Synthesis of Allenyl Esters by Horner-Wadsworth-Emmons Reactions of Ketenes Mediated by *i*-PrMgBr

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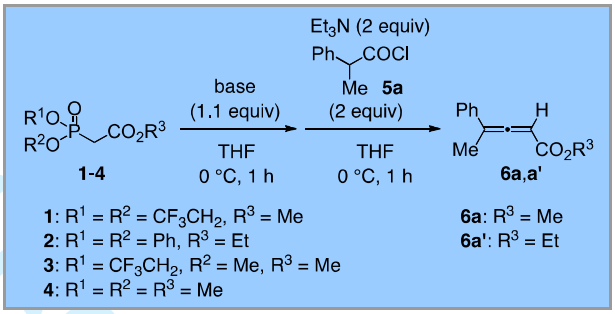
Abstract: The synthesis of conjugated allenyl esters (tri-substituted allenes) was achieved by the Mg(II)-mediated Horner-Wadsworth-Emmons reaction of methyl bis(2,2,2-trifluoroethyl)phosphonoacetate with di-substituted ketenes. In addition, a novel access to α-fluorinated allenyl carboxamides (tetra-substituted allenes) is presented.

Key words: Horner-Wadsworth-Emmons reaction, allene, ketene, Grignard reagent, fluorine

Since the first synthesis of glutinic acid (allene-1,3-dicarboxylic acid) in 1887,[1] allenes have attracted considerable attention as chemical curiosities.[2] Furthermore, allene derivatives have recently been established as versatile building blocks in organic synthesis, including asymmetric synthesis.[3] Allenic structures are also found in natural products and pharmaceutical agents.[4] We have already established a characteristic method of synthesizing conjugated allenyl esters from diethyl α-alkynyl-α-methoxy malonates via a cascade reaction,[5] and suggested the possibility of developing novel inhibitors of cysteine protease based on several biomimetic reactions using the conjugated allenyl compounds and their precursors.[6] On the other hand, the Horner-Wadsworth-Emmons (HWE) reaction of phosphonoacetates with aldehydes (or ketones) is one of the most useful methods of synthesizing α,β-unsaturated esters.[7] There are, however, only a limited number of reports concerning the HWE reaction of ketene for the preparation of allenyl esters.[8,9] We now describe a facile one-pot synthesis of allenyl esters (tri- or tetra-substituted allenes) by HWE reactions of ketenes using *i*-PrMgBr as a base.

We first investigated HWE reactions of methyl bis(2,2,2-trifluoroethyl)phosphonoacetate (Still-Gennari reagent, **1**)[10,11] with a di-substituted ketene, which was prepared in situ from 2-phenylpropionyl chloride (**5a**) and triethylamine,[12] as shown in Table 1. Phosphonoacetate **1** is a typical *Z*-selective HWE reagent due to an electron-withdrawing effect of two trifluoroethoxy groups on its phosphorus atom. As expected, the desired conjugated allenyl ester **6a** (tri-substituted allene) was obtained by the HWE reaction of **1** in good to excellent yields using bases such as *n*-BuLi, NaH, and *i*-PrMgBr (Table 1, entries 1-3). Among these, *i*-PrMgBr afforded allenyl ester **6a** in an almost quantitative yield (98%).[13,14] We have already reported stereoselective HWE reactions for the preparation of α,β-unsaturated esters using *i*-PrMgBr.[15] Thus, HWE reagents **2-4** were investigated in the HWE reaction mediated by *i*-PrMgBr for the preparation of conjugated allenyl esters **6a** and **6a'** (Table 1, entries 4-6). As a result, *Z*-selective HWE reagent **2** (Ando reagent)[16,17] also furnished **6a'** in an excellent yield (96%). It appears that increasing the *Z*-selectivity of HWE reagents in the reaction with aldehydes and ketones tends to increase the chemical yields of allenyl ester **6a** (Table 1, entries 3, 5, 6).

Table 1 HWE reactions of phosphonoacetates **1-4** with phenyl methyl ketene prepared in situ from 2-phenylpropionyl chloride (**5a**)



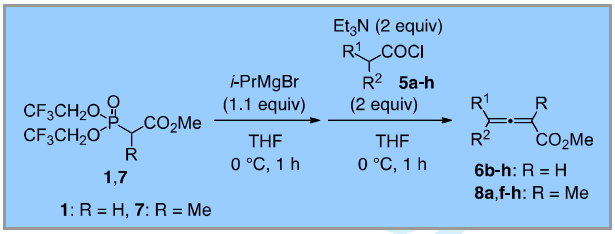
Entry	HWE reagent	Base	Yield (%)[a]
1	**1**	*n*-BuLi	68 (**6a**)
2	**1**	NaH	5 (**6a**)
3	**1**	*i*-PrMgBr	98 (**6a**)
4	**2**	*i*-PrMgBr	96 (**6a'**)
5	**3**	*i*-PrMgBr	81 (**6a**)
6	**4**	*i*-PrMgBr	72 (**6a**)

[a] Isolated yields.

To explore the substrate scope of the HWE reaction, a range of in situ−generated ketenes from the corresponding acyl chlorides **5a-h** were subjected to reaction with HWE reagent **1** as shown in Table 2. In all cases investigated, HWE reactions of di-substituted ketenes derived from acyl chlorides **5b-e** proceeded smoothly to afford 90-100% yields of the desired allenyl esters **6b-e** (tri-substituted allenes) (Table 2, entries 1-4). On the other hand, the HWE reaction of mono-substituted ketenes derived from acyl chlorides **5f-h** resulted in the formation of allenyl esters **6f-h** (di-substituted allenes) in low yields (Table 2, entries

5-7). It is interesting to note that a similar HWE reaction of ketenes derived from **5f-h** with α-methylated Still-Gennari reagent (**7**)[18] afforded the corresponding allenyl esters **8f-h** (tri-substituted allenes) in higher yields than those of **6f-h** (Table 2, entries 8-10). The HWE reaction of **7** with phenyl methyl ketene derived from acyl chloride **5a** furnished allenyl esters **8a** (tetra-substituted allene) in 89% yield (Table 2, entry 11).

Table 2 HWE reactions of phosphonoacetates **1**,**7** with various ketenes prepared in situ from acid chlorides **5a-h**

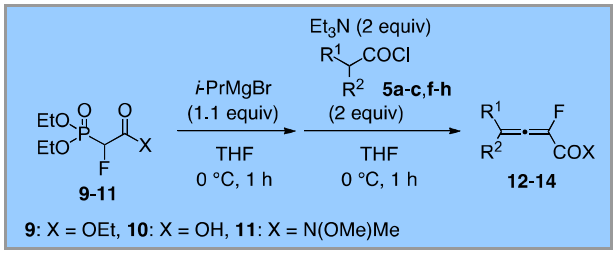


Entry	HWE reagent	R^1	R^2	Yield (%)[a]
1	**1** (R = H)	Ph	Et	100 (**6b**)
2	**1** (R = H)	Ph	Ph	100 (**6c**)
3	**1** (R = H)	4-NO_2Ph	Me	90 (**6d**)
4	**1** (R = H)	4-MeOPh	Me	97 (**6e**)
5	**1** (R = H)	Ph	H	29 (**6f**)
6	**1** (R = H)	Bn	H	38 (**6g**)
7	**1** (R = H)	*n*-C_6H_{13}	H	22 (**6h**)
8	**7** (R = Me)	Ph	H	40 (**8f**)
9	**7** (R = Me)	Bn	H	69 (**8g**)
10	**7** (R = Me)	*n*-C_6H_{13}	H	65 (**8h**)
11[b]	**7** (R = Me)	Ph	Me	89 (**8a**)

[a] Isolated yields.
[b] Reaction mixture was stirred for 3 h.

We next investigated the use of ethyl 2-fluoro-2-diethylphosphonoacetate (**9**)[19,20] in place of **1** as the HWE reagent in order to obtain a fluorinated allenyl ester. To the best of our knowledge, there are very few examples of the synthesis of α-fluorinated allenyl esters.[21] As a result, the desired product **12a** (tetra-substituted allene) was obtained in moderate yield (Table 3, entry 1). However, the HWE reaction of phosphonoacetic acid **10** using a 2.1 equivalent of *i*-PrMgBr did not proceed at all (Table 3, entry 2). Finally, it appeared that the HWE reaction of Weinreb amide **11**[22] with di-substituted ketenes derived from acyl chlorides **5a-c** afforded fluorinated allenyl carboxamides **14a-c** (tetra-substituted allenes) in 71-100% yields (Table 3, entries 3-8).[23] Unfortunately, poor yields of fluorinated allenyl carboxamides **14f-h** (tri-substituted allenes) were obtained in the HWE reaction of Weinreb amide **11** with mono-substituted ketenes derived from acyl chlorides **5f-h** (Table 3, entries 9-12).

Table 3 HWE reactions of α-fluorophosphonoacetates **9**-**11** with various ketenes prepared in situ from acid chlorides **5a-c**,**f-h**



Entry	HWE reagent	R^1	R^2	Yield (%)[a]
1	**9** (X = OEt)	Ph	Me	ca. 57 (**12a**)[b]
2[c]	**10** (X = OH)	Ph	Me	0 (**13a**)
3	**11** [X = N(OMe)Me]	Ph	Me	71 (**14a**)
4[d]	**11** [X = N(OMe)Me]	Ph	Me	90 (**14a**)
5[e]	**11** [X = N(OMe)Me]	Ph	Me	100 (**14a**)
6	**11** [X = N(OMe)Me]	Ph	Et	71 (**14b**)
7[e]	**11** [X = N(OMe)Me]	Ph	Et	94 (**14b**)
8	**11** [X = N(OMe)Me]	Ph	Ph	92 (**14c**)
9	**11** [X = N(OMe)Me]	Ph	H	0 (**14f**)[f]
10	**11** [X = N(OMe)Me]	Bn	H	0 (**14g**)[g]
11[e]	**11** [X = N(OMe)Me]	Bn	H	ca. 14 (**14g**)[b,h]
12	**11** [X = N(OMe)Me]	*n*-C_6H_{13}	H	0 (**14h**)[i]

[a] Isolated yields.
[b] Small amount of impurities were included.
[c] 2.1 equiv of *i*-PrMgBr was used.
[d] Reaction mixture was stirred for 3 h.
[e] Reaction mixture was stirred for 18 h.
[f] HWE reagent **11** was recovered (ca. 54%).
[g] HWE reagent **11** was recovered (ca. 40%).
[h] HWE reagent **11** was recovered (ca. 20%).
[i] HWE reagent **11** was not recovered.

In conclusion, we have developed a facile method of synthesizing conjugated allenyl esters **6** and **8** by the Mg(II)-mediated HWE reaction of **1** and **7** with di-substituted ketenes, which were prepared in situ from the corresponding acid chlorides. For the first time, α-fluorinated allenyl carboxamides **14** have also been prepared successfully using the Mg(II)-mediated HWE reaction of **11** with di-substituted ketenes. We believe that the proposed method of synthesizing conjugated allenyl carboxylic acid derivatives is a valuable addition to the chemistry of allenes.

Acknowledgment

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Supporting Information

Supporting information for this article is available online at http://

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(13) **Typical Procedure:** To a solution of methyl bis(2,2,2-trifluoroethyl)phosphonoacetate (**1**) (40 μL, 0.188 mmol) in anhydrous THF (1.9 mL) was added *i*-PrMgBr (0.77 mol/L in THF, 269 μL, 0.207 mmol), and the solution was stirred at 0 °C for 1 h under argon. After adding triethylamine (53 μL, 0.377 mmol) and 2-phenylpropionyl chloride (**5a**) (56 μL, 0.377 mmol), the mixture was stirred at 0 °C for 1 h under argon. The reaction mixture was treated with sat. NH_4Cl aq (2 mL) and then extracted with $CHCl_3$ (20 mL x 3). The extract was dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The oily residue was purified by silica gel column chromatography [*n*-hexane–AcOEt (12.5:1 to 11:1)] to afford allenyl ester **6a** (34.7 mg, 98%).

(14) The spectroscopic data of **6a** are as follows: Pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.21 (d, J = 2.9 Hz, 3H), 3.75 (s, 3H), 5.90 (q, J = 2.9 Hz, 1H), 7.27-7.28 (m, 1H), 7.33-7.40 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.2, 52.1, 89.5, 105.5, 126.2, 127.9, 128.6, 134.3, 166.1, 214.0; IR (neat) 2951, 1948, 1722, 1495, 1437, 1392, 1263, 1209, 1151 cm^{-1}; ESIMS *m/z*: calcd for $C_{12}H_{12}NaO_2$ $[M+Na]^+$, 211.0735; found, 211.0732. Anal. Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 76.27; H, 6.54%.

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(23) The spectroscopic data of **14a** are as follows: Yellow oil (37.6 mg, 100%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.35 (d, $^{5}J_{C,F}$ = 8.3 Hz, 3H), 3.26 (s, 3H), 3.51 (s, 3H), 7.31-7.40 (m, 3H), 7.49-7.53 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.3, 33.7, 61.6, 118.9 (d, $^{3}J_{C,F}$ = 12.0 Hz), 126.8 (d, $^{5}J_{C,F}$ = 2.7 Hz), 128.7, 129.1 (d, $^{6}J_{C,F}$ = 1.7 Hz), 129.6 (d, $^{1}J_{C,F}$ = 234.8 Hz), 134.4 (d, $^{4}J_{C,F}$ = 1.7 Hz), 162.0 (d, $^{2}J_{C,F}$ = 40.1 Hz), 193.2 (d, $^{2}J_{C,F}$ = 18.7 Hz); IR (neat) 2937, 1954, 1652, 1462, 1444, 1417, 1386, 1155 cm^{-1}; ESIMS *m/z*: calcd for $C_{13}H_{14}FNNaO_2$ $[M+Na]^+$, 258.0906; found, 258.0896. Anal. Calcd for $C_{13}H_{14}FNO_2$: C, 66.37; H, 6.00; N, 5.95. Found: C, 66.08; H, 6.02; N, 5.89%.

Supporting Information

for

Facile Synthesis of Allenyl Esters by Horner-Wadsworth-Emmons Reactions of Ketenes Mediated by *i*-PrMgBr

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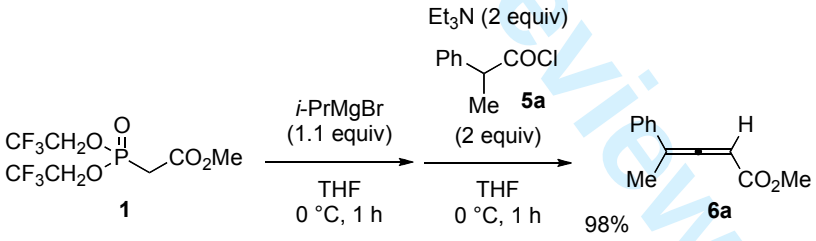
1. General Information

IR spectra were obtained using a JASCO FT/IR-6200 IR Fourier transform spectrometer. ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were recorded on a Bruker AV500 spectrometers. Chemical shifts are given in δ values (parts per million) using tetramethylsilane (TMS) as an internal standard. Electron spray ionization mass spectra (ESIMS) were recorded on a Waters LCT Premier spectrometer. Elemental combustion analyses were performed using a J-SCIENCE LAB JM10. All reactions were monitored by TLC employing 0.25-mm silica gel plates (Merck 5715; 60 F_{254}). Column chromatography was carried out on silica gel [Kanto Chemical 60N (spherical, neutral); 63-210 μm]. Anhydrous THF was used as purchased from Kanto Chemical. Triethylamine was distilled prior to use. All other reagents were used as purchased.

2. Experimental Procedures and Compound Characterizations

2.1 General procedure for the preparation of allenyl esters 6a-e, 8a,f-h

Methyl 4-Phenylpenta-2,3-dienoate (**6a**)



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Methyl 4-Phenylhexa-2,3-dienoate (**6b**)

Pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.18 (t, *J* = 7.3 Hz, 3H), 2.50-2.63 (m, 2H), 3.75 (s, 3H), 5.97 (t, *J* = 3.4 Hz, 1H), 7.25-7.28 (m, 1H), 7.33-7.40 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.2, 23.0, 52.0, 91.3, 112.4, 126.4, 127.8, 128.6, 134.1, 166.3, 213.7; IR (neat) 2970, 1945, 1720, 1592, 1495, 1453, 1436, 1398, 1258, 1209, 1151, 1032 cm^{-1}; ESIMS *m*/*z*: calcd for $C_{13}H_{14}NaO_2$ $[M+Na]^+$, 225.0891; found, 225.0889.

Methyl 4,4-Diphenylbuta-2,3-dienoate (**6c**)

Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.78 (s, 3H), 6.10 (s, 1H), 7.33-7.38 (m, 10H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 52.2, 90.4, 114.2, 128.3, 128.7, 128.8, 134.2, 165.8, 214.7; IR (neat) 3420, 3058, 2950, 1942, 1723, 1493, 1435, 1386 cm^{-1}; ESIMS *m*/*z*: calcd for $C_{17}H_{14}NaO_2$ $[M+Na]^+$, 273.0891; found, 273.0871.

Methyl 4-(4-Nitrophenyl)penta-2,3-dienoate (**6d**)

Pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.25 (d, *J* = 2.8 Hz, 3H), 3.78 (s, 3H), 6.00 (q, *J* = 2.8 Hz, 1H), 7.53 (d, *J* = 8.8 Hz, 2H), 8.21 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.1, 52.3, 90.5, 104.5, 123.9, 126.9, 141.3, 147.2, 165.3, 214.5; IR (neat) 2953, 1948, 1721, 1593, 1518, 1437, 1346, 1297, 1262 cm^{-1}; ESIMS *m*/*z*: calcd for $C_{12}H_{11}NNaO_4$ $[M+Na]^+$, 256.0586; found,

256.0577.

Methyl 4-(4-Methoxyphenyl)penta-2,3-dienoate (**6e**)

Pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.18 (d, J = 2.9 Hz, 3H), 3.75 (s, 3H), 3.81 (s, 3H), 5.89 (q, J = 2.9 Hz, 1H), 6.87-6.90 (m, 2H), 7.30-7.33 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.3, 52.1, 55.3, 89.4, 105.0, 114.0, 126.2, 127.4, 159.3, 166.3, 214.0; IR (neat) 2952, 2838, 2551, 2052, 1946, 1715, 1606, 1513, 1437, 1390, 1255, 1113 cm^{-1}; ESIMS *m/z*: calcd for $C_{13}H_{14}NaO_3$ $[M+Na]^+$, 241.0841; found, 241.0824.

Methyl 2-Methyl-4-phenylpenta-2,3-dienoate (**8a**)

Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.97 (s, 3H), 2.17 (s, 3H), 3.73 (s, 3H), 7.23-7.25 (m, 1H), 7.34-7.38 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.2, 16.4, 52.2, 96.9, 103.6, 126.1, 127.4, 128.5, 135.5, 168.1, 211.4; IR (neat) 2989, 2952, 1947, 1715, 1598, 1494, 1436, 1372, 1207, 1191, 1120, 1067 cm^{-1}; ESIMS *m/z*: calcd for $C_{13}H_{14}NaO_2$ $[M+Na]^+$, 225.0891; found, 225.0882.

Methyl 2-Methyl-4-phenylbuta-2,3-dienoate (**8f**)

Pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.00 (d, J = 3.0 Hz, 3H), 3.74 (s, 3H), 6.47 (q, J = 2.9 Hz, 1H), 7.22-7.34 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.1, 52.3, 97.3, 99.1, 127.4, 127.7, 128.8, 132.4, 167.5, 212.4; IR (neat) 2951, 1949, 1716, 1435, 1274, 1122 cm^{-1}.

Methyl 2-Methyl-5-phenylpenta-2,3-dienoate (**8g**)

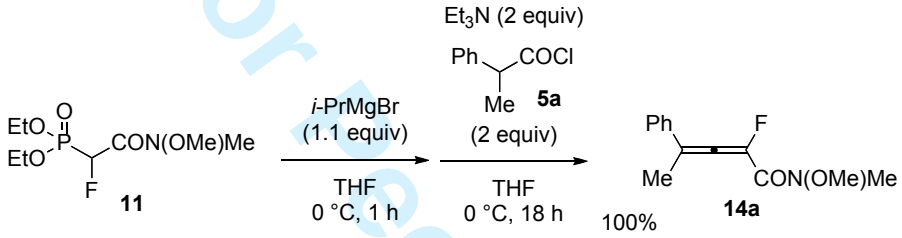
Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.86 (d, J = 2.9 Hz, 3H), 3.39-3.49 (m, 2H), 3.74 (s, 3H), 5.58-5.64 (m, 1H), 7.18-7.33 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.1, 34.7, 52.1, 93.3, 95.8, 126.5, 128.4, 128.5, 139.2, 168.2, 210.7; IR (neat) 2951, 1960, 1716, 1435, 1275, 1122 cm^{-1}.

Methyl 2-Methyldeca-2,3-dienoate (**8h**)

Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.89 (t, J = 6.8 Hz, 3H), 1.23-1.39 (m, 6H), 1.40-1.47 (m, 2H), 1.86 (d, J = 2.9 Hz, 3H), 2.10 (q, J = 7.1 Hz, 2H), 3.73 (s, 3H), 5.43-5.48 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 15.3, 22.7, 28.0, 28.6, 28.8, 31.6, 52.0, 93.9, 95.3, 168.5, 210.1; IR (neat) 2928, 2857, 1960, 1717, 1436, 1275, 1123 cm^{-1}.

2.2 General procedure for the preparation of allenyl carboxamides 14a-c

2-Fluoro-*N*-methoxy-*N*-methyl-4-phenylpenta-2,3-dienamide (**14a**)



To a solution of diethyl {1-fluoro-2-[methoxy(methyl)amino]-2-oxoethyl}phosphonate (**11**) (40.0 mg, 0.156 mmol) in anhydrous THF (1.6 mL) was added *i*-PrMgBr (0.74 mol/L in THF, 231 μL, 0.171 mmol), and the solution was stirred at 0 °C for 1 h under argon. After adding triethylamine (43 μL, 0.311 mmol) and 2-phenylpropionyl chloride (**5a**) (46 μL, 0.311 mmol), the mixture was stirred at 0 °C for 18 h under argon. The reaction mixture was treated with sat. NH_4Cl aq (5 mL) and then extracted with $CHCl_3$ (50 mL x 3). The extract was dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The oily residue was purified by silica gel column chromatography [$CHCl_3$–AcOEt (50:1)] to afford α-fluorinated allenyl carboxamide **14a** (37.6 mg, 100%). Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.35 (d, $^{5}J_{C,F}$ = 8.3 Hz, 3H), 3.26 (s, 3H), 3.51 (s, 3H), 7.31-7.40 (m, 3H), 7.49-7.53 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.3, 33.6, 61.6, 118.9 (d, $^{3}J_{C,F}$ = 12.0 Hz), 126.8 (d, $^{5}J_{C,F}$ = 2.7 Hz), 128.7, 129.1 (d, $^{6}J_{C,F}$ = 1.7 Hz), 129.6 (d, $^{1}J_{C,F}$ = 234.8 Hz), 134.4 (d, $^{4}J_{C,F}$ = 1.7 Hz), 162.0 (d, $^{2}J_{C,F}$ = 40.1 Hz), 193.2 (d, $^{2}J_{C,F}$ = 18.7 Hz); IR (neat) 2937, 1954, 1652, 1462, 1444, 1417, 1386, 1155 cm^{-1}; ESIMS *m*/*z*: calcd for $C_{13}H_{14}FNNaO_2$ $[M+Na]^+$, 258.0906;

found, 258.0896. Anal. Calcd for $C_{13}H_{14}FNO_2$: C, 66.37; H, 6.00; N, 5.95. Found: C, 66.08; H, 6.02; N, 5.89%.

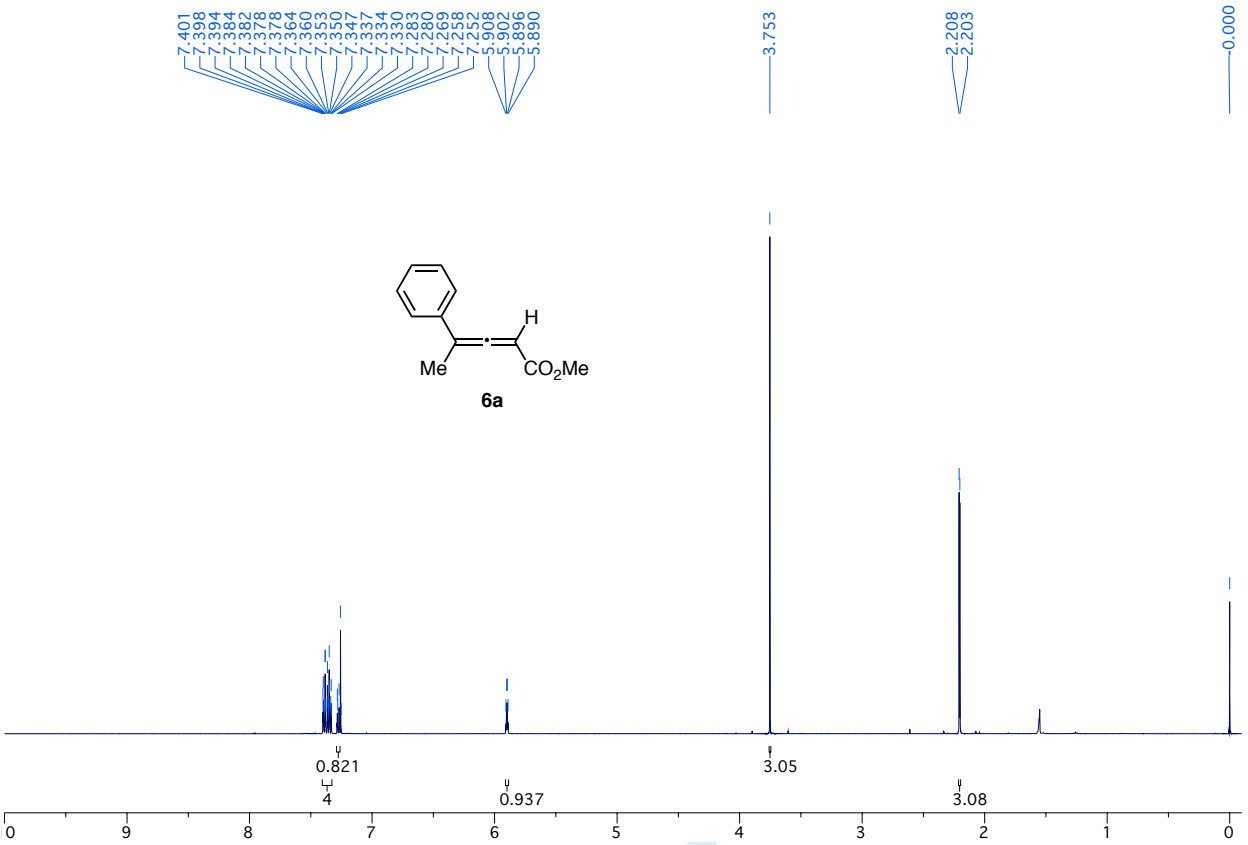
2-Fluoro-*N*-methoxy-*N*-methyl-4-phenylhexa-2,3-dienamide (**14b**)

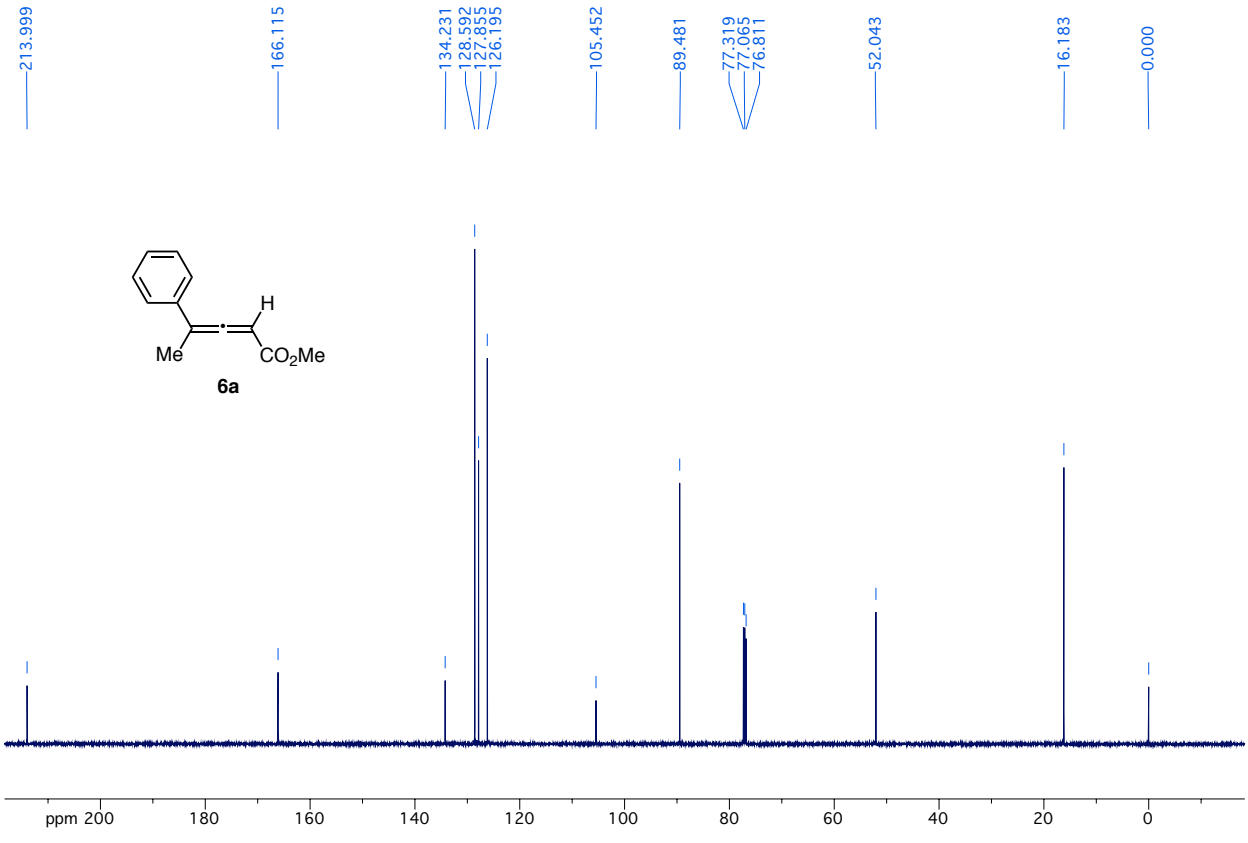
Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.23 (t, J = 7.3 Hz, 3H), 2.63-2.79 (m, 2H), 3.25 (s, 3H), 3.48 (s, 3H), 7.30-7.40 (m, 3H), 7.49-7.53 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.0 (d, $^5J_{C,F}$ = 1.8 Hz), 25.0, 33.7, 61.5, 125.9 (d, $^3J_{C,F}$ = 12.1 Hz), 126.9 (d, $^5J_{C,F}$ = 2.6 Hz), 128.8, 129.1 (d, $^6J_{C,F}$ = 1.7 Hz), 132.2 (d, $^1J_{C,F}$ = 234.6 Hz), 134.3 (d, $^4J_{C,F}$ = 1.7 Hz), 162.2 (d, $^2J_{C,F}$ = 40.2 Hz), 192.8 (d, $^2J_{C,F}$ = 18.8 Hz); IR (neat) 2972, 2937, 1950, 1660, 1456, 1384, 1153 cm^{-1}; ESIMS *m*/*z*: calcd for $C_{14}H_{16}FNNaO_2$ $[M+Na]^+$, 272.1063; found, 272.1061. Anal. Calcd for $C_{14}H_{16}FNO_2$: C, 67.45; H, 6.47; N, 5.62. Found: C, 67.16; H, 6.54; N, 5.47%.

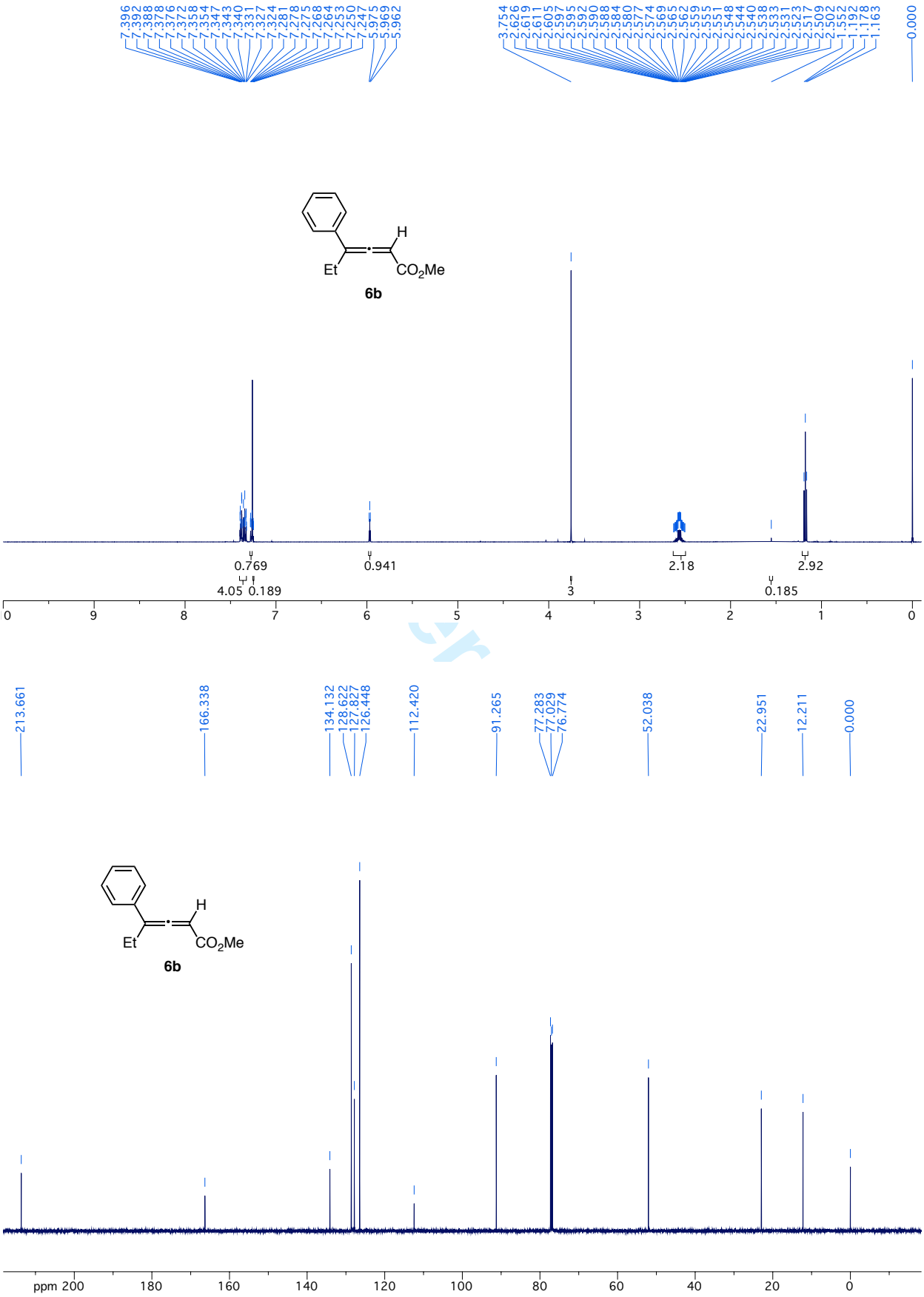
2-Fluoro-*N*-methoxy-*N*-methyl-4,4-diphenylbuta-2,3-dienamide (**14c**)

Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.28 (s, 3H), 3.40 (s, 3H), 7.38-7.42 (m, 6H), 7.44-7.47 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 33.7, 61.7, 125.6 (d, $^3J_{C,F}$ = 12.1 Hz), 128.7 129.1 (d, $^5J_{C,F}$ = 3.1 Hz), 129.2, 131.0 (d, $^1J_{C,F}$ = 235.1 Hz), 134.7, 161.5 (d, $^2J_{C,F}$ = 39.9 Hz), 195.6 (d, $^2J_{C,F}$ = 19.2 Hz); IR (neat) 2936, 1945, 1660, 1444, 1385, 1155 cm^{-1}; ESIMS *m*/*z*: calcd for $C_{18}H_{16}FNNaO_2$ $[M+Na]^+$, 320.1063; found, 320.1060.

3. NMR spectra



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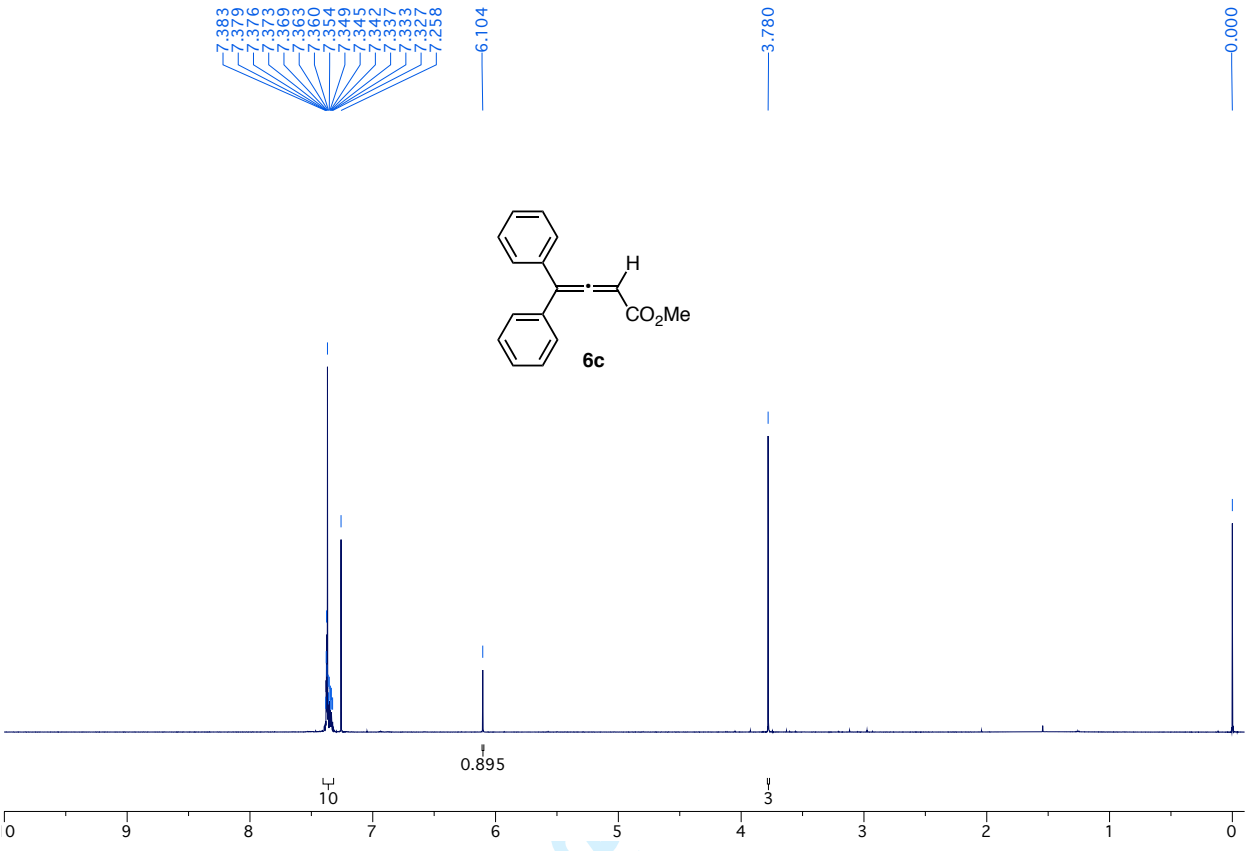
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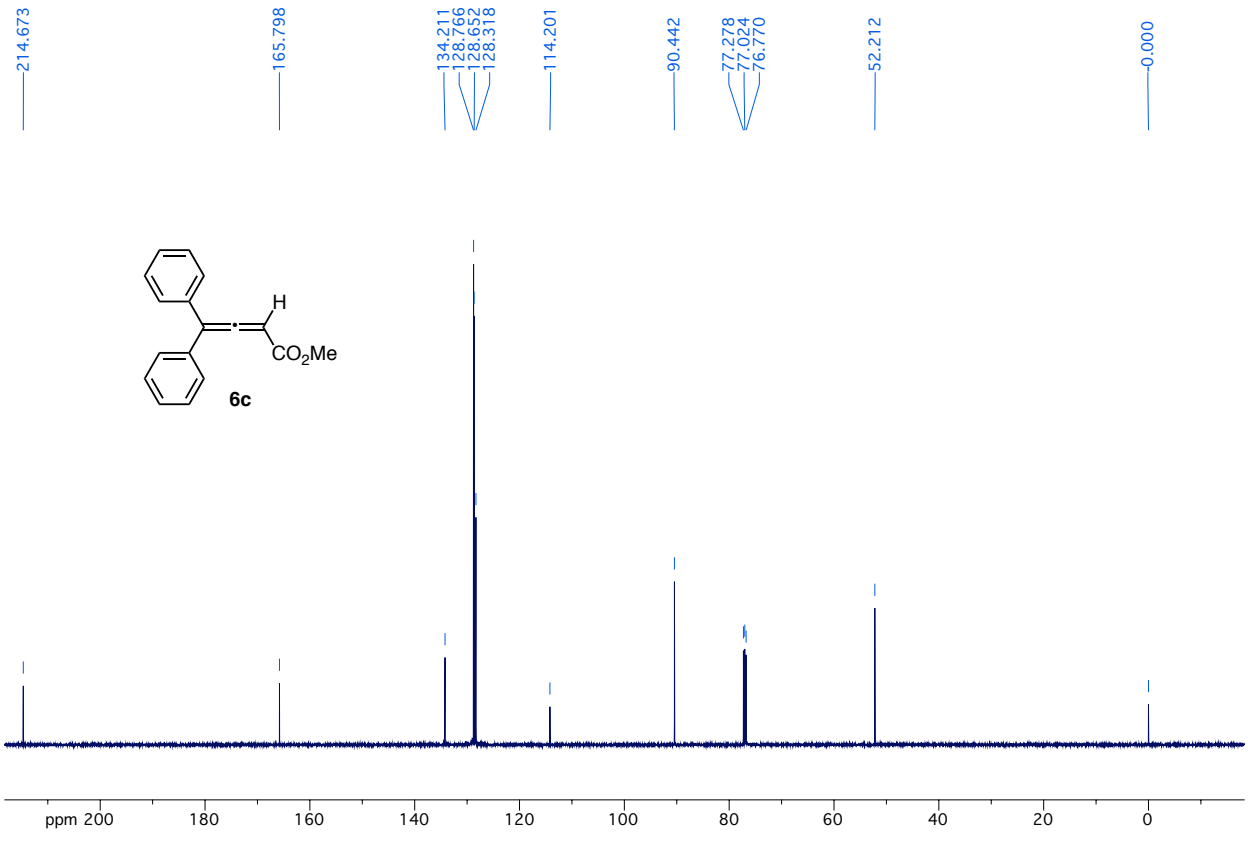
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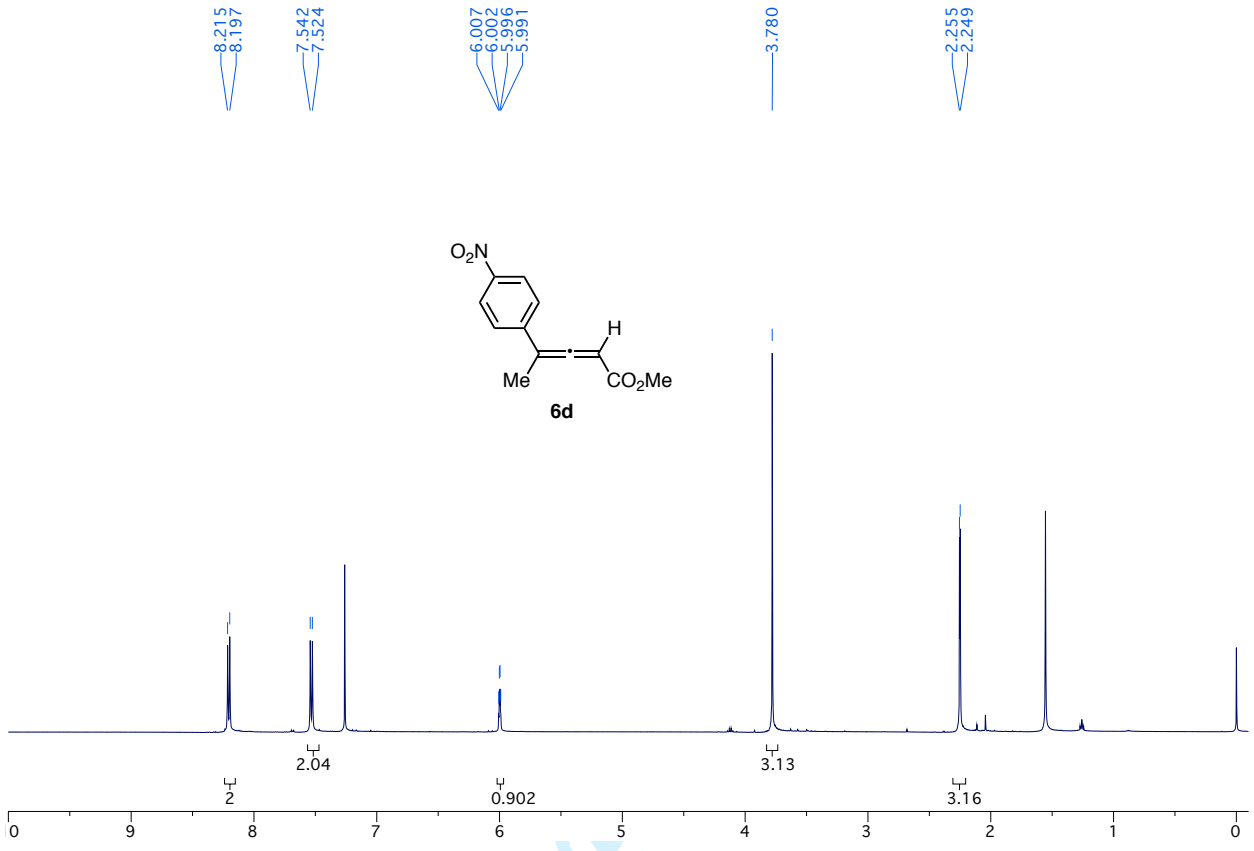
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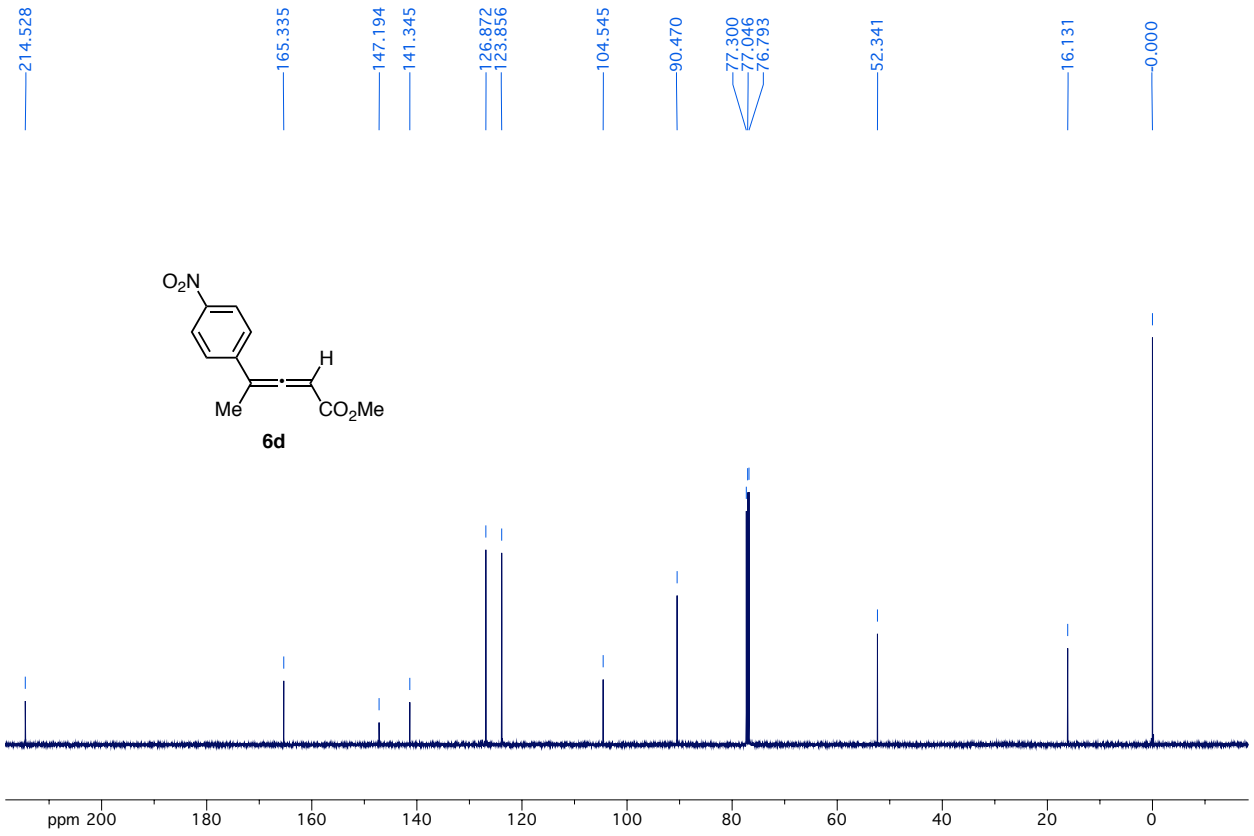
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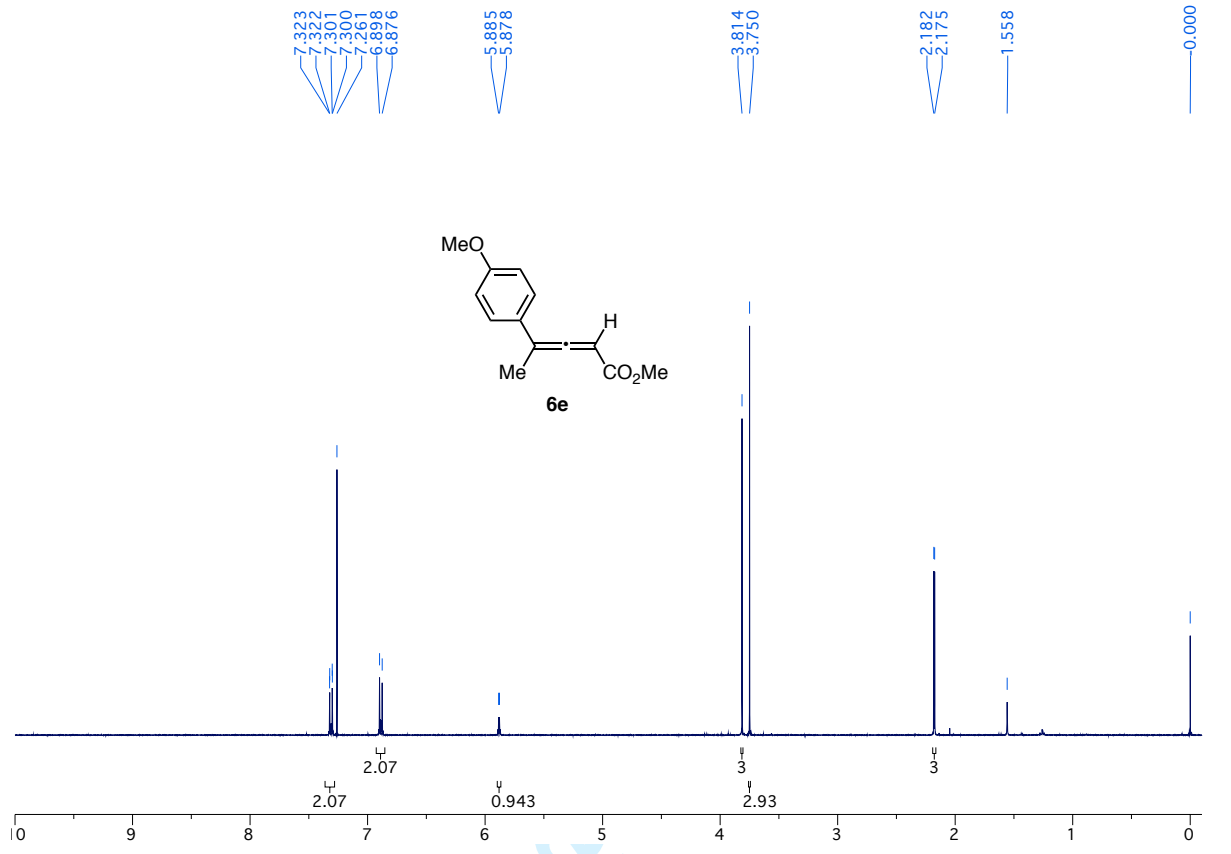
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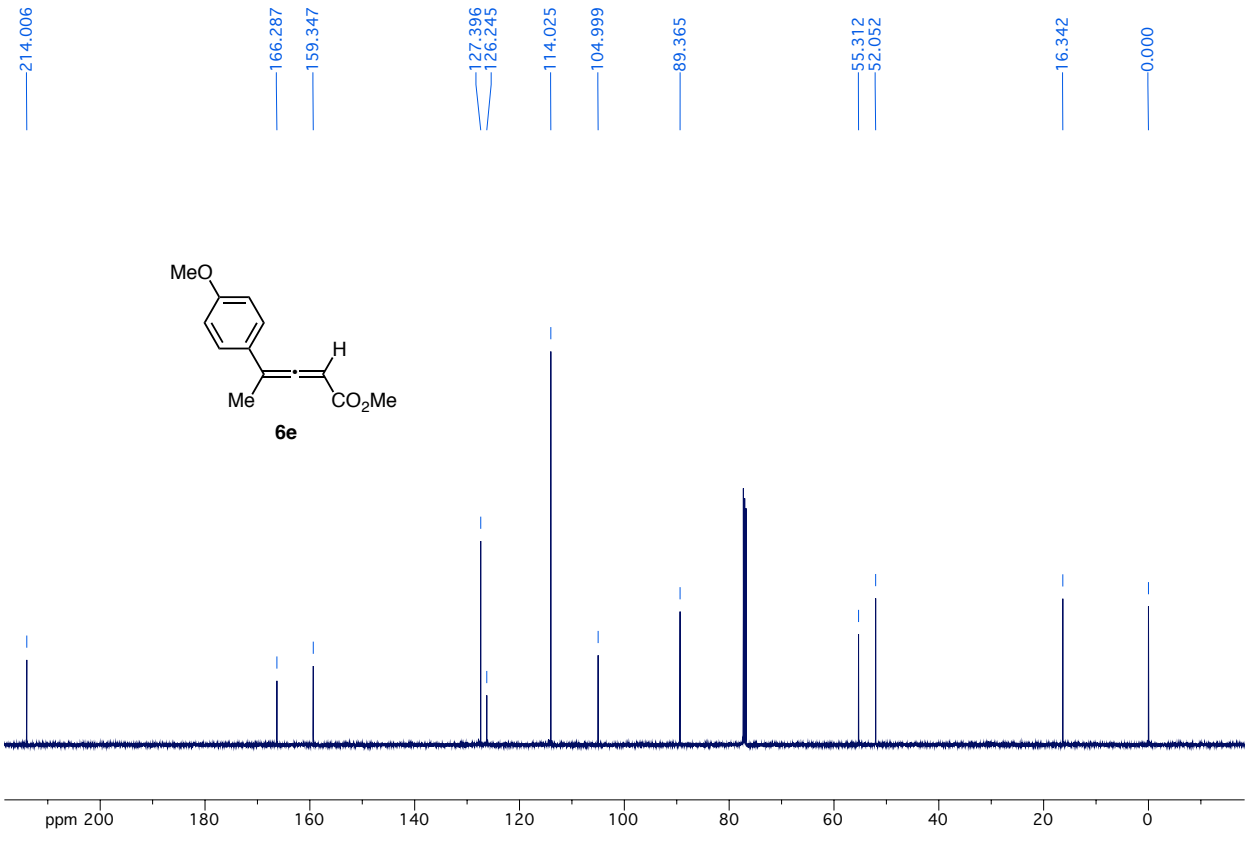
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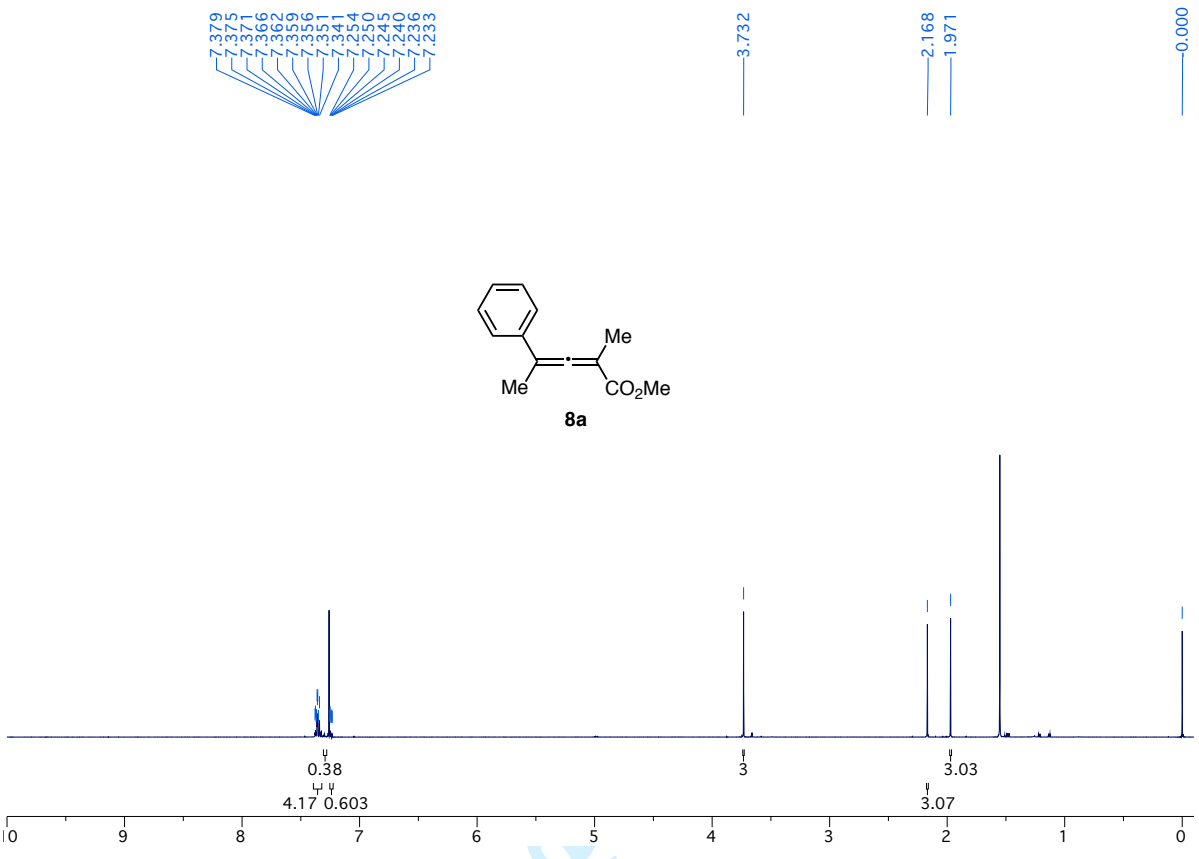
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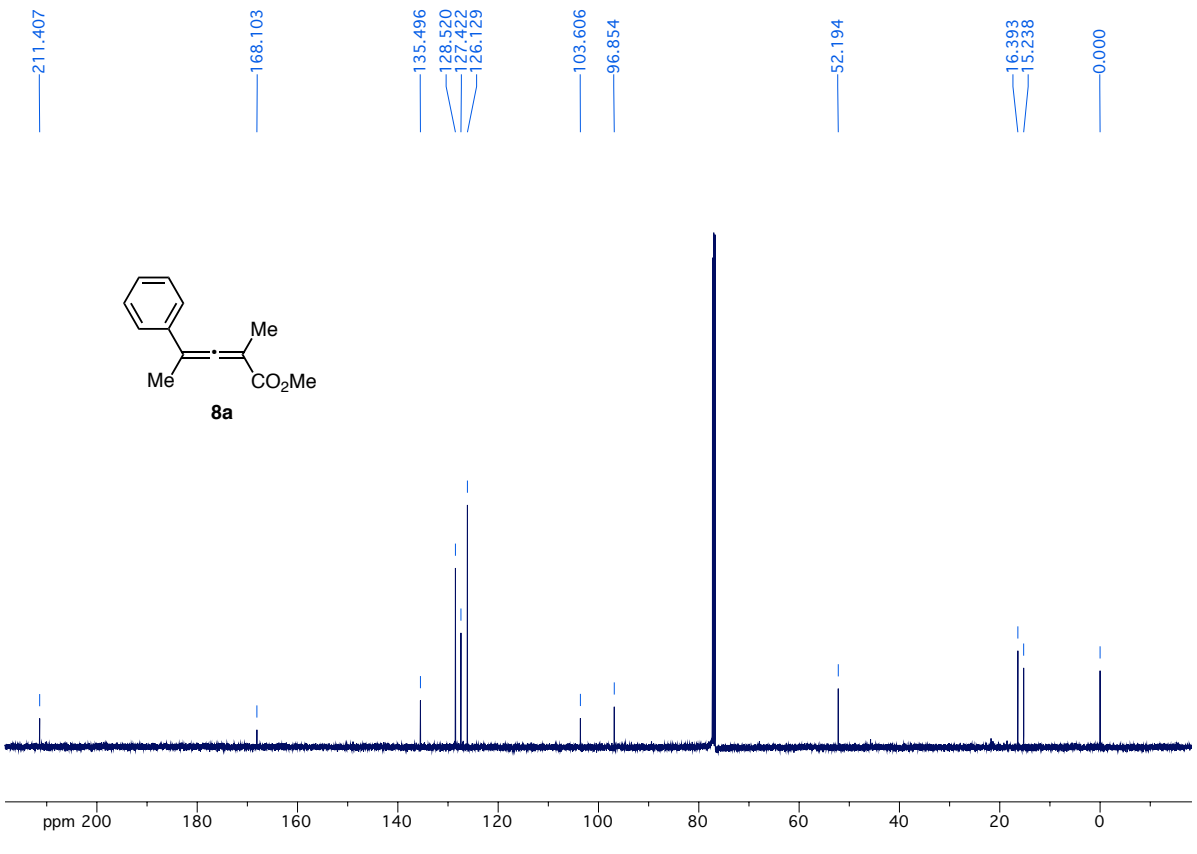
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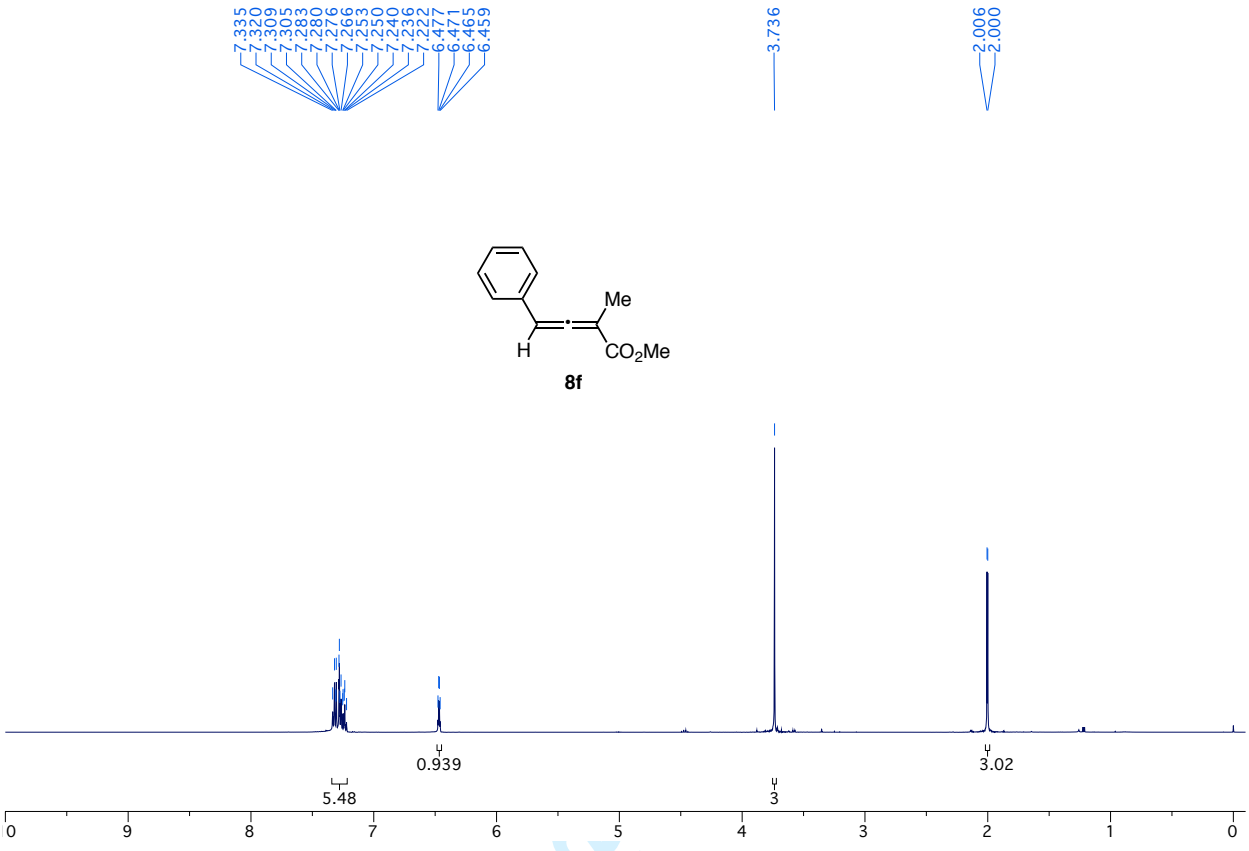
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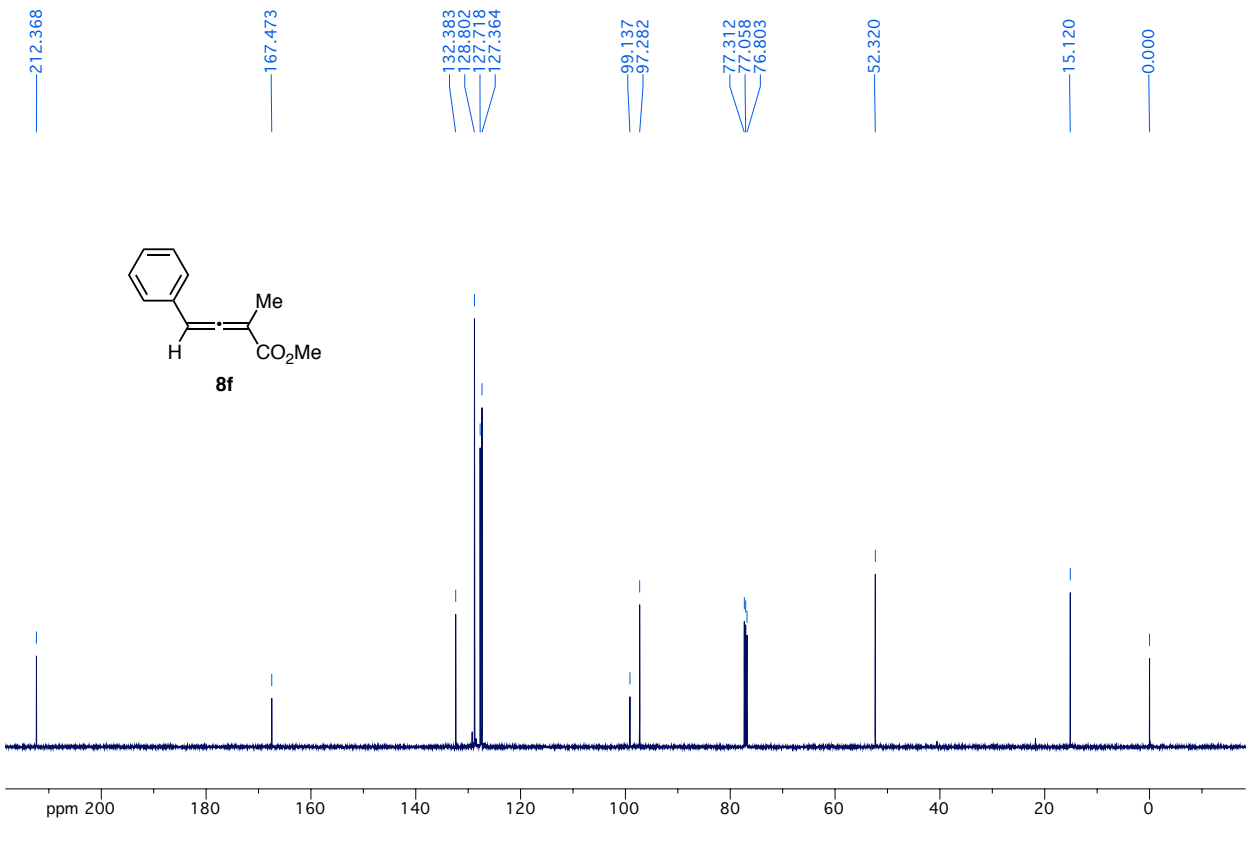
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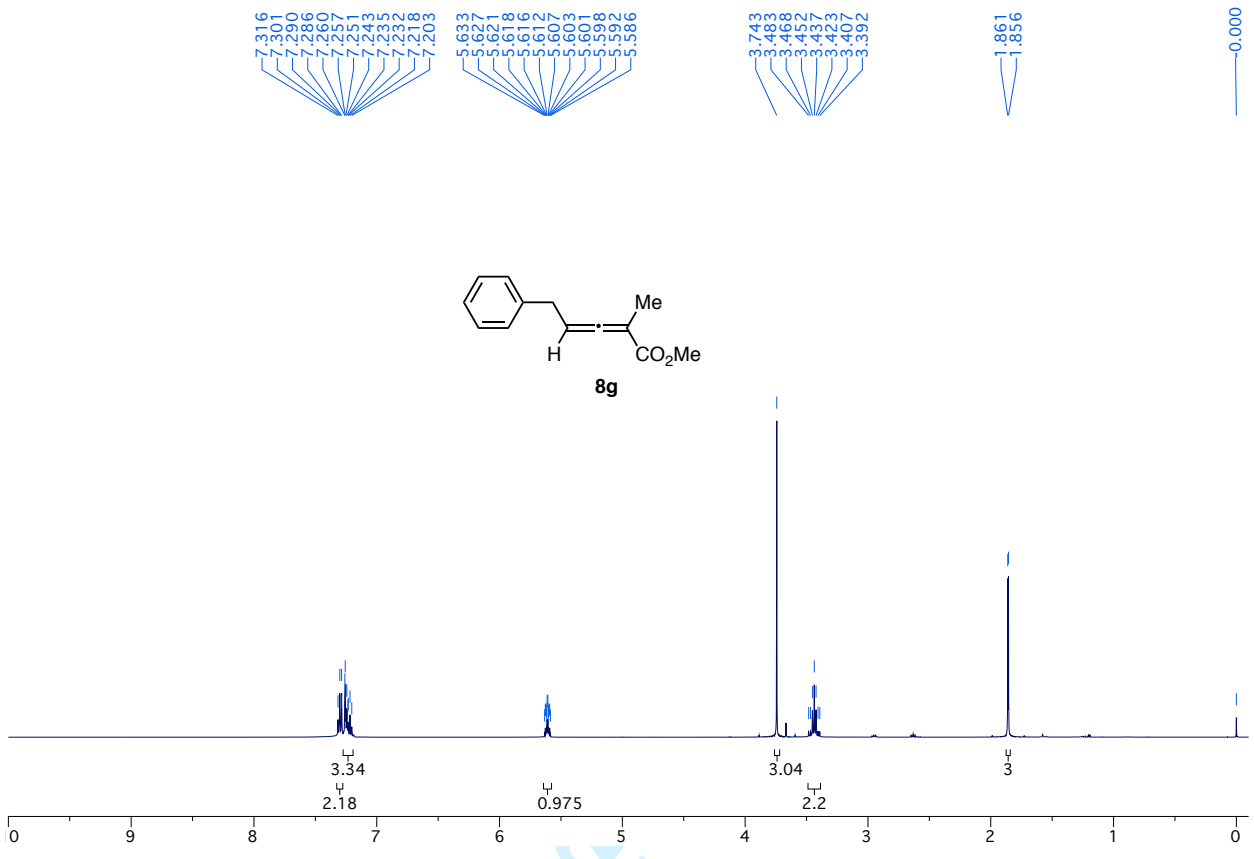
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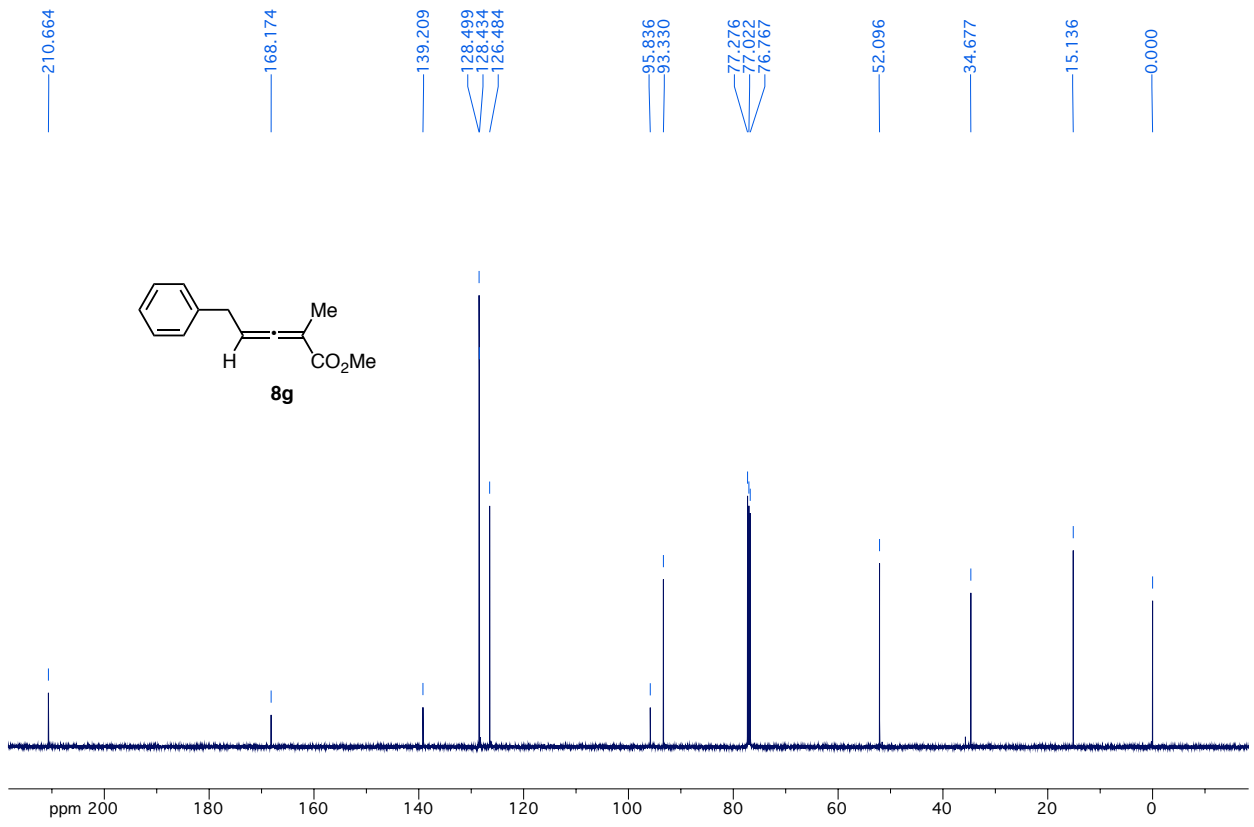
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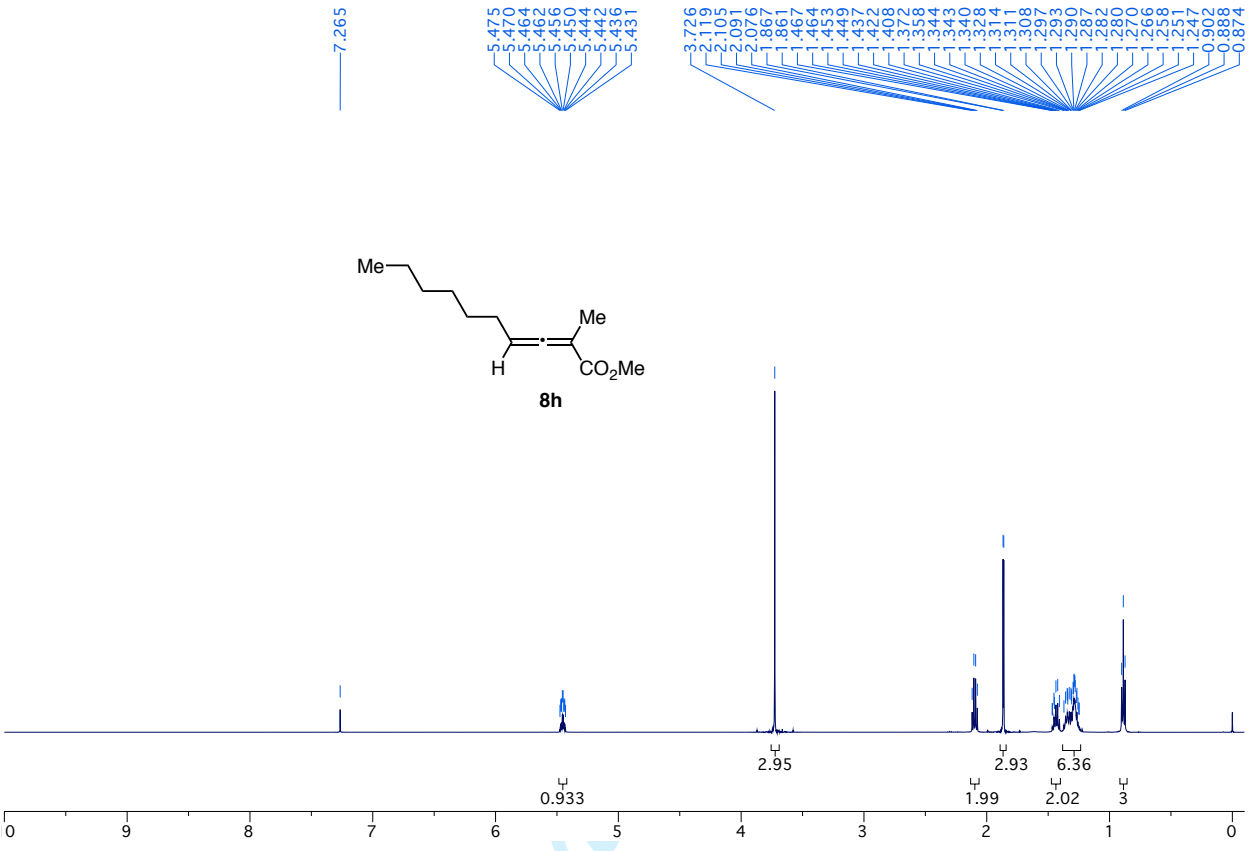
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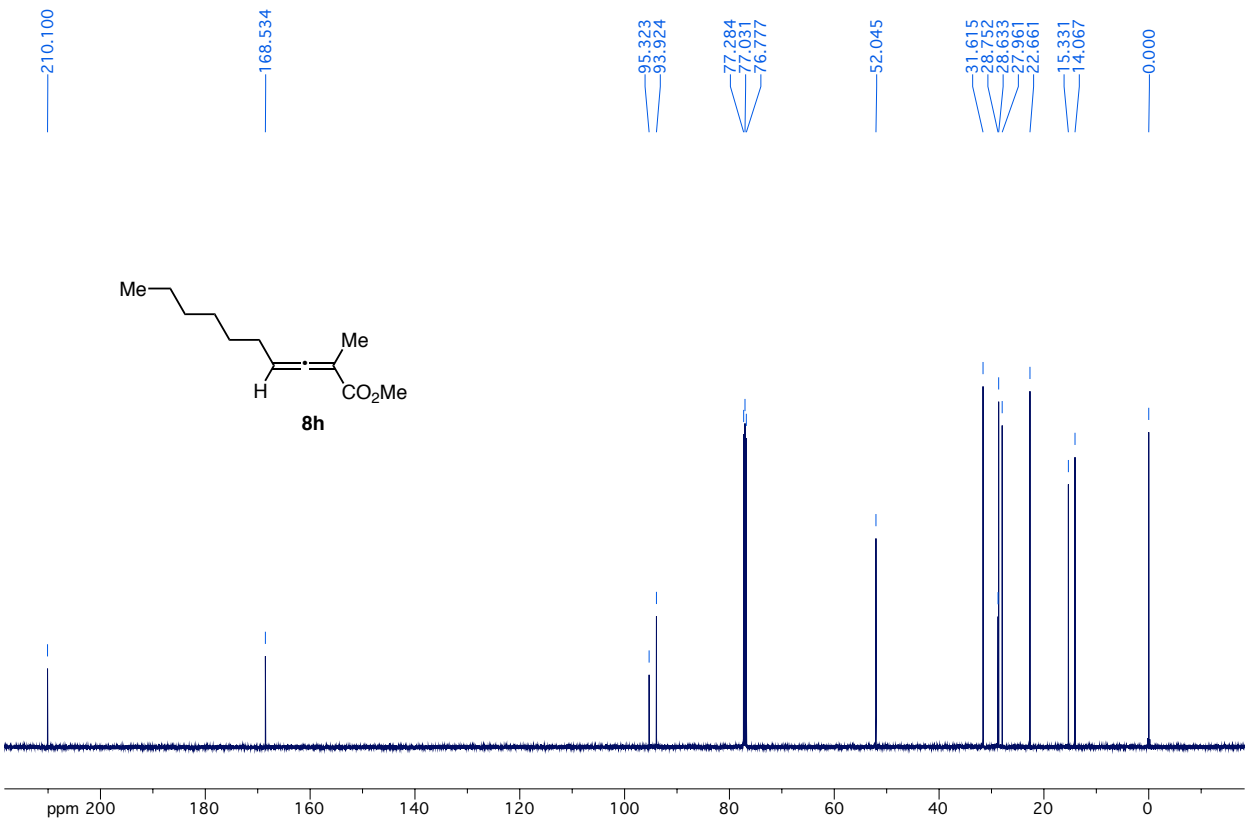
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15.331
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Me
H
CO2Me
8h
ppm 200
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140
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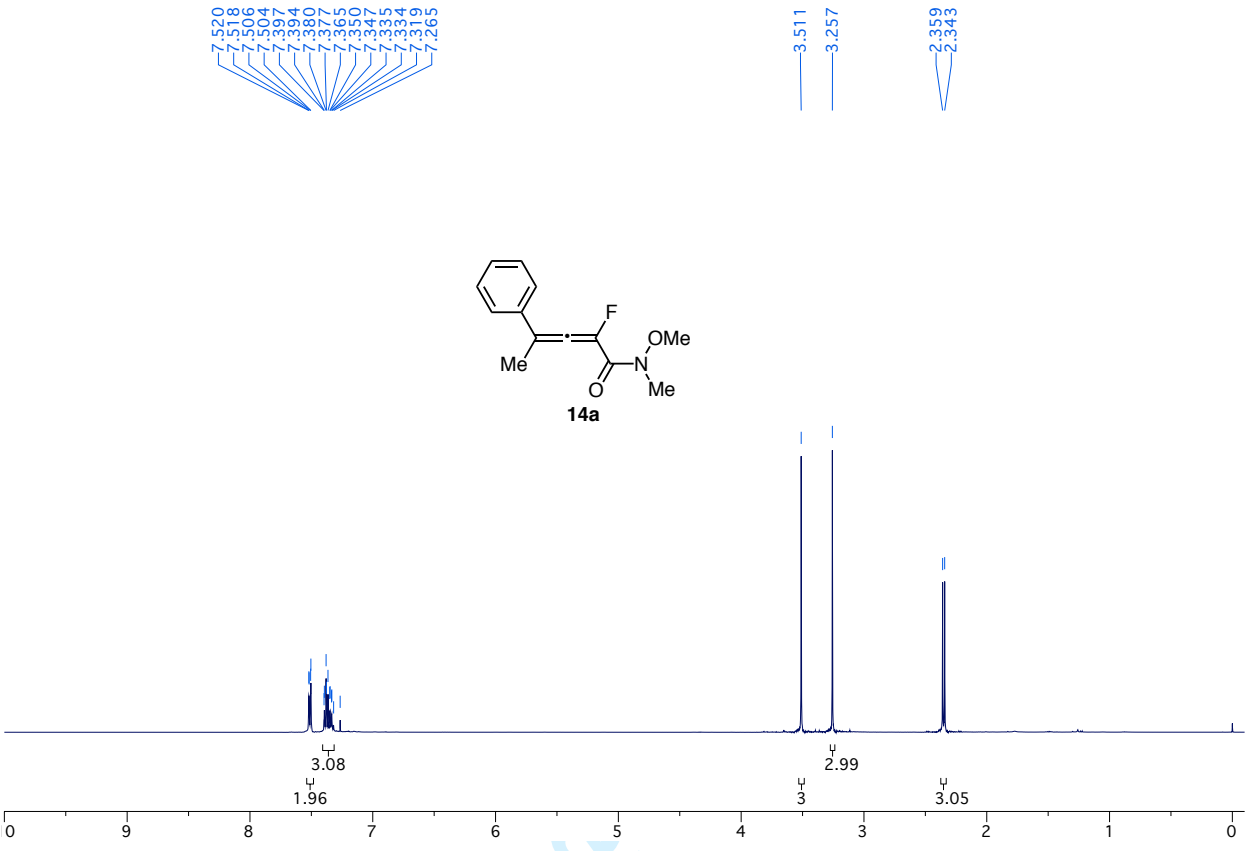
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7.377
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7.334
7.319
7.265
3.511
3.257
2.359
2.343
F
OMe
Me
N
O
Me
14a
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3
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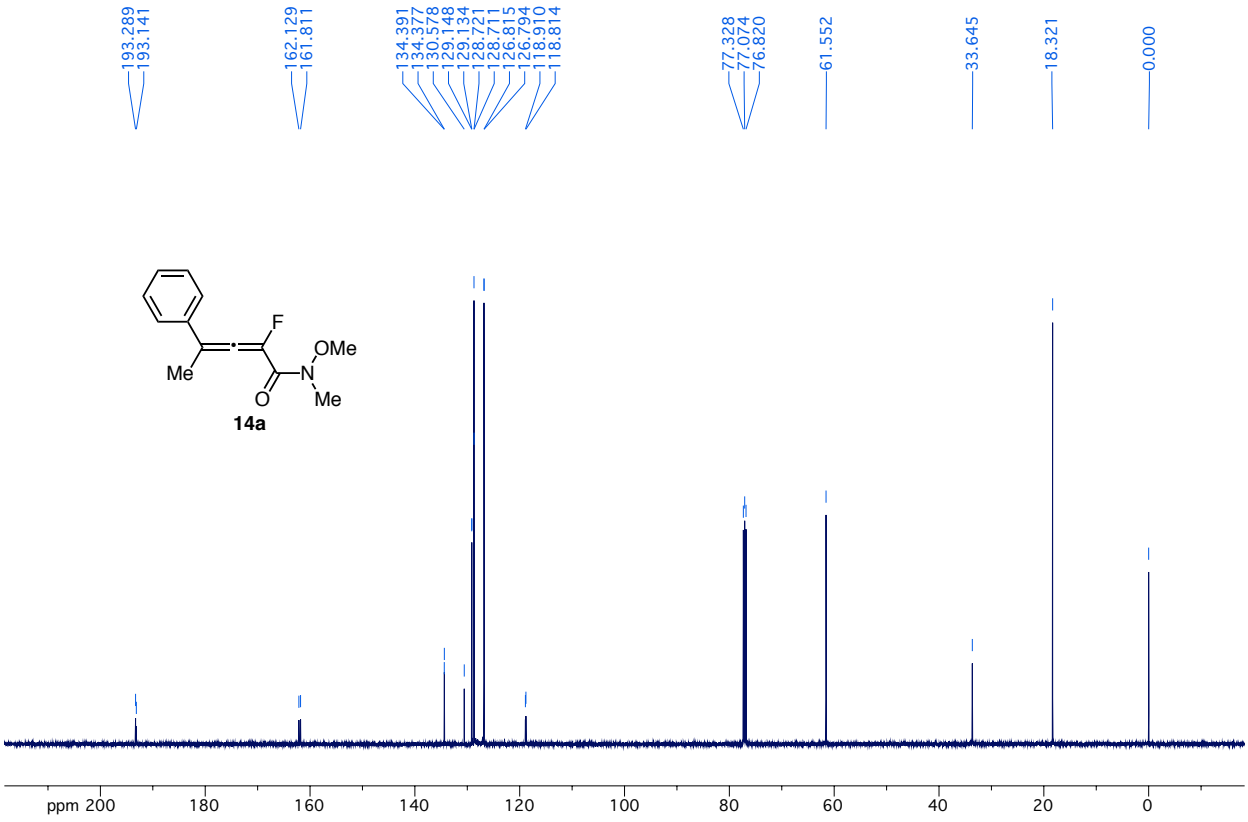
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128.711
126.815
126.794
118.910
118.814
77.328
77.074
76.820
61.552
33.645
18.321
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Me
N
O
Me
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ppm 200
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140
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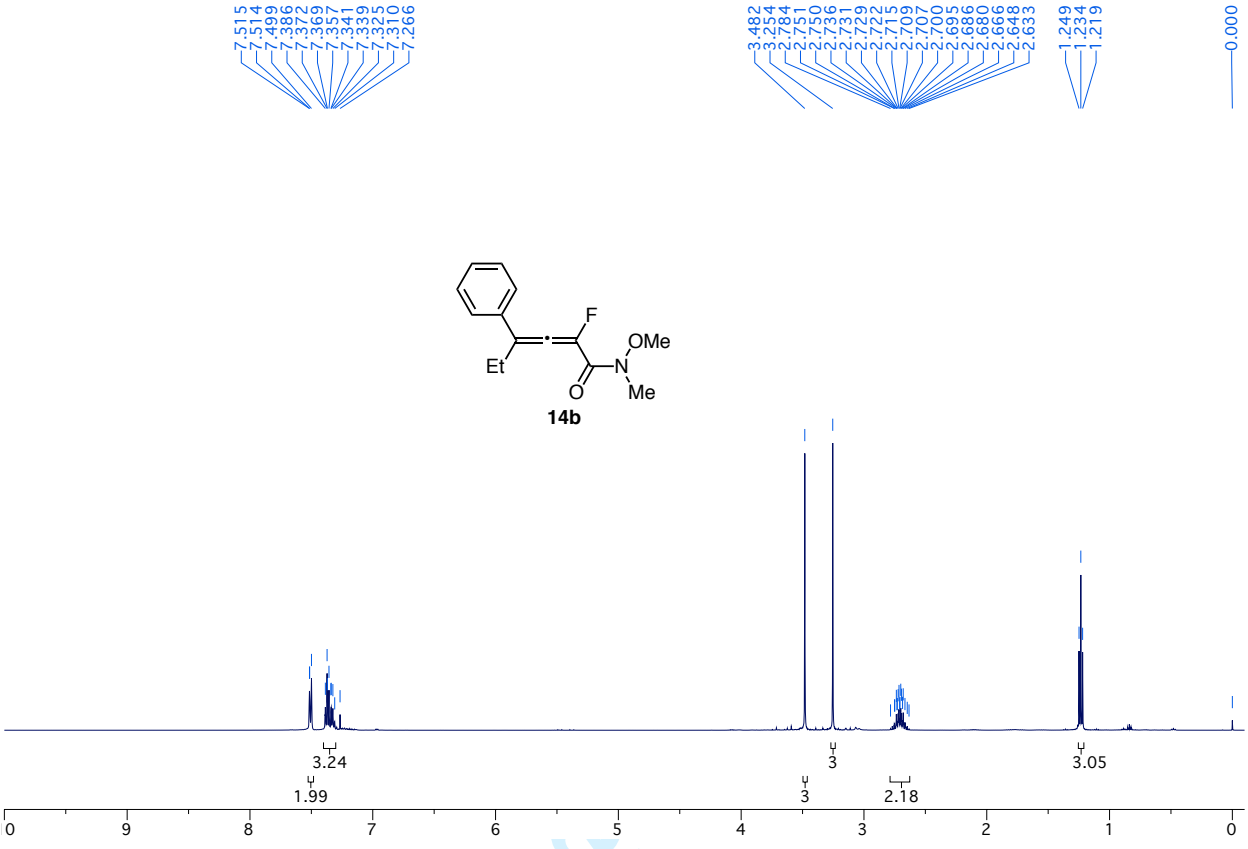
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7.514
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7.369
7.357
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7.325
7.310
7.266
3.482
3.254
2.784
2.751
2.750
2.736
2.731
2.729
2.722
2.715
2.709
2.707
2.700
2.695
2.686
2.680
2.666
2.648
2.633
1.249
1.234
1.219
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OMe
Et
N
O
Me
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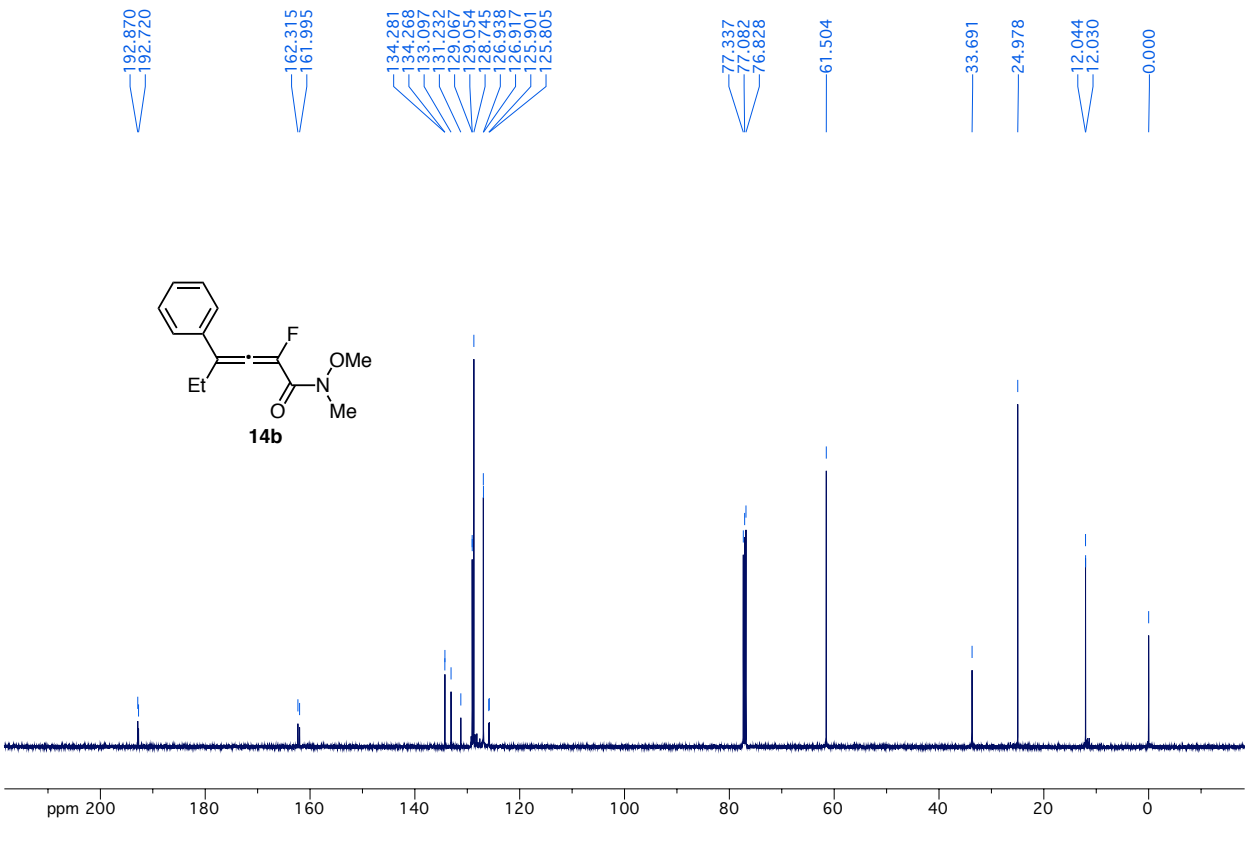
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125.901
125.805
77.337
77.082
76.828
61.504
33.691
24.978
12.044
12.030
0.000
F
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Et
N
O
Me
14b
ppm 200
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140
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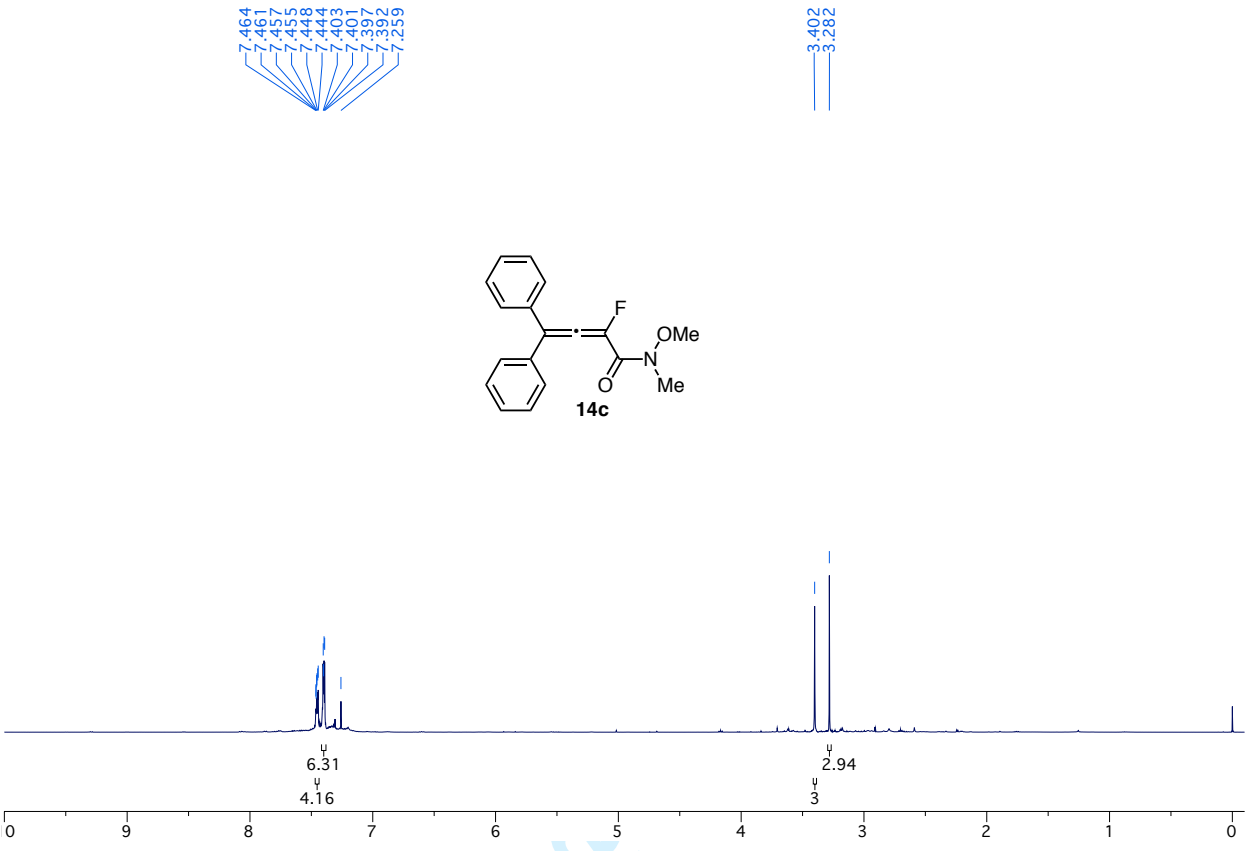
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3.402
3.282
F
OMe
N
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7
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3
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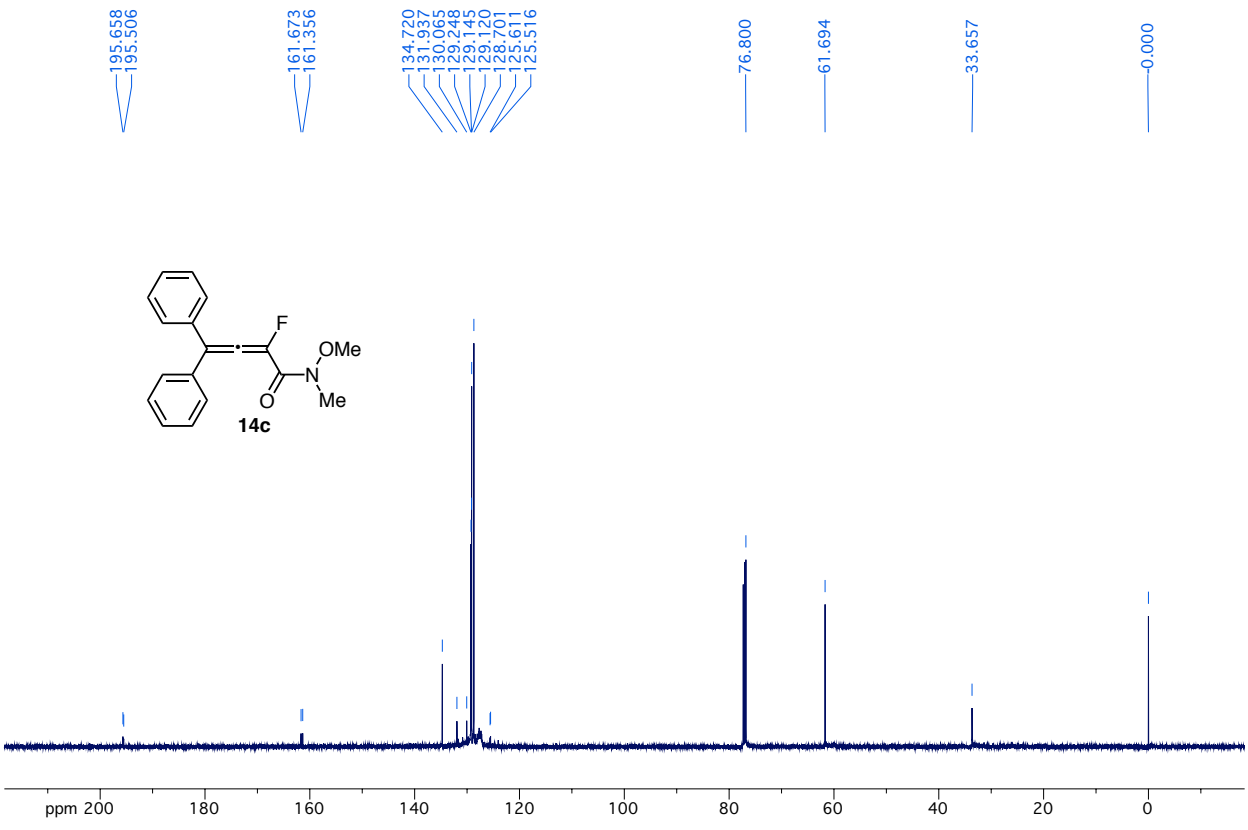
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125.516
76.800
61.694
33.657
0.000
F
OMe
N
Me
O
14c
ppm 200
180
160
140
120
100
80
60
40
20
0