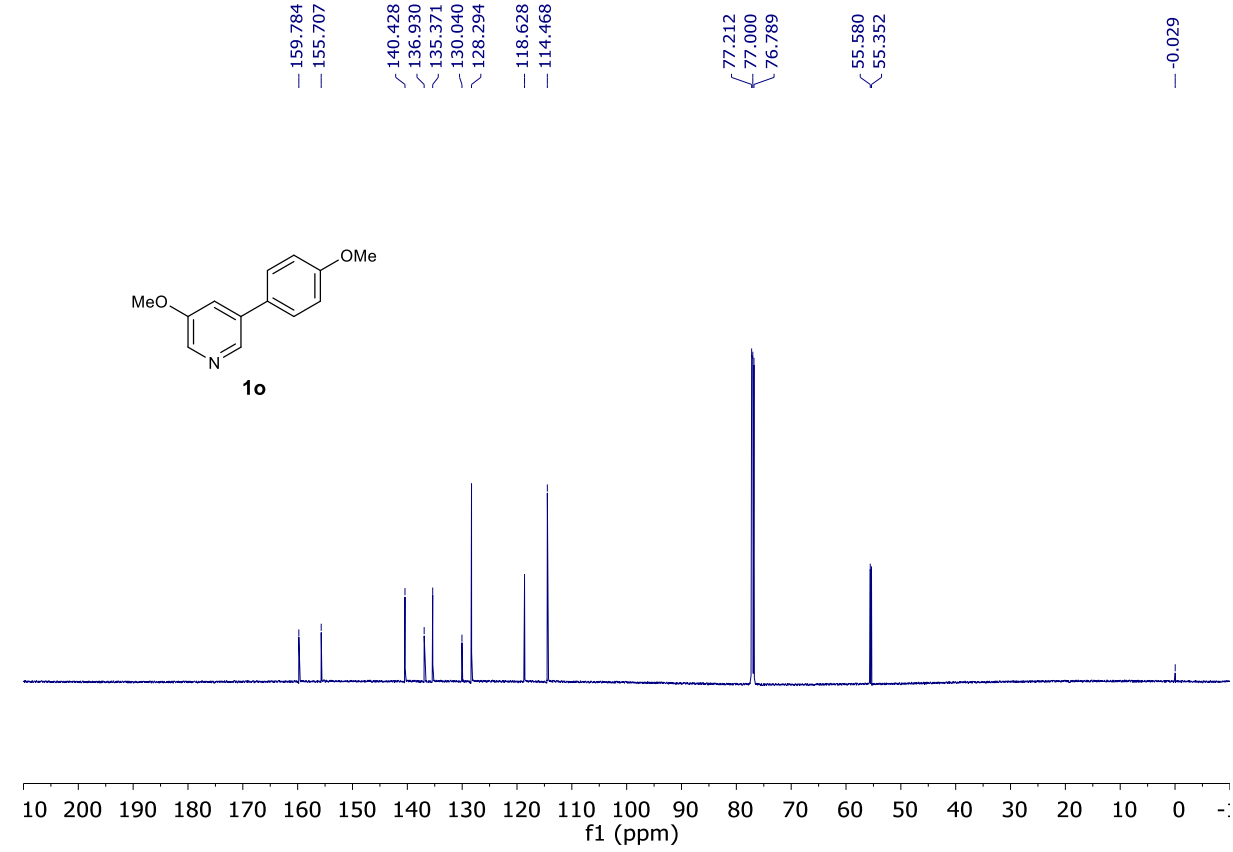

8.995
8.991
8.815
8.813
8.807
8.805
8.228
8.225
8.224
8.221
8.214
8.212
8.210
8.208
7.662
7.661
7.654
7.653
7.648
7.647
7.640
7.639
7.577
2.506
2.503
2.500
2.497
2.494
1.067
T8
f1 (ppm)
2.00
1.98
2.02
2.03
1.95
12.15

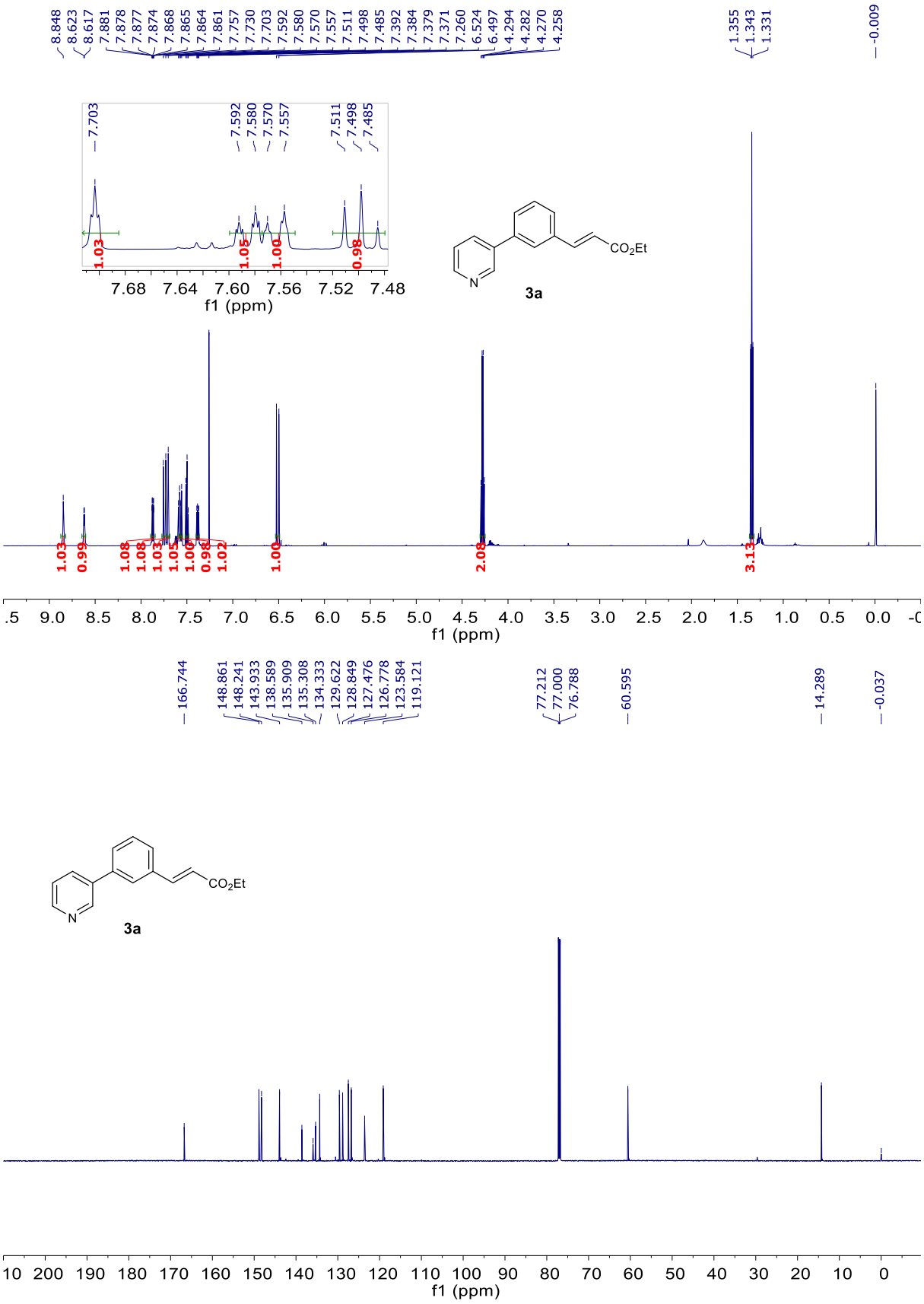

152.832
146.935
140.255
134.291
124.359
62.143
39.918
39.778
39.639
39.500
39.361
39.222
39.082
22.140
T8
f1 (ppm)


8.618
8.614
8.378
8.375
7.629
7.516
7.502
7.260
7.007
6.992
3.857
2.389
-0.002
OMe
Me
N
1m
0.98
0.98
1.00
2.00
1.99
3.05
3.02
f1 (ppm)

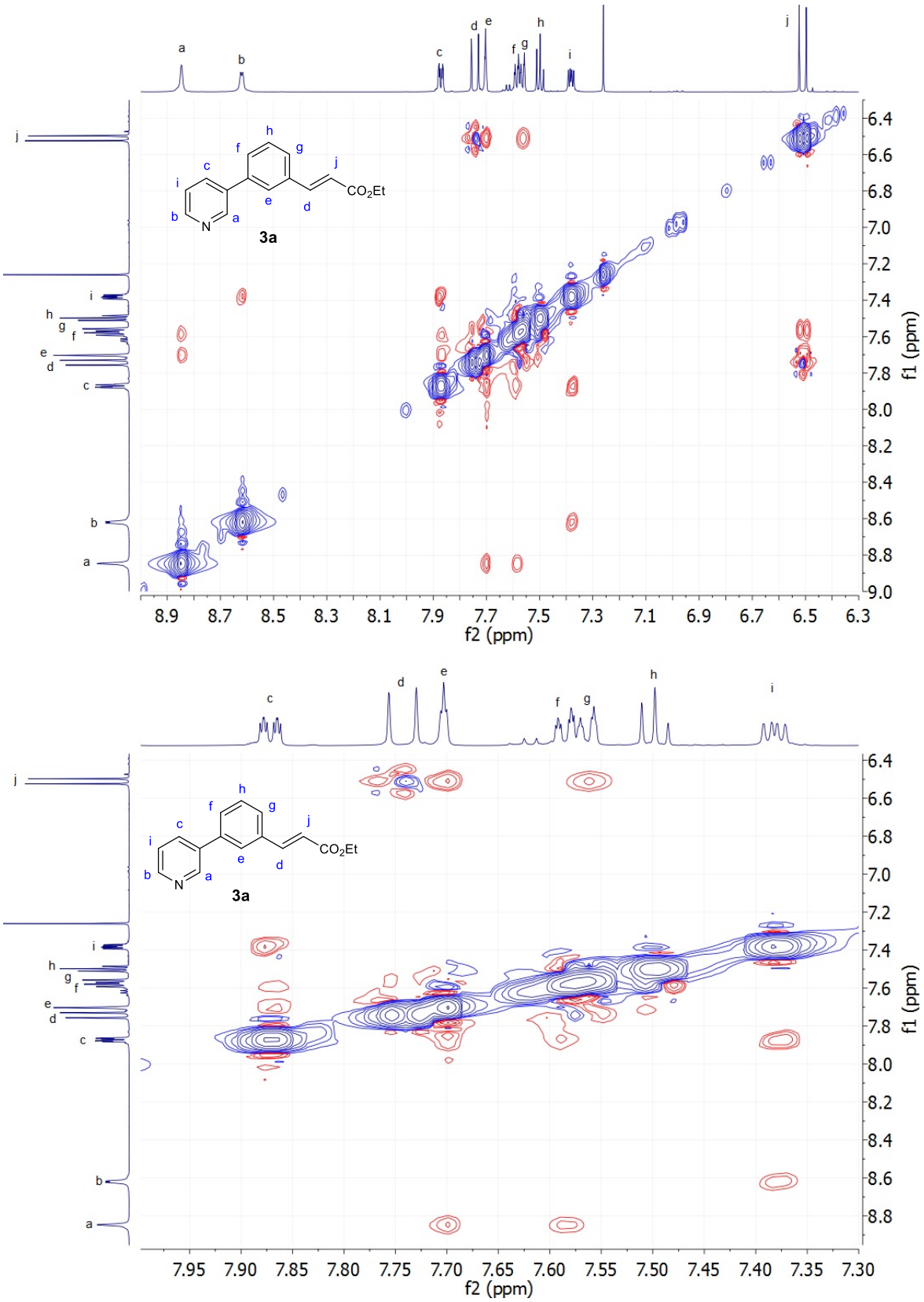

159.629
148.386
145.201
135.710
134.462
132.867
130.354
128.183
114.452
77.211
77.000
76.788
55.350
18.461
-0.021
OMe
Me
N
1m
f1 (ppm)

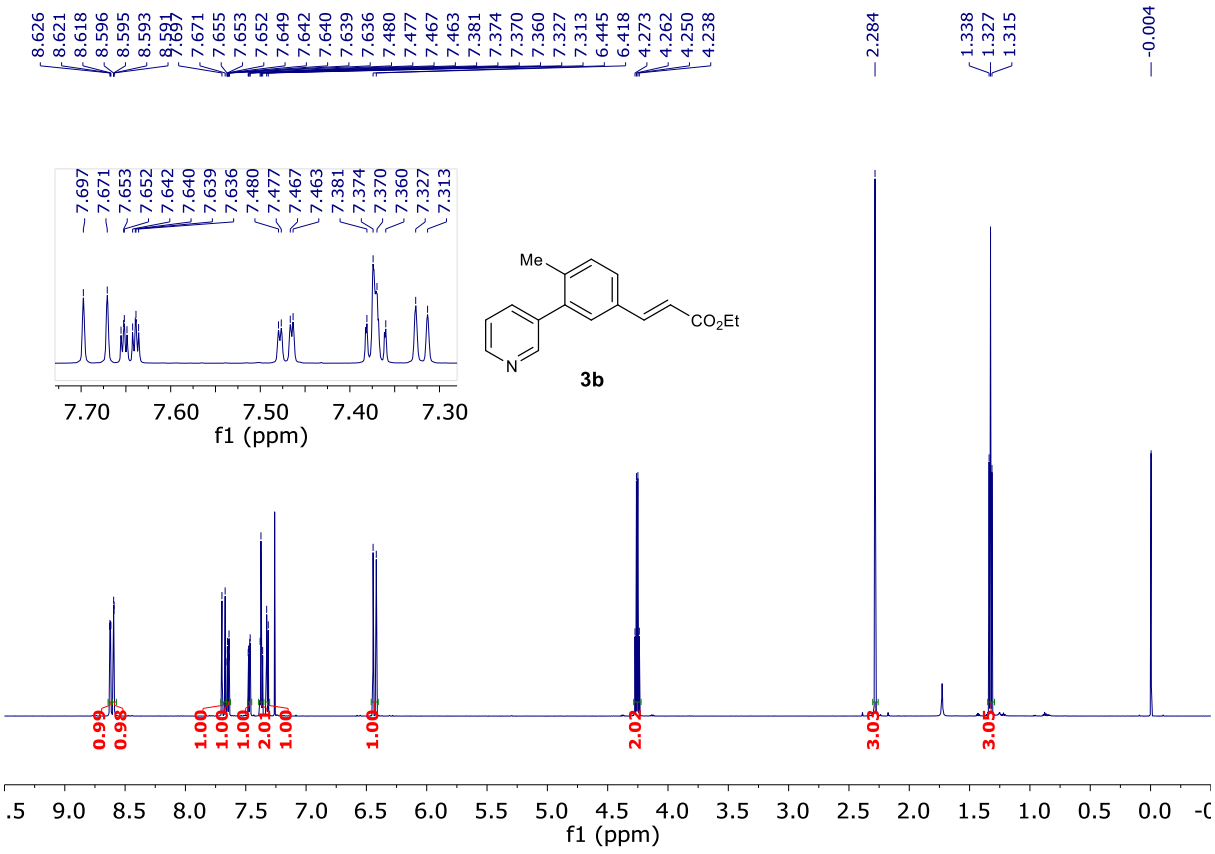

8.426
8.423
8.252
8.247
7.521
7.506
7.325
7.322
7.320
7.317
7.260
7.008
6.994
3.909
3.856
-0.003
OMe
MeO
N
1o
1.00
0.98
2.12
1.02
2.07
3.12
2.99
f1 (ppm)

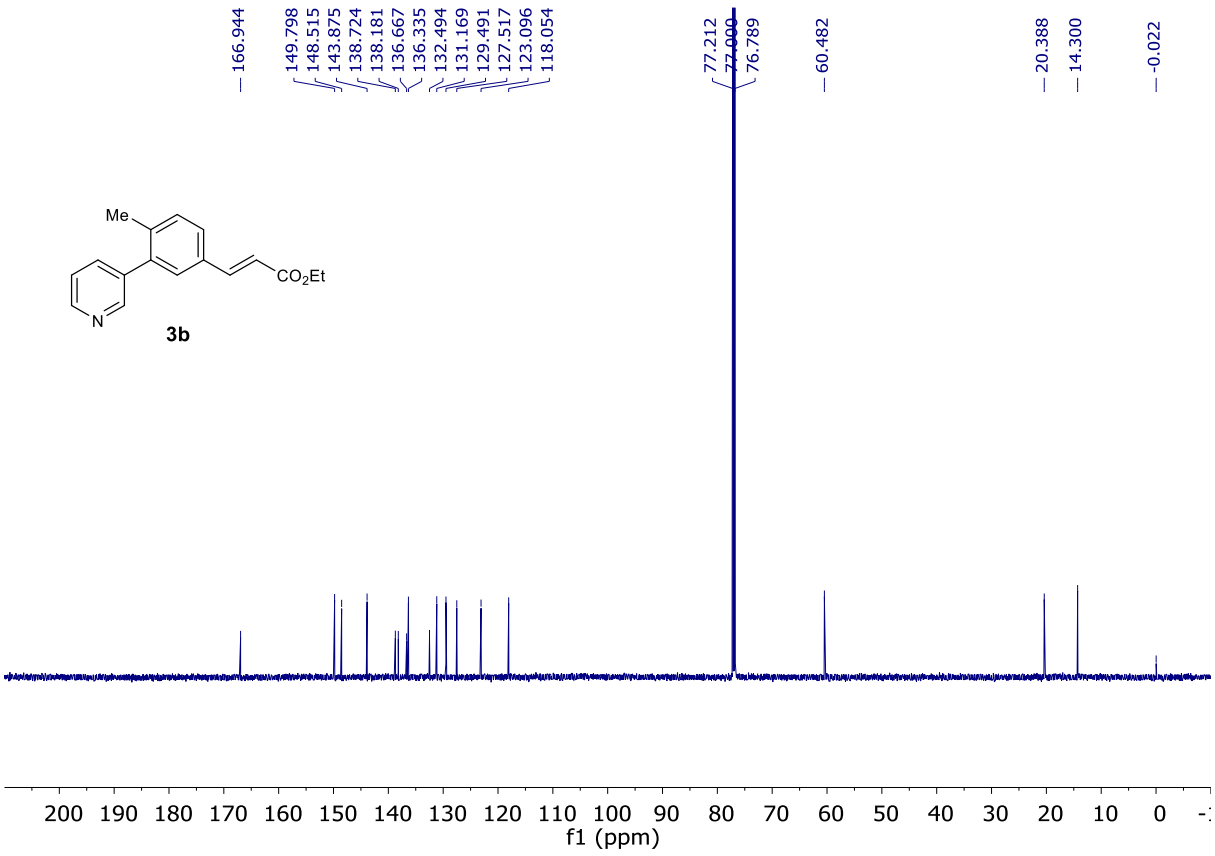

159.784
155.707
140.428
136.930
135.371
130.040
128.294
118.628
114.468
77.212
77.000
76.789
55.580
55.352
-0.029
OMe
MeO
N
1o
f1 (ppm)


8.848
8.623
8.617
7.881
7.878
7.877
7.874
7.868
7.865
7.864
7.861
7.757
7.730
7.703
7.592
7.580
7.570
7.557
7.511
7.498
7.485
7.392
7.384
7.379
7.371
7.260
6.524
6.497
4.294
4.282
4.270
4.258
1.355
1.343
1.331
-0.009
1.03
1.05
1.00
0.98
7.68 7.64 7.60 7.56 7.52 7.48
f1 (ppm)
CO2Et
N
3a
1.03
0.99
1.08
1.08
1.03
1.05
1.00
0.98
1.02
1.00
2.08
3.13
.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
166.744
148.861
148.241
143.933
138.589
135.909
135.308
134.333
129.622
128.849
127.476
126.778
123.584
119.121
77.212
77.000
76.788
60.595
14.289
-0.037
CO2Et
N
3a
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

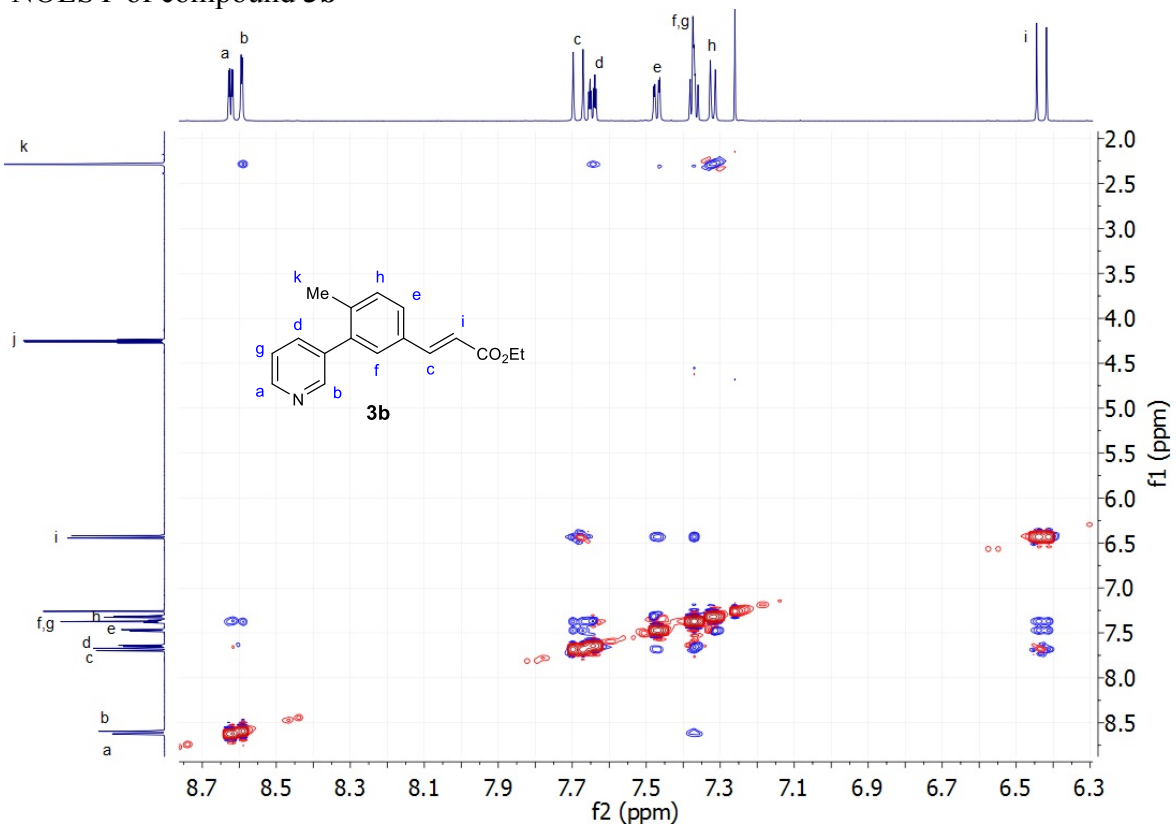
2D NOESY of compound **3a**

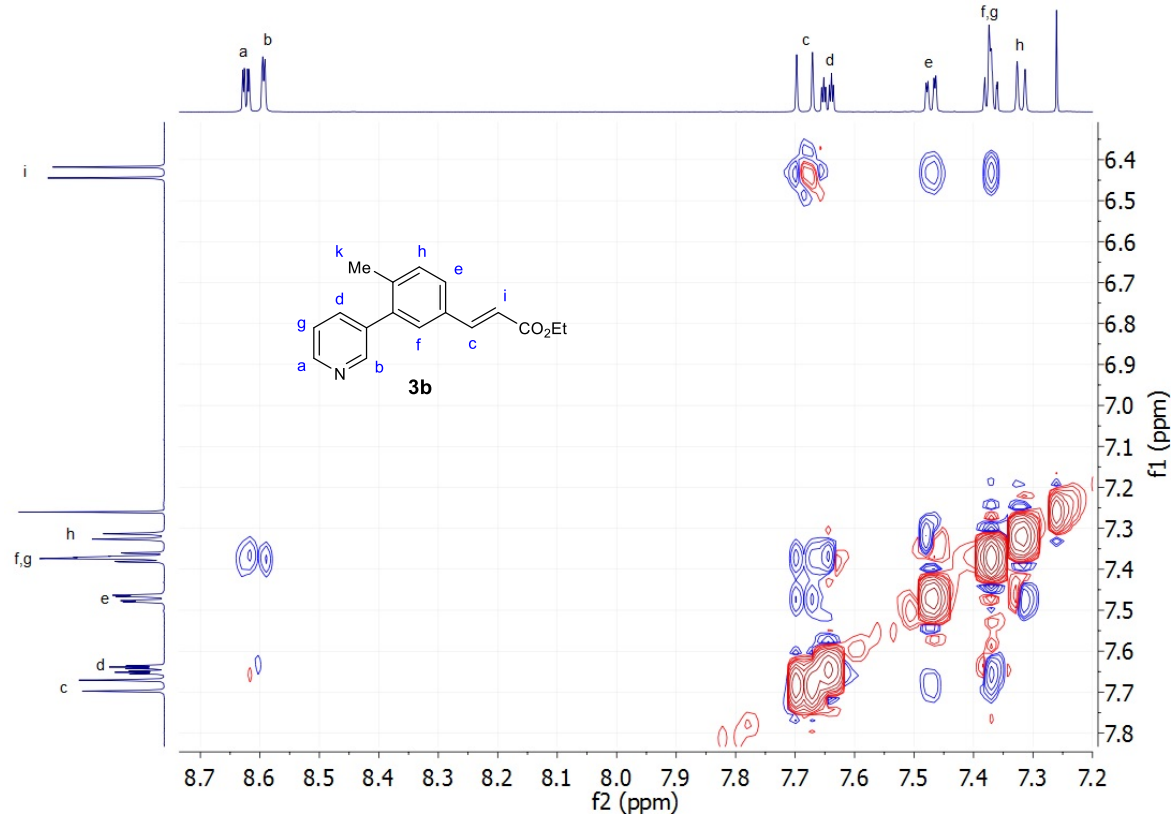


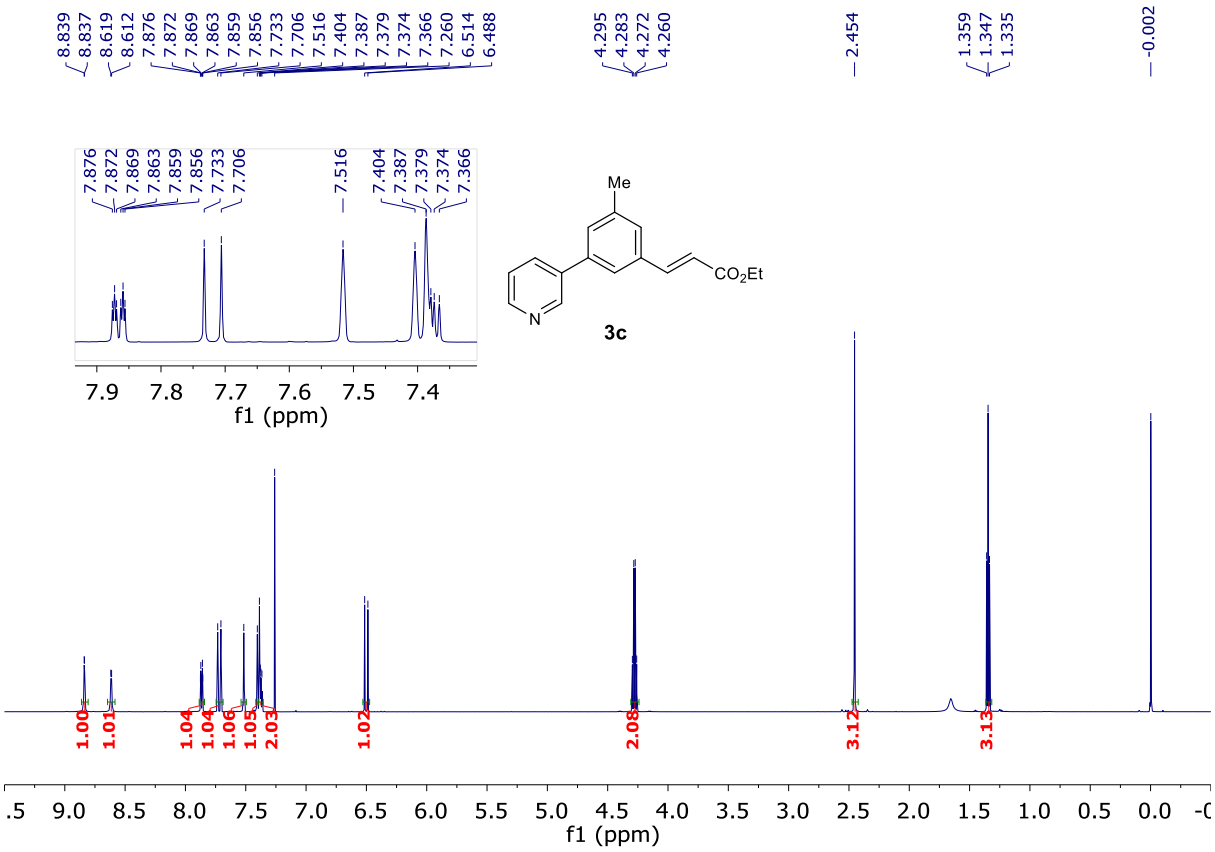

8.626
8.621
8.618
8.596
8.595
8.593
8.591
7.697
7.671
7.655
7.653
7.652
7.649
7.642
7.640
7.639
7.636
7.480
7.477
7.467
7.463
7.381
7.374
7.370
7.360
7.327
7.313
6.445
6.418
4.273
4.262
4.250
4.238
2.284
1.338
1.327
1.315
-0.004
Me
CO2Et
N
3b
7.70
7.60
7.50
7.40
7.30
f1 (ppm)
0.99
0.98
1.00
1.00
1.00
2.01
1.00
1.00
2.02
3.03
3.05
f1 (ppm)

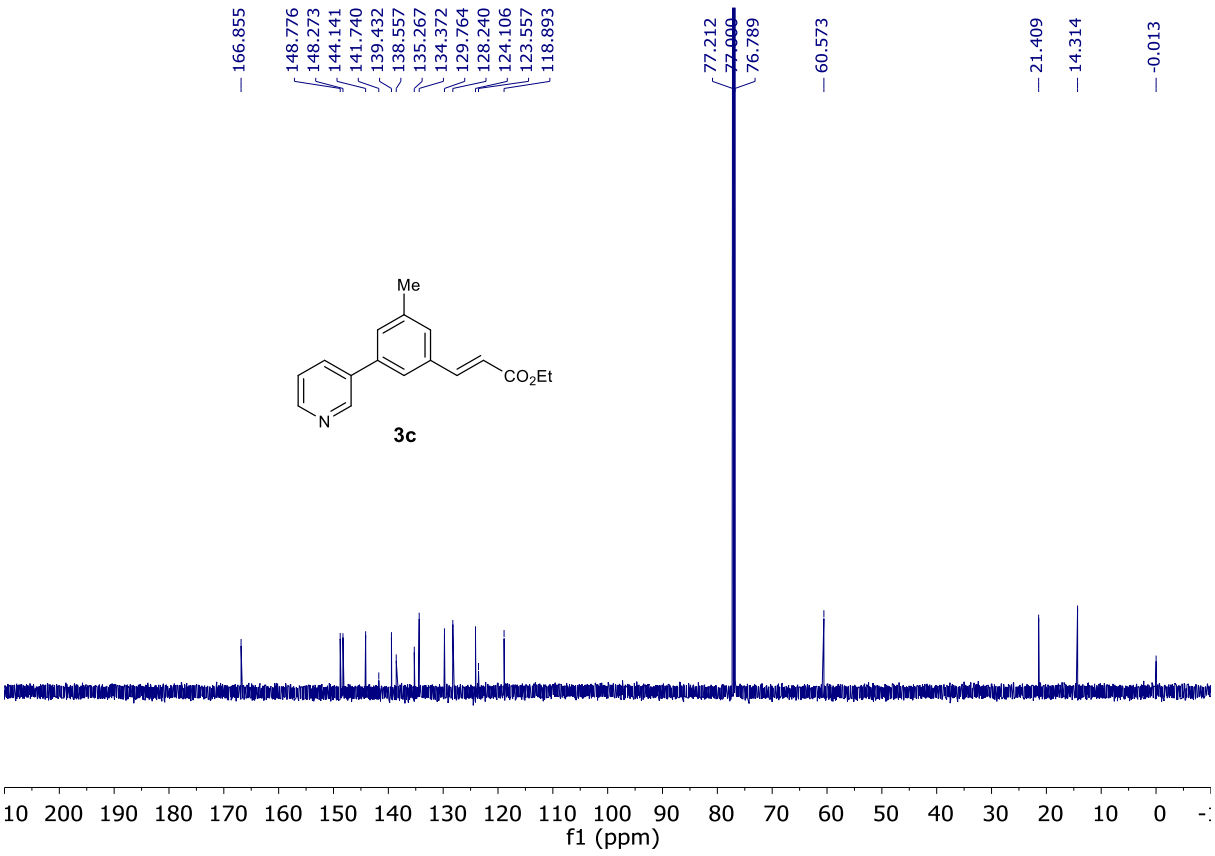

166.944
149.798
148.515
143.875
138.724
138.181
136.667
136.335
132.494
131.169
129.491
127.517
123.096
118.054
77.212
77.000
76.789
60.482
20.388
14.300
-0.022
Me
CO2Et
N
3b
f1 (ppm)

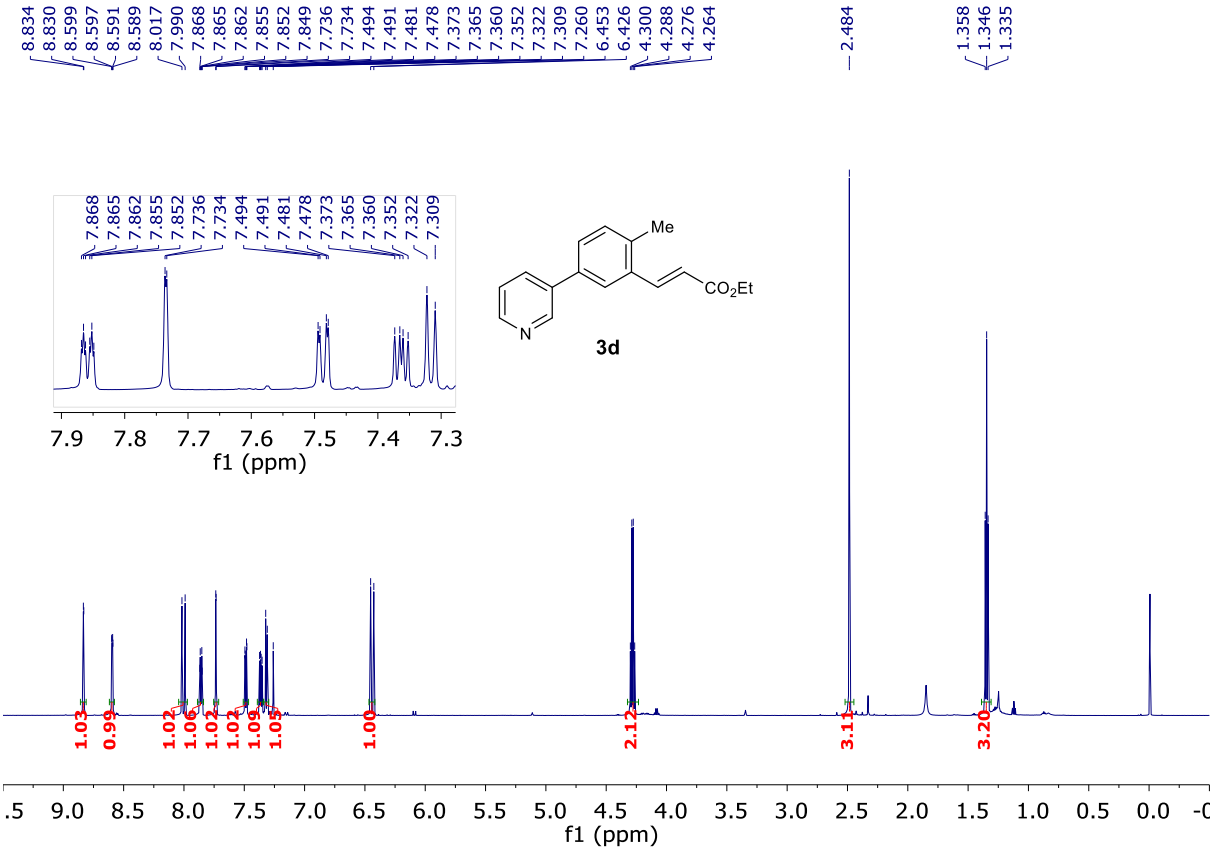
2D NOESY of compound **3b**

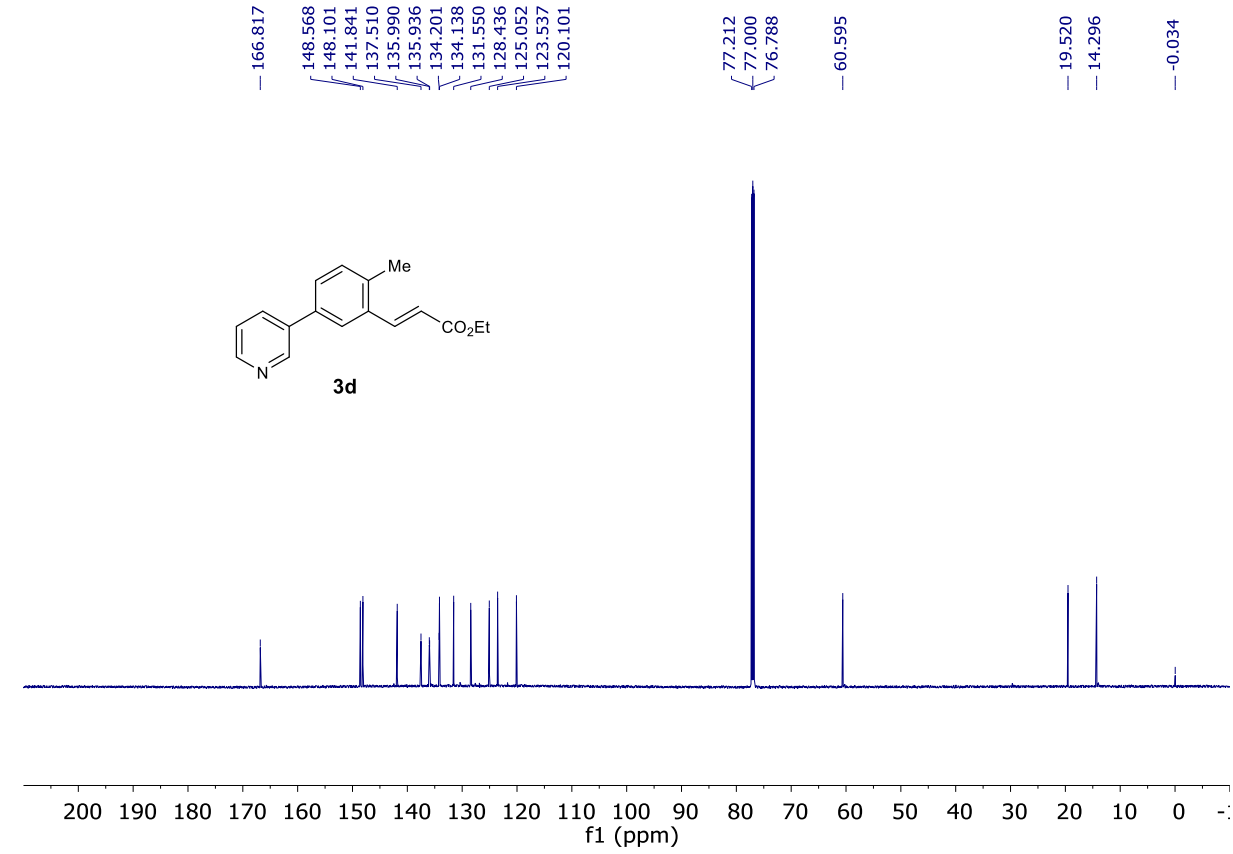


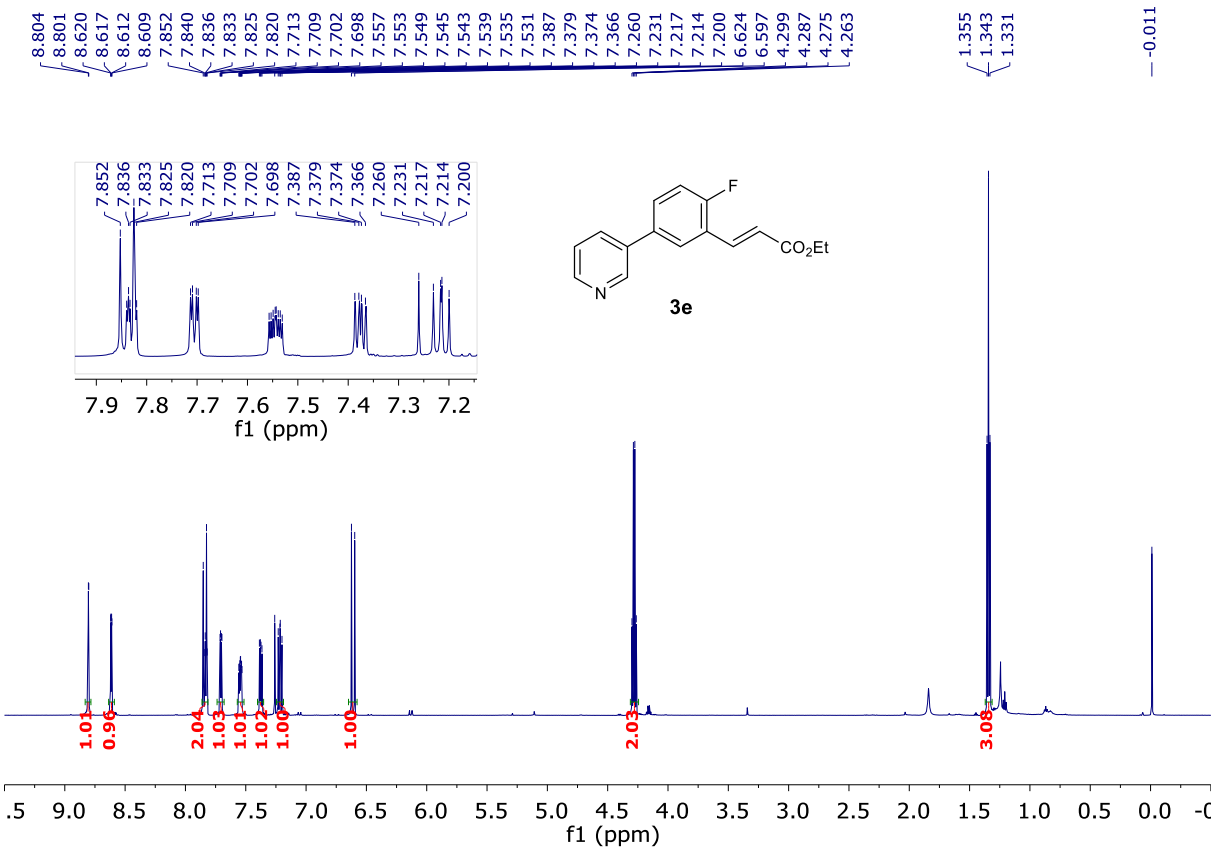


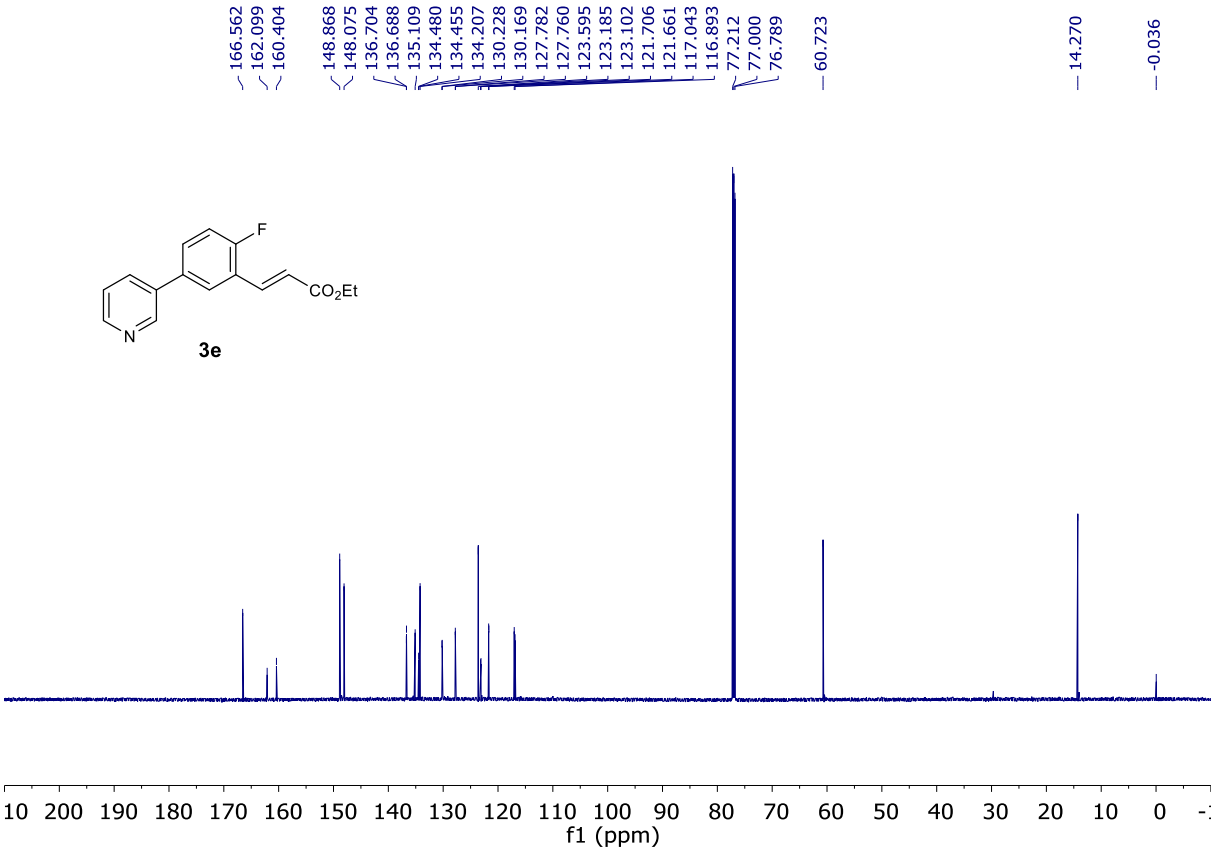

8.839
8.837
8.619
8.612
7.876
7.872
7.869
7.863
7.859
7.856
7.733
7.706
7.516
7.404
7.387
7.379
7.374
7.366
7.260
6.514
6.488
4.295
4.283
4.272
4.260
2.454
1.359
1.347
1.335
-0.002
Me
CO2Et
N
3c
f1 (ppm)
1.00
1.01
1.04
1.04
1.06
1.05
2.03
1.02
2.08
3.12
3.13

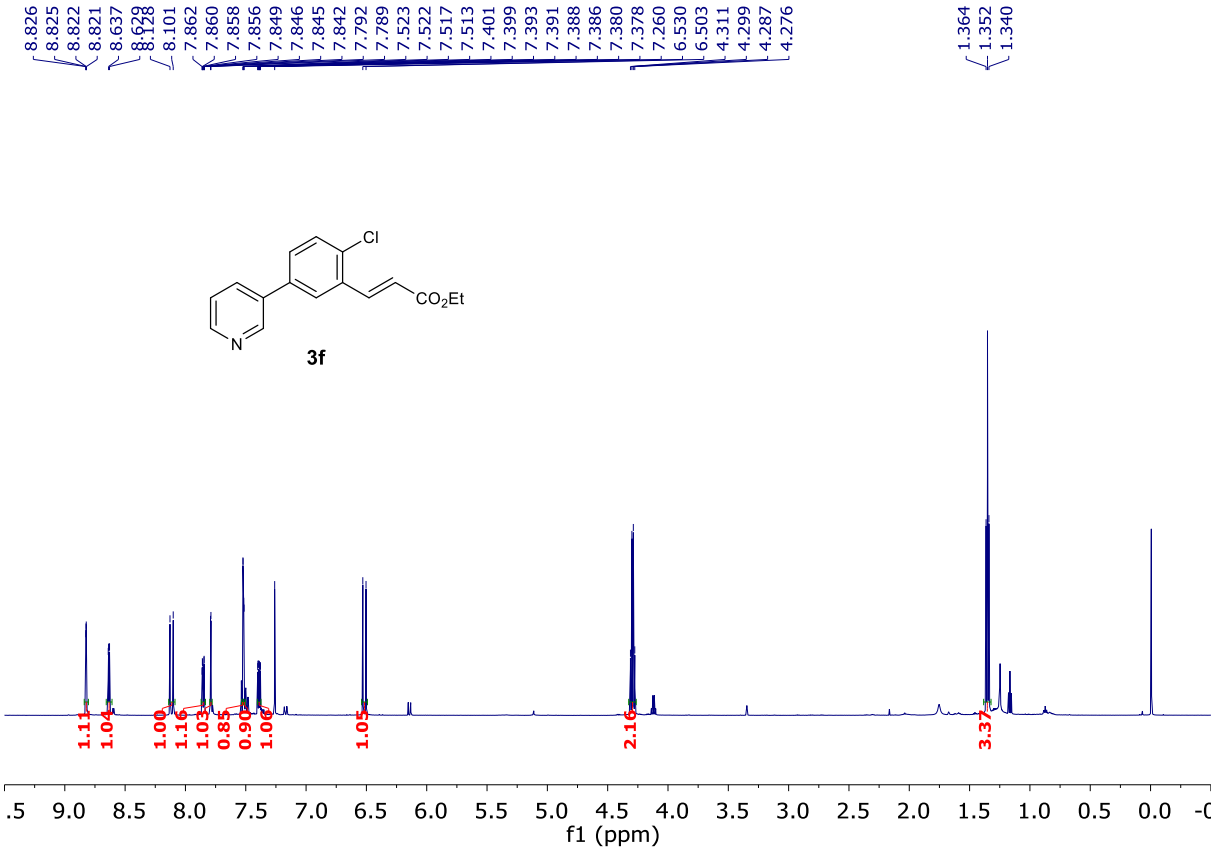

166.855
148.776
148.273
144.141
141.740
139.432
138.557
135.267
134.372
129.764
128.240
124.106
123.557
118.893
77.212
77.000
76.789
60.573
21.409
14.314
-0.013
Me
CO2Et
N
3c
f1 (ppm)

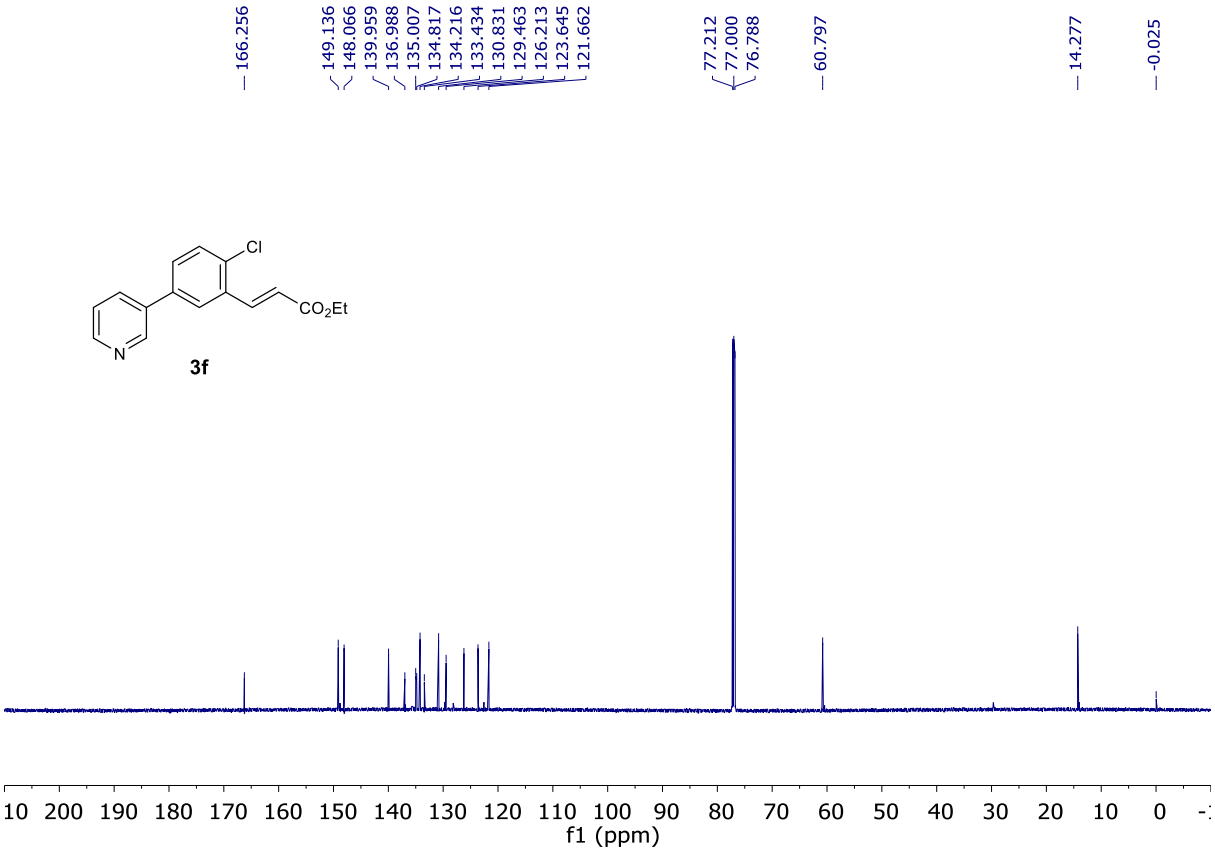

8.834
8.830
8.599
8.597
8.591
8.589
8.017
7.990
7.868
7.865
7.862
7.855
7.852
7.849
7.736
7.734
7.494
7.491
7.481
7.478
7.373
7.365
7.360
7.352
7.322
7.309
7.260
6.453
6.426
4.300
4.288
4.276
4.264
2.484
1.358
1.346
1.335
Me
CO2Et
N
3d
f1 (ppm)
1.03
0.99
1.02
1.06
1.02
1.02
1.09
1.05
1.00
2.12
3.11
3.20

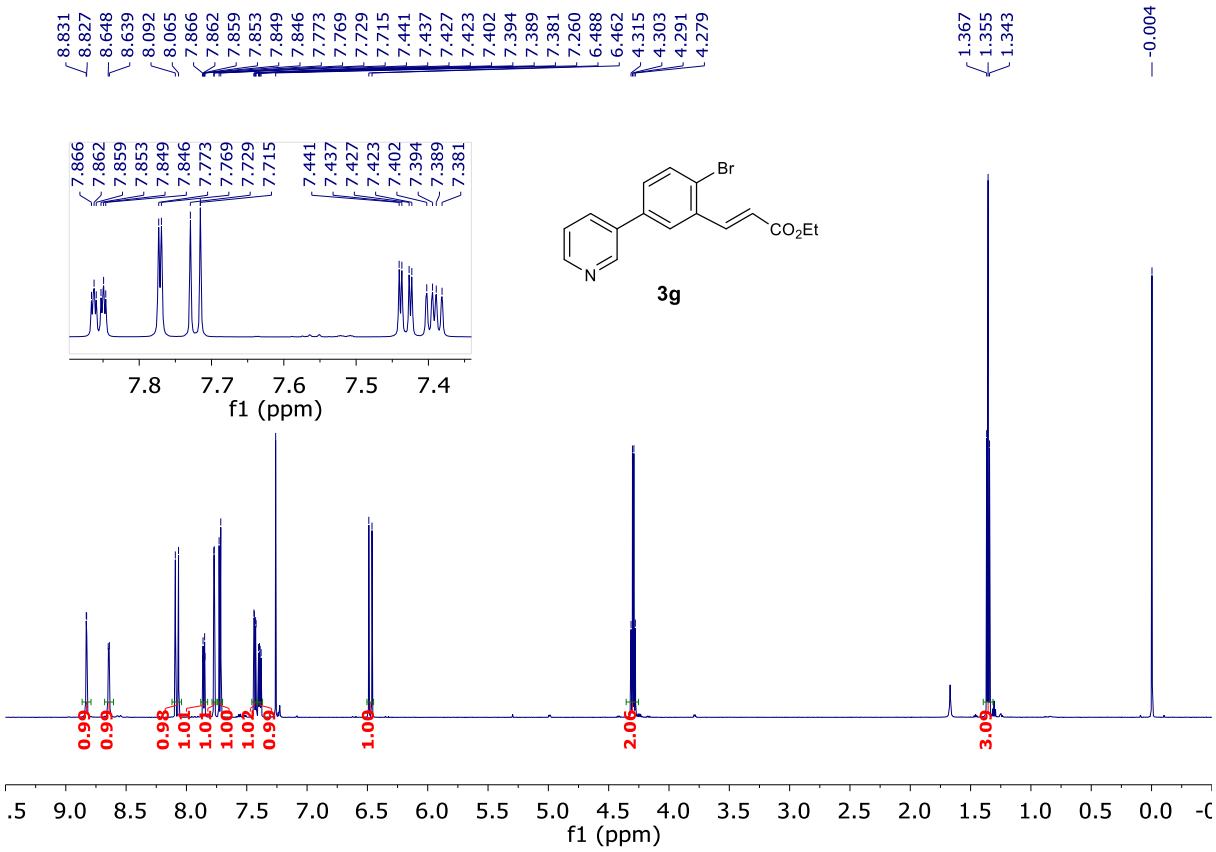

166.817
148.568
148.101
141.841
137.510
135.990
135.936
134.201
134.138
131.550
128.436
125.052
123.537
120.101
77.212
77.000
76.788
60.595
19.520
14.296
-0.034
Me
CO2Et
N
3d
f1 (ppm)

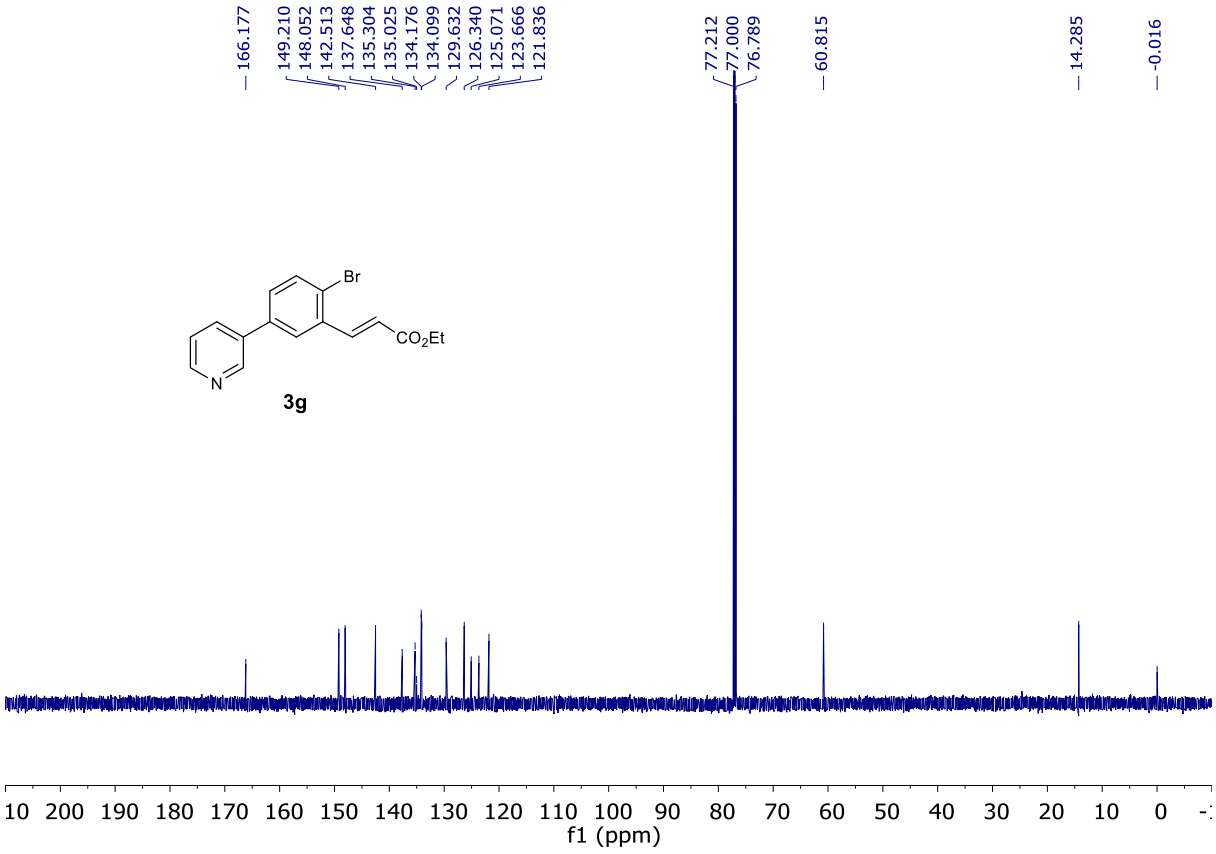

8.804 8.801 8.620 8.617 8.612 8.609 7.852 7.840 7.836 7.833 7.825 7.820 7.713 7.709 7.702 7.698 7.557 7.553 7.549 7.545 7.543 7.539 7.535 7.531 7.387 7.379 7.374 7.366 7.260 7.231 7.217 7.214 7.200 6.624 6.597 4.299 4.287 4.275 4.263 1.355 1.343 1.331 -0.011
7.852 7.836 7.833 7.825 7.820 7.713 7.709 7.702 7.698 7.387 7.379 7.374 7.366 7.260 7.231 7.217 7.214 7.200
7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2
f1 (ppm)
F
CO2Et
N
3e
1.01 0.96 2.04 1.03 1.01 1.02 1.00 1.00 2.03 3.08
.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0
f1 (ppm)

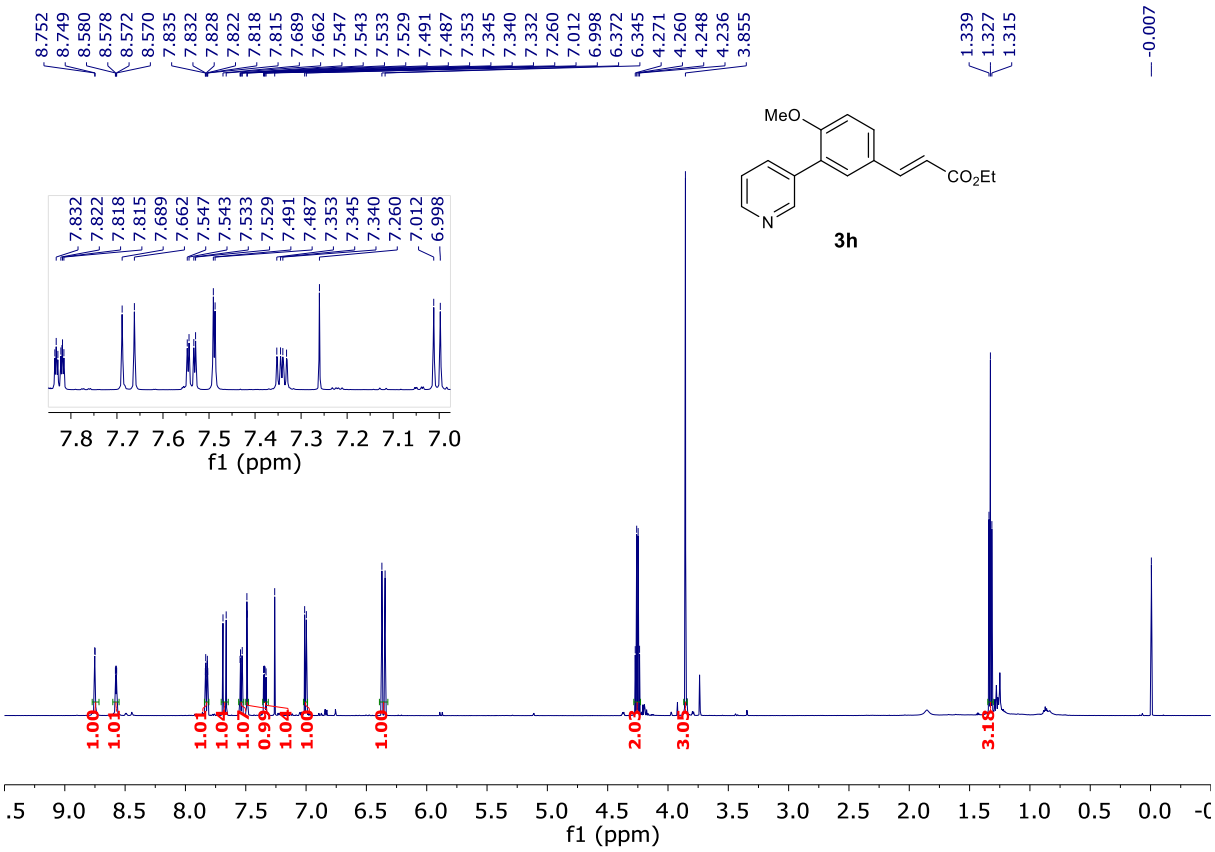

166.562 162.099 160.404 148.868 148.075 136.704 136.688 135.109 134.480 134.455 134.207 130.228 130.169 127.782 127.760 123.595 123.185 123.102 121.706 121.661 117.043 116.893 77.212 77.000 76.789 60.723 14.270 -0.036
F
CO2Et
N
3e
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

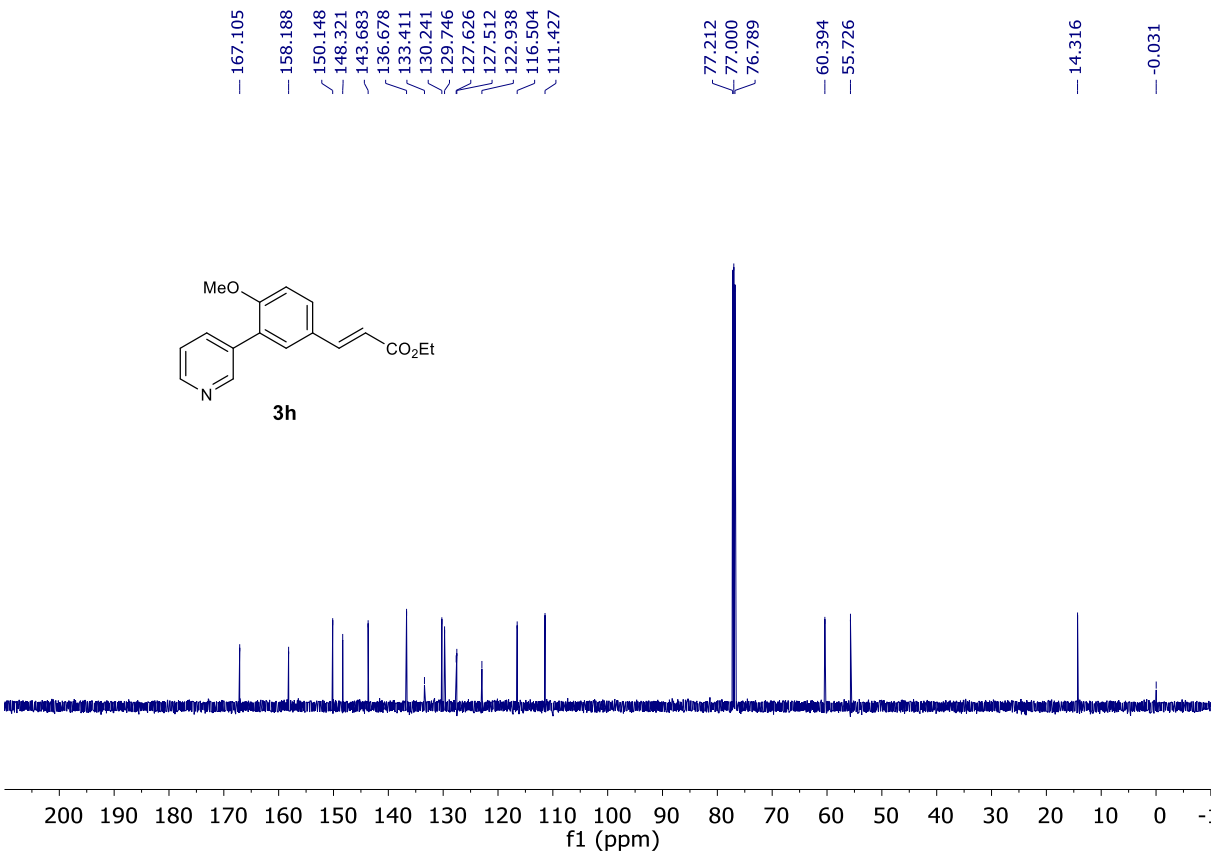

8.826
8.825
8.822
8.821
8.637
8.629
8.128
8.101
7.862
7.860
7.858
7.856
7.849
7.846
7.845
7.842
7.792
7.789
7.523
7.522
7.517
7.513
7.401
7.399
7.393
7.391
7.388
7.386
7.380
7.378
7.260
6.530
6.503
4.311
4.299
4.287
4.276
1.364
1.352
1.340
Cl
CO2Et
N
3f
1.11
1.04
1.00
1.16
1.03
0.85
0.90
1.06
1.05
2.16
3.37
f1 (ppm)


166.256
149.136
148.066
139.959
136.988
135.007
134.817
134.216
133.434
130.831
129.463
126.213
123.645
121.662
77.212
77.000
76.788
60.797
14.277
-0.025
Cl
CO2Et
N
3f
f1 (ppm)

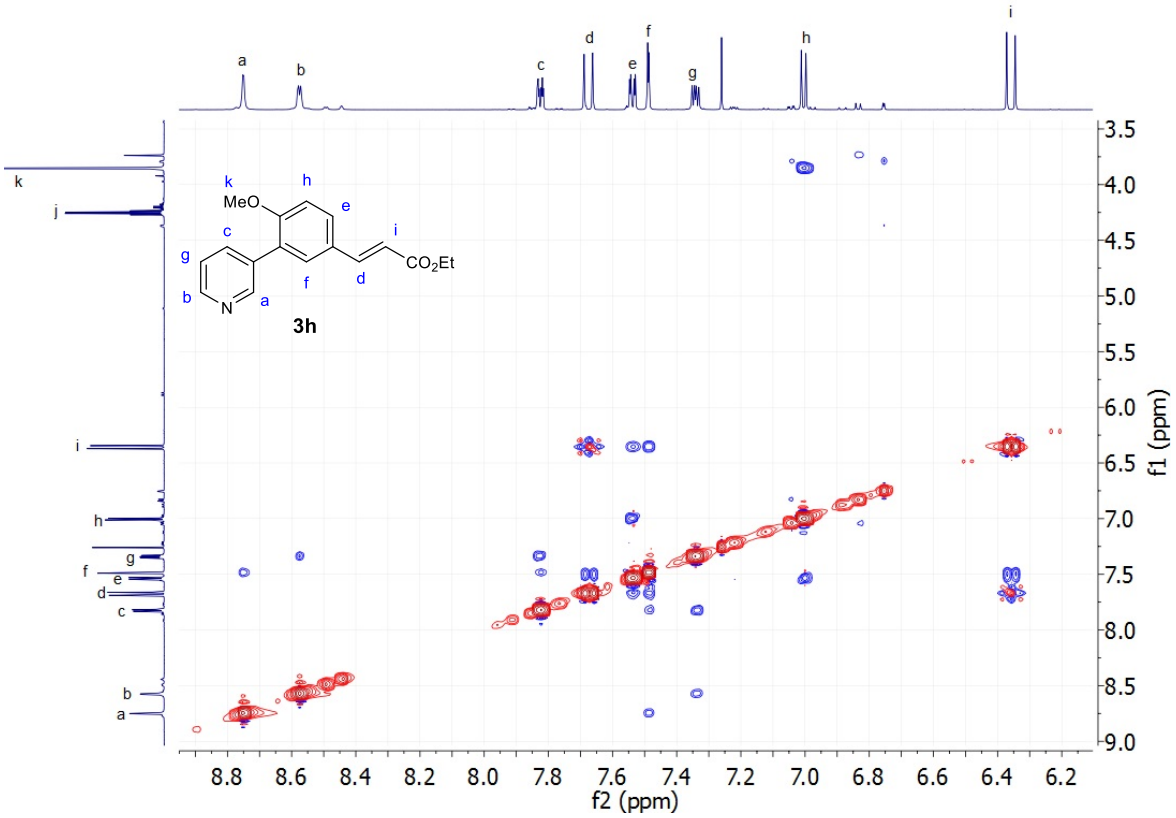

8.831
8.827
8.648
8.639
8.092
8.065
7.866
7.862
7.859
7.853
7.849
7.846
7.773
7.769
7.729
7.715
7.441
7.437
7.427
7.423
7.402
7.394
7.389
7.381
7.260
6.488
6.462
4.315
4.303
4.291
4.279
1.367
1.355
1.343
-0.004
Br
CO2Et
N
3g
f1 (ppm)
0.99
0.99
0.98
1.01
1.01
1.00
1.02
0.99
1.08
2.06
3.09

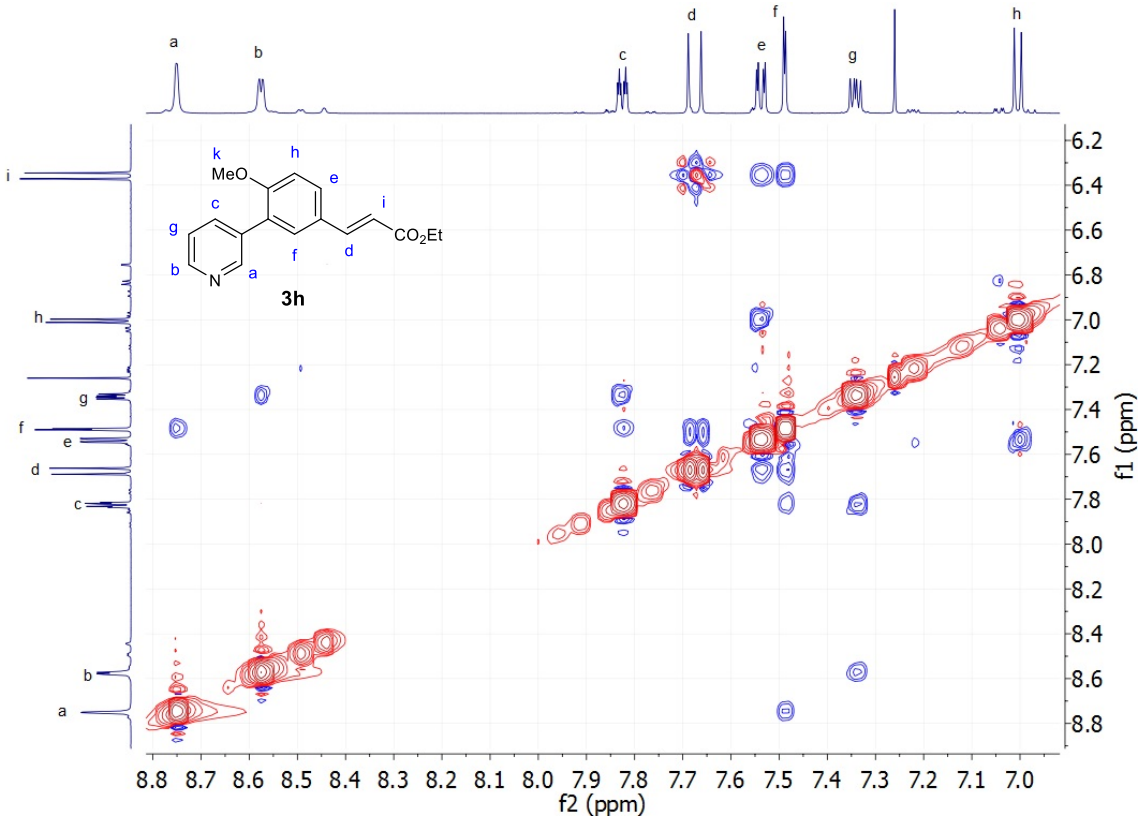

166.177
149.210
148.052
142.513
137.648
135.304
135.025
134.176
134.099
129.632
126.340
125.071
123.666
121.836
77.212
77.000
76.789
60.815
14.285
-0.016
Br
CO2Et
N
3g
f1 (ppm)

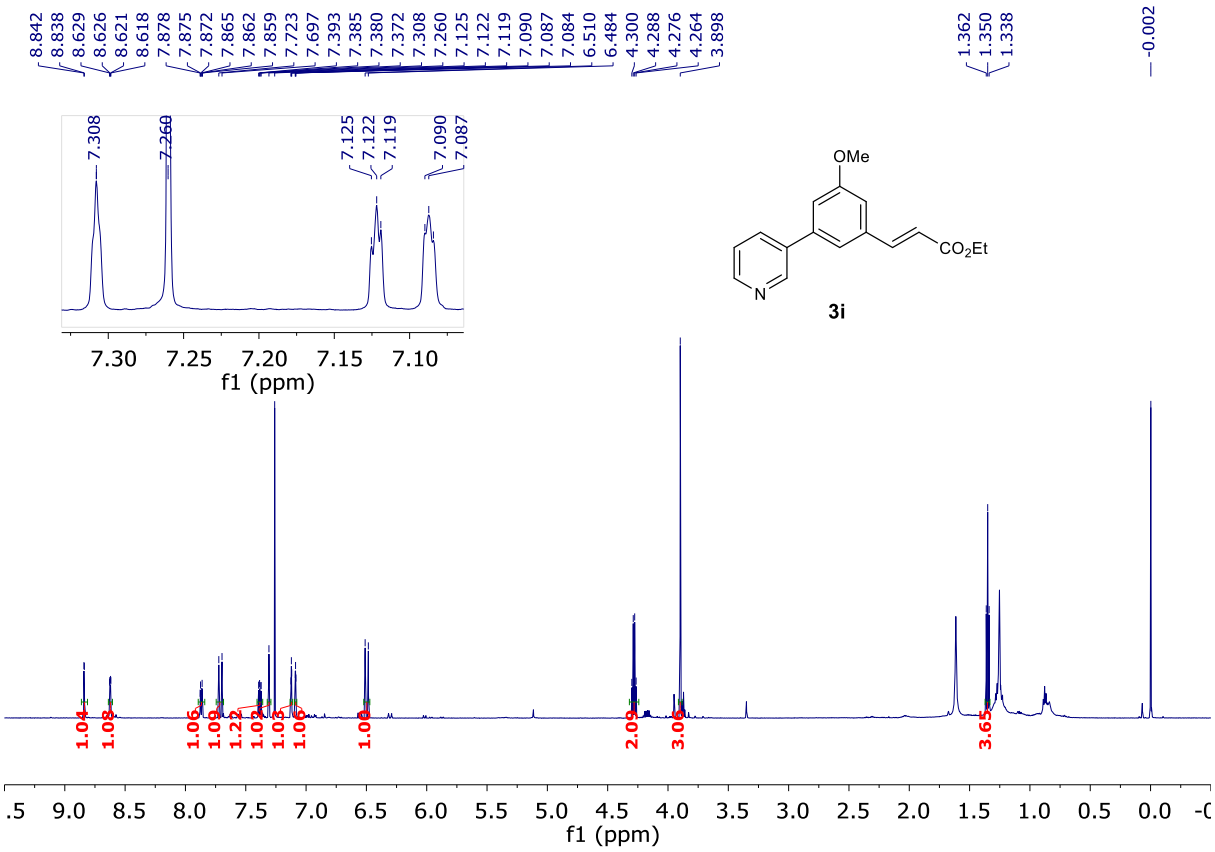

8.752 8.749 8.580 8.578 8.572 8.570 7.835 7.832 7.828 7.822 7.818 7.815 7.689 7.662 7.547 7.543 7.533 7.529 7.491 7.487 7.353 7.345 7.340 7.332 7.260 7.012 6.998 6.372 6.345 4.271 4.260 4.248 4.236 3.855
1.339 1.327 1.315
-0.007
MeO
CO2Et
N
3h
7.832 7.822 7.818 7.815 7.689 7.662 7.547 7.543 7.533 7.529 7.491 7.487 7.353 7.345 7.340 7.260 7.012 6.998
7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0
f1 (ppm)
1.00 1.01 1.01 1.04 1.07 0.99 1.04 1.00 1.00 2.03 3.05 3.18
.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

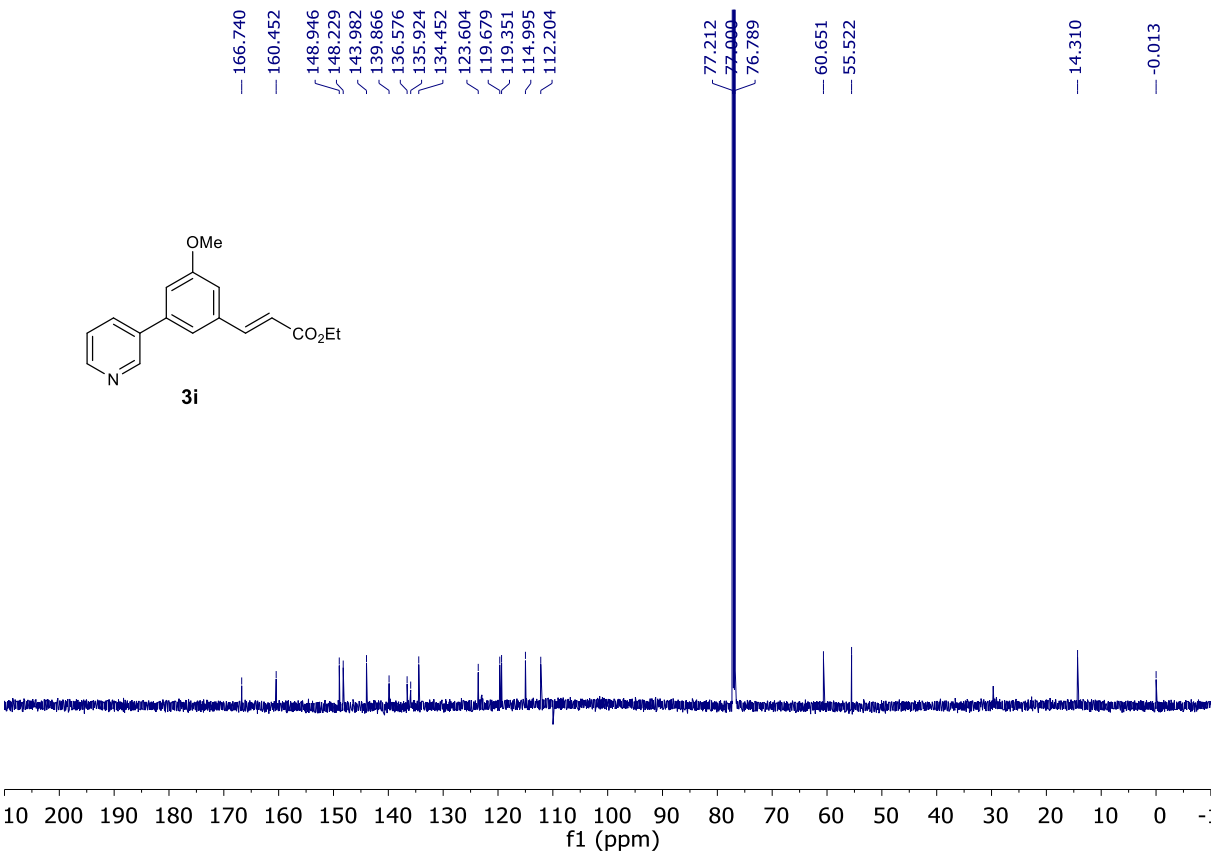

167.105 158.188 150.148 148.321 143.683 136.678 133.411 130.241 129.746 127.626 127.512 122.938 116.504 111.427
77.212 77.000 76.789
60.394 55.726
14.316
-0.031
MeO
CO2Et
N
3h
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

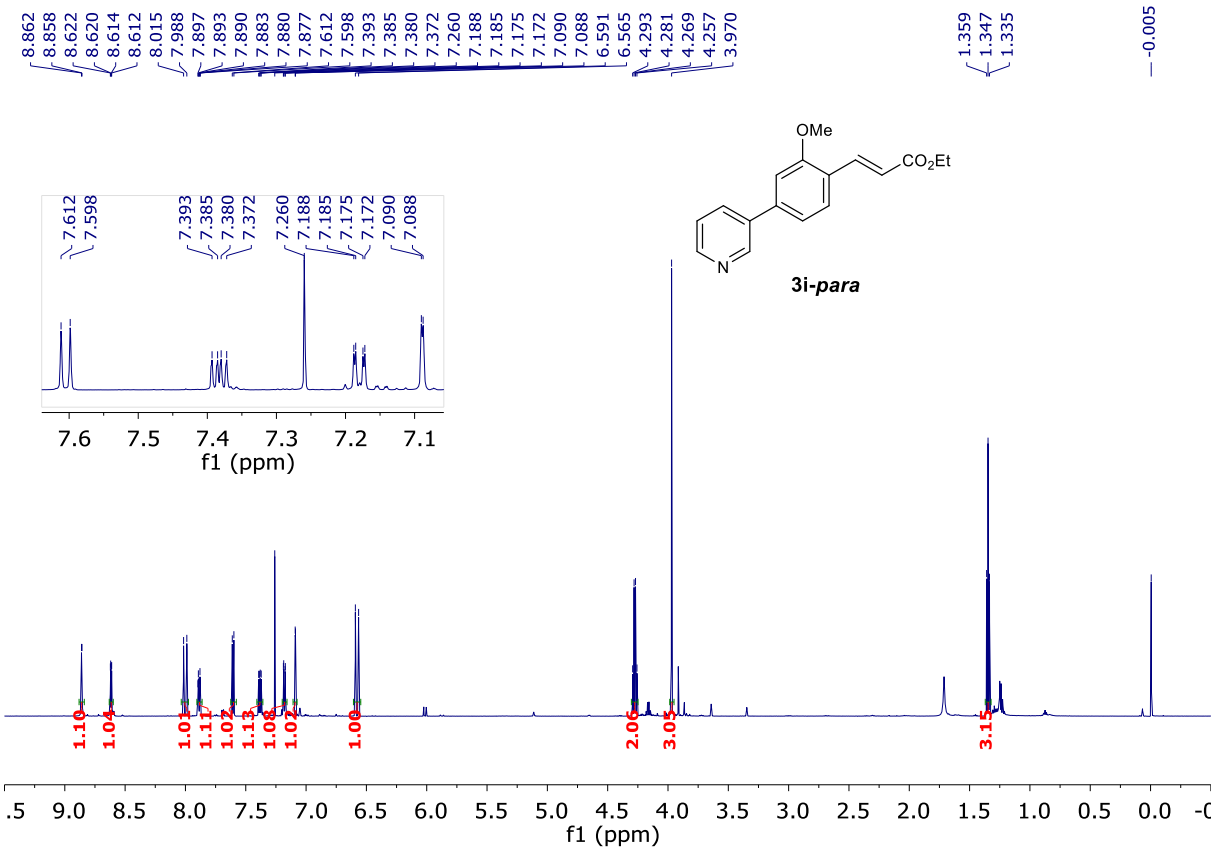
2D NOESY of compound **3h**

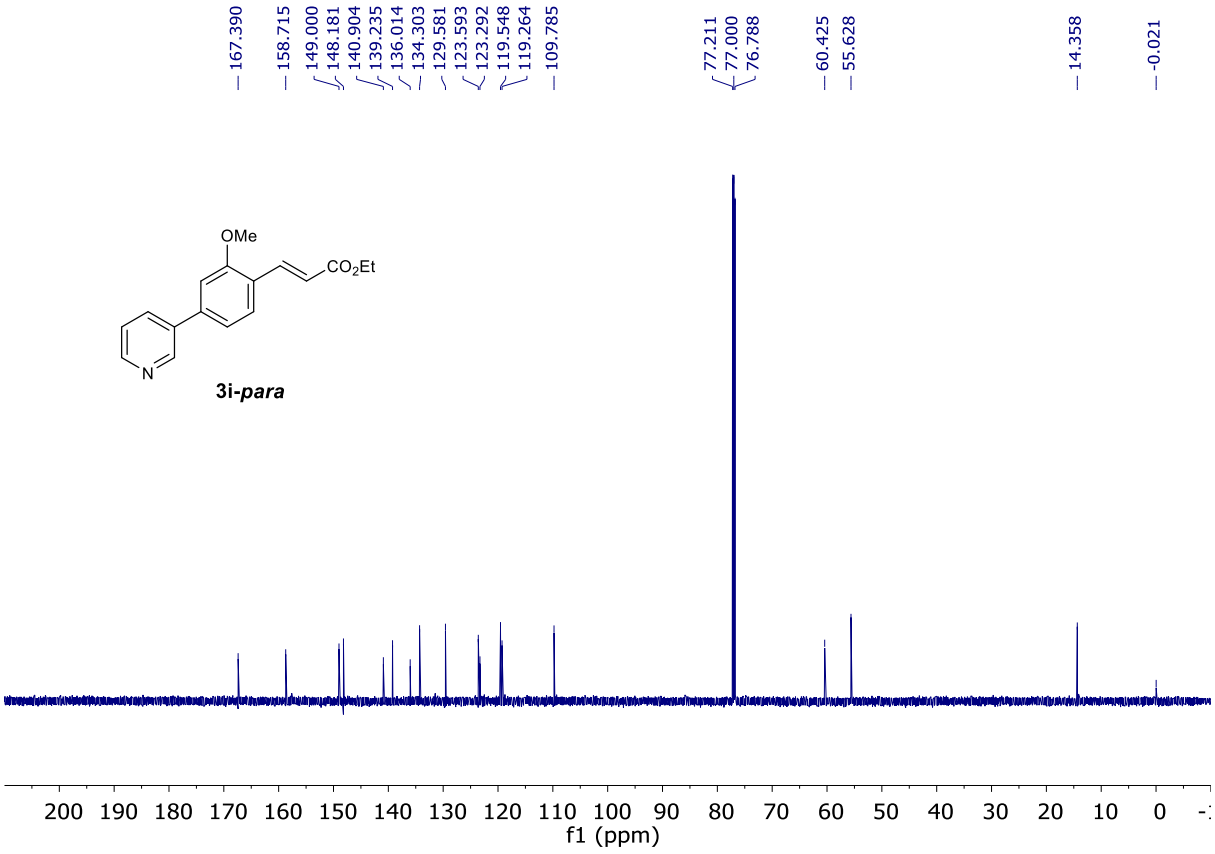


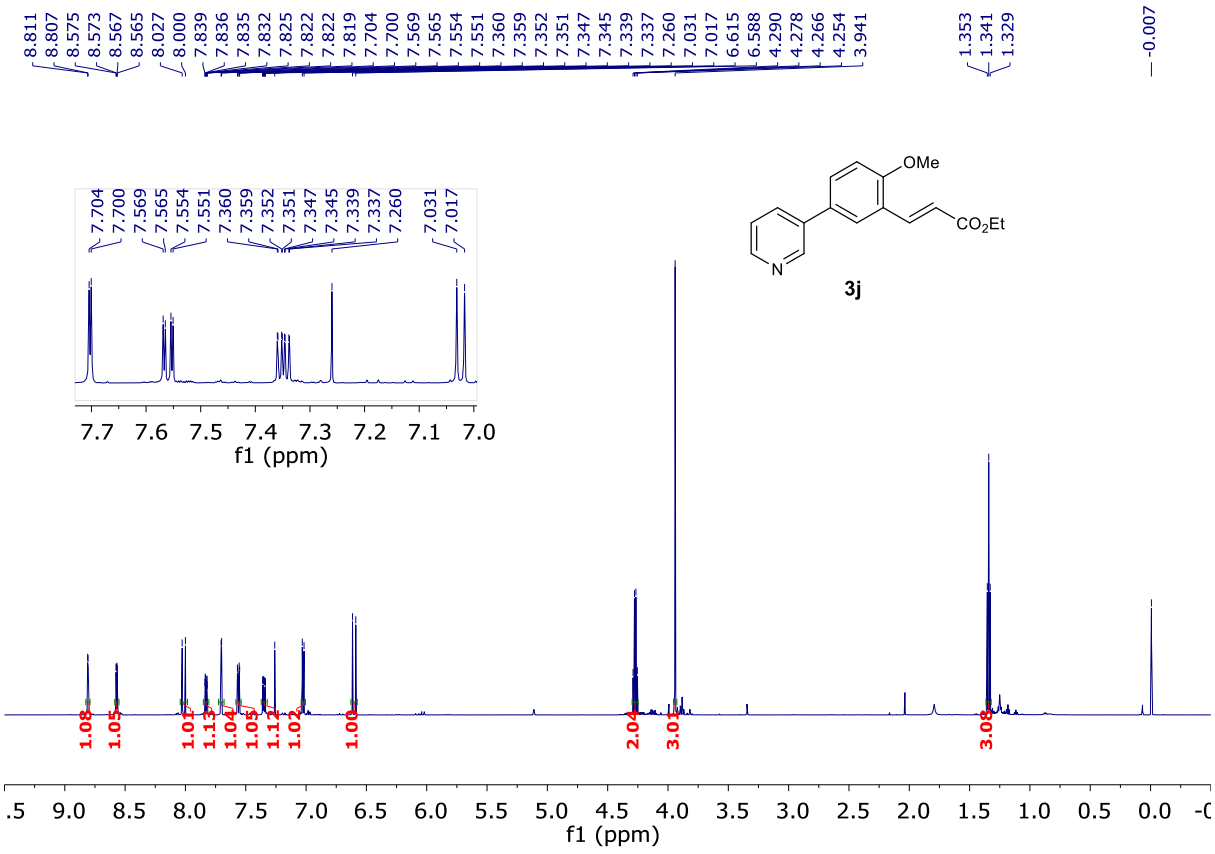


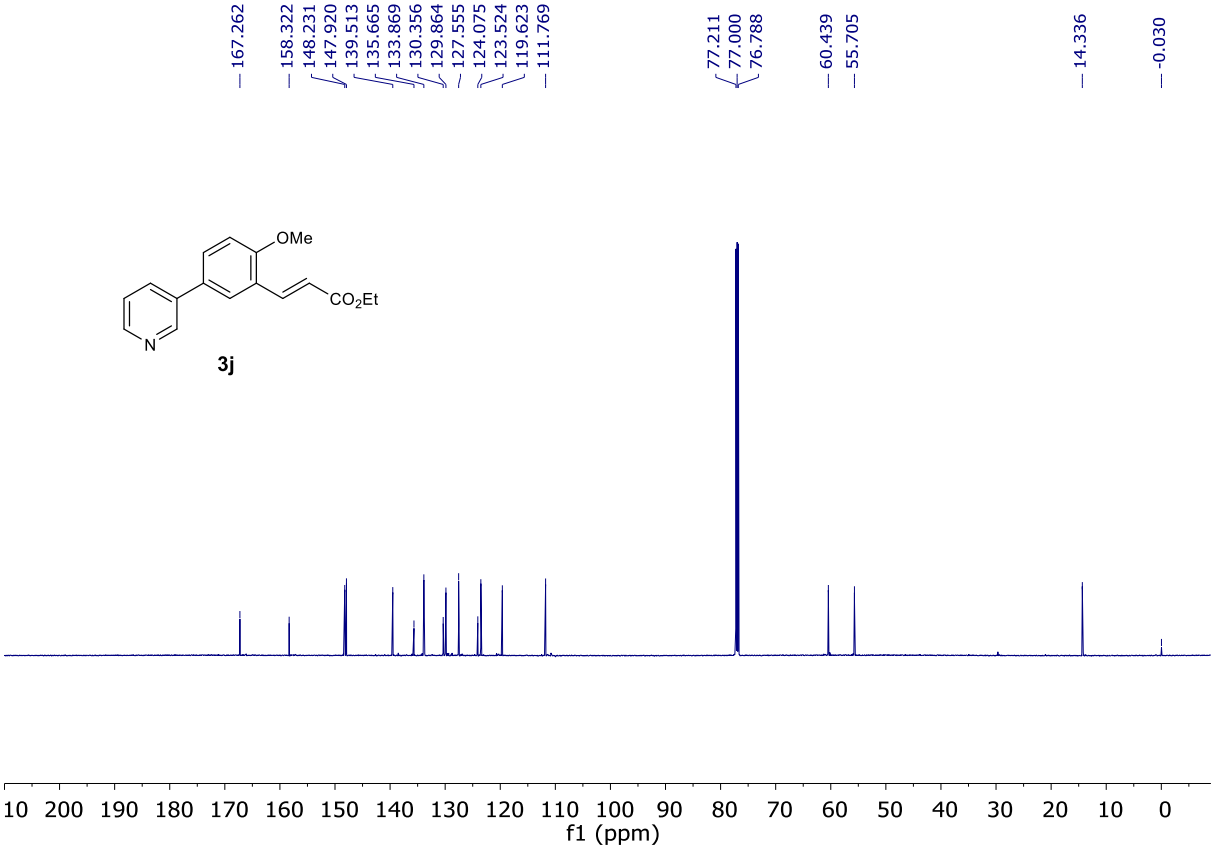

8.842
8.838
8.629
8.626
8.621
8.618
7.878
7.875
7.872
7.865
7.862
7.859
7.723
7.697
7.393
7.385
7.380
7.372
7.308
7.260
7.125
7.122
7.119
7.090
7.087
7.084
6.510
6.484
4.300
4.288
4.276
4.264
3.898
1.362
1.350
1.338
-0.002
7.308
7.260
7.125
7.122
7.119
7.090
7.087
7.30 7.25 7.20 7.15 7.10
f1 (ppm)
OMe
CO2Et
N
3i
1.04
1.08
1.06
1.09
1.22
1.02
1.03
1.06
1.00
2.09
3.00
3.65
.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

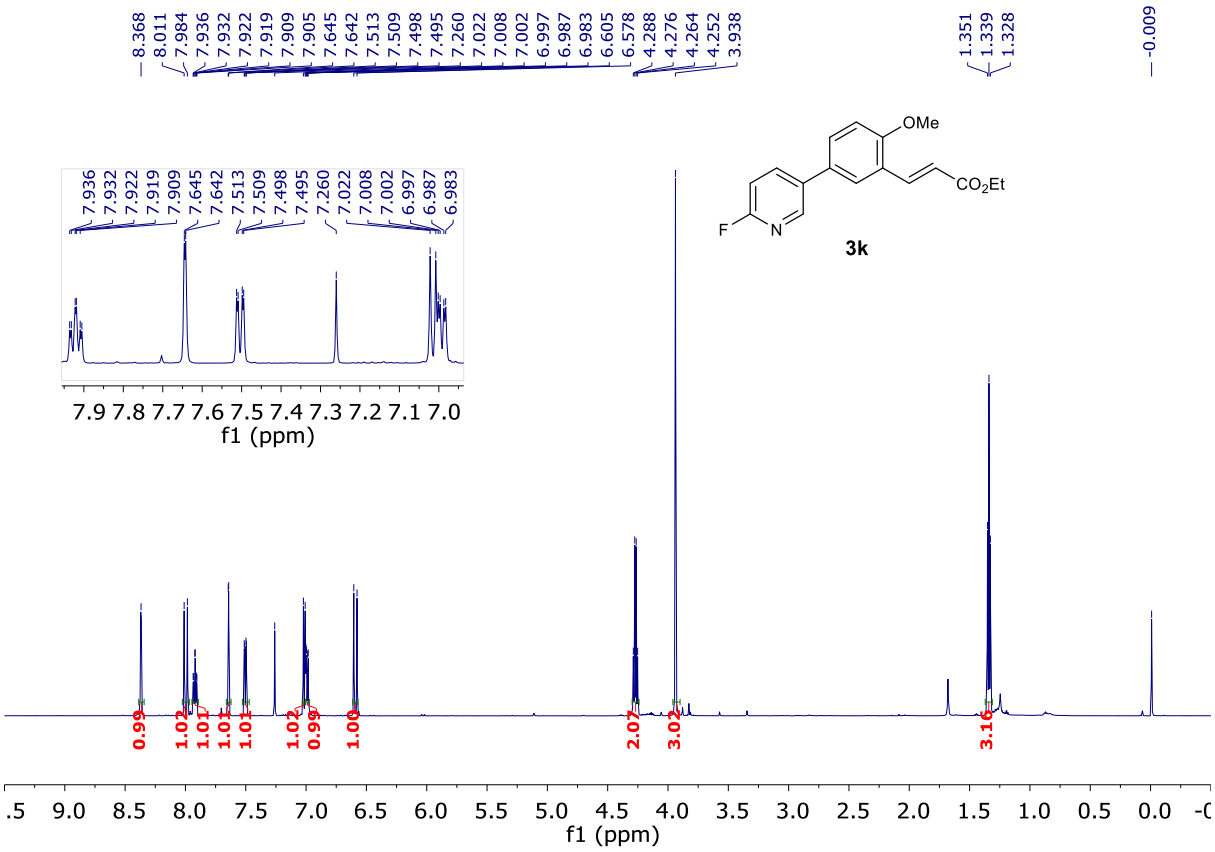

166.740
160.452
148.946
148.229
143.982
139.866
136.576
135.924
134.452
123.604
119.679
119.351
114.995
112.204
77.212
77.000
76.789
60.651
55.522
14.310
-0.013
OMe
CO2Et
N
3i
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

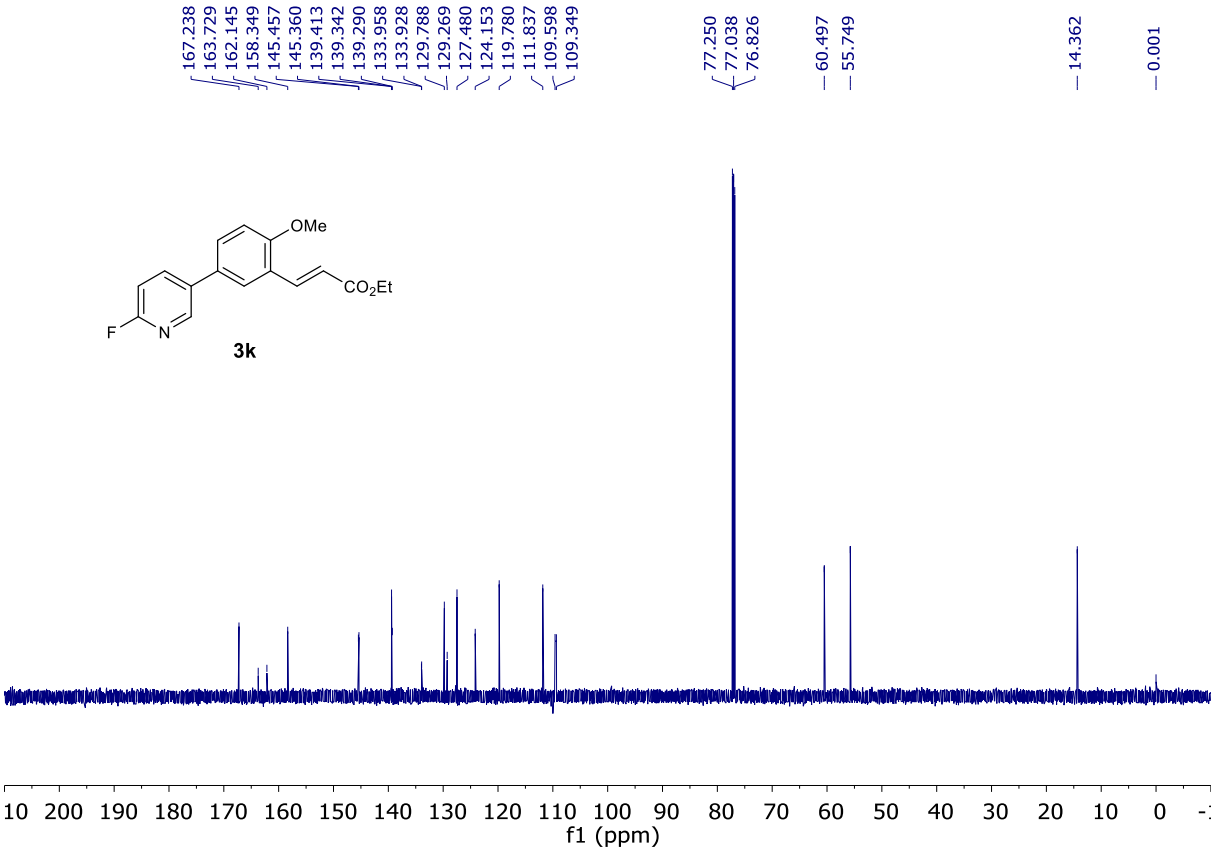

8.862
8.858
8.622
8.620
8.614
8.612
8.015
7.988
7.897
7.893
7.890
7.883
7.880
7.877
7.612
7.598
7.393
7.385
7.380
7.372
7.260
7.188
7.185
7.175
7.172
7.090
7.088
6.591
6.565
4.293
4.281
4.269
4.257
3.970
1.359
1.347
1.335
-0.005
OMe
CO2Et
N
3i-para
f1 (ppm)
1.10
1.04
1.01
1.11
1.02
1.13
1.08
1.07
1.00
2.06
3.03
3.15

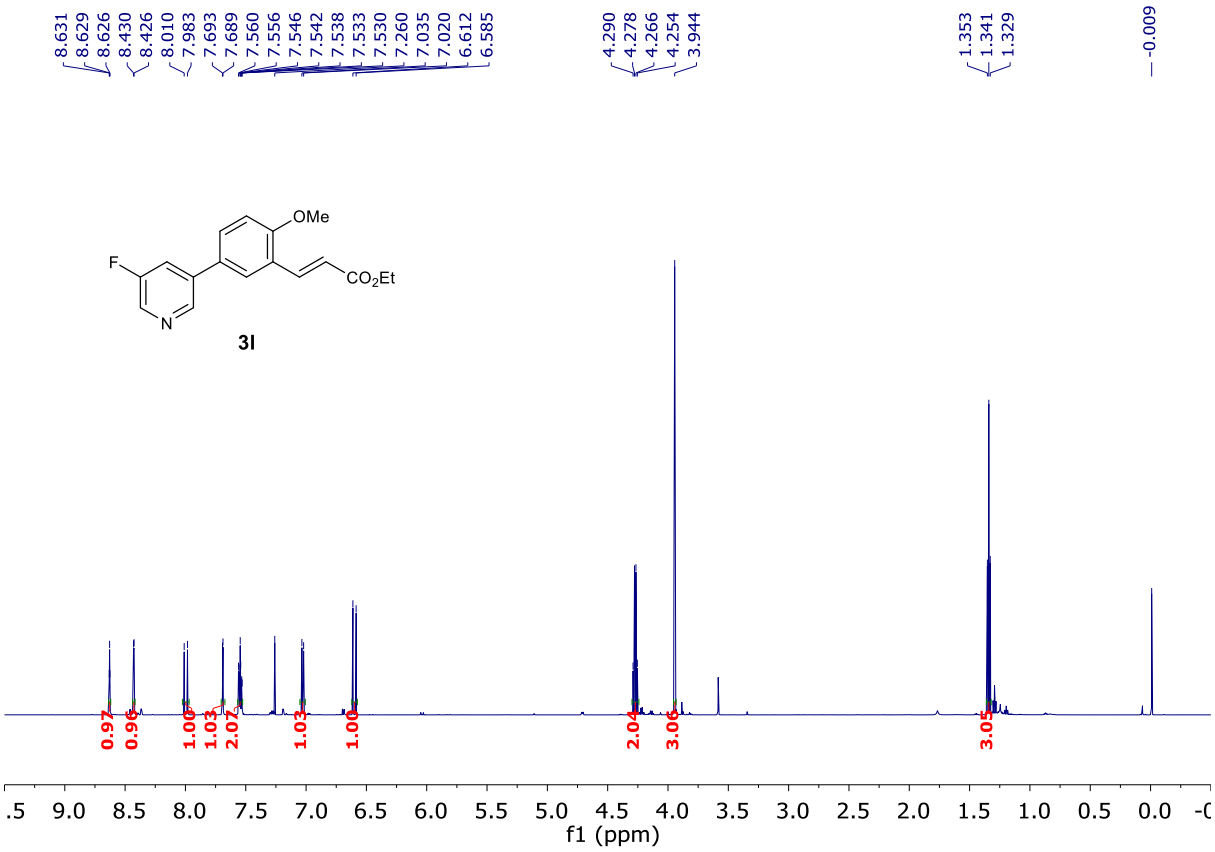

167.390
158.715
149.000
148.181
140.904
139.235
136.014
134.303
129.581
123.593
123.292
119.548
119.264
109.785
77.211
77.000
76.788
60.425
55.628
14.358
-0.021
OMe
CO2Et
N
3i-para
f1 (ppm)

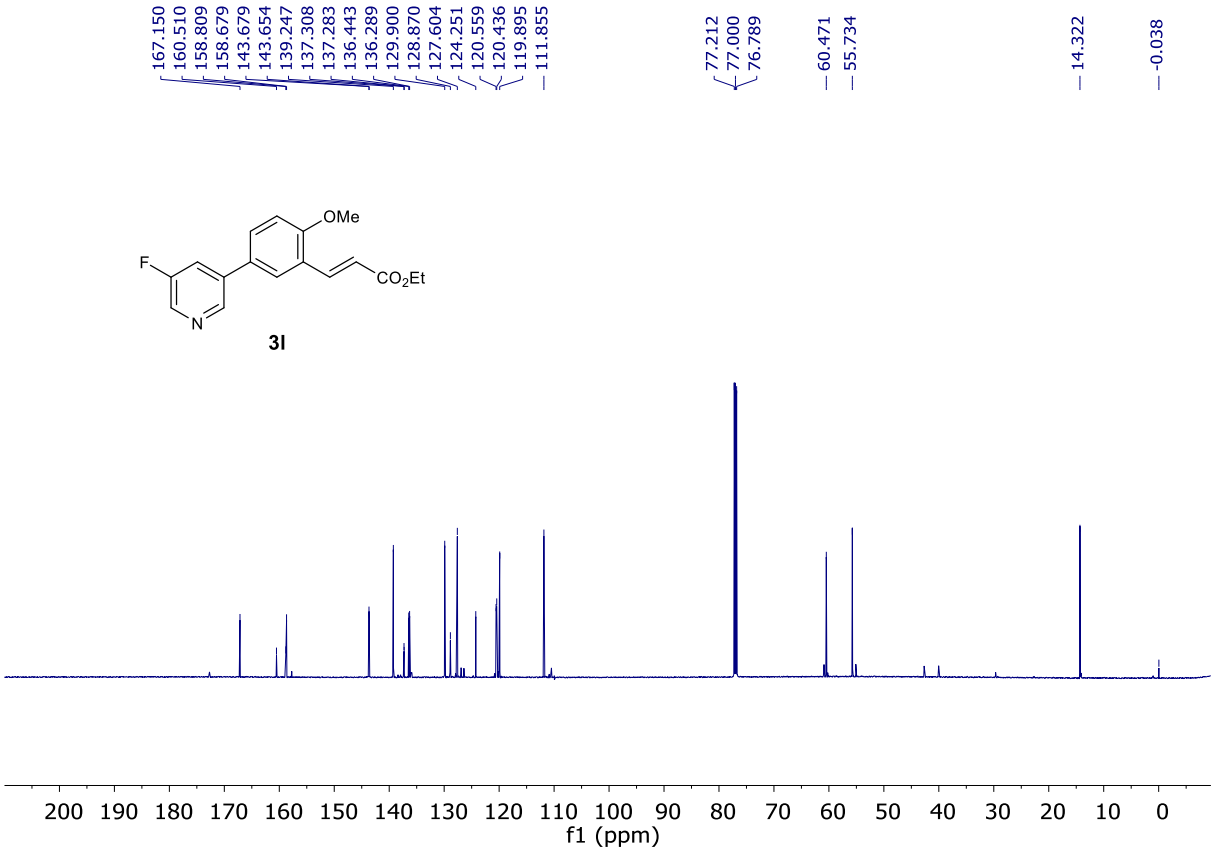

8.811
8.807
8.575
8.573
8.567
8.565
8.027
8.000
7.839
7.836
7.835
7.832
7.825
7.822
7.822
7.819
7.704
7.700
7.569
7.565
7.554
7.551
7.360
7.359
7.352
7.351
7.347
7.345
7.339
7.337
7.260
7.031
7.017
6.615
6.588
4.290
4.278
4.266
4.254
3.941
1.353
1.341
1.329
-0.007
OMe
CO2Et
N
3j
7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0
f1 (ppm)
1.08
1.05
1.01
1.13
1.04
1.05
1.12
1.02
1.00
2.04
3.01
3.08
f1 (ppm)

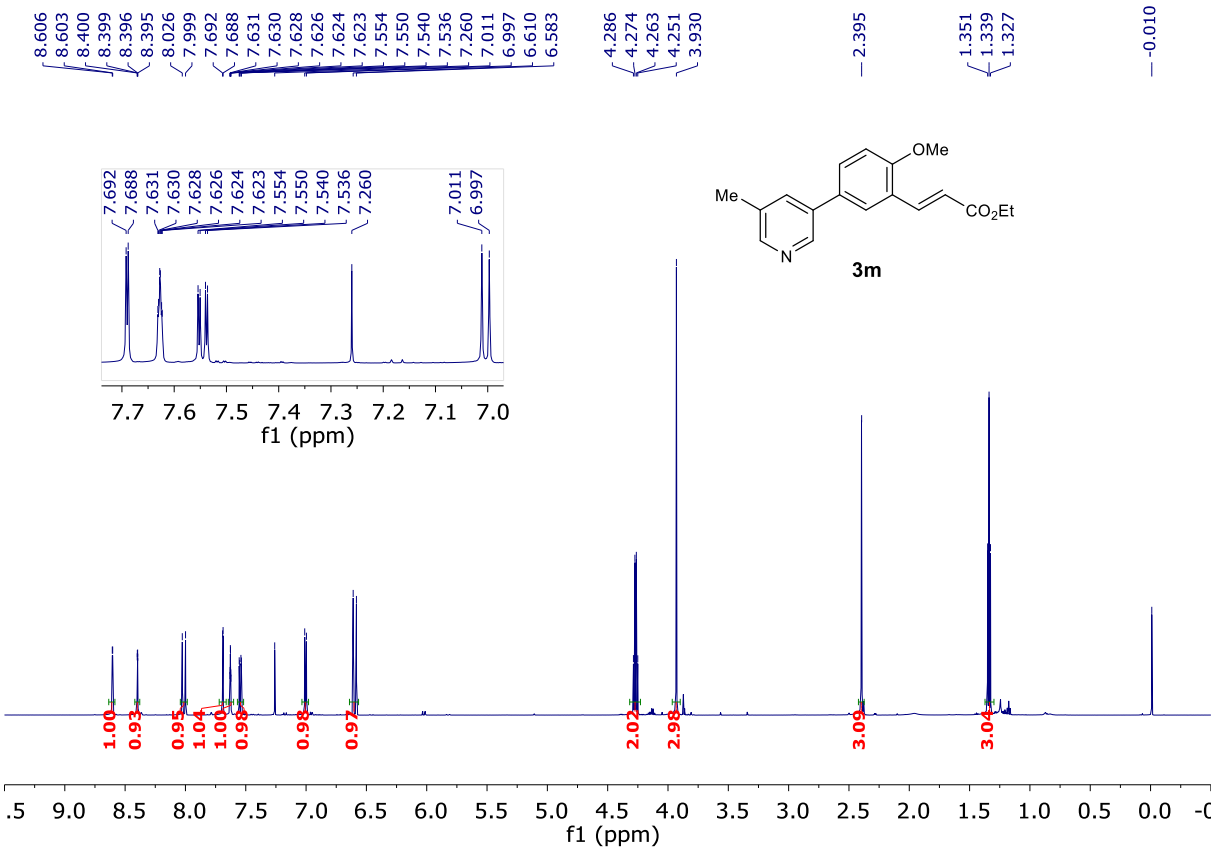

167.262
158.322
148.231
147.920
139.513
135.665
133.869
130.356
129.864
127.555
124.075
123.524
119.623
111.769
77.211
77.000
76.788
60.439
55.705
14.336
-0.030
OMe
CO2Et
N
3j
f1 (ppm)

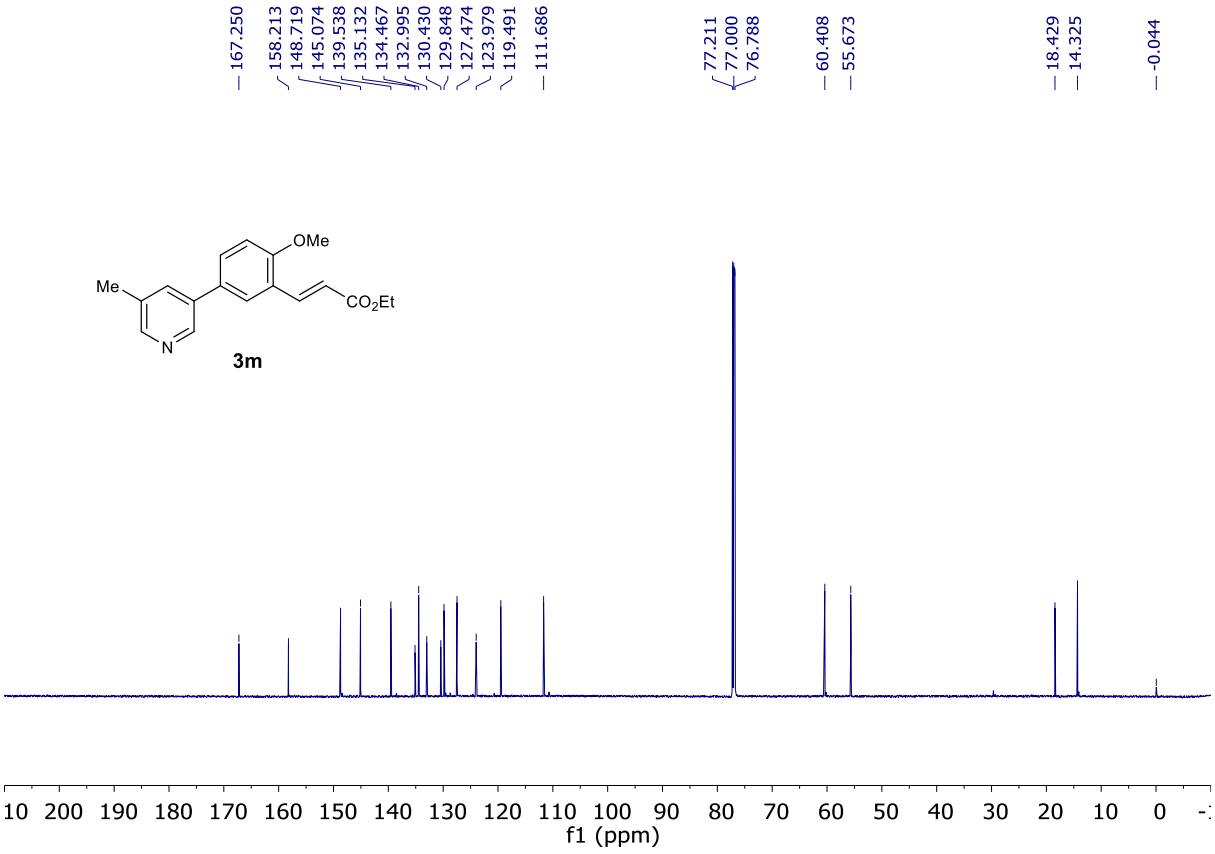

8.368
8.011
7.984
7.936
7.932
7.922
7.919
7.909
7.905
7.645
7.642
7.513
7.509
7.498
7.495
7.260
7.022
7.008
7.002
6.997
6.987
6.983
6.605
6.578
4.288
4.276
4.264
4.252
3.938
1.351
1.339
1.328
-0.009
OMe
CO2Et
F
N
3k
7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0
f1 (ppm)
0.99
1.02
1.01
1.01
1.01
1.02
0.99
1.00
2.07
3.02
3.16
f1 (ppm)

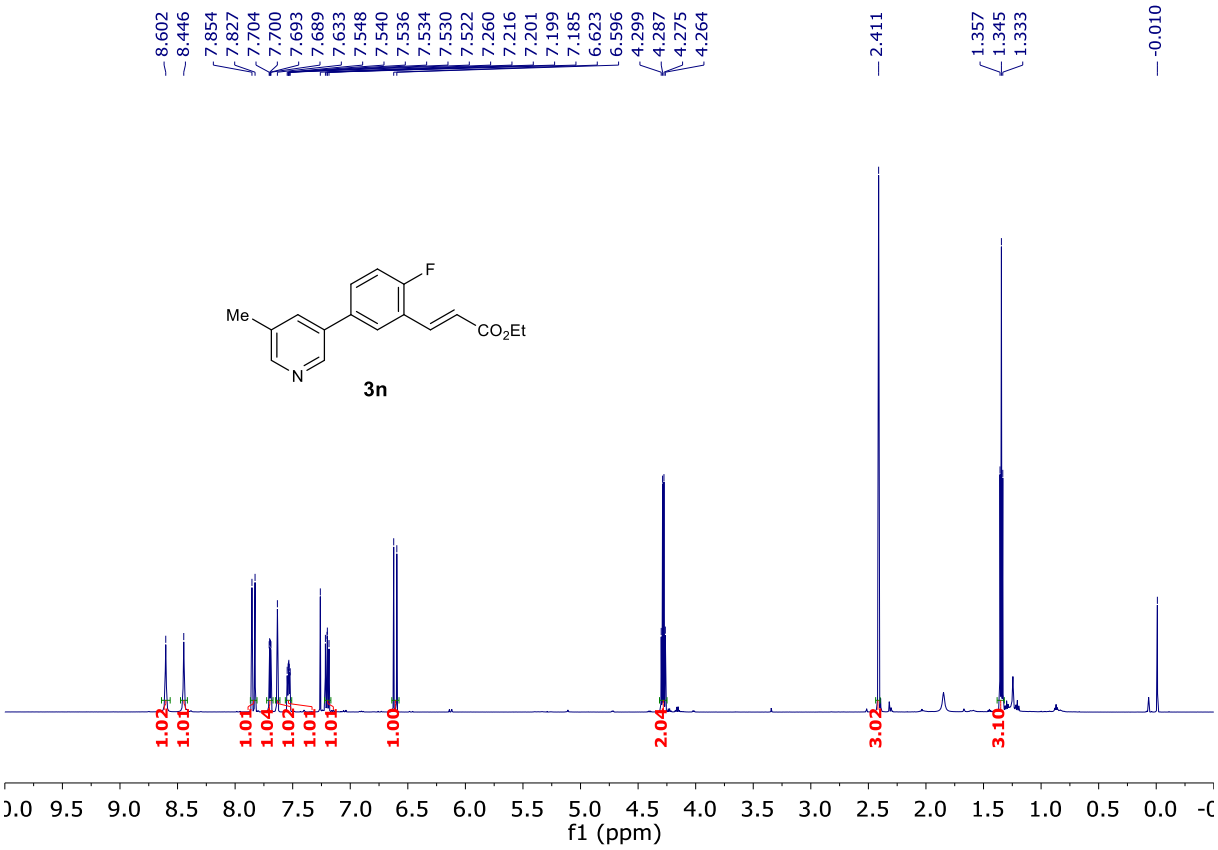

167.238
163.729
162.145
158.349
145.457
145.360
139.413
139.342
139.290
133.958
133.928
129.788
129.269
127.480
124.153
119.780
111.837
109.598
109.349
77.250
77.038
76.826
60.497
55.749
14.362
0.001
OMe
CO2Et
F
N
3k
f1 (ppm)

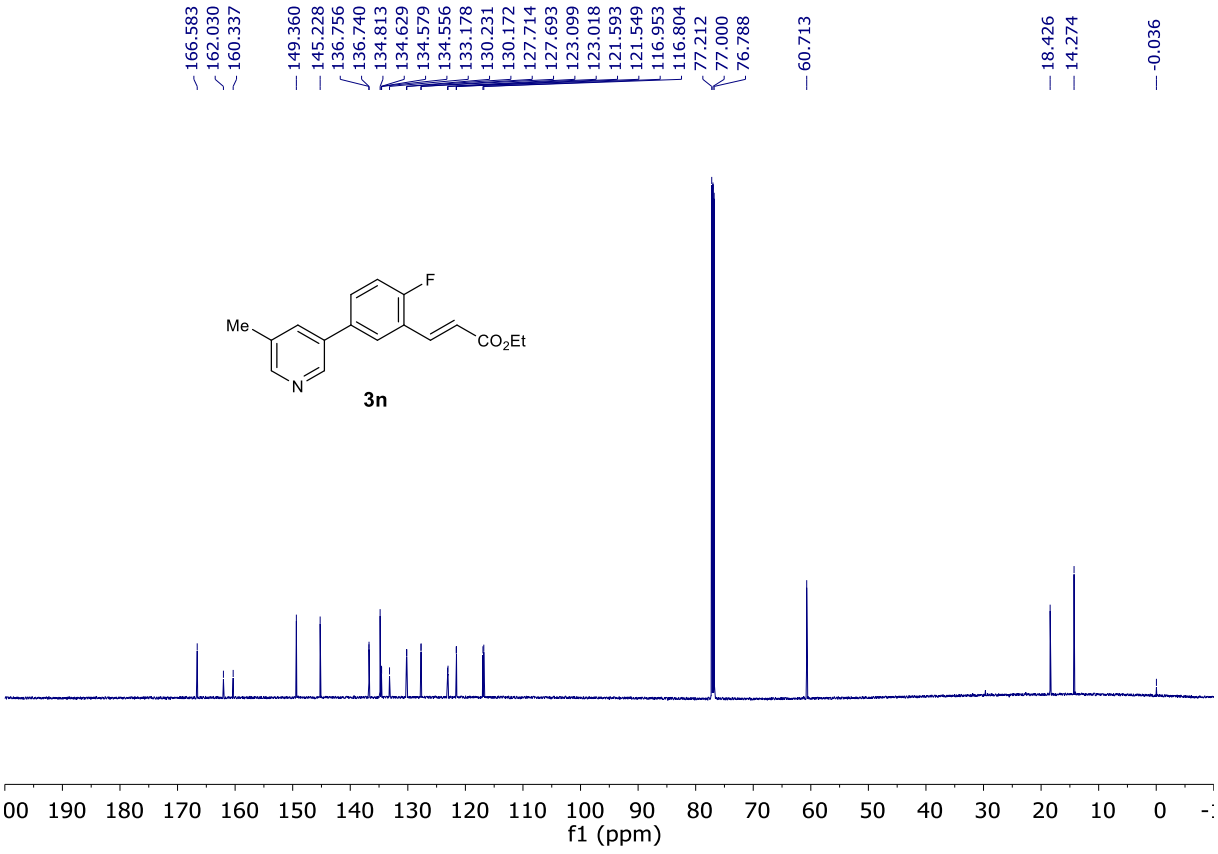

8.631
8.629
8.626
8.430
8.426
8.010
7.983
7.693
7.689
7.560
7.556
7.546
7.542
7.538
7.533
7.530
7.260
7.035
7.020
6.612
6.585
4.290
4.278
4.266
4.254
3.944
1.353
1.341
1.329
-0.009
OMe
F
CO2Et
N
3l
0.97
0.96
1.00
1.03
2.07
1.03
1.00
2.04
3.06
3.05
f1 (ppm)

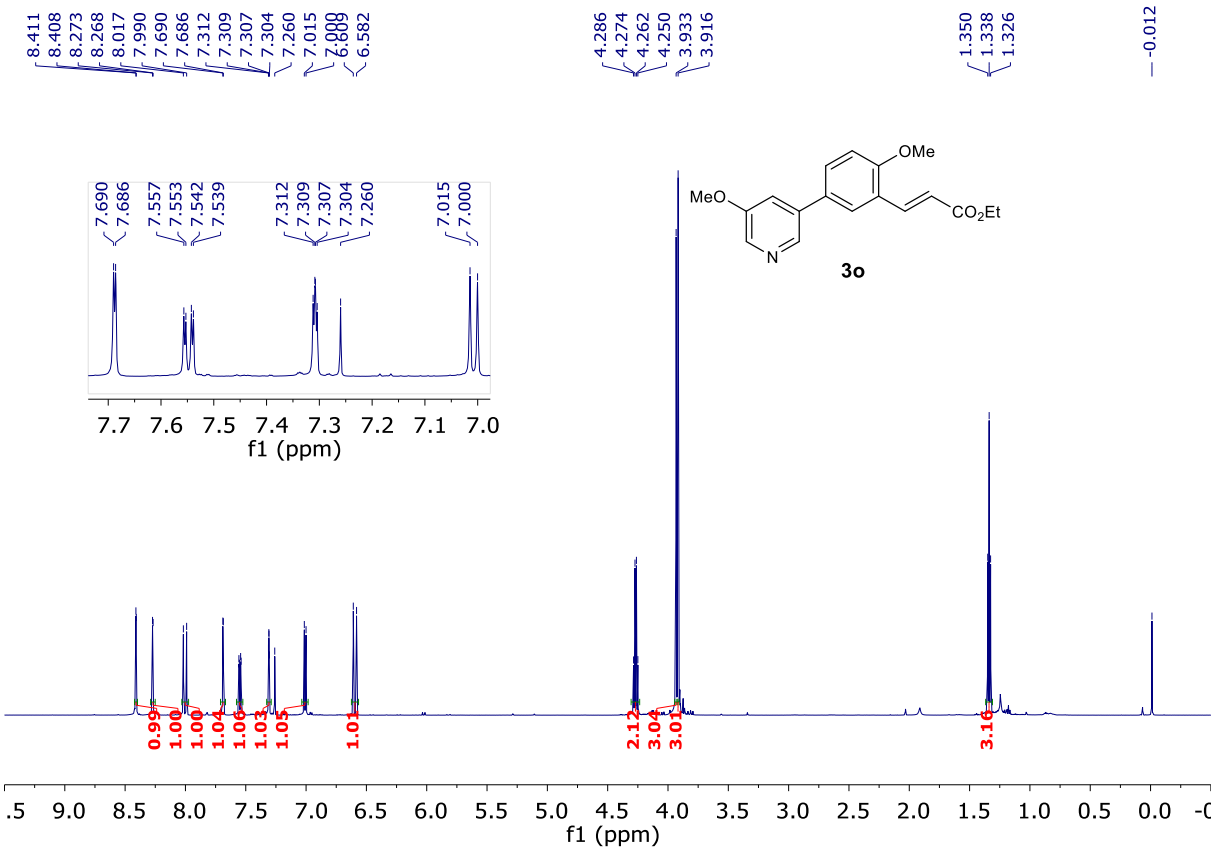

167.150
160.510
158.809
158.679
143.679
143.654
139.247
137.308
137.283
136.443
136.289
129.900
128.870
127.604
124.251
120.559
120.436
119.895
111.855
77.212
77.000
76.789
60.471
55.734
14.322
-0.038
OMe
F
CO2Et
N
3l
f1 (ppm)

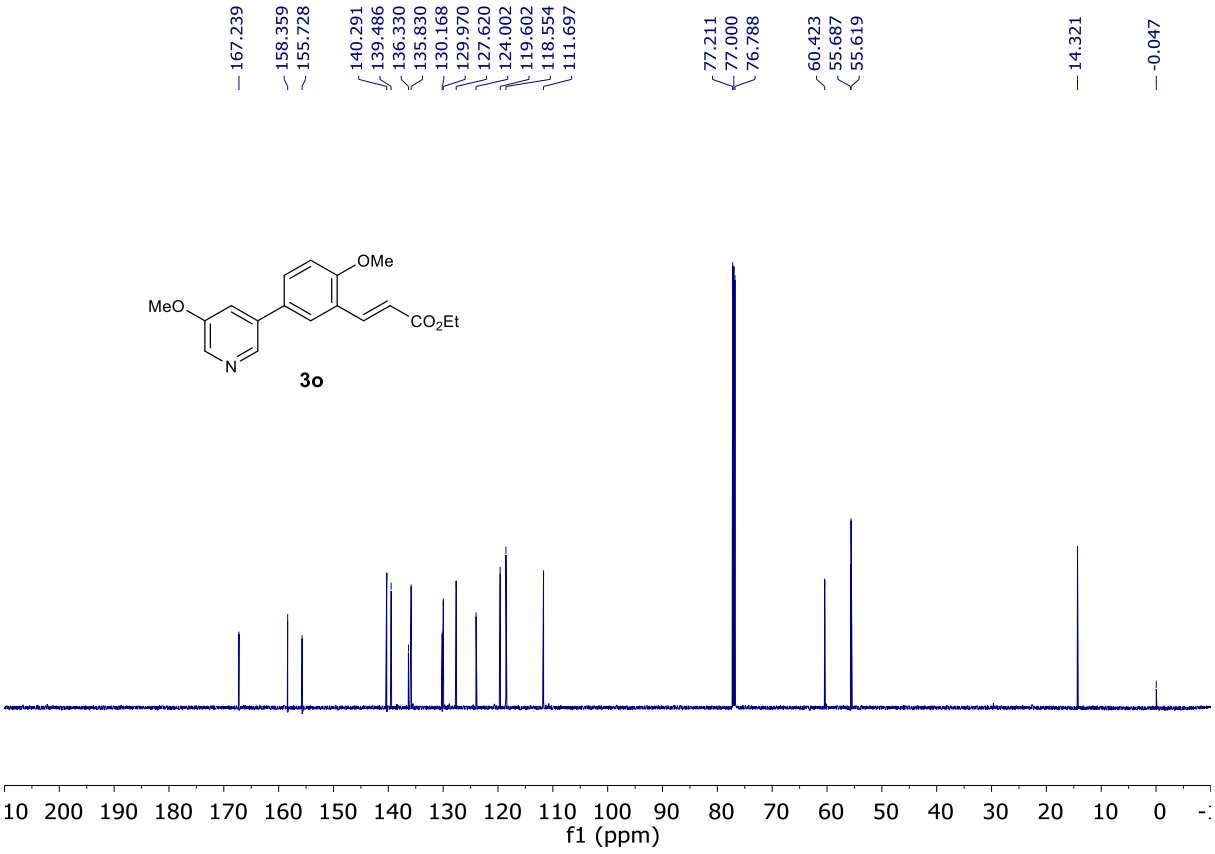

8.606 8.603 8.400 8.399 8.396 8.395 8.026 7.999 7.692 7.688 7.631 7.630 7.628 7.626 7.624 7.623 7.554 7.550 7.540 7.536 7.260 7.011 6.997 6.610 6.583
4.286 4.274 4.263 4.251 3.930
2.395
1.351 1.339 1.327
-0.010
7.692 7.688 7.631 7.630 7.628 7.626 7.624 7.623 7.554 7.550 7.540 7.536 7.260 7.011 6.997
7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0
f1 (ppm)
OMe
Me
CO2Et
N
3m
1.00 0.93 0.95 1.04 1.00 0.98 0.98 0.97 2.02 2.98 3.09 3.04
.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0
f1 (ppm)

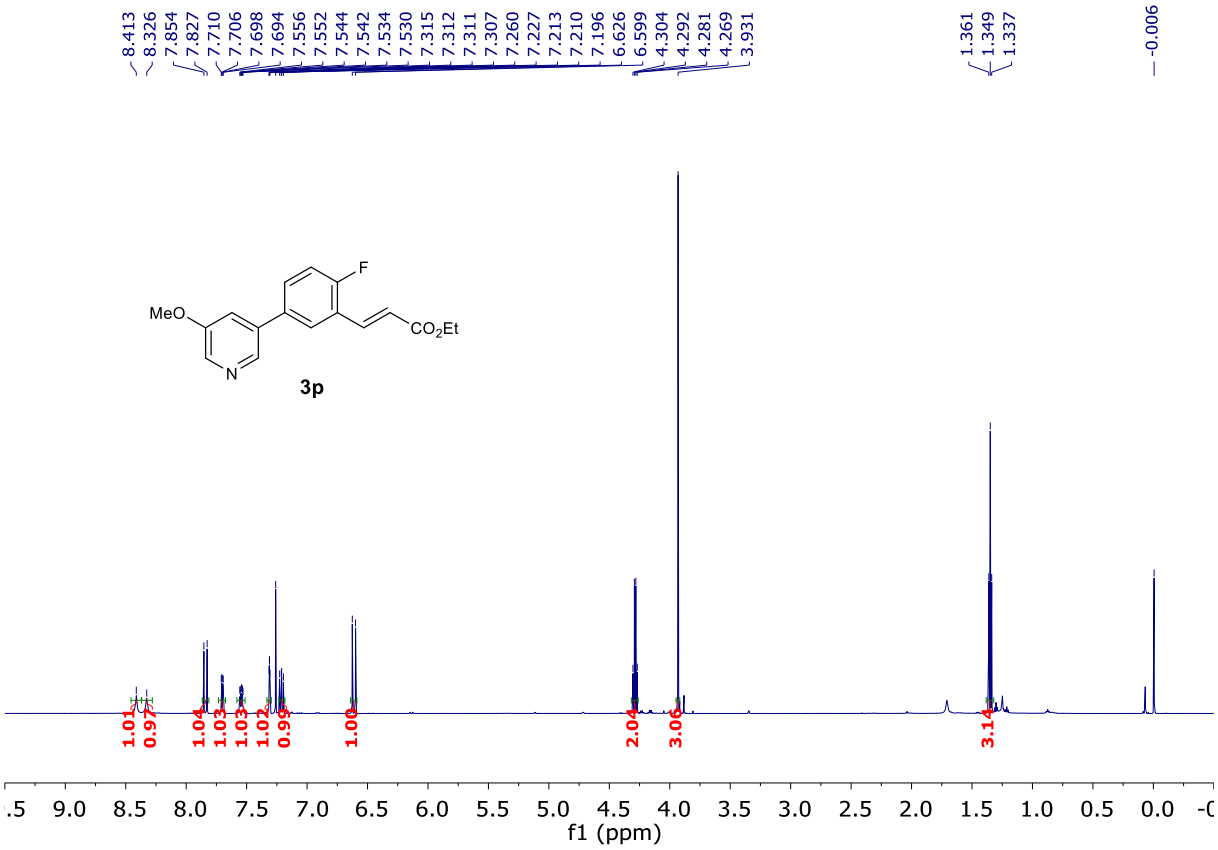

167.250 158.213 148.719 145.074 139.538 135.132 134.467 132.995 130.430 129.848 127.474 123.979 119.491 111.686
77.211 77.000 76.788
60.408 55.673
18.429 14.325
-0.044
OMe
Me
CO2Et
N
3m
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

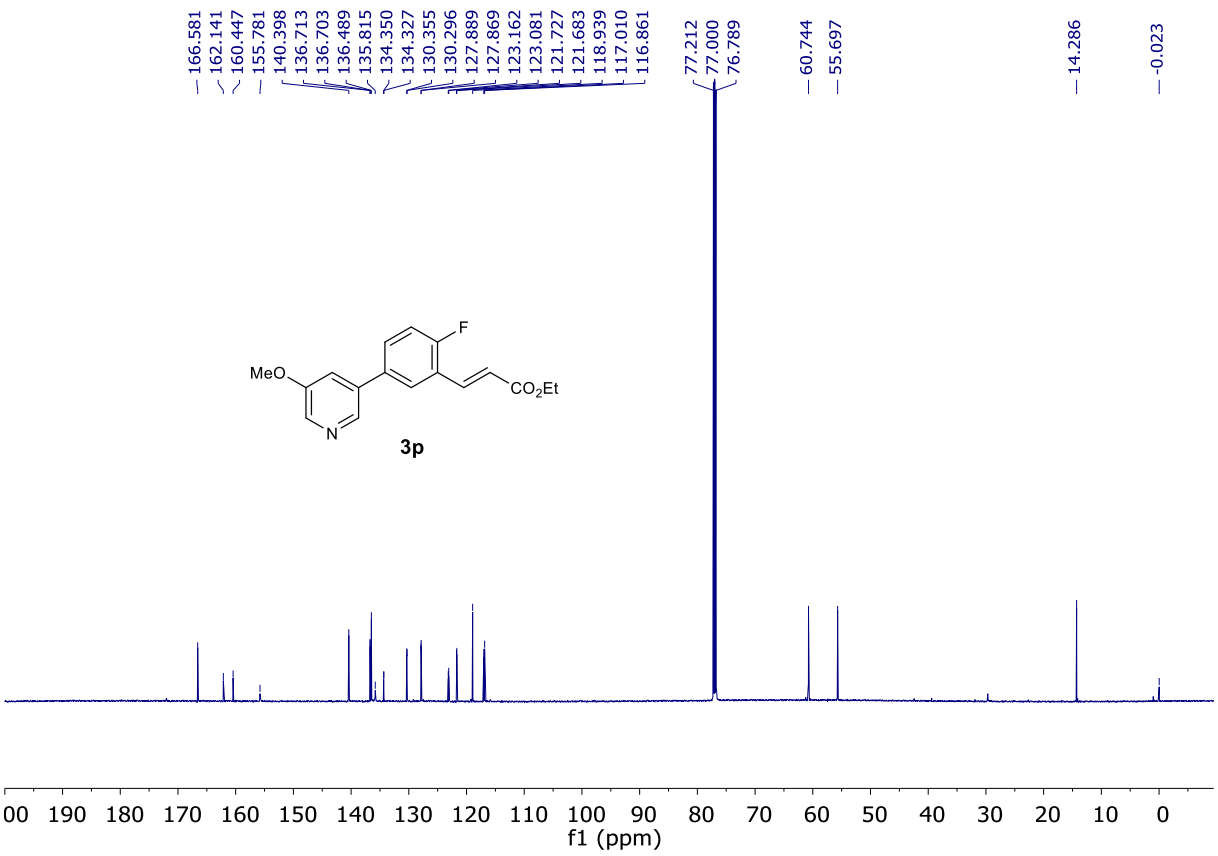

8.602
8.446
7.854
7.827
7.704
7.700
7.693
7.689
7.633
7.548
7.540
7.536
7.534
7.530
7.522
7.260
7.216
7.201
7.199
7.185
6.623
6.596
4.299
4.287
4.275
4.264
2.411
1.357
1.345
1.333
-0.010
F
Me
CO2Et
N
3n
1.02
1.01
1.01
1.04
1.02
1.01
1.01
1.00
2.04
3.02
3.10
f1 (ppm)


166.583
162.030
160.337
149.360
145.228
136.756
136.740
134.813
134.629
134.579
134.556
133.178
130.231
130.172
127.714
127.693
123.099
123.018
121.593
121.549
116.953
116.804
77.212
77.000
76.788
60.713
18.426
14.274
-0.036
F
Me
CO2Et
N
3n
f1 (ppm)


8.411
8.408
8.273
8.268
8.017
7.990
7.690
7.686
7.312
7.309
7.307
7.304
7.260
7.015
7.000
6.809
6.582
4.286
4.274
4.262
4.250
3.933
3.916
1.350
1.338
1.326
-0.012
7.690
7.686
7.557
7.553
7.542
7.539
7.312
7.309
7.307
7.304
7.260
7.015
7.000
7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0
f1 (ppm)
OMe
MeO
CO2Et
N
3o
0.99
1.00
1.00
1.04
1.06
1.03
1.05
1.01
2.12
3.04
3.01
3.16
.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0
f1 (ppm)


167.239
158.359
155.728
140.291
139.486
136.330
135.830
130.168
129.970
127.620
124.002
119.602
118.554
111.697
77.211
77.000
76.788
60.423
55.687
55.619
14.321
-0.047
OMe
MeO
CO2Et
N
3o
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)


8.413
8.326
7.854
7.827
7.710
7.706
7.698
7.694
7.556
7.552
7.544
7.542
7.534
7.530
7.315
7.312
7.311
7.307
7.260
7.227
7.213
7.210
7.196
6.626
6.599
4.304
4.292
4.281
4.269
3.931
1.361
1.349
1.337
-0.006
F
MeO
CO2Et
N
3p
1.01
0.97
1.04
1.03
1.03
1.02
0.99
1.00
2.04
3.06
3.14
f1 (ppm)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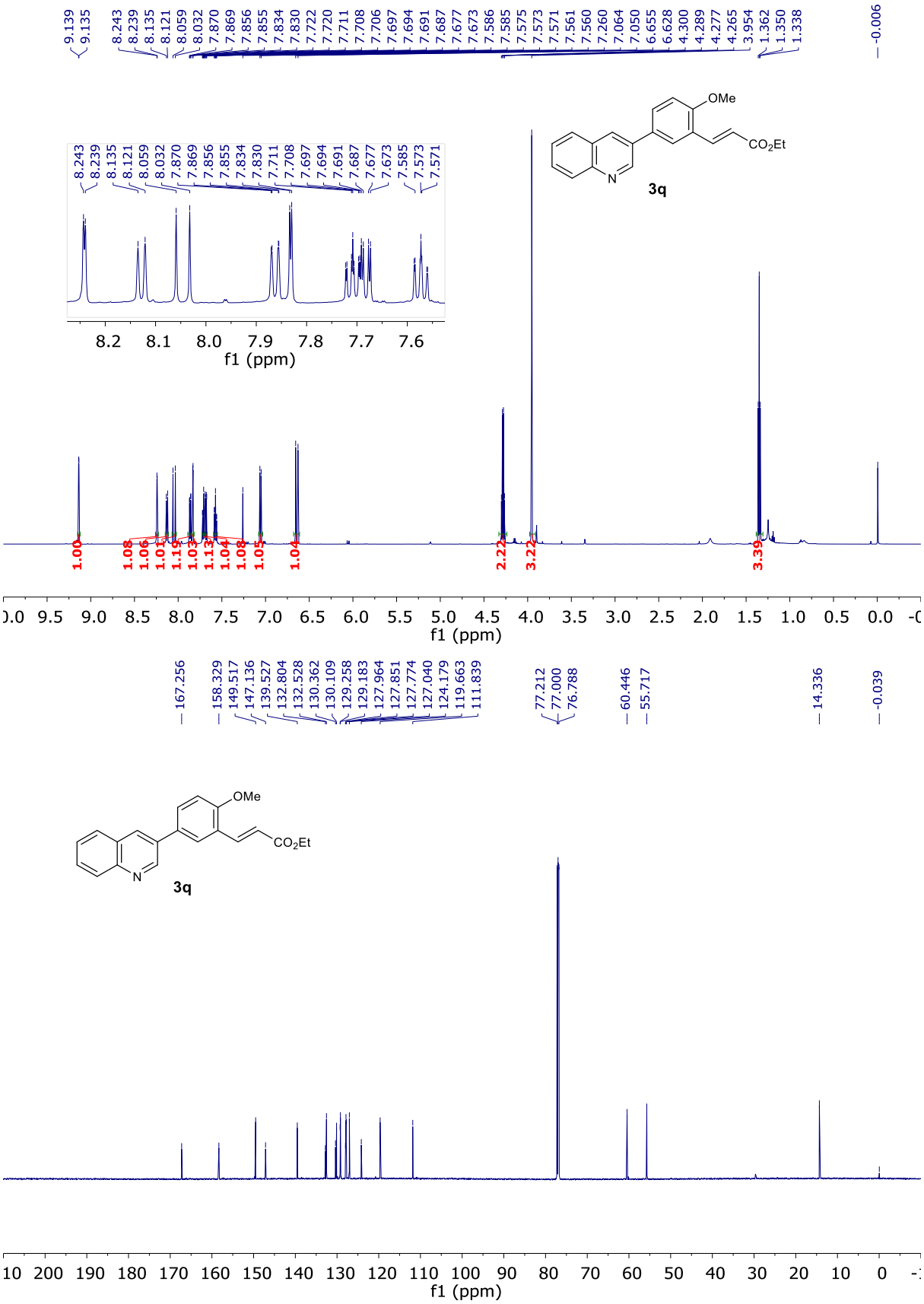
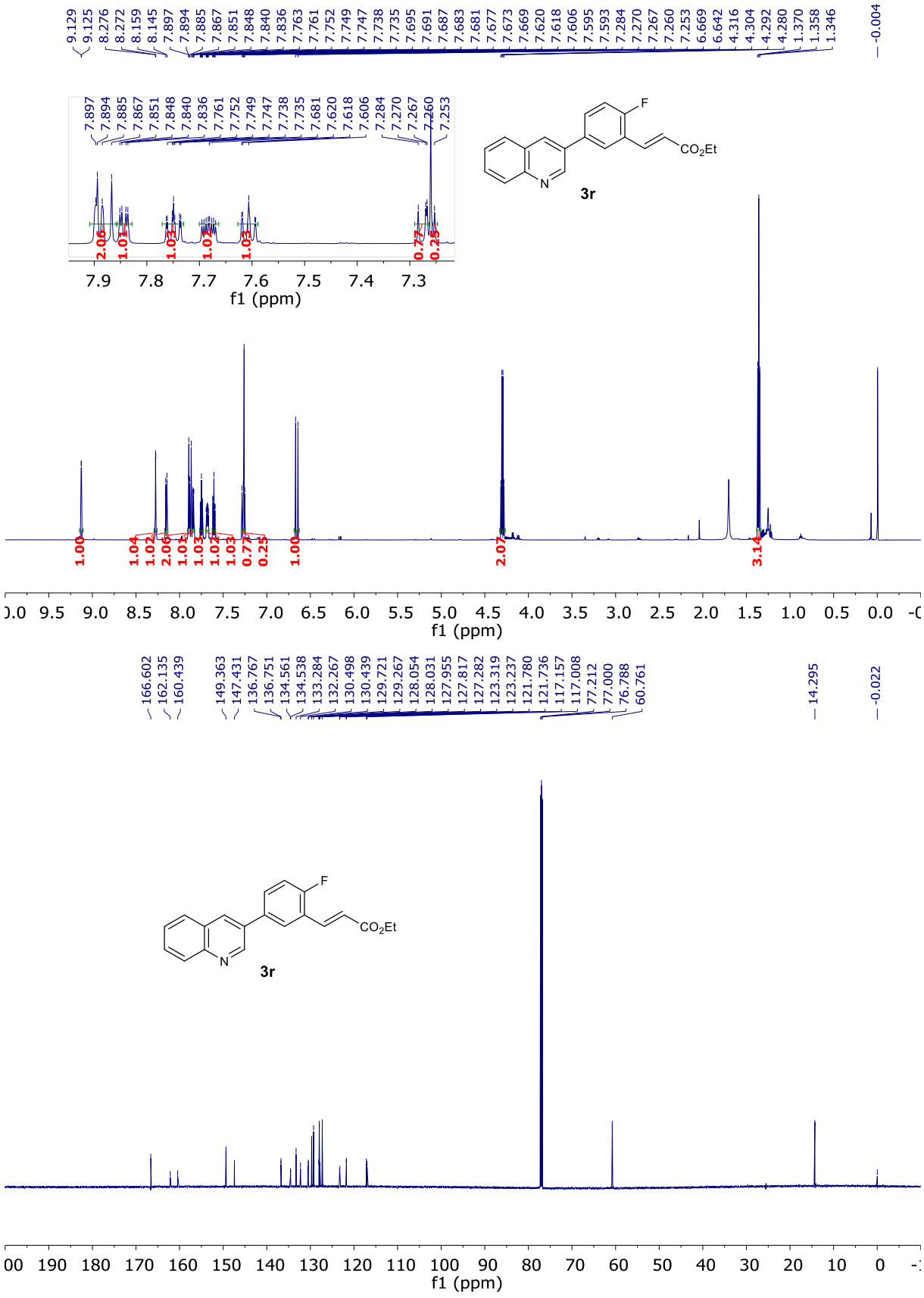
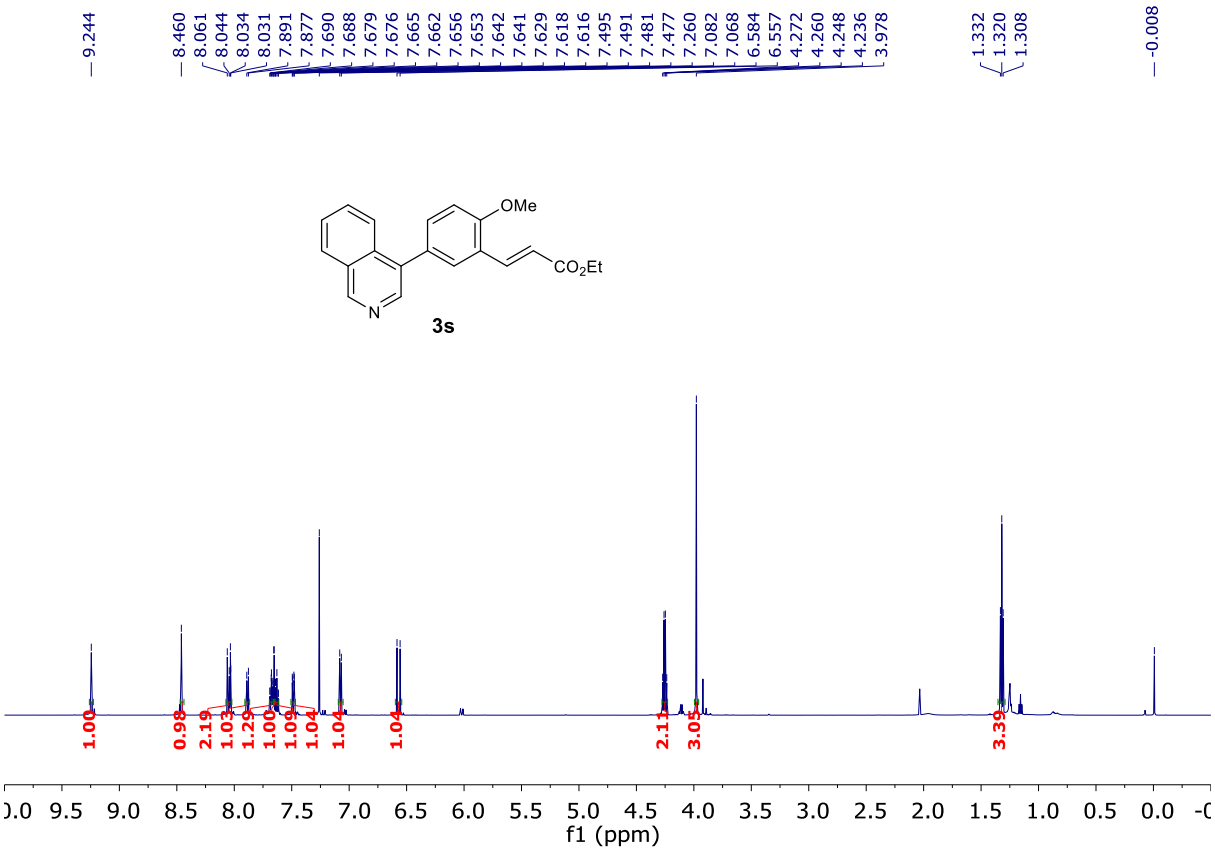
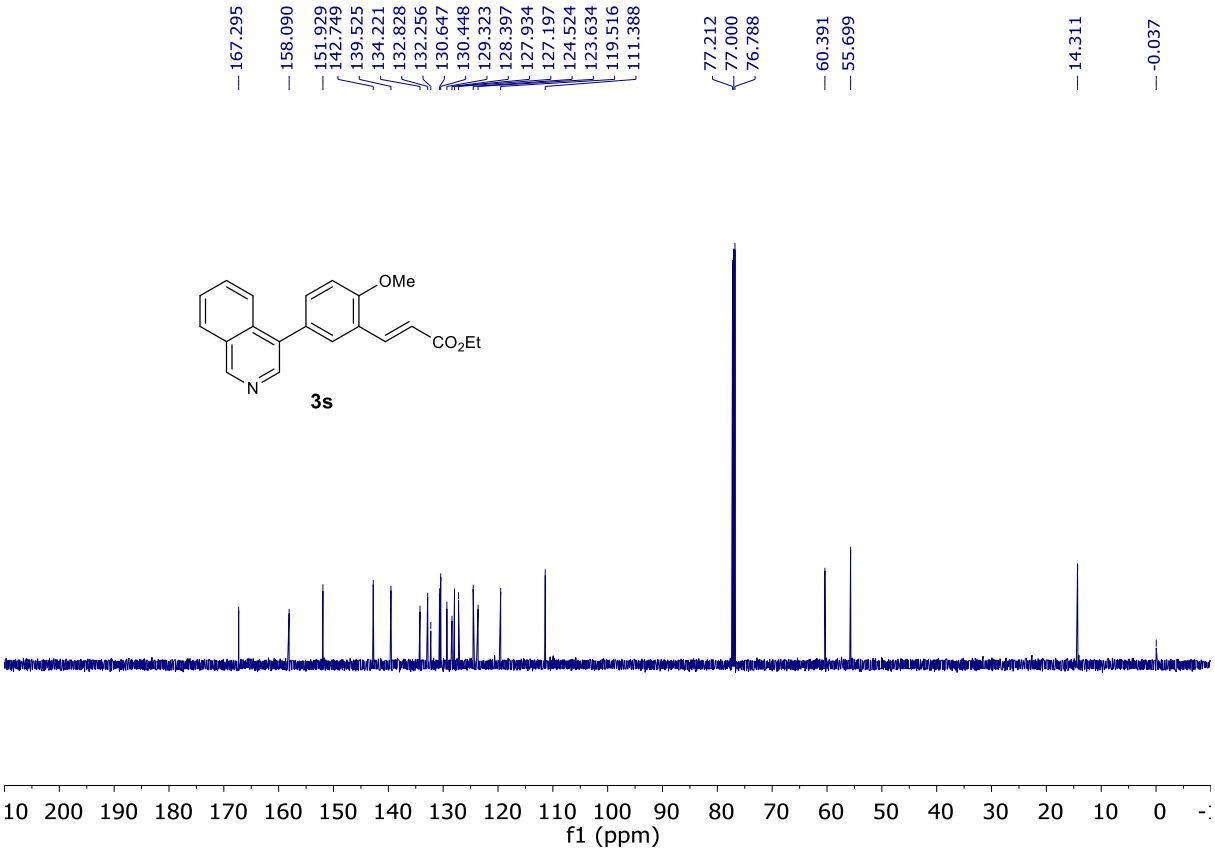
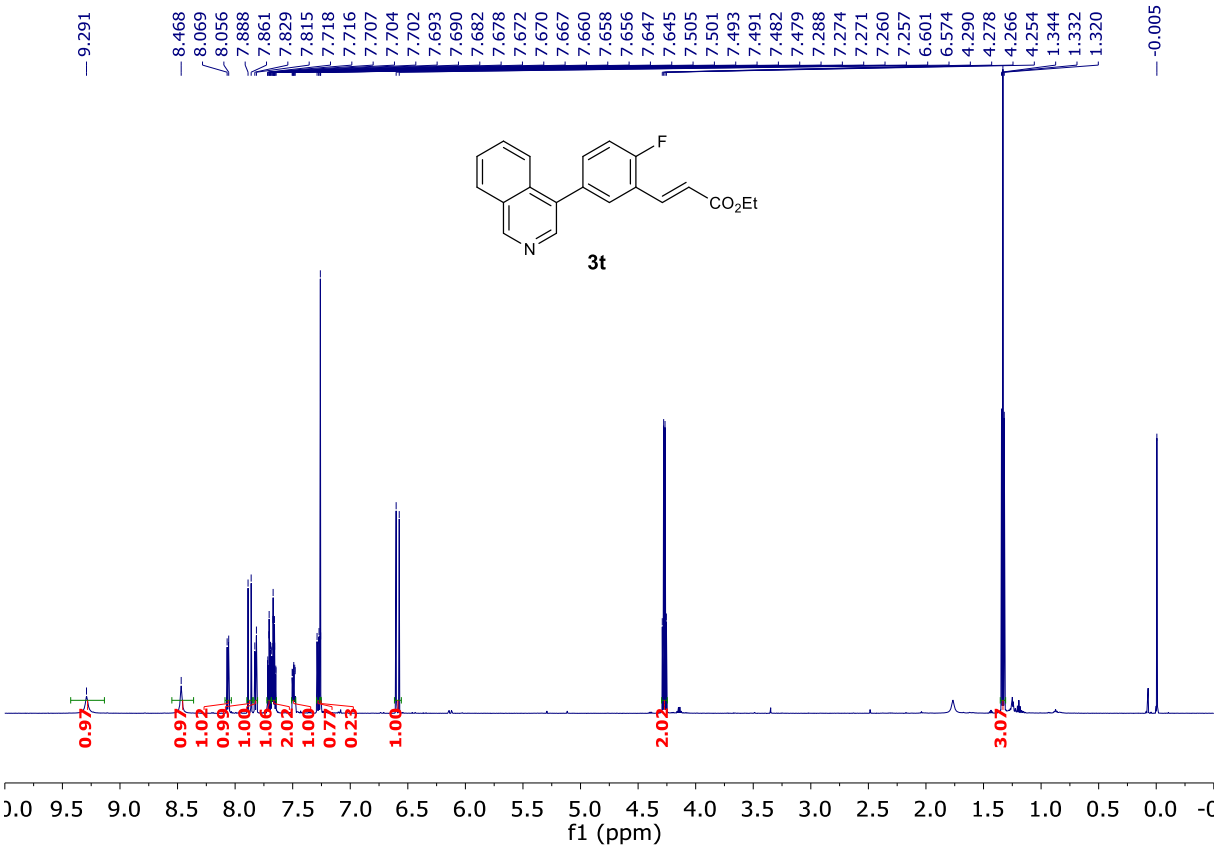
162.141
160.447
155.781
140.398
136.713
136.703
136.489
135.815
134.350
134.327
130.355
130.296
127.889
127.869
123.162
123.081
121.727
121.683
118.939
117.010
116.861
77.212
77.000
76.789
60.744
55.697
14.286
-0.023
F
MeO
CO2Et
N
3p
f1 (ppm)

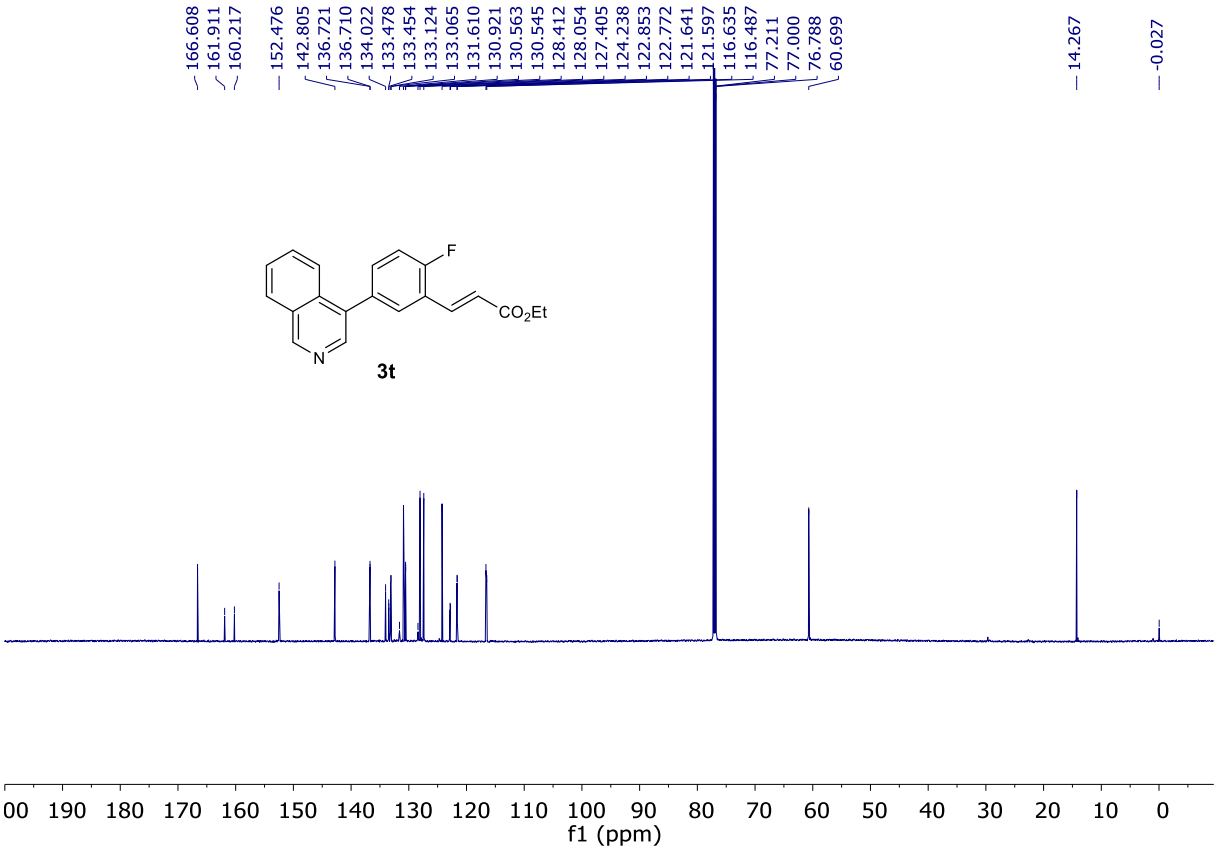

9.139
9.135
8.243
8.239
8.135
8.121
8.059
8.032
7.870
7.869
7.856
7.855
7.834
7.830
7.722
7.720
7.711
7.708
7.706
7.697
7.694
7.691
7.687
7.677
7.673
7.586
7.585
7.575
7.573
7.571
7.561
7.560
7.260
7.064
7.050
6.655
6.628
4.300
4.289
4.277
4.265
3.954
1.362
1.350
1.338
-0.006
OMe
CO2Et
N
3q
f1 (ppm)
1.00
1.08
1.06
1.01
1.19
1.03
1.13
1.04
1.08
1.05
1.04
2.22
3.22
3.39
f1 (ppm)
167.256
158.329
149.517
147.136
139.527
132.804
132.528
130.362
130.109
129.258
129.183
127.964
127.851
127.774
127.040
124.179
119.663
111.839
77.212
77.000
76.788
60.446
55.717
14.336
-0.039
OMe
CO2Et
N
3q
f1 (ppm)

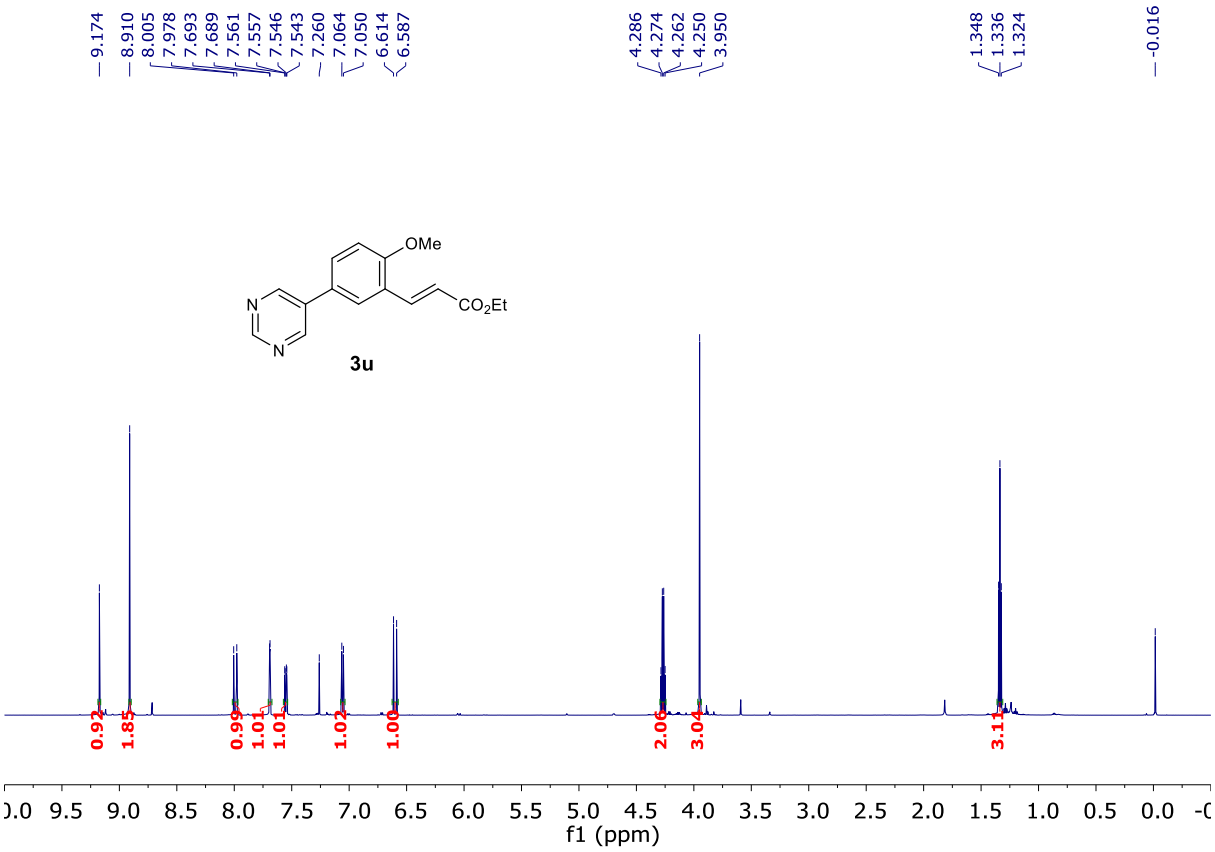

9.129
9.125
8.276
8.272
8.159
8.145
7.897
7.894
7.885
7.867
7.851
7.848
7.840
7.836
7.763
7.761
7.752
7.749
7.747
7.738
7.735
7.695
7.691
7.687
7.683
7.681
7.677
7.673
7.669
7.620
7.618
7.606
7.595
7.593
7.284
7.270
7.267
7.260
7.253
6.669
6.642
4.316
4.304
4.292
4.280
1.370
1.358
1.346
-0.004
F
CO2Et
N
3r
2.06
1.01
1.03
1.02
1.03
0.77
0.25
7.9 7.8 7.7 7.6 7.5 7.4 7.3
f1 (ppm)
1.00
1.04
1.02
2.06
1.01
1.03
1.02
1.03
0.77
0.25
1.00
2.07
3.14
f1 (ppm)
166.602
162.135
160.439
149.363
147.431
136.767
136.751
134.561
134.538
133.284
132.267
130.498
130.439
129.721
129.267
128.054
128.031
127.955
127.817
127.282
123.319
123.237
121.780
121.736
117.157
117.008
77.212
77.000
76.788
60.761
14.295
-0.022
F
CO2Et
N
3r
f1 (ppm)

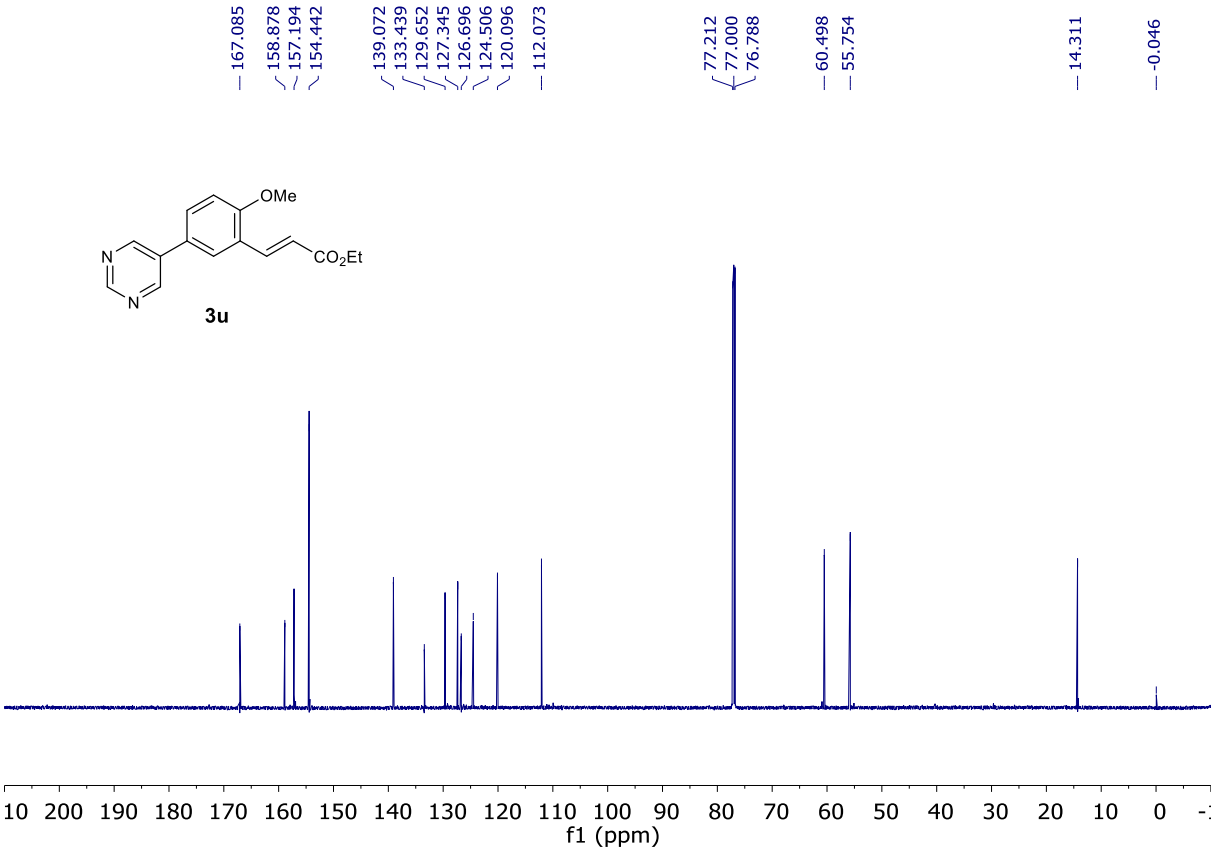

9.244
8.460
8.061
8.044
8.034
8.031
7.891
7.877
7.690
7.688
7.679
7.676
7.665
7.662
7.656
7.653
7.642
7.641
7.629
7.618
7.616
7.495
7.491
7.481
7.477
7.260
7.082
7.068
6.584
6.557
4.272
4.260
4.248
4.236
3.978
1.332
1.320
1.308
-0.008
OMe
CO2Et
N
3s
1.00
0.98
2.19
1.03
1.29
1.00
1.09
1.04
1.04
1.04
2.11
3.05
3.39
f1 (ppm)

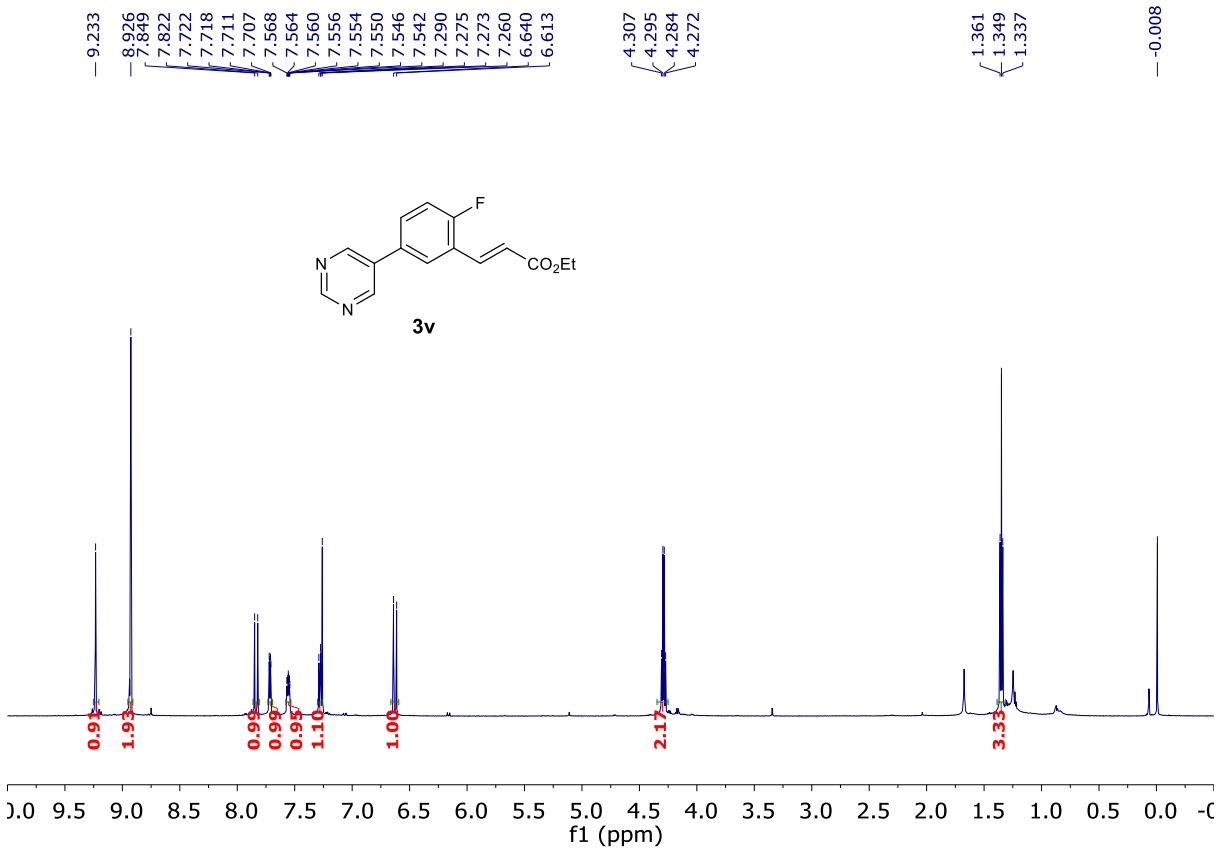

167.295
158.090
151.929
142.749
139.525
134.221
132.828
132.256
130.647
130.448
129.323
128.397
127.934
127.197
124.524
123.634
119.516
111.388
77.212
77.000
76.788
60.391
55.699
14.311
-0.037
OMe
CO2Et
N
3s
f1 (ppm)

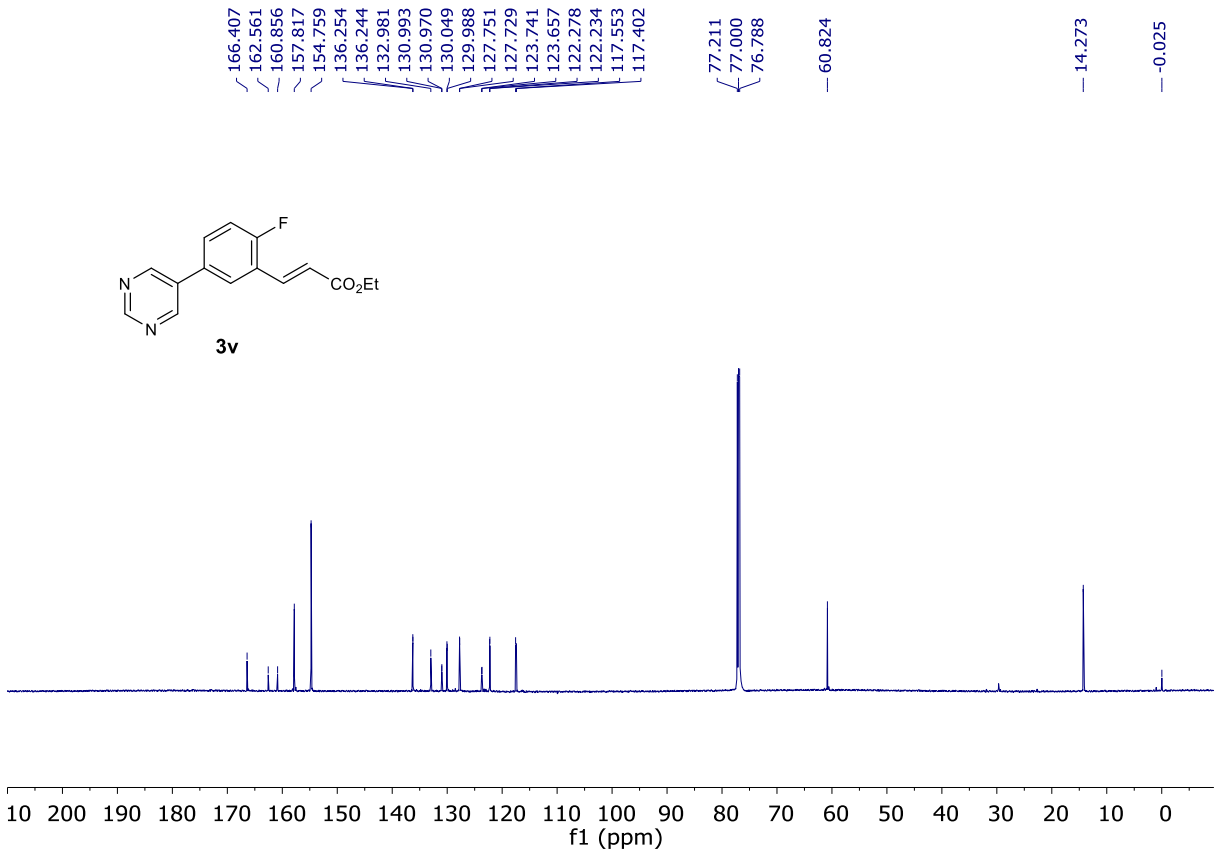

9.291
8.468
8.069
8.056
7.888
7.861
7.829
7.815
7.718
7.716
7.707
7.704
7.702
7.693
7.690
7.682
7.678
7.672
7.670
7.667
7.660
7.658
7.656
7.647
7.645
7.505
7.501
7.493
7.491
7.482
7.479
7.288
7.274
7.271
7.260
7.257
6.601
6.574
4.290
4.278
4.266
4.254
1.344
1.332
1.320
-0.005
F
CO2Et
N
3t
0.97
0.97
1.02
0.99
1.00
1.06
2.02
1.06
0.77
0.23
1.00
2.02
3.07
f1 (ppm)

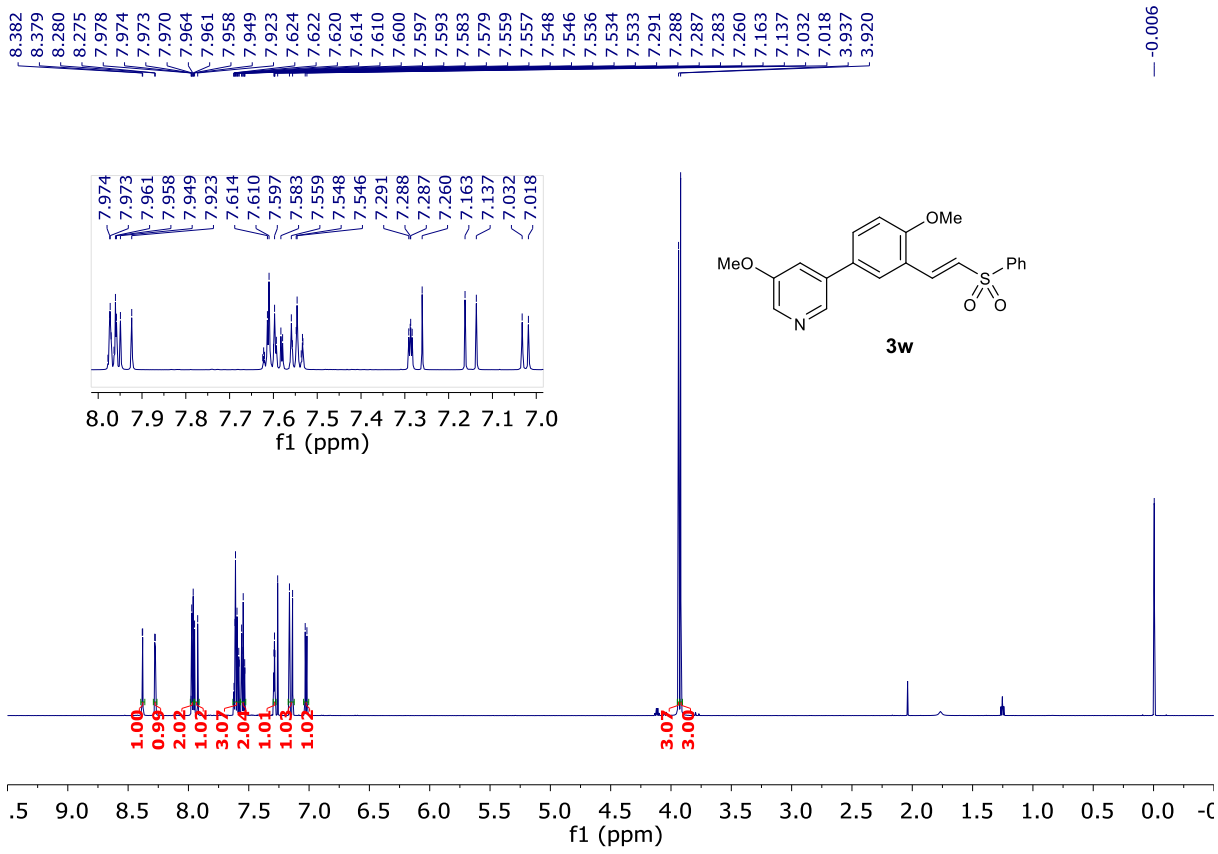

166.608
161.911
160.217
152.476
142.805
136.721
136.710
134.022
133.478
133.454
133.124
133.065
131.610
130.921
130.563
130.545
128.412
128.054
127.405
124.238
122.853
122.772
121.641
121.597
116.635
116.487
77.211
77.000
76.788
60.699
14.267
-0.027
F
CO2Et
N
3t
f1 (ppm)


9.174
8.910
8.005
7.978
7.693
7.689
7.561
7.557
7.546
7.543
7.260
7.064
7.050
6.614
6.587
4.286
4.274
4.262
4.250
3.950
1.348
1.336
1.324
-0.016
OMe
N
N
CO2Et
3u
0.92
1.85
0.99
1.01
1.01
1.02
1.00
2.06
3.04
3.11
f1 (ppm)


167.085
158.878
157.194
154.442
139.072
133.439
129.652
127.345
126.696
124.506
120.096
112.073
77.212
77.000
76.788
60.498
55.754
14.311
-0.046
OMe
N
N
CO2Et
3u
f1 (ppm)


9.233
8.926
7.849
7.822
7.722
7.718
7.711
7.707
7.568
7.564
7.560
7.556
7.554
7.550
7.546
7.542
7.290
7.275
7.273
7.260
6.640
6.613
4.307
4.295
4.284
4.272
1.361
1.349
1.337
-0.008
F
N
N
CO2Et
3v
0.91
1.93
0.99
0.99
0.95
1.10
1.00
2.17
3.33
f1 (ppm)


166.407
162.561
160.856
157.817
154.759
136.254
136.244
132.981
130.993
130.970
130.049
129.988
127.751
127.729
123.741
123.657
122.278
122.234
117.553
117.402
77.211
77.000
76.788
60.824
14.273
-0.025
F
N
N
CO2Et
3v
f1 (ppm)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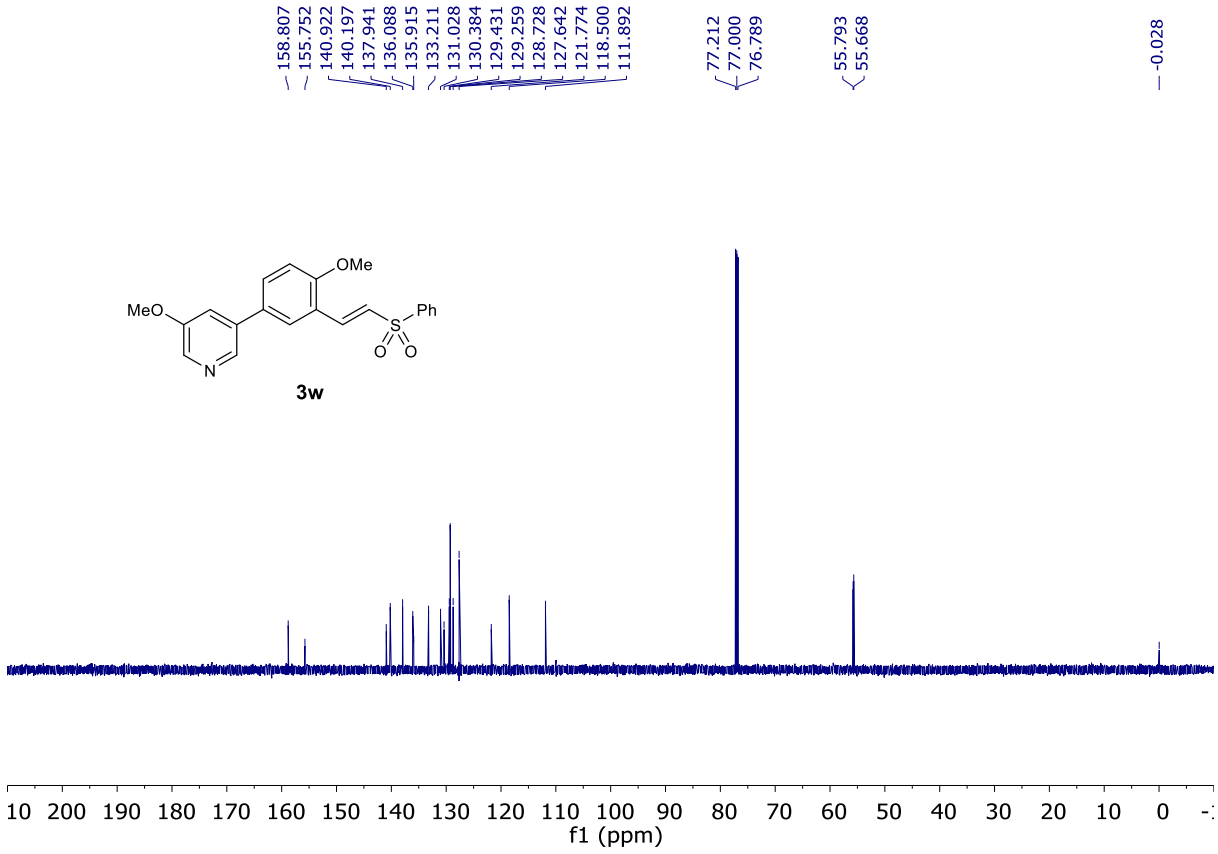
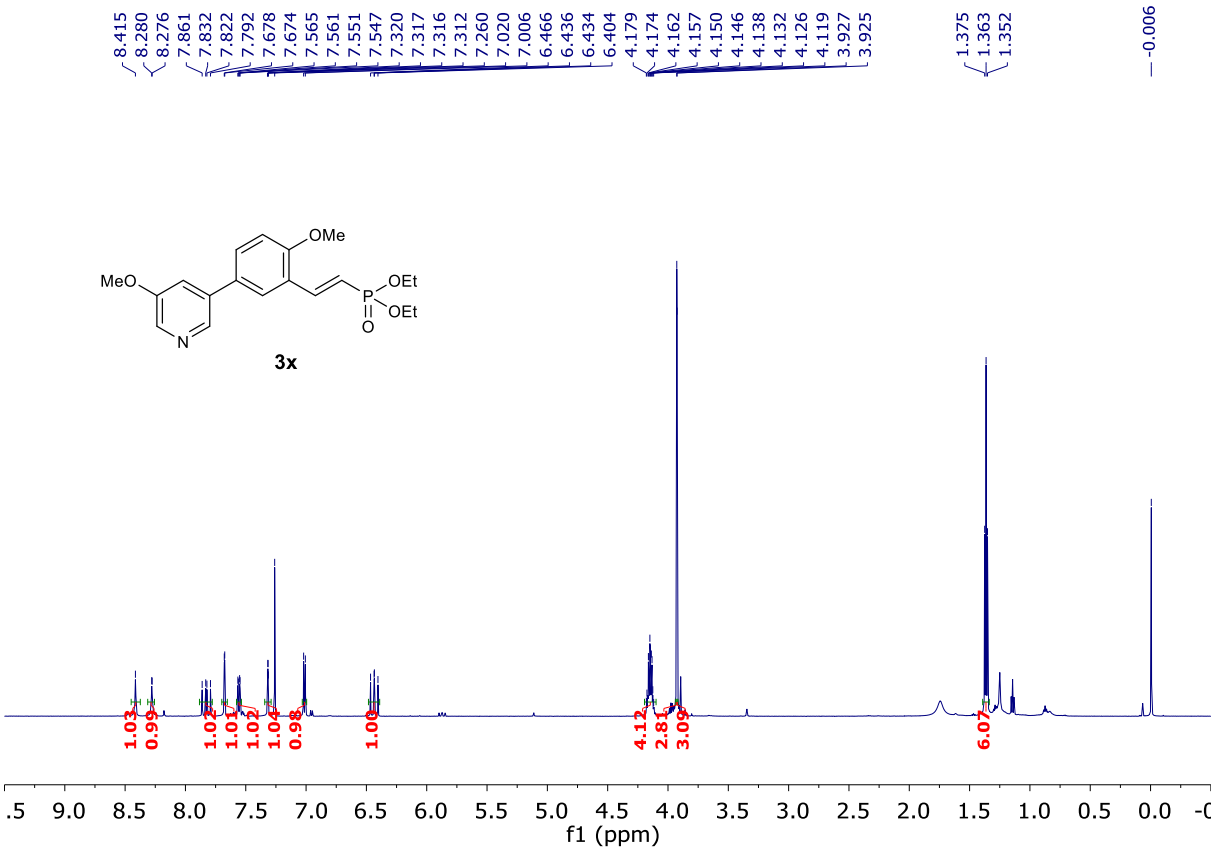
8.379
8.280
8.275
7.978
7.974
7.973
7.970
7.964
7.961
7.958
7.949
7.923
7.624
7.622
7.620
7.614
7.610
7.600
7.597
7.593
7.583
7.579
7.559
7.557
7.548
7.546
7.536
7.534
7.533
7.291
7.288
7.287
7.283
7.260
7.163
7.137
7.032
7.018
3.937
3.920
-0.006
7.974
7.973
7.961
7.958
7.949
7.923
7.614
7.610
7.597
7.583
7.559
7.548
7.546
7.291
7.288
7.287
7.260
7.163
7.137
7.032
7.018
8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0
f1 (ppm)
OMe
MeO
Ph
S
O
O
N
3w
1.00
0.99
2.02
1.02
3.07
2.04
1.01
1.03
1.02
3.07
3.00
.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


158.807
155.752
140.922
140.197
137.941
136.088
135.915
133.211
131.028
130.384
129.431
129.259
128.728
127.642
121.774
118.500
111.892
77.212
77.000
76.789
55.793
55.668
-0.028
OMe
MeO
Ph
S
O
O
N
3w
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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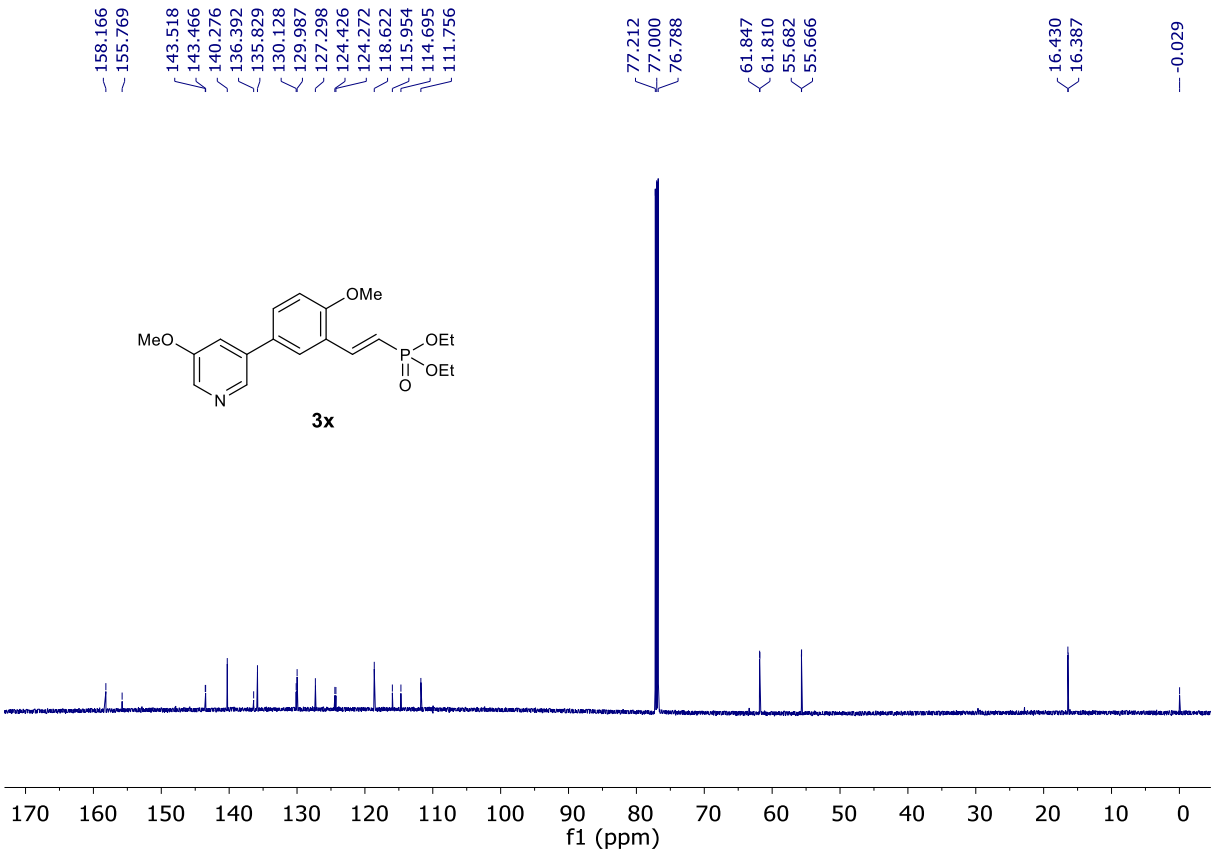
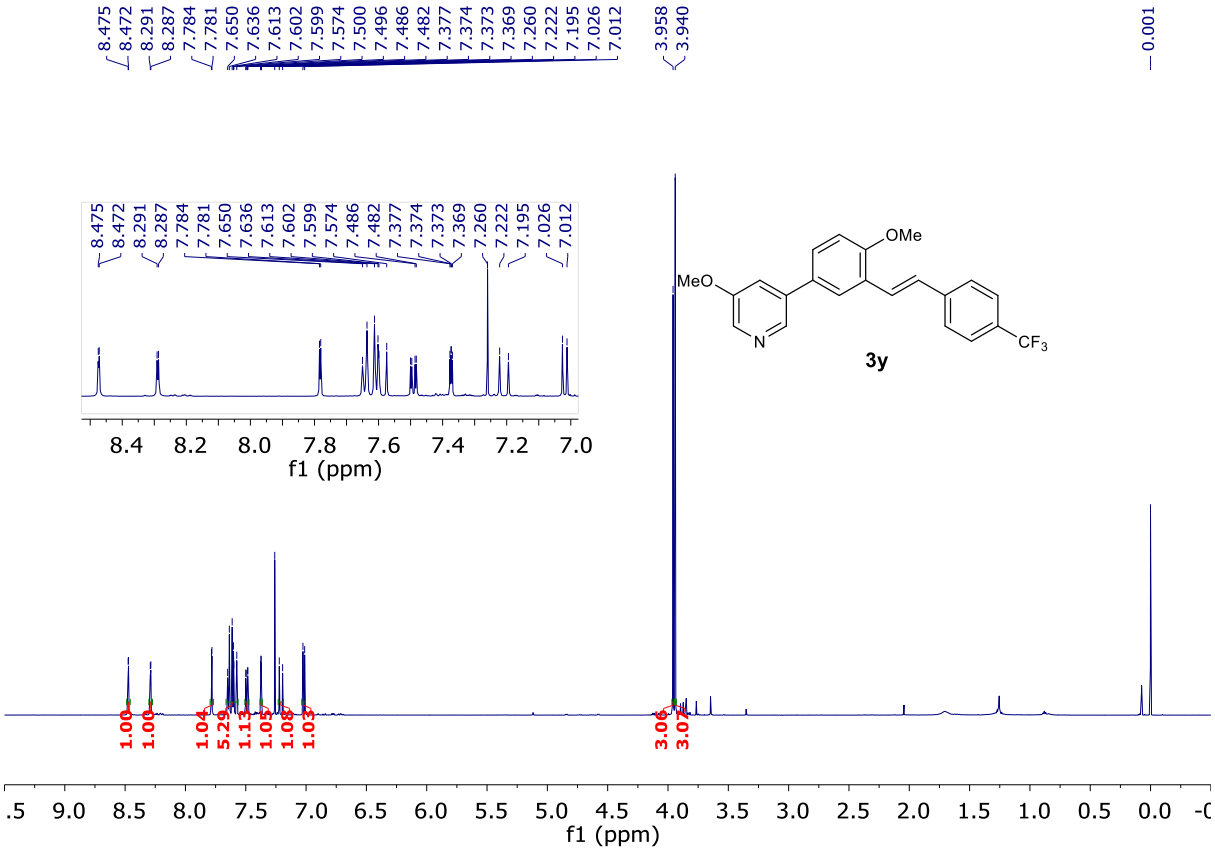
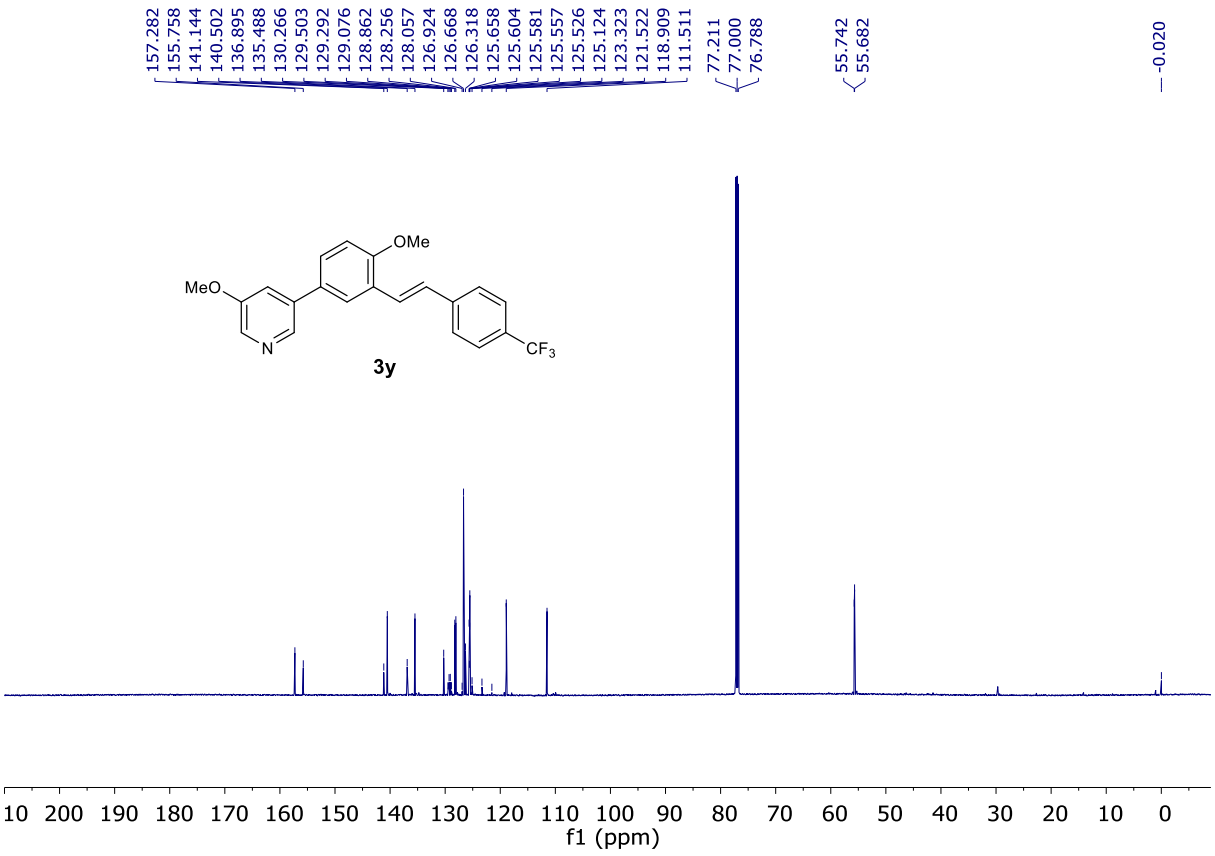
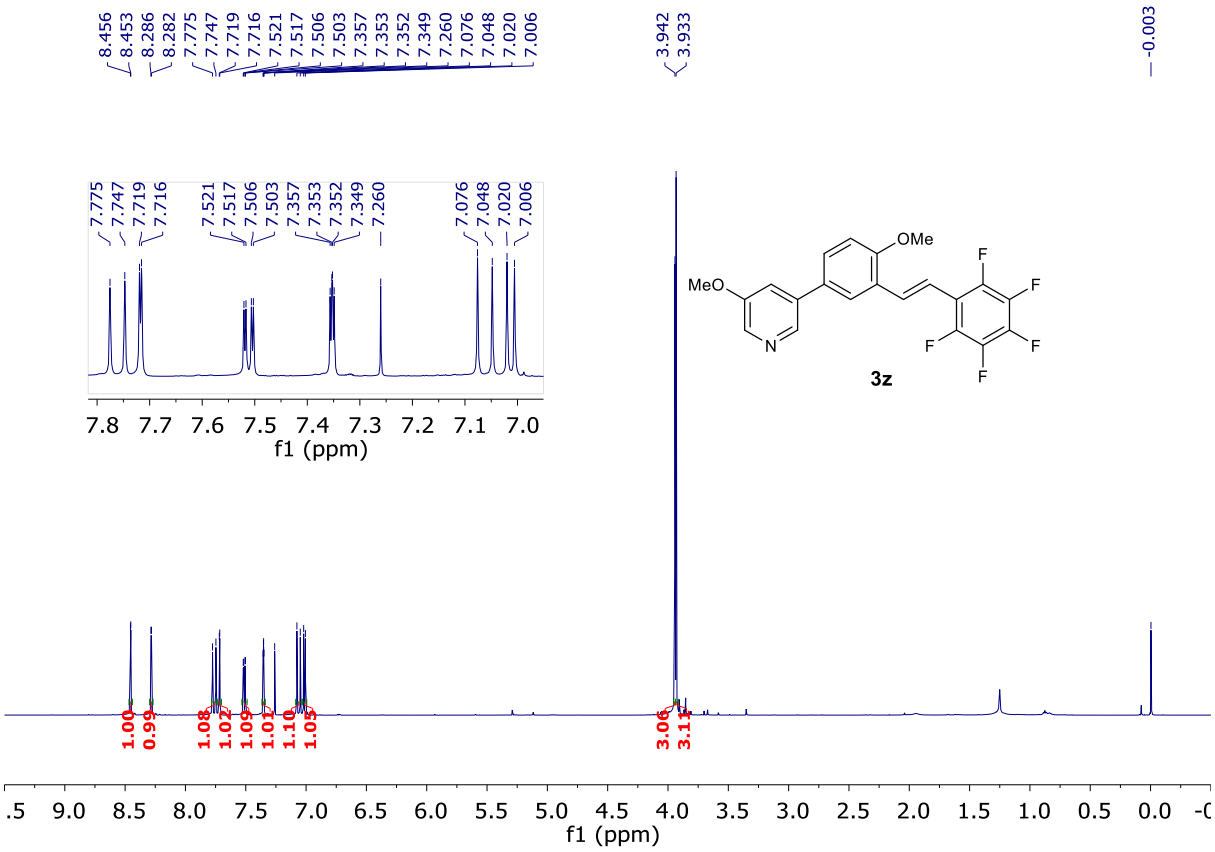
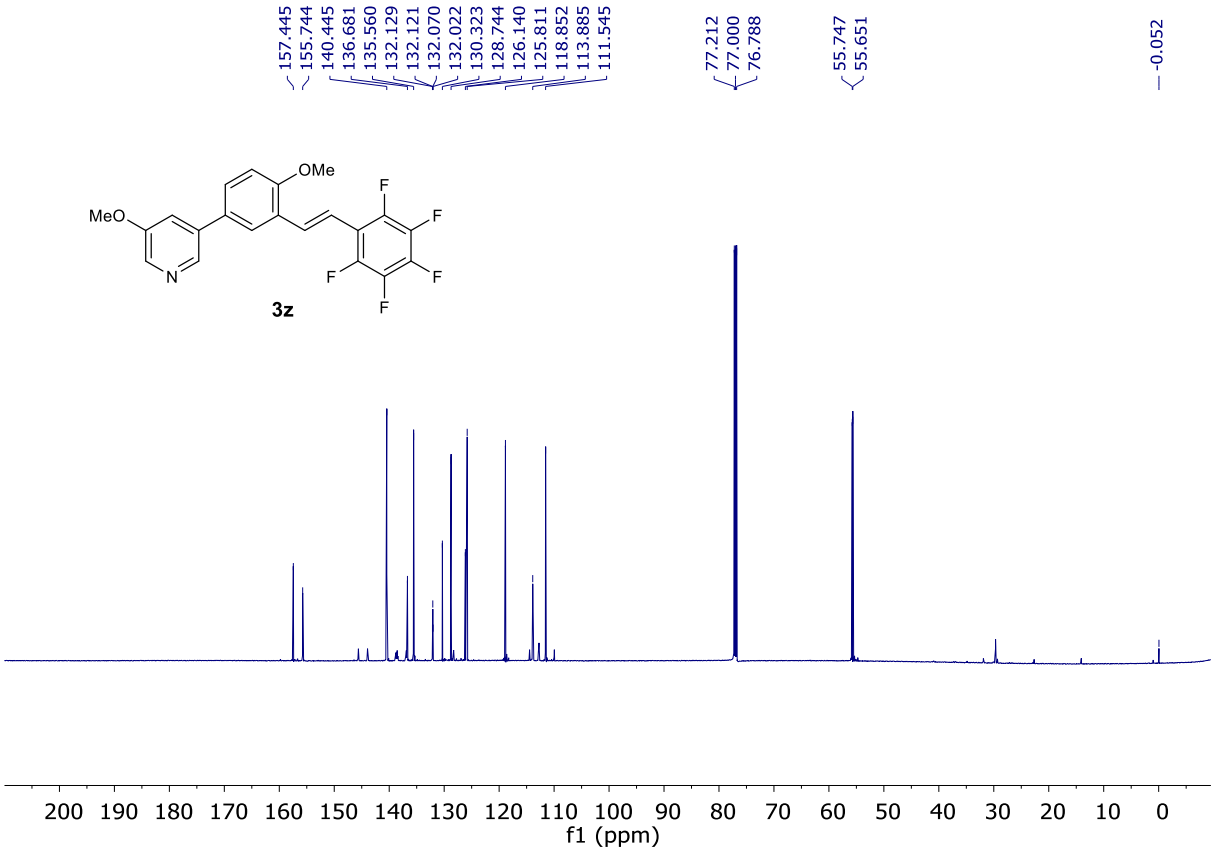
8.280
8.276
7.861
7.832
7.822
7.792
7.678
7.674
7.565
7.561
7.551
7.547
7.320
7.317
7.316
7.312
7.260
7.020
7.006
6.466
6.436
6.434
6.404
4.179
4.174
4.162
4.157
4.150
4.146
4.138
4.132
4.126
4.119
3.927
3.925
1.375
1.363
1.352
-0.006
OMe
MeO
OEt
OEt
P
O
N
3x
1.03
0.99
1.02
1.01
1.02
1.04
0.98
1.00
4.12
2.81
3.09
6.07
f1 (ppm)


158.166
155.769
143.518
143.466
140.276
136.392
135.829
130.128
129.987
127.298
124.426
124.272
118.622
115.954
114.695
111.756
77.212
77.000
76.788
61.847
61.810
55.682
55.666
16.430
16.387
-0.029
OMe
MeO
OEt
OEt
P
O
N
3x
f1 (ppm)


8.475
8.472
8.291
8.287
7.784
7.781
7.650
7.636
7.613
7.602
7.599
7.574
7.500
7.496
7.486
7.482
7.377
7.374
7.373
7.369
7.260
7.222
7.195
7.026
7.012
3.958
3.940
0.001
OMe
MeO
N
CF3
3y
8.4
8.2
8.0
7.8
7.6
7.4
7.2
7.0
f1 (ppm)
1.00
1.00
1.04
5.29
1.13
1.05
1.08
1.03
3.06
3.07
f1 (ppm)


157.282
155.758
141.144
140.502
136.895
135.488
130.266
129.503
129.292
129.076
128.862
128.256
128.057
126.924
126.668
126.318
125.658
125.604
125.581
125.557
125.526
125.124
123.323
121.522
118.909
111.511
77.211
77.000
76.788
55.742
55.682
-0.020
OMe
MeO
N
CF3
3y
f1 (ppm)


8.456
8.453
8.286
8.282
7.775
7.747
7.719
7.716
7.521
7.517
7.506
7.503
7.357
7.353
7.352
7.349
7.260
7.076
7.048
7.020
7.006
3.942
3.933
-0.003
OMe
MeO
F
N
3z
7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0
f1 (ppm)
1.00
0.99
1.08
1.02
1.09
1.01
1.10
1.05
3.06
3.11
.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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140.445
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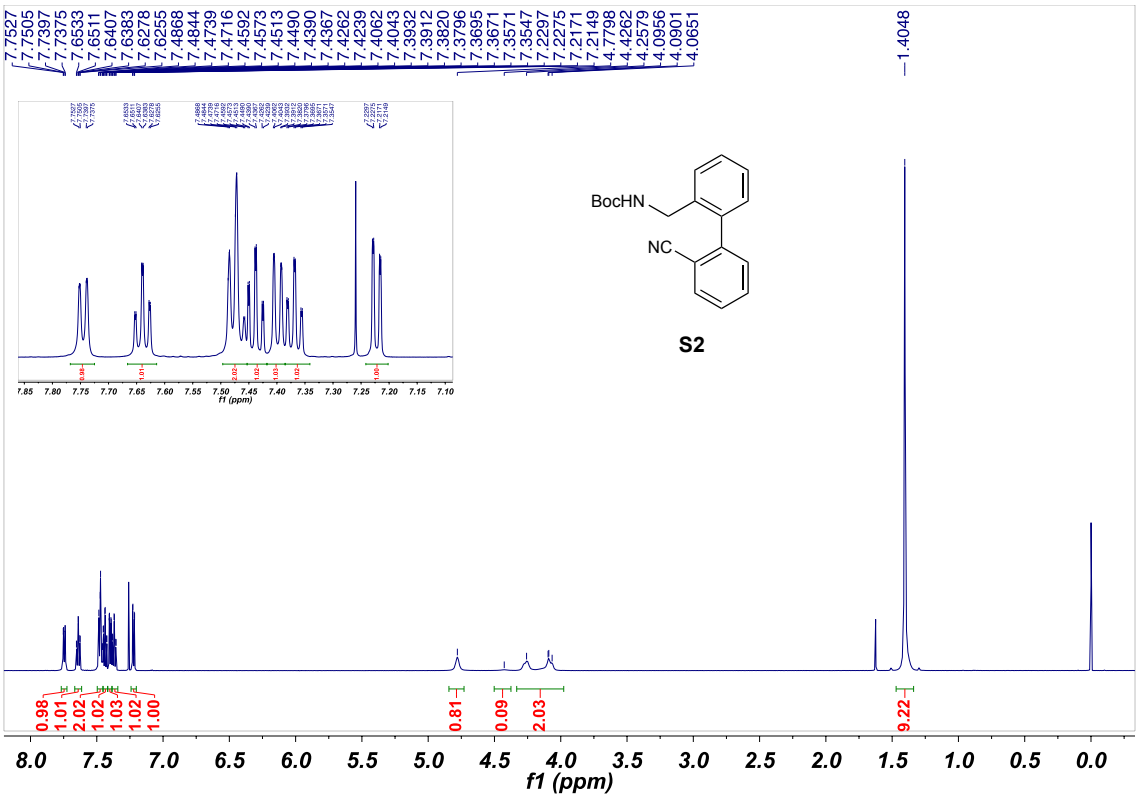
132.121
132.070
132.022
130.323
128.744
126.140
125.811
118.852
113.885
111.545
77.212
77.000
76.788
55.747
55.651
-0.052
OMe
MeO
F
N
3z
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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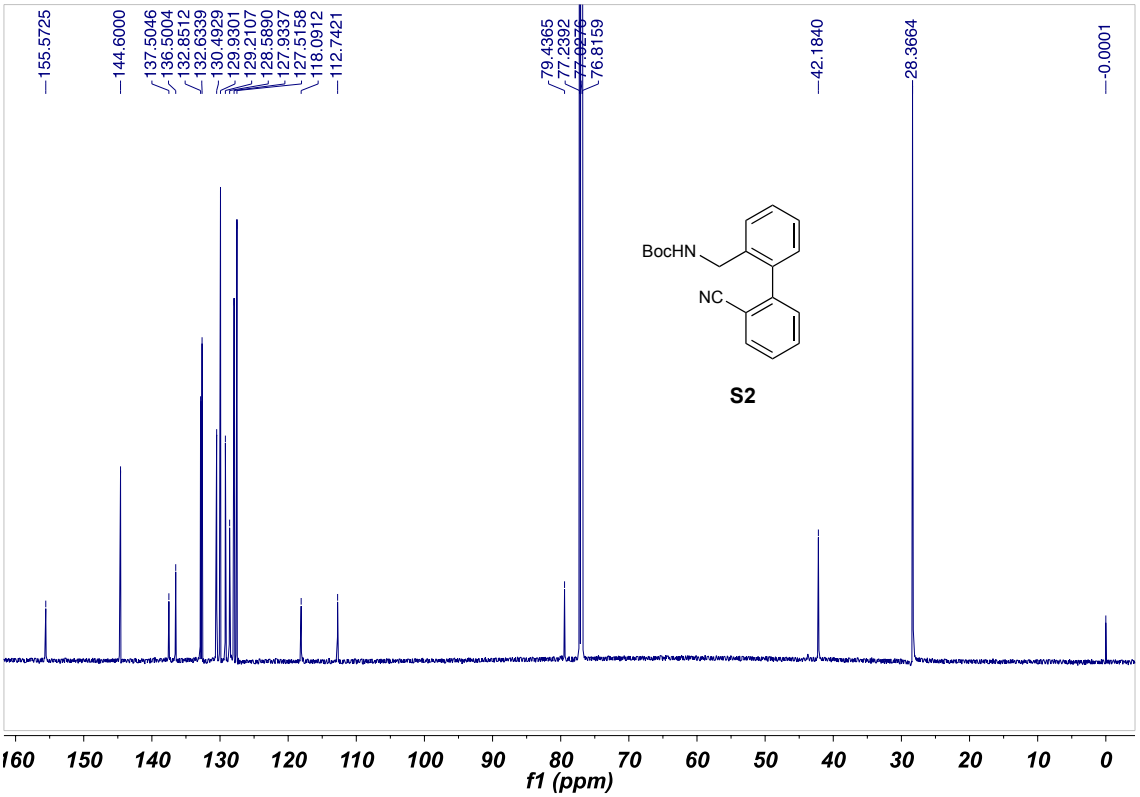
7.7505
7.7397
7.7375
7.6533
7.6511
7.6407
7.6383
7.6278
7.6255
7.4868
7.4844
7.4739
7.4716
7.4592
7.4573
7.4513
7.4490
7.4390
7.4367
7.4262
7.4239
7.4062
7.4043
7.3932
7.3912
7.3820
7.3796
7.3695
7.3671
7.3571
7.3547
7.2297
7.2275
7.2171
7.2149
4.7798
4.4262
4.2579
4.0956
4.0901
4.0651
1.4048
BocHN
NC
S2
0.98
1.01
2.02
1.02
1.03
1.02
1.00
0.81
0.09
2.03
9.22
f1 (ppm)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144.6000
137.5046
136.5004
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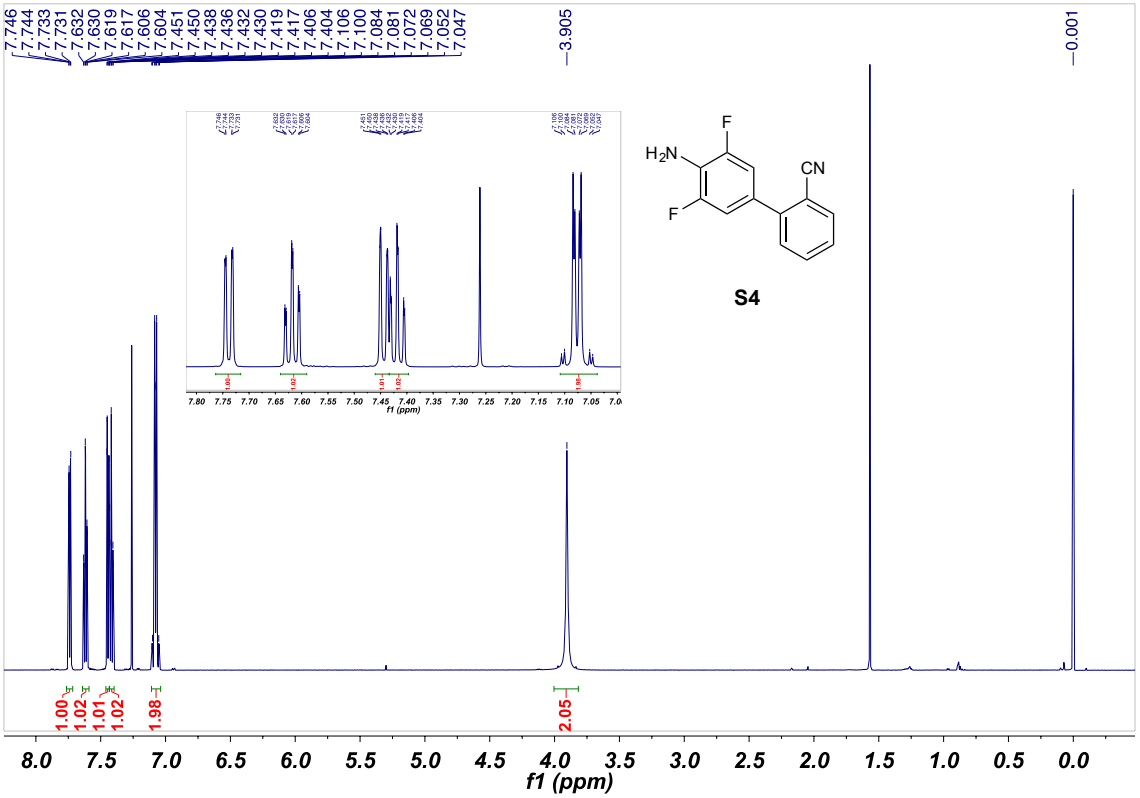
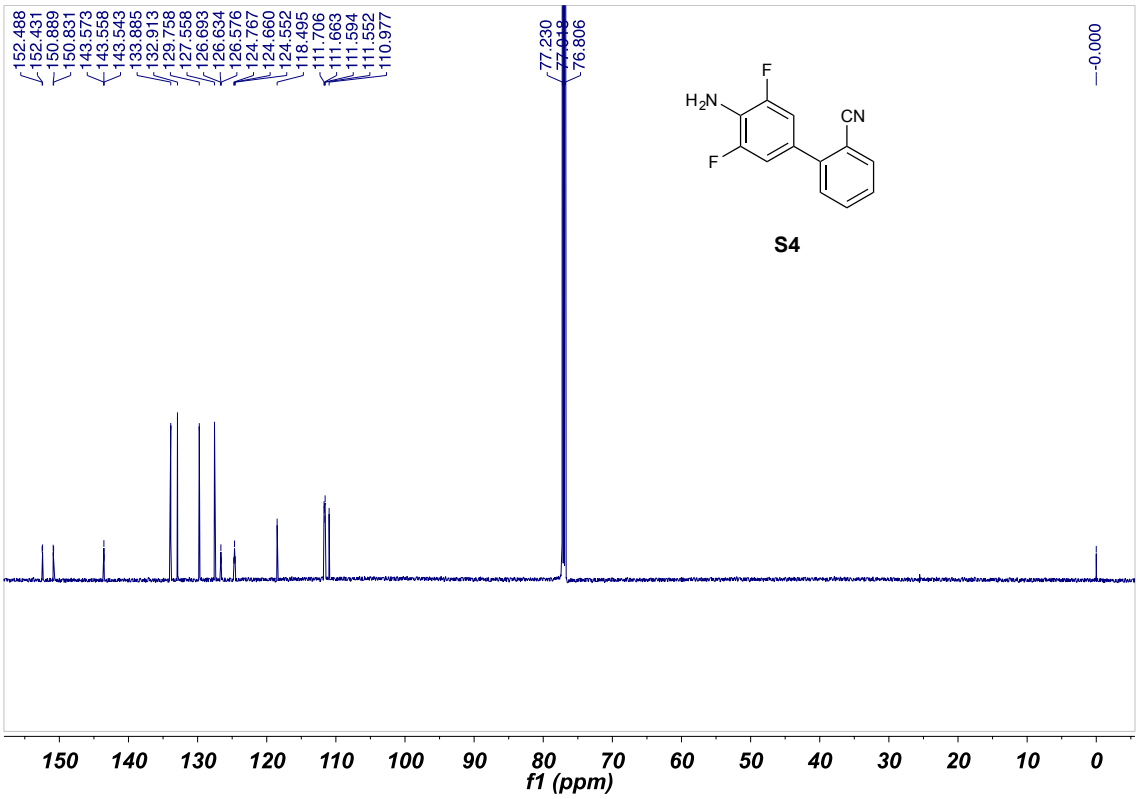
130.4929
129.9301
129.2107
128.5890
127.9337
127.5158
118.0912
112.7421
79.4365
77.2392
76.8159
42.1840
28.3664
0.0001
BocHN
NC
S2
f1 (ppm)


7.746
7.744
7.733
7.731
7.632
7.630
7.619
7.617
7.606
7.604
7.451
7.450
7.438
7.436
7.432
7.430
7.419
7.417
7.406
7.404
7.106
7.100
7.084
7.081
7.072
7.069
7.052
7.047
3.905
0.001
F
H2N
CN
F
S4
1.00
1.02
1.01
1.02
1.98
2.05
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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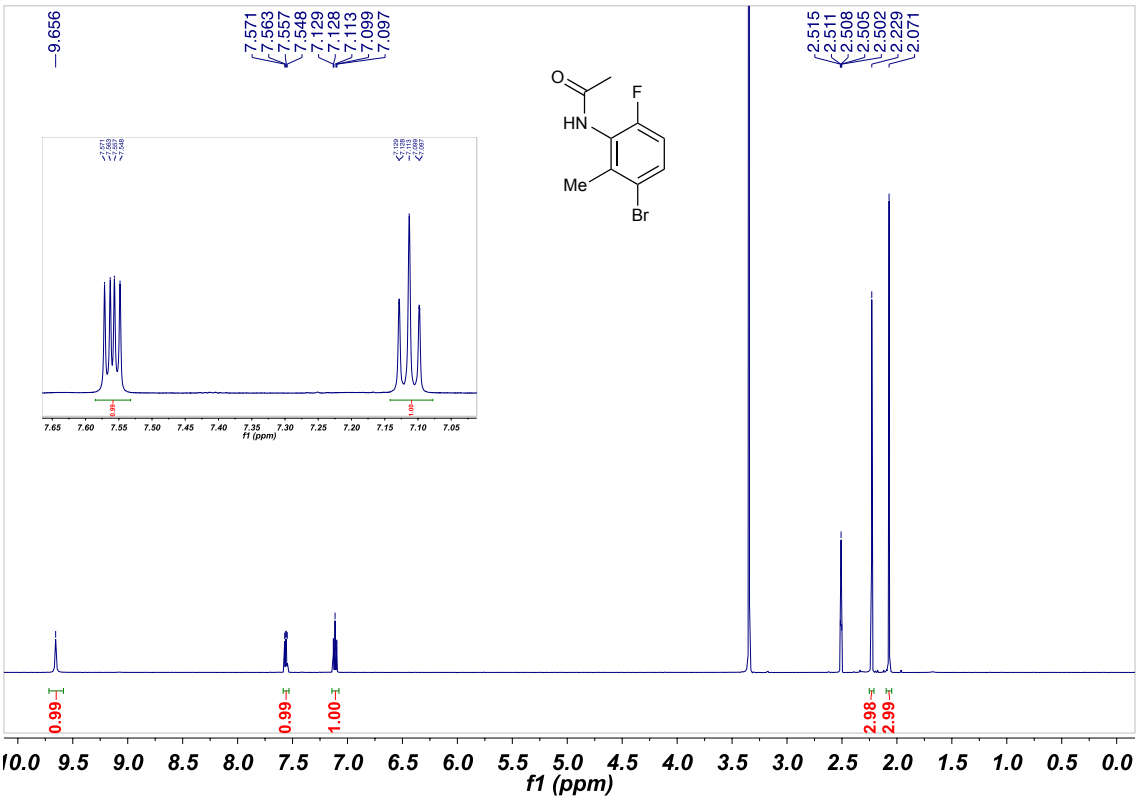
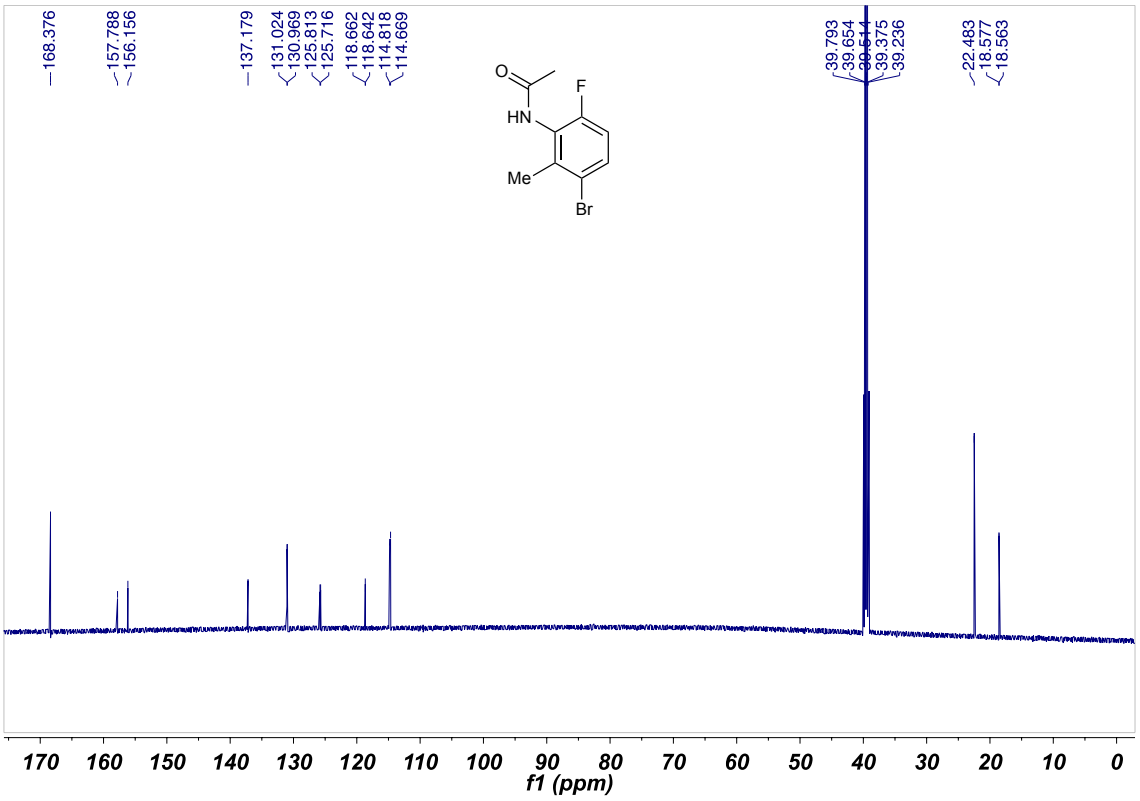
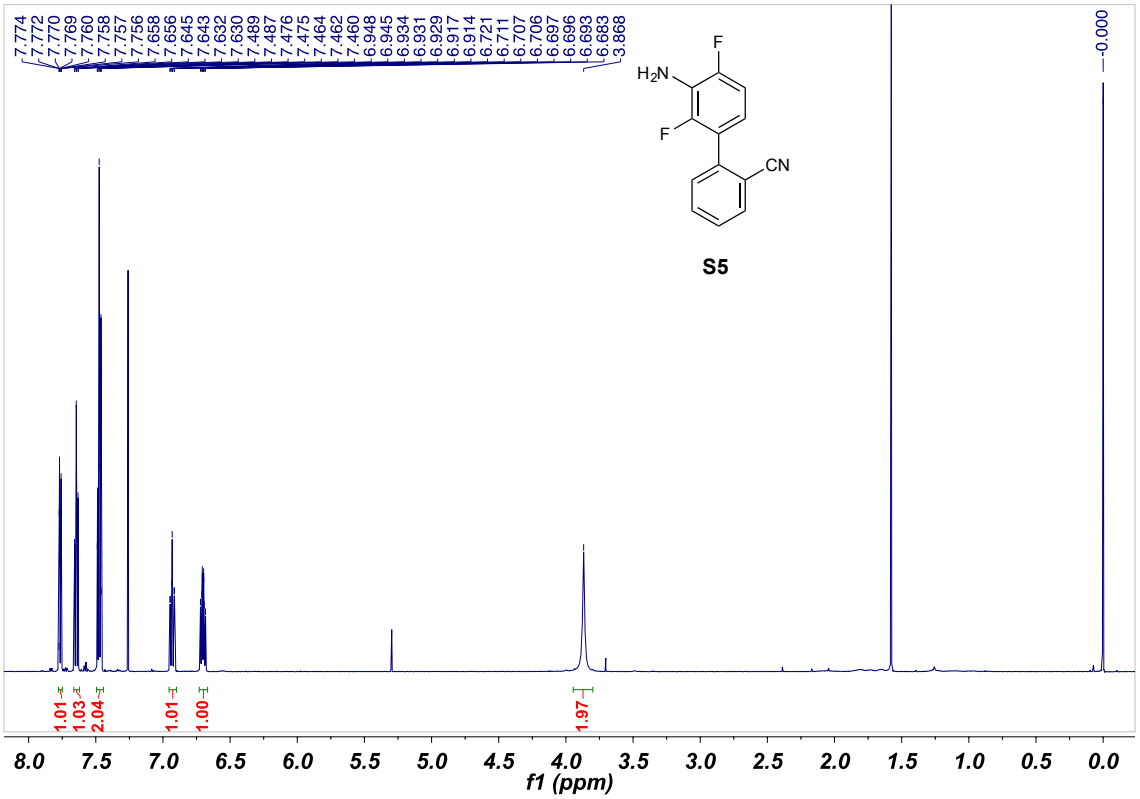
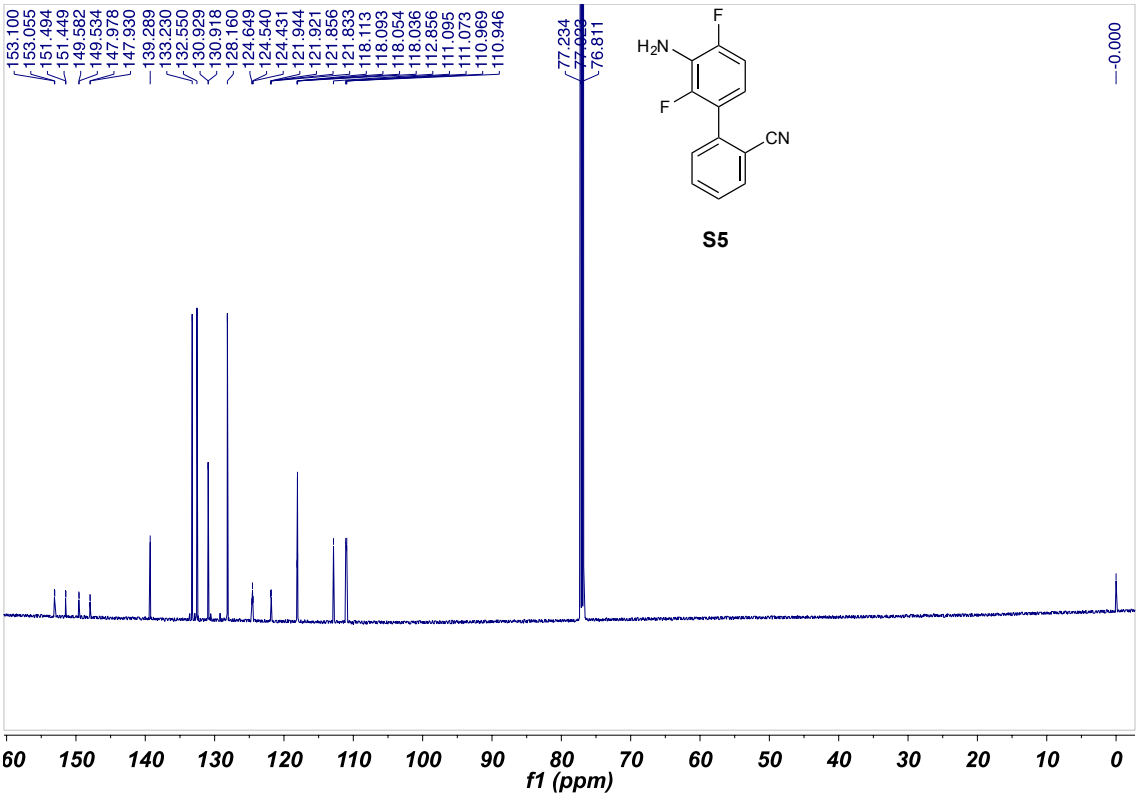
152.431
150.889
150.831
143.573
143.558
143.543
133.885
132.913
129.758
127.558
126.693
126.634
126.576
124.767
124.660
124.552
118.495
111.706
111.663
111.594
111.552
110.977
77.230
77.019
76.806
0.000
F
H2N
CN
F
S4
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


9.656
7.571
7.563
7.557
7.548
7.129
7.128
7.113
7.099
7.097
2.515
2.511
2.508
2.505
2.502
2.229
2.071
O
HN
F
Me
Br
0.99
0.99
1.00
2.98
2.99
f1 (ppm)


168.376
157.788
156.156
137.179
131.024
130.969
125.813
125.716
118.662
118.642
114.818
114.669
39.793
39.654
39.514
39.375
39.236
22.483
18.577
18.563
O
HN
F
Me
Br
f1 (ppm)


7.774
7.772
7.770
7.769
7.760
7.758
7.757
7.756
7.658
7.656
7.645
7.643
7.632
7.630
7.489
7.487
7.476
7.475
7.464
7.462
7.460
6.948
6.945
6.934
6.931
6.929
6.917
6.914
6.721
6.711
6.707
6.706
6.697
6.696
6.693
6.683
3.868
-0.000
F
H2N
F
CN
S5
1.01
1.03
2.04
1.01
1.00
1.97
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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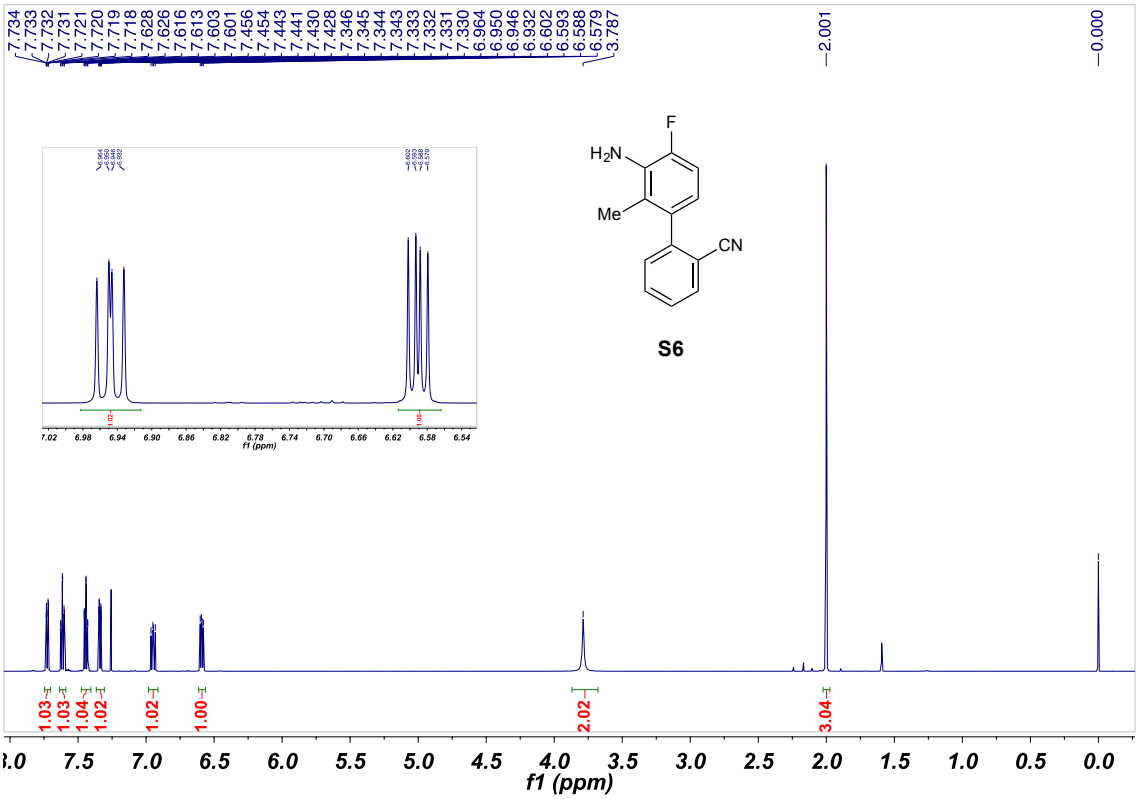
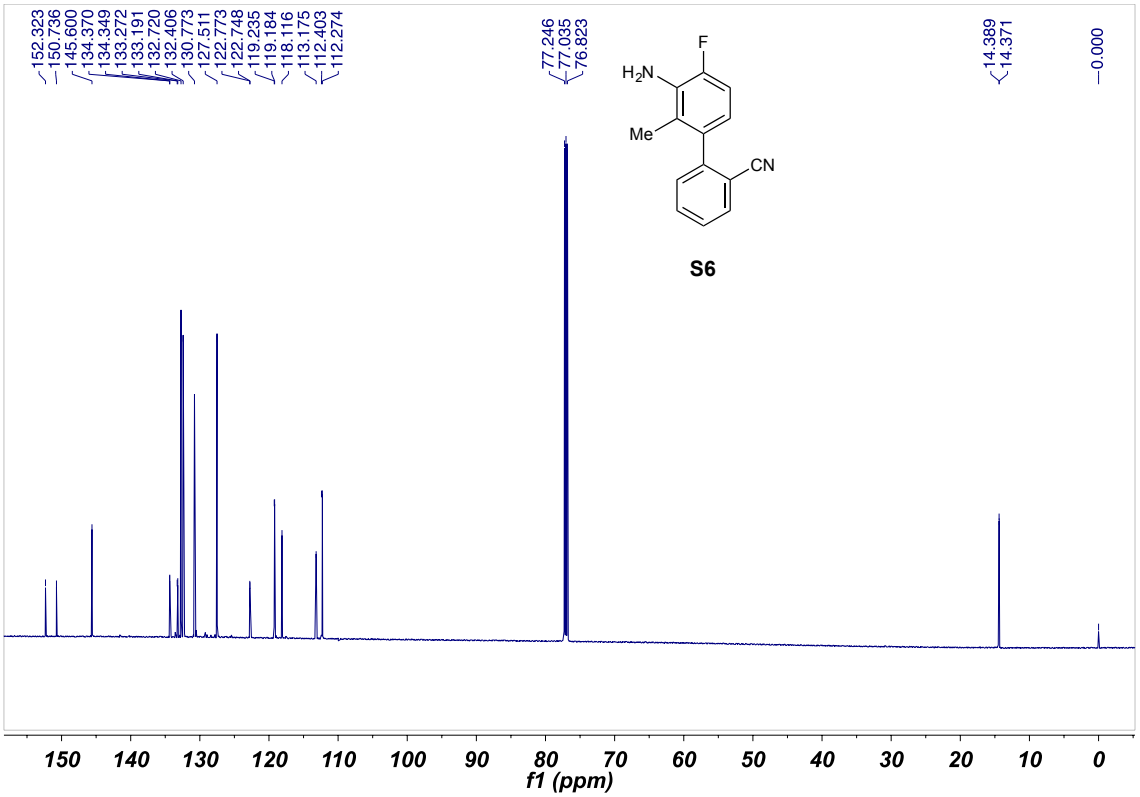
151.494
151.449
149.582
149.534
147.978
147.930
139.289
133.230
132.550
130.929
130.918
128.160
124.649
124.540
124.431
121.944
121.921
121.856
121.833
118.113
118.093
118.054
118.036
112.856
111.095
111.073
110.969
110.946
77.234
77.023
76.811
-0.000
F
H2N
F
CN
S5
60
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.734
7.733
7.732
7.731
7.721
7.720
7.719
7.718
7.628
7.626
7.616
7.613
7.603
7.601
7.456
7.454
7.443
7.441
7.430
7.428
7.346
7.345
7.344
7.343
7.333
7.332
7.331
7.330
6.964
6.950
6.946
6.932
6.602
6.593
6.588
6.579
3.787
2.001
0.000
F
H2N
Me
CN
S6
1.03
1.03
1.04
1.02
1.02
1.00
2.02
3.04
f1 (ppm)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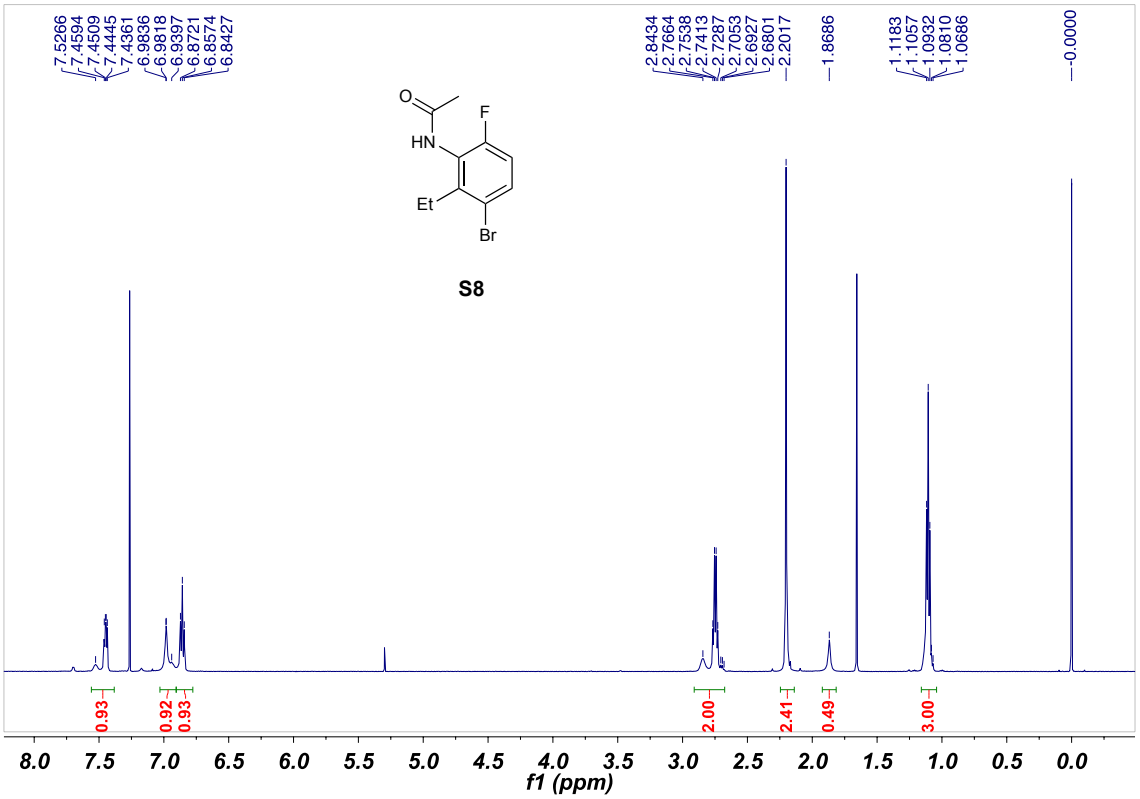
150.736
145.600
134.370
134.349
133.272
133.191
132.720
132.406
130.773
127.511
122.773
122.748
119.235
119.184
118.116
113.175
112.403
112.274
77.246
77.035
76.823
14.389
14.371
0.000
F
H2N
Me
CN
S6
f1 (ppm)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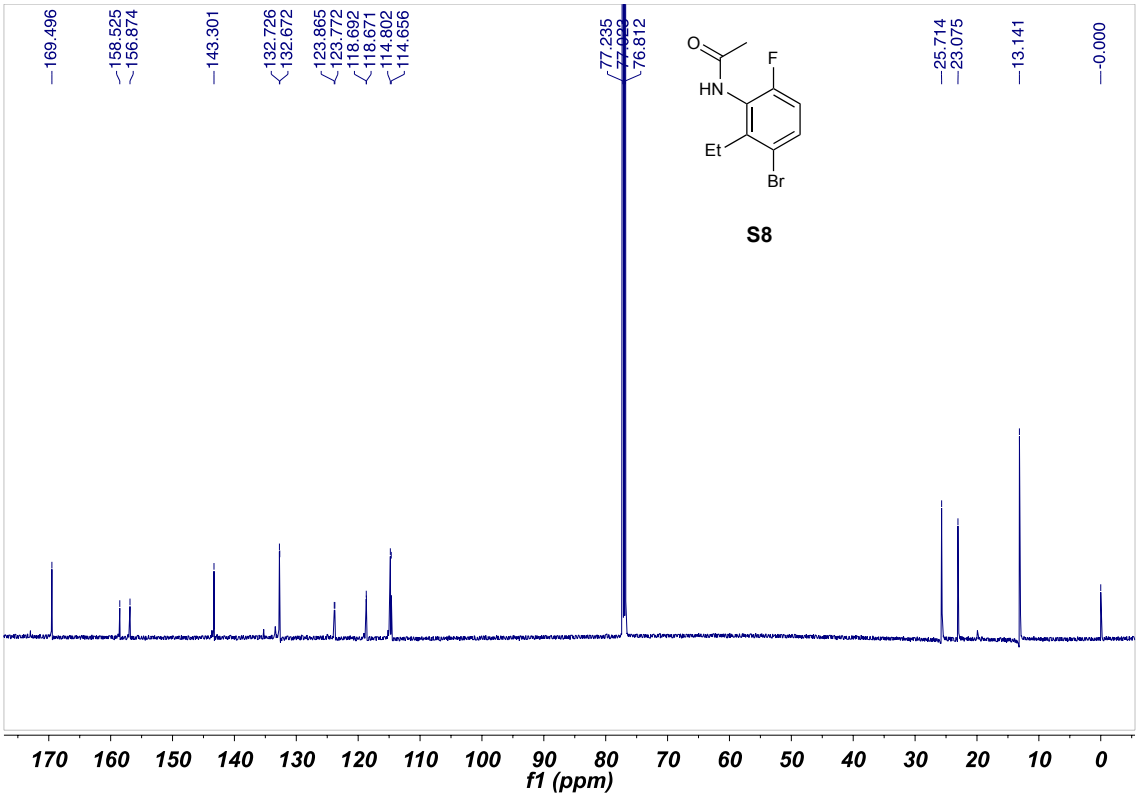
7.4509
7.4445
7.4361
6.9836
6.9818
6.9397
6.8721
6.8574
6.8427
2.8434
2.7664
2.7538
2.7413
2.7287
2.7053
2.6927
2.6801
2.2017
1.8686
1.1183
1.1057
1.0932
1.0810
1.0686
0.0000
O
HN
F
Et
Br
S8
0.93
0.92
0.93
2.00
2.41
0.49
3.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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123.772
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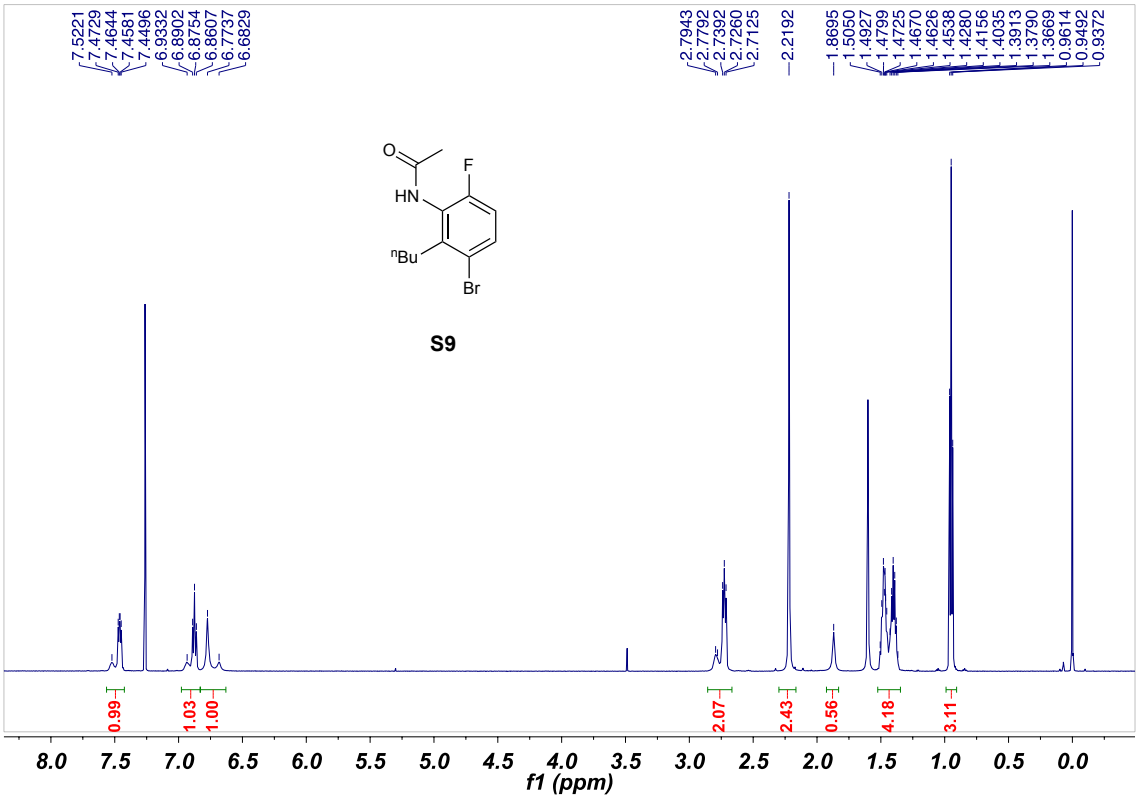
118.671
114.802
114.656
77.235
77.023
76.812
25.714
23.075
13.141
0.000
O
HN
F
Et
Br
S8
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.5221
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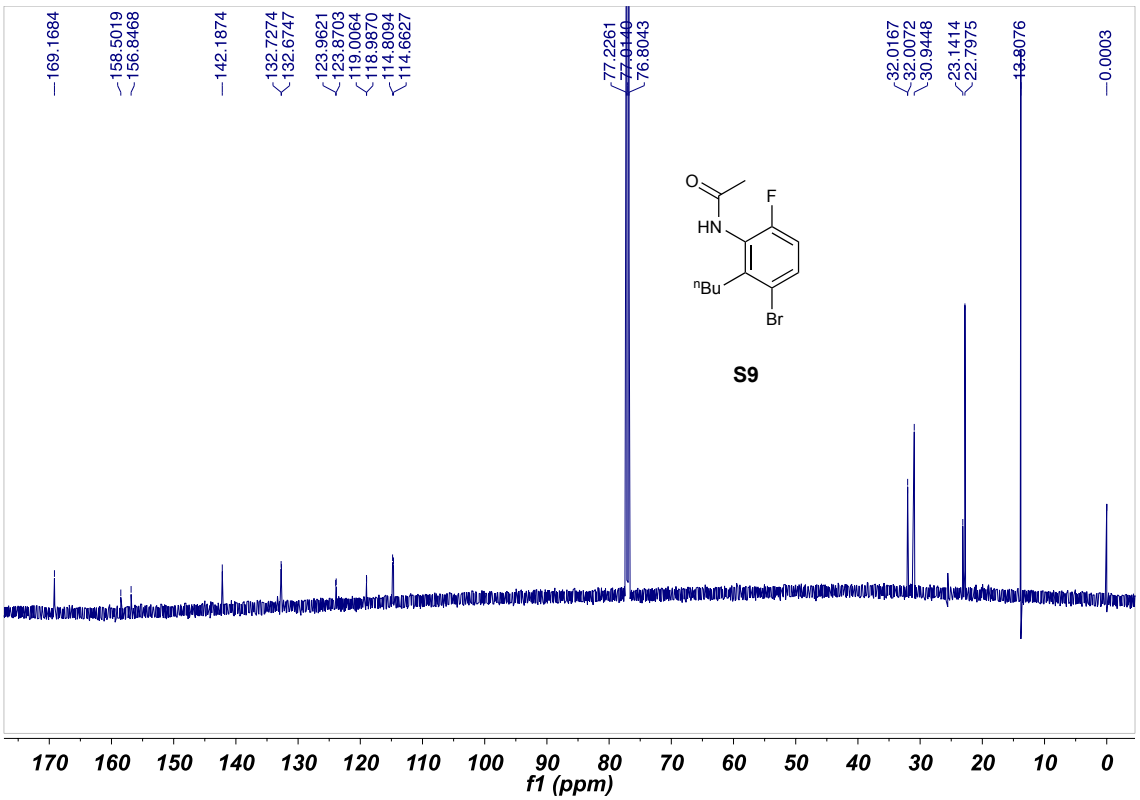
7.4644
7.4581
7.4496
6.9332
6.8902
6.8754
6.8607
6.7737
6.6829
2.7943
2.7792
2.7392
2.7260
2.7125
2.2192
1.8695
1.5050
1.4927
1.4799
1.4725
1.4670
1.4626
1.4538
1.4280
1.4156
1.4035
1.3913
1.3790
1.3669
0.9614
0.9492
0.9372
O
HN
F
nBu
Br
S9
0.99
1.03
1.00
2.07
2.43
0.56
4.18
3.11
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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156.8468
142.1874
132.7274
132.6747
123.9621
123.8703
119.0064
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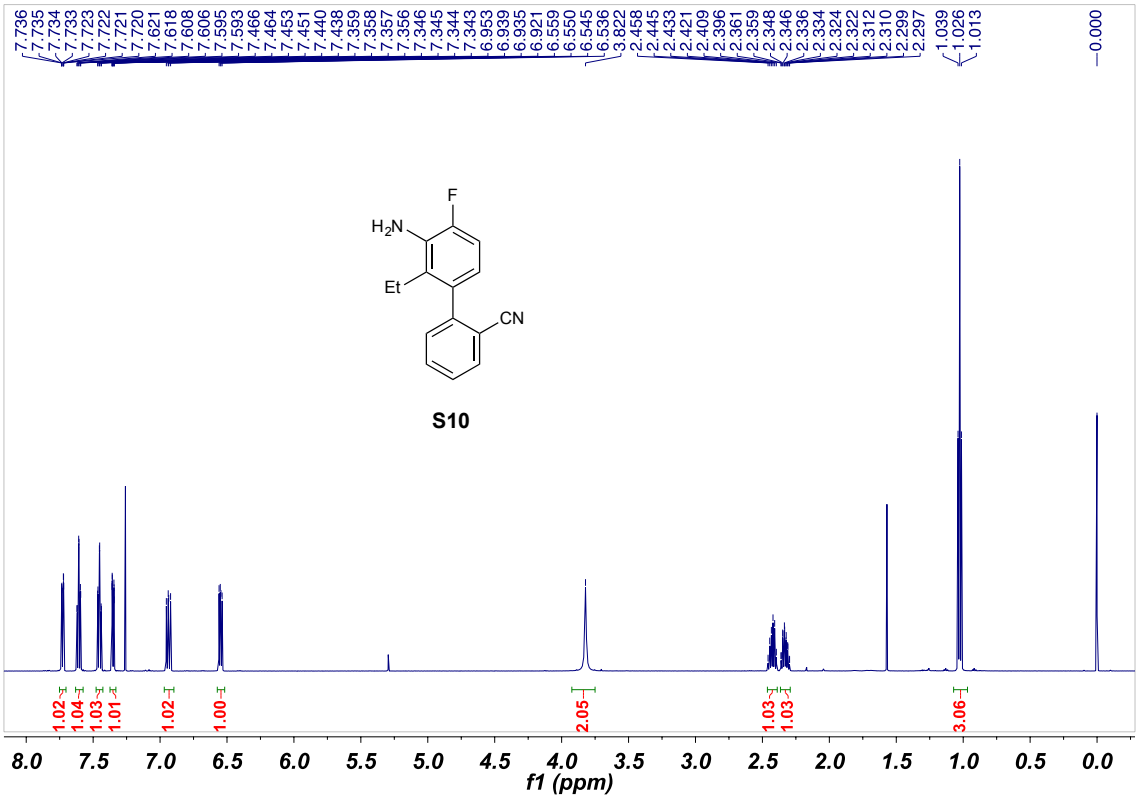
114.6627
77.2261
77.0140
76.8043
32.0167
32.0072
30.9448
23.1414
22.7975
13.8076
0.0003
O
HN
F
nBu
Br
S9
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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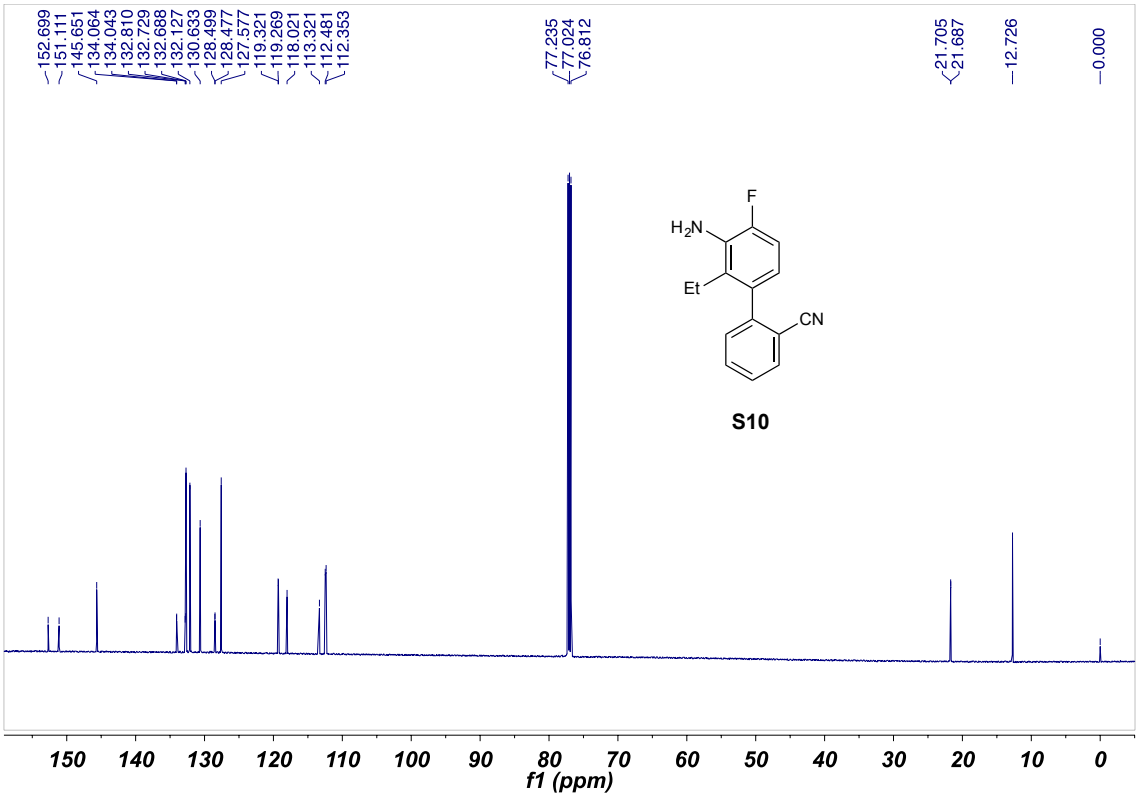
7.734
7.733
7.723
7.722
7.721
7.720
7.621
7.618
7.608
7.606
7.595
7.593
7.466
7.464
7.453
7.451
7.440
7.438
7.359
7.358
7.357
7.356
7.346
7.345
7.344
7.343
6.953
6.939
6.935
6.921
6.559
6.550
6.545
6.536
3.822
2.458
2.445
2.433
2.421
2.409
2.396
2.361
2.359
2.348
2.346
2.336
2.334
2.324
2.322
2.312
2.310
2.299
2.297
1.039
1.026
1.013
0.000
F
H2N
Et
CN
S10
1.02
1.04
1.03
1.01
1.02
1.00
2.05
1.03
1.03
3.06
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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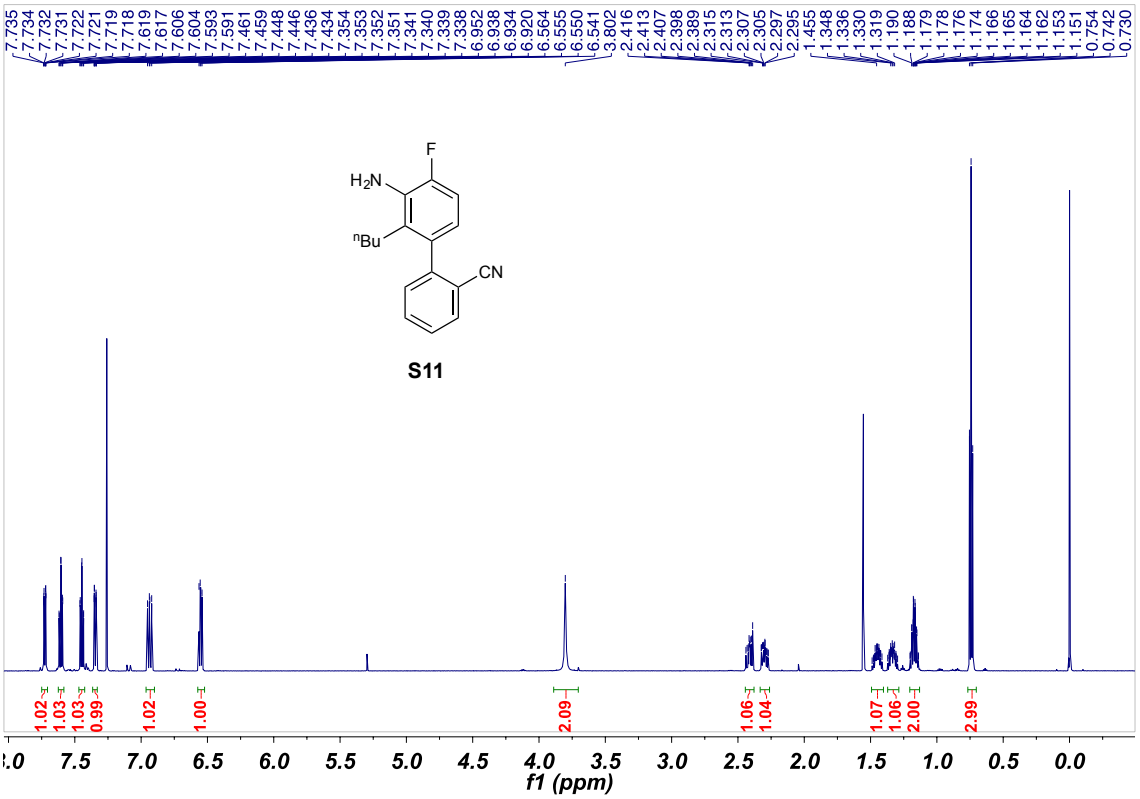
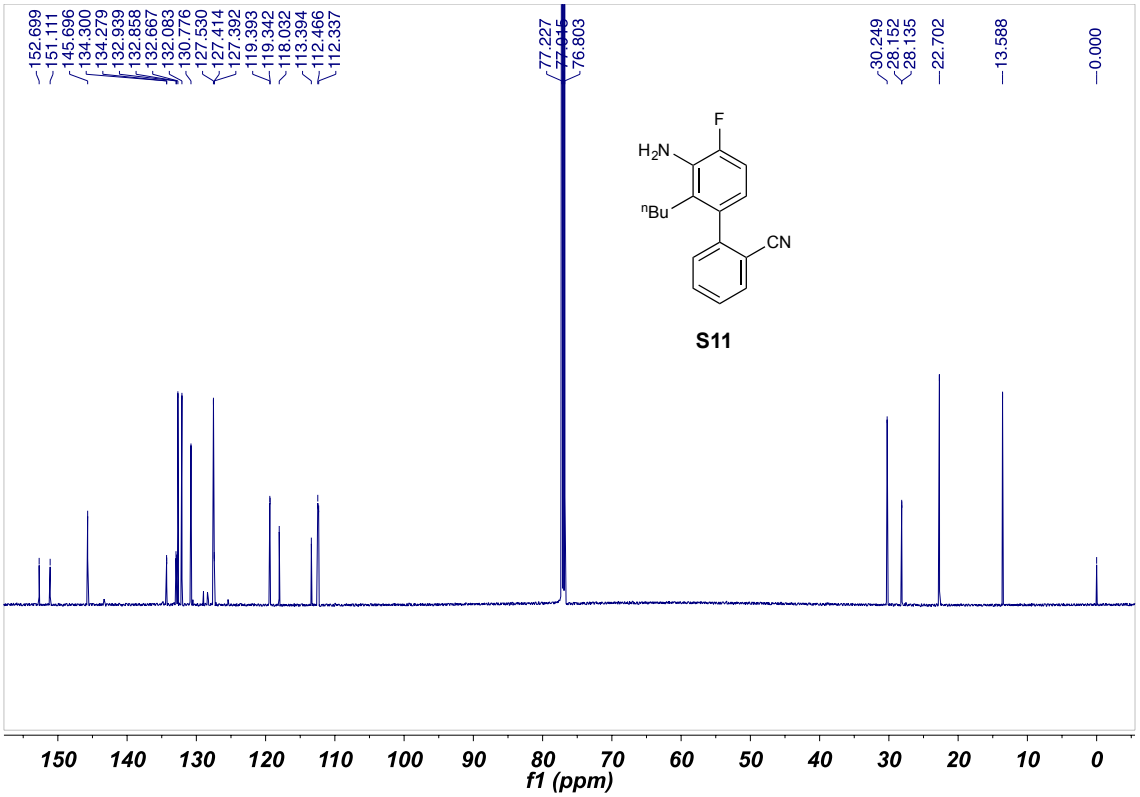
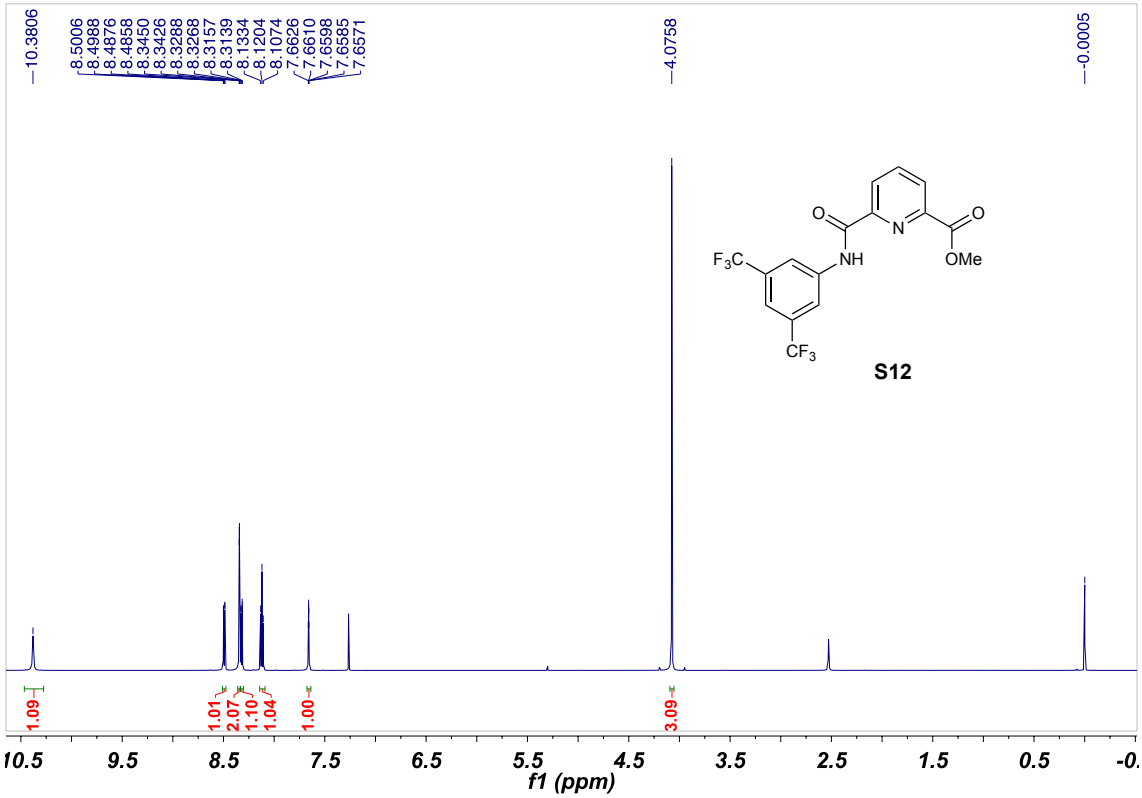
134.064
134.043
132.810
132.729
132.688
132.127
130.633
128.499
128.477
127.577
119.321
119.269
118.021
113.321
112.481
112.353
77.235
77.024
76.812
21.705
21.687
12.726
0.000
F
H2N
Et
CN
S10
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


F
H2N
nBu
CN
S11
f1 (ppm)


F
H2N
nBu
CN
S11
f1 (ppm)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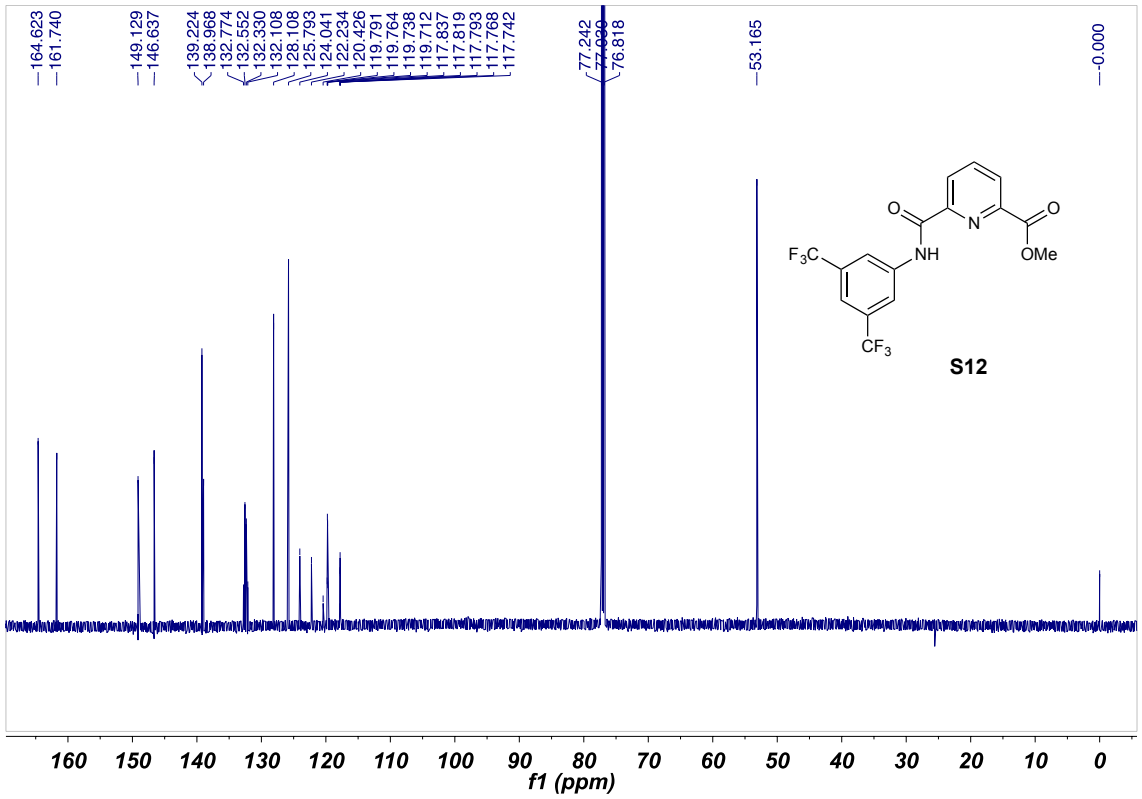
8.5006
8.4988
8.4876
8.4858
8.3450
8.3426
8.3288
8.3268
8.3157
8.3139
8.1334
8.1204
8.1074
7.6626
7.6610
7.6598
7.6585
7.6571
4.0758
-0.0005
1.09
1.01
2.07
1.10
1.04
1.00
3.09
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)
O
N
O
NH
OMe
F3C
CF3
S12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149.129
146.637
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138.968
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132.552
132.330
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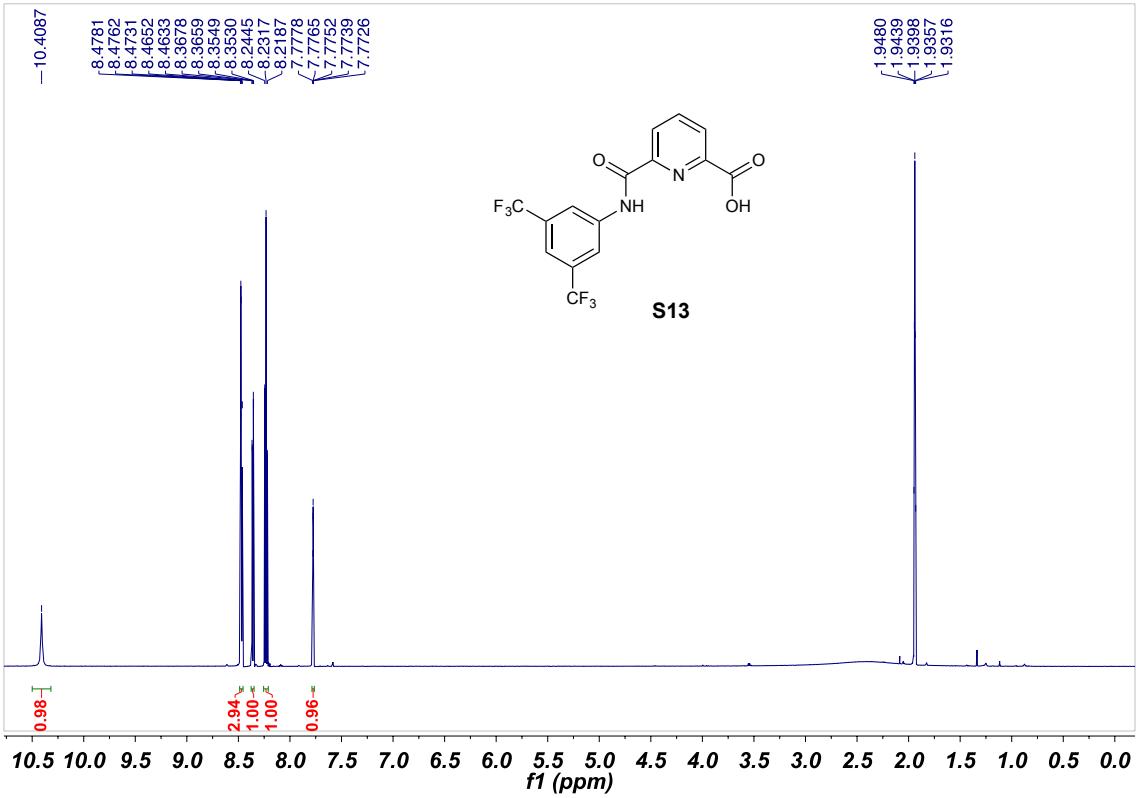
128.108
125.793
124.041
122.234
120.426
119.791
119.764
119.738
119.712
117.837
117.819
117.793
117.768
117.742
77.242
77.000
76.818
53.165
-0.000
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
O
N
O
NH
OMe
F3C
CF3
S12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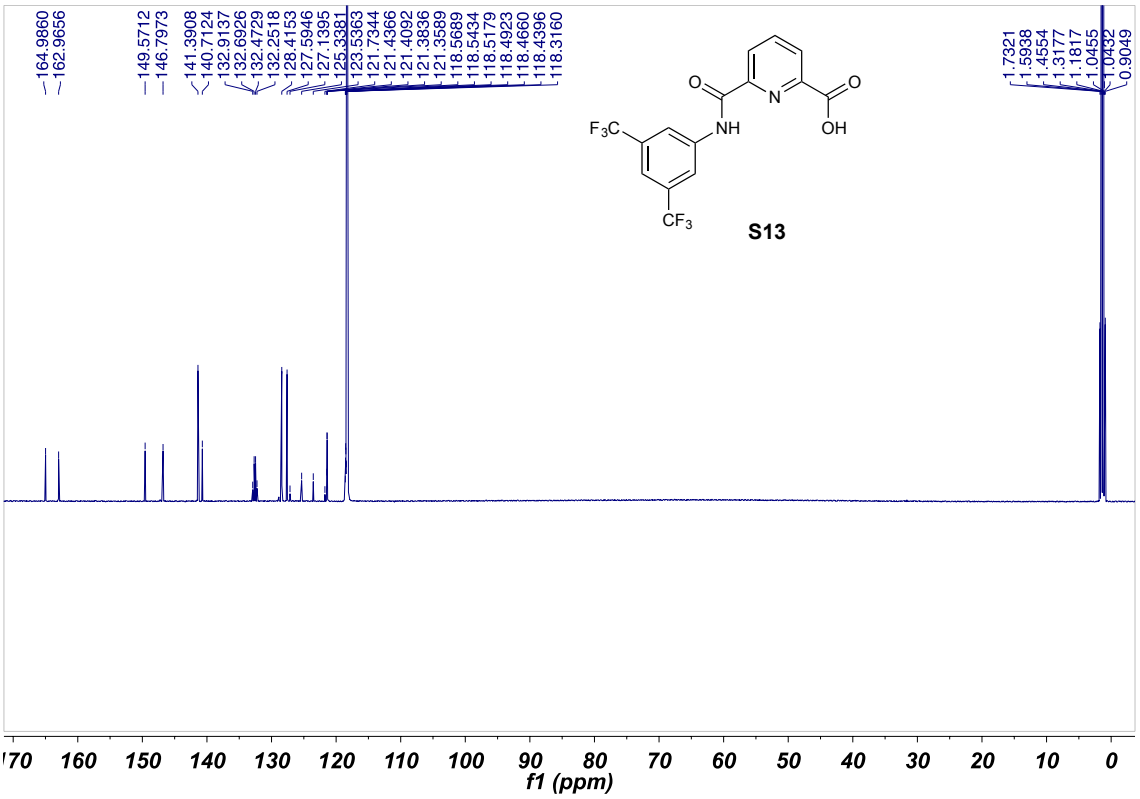
8.4762
8.4731
8.4652
8.4633
8.3678
8.3659
8.3549
8.3530
8.2445
8.2317
8.2187
7.7778
7.7765
7.7752
7.7739
7.7726
1.9480
1.9439
1.9398
1.9357
1.9316
F3C
NH
O
N
OH
CF3
S13
0.98
2.94
1.00
1.00
0.96
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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146.7973
141.3908
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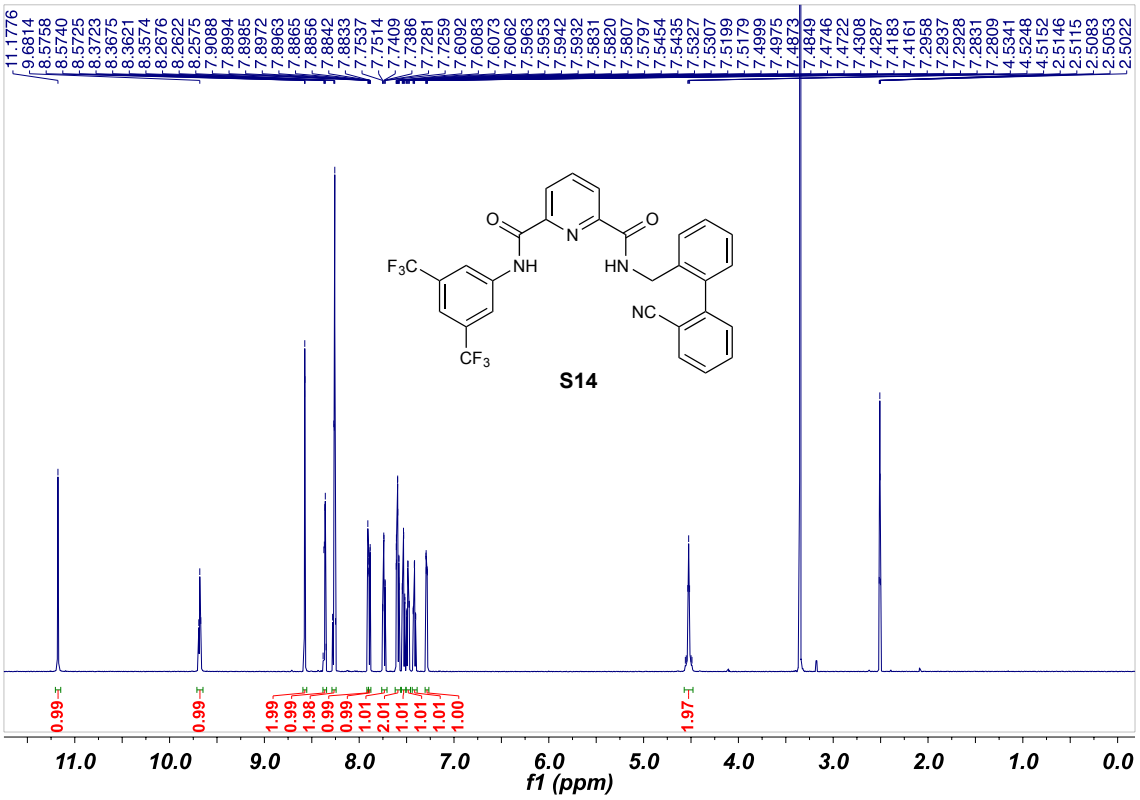
132.4729
132.2518
128.4153
127.5946
127.1395
125.3381
123.5363
121.7344
121.4366
121.4092
121.3836
121.3589
118.5689
118.5434
118.5179
118.4923
118.4660
118.4396
118.3160
1.7321
1.5938
1.4554
1.3177
1.1817
1.0455
1.0432
0.9049
F3C
NH
O
N
OH
CF3
S13
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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8.2622
8.2575
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7.8985
7.8972
7.8963
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7.8856
7.8842
7.8833
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7.7514
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7.7281
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7.6083
7.6073
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7.5963
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7.5831
7.5820
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7.5797
7.5454
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7.5327
7.5307
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7.5179
7.4999
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7.4849
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7.4722
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7.2831
7.2809
4.5341
4.5248
4.5152
2.5146
2.5115
2.5083
2.5053
2.5022
O
N
O
NH
HN
F3C
CF3
NC
S14
0.99
0.99
1.99
0.99
1.98
0.99
0.99
1.01
2.01
1.01
1.01
1.01
1.00
1.97
11.0
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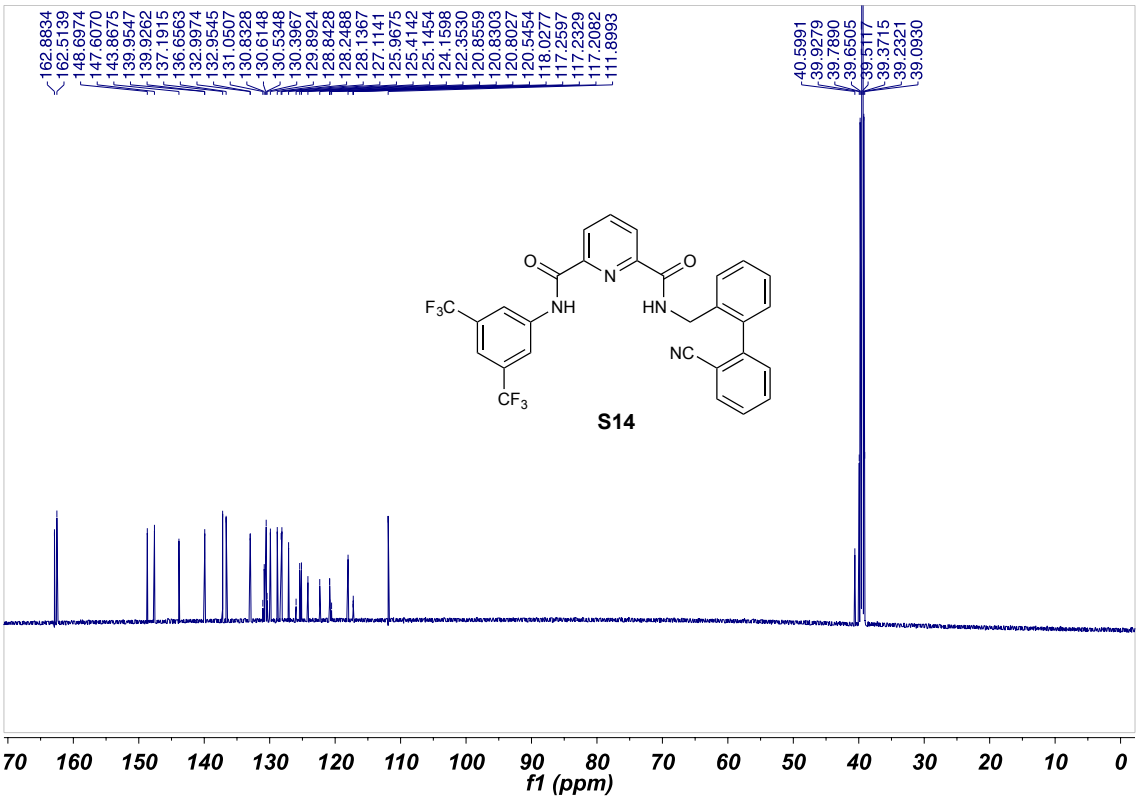
f1 (ppm)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132.9545
131.0507
130.8328
130.6148
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129.8924
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127.1141
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125.4142
125.1454
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117.2329
117.2082
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40.5991
39.9279
39.7890
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39.5117
39.3715
39.2321
39.0930
O
N
O
NH
HN
F3C
CF3
NC
S14
70
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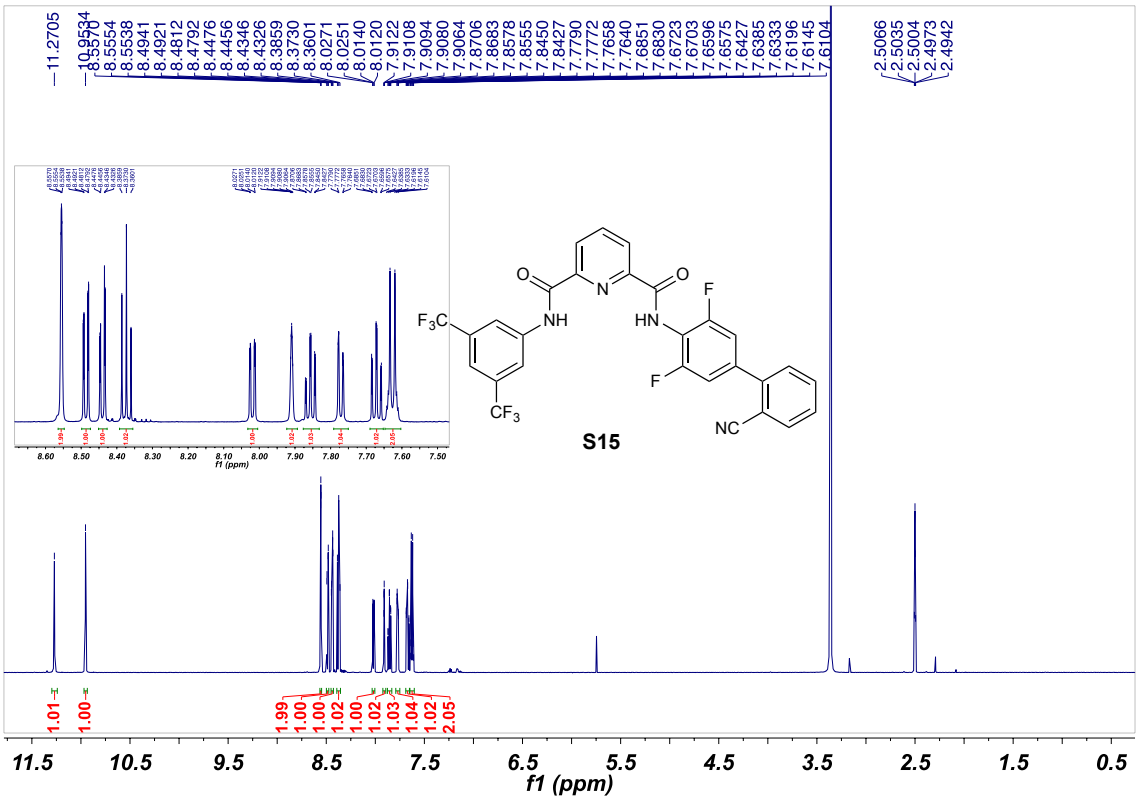
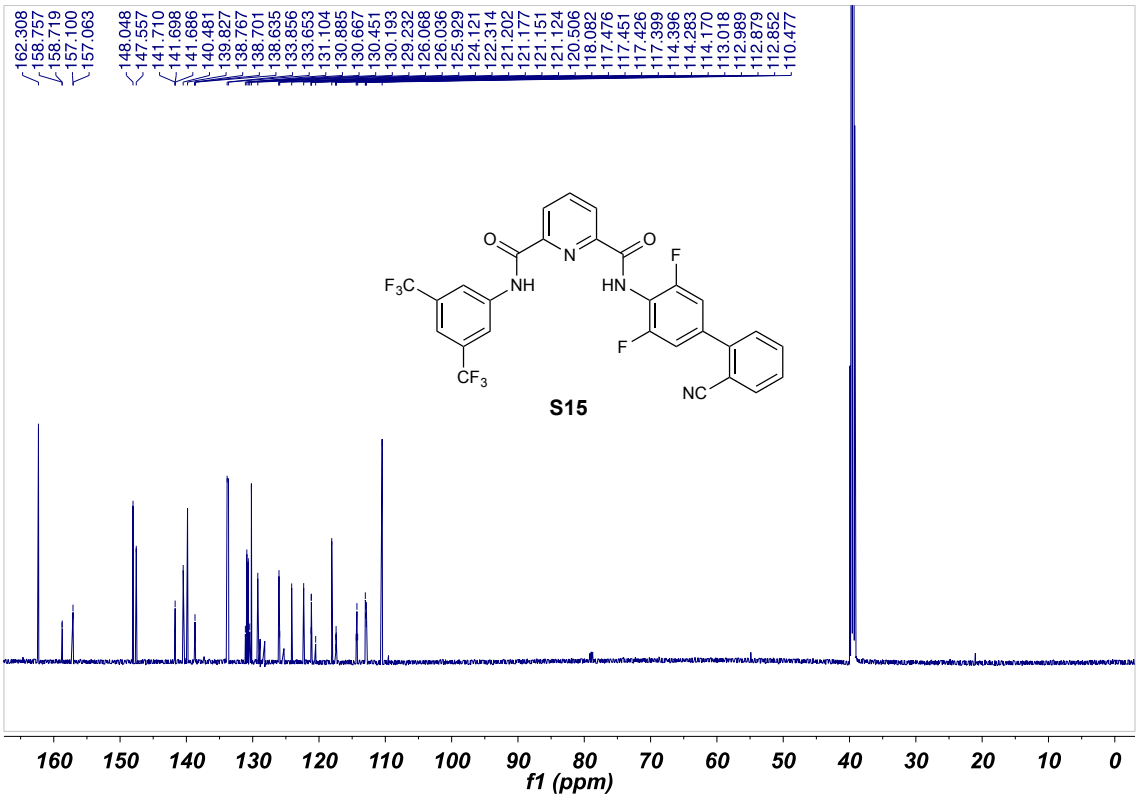
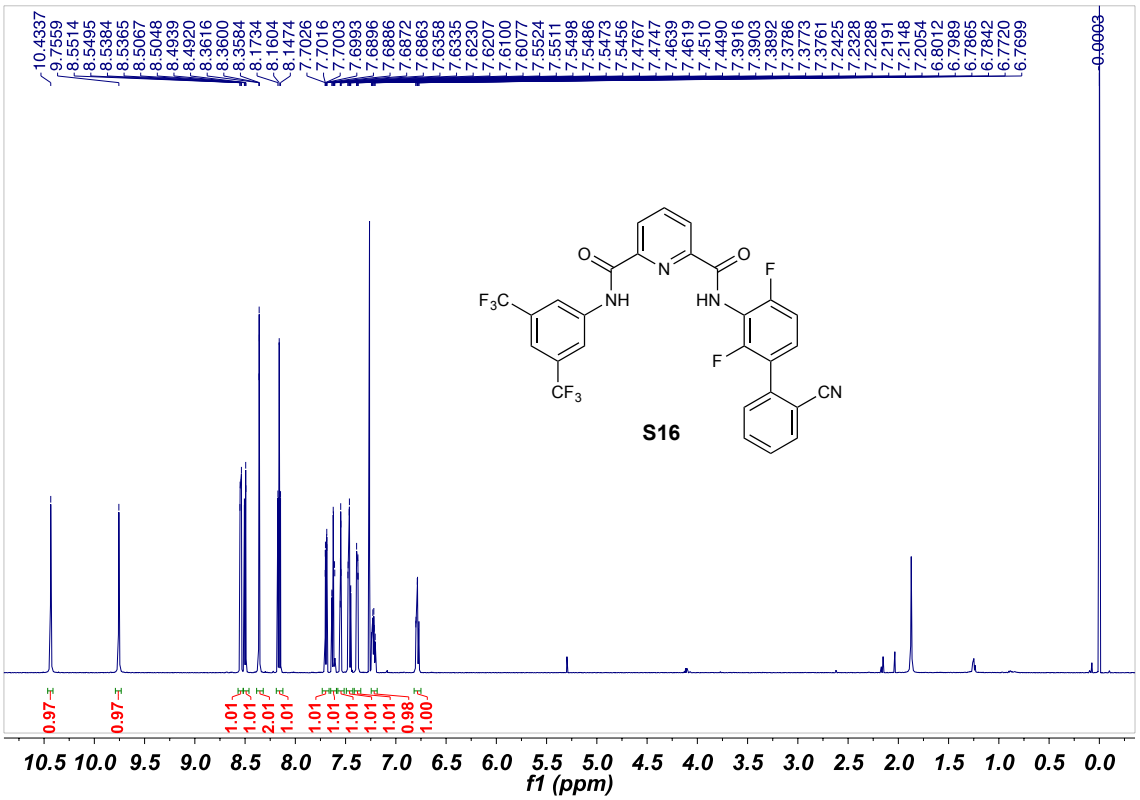
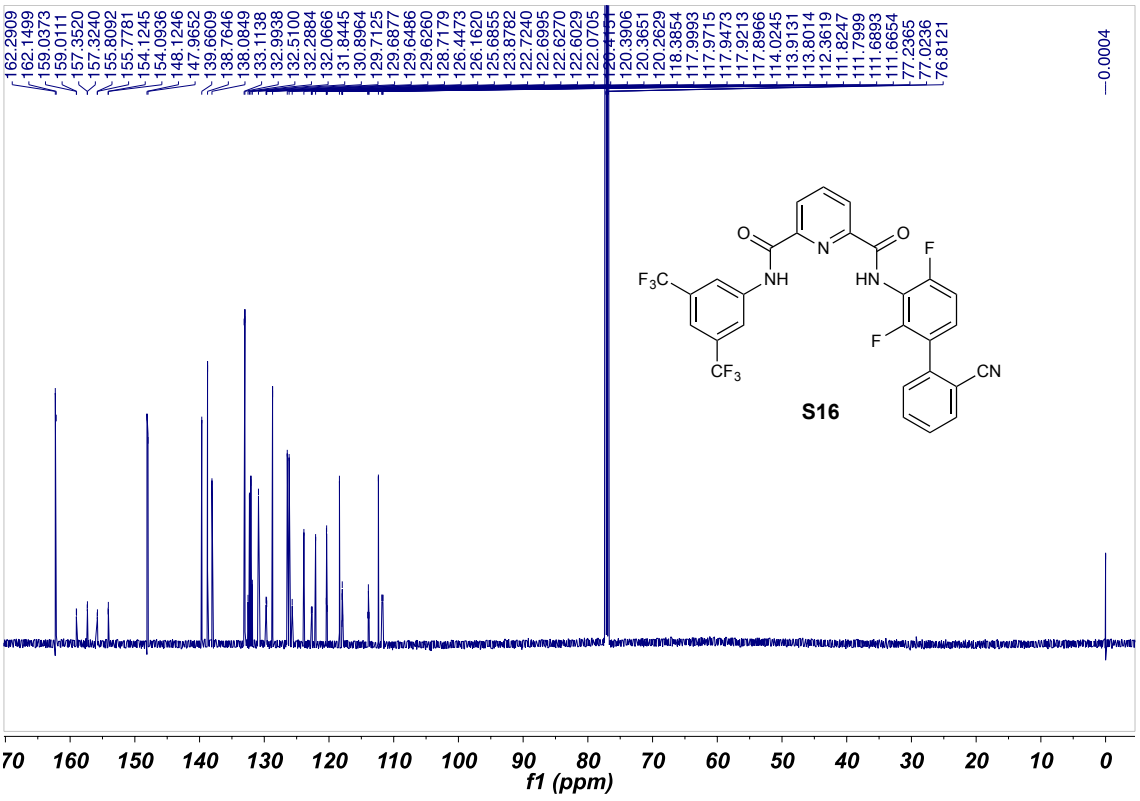
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


S15
f1 (ppm)


S15
f1 (ppm)


S16
f1 (ppm)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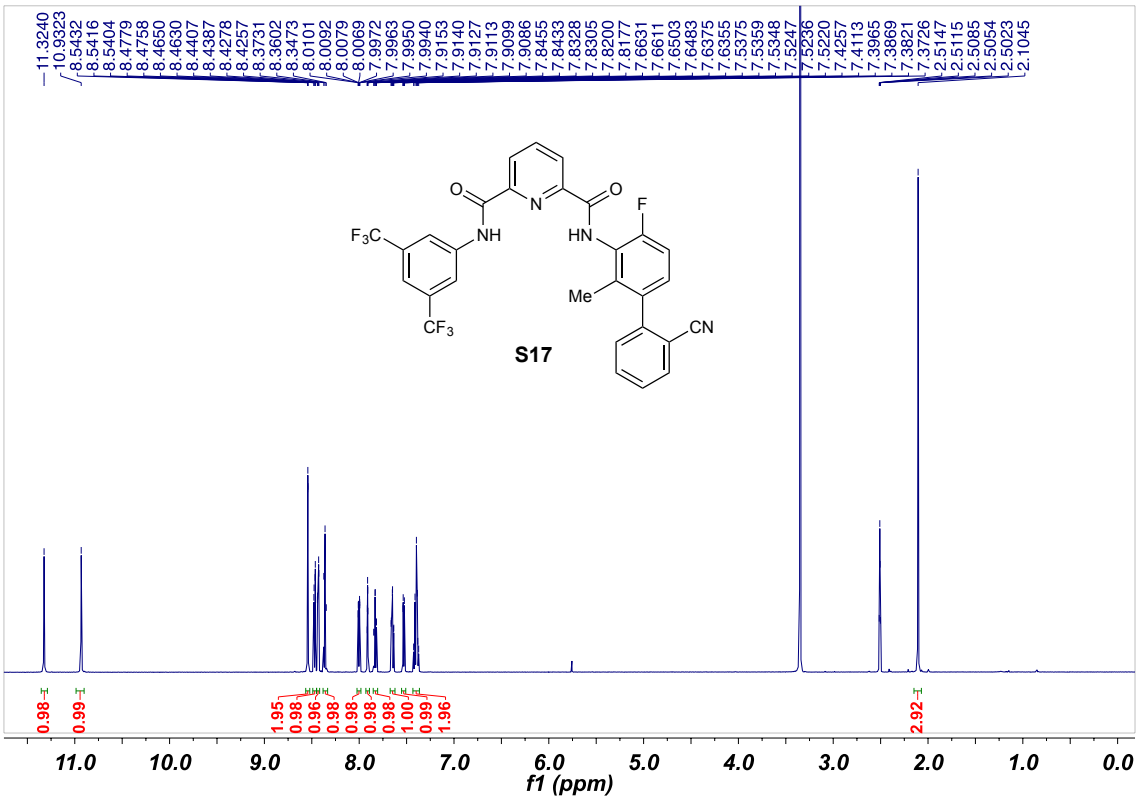
f1 (ppm)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8.4387
8.4278
8.4257
8.3731
8.3602
8.3473
8.0101
8.0092
8.0079
8.0069
7.9972
7.9963
7.9950
7.9940
7.9153
7.9140
7.9127
7.9113
7.9099
7.9086
7.8455
7.8433
7.8328
7.8305
7.8200
7.8177
7.6631
7.6611
7.6503
7.6483
7.6375
7.6355
7.5375
7.5359
7.5348
7.5247
7.5236
7.5220
7.4257
7.4113
7.3965
7.3869
7.3821
7.3726
2.5147
2.5115
2.5085
2.5054
2.5023
2.1045
F3C
NH
N
O
O
HN
F
Me
CF3
CN
S17
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0.99
1.95
0.98
0.96
0.98
0.98
0.98
1.00
0.99
1.96
2.92
11.0
10.0
9.0
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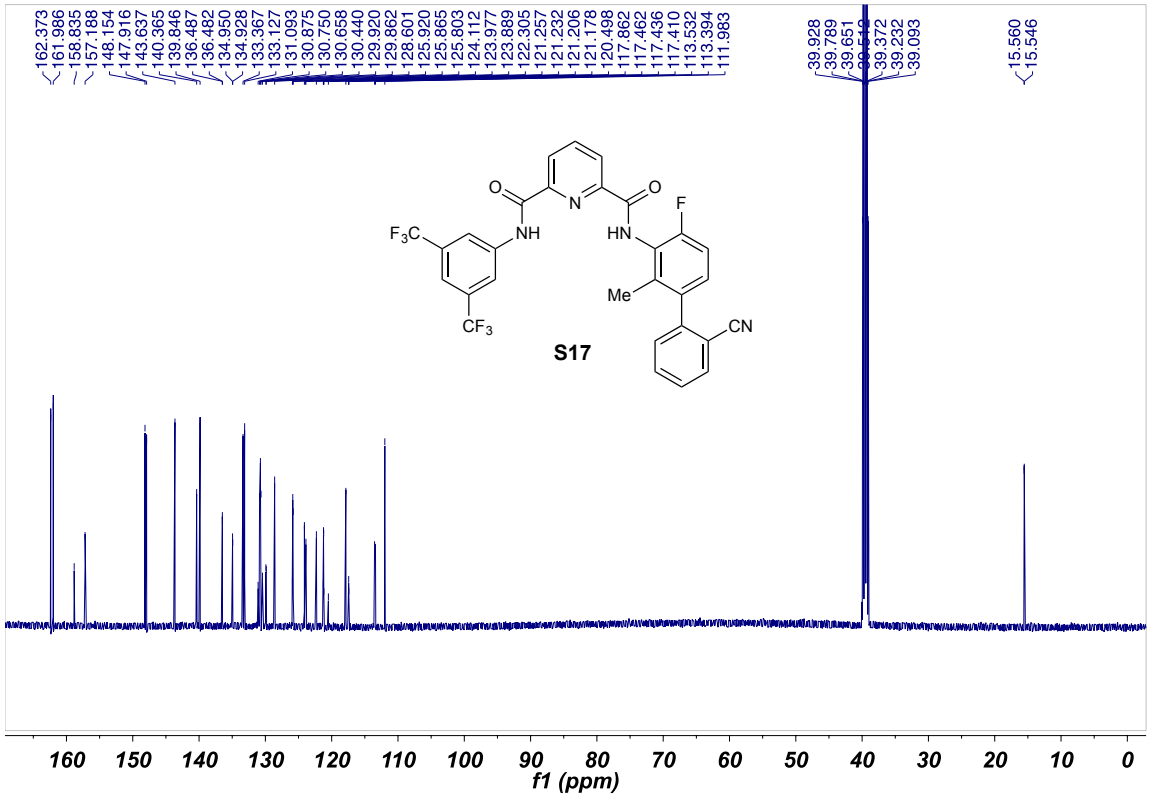
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)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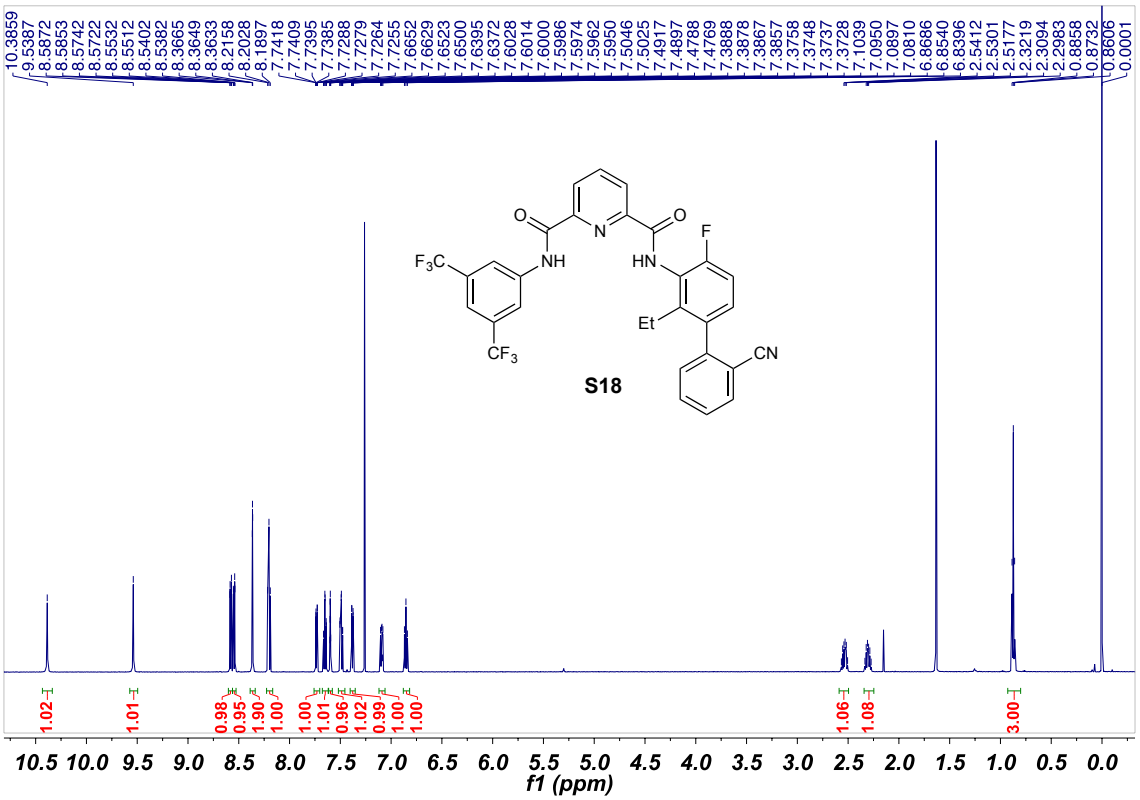
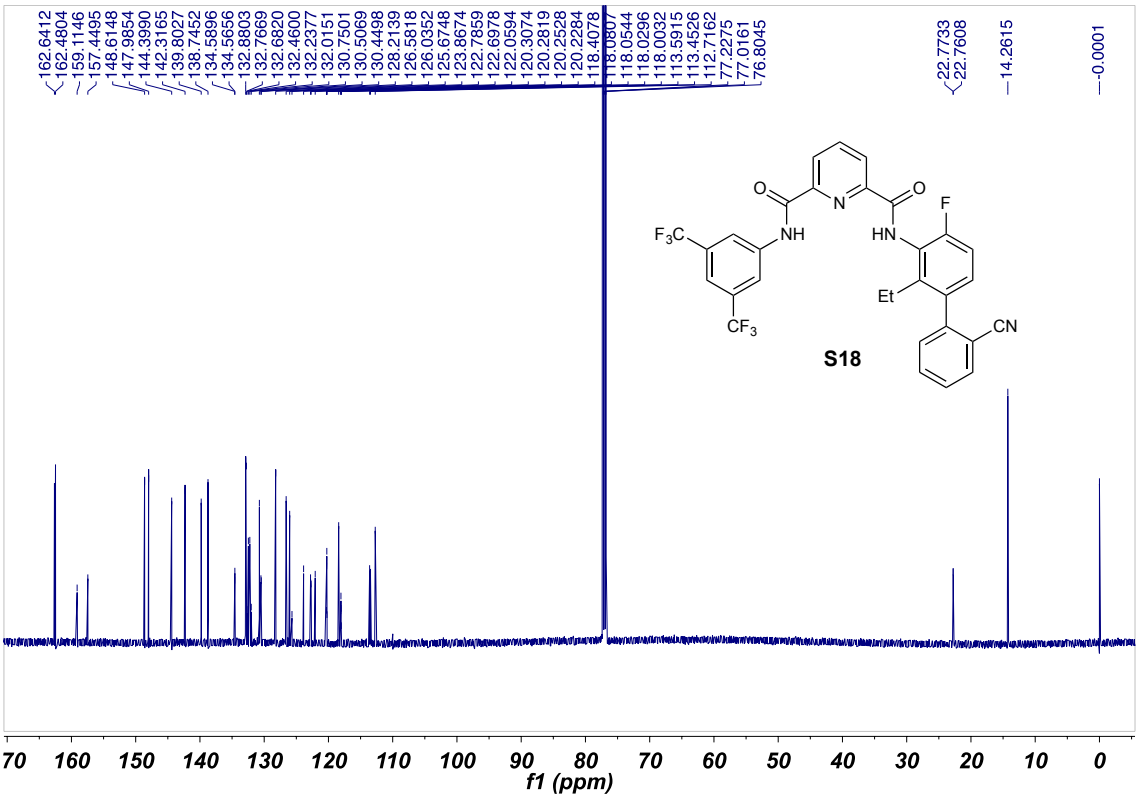
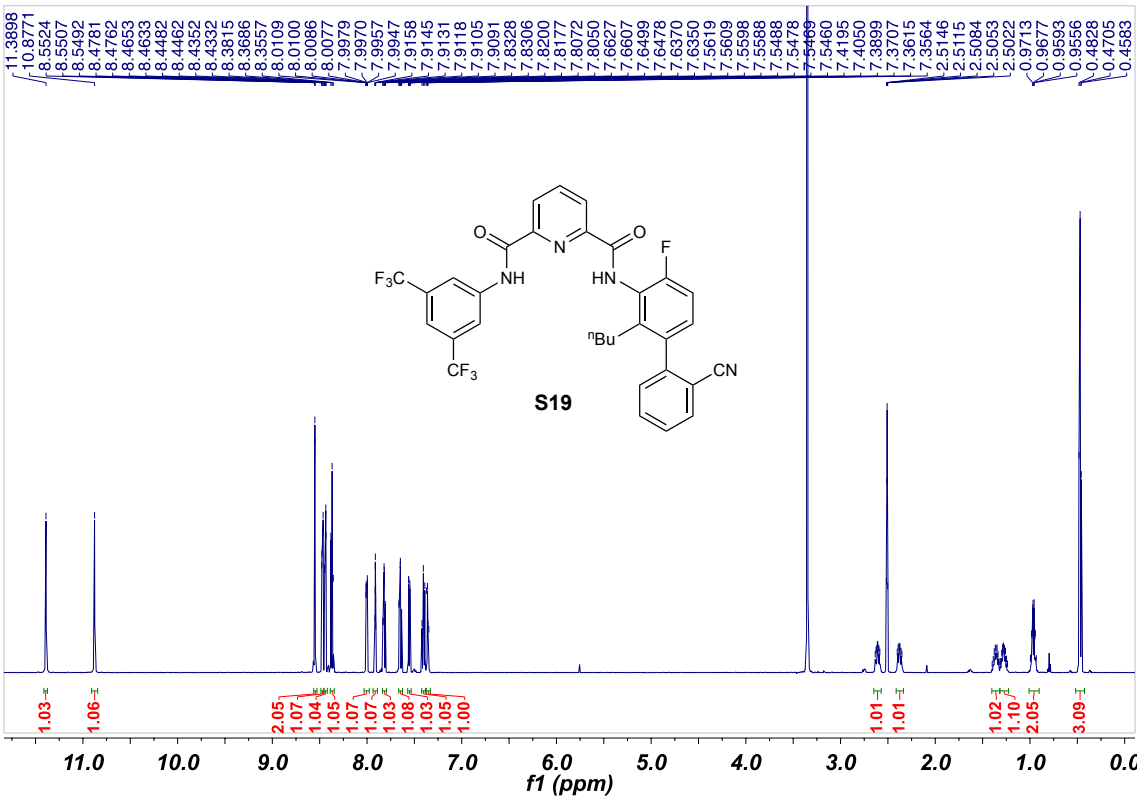
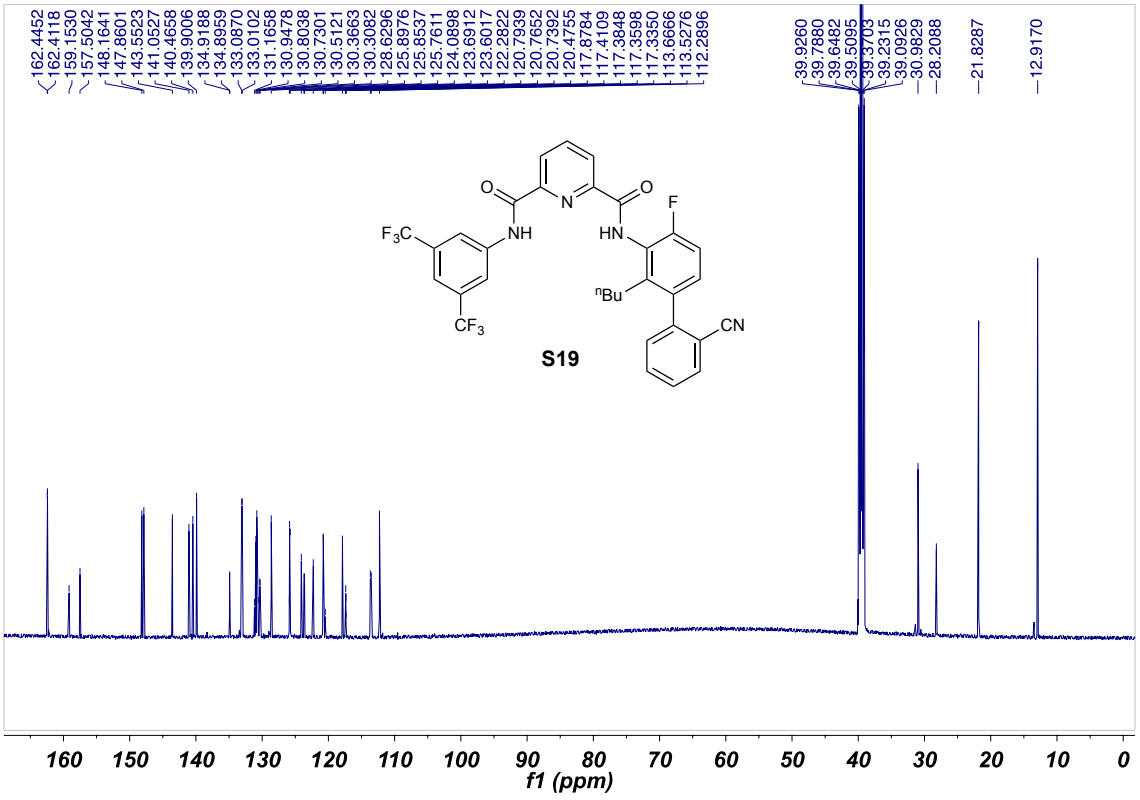
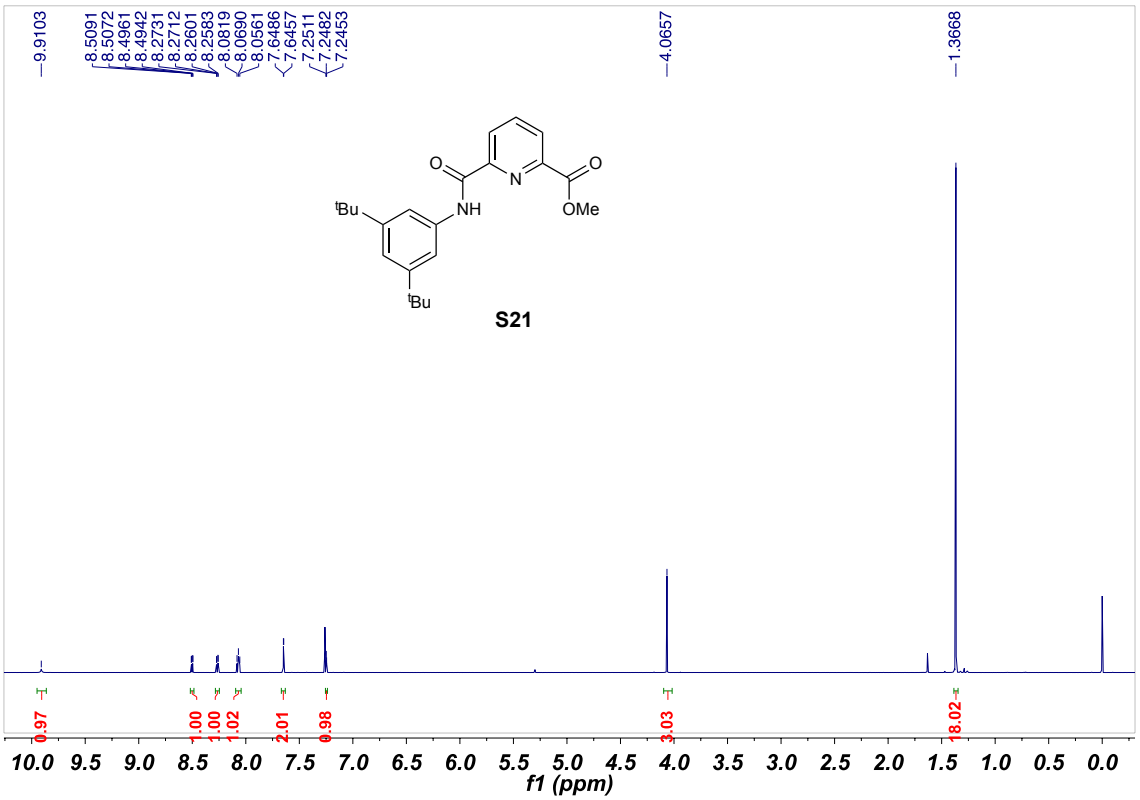
136.482
134.950
134.928
133.367
133.127
131.083
130.875
130.750
130.658
130.440
129.920
129.862
128.601
125.920
125.865
125.803
124.112
123.977
123.889
122.305
121.257
121.232
121.206
121.178
120.498
117.862
117.462
117.436
117.410
113.532
113.394
111.983
39.928
39.789
39.651
39.372
39.232
39.093
15.560
15.546
F3C
NH
N
O
O
HN
F
Me
CF3
CN
S17
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


S18
f1 (ppm)


S18
f1 (ppm)


S19
f1 (ppm)


S19
f1 (ppm)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8.2712
8.2601
8.2583
8.0819
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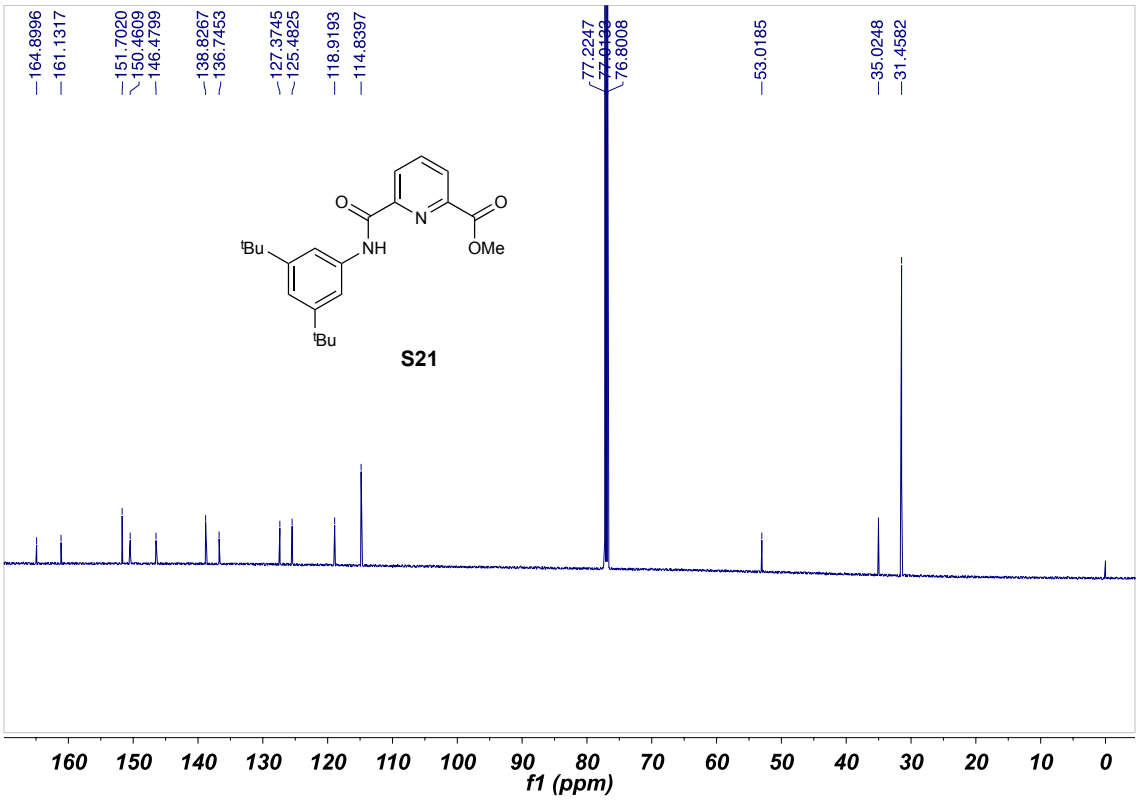
8.0561
7.6486
7.6457
7.2511
7.2482
7.2453
4.0657
1.3668
tBu
NH
OMe
tBu
S21
0.97
1.00
1.00
1.02
2.01
0.98
3.03
18.02
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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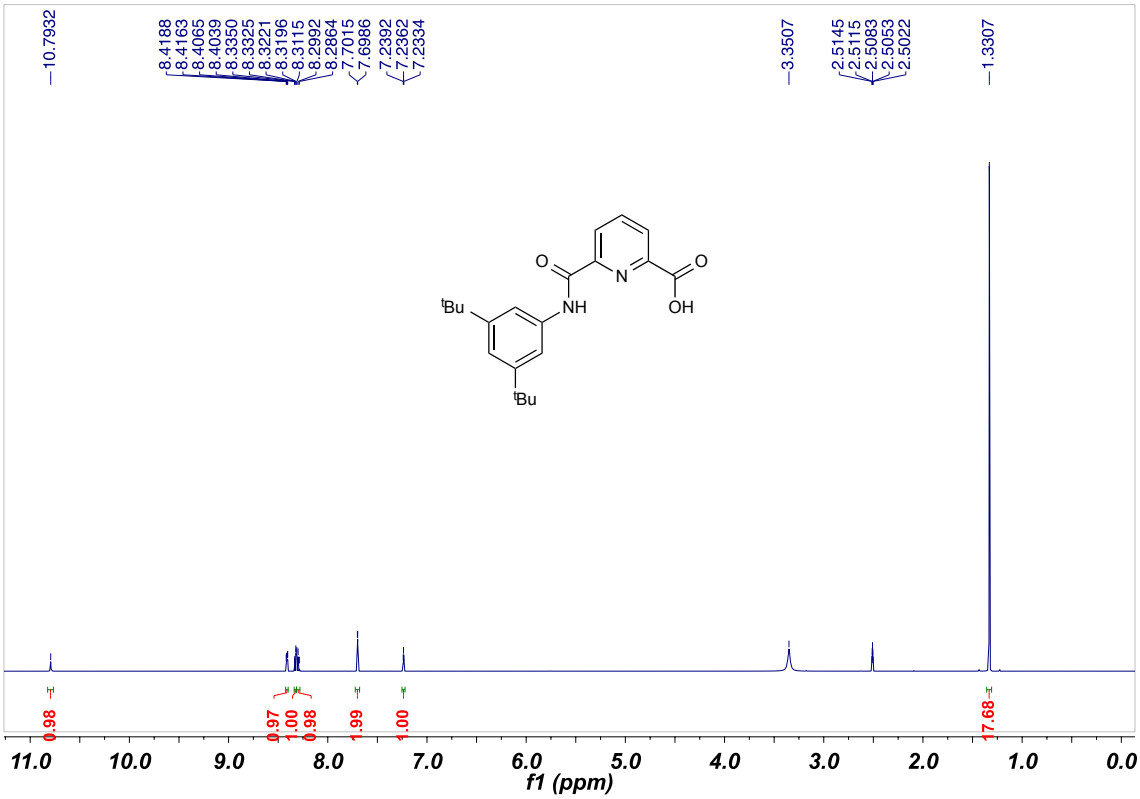
136.7453
127.3745
125.4825
118.9193
114.8397
77.2247
77.0129
76.8008
53.0185
35.0248
31.4582
tBu
NH
OMe
tBu
S21
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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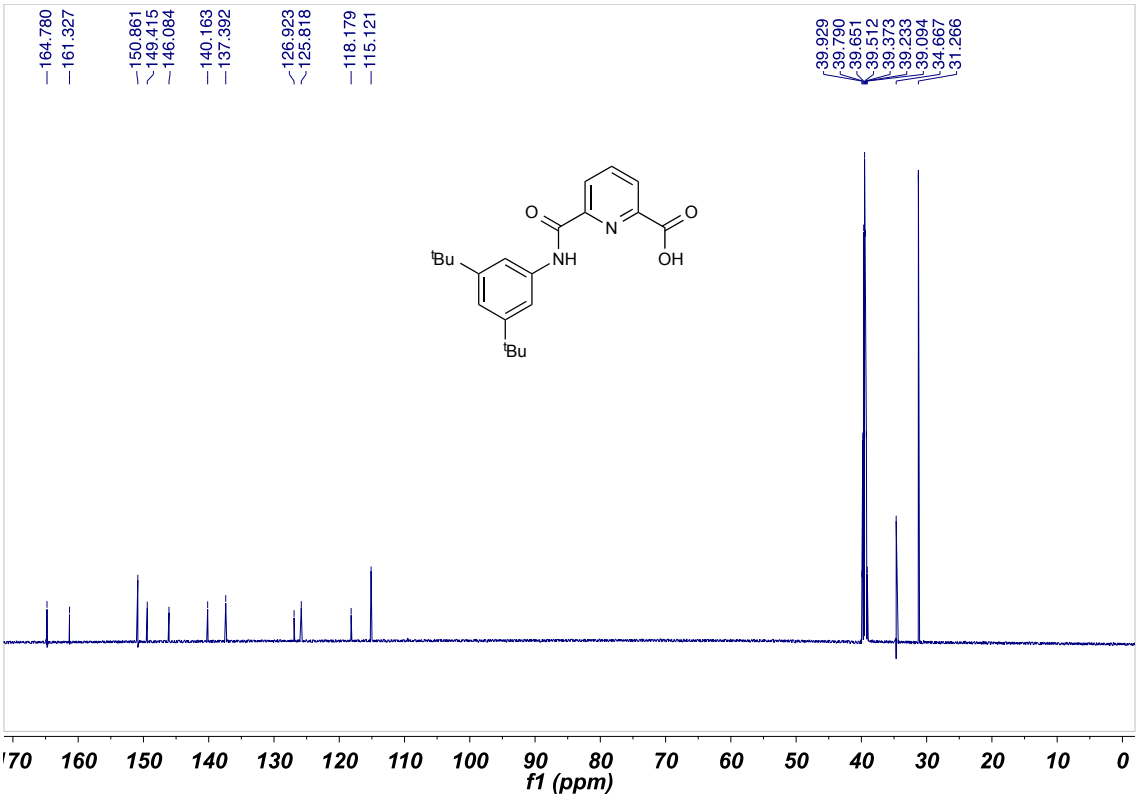
8.4039
8.3350
8.3325
8.3221
8.3196
8.3115
8.2992
8.2864
7.7015
7.6986
7.2392
7.2362
7.2334
3.3507
2.5145
2.5115
2.5083
2.5053
2.5022
1.3307
0.98
0.97
1.00
0.98
1.99
1.00
17.68
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)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146.084
140.163
137.392
126.923
125.818
118.179
115.121
39.929
39.790
39.651
39.512
39.373
39.233
39.094
34.667
31.266
170
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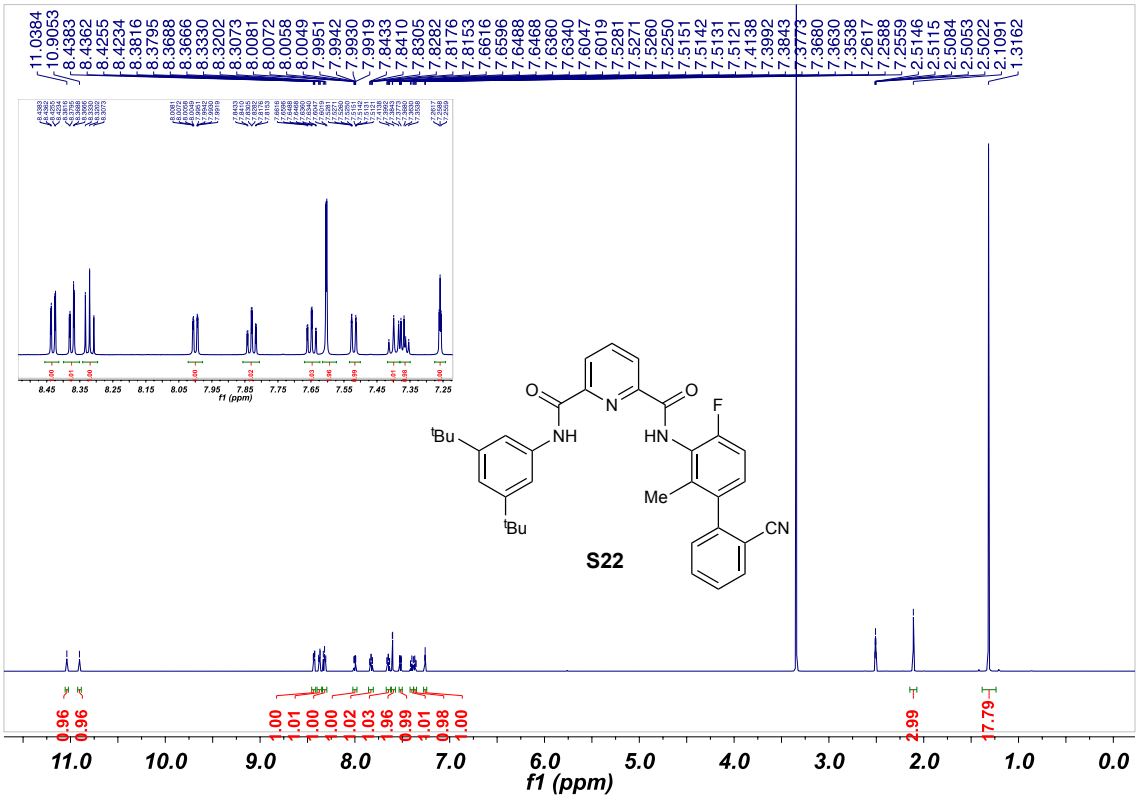
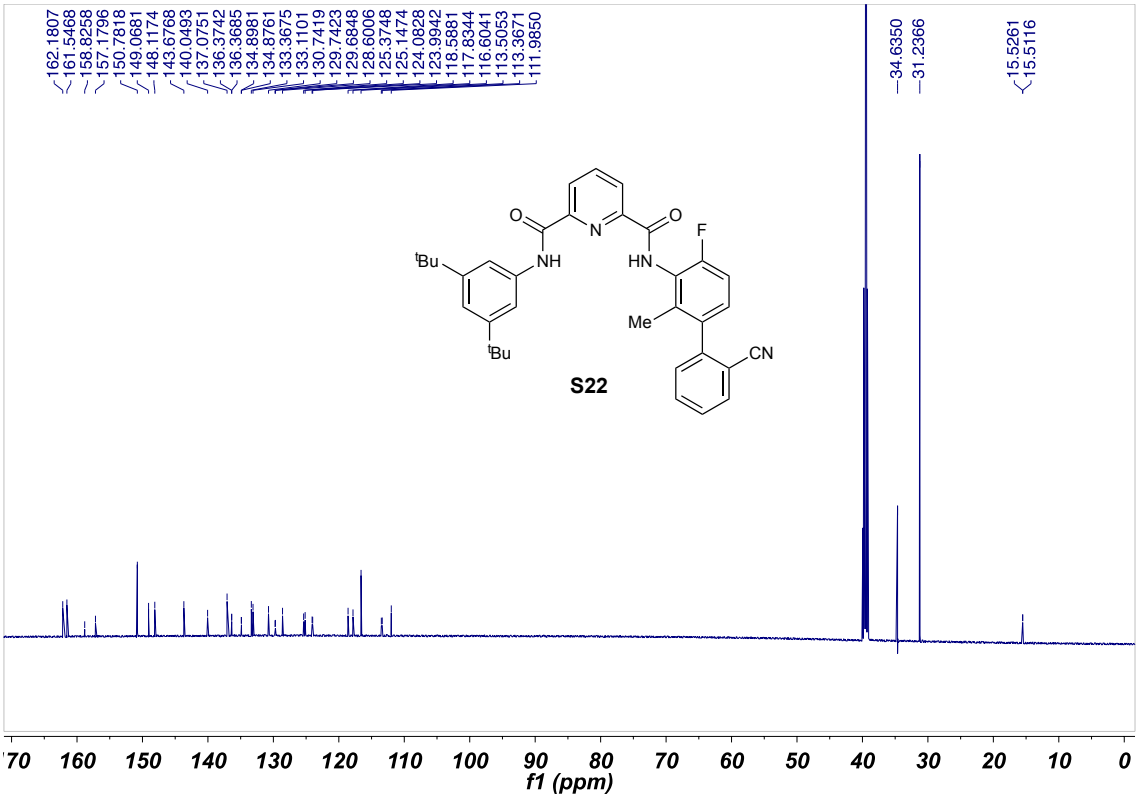
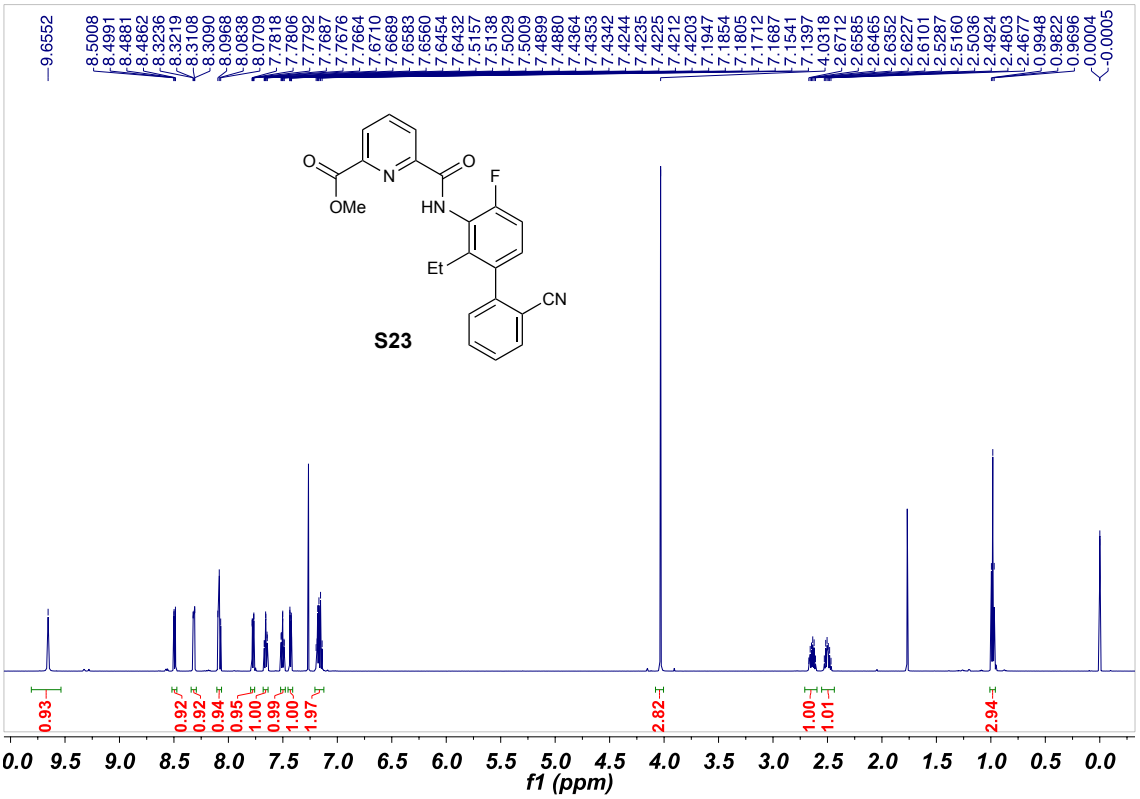
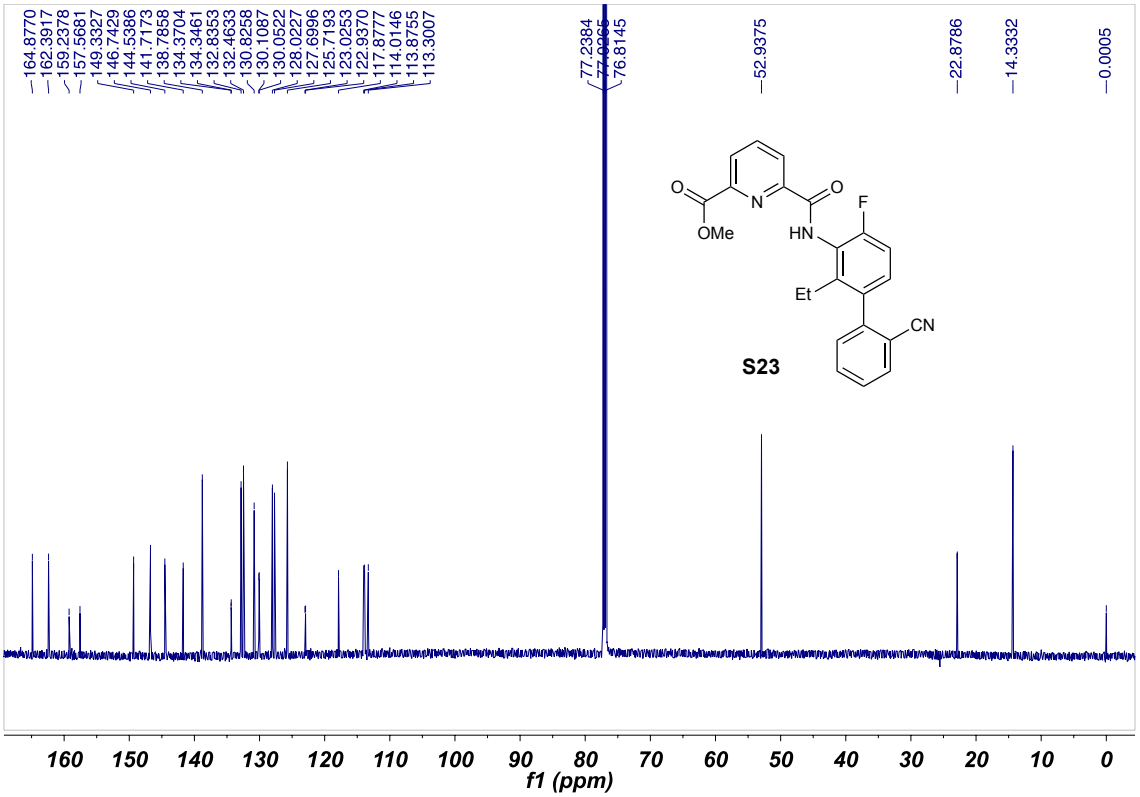
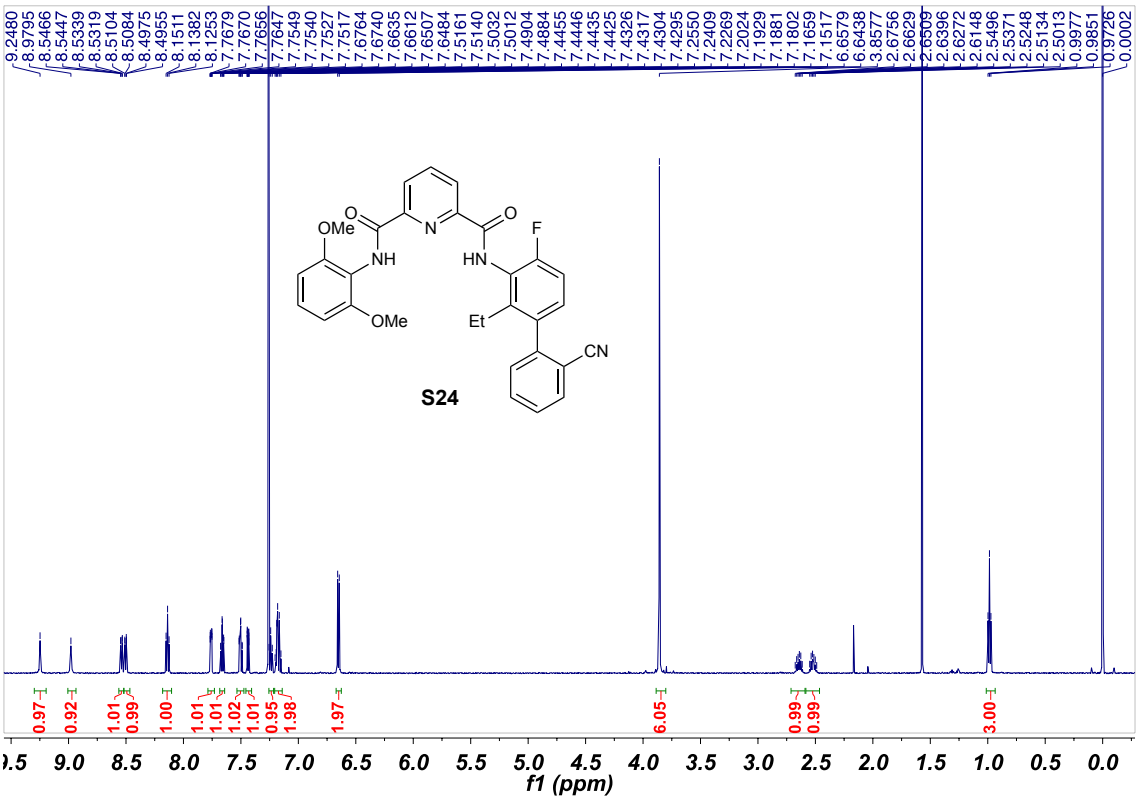
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


S22
f1 (ppm)


S22
f1 (ppm)


S23
f1 (ppm)


S23
f1 (ppm)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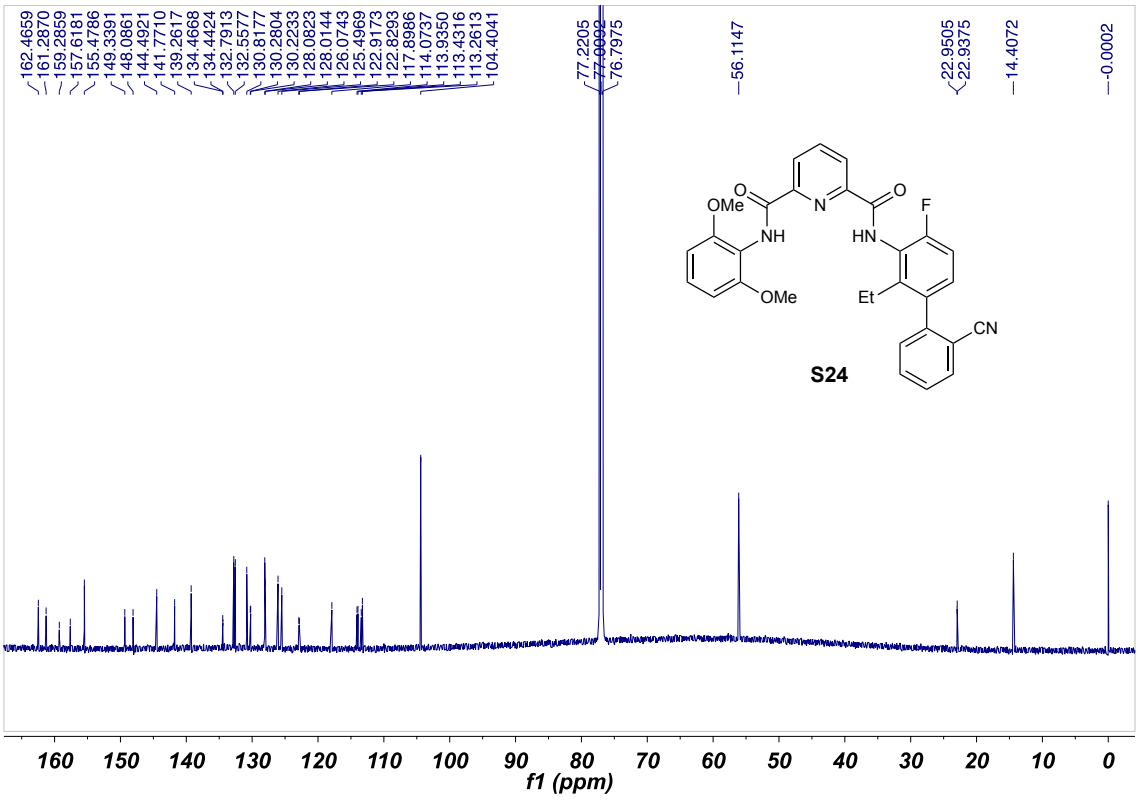
f1 (ppm)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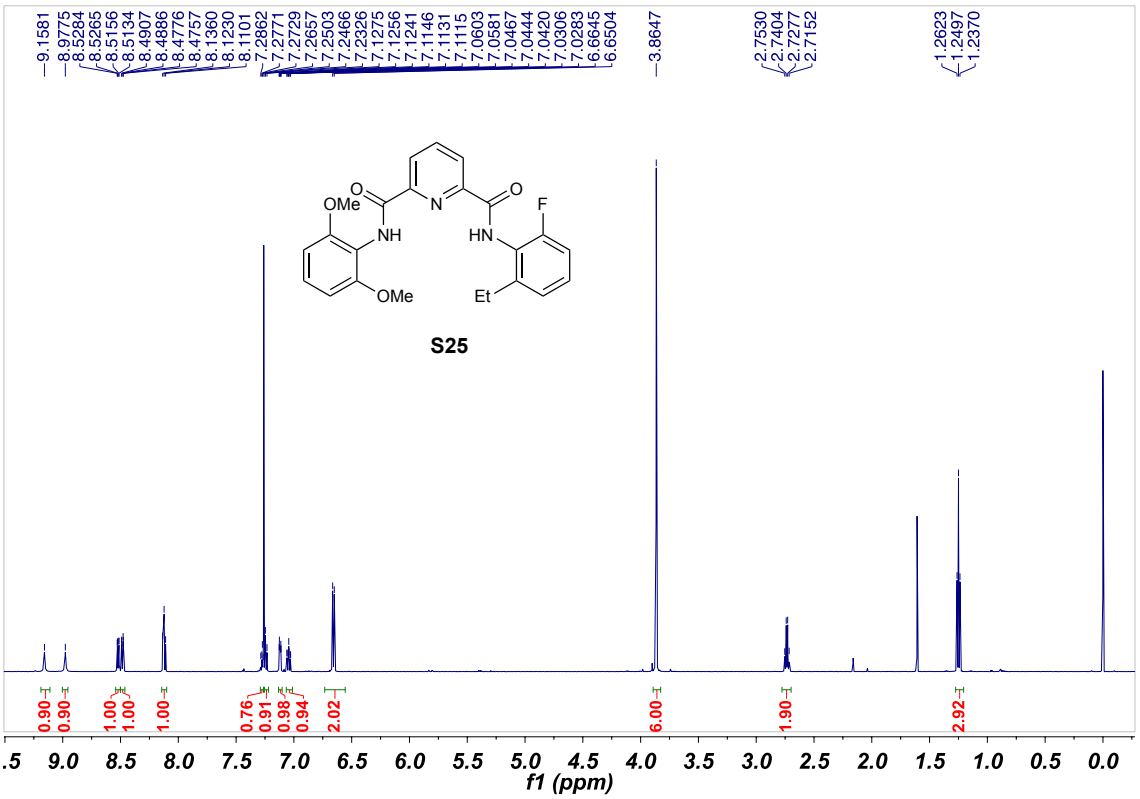
f1 (ppm)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8.1360
8.1230
8.1101
7.2862
7.2771
7.2729
7.2657
7.2503
7.2466
7.2326
7.1275
7.1256
7.1241
7.1146
7.1131
7.1115
7.0603
7.0581
7.0467
7.0444
7.0420
7.0306
7.0283
6.6645
6.6504
3.8647
2.7530
2.7404
2.7277
2.7152
1.2623
1.2497
1.2370
OMe
NH
N
O
HN
F
OMe
Et
S25
0.90
0.90
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1.00
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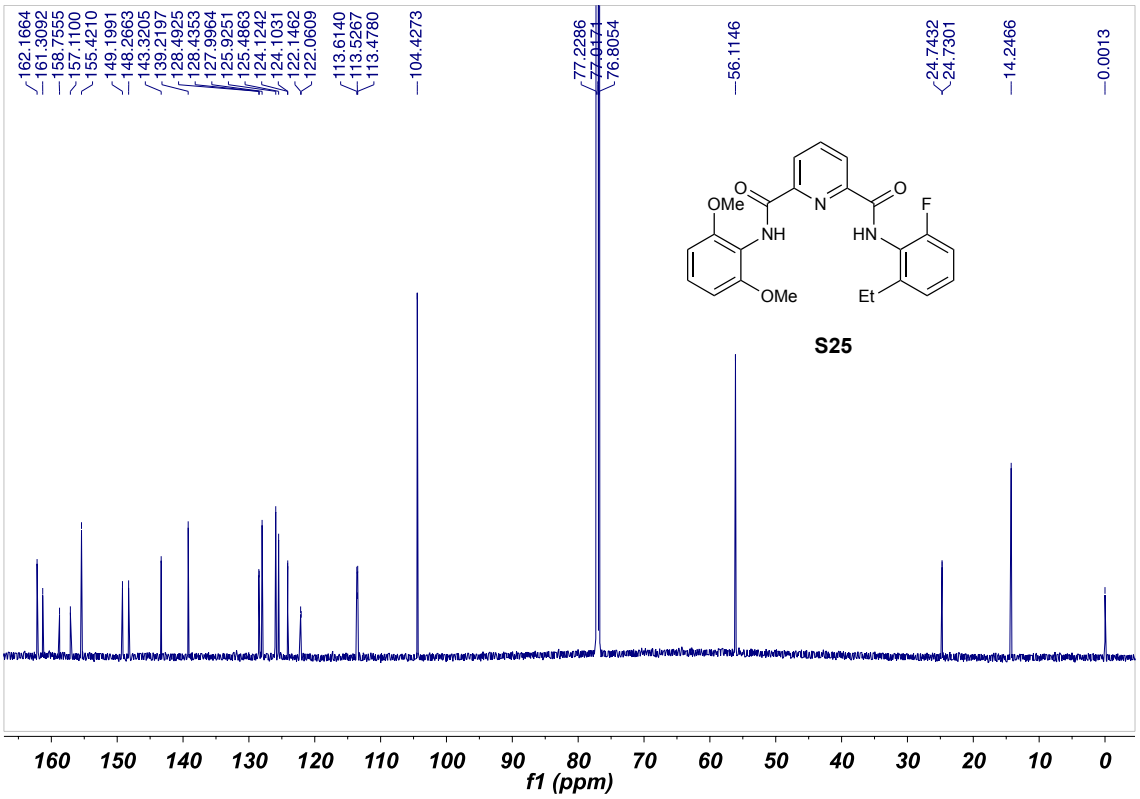
0.76
0.91
0.98
0.94
2.02
6.00
1.90
2.92
f1 (ppm)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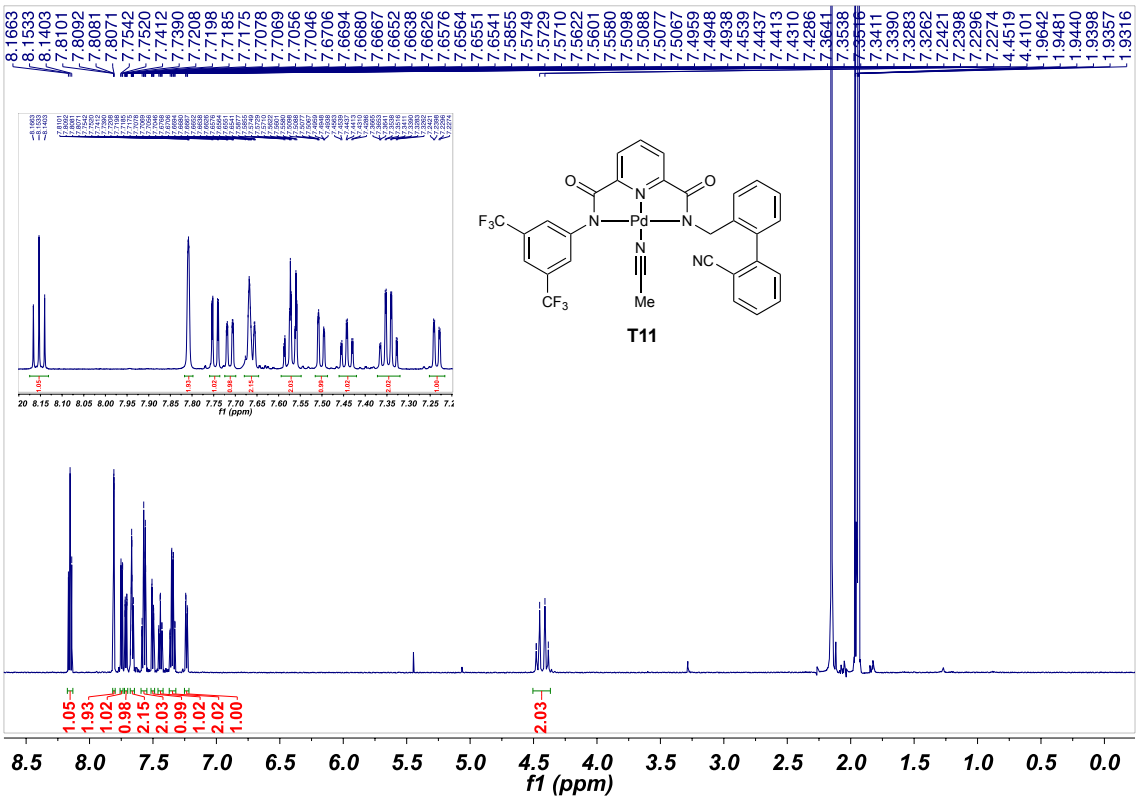
125.4863
124.1242
124.1031
122.1462
122.0609
113.6140
113.5267
113.4780
104.4273
77.2286
77.0171
76.8054
56.1146
24.7432
24.7301
14.2466
-0.0013
OMe
NH
N
O
HN
F
OMe
Et
S25
f1 (ppm)


T11
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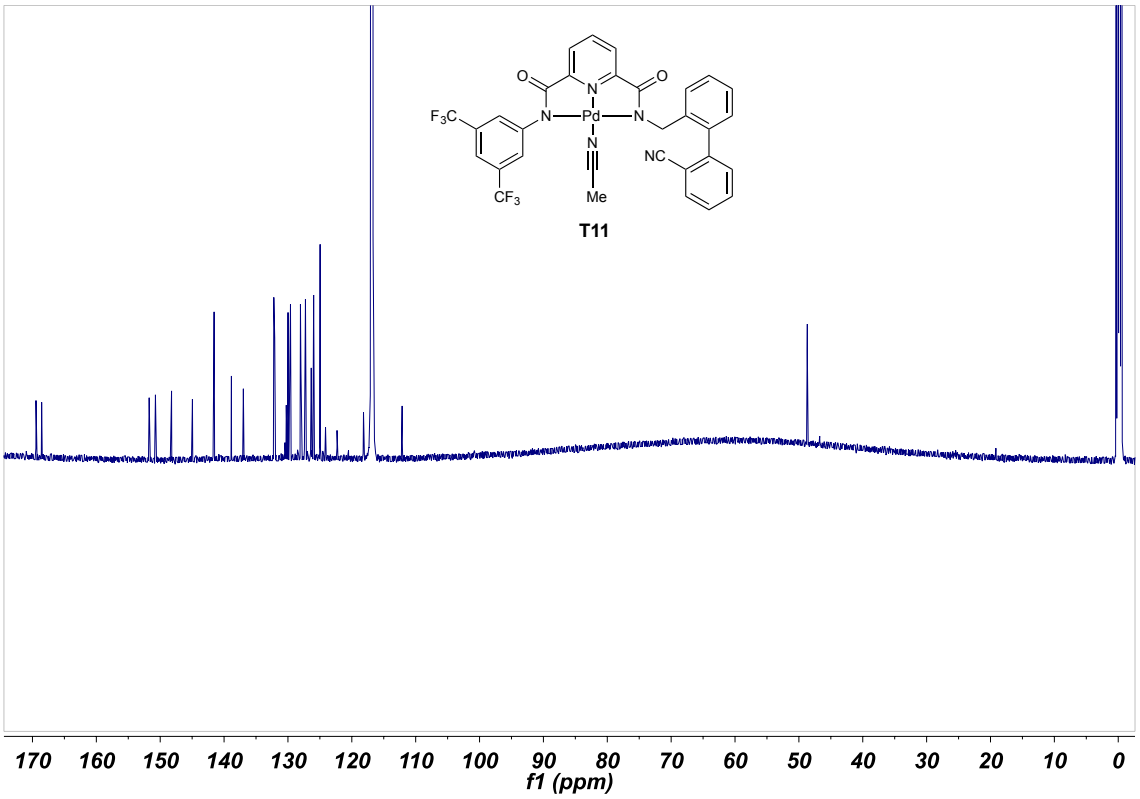
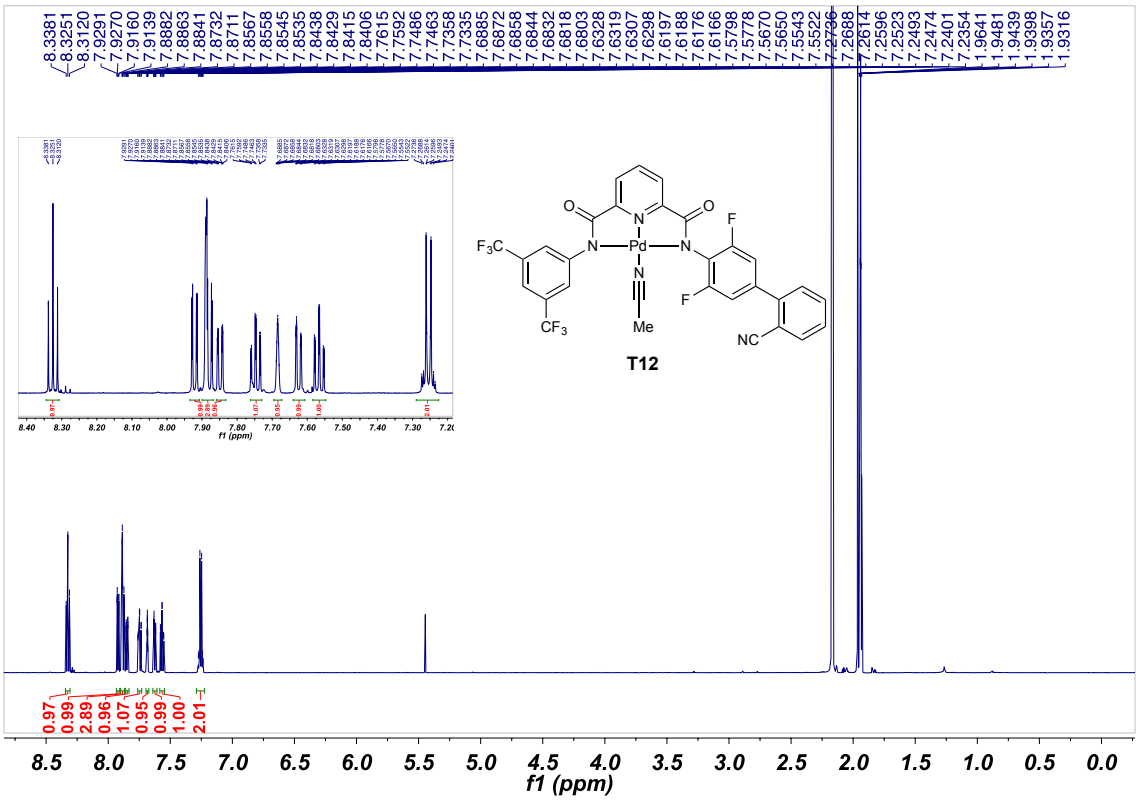
1.02
0.98
2.15
2.03
0.99
1.02
2.02
1.00
2.03
f1 (ppm)


T11
f1 (ppm)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7.8863
7.8841
7.8732
7.8711
7.8567
7.8558
7.8545
7.8535
7.8438
7.8429
7.8415
7.8406
7.7615
7.7592
7.7486
7.7463
7.7358
7.7335
7.6885
7.6872
7.6858
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7.6319
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7.2688
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7.2596
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7.2474
7.2401
7.2354
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1.9481
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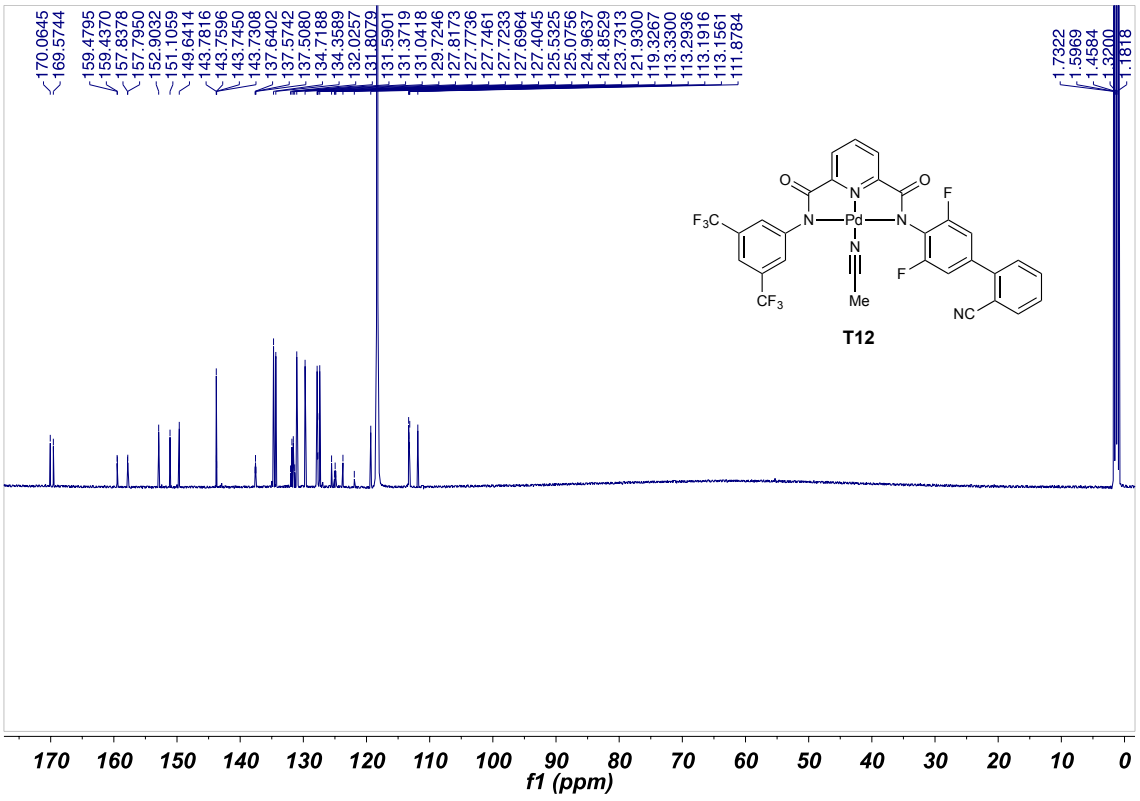
1.9398
1.9357
1.9316
0.97
0.99
2.89
0.96
1.07
0.95
0.99
1.00
2.01
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
T12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143.7450
143.7308
137.6402
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134.7188
134.3589
132.0257
131.8079
131.5901
131.3719
131.0418
129.7246
127.8173
127.7736
127.7461
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127.6964
127.4045
125.5325
125.0756
124.9637
124.8529
123.7313
121.9300
119.3267
113.3300
113.2936
113.1916
113.1561
111.8784
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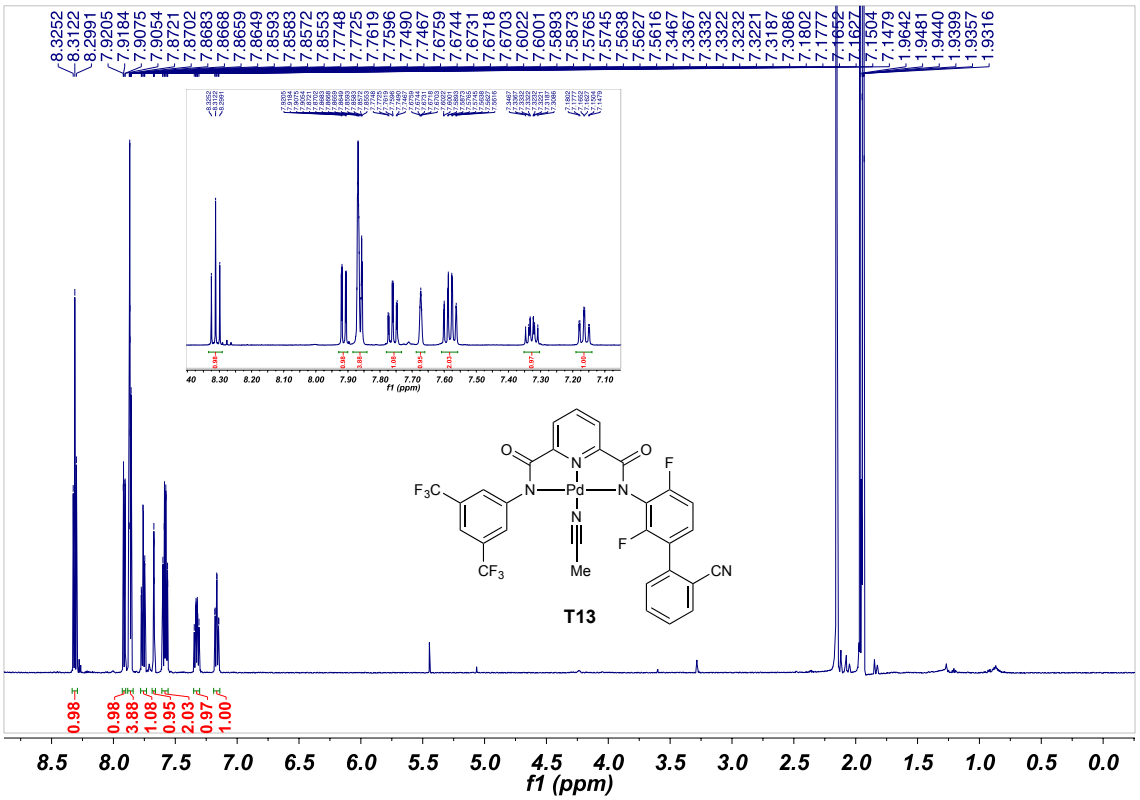
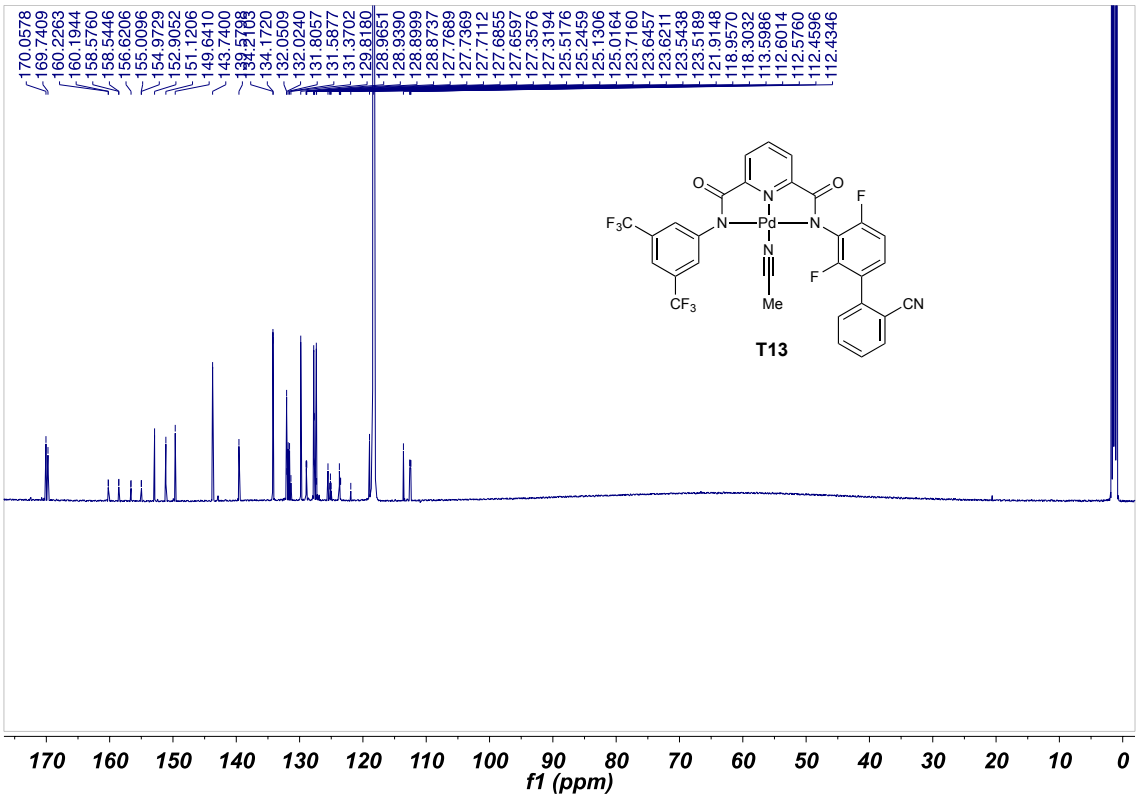
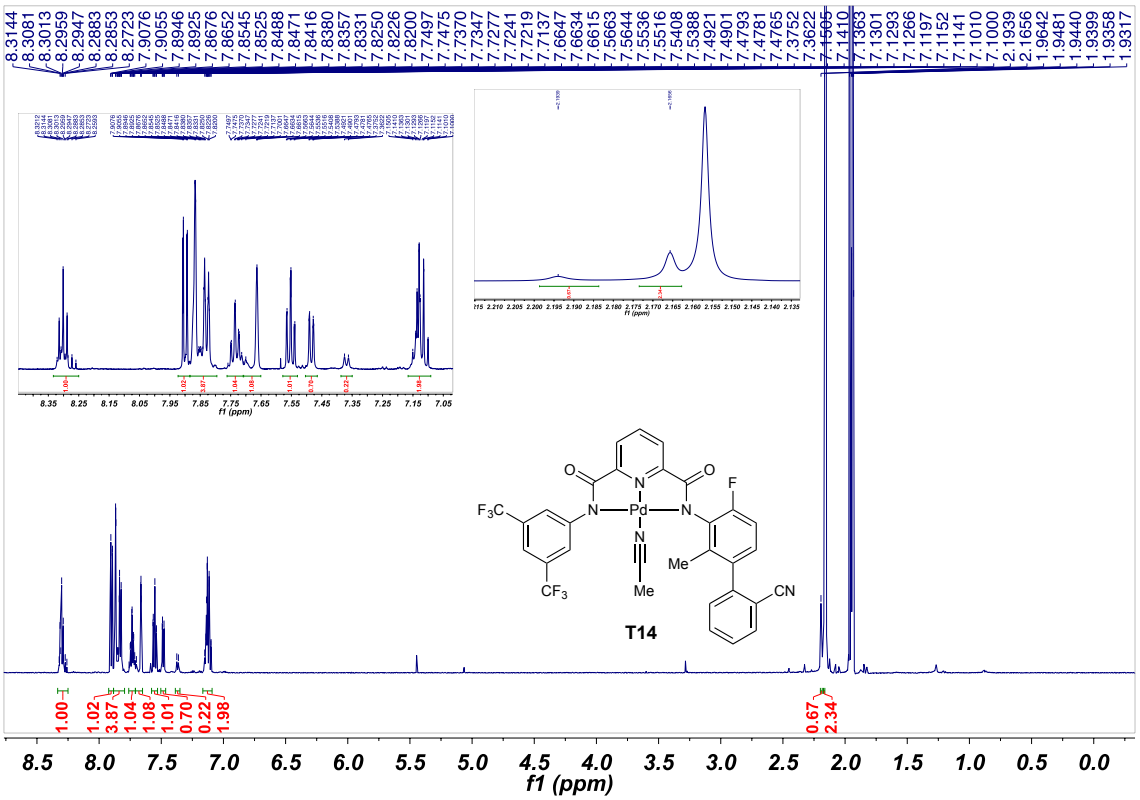
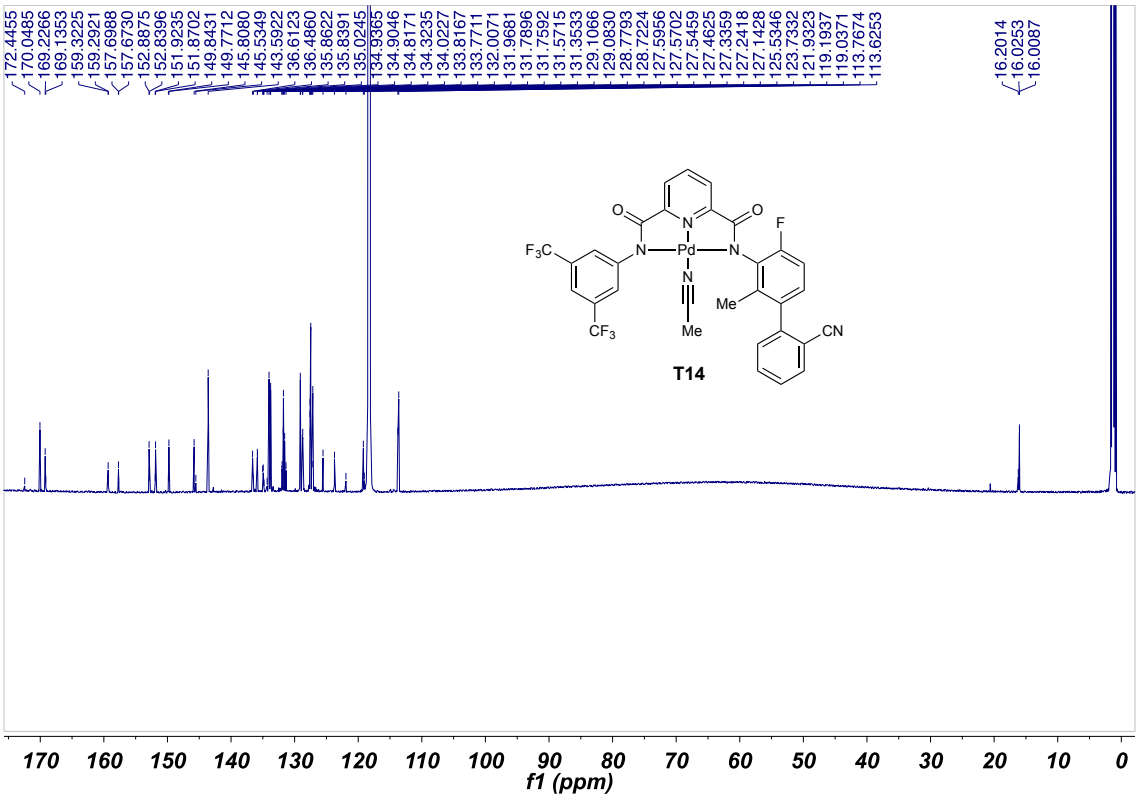
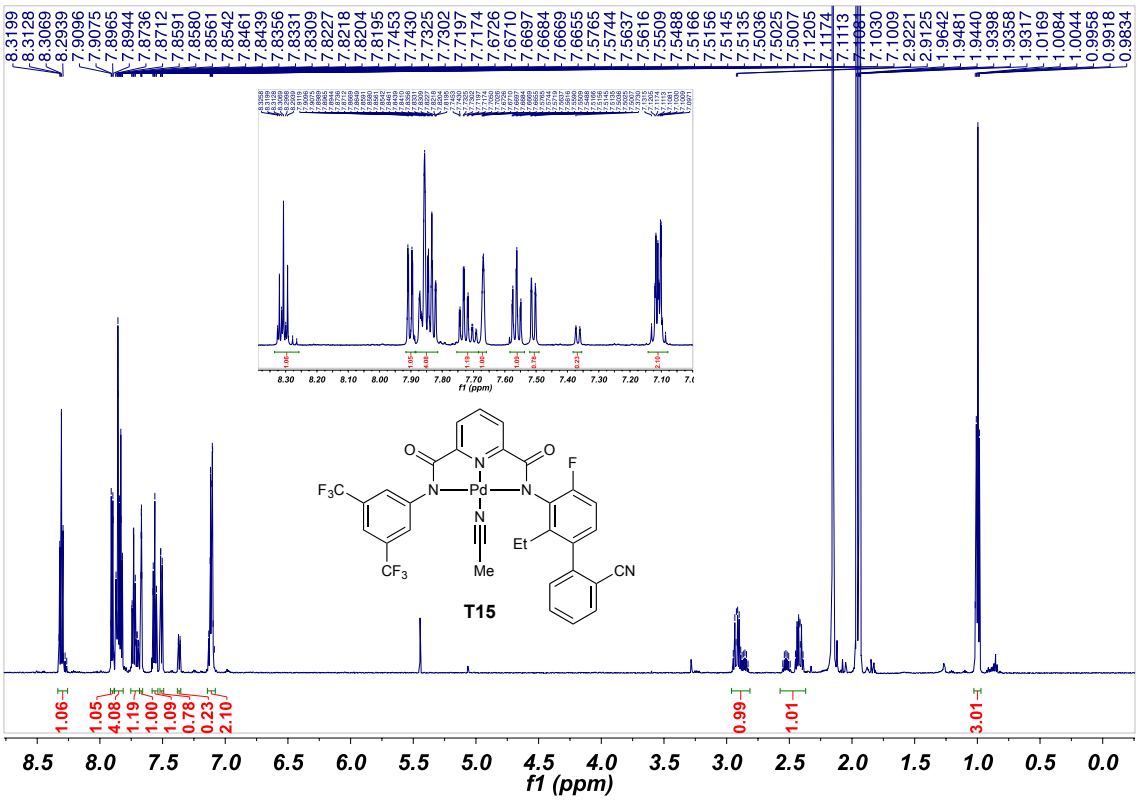
1.5969
1.4584
1.3200
1.1818
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
T12

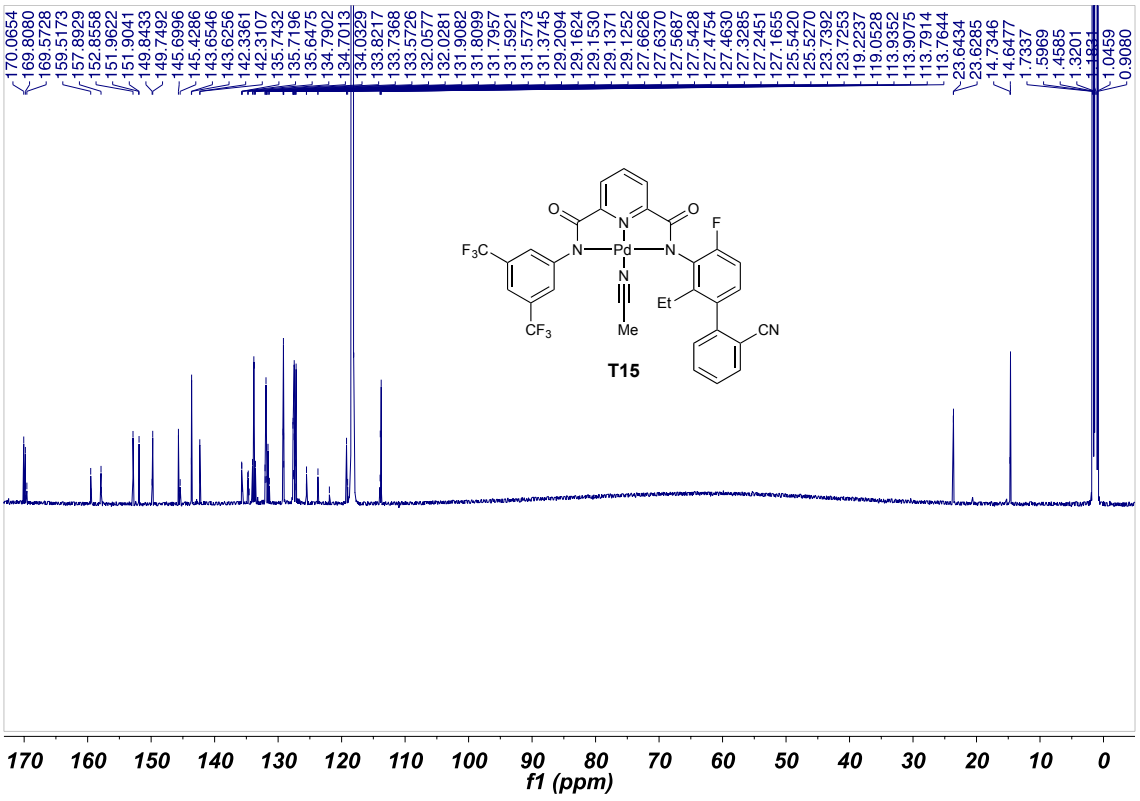

T13
f1 (ppm)

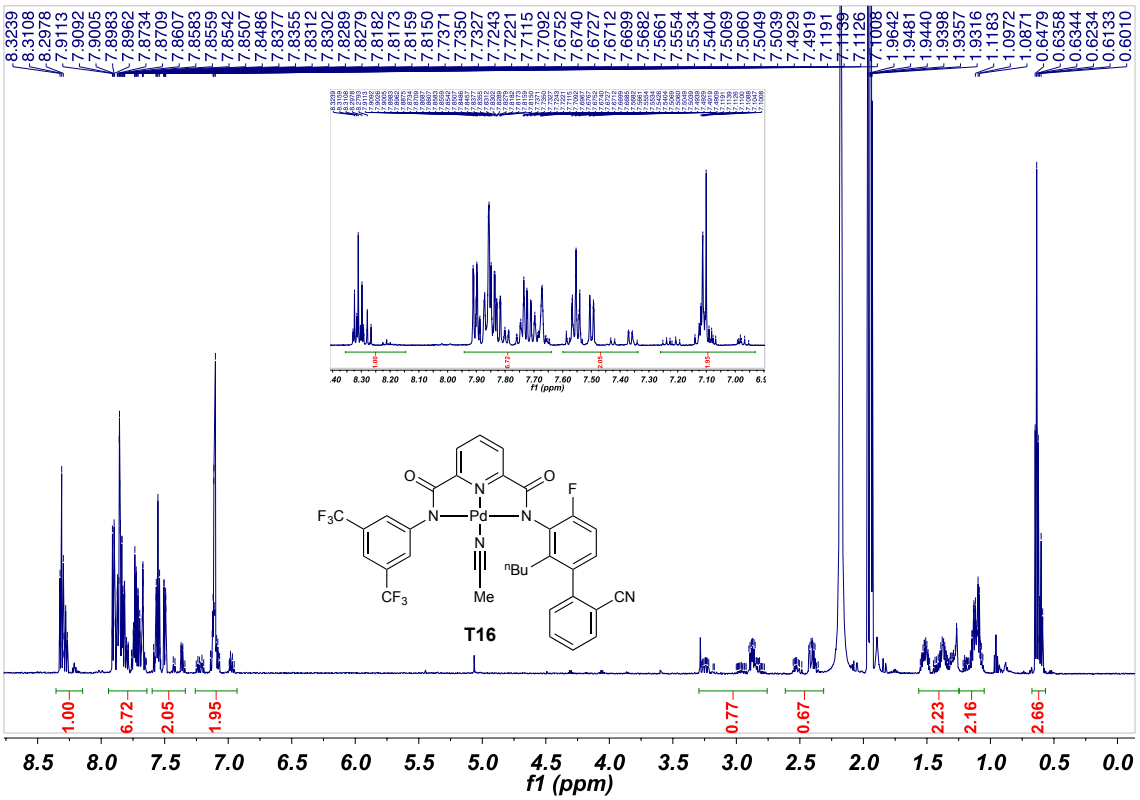

T13
f1 (ppm)

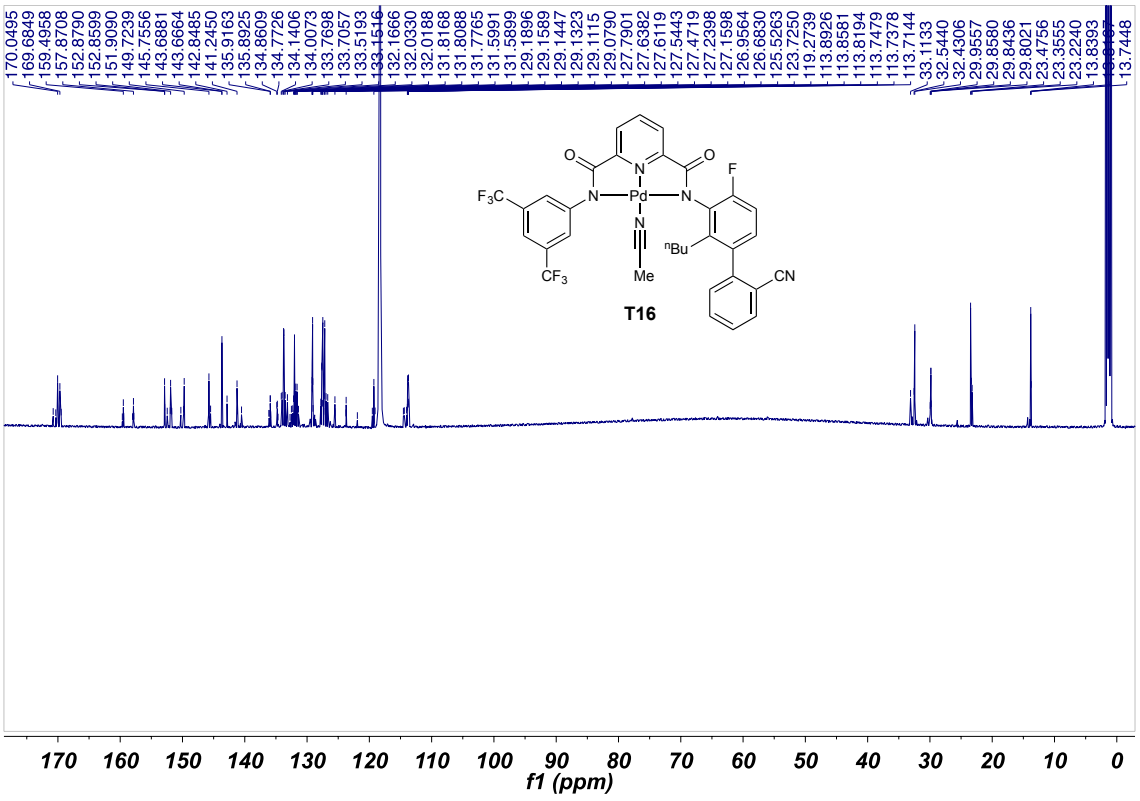

T14
f1 (ppm)

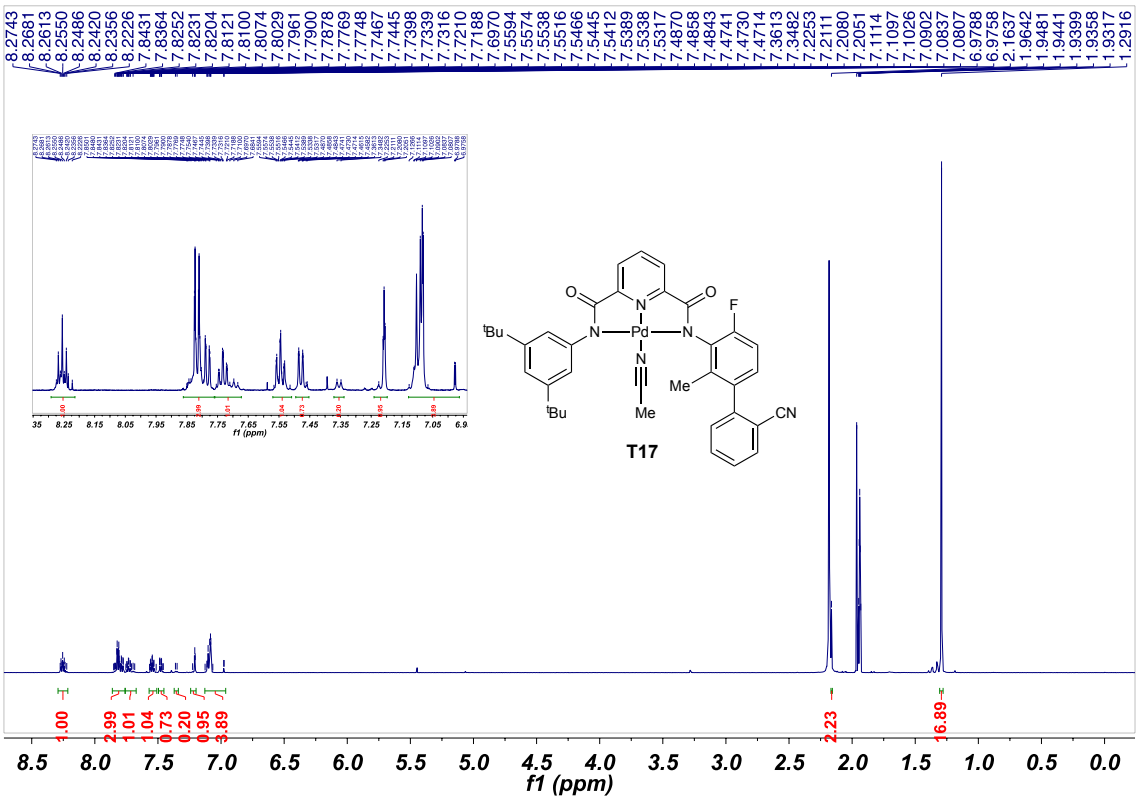

T14
f1 (ppm)

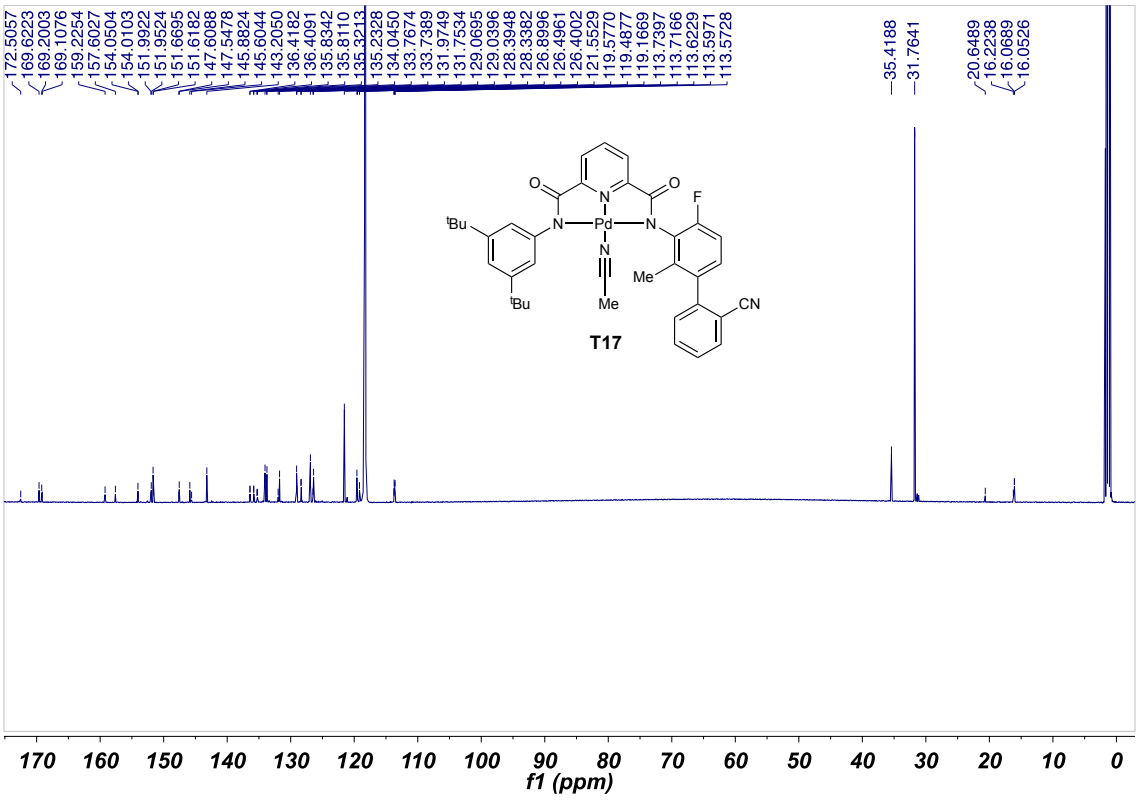

T15
f1 (ppm)

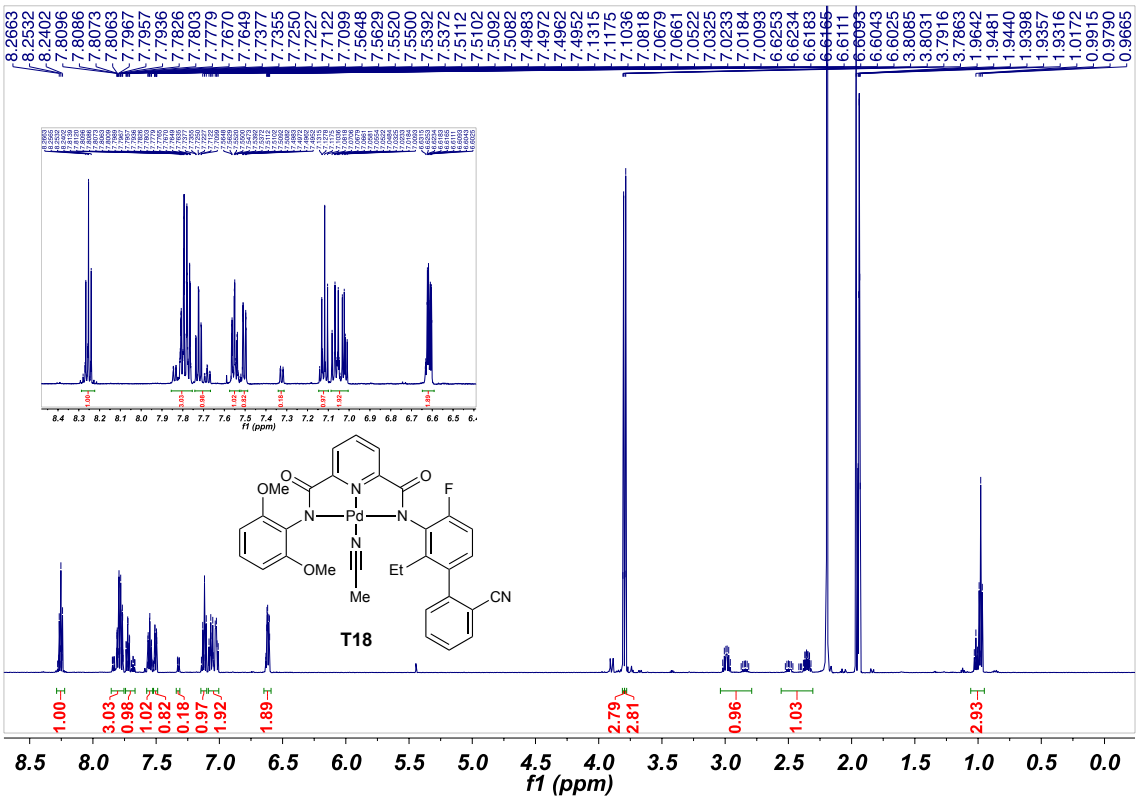

T15
f1 (ppm)

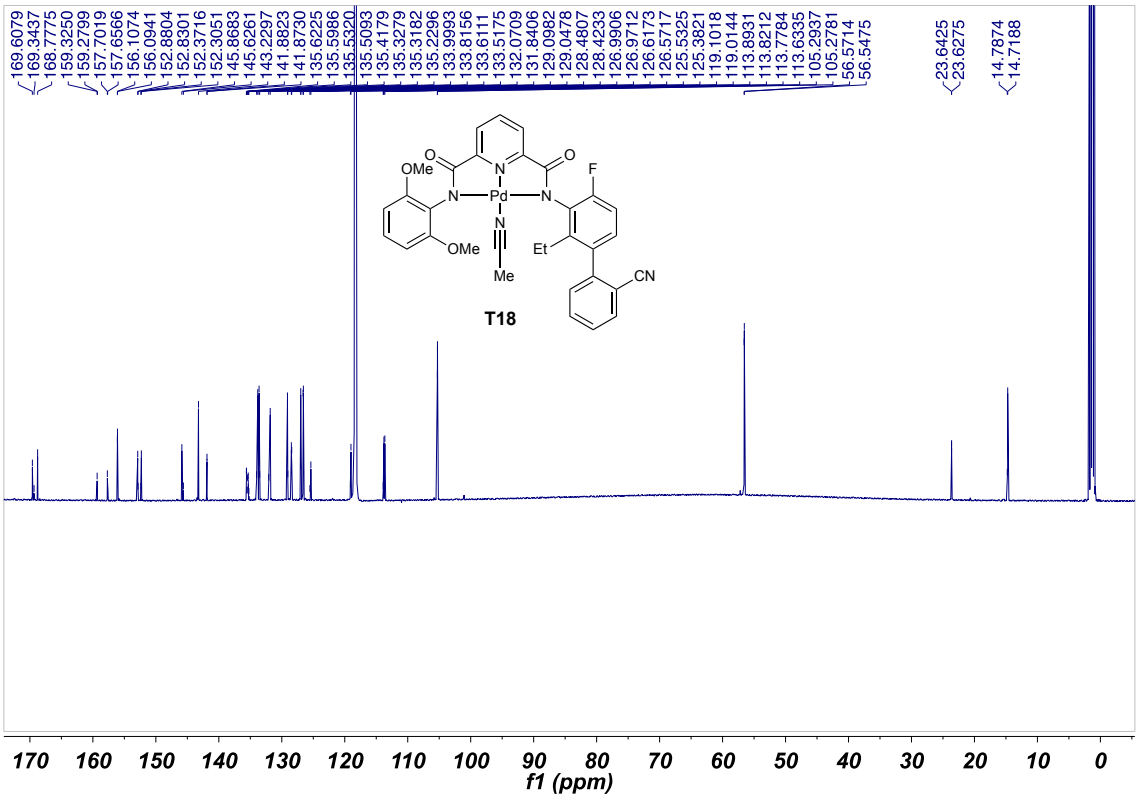

T16
1.00
6.72
2.05
1.95
0.77
0.67
2.23
2.16
2.66
f1 (ppm)

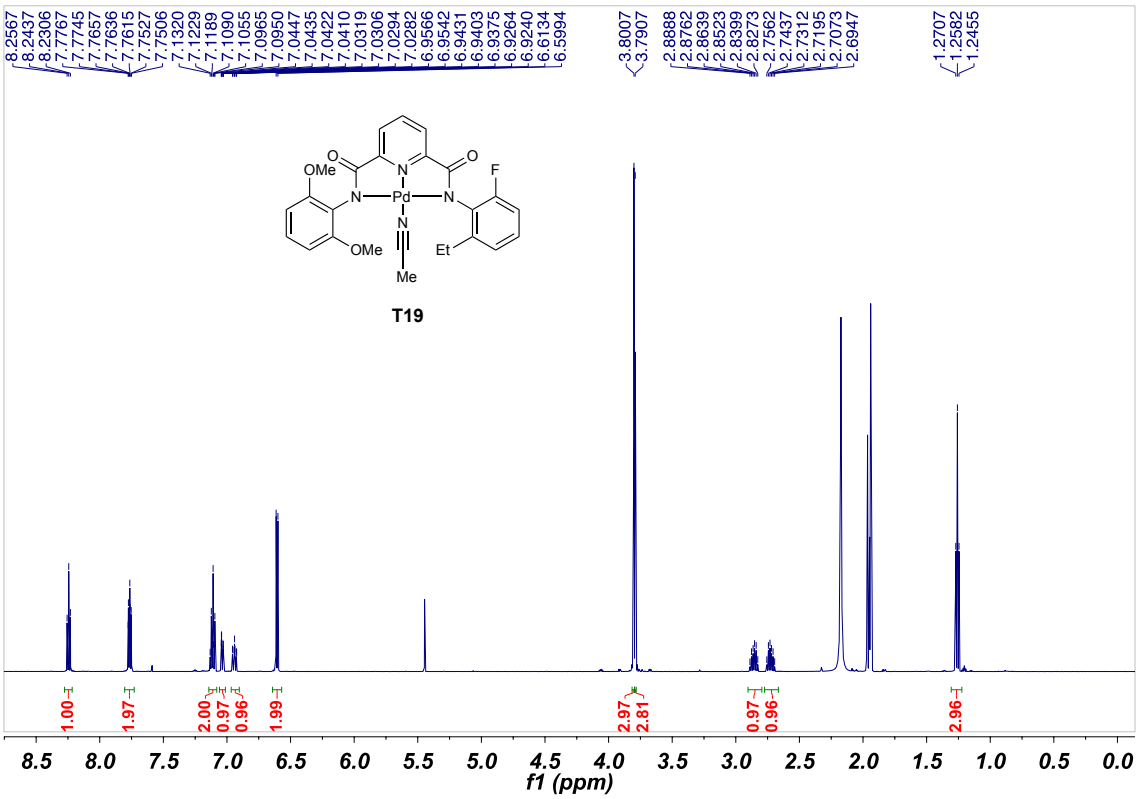

T16
f1 (ppm)

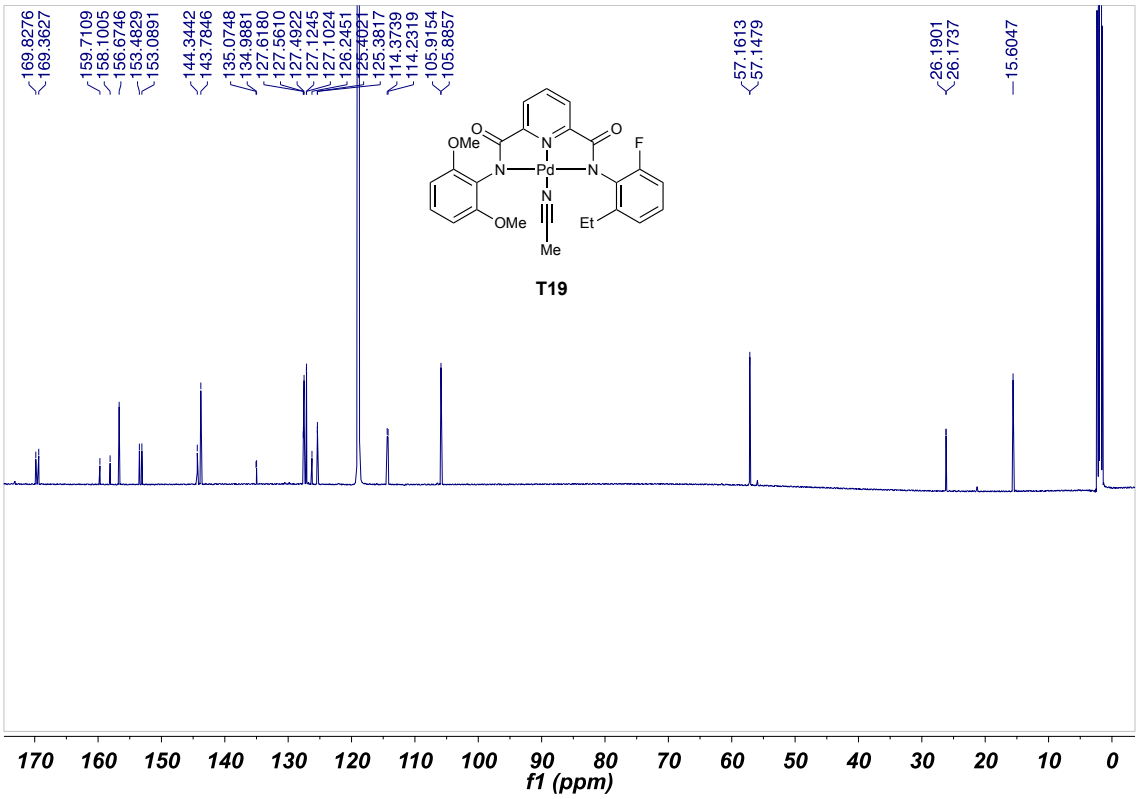

T17
1.00
2.99
1.01
1.04
0.73
0.20
0.95
3.89
2.23
16.89
f1 (ppm)

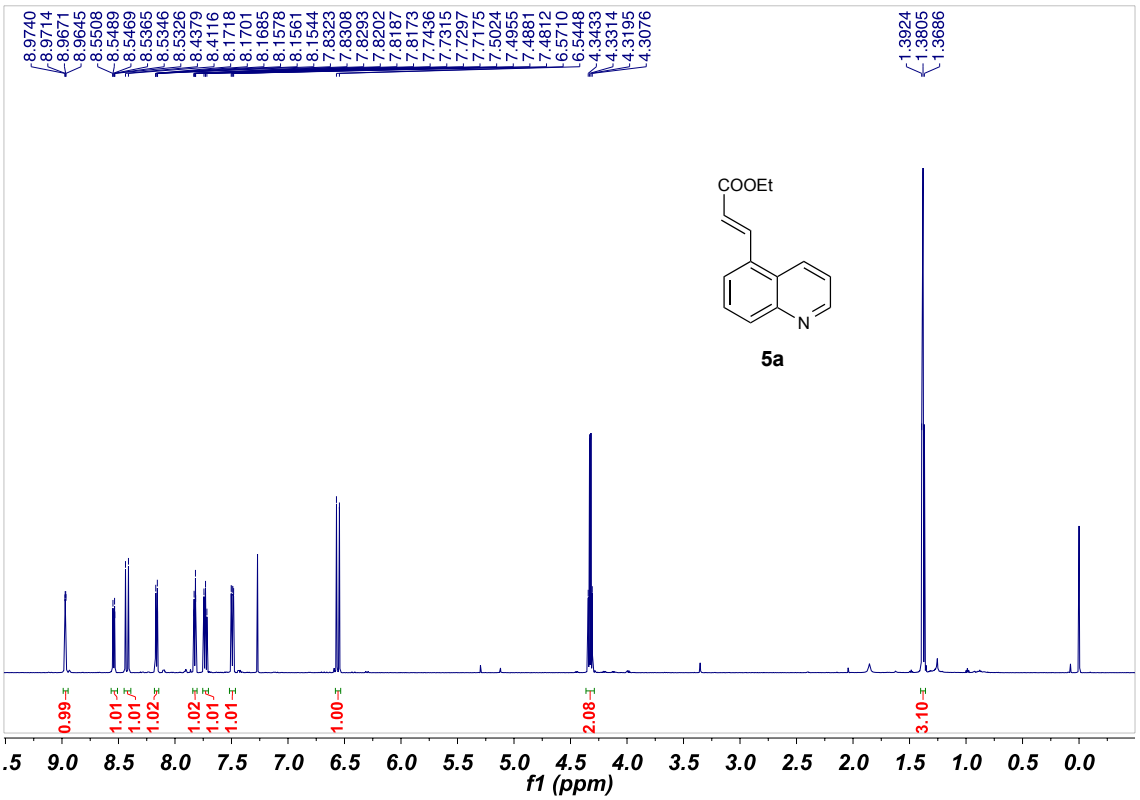

T17
f1 (ppm)

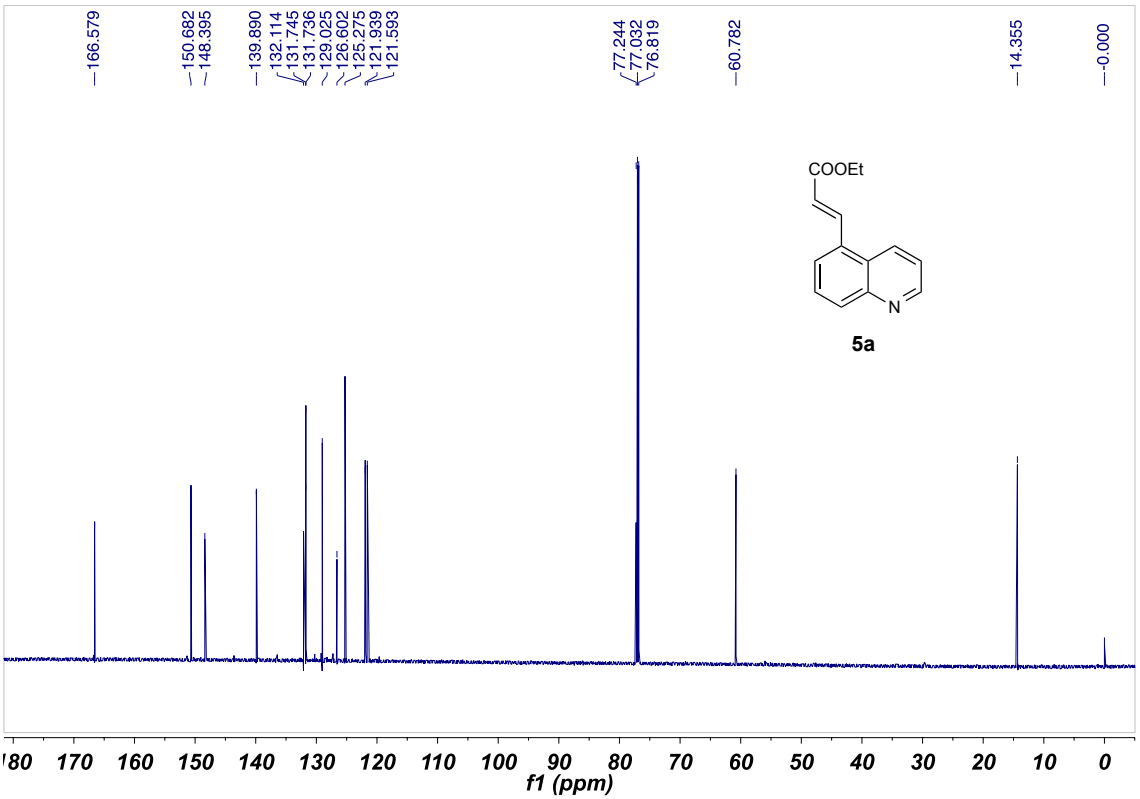

T18
f1 (ppm)

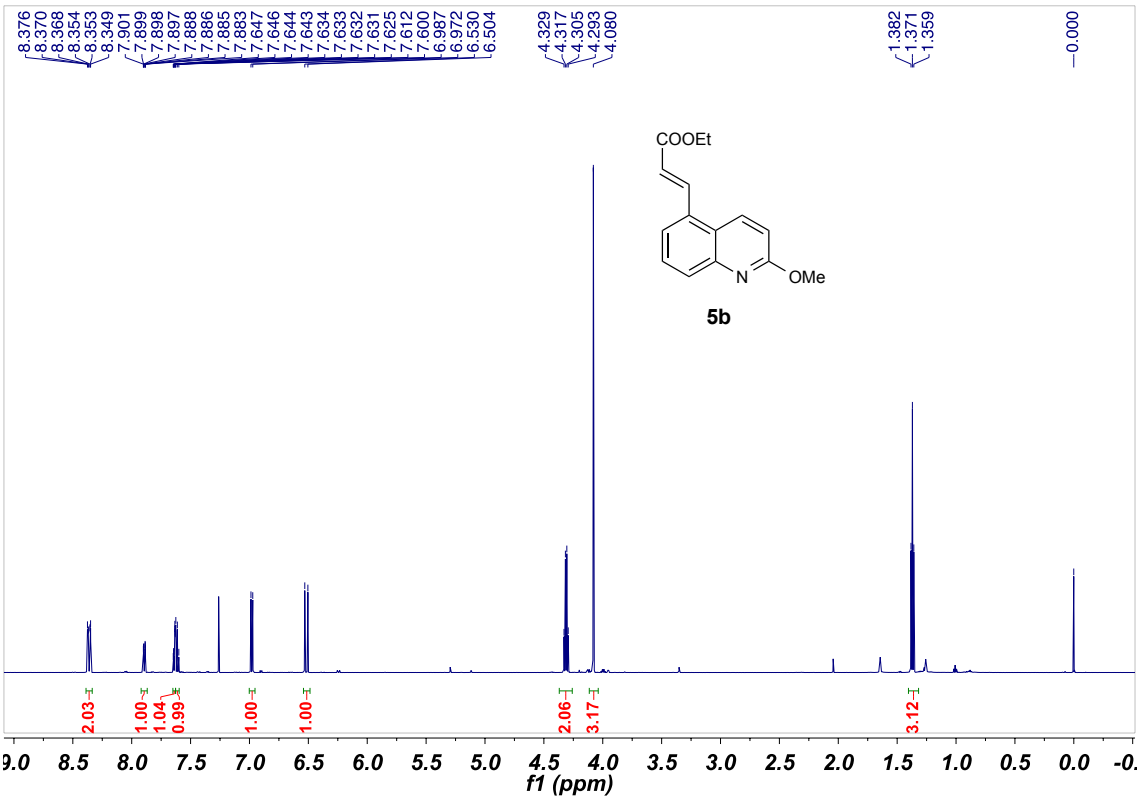

T18
f1 (ppm)

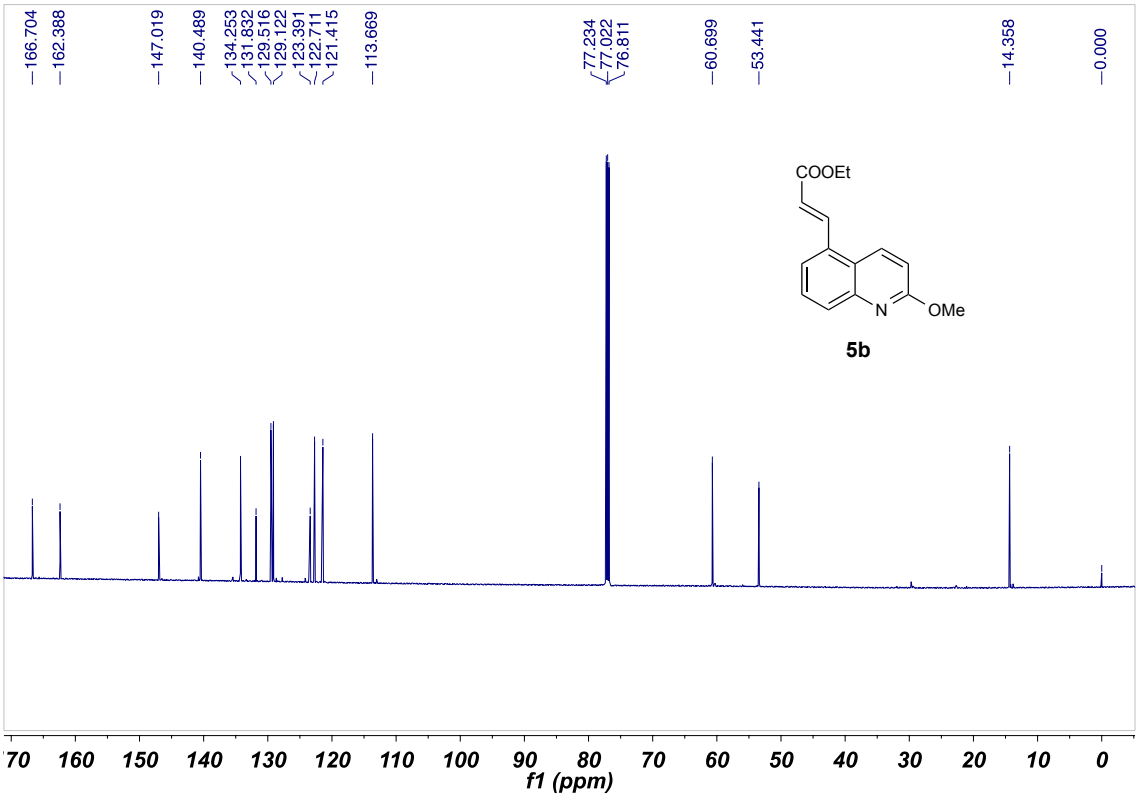

8.2567
8.2437
8.2306
7.7767
7.7745
7.7657
7.7636
7.7615
7.7527
7.7506
7.1320
7.1229
7.1189
7.1090
7.1055
7.0965
7.0950
7.0447
7.0435
7.0422
7.0410
7.0319
7.0306
7.0294
7.0282
6.9566
6.9542
6.9431
6.9403
6.9375
6.9264
6.9240
6.6134
6.5994
3.8007
3.7907
2.8888
2.8762
2.8639
2.8523
2.8399
2.8273
2.7562
2.7437
2.7312
2.7195
2.7073
2.6947
1.2707
1.2582
1.2455
OMe
O
N
O
F
N
Pd
N
N
OMe
Et
Me
T19
1.00
1.97
2.00
0.97
0.96
1.99
2.97
2.81
0.97
0.96
2.96
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

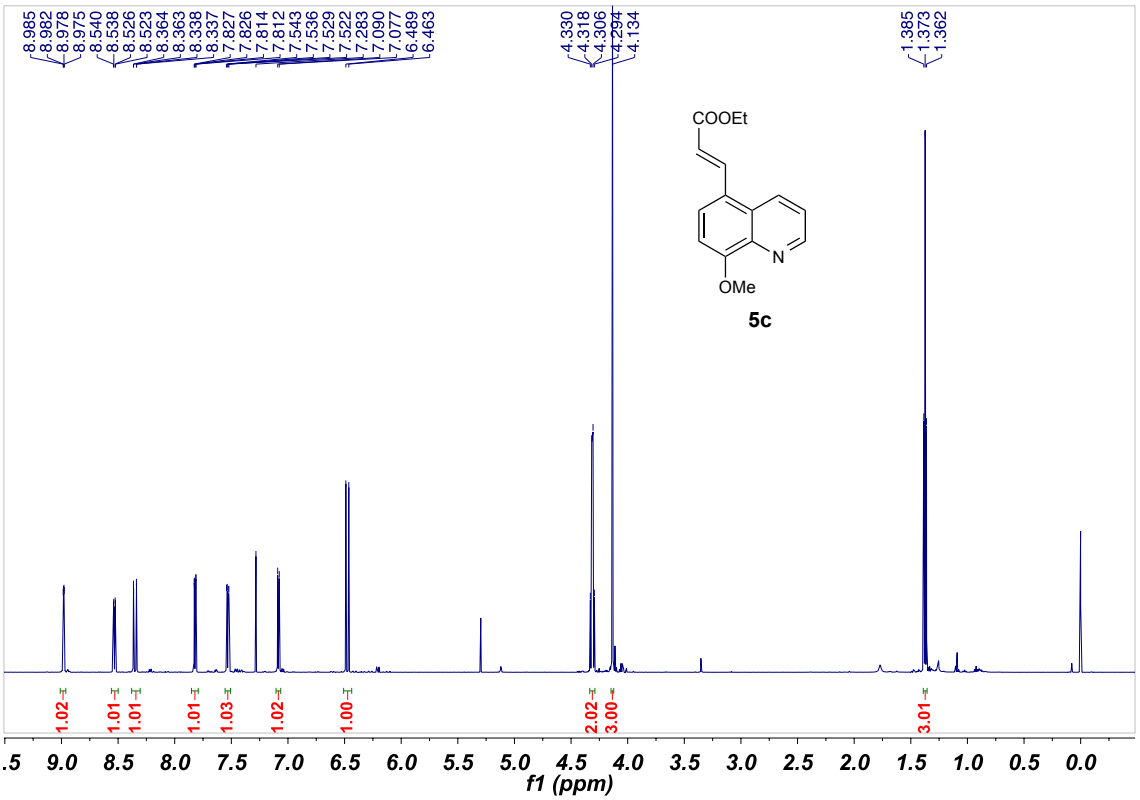

169.8276
169.3627
159.7109
158.1005
156.6746
153.4829
153.0891
144.3442
143.7846
135.0748
134.9881
127.6180
127.5610
127.4922
127.1245
127.1024
126.2451
125.4021
125.3817
114.3739
114.2319
105.9154
105.8857
57.1613
57.1479
26.1901
26.1737
15.6047
OMe
O
N
O
F
N
Pd
N
N
OMe
Et
Me
T19
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

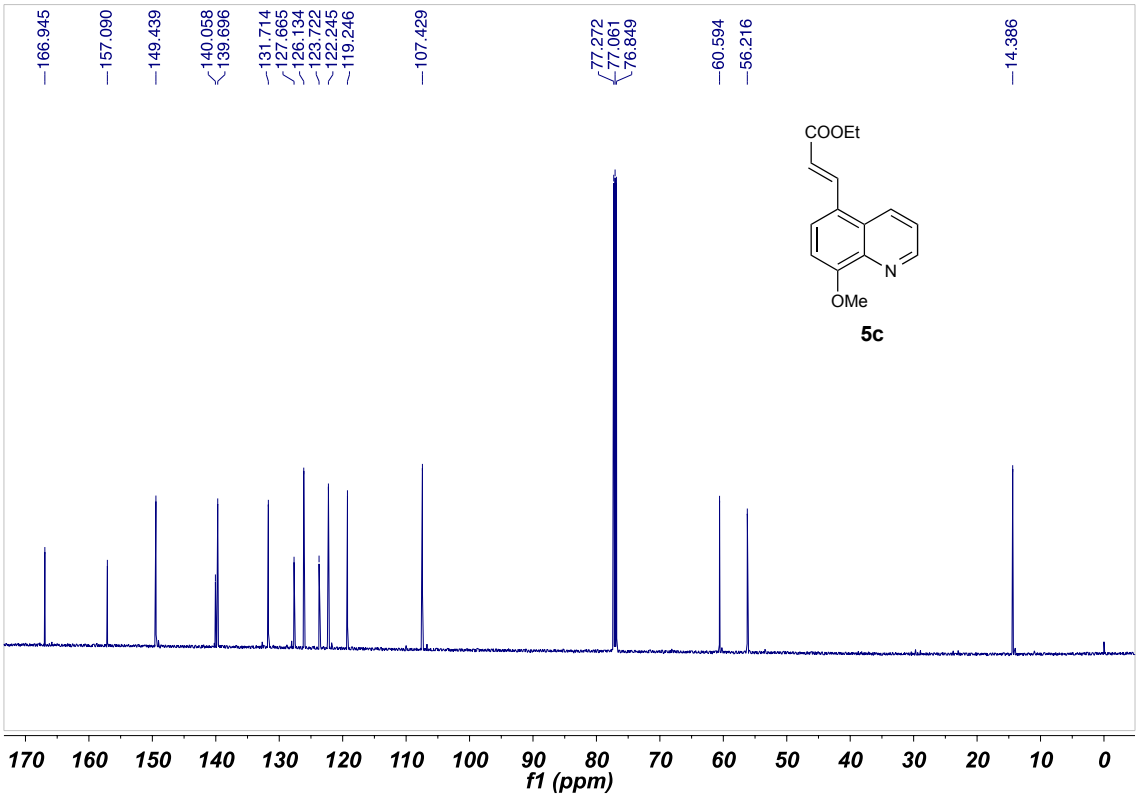

8.9740
8.9714
8.9671
8.9645
8.5508
8.5489
8.5469
8.5365
8.5346
8.5326
8.4379
8.4116
8.1718
8.1701
8.1685
8.1578
8.1561
8.1544
7.8323
7.8308
7.8293
7.8202
7.8187
7.8173
7.7436
7.7315
7.7297
7.7175
7.5024
7.4955
7.4881
7.4812
6.5710
6.5448
4.3433
4.3314
4.3195
4.3076
1.3924
1.3805
1.3686
COOEt
N
5a
0.99
1.01
1.01
1.02
1.02
1.01
1.01
1.00
2.08
3.10
f1 (ppm)


166.579
150.682
148.395
139.890
132.114
131.745
131.736
129.025
126.602
125.275
121.939
121.593
77.244
77.032
76.819
60.782
14.355
0.000
COOEt
N
5a
f1 (ppm)

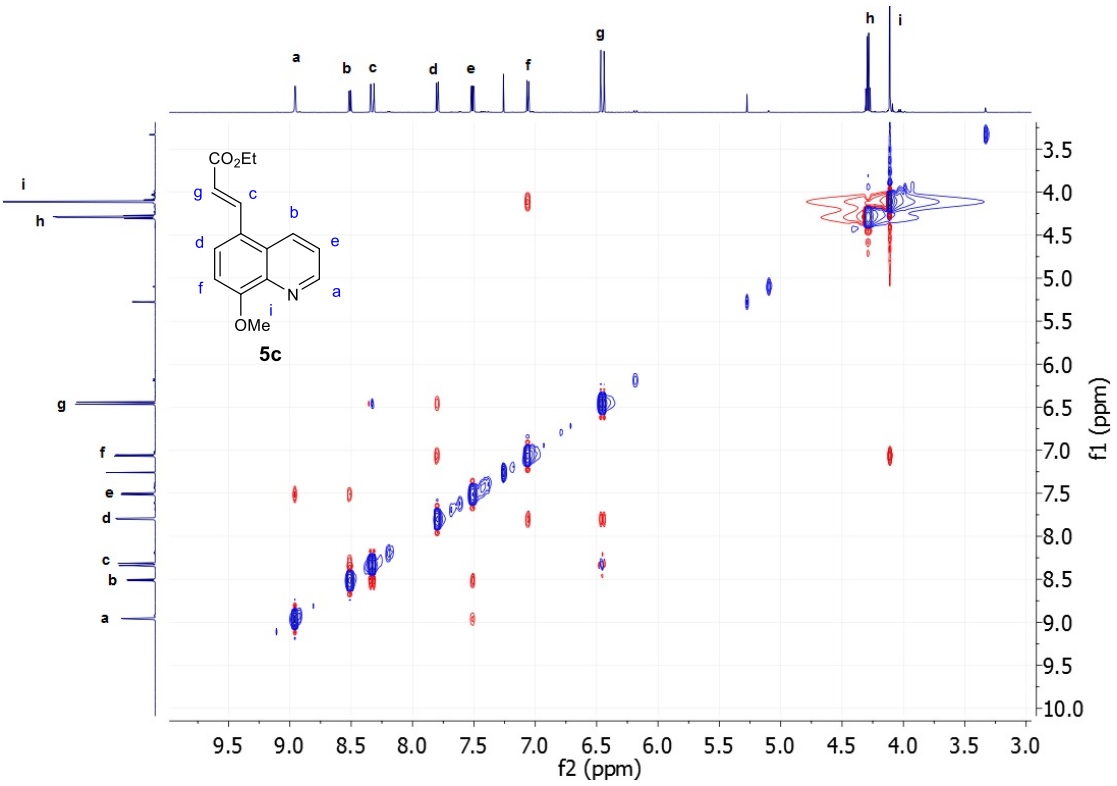

8.376
8.370
8.368
8.354
8.353
8.349
7.901
7.899
7.898
7.897
7.888
7.886
7.885
7.883
7.647
7.646
7.644
7.643
7.634
7.633
7.632
7.631
7.625
7.612
7.600
6.987
6.972
6.530
6.504
4.329
4.317
4.305
4.293
4.080
1.382
1.371
1.359
0.000
COOEt
N
OMe
5b
2.03
1.00
1.04
0.99
1.00
1.00
2.06
3.17
3.12
f1 (ppm)

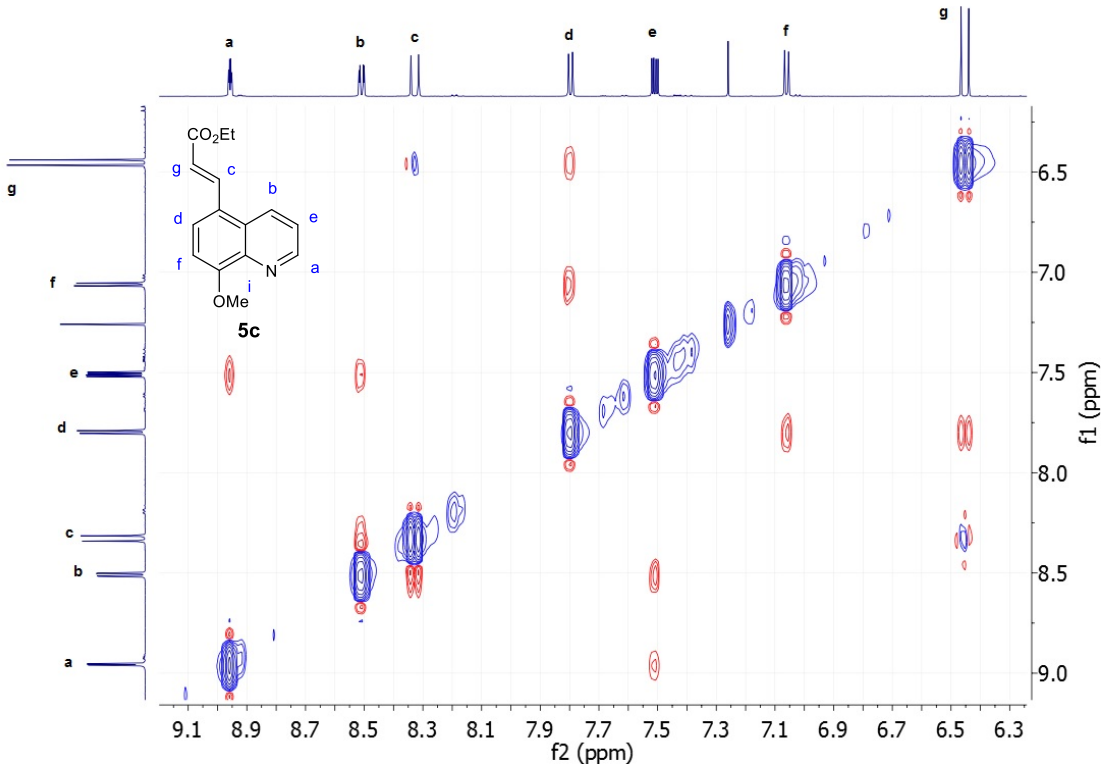

166.704
162.388
147.019
140.489
134.253
131.832
129.516
129.122
123.391
122.711
121.415
113.669
77.234
77.022
76.811
60.699
53.441
14.358
0.000
COOEt
N
OMe
5b
f1 (ppm)

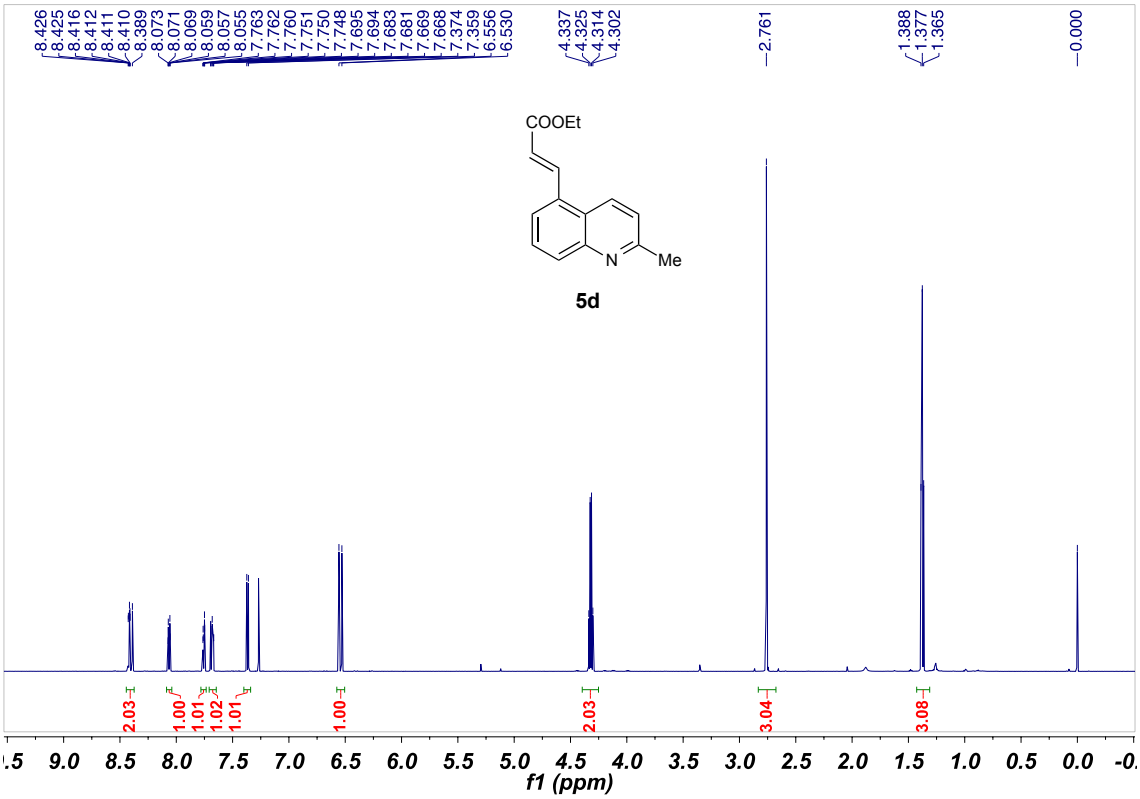

8.985
8.982
8.978
8.975
8.540
8.538
8.526
8.523
8.364
8.363
8.338
8.337
7.827
7.826
7.814
7.812
7.543
7.536
7.529
7.522
7.283
7.090
7.077
6.489
6.463
4.330
4.318
4.306
4.294
4.134
1.385
1.373
1.362
COOEt
N
OMe
5c
1.02
1.01
1.01
1.01
1.03
1.02
1.00
2.02
3.00
3.01
f1 (ppm)

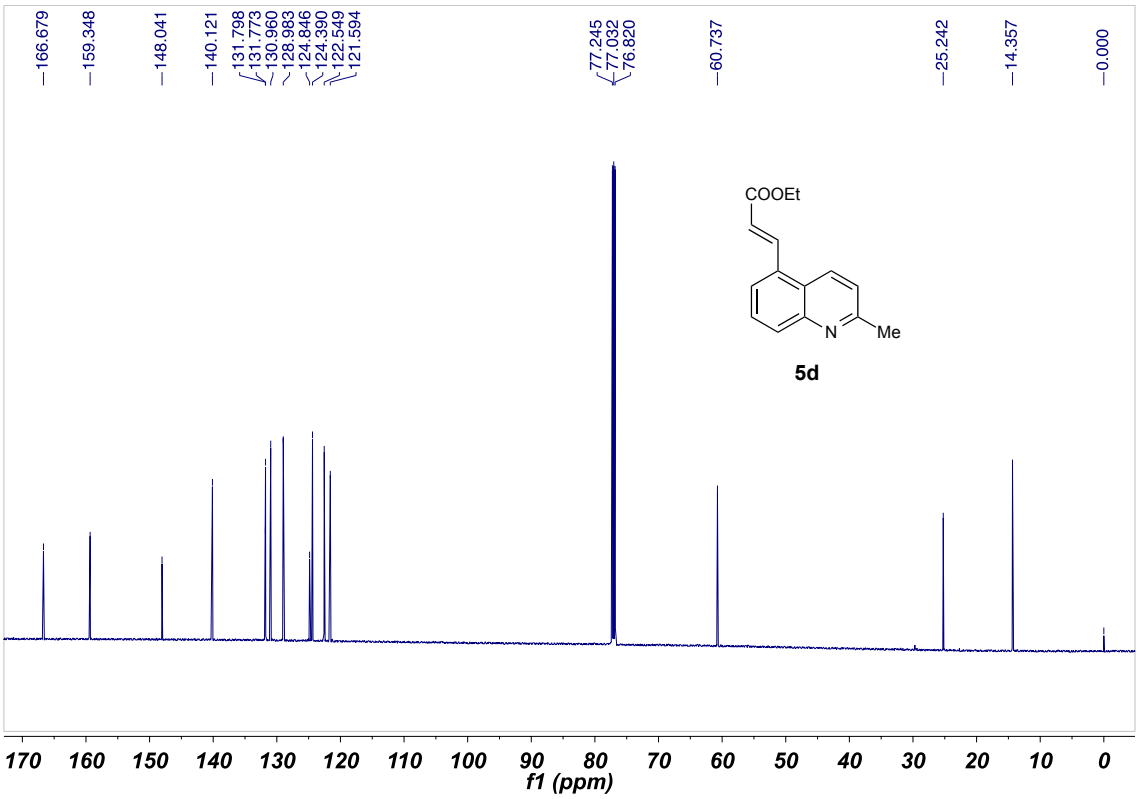

166.945
157.090
149.439
140.058
139.696
131.714
127.665
126.134
123.722
122.245
119.246
107.429
77.272
77.061
76.849
60.594
56.216
14.386
COOEt
N
OMe
5c
f1 (ppm)

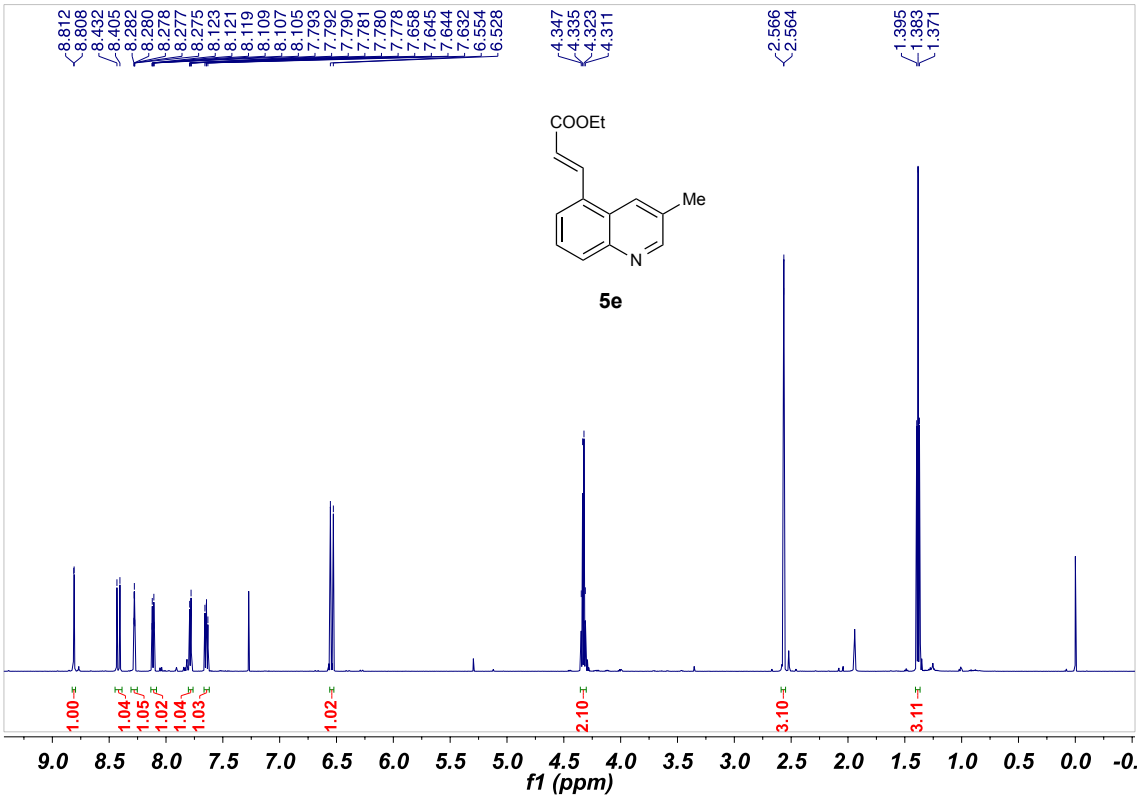
2D NOESY of compound **5c**

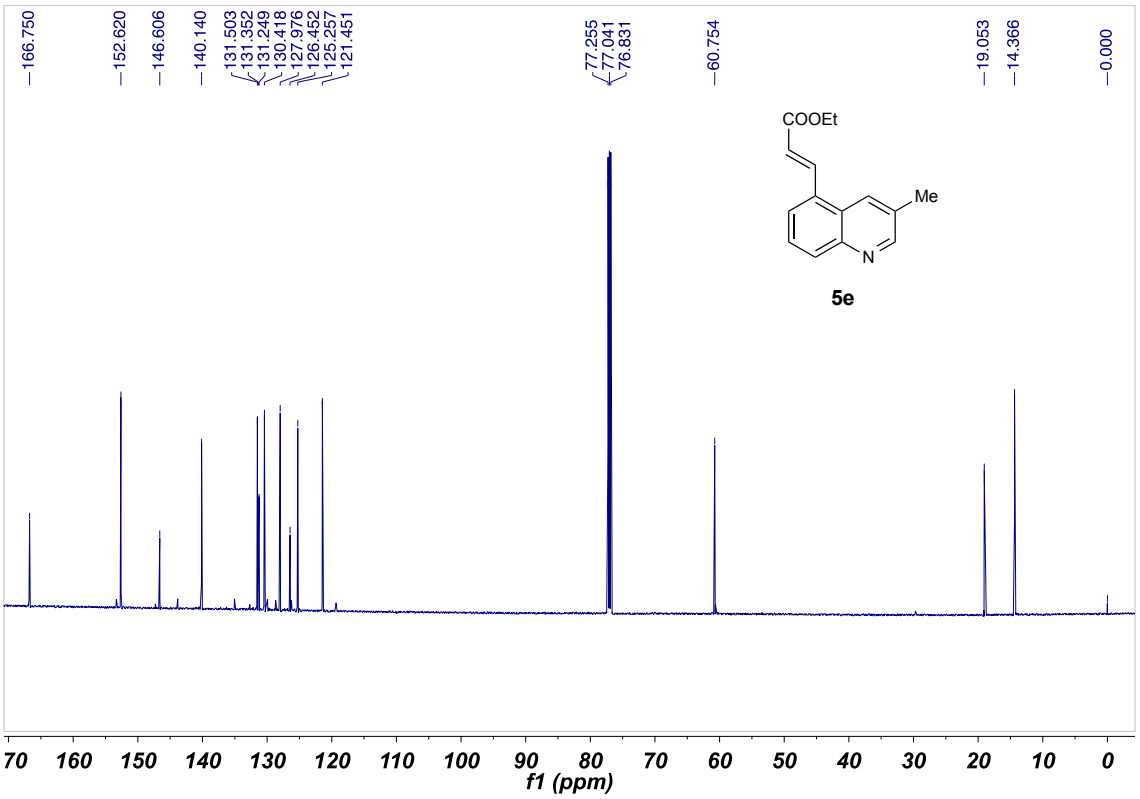


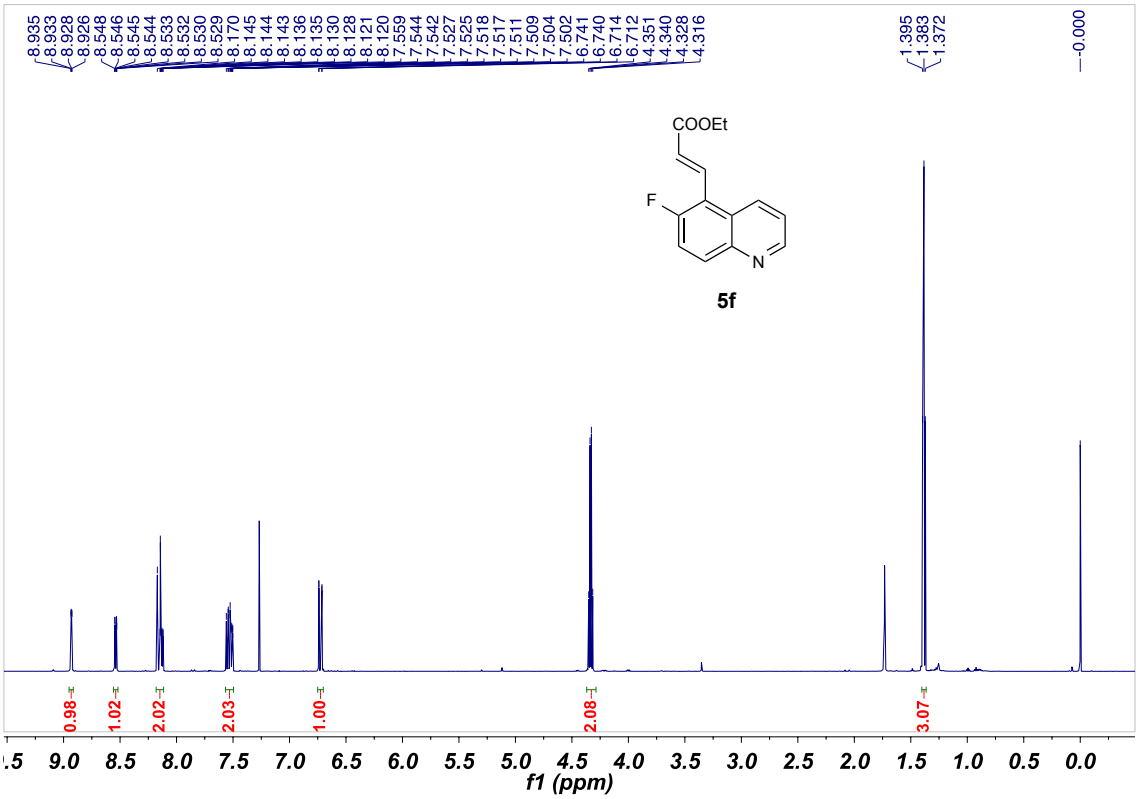


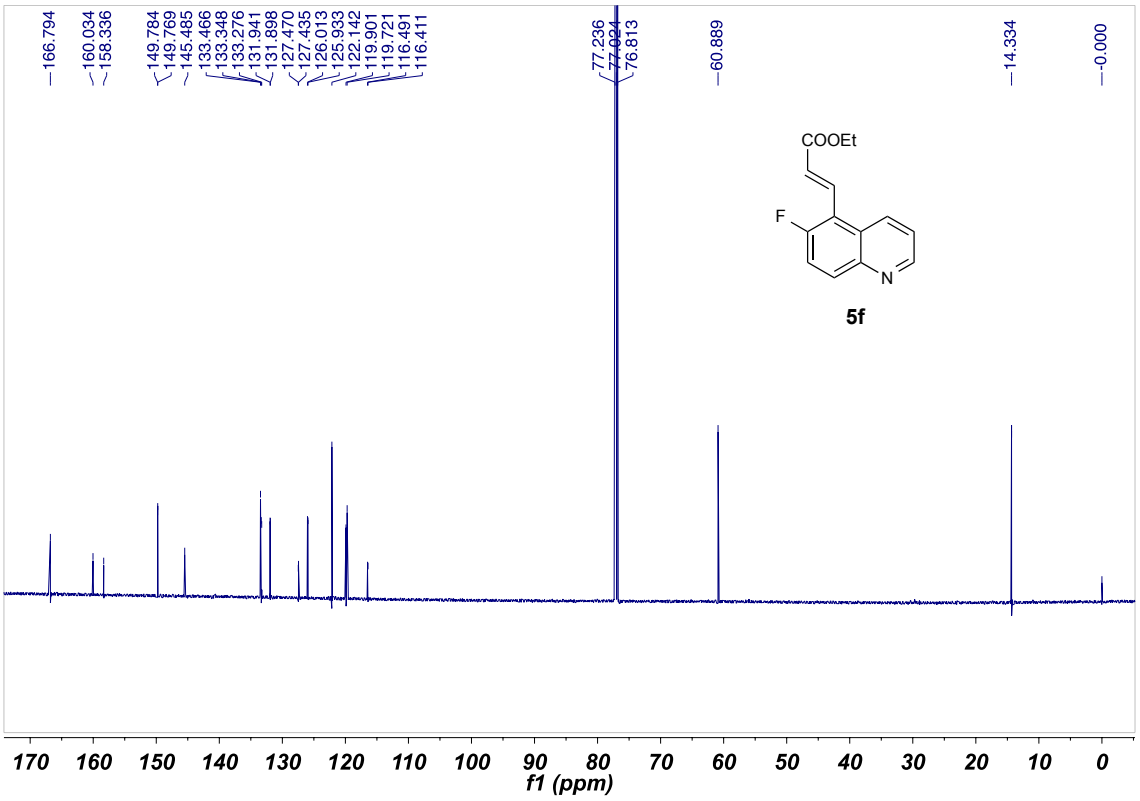

8.426
8.425
8.416
8.412
8.411
8.410
8.389
8.073
8.071
8.069
8.059
8.057
8.055
7.763
7.762
7.760
7.751
7.750
7.748
7.695
7.694
7.683
7.681
7.669
7.668
7.374
7.359
6.556
6.530
4.337
4.325
4.314
4.302
2.761
1.388
1.377
1.365
0.000
COOEt
N
Me
5d
2.03
1.00
1.01
1.02
1.01
1.00
2.03
3.04
3.08
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

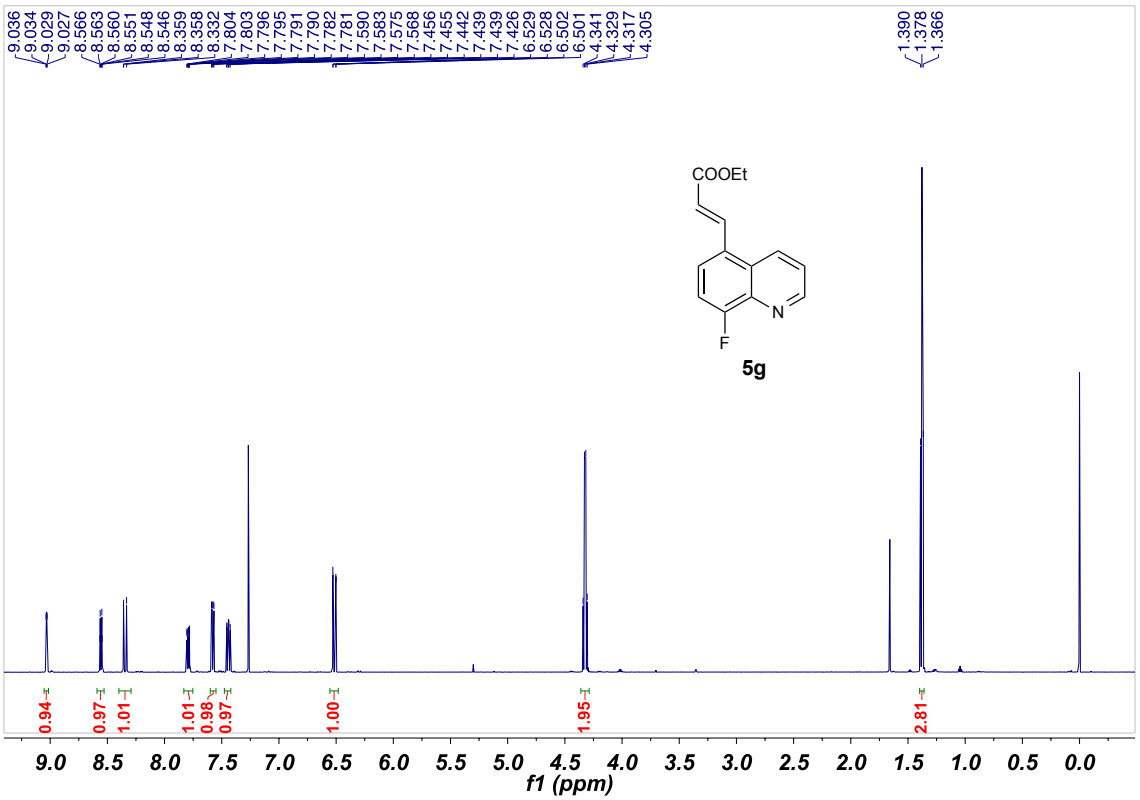

166.679
159.348
148.041
140.121
131.798
131.773
130.960
128.983
124.846
124.390
122.549
121.594
77.245
77.032
76.820
60.737
25.242
14.357
0.000
COOEt
N
Me
5d
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.812
8.808
8.432
8.405
8.282
8.280
8.278
8.277
8.275
8.123
8.121
8.119
8.109
8.107
8.105
7.793
7.792
7.790
7.781
7.780
7.778
7.658
7.645
7.644
7.632
6.554
6.528
4.347
4.335
4.323
4.311
2.566
2.564
1.395
1.383
1.371
COOEt
Me
N
5e
1.00
1.04
1.05
1.02
1.04
1.03
1.02
2.10
3.10
3.11
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.
f1 (ppm)


166.750
152.620
146.606
140.140
131.503
131.352
131.249
130.418
127.976
126.452
125.257
121.451
77.255
77.041
76.831
60.754
19.053
14.366
0.000
COOEt
Me
N
5e
70 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.935
8.933
8.928
8.926
8.548
8.546
8.545
8.544
8.533
8.532
8.530
8.529
8.170
8.145
8.144
8.143
8.136
8.135
8.130
8.128
8.121
8.120
7.559
7.544
7.542
7.527
7.525
7.518
7.517
7.511
7.509
7.504
7.502
6.741
6.740
6.714
6.712
4.351
4.340
4.328
4.316
1.395
1.383
1.372
0.000
COOEt
F
N
5f
0.98
1.02
2.02
2.03
1.00
2.08
3.07
f1 (ppm)


166.794
160.034
158.336
149.784
149.769
145.485
133.466
133.348
133.276
131.941
131.898
127.470
127.435
126.013
125.933
122.142
119.901
119.721
116.491
116.411
77.236
77.024
76.813
60.889
14.334
0.000
COOEt
F
N
5f
f1 (ppm)


9.036
9.034
9.029
9.027
8.566
8.563
8.560
8.551
8.548
8.546
8.359
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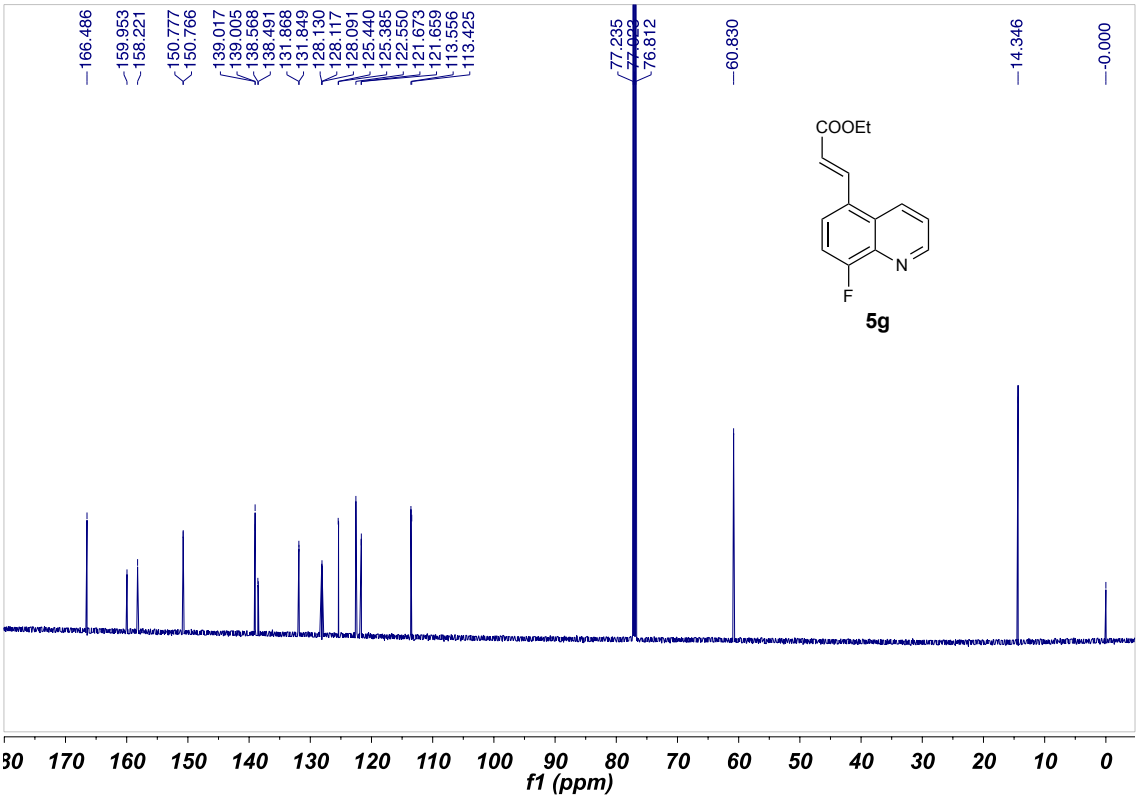
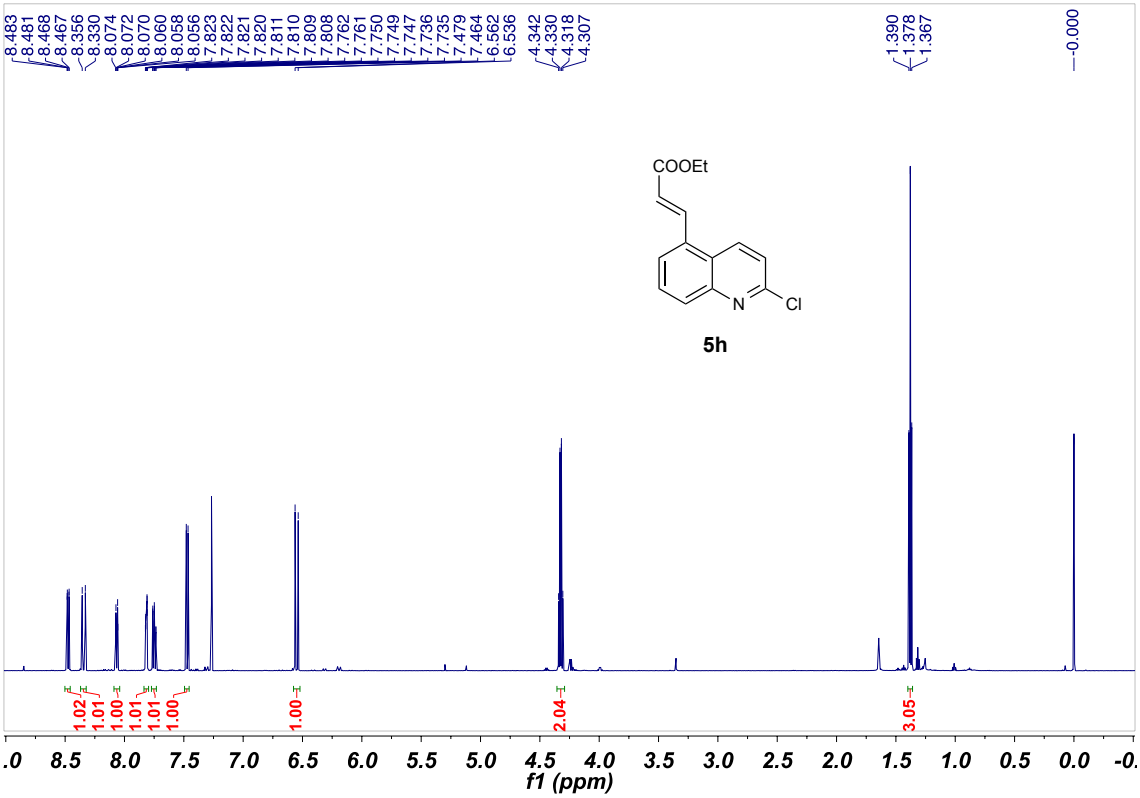
8.332
7.804
7.803
7.796
7.795
7.791
7.790
7.782
7.781
7.590
7.583
7.575
7.568
7.456
7.455
7.442
7.439
7.439
7.426
6.529
6.528
6.502
6.501
4.341
4.329
4.317
4.305
1.390
1.378
1.366
COOEt
N
F
5g
0.94
0.97
1.01
1.01
0.98
0.97
1.00
1.95
2.81
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


166.486
159.953
158.221
150.777
150.766
139.017
139.005
138.568
138.491
131.868
131.849
128.130
128.117
128.091
125.440
125.385
122.550
121.673
121.659
113.556
113.425
77.235
77.000
76.812
60.830
14.346
-0.000
COOEt
N
F
5g
30 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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8.481
8.468
8.467
8.356
8.330
8.074
8.072
8.070
8.060
8.058
8.056
7.823
7.822
7.821
7.820
7.811
7.810
7.809
7.808
7.762
7.761
7.750
7.749
7.747
7.736
7.735
7.479
7.464
6.562
6.536
4.342
4.330
4.318
4.307
1.390
1.378
1.367
0.000
COOEt
N
Cl
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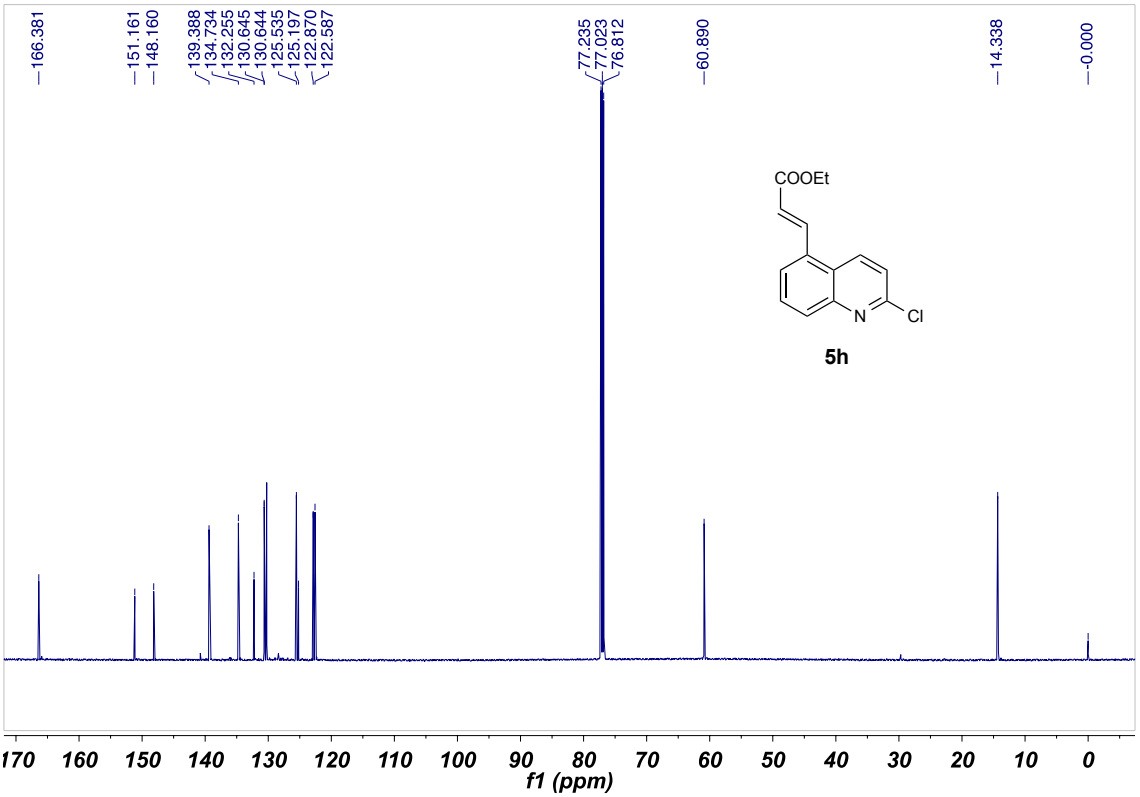
1.01
1.00
1.01
1.01
1.00
1.00
2.04
3.05
f1 (ppm)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139.388
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130.644
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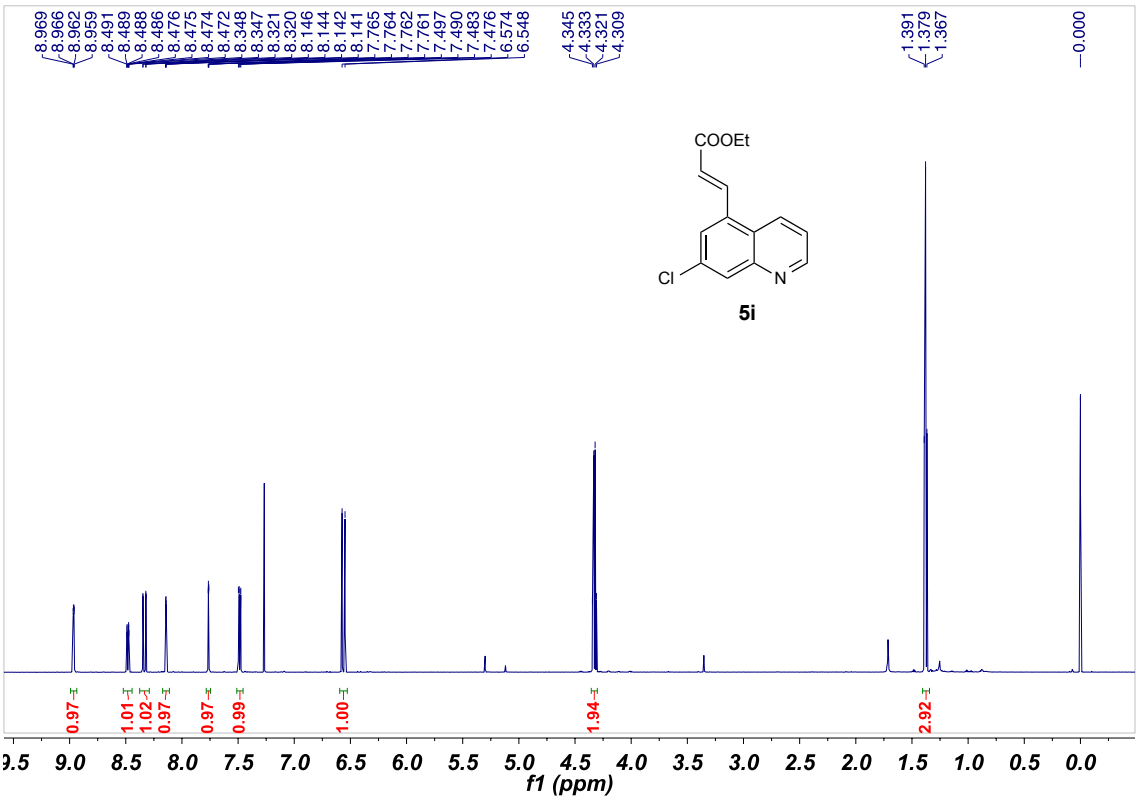
77.023
76.812
60.890
14.338
0.000
COOEt
N
Cl
5h
f1 (ppm)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8.962
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8.491
8.489
8.488
8.486
8.476
8.475
8.474
8.472
8.348
8.347
8.321
8.320
8.146
8.144
8.142
8.141
7.765
7.764
7.762
7.761
7.497
7.490
7.483
7.476
6.574
6.548
4.345
4.333
4.321
4.309
1.391
1.379
1.367
0.000
COOEt
Cl
N
5i
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1.01
1.02
0.97
0.97
0.99
1.00
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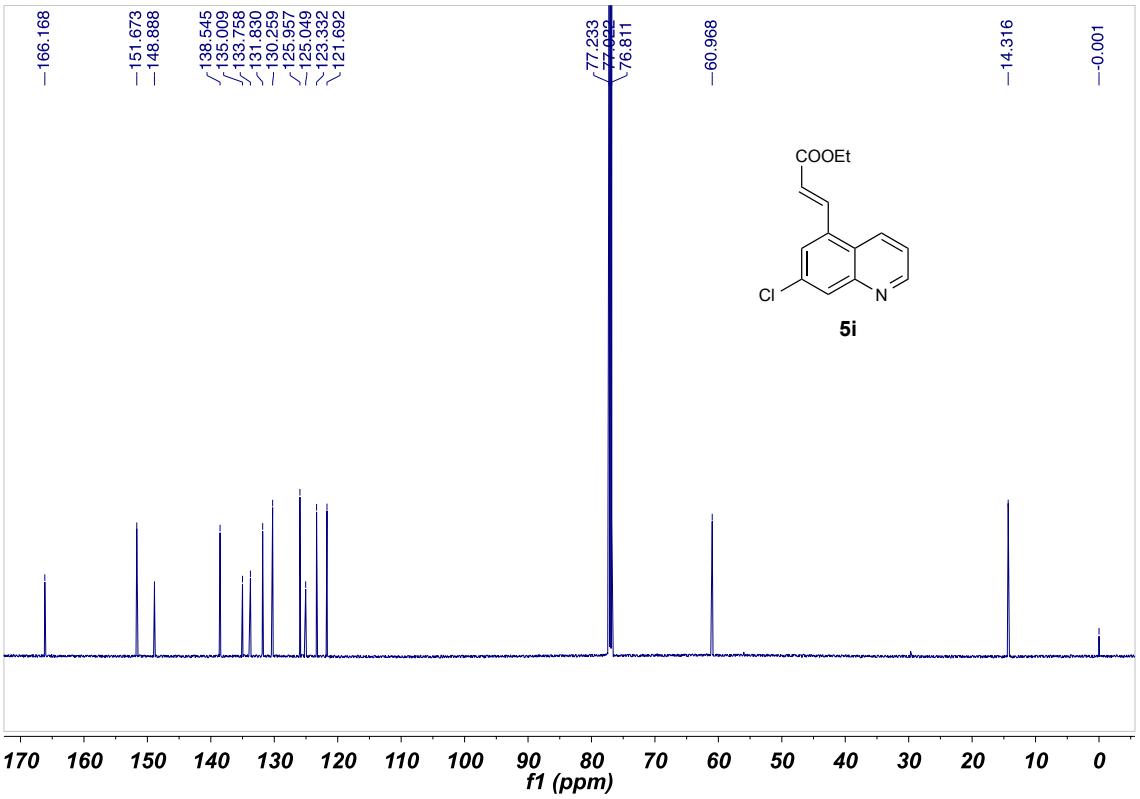
f1 (ppm)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151.673
148.888
138.545
135.009
133.758
131.830
130.259
125.957
125.049
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77.233
76.811
60.968
14.316
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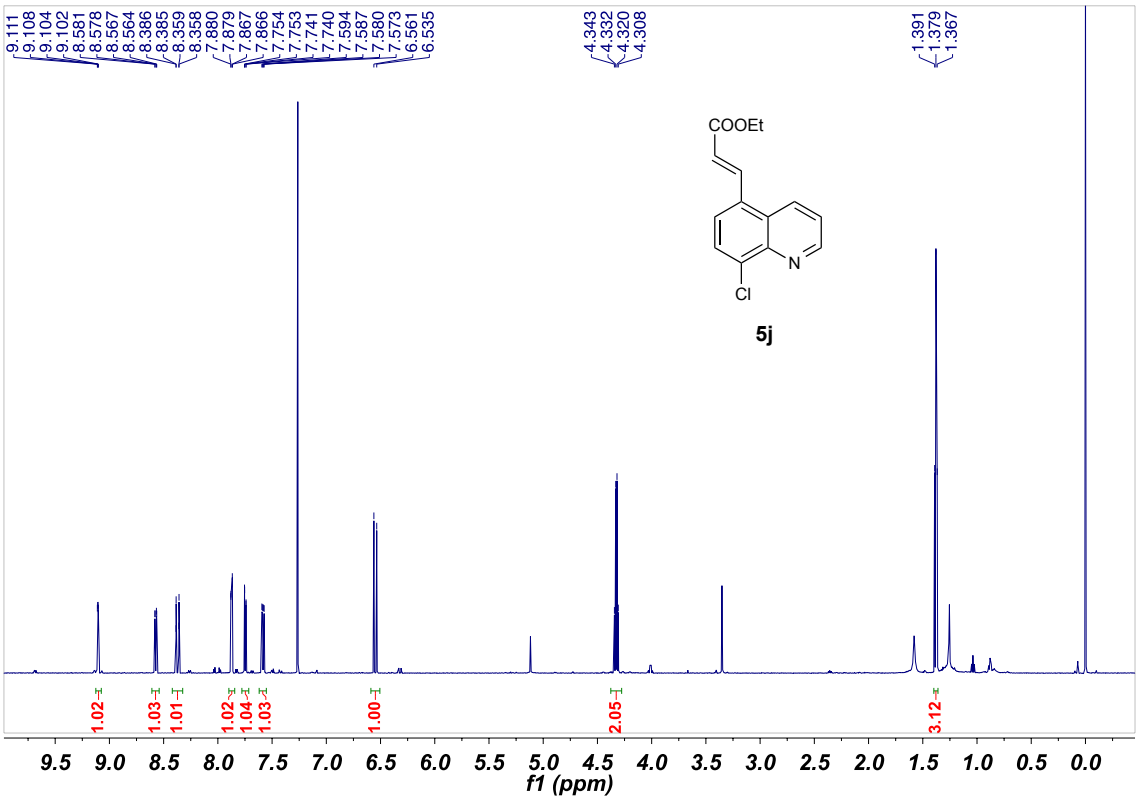
COOEt
Cl
N
5i
f1 (ppm)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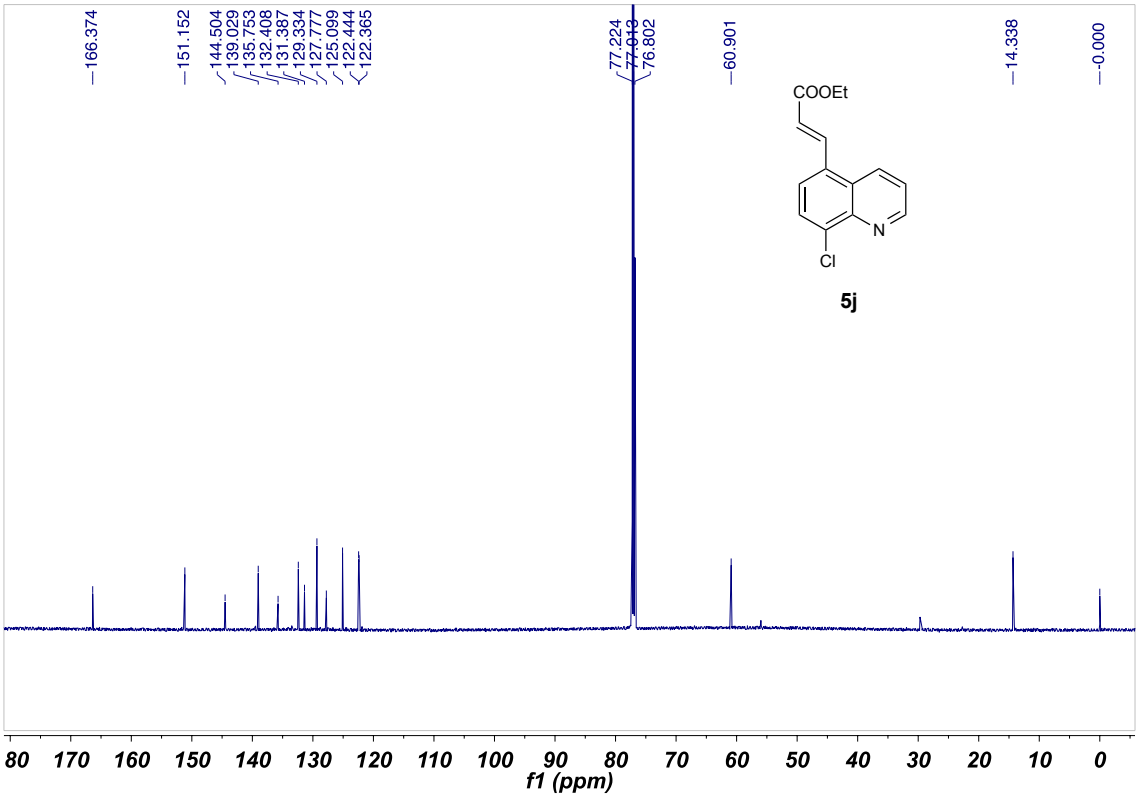
9.108
9.104
9.102
8.581
8.578
8.567
8.564
8.386
8.385
8.359
8.358
7.880
7.879
7.867
7.866
7.754
7.753
7.741
7.740
7.594
7.587
7.580
7.573
6.561
6.535
4.343
4.332
4.320
4.308
1.391
1.379
1.367
COOEt
N
Cl
5j
1.02
1.03
1.01
1.02
1.04
1.03
1.00
2.05
3.12
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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135.753
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131.387
129.334
127.777
125.099
122.444
122.365
77.224
77.013
76.802
60.901
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0.000
COOEt
N
Cl
5j
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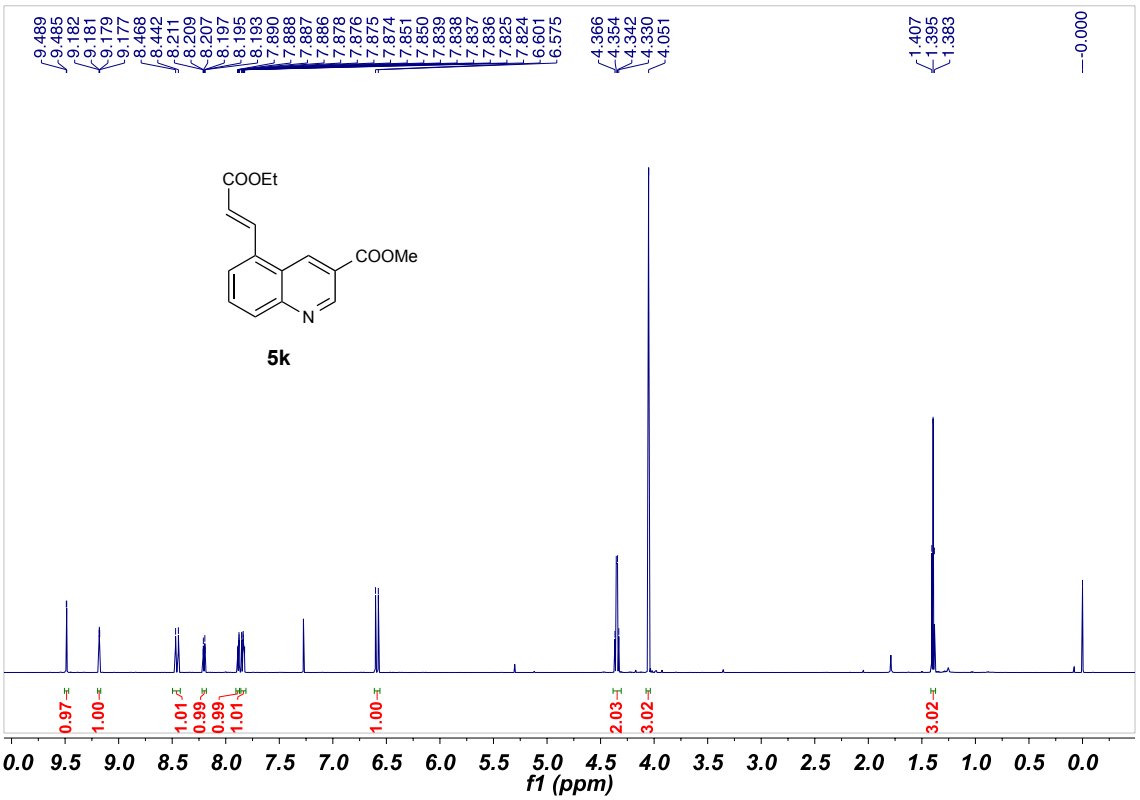
f1 (ppm)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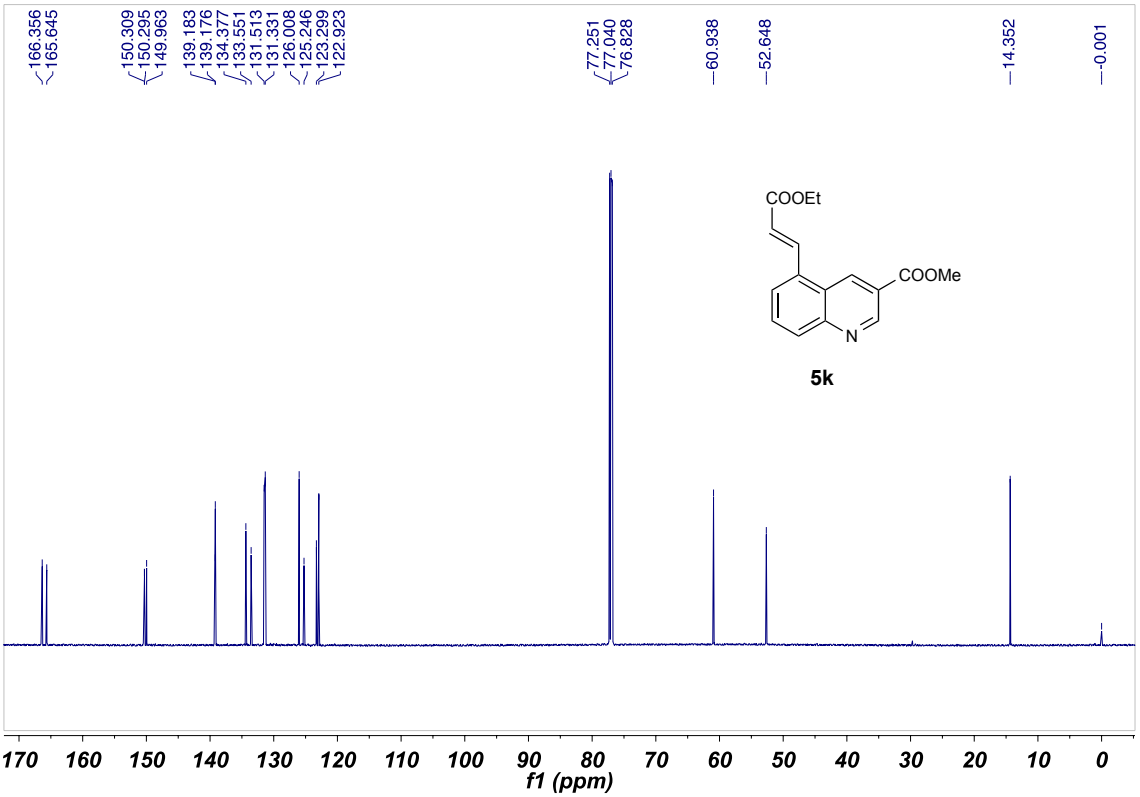
9.485
9.182
9.181
9.179
9.177
8.468
8.442
8.211
8.209
8.207
8.197
8.195
8.193
7.890
7.888
7.887
7.886
7.878
7.876
7.875
7.874
7.851
7.850
7.839
7.838
7.837
7.836
7.825
7.824
6.601
6.575
4.366
4.354
4.342
4.330
4.051
1.407
1.395
1.383
-0.000
COOEt
COOMe
N
5k
0.97
1.00
1.01
0.99
0.99
1.01
1.00
2.03
3.02
3.02
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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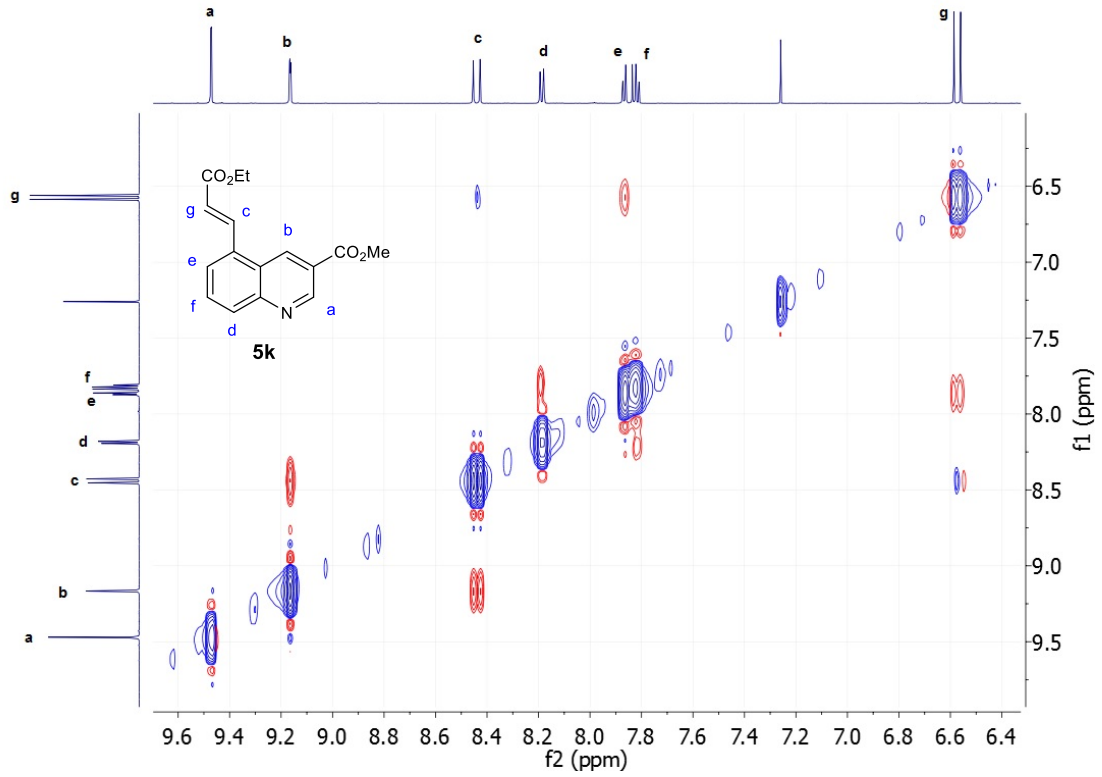
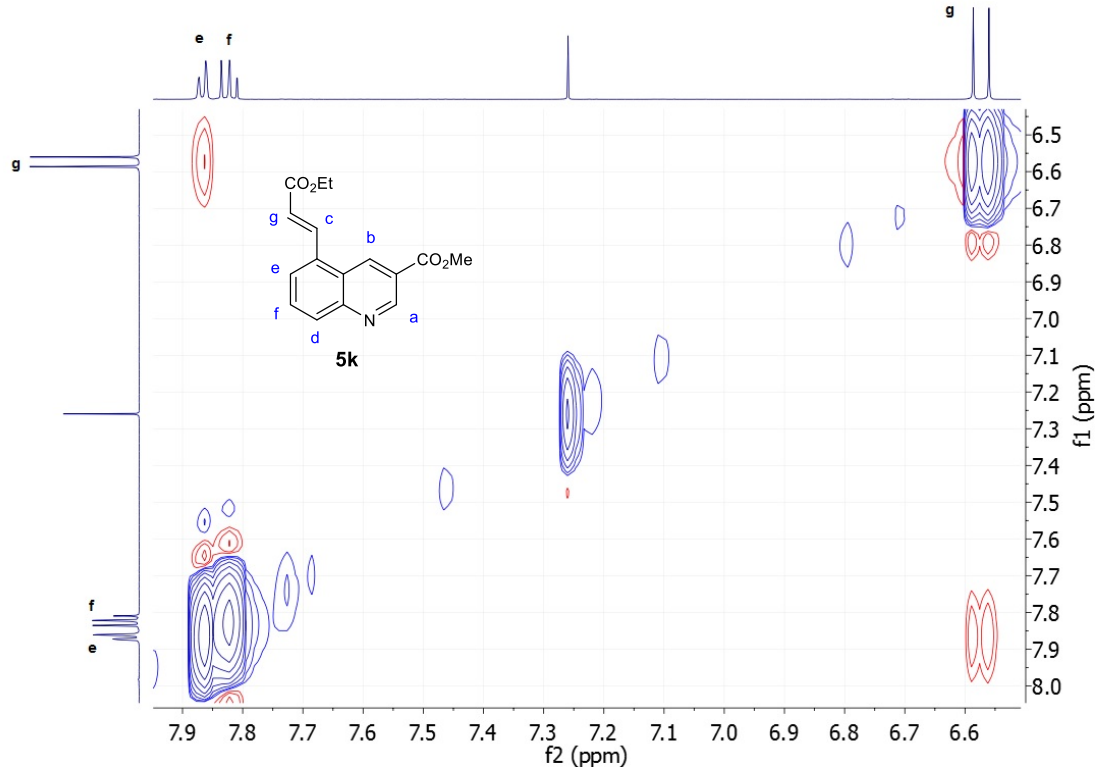
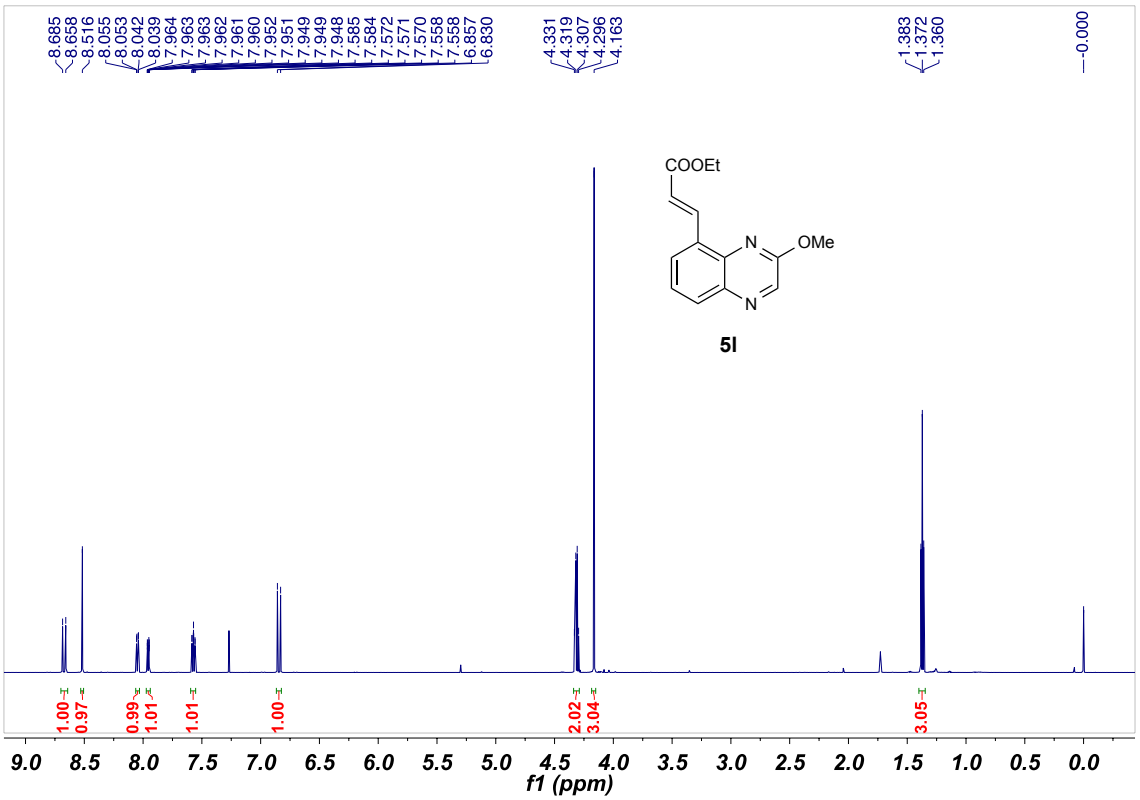
150.295
149.963
139.183
139.176
134.377
133.551
131.513
131.331
126.008
125.246
123.299
122.923
77.251
77.040
76.828
60.938
52.648
14.352
-0.001
COOEt
COOMe
N
5k
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

2D NOESY of compound **5k**



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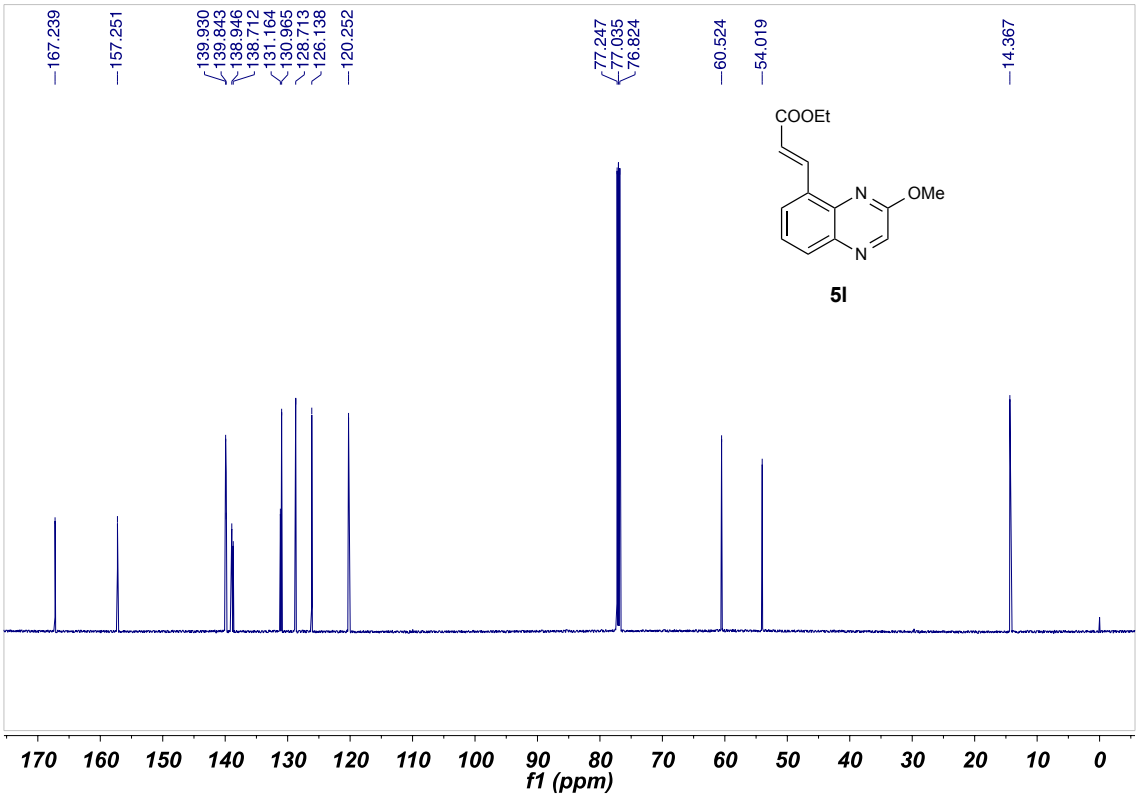
8.516
8.055
8.053
8.042
8.039
7.964
7.963
7.963
7.962
7.961
7.960
7.952
7.951
7.949
7.949
7.948
7.585
7.584
7.572
7.571
7.570
7.558
7.558
6.857
6.830
4.331
4.319
4.307
4.296
4.163
1.383
1.372
1.360
-0.000
COOEt
N
OMe
N
5l
1.00
0.97
0.99
1.01
1.01
1.00
2.02
3.04
3.05
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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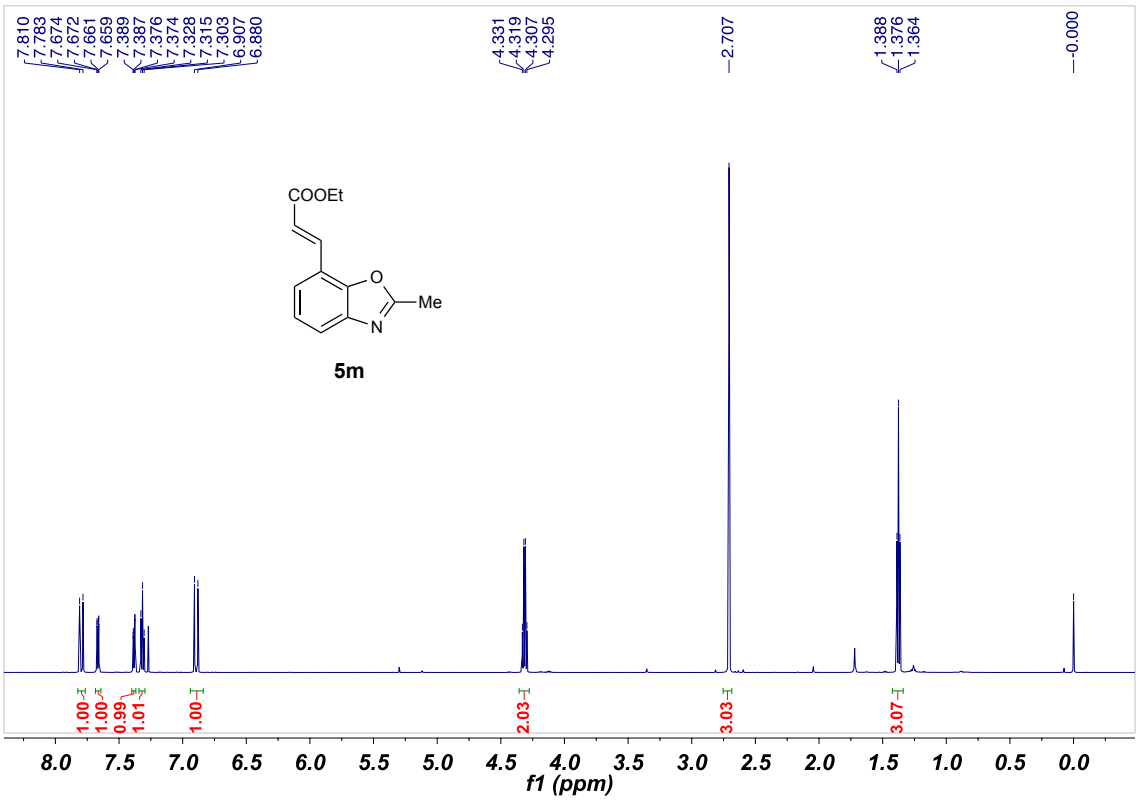
157.251
139.930
139.843
138.946
138.712
131.164
130.965
128.713
126.138
120.252
77.247
77.035
76.824
60.524
54.019
14.367
COOEt
N
OMe
N
5l
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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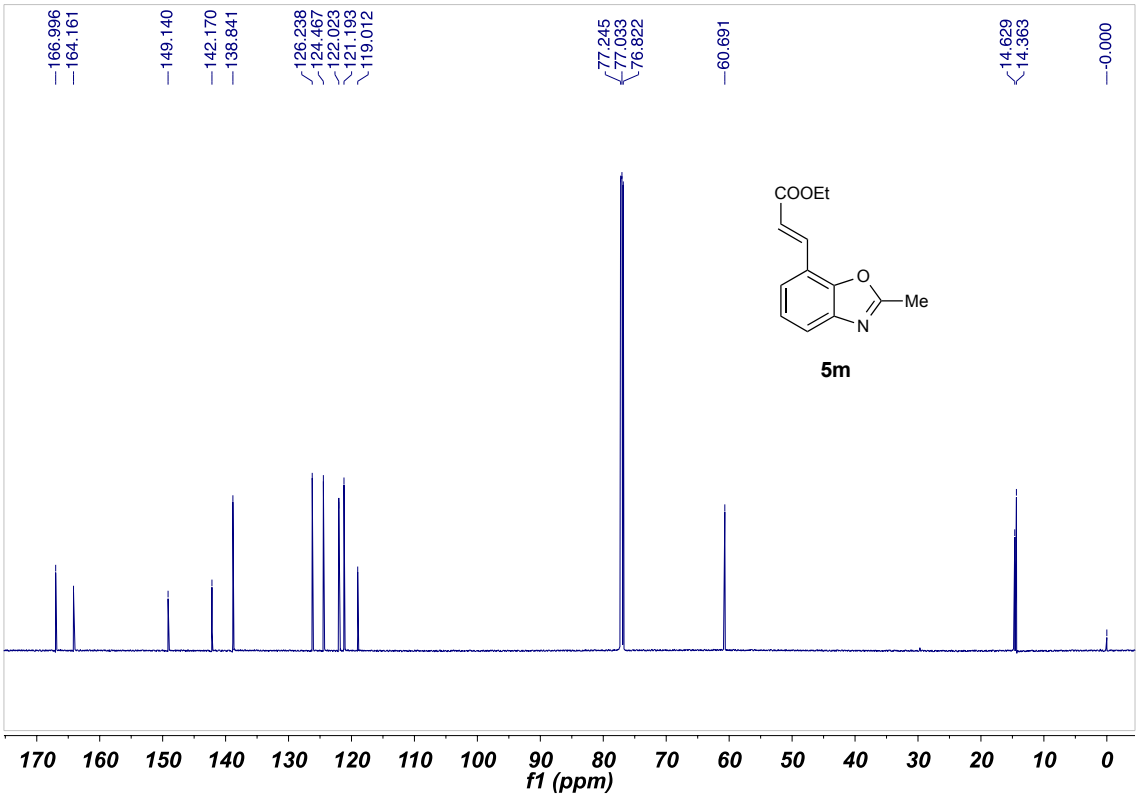
7.783
7.674
7.672
7.661
7.659
7.389
7.387
7.376
7.374
7.328
7.315
7.303
6.907
6.880
4.331
4.319
4.307
4.295
2.707
1.388
1.376
1.364
0.000
COOEt
O
Me
N
5m
1.00
1.00
0.99
1.01
1.00
2.03
3.03
3.07
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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138.841
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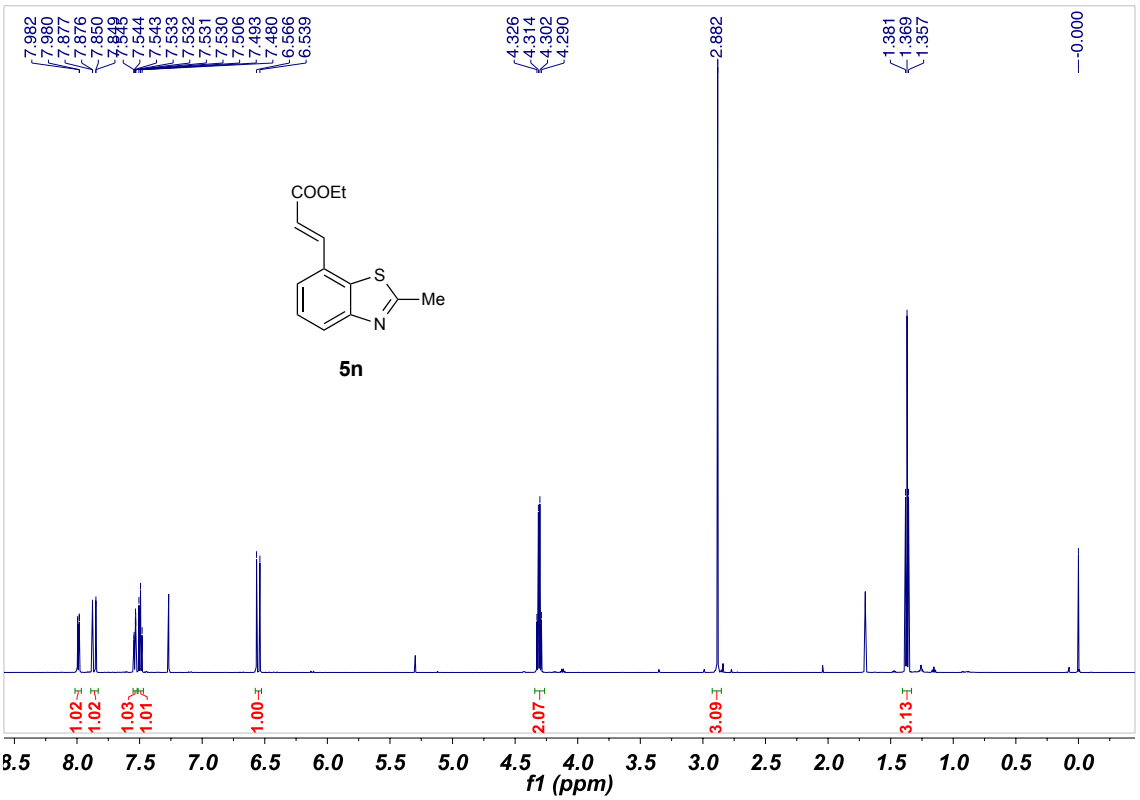
124.467
122.023
121.193
119.012
77.245
77.033
76.822
60.691
14.629
14.363
0.000
COOEt
O
Me
N
5m
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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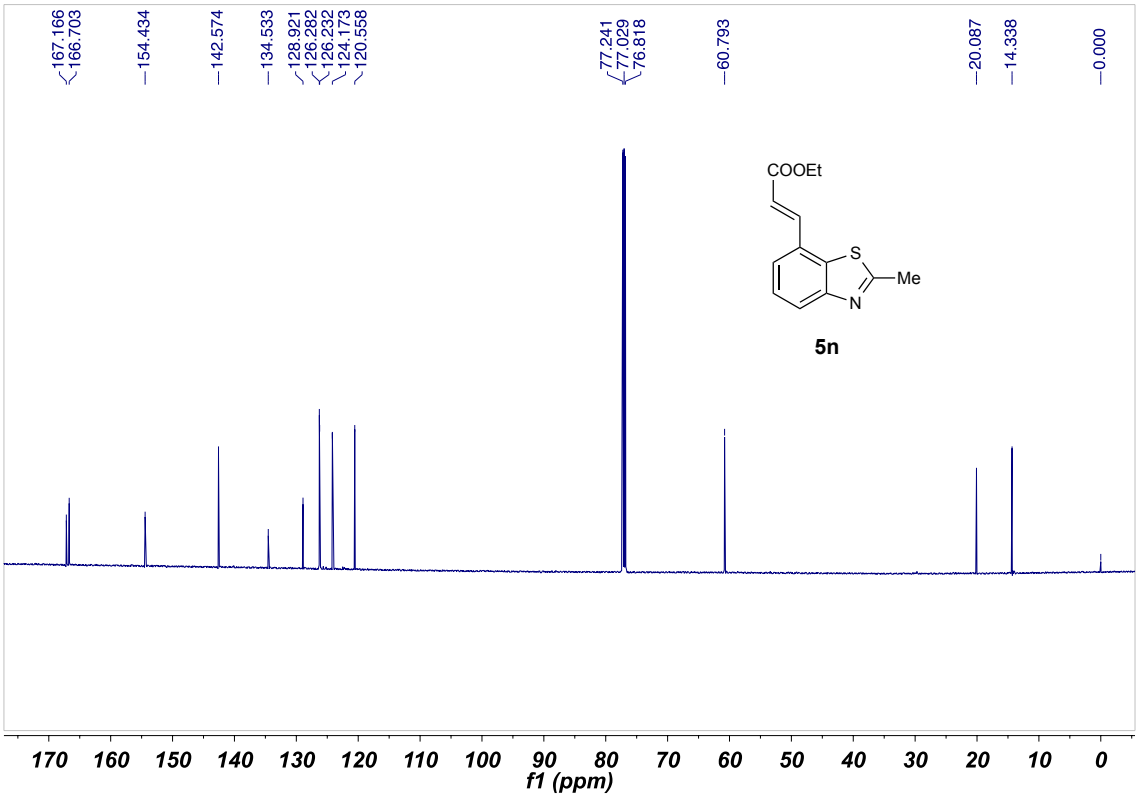
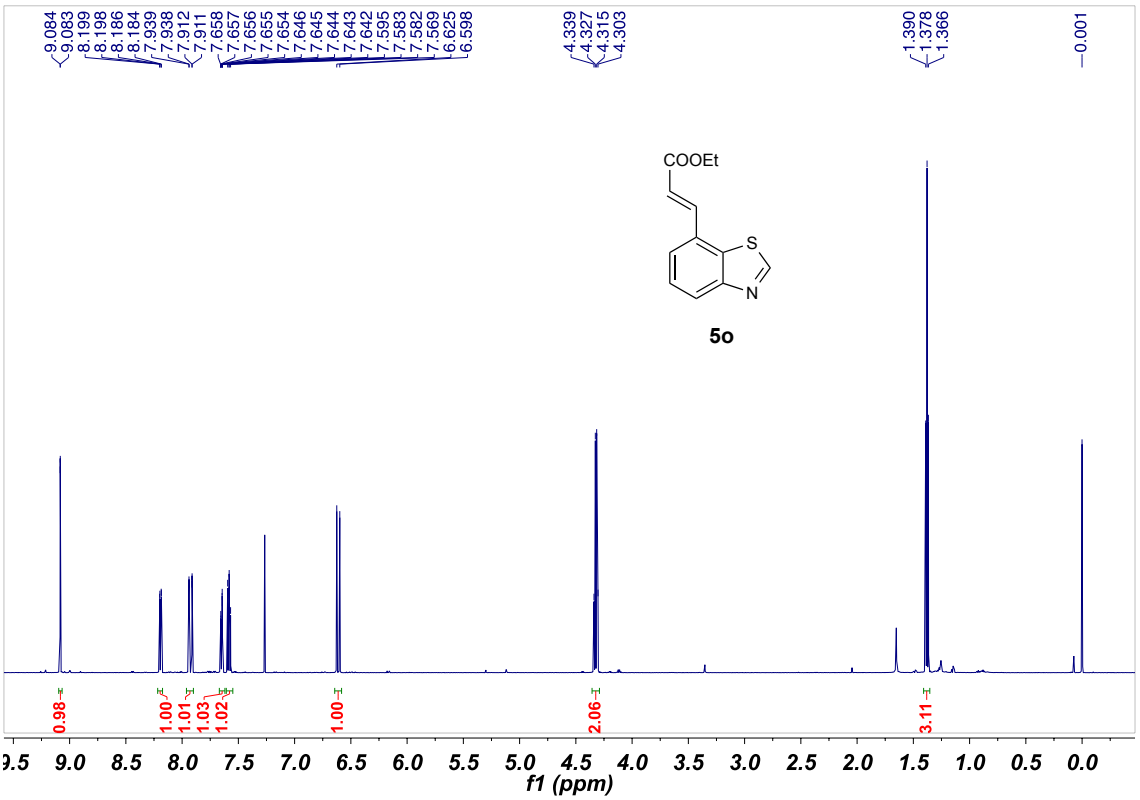
7.877
7.876
7.850
7.544
7.543
7.533
7.532
7.531
7.530
7.506
7.493
7.480
6.566
6.539
4.326
4.314
4.302
4.290
2.882
1.381
1.369
1.357
0.000
COOEt
S
Me
N
5n
1.02
1.02
1.03
1.01
1.00
2.07
3.09
3.13
f1 (ppm)


167.166
166.703
154.434
142.574
134.533
128.921
126.282
126.232
124.173
120.558
77.241
77.029
76.818
60.793
20.087
14.338
0.000
COOEt
S
Me
N
5n
f1 (ppm)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9.083
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8.198
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8.184
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7.938
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7.911
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7.656
7.655
7.654
7.646
7.645
7.644
7.643
7.642
7.595
7.583
7.582
7.569
6.625
6.598
4.339
4.327
4.315
4.303
1.390
1.378
1.366
0.001
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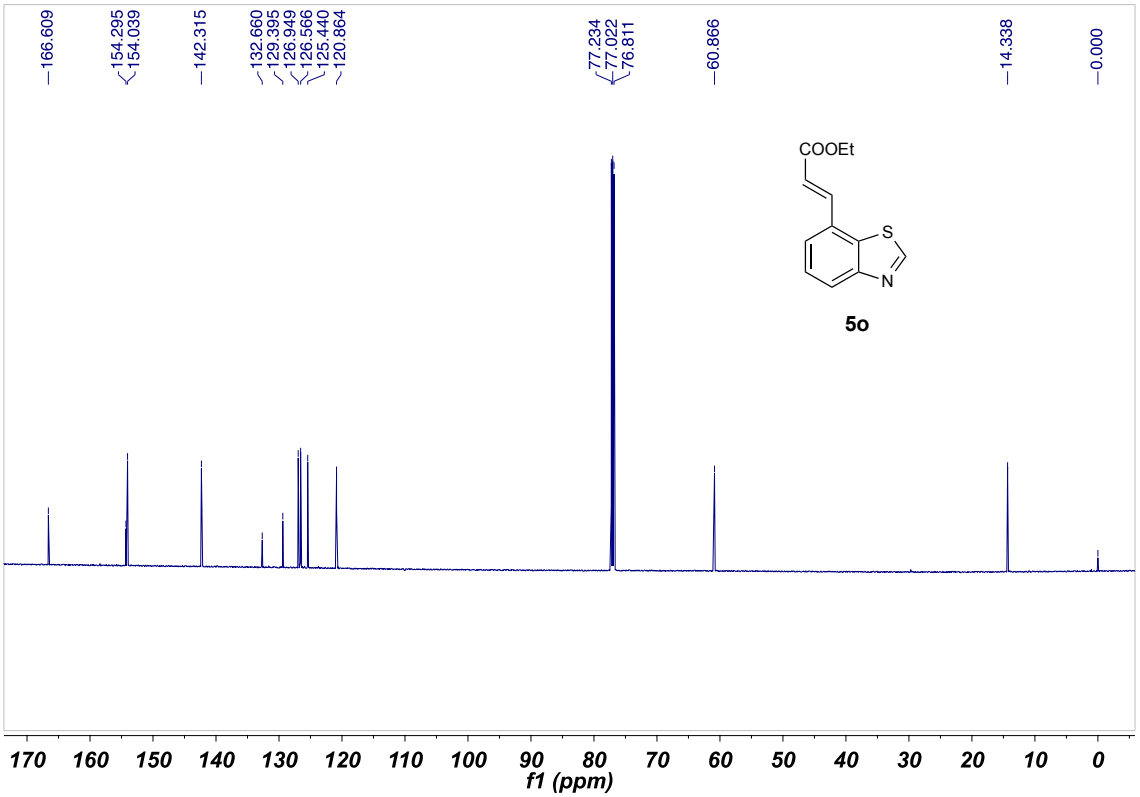
S
N
5o
0.98
1.00
1.01
1.03
1.02
1.00
2.06
3.11
f1 (ppm)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154.039
142.315
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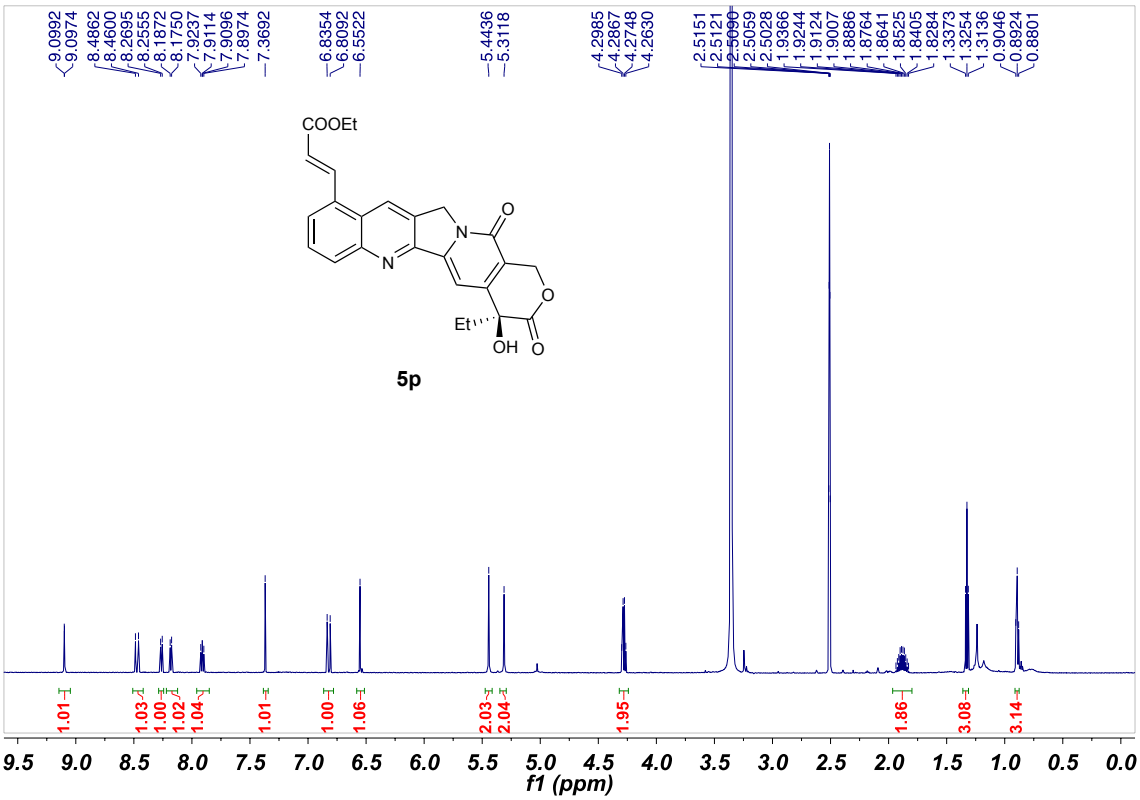
129.395
126.949
126.566
125.440
120.864
77.234
77.022
76.811
60.866
14.338
0.000
COOEt
S
N
5o
f1 (ppm)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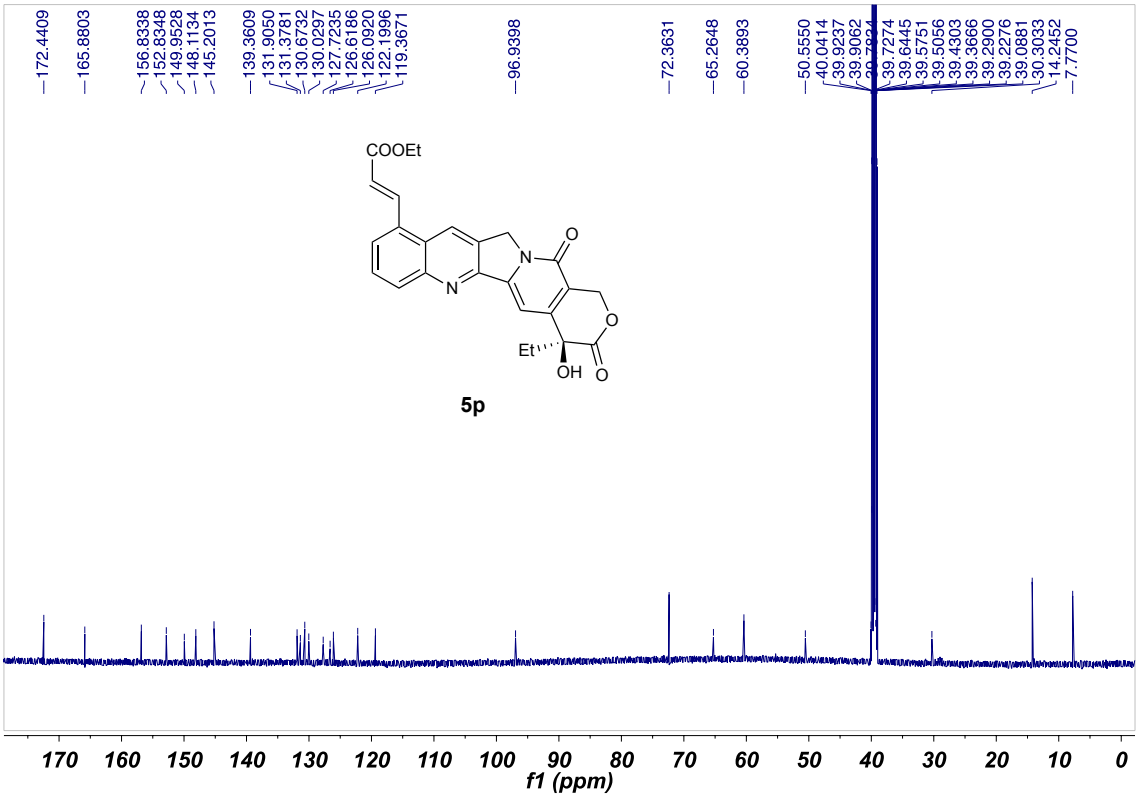
8.4862
8.4600
8.2695
8.2555
8.1872
8.1750
7.9237
7.9114
7.9096
7.8974
7.3692
6.8354
6.8092
6.5522
5.4436
5.3118
4.2985
4.2867
4.2748
4.2630
2.5151
2.5121
2.5090
2.5059
2.5028
1.9366
1.9244
1.9124
1.9007
1.8886
1.8764
1.8641
1.8525
1.8405
1.8284
1.3373
1.3254
1.3136
0.9046
0.8924
0.8801
COOEt
O
N
N
O
Et
OH
O
5p
1.01
1.03
1.00
1.02
1.04
1.01
1.00
1.06
2.03
2.04
1.95
1.86
3.08
3.14
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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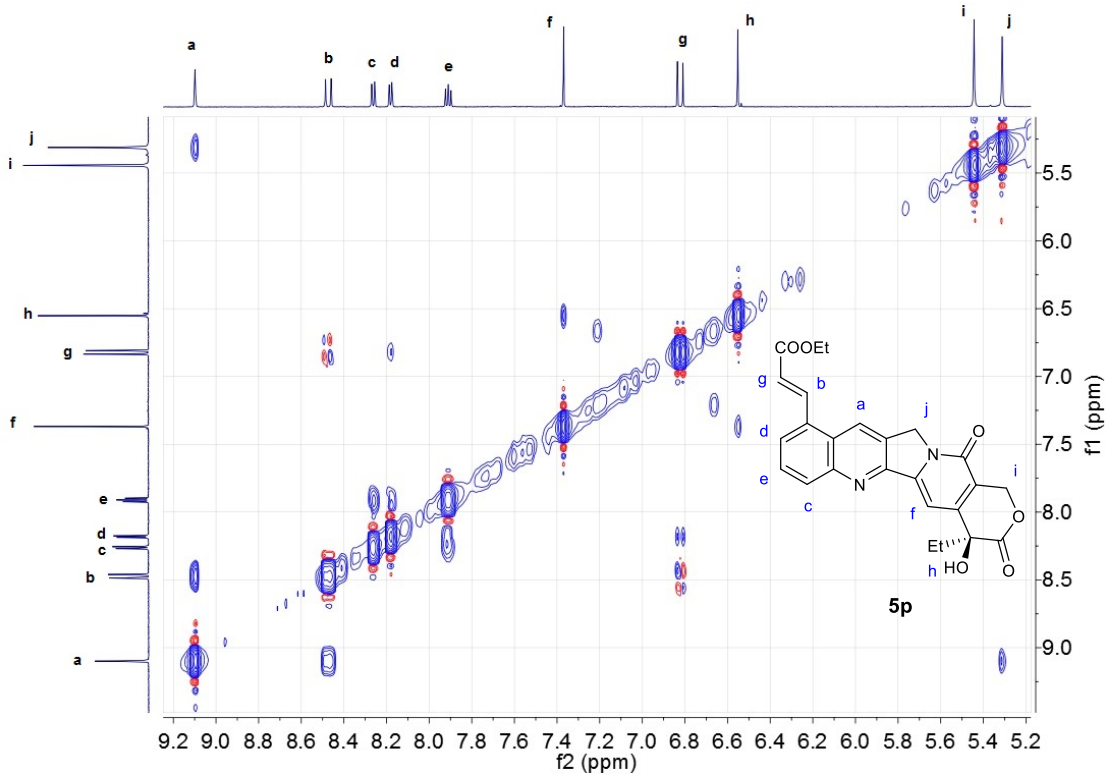
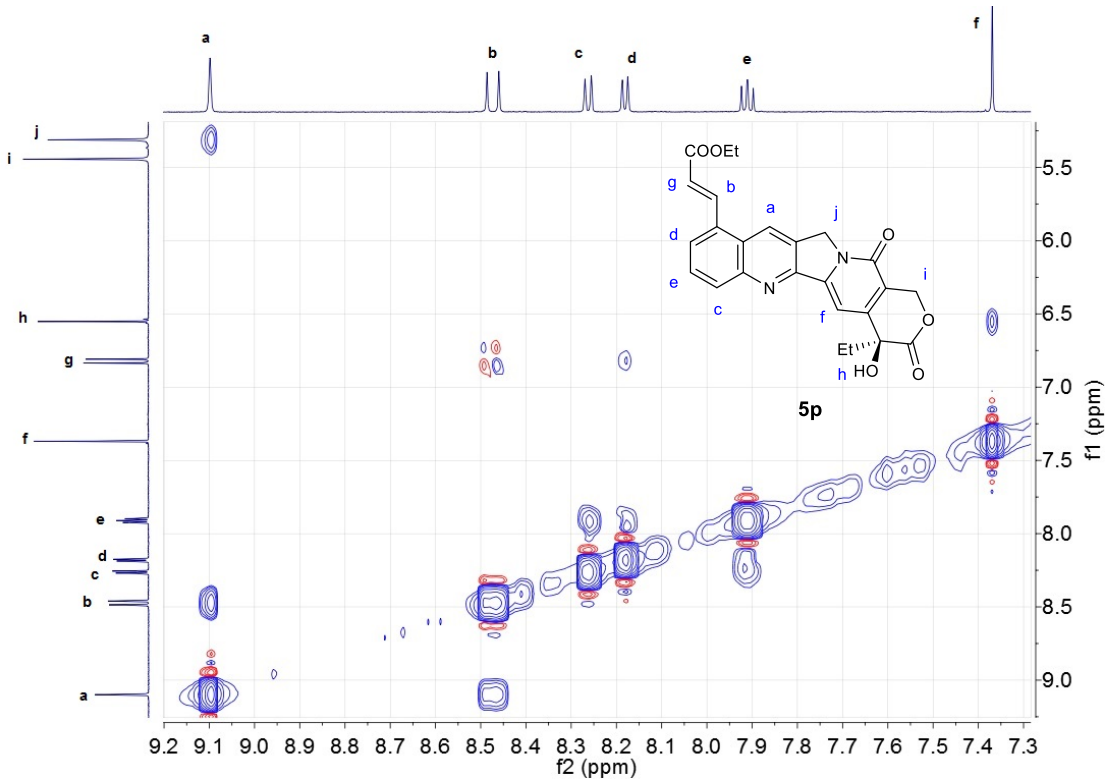
156.8338
152.8348
149.9528
148.1134
145.2013
139.3609
131.9050
131.3781
130.6732
130.0297
127.7235
126.6186
126.0920
122.1996
119.3671
96.9398
72.3631
65.2648
60.3893
50.5550
40.0414
39.9237
39.9062
39.7274
39.6445
39.5751
39.5056
39.4303
39.3666
39.2900
39.2276
39.0881
30.3033
14.2452
7.7700
COOEt
O
N
N
O
Et
OH
O
5p
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

2D NOESY of compound **5p**



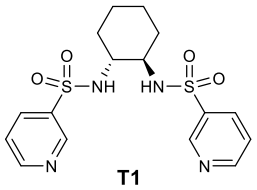


10. X-Ray Crystallographic Data

Experimental Summary

The single crystal X-ray diffraction studies were carried out on a Bruker Kappa APEX-II CCD diffractometer equipped with Mo K_α radiation (λ = 0.71073 Å). A 0.217 x 0.183 x 0.155 mm piece of a colorless block was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using ϕ and ϖ scans. Crystal-to-detector distance was 40 mm and exposure time was 5 seconds per frame using a scan width of 1.0°. Data collection was 99.8% complete to 25.00° in θ. A total of 13470 reflections were collected covering the indices, -20<=h<=20, -10<=k<=10, -12<=l<=18. 4124 reflections were found to be symmetry independent, with a R_{int} of 0.0336. Indexing and unit cell refinement indicated a *C*-centered, monoclinic lattice. The space group was found to be *C*2. The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by direct methods (SHELXT) produced a complete phasing model consistent with the proposed structure.

All nonhydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014.



T1

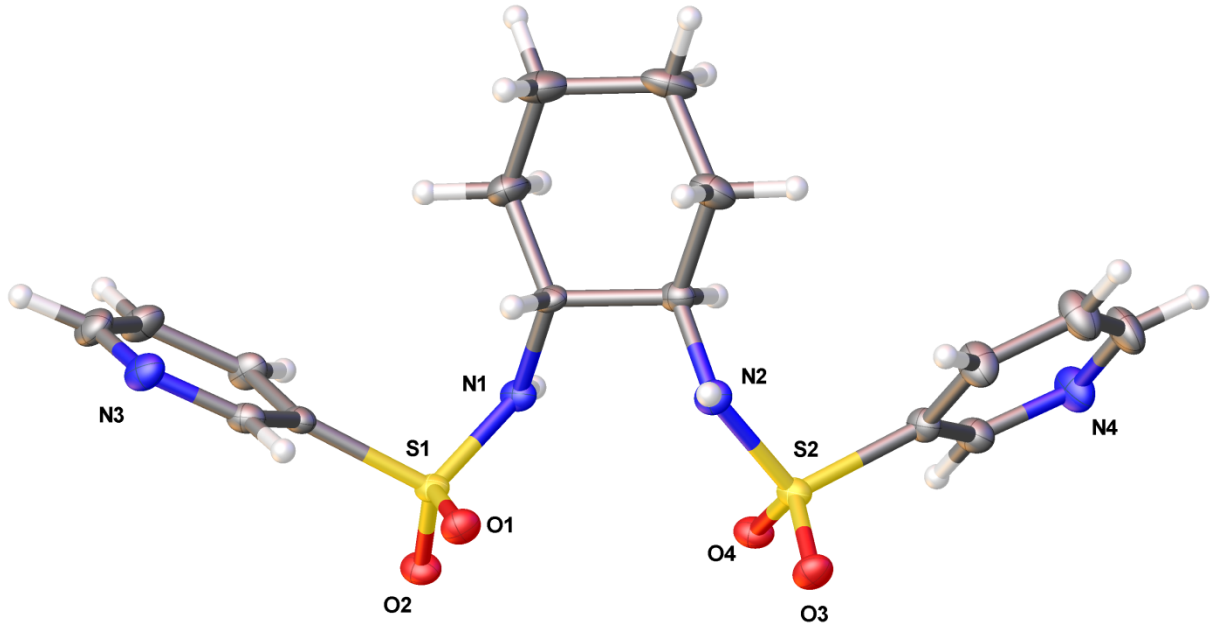


Table S7. Crystal data and structure refinement for Yu38.

Report date	2015-02-20	
Identification code	ZHG-2-16	
Empirical formula	C16.50 H21 Cl N4 O4 S2	
Molecular formula	C16 H20 N4 O4 S2, 0.5(C H2 Cl2)	
Formula weight	438.94	
Temperature	100 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C 1 2 1	
Unit cell dimensions	a = 16.294(2) Å	α= 90°.
	b = 8.7028(12) Å	β= 97.723(4)°.
	c = 14.4268(19) Å	γ = 90°.
Volume	2027.2(5) Å^3	
Z	4	

Density (calculated)	1.438 Mg/m^3
Absorption coefficient	0.425 mm^{-1}
F(000)	916
Crystal size	0.217 x 0.183 x 0.155 mm^3
Crystal color, habit	Colorless Block
Theta range for data collection	2.523 to 26.403°.
Index ranges	-20<=h<=20, -10<=k<=10, -12<=l<=18
Reflections collected	13470
Independent reflections	4124 [R(int) = 0.0336]
Completeness to theta = 25.000°	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.2602 and 0.2291
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4124 / 3 / 257
Goodness-of-fit on F^2	1.021
Final R indices [I>2sigma(I)]	R1 = 0.0405, wR2 = 0.0918
R indices (all data)	R1 = 0.0517, wR2 = 0.0989
Absolute structure parameter	0.06(3)
Extinction coefficient	n/a
Largest diff. peak and hole	0.606 and -0.909 $e.Å^{-3}$

Table S8. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for Yu38. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S(1)	3889(1)	4576(1)	3259(1)	15(1)
S(2)	6058(1)	4696(1)	1789(1)	16(1)
O(1)	4623(2)	4035(3)	3823(2)	20(1)
O(2)	3364(2)	3502(3)	2699(2)	20(1)
O(3)	6632(2)	3597(3)	2251(2)	21(1)
O(4)	5293(2)	4160(3)	1285(2)	19(1)
N(1)	4101(2)	5899(4)	2573(2)	16(1)
N(2)	5894(2)	5937(4)	2560(2)	18(1)
N(3)	3105(2)	5964(4)	5641(2)	22(1)
N(4)	6660(2)	6299(5)	-639(2)	27(1)
C(1)	3281(2)	5430(4)	4057(3)	15(1)
C(2)	2526(3)	6092(5)	3737(3)	20(1)
C(3)	2054(3)	6681(5)	4386(3)	24(1)
C(4)	2365(3)	6574(5)	5326(3)	25(1)
C(5)	3554(3)	5396(4)	5012(3)	18(1)
C(6)	4621(3)	7215(5)	2901(3)	18(1)
C(7)	4111(3)	8697(5)	2802(3)	27(1)
C(8)	4637(3)	10097(5)	3116(3)	34(1)
C(9)	5366(3)	10203(5)	2560(3)	30(1)
C(10)	5892(3)	8743(5)	2658(3)	26(1)
C(11)	5378(3)	7307(5)	2377(3)	18(1)
C(12)	6570(3)	5694(5)	963(3)	18(1)
C(13)	7281(3)	6530(5)	1253(3)	26(1)
C(14)	7668(3)	7261(6)	583(3)	32(1)
C(15)	7343(3)	7109(6)	-348(3)	31(1)
C(16)	6277(3)	5611(5)	13(3)	21(1)
Cl(1S)	4117(1)	-166(3)	-107(1)	81(1)
C(1S)	5000	1022(9)	0	63(3)

Table S9. Bond lengths [Å] and angles [°] for Yu38.

S(1)-O(1)	1.432(3)
S(1)-O(2)	1.439(3)
S(1)-N(1)	1.585(3)
S(1)-C(1)	1.780(4)
S(2)-O(3)	1.436(3)
S(2)-O(4)	1.434(3)
S(2)-N(2)	1.599(3)
S(2)-C(12)	1.772(4)
N(1)-H(1)	0.89(3)
N(1)-C(6)	1.465(5)
N(2)-H(2)	0.87(2)
N(2)-C(11)	1.463(5)
N(3)-C(4)	1.339(6)
N(3)-C(5)	1.335(5)
N(4)-C(15)	1.336(6)
N(4)-C(16)	1.338(5)
C(1)-C(2)	1.381(5)
C(1)-C(5)	1.390(5)
C(2)-H(2A)	0.9500
C(2)-C(3)	1.387(6)
C(3)-H(3)	0.9500
C(3)-C(4)	1.385(6)
C(4)-H(4)	0.9500
C(5)-H(5)	0.9500
C(6)-H(6)	1.0000
C(6)-C(7)	1.529(6)
C(6)-C(11)	1.533(6)
C(7)-H(7A)	0.9900
C(7)-H(7B)	0.9900
C(7)-C(8)	1.523(6)
C(8)-H(8A)	0.9900
C(8)-H(8B)	0.9900
C(8)-C(9)	1.524(7)
C(9)-H(9A)	0.9900

C(9)-H(9B)	0.9900
C(9)-C(10)	1.528(6)
C(10)-H(10A)	0.9900
C(10)-H(10B)	0.9900
C(10)-C(11)	1.529(6)
C(11)-H(11)	1.0000
C(12)-C(13)	1.383(6)
C(12)-C(16)	1.392(5)
C(13)-H(13)	0.9500
C(13)-C(14)	1.379(6)
C(14)-H(14)	0.9500
C(14)-C(15)	1.382(6)
C(15)-H(15)	0.9500
C(16)-H(16)	0.9500
Cl(1S)-C(1S)	1.761(5)
C(1S)-Cl(1S)#1	1.761(5)
C(1S)-H(1SA)	0.9900
C(1S)-H(1SB)	0.9900

O(1)-S(1)-O(2)	119.53(18)
O(1)-S(1)-N(1)	110.98(18)
O(1)-S(1)-C(1)	105.33(17)
O(2)-S(1)-N(1)	106.52(17)
O(2)-S(1)-C(1)	107.08(18)
N(1)-S(1)-C(1)	106.68(18)
O(3)-S(2)-N(2)	106.63(17)
O(3)-S(2)-C(12)	107.64(18)
O(4)-S(2)-O(3)	119.06(18)
O(4)-S(2)-N(2)	110.93(17)
O(4)-S(2)-C(12)	105.90(18)
N(2)-S(2)-C(12)	105.92(18)
S(1)-N(1)-H(1)	121(4)
C(6)-N(1)-S(1)	122.1(3)
C(6)-N(1)-H(1)	114(4)
S(2)-N(2)-H(2)	116(3)
C(11)-N(2)-S(2)	124.8(3)

C(11)-N(2)-H(2)	116(3)
C(5)-N(3)-C(4)	117.8(3)
C(15)-N(4)-C(16)	117.5(4)
C(2)-C(1)-S(1)	120.4(3)
C(2)-C(1)-C(5)	119.5(4)
C(5)-C(1)-S(1)	120.0(3)
C(1)-C(2)-H(2A)	120.7
C(1)-C(2)-C(3)	118.5(4)
C(3)-C(2)-H(2A)	120.7
C(2)-C(3)-H(3)	120.9
C(4)-C(3)-C(2)	118.2(4)
C(4)-C(3)-H(3)	120.9
N(3)-C(4)-C(3)	123.6(4)
N(3)-C(4)-H(4)	118.2
C(3)-C(4)-H(4)	118.2
N(3)-C(5)-C(1)	122.3(4)
N(3)-C(5)-H(5)	118.9
C(1)-C(5)-H(5)	118.9
N(1)-C(6)-H(6)	108.0
N(1)-C(6)-C(7)	110.2(3)
N(1)-C(6)-C(11)	110.5(3)
C(7)-C(6)-H(6)	108.0
C(7)-C(6)-C(11)	111.9(3)
C(11)-C(6)-H(6)	108.0
C(6)-C(7)-H(7A)	109.3
C(6)-C(7)-H(7B)	109.3
H(7A)-C(7)-H(7B)	107.9
C(8)-C(7)-C(6)	111.7(4)
C(8)-C(7)-H(7A)	109.3
C(8)-C(7)-H(7B)	109.3
C(7)-C(8)-H(8A)	109.7
C(7)-C(8)-H(8B)	109.7
C(7)-C(8)-C(9)	109.8(4)
H(8A)-C(8)-H(8B)	108.2
C(9)-C(8)-H(8A)	109.7
C(9)-C(8)-H(8B)	109.7

C(8)-C(9)-H(9A)	109.3
C(8)-C(9)-H(9B)	109.3
C(8)-C(9)-C(10)	111.6(4)
H(9A)-C(9)-H(9B)	108.0
C(10)-C(9)-H(9A)	109.3
C(10)-C(9)-H(9B)	109.3
C(9)-C(10)-H(10A)	109.2
C(9)-C(10)-H(10B)	109.2
C(9)-C(10)-C(11)	112.0(4)
H(10A)-C(10)-H(10B)	107.9
C(11)-C(10)-H(10A)	109.2
C(11)-C(10)-H(10B)	109.2
N(2)-C(11)-C(6)	110.5(3)
N(2)-C(11)-C(10)	109.7(3)
N(2)-C(11)-H(11)	108.5
C(6)-C(11)-H(11)	108.5
C(10)-C(11)-C(6)	111.1(3)
C(10)-C(11)-H(11)	108.5
C(13)-C(12)-S(2)	120.3(3)
C(13)-C(12)-C(16)	119.2(4)
C(16)-C(12)-S(2)	120.4(3)
C(12)-C(13)-H(13)	120.9
C(14)-C(13)-C(12)	118.2(4)
C(14)-C(13)-H(13)	120.9
C(13)-C(14)-H(14)	120.5
C(13)-C(14)-C(15)	119.1(4)
C(15)-C(14)-H(14)	120.5
N(4)-C(15)-C(14)	123.4(4)
N(4)-C(15)-H(15)	118.3
C(14)-C(15)-H(15)	118.3
N(4)-C(16)-C(12)	122.5(4)
N(4)-C(16)-H(16)	118.7
C(12)-C(16)-H(16)	118.7
Cl(1S)-C(1S)-Cl(1S)#1	108.1(4)
Cl(1S)-C(1S)-H(1SA)	110.1
Cl(1S)#1-C(1S)-H(1SA)	110.1

Cl(1S)#1-C(1S)-H(1SB)	110.1
Cl(1S)-C(1S)-H(1SB)	110.1
H(1SA)-C(1S)-H(1SB)	108.4

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,y,-z

Table S10. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for Yu38. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S(1)	20(1)	13(1)	12(1)	-2(1)	0(1)	0(1)
S(2)	21(1)	14(1)	11(1)	0(1)	0(1)	-1(1)
O(1)	22(2)	19(1)	18(2)	1(1)	-1(1)	4(1)
O(2)	27(2)	17(2)	16(1)	-4(1)	0(1)	-4(1)
O(3)	26(2)	19(2)	18(2)	2(1)	1(1)	6(1)
O(4)	23(2)	16(1)	16(1)	-2(1)	-2(1)	-3(1)
N(1)	22(2)	16(2)	10(2)	-1(1)	-1(1)	0(1)
N(2)	22(2)	19(2)	10(2)	-1(1)	-2(1)	0(2)
N(3)	31(2)	22(2)	13(2)	-2(2)	2(2)	4(2)
N(4)	36(2)	32(2)	12(2)	-1(2)	3(2)	-8(2)
C(1)	20(2)	12(2)	14(2)	0(2)	2(2)	-2(2)
C(2)	25(2)	22(2)	11(2)	2(2)	-2(2)	5(2)
C(3)	28(2)	22(2)	23(2)	-2(2)	0(2)	8(2)
C(4)	34(3)	23(2)	20(2)	-5(2)	8(2)	5(2)
C(5)	24(2)	14(2)	14(2)	0(2)	-1(2)	0(2)
C(6)	26(2)	12(2)	14(2)	-3(2)	3(2)	0(2)
C(7)	30(2)	18(2)	34(3)	-3(2)	9(2)	3(2)
C(8)	45(3)	17(2)	39(3)	-4(2)	2(2)	2(2)
C(9)	38(3)	14(2)	36(3)	5(2)	-5(2)	-5(2)

C(10)	33(3)	19(2)	24(2)	4(2)	0(2)	-5(2)
C(11)	25(2)	15(2)	14(2)	0(2)	2(2)	0(2)
C(12)	23(2)	18(2)	12(2)	0(2)	1(2)	-1(2)
C(13)	29(2)	33(2)	15(2)	-4(2)	0(2)	-9(2)
C(14)	34(3)	39(3)	23(2)	-1(2)	3(2)	-16(2)
C(15)	39(3)	34(3)	20(2)	3(2)	9(2)	-14(2)
C(16)	26(2)	19(2)	17(2)	0(2)	1(2)	-3(2)
Cl(1S)	55(1)	132(2)	56(1)	-28(1)	10(1)	4(1)
C(1S)	128(9)	20(4)	31(4)	0	-20(5)	0

Table S11. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for Yu38.

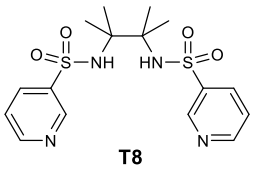
	x	y	z	U(eq)
H(1)	3800(30)	6040(70)	2020(30)	58(18)
H(2)	6260(20)	5950(50)	3060(20)	25(13)
H(2A)	2333	6142	3086	24
H(3)	1532	7146	4191	29
H(4)	2036	6953	5771	30
H(5)	4079	4953	5224	21
H(6)	4823	7059	3580	21
H(7A)	3868	8829	2140	32
H(7B)	3651	8615	3182	32
H(8A)	4843	10013	3792	41
H(8B)	4295	11038	3018	41
H(9A)	5715	11094	2784	36
H(9B)	5156	10373	1892	36
H(10A)	6154	8639	3315	31
H(10B)	6339	8832	2260	31
H(11)	5180	7360	1691	22
H(13)	7496	6598	1897	31
H(14)	8151	7861	758	38
H(15)	7619	7606	-804	37
H(16)	5786	5043	-180	25
H(1SA)	5013	1687	558	75
H(1SB)	4987	1687	-558	75

Table S12. Hydrogen bonds for Yu38 [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(1)-H(1)...N(4)#1	0.89(3)	2.04(3)	2.918(5)	167(5)
N(2)-H(2)...N(3)#2	0.87(2)	2.02(3)	2.873(5)	168(4)

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,y,-z #2 -x+1,y,-z+1



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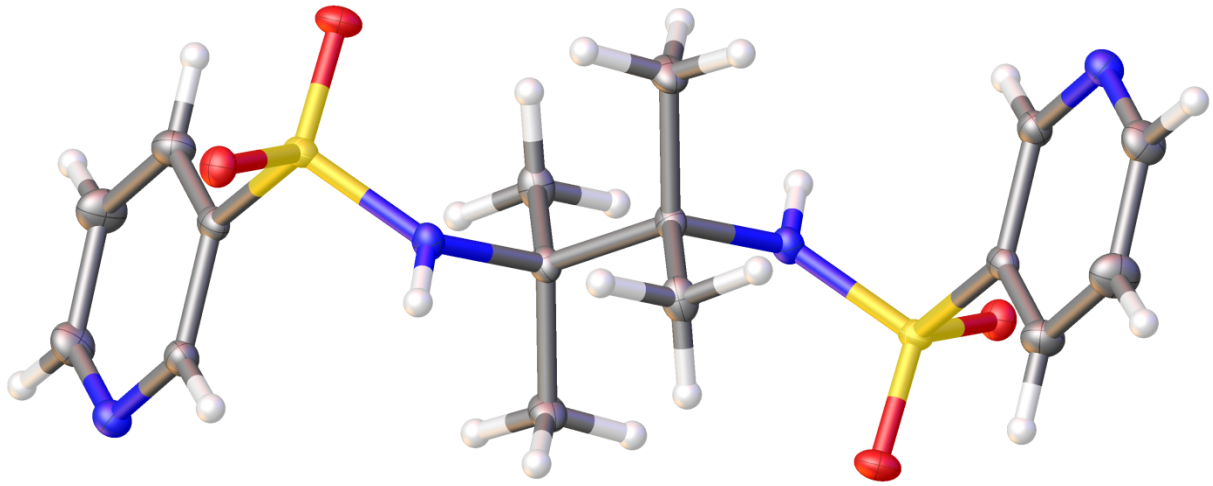


Table S13. Crystal data and structure refinement for yu50.

Identification code	yu50	
Empirical formula	C16 H22 N4 O4 S2	
Formula weight	398.49	
Temperature	100.0 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21/n	
Unit cell dimensions	a = 10.4117(10) Å	α= 90°.
	b = 6.0842(5) Å	β= 94.632(5)°.
	c = 14.2796(13) Å	γ = 90°.
Volume	901.61(14) Å^3	
Z	2	
Density (calculated)	1.468 Mg/m^3	
Absorption coefficient	0.326 mm^{-1}	
F(000)	420	
Crystal size	0.34 x 0.3 x 0.24 mm^3	
Theta range for data collection	2.334 to 28.329°.	
Index ranges	-10<=h<=13, -7<=k<=8, -19<=l<=15	
Reflections collected	6520	
Independent reflections	2228 [R(int) = 0.0370]	
Completeness to theta = 25.242°	99.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.1525 and 0.1227	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2228 / 0 / 124	
Goodness-of-fit on F^2	1.096	
Final R indices [I>2sigma(I)]	R1 = 0.0364, wR2 = 0.1009	

R indices (all data)	R1 = 0.0392, wR2 = 0.1030
Extinction coefficient	n/a
Largest diff. peak and hole	0.476 and -0.389 e.Å^{-3}

Table S14. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for yu50. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S(1)	-96(1)	7356(1)	2040(1)	13(1)
O(1)	655(1)	9241(2)	2351(1)	16(1)
O(2)	-1464(1)	7578(2)	1866(1)	19(1)
N(1)	1714(1)	3077(2)	3819(1)	17(1)
N(2)	530(1)	6489(2)	1117(1)	14(1)
C(1)	743(2)	2371(3)	4303(1)	21(1)
C(2)	1420(2)	4544(3)	3137(1)	15(1)
C(3)	173(1)	5331(2)	2927(1)	13(1)
C(4)	149(1)	4549(2)	516(1)	13(1)
C(5)	-519(2)	3047(3)	4129(1)	22(1)
C(6)	-823(2)	4575(3)	3423(1)	18(1)
C(7)	-1020(2)	3337(3)	855(1)	17(1)
C(8)	1297(2)	2969(3)	579(1)	18(1)

Table S15. Bond lengths [Å] and angles [°] for yu50.

S(1)-O(1)	1.4383(11)
S(1)-O(2)	1.4327(12)
S(1)-N(2)	1.6056(13)
S(1)-C(3)	1.7734(15)
N(1)-C(1)	1.341(2)
N(1)-C(2)	1.338(2)
N(2)-C(4)	1.4945(19)
N(2)-H(2)	0.82(2)
C(1)-H(1)	0.9500
C(1)-C(5)	1.381(2)
C(2)-H(2A)	0.9500
C(2)-C(3)	1.393(2)
C(3)-C(6)	1.380(2)
C(4)-C(4)#1	1.579(3)
C(4)-C(7)	1.534(2)
C(4)-C(8)	1.531(2)
C(5)-H(5)	0.9500
C(5)-C(6)	1.389(2)
C(6)-H(6)	0.9500
C(7)-H(7A)	0.9800
C(7)-H(7B)	0.9800
C(7)-H(7C)	0.9800
C(8)-H(8A)	0.9800
C(8)-H(8B)	0.9800
C(8)-H(8C)	0.9800

O(1)-S(1)-N(2)	105.59(7)
O(1)-S(1)-C(3)	106.45(7)
O(2)-S(1)-O(1)	119.10(7)
O(2)-S(1)-N(2)	110.62(7)
O(2)-S(1)-C(3)	106.70(7)
N(2)-S(1)-C(3)	107.89(7)
C(2)-N(1)-C(1)	116.82(14)
S(1)-N(2)-H(2)	112.9(16)

C(4)-N(2)-S(1)	128.64(11)
C(4)-N(2)-H(2)	114.5(16)
N(1)-C(1)-H(1)	118.0
N(1)-C(1)-C(5)	123.96(15)
C(5)-C(1)-H(1)	118.0
N(1)-C(2)-H(2A)	118.7
N(1)-C(2)-C(3)	122.69(14)
C(3)-C(2)-H(2A)	118.7
C(2)-C(3)-S(1)	118.87(12)
C(6)-C(3)-S(1)	121.06(12)
C(6)-C(3)-C(2)	120.05(14)
N(2)-C(4)-C(4)#1	106.50(14)
N(2)-C(4)-C(7)	112.27(12)
N(2)-C(4)-C(8)	106.96(12)
C(7)-C(4)-C(4)#1	111.16(15)
C(8)-C(4)-C(4)#1	111.53(15)
C(8)-C(4)-C(7)	108.37(12)
C(1)-C(5)-H(5)	120.4
C(1)-C(5)-C(6)	119.16(15)
C(6)-C(5)-H(5)	120.4
C(3)-C(6)-C(5)	117.31(15)
C(3)-C(6)-H(6)	121.3
C(5)-C(6)-H(6)	121.3
C(4)-C(7)-H(7A)	109.5
C(4)-C(7)-H(7B)	109.5
C(4)-C(7)-H(7C)	109.5
H(7A)-C(7)-H(7B)	109.5
H(7A)-C(7)-H(7C)	109.5
H(7B)-C(7)-H(7C)	109.5
C(4)-C(8)-H(8A)	109.5
C(4)-C(8)-H(8B)	109.5
C(4)-C(8)-H(8C)	109.5
H(8A)-C(8)-H(8B)	109.5
H(8A)-C(8)-H(8C)	109.5
H(8B)-C(8)-H(8C)	109.5

Symmetry transformations used to generate equivalent atoms:

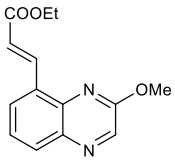
#1 -x,-y+1,-z

Table S16. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for yu50. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S(1)	12(1)	12(1)	14(1)	0(1)	0(1)	1(1)
O(1)	18(1)	13(1)	18(1)	-2(1)	1(1)	-2(1)
O(2)	12(1)	20(1)	23(1)	2(1)	-1(1)	4(1)
N(1)	16(1)	16(1)	18(1)	1(1)	-1(1)	0(1)
N(2)	13(1)	14(1)	14(1)	-2(1)	0(1)	-3(1)
C(1)	22(1)	20(1)	20(1)	7(1)	1(1)	0(1)
C(2)	14(1)	16(1)	14(1)	0(1)	0(1)	-1(1)
C(3)	14(1)	13(1)	13(1)	-1(1)	-1(1)	-1(1)
C(4)	15(1)	10(1)	13(1)	0(1)	-1(1)	-1(1)
C(5)	20(1)	23(1)	25(1)	7(1)	7(1)	-3(1)
C(6)	15(1)	19(1)	21(1)	1(1)	2(1)	0(1)
C(7)	20(1)	16(1)	15(1)	1(1)	-1(1)	-6(1)
C(8)	22(1)	14(1)	18(1)	1(1)	-3(1)	4(1)

Table S17. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for yu50.

	x	y	z	U(eq)
H(1)	936	1344	4795	25
H(2A)	2089	5071	2781	18
H(5)	-1172	2473	4488	27
H(6)	-1681	5080	3287	22
H(7A)	-808	2783	1493	26
H(7B)	-1248	2102	433	26
H(7C)	-1751	4351	855	26
H(8A)	2085	3782	472	27
H(8B)	1155	1819	102	27
H(8C)	1387	2296	1205	27
H(2)	1280(20)	6880(40)	1095(16)	25(6)



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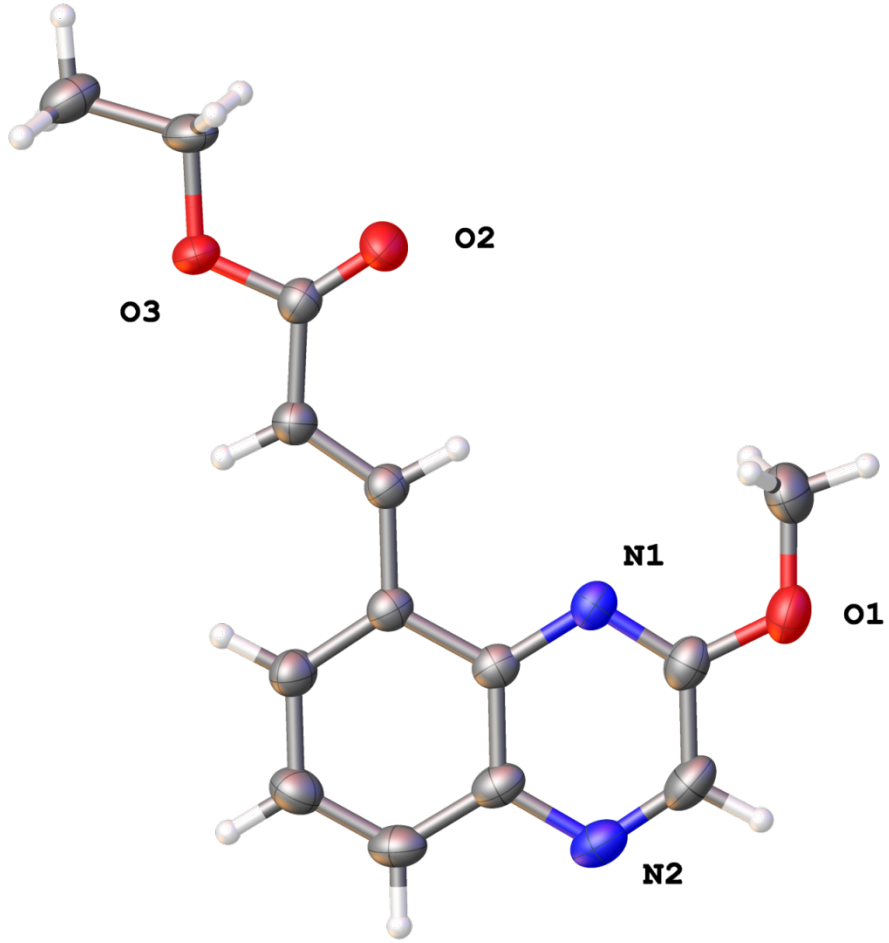


Table S18. Crystal data and structure refinement for Yu83.

Report date	2016-11-16	
Identification code	yu83	
Empirical formula	C14 H14 N2 O3	
Molecular formula	C14 H14 N2 O3	
Formula weight	258.27	
Temperature	100.0 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 1 21/c 1	
Unit cell dimensions	a = 4.5660(3) Å	α= 90°.
	b = 26.0435(11) Å	β= 91.036(2)°.
	c = 10.8149(5) Å	γ = 90°.
Volume	1285.84(12) $Å^3$	
Z	4	
Density (calculated)	1.334 Mg/m^3	
Absorption coefficient	0.095 mm^{-1}	
F(000)	544	
Crystal size	0.22 x 0.08 x 0.08 mm^3	
Crystal color, habit	colorless needle	
Theta range for data collection	1.564 to 25.347°.	
Index ranges	-5<=h<=5, -31<=k<=25, -12<=l<=13	
Reflections collected	9029	
Independent reflections	2354 [R(int) = 0.0274]	
Completeness to theta = 25.242°	99.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.6463 and 0.6125	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2354 / 0 / 174	
Goodness-of-fit on F^2	1.038	
Final R indices [I>2sigma(I)]	R1 = 0.0444, wR2 = 0.0990	
R indices (all data)	R1 = 0.0607, wR2 = 0.1065	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.151 and -0.175 $e.Å^{-3}$	

Table S19. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for Yu83. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(3)	9390(3)	6042(1)	1371(1)	40(1)
O(1)	-2599(3)	5798(1)	6904(1)	47(1)
O(2)	6637(3)	5501(1)	2472(1)	48(1)
N(1)	688(3)	6272(1)	5776(1)	32(1)
N(2)	-861(4)	7117(1)	7280(2)	42(1)
C(4)	1152(4)	7170(1)	6357(2)	35(1)
C(11)	6729(4)	6393(1)	2967(2)	34(1)
C(14)	12273(5)	5822(1)	-358(2)	49(1)
C(2)	-1230(4)	6241(1)	6645(2)	36(1)
C(3)	-2026(5)	6666(1)	7396(2)	44(1)
C(7)	5181(4)	7302(1)	4500(2)	36(1)
C(8)	3985(4)	6818(1)	4644(2)	30(1)
C(5)	2454(4)	7650(1)	6175(2)	41(1)
C(9)	1909(4)	6748(1)	5599(2)	29(1)
C(13)	10356(5)	5610(1)	631(2)	42(1)
C(12)	7516(4)	5929(1)	2283(2)	32(1)
C(1)	-1833(5)	5360(1)	6163(2)	54(1)
C(10)	4819(4)	6382(1)	3875(2)	31(1)
C(6)	4440(5)	7714(1)	5262(2)	42(1)

Table S20. Bond lengths [Å] and angles [°] for Yu83.

O(3)-C(13)	1.453(2)		
O(3)-C(12)	1.349(2)	C(12)-O(3)-C(13)	116.00(15)
O(1)-C(2)	1.343(2)	C(2)-O(1)-C(1)	116.45(16)
O(1)-C(1)	1.441(3)	C(2)-N(1)-C(9)	115.92(16)
O(2)-C(12)	1.205(2)	C(3)-N(2)-C(4)	116.23(17)
N(1)-C(2)	1.299(2)	N(2)-C(4)-C(5)	118.83(17)
N(1)-C(9)	1.376(2)	N(2)-C(4)-C(9)	121.01(18)
N(2)-C(4)	1.376(3)	C(5)-C(4)-C(9)	120.16(18)
N(2)-C(3)	1.296(3)	C(12)-C(11)-H(11)	119.1
C(4)-C(5)	1.401(3)	C(10)-C(11)-H(11)	119.1
C(4)-C(9)	1.417(3)	C(10)-C(11)-C(12)	121.84(17)
C(11)-H(11)	0.9500	H(14A)-C(14)-H(14B)	109.5
C(11)-C(12)	1.464(3)	H(14A)-C(14)-H(14C)	109.5
C(11)-C(10)	1.325(3)	H(14B)-C(14)-H(14C)	109.5
C(14)-H(14A)	0.9800	C(13)-C(14)-H(14A)	109.5
C(14)-H(14B)	0.9800	C(13)-C(14)-H(14B)	109.5
C(14)-H(14C)	0.9800	C(13)-C(14)-H(14C)	109.5
C(14)-C(13)	1.500(3)	O(1)-C(2)-C(3)	115.10(18)
C(2)-C(3)	1.425(3)	N(1)-C(2)-O(1)	121.79(18)
C(3)-H(3)	0.9500	N(1)-C(2)-C(3)	123.11(19)
C(7)-H(7)	0.9500	N(2)-C(3)-C(2)	122.68(19)
C(7)-C(8)	1.384(3)	N(2)-C(3)-H(3)	118.7
C(7)-C(6)	1.398(3)	C(2)-C(3)-H(3)	118.7
C(8)-C(9)	1.426(3)	C(8)-C(7)-H(7)	118.9
C(8)-C(10)	1.462(2)	C(8)-C(7)-C(6)	122.15(19)
C(5)-H(5)	0.9500	C(6)-C(7)-H(7)	118.9
C(5)-C(6)	1.363(3)	C(7)-C(8)-C(9)	117.81(16)
C(13)-H(13A)	0.9900	C(7)-C(8)-C(10)	122.38(17)
C(13)-H(13B)	0.9900	C(9)-C(8)-C(10)	119.80(16)
C(1)-H(1A)	0.9800	C(4)-C(5)-H(5)	120.0
C(1)-H(1B)	0.9800	C(6)-C(5)-C(4)	120.02(18)
C(1)-H(1C)	0.9800	C(6)-C(5)-H(5)	120.0
C(10)-H(10)	0.9500	N(1)-C(9)-C(4)	121.01(17)
C(6)-H(6)	0.9500	N(1)-C(9)-C(8)	119.46(16)

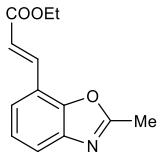
C(4)-C(9)-C(8)	119.53(17)
O(3)-C(13)-C(14)	107.18(16)
O(3)-C(13)-H(13A)	110.3
O(3)-C(13)-H(13B)	110.3
C(14)-C(13)-H(13A)	110.3
C(14)-C(13)-H(13B)	110.3
H(13A)-C(13)-H(13B)	108.5
O(3)-C(12)-C(11)	110.84(15)
O(2)-C(12)-O(3)	122.79(17)
O(2)-C(12)-C(11)	126.37(18)
O(1)-C(1)-H(1A)	109.5
O(1)-C(1)-H(1B)	109.5
O(1)-C(1)-H(1C)	109.5
H(1A)-C(1)-H(1B)	109.5
H(1A)-C(1)-H(1C)	109.5
H(1B)-C(1)-H(1C)	109.5
C(11)-C(10)-C(8)	125.93(17)
C(11)-C(10)-H(10)	117.0
C(8)-C(10)-H(10)	117.0
C(7)-C(6)-H(6)	119.8
C(5)-C(6)-C(7)	120.32(19)
C(5)-C(6)-H(6)	119.8

Table S21. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for Yu83. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(3)	46(1)	34(1)	40(1)	-10(1)	16(1)	-3(1)
O(1)	45(1)	52(1)	45(1)	6(1)	13(1)	-6(1)
O(2)	59(1)	30(1)	56(1)	0(1)	20(1)	-2(1)
N(1)	29(1)	37(1)	29(1)	3(1)	1(1)	3(1)
N(2)	38(1)	52(1)	36(1)	-8(1)	4(1)	7(1)
C(4)	31(1)	43(1)	30(1)	-5(1)	0(1)	8(1)
C(11)	38(1)	31(1)	33(1)	-2(1)	5(1)	-2(1)
C(14)	56(1)	54(1)	38(1)	-5(1)	11(1)	11(1)
C(2)	29(1)	47(1)	33(1)	5(1)	2(1)	2(1)
C(3)	35(1)	62(1)	34(1)	-1(1)	10(1)	6(1)
C(7)	42(1)	33(1)	33(1)	3(1)	5(1)	3(1)
C(8)	32(1)	32(1)	28(1)	2(1)	1(1)	4(1)
C(5)	42(1)	38(1)	43(1)	-11(1)	1(1)	7(1)
C(9)	28(1)	33(1)	28(1)	1(1)	-2(1)	5(1)
C(13)	44(1)	37(1)	47(1)	-16(1)	9(1)	2(1)
C(12)	32(1)	34(1)	31(1)	1(1)	3(1)	0(1)
C(1)	61(2)	41(1)	60(1)	8(1)	12(1)	-8(1)
C(10)	32(1)	29(1)	30(1)	2(1)	2(1)	2(1)
C(6)	49(1)	30(1)	46(1)	-2(1)	1(1)	1(1)

Table S22. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for Yu83.

	x	y	z	U(eq)
H(11)	7612	6710	2754	40
H(14A)	12924	5542	-892	74
H(14B)	13983	5990	25	74
H(14C)	11165	6073	-854	74
H(3)	-3470	6617	8007	52
H(7)	6549	7356	3861	44
H(5)	1953	7932	6689	49
H(13A)	8649	5431	255	51
H(13B)	11467	5363	1153	51
H(1A)	-2197	5438	5287	81
H(1B)	-3027	5064	6402	81
H(1C)	244	5278	6296	81
H(10)	3910	6062	4041	37
H(6)	5326	8040	5143	50



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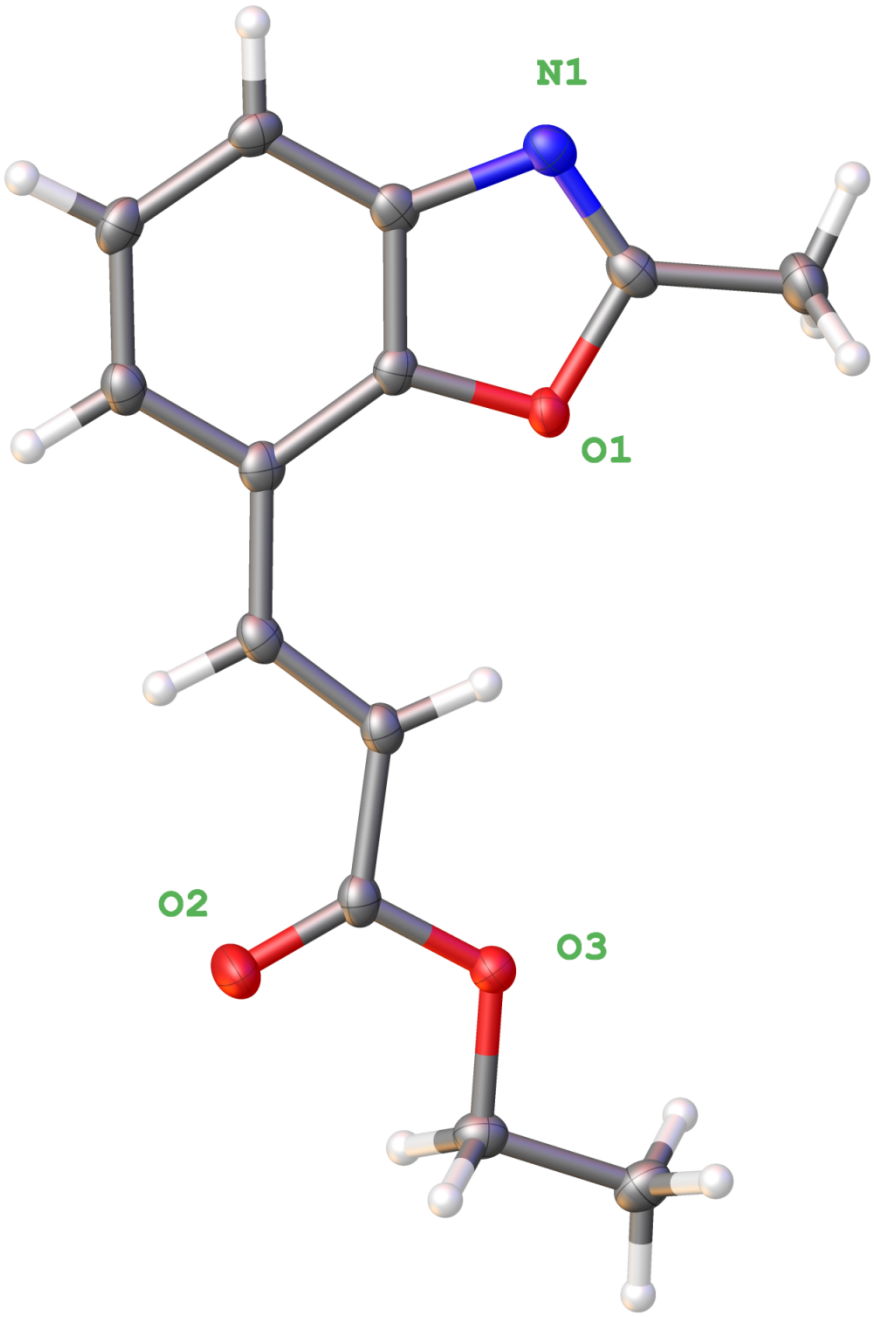


Table S23. Crystal data and structure refinement for Yu80.

Report date	2016-10-16	
Identification code	yu80_a	
Empirical formula	C13 H13 N O3	
Molecular formula	C13 H13 N O3	
Formula weight	231.24	
Temperature	100.0 K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P 1 21/n 1	
Unit cell dimensions	a = 7.3728(16) Å	α= 90°.
	b = 21.871(4) Å	β= 116.594(5)°.
	c = 7.9223(17) Å	γ = 90°.
Volume	1142.3(4) $Å^3$	
Z	4	
Density (calculated)	1.345 Mg/m^3	
Absorption coefficient	0.792 mm^{-1}	
F(000)	488	
Crystal size	0.1 x 0.02 x 0.02 mm^3	
Crystal color, habit	colorless needle	
Theta range for data collection	4.042 to 66.596°.	
Index ranges	-7<=h<=8, -25<=k<=26, -8<=l<=9	
Reflections collected	7761	
Independent reflections	2016 [R(int) = 0.0572]	
Completeness to theta = 66.597°	99.4 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.5210 and 0.3801	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2016 / 0 / 156	
Goodness-of-fit on F^2	1.031	
Final R indices [I>2sigma(I)]	R1 = 0.0445, wR2 = 0.1067	
R indices (all data)	R1 = 0.0682, wR2 = 0.1167	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.179 and -0.242 e.$Å^{-3}$	

Table S24. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for Yu80_a. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	2209(2)	4321(1)	2588(2)	18(1)
O(2)	3070(3)	5704(1)	8578(2)	30(1)
O(3)	1372(2)	6112(1)	5685(2)	19(1)
N(1)	2750(3)	3437(1)	1410(2)	21(1)
C(1)	635(4)	4251(1)	-823(3)	27(1)
C(2)	1895(3)	3964(1)	1025(3)	20(1)
C(3)	3408(3)	3961(1)	4105(3)	16(1)
C(4)	3761(3)	3416(1)	3399(3)	18(1)
C(5)	4933(3)	2959(1)	4615(3)	19(1)
C(6)	5714(3)	3077(1)	6534(3)	21(1)
C(7)	5331(3)	3628(1)	7210(3)	20(1)
C(8)	4156(3)	4094(1)	6023(3)	17(1)
C(9)	3771(3)	4656(1)	6805(3)	18(1)
C(10)	2646(3)	5128(1)	5857(3)	18(1)
C(11)	2412(3)	5664(1)	6873(3)	19(1)
C(12)	1220(3)	6686(1)	6537(3)	20(1)
C(13)	35(3)	7118(1)	4943(3)	23(1)

Table S25. Bond lengths [Å] and angles [°] for Yu80_a.

O(1)-C(2)	1.393(2)	C(2)-N(1)-C(4)	104.65(17)
O(1)-C(3)	1.377(2)	H(1A)-C(1)-H(1B)	109.5
O(2)-C(11)	1.217(2)	H(1A)-C(1)-H(1C)	109.5
O(3)-C(11)	1.337(2)	H(1B)-C(1)-H(1C)	109.5
O(3)-C(12)	1.453(2)	C(2)-C(1)-H(1A)	109.5
N(1)-C(2)	1.285(3)	C(2)-C(1)-H(1B)	109.5
N(1)-C(4)	1.410(3)	C(2)-C(1)-H(1C)	109.5
C(1)-H(1A)	0.9800	O(1)-C(2)-C(1)	115.09(18)
C(1)-H(1B)	0.9800	N(1)-C(2)-O(1)	115.05(18)
C(1)-H(1C)	0.9800	N(1)-C(2)-C(1)	129.86(19)
C(1)-C(2)	1.477(3)	O(1)-C(3)-C(4)	107.61(16)
C(3)-C(4)	1.390(3)	O(1)-C(3)-C(8)	128.12(18)
C(3)-C(8)	1.395(3)	C(4)-C(3)-C(8)	124.27(19)
C(4)-C(5)	1.388(3)	C(3)-C(4)-N(1)	108.72(18)
C(5)-H(5)	0.9500	C(5)-C(4)-N(1)	130.74(19)
C(5)-C(6)	1.388(3)	C(5)-C(4)-C(3)	120.53(18)
C(6)-H(6)	0.9500	C(4)-C(5)-H(5)	121.6
C(6)-C(7)	1.396(3)	C(6)-C(5)-C(4)	116.74(19)
C(7)-H(7)	0.9500	C(6)-C(5)-H(5)	121.6
C(7)-C(8)	1.394(3)	C(5)-C(6)-H(6)	119.2
C(8)-C(9)	1.460(3)	C(5)-C(6)-C(7)	121.7(2)
C(9)-H(9)	0.9500	C(7)-C(6)-H(6)	119.2
C(9)-C(10)	1.328(3)	C(6)-C(7)-H(7)	118.6
C(10)-H(10)	0.9500	C(8)-C(7)-C(6)	122.88(18)
C(10)-C(11)	1.474(3)	C(8)-C(7)-H(7)	118.6
C(12)-H(12A)	0.9900	C(3)-C(8)-C(9)	125.46(18)
C(12)-H(12B)	0.9900	C(7)-C(8)-C(3)	113.89(18)
C(12)-C(13)	1.505(3)	C(7)-C(8)-C(9)	120.65(17)
C(13)-H(13A)	0.9800	C(8)-C(9)-H(9)	116.3
C(13)-H(13B)	0.9800	C(10)-C(9)-C(8)	127.33(18)
C(13)-H(13C)	0.9800	C(10)-C(9)-H(9)	116.3
		C(9)-C(10)-H(10)	119.8
C(3)-O(1)-C(2)	103.97(15)	C(9)-C(10)-C(11)	120.40(17)
C(11)-O(3)-C(12)	116.47(15)	C(11)-C(10)-H(10)	119.8

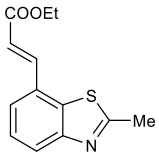
O(2)-C(11)-O(3)	123.13(19)
O(2)-C(11)-C(10)	125.23(19)
O(3)-C(11)-C(10)	111.64(16)
O(3)-C(12)-H(12A)	110.4
O(3)-C(12)-H(12B)	110.4
O(3)-C(12)-C(13)	106.81(16)
H(12A)-C(12)-H(12B)	108.6
C(13)-C(12)-H(12A)	110.4
C(13)-C(12)-H(12B)	110.4
C(12)-C(13)-H(13A)	109.5
C(12)-C(13)-H(13B)	109.5
C(12)-C(13)-H(13C)	109.5
H(13A)-C(13)-H(13B)	109.5
H(13A)-C(13)-H(13C)	109.5
H(13B)-C(13)-H(13C)	109.5

Table S26. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for Yu80_a. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	15(1)	21(1)	14(1)	0(1)	4(1)	0(1)
O(2)	40(1)	29(1)	16(1)	-2(1)	7(1)	8(1)
O(3)	20(1)	19(1)	16(1)	-1(1)	6(1)	2(1)
N(1)	18(1)	25(1)	20(1)	-3(1)	10(1)	-2(1)
C(1)	29(1)	33(1)	17(1)	1(1)	8(1)	1(1)
C(2)	18(1)	24(1)	18(1)	-4(1)	9(1)	-5(1)
C(3)	11(1)	19(1)	18(1)	1(1)	6(1)	-1(1)
C(4)	11(1)	24(1)	19(1)	-2(1)	7(1)	-2(1)
C(5)	13(1)	19(1)	25(1)	-1(1)	9(1)	1(1)
C(6)	12(1)	24(1)	24(1)	4(1)	6(1)	1(1)
C(7)	16(1)	26(1)	16(1)	0(1)	6(1)	-1(1)
C(8)	11(1)	20(1)	18(1)	-1(1)	5(1)	-3(1)
C(9)	15(1)	22(1)	16(1)	-3(1)	6(1)	-4(1)
C(10)	14(1)	22(1)	15(1)	0(1)	5(1)	-2(1)
C(11)	14(1)	23(1)	16(1)	1(1)	5(1)	-1(1)
C(12)	19(1)	20(1)	23(1)	-3(1)	11(1)	-1(1)
C(13)	21(1)	23(1)	28(1)	2(1)	13(1)	3(1)

Table S27. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for Yu80_a.

	x	y	z	U(eq)
H(1A)	-714	4341	-928	40
H(1B)	505	3971	-1836	40
H(1C)	1277	4631	-932	40
H(5)	5188	2584	4157	23
H(6)	6530	2777	7410	25
H(7)	5897	3687	8536	24
H(9)	4397	4687	8142	22
H(10)	1988	5121	4516	21
H(12A)	2587	6853	7338	24
H(12B)	513	6623	7332	24
H(13A)	690	7149	4108	35
H(13B)	-5	7523	5455	35
H(13C)	-1351	6964	4226	35



5n

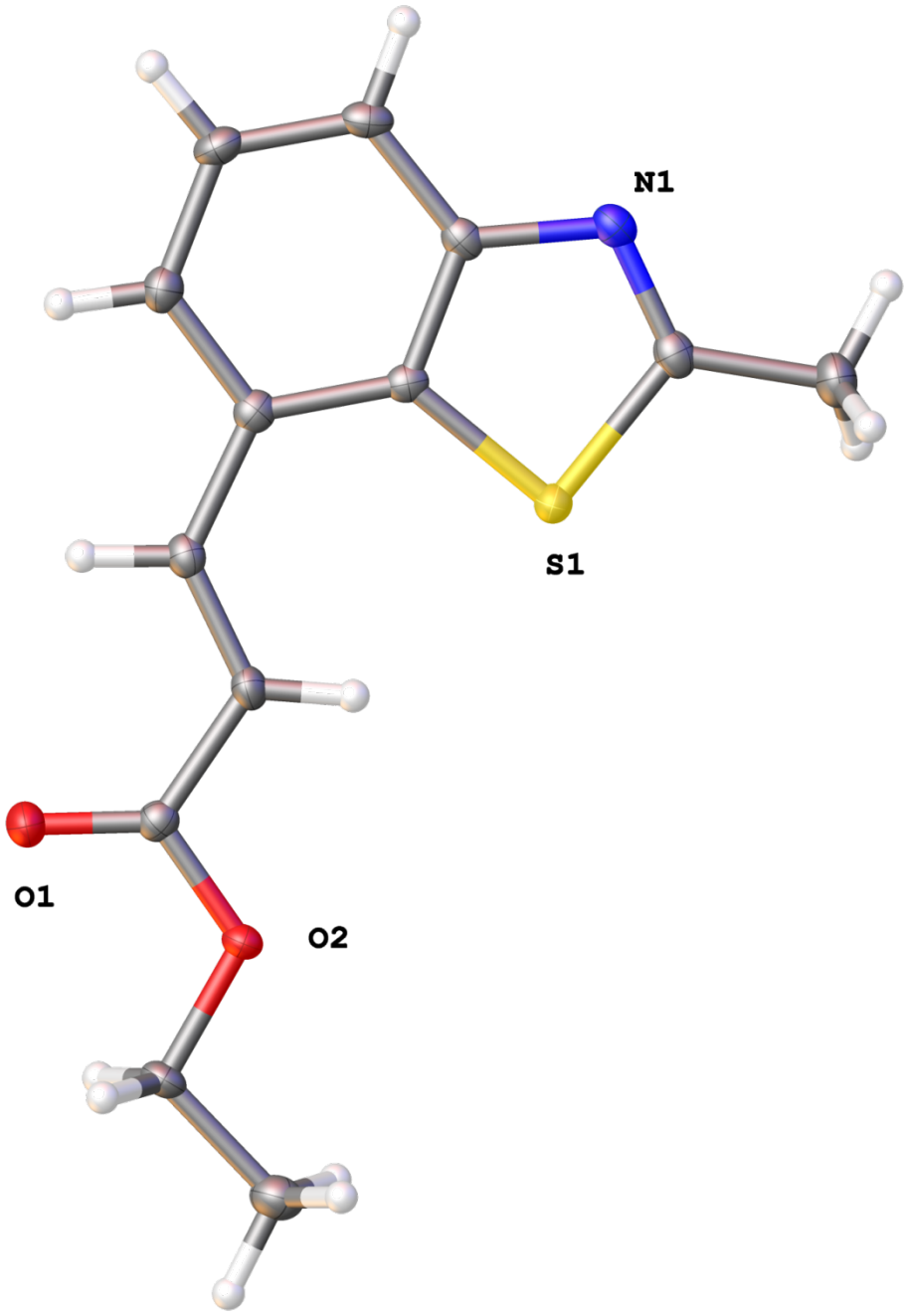


Table S28. Crystal data and structure refinement for Yu82.

Report date	2016-11-09	
Identification code	yu82	
Empirical formula	C13 H13 N O2 S	
Molecular formula	C13 H13 N O2 S	
Formula weight	247.30	
Temperature	100.0 K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 7.3791(8) Å	α= 71.415(3)°.
	b = 7.9026(8) Å	β= 79.346(3)°.
	c = 11.8080(12) Å	γ = 66.702(3)°.
Volume	598.08(11) Å^3	
Z	2	
Density (calculated)	1.373 Mg/m^3	
Absorption coefficient	0.259 mm^{-1}	
F(000)	260	
Crystal size	0.25 x 0.2 x 0.08 mm^3	
Crystal color, habit	colorless plate	
Theta range for data collection	1.824 to 25.364°.	
Index ranges	-8<=h<=8, -6<=k<=9, -12<=l<=14	
Reflections collected	6836	
Independent reflections	2194 [R(int) = 0.0403]	
Completeness to theta = 25.242°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.5619 and 0.5134	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2194 / 0 / 156	
Goodness-of-fit on F^2	1.052	
Final R indices [I>2sigma(I)]	R1 = 0.0336, wR2 = 0.0785	
R indices (all data)	R1 = 0.0422, wR2 = 0.0839	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.257 and -0.245 e.Å^{-3}	

Table S29. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for Yu82. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S(1)	1934(1)	8359(1)	3857(1)	16(1)
O(1)	3399(2)	664(2)	6446(1)	23(1)
O(2)	1450(2)	3031(2)	7277(1)	17(1)
N(1)	3044(2)	10013(2)	1723(1)	18(1)
C(1)	894(3)	12327(3)	2844(2)	24(1)
C(2)	2006(3)	10369(2)	2688(2)	17(1)
C(3)	3441(2)	6887(2)	2970(1)	14(1)
C(4)	3878(2)	8045(2)	1856(2)	15(1)
C(5)	5082(2)	7217(3)	967(2)	18(1)
C(6)	5828(3)	5247(3)	1208(2)	18(1)
C(7)	5387(2)	4097(3)	2310(2)	18(1)
C(8)	4193(2)	4870(2)	3221(2)	15(1)
C(9)	3842(2)	3541(2)	4344(2)	16(1)
C(10)	2718(2)	3926(2)	5323(1)	16(1)
C(11)	2593(2)	2348(2)	6376(2)	15(1)
C(12)	1250(3)	1595(3)	8374(2)	18(1)
C(13)	-51(3)	2655(3)	9249(2)	24(1)

Table S30. Bond lengths [Å] and angles [°] for Yu82.

S(1)-C(2)	1.7533(18)	N(1)-C(4)-C(3)	115.59(14)
S(1)-C(3)	1.7346(16)	N(1)-C(4)-C(5)	123.96(15)
O(1)-C(11)	1.206(2)	C(5)-C(4)-C(3)	120.45(16)
O(2)-C(11)	1.3439(19)	C(4)-C(5)-H(5)	120.8
O(2)-C(12)	1.454(2)	C(6)-C(5)-C(4)	118.50(16)
N(1)-C(2)	1.294(2)	C(6)-C(5)-H(5)	120.8
N(1)-C(4)	1.395(2)	C(5)-C(6)-H(6)	119.4
C(1)-H(1A)	0.9800	C(5)-C(6)-C(7)	121.15(15)
C(1)-H(1B)	0.9800	C(7)-C(6)-H(6)	119.4
C(1)-H(1C)	0.9800	C(6)-C(7)-H(7)	119.0
C(1)-C(2)	1.491(2)	C(6)-C(7)-C(8)	122.04(16)
C(3)-C(4)	1.408(2)	C(8)-C(7)-H(7)	119.0
C(3)-C(8)	1.413(2)	C(3)-C(8)-C(9)	125.80(15)
C(4)-C(5)	1.397(2)	C(7)-C(8)-C(3)	116.51(16)
C(5)-H(5)	0.9500	C(7)-C(8)-C(9)	117.69(16)
C(5)-C(6)	1.381(3)	C(8)-C(9)-H(9)	115.6
C(6)-H(6)	0.9500	C(10)-C(9)-C(8)	128.89(16)
C(6)-C(7)	1.396(2)	C(10)-C(9)-H(9)	115.6
C(7)-H(7)	0.9500	C(9)-C(10)-H(10)	120.0
C(7)-C(8)	1.397(2)	C(9)-C(10)-C(11)	120.00(15)
C(8)-C(9)	1.459(2)	C(11)-C(10)-H(10)	120.0
C(9)-H(9)	0.9500	O(1)-C(11)-O(2)	123.49(15)
C(9)-C(10)	1.336(2)	O(1)-C(11)-C(10)	125.68(15)
C(10)-H(10)	0.9500	O(2)-C(11)-C(10)	110.83(14)
C(10)-C(11)	1.473(2)	O(2)-C(12)-H(12A)	110.4
C(12)-H(12A)	0.9900	O(2)-C(12)-H(12B)	110.4
C(12)-H(12B)	0.9900	O(2)-C(12)-C(13)	106.71(14)
C(12)-C(13)	1.497(2)	H(12A)-C(12)-H(12B)	108.6
C(13)-H(13A)	0.9800	C(13)-C(12)-H(12A)	110.4
C(13)-H(13B)	0.9800	C(13)-C(12)-H(12B)	110.4
C(13)-H(13C)	0.9800	C(12)-C(13)-H(13A)	109.5
		C(12)-C(13)-H(13B)	109.5
C(3)-S(1)-C(2)	89.62(8)	C(12)-C(13)-H(13C)	109.5
C(11)-O(2)-C(12)	115.62(13)	H(13A)-C(13)-H(13B)	109.5
C(2)-N(1)-C(4)	110.56(14)	H(13A)-C(13)-H(13C)	109.5
H(1A)-C(1)-H(1B)	109.5	H(13B)-C(13)-H(13C)	109.5
H(1A)-C(1)-H(1C)	109.5		
H(1B)-C(1)-H(1C)	109.5		
C(2)-C(1)-H(1A)	109.5		
C(2)-C(1)-H(1B)	109.5		
C(2)-C(1)-H(1C)	109.5		
N(1)-C(2)-S(1)	115.68(13)		
N(1)-C(2)-C(1)	124.49(16)		
C(1)-C(2)-S(1)	119.83(13)		
C(4)-C(3)-S(1)	108.55(12)		
C(4)-C(3)-C(8)	121.35(15)		
C(8)-C(3)-S(1)	130.10(13)		

Table S31. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for Yu82. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S(1)	18(1)	13(1)	15(1)	-4(1)	1(1)	-4(1)
O(1)	29(1)	14(1)	21(1)	-4(1)	3(1)	-5(1)
O(2)	21(1)	14(1)	13(1)	-2(1)	2(1)	-6(1)
N(1)	18(1)	16(1)	18(1)	-2(1)	-2(1)	-7(1)
C(1)	27(1)	16(1)	28(1)	-6(1)	-2(1)	-7(1)
C(2)	18(1)	15(1)	19(1)	-3(1)	-5(1)	-6(1)
C(3)	12(1)	17(1)	13(1)	-4(1)	-2(1)	-6(1)
C(4)	14(1)	15(1)	16(1)	-2(1)	-4(1)	-7(1)
C(5)	17(1)	24(1)	12(1)	-2(1)	-1(1)	-10(1)
C(6)	18(1)	23(1)	16(1)	-9(1)	3(1)	-8(1)
C(7)	16(1)	16(1)	20(1)	-6(1)	-2(1)	-4(1)
C(8)	14(1)	17(1)	16(1)	-5(1)	-3(1)	-5(1)
C(9)	17(1)	14(1)	17(1)	-4(1)	-3(1)	-5(1)
C(10)	17(1)	12(1)	18(1)	-3(1)	-2(1)	-4(1)
C(11)	14(1)	16(1)	16(1)	-5(1)	-1(1)	-6(1)
C(12)	22(1)	16(1)	14(1)	1(1)	0(1)	-9(1)
C(13)	27(1)	25(1)	20(1)	-4(1)	2(1)	-12(1)

Table S32. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for Yu82.

	x	y	z	U(eq)
H(1A)	-528	12620	2857	36
H(1B)	1278	13265	2178	36
H(1C)	1203	12383	3601	36
H(5)	5380	7993	213	21
H(6)	6656	4663	614	22
H(7)	5916	2746	2444	21
H(9)	4503	2221	4385	19
H(10)	1999	5216	5339	19
H(12A)	2562	772	8691	21
H(12B)	647	776	8223	21
H(13A)	-1333	3483	8917	37
H(13B)	576	3441	9402	37
H(13C)	-247	1738	10001	37

11. References

1. Ye, M. *et al.* Ligand-promoted C3-selective arylation of pyridines with Pd catalysts: gram-scale synthesis of (±)-Preclamol. *J. Am. Chem. Soc.* **133,** 19090–19093 (2011).
2. Kudo, N., Perseghini, M. & Fu, G. C. A versatile method for Suzuki cross-coupling reactions of nitrogen heterocycles. *Angew. Chem. Int. Ed.* **45,** 1282–1284 (2006).
3. Gran, U., Wennerström, O. & Westman, G. Stereoselective reductions with macrocyclic NADH models. *Tetrahedron: Asymmetry* **11,** 3027–3040 (2000).
4. Rudolf, S., Goebel, W. & Neumann, W. Reactions of pyridine-3-sulfonyl chloride with amines. *Acta Chim. Acad. Sci. Hung.* **64,** 267–271 (1970).
5. Thelemann, J. *et al.* Aryl bis-sulfonamide inhibitors of IspF from Arabidopsis thaliana and Plasmodium falciparum. *ChemMedChem* **10,** 2090–2098 (2015).
6. Planas, O., Whiteoak, C. J., Company, A. & Ribas, X. Regioselective access to sultam motifs through cobalt-catalyzed annulation of aryl sulfonamides and alkynes using an 8-aminoquinoline directing group. *Adv. Synth. Catal.* **357,** 4003–4012 (2015).
7. Royo, E., Betancort, J. M., Davis, T. J., Carroll, P. & Walsh, P. J. Synthesis, structure, and catalytic properties of bis[bis(sulfonamido)] titanium complexes. *Organometallics* **19,** 4840–4851 (2000).
8. Chen, L. *et al.* Structure–based design of 3-carboxy-substituted 1,2,3,4-tetrahydroquinolines as inhibitors of myeloid cell leukemia-1 (Mcl-1). *Org. Biomol. Chem.* **14,** 5505–5510 (2016).
9. Mcnab, H. ^{13}C Nuclear Magnetic Resonance Spectra of Quinoxaline Derivatives. *J. Chem. Soc., Perkin Trans.* **1,** 357–363 (1982).
10. Kimura, H., Torikai, K. & Ueda, I. Termal Cyclization of Nonconjugated Aryl-Yne-Carbodiimide Furnishing a Dibenzonaphthyridine Derivative. *Chem. Pharm. Bull.* **57,** 393–396 (2009).
11. Thansandote, P., Hulcoop, D. G., Langer, M. & Lautens, M. Palladium–Catalyzed Annulation of Haloanilines and Halobenzamides Using Norbornadiene as an Acetylene Synthon: A Route to Functionalized Indolines, Isoquinolinones, and Indoles. *J. Org. Chem.* **74,** 1673–1678 (2009).
12. Ong, W. Q. *et al.* Conputational prediction and experimental verification of pyridine–based helical oligoamides containing four repeating units per helical turn. *Chem. Commun.* **47,** 6416–6418 (2011).