Iron-Catalyzed Regioselective Remote C(sp^2)-H Carboxylation of Naphthyl and Quinoline Amides

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Table of Contents

Scheme S1. Metal-Catalyzed Direct C-H Carboxylation Using C1 Sources	S2
Figure S1. Examples of Some Biologically Important Naphthalene and Quinoline Based Carboxylic Acid Scaffolds.	S2
Table S1. Optimization of Reaction Conditions	S3
Scheme S2. Effect of DG's on Carboxylation	S4
Crystal Data and Structure Refinement for **2b**	S4-5
ESI-MS analysis of the reaction mixture in the presence of TEMPO	S5
^{1}H and ^{13}C NMR Spectra	S6-S52

Scheme S1. Metal-Catalyzed Direct C-H Carboxylation Using C1 Sources

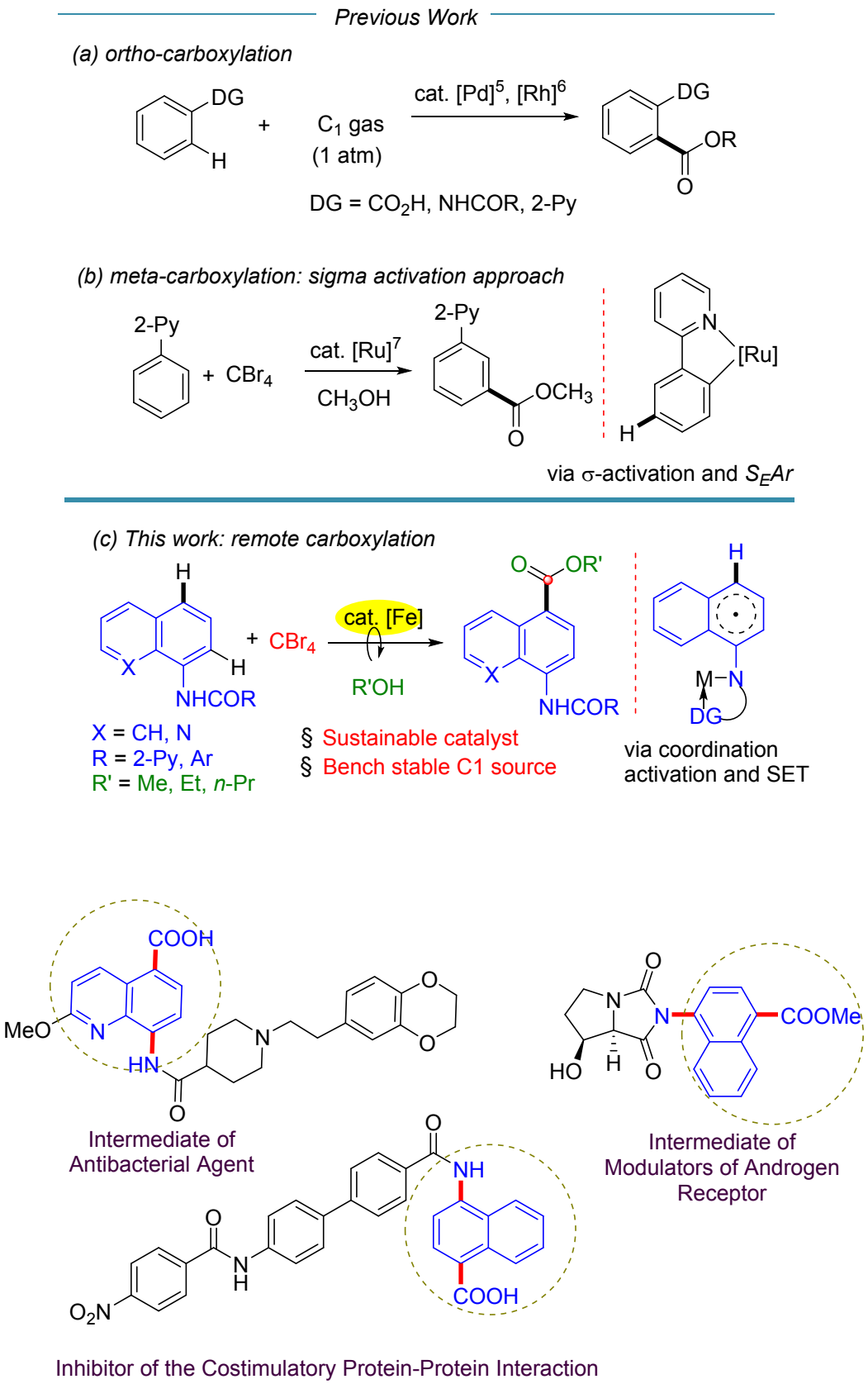
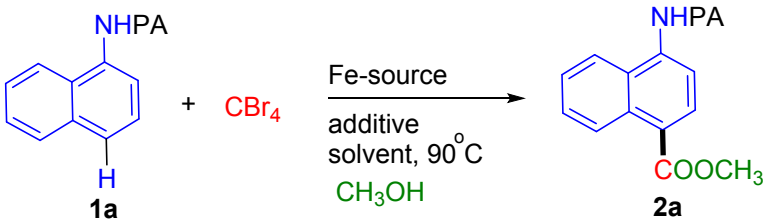


Figure S1. Examples of Some Biologically Important Naphthalene and Quinoline Based Carboxylic Acid Scaffolds.

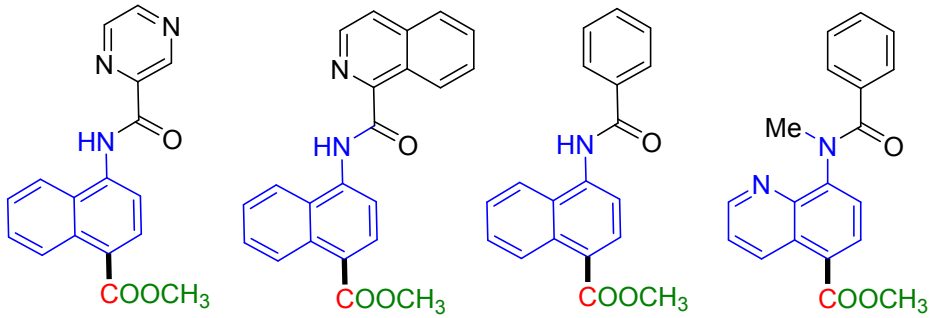
Table S1. Optimization of Reaction Conditions[a]



entry	Fe-source	additive	solvent	yield[b] (%)
1	$Fe(acac)_3$	-	1,4-Dioxane	47
2	$Fe(acac)_3$	-	DMA	21
3	$Fe(acac)_3$	-	CH_3CN	43
4	$Fe(acac)_3$		$(CH_2Cl)_2$	37
5	$Fe(acac)_3$	-	CH_3OH	51
6	$Fe(acac)_3$	-	CF_3CH_2OH	39
7	$Fe(acac)_3$		H_2O	41
8	$FeCl_3$	-	CH_3OH	45
9	$FeSO_4$•$7H_2O$	-	CH_3OH	41
10	Ferrocene	-	CH_3OH	43
11	$Fe(NO_3)_3$•$9H_2O$	-	CH_3OH	n.d.
12[c]	$Fe(acac)_3$	PivOH	CH_3OH	53
13	**$Fe(acac)_3$**	**PivOH**	**CH_3OH**	**65**
14	$Fe(acac)_3$	1-Ad-OH	CH_3OH	61
15	$Fe(acac)_3$	$MesCO_2H$	CH_3OH	63
16[d]	$Fe(acac)_3$	PivOH	CH_3OH	39
17[e]	$Fe(acac)_3$	PivOH	CH_3OH	trace
18[f]	$Fe(acac)_3$	PivOH	CH_3OH	27
19	-	PivOH	CH_3OH	n.d.

[a]Reaction conditions: **1a** (0.2 mmol), CBr_4 (0.6 mmol), Fe-source (10 mol %), additive (0.2 mmol), CH_3OH:solvent (1:1), 90 °C, 24 h. [b]Isolated yield. [c]50 mol% PivOH, [d]5 mol % $Fe(acac)_3$. [e]60 °C. [f]0.2 mmol CBr_4. PivOH = pivalic acid; 1-Ad-OH = adamantanecarboxylic acid; $MesCO_2H$ = mesitylenecarboxylic acid. n.d. = not detected.

Scheme S2. Effect of DG's on Carboxylation[a,b]



2p, 57% **2q**, 58% **2r**, n.d. **2s**, n.d.

[a]Reaction conditions: **1l-o** (0.2 mmol), CBr_4 (0.6 mmol), MeOH (1.5 mL), PivOH (0.2 mmol), $Fe(acac)_3$ (10 mol %), 90 °C, 24 h. [b]Isolated yield. n.d. = not detected.

Crystal data and Structure Refinement

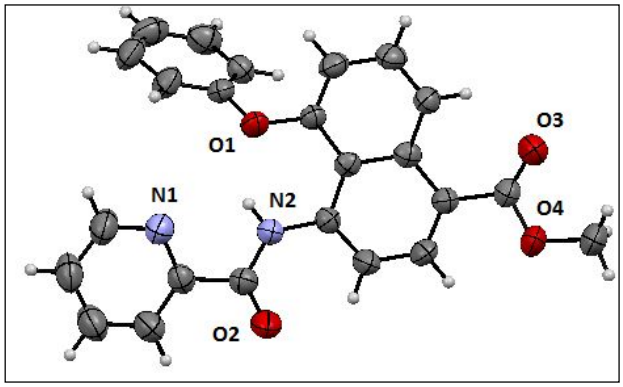
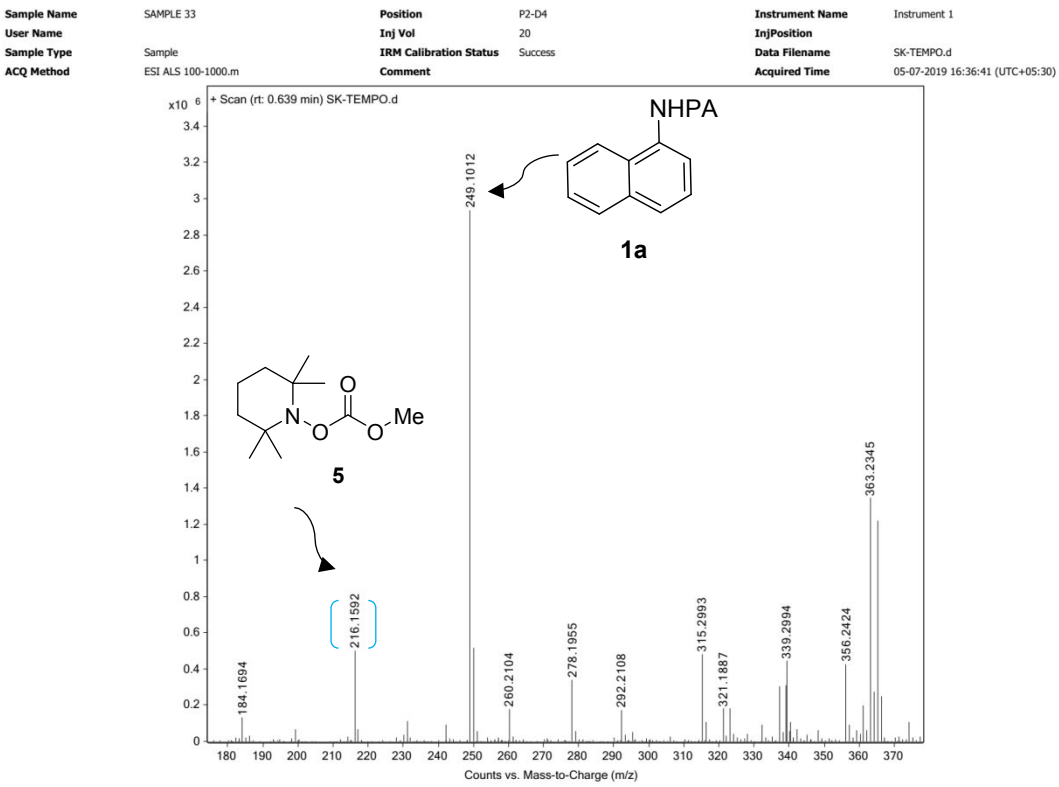


Figure S2. ORTEP diagram of methyl 5-phenoxy-4-(picolinamido)-1-naphthoate **2b** with 50% ellipsoid (CCDC 1910785).

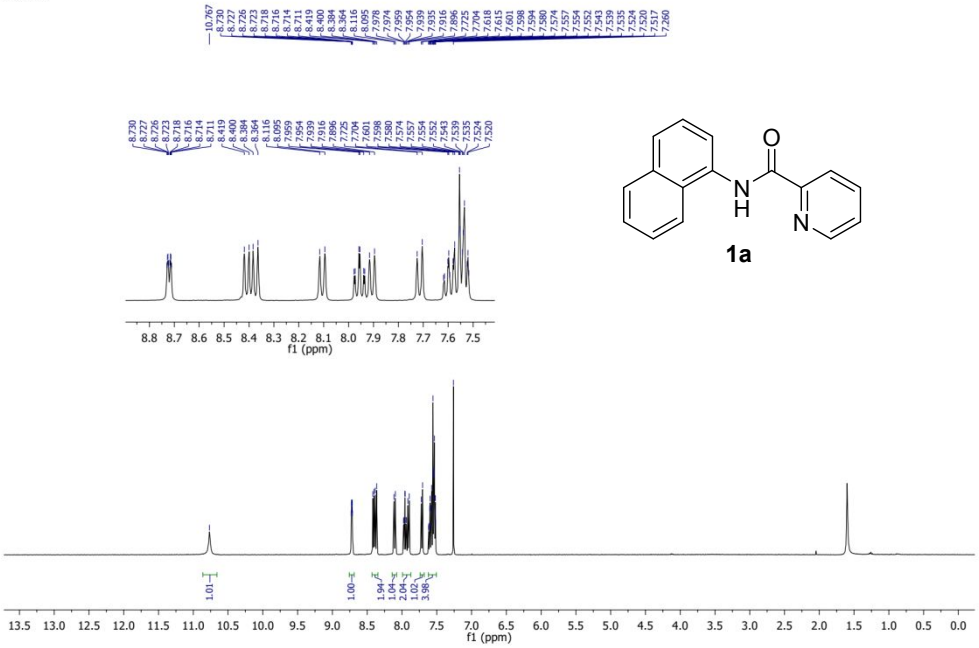
Identification code	**2b**
Empirical formula	$C_{24}H_{18}N_2O_4$
Formula weight	398.42
Crystal habit, color	Needle / colorless
Temperature, *T*/K	293(2)
Wavelength, *λ*/Å	0.71073

Crystal system	monoclinic
Space group	P 21/c
Unit cell dimensions	a = 29.2218(9)Å b = 9.7598(4)Å c = 20.4945(8)Å α = 90.000 β = 91.601(3) γ = 90.000
Volume, V/Å^3	5842.7(4)
Z	4
Calculated density, Mg·m^{-3}	1.347
Absorption coefficient, μ/mm^{-1}	0.089
F(000)	2496
θ range for data collection	2.311 to 24.999°
Limiting indices	$-34 \leq h \leq 23$, $-8 \leq k \leq 11$, $-23 \leq l \leq 23$
Reflection collected	5683
Completeness to θ	99.9 % (θ = 24.999°)
Absorption correction	0.089
Refinement method	'SHELXL-2014/7'
Data / restraints / parameters	10288/0/ 814
Goodness–of–fit on F^2	1.001
Final R indices [I>2sigma(I)]	$R1$ = 0.0687, $wR2$ = 0.1901
R indices (all data)	$R1$ = 0.1239, $wR2$ = 0.1901

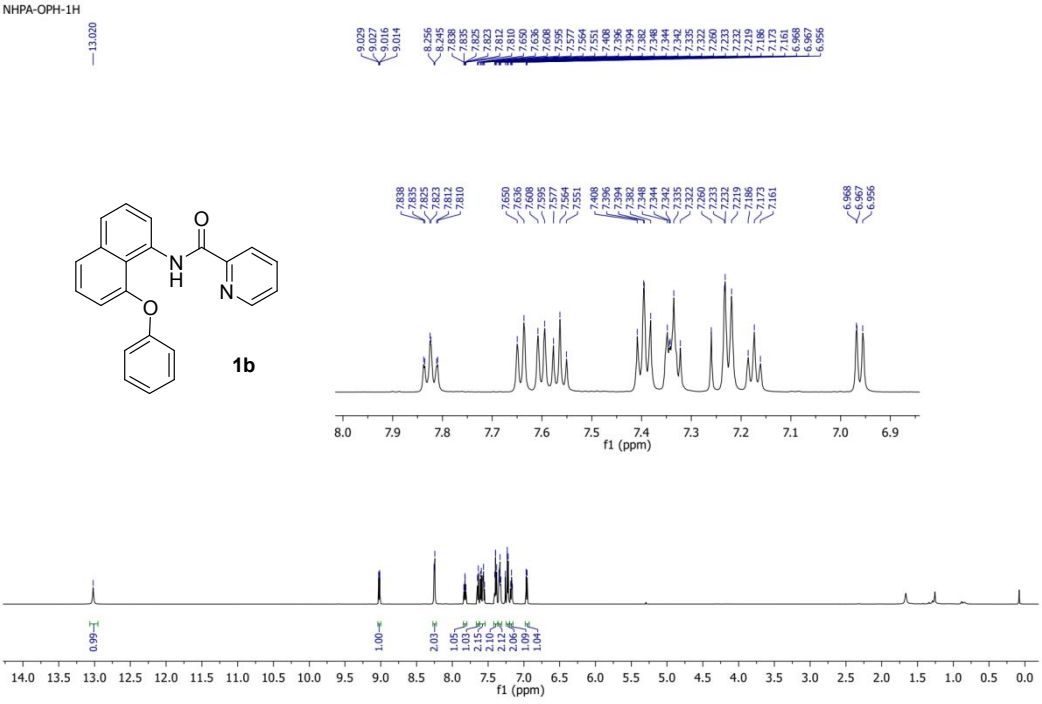
ESI-MS analysis of the reaction mixture in the presence of TEMPO



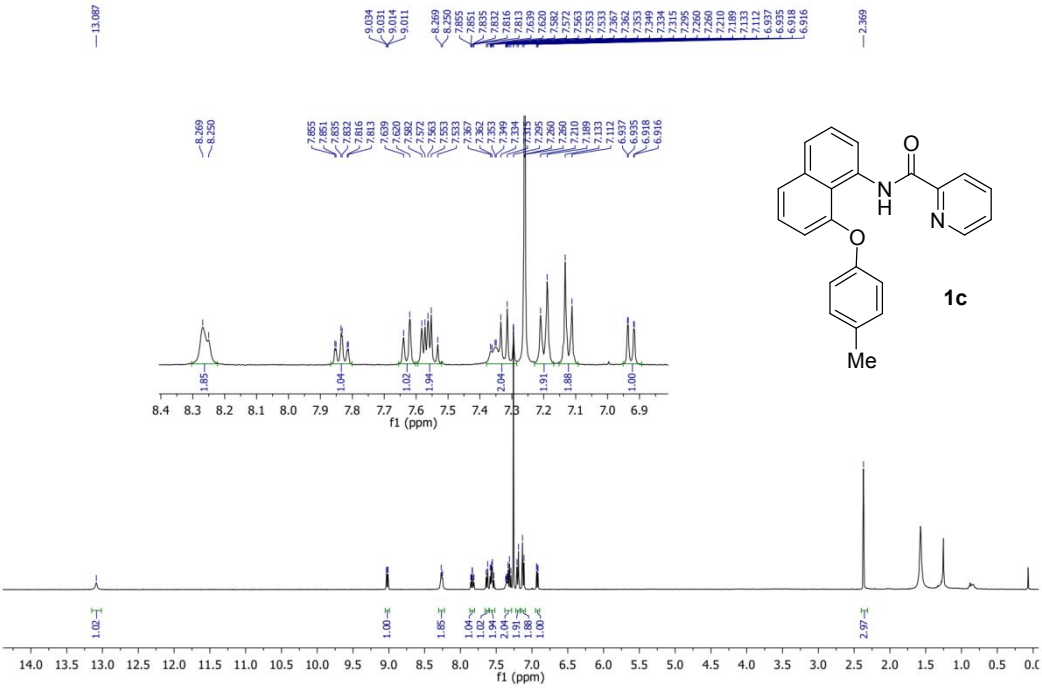
NHPA-1H



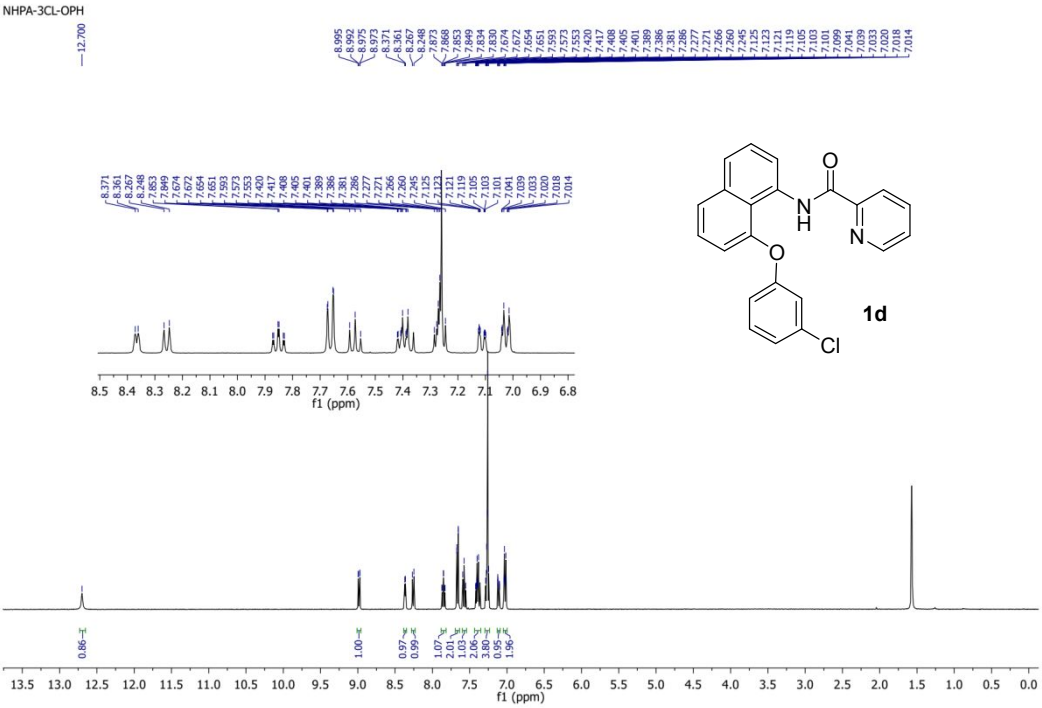
NHPA-OPH-1H



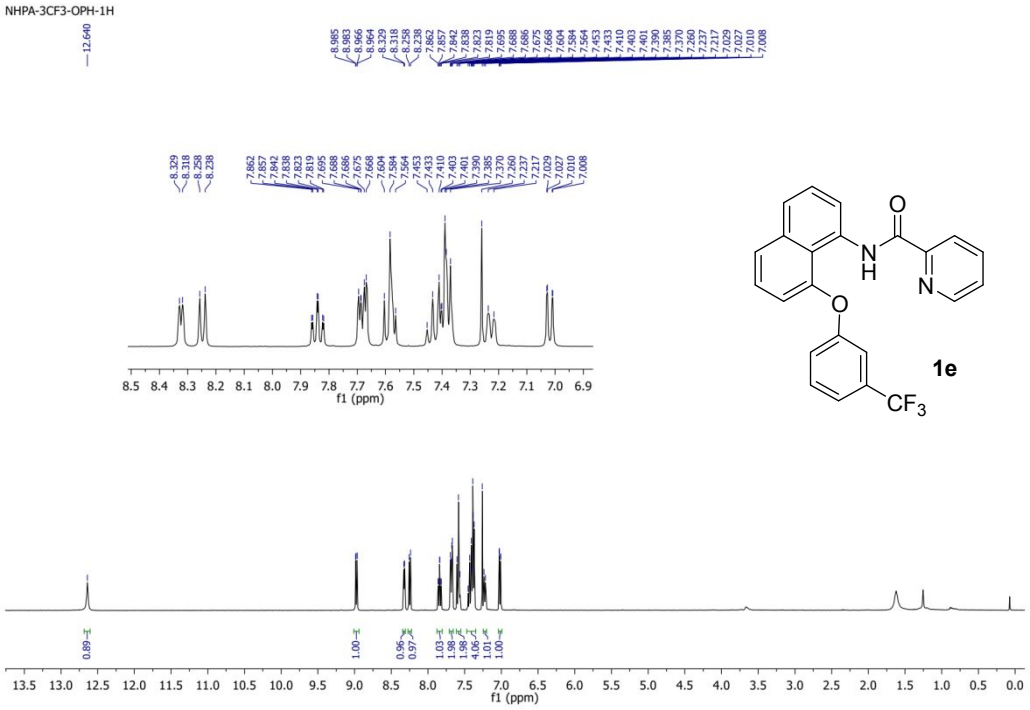
NHPA-4ME-OPH



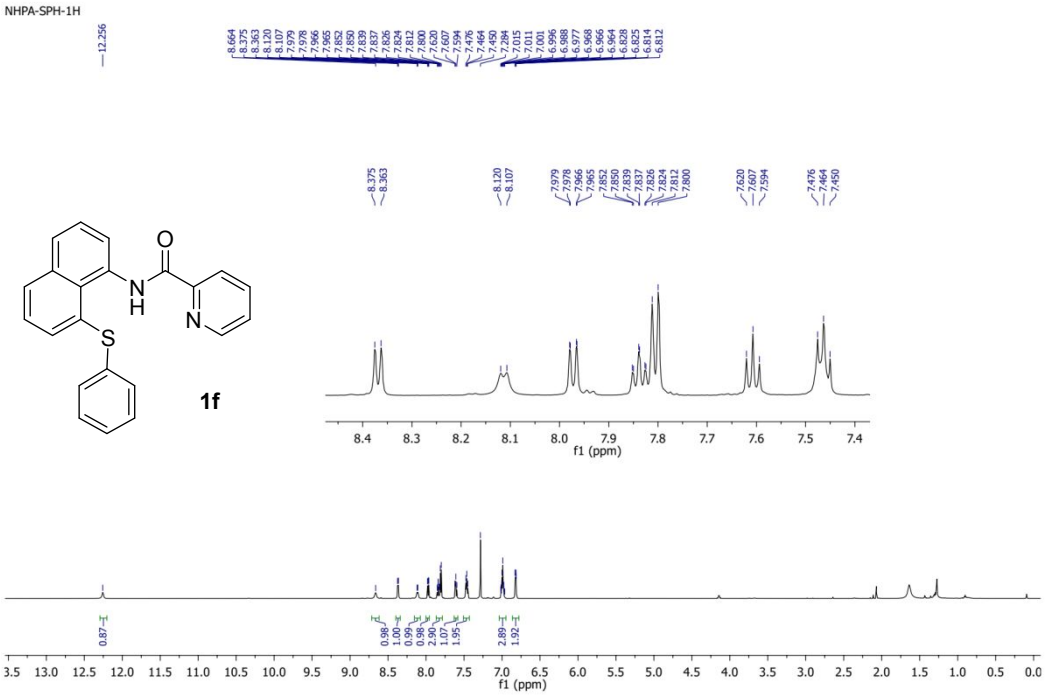
NHPA-3CL-OPH



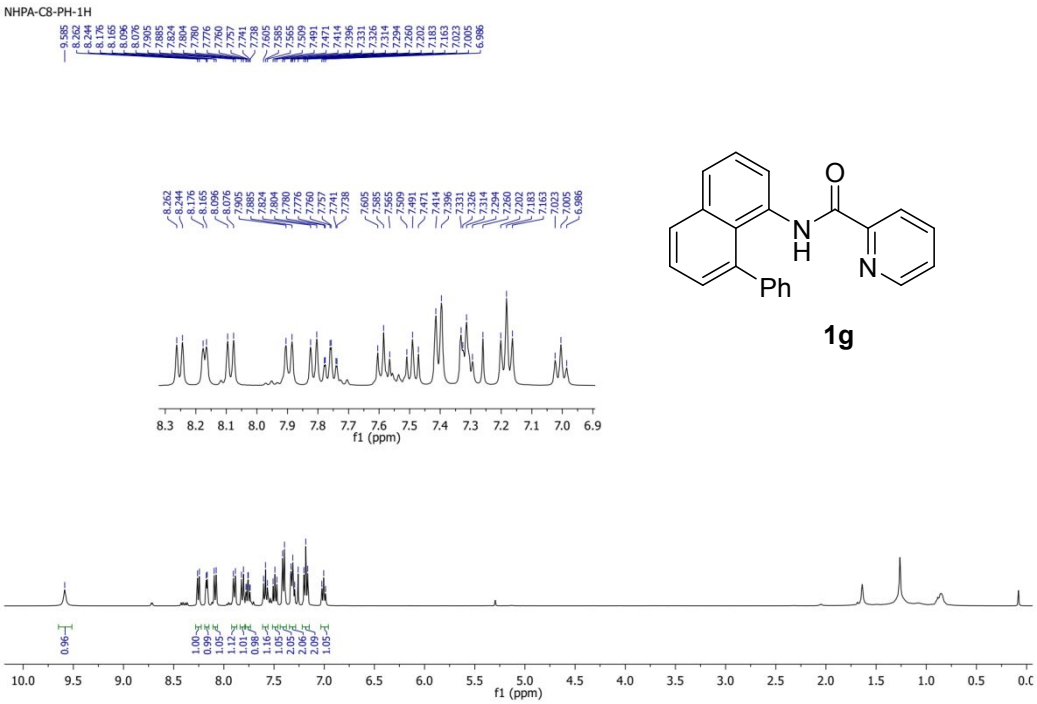
NHPA-3CF3-OPH-1H



NHPA-SPH-1H

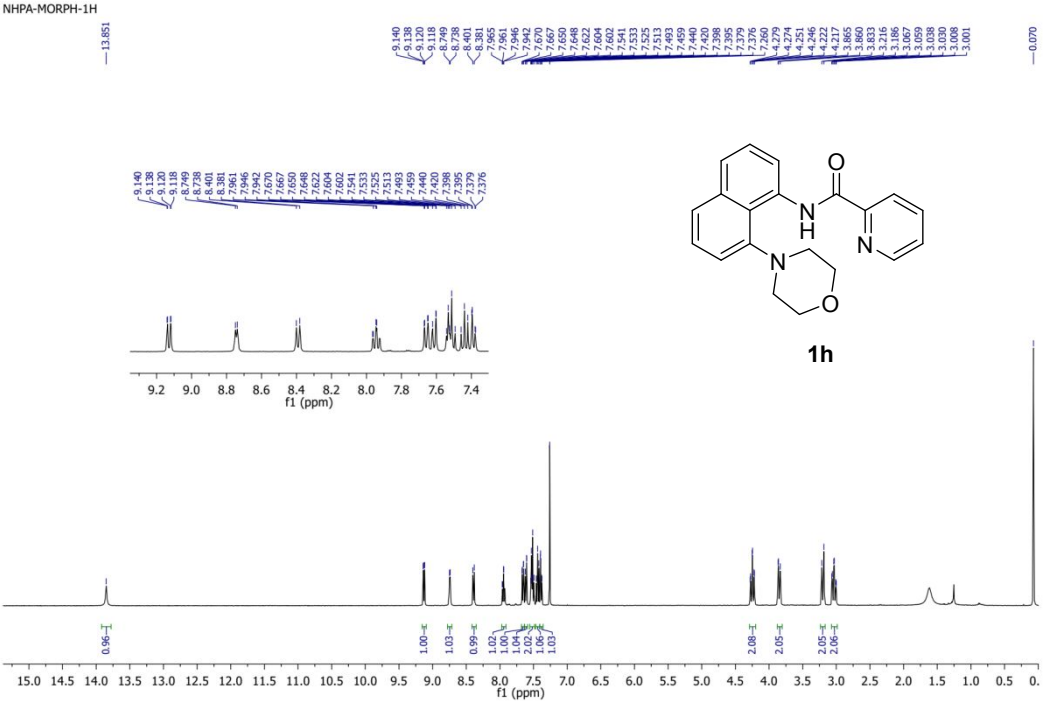


NHPA-C8-PH-1H



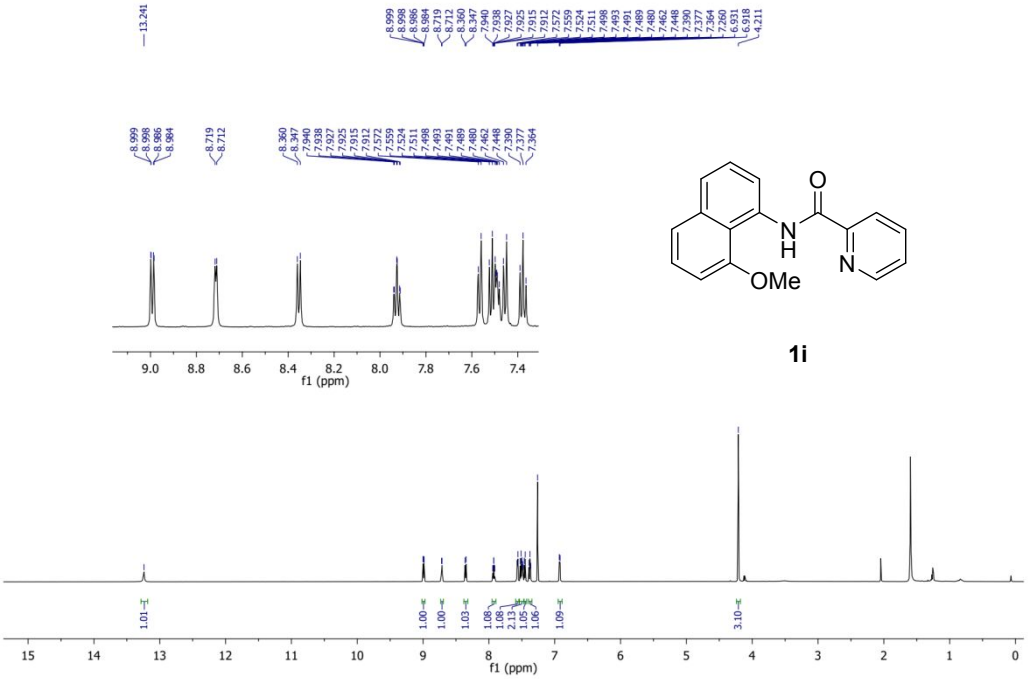
1g

NHPA-MORPH-1H



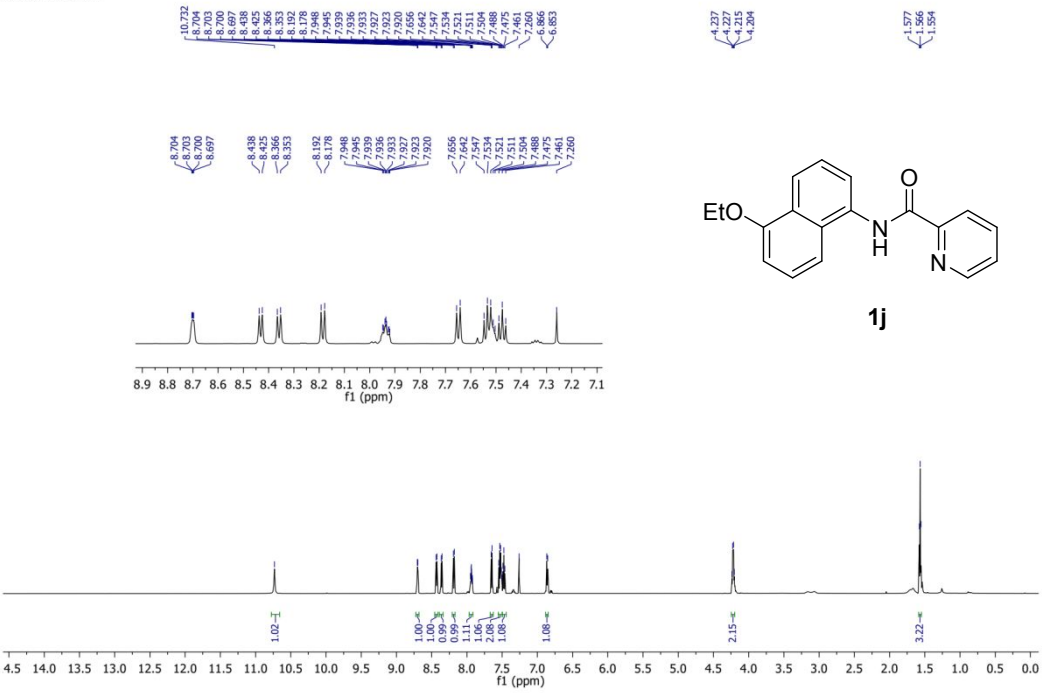
1h

SK-P-OME-SM-1H



1i

SK-OET-PA-SM-1H



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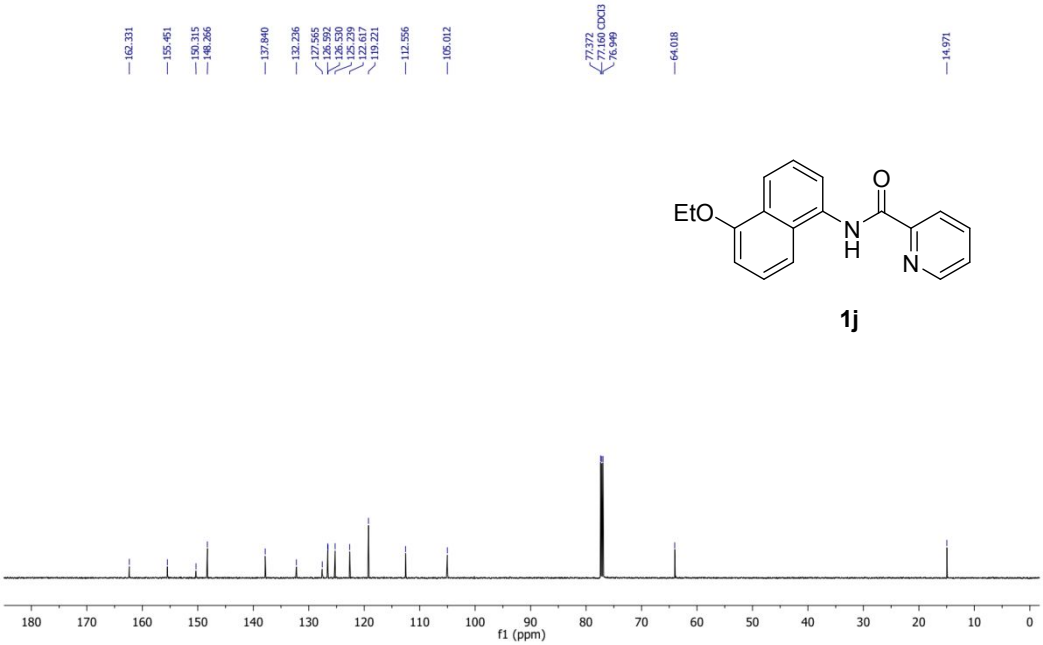
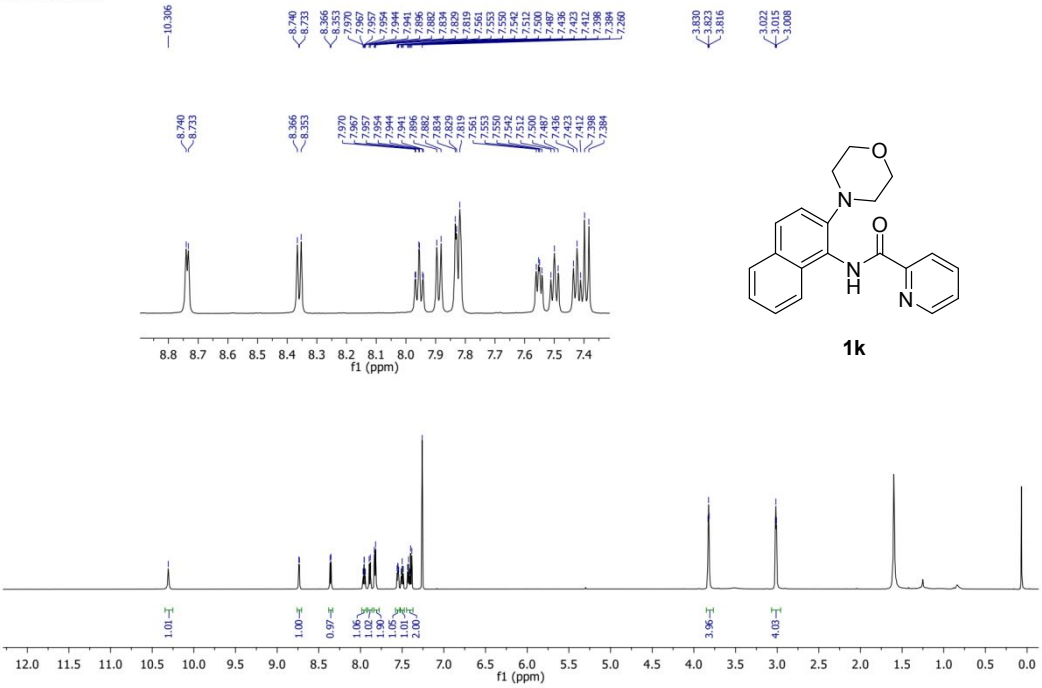
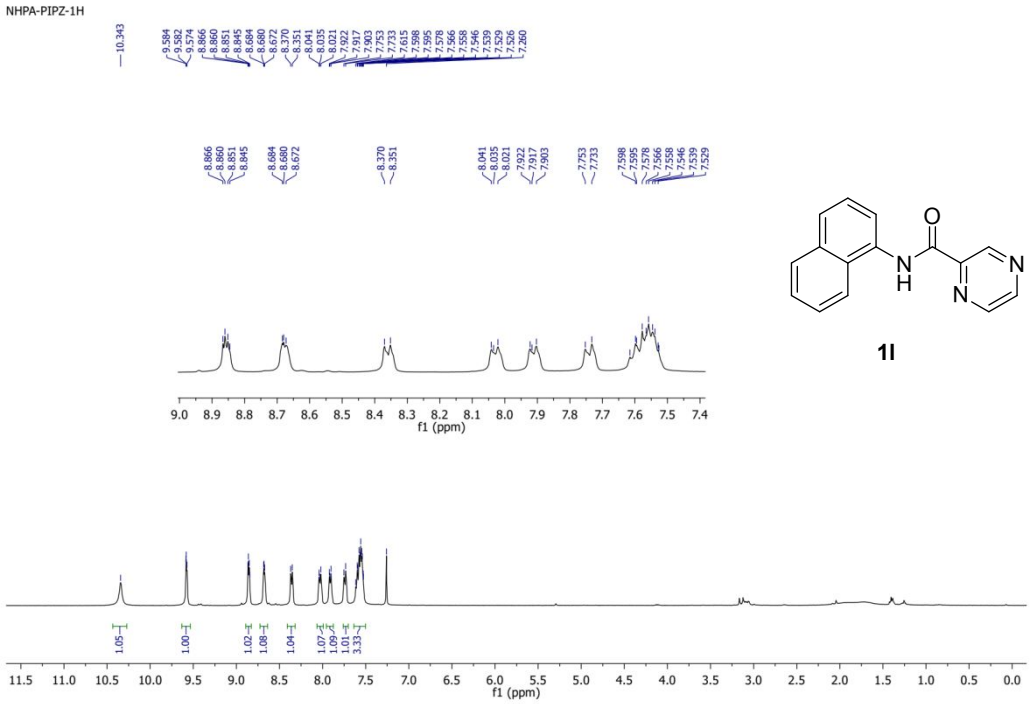


SK-MOR-PA-SM-1H

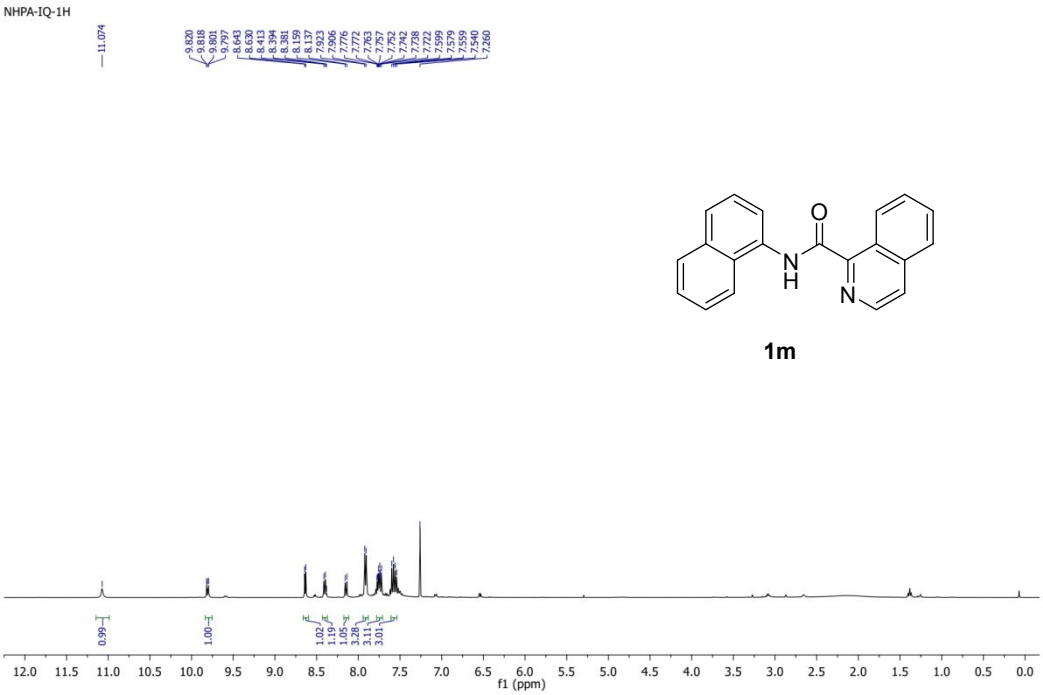


NHPA-PIPZ-1H

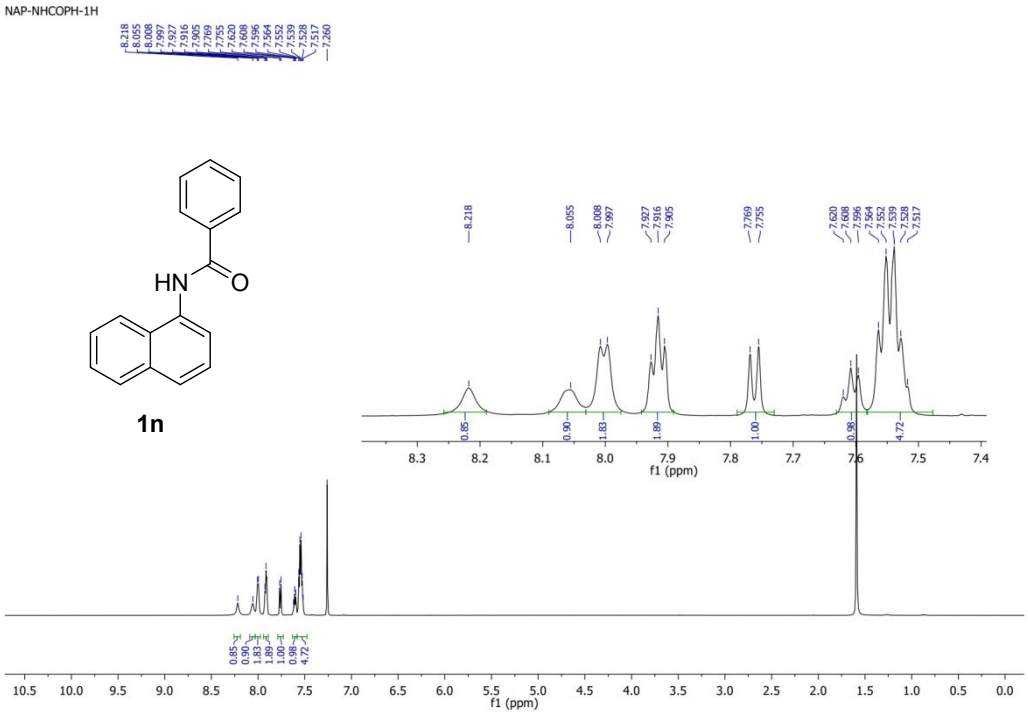


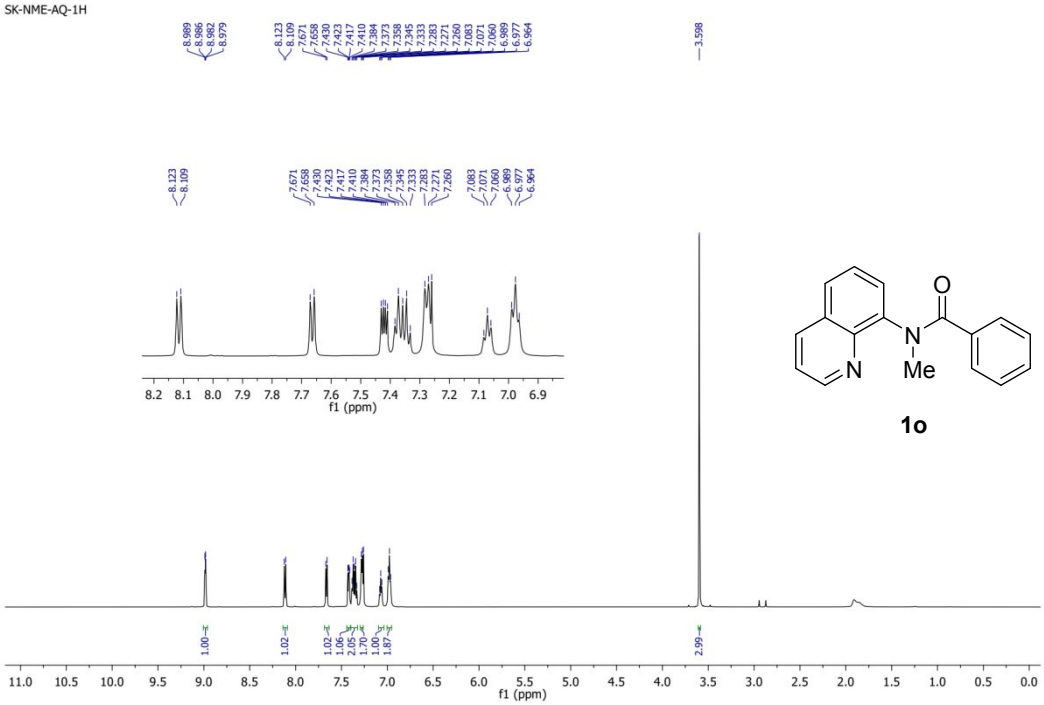
1l

NHPA-IQ-1H

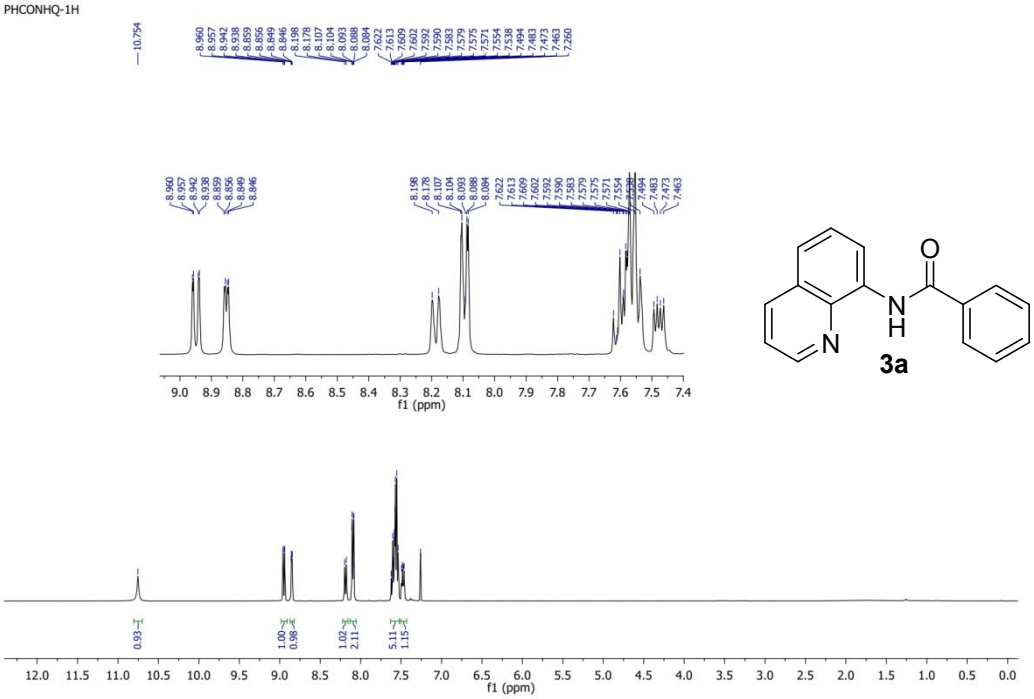


1m

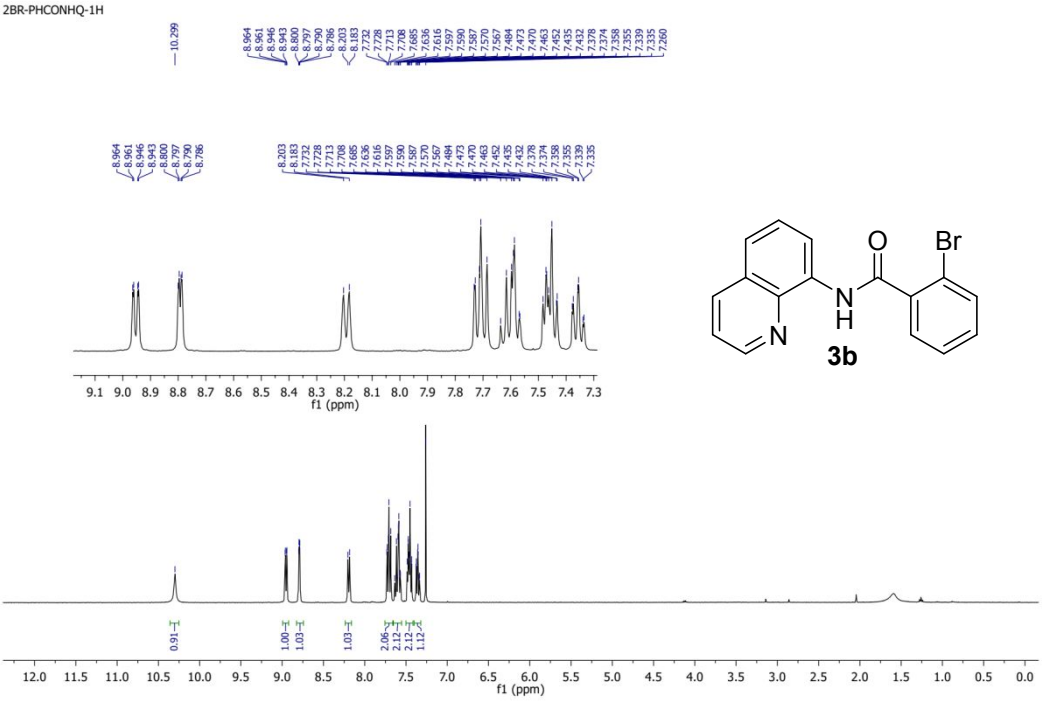

NAP-NHCOPH-1H
HN
O
1n
f1 (ppm)


SK-NME-AQ-1H
N
N
Me
O
1o
f1 (ppm)

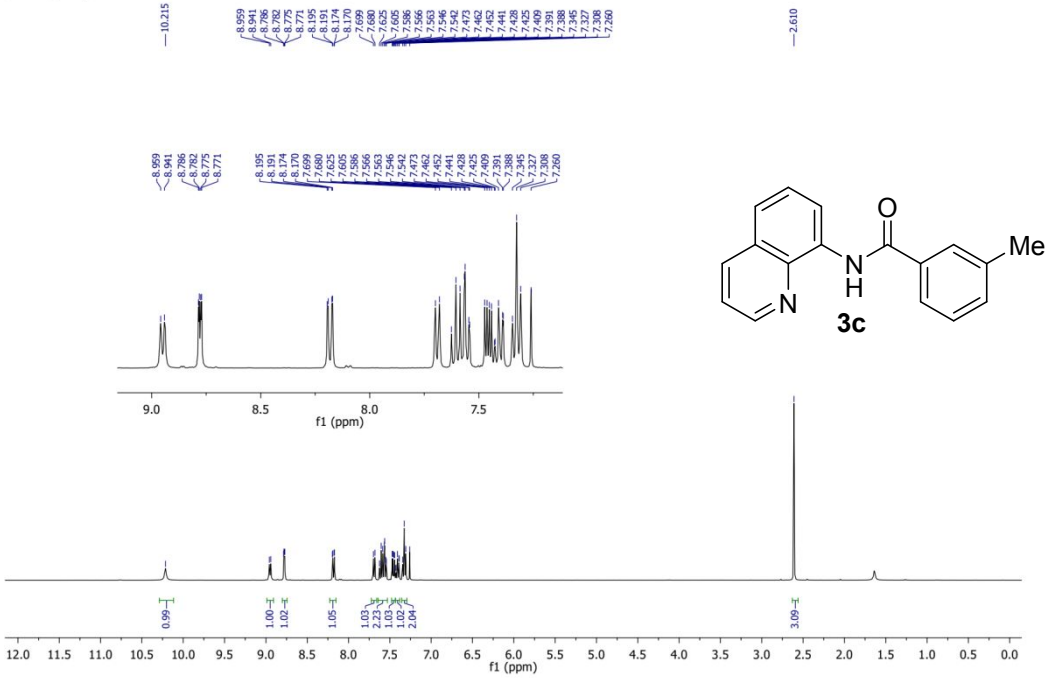
PHCONHQ-1H



2BR-PHCONHQ-1H



3ME-PHCONHQ-1H



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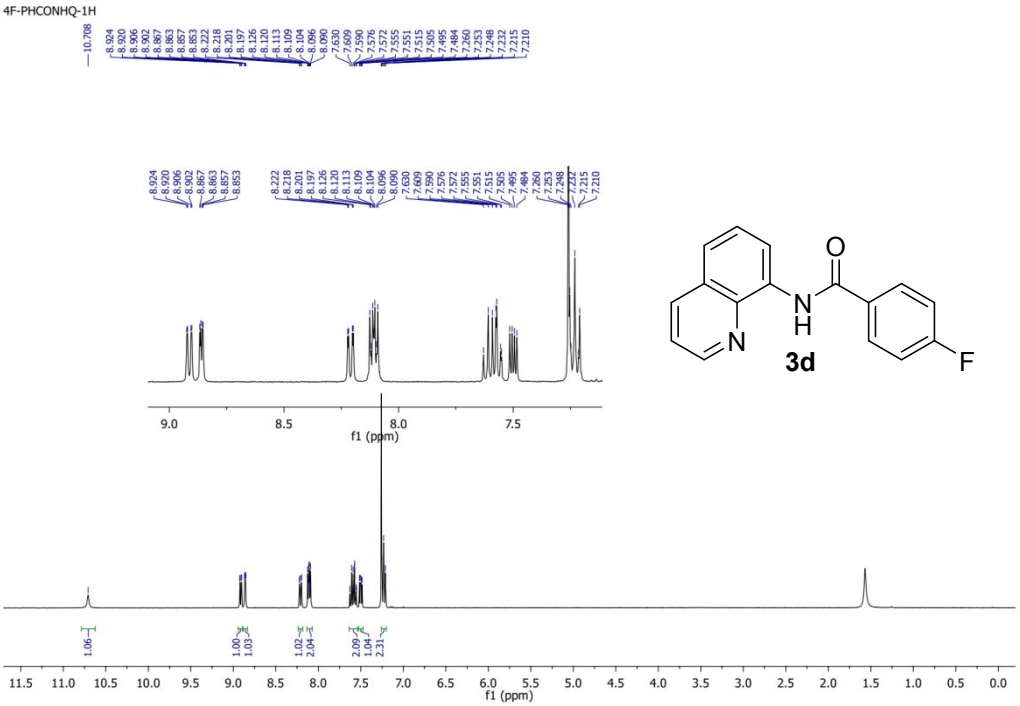
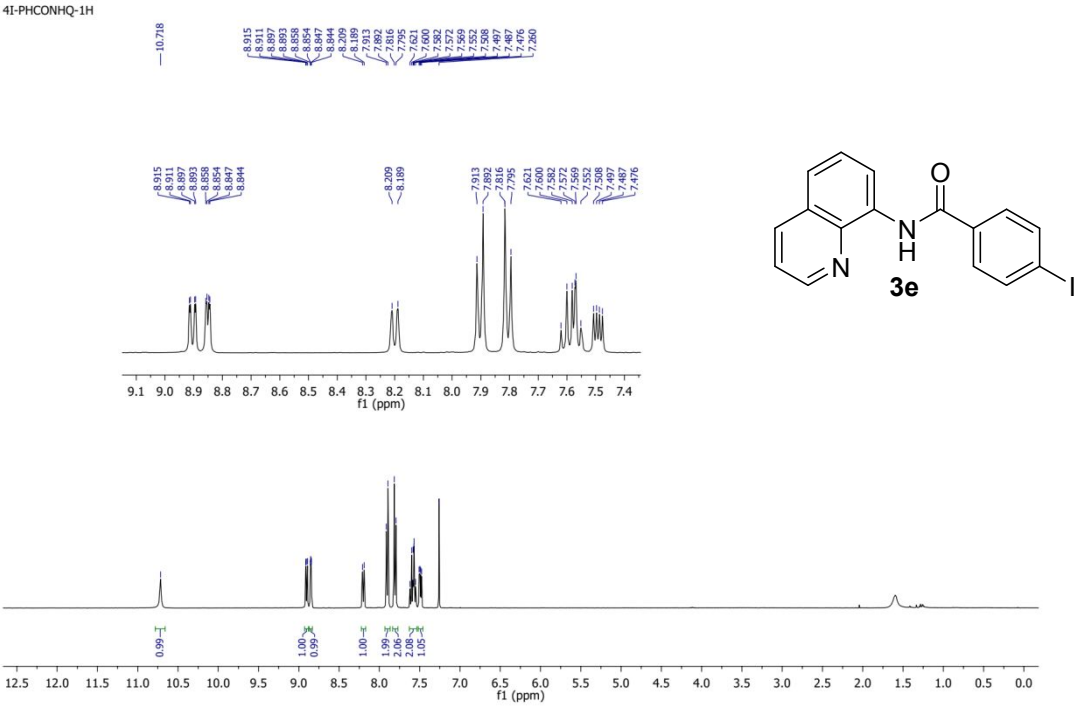
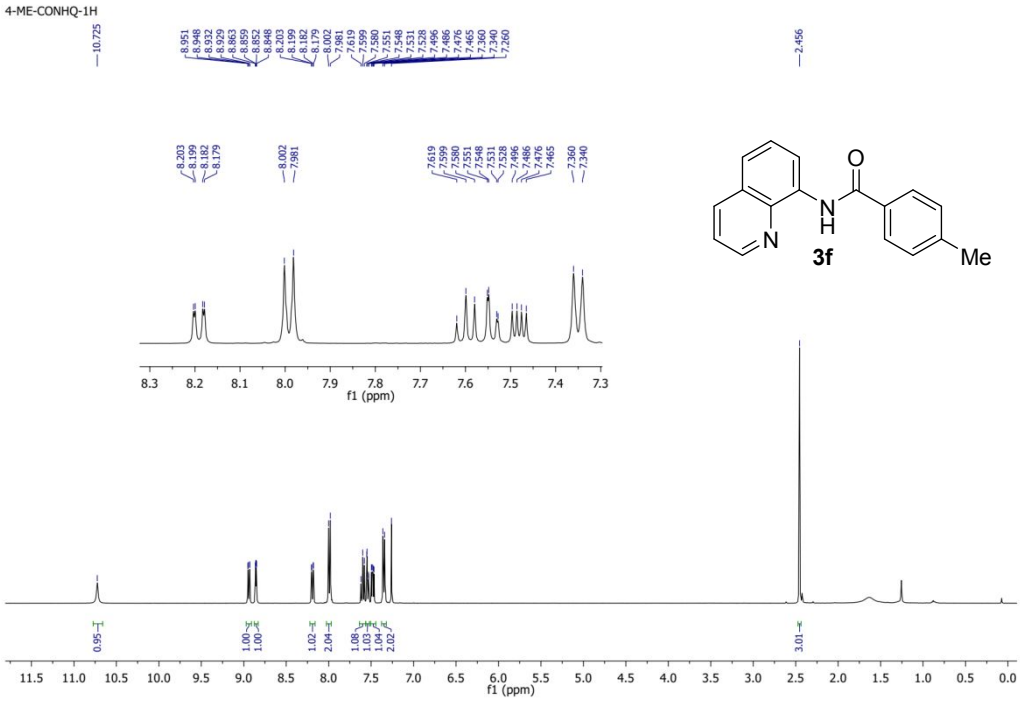


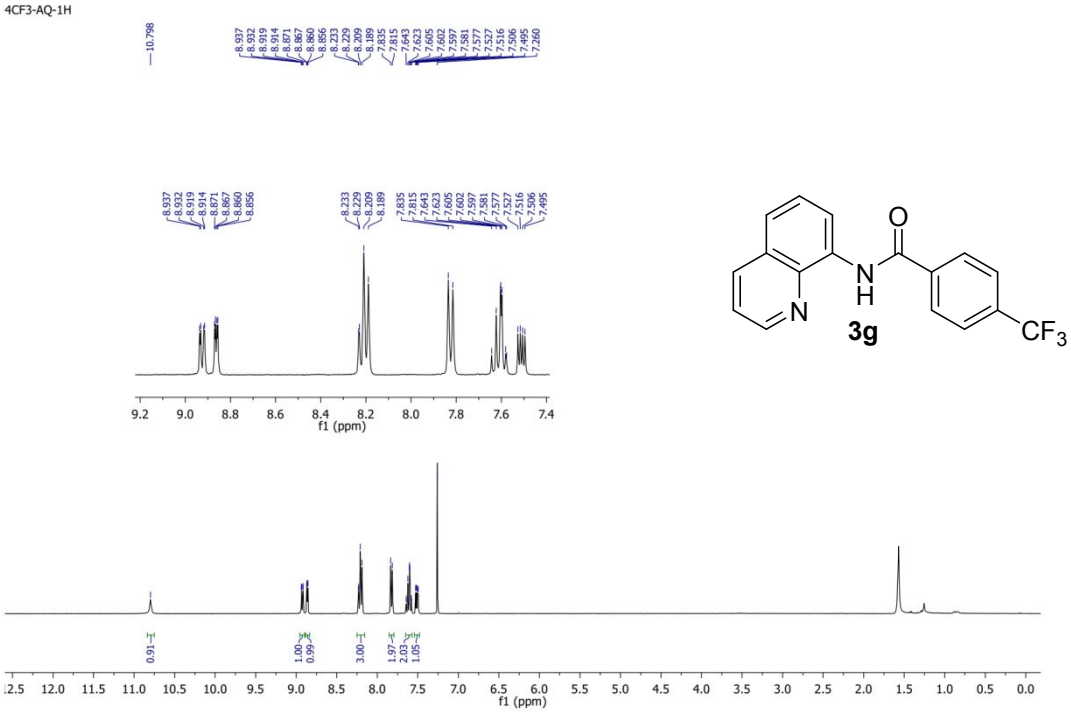
4I-PHCONHQ-1H



4-ME-CONHQ-1H



4CF3-AQ-1H



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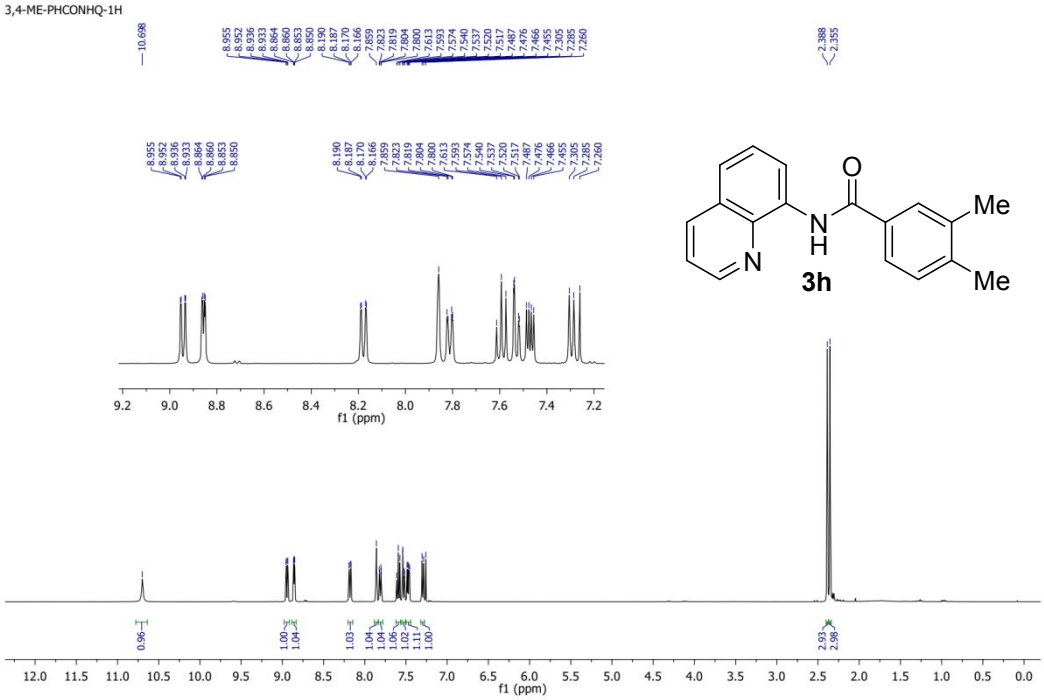
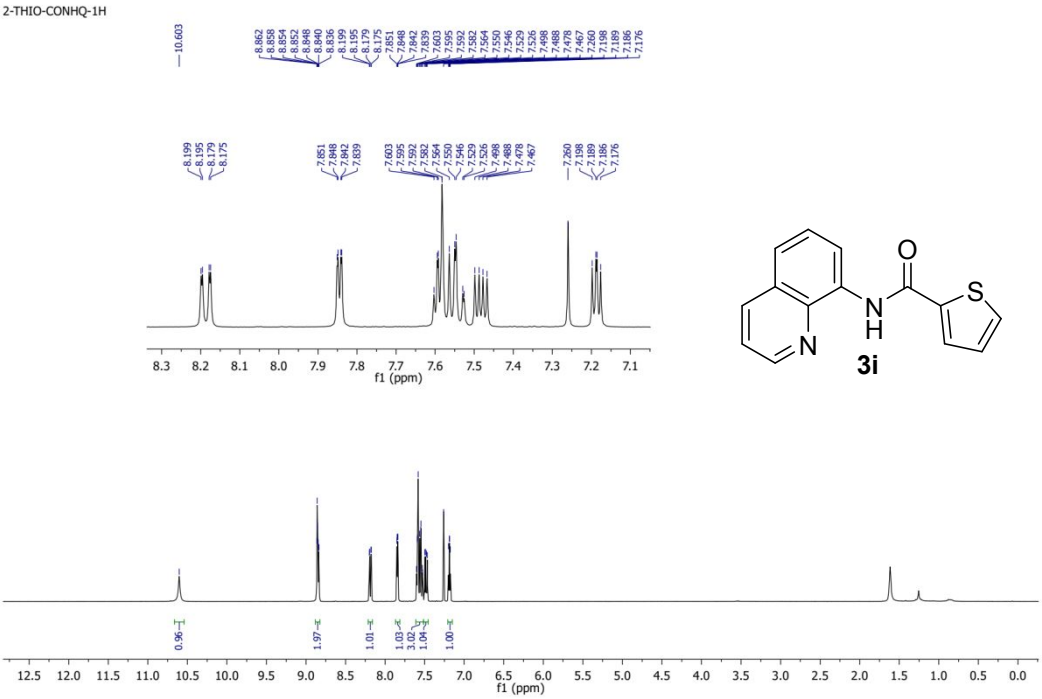
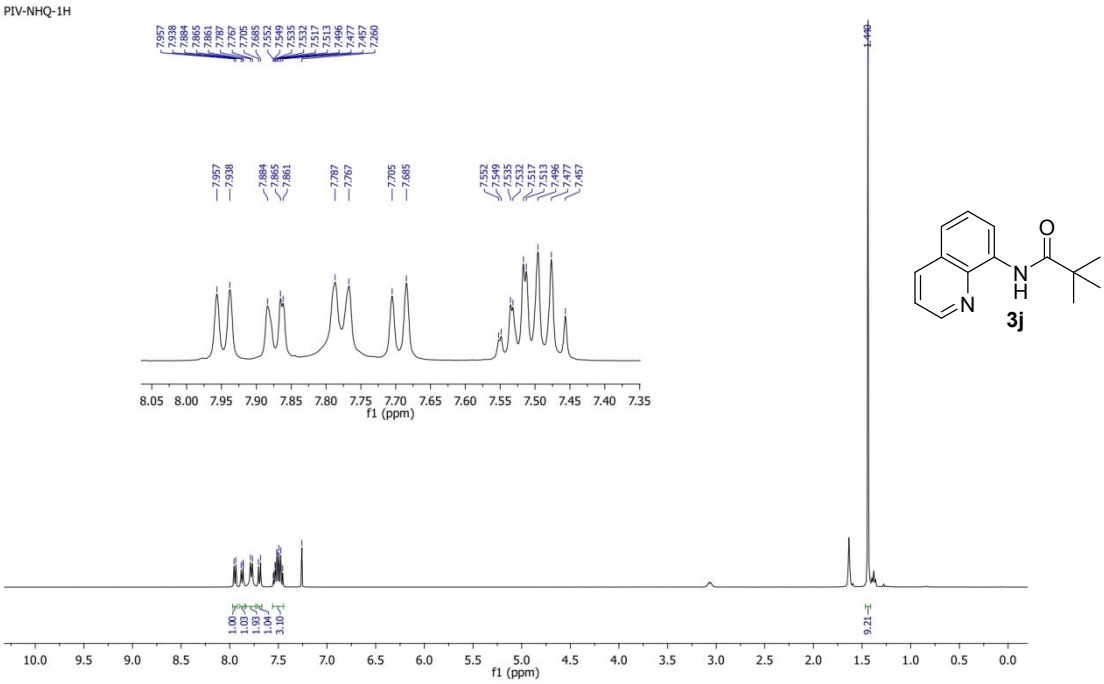


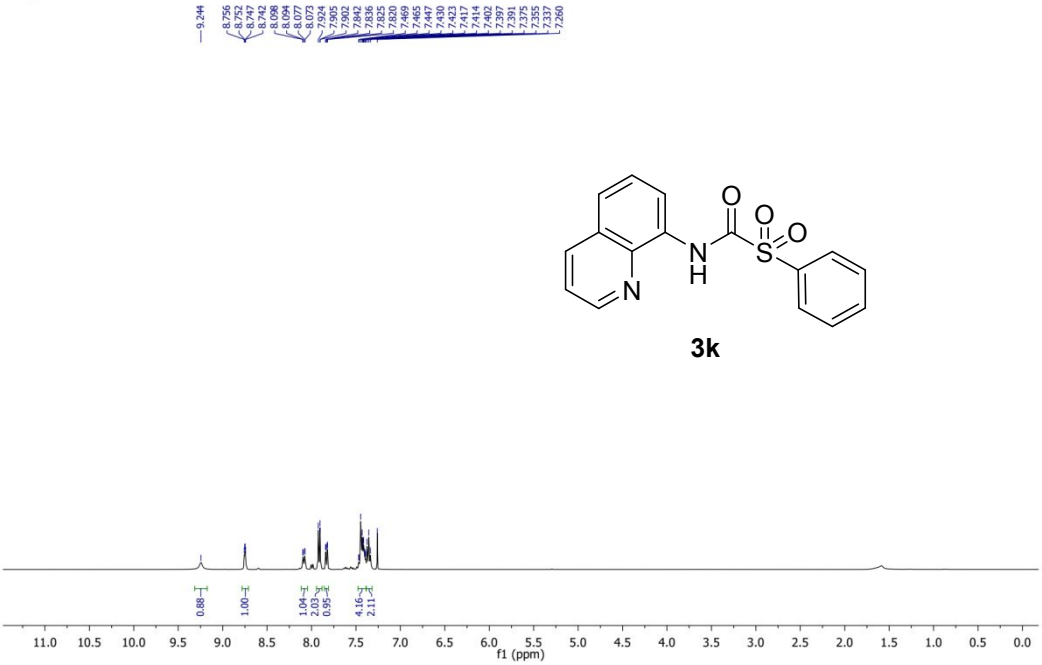
2-THIO-CONHQ-1H



PIV-NHQ-1H

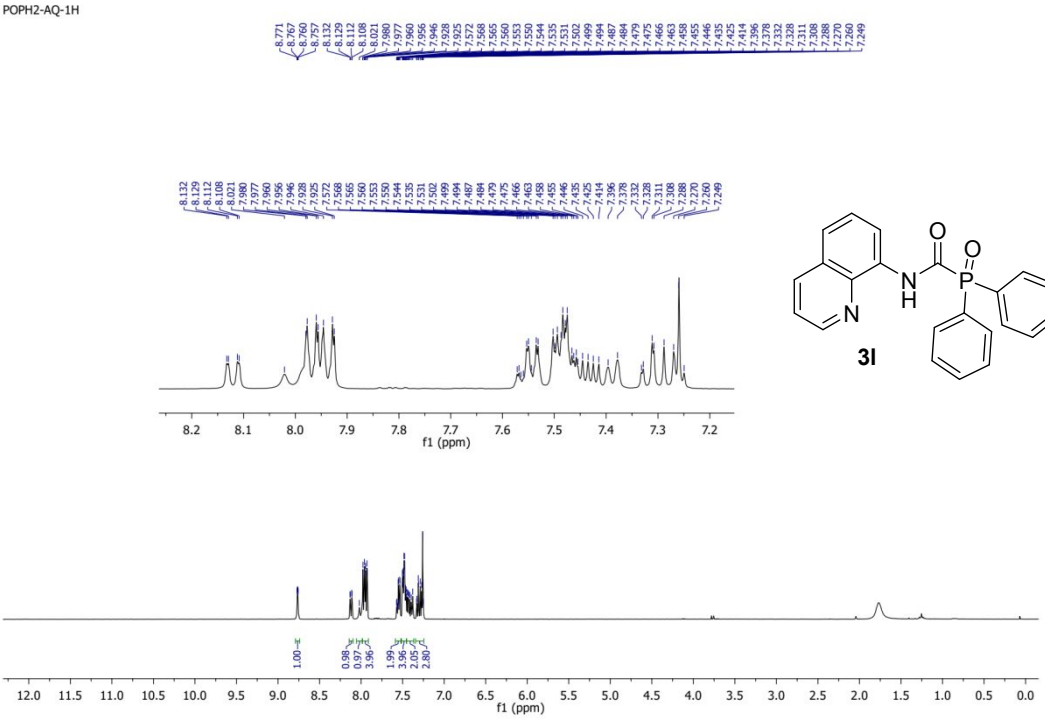


SNHQ-1HA



3k

POPH2-AQ-1H



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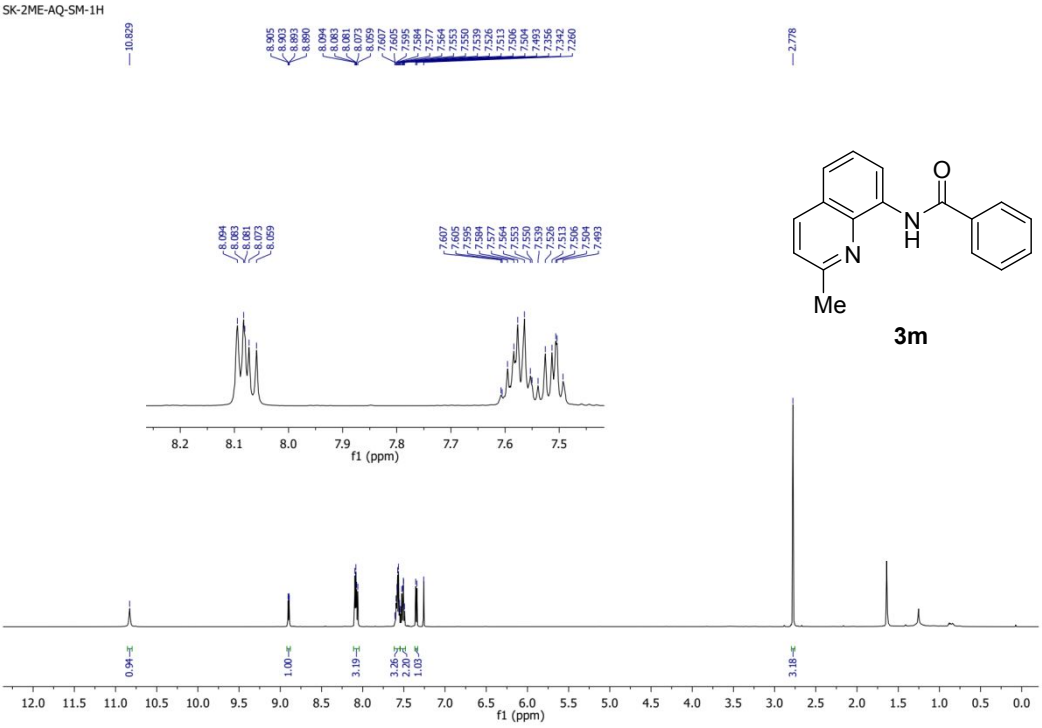
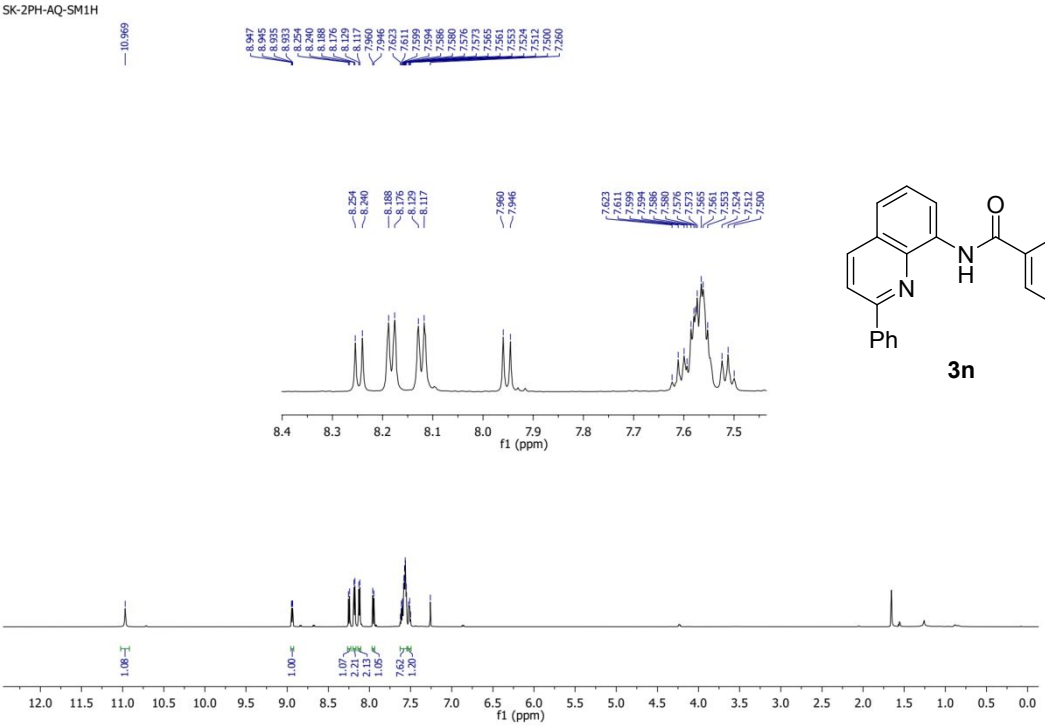
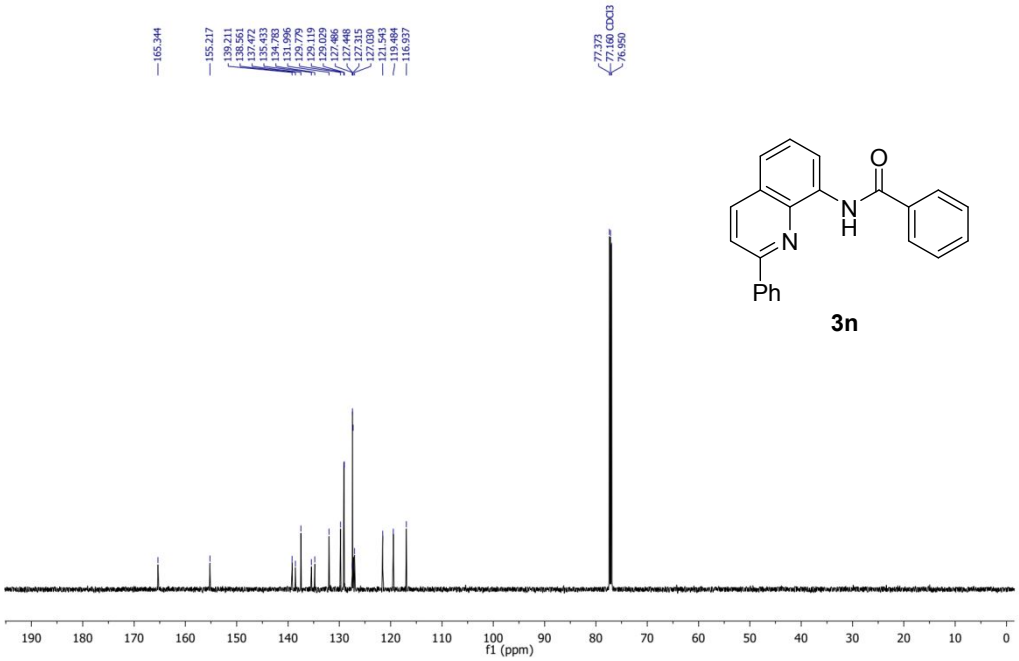

SK-2ME-AQ-SM-1H
10.829
8.905
8.903
8.893
8.890
8.094
8.083
8.081
8.073
8.069
7.607
7.605
7.595
7.584
7.577
7.564
7.553
7.550
7.539
7.526
7.513
7.506
7.504
7.493
7.356
7.342
7.260
2.778
0.94
1.00
3.19
3.26
2.20
1.03
3.18
f1 (ppm)

3m


SK-2PH-AQ-SM1H
10.969
8.947
8.945
8.935
8.931
8.254
8.240
8.188
8.176
8.129
8.117
7.960
7.946
7.623
7.611
7.599
7.594
7.586
7.580
7.576
7.573
7.565
7.561
7.553
7.524
7.512
7.500
7.260
1.08
1.00
1.07
2.21
2.13
1.05
7.62
1.28
f1 (ppm)

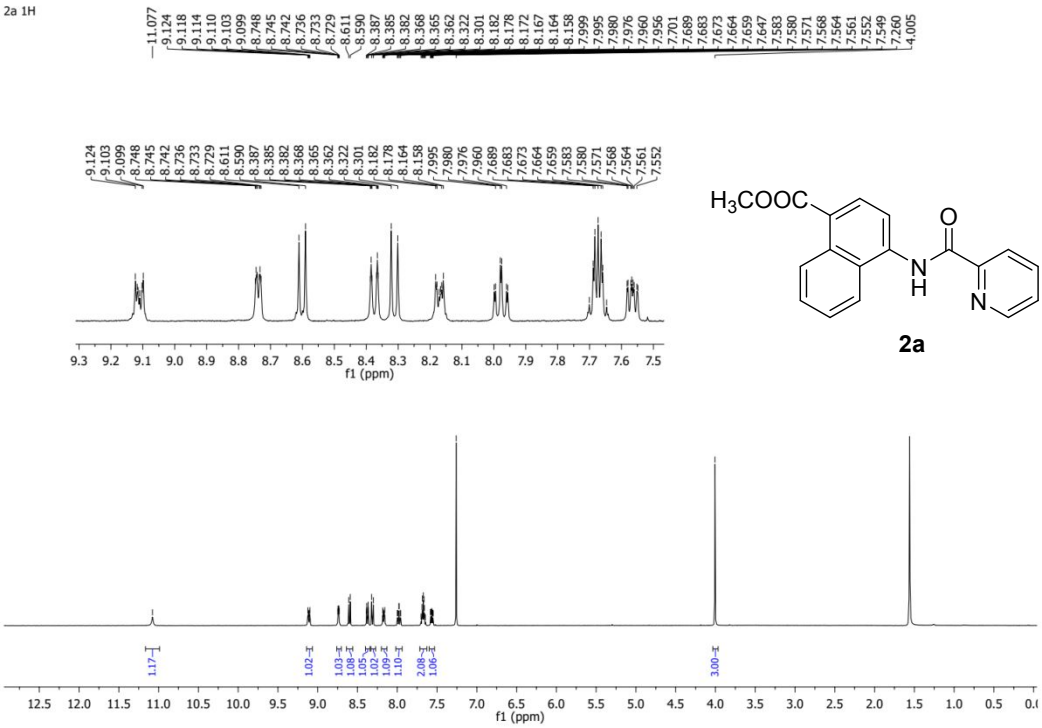
3n

SK-2-PH-AQ-SM-13C



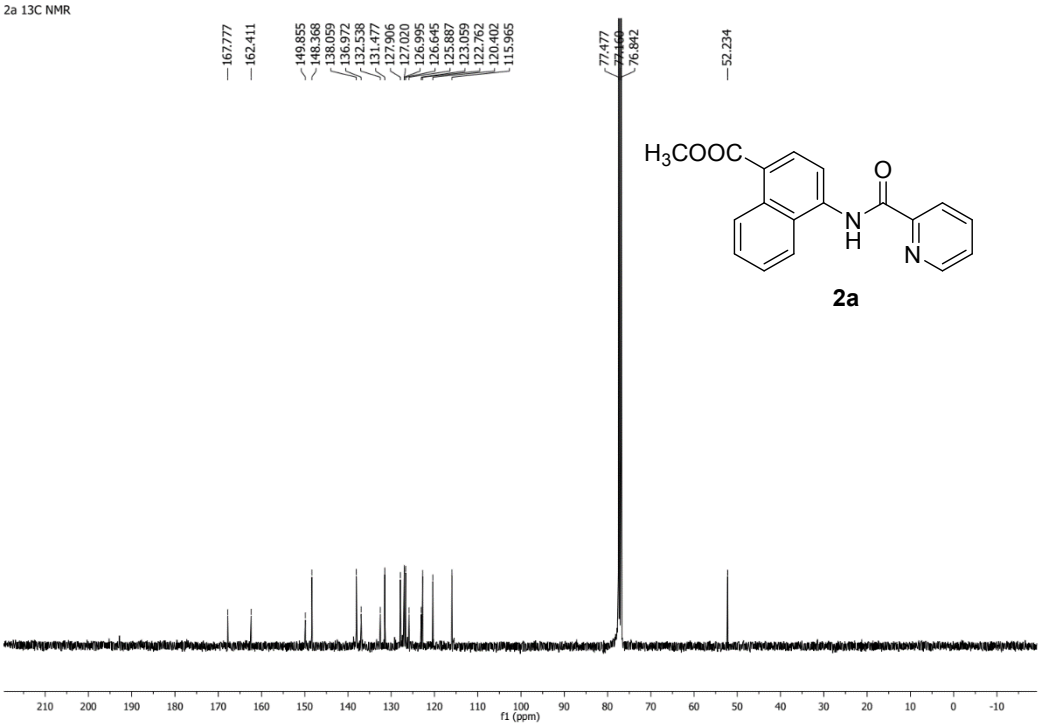
3n

2a 1H

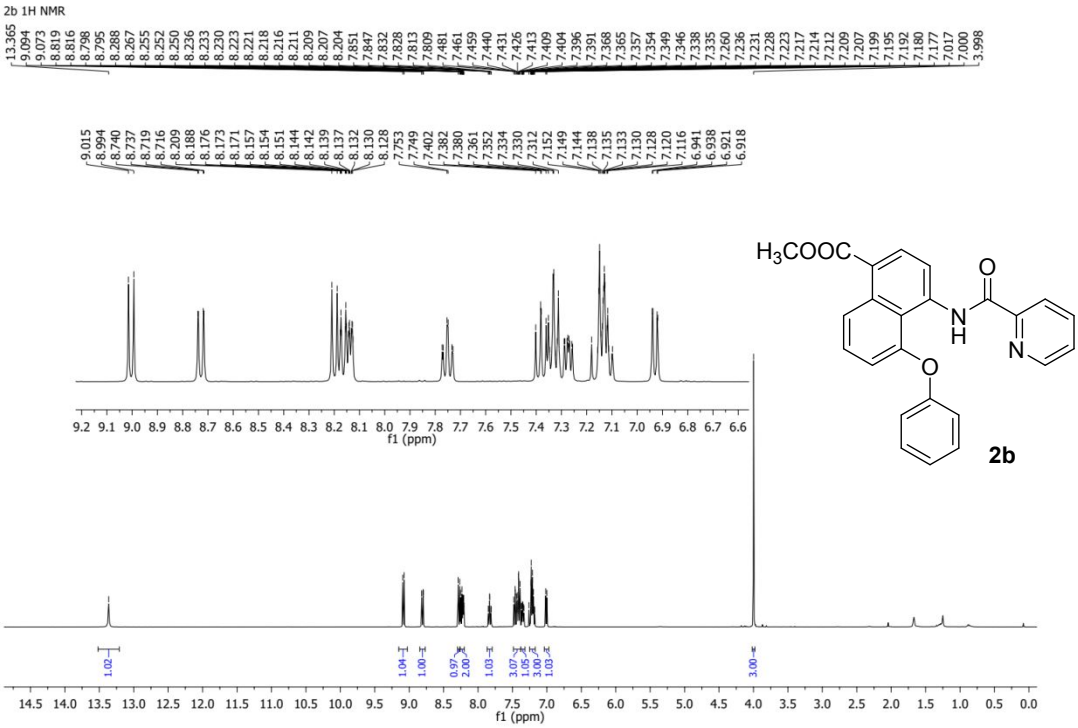


2a

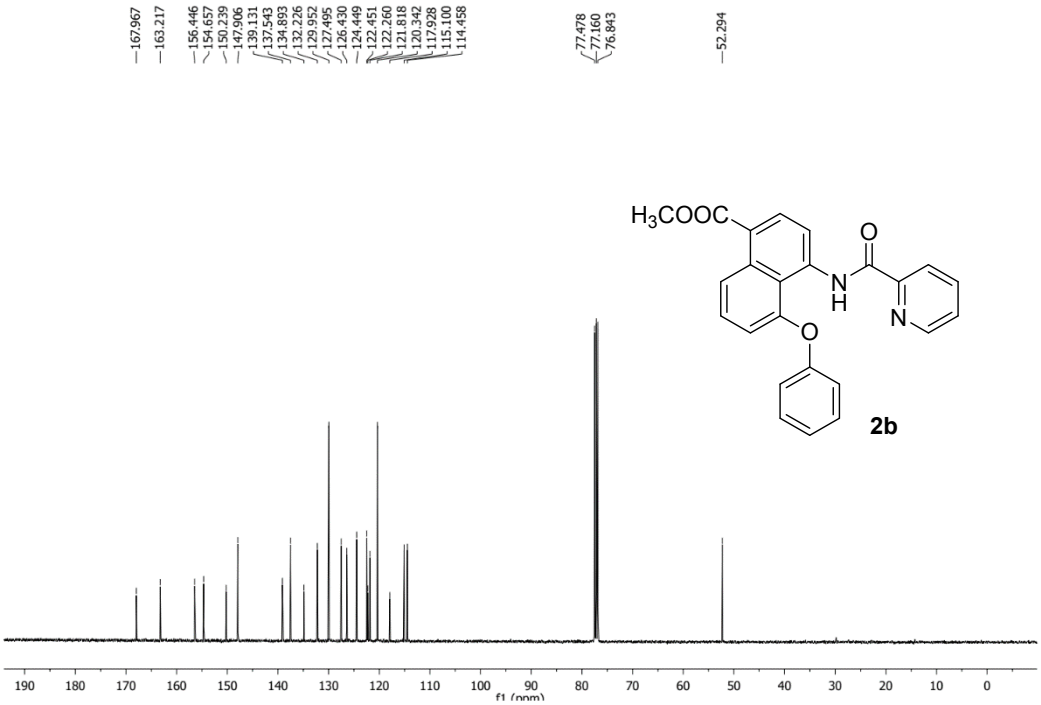
2a 13C NMR



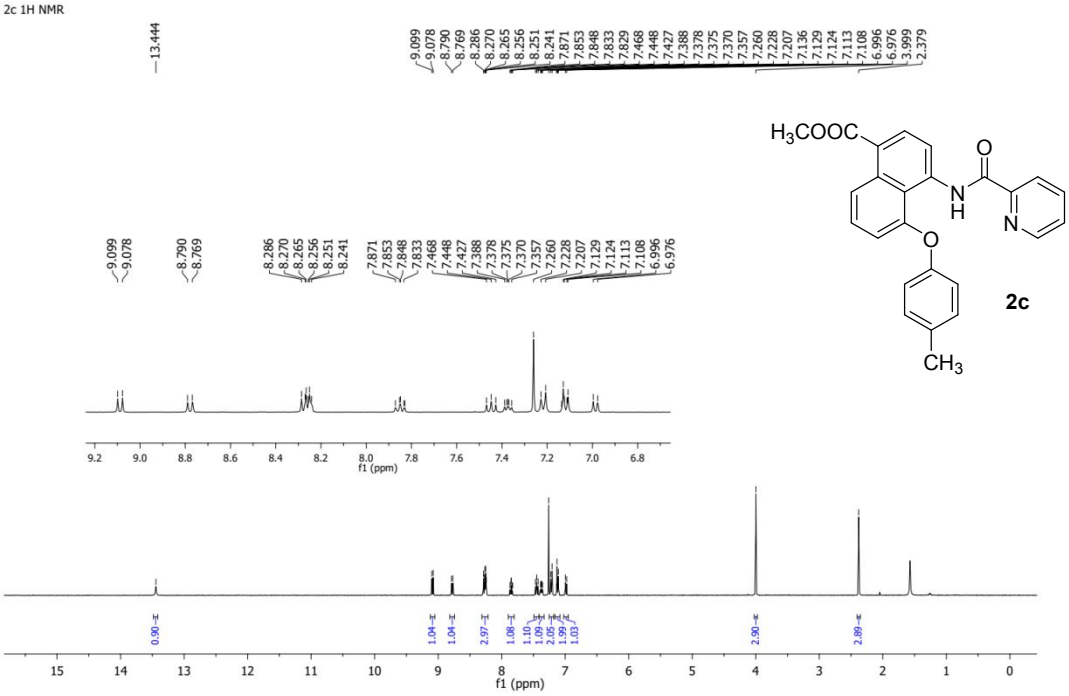
2b 1H NMR

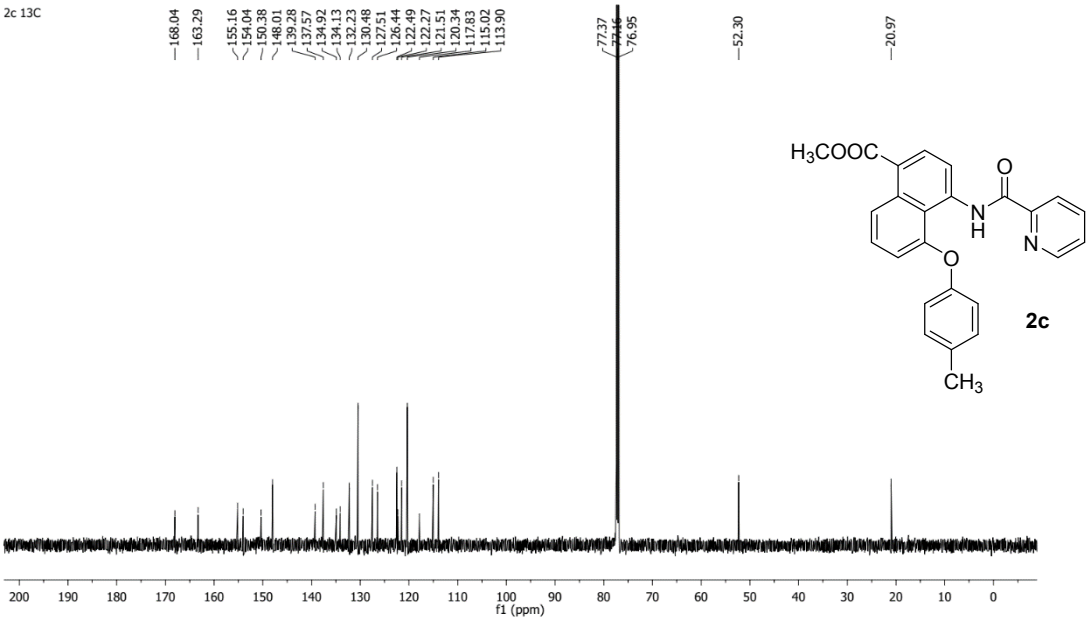


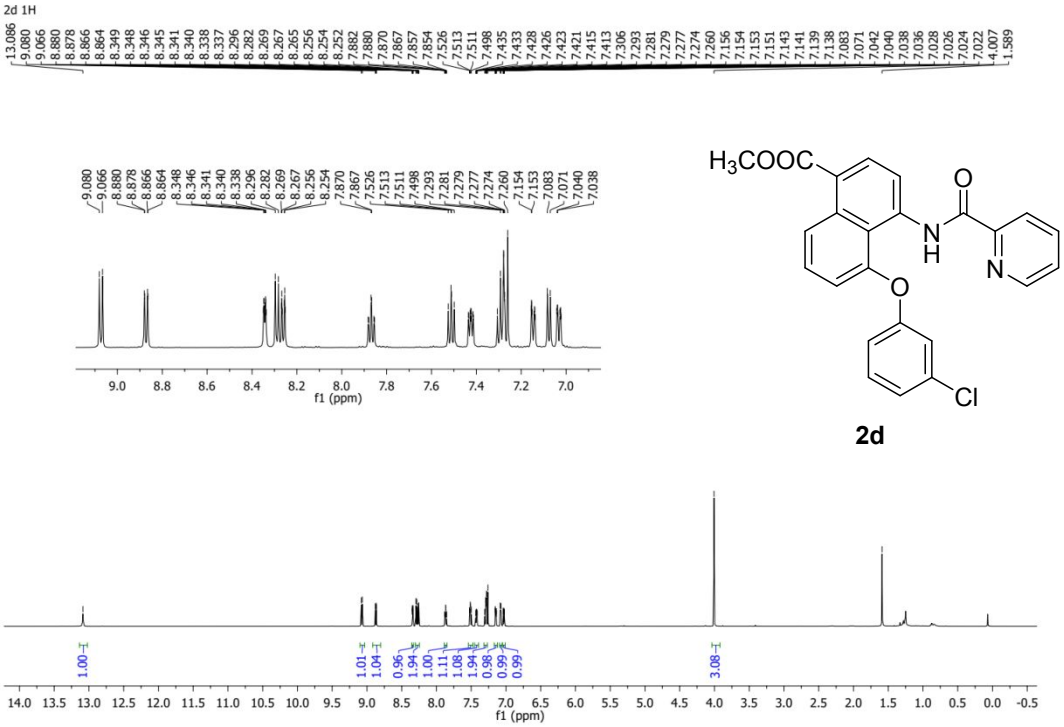
2b 13C NMR



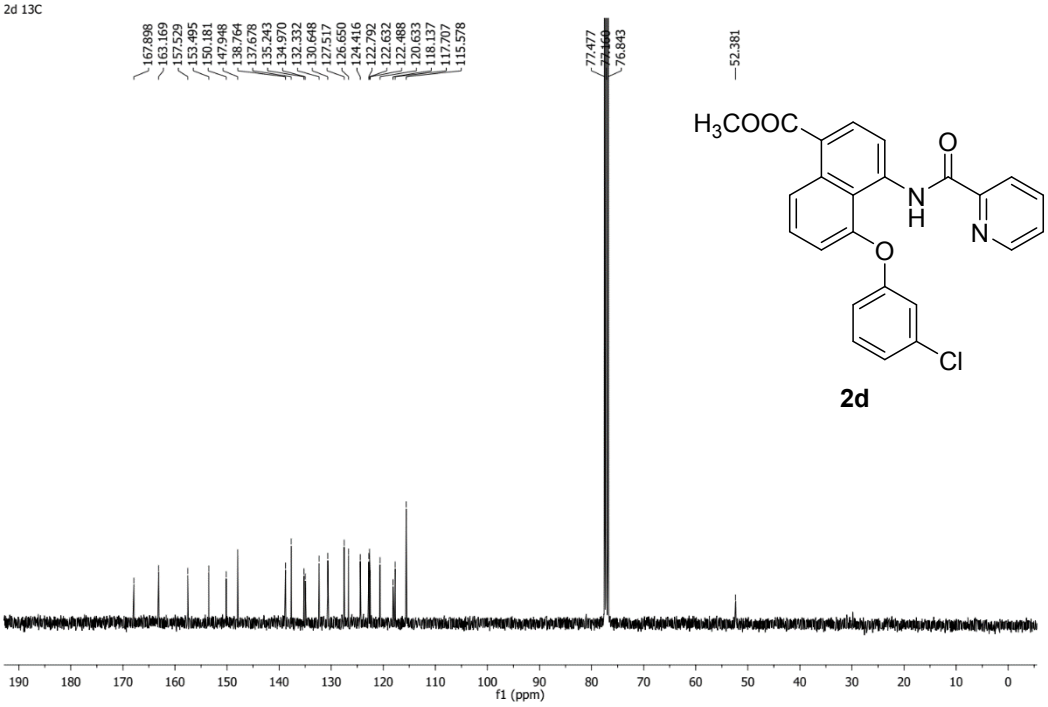
2c 1H NMR




2c 13C
168.04
163.29
155.16
154.04
150.38
148.01
139.28
137.57
134.92
134.13
132.23
130.48
127.51
126.44
122.49
122.27
121.51
120.34
117.83
115.02
113.90
77.37
77.16
76.95
52.30
20.97
H3COOC
O
N
H
N
O
CH3
2c
f1 (ppm)

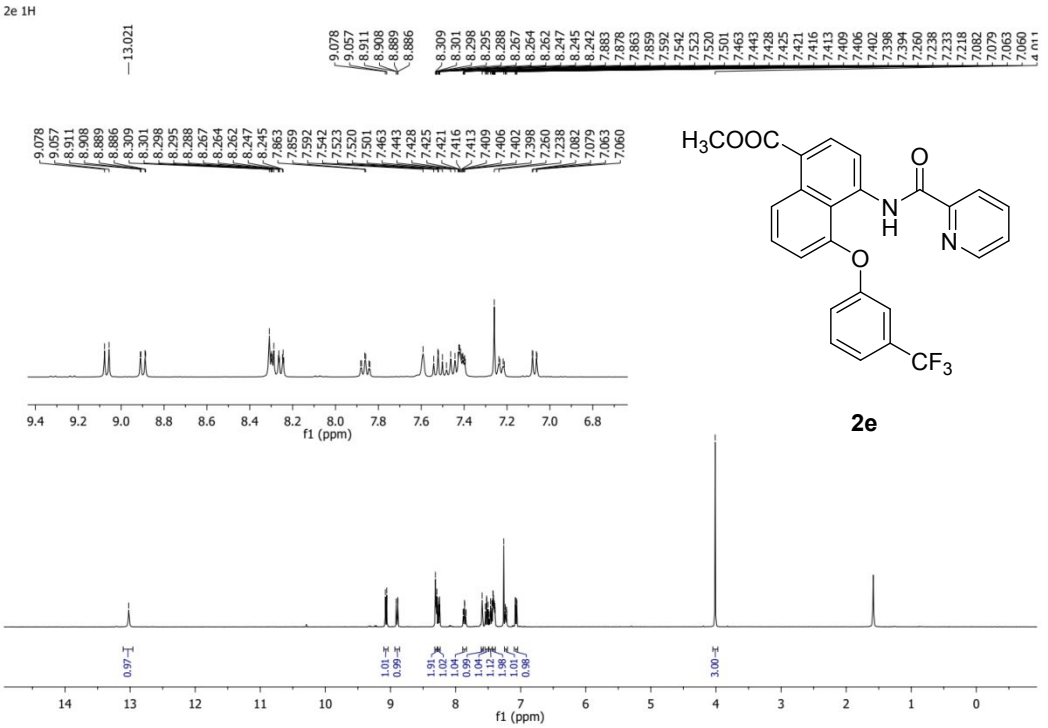

2d 1H
H3COOC
O
N
H
N
O
Cl
2d
f1 (ppm)

2d 13C

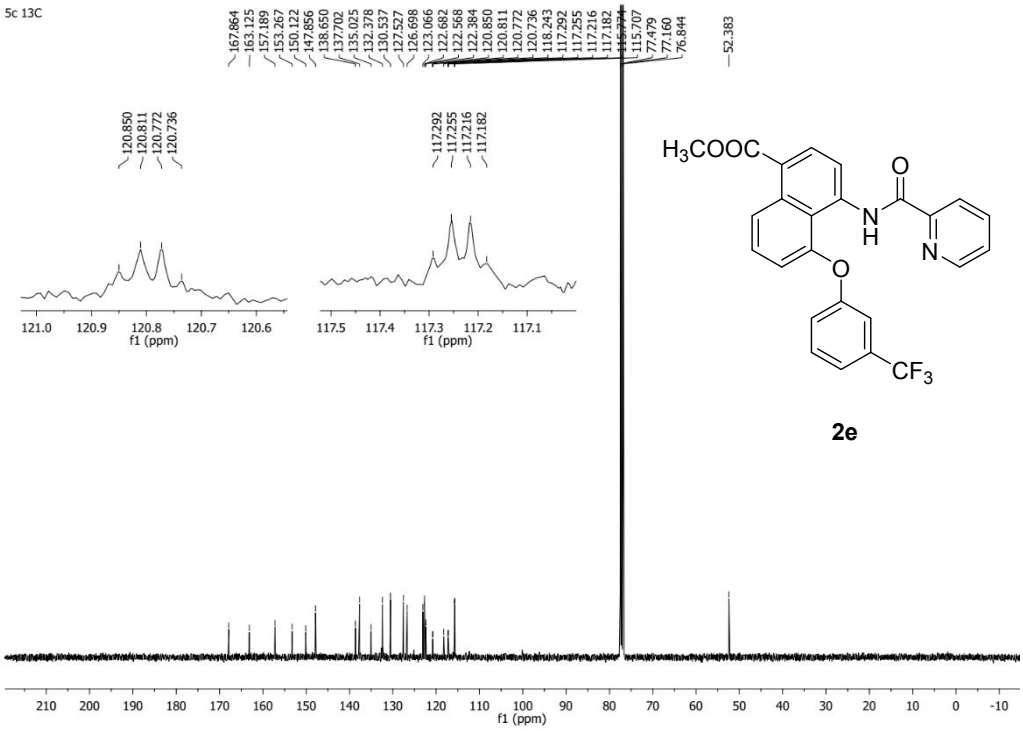


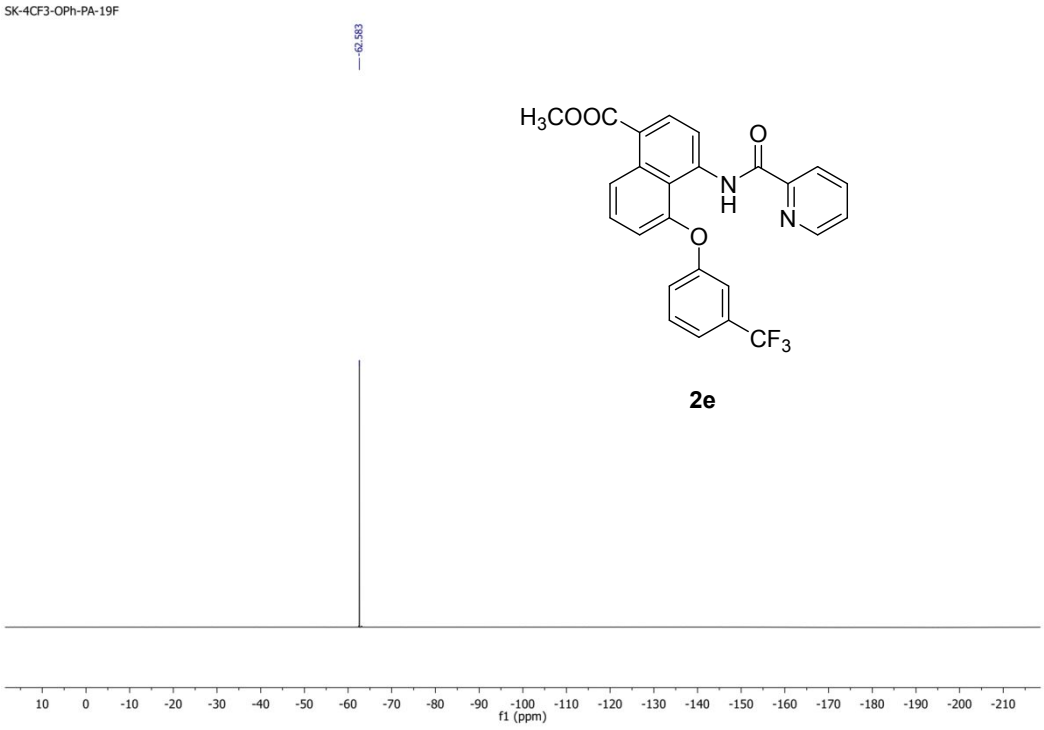
2d

2e 1H

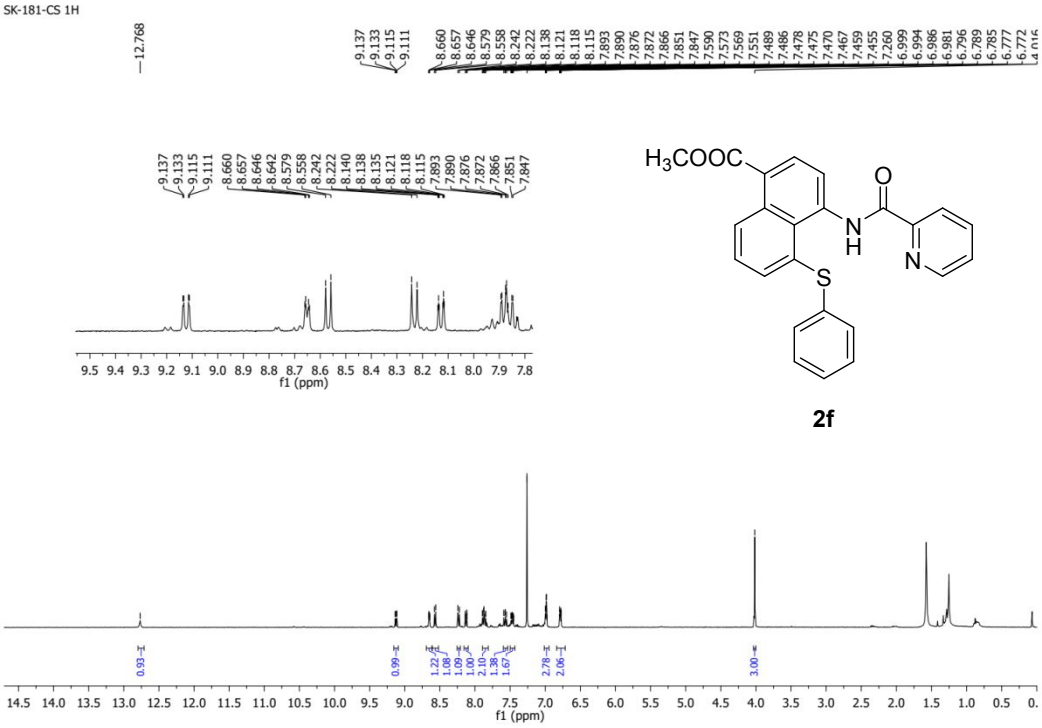


2e

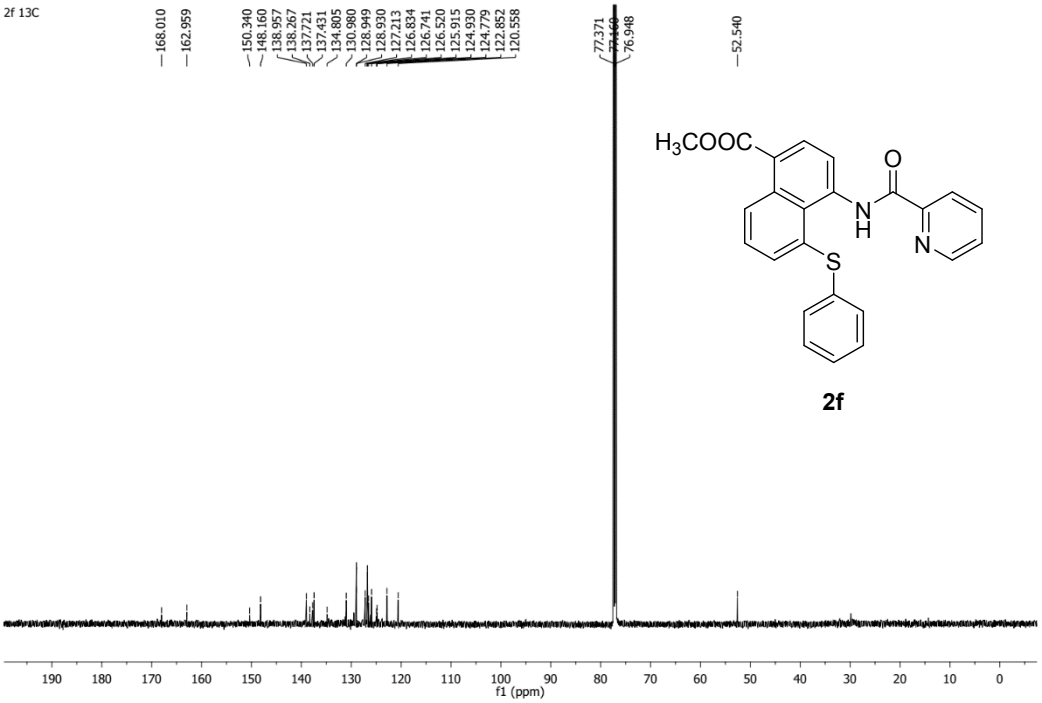

5c 13C
167.864
163.125
157.189
153.267
150.122
147.856
138.650
137.702
135.025
132.378
130.537
127.527
126.698
123.066
122.682
122.568
122.384
120.850
120.811
120.772
120.736
118.243
117.292
117.255
117.216
117.182
115.707
77.479
77.160
76.844
52.383
120.850
120.811
120.772
120.736
117.292
117.255
117.216
117.182
121.0 120.9 120.8 120.7 120.6
f1 (ppm)
117.5 117.4 117.3 117.2 117.1
f1 (ppm)
H3COOC
O
N
H
N
O
CF3
2e
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

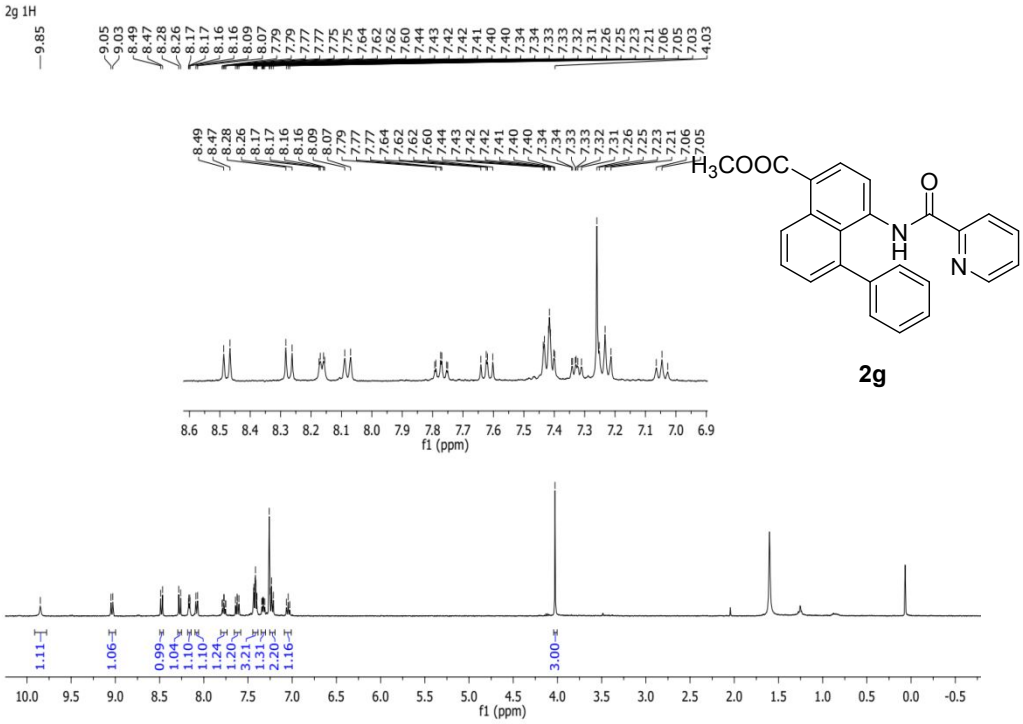

SK-4CF3-OPh-PA-19F
-62.563
H3COOC
O
N
H
N
O
CF3
2e
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

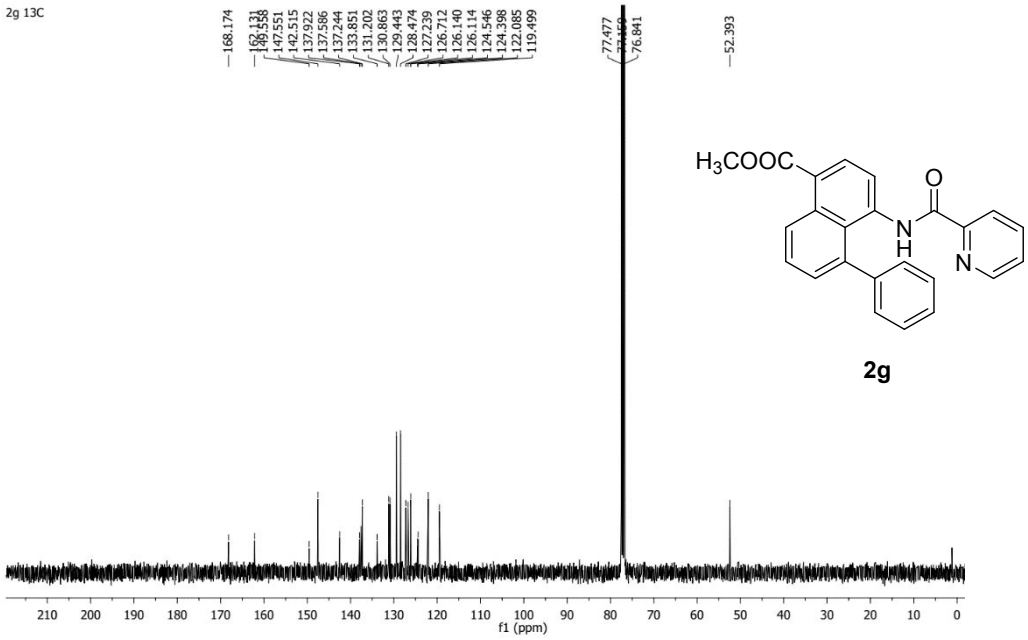
SK-181-CS 1H

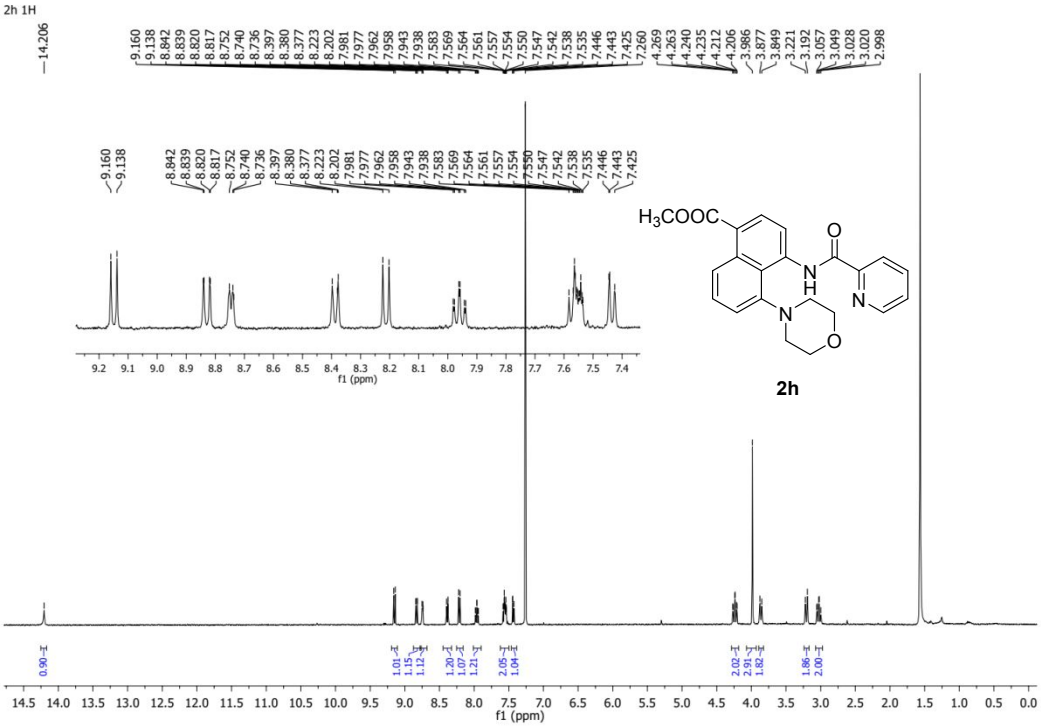


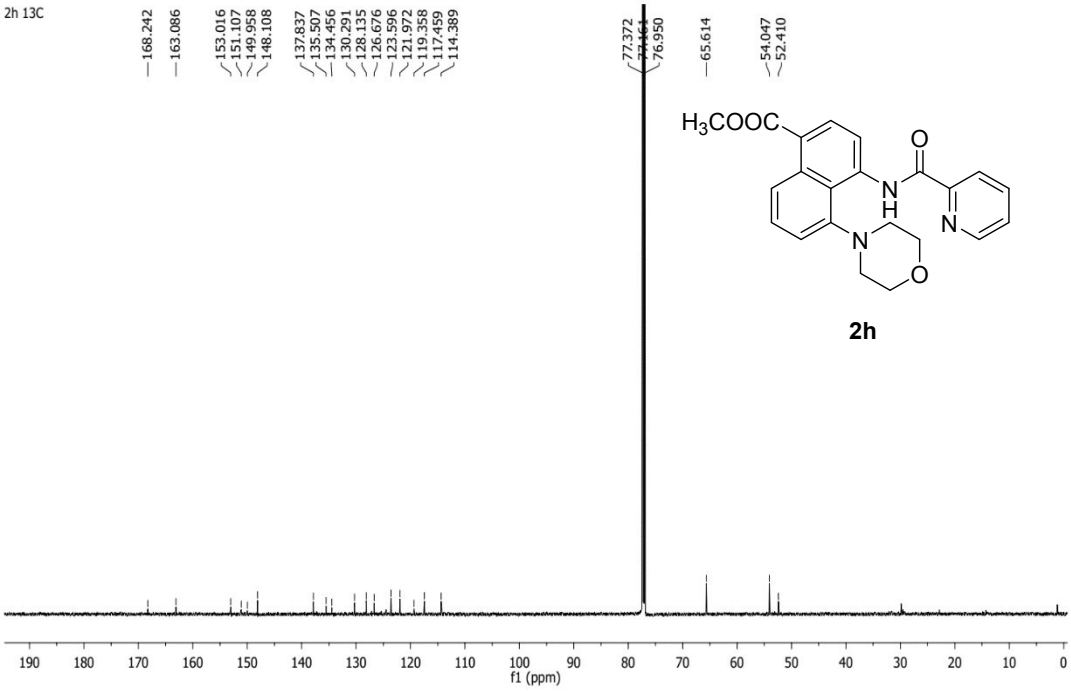
2f 13C



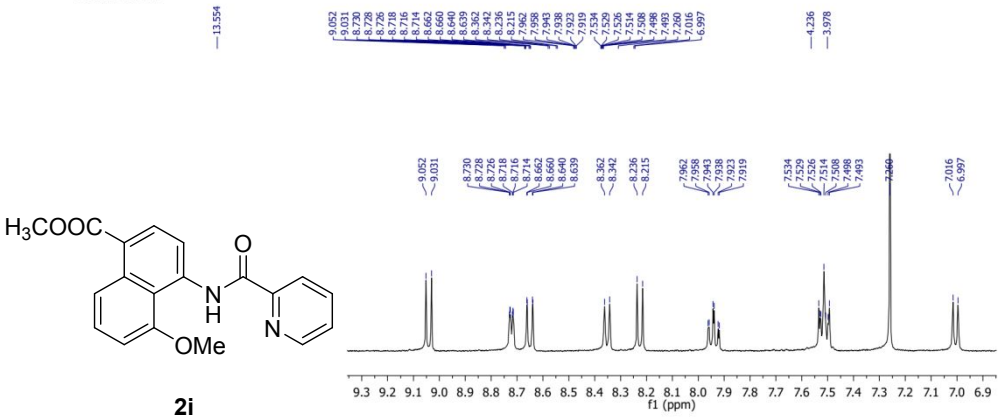

2g 1H
H3COOC
O
N
H
N
2g
f1 (ppm)


2g 13C
H3COOC
O
N
H
N
2g
f1 (ppm)

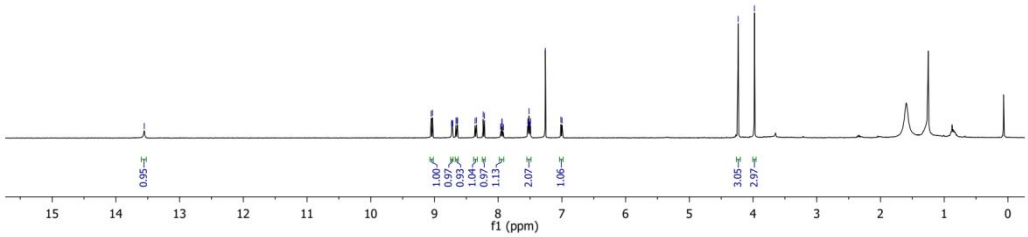

2h 1H
14.206
9.160
9.138
8.842
8.839
8.820
8.817
8.752
8.740
8.736
8.397
8.380
8.377
8.223
8.202
7.981
7.977
7.962
7.958
7.943
7.938
7.583
7.569
7.564
7.561
7.557
7.554
7.550
7.547
7.542
7.538
7.535
7.446
7.443
7.425
7.260
4.269
4.263
4.240
4.235
4.212
4.206
3.986
3.877
3.849
3.221
3.192
3.057
3.049
3.028
3.020
2.998
f1 (ppm)
H3COOC
O
N
H
N
N
O
2h


2h 13C
168.242
163.086
153.016
151.107
149.958
148.108
137.837
135.507
134.456
130.291
128.135
126.676
123.596
121.972
119.358
117.459
114.389
77.372
76.950
65.614
54.047
52.410
f1 (ppm)
H3COOC
O
N
H
N
N
O
2h

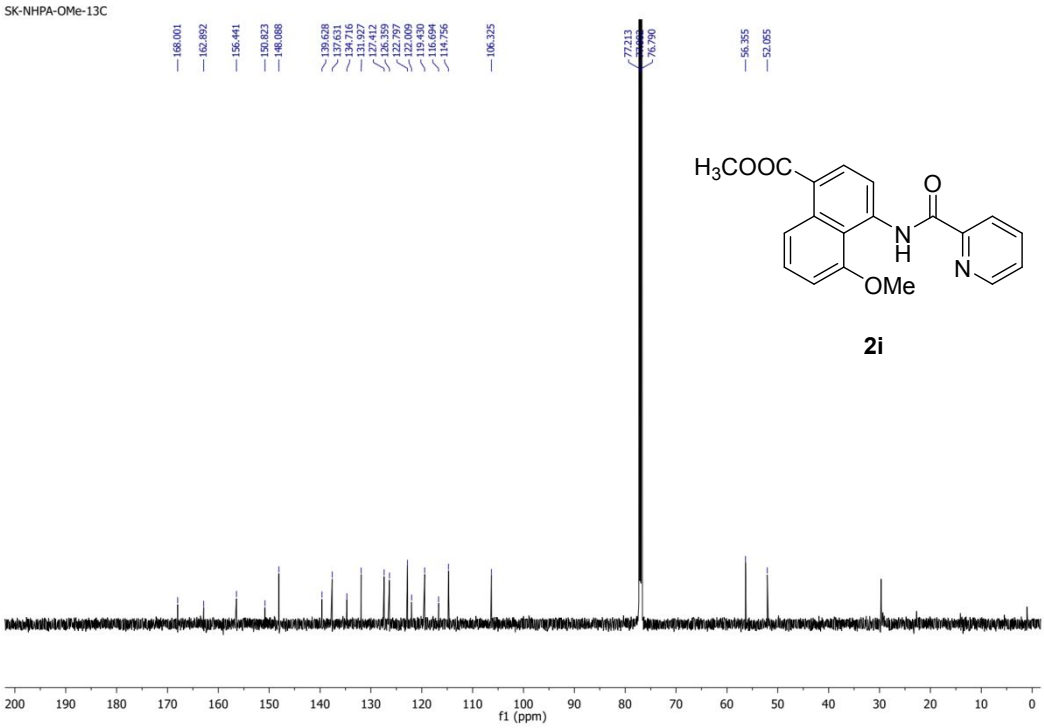
SK-PA-OME-1H



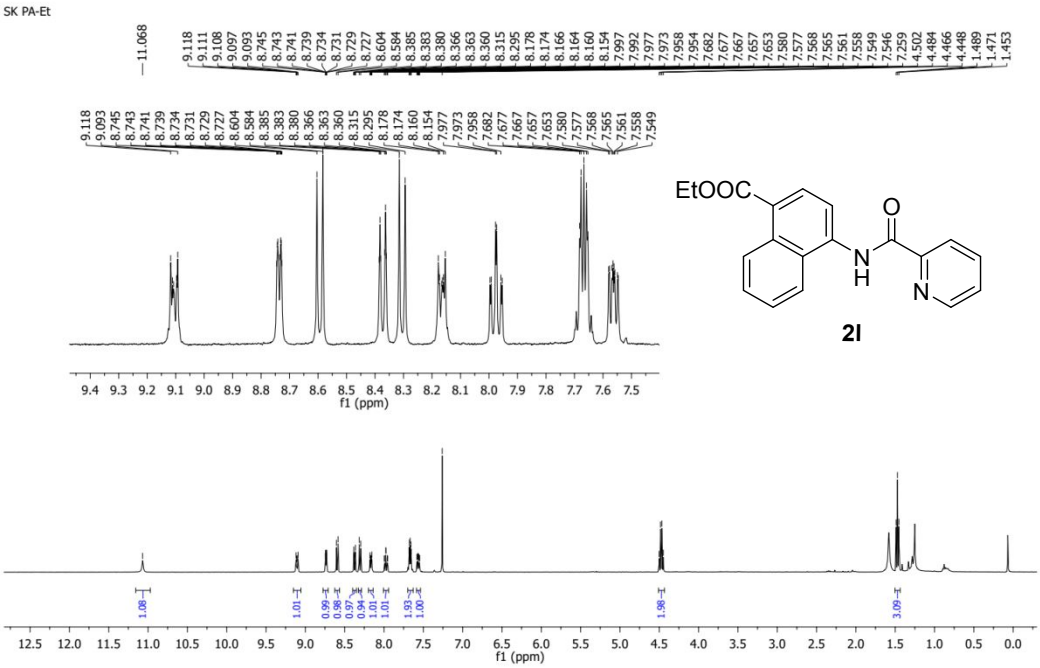
2i

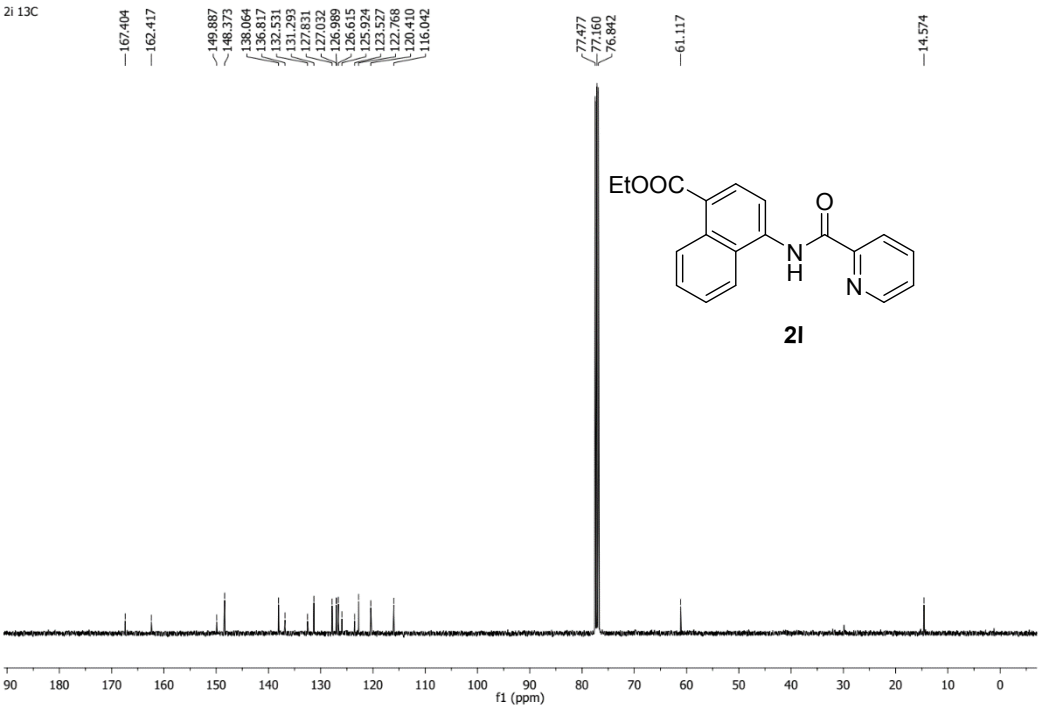


SK-NHPA-OMe-13C

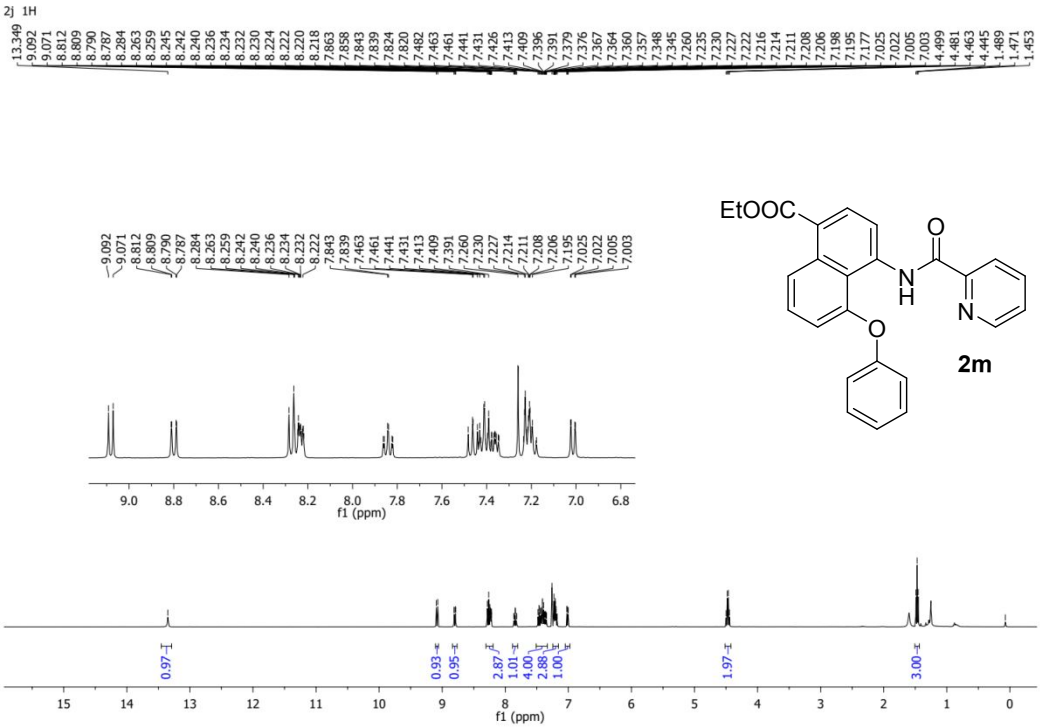


2i

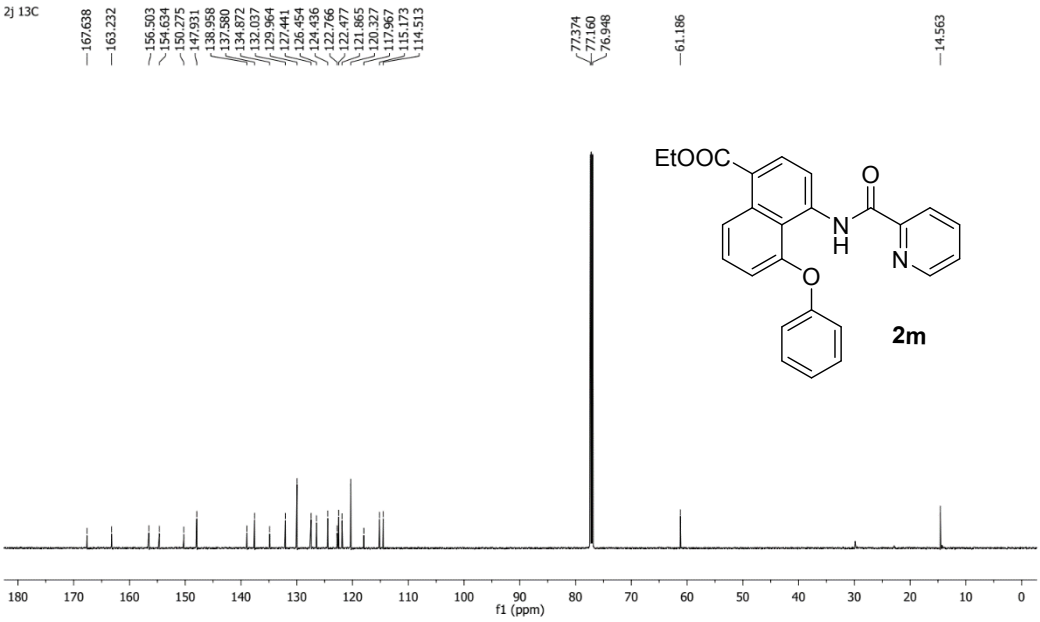

SK PA-Et
EtOOC
O
N
H
N
2l
f1 (ppm)


2i 13C
EtOOC
O
N
H
N
2l
f1 (ppm)

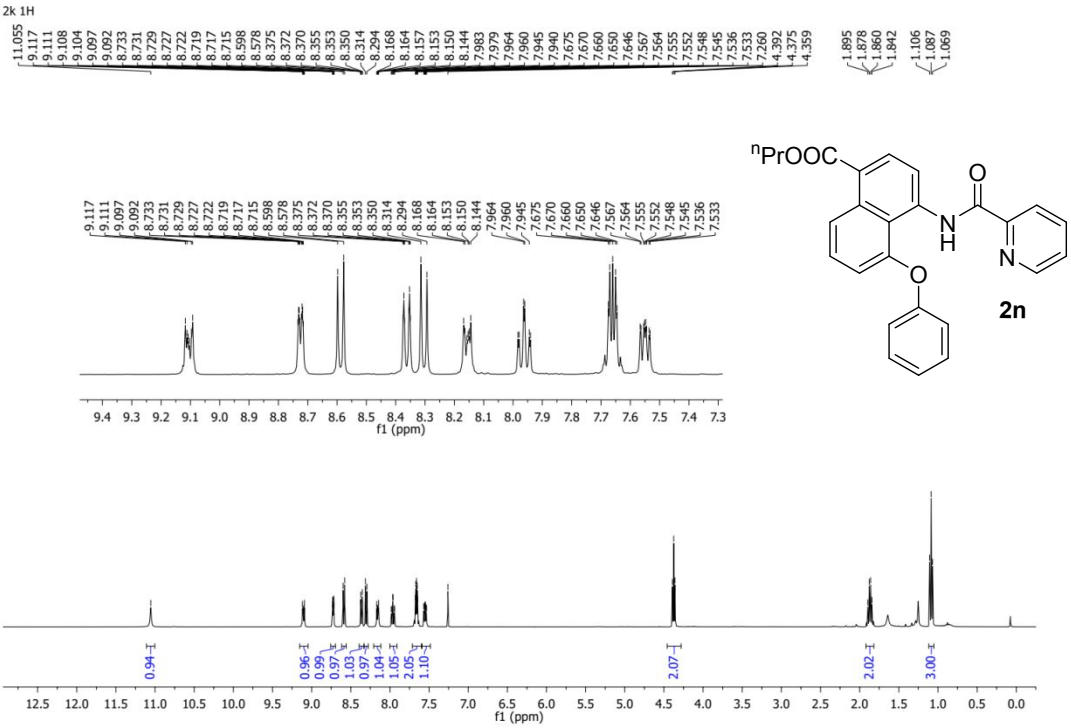
2j 1H



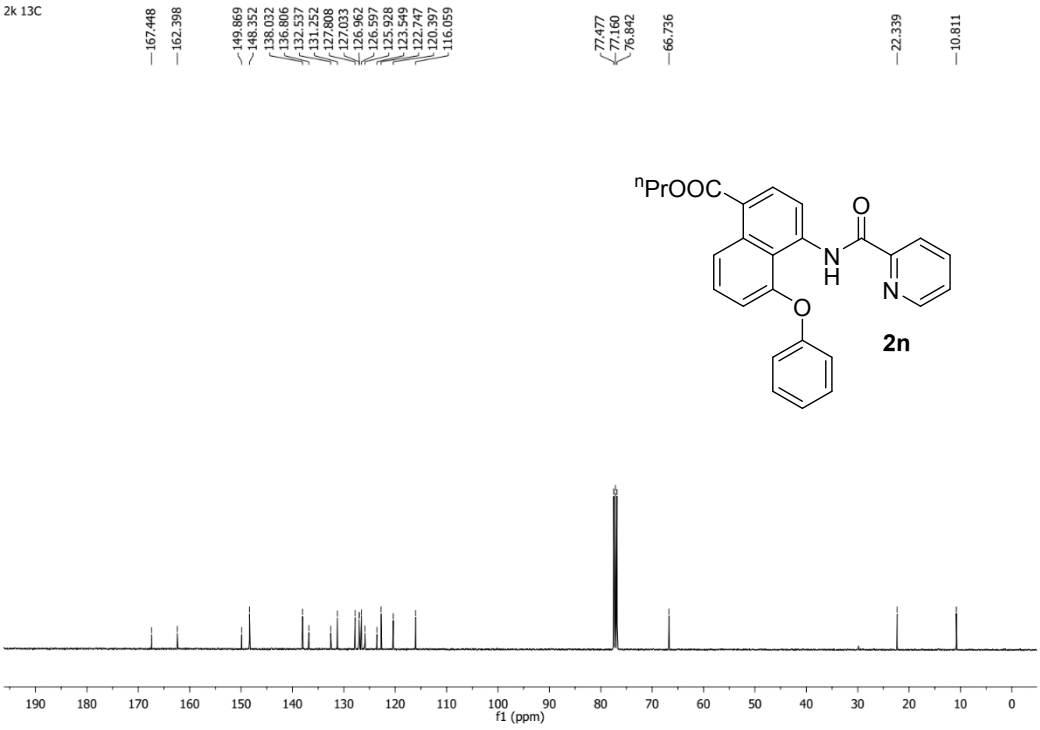
2j 13C

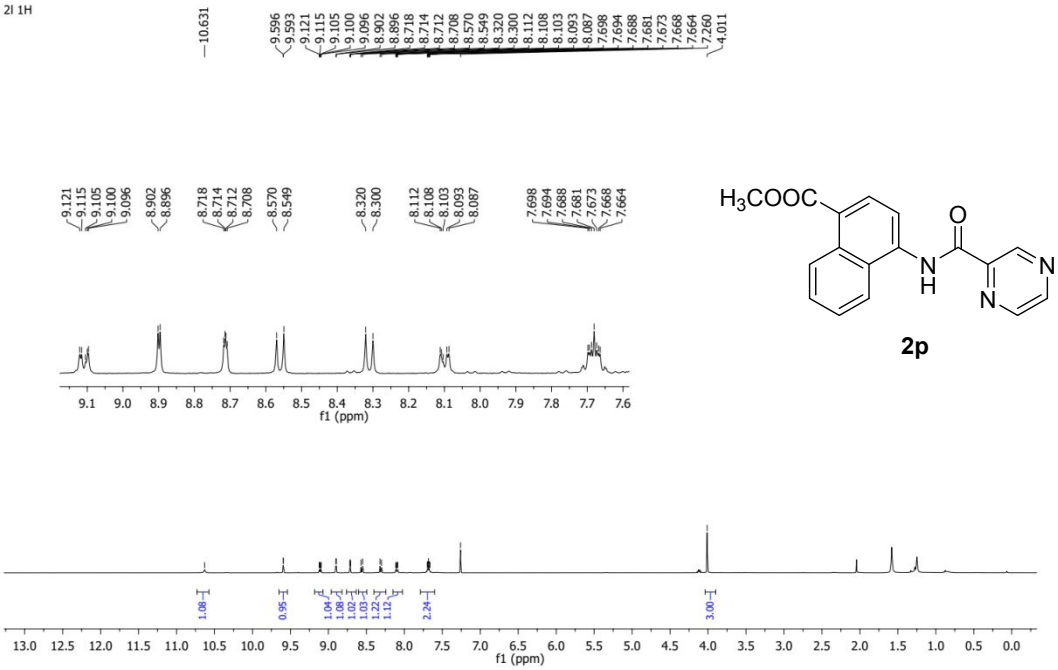


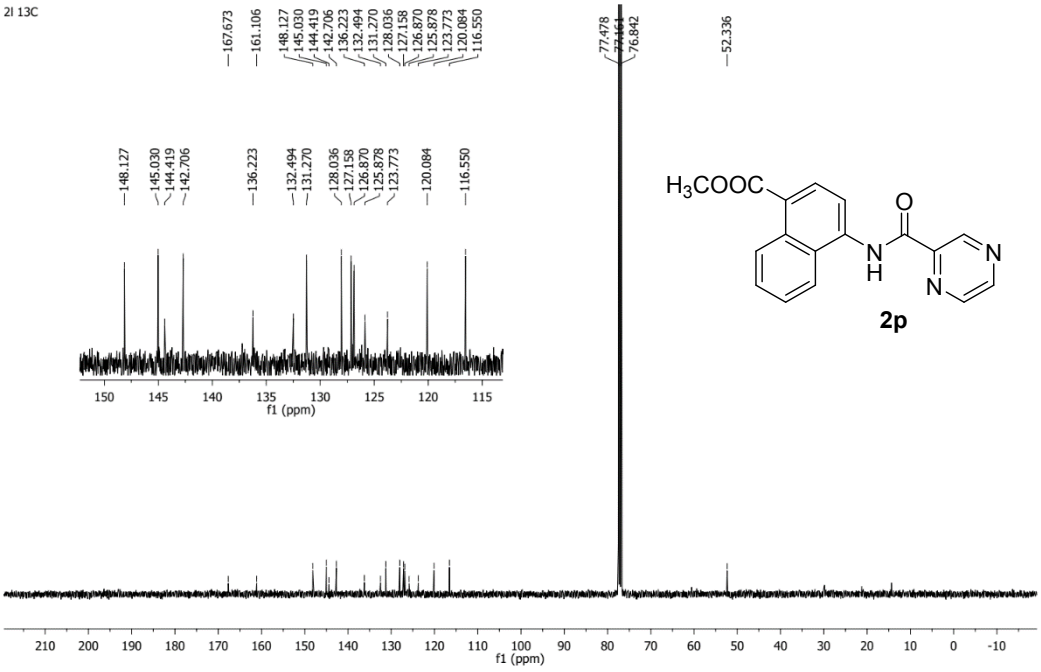
2k 1H

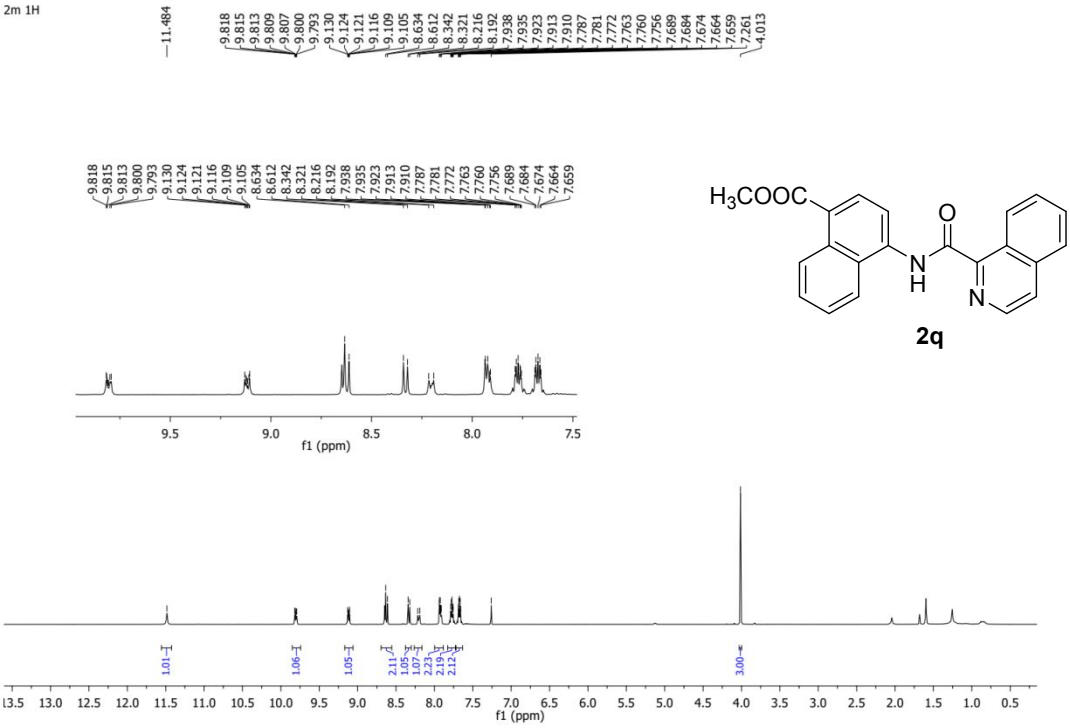


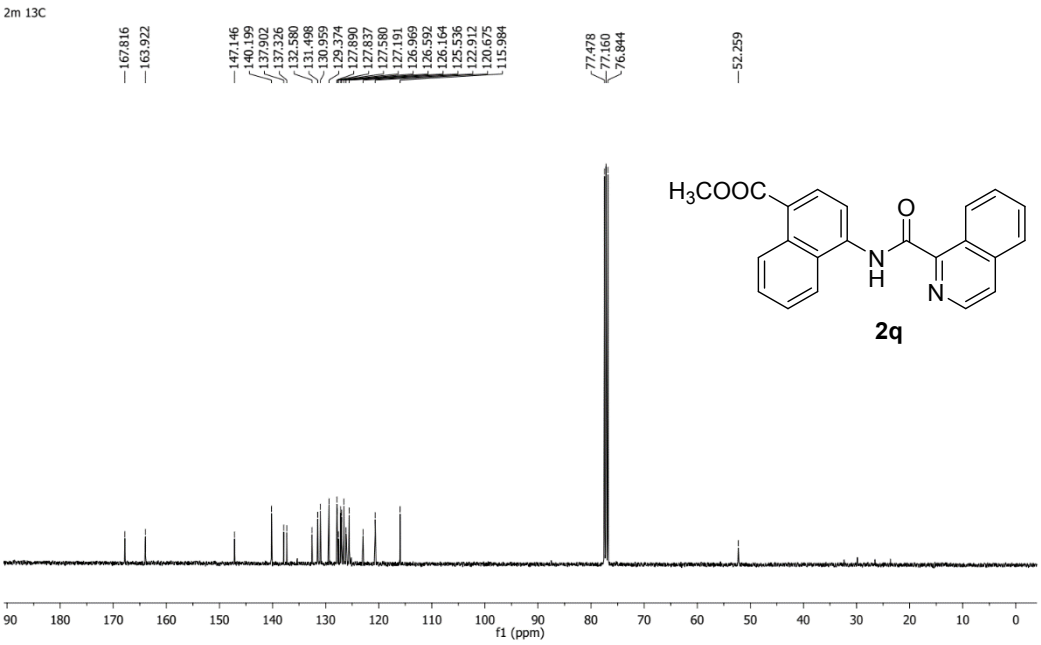
2k 13C



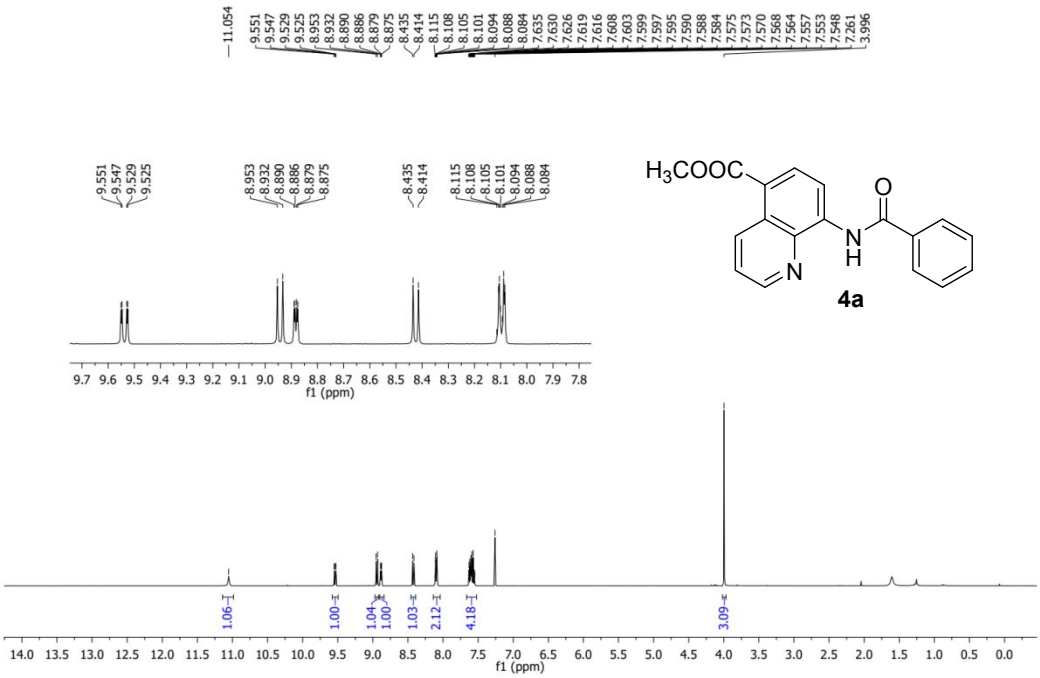

2l 1H
f1 (ppm)
H3COOC
O
N
H
N
N
2p


2l 13C
f1 (ppm)
H3COOC
O
N
H
N
N
2p

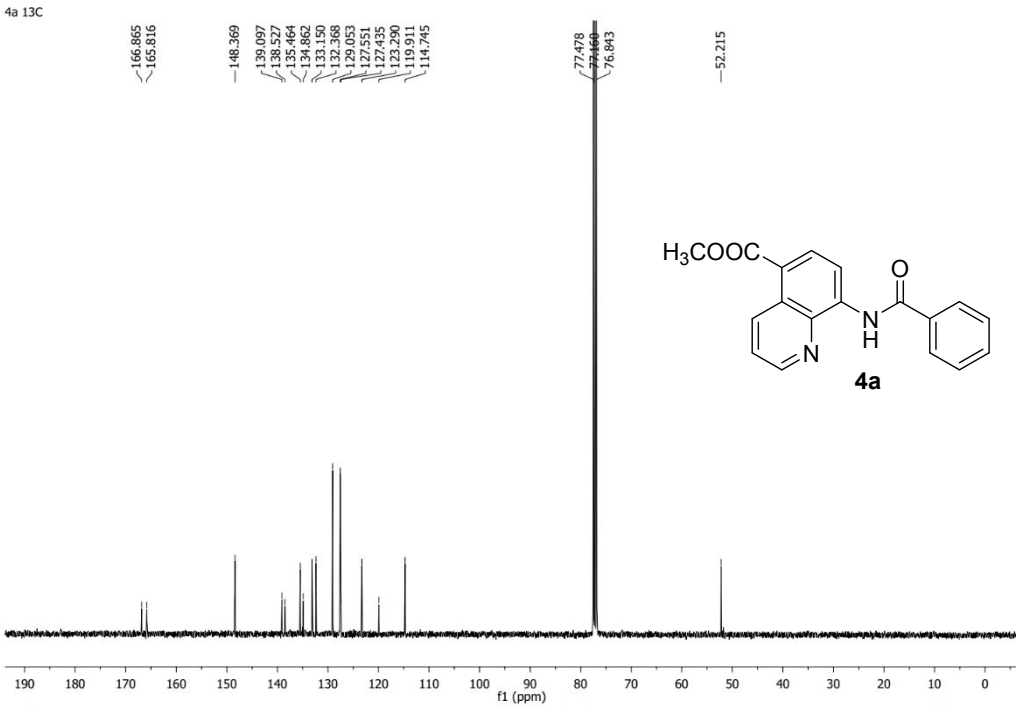

2m 1H
11.484
9.818
9.815
9.813
9.809
9.807
9.800
9.793
9.130
9.124
9.121
9.116
9.109
9.105
8.634
8.612
8.342
8.321
8.216
8.192
7.938
7.935
7.923
7.913
7.910
7.787
7.781
7.772
7.763
7.760
7.756
7.689
7.684
7.674
7.664
7.659
7.261
4.013
H3COOC
O
N
H
N
2q
f1 (ppm)
1.01
1.06
1.05
2.11
1.05
1.07
2.23
2.19
2.12
3.00


2m 13C
167.816
163.922
147.146
140.199
137.902
137.326
132.580
131.498
130.959
129.374
127.890
127.837
127.580
127.191
126.969
126.592
126.164
125.536
122.912
120.675
115.984
77.478
77.160
76.844
52.259
H3COOC
O
N
H
N
2q
f1 (ppm)

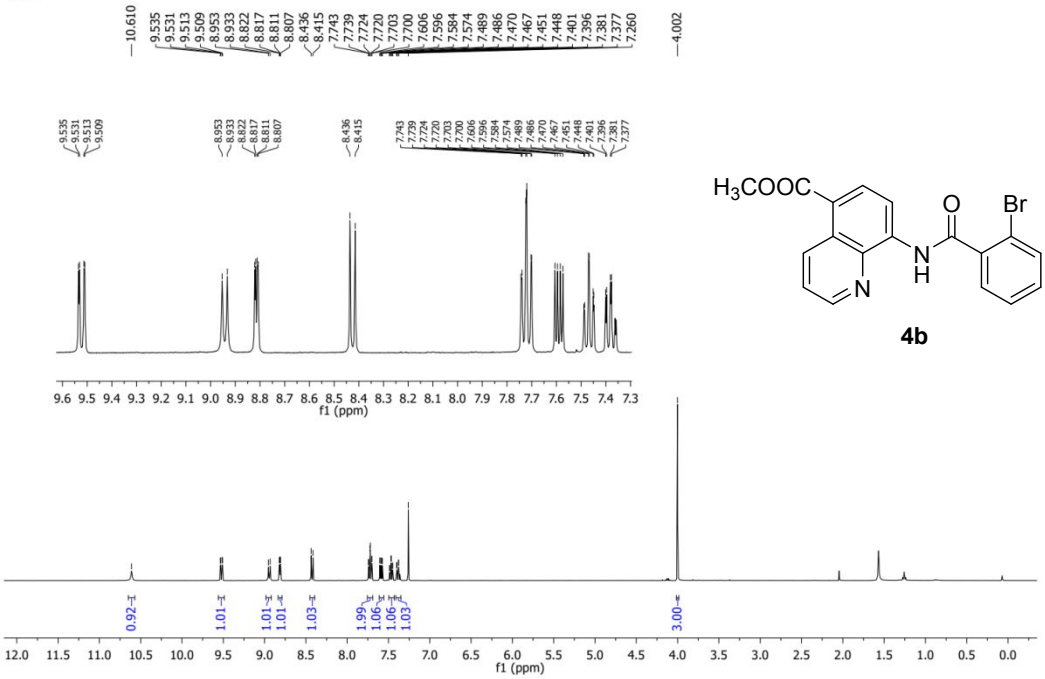
4a-1H


11.054
9.551
9.547
9.529
9.525
8.953
8.932
8.890
8.886
8.879
8.875
8.435
8.414
8.115
8.108
8.105
8.101
8.094
8.088
8.084
7.635
7.630
7.626
7.619
7.616
7.608
7.603
7.599
7.597
7.595
7.590
7.588
7.584
7.575
7.573
7.570
7.568
7.564
7.557
7.553
7.548
7.261
3.996
f1 (ppm)
1.06
1.00
1.04
1.00
1.03
2.12
4.18
3.09
H3COOC
O
N
H
N
4a

4a 13C

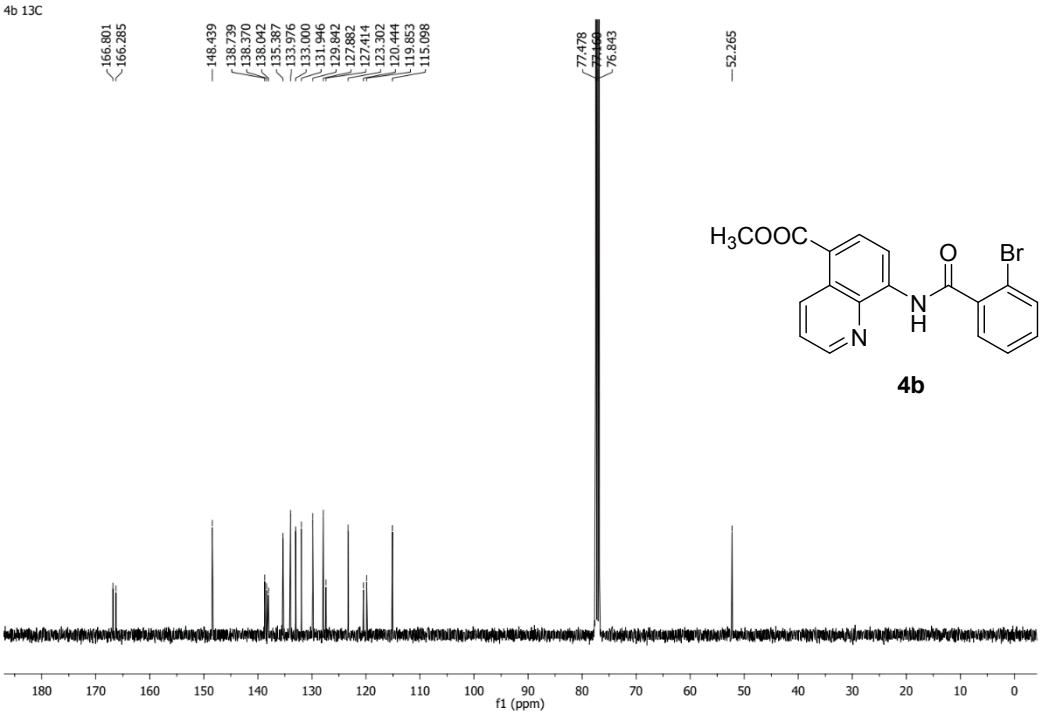

166.865
165.816
148.369
139.097
138.527
135.464
134.862
133.150
132.368
129.053
127.551
127.435
123.290
119.911
114.745
77.478
77.160
76.843
52.215
f1 (ppm)
H3COOC
O
N
H
N
4a

4b 1H

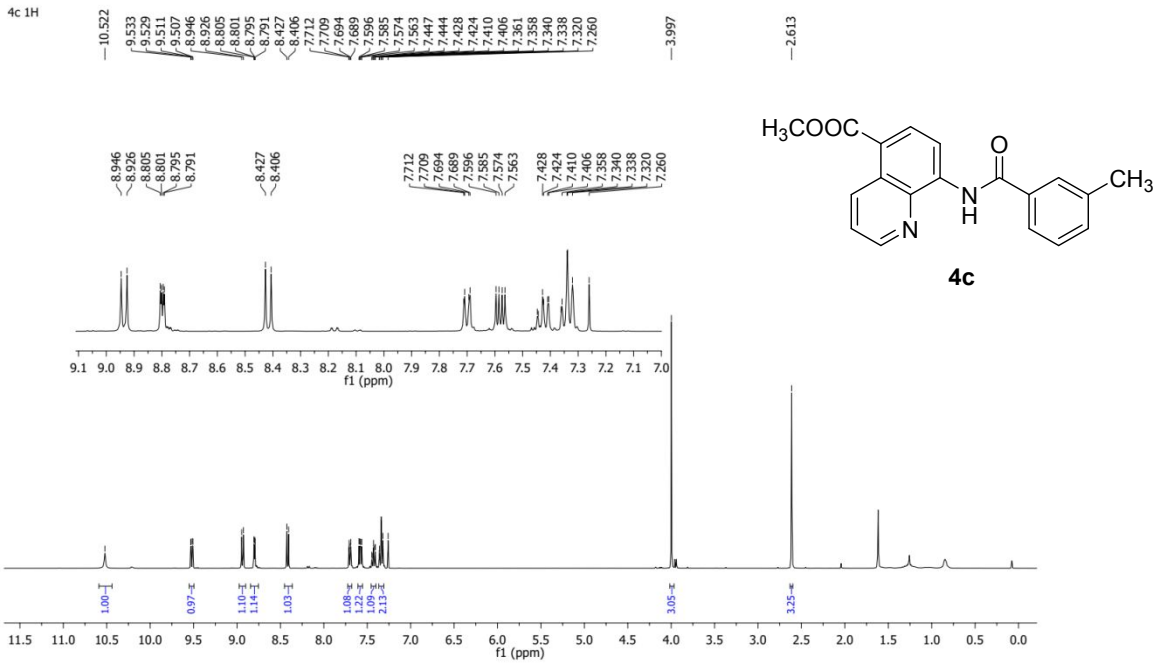


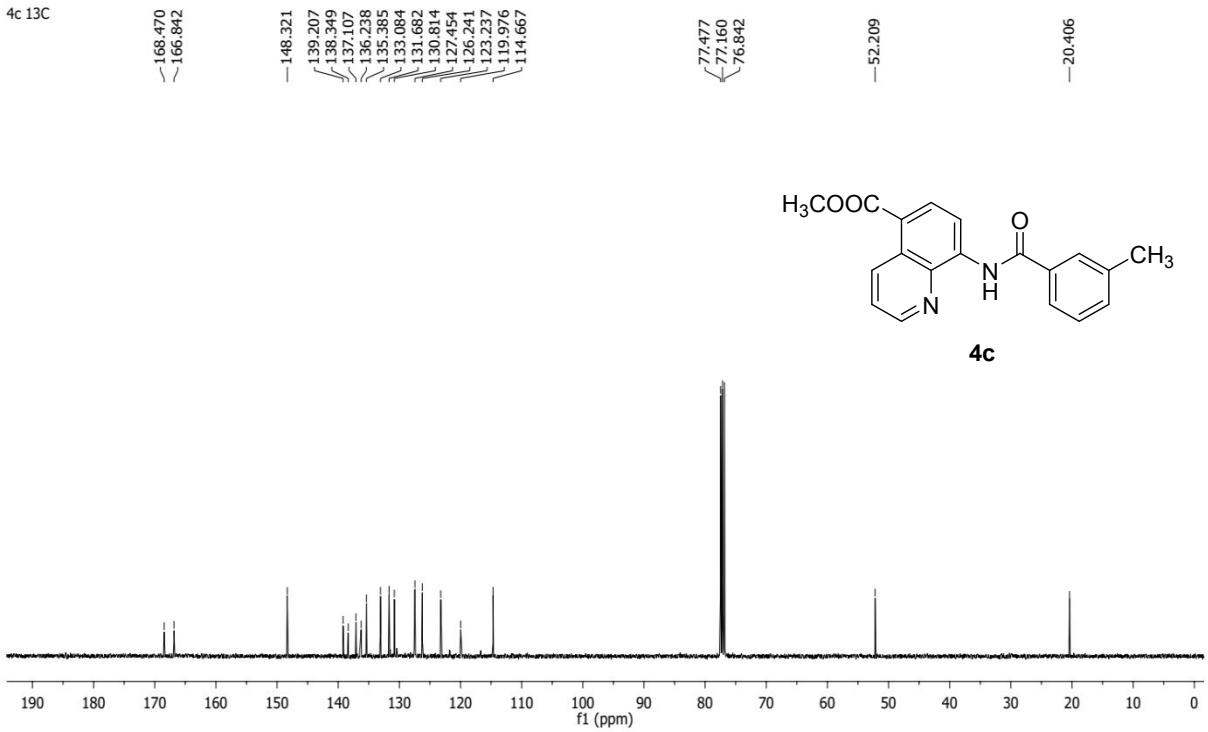
4b

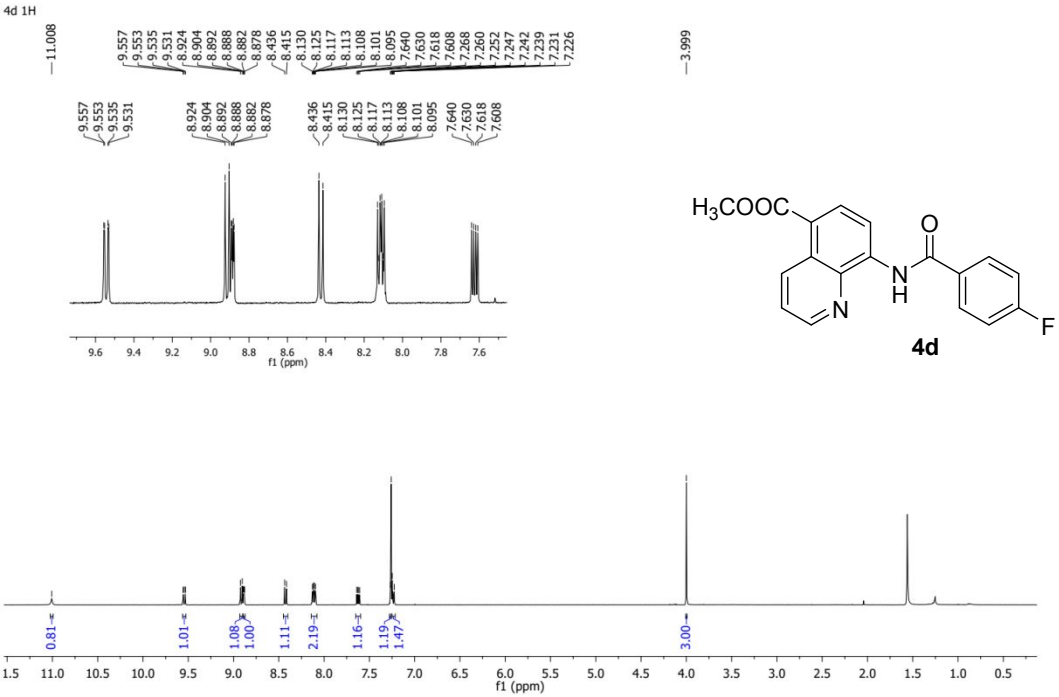
4b 13C

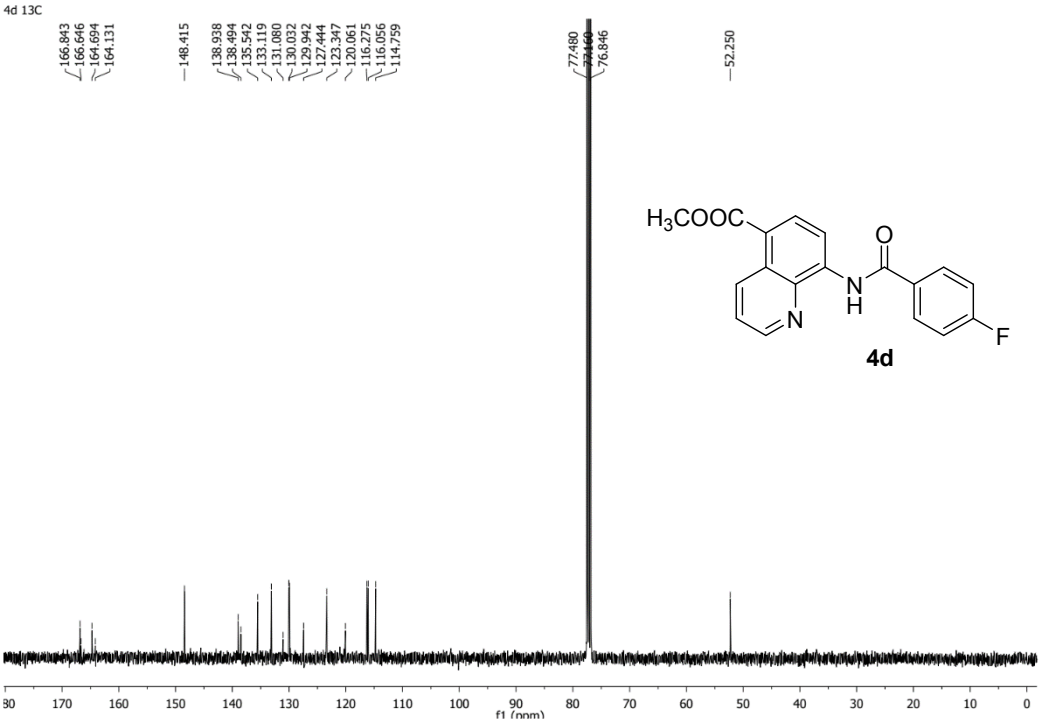


4b

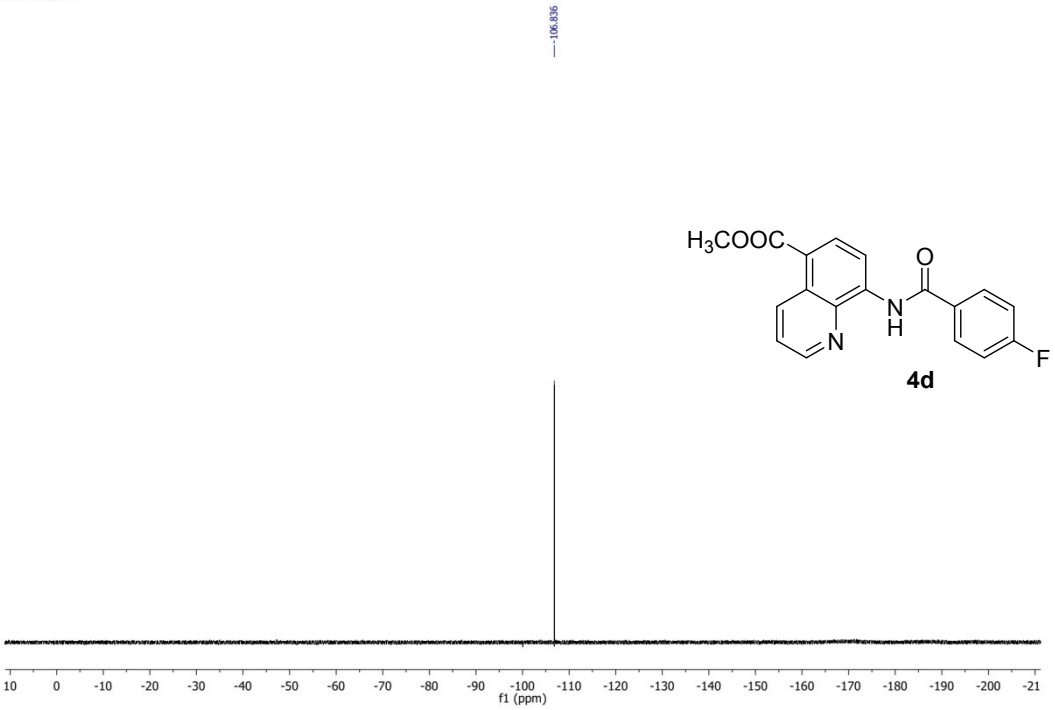

4c 1H
10.522
9.533
9.529
9.511
9.507
8.946
8.926
8.805
8.801
8.795
8.791
8.427
8.406
7.712
7.709
7.694
7.689
7.596
7.585
7.574
7.563
7.447
7.444
7.428
7.424
7.410
7.406
7.361
7.358
7.340
7.338
7.320
7.260
3.997
2.613
f1 (ppm)
H3COOC
O
N
H
CH3
4c


4c 13C
168.470
166.842
148.321
139.207
138.349
137.107
136.238
135.385
133.084
131.682
130.814
127.454
126.241
123.237
119.976
114.667
77.477
77.160
76.842
52.209
20.406
f1 (ppm)
H3COOC
O
N
H
CH3
4c


4d 1H
11.008
9.557
9.553
9.535
9.531
8.924
8.904
8.892
8.888
8.882
8.878
8.436
8.415
8.130
8.125
8.117
8.113
8.108
8.101
8.095
7.640
7.630
7.618
7.608
7.268
7.260
7.252
7.247
7.242
7.239
7.231
7.226
3.999
f1 (ppm)
H3COOC
O
N
H
N
F
4d
0.81
1.01
1.08
1.00
1.11
2.19
1.16
1.19
1.47
3.00

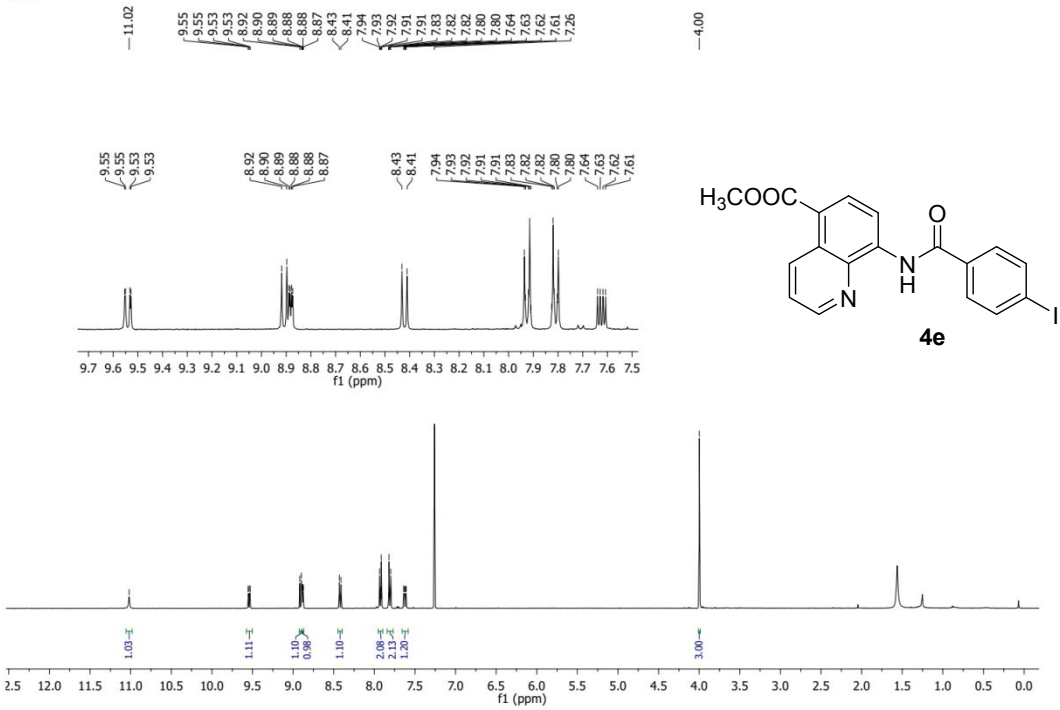

4d 13C
166.843
166.646
164.694
164.131
148.415
138.938
138.494
135.542
133.119
131.080
130.032
129.942
127.444
123.347
120.061
116.275
116.056
114.759
77.480
77.160
76.846
52.250
f1 (ppm)
H3COOC
O
N
H
N
F
4d

SK-4F-AQ-19F

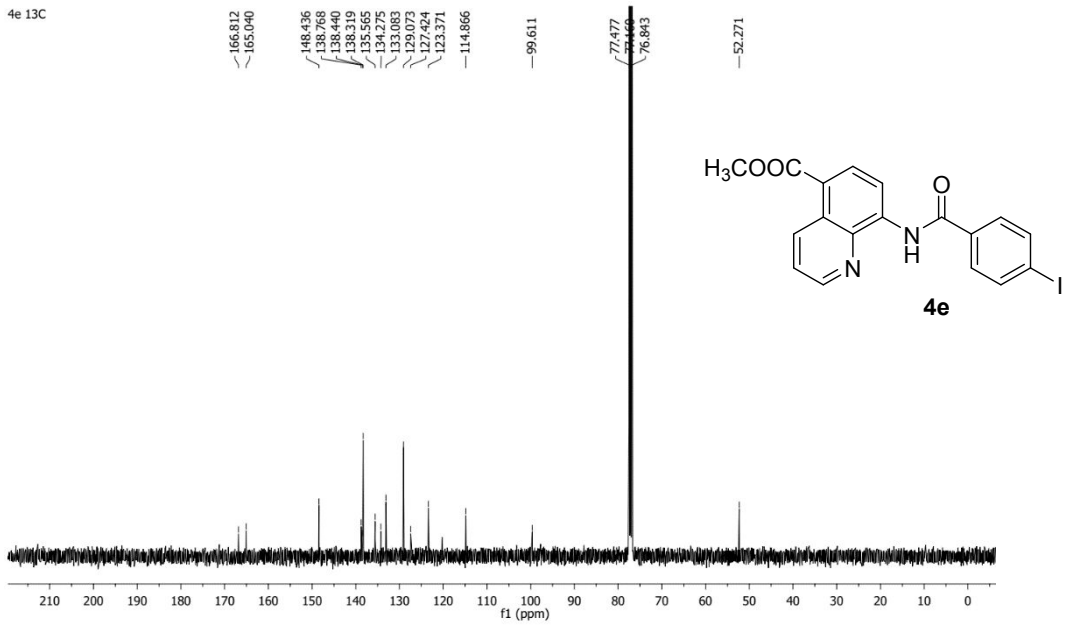


4d

4e-1H

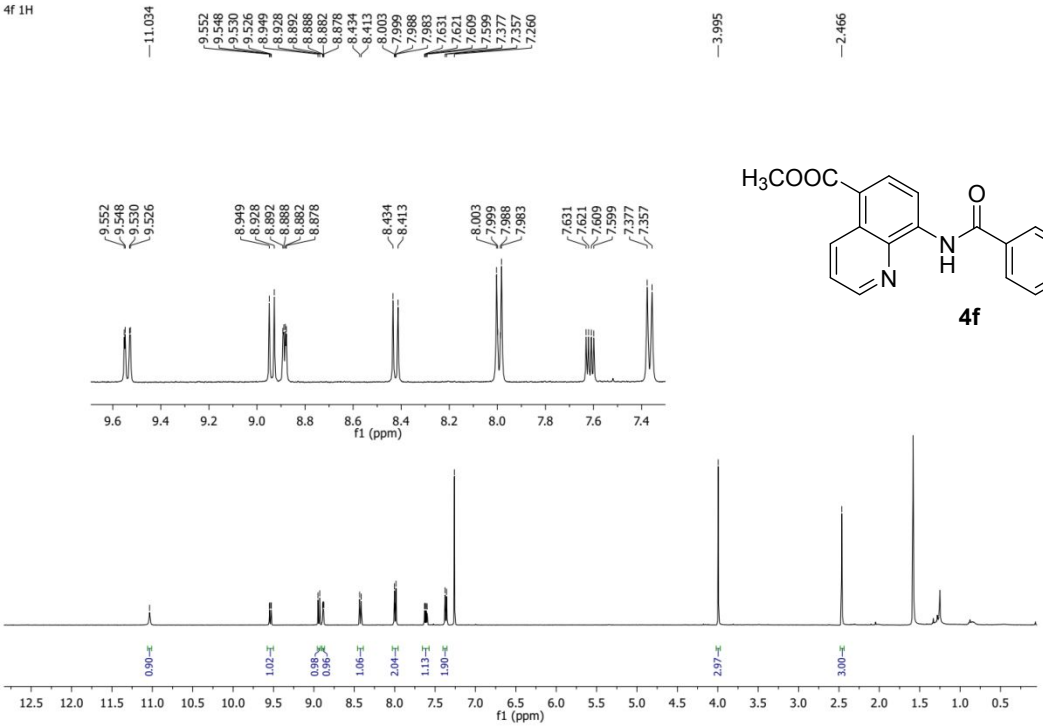


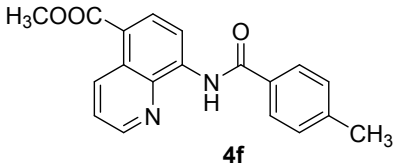
4e


4e 13C
166.812
165.040
148.436
138.768
138.440
138.319
135.565
134.275
133.083
129.073
127.424
123.371
114.866
99.611
77.477
77.160
76.843
52.271
f1 (ppm)

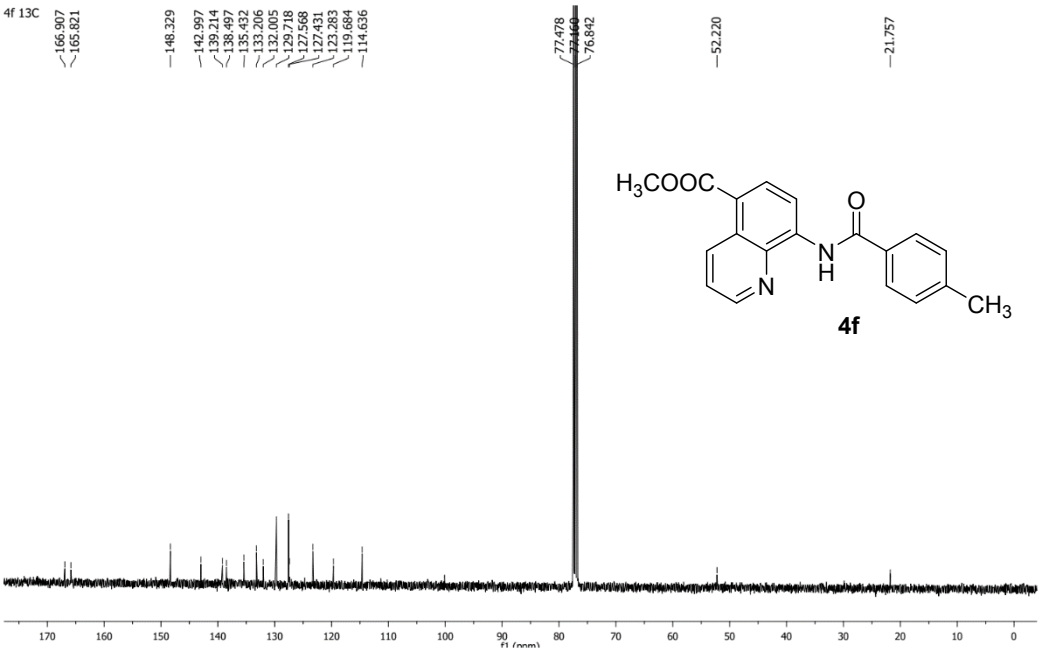
H3COOC
O
N
H
N
I

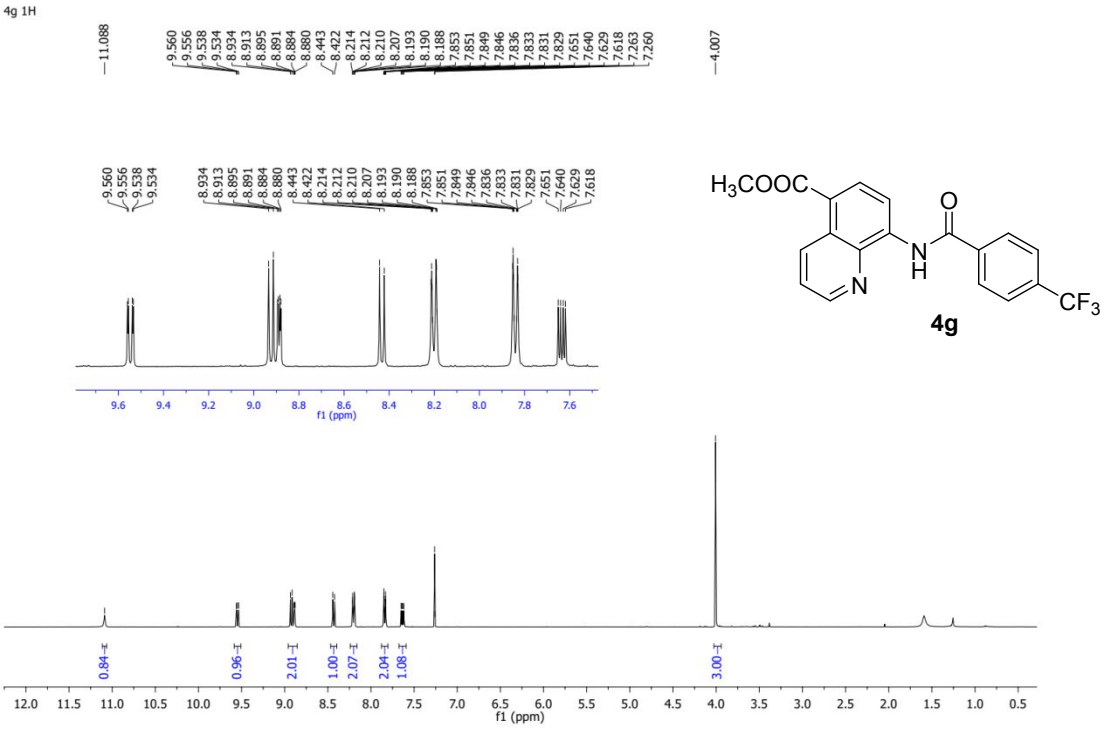
4e

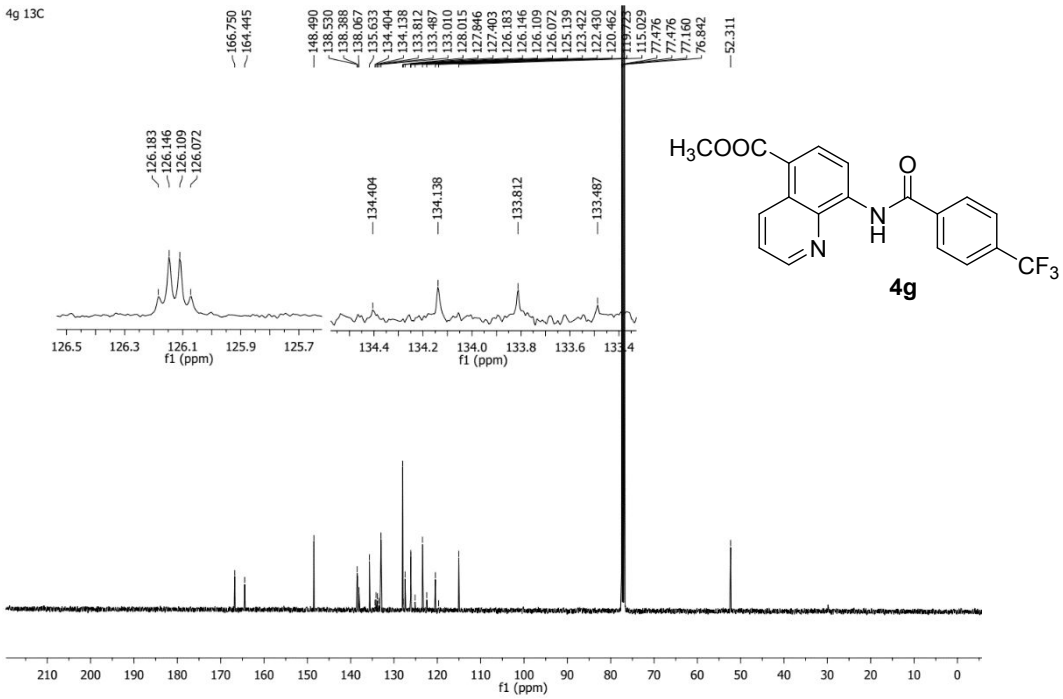

4f 1H
11.034
9.552
9.548
9.530
9.526
8.949
8.928
8.892
8.888
8.882
8.878
8.434
8.413
8.003
7.999
7.988
7.983
7.631
7.621
7.609
7.599
7.377
7.357
7.260
3.995
2.466
0.90
1.02
0.98
0.96
1.06
2.04
1.13
1.90
2.97
3.00
f1 (ppm)

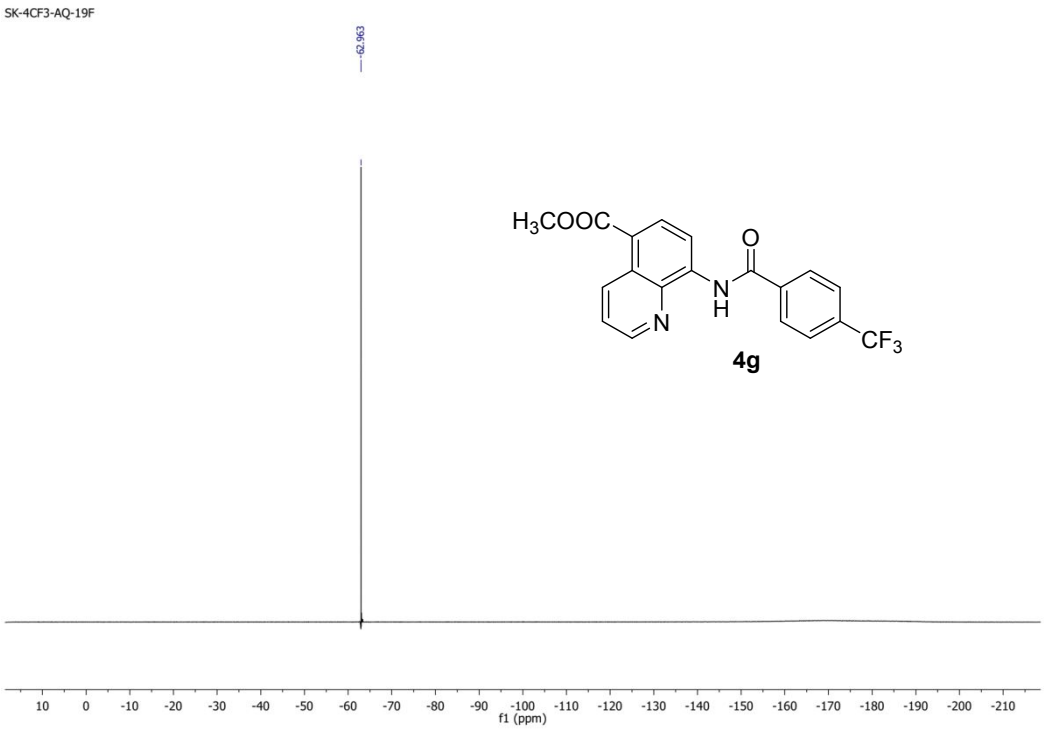

H3COOC
O
N
H
N
CH3

4f

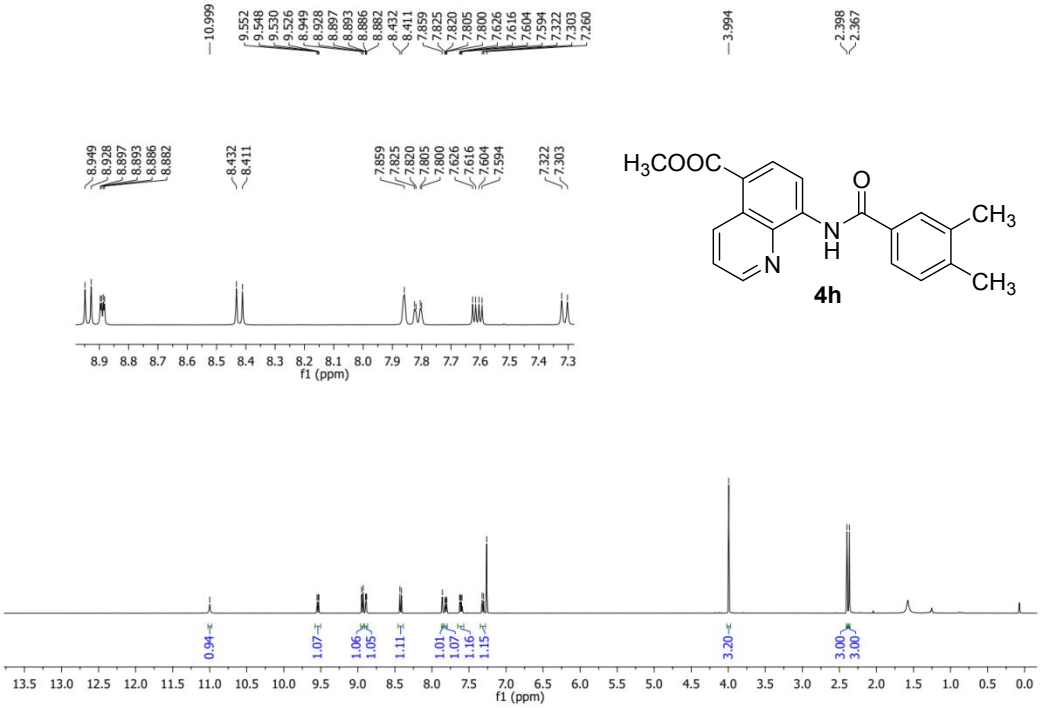

4f 13C
166.907
165.821
148.329
142.997
139.214
138.497
135.432
133.206
132.005
129.718
127.568
127.431
123.283
119.684
114.636
77.478
77.160
76.842
52.220
21.757
H3COOC
O
N
H
N
CH3
4f
f1 (ppm)


4g 1H
11.088
9.560
9.556
9.538
9.534
8.934
8.913
8.895
8.891
8.884
8.880
8.443
8.422
8.214
8.212
8.210
8.207
8.193
8.190
8.188
7.853
7.851
7.849
7.846
7.836
7.833
7.831
7.829
7.651
7.640
7.629
7.618
7.263
7.260
4.007
H3COOC
O
N
H
N
CF3
4g
0.84
0.96
2.01
1.00
2.07
2.04
1.08
3.00
f1 (ppm)

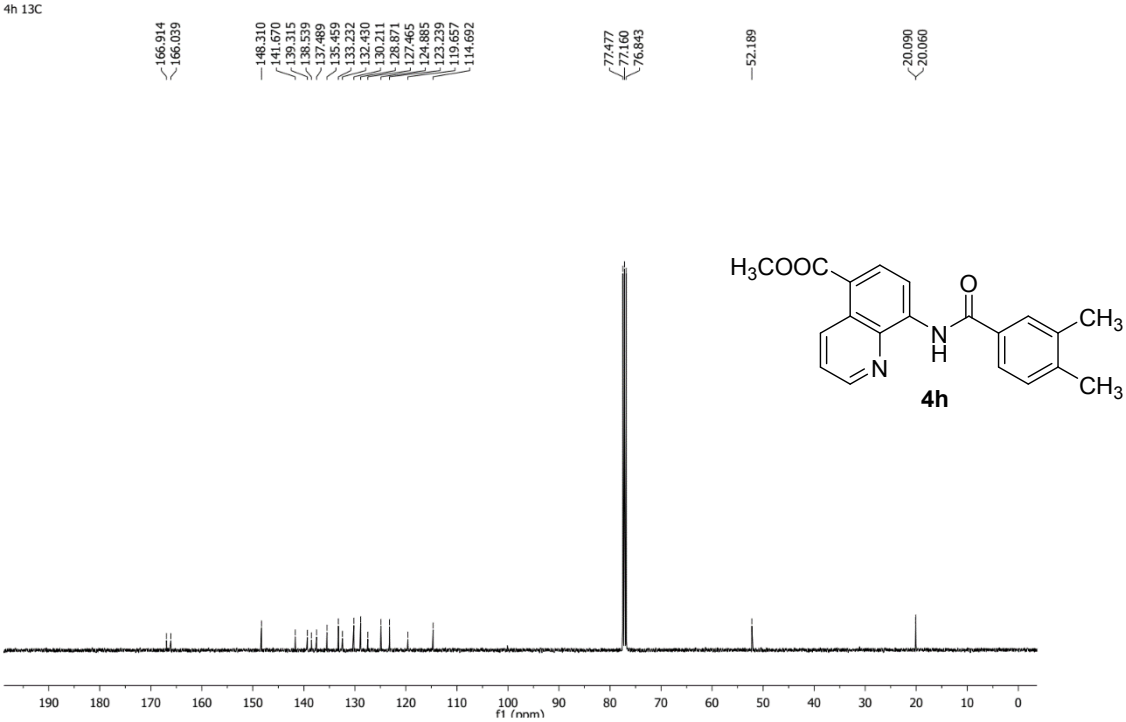

4g 13C
166.750
164.445
148.490
138.530
138.388
138.067
135.633
134.404
134.138
133.812
133.487
133.010
128.015
127.846
127.403
126.183
126.146
126.109
126.072
126.072
125.139
123.422
122.430
120.462
115.029
77.476
77.476
77.160
76.842
52.311
126.183
126.146
126.109
126.072
134.404
134.138
133.812
133.487
f1 (ppm)
f1 (ppm)
f1 (ppm)
H3COOC
O
N
H
N
CF3
4g


SK-4CF3-AQ-19F
-62.963
f1 (ppm)
H3COOC
O
N
H
N
CF3
4g

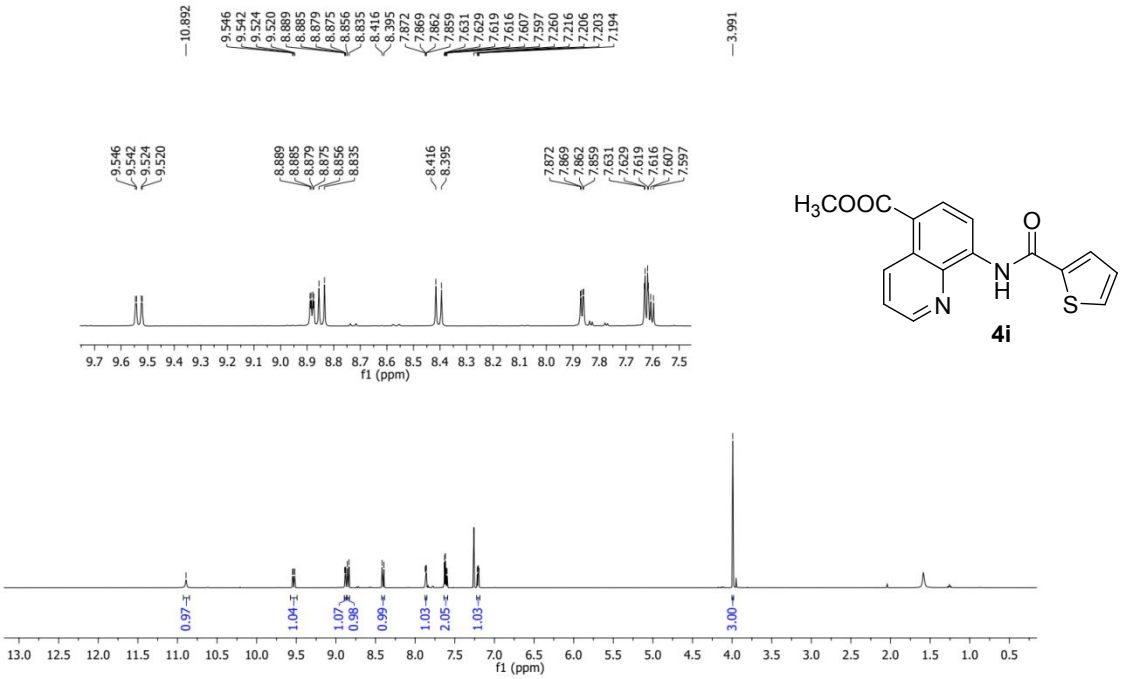
4h 1H


10.999
9.552
9.548
9.530
9.526
8.949
8.928
8.897
8.893
8.886
8.882
8.432
8.411
7.859
7.825
7.820
7.805
7.800
7.626
7.616
7.604
7.594
7.322
7.303
7.260
3.994
2.398
2.367
f1 (ppm)
0.94
1.07
1.06
1.05
1.11
1.01
1.07
1.16
1.15
3.20
3.00
3.00
H3COOC
O
N
H
N
CH3
CH3
4h

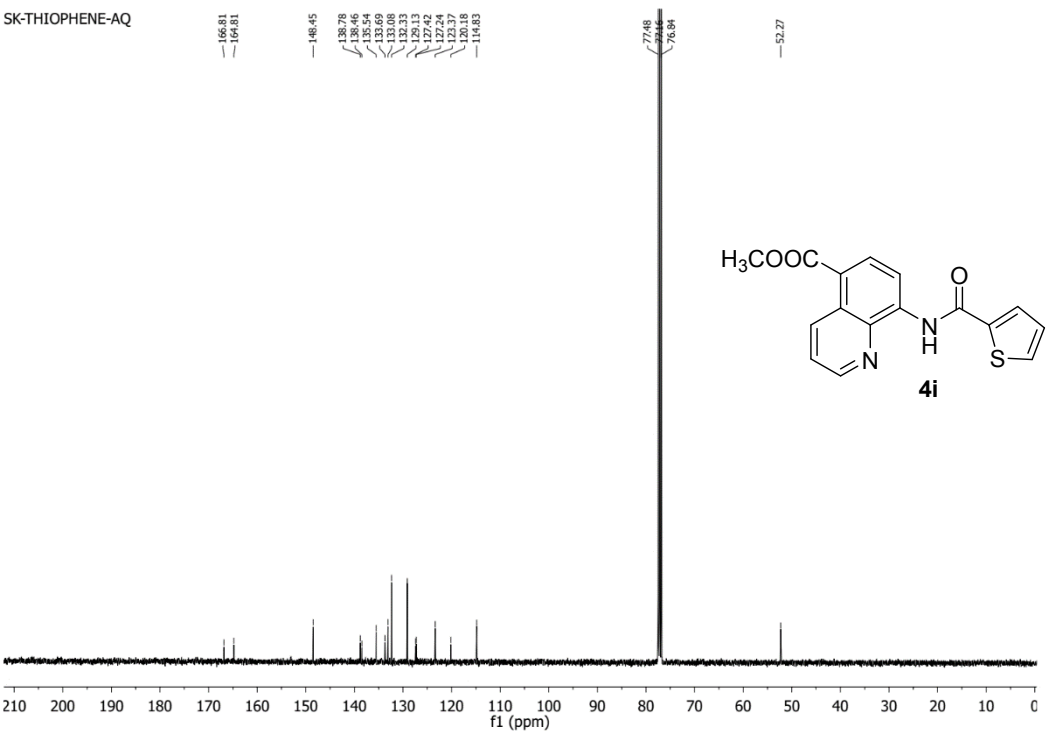
4h 13C


166.914
166.039
148.310
141.670
139.315
138.539
137.489
135.459
133.232
132.430
130.211
128.871
127.465
124.885
123.239
119.657
114.692
77.477
77.160
76.843
52.189
20.090
20.060
f1 (ppm)
H3COOC
O
N
H
N
CH3
CH3
4h

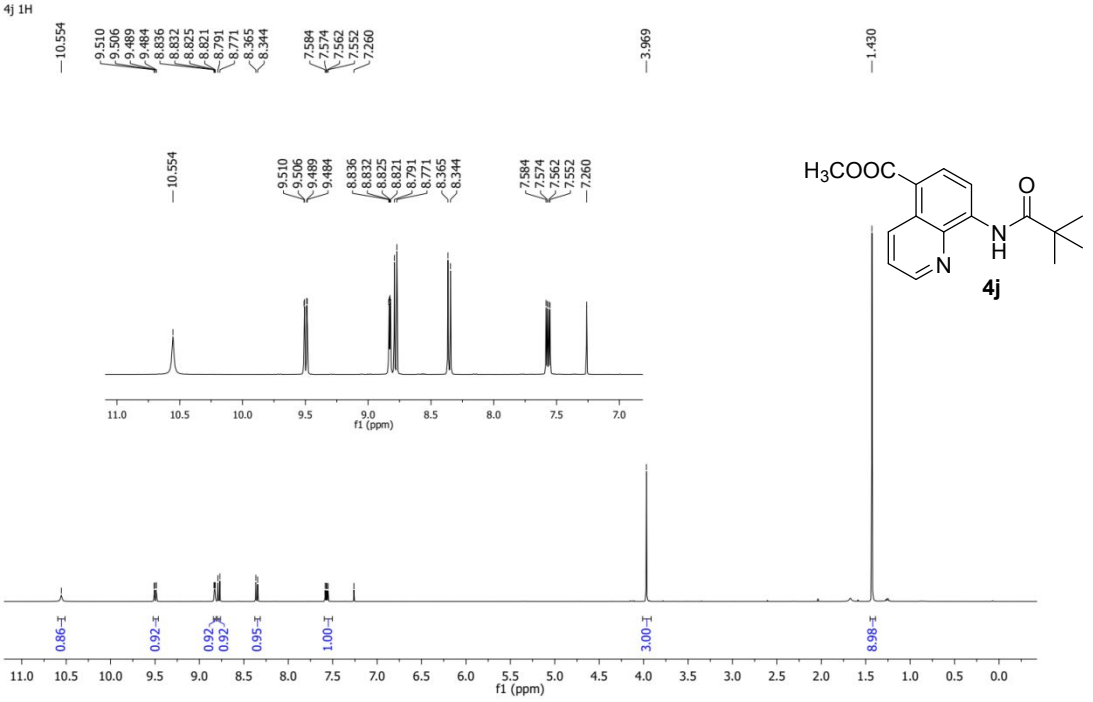
4i 1H



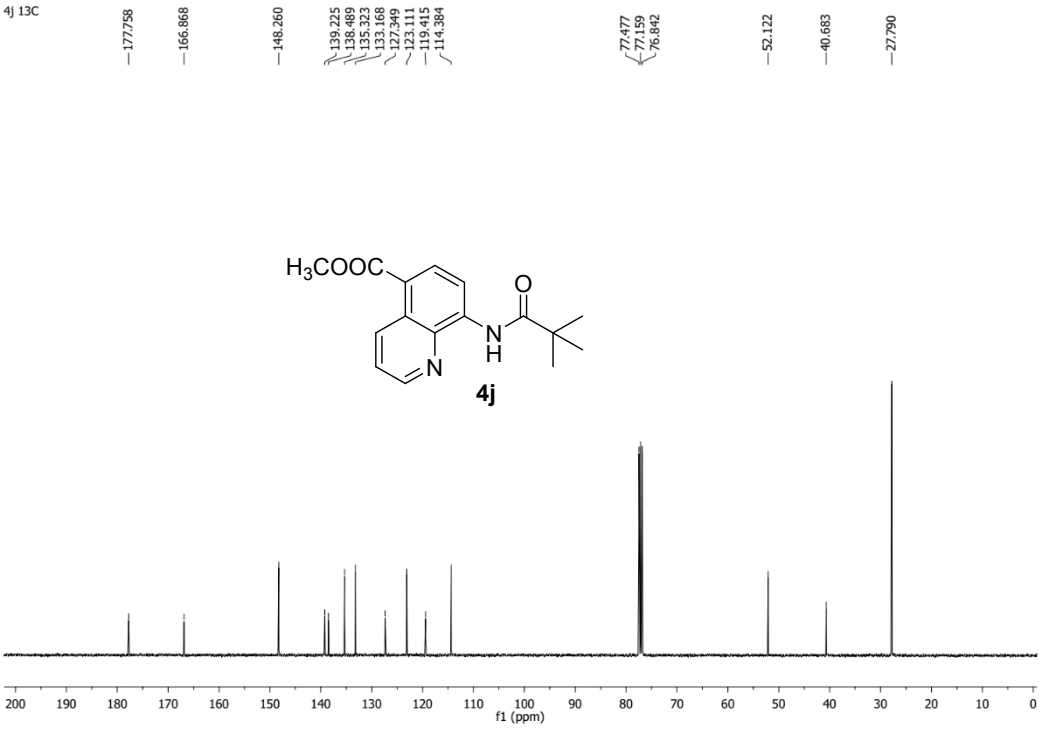
SK-THIOPHENE-AQ

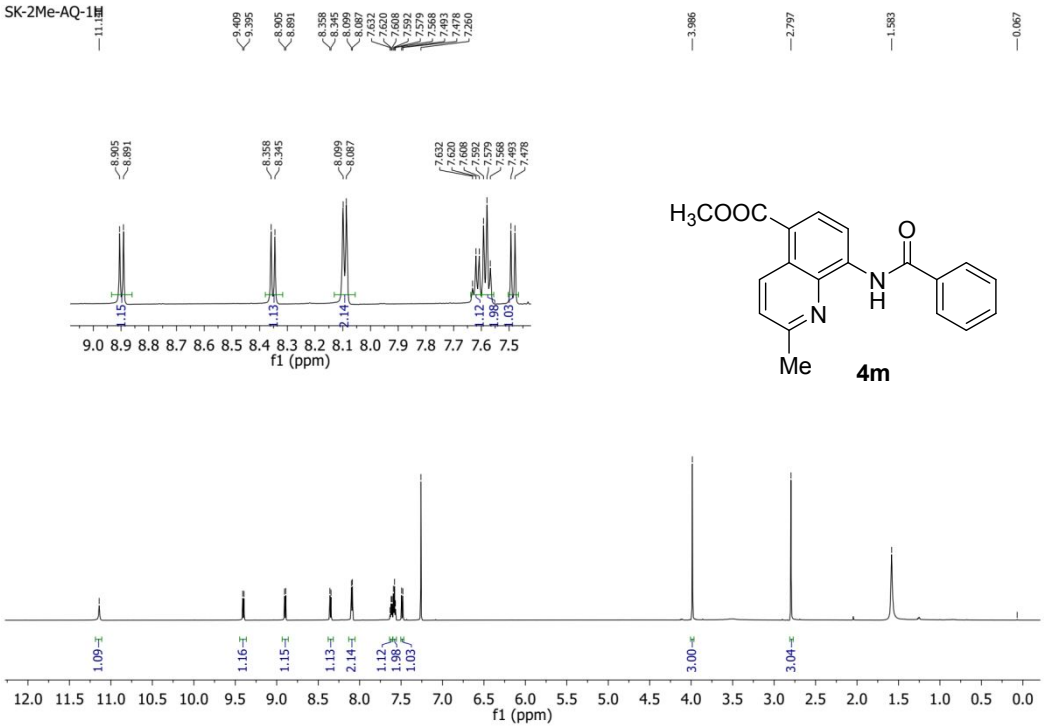


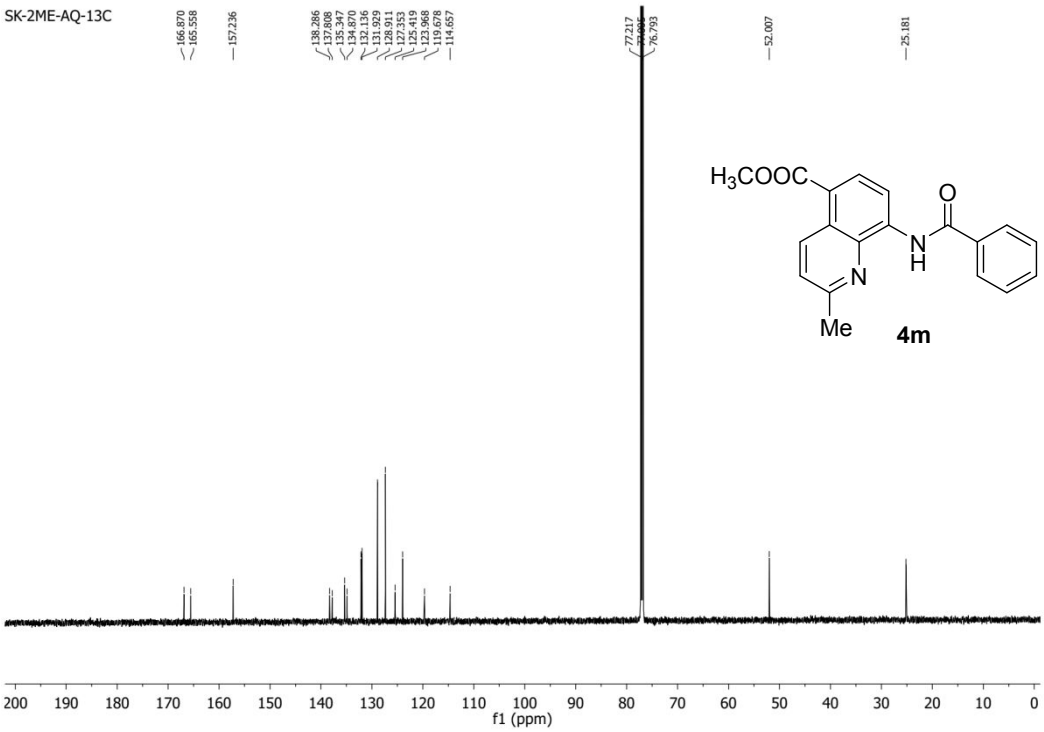
4j 1H


10.554
9.510
9.506
9.489
9.484
8.836
8.832
8.825
8.821
8.791
8.771
8.365
8.344
7.584
7.574
7.562
7.552
7.260
3.969
1.430
H3COOC
O
N
H
N
4j
0.86
0.92
0.92
0.92
0.95
1.00
3.00
8.98
f1 (ppm)

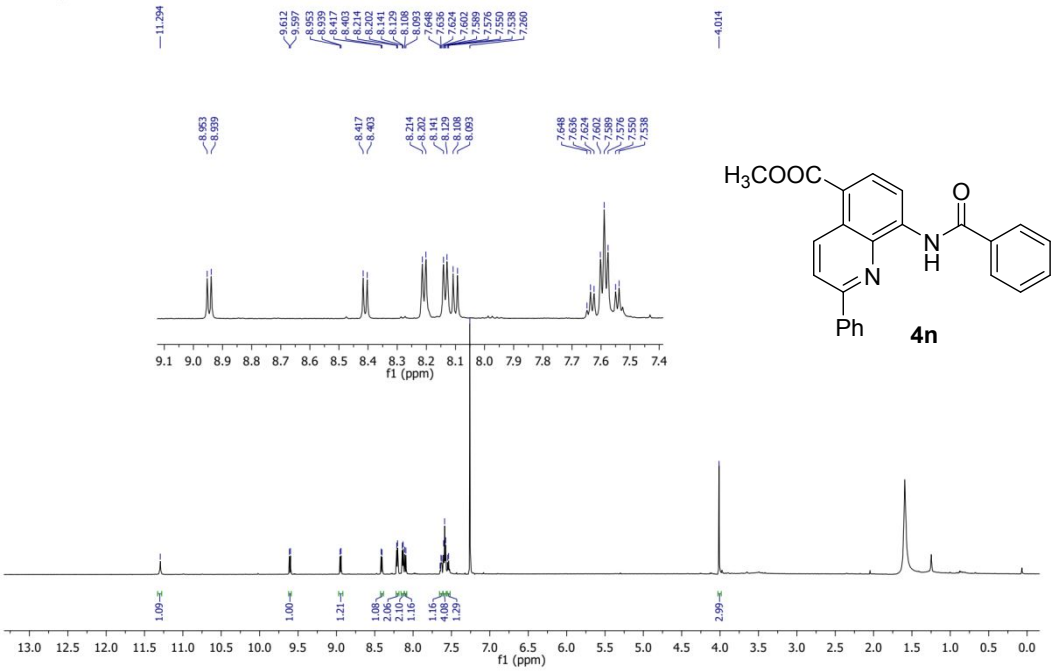
4j 13C


177.758
166.868
148.260
139.225
138.489
135.323
133.168
127.349
123.111
119.415
114.384
77.477
77.159
76.842
52.122
40.683
27.790
H3COOC
O
N
H
N
4j
f1 (ppm)

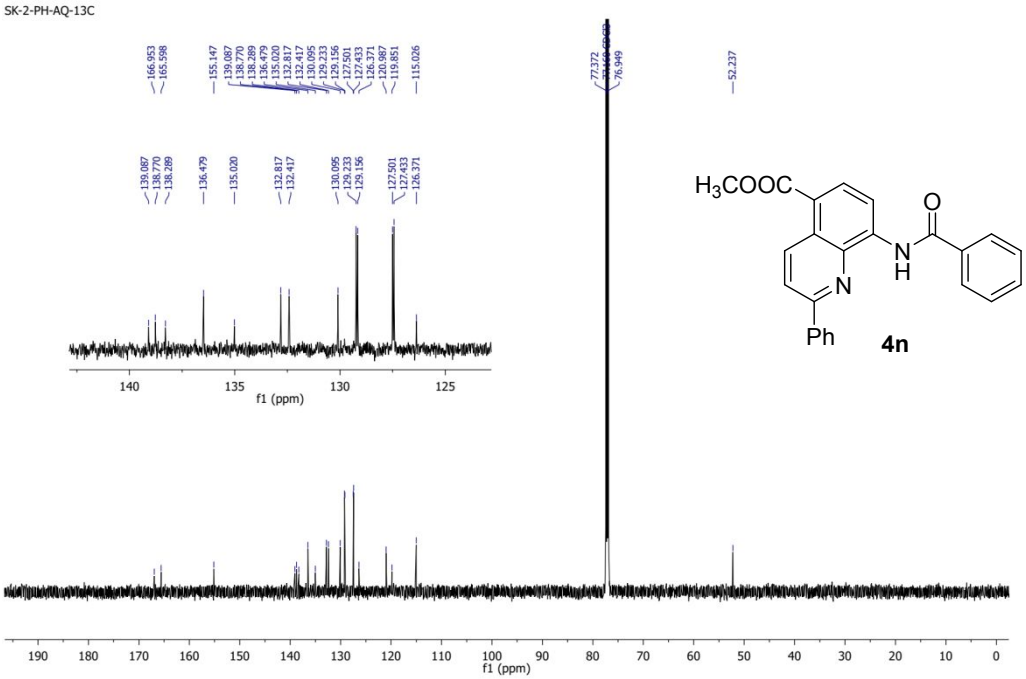

SK-2Me-AQ-1H
11.112
9.409
9.395
8.905
8.891
8.358
8.345
8.099
8.087
7.632
7.620
7.608
7.592
7.579
7.568
7.493
7.478
7.260
3.986
2.797
1.583
0.067
1.15
1.13
2.14
1.12
1.98
1.03
9.0 8.9 8.8 8.7 8.6 8.5 8.4 8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5
f1 (ppm)
H3COOC
O
N
H
N
Me
4m
1.09
1.16
1.15
1.13
2.14
1.12
1.98
1.03
3.00
3.04
12.0 11.5 11.0 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)


SK-2ME-AQ-13C
166.870
165.558
157.236
138.286
137.808
135.347
134.870
132.136
131.929
128.911
127.253
125.419
123.968
119.678
114.657
77.217
76.793
52.007
25.181
H3COOC
O
N
H
N
Me
4m
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

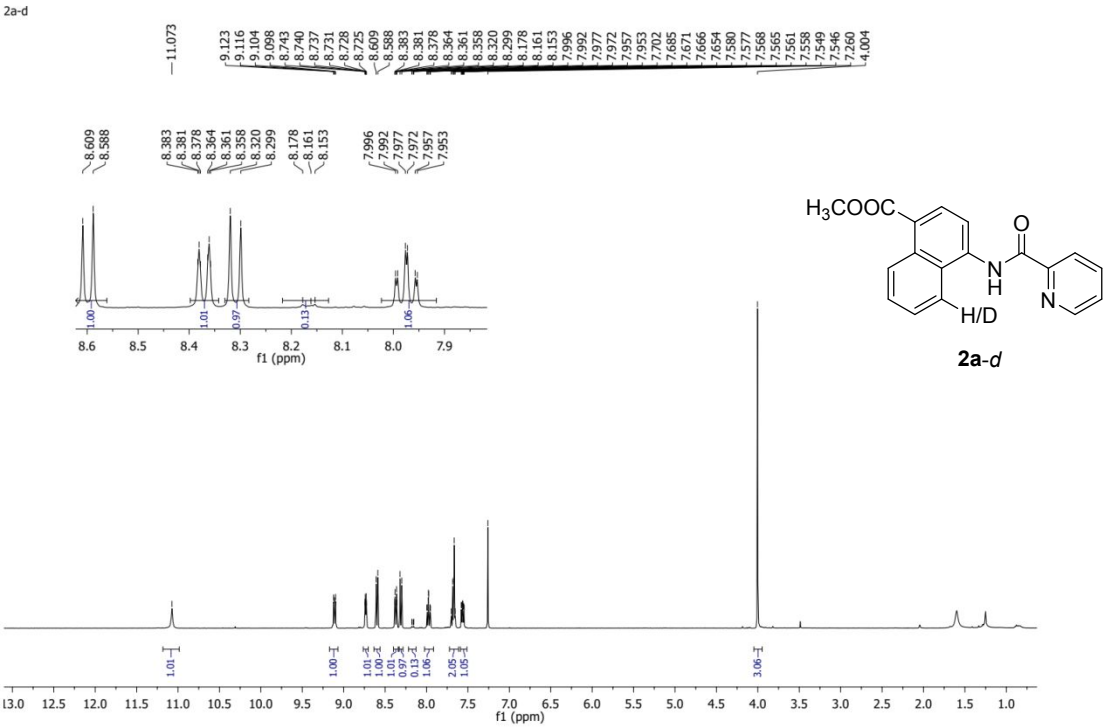
SK-2PH-AQ-1H



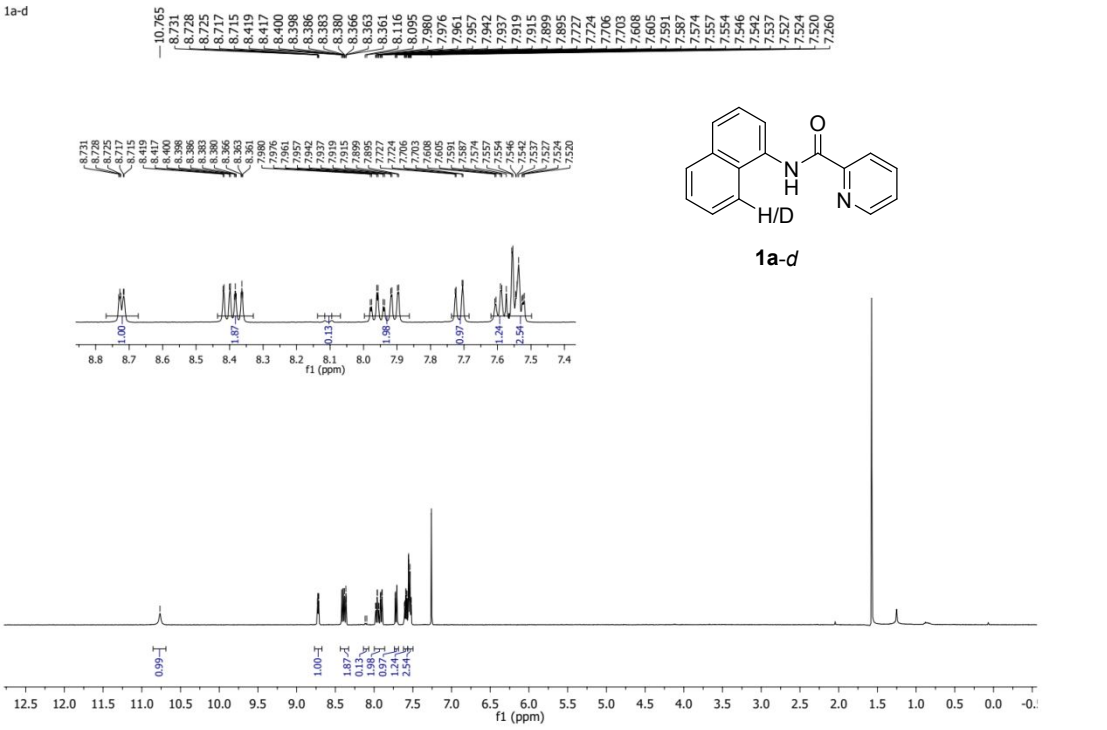
SK-2-PH-AQ-13C



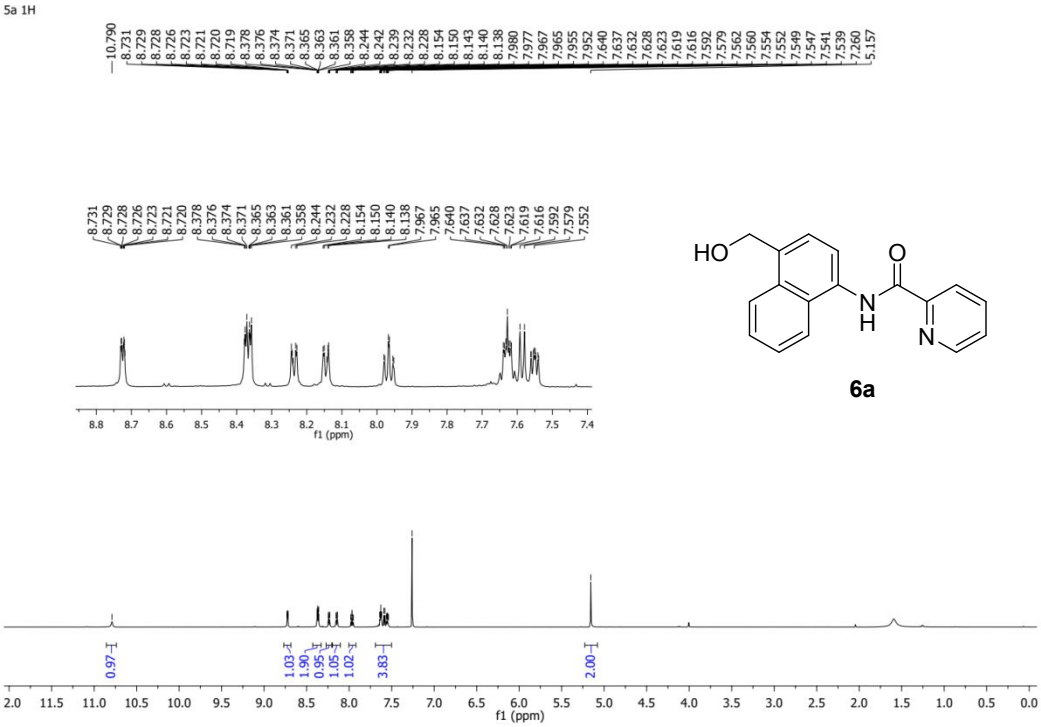
2a-d



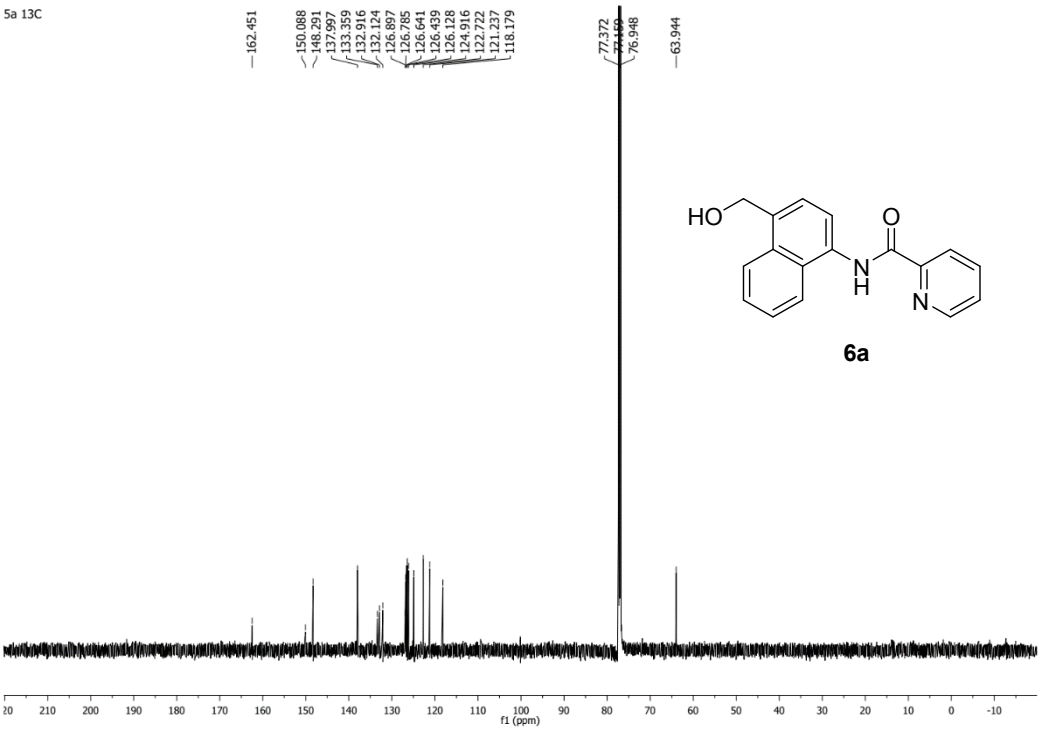
1a-d



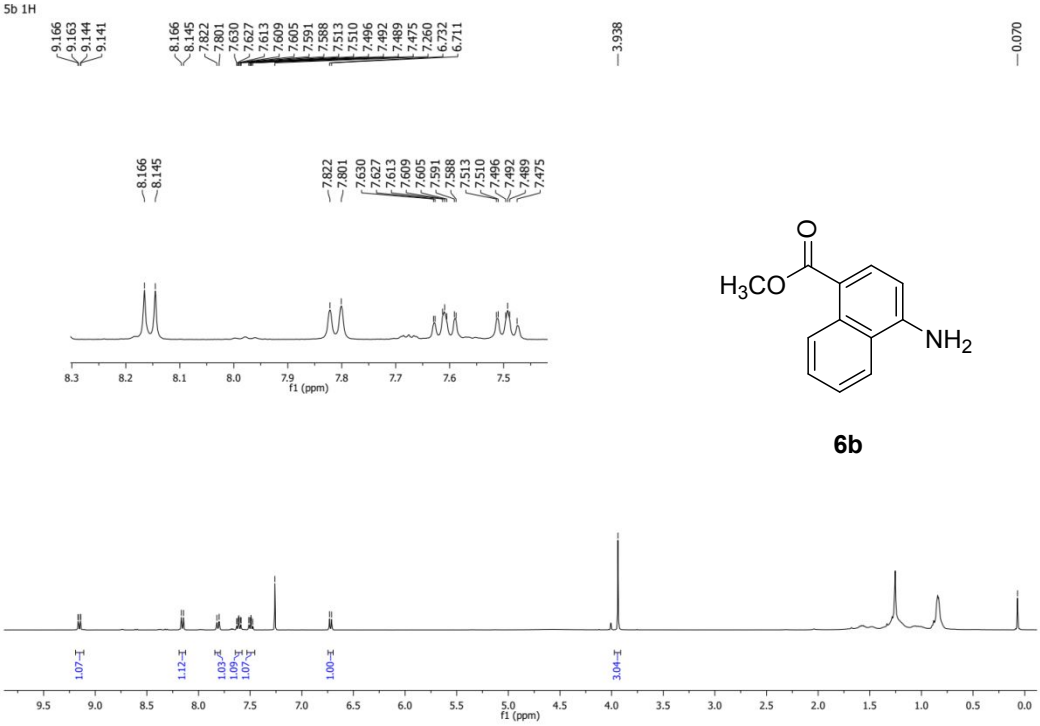
5a 1H


10.790
8.731
8.729
8.728
8.726
8.723
8.721
8.720
8.719
8.378
8.376
8.374
8.371
8.365
8.363
8.361
8.358
8.244
8.242
8.239
8.232
8.228
8.154
8.150
8.143
8.140
8.138
7.980
7.977
7.967
7.965
7.955
7.952
7.640
7.637
7.632
7.628
7.623
7.619
7.616
7.592
7.579
7.562
7.560
7.554
7.552
7.549
7.547
7.541
7.539
7.260
5.157
HO
O
N
H
N
6a
0.97
1.03
1.90
0.95
1.05
1.02
3.83
2.00
f1 (ppm)

5a 13C

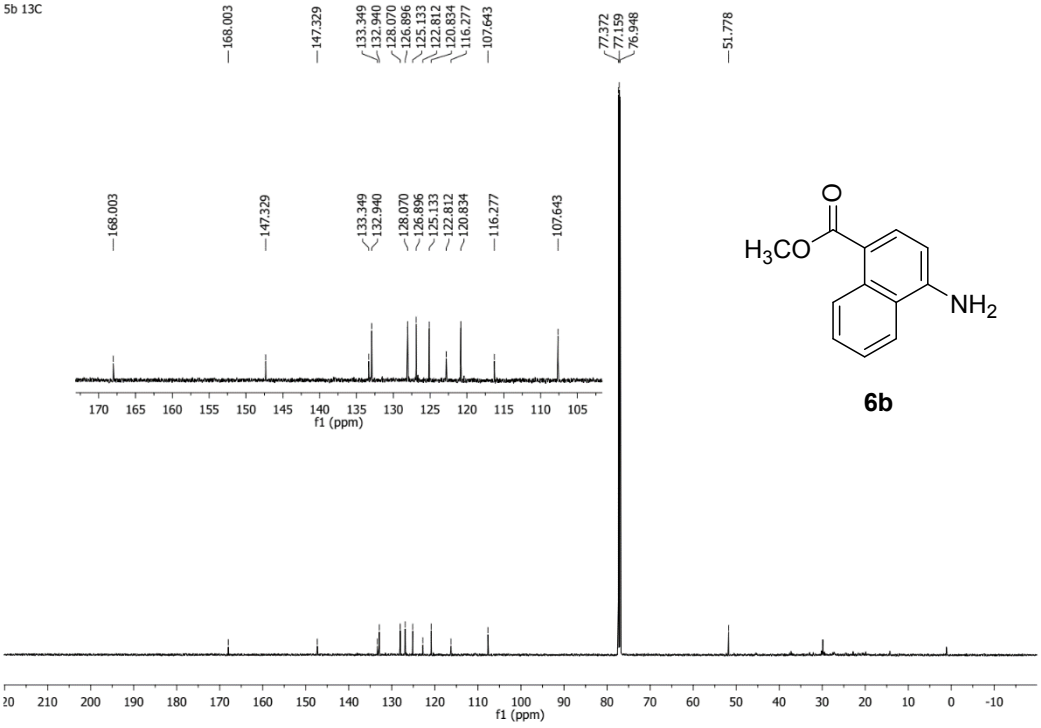

162.451
150.088
148.291
137.997
133.359
132.916
132.124
126.897
126.785
126.641
126.439
126.128
124.916
122.722
121.237
118.179
77.372
77.160
76.948
63.944
HO
O
N
H
N
6a
f1 (ppm)

5b 1H



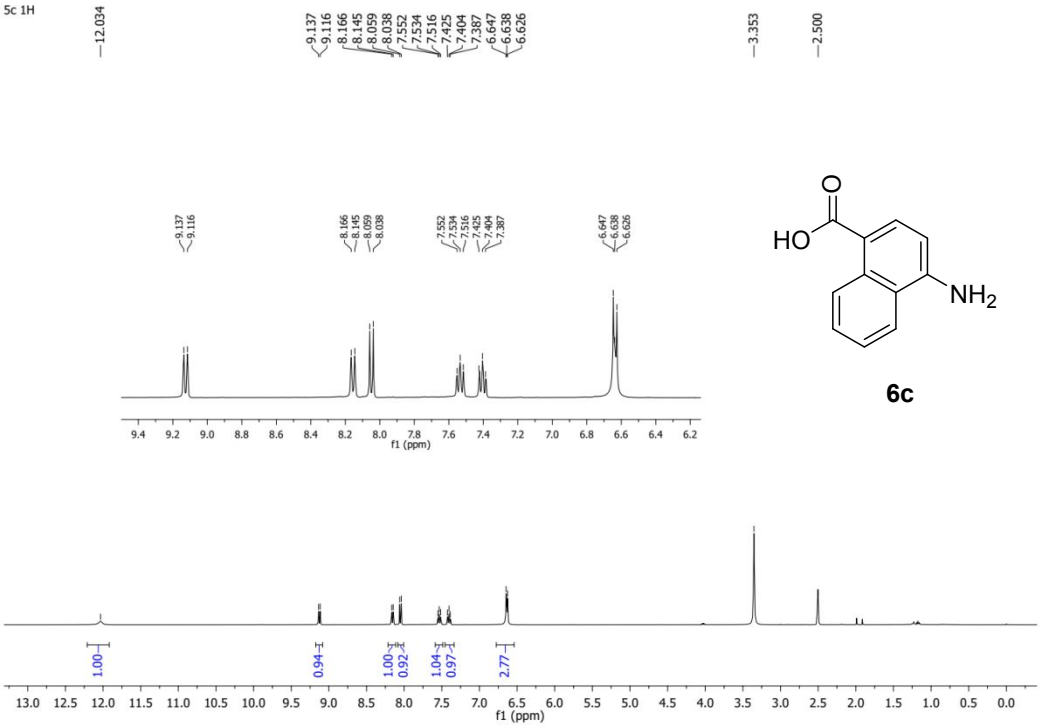
6b

5b 13C

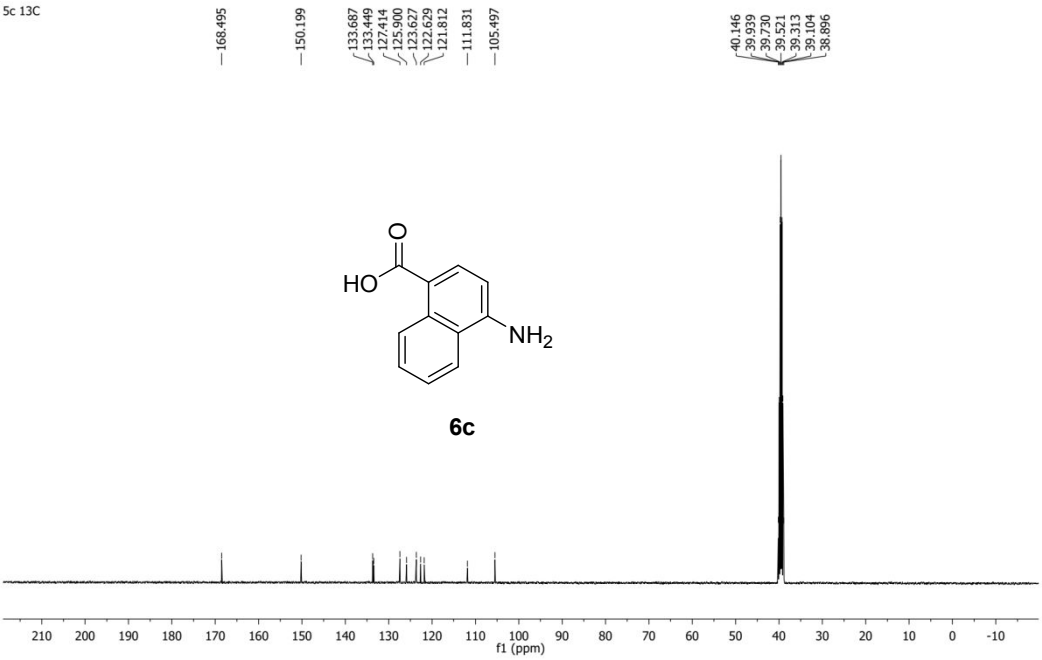


6b

5c 1H


12.034
9.137
9.116
8.166
8.145
8.059
8.038
7.552
7.534
7.516
7.425
7.404
7.387
6.647
6.638
6.626
3.353
2.500
HO
O
NH2
6c
f1 (ppm)
1.00
0.94
1.00
0.92
1.04
0.97
2.77

5c 13C


168.495
150.199
133.687
133.449
127.414
125.900
123.627
122.629
121.812
111.831
105.497
40.146
39.939
39.730
39.521
39.313
39.104
38.896
HO
O
NH2
6c
f1 (ppm)