SUPPORTING INFORMATION

for

Biomimetic Aerobic C–H Olefination of Cyclic Enaminones at Room Temperature: Development toward the Synthesis of 1,3,5-Trisubstituted Benzenes

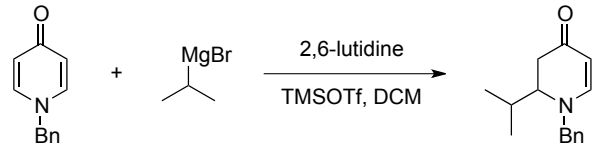
Yi-Yun Yu and Gunda I. Georg*

Department of Chemistry and Department of Medicinal Chemistry and
the Institute for Therapeutics Discovery and Development, University of Minnesota
717 Delaware Street SE, Minneapolis, Minnesota 55414 USA

Table of Contents

1. Preparation of the starting materials

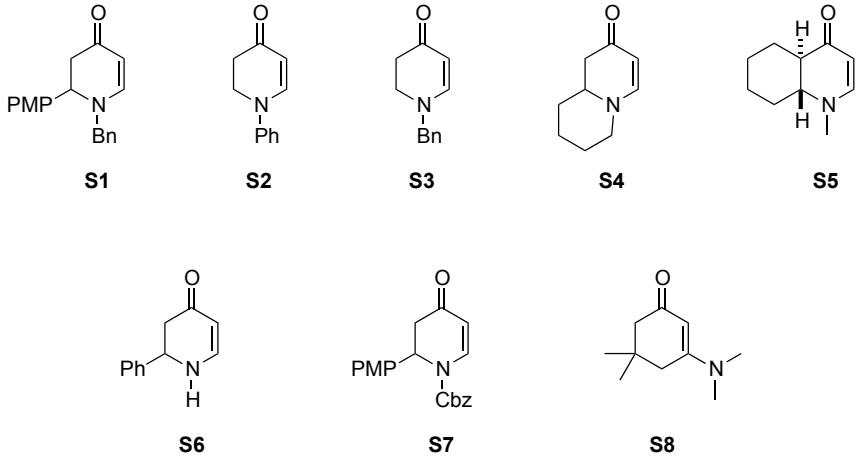
1) Preparation of *N*-benzyl-2-isopropyl-2,3-dihydropyridin-4(1*H*)-one



N-Benzyl-4-pyridone (3.0 g, 16.20 mmol) in dry CH_2Cl_2 (30 mL) was treated with TMSOTf (6.3 mL, 32.39 mmol) at room temperature under a N_2 atmosphere. After the reaction was stirred for 1 h, 2,6-lutidine (3.8 mL, 32.39 mmol) was added, followed by slow addition of a 2.0 M solution of isopropylmagnesium bromide in THF (12.2 mL, 24.29 mmol) with a syringe pump. The reaction was stirred for another 2 h and then quenched with saturated NH_4Cl (15 mL). The mixture was extracted with CH_2Cl_2 (15 mL × 4). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Further purification was carried out by flash column chromatography (3:1 EtOAc/hexanes) to produce 2.1 g (57%) of *N*-benzyl-2-isopropyl-2,3-dihydropyridin-4(1*H*)-one as an orange oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.30 (m, 3H), 7.29–7.24 (m, 2H), 7.12 (d, *J* = 7.4 Hz, 1H), 4.91 (d, *J* = 7.4 Hz, 1H), 4.47 (d, *J* = 15.4 Hz, 1H), 4.39 (d, *J* = 15.4 Hz, 1H), 3.22 (td, *J* = 6.9, 4.0 Hz, 1H), 2.60 (dd, *J* = 16.7, 7.5 Hz, 1H), 2.39 (dd, *J* = 16.7, 3.8 Hz, 1H), 2.28 (dq, *J* = 13.4, 6.7 Hz, 1H), 0.95 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.3, 153.7, 137.0, 129.2, 128.4, 127.4, 97.5, 61.4, 58.8, 36.5, 29.1, 19.8, 18.1; FTIR (Film, cm^{-1}) 3054, 2984, 2876, 1635, 1591, 1496, 1455, 1441, 1421, 1387, 1357, 1344, 1204, 1166, 1094, 1077, 1029, 1014, 1002, 955, 896; HRMS (ESI+) *m/z* calculated for $[M+Na]^+$ $C_{15}H_{19}NONa$: 252.1359, found 252.1354.

2) Synthesis of other cyclic enaminones

Other cyclic enaminones were prepared according to the reported procedures as follows (Scheme S1): **S1**,[1] **S2**,[2] **S3**,[3] **S4**,[4] **S5**,[4] **S6**,[2] **S7**,[5] **S8**.[6]

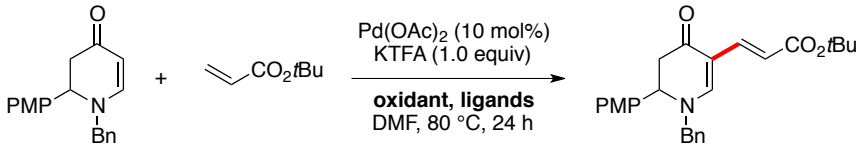


Scheme S1. Preparation of cyclic enaminones.

2. Optimization data for the aerobic dehydrogenative alkenylation

1) Initial trials

Table S1. Initial attempts of aerobic oxidative alkenylation of cyclic enaminones



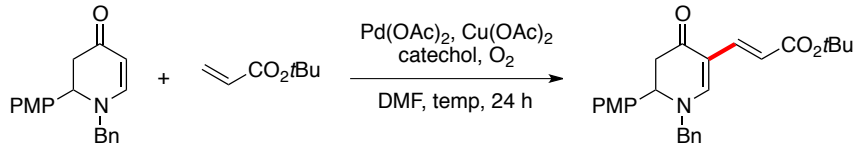
S1 **S9** **S10**

Entry[a]	Cu^{II} (0.2)	Oxidant[b]	Ligand (0.2)	% Consumption[c]	% Yield[d]
1	–	air	–	50	27
2	–	O_2	–	71	44
3	$Cu(OAc)_2$	O_2	–	91	41
4	–	O_2	Boc-β-Ala-OH	85	49
5	–	O_2	Boc-Phe-OH	76	45

[a] Other conditions: **S1** (0.2 M), **S9** (2 equiv), $Pd(OAc)_2$ (10 mol %), KTFA (1 equiv) in DMF (0.5 mL) at 80 ºC through 24 h. [b] The pressure was 1 atm. [c] NMR % conversion of the starting enaminone with Ph_3SiMe (1.0 equiv) as the internal standard. [d] NMR % yield with Ph_3SiMe (1.0 equiv) as the internal standard.

2) Introduction of catechol

Table S2. Aerobic oxidative alkenylation of cyclic enaminones with catechol



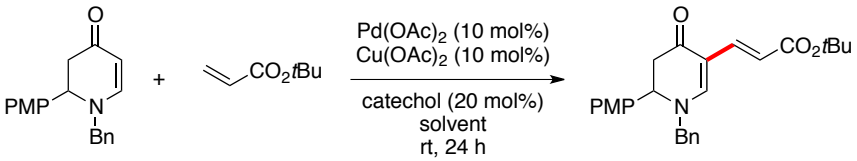
S1 **S9** **S10**

Entry[a]	$Pd(OAc)_2$ (mol %)	$Cu(OAc)_2$ (mol %)	Catechol (mol %)	Oxidant (1 atm)	Temp (ºC)	% Consumption[b]	% Yield[c]
1	5	5	10	O_2	80	69	40
2	5	5	10	O_2	rt	49	36
3	5	10	20	O_2	rt	47	47
4	10	10	20	O_2	rt	**85**	**78**
5	5	10	20	air	rt	49	44
6	10	10	20	air	rt	79	72
7	10	10	10	O_2	rt	78	72
8	10	20	40	O_2	rt	77	69

[a] Other conditions: **S1** (0.2 M), **S9** (4 equiv) in DMF (0.5 mL) through 24 h. [b] NMR % conversion of the starting enaminone with Ph_3SiMe (1.0 equiv) as the internal standard. [c] NMR % yield with Ph_3SiMe (1.0 equiv) as the internal standard.

3) Solvent screen

Table S3. Solvent effect on the aerobic oxidative alkenylation of cyclic enaminones



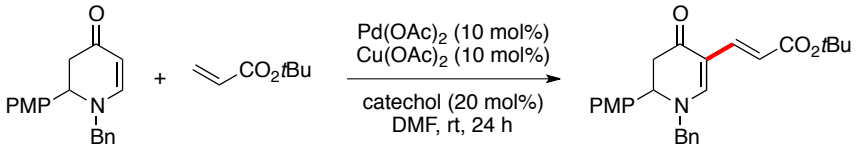
S1 **S9** **S10**

Entry[a]	Solvent	% Consumption[b]	% Yield[c]
1	DMF	**85**	**78**
2	MeCN	73	65
3	DMSO	70	62
4	NMP	51	43
5	THF	42	39
6	toluene	65	57

[a] Other conditions: **S1** (0.2 M), **S9** (4 equiv), $Pd(OAc)_2$ (10 mol %), $Cu(OAc)_2$ (10 mol %), catechol (20 mol %) in DMF (0.5 mL) at rt under O_2 (1 atm) through 24 h. [b] NMR % conversion of the starting enaminone with Ph_3SiMe (1.0 equiv) as the internal standard. [c] NMR % yield with Ph_3SiMe (1.0 equiv) as the internal standard.

4) Alkene concentration

Table S4. Alkene concentration on the aerobic oxidative alkenylation of cyclic enaminones



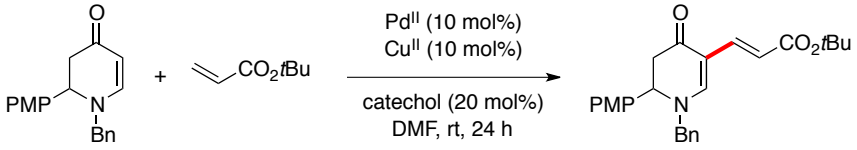
S1 **S9** **S10**

Entry[a]	**S9** (equiv)	% Consumption[b]	% Yield[c]
1	1.0	59	57
2	2.0	72	69
3	3.0	69	62
4	4.0	**85**	**78**
5	5.0	77	74
6	6.0	82	74
7	8.0	77	77

[a] Other conditions: **S1** (0.2 M), $Pd(OAc)_2$ (10 mol %), $Cu(OAc)_2$ (10 mol %), catechol (20 mol %) in DMF (0.5 mL) at rt under O_2 (1 atm) through 24 h. [b] NMR % conversion of the starting enaminone with Ph_3SiMe (1.0 equiv) as the internal standard. [c] NMR % yield with Ph_3SiMe (1.0 equiv) as the internal standard.

5) Catalyst combination

Table S5. Catalyst screen for the aerobic oxidative alkenylation of cyclic enaminones



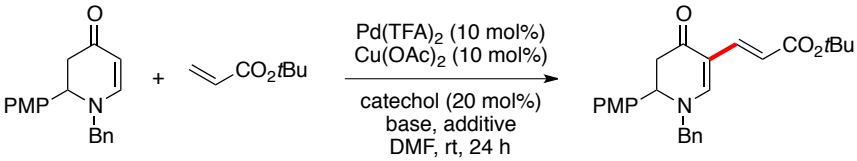
S1 **S9** **S10**

Entry[a]	Pd^{II} (10 mol %)	Cu^{II} (10 mol %)	% Consumption[b]	% Yield[c]
1	$Pd(OAc)_2$	$Cu(OAc)_2$	85	78
2	$Pd(TFA)_2$	$Cu(TFA)_2$	73	63
3	$PdCl_2$	$CuCl_2$	53	55
4	$Pd(TFA)_2$	$Cu(OAc)_2$	**90**	**81**
5	$Pd(OAc)_2$	$Cu(TFA)_2$	86	81
6	$PdCl_2$	$Cu(OAc)_2$	61	57
7	$Pd(OAc)_2$	$CuCl_2$	48	37
8	$PdCl_2$	$Cu(TFA)_2$	43	33
9	$Pd(TFA)_2$	$CuCl_2$	38	27

[a] Other conditions: **S1** (0.2 M), **S9** (4 equiv), catechol (20 mol %) in DMF (0.5 mL) at rt under O_2 (1 atm) through 24 h. [b] NMR % conversion of the starting enaminone with Ph_3SiMe (1.0 equiv) as the internal standard. [c] NMR % yield with Ph_3SiMe (1.0 equiv) as the internal standard.

6) Additional optimization

Table S6. Further study on the aerobic oxidative alkenylation of cyclic enaminones



S1 **S9** **S10**

Entry[a]	**S1** (M)	Base (0.2 equiv)	Additive	% Consumption[b]	% Yield[c]
1	0.2	–	–	90	81
2	0.2	pyridine	–	20	16
3	0.2	Et_3N	–	52	51
4	0.2	Na_2CO_3	–	72	69
5	0.2	$NaHCO_3$	–	77	73
6	0.4	–	–	100	86
7	0.1	–	–	58	43

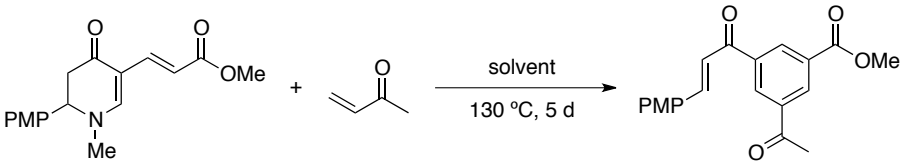
8	0.05	–	–	77	68
9	0.03	–	–	61	52
10	0.2	–	4Å MS	**100**	**91** (**89**[d])

[a] Other conditions: **S9** (4 equiv), $Pd(TFA)_2$ (10 mol %), $Cu(OAc)_2$ (10 mol %), catechol (20 mol %) in DMF (0.5 mL) at rt under O_2 (1 atm) through 24 h. [b] NMR % conversion of the starting enaminone with Ph_3SiMe (1.0 equiv) as the internal standard. [c] NMR % yield with Ph_3SiMe (1.0 equiv) as the internal standard. [d] Isolated yield.

3. Condition optimization for the Diels-Alder tandem reaction

1) Solvent screen

Table S7. Solvent effect on the Diels-Alder tandem reaction



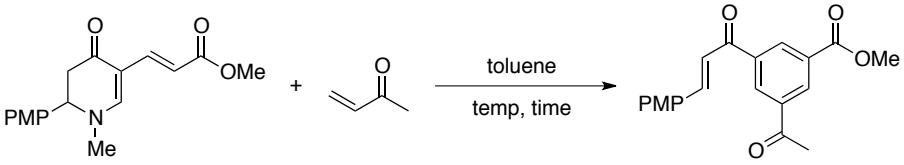
S11 **S12** **S13**

Entry[a]	Solvent (1 mL)	% Yield
1	toluene	44
2	DCE	45
3	MeCN	36
4	dioxane	35
5	DMAc	28
6	THF	0

[a] Conditions: Enaminone **S11** (0.07 M), alkene **S12** (2 equiv) at 130 °C for 5 d. ^1H NMR yield based on 1.0 equiv of Ph_3SiMe as the internal standard.

2) Reaction time and temperature

Table S8. Reaction time and temperature effect on the Diels-Alder tandem reaction



S11 **S12** **S13**

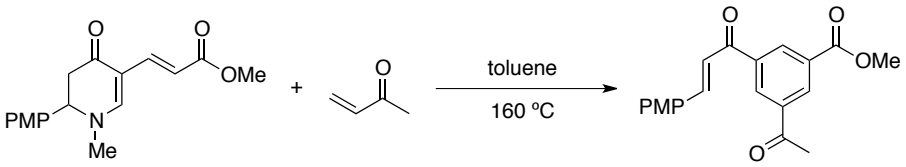
Entry[a]	Time (h)	Temp (ºC)	% Yield
1[b]	0.5	180	17
2[b]	2	180	44
3[b]	4	180	48
4[b]	8	180	51

5[b]	10	180	52
6[b]	2	200	46
7[b]	4	200	19
8	24	150	31
9	24	160	56
10	24	170	40
11	24	180	45
12	15	180	43

[a] Conditions: Enaminone **S11** (0.07 M), alkene **S12** (4 equiv) in toluene (1 mL). ^{1}H NMR yield based on 1.0 equiv of Ph_3SiMe as the internal standard. [b] Under microwave.

3) Stoichiometry

Table S9. Effect of reagent stoichiometry on the Diels-Alder tandem reaction



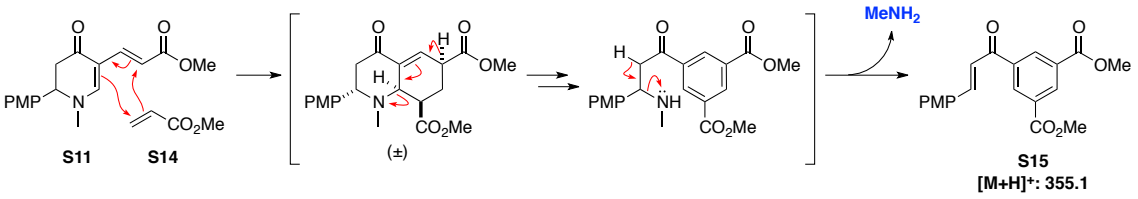
S11 **S12** **S13**

Entry[a]	**S12** (equiv)	Time (h)	% Yield
1	1.1	24	27
2	2.0	24	42
3	4.0	24	56
4	8.0	24	**63** (**66**[b])
5	15.0	24	59
6	30.0	24	61
7	2.0	48	43
8[c]	2.0	24	17

[a] Other conditions: Enaminone **S11** (0.07 M) in toluene (1 mL) at 160 °C. ^{1}H NMR yield based on 1.0 equiv of Ph_3SiMe as the internal standard. [b] Isolated yield. [c] Under 1 atm O_2.

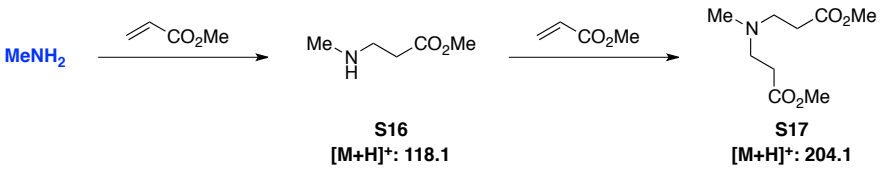
4. Mechanistic study of the Diels-Alder tandem reaction

We proposed that methylamine was released during retro-Michael fragmentation in the Diels-Alder tandem sequence of synthesizing 1,3,5-trisubstituted benzenes. In order to support our hypothesis, diene **S11** (2.5 mg, 8.3 μmol) was treated with dienophile **S14** (6.0 μL, 66.4 μmol) in toluene (0.5 mL) at 160 °C for 15 h (Eq. 1). The crude mixture from the tandem reaction was initially subjected to a GC-MS analysis to detect methylamine. However, no methylamine was found.



Eq. 1

In light of the excess amount of dienophile in presence (*i.e.* 8.0 equiv of acrylate **S14**), we postulated that the release of a stoichiometric amount of methylamine could be readily trapped by acrylate **S14** to yield aza-Michael adducts **S16** and/or **S17** in Eq. 2.



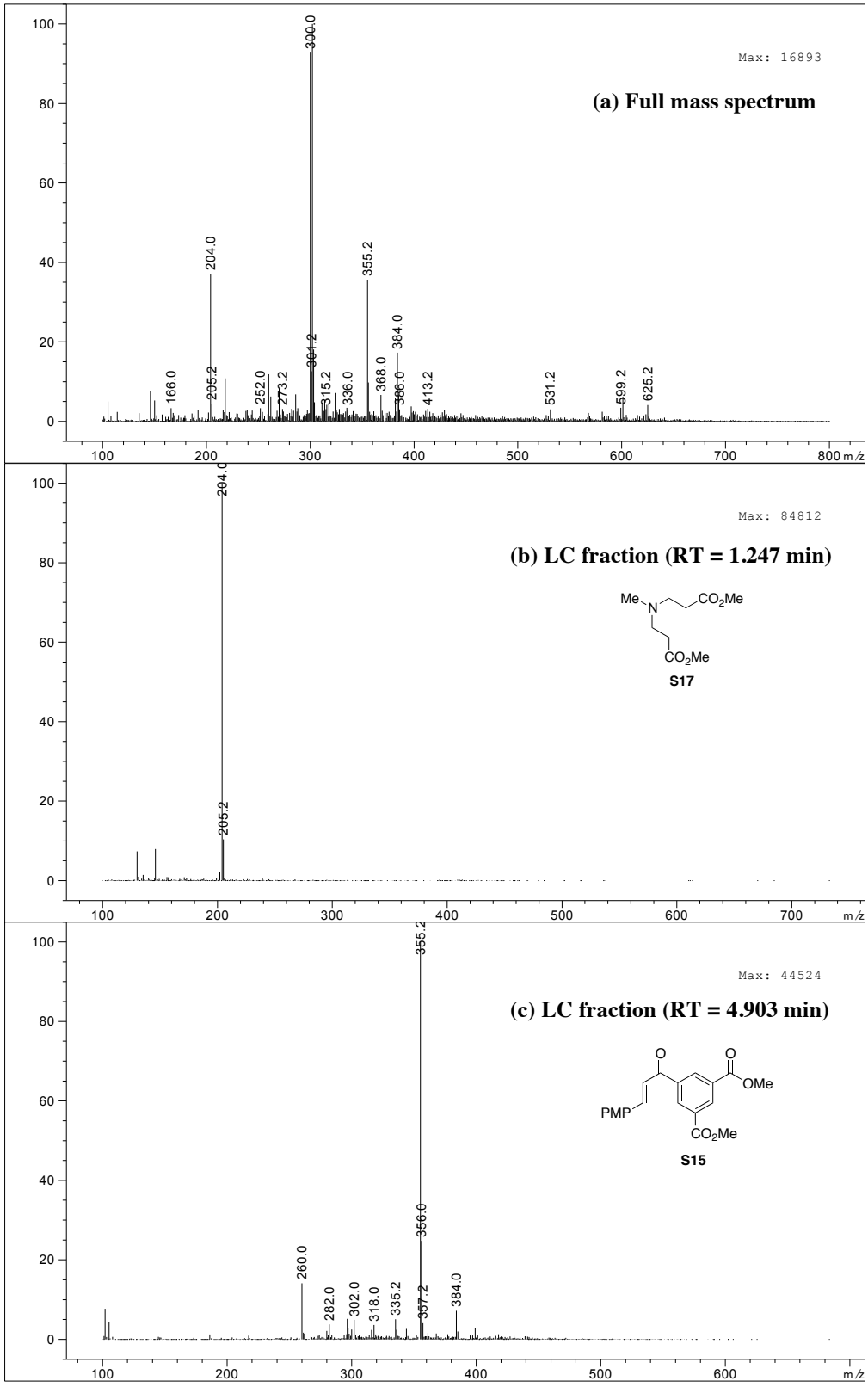
Eq. 2

Hence, an LC-MS analysis was conducted on an Agilent LC-MSD ChemStation (Figure S1). An initial full MS scan of the crude mixture confirmed the product peak at *m/z* 355.2 ([**S15**+H]$^+$, Figure S1-a). In addition, another prominent peak at *m/z* 204.0 ([**S17**+H]$^+$) was also detected corresponding to the aza-Michael adduct **S17** (Figure S1-a). No peak from the possible adduct **S16** was observed. To our delight, the LC-MS separation reconfirmed the two distinct peaks from **S17** (Figure S1-b, RT = 1.247 min) and **S15** (Figure S1-c, RT = 4.903 min) respectively, which provides strong evidence for our proposed mechanism. In fact, the fast scavenging of byproduct methylamine may be one driving force for the tandem reaction to proceed smoothly.

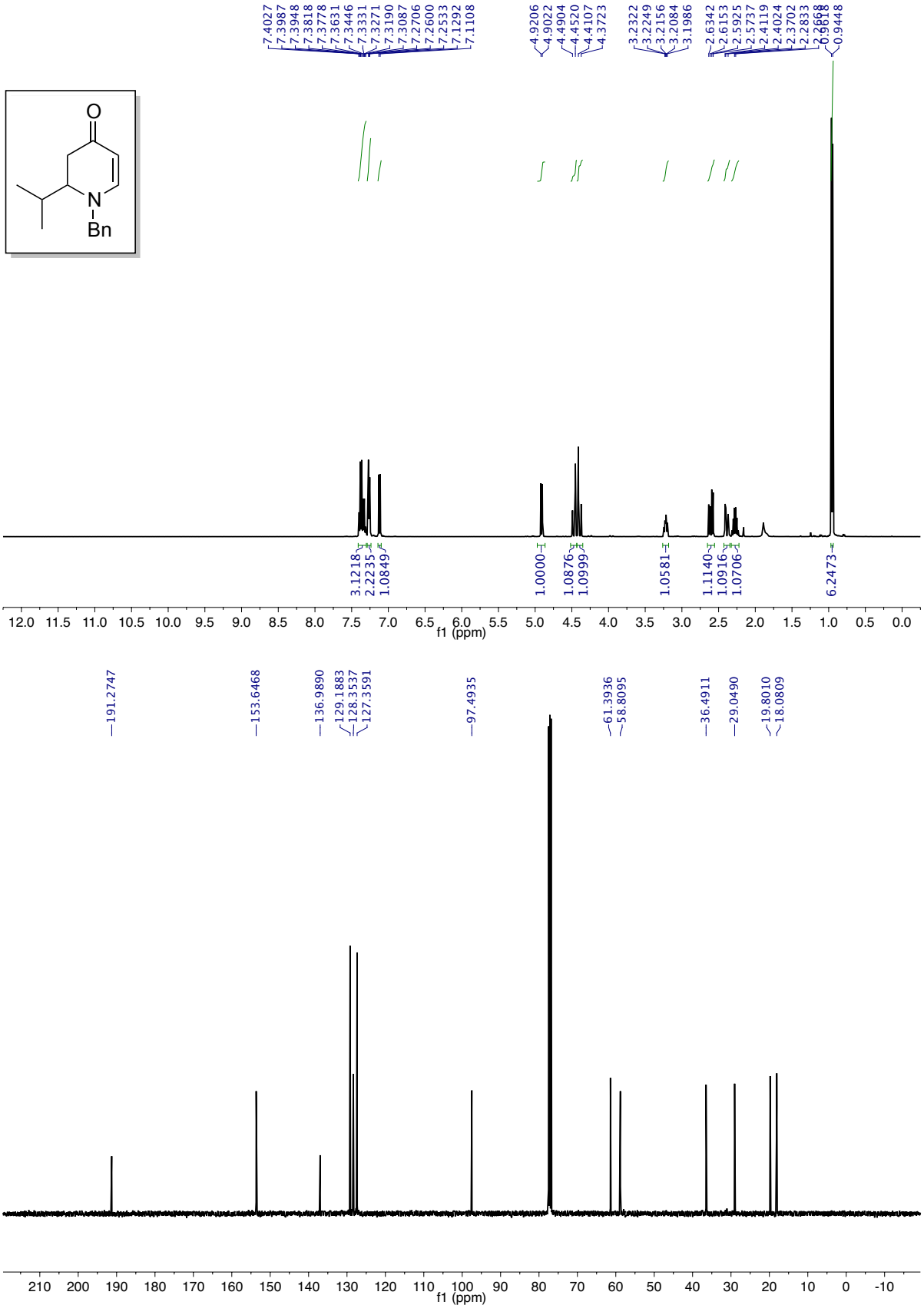
5. References

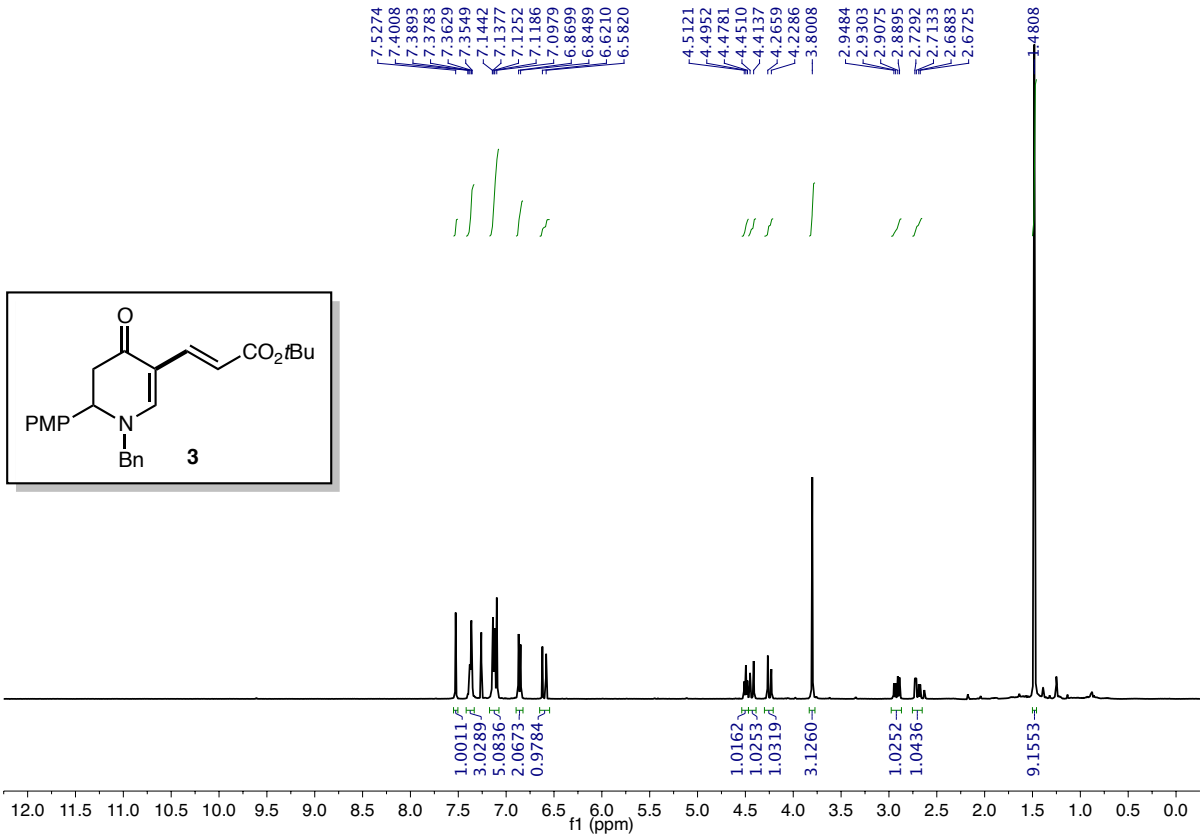
[1] Y.-Y. Yu, M. J. Niphakis, G. I. Georg, *Org. Lett.* **2011**, *13*, 5932-5935.
[2] M. J. Niphakis, B. J. Turunen, G. I. Georg, *J. Org. Chem.* **2010**, *75*, 6793-6805.
[3] P. Guerry, R. Neier, *Synthesis* **1984**, *1984*, 485-488.
[4] B. J. Turunen, G. I. Georg, *J. Am. Chem. Soc.* **2006**, *128*, 8702-8703.
[5] R. Sebesta, M. G. Pizzuti, A. J. Boersma, A. J. Minnaard, B. L. Feringa, *Chem. Commun.* **2005**, 1711-1713.
[6] C. J. Kowalski, K. W. Fields, *J. Org. Chem.* **1981**, *46*, 197-201.

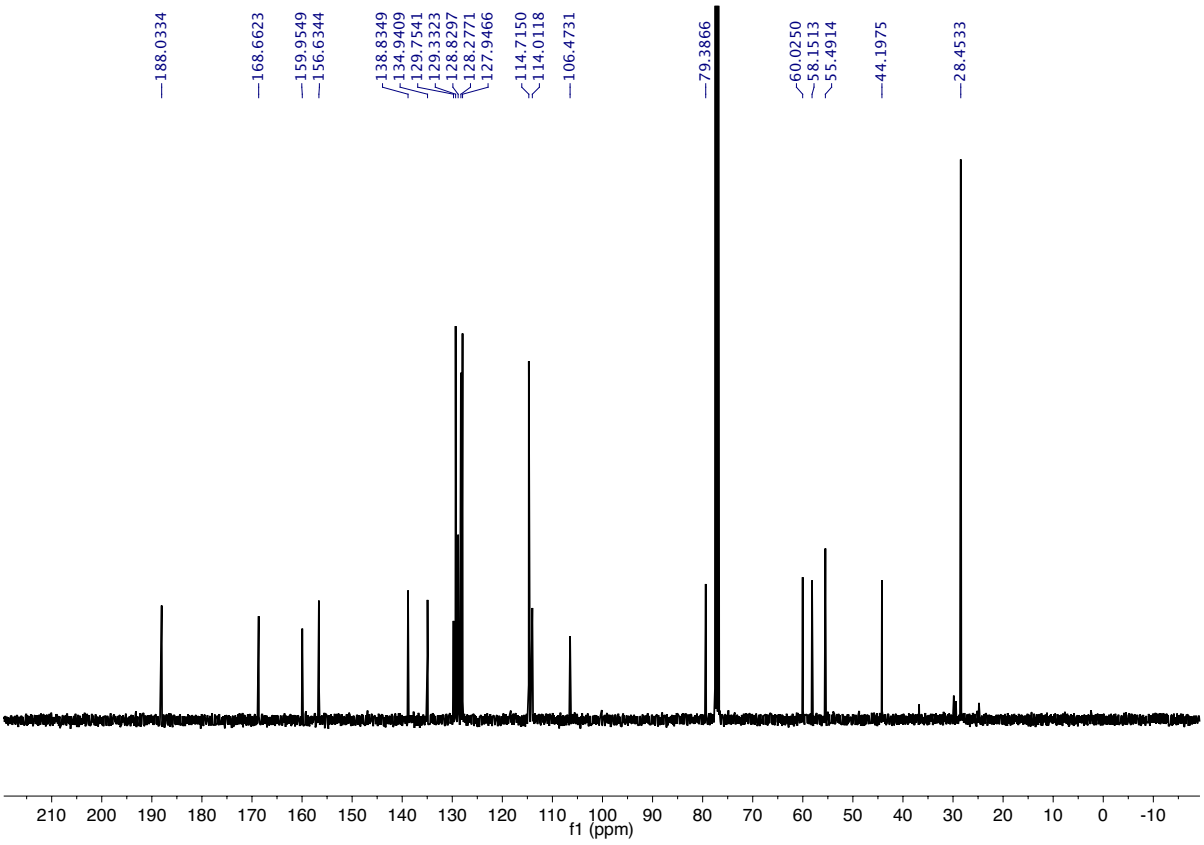
Figure S1. LC-MS analysis of a Diels-Alder tandem reaction between **S11** and **S14**

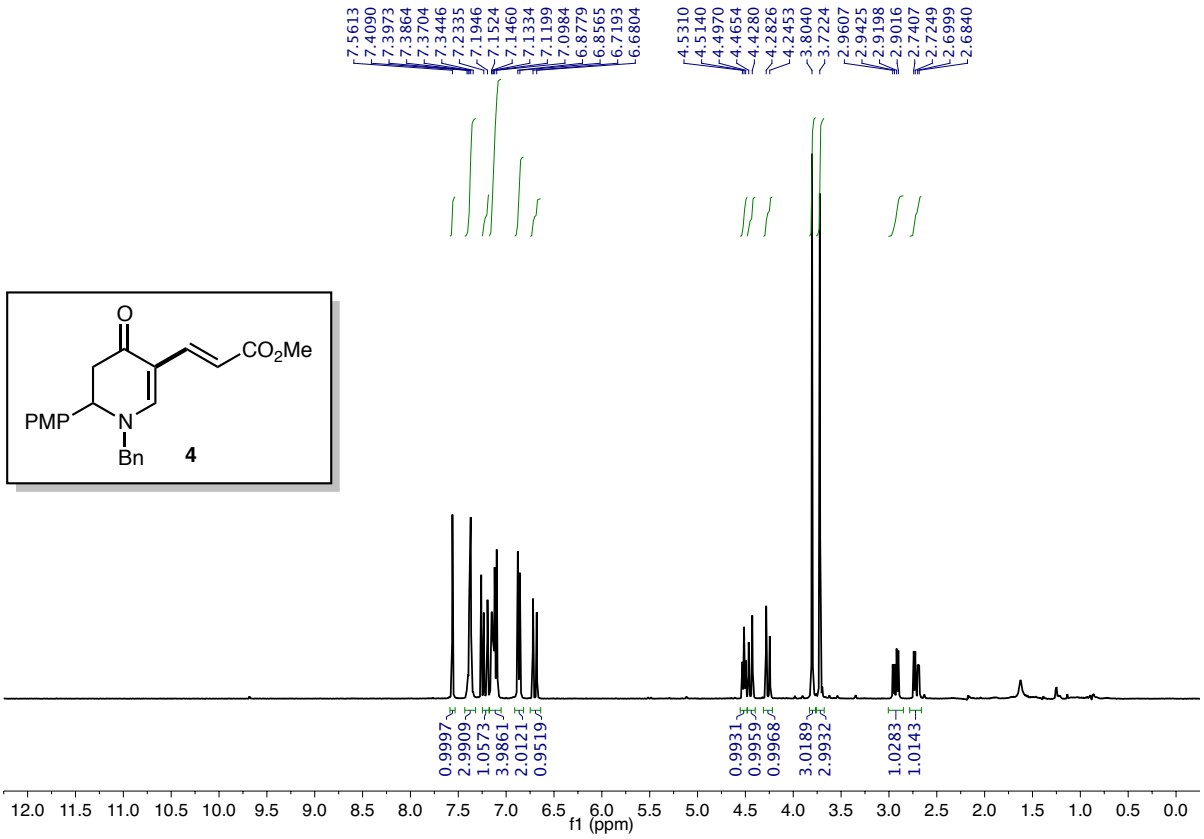


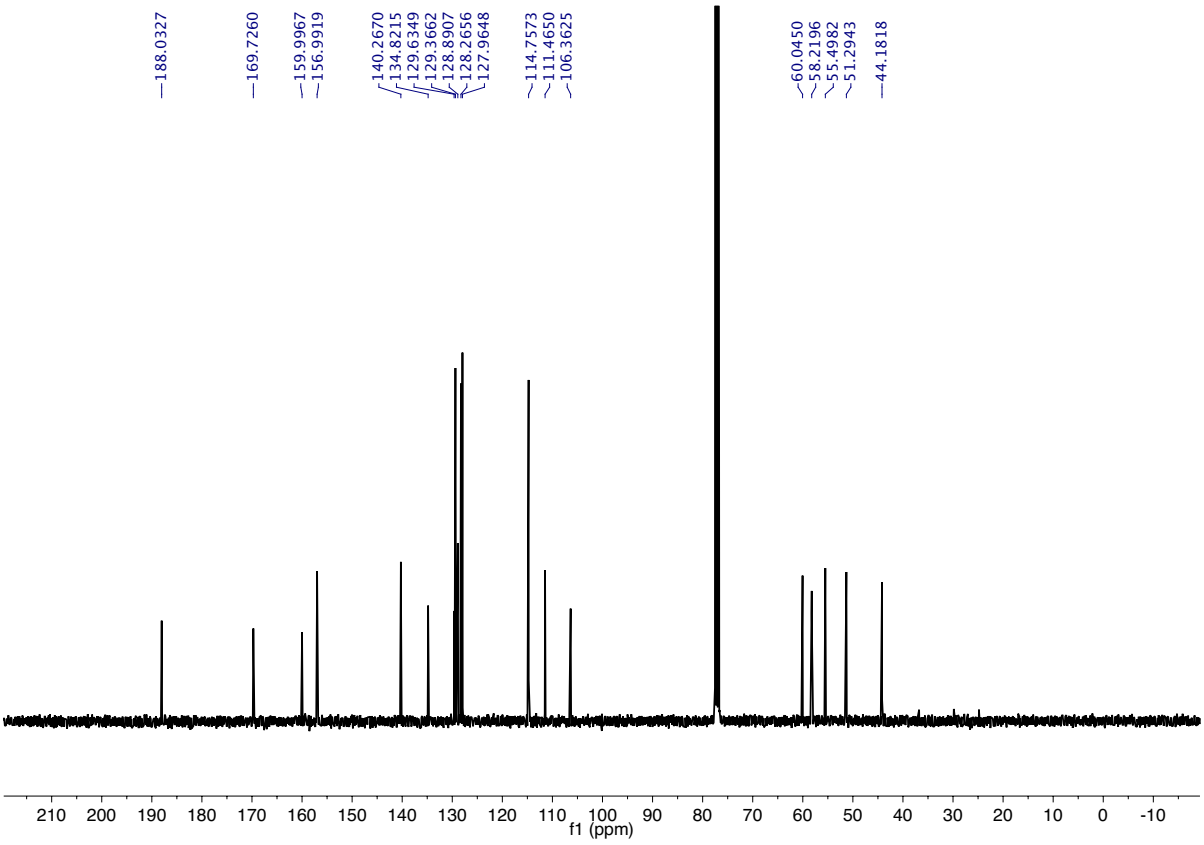
6. ^{1}H NMR and ^{13}C NMR spectra for new compounds

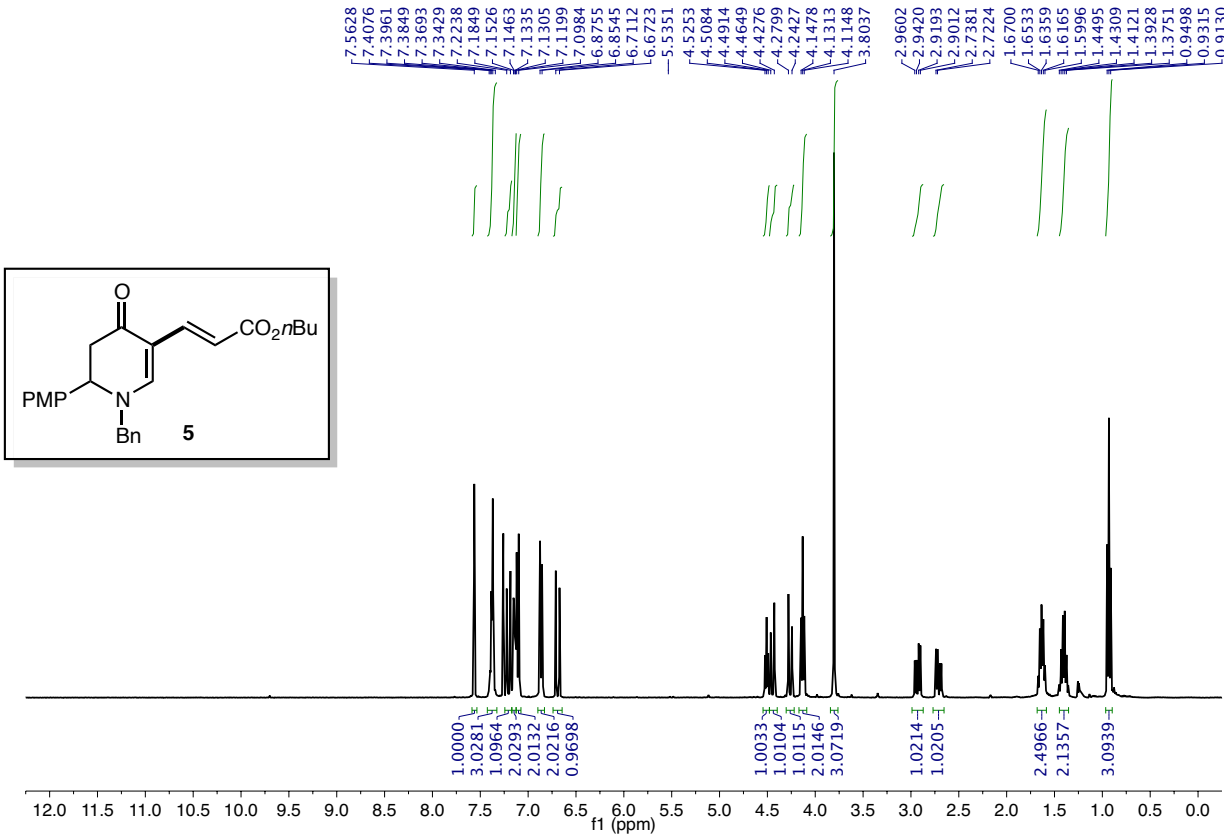


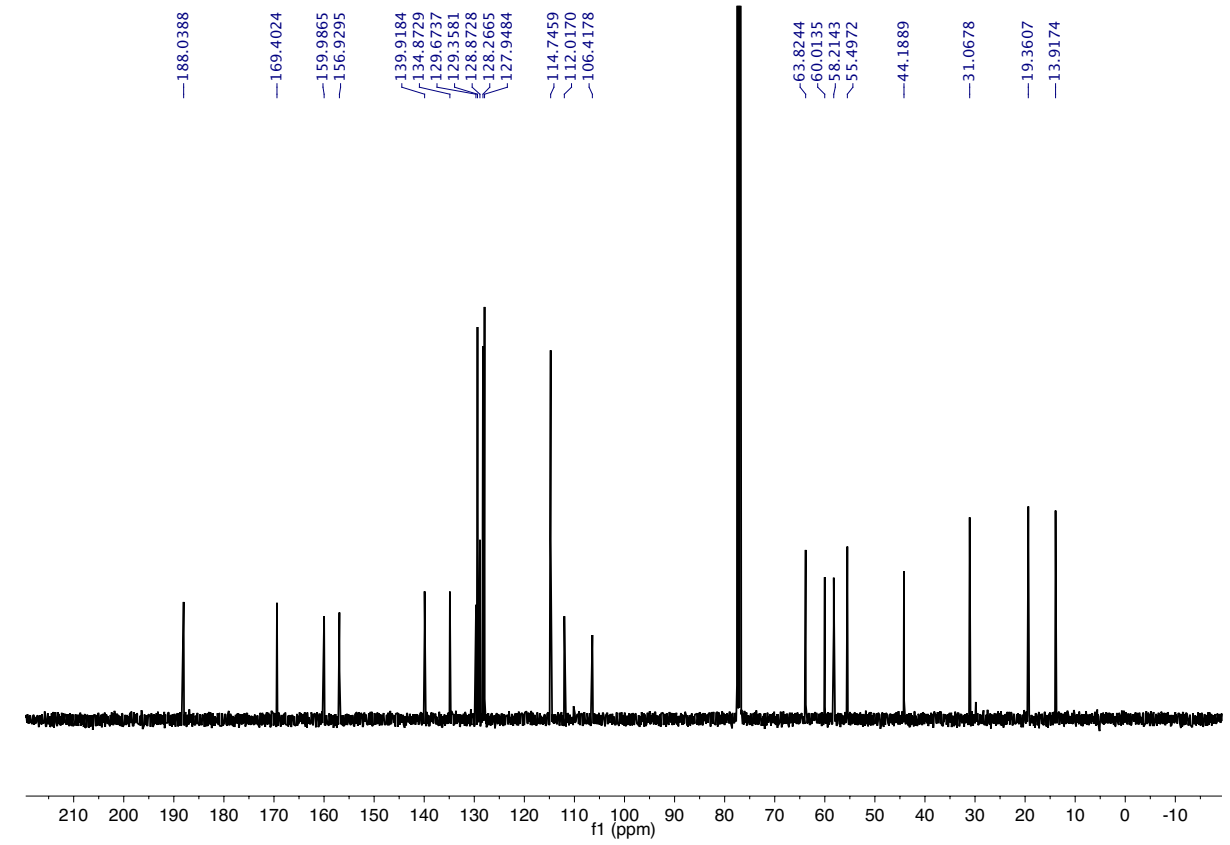

7.5274
7.4008
7.3893
7.3783
7.3629
7.3549
7.1442
7.1377
7.1252
7.1186
7.0979
6.8699
6.8489
6.6210
6.5820
4.5121
4.4952
4.4781
4.4510
4.4137
4.2659
4.2286
3.8008
2.9484
2.9303
2.9075
2.8895
2.7292
2.7133
2.6883
2.6725
1.4808
O
CO2tBu
PMP
N
Bn
3
1.0011
3.0289
5.0836
2.0673
0.9784
1.0162
1.0253
1.0319
3.1260
1.0252
1.0436
9.1553
f1 (ppm)

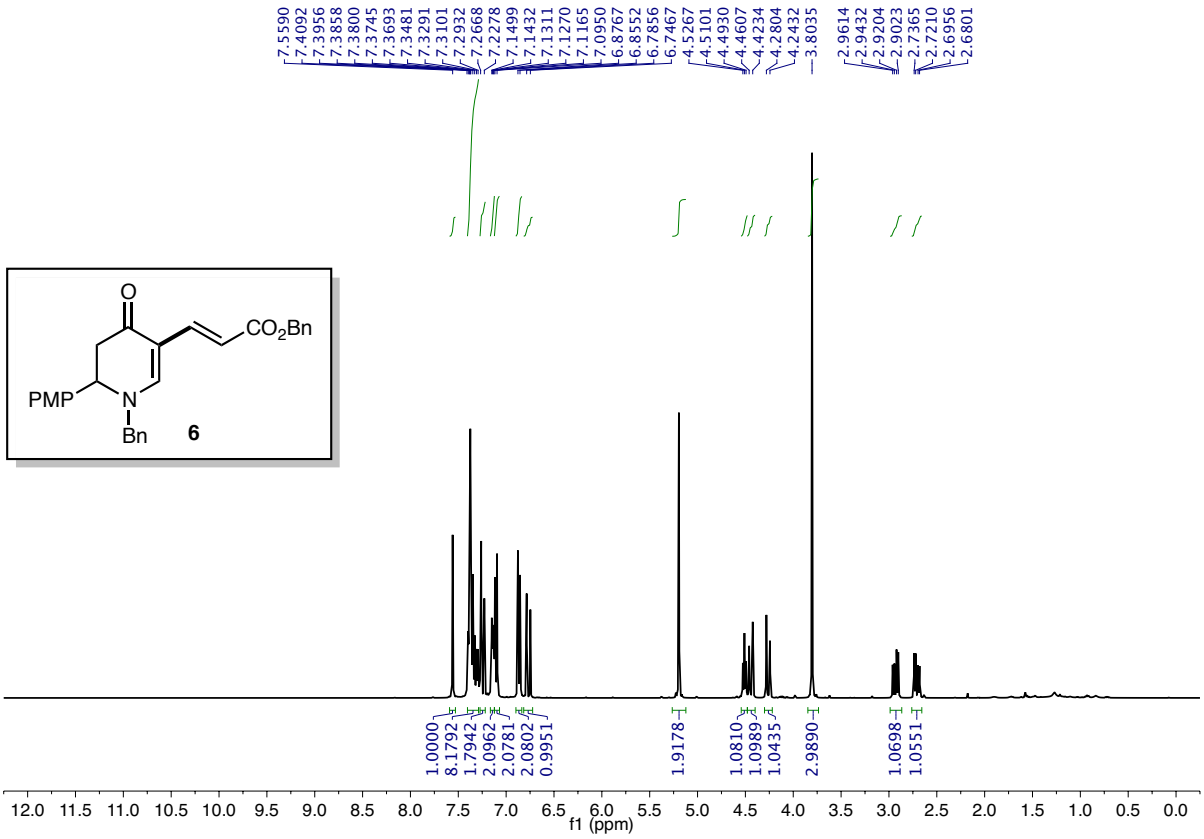

188.0334
168.6623
159.9549
156.6344
138.8349
134.9409
129.7541
129.3323
128.8297
128.2771
127.9466
114.7150
114.0118
106.4731
79.3866
60.0250
58.1513
55.4914
44.1975
28.4533
f1 (ppm)

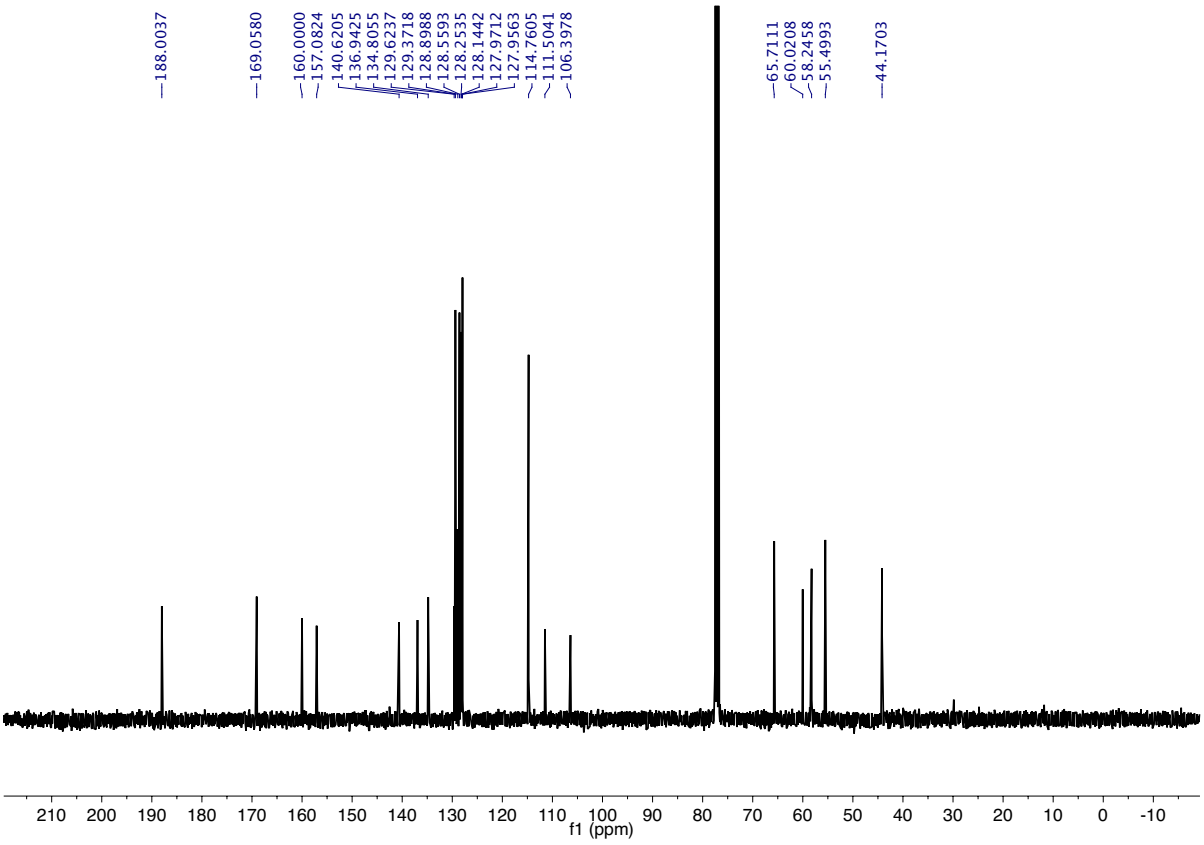

7.5613
7.4090
7.3973
7.3864
7.3704
7.3446
7.2335
7.1946
7.1524
7.1460
7.1334
7.1199
7.0984
6.8779
6.8565
6.7193
6.6804
4.5310
4.5140
4.4970
4.4654
4.4280
4.2826
4.2453
3.8040
3.7224
2.9607
2.9425
2.9198
2.9016
2.7407
2.7249
2.6999
2.6840
O
CO2Me
PMP
N
Bn
4
0.9997
2.9909
1.0573
3.9861
2.0121
0.9519
0.9931
0.9959
0.9968
3.0189
2.9932
1.0283
1.0143
f1 (ppm)

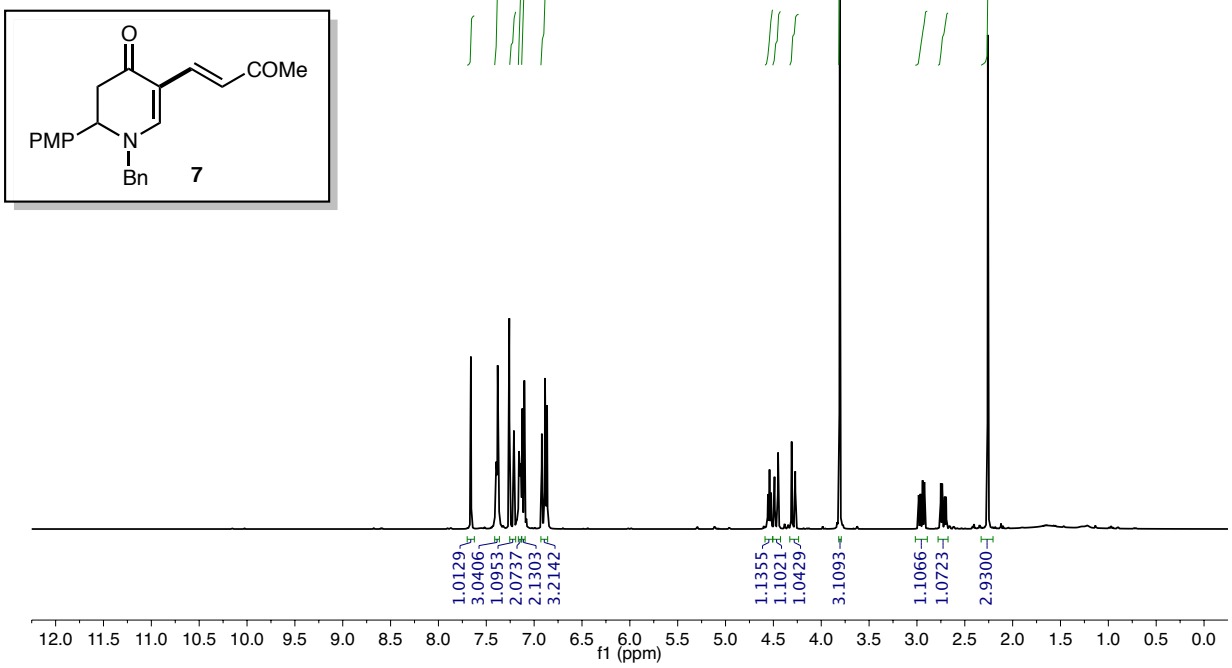

188.0327
169.7260
159.9967
156.9919
140.2670
134.8215
129.6349
129.3662
128.8907
128.2656
127.9648
114.7573
111.4650
106.3625
60.0450
58.2196
55.4982
51.2943
44.1818
f1 (ppm)

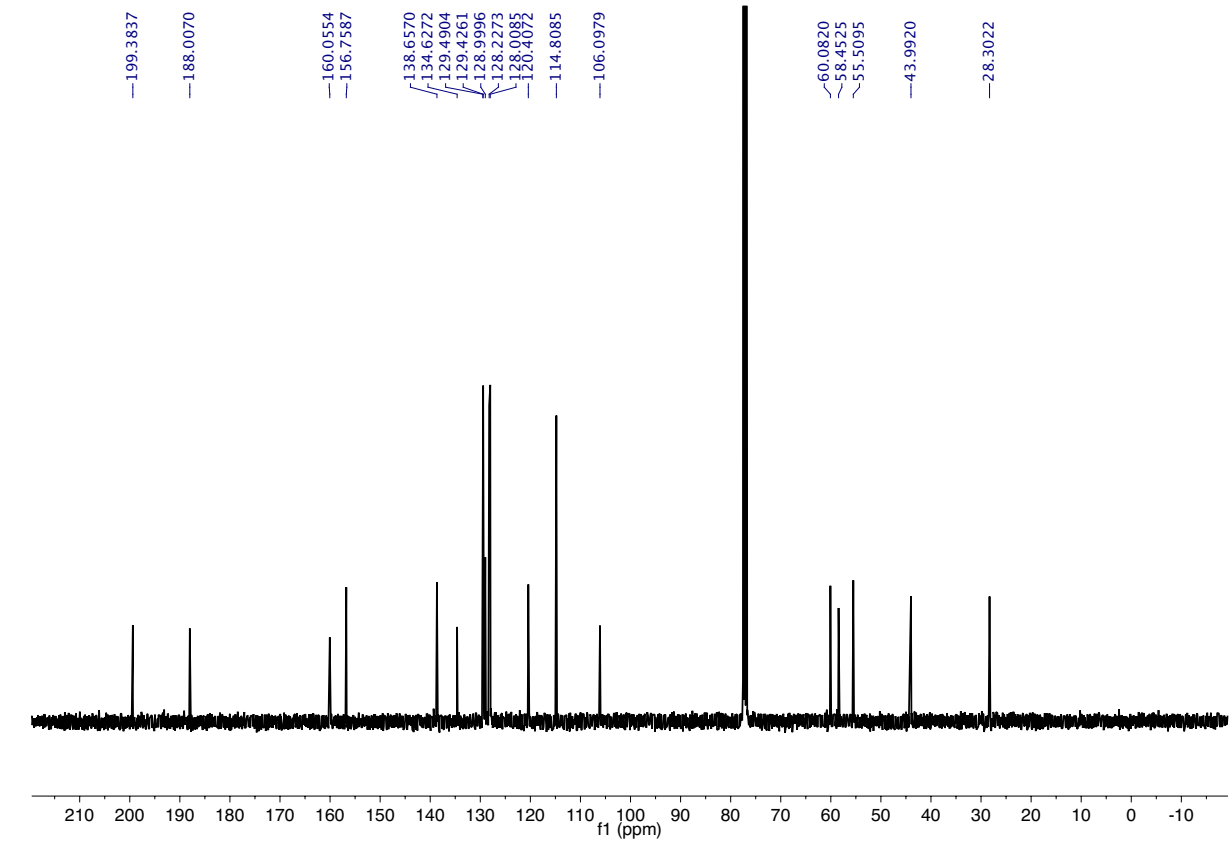

O
CO2nBu
PMP
N
Bn
5
f1 (ppm)

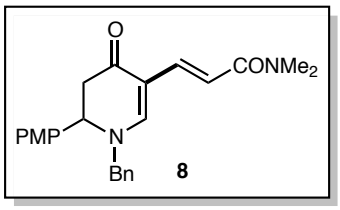

f1 (ppm)


7.5590
7.4092
7.3956
7.3858
7.3800
7.3745
7.3693
7.3481
7.3291
7.3101
7.2932
7.2668
7.2278
7.1499
7.1432
7.1311
7.1270
7.1165
7.0950
6.8767
6.8552
6.7856
6.7467
4.5267
4.5101
4.4930
4.4607
4.4234
4.2804
4.2432
3.8035
2.9614
2.9432
2.9204
2.9023
2.7365
2.7210
2.6956
2.6801
O
CO2Bn
PMP
N
Bn
6
1.0000
8.1792
1.7942
2.0962
2.0781
2.0802
0.9951
1.9178
1.0810
1.0989
1.0435
2.9890
1.0698
1.0551
f1 (ppm)

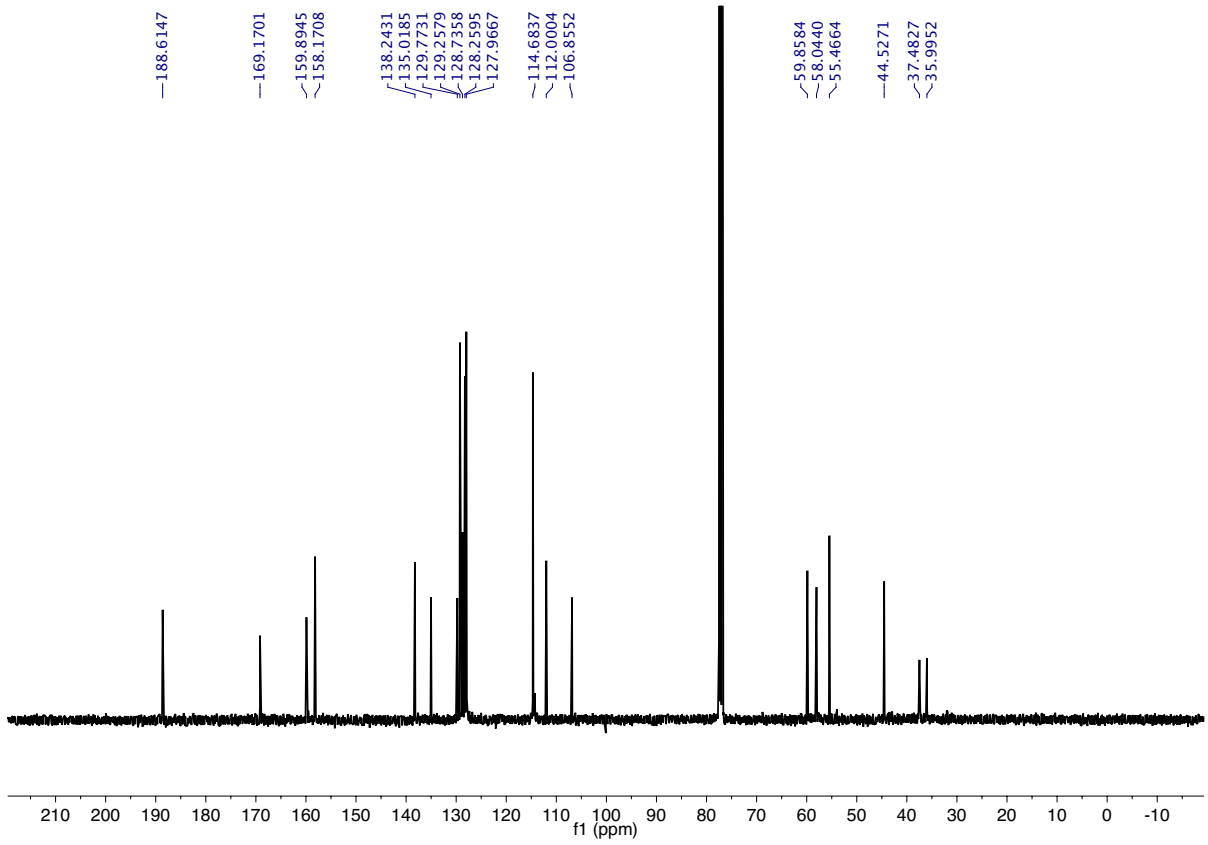

188.0037
169.0580
160.0000
157.0824
140.6205
136.9425
134.8055
129.6237
129.3718
128.8988
128.5593
128.2535
128.1442
127.9712
127.9563
114.7605
111.5041
106.3978
65.7111
60.0208
58.2458
55.4993
44.1703
f1 (ppm)

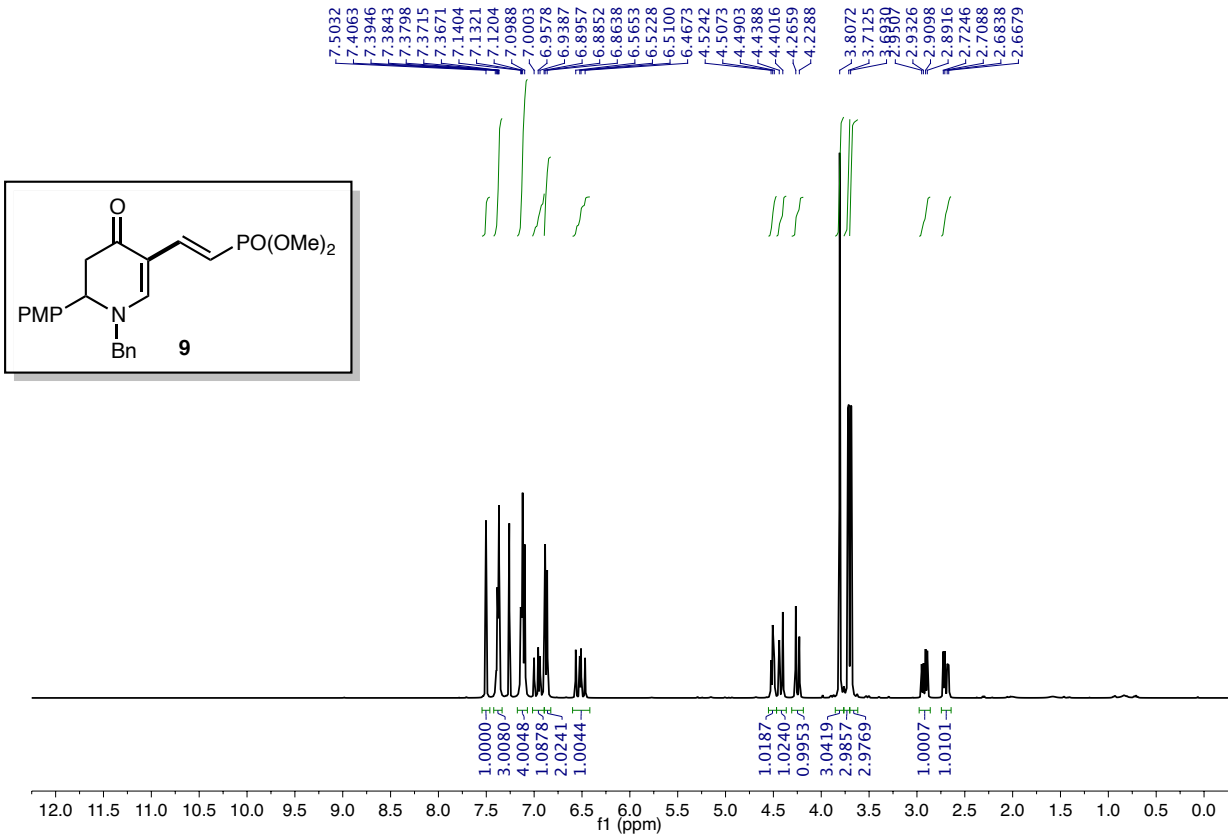

7.6611
7.4043
7.3937
7.3897
7.3810
7.3768
7.2510
7.2116
7.1587
7.1519
7.1397
7.1364
7.1239
7.1024
7.0806
6.9195
6.8859
6.8804
6.8645
4.5570
4.5404
4.5237
4.4882
4.4509
4.3091
4.2718
3.8070
2.9817
2.9633
2.9407
2.9224
2.7509
2.7359
2.2995
1.0129
3.0406
1.0953
2.0737
2.1303
3.2142
1.1355
1.1021
1.0429
3.1093
1.1066
1.0723
2.9300
f1 (ppm)

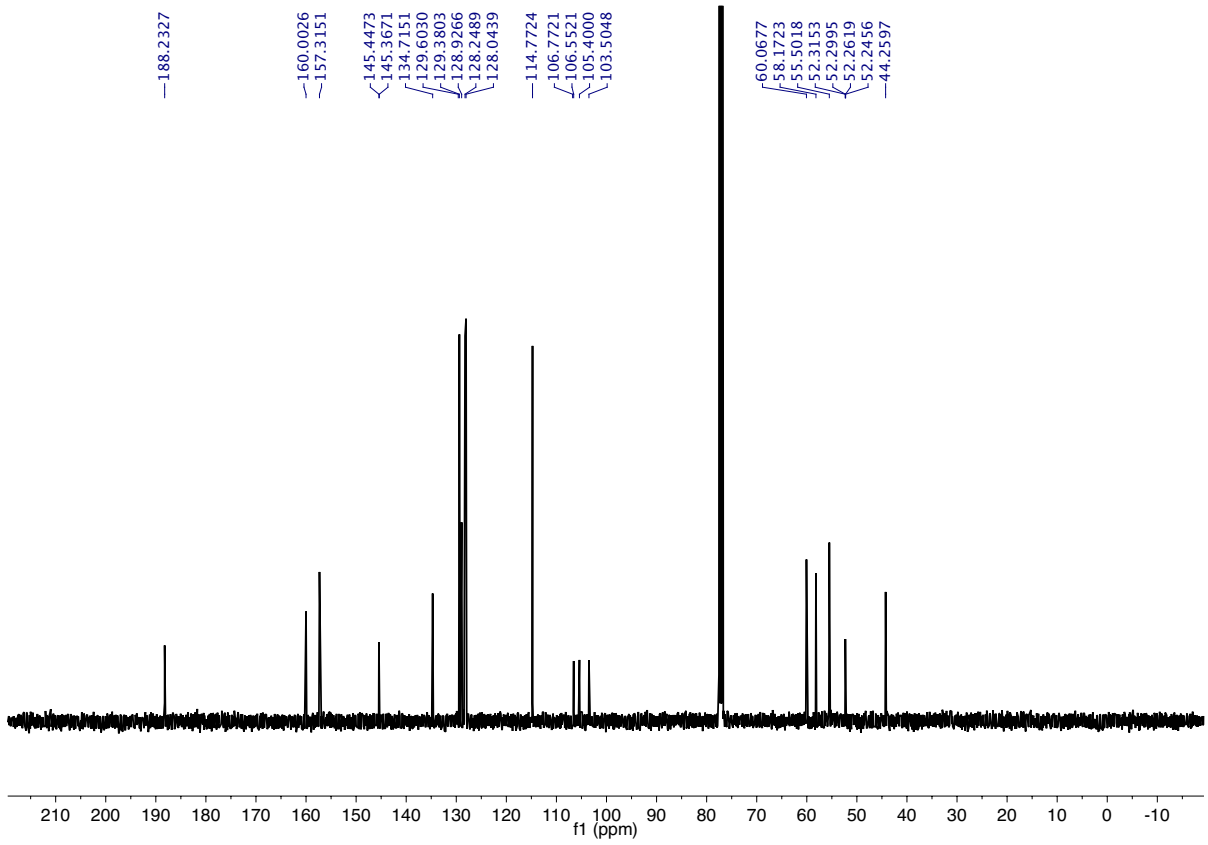

199.3837
188.0070
160.0554
156.7587
138.6570
134.6272
129.4904
129.4261
128.9996
128.2273
120.4072
114.8085
106.0979
60.0820
58.4525
55.5095
43.9920
28.3022
f1 (ppm)

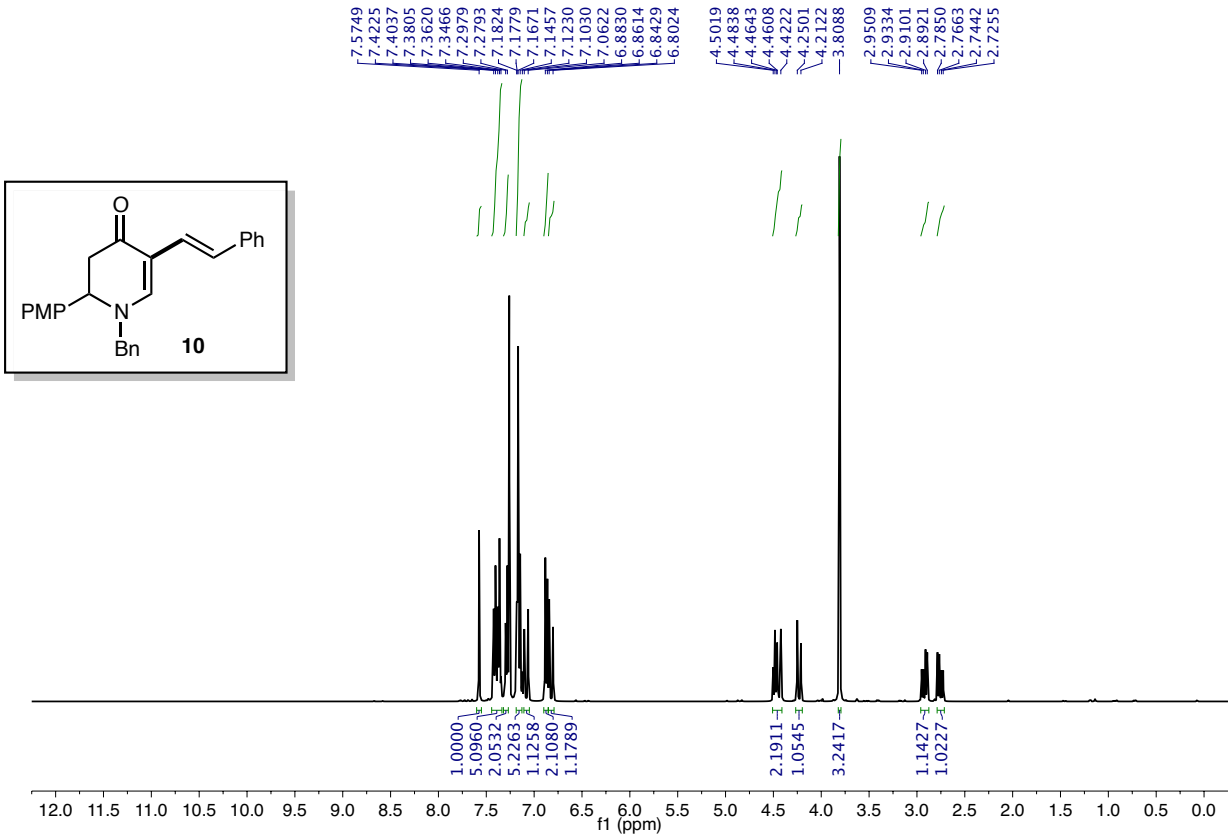

O
CONMe2
PMP
N
Bn
8

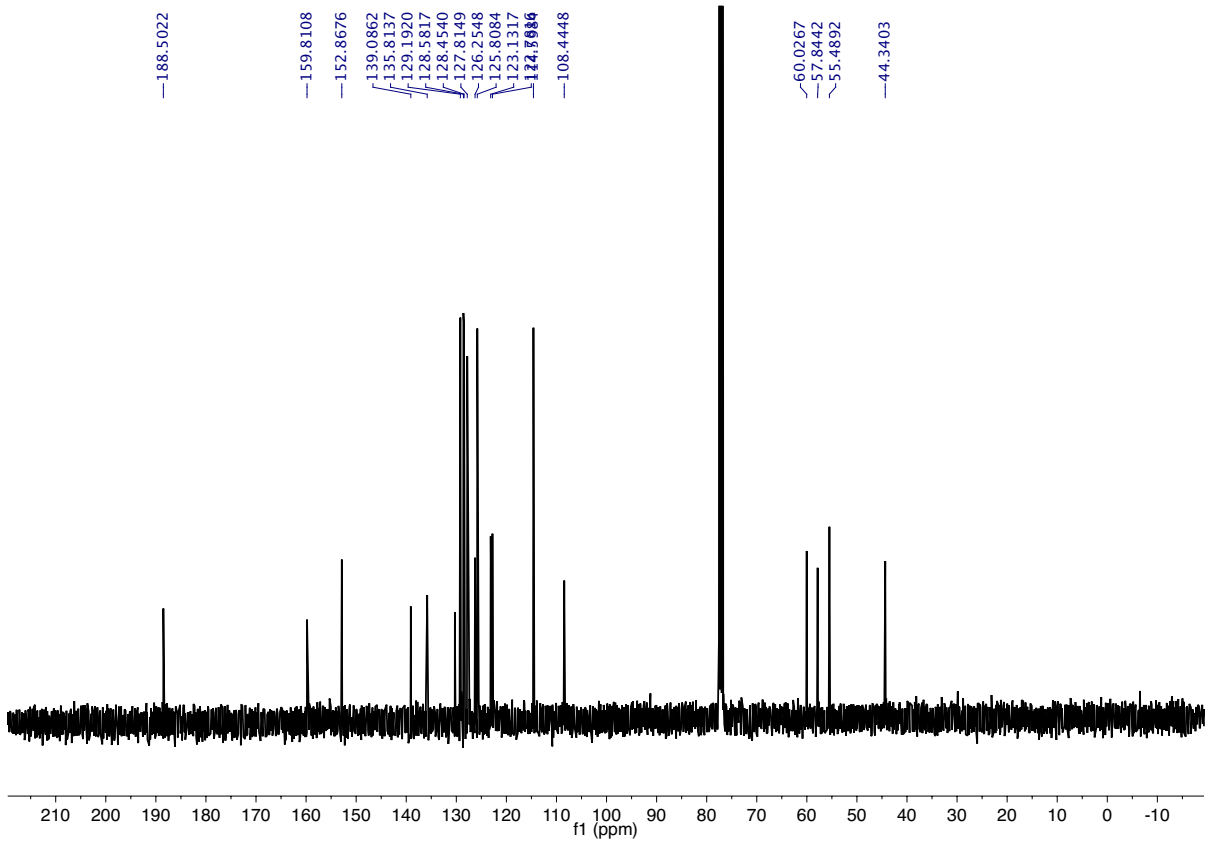
7.5507
7.4179
7.3807
7.3634
7.3581
7.3501
7.3461
7.3391
7.3217
7.1393
7.1336
7.1199
7.1116
7.0986
7.0733
6.8686
6.8470
4.4985
4.4815
4.4653
4.4289
4.2410
4.2037
3.7954
3.1003
3.0123
2.9507
2.9326
2.9098
2.8917
2.7240
2.7075
2.6834
2.6669
0.9600
1.1469
2.9240
5.1503
1.9989
1.9482
1.0177
3.2278
3.0077
3.0100
1.2065
1.0529
f1 (ppm)

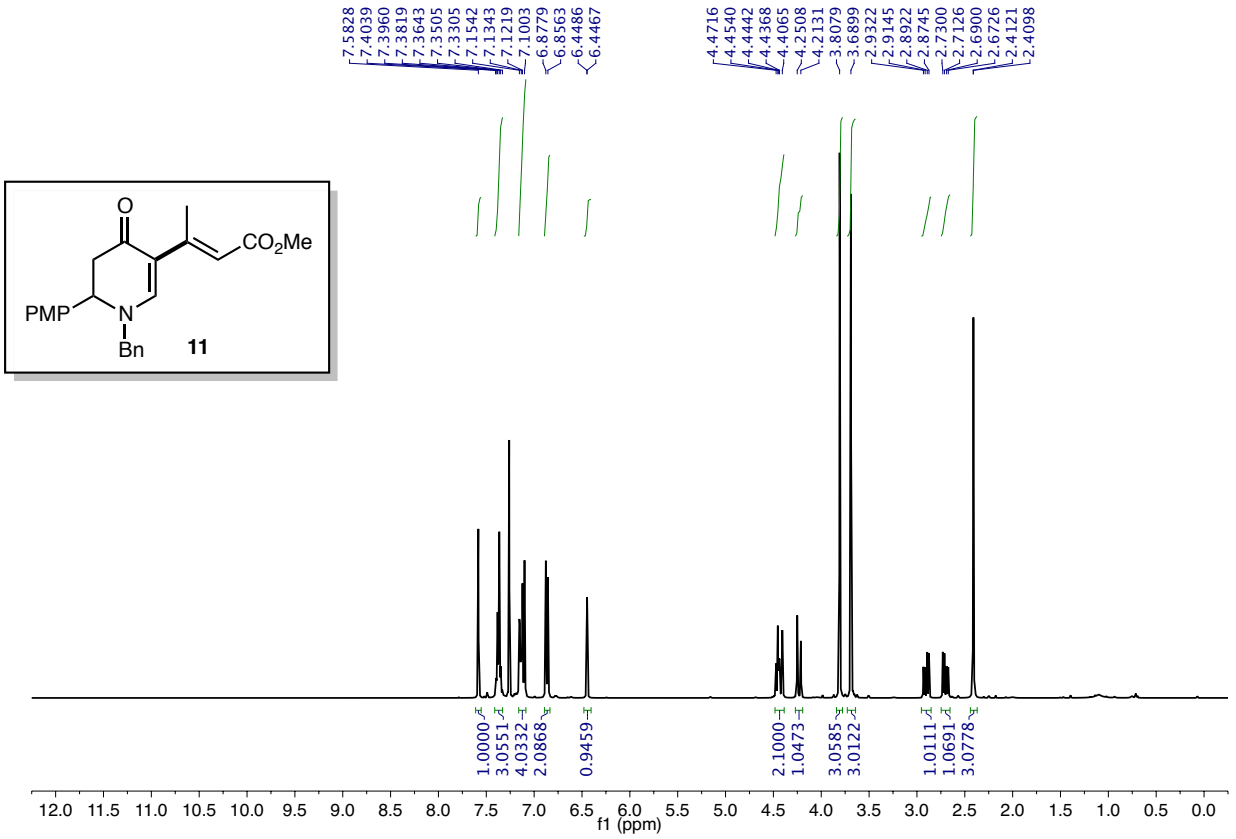

188.6147
169.1701
159.8945
158.1708
138.2431
135.0185
129.7731
129.2579
128.7358
128.2595
127.9667
114.6837
112.0004
106.8552
59.8584
58.0440
55.4664
44.5271
37.4827
35.9952
f1 (ppm)

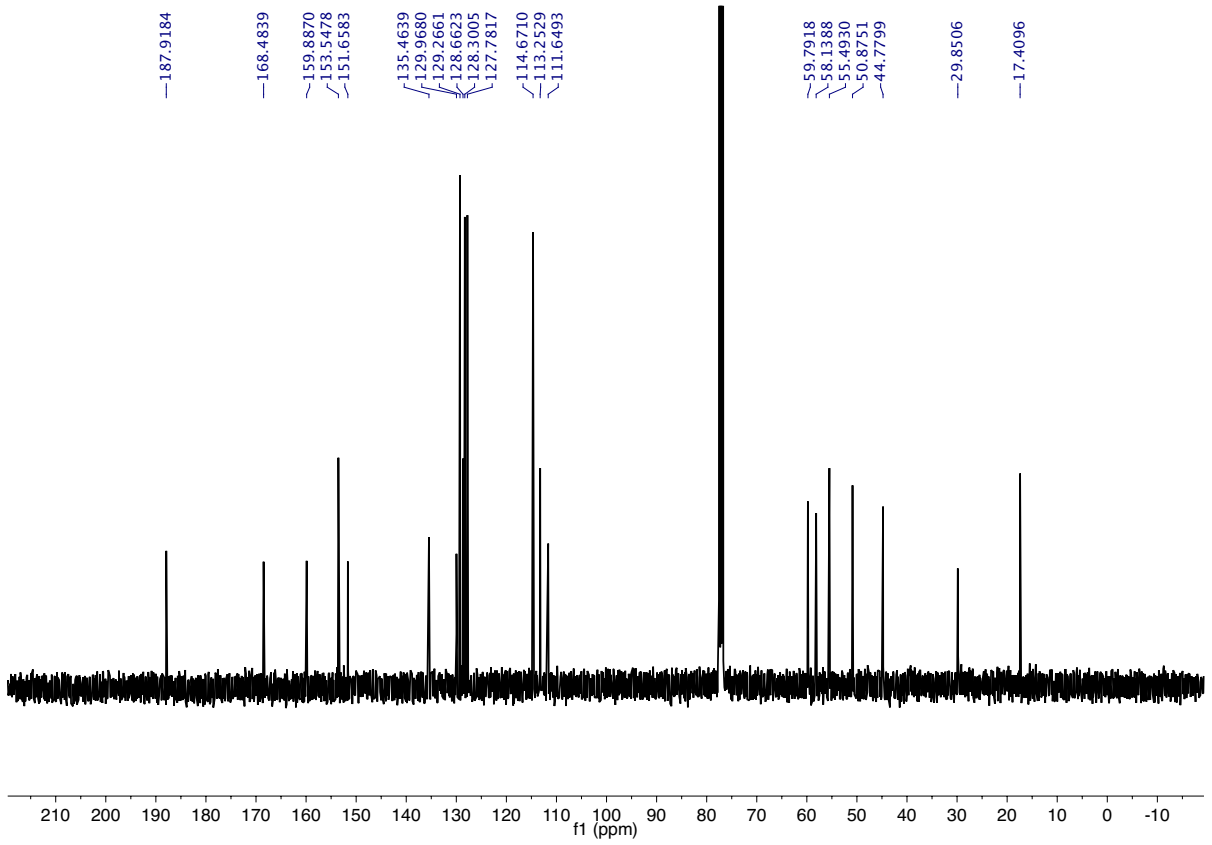

7.5032
7.4063
7.3946
7.3843
7.3798
7.3715
7.3671
7.1404
7.1321
7.1204
7.0988
7.0003
6.9578
6.9387
6.8957
6.8852
6.8638
6.5653
6.5228
6.5100
6.4673
4.5242
4.5073
4.4903
4.4388
4.4016
4.2659
4.2288
3.8072
3.7125
3.6930
3.6907
2.9326
2.9098
2.8916
2.7246
2.7088
2.6838
2.6679
O
PO(OMe)2
PMP
N
Bn
9
1.0000
3.0080
4.0048
1.0878
2.0241
1.0044
1.0187
1.0240
0.9953
3.0419
2.9857
2.9769
1.0007
1.0101
f1 (ppm)

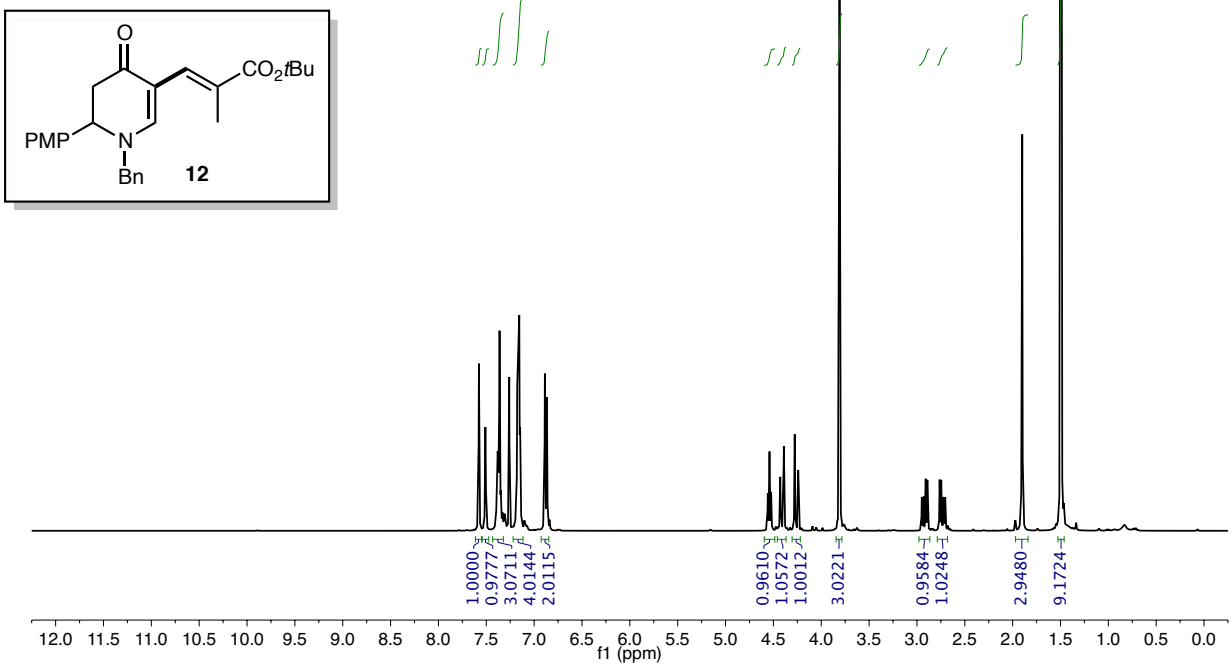

188.2327
160.0026
157.3151
145.4473
145.3671
134.7151
129.6030
129.3803
128.9266
128.2489
128.0439
114.7724
106.7721
106.5521
105.4000
103.5048
60.0677
58.1723
55.5018
52.3153
52.2995
52.2619
52.2456
44.2597
f1 (ppm)

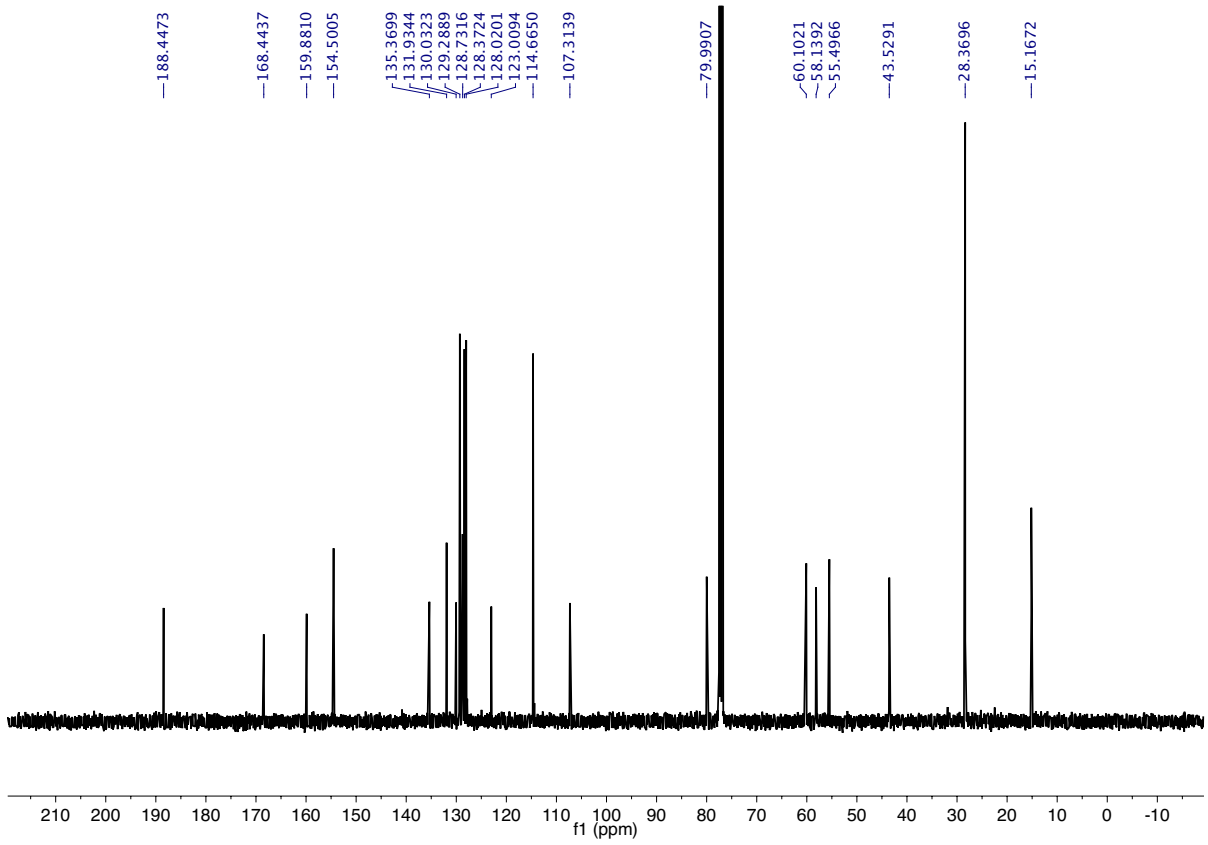

O
Ph
PMP
N
Bn
10
7.5749
7.4225
7.4037
7.3805
7.3620
7.3466
7.2979
7.2793
7.1824
7.1779
7.1671
7.1457
7.1230
7.1030
7.0622
6.8830
6.8614
6.8429
6.8024
4.5019
4.4838
4.4643
4.4608
4.4222
4.2501
4.2122
3.8088
2.9509
2.9334
2.9101
2.8921
2.7850
2.7663
2.7442
2.7255
1.0000
5.0960
2.0532
5.2263
1.1258
2.1080
1.1789
2.1911
1.0545
3.2417
1.1427
1.0227
f1 (ppm)

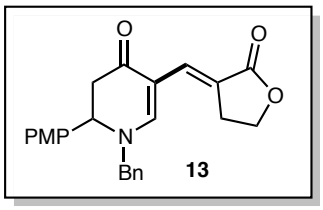

188.5022
159.8108
152.8676
139.0862
135.8137
129.1920
128.5817
128.4540
127.8149
126.2548
125.8084
123.1317
108.4448
60.0267
57.8442
55.4892
44.3403
f1 (ppm)


7.5828
7.4039
7.3960
7.3819
7.3643
7.3505
7.3305
7.1542
7.1343
7.1219
7.1003
6.8779
6.8563
6.4486
6.4467
4.4716
4.4540
4.4442
4.4368
4.4065
4.2508
4.2131
3.8079
3.6899
2.9322
2.9145
2.8922
2.8745
2.7300
2.7126
2.6900
2.6726
2.4121
2.4098
O
CO2Me
PMP
N
Bn
11
1.0000
3.0551
4.0332
2.0868
0.9459
2.1000
1.0473
3.0585
3.0122
1.0111
1.0691
3.0778
f1 (ppm)

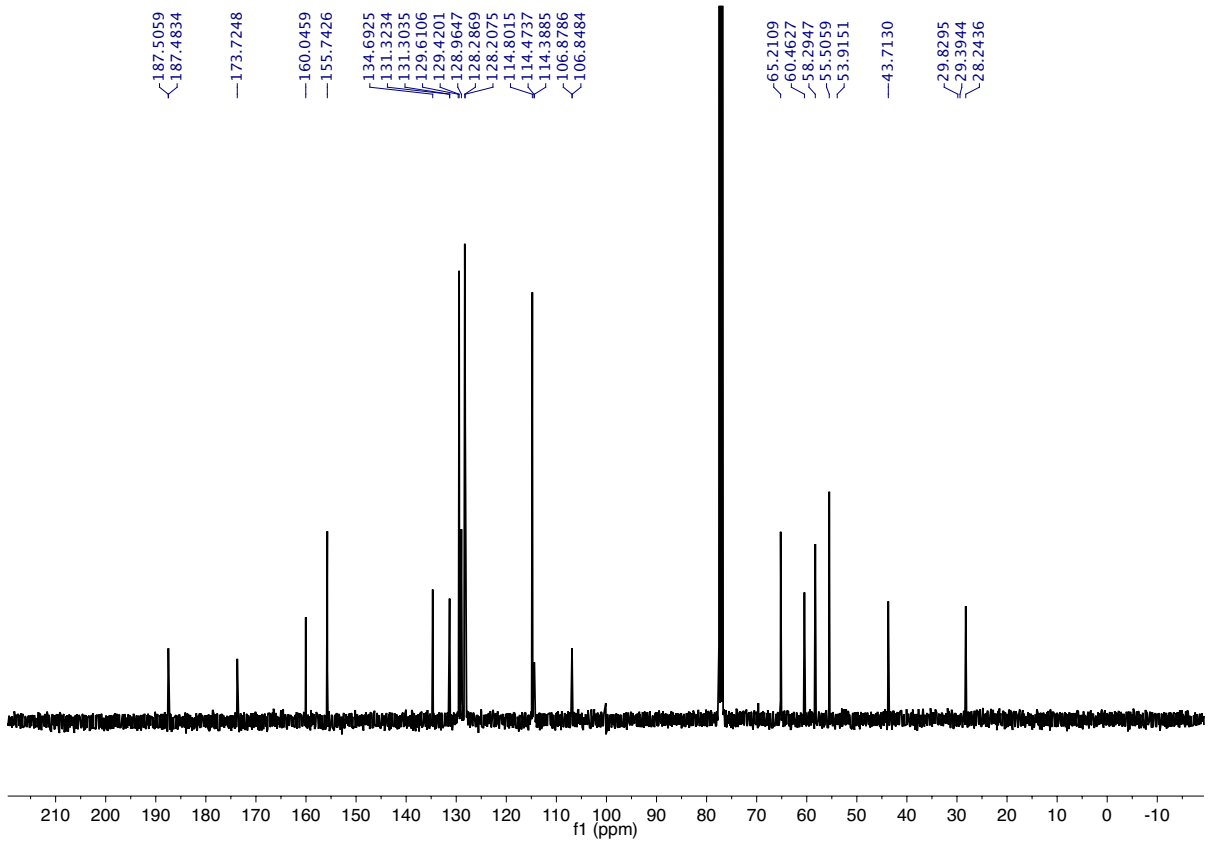

187.9184
168.4839
159.8870
153.5478
151.6583
135.4639
129.9680
129.2661
128.6623
128.3005
127.7817
114.6710
113.2529
111.6493
59.7918
58.1388
55.4930
50.8751
44.7799
29.8506
17.4096
f1 (ppm)

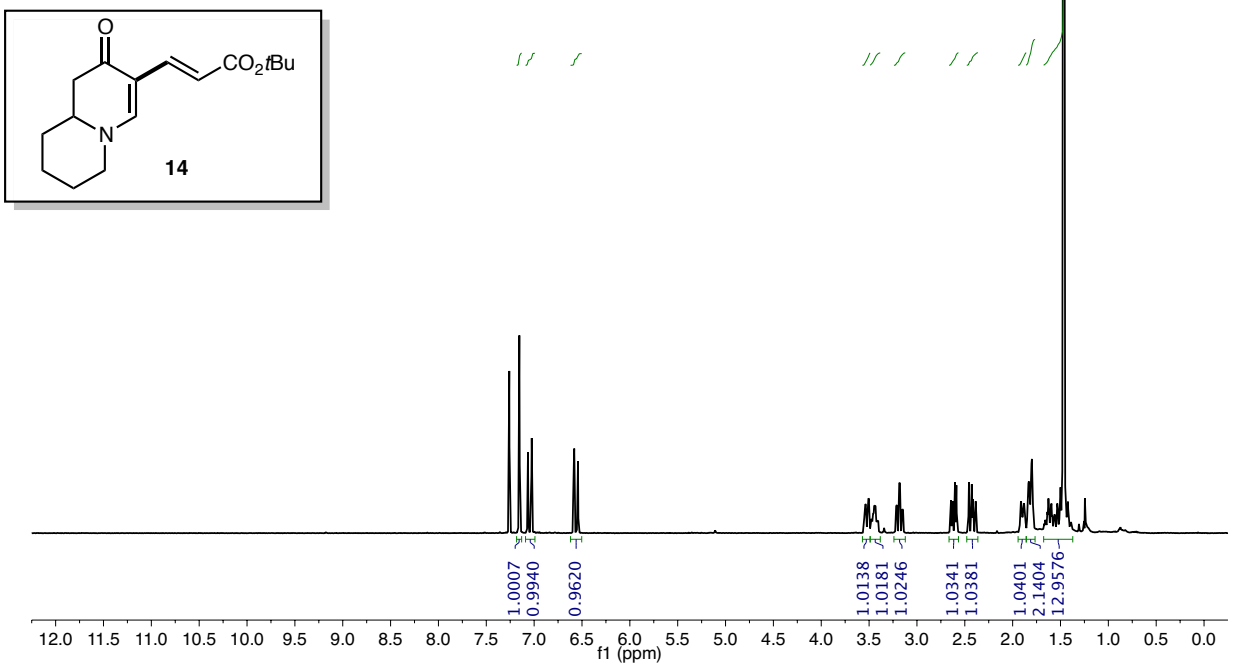

O
CO2tBu
PMP
N
Bn
12
7.5775
7.5094
7.5072
7.3995
7.3914
7.3784
7.3613
7.3487
7.3312
7.1766
7.1591
7.1552
7.1461
6.8879
6.8664
4.5581
4.5407
4.5234
4.4280
4.3907
4.2773
4.2402
3.8095
2.9494
2.9317
2.9084
2.8907
2.7630
2.7458
2.7218
2.7046
1.9025
1.8995
1.4957
1.0000
0.9777
3.0711
4.0144
2.0115
0.9610
1.0572
1.0012
3.0221
0.9584
1.0248
2.9480
9.1724
f1 (ppm)

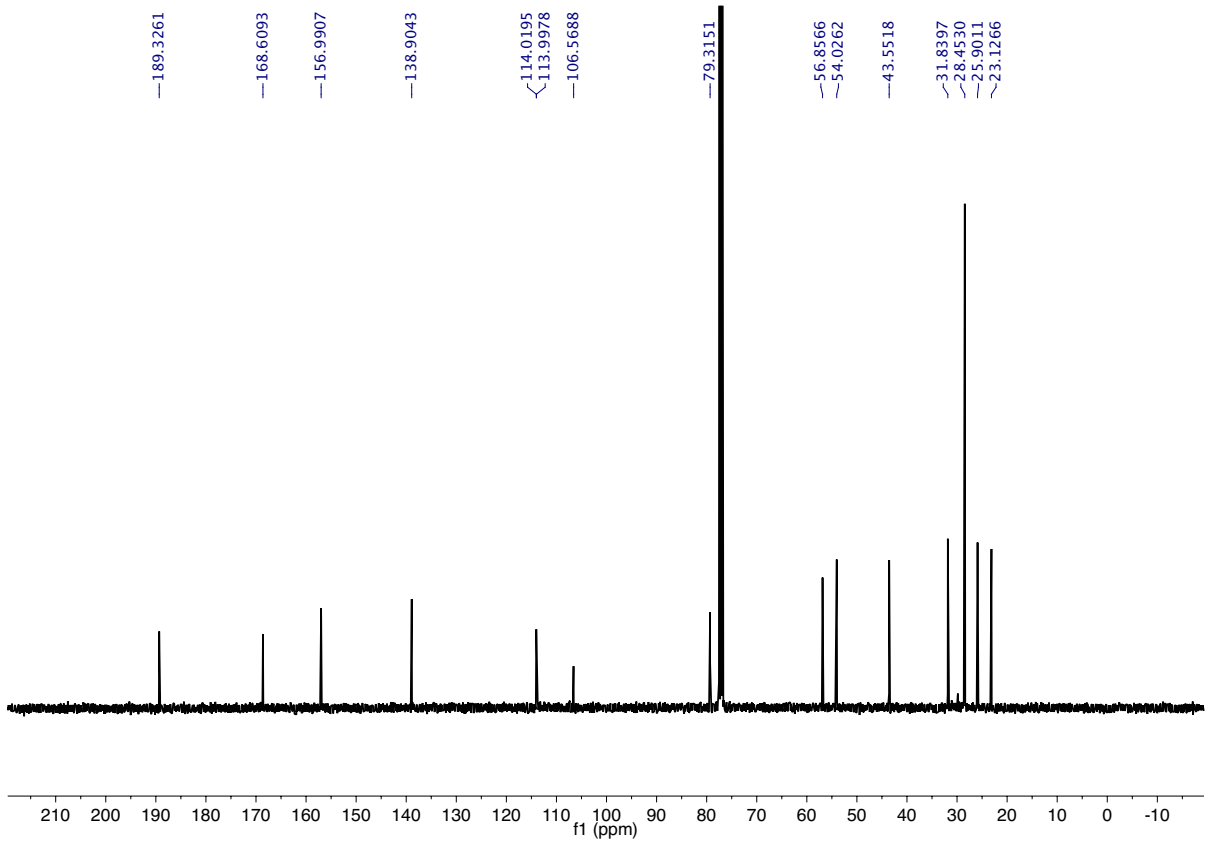

188.4473
168.4437
159.8810
154.5005
135.3699
131.9344
130.0323
129.2889
128.7316
128.3724
128.0201
123.0094
114.6650
107.3139
79.9907
60.1021
58.1392
55.4966
43.5291
28.3696
15.1672
f1 (ppm)

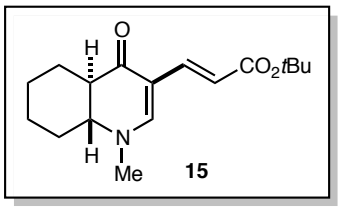

O
O
O
PMP
N
Bn
13

7.6254
7.4207
7.4148
7.4116
7.3994
7.3824
7.3519
7.3483
7.1750
7.1695
7.1531
7.1309
6.8968
6.8752
4.5995
4.5823
4.5653
4.4690
4.4322
4.3143
4.3011
4.2980
4.2773
3.8094
2.9885
2.9687
2.9460
2.9287
2.9051
2.8814
2.8631
2.7640
2.7477
2.7232
2.7070
1.0000
4.1192
4.1723
2.1840
1.0758
1.1446
3.0522
3.2792
3.1672
1.0875
f1 (ppm)


187.5059
187.4834
173.7248
160.0459
155.7426
134.6925
131.3234
131.3035
129.6106
129.4201
128.9647
128.2869
128.2075
114.8015
114.4737
114.3885
106.8786
106.8484
65.2109
60.4627
58.2947
55.5059
53.9151
43.7130
29.8295
29.3944
28.2436
f1 (ppm)

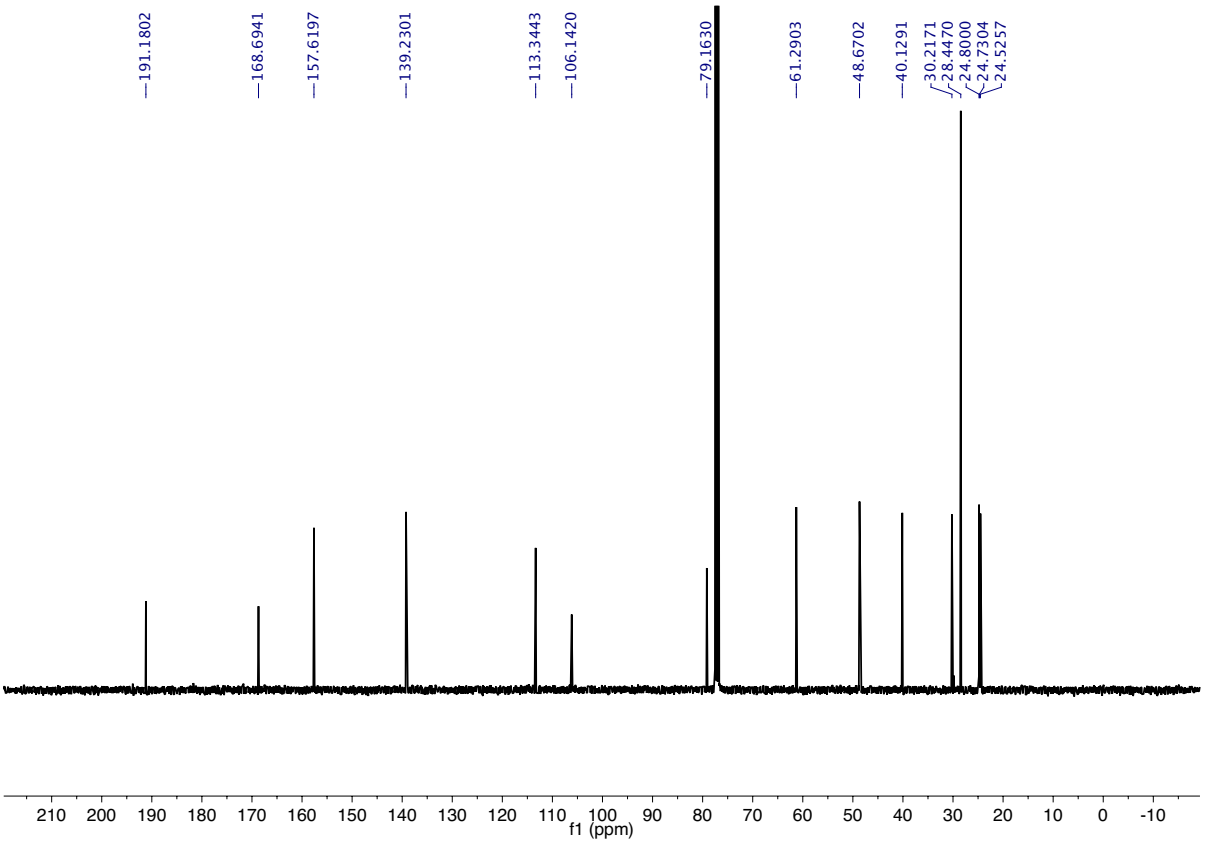

O
CO2tBu
N
14
7.1544
7.0643
7.0253
6.5808
6.5418
3.5445
3.5392
3.5344
3.5123
3.5070
3.5023
3.4759
3.4553
3.4470
3.4421
3.4328
3.4188
3.2168
3.2096
3.1848
3.1774
3.1525
3.1452
2.6023
2.5879
2.4567
2.4273
1.9136
1.8816
1.8308
1.7987
1.6260
1.5946
1.5337
1.5277
1.4995
1.4668
1.4457
1.4297
1.0007
0.9940
0.9620
1.0138
1.0181
1.0246
1.0341
1.0381
1.0401
2.1404
12.9576
f1 (ppm)

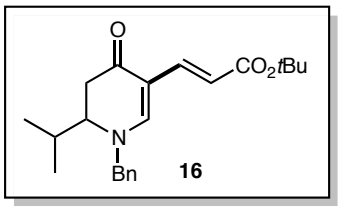

189.3261
168.6093
156.9907
138.9043
114.0195
113.9978
106.5688
79.3151
56.8566
54.0262
43.5518
31.8397
28.4530
25.9011
23.1266
f1 (ppm)


O
H
CO2tBu
N
H
Me

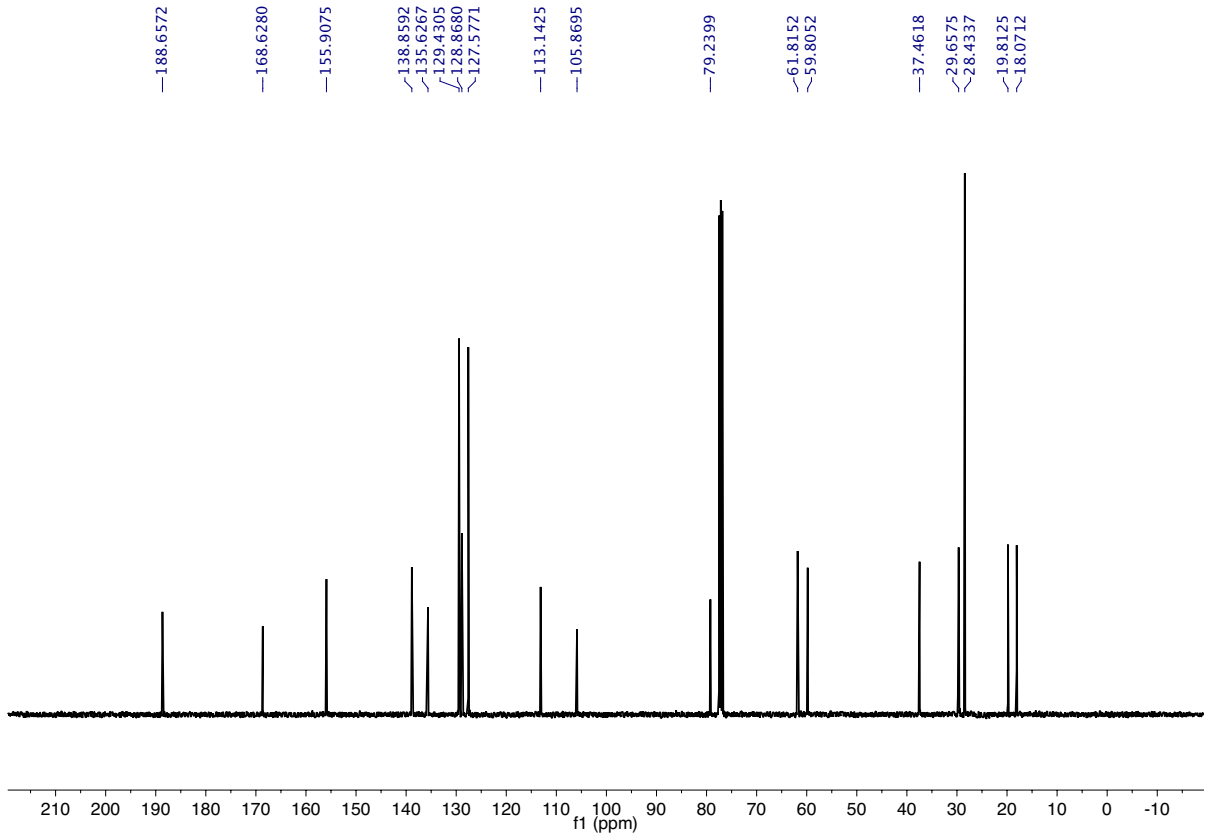
15

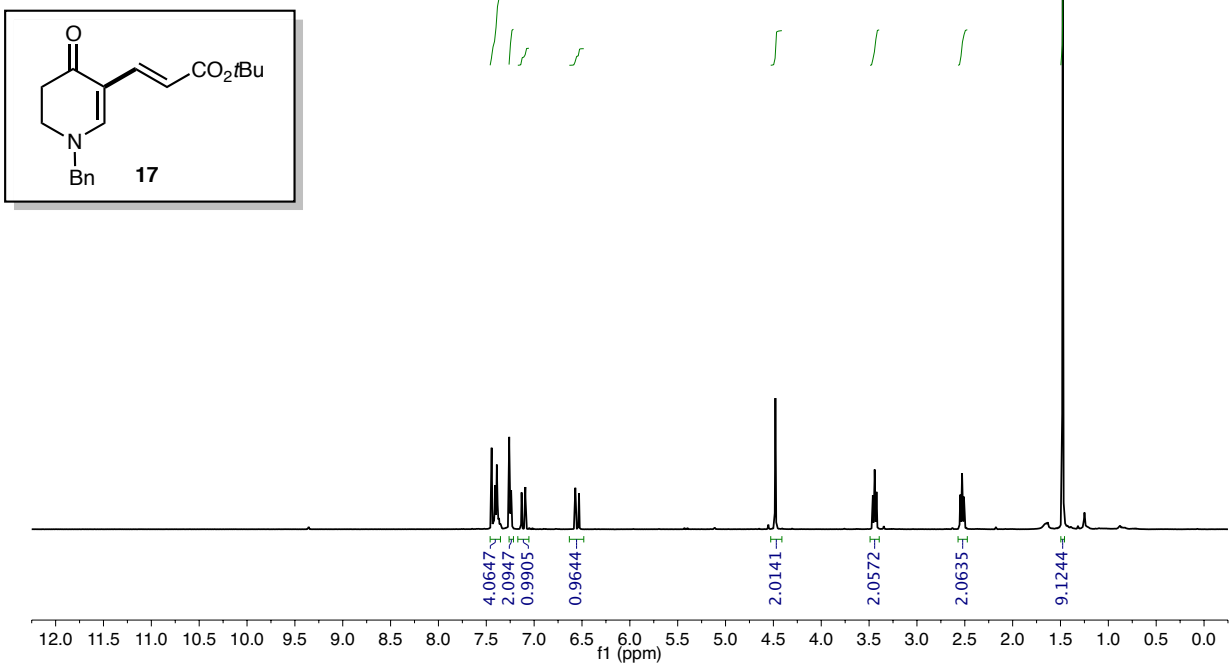
7.2657
7.1031
7.0641
6.5605
6.5215
3.1694
3.1602
3.1398
3.1321
3.1247
3.1041
3.0876
2.4521
2.2474
2.2258
2.2171
2.1643
2.1292
1.8744
1.8696
1.8459
1.4388
1.4297
1.4079
1.3993
1.2590
1.2144
1.0221
0.9999
0.9775
4.0944
1.0298
1.0420
1.1070
2.0867
10.4985
3.4786
f1 (ppm)


191.1802
168.6941
157.6197
139.2301
113.3443
106.1420
79.1630
61.2903
48.6702
40.1291
30.2171
28.4470
24.8000
24.7304
24.5257
f1 (ppm)

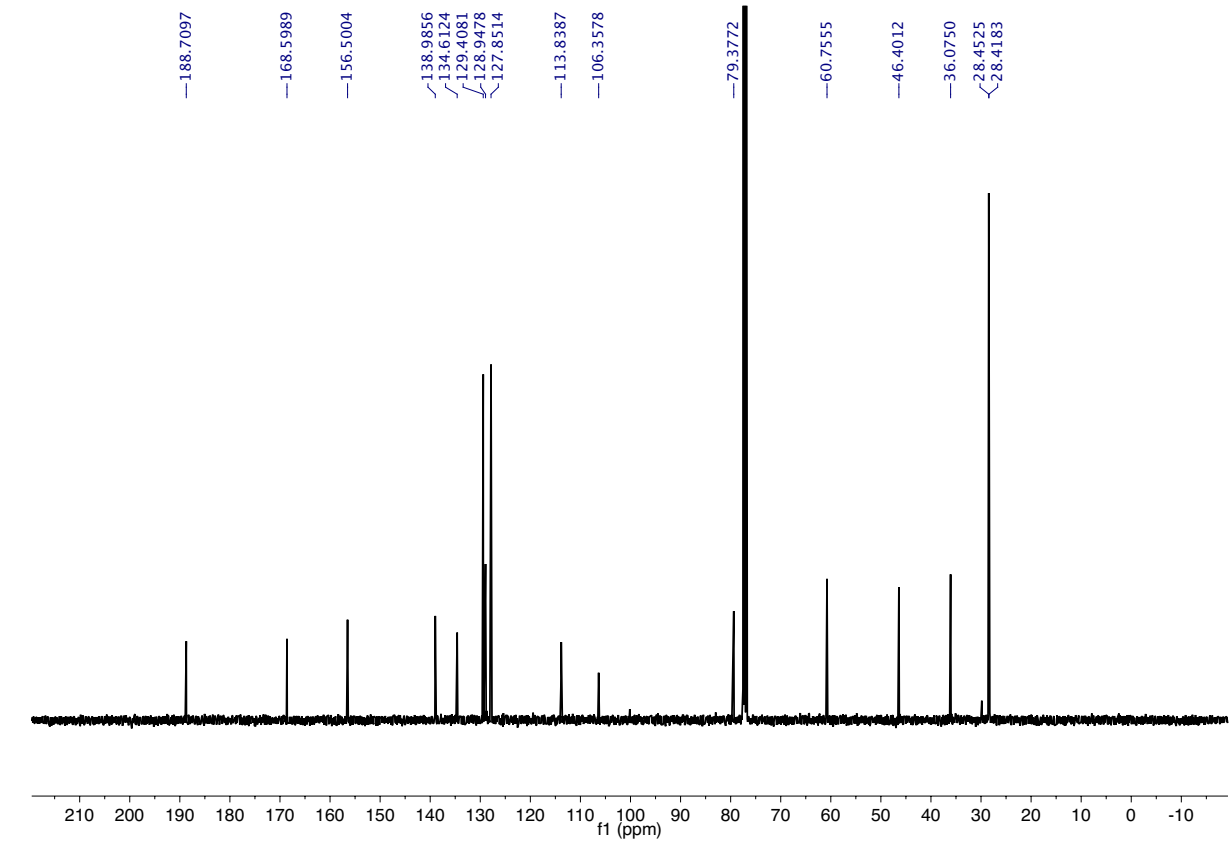

O
CO2tBu
N
Bn
16

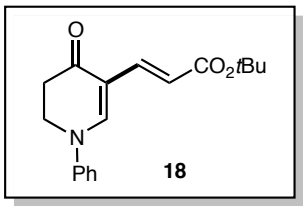
7.4053
7.3827
7.3617
7.3437
7.2596
7.2420
7.0956
7.0566
6.5177
6.4788
4.5977
4.5601
4.4951
4.4575
3.2948
3.2892
3.2753
3.2612
3.2557
2.6236
2.6047
2.4974
2.4915
2.4558
2.2271
2.2104
1.4623
0.9840
0.9669
0.9312
0.9143
4.1804
2.1553
1.0456
1.0005
1.0394
1.0842
1.0608
1.1007
1.0604
1.0782
9.4134
3.1373
3.0525
f1 (ppm)


188.6572
168.6280
155.9075
138.8592
135.6267
129.4305
128.8680
127.5771
113.1425
105.8695
79.2399
61.8152
59.8052
37.4618
29.6575
28.4337
19.8125
18.0712
f1 (ppm)


7.4440
7.4241
7.4082
7.3900
7.3693
7.3539
7.2603
7.2401
7.1309
7.0919
6.5698
6.5307
4.4789
3.4610
3.4418
3.4223
2.5475
2.5282
2.5089
1.4767
4.0647
2.0947
0.9905
0.9644
2.0141
2.0572
2.0635
9.1244
f1 (ppm)

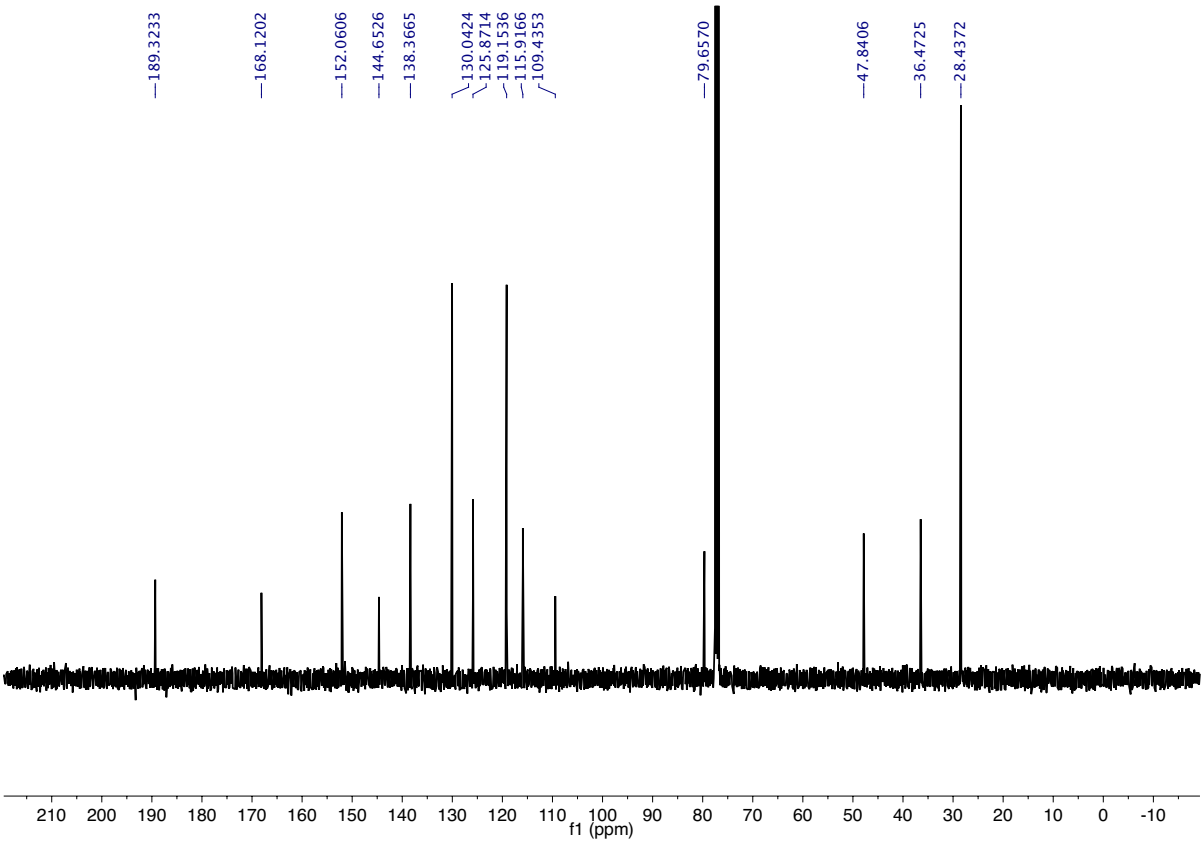
O
CO2tBu
N
Bn
17

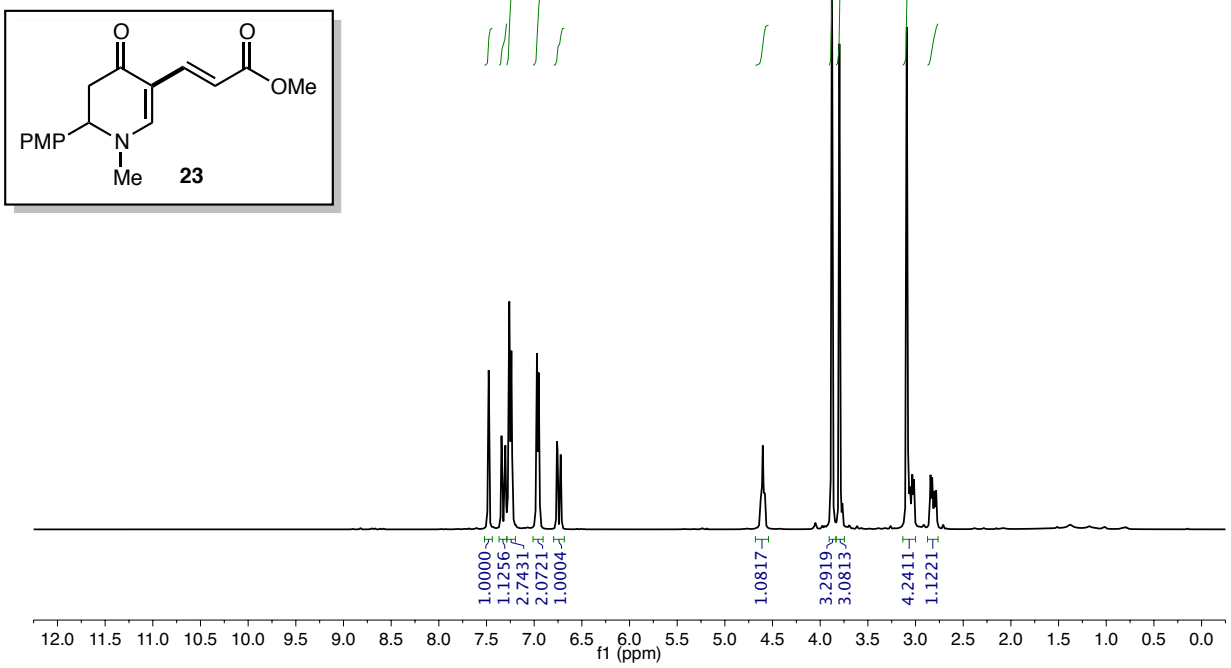

188.7097
168.5989
156.5004
138.9856
134.6124
129.4081
128.9478
127.8514
113.8387
106.3578
79.3772
60.7555
46.4012
36.0750
28.4525
28.4183
f1 (ppm)

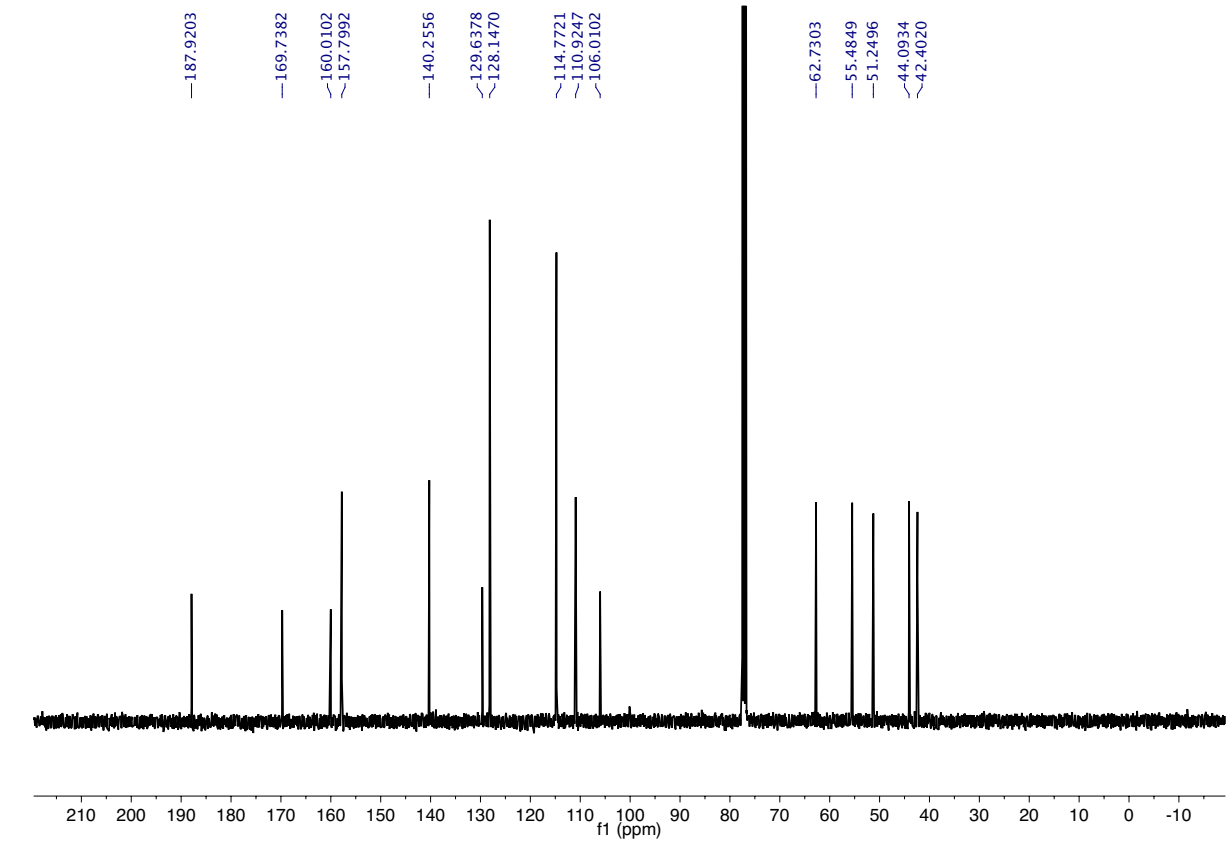

O
CO2tBu
N
Ph

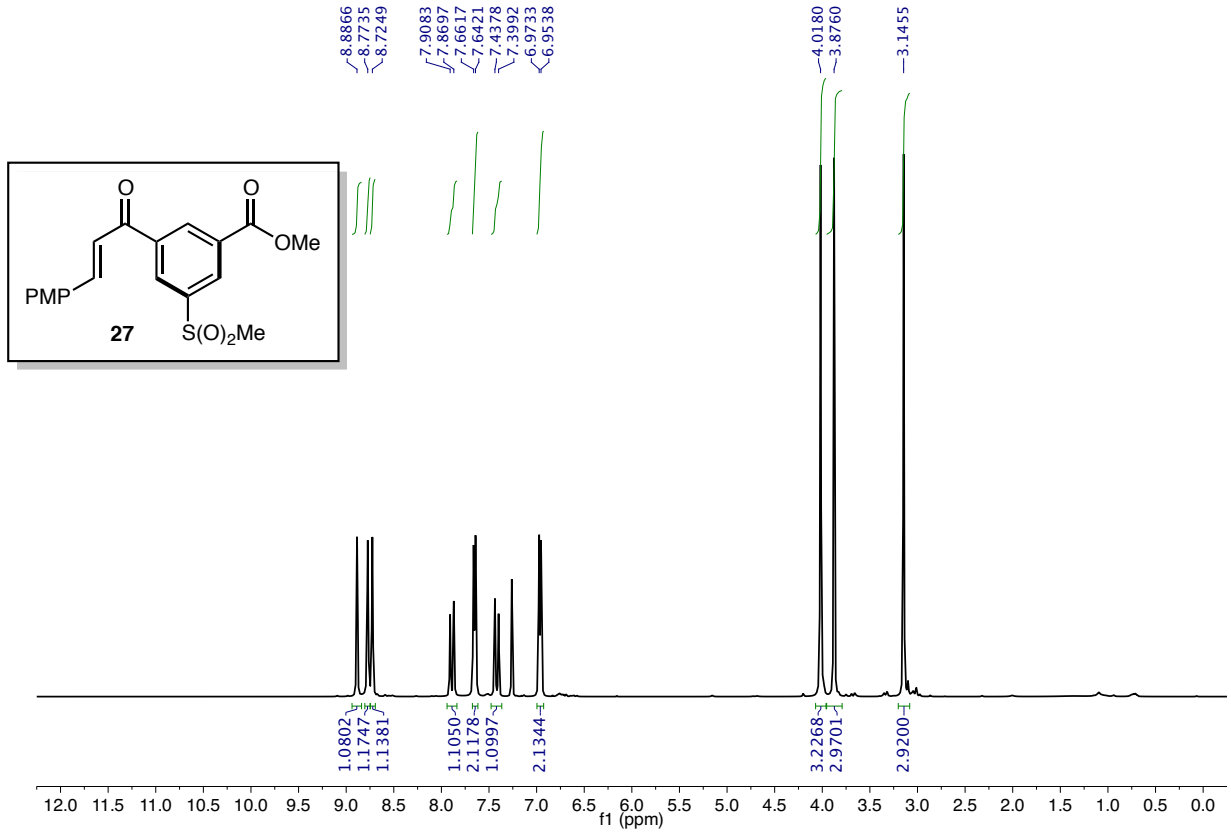
18

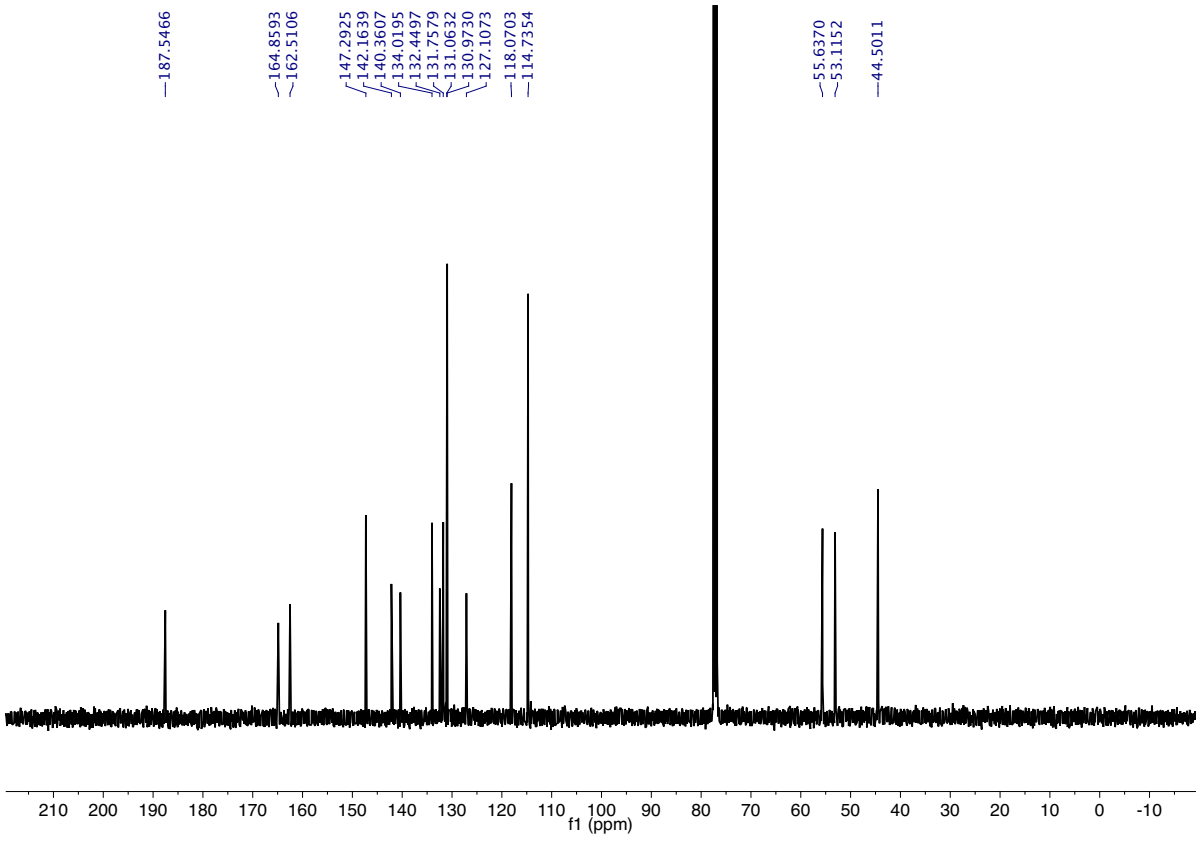
7.6926
7.4532
7.4336
7.4139
7.2596
7.2431
7.2179
7.1784
7.1679
7.1475
6.6187
6.5795
4.0769
4.0583
4.0394
2.7613
2.7426
2.7239
1.4886
0.9996
2.0051
4.0370
0.9734
2.0103
2.0146
9.0848
f1 (ppm)

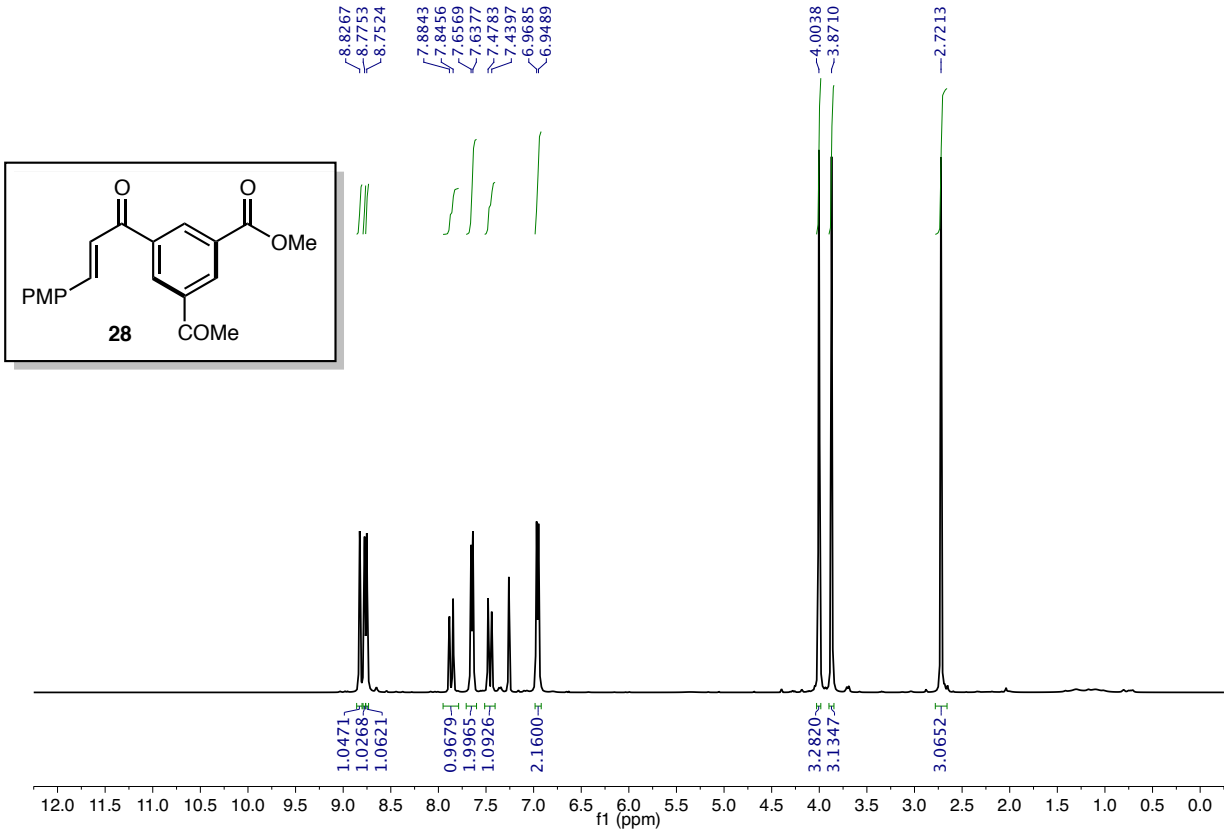

189.3233
168.1202
152.0606
144.6526
138.3665
130.0424
125.8714
119.1536
115.9166
109.4353
79.6570
47.8406
36.4725
28.4372
f1 (ppm)

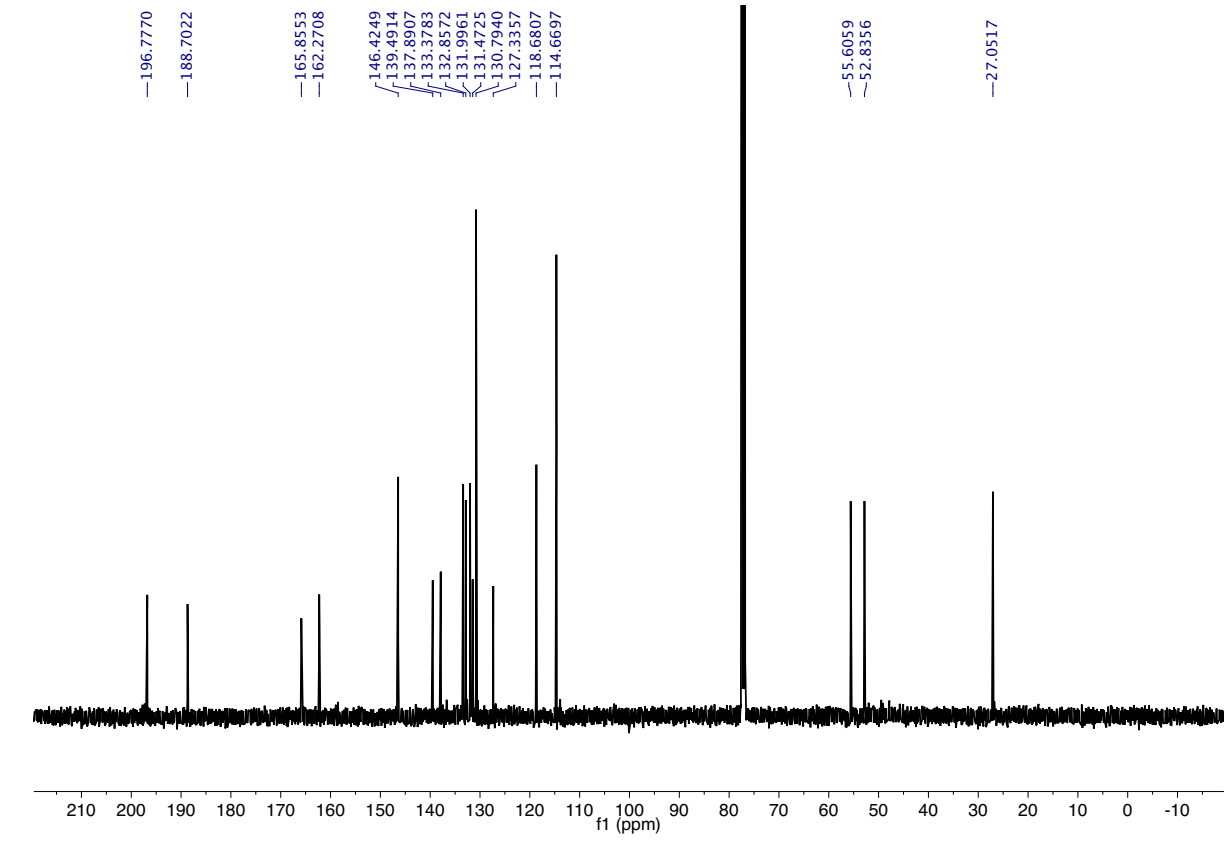

7.4771
7.3428
7.3026
7.2604
7.2388
6.9709
6.9525
6.7567
6.7219
4.6196
4.6023
4.5855
3.8783
3.7987
3.0919
3.0725
3.0595
3.0342
3.0186
2.8428
2.8251
2.8017
2.7839
1.0000
1.1256
2.7431
2.0721
1.0004
1.0817
3.2919
3.0813
4.2411
1.1221
f1 (ppm)

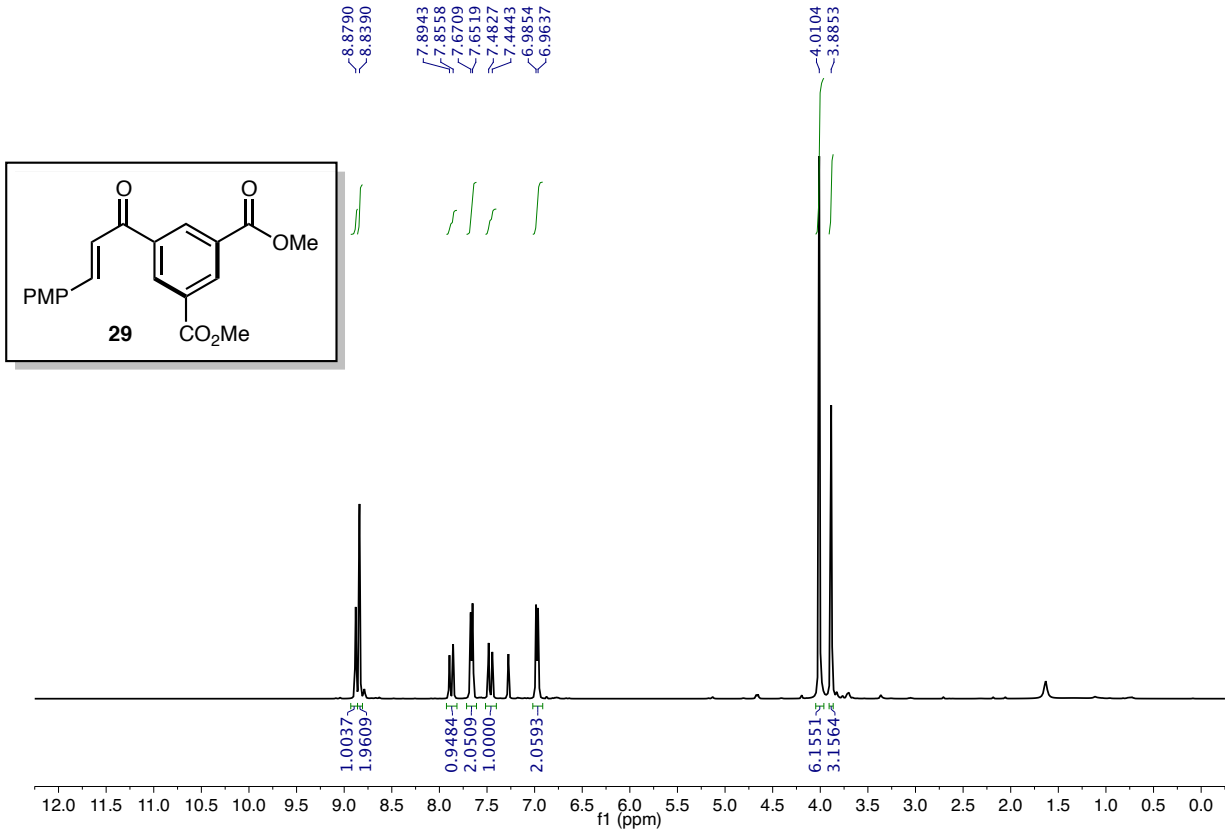

187.9203
169.7382
160.0102
157.7992
140.2556
129.6378
128.1470
114.7721
110.9247
106.0102
62.7303
55.4849
51.2496
44.0934
42.4020
f1 (ppm)

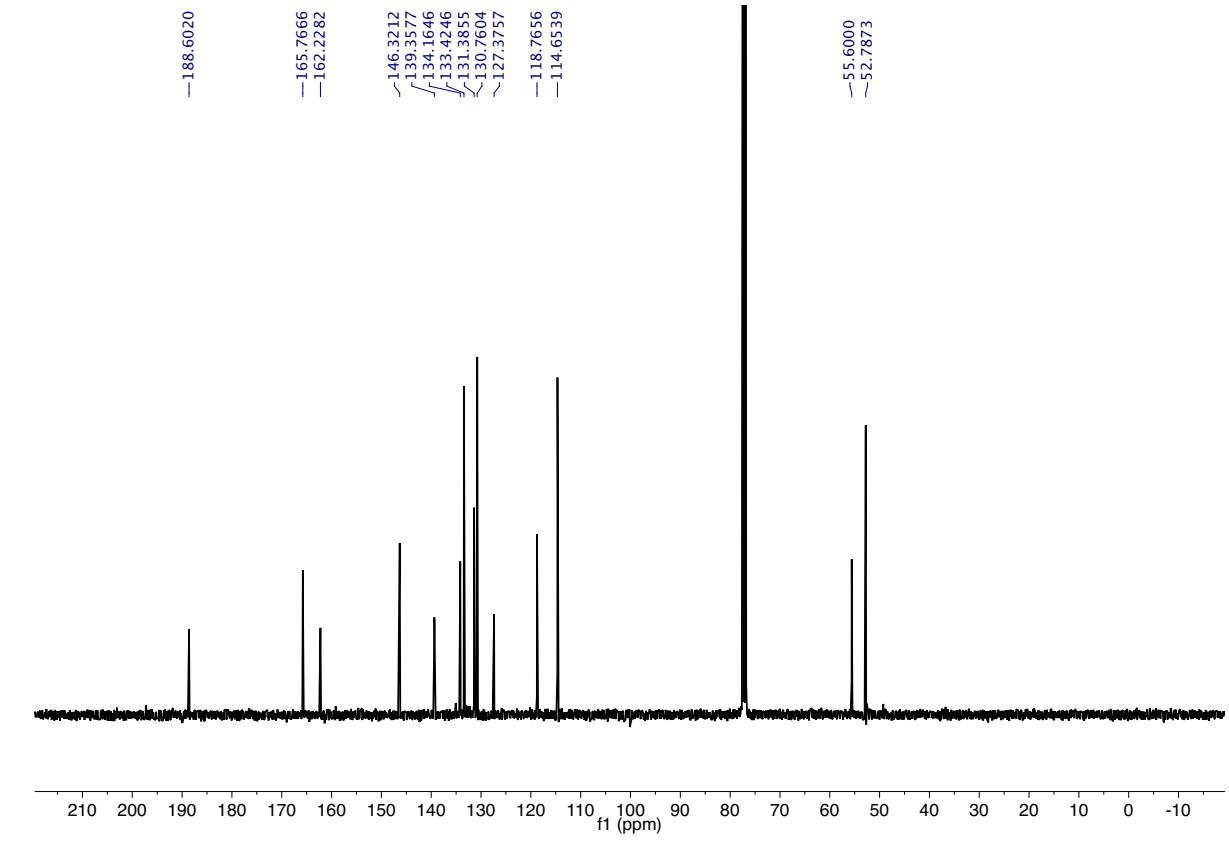

8.8866
8.7735
8.7249
7.9083
7.8697
7.6617
7.6421
7.4378
7.3992
6.9733
6.9538
4.0180
3.8760
3.1455
O
O
OMe
PMP
27
S(O)2Me
1.0802
1.1747
1.1381
1.1050
2.1178
1.0997
2.1344
3.2268
2.9701
2.9200
f1 (ppm)

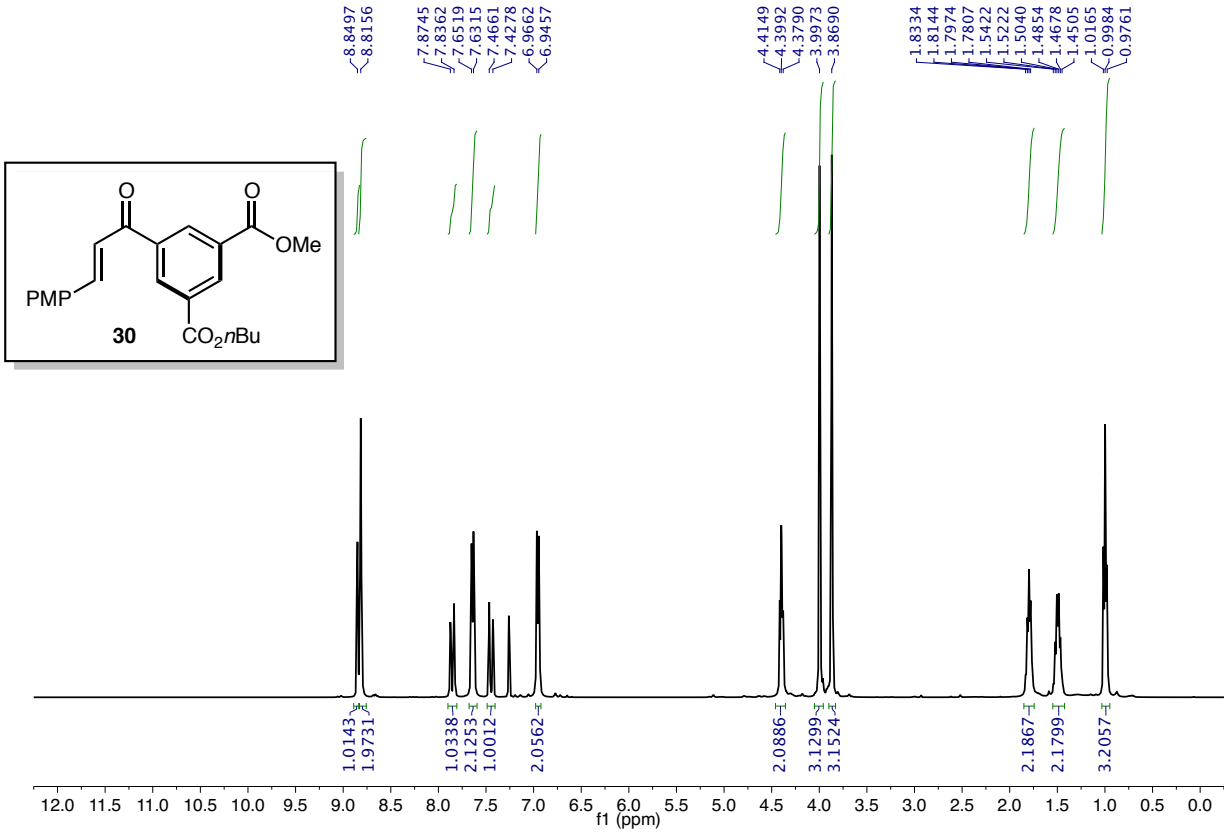

187.5466
164.8593
162.5106
147.2925
142.1639
140.3607
134.0195
132.4497
131.7579
131.0632
130.9730
127.1073
118.0703
114.7354
55.6370
53.1152
44.5011
f1 (ppm)

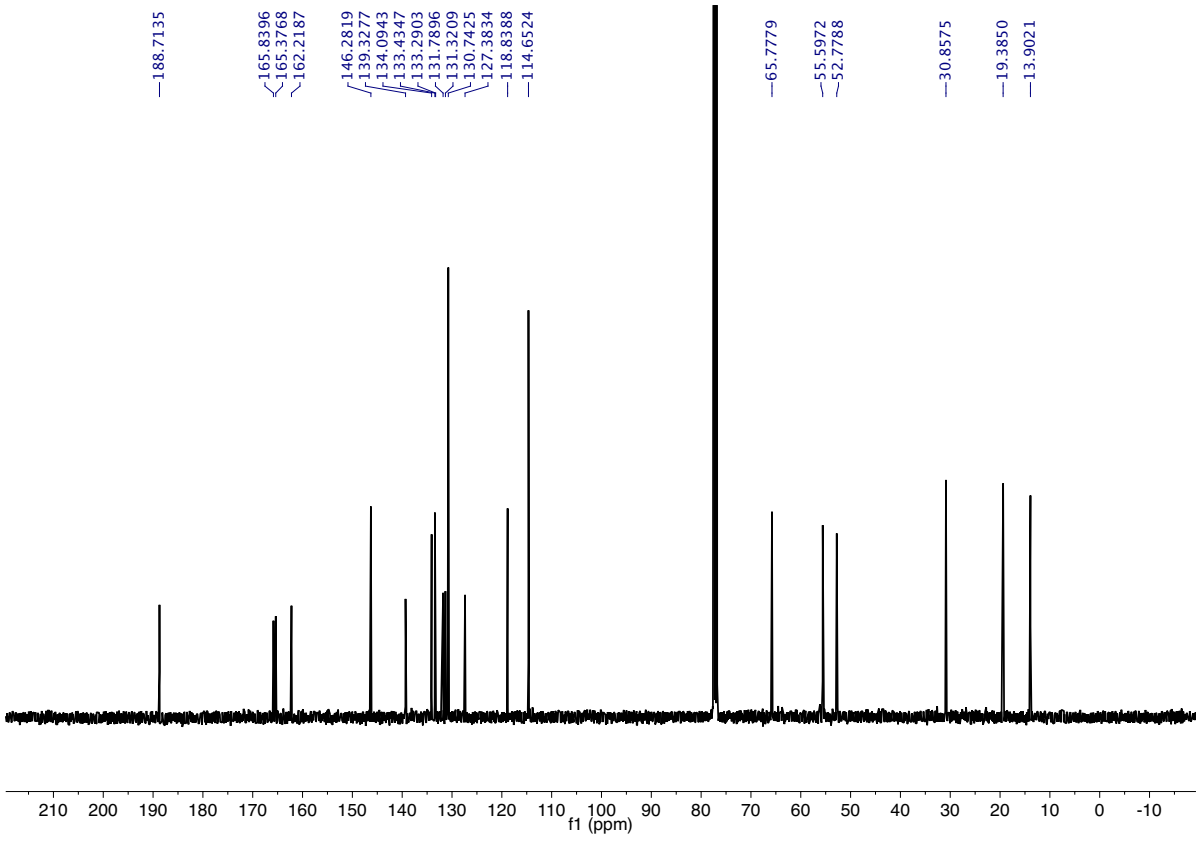

8.8267
8.8753
8.7524
7.8843
7.8456
7.6569
7.6377
7.4783
7.4397
6.9685
6.9489
4.0038
3.8710
2.7213
O
O
OMe
PMP
28
COMe
1.0471
1.0268
1.0621
0.9679
1.9965
1.0926
2.1600
3.2820
3.1347
3.0652
f1 (ppm)

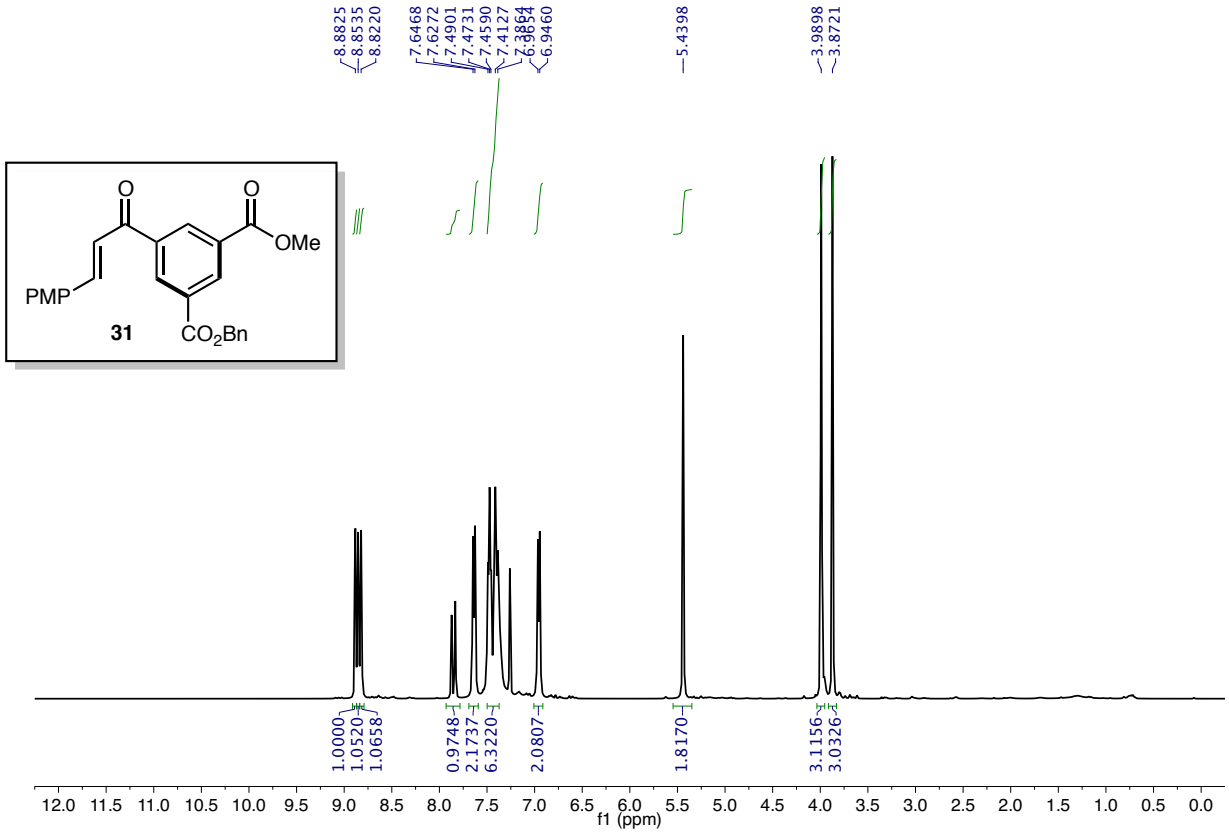

196.7770
188.7022
165.8553
162.2708
146.4249
139.4914
137.8907
133.3783
132.8572
131.9961
131.4725
130.7940
127.3357
118.6807
114.6697
55.6059
52.8356
27.0517
f1 (ppm)

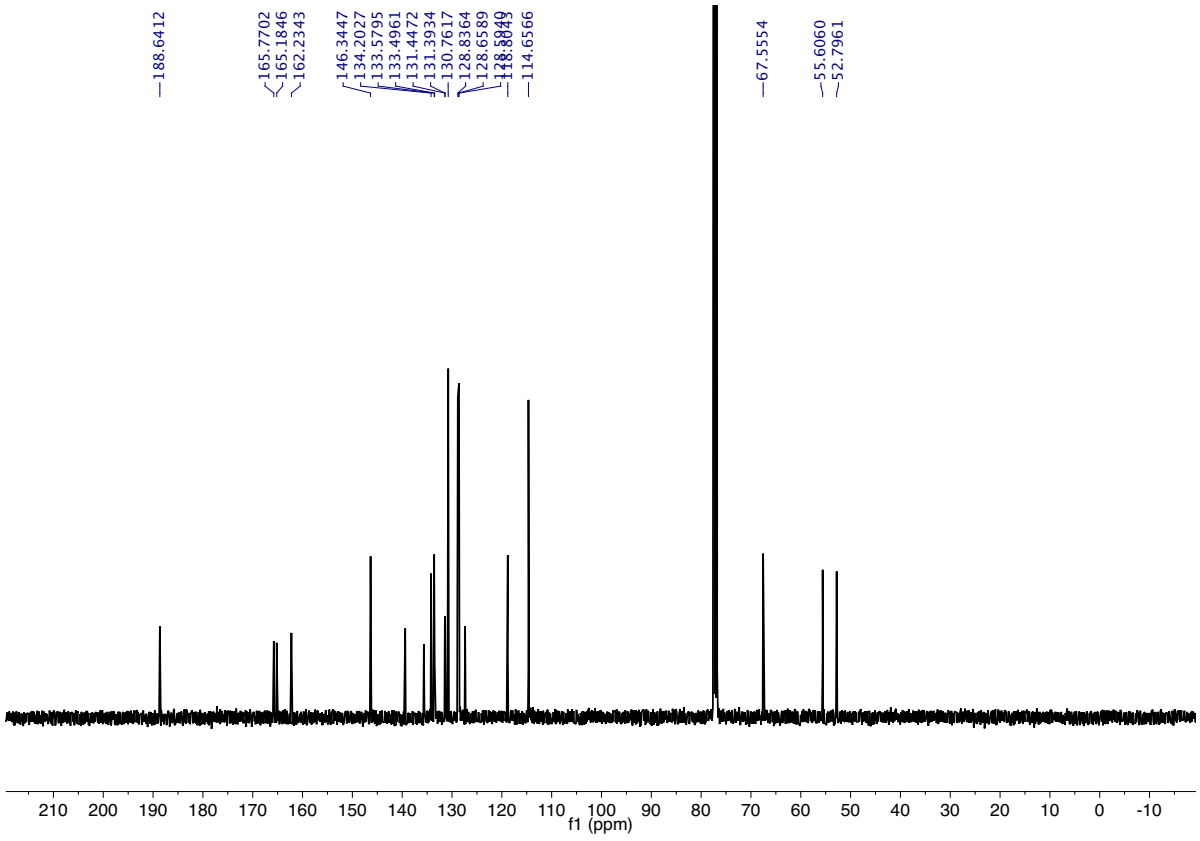

8.8790
8.8390
7.8943
7.8558
7.6709
7.6519
7.4827
7.4443
6.9854
6.9637
4.0104
3.8853
O
O
OMe
PMP
29
CO2Me
1.0037
1.9609
0.9484
2.0509
1.0000
2.0593
6.1551
3.1564
f1 (ppm)

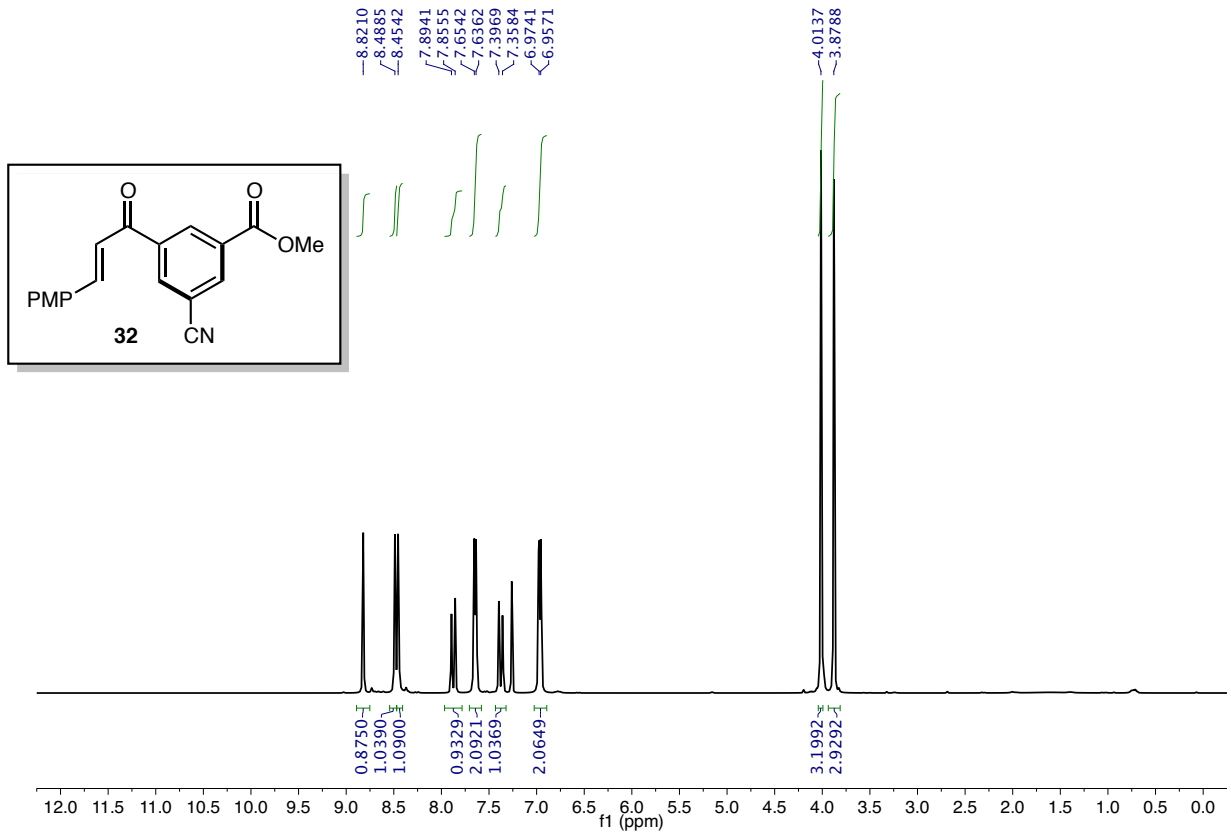

188.6020
165.7666
162.2282
146.3212
139.3577
134.1646
133.4246
131.3855
130.7604
127.3757
118.7656
114.6539
55.6000
52.7873
f1 (ppm)

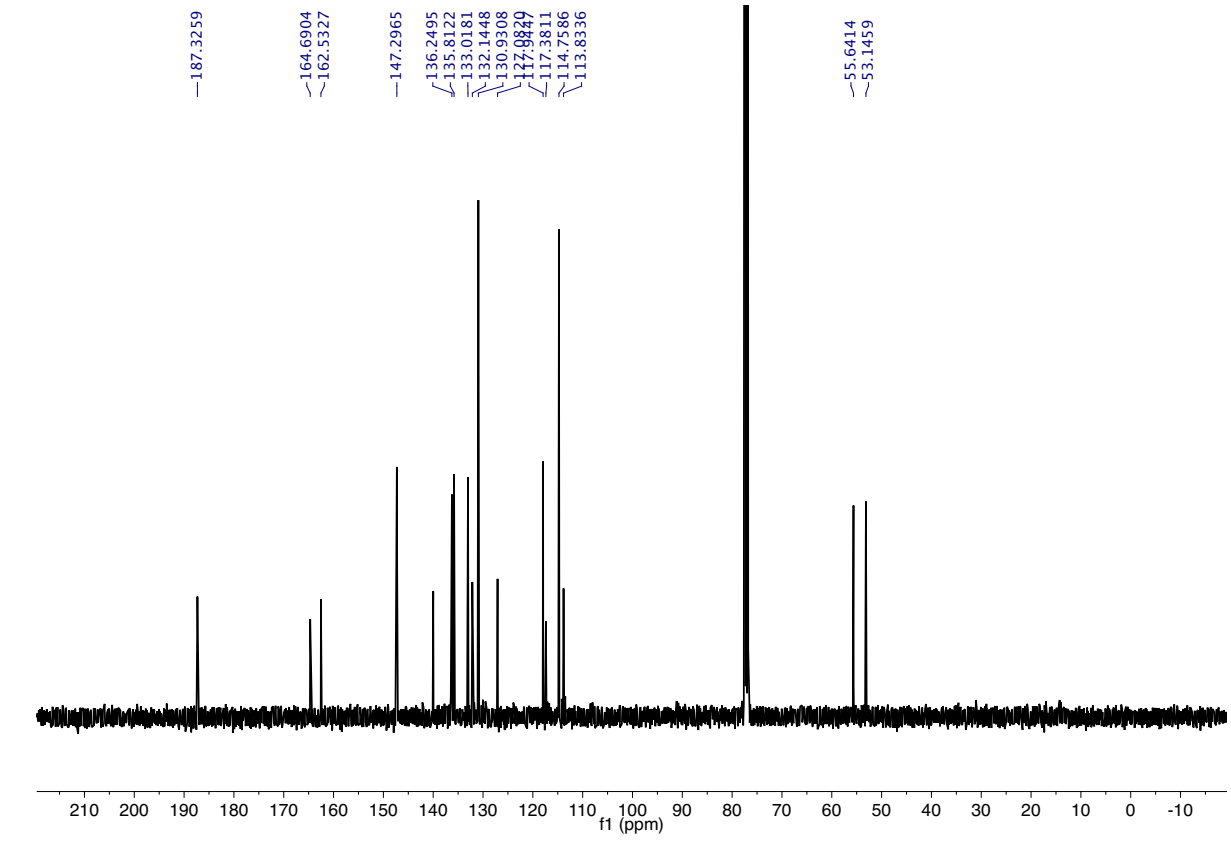

8.8497
8.8156
7.8745
7.8362
7.6519
7.6315
7.4661
7.4278
6.9662
6.9457
4.4149
4.3992
4.3790
3.9973
3.8690
1.8334
1.8144
1.7974
1.7807
1.5422
1.5222
1.5040
1.4854
1.4678
1.4505
1.0165
0.9984
0.9761
1.0143
1.9731
1.0338
2.1253
1.0012
2.0562
2.0886
3.1299
3.1524
2.1867
2.1799
3.2057
O
O
OMe
PMP
30
CO2nBu
f1 (ppm)

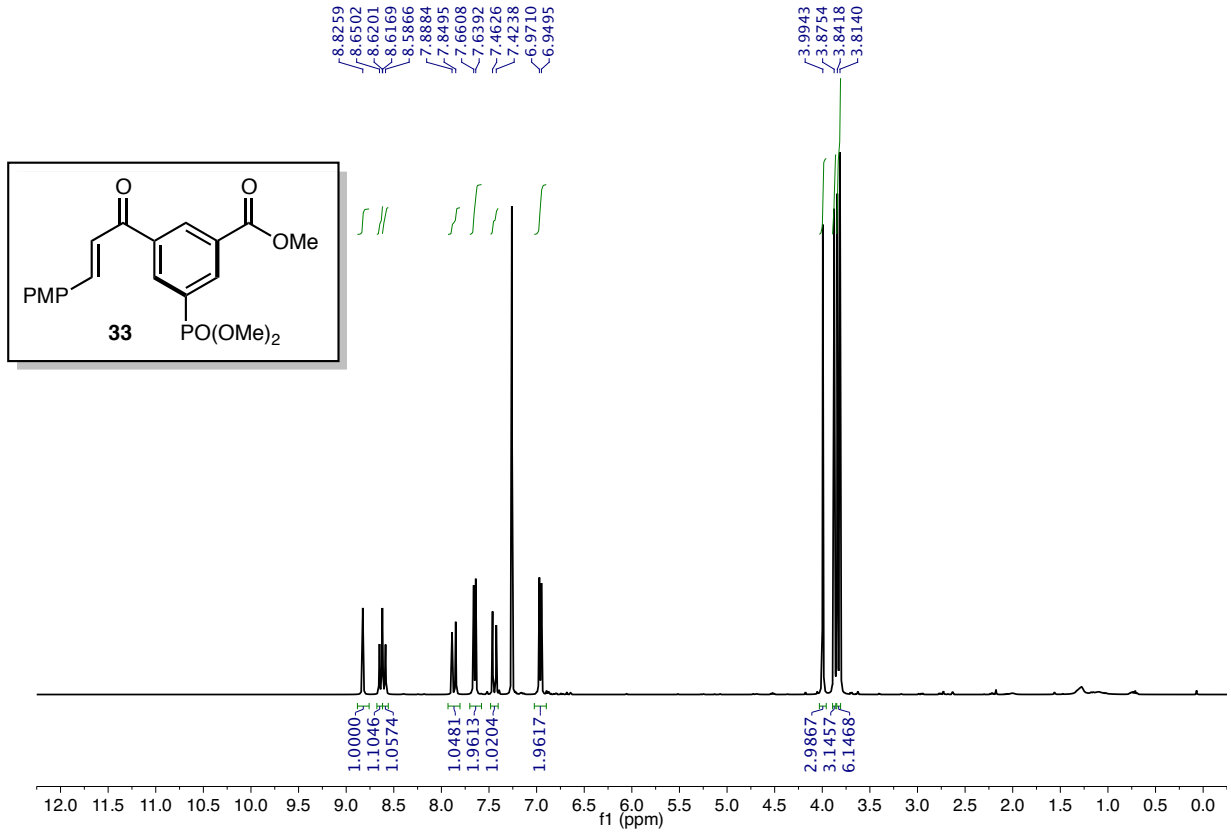

188.7135
165.8396
165.3768
162.2187
146.2819
139.3277
134.0943
133.4347
133.2903
131.7896
131.3209
130.7425
127.3834
118.8388
114.6524
65.7779
55.5972
52.7788
30.8575
19.3850
13.9021
f1 (ppm)

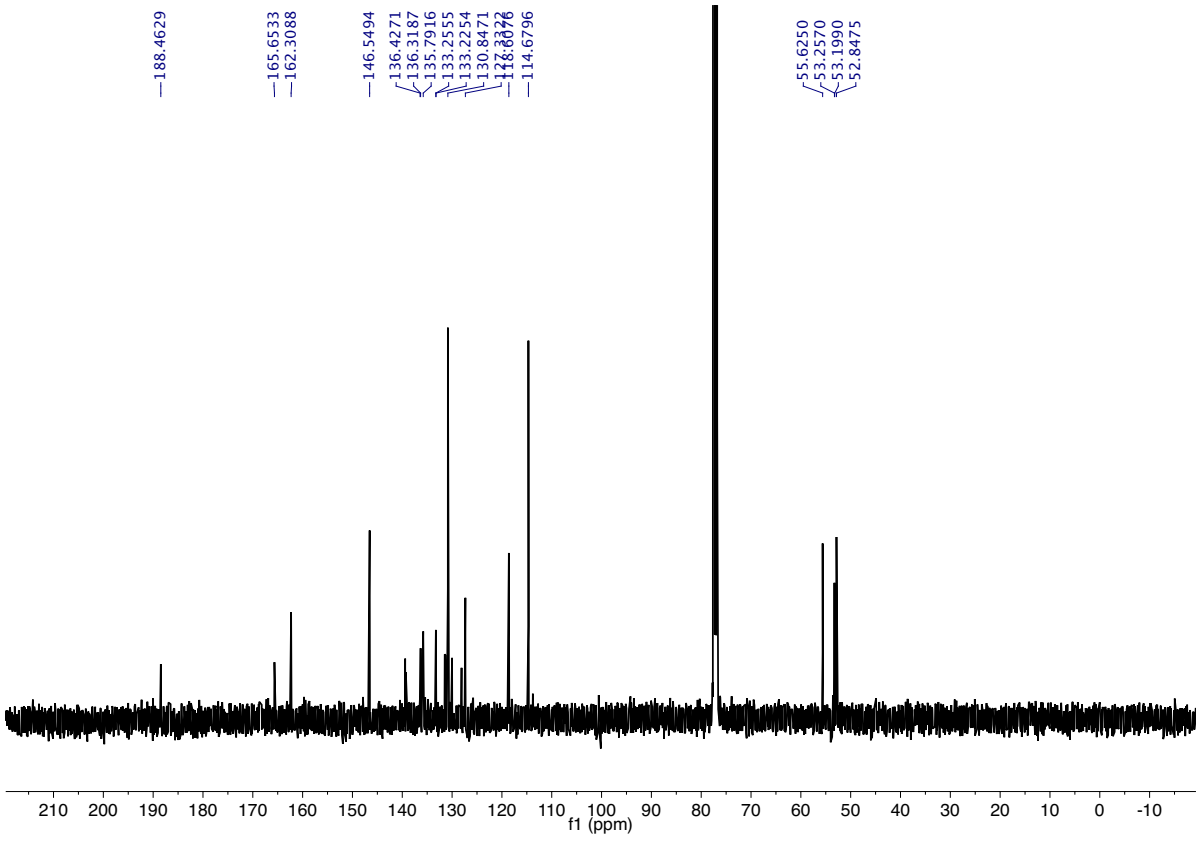

8.8825
8.8535
8.8220
7.6468
7.6272
7.4901
7.4731
7.4590
7.4127
6.9460
5.4398
3.9898
3.8721
O
O
OMe
PMP
31
CO2Bn
1.0000
1.0520
1.0658
0.9748
2.1737
6.3220
2.0807
1.8170
3.1156
3.0326
f1 (ppm)

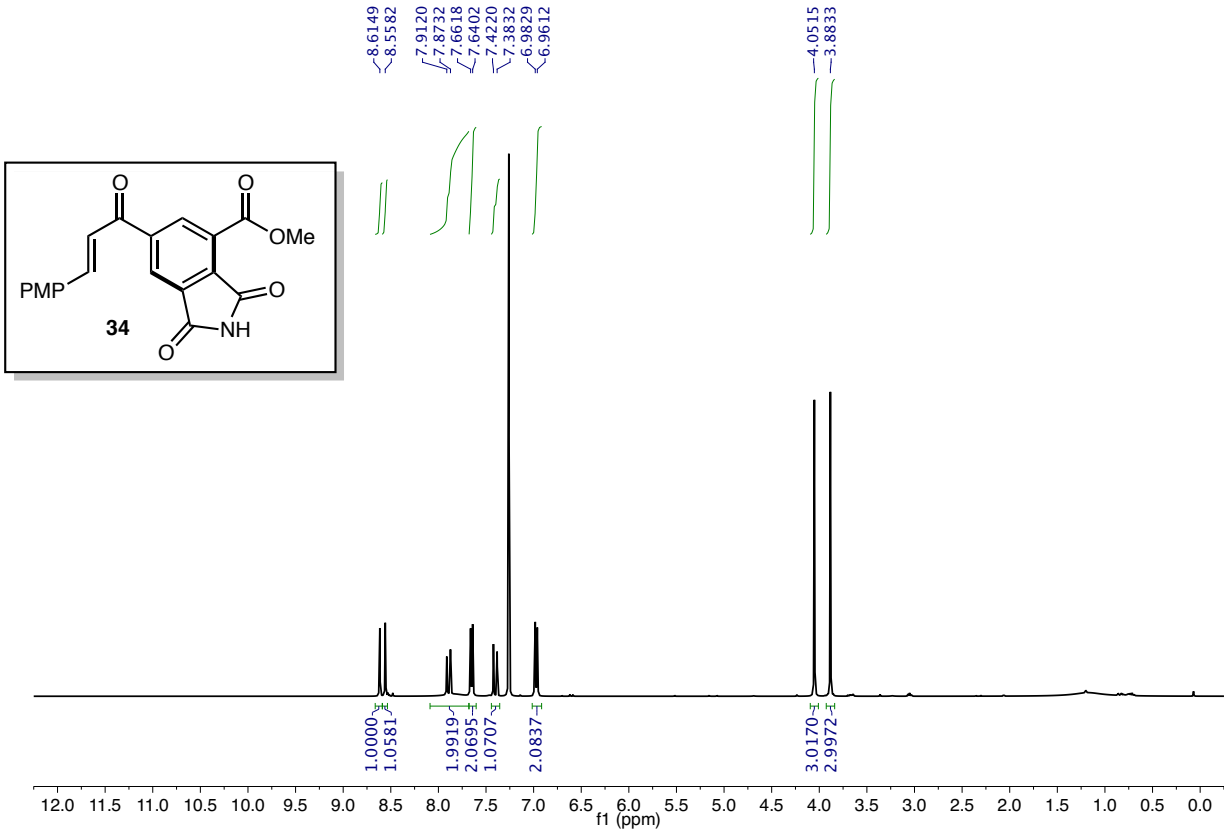

188.6412
165.7702
165.1846
162.2343
146.3447
134.2027
133.5795
133.4961
131.4472
131.3934
130.7617
128.8364
128.6589
114.6566
67.5554
55.6060
52.7961
f1 (ppm)

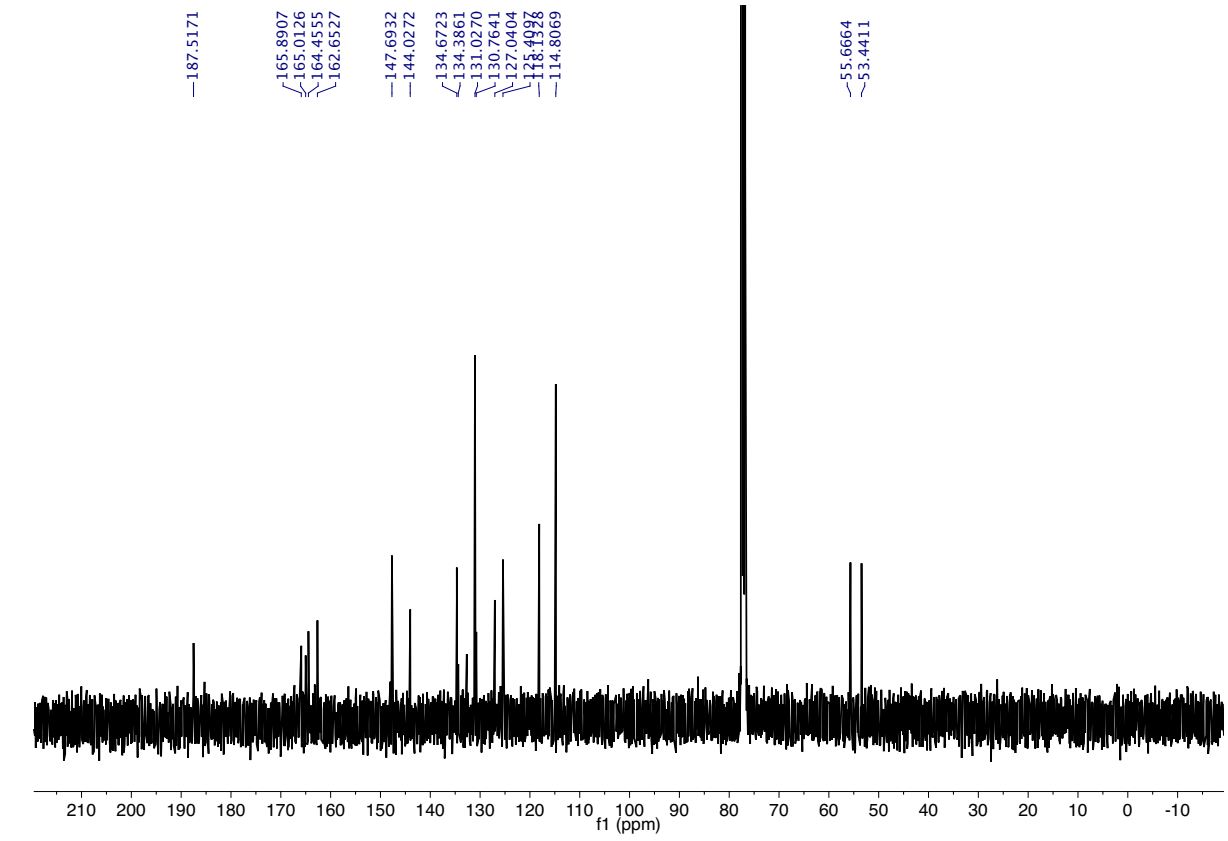

8.8210
8.4885
8.4542
7.8941
7.8555
7.6542
7.6362
7.3969
7.3584
6.9741
6.9571
4.0137
3.8788
O
O
OMe
PMP
32
CN
0.8750
1.0390
1.0900
0.9329
2.0921
1.0369
2.0649
3.1992
2.9292
f1 (ppm)

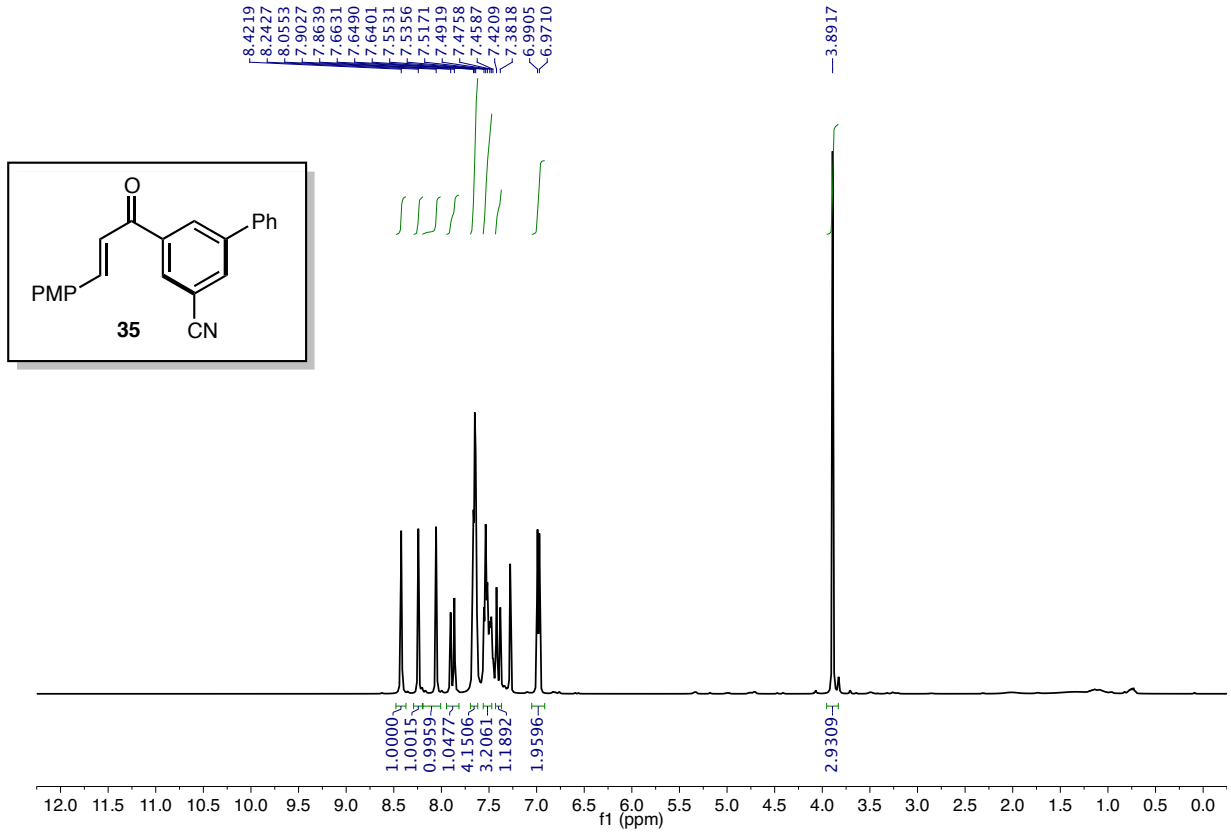

187.3259
164.6904
162.5327
147.2965
136.2495
135.8122
133.0181
132.1448
130.9308
117.3811
114.7586
113.8336
55.6414
53.1459
f1 (ppm)

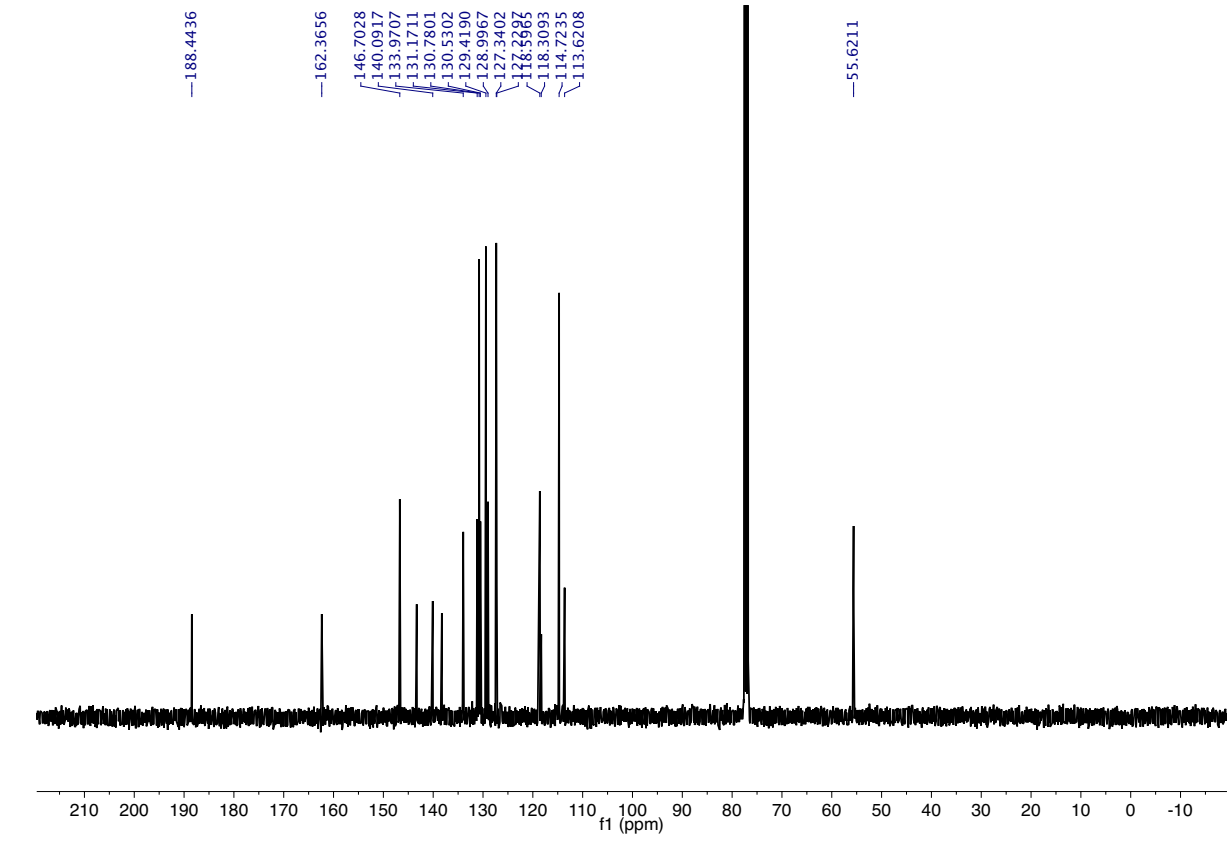

8.8259
8.6502
8.6201
8.6169
8.5866
7.8884
7.8495
7.6608
7.6392
7.4626
7.4238
6.9710
6.9495
3.9943
3.8754
3.8418
3.8140
O
O
OMe
PMP
33
PO(OMe)2
1.0000
1.1046
1.0574
1.0481
1.9613
1.0204
1.9617
2.9867
3.1457
6.1468
f1 (ppm)

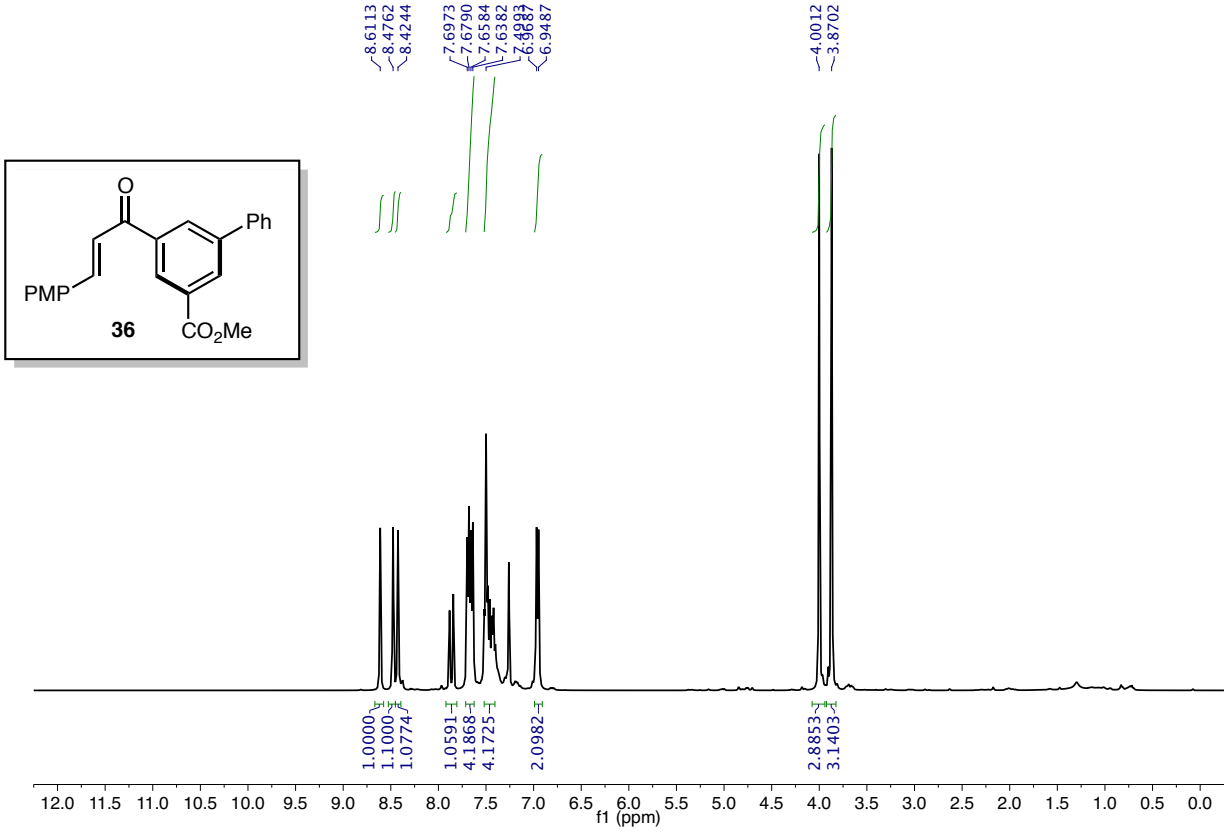

188.4629
165.6533
162.3088
146.5494
136.4271
136.3187
135.7916
133.2555
133.2254
130.8471
118.8078
114.6796
55.6250
53.2570
53.1990
52.8475
f1 (ppm)

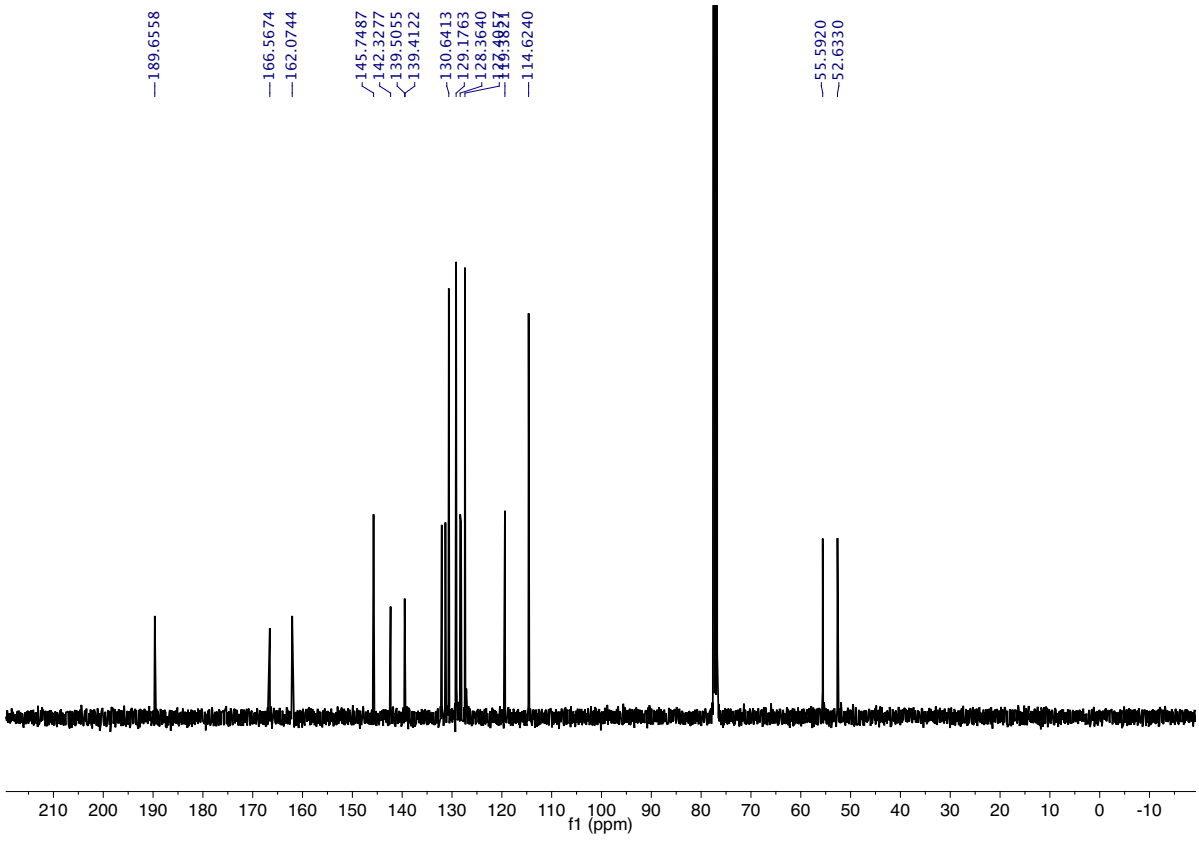

8.6149
8.5582
7.9120
7.8732
7.6618
7.6402
7.4220
7.3832
6.9829
6.9612
4.0515
3.8833
PMP
O
O
OMe
O
NH
O
34
1.0000
1.0581
1.9919
2.0695
1.0707
2.0837
3.0170
2.9972
f1 (ppm)

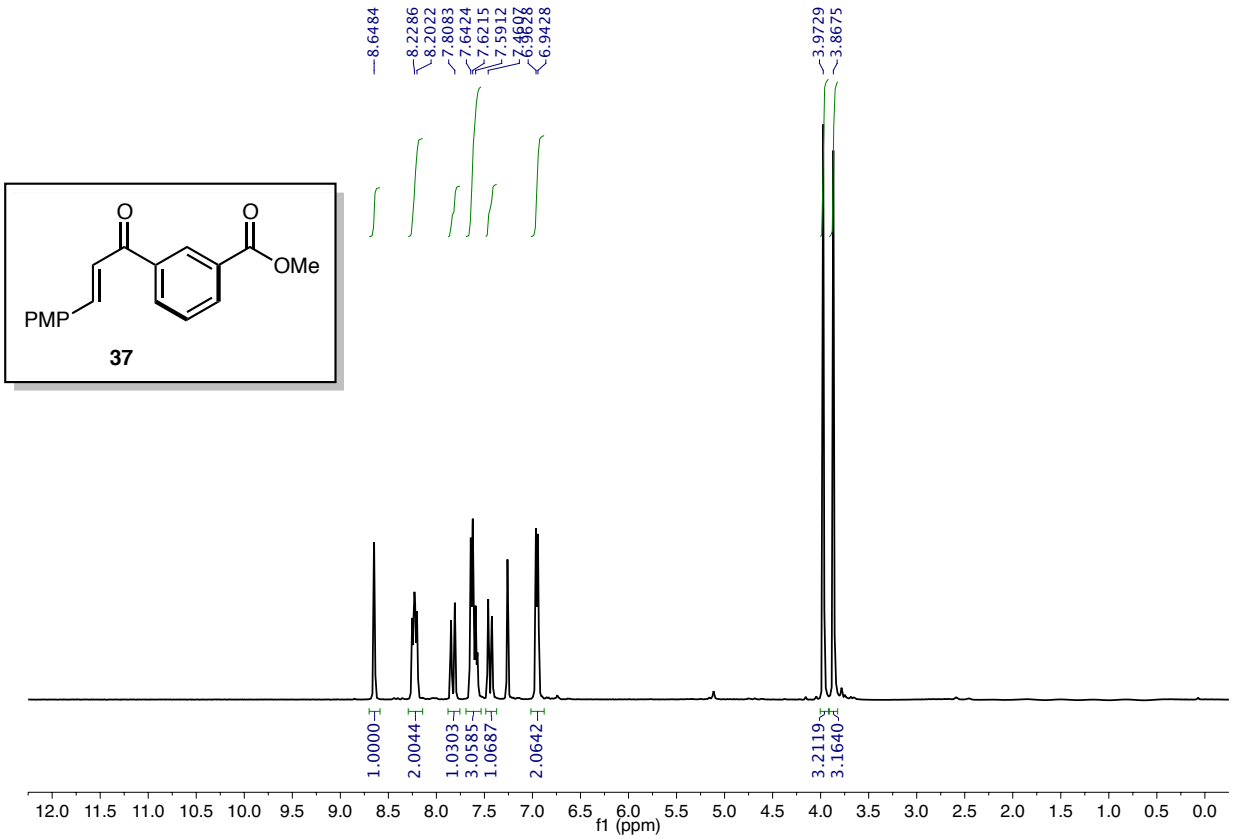

187.5171
165.8907
165.0126
164.4555
162.6527
147.6932
144.0272
134.6723
134.3861
131.0270
130.7641
127.0404
125.4097
118.1328
114.8069
55.6664
53.4411
f1 (ppm)

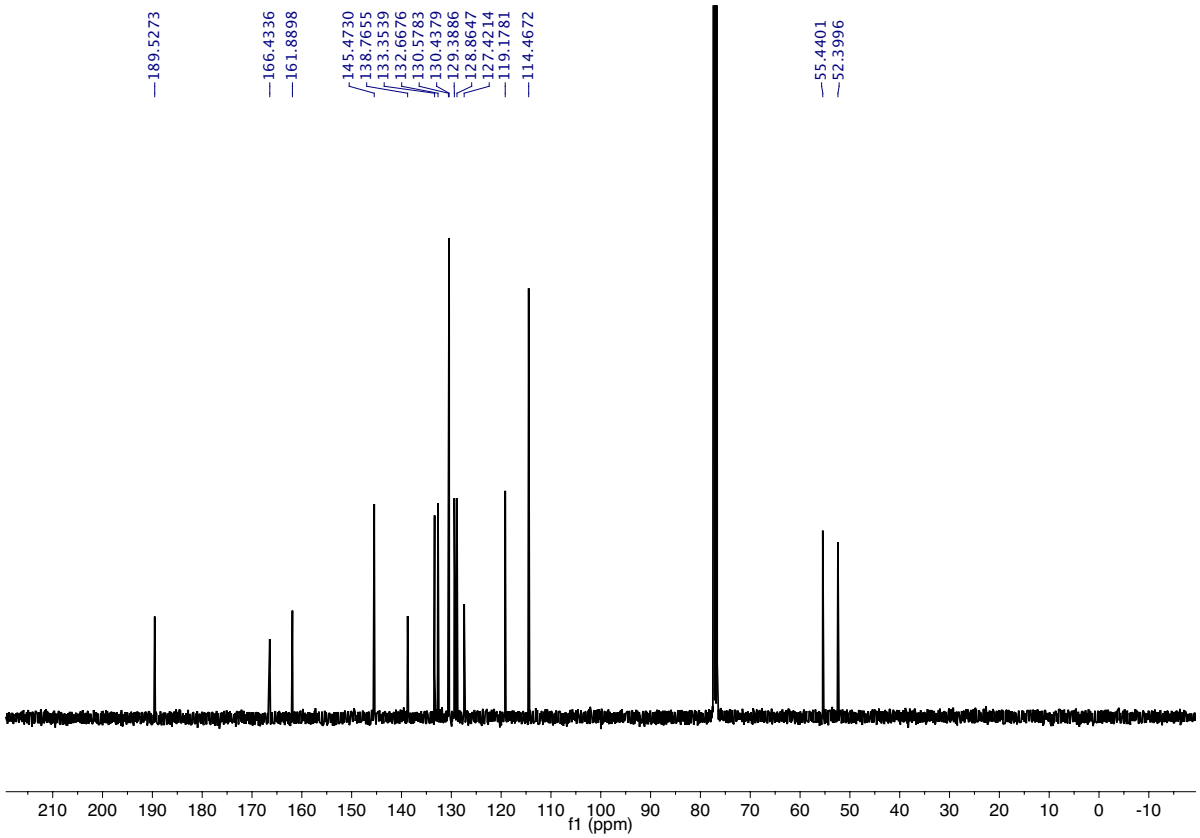

8.4219
8.2427
8.0553
7.9027
7.8639
7.6631
7.6490
7.6401
7.5531
7.5356
7.5171
7.4919
7.4758
7.4587
7.4209
7.3818
6.9905
6.9710
3.8917
O
Ph
PMP
35
CN
1.0000
1.0015
0.9959
1.0477
4.1506
3.2061
1.1892
1.9596
2.9309
f1 (ppm)

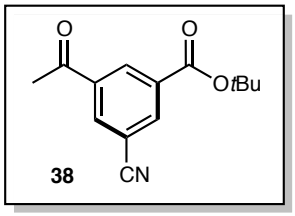

188.4436
162.3656
146.7028
140.0917
133.9707
131.1711
130.7801
130.5302
129.4190
128.9967
127.3402
118.3093
114.7235
113.6208
55.6211
f1 (ppm)


8.6113
8.4762
8.4244
7.6973
7.6790
7.6584
7.6382
7.4993
6.9687
6.9487
4.0012
3.8702
O
Ph
PMP
36
CO2Me
1.0000
1.1000
1.0774
1.0591
4.1868
4.1725
2.0982
2.8853
3.1403
f1 (ppm)


189.6558
166.5674
162.0744
145.7487
142.3277
139.5055
139.4122
130.6413
129.1763
128.3640
114.6240
55.5920
52.6330
f1 (ppm)

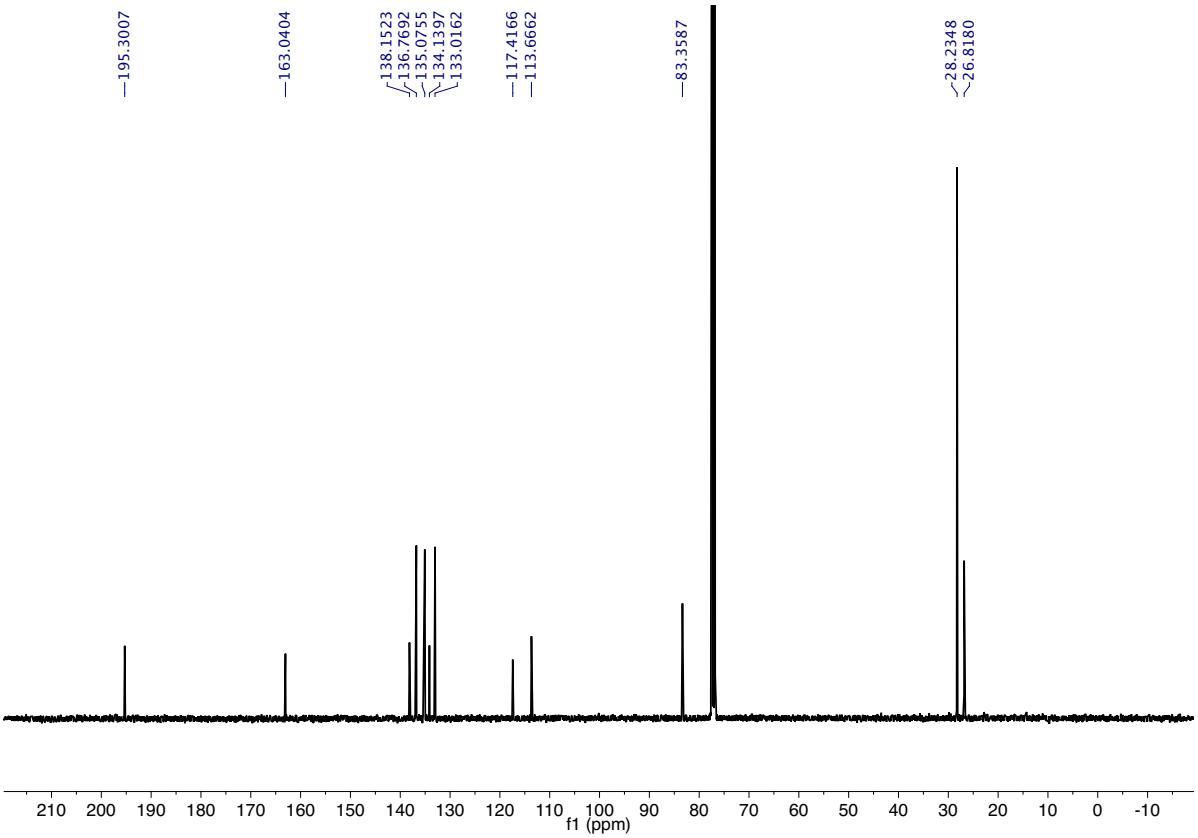

8.6484
8.2286
8.2022
7.8083
7.6424
7.6215
7.5912
7.4607
6.9628
6.9428
3.9729
3.8675
O
O
OMe
PMP
37
1.0000
2.0044
1.0303
3.0585
1.0687
2.0642
3.2119
3.1640
f1 (ppm)

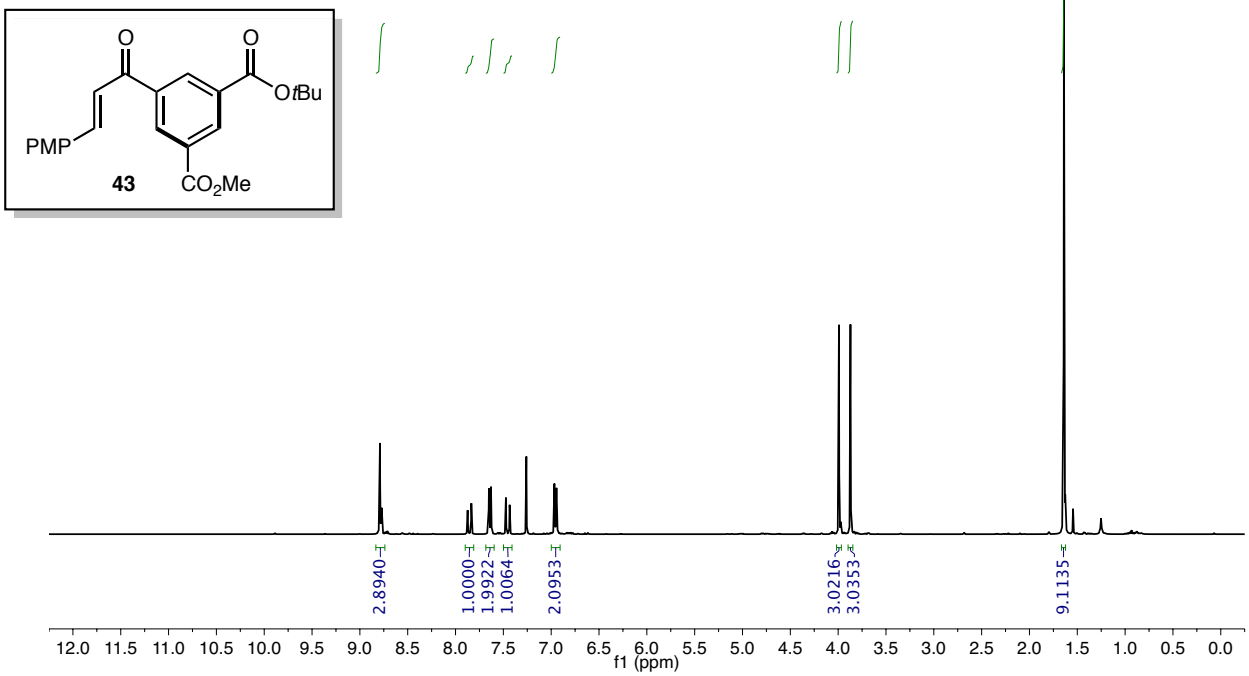

189.5273
166.4336
161.8898
145.4730
138.7655
133.3539
132.6676
130.5783
130.4379
129.3886
128.8647
127.4214
119.1781
114.4672
55.4401
52.3996
f1 (ppm)

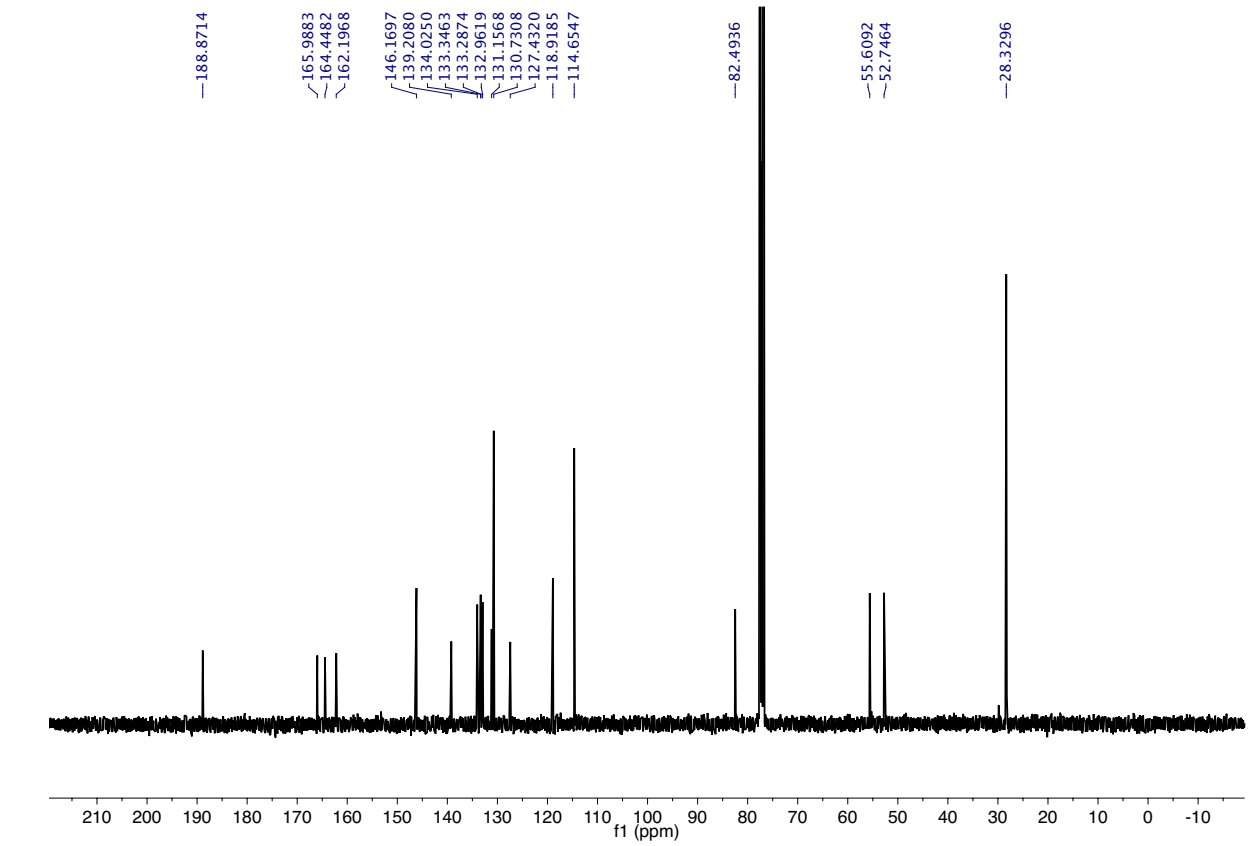

O
O
O*t*Bu
CN

38

8.7073
8.4161
8.3683
2.6737
1.6267
1.0058
1.1023
1.0866
3.0434
9.1456
f1 (ppm)


195.3007
163.0404
138.1523
136.7692
135.0755
134.1397
133.0162
117.4166
113.6662
83.3587
28.2348
26.8180
f1 (ppm)


8.7941
8.7898
8.7778
8.7737
8.7697
7.8736
7.8347
7.6510
7.6294
7.4734
7.4345
6.9663
6.9446
3.9915
3.8713
1.6398
O
O
OtBu
PMP
43
CO2Me
2.8940
1.0000
1.9922
1.0064
2.0953
3.0216
3.0353
9.1135
f1 (ppm)


188.8714
165.9883
164.4482
162.1968
146.1697
139.2080
134.0250
133.3463
133.2874
132.9619
131.1568
130.7308
127.4320
118.9185
114.6547
82.4936
55.6092
52.7464
28.3296
f1 (ppm)