Supporting Information

for

Water-Accelerated Nickel-Catalyzed α-Crotylation of Simple Ketones with 1,3-Butadiene under pH and Redox-Neutral Conditions

Tiantian Chen,[†] Haijian Yang,[†] Yang Yang,[†] Guangbin Dong*[,‡] and Dong Xing*[,†]

[†]Shanghai Engineering Research Center of Molecular Therapeutics and New Drug Development, School of Chemistry and Molecular Engineering, East China Normal University, Shanghai, China 200062

[‡]Department of Chemistry, University of Chicago, Chicago, IL 60637 (USA)

E-mail: gbdong@uchicago.edu; dxing@sat.ecnu.edu.cn

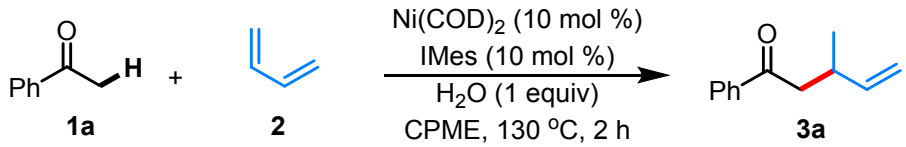
Table of Contents

1. General Information

Unless noted otherwise, all ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on Brucker spectrometers in $CDCl_3$. Tetramethylsilane (TMS) served as an internal standard ($\delta = 0$) for ^{1}H NMR, and $CDCl_3$ was used as internal standard ($\delta = 77.0$) for ^{13}C NMR. Chemical shifts are reported in parts per million as follows: chemical shift, multiplicity (s =singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad). Infrared (IR) spectra were obtained using a Bruker tensor 27 infrared spectrometer. High-resolution mass spectrometry (HRMS) was performed on either a Bruker Maxis Impact QTOF MS with ESI source or a Waters GCT-Premier TOF MS with EI source. Unless otherwise noted, solvents used for the key reactions were freshly distilled over calcium hydride or sodium. Cyclopentyl methyl ether (CPME) (99.5%, Extra Dry, stabilized) used for the key reactions was purchased from Acros and degassed with nitrogen before use. All the key reactions were carried out under nitrogen atmosphere with a stir bar in a sealed vial. Reaction temperatures were reported as the temperatures of the bather surrounding the vials. Sensitive ligands and metal catalysts and solvents were transferred under nitrogen into a nitrogen-filled glovebox with standard techniques. $Ni(COD)_2$ and NHC ligands were purchased from Strem Chemicals. ^{Me}IMes and ^{CP}IMes were synthesized according to literature procedure.[1] Ketones used for the key reactions were purified by fractional distillation (lower boiling point ketones), column isolation (liquid ketones) or recrystallization (solid ketones). 1,3-Butadiene (2 mol/L solution in THF) used for the key reactions was purchased from TCI Chemicals. All other materials were obtained from commercial sources and were used as received.

2. Experimental Procedure for the Key Reaction

2.1 The general procedure for the synthesis of α-allylic alkylation product 3 from 1 and 2.



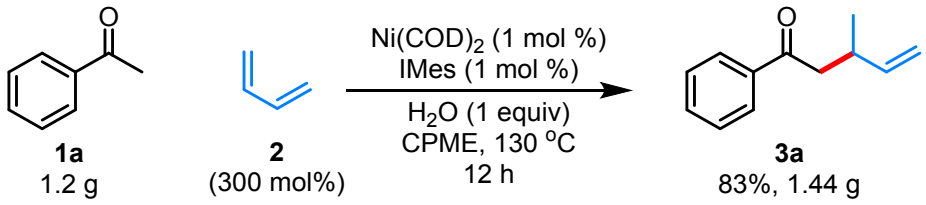
A 4-mL baked vial charged with a stir bar was transferred into glove box. To this vial was added $Ni(COD)_2$ (5.5 mg, 10 mol%), IMes (6.1 mg, 10 mol%) and 0.4 mL of CPME. This mixture was stirred for 5 min. **1a** (24 μL, 0.2 mmol) and **2** (2 M solution in THF) (300 μL, 0.6 mmol, 3 equiv) was then subsequently added followed by the addition of H_2O (3.6 μL, 0.2 mmol). The vial was tightly capped,

removed from glove box and heated at 130 °C for 2 h. After the completion of the reaction, the mixture was cooled to room temperature, diluted with ethyl acetate and passed through a short pad of silica gel. After concentration under vacuum, the crude mixture was subjected to flash chromatography (silica gel, PE/Et_2O=200:1 to 100:1) to give the desired product **3a**.

2.2 Parallel experiments with or without H_2O.

Parallel experiments between **1a** and **2** with or without H_2O were conducted under standard reaction conditions, and the reactions in different vials were stopped at 5 min, 10 min, 15 min, 30 min, 1 h, 2 h, accordingly. The yield of the product was determined by ^1H NMR by adding 1,1,2,2-tetrachloroethane as the internal standard. The reactions without H_2O were run under strictly anhydrous conditions: CPME was distilled from sodium and treated with freeze-pump-thaw technique before use. **1a** and **2** were treated with activated 4 Å molecule sieves before use.

2.3 Gram-scale synthesis of 3a



1a
1.2 g

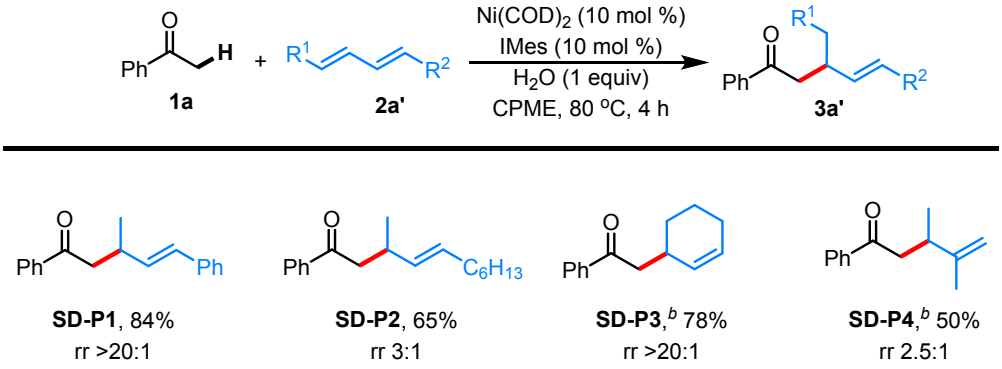
2
(300 mol%)

3a
83%, 1.44 g

A 150 mL round bottom pressure vessel charged with a stir bar was transferred into glove box. To this vessel was added $Ni(COD)_2$ (27.5 mg, 1 mol%), IMes (30 mg, 1 mol%) and 20 mL of CPME. This mixture was stirred for 5 min. **1a** (1.2 g, 10 mmol) and **2** (2 M solution in THF) (15 mL, 30 mmol, 3 equiv) was then subsequently added followed by the addition of H_2O (180 μL, 1 equiv). The vessel was tightly capped, removed from glove box and heated at 130 °C for 12 h. After the completion of the reaction, the mixture was cooled to room temperature, diluted with ethyl acetate and passed through a short pad of silica gel. After concentration under vacuum, the crude mixture was subjected to flash chromatography (silica gel, PE/Et_2O=200:1 to 100:1) to give the desired product.

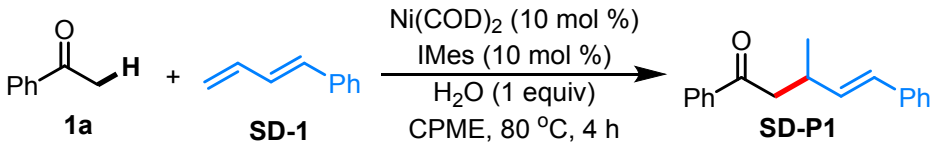
2.4 Results of substituted 1,3-dienes

Scheme S1. Substrate scope of substituted 1,3-dienes[a]



[a]Unless otherwise noted, all reactions were run on a 0.2 mmol scale of 2; reaction time = 4 h; **1a**:**2** = 1.2:1; all yields are isolated yields; regioselectivity ratio (rr) was determined by ^{1}H NMR of the reaction mixture. [b]5 equiv of 1,3-diene used.

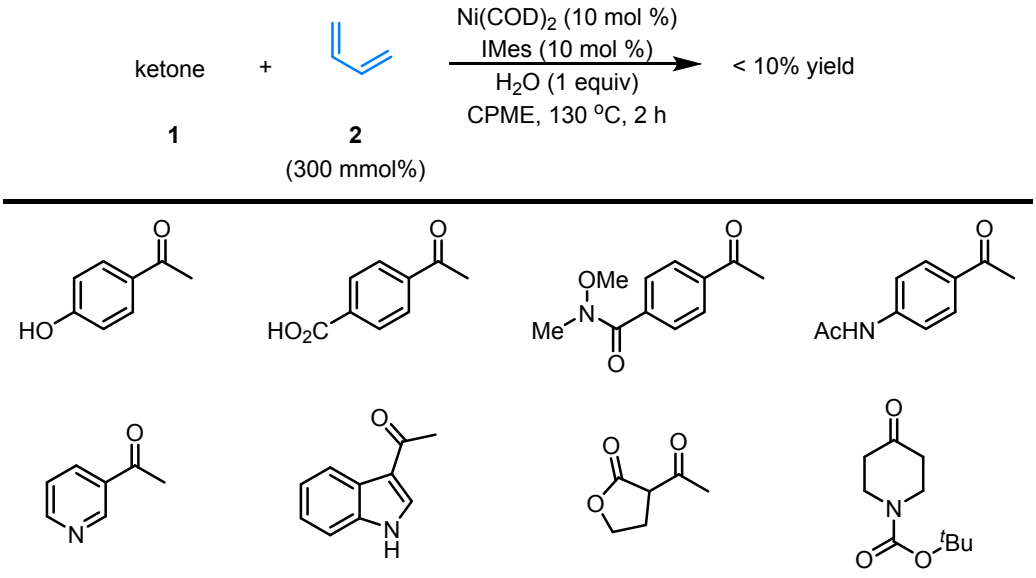
General procedure for the synthesis of α-allylic alkylation product SD-P1 from 1 and substituted diene SD-1.



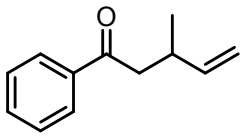
A 4-mL baked vial charged with a stir bar was transferred into glove box. To this vial was added $Ni(COD)_2$ (5.5 mg, 10 mol%), IMes (6.1 mg, 10 mol%) and 0.4 mL of CPME. This mixture was stirred for 5 min. **1a** (28.8 μL, 0.24 mmol) and **SD-1** (26 mg, 0.2 mmol) was then subsequently added followed by the addition of H_2O (3.6 μL, 0.2 mmol). The vial was tightly capped, removed from glove box and heated at 80 °C for 4 h. After the completion of the reaction, the mixture was cooled to room temperature, diluted with ethyl acetate and passed through a short pad of silica gel. After concentration in vacuum, the crude mixture was subjected to flash chromatography (silica gel, PE/Et_2O=100:1 to 70:1) to give the desired product **SD-P1**.

2.5 Results of other tested unreactive ketone substrates

Scheme S2. Unreactive Ketone Substrates (less than 10% yield).

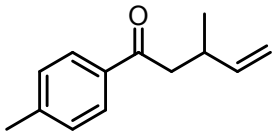


3. Characterization Data



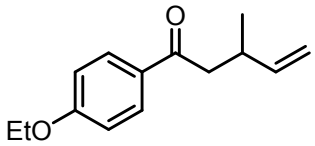
3-methyl-1-phenylpent-4-en-1-one (3a)[2]

Synthesized from acetophenone and 1,3-butadiene by following the general procedure on a 0.2 mmol scale. Yield: 84%. Colorless liquid. R_f = 0.4 (PE:Et_2O=20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 – 7.90 (m, 2H), 7.59 – 7.52 (m, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 5.95 – 5.79 (m, 1H), 5.09 – 4.92 (m, 2H), 3.09 – 2.85 (m, 3H), 1.10 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.3, 143.1, 137.3, 133.0, 128.6, 128.1, 113.0, 45.1, 33.6, 19.8.



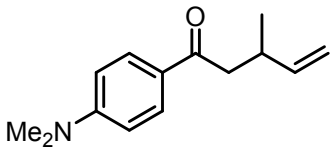
3-methyl-1-(*p*-tolyl)pent-4-en-1-one (3b)[3]

Synthesized from 1-(*p*-tolyl)ethan-1-one and 1,3-butadiene by following the general procedure on a 0.2 mmol scale. Yield: 79%. Colorless liquid. R_f = 0.6 (PE:Et_2O=20:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 10.7 Hz, 2H), 7.26 (d, J = 7.5 Hz, 2H), 5.95 – 5.73 (m, 1H), 5.08 – 4.90 (m, 2H), 3.09 – 2.77 (m, 3H), 2.41 (s, 3H), 1.09 (d, J = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.0, 143.7, 143.2, 134.8, 129.3, 128.3, 113.0, 45.0, 33.7, 21.6, 19.8.



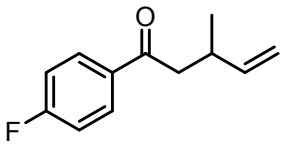
1-(4-ethoxyphenyl)-3-methylpent-4-en-1-one (3c)

Synthesized from 1-(4-ethoxyphenyl)-3-methylpent-4-en-1-one and 1,3-butadiene by following the general procedure on a 0.2 mmol scale of ketone. Yield: 74%. Colorless liquid. R_f = 0.5 (PE:Et_2O=20:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.9 Hz, 2H), 6.91 (d, J = 8.9 Hz, 2H), 5.94 – 5.79 (m, 1H), 5.06 – 4.92 (m, 2H), 4.09 (q, *J* = 7.0 Hz, 2H), 3.04 – 2.78 (m, 3H), 1.44 (t, *J* = 7.0 Hz, 3H), 1.09 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.9, 162.8, 143.2, 130.4, 130.2, 114.1, 112.9, 63.7, 44.8, 33.8, 19.8, 14.7. IR (KBr) 2970, 2930, 1672, 1639, 1598, 1575, 1508, 1419, 1305, 1169, 992 cm^{-1}. HRMS: calcd. $C_{14}H_{18}O_2Na$ $[M+Na]^+$: 241.1199. Found: 241.1200.



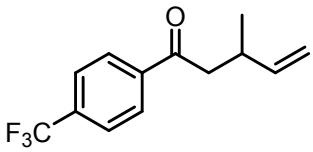
1-(4-(dimethylamino)phenyl)-3-methylpent-4-en-1-one (3d)

Synthesized from 1-(4-(dimethylamino)phenyl)ethan-1-one and 1,3-butadiene by following the general procedure on a 0.2 mmol scale. Yield: 46%. Colorless liquid. R_f = 0.45 (PE:Et_2O=20:1). ^{1}NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 9.1 Hz, 2H), 6.67 (d, *J* = 9.1 Hz, 2H), 5.95 – 5.79 (m, 1H), 5.19 – 4.85 (m, 2H), 3.08 (s, 6H), 3.01 – 2.75 (m, 3H), 1.10 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.5, 153.3, 143.6, 130.4, 125.4, 112.6, 110.6, 44.4, 40.0, 34.1, 19.8. IR (KBr) 2921, 2906, 2355, 1659, 1597, 1522, 1368, 1186, 946, 814 cm^{-1}. HRMS: calcd. $C_{14}H_{19}NONa$ $[M+Na]^+$: 240.1359. Found: 240.1376.



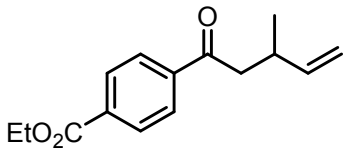
1-(4-fluorophenyl)-3-methylpent-4-en-1-one (3e)

Synthesized from 1-(4-fluorophenyl)ethan-1-one and 1,3-butadiene by following the general procedure on a 0.2 mmol scale. Yield: 77%. Colorless liquid. R_f = 0.6 (PE:Et_2O=20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 – 7.95 (m, 2H), 7.21 – 7.09 (m, 2H), 5.94 – 5.78 (m, 1H), 5.11 – 4.89 (m, 2H), 3.10 – 2.83 (m, 3H), 1.10 (d, J = 6.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.7, 165.7 (d, *J* = 254.5 Hz), 142.9, 133.7 (d, *J* = 2.9 Hz), 130.7 (d, *J* = 9.2 Hz), 115.6 (d, *J* = 21.8 Hz), 113.1, 45.0, 33.6, 19.8. IR (KBr) 2969, 2960, 2924, 2177, 1978, 1685, 1596, 1229, 996, 833 cm^{-1}. HRMS: calcd. $C_{12}H_{13}FONa$ $[M+Na]^+$: 215.0843. Found: 215.0841.



3-methyl-1-(4-(trifluoromethyl)phenyl)pent-4-en-1-one (3f)

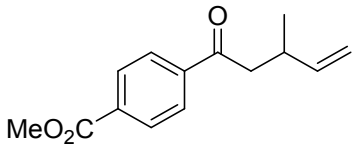
Synthesized from 1-(4-(trifluoromethyl)phenyl)ethan-1-one and 1,3-butadiene by following the general procedure on a 0.2 mmol scale. Yield: 82%. Colorless liquid. R_f = 0.6 (PE:Et_2O=20:1). ^{1}NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.0 Hz, 2H), 7.73 (d, *J* = 8.1 Hz, 2H), 5.92 – 5.74 (m, 1H), 5.10 – 4.91 (m, 2H), 3.11 – 2.85 (m, 3H), 1.11 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.3, 142.6, 139.9, 134.3 (q, *J* = 32.8 Hz), 128.4, 125.7 (q, *J* = 3.7 Hz), 123.6 (q, *J* = 272.8 Hz), 113.4, 45.4, 33.5, 19.8. IR (KBr) 2957, 2920, 2338, 2163, 1691, 1409, 1322, 1015, 993, 827 cm^{-1}. HRMS: calcd. $C_{13}H_{13}F_3ONa$ $[M+Na]^+$: 265.0811. Found: 265.0804.



ethyl 4-(3-methylpent-4-enoyl)benzoate (3g)

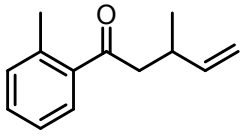
Synthesized from ethyl 4-acetylbenzoate and 1,3-butadiene by following the general procedure on a 0.2 mmol scale. Yield: 88%. Colorless liquid. R_f = 0.4 (PE:Et_2O=20:1). ^{1}NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.1 Hz, 2H), 7.99 (d, *J* = 8.0 Hz, 2H), 5.92 – 5.78 (m, 1H), 5.08 – 4.91 (m, 2H), 4.41 (q, *J*

= 7.1 Hz, 2H), 3.12 – 2.84 (m, 3H), 1.42 (t, *J* = 7.1 Hz, 3H), 1.11 (d, *J* = 6.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.9, 165.7, 142.8, 140.4, 134.1, 129.8, 128.0, 113.3, 61.4, 45.5, 33.6, 19.8, 14.3. IR (KBr). 2969, 2158, 1717, 1686, 1406, 1209, 996, 853 cm^{-1}. HRMS: calcd. $C_{15}H_{18}O_3Na$ $[M+Na]^+$: 269.1148. Found: 269.1153.



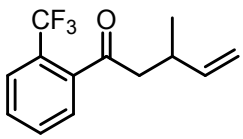
methyl 4-(3-methylpent-4-enoyl)benzoate (3h)

Synthesized from methyl 4-acetylbenzoate and 1,3-butadiene by following the general procedure on a 0.2 mmol scale. Yield: 80%. Colorless liquid. R_f = 0.5 (PE:Et_2O=5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 7.8 Hz, 2H), 7.99 (d, *J* = 7.6 Hz, 2H), 5.92 – 5.74 (m, 1H), 5.00 (dd, *J* = 25.5, 13.4 Hz, 2H), 3.95 (s, 2H), 3.11 – 3.00 (m, 1H), 2.98 – 2.86 (m, 3H), 1.11 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.8, 166.2, 142.7, 140.5, 133.7, 129.8, 128.0, 113.3, 52.4, 45.5, 33.5, 19.8. IR (KBr) 3053, 1730, 1436, 1267, 1006, 910, 704cm^{-1}. HRMS: calcd. $C_{14}H_{16}O_3$ $[M]^+$: 232.1099. Found: 232.1096.



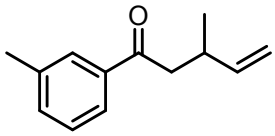
3-methyl-1-(o-tolyl)pent-4-en-1-one (3i)

Synthesized from 1-(o-tolyl)ethan-1-one and 1,3-butadiene by following the general procedure on a 0.2 mmol scale. Yield: 64%. Colorless liquid. R_f = 0.4 (PE:Et_2O=20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.70 (m, 2H), 7.40 – 7.31 (m, 2H), 5.93 – 5.80 (m, 1H), 5.09 – 4.87 (m, 2H), 3.09 – 2.80 (m, 3H), 2.41 (s, 3H), 1.09 (d, J = 6.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.6, 143.1, 138.4, 137.3, 133.7, 128.6, 128.4, 125.3, 113.0, 45.2, 33.6, 21.4, 19.8. IR (KBr) 2960, 2926, 1683, 1603, 1456, 1355, 1275, 1181, 1159, 921 cm^{-1}. HRMS: calcd. $C_{13}H_{16}ONa$ $[M+Na]^+$: 211.1093. Found: 211.1095.



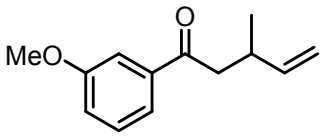
3-methyl-1-(2-(trifluoromethyl)phenyl)pent-4-en-1-one (3j)

Synthesized from 1-(2-(trifluoromethyl)phenyl)ethan-1-one and 1,3-butadiene by following the general procedure on a 0.2 mmol scale. Yield: 79%. Colorless liquid. R_f = 0.7 (PE:Et_2O=20:1). ^{1}NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.65 (m, 1H), 7.63 – 7.49 (m, 2H), 7.46 – 7.35 (m, 1H), 5.91 – 5.74 (m, 1H), 5.10 – 4.93 (m, 2H), 2.99 – 2.73 (m, 3H), 1.11 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.1, 142.6, 140.6 (q, J = 1.7 Hz), 131.8, 123.0, 127.1, 126.8 (d, *J* = 32.4 Hz), 126.7 (q, *J* = 5.0 Hz), 123.6 (q, *J* = 273.7 Hz), 113.4, 49.7 (d, *J* = 1.3 Hz), 32.9, 19.5. IR (KBr) 2990, 2921, 2204, 1709, 1312, 1273, 1167, 1129, 916 cm^{-1}. HRMS: calcd. $C_{13}H_{13}F_3ONa$ $[M+Na]^+$: 265.0811. Found: 265.0829.



3-methyl-1-(*m*-tolyl)pent-4-en-1-one (3k)

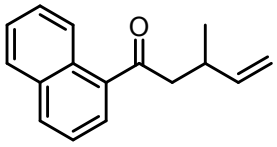
Synthesized from 1-(*m*-tolyl)ethan-1-one and 1,3-butadiene by following the general procedure on a 0.2 mmol scale. Yield: 68%. Colorless liquid. R_f = 0.6 (PE:Et_2O=20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 11.0 Hz, 2H), 7.34 – 7.22 (m, 2H), 5.87 – 5.70 (m, 1H), 5.03 – 4.82 (m, 2H), 2.99 – 2.74 (m, 3H), 2.33 (s, 3H), 1.02 (d, *J* = 6.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.6, 143.1, 138.4, 137.3, 133.7, 128.6, 128.4, 125.3, 113.0, 45.2, 33.6, 21.4, 19.8. IR (KBr) 2960, 2926, 1683, 1604, 1586, 1280, 1182, 1160 cm^{-1}. HRMS: calcd. $C_{13}H_{16}ONa$ $[M+Na]^+$: 211.1093. Found: 211.1095.



1-(3-methoxyphenyl)-3-methylpent-4-en-1-one (3l)

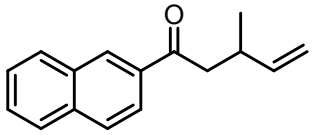
Synthesized from 1-(3-methoxyphenyl)ethan-1-one and 1,3-butadiene by following the general procedure on a 0.2 mmol scale. Yield: 69%. Colorless liquid. R_f = 0.5 (PE:Et_2O=20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 – 7.46 (m, 2H), 7.41 – 7.33 (m, 1H), 7.14 – 7.07 (m, 1H), 5.94 – 5.77 (m, 1H), 4.99 (dd, *J* = 28.0, 13.8 Hz, 2H), 3.91 – 3.79 (m, 3H), 3.09 – 2.77 (m, 3H), 1.10 (d, *J* = 5.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.2, 159.8, 143.0, 138.7, 129.5, 120.8, 119.5, 113.1, 112.3, 55.4,

45.3, 33.7, 19.8. IR (KBr) 2961, 1684, 1597, 1486, 1275, 1253, 1194, 1046 cm^{-1}. HRMS: calcd. $C_{13}H_{16}O_2Na$ $[M+Na]^+$: 227.1043. Found: 227.1046.



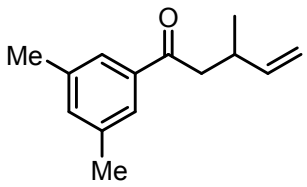
3-methyl-1-(naphthalen-1-yl)pent-4-en-1-one (3m)

Synthesized from 1-(naphthalen-1-yl)ethan-1-one and 1,3-butadiene by following the general procedure on a 0.2 mmol scale. Yield: 75%. Colorless liquid. R_f = 0.6 (PE:Et_2O=20:1). ^1H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, *J* = 8.5 Hz, 1H), 7.98 (d, *J* = 8.2 Hz, 1H), 7.93 – 7.78 (m, 2H), 7.64 – 7.43 (m, 3H), 5.94 – 5.78 (m, 1H), 5.11 – 4.87 (m, 2H), 3.19 – 2.88 (m, 3H), 1.13 (d, *J* = 4.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.9, 142.9, 136.6, 134.0, 132.4, 130.1, 128.4, 127.8, 127.3, 126.4, 125.8, 124.3, 113.3, 48.8, 34.2, 19.9. IR (KBr) 2961, 1681, 1507, 1459, 1349, 1279, 1230, 1175, 1086, 995, 914 cm^{-1}. HRMS: calcd. $C_{16}H_{16}ONa$ $[M+Na]^+$: 247.1093. Found: 247.1092.



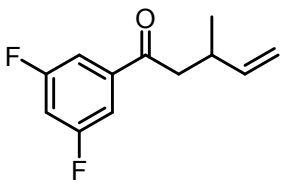
3-methyl-1-(naphthalen-2-yl)pent-4-en-1-one (3n)

Synthesized from 1-(naphthalen-2-yl)ethan-1-one and 1,3-butadiene by following the general procedure on a 0.2 mmol scale. Yield: 50%. Colorless liquid. R_f = 0.55 (PE:Et_2O=20:1). ^1H NMR (400 MHz, $CDCl_3$) δ 8.45 (s, 1H), 8.02 (d, *J* = 8.6 Hz, 1H), 7.96 (d, *J* = 8.0 Hz, 1H), 7.92 – 7.83 (m, 2H), 7.69 – 7.45 (m, 2H), 5.99 – 5.80 (m, 1H), 5.14 – 4.92 (m, 2H), 3.24 – 2.91 (m, 3H), 1.14 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.3, 143.1, 135.5, 134.6, 132.5, 129.7, 129.6, 128.5, 128.4, 127.8, 126.8, 124.0, 113.1, 45.2, 33.8, 19.9. IR (KBr) 3059, 2961, 2928, 1677, 1627, 1596, 1577, 1468, 1357, 1278, 1183, 1123, 933, 912 cm^{-1}. HRMS: calcd. $C_{16}H_{16}ONa$ $[M+Na]^+$: 247.1093. Found: 247.1101



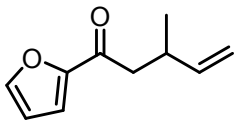
1-(3,5-dimethylphenyl)-3-methylpent-4-en-1-one (3o)

Synthesized from 1-(3,5-dimethylphenyl)ethan-1-one and 1,3-butadiene by following the general procedure on a 0.2 mmol scale. Yield: 83%. Colorless liquid. R_f = 0.55 (PE:Et_2O=20:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.55 (s, 2H), 7.19 (s, 1H), 5.94 – 5.78 (m, 1H), 5.11 – 4.89 (m, 2H), 3.07 – 2.80 (m, 3H), 2.37 (s, 6H), 1.09 (d, J = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.8, 143.2, 138.2, 137.4, 134.6, 125.9, 112.9, 45.2, 33.6, 21.3, 19.8. IR (KBr)2955, 2920, 2859, 1683, 1641, 1605, 1357, 1181, 994 cm^{-1}. HRMS: calcd. $C_{14}H_{18}ONa$ $[M+Na]^+$: 225.1250. Found: 225.1251.



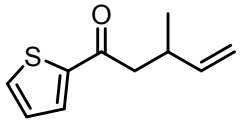
1-(3,5-difluorophenyl)-3-methylpent-4-en-1-one (3p)

Synthesized from 1-(3,5-difluorophenyl)ethan-1-one and 1,3-butadiene by following the general procedure on a 0.2 mmol scale. Yield: 81%. Colorless liquid. R_f = 0.55 (PE:Et_2O=20:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.52 – 7.41 (m, 2H), 7.07 – 6.96 (m, 1H), 5.90 – 5.75 (m, 1H), 5.11 – 4.82 (m, 2H), 3.05 – 2.78 (m, 3H), 1.10 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.6 (d, J = 2.3 Hz), 163.1 (d, *J* = 249.0 Hz), 163.0 (d, *J* = 249.0 Hz), 142.5, 140.1 (t, *J* = 8.0 Hz), 113.5, 111.0 (d, *J* = 29.0 Hz), 111.0 (d, *J* = 18.0 Hz), 108.3 (t, *J* = 25.0 Hz), 45.2, 33.5, 19.8. IR (KBr) 2949, 2926, 2361, 2015, 1693, 1617, 1438, 1310, 1120, 984 cm^{-1}. HRMS: calcd. $C_{12}H_{12}F_2ONa$ $[M+Na]^+$: 233.0748. Found: 233.0742.



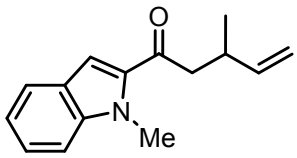
1-(furan-2-yl)-3-methylpent-4-en-1-one (3q)

Synthesized from 1-(furan-2-yl)ethan-1-one and 1,3-butadiene by following the general procedure on a 0.2 mmol scale. Yield: 84%. Colorless liquid. R_f = 0.5 (PE:Et_2O=20:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 1.6 Hz, 1H), 7.18 (d, *J* = 3.7 Hz, 1H), 6.57 – 6.49 (m, 1H), 5.90 – 5.76 (m, 1H), 5.12 – 4.89 (m, 2H), 2.94 – 2.82 (m, 2H), 2.80 – 2.70 (m, 1H), 1.09 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 188.6, 153.1, 146.3, 142.8, 117.1, 113.2, 112.2, 45.0, 33.8, 19.8. IR (KBr) 2920, 2850, 1666, 1641, 1467, 1373, 1263, 913 cm^{-1}. HRMS: calcd. $C_{10}H_{12}O_2$ $[M]^+$: 164.0832. Found: 164.0833.



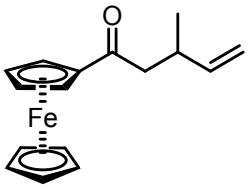
3-methyl-1-(thiophen-2-yl)pent-4-en-1-one (3r)

Synthesized from 1-(thiophen-2-yl)ethan-1-one and 1,3-butadiene by following the general procedure on a 0.2 mmol scale. Yield: 68%. Colorless liquid. R_f = 0.35 (PE:Et_2O=20:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.69 (m, 1H), 7.63 (d, *J* = 4.9 Hz, 1H), 7.13 (dd, *J* = 5.0, 3.8 Hz, 1H), 5.93 – 5.78 (m, 1H), 5.11 – 4.89 (m, 2H), 3.01 – 2.75 (m, 3H), 1.10 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.3, 144.8, 142.8, 133.6, 131.9, 128.1, 113.2, 46.0, 34.1, 19.7. IR (KBr) 2957, 2356, 1654, 1600, 1518, 1413, 1316, 1058, 994 cm^{-1}. HRMS: calcd. $C_{10}H_{12}OSNa$ $[M+Na]^+$: 203.0501. Found: 203.0509.



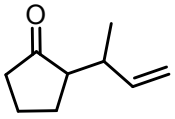
3-methyl-1-(1-methyl-1H-indol-3-yl)pent-4-en-1-one(3s)

Synthesized from 1-(1-methyl-1H-indol-3-yl)ethan-1-one and 1,3-butadiene by following the general procedure on a 0.2 mmol scale. Yield: 84%. Colorless liquid. R_f = 0.4 (PE:Et_2O=5:1). 1H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 7.6 Hz, 1H), 7.28 (d, *J* = 3.8 Hz, 2H), 7.19 (d, *J* = 3.1 Hz, 1H), 7.13 – 7.01 (m, 1H), 5.84 – 5.72 (m, 1H), 4.92 (dd, *J* = 33.8, 13.7 Hz, 2H), 3.97 (s, 3H), 3.02 – 2.73 (m, 3H), 1.03 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.4, 143.1, 140.1, 135.3, 125.9, 125.8, 122.9, 120.7, 113.1, 111.4, 110.4, 46.6, 34.6, 32.2, 19.9. IR (KBr) 2990, 1712, 1658, 1514, 1222, 912, 736cm^{-1}. HRMS: calcd. $C_{15}H_{17}NO$ $[M+H]^+$: 228.1388. Found: 228.1391.



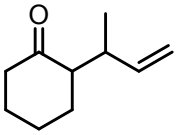
3-methyl-1-(ferrocene-2-yl)pent-4-en-1-one (3t)

Synthesized from acetylferrocene and 1,3-butadiene by following the general procedure on a 0.2 mmol scale. Yield: 58%. Colorless liquid. R_f = 0.2 (PE:Et_2O=20:1). ^1H NMR (400 MHz, $CDCl_3$) δ 5.94 – 5.80 (m, 1H), 5.12 – 4.94 (m, 2H), 4.81 – 4.73 (m, 2H), 4.52 – 4.45 (m, 2H), 4.20 (s, 5H), 2.94 – 2.83 (m, 1H), 2.77 (dd, *J* = 15.8, 6.3 Hz, 1H), 2.63 (dd, *J* = 15.9, 7.5 Hz, 1H), 1.10 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.3, 143.4, 113.0, 79.4, 72.2, 72.2, 69.8, 69.3, 46.4, 33.4, 19.8. IR (KBr) 2961, 2920, 1715, 1665, 1601, 1452, 1275, 1106, 1000, 912 cm^{-1}. HRMS: calcd. $C_{16}H_{18}FeONa$ $[M+Na]^+$: 305.0599. Found: 305.0610.



2-(but-3-en-2-yl)cyclopentan-1-one (4a)[4]

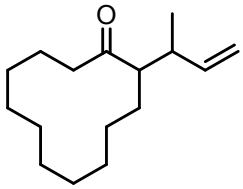
Synthesized from cyclopentanone and 1,3-butadiene by following the general procedure on a 0.2 mmol scale with 20 mol% loading of the catalyst. 1 equivalent of 1,3-butadiene was used. Yield: 35%. Colorless liquid. R_f = 0.3 (PE:Et_2O=20:1). Isolated as a mixture with 1:1 dr, and the pure product contains 17% of the regioisomer (linear product). ^1H NMR (400 MHz, $CDCl_3$) δ 5.90 – 5.74 (m, 0.5H), 5.72 – 5.58 (m, 0.5H), 5.01 (dd, *J* = 17.3, 8.6 Hz, 2H), 2.81 – 2.67 (m, 1H), 2.36 – 2.25 (m, 1H), 2.13 – 1.94 (m, 4H), 1.78 – 1.66 (m, 2H), 1.10 (d, *J* = 7.0 Hz, 1.5H), 0.94 (d, *J* = 7.0 Hz, 1.5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 220.4, 220.3, 142.2, 140.2, 115.0, 113.5, 54.1, 53.5, 39.1, 39.1, 36.8, 36.4, 25.1, 24.7, 20.7, 17.9, 15.1.



2-(but-3-en-2-yl)cyclohexan-1-one(4b)[5]

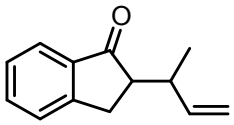
Synthesized from cyclohexanone and 1,3-butadiene by following the general procedure on a 0.2 mmol scale with 20 mol% loading of the catalyst. 1 equivalent of 1,3-butadiene was used. Yield: 60%.

Colorless liquid. R_f = 0.6 (PE:Et_2O=20:1). Isolated as a mixture with 1:1 dr, and the pure product contains 16% of the regioisomer (linear product). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.88 – 5.74 (m, 0.5H), 5.74 – 5.59 (m, 0.5H), 5.07 – 4.94 (m, 2H), 2.78 – 2.62 (m, 1H), 2.45 – 2.33 (m, 1H), 2.32 – 2.23 (m, 2H), 2.06 – 1.82 (m, 3H), 1.79 – 1.52 (m, 3H), 1.01 (d, *J* = 2.0 Hz, 1.5H), 0.99 (d, *J* = 1.9 Hz, 1.5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 213.0, 212.2, 142.5, 141.6, 114.4, 113.6, 55.8, 55.2, 42.2, 42.0, 36.7, 35.9, 30.8, 28.7, 28.1, 27.6, 24.5, 24.0, 18.4, 15.7.



2-(but-3-en-2-yl)cyclododecan-1-one(4c)[6]

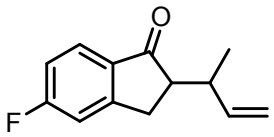
Synthesized from cyclododecanone and 1,3-butadiene by following the general procedure on a 0.2 mmol scale. Yield: 50%. Colorless liquid. R_f = 0.6 (PE:Et_2O=20:1). Isolated as a mixture with 2:1 dr, and the pure product contains 20% of the regioisomer (linear product). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.71 – 5.50 (m, 1H), 5.05 – 4.78 (m, 2H), 2.49 – 2.26 (m, 4H), 1.73 – 1.59 (m, 2H), 1.32 – 1.13 (m, 16H), 0.93 (d, *J* = 6.7 Hz, 1H), 0.87 (d, *J* = 6.2 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 213.2, 213.1, 141.3, 140.8, 113.7, 113.1, 57.1, 56.5, 38.2, 37.9, 37.6, 36.7, 28.7, 27.0, 25.4, 25.0, 24.7, 23.2, 23.1, 23.1, 22.7, 22.5, 21.7, 21.7, 21.2, 21.1, 20.8, 18.3.



2-(but-3-en-2-yl)-2,3-dihydro-1H-inden-1-one (4d)

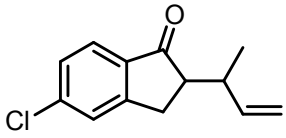
Synthesized from 2,3-dihydro-1H-inden-1-one and 1,3-butadiene by following the general procedure on a 0.2 mmol scale. Yield: 78%. Colorless liquid. R_f = 0.4 (PE:Et_2O=20:1). dr: 1:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 – 7.72 (m, 1H), 7.63 – 7.52 (m, 1H), 7.51 – 7.42 (m, 1H), 7.40 – 7.30 (m, 1H), 5.98 – 5.81 (m, 0.5H), 5.70 – 5.52 (m, 0.5H), 5.17 – 4.90 (m, 2H), 3.23 – 2.68 (m, 4H), 1.20 (d, *J* = 6.9 Hz, 1.5H), 0.89 (d, *J* = 6.9 Hz, 1.5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 208.2, 208.1, 154.3, 154.1, 141.8, 139.0, 137.5, 137.3, 134.7, 134.7, 127.3, 126.5, 123.7, 123.7, 115.5, 114.0, 52.3, 51.2, 37.9,

37.8, 28.6, 28.4, 17.6, 13.7. IR (KBr) 2961, 2925, 1705, 1607, 1588, 1463, 1327, 1279, 1202, 1150, 997 cm^{-1}. HRMS: calcd. $C_{13}H_{14}ONa$ $[M+Na]^+$: 209.0937. Found: 209.0947.



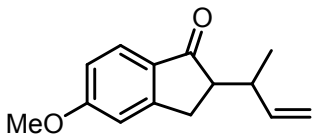
2-(but-3-en-2-yl)-5-fluoro-2,3-dihydro-1H-inden-1-one (4e)

Synthesized from 5-fluoro-2,3-dihydro-1H-inden-1-one and 1,3-butadiene by following the general procedure on a 0.2 mmol scale. Yield: 84%. Colorless liquid. R_f = 0.55 (PE:Et_2O=20:1). dr: 1:1. ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.70 (m, 1H), 7.16 – 6.98 (m, 2H), 5.94 – 5.81 (m, 0.5H), 5.67 – 5.53 (m, 0.5H), 5.16 – 4.91 (m, 2H), 3.21 – 2.70 (m, 4H), 1.19 (d, *J* = 6.9 Hz, 1.5H), 0.90 (d, *J* = 6.9 Hz, 1.5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.1, 206.0, 168.5, 166.0, 157.1 (d, *J* = 9.9 Hz), 156.9 (d, *J* = 9.9 Hz), 141.4, 138.7, 133.9, 133.7, 126.0 (d, *J* = 2.3 Hz), 125.9 (d, *J* = 2.2 Hz), 115.8, 115.7 (d, *J* = 3.0 Hz), 115.7, 115.5 (d, *J* = 3.0 Hz), 114.1, 113.12, 113.0, 52.5, 53.4, 37.9, 37.7, 28.6 (d, *J* = 2.2 Hz), 28.4 (d, *J* = 2.1 Hz), 17.6, 13.7. IR (KBr) 2956, 1708, 1615, 1592, 1480, 1434, 1330, 1126, 996 cm^{-1}. HRMS: calcd. $C_{13}H_{13}FONa$ $[M+Na]^+$: 227.0843. Found: 227.0852



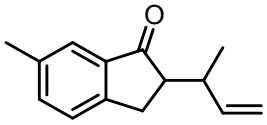
2-(but-3-en-2-yl)-5-chloro-2,3-dihydro-1H-inden-1-one (4f)

Synthesized from 5-chloro-2,3-dihydro-1H-inden-1-one and 1,3-butadiene by following the general procedure on a 0.2 mmol scale. Yield: 46%. Colorless liquid. R_f = 0.65 (PE:Et_2O=20:1). Isolated as a mixture with 1.1:1 dr, and the pure product contains 11% of the regioisomer (linear product). ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.61 (m, 1H), 7.52 – 7.40 (m, 1H), 7.38 – 7.29 (m, 1H), 5.95 – 5.80 (m, 0.4H), 5.67 – 5.53 (m, 0.6H), 5.17 – 4.90 (m, 2H), 3.18 – 2.69 (m, 4H), 1.19 (d, *J* = 6.9 Hz, 1.7H), 0.89 (d, *J* = 6.9 Hz, 1.3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.6, 206.6, 155.7, 155.5, 141.4, 141.2, 141.2, 138.6, 136.0, 135.8, 128.2, 128.1, 126.7, 124.8, 124.8, 115.8, 114.6, 114.2, 52.4, 51.3, 38.0, 37.9, 28.4, 28.3, 17.6, 13.7. IR (KBr) 2920, 1709, 1599, 1578, 1318, 1265, 1198, 1068, 997, 878 cm^{-1}. HRMS: calcd. $C_{13}H_{13}ClONa$ $[M+Na]^+$: 243.0547. Found: 243.0543



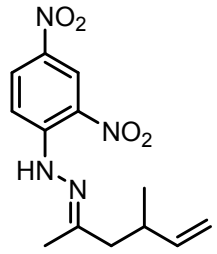
2-(but-3-en-2-yl)-5-methoxy-2,3-dihydro-1H-inden-1-one (4g)

Synthesized from 5-methoxy-2,3-dihydro-1H-inden-1-one and 1,3-butadiene by following the general procedure on a 0.2 mmol scale. Yield: 86%. Colorless liquid. R_f = 0.4 (PE:Et_2O=20:1). dr:1.3:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 – 7.62 (m, 1H), 6.89 (dd, *J* = 8.0, 4.0 Hz, 2H), 5.97 – 5.83 (m, 0.6H), 5.68 – 5.54 (m, 0.4H), 5.14 – 4.90 (m, 2H), 3.88 (d, *J* = 2.5 Hz, 3H), 3.15 – 2.92 (m, 2H), 2.92 – 2.65 (m, 2H), 1.18 (d, *J* = 6.9 Hz, 1.3H), 0.87 (d, *J* = 6.9 Hz, 1.7H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.3 , 206.2, 165.3, 165.3, 157.3, 157.0, 141.9, 138.9, 130.9, 130.7, 125.4, 115.4, 115.3, 115.3, 113.8, 109.6, 55.6, 55.6, 52.4, 51.3, 37.9, 37.7, 28.6, 28.4, 17.6, 13.5. IR (KBr) 2955, 1695, 1597, 1558, 1455, 1336, 1104, 1087, 918 cm^{-1}. HRMS: calcd. $C_{14}H_{16}O_2Na$ $[M+Na]^+$: 239.1043. Found: 239.1049.



2-(but-3-en-2-yl)-6-methyl-2,3-dihydro-1H-inden-1-one (4h)

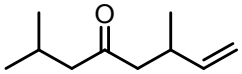
Synthesized from 6-methyl-2,3-dihydro-1H-inden-1-one and 1,3-butadiene by following the general procedure on a 0.2 mmol scale. Yield: 80%. Colorless liquid. R_f = 0.65 (PE:Et_2O=20:1). dr :1:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 4.5 Hz, 1H), 7.42 – 7.37 (m, 1H), 7.33 (t, *J* = 6.9 Hz, 1H), 5.96 – 5.82 (m, 0.5H), 5.67 – 5.53 (m, 0.5H), 5.15 – 4.88 (m, 2H), 3.14 – 2.96 (m, 2H), 2.90 – 2.66 (m, 2H), 2.39 (d, *J* = 2.6 Hz, 3H), 1.19 (d, *J* = 6.9 Hz, 1.5H), 0.88 (d, *J* = 6.9 Hz, 1.5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 208.3, 208.2, 151.7, 151.4, 141.8, 139.0, 137.7, 137.5, 137.2, 137.2, 136.0, 135.9, 126.2, 123.6, 123.6, 115.4, 113.9, 52.6, 51.5, 38.0, 37.8, 28.2, 28.0, 21.1, 17.6, 13.6. IR (KBr) 2961, 2919, 1704, 1616, 1491, 1417, 1280, 1155, 994 cm^{-1}. HRMS: calcd. $C_{14}H_{16}ONa$ $[M+Na]^+$: 223.1093. Found: 223.1097.



4i-2

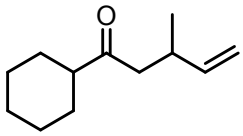
1-(2,4-dinitrophenyl)-2-(4-methylhex-5-en-2-ylidene)hydrazine (4i-2)

The reaction between acetone and 1,3-butadiene was conducted by following the general procedure with 0.25 mL of acetone and 0.3 mL of the 1,3-butadiene solution (2 M in THF). After the reaction was finished, to this reaction mixture was added 2,4-dinitrophenylhydrazine (700 mg, 3.5 mmol), MeOH (2 mL) and 0.3 mL of concentrated HCl. The resulted reaction mixture was stirred at room temperature overnight. The solvent was removed under vacuum. The residue was purified by flash column chromatography to give **4i-2** as a yellow solid. R_f = 0.3 (PE:EA=5:1). ^{1}H NMR(400 MHz, $CDCl_3$) δ 10.96 (s, 1H), 9.05 (s, 1H), 8.23 (d, J = 7.2 Hz, 1H), 7.89 (d, *J* = 9.6 Hz, 1H), 5.80 – 5.65 (m, 1H), 4.94 (dd, *J* = 26.1, 13.8 Hz, 2H), 2.65 – 2.51 (m, 1H), 2.49 – 2.29 (m, 2H), 1.98 (s, 3H), 1.02 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156. 9, 145.2, 142.9, 137.7, 130.0, 123.6, 116.5, 113.6, 45.9, 35.5, 20.1, 16.2. IR (KBr) 2923, 1616, 1591, 1506, 1420, 1329, 1309, 1134, 1074 cm^{-1}. HRMS: calcd. $C_{13}H_{16}N_4O_4Na$ $[M+Na]^+$: 315.1064. Found: 315.1052.



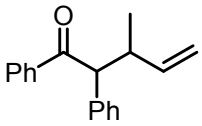
2,6-dimethyloct-7-en-4-one (4j)[7]

Synthesized from 4-methylpentan-2-one and 1,3-butadiene by following the general procedure on a 0.2 mmol scale with 20 mol% loading of the catalyst. 5 equivalents of 1,3-butadiene were used. Yield: 30%. Colorless liquid. R_f = 0.55 (PE:Et_2O=20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.82 – 5.69 (m, 1H), 5.04 – 4.89 (m, 2H), 2.80 – 2.66 (m, 1H), 2.48 – 2.38 (m, 1H), 2.37 – 2.22 (m, 3H), 2.22 – 2.08 (m, 1H), 1.01 (d, *J* = 6.7 Hz, 3H), 0.92 (s, 3H), 0.90 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 209.9, 143.0, 113.0, 52. 5, 49.9, 33.2, 24.4, 22.6, 22.6, 19.7.



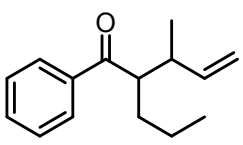
1-cyclohexyl-3-methylpent-4-en-1-one (4k)[8]

Synthesized from 1-cyclohexylethan-1-one and 1,3-butadiene by following the general procedure on a 0.2 mmol scale with 20 mol% loading of the catalyst. 5 equivalents of 1,3-butadiene were used. Yield: 44%. Colorless liquid. R_f = 0.6 (PE:Et_2O=20:1). ^1H NMR (400 MHz, $CDCl_3$) δ 5.76 – 5.62 (m, 1H), 4.97 – 4.79 (m, 2H), 2.76 – 2.47 (m, 1H), 2.45 – 2.36 (m, 1H), 2.35 – 2.27 (m, 1H), 2.26 – 2.18 (m, 1H), 1.80 – 1.69 (m, 4H), 1.32 – 1.11 (m, 6H), 0.93 (d, *J* = 6.8, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 213.1, 143.2, 112.8, 51.2, 47.3, 33.0, 28.3, 28.3, 25.9, 25.7, 25.7, 19.7.



3-methyl-1,2-diphenylpent-4-en-1-one (4l)

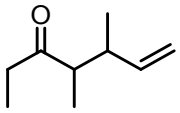
Synthesized from 1,2-diphenylethan-1-one and 1,3-butadiene by following the general procedure on a 0.2 mmol scale. Yield: 50%. Colorless liquid. R_f = 0.55 (PE:Et_2O=20:1). Isolated as a mixture with 1.4:1 dr. ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.8 Hz, 2H), 7.53 – 7.16 (m, 8H), 5.53 – 5.28 (m, 2H), 4.57 (q, *J* = 7.2 Hz, 1H), 2.97 – 2.79 (m, 1H), 2.65 – 2.54 (m, 0.4H), 2.53 – 2.42 (m, 0.6H), 1.61 – 1.51 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.6, 199.5, 139.3, 136.9, 132.8, 132.8, 128.9, 128.70 , 128.7, 128.5, 128.4, 128.3, 128.2, 127.4, 127.3, 127.0, 127.0, 126.0, 54.1, 53.7, 37.1, 31.5, 18.0, 12.8. IR (KBr) 2920, 1680, 1597, 1580, 1492, 1447, 1260, 1202, 1174, 966 cm^{-1}. HRMS: calcd. $C_{18}H_{18}ONa$ $[M+Na]^+$: 273.1250. Found: 273.1251.



3-methyl-1-phenyl-2-propylpent-4-en-1-one (4m)

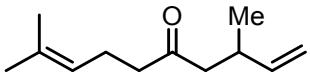
Synthesized from 1-phenylpentan-1-one and 1,3-butadiene by following the general procedure on a 0.2 mmol scale. Yield: 53%. R_f = 0.6 (PE:Et_2O=20:1). Isolated as a mixture with 1:1 dr, and the pure product contains 24% of the regioisomer (linear product). Colorless liquid. ^1H NMR (400 MHz, $CDCl_3$)

δ 7.92 – 7.84 (m, 2H), 7.52 – 7.44 (m, 1H), 7.43 – 7.34 (m, 2H), 5.79 – 5.55 (m, 1H), 5.01 – 4.79 (m, 2H), 3.44 – 3.22 (m, 1H), 2.55 – 2.44 (m, 1H), 1.77 – 1.57 (m, 1H), 1.49 – 1.35 (m, 1H), 1.26 – 1.04 (m, 2H), 0.91 (dd, *J* = 11.8, 6.8 Hz, 3H), 0.84 – 0.67 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 204.8, 203.8, 141.9, 141.7, 132.9, 132.8, 128.0, 128.6, 128.2, 128.2, 114.8, 114.2, 51.0, 50.8, 41.2, 39.9,, 33.06, 30.7, 21.1, 20.8, 19.1, 16.2, 14.4, 14.4. IR (KBr) 2959, 1677, 1596, 1447, 1375, 1276, 1208, 913 cm^{-1}. HRMS: calcd. $C_{15}H_{20}ONa$ $[M+Na]^+$: 239.1406. Found: 239.1401.



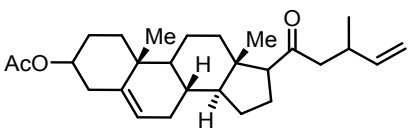
4,5-dimethylhept-6-en-3-one (4n)[9]

Synthesized from pentan-3-one and 1,3-butadiene by following the general procedure on a 0.2 mmol scale of 1,3-butadiene with 20 mol% loading of the catalyst. 5 equivalents of pentan-3-one were used. Yield: 32%. Colorless liquid. R_f = 0.45 (PE:Et_2O=20:1). Isolated as a mixture with 1.5:1 dr, and the pure product contains ca. 30% of the regioisomers (linear products). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.74 – 5.53 (m, 1H), 5.07 – 4.92 (m, 2H), 2.54 – 2.37 (m, 4H), 1.12 – 0.93 (m, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 214.9, 214.6, 142.0, 141.1, 114.8, 114.1, 51.2, 51.1, 40.6, 39.8, 35.4, 35.2, 18.6, 16.0, 14.6, 13.0, 7.6, 7.5.



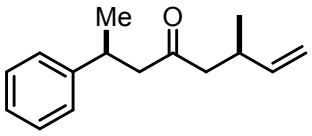
3,9-dimethyldeca-1,8-dien-5-one (4o)

Synthesized from 6-methylhept-5-en-2-one and 1,3-butadiene by following the general procedure on a 0.2 mmol scale. Yield: 62%. Colorless liquid. R_f = 0.6 (PE:Et_2O=20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.81 – 5.70 (m, 1H), 5.09 – 4.89 (m, 3H), 2.79 – 2.68 (m, 1H), 2.49 – 2.29 (m, 4H), 2.29 – 2.19 (m, 2H), 1.67 (s, 3H), 1.61 (s, 3H), 1.01 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 209.9, 142.9, 132.6, 122.8, 112.9, 49.5, 43.4, 33.3, 25.7, 22.4, 19.8, 17.6. IR (KBr) 2938, 1731, 1558, 1540, 1507, 1472, 1457, 1363, 1275, 1250, 1039 cm^{-1}. HRMS: calcd. $C_{12}H_{20}O$ $[M]^+$: 180.1509. Found: 180.1515.



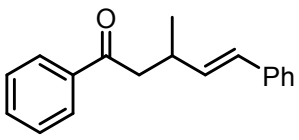
(8*S*,10*R*,13*S*,14*S*)-10,13-dimethyl-17-(3-methylpent-4-enoyl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl acetate (4p)

Synthesized from pregnenolone acetate and 1,3-butadiene by following the general procedure on a 0.2 mmol scale with 20 mol% loading of the catalyst. 5 equivalents of 1,3-butadiene were used. Yield: 50%. White solid. Mp = 81 – 83 °C. R_f = 0.2 (PE:Et_2O=20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.82 – 5.69 (m, 1H), 5.38 (d, *J* = 5.0 Hz, 1H), 5.05 – 4.88 (m, 2H), 4.67 – 4.54 (m, 1H), 2.82 – 2.71 (m, 1H), 2.55 – 2.11 (m, 6H), 2.07 – 1.95 (m, 5H), 1.91 – 1.81 (m, 2H), 1.70 – 1.41 (m, 9H), 1.30 – 1.10 (m, 3H), 1.01 (d, *J* = 7.3 Hz, 6H), 0.62 (d, *J* = 3.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.5, 210.4, 170.6, 143.3, 143.3, 139.6, 122.4, 112.9, 112.8, 73.8, 63.2, 63.1, 56.9, 51.1, 51.1, 49.9, 44.3, 44.3, 38.1, 37.0, 36.6, 33.2, 33.1, 31.8, 31.8, 27.7, 24.5, 22.9, 21.5, 21.1, 19.8, 19.7, 19.3, 13.5, 13.4. IR (KBr) 2938, 1731, 1558, 1540, 1507, 1472, 1457, 1363, 1275, 1250, 1039 cm^{-1}. HRMS: calcd. $C_{27}H_{40}O_3Na$ [M+Na]$^+$: 435.2870. Found: 435.2879.



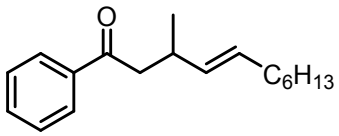
6-methyl-2-phenyloct-7-en-4-one (4q)

Synthesized from (*S*)-4-phenylpentan-2-one (*S*)-**1q**[10] (ee: 88%) and 1,3-butadiene by following the general procedure on a 0.2 mmol scale. Yield: 70%. Colorless liquid. R_f = 0.55 (PE:Et_2O=20:1). dr: 1:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.11 (m, 5H), 5.78 – 5.59 (m, 1H), 5.01 – 4.84 (m, 2H), 3.38 – 3.25 (m, 1H), 2.77 – 2.53 (m, 3H), 2.40 – 2.16 (m, 2H), 1.25 (d, *J* = 6.8 Hz, 3H), 0.94 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 208.8, 208.8, 146.3, 142.9, 142.8, 128.5, 126.8, 126.3, 112.9, 100.0, 51.8, 51.7, 50.1, 50.1, 35.3, 35.3, 33.1, 33.1, 22.0, 19.7. IR (KBr) 2961, 2923, 1709, 1452, 1373, 911, 760, 699 cm^{-1}. HRMS: calcd. $C_{15}H_{20}O$ [M]$^+$: 216.1509. Found: 216.1512. HPLC analysis of *ent*-**4q**: dr: 1:1; ee: 88%/90%, Chiralcel IG, *n*-hexane/*i*-PrOH = 600:1, 0.8 mL/min, λ = 190 nm, t_R (major) = 19.111 min, t_R (minor) = 21.685 min, t_R (major) = 20.707 min, t_R (minor) = 22.050 min.



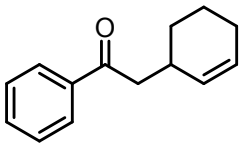
(*E*)-3-methyl-1,5-diphenylpent-4-en-1-one (SD-P1)[11]

Synthesized from acetophenone and (*E*)-buta-1,3-dien-1-ylbenzene by following general procedure on a 0.2 mmol scale. Yield: 84%. Colorless liquid. R_f = 0.46 (PE:Et_2O=10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 – 7.93 (m, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.35 – 7.23 (m, 4H), 7.18 (t, *J* = 7.1 Hz, 1H), 6.41 (d, *J* = 15.9 Hz, 1H), 6.22 (dd, *J* = 15.9, 6.7 Hz, 1H), 3.16 – 2.94 (m, 3H), 1.19 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.2, 137.5, 137.3, 134.9, 133.0, 128.6, 128.6, 128.49, 128.1, 127.1, 126.1, 45.6, 33.2, 20.3.



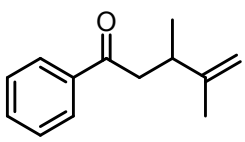
(*E*)-3-methyl-1-phenylundec-4-en-1-one (SD-P2)[12]

Synthesized from acetophenone and (*E*)-deca-1,3-diene by following general procedure on a 0.2 mmol scale. Yield: 65%. Colorless liquid. R_f = 0.3 (PE:Et_2O=20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 – 7.82 (m, 2H), 7.50 – 7.44 (m, 1H), 7.37 (t, *J* = 7.6 Hz, 2H), 5.43 – 4.87 (m, 2H), 3.01 – 2.54 (m, 3H), 1.89 – 1.46 (m, 3H), 1.37 – 1.09 (m, 7H), 0.98 (t, *J* = 6.8 Hz, 1H), 1.03 – 0.72 (m, 5H).



2-(cyclohex-2-en-1-yl)-1-phenylethan-1-one (SD-P3)[13]

Synthesized from acetophenone and cyclohexa-1,3-diene by following general procedure on a 0.2 mmol scale, 5 equivalents of cyclohexa-1,3-diene were used. Yield: 78%. Colorless liquid. R_f = 0.76 (PE:Et_2O=10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, 2H), 7.53 – 7.43 (m, 1H), 7.38 (t, *J* = 7.8 Hz, 2H), 5.72 – 5.59 (m, 1H), 5.57 – 5.47 (m, 1H), 2.91 – 2.84 (m, 2H), 2.81 – 2.67 (m, 1H), 2.00 – 1.87 (m, 2H), 1.83 – 1.73 (m, 1H), 1.70 – 1.60 (m, 1H), 1.56 – 1.42 (m, 1H), 1.30 – 1.14 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.7, 137.3, 132.9, 130.8, 128.6, 128.1, 127.9, 44.8, 31.6, 29.1, 25.1, 21.1.

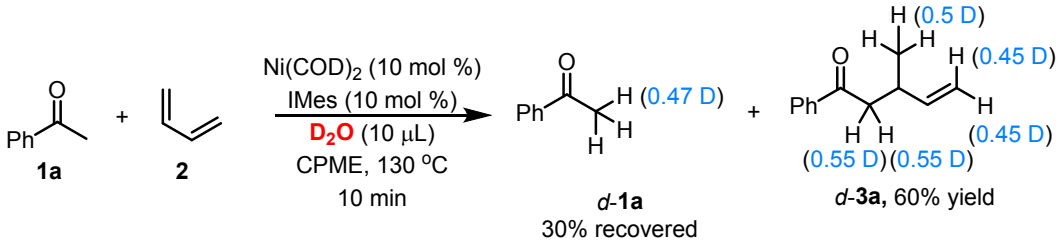


3,4-dimethyl-1-phenylpent-4-en-1-one(SD-P4)

Synthesized from acetophenone and isoprene by following general procedure on a 0.1 mmol scale of 1-(naphthalen-1-yl)ethan-1-one, 5 equivalents of isoprene were used. Yield: 50%. Colorless liquid. R_f = 0.6 (PE:Et_2O=20:1). ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 – 7.92 (m, 2H), 7.62 – 7.53 (m, 1H), 7.52 – 7.42 (m, 2H), 4.73 (s, 2H), 3.20 – 2.84 (m, 3H), 1.77 (s, 3H), 1.10 (d, J = 5.3, 4.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.6, 149.4, 137.3, 132.9, 128.6, 128.1, 109.5, 44.3, 36.9, 20.3, 19.6. IR (KBr) 2964, 2930, 1683, 1645, 1579, 1447, 1319, 1276, 1210, 1100, 890. HRMS: calcd. $C_{13}H_{16}ONa$ $[M+Na]^+$: 211.1093. Found: 211.1104.

4. Deuterium Experiments

Deuterium-labelling experiment of 1a and 2a in the presence of D_2O.

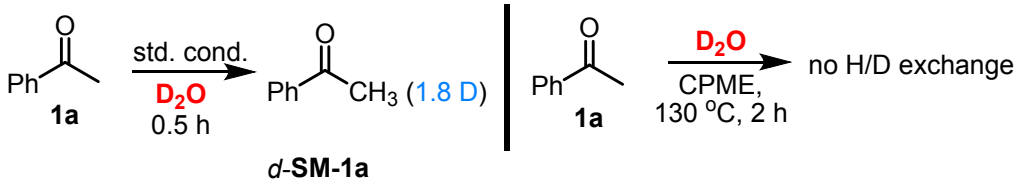


Substrate **1a** (0.2 mmol) and **2** (0.6 mmol, 3 equiv) were subjected to standard reaction condition but H_2O was replaced with D_2O (10 μL), the reaction was stopped after heating at 130 °C for 10 min. The crude reaction mixture was then subjected to column chromatography to isolate recovered *d*-**1a** and the product *d*-**3a**.

Recovered *d*-**1a** (yield: 30%): ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 8.1 Hz, 2H), 7.61 – 7.51 (m, 1H), 7.49 – 7.45 (m, 2H), 2.65 – 2.56 (m, 1.6H).

Isolated *d*-**3a** (yield: 60%): ^1H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 7.8 Hz, 2H), 7.54 – 7.44 (m, 1H), 7.44 – 7.33 (m, 2H), 5.84 – 5.69 (m, 0.91H), 5.03 – 4.79 (m, 1.13H), 3.00 – 2.88 (m, 0.54H), 2.88 – 2.75 (m, 1.34H), 1.08 – 0.93 (m, 1.52H).

Control experiment of 1a with D_2O.

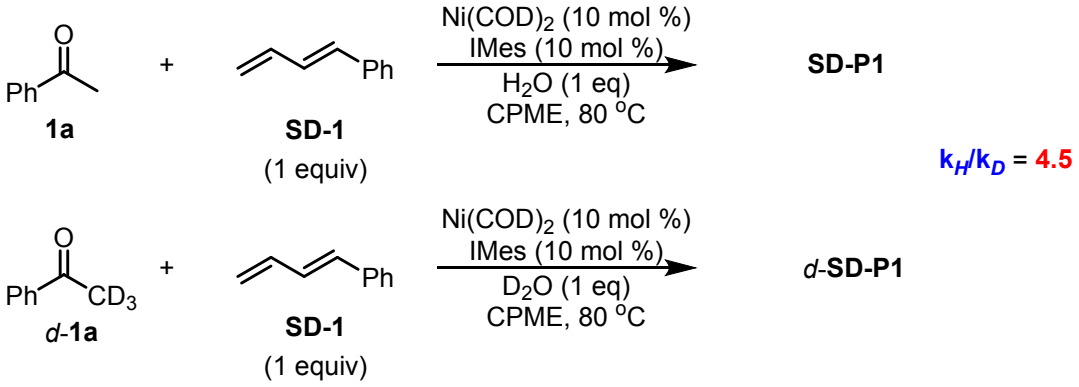


Substrate **1a** (0.2 mmol) was subjected to the standard reaction condition but without the addition of **2** and H_2O, instead, D_2O (10 μL) was added. The reaction mixture was heated at 130 °C for 0.5 h. The reaction mixture was then filtered with a short pad of silica gel and the crude product was subjected to ^1H NMR analysis.

Recovered *d*-**SM-1a**: ^1H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, 2H), 7.62 – 7.52 (m, 1H), 7.46 (t, J = 7.7 Hz, 2H), 2.64 – 2.54 (m, 1.2H).

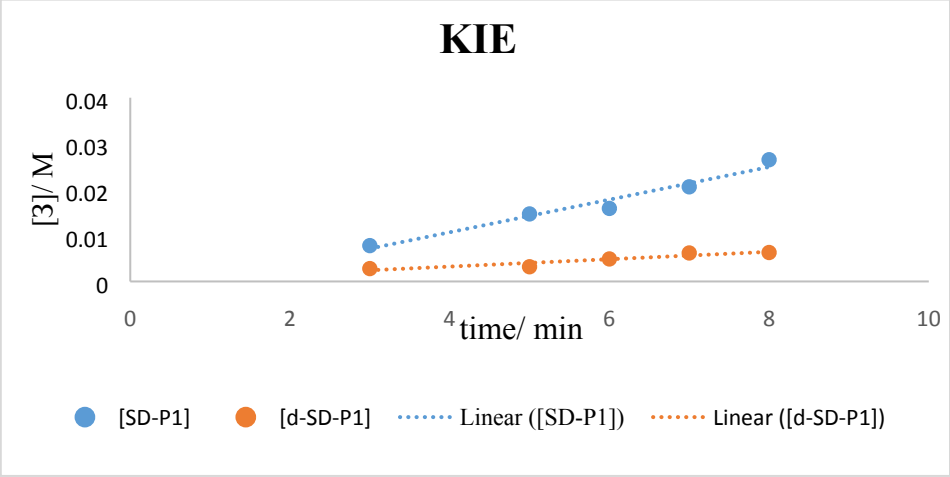
An experiment without the addition of $Ni(COD)_2$ and IMes was also conducted, no H/D exchange was observed after the reaction mixture was heated at 130 °C for 2 h.

Side-by-side reactions between 1a and *d*-1a with SD-1 (KIE study)

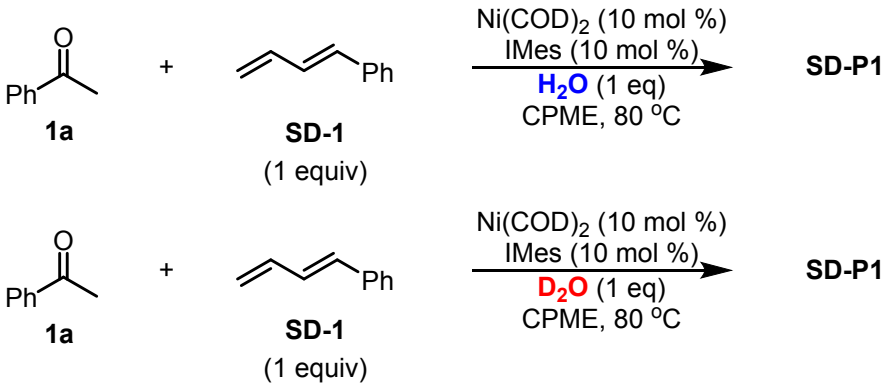


The side-by-side reactions between **1a** and ***d*-1a** with **SD-1** were conducted under standard reaction condition while the reaction temperature was 80 °C. For the reaction between **1a** and **SD-1**, 1 equivalent of H_2O was used as the additive, for the reaction between *d*-**1a** and **SD-1**, 1 equivalent of D_2O was used as the additive. Authentic samples from these two vials were picked at 3 min, 5 min, 6 min, 7 min, 8 min accordingly. The concentration of the product was determined by GC with *n*-dodecane as the internal standard.

Time (min)	[SD-P1]	[*d* -SD-P1]
3	0.0078	0.0028
5	0.0147	0.0032
6	0.0159	0.0049
7	0.0206	0.0062
8	0.0265	0.0063

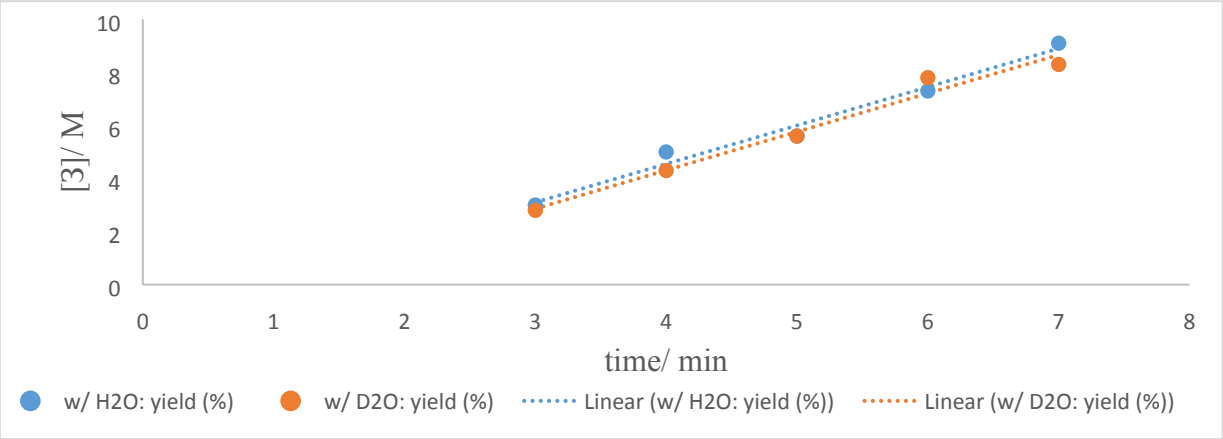


Competitive experiments between 1a and SD-1 with either H_2O or D_2O as the additive



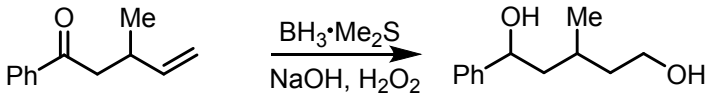
According to the control experiment between **1a** and D_2O, D_2O would incorporate with the acetophenone substrate during the reaction, therefore would make the KIE study less accurate if H_2O was used as the additive for the reaction with deuterium-labelled acetophenone substrate. As a result, the side-by-side reactions between **1a** and **SD-1** with either H_2O or D_2O as the additive were conducted under standard reaction conditions while the reaction temperature was 80 °C. Authentic samples were picked at 3 min, 4 min, 5 min, 6 min, 7 min accordingly. The reaction rate between these two reactions were compared by GC analysis with *n*-dodecane as the internal standard, and no rate difference was observed. Therefore, for the KIE study, H_2O was used as the additive for the reaction between **1a** and **SD-P1** while D_2O was used as the additive for the reaction between *d*-**1a** and **SD-P1** to make sure there were no deuterium lost of *d*-**1a**.

Time (min)	w/ H_2O: yield (%)	w/ D_2O: yield (%)
3	3	2.8
4	5	4.3
5	5.6	5.6
6	7.3	7.8
7	9.1	8.3



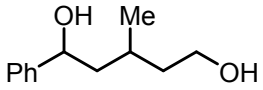
5. Experimental Procedure for the Synthetic Applications

5.1 Conversion of 3a into diol 5



5, 68%, dr 6:1

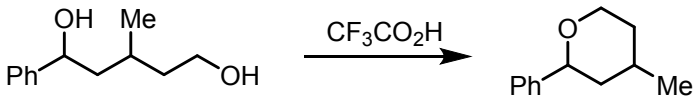
Under nitrogen atmosphere, a flame-dried flask charged with a stir bar was added **3a** (34.8 mg, 0.2 mmol) and dry THF (0.5 mL), the reaction mixture was cooled to 0 °C. A BH_3•SMe_2 solution (10 M in THF) (100 µL, 1.0 mmol, 5 equiv) was slowly added at 0 °C. After addition, the reaction mixture was warmed to room temperature and allowed to stir for 1 hour. The reaction mixture was then cooled to 0 °C and aqueous NaOH solution (3 M) (5 equiv) was slowly added, followed by the addition of H_2O_2 (1 mL). The reaction was stirred at 0 °C for 1 hour. After cooling to room temperature, the reaction mixture was extracted with Et_2O (3×20 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated under vacuum. The crude mixture was purified by flash column chromatography to give product **5** (yield: 68%).



3-methyl-1-phenylpentane-1,5-diol (5)[14]

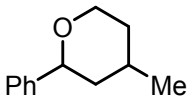
Yield: 68%. Colorless liquid. R_f = 0.45 (PE:EA=1:1). dr 5:1. ^{1}H NMR (400 MHz, $CDCl_3$) 7.38 – 7.19 (m, 5H), 4.73 (q, *J* = 9.3, 8.0 Hz, 1H), 3.70 – 3.54 (m, 2H), 3.45 (s, 1H), 2.86 (s, 1H), 1.77 – 1.54 (m, 3H), 1.51 – 1.23 (m, 2H), 0.97 (d, *J* = 6.7 Hz, 0.5H), 0.91 (d, *J* = 5.7 Hz, 2.5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.9, 127.5, 126.5, 124.9, 71.4, 59.9, 45.4, 37.9, 25.4, 19.5.

5.2 Application of diol 5 to the synthesis of heterocycles



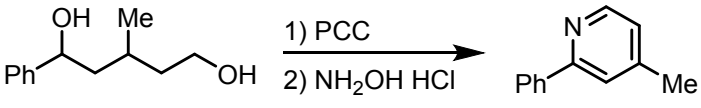
5 **6**, 75%

To a flame-dried flask charged with a stir bar was added **5** (19.4 mg, 0.1 mmol) and dry CH_2Cl_2 (2 mL), this mixture was cooled to 0 °C under a nitrogen atmosphere. To this solution was added CF_3SO_3H (17.6 μl, 0.2 mmol, 2 equiv) and the resulting reaction mixture was stirred at 0 °C for 1 h. After completion of the reaction, saturated aqueous $NaHCO_3$ (10 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated under vacuum. The crude product was purified by flash chromatography to give the desired product **6** (yield: 75%).



4-methyl-2-phenyltetrahydro-2H-pyran (6)[15]

Yield: 75%. Colorless liquid. R_f = 0.6 (PE:Et_2O=20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.23 (m, 5H), 4.24 (d, *J* = 11.3 Hz, 1H), 4.08 (dd, *J* = 12.4, 4.2 Hz, 1H), 3.53 (t, *J* = 12.0 Hz, 1H), 1.80 – 1.74 (m, 1H), 1.71 (s, 1H), 1.58 – 1.55 (m, 1H), 1.32 – 1.24 (m, 2H), 0.91 (d, *J* = 6.5 Hz, 3H).

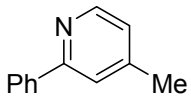


5 **7**

59% (2 steps)

To a flame-dried flask charged with a stir bar was added PCC (216 mg, 0.3 mmol) and CH_2Cl_2 (20 mL). To this solution was added **5** (19.4 mg, 0.1 mmol) in 2 mL of CH_2Cl_2 dropwisely. The reaction mixture was stirred for 2 h. After completion of the reaction, the reaction mixture was filtered through a plug of Celite and washed with CH_2Cl_2. The filtrate was concentrated under vacuum. The crude product is directly subjected to the next reaction without further purification.

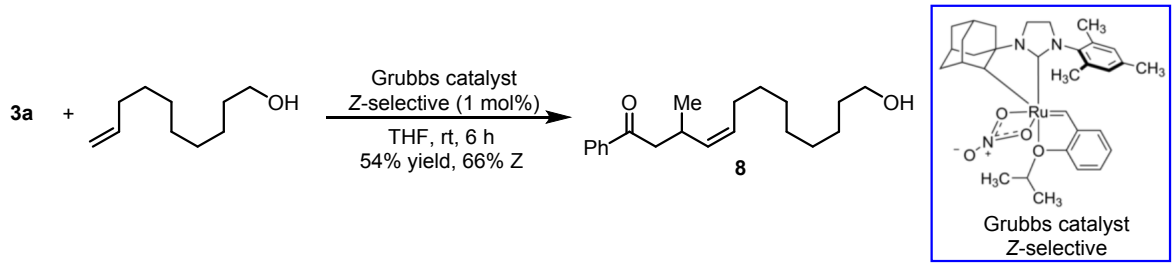
To a 4 mL reaction vial was added the above-obtained aldehyde and acetonitrile (1.2 mL), a solution of hydroxylamine hydrochloride (3.0 mmol) was added and the vial was capped and heated at 80 °C overnight. After completion of the reaction, the solvent was removed under vacuum. The crude mixture was then dissolved in 2 mL of saturated aqueous K_2CO_3/H_2O (1:1) and was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under vacuum. The crude product was purified by flash chromatography to give the desired product **7** (yield: 59% for 2 steps).



4-methyl-2-phenylpyridine (7)[16]

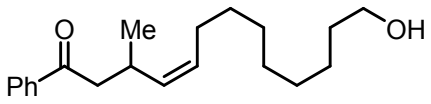
Yield: 59% (2 steps). White solid. R_f = 0.4 (PE:Et_2O=20:1). ^1H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, *J* = 4.9 Hz, 1H), 7.97 (d, *J* = 7.6 Hz, 2H), 7.54 (s, 1H), 7.51 – 7.34 (m, 3H), 7.04 (d, *J* = 4.9 Hz, 1H), 2.40 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.4, 149.4, 147.7, 139.5, 128.8, 128.7, 126.9, 123.1, 121.5, 21.2.

5.3 Olefin metathesis of 3a into enol 8



To a 4 mL vial was charged with **3a** (34.8 mg, 0.2 mmol), 8-nonen-1-ol (180 µl, 1.0 mmol, 5 equiv) and THF (0.2 mL), a solution of the Grubbs *Z*-selective catalyst® (CAS: 1352916-84-7) (40 µL, 0.002 mmol) (0.05 M in THF) was added. The resulting solution was stirred in an open vial for 5 h. After

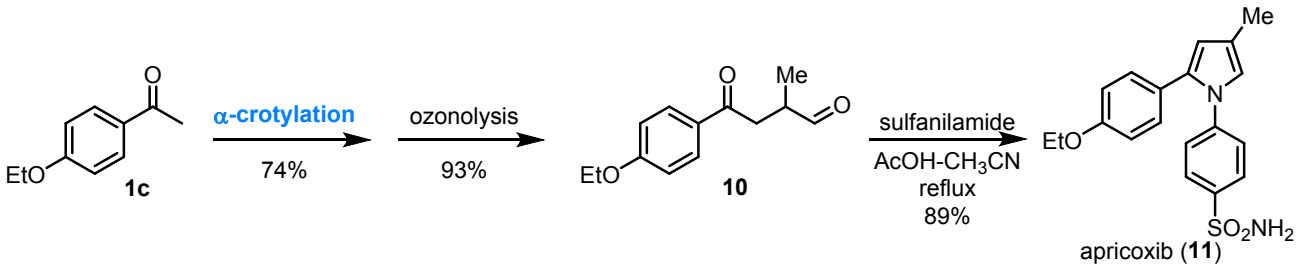
completion of the reaction, the reaction was quenched with excess amount of ethyl vinyl ether (0.1 mL). The solvent was removed under vacuum. The crude product was purified by flash chromatography to give the desired product **8** (yield: 54%).



(*Z*)-13-hydroxy-3-methyl-1-phenyltridec-4-en-1-one (8)

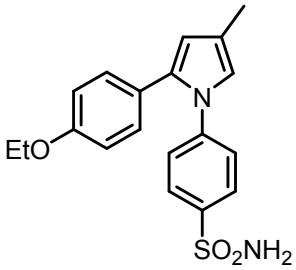
Yield: 54%. Colorless liquid. R_f = 0.35 (PE:Et_2O=10:1). 66% *Z*. ^{1}H NMR (400 MHz, $CDCl_3$) δ ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 9.0 Hz, 2H), 7.61 – 7.50 (m, 1H), 7.45 (d, *J* = 7.7 Hz, 2H), 5.46 – 5.16 (m, 2H), 3.68 – 3.58 (m, 2H), 3.26 – 2.80 (m, 3H), 2.10 – 1.89 (m, 2H), 1.63 – 1.51 (m, 2H), 1.43 – 1.20 (m, 11H), 1.05 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.7, 137.3, 134.2, 132.9, 129.4, 128.5, 128.2, 63.0, 46.1, 32.8, 29.7, 29.4, 29.4, 29.2, 28.7, 27.4, 25.7, 21.3. Observed ^{13}C NMR of the *E* isomer: 134.52, 129.30, 45.88, 33.07, 20.61. IR (KBr) 2923, 2851, 1681, 1448, 1260, 1019, 799, 689 cm^{-1}. HRMS: calcd. $C_{20}H_{31}O_2Na$ $[M+Na]^+$: 303.2324. Found: 303.2318.

5.4 Synthesis of apricoxib:[17]



Compound **3c** was obtained by the key reaction from **1c** and **2** (74% yield, Table 2). Compound **3c** (0.2 mmol, 43.6 mg) in 2 mL of CH_2Cl_2/MeOH (1:5) was treated with ozone bubbles at –78 °C until a blue coloration persisted. Me_2S (80 μL, 0.22 mmol) was then added and the reaction mixture was warmed slowly to room temperature. The solvent was evaporated under vacuum to give the crude aldehyde (93%), which was then diluted with 2 mL of 40% acetic acid in acetonitrile and sulfanilamide (0.23 mmol) was added. The mixture was refluxed until complete consumption of the aldehyde as monitored by TLC. After cooling to room temperature, the mixture was concentrated under vacuum and diluted with 10 mL of EtOAc. The organic layer was then washed with saturated Na_2CO_3, followed

by brine, dried over $MgSO_4$ and concentrated. The crude mixture was purified by silica gel flash chromatography to give apricoxib (**11**) as a light yellow solid (yield: 89%).

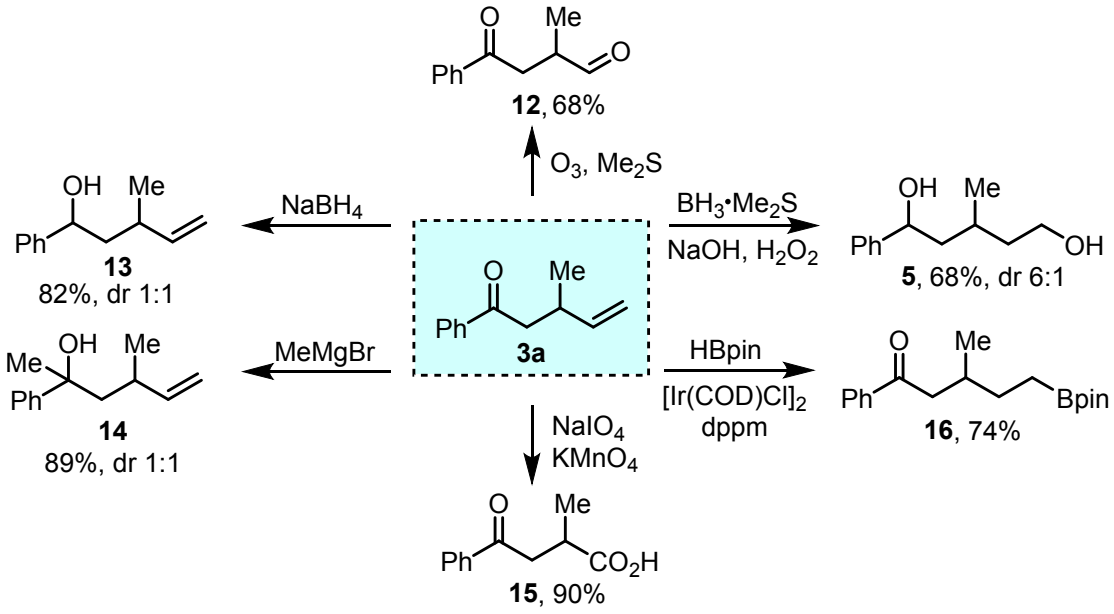


apricoxib
(**11**)

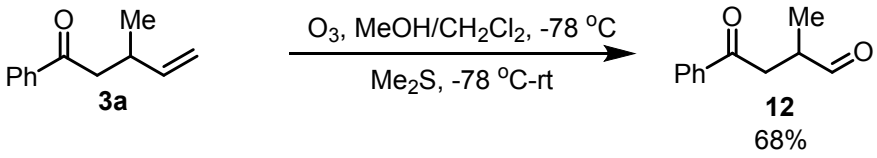
4-(2-(4-ethoxyphenyl)-4-methyl-1H-pyrrol-1-yl)benzenesulfonamide (apricoxib) (11)[18]

Yield: 89%. light yellow solid. R_f = 0.30 (PE:EA=3:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 – 7.76 (m, 2H), 7.22 (d, *J* = 8.9 Hz, 2H), 7.06 – 6.97 (m, 2H), 6.83 – 6.75 (m, 2H), 6.72 (s, 1H), 6.23 (d, *J* = 1.9 Hz, 1H), 4.89 – 4.75 (m, 2H), 4.01 (q, *J* = 7.0 Hz, 2H), 2.17 (s, 3H), 1.40 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ158.0, 144.3, 138.6, 133.6, 129.7, 127.5, 125.2, 124.9, 121.1, 121.0, 114.4, 113.2, 63.4, 14.8, 11.7.

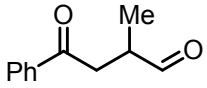
5.5 Other synthetic elaborations of 3a



5.5.1 Oxidation of 3a into carboxylic aldehyde 12.



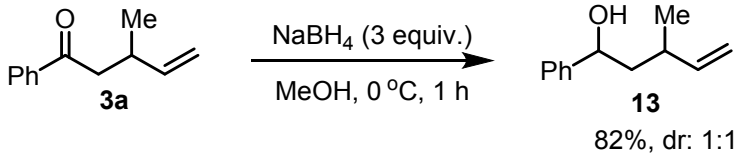
Under nitrogen atmosphere, to a flame-dried flask charged with a stir bar was added **3a** (69 mg, 0.4 mmol), pyridine (0.18 mL) and MeOH (3.9 mL). The mixture was cooled to –78 °C. Ozone was bubbled through until the starting material was consumed as determined by TLC analysis. Dimethylsulfide (0.32 mL) was added to quench the reaction and the resultant solution was then allowed to warm to room temperature and was stirred for 4 h. The reaction mixture was concentrated under reduced pressure. The organic residue was diluted with Et_2O (20 mL) and washed with a saturated aqueous $NaHCO_3$ solution (20 mL). Layers were separated and the aqueous layer was extracted with Et_2O (2×10 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated in vacuum. The crude product was purified by flash chromatography to give the desired product **12** (yield: 68%).



2-methyl-4-oxo-4-phenylbutanal (12)[19]

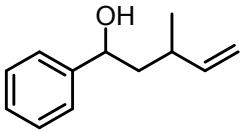
Yield: 68%. Colorless liquid. R_f = 0.55 (PE:Et_2O=10:1). ^1H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 7.98 (d, J = 7.0 Hz, 2H), 7.64 – 7.54 (m, 1H), 7.48 (t, *J* = 7.8 Hz, 2H), 3.50 (dd, *J* = 17.7, 6.5 Hz, 1H), 3.13 (q, *J* = 6.8 Hz, 1H), 3.01 (dd, *J* = 17.7, 5.8 Hz, 1H), 1.25 (d, *J* = 7.3 Hz, 3H). HRMS: calcd. $C_{11}H_{12}O_2Na$ $[M+Na]^+$: 199.0730. Found: 199.0723.

5.5.2 Reduction of 3a into 13.



To a flame-dried flask equipped with a stir bar was added **3a** (0.1 mmol, 17.4 mg) and anhydrous MeOH (0.5 mL). The flask was placed in an ice bath. $NaBH_4$ (0.3 mmol, 3 equiv) was added portion-wise and the reaction mixture was allowed to stir at 0 °C for 1 h. The reaction was quenched with saturated $NaHCO_3$ and extracted with CH_2Cl_2 (3 × 10 mL), dried with $MgSO_4$, and concentrated under

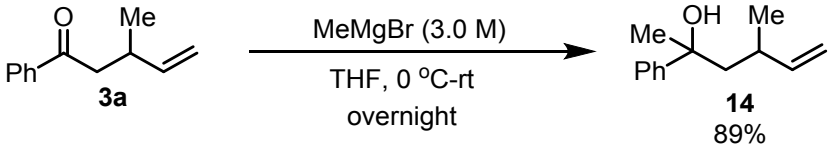
reduced pressure. The crude mixture was purified by silica flash chromatography to afford 15.3 mg of the product **13** (yield: 82%).



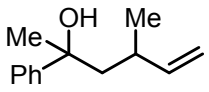
3-methyl-1-phenylpent-4-en-1-ol (13)[20]

Yield: 82%. Colorless liquid. R_f = 0.5 (PE:Et_2O=10:1). dr: 1:1. ^1H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.20 (m, 5H), 5.85 – 5.64 (m, 1H), 5.12 – 4.93 (m, 2H), 4.76 – 4.65 (m, 1H), 2.46 – 2.35 (m, 0.5H), 2.26 – 2.15 (m, 0.5H), 2.11 – 1.95 (m, 1H), 1.91 – 1.74 (m, 1H), 1.70 – 1.56 (m, 1H), 1.03 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.2, 144.7, 144.6, 143.9, 128.5, 127.6, 127.4, 126.1, 125.8, 113.7, 113.3, 73.0, 72.3, 46.1, 45.9, 35.2, 34.9, 21.0, 20.5.

5.5.3 Reaction of 3a with MeMgBr to 14.



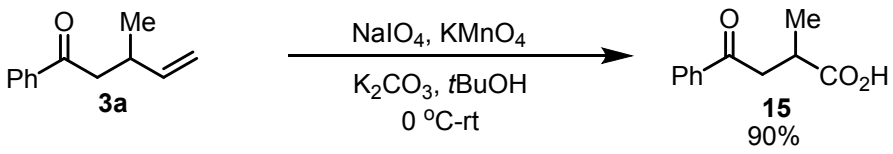
Under nitrogen atmosphere, to a flame-dried flask charged with a stir bar was added **3a** (0.1 mmol, 17.4 mg) and dry THF (3 mL). The solution was cooled to 0 °C and a THF solution of MeMgBr (3.0 M in THF) (2.5 equiv) was added dropwise and the flask was slowly warmed to room temperature and allowed to stir overnight. The reaction was then cooled to 0 °C and quenched with sat. NH_4Cl. The partitions were warmed to room temperature and the two layers were separated. The aqueous layer was extracted twice with Et_2O and the combined organic layers were dried over $MgSO_4$, filtered and concentrated. The crude mixture was purified by flash column chromatography to give 9.5 mg of the desired product **14** (yield: 89%).



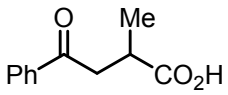
4-methyl-2-phenylhex-5-en-2-ol (14)

Yield: 89%. Colorless liquid. R_f = 0.45 (PE:Et_2O=10:1). dr: 1:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.11 (m, 5H), 5.81 – 5.59 (m, 1H), 4.95 – 4.73 (m, 2H), 2.34 – 2.22 (m, 0.5H), 2.10 – 1.89 (m, 1.5H), 1.88 – 1.68 (m, 2H), 1.52 (s, 1.8H), 1.40 (s, 1.2H), 0.92 (d, *J* = 6.9, 2.2 Hz, 1.7H), 0.83 (d, *J* = 6.8, 2.1 Hz, 1.3H). One of the two diastereomers was isolated and characterized. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 7.2 Hz, 2H), 7.25 (t, *J* = 7.5 Hz, 2H), 7.18 – 7.08 (m, 1H), 5.73 – 5.57 (m, 1H), 4.94 – 4.80 (m, 2H), 2.32 – 2.21 (m, 1H), 2.07 (s, 1H), 1.81 (dd, *J* = 14.4, 8.3 Hz, 1H), 1.71 (dd, *J* = 14.3, 4.7 Hz, 1H), 1.54 – 1.45 (m, 3H), 0.91 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.5, 145.8, 128.1, 126.5, 124.7, 113.0, 75.1, 50.9, 34.9, 30.0, 22.3. IR (KBr) 3446, 2967, 2926, 1636, 1494, 1446, 1374, 1275, 1098, 1028, 997, 908. HRMS: calcd. $C_{13}H_{18}O$ $[M]^+$: 190.1352. Found: 190.1360.

5.5.4 Oxidation of 3a into carboxylic acid 15.



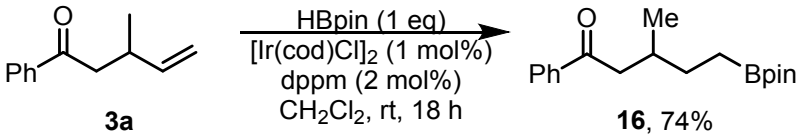
To a solution of **3a** (34.8 mg, 0.2 mmol) and K_2CO_3 (9.12 mg, 0.06 mmol, 0.33 equiv) in *t*-butyl alcohol (16 mL) and water (3 mL) was added an aqueous solution (13 mL) of sodium periodate (214 mg, 1 mmol, 5 equiv), potassium permanganate (9 mg, 0.06 mmol, 0.33 equiv) and K_2CO_3 (9.12 mg, 0.06 mmol, 0.33 equiv.) at 0 ºC in a dropwise manner. The resulting mixture was stirred at the same temperature for 30 min and then warmed to room temperature and further stirred overnight. The reaction mixture was acidified with 1 M of hydrochloric acid at 0 ºC to pH ca. 2, and solid sodium pyrosulfite was added until reddish color disappeared. The mixture was then concentrated under reduced pressure to remove *t*-butyl alcohol. The resulting aqueous solution was extracted with CH_2Cl_2 (3×20 mL). The combined organic layer was washed with brine (20 mL), dried over $MgSO_4$, and concentrated. The crude mixture was purified by flash column chromatography to give product **15** (yield: 90%).



2-methyl-4-oxo-4-phenylbutanoic acid (15)[21]

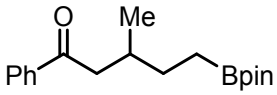
Yield: 90%. White solid. R_f = 0.34 (PE:EA=5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J = 7.1 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 3.48 (dd, *J* = 17.7, 7.7 Hz, 1H), 3.24 – 3.11 (m, 1H), 3.06 (dd, *J* = 17.7, 5.4 Hz, 1H), 1.33 (d, *J* = 7.1 Hz, 3H). HRMS: calcd. $C_{11}H_{12}O_3Na$ $[M+Na]^+$: 215.0679. Found: 215.0676.

5.5.5 Borohydride of 3a into borane 16



3a **16**, 74%

In a glovebox filled with nitrogen, a flame-dried vessel equipped with a magnetic stir bar was charged with $[Ir(cod)Cl]_2$ (1.34 mg, 0.002 mmol, 1 mol%) and 1,1-bis(diphenylphosphino)methane (dppm) (1.54 mg, 0.004 mmol, 2 mol%). The solids were dissolved in anhydrous DCM (0.3 mL) and allowed to stir for five minutes. To this solution was added **3a** (34.8 mg, 0.2 mmol), followed by dropwise addition of 4,4,5,5-tetramethyl-1,3,2dioxaborolane (pinacolborane, HBpin) (29 μL, 0.2 mmol, 1 equiv). The vessel was sealed, removed from the glove box, and was allowed to stir at room temperature for 18 hours. Upon completion, the reaction was quenched with methanol and water and then partitioned between brine and DCM. The aqueous layer was extracted with CH_2Cl_2 (3×10 mL) and the combined organic phases were dried over anhydrous $MgSO_4$, filtered, and concentrated under vacuum. The crude product was purified by flash chromatography to give the desired product **16** (yield: 74%).



3-methyl-1-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentan-1-one (16)

Yield: 74%. Colorless liquid. R_f = 0.5 (PE:Et_2O=20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.5 Hz, 2H), 7.57 – 7.51 (m, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 3.05 – 2.93 (m, 1H), 2.69 (dd, *J* = 15.7, 8.6 Hz, 1H), 2.15 – 2.04 (m, 1H), 1.44 – 1.34 (m, 2H), 1.24 (s, 12H), 0.94 (d, *J* = 6.5 Hz, 3H), 0.86 – 0.76 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.5, 137.4, 132.8, 128.5, 128.1, 83.0, 45.7, 31.9, 31.3, 24.8, 24.8, 19.5. IR (KBr) 2975, 2927, 1682, 1370, 1316, 1143, 690 cm^{-1}. HRMS: calcd. $C_{18}H_{27}O_3NaB[M+Na]^+$: 325.1945. Found: 325.1957.

6. References:

[1] Kinuta, H.; Tobisu, M.; Chatani, N. Rhodium Catalyzed Borylation of Aryl 2-Pyridyl Ethers through Cleavage of the Carbon−Oxygen Bond: Borylative Removal of the Directing Group. *J. Am. Chem. Soc*. **2015**, *137*, 1593−1600.

[2] Evans, P. A.; Uraguchi, D. Regio- and Enantiospecific Rhodium-Catalyzed Arylation of Unsymmetrical Fluorinated Acyclic Allylic Carbonates: Inversion of Absolute Configuration.*J. Am. Chem. Soc*. **2003**, *125*, 7158−7159

[3] Li, J.; Ji, K.; Zheng, R.; Nelson, J.; Zhang, L. Expanding the Horizon of Intermolecular Trapping of *in situ* Generated α-Oxo Gold Carbenes: Efficient Oxidative Union of Allylic Sulfides and Terminal Alkynes *via* C–C Bond Formation. *Chem. Commun*, **2014**, *50*, 4130-4133.

[4] Mikami, K.; Takahashi, K.; Nakai, T. Diastereocontrol via the Phenol- and Palladium(II)-Catalyzed Claisen Rearrangement with Cyclic Enol Ethers. *Tetrahedron Lett*. **1987**, *28*, 5879-5882.

[5] Usui, I.; Schmidt, S.; Breit, B. Dual Palladium- and Proline-Catalyzed Allylic Alkylation of Enolizable Ketones and Aldehydes with Allylic Alcohols. *Org. Lett*. **2009**, *11*, 1453-1456.

[6] Takahashi, K.; Miyake, A.; Hata, G. Palladium-Catalyzed Reactions of 1,3-Dienes with Active Methylene Compounds. IV. Palladium-diphosphine Complex Catalysts. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 1183-1191.

[7] Sinha, A. K.; Sinha, B. P.; Sharma, A.; Kumar, V.; Acharya, R. Microwave-Assisted Mild Conversion of Natural Dihydrotagetone into 5-Isobutyl-3-methyl-4,5-dihydro-2(3*H*)-furanone, an Analogue of Whisky Lactone. *Aust. J. Chem.* **2007**, *60*, 124-127.

[8] Chen, Q.-A.; Kim, D. K.; Dong, V. M. Regioselective Hydroacylation of 1,3-Dienes by Cobalt Catalysis. *J. Am. Chem. Soc*. **2014**, *136*, 3772−3775

[9] van der Baan, J. L.; Bickelhaupt, F. Palladium(II)-Catalyzed Claisen Rearrangement of Allyl Vinyl Ethers. *Tetrahedron Lett.* **1986**, *27*, 6267-6270.

[10] López, F.; Harutyunyan, S. R.; Minnaard, A. J.; Feringa, B. L. Copper-Catalyzed Enantioselective Conjugate Addition of Grignard Reagents to Acyclic Enones. *J. Am. Chem. Soc*. **2004**, *126*, 12784−12785.

[11] Ogoshi, S.; Haba, T.; Ohashi, M. Nickel-Catalyzed Direct Conjugate Addition of Simple Alkenes to Enones. *J. Am. Chem. Soc*. **2009**, *131*, 10350−10351.

[12] Wu, T. R.; Chong, J. M. Asymmetric Conjugate Alkenylation of Enones Catalyzed by Chiral Diols. *J. Am. Chem. Soc*. **2007**, *129*, 4908−4909

[13] Arava, S.; Kumar, J. N.; Maksymenko, S.; Iron, M. A.; Parida, K. N.; Fristrup, P.; Szpilman, A. M. Enolonium Species—Umpoled Enolates. *Angew. Chem., Int. Ed*. **2017**, *56*, 2599-2603.

[14] Liu, C.; Wang, X.; Li, Z.; Cui, L.; Li, C. Silver-Catalyzed Decarboxylative Radical Azidation of Aliphatic Carboxylic Acids in Aqueous Solution. *J. Am. Chem. Soc.* **2015**, *137*, 9820-9823.

[15] Berthiol, F.; Matsubara, R.; Kawai, N.; Kobayashi, S. Catalytic Asymmetric Michael Reactions with Enamides as Nucleophiles. *Angew. Chem. Int. Ed.* **2007**, *46*, 7803-7805.

[16] Zou, B.; Wei, J.; Cai, G.; Ma, D. Synthesis of an Oxazoline Analogue of Apratoxin A. *Org. Lett.* **2003**, *5*, 3503-3506.

[17] Hilf, J. A.; Holzwarth, M. S.; Rychnovsky, S. D. Route to Highly Substituted Pyridines. *J. Org. Chem.* **2016**, *81*, 10376-10382.

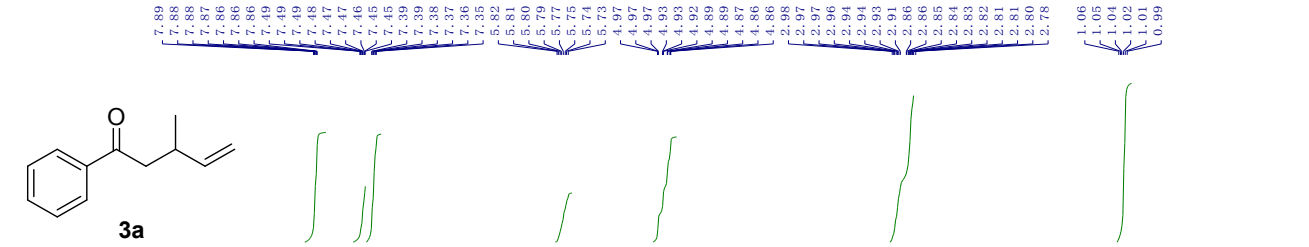
[18] Mandal, P. K.; Freiter, E. M.; Bagsby, A. L.; Robertson, F. M.; McMurray, J. S. Efficient Synthesis of Apricoxib, CS-706, a Selective Cyclooxygenase-2 Inhibitor, and Evaluation of Inhibition of Prostaglandin E2 Production in Inflammatory Breast Cancer Cells. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 6071-6073.

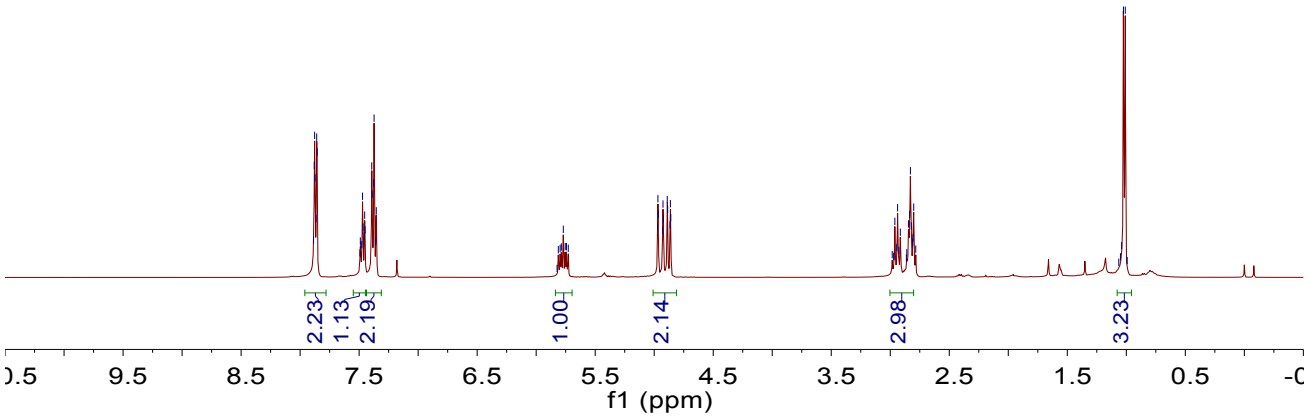
[19] Barluenga, J.; Álvarez-Rodrigo, L.; Rodríguez, F.; Fañanás, F. J. Zirconocene-Catalyzed Reactions of Alkenyl-Substituted Enol Ethers. *Angew. Chem. Int. Ed.* **2006**, *45*, 6362-6365.

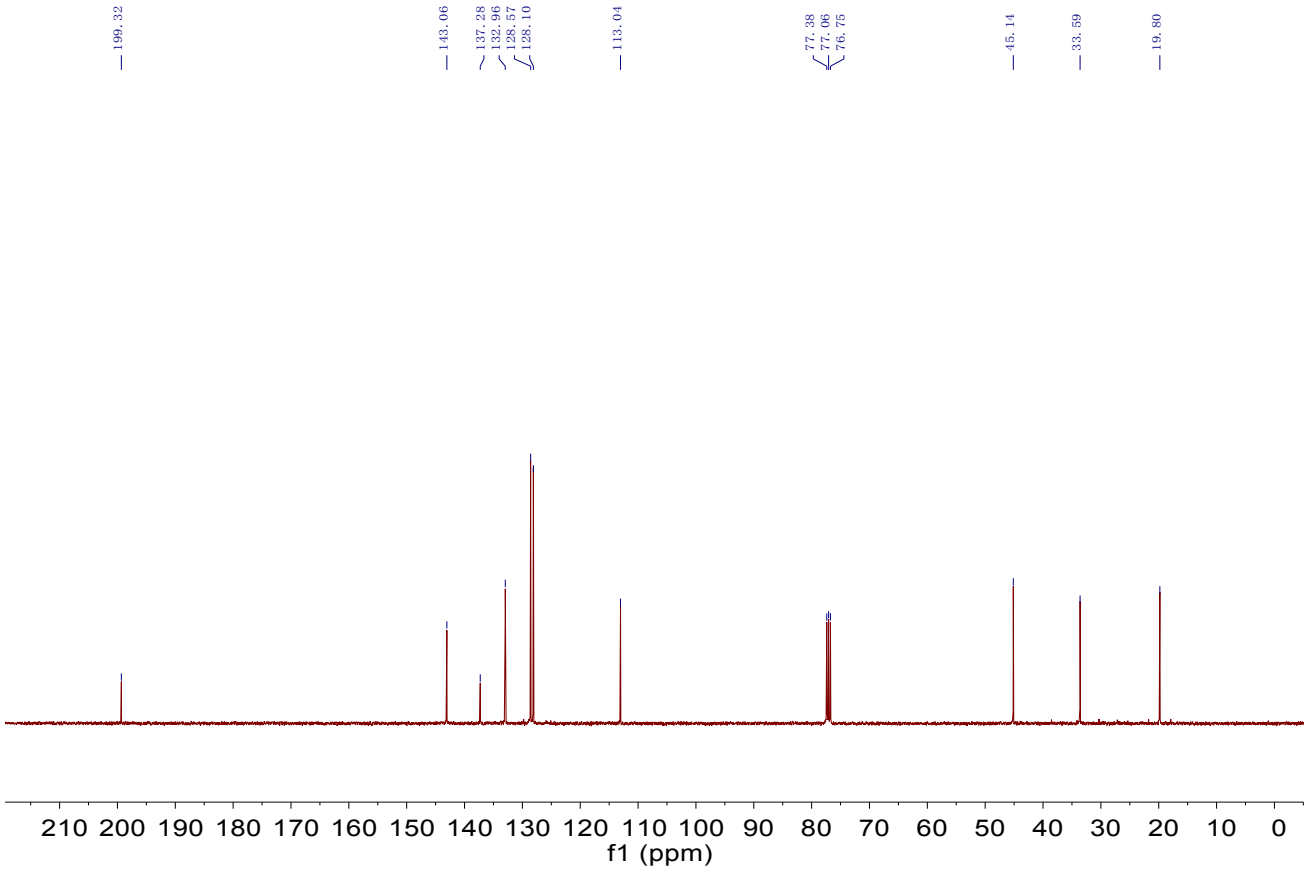
[20] López, F.; Harutyunyan, S. R.; Minnaard, A. J.; Feringa, B. L. Copper-Catalyzed Enantioselective Conjugate Addition of Grignard Reagents to Acyclic Enones. *J. Am. Chem. Soc.* **2004**, *126*, 12784-12785.

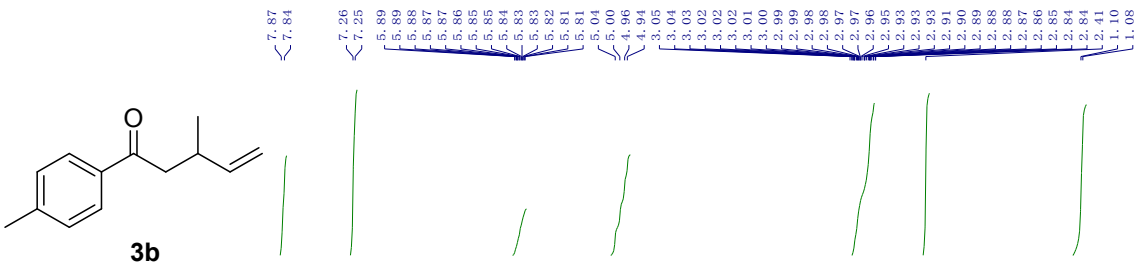
[21] Xie, J.; Huang, Z.-Z. The Cascade Carbo-Carbonylation of Unactivated Alkenes Catalyzed by an Organocatalyst and a Transition Metal Catalyst: a facile approach to γ-diketones and γ-carbonyl aldehydes from arylalkenes under air. *Chem. Commun.* **2010**, *46*, 1947-1949.

7. NMR Spectra

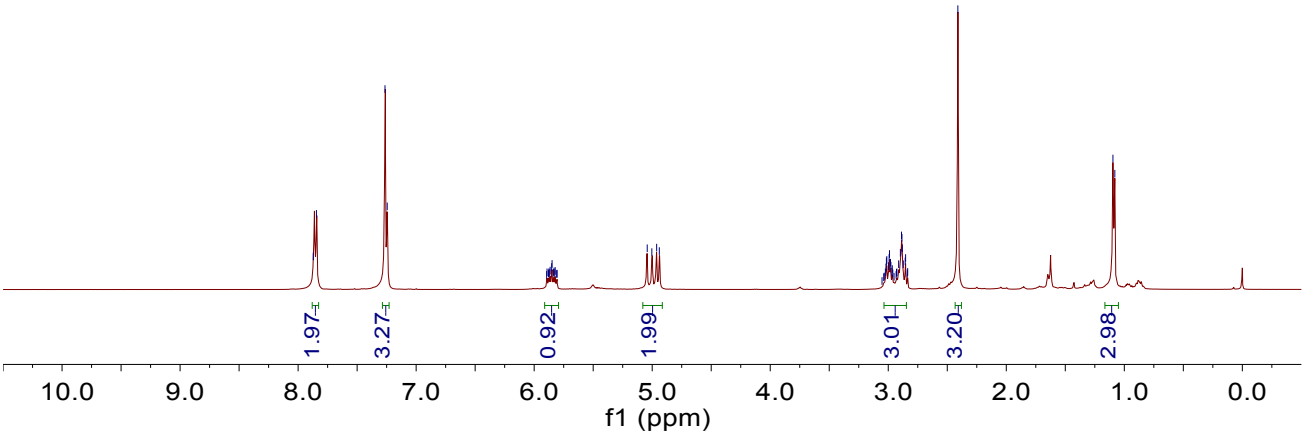


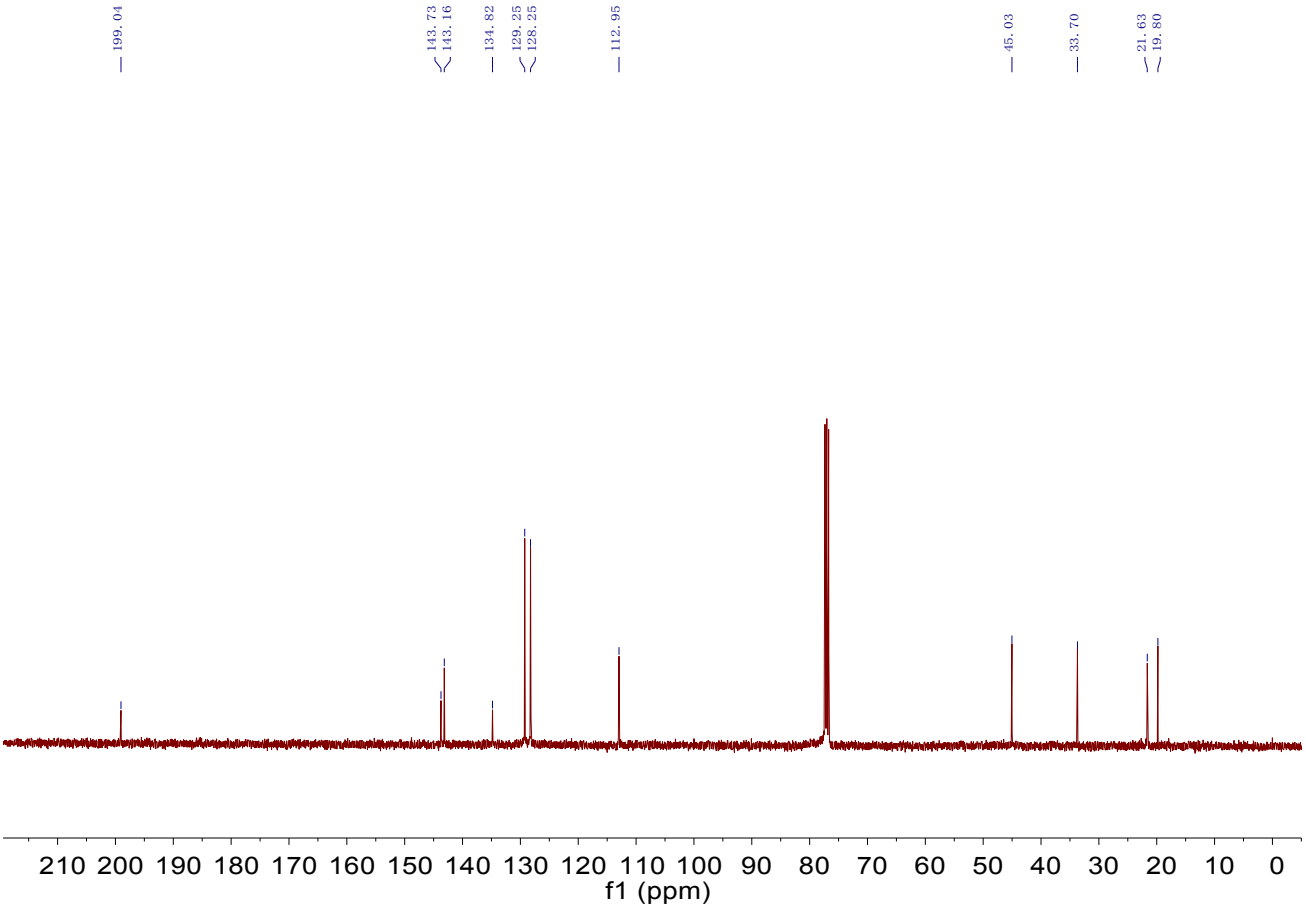


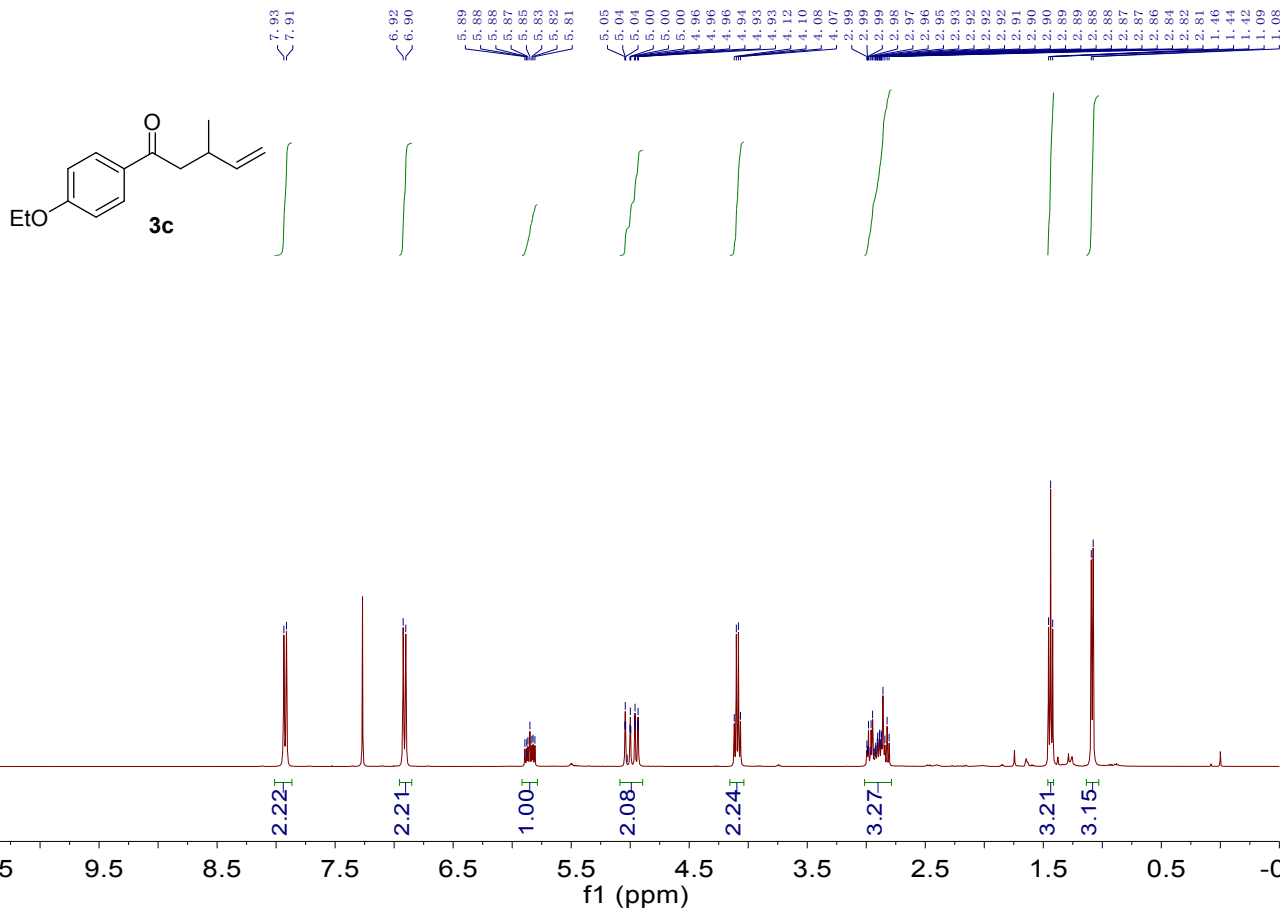


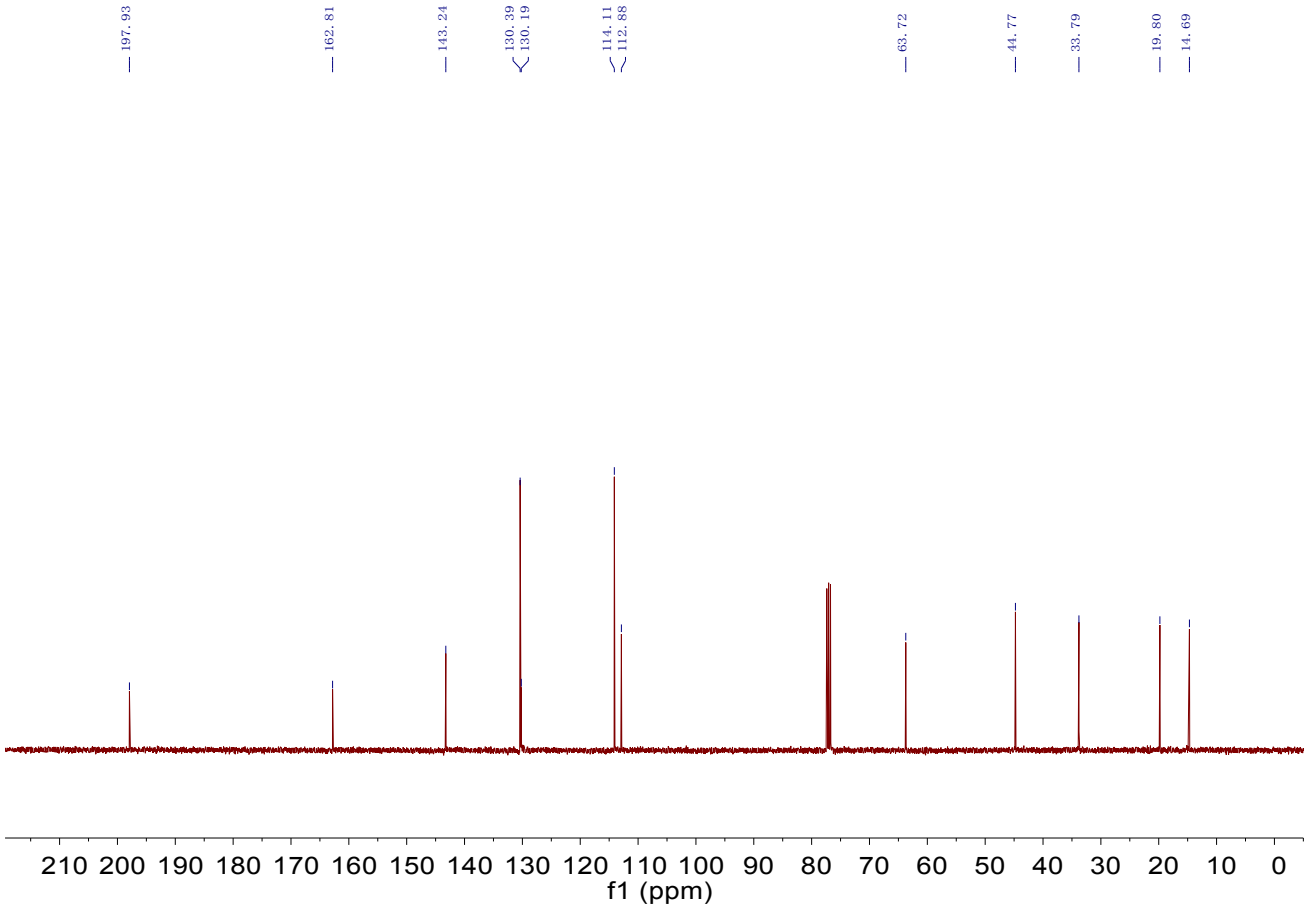

7.87
7.84
7.26
7.25
5.89
5.88
5.87
5.86
5.85
5.84
5.83
5.82
5.81
5.04
5.00
4.96
4.94
3.05
3.04
3.03
3.02
3.02
3.01
3.00
2.99
2.99
2.98
2.98
2.97
2.97
2.96
2.95
2.93
2.93
2.91
2.90
2.89
2.88
2.88
2.87
2.86
2.85
2.84
2.84
2.41
1.10
1.08
O

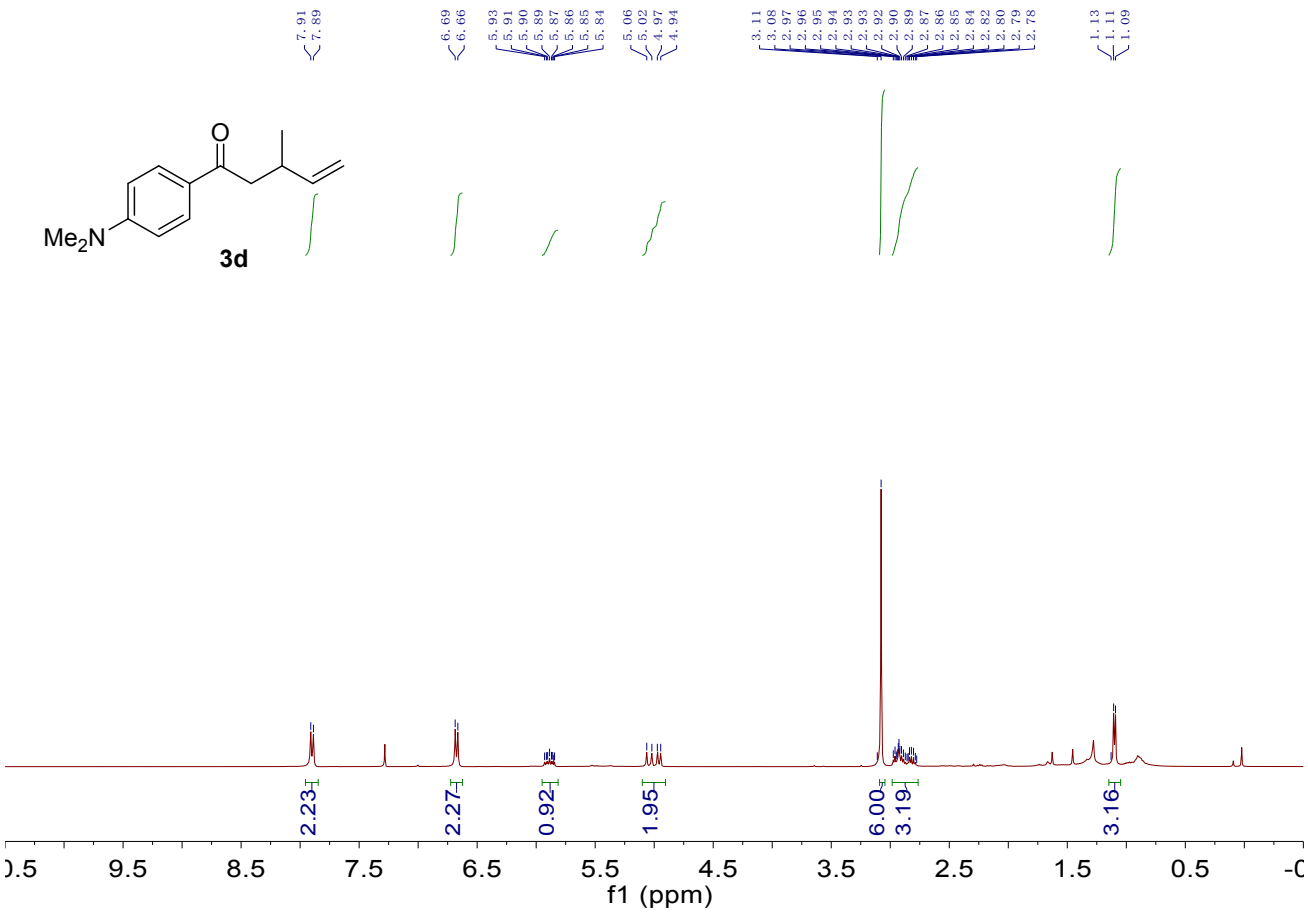
3b

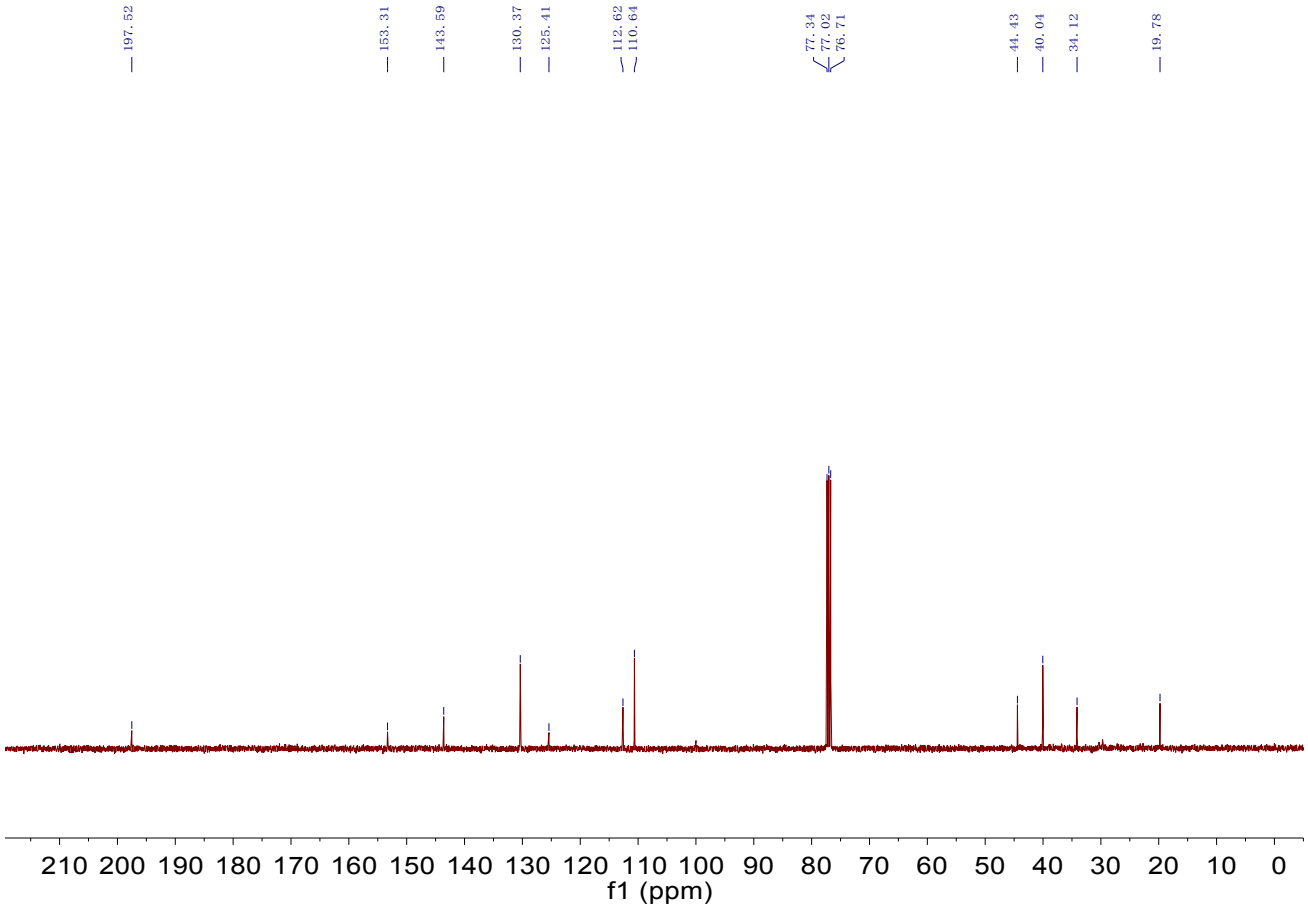

1.97
3.27
0.92
1.99
3.01
3.20
2.98
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

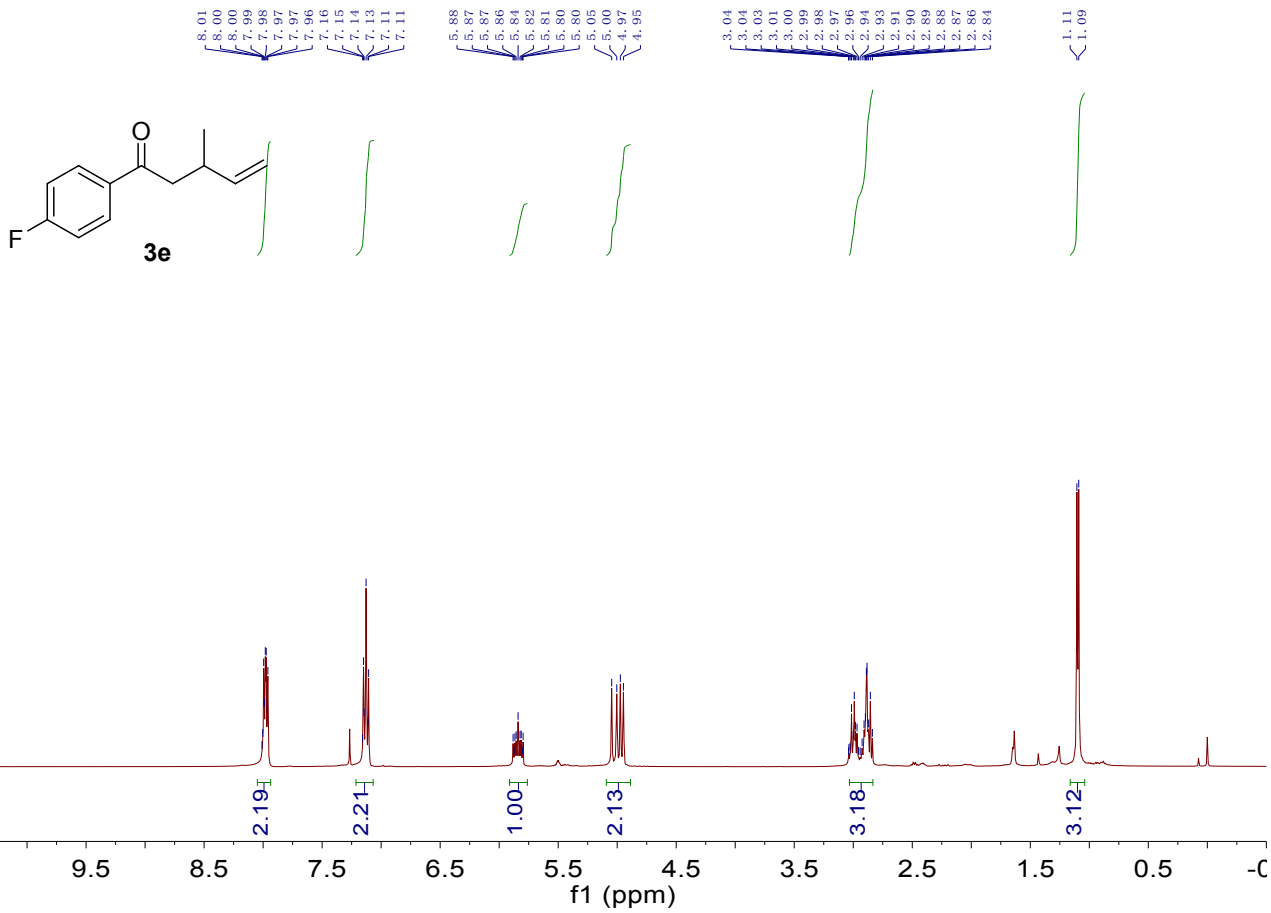

199.04
143.73
143.16
134.82
129.25
128.25
112.95
45.03
33.70
21.63
19.80
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

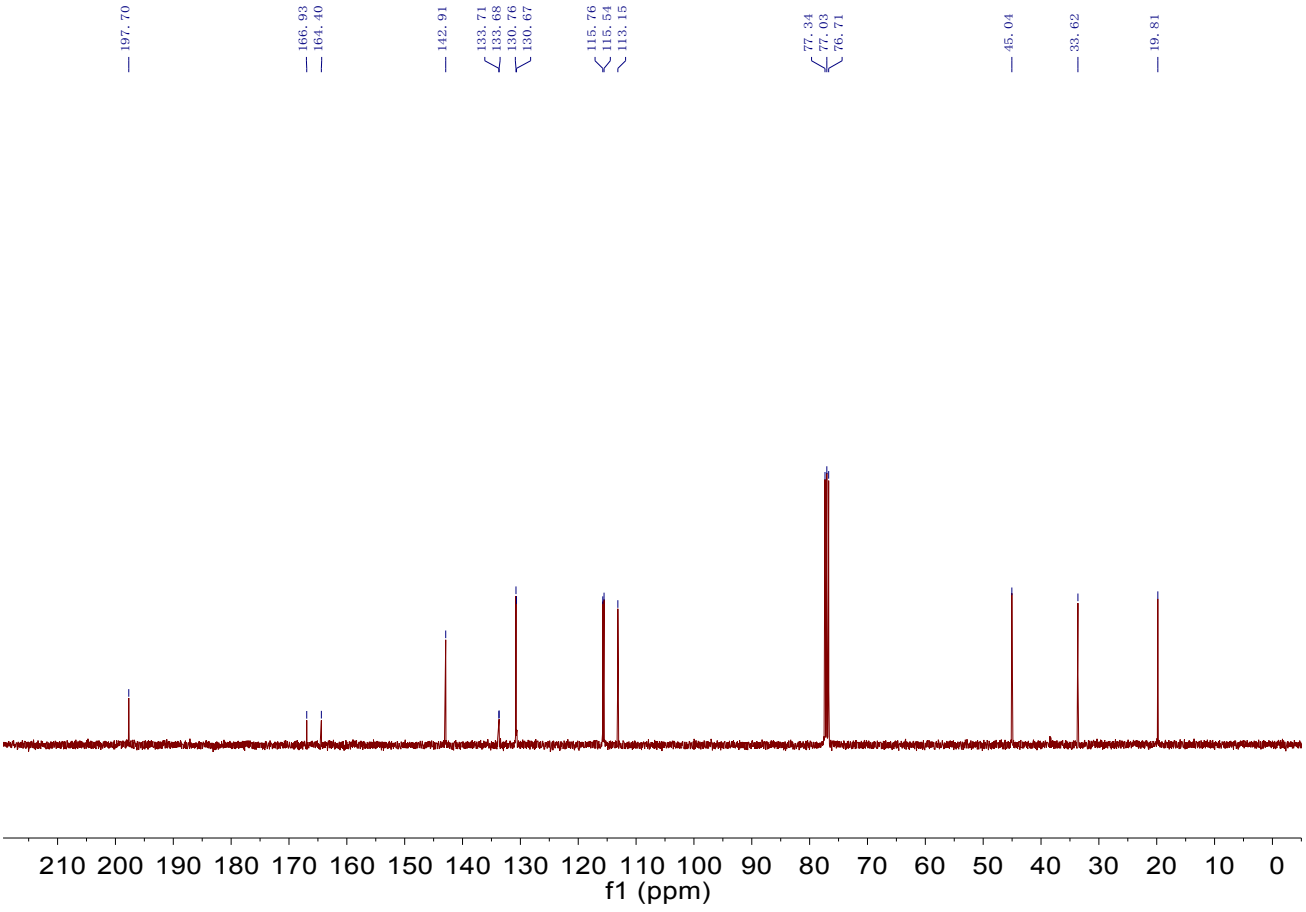

7.93
7.91
6.92
6.90
5.89
5.88
5.88
5.87
5.85
5.83
5.82
5.81
5.05
5.04
5.04
5.00
5.00
5.00
4.96
4.96
4.96
4.94
4.93
4.12
4.10
4.08
4.07
2.99
2.99
2.99
2.98
2.97
2.96
2.95
2.93
2.92
2.92
2.92
2.91
2.90
2.90
2.89
2.89
2.88
2.88
2.87
2.87
2.86
2.84
2.82
2.81
1.46
1.44
1.42
1.09
1.08
O
EtO
3c
2.22
2.21
1.00
2.08
2.24
3.27
3.21
3.15
f1 (ppm)

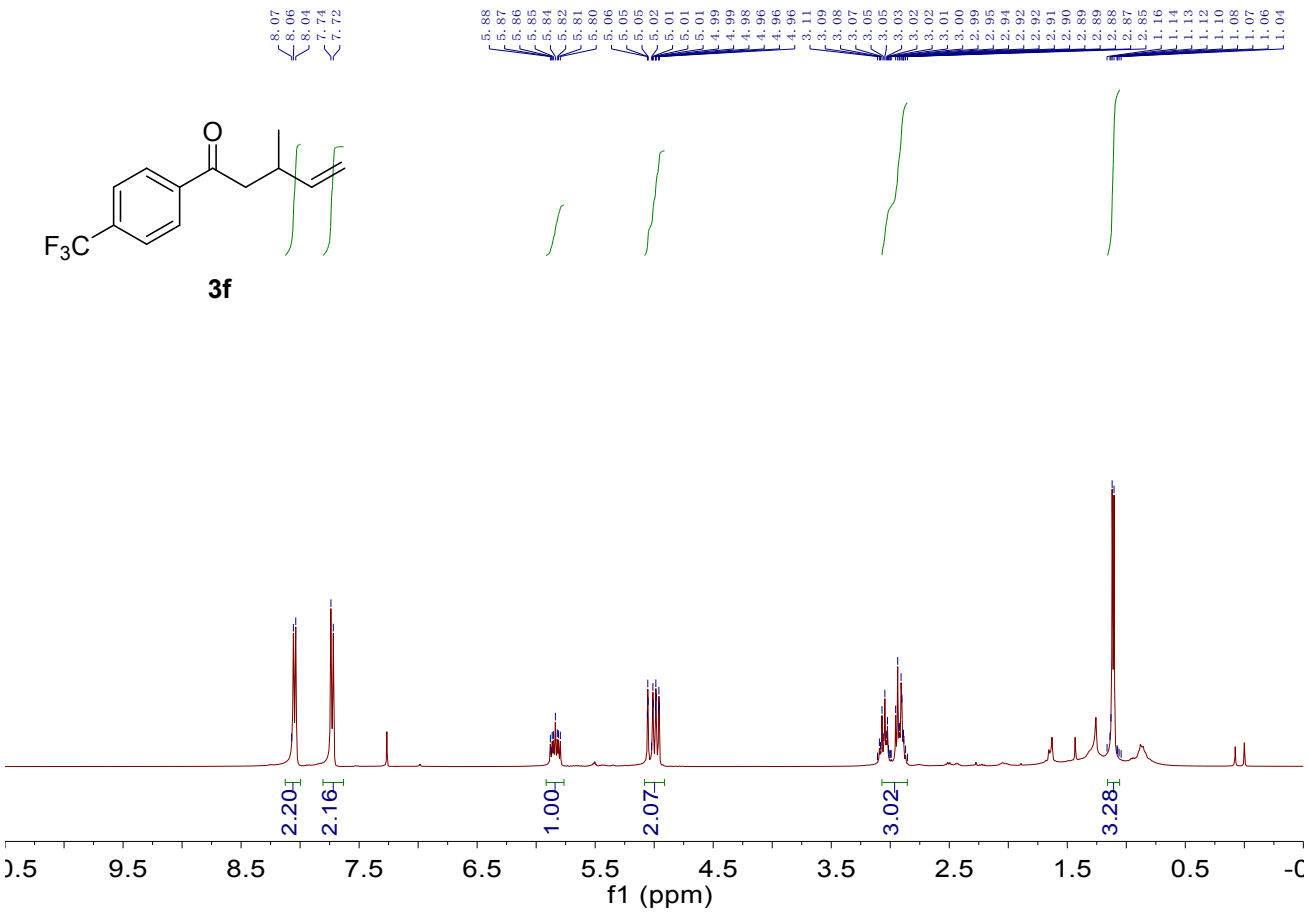

197.93
162.81
143.24
130.39
130.19
114.11
112.88
63.72
44.77
33.79
19.80
14.69
f1 (ppm)

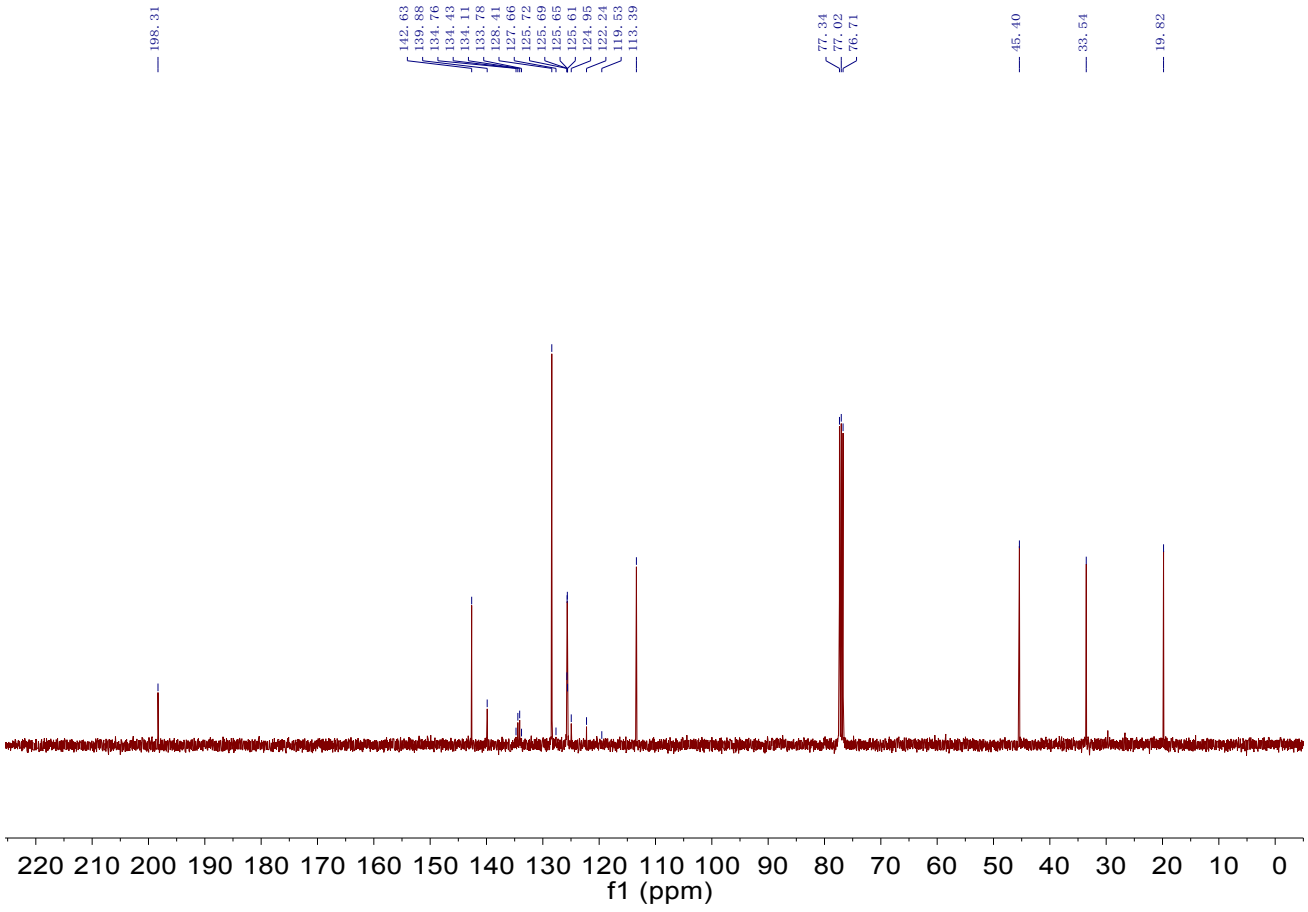

7.91
7.89
6.69
6.66
5.93
5.91
5.90
5.89
5.87
5.86
5.85
5.84
5.06
5.02
4.97
4.94
3.11
3.08
2.97
2.96
2.95
2.94
2.93
2.93
2.92
2.90
2.89
2.87
2.86
2.85
2.84
2.82
2.80
2.79
2.78
1.13
1.11
1.09
O
Me2N
3d
2.23
2.27
0.92
1.95
6.00
3.19
3.16
f1 (ppm)

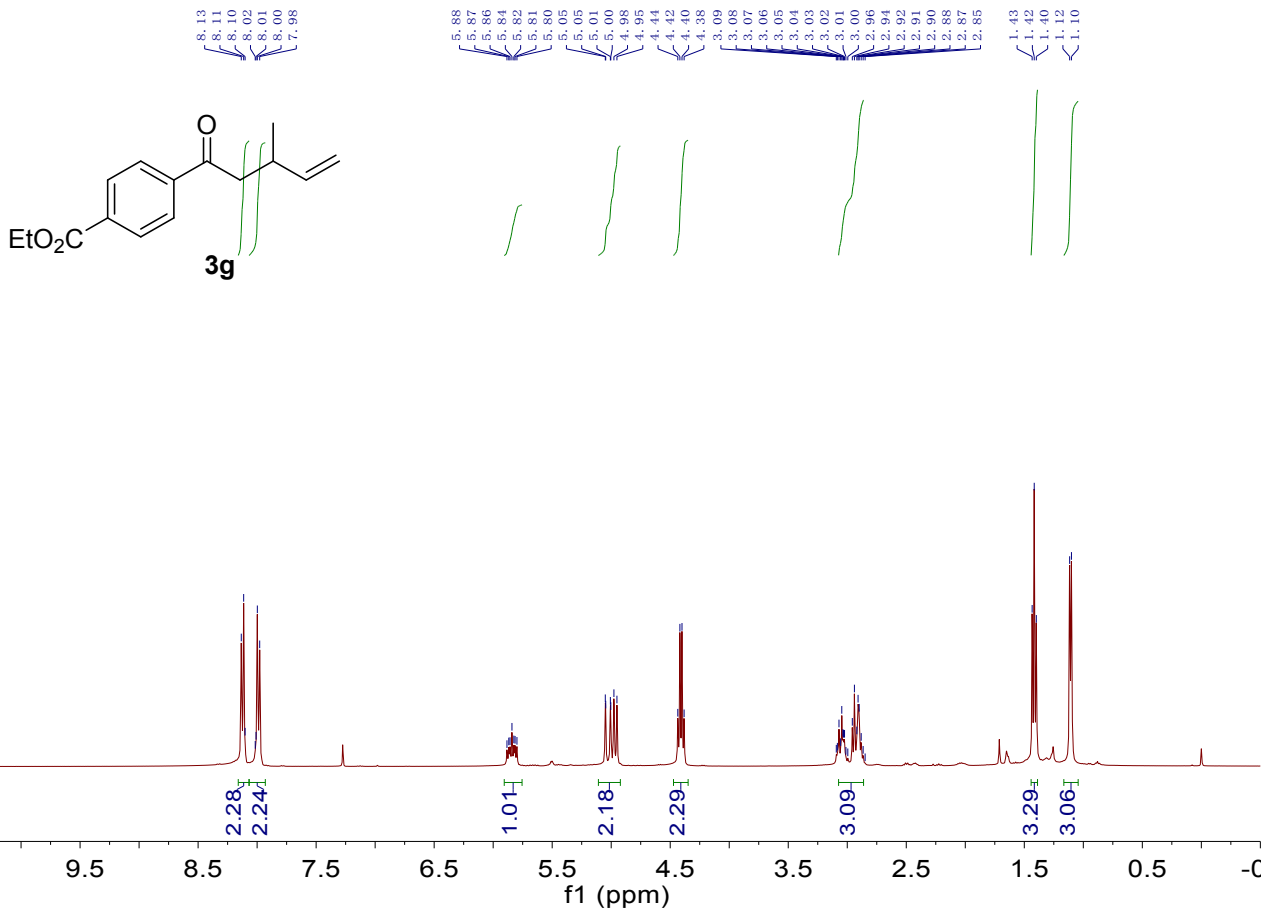

197.52
153.31
143.59
130.37
125.41
112.62
110.64
77.34
77.02
76.71
44.43
40.04
34.12
19.78
f1 (ppm)

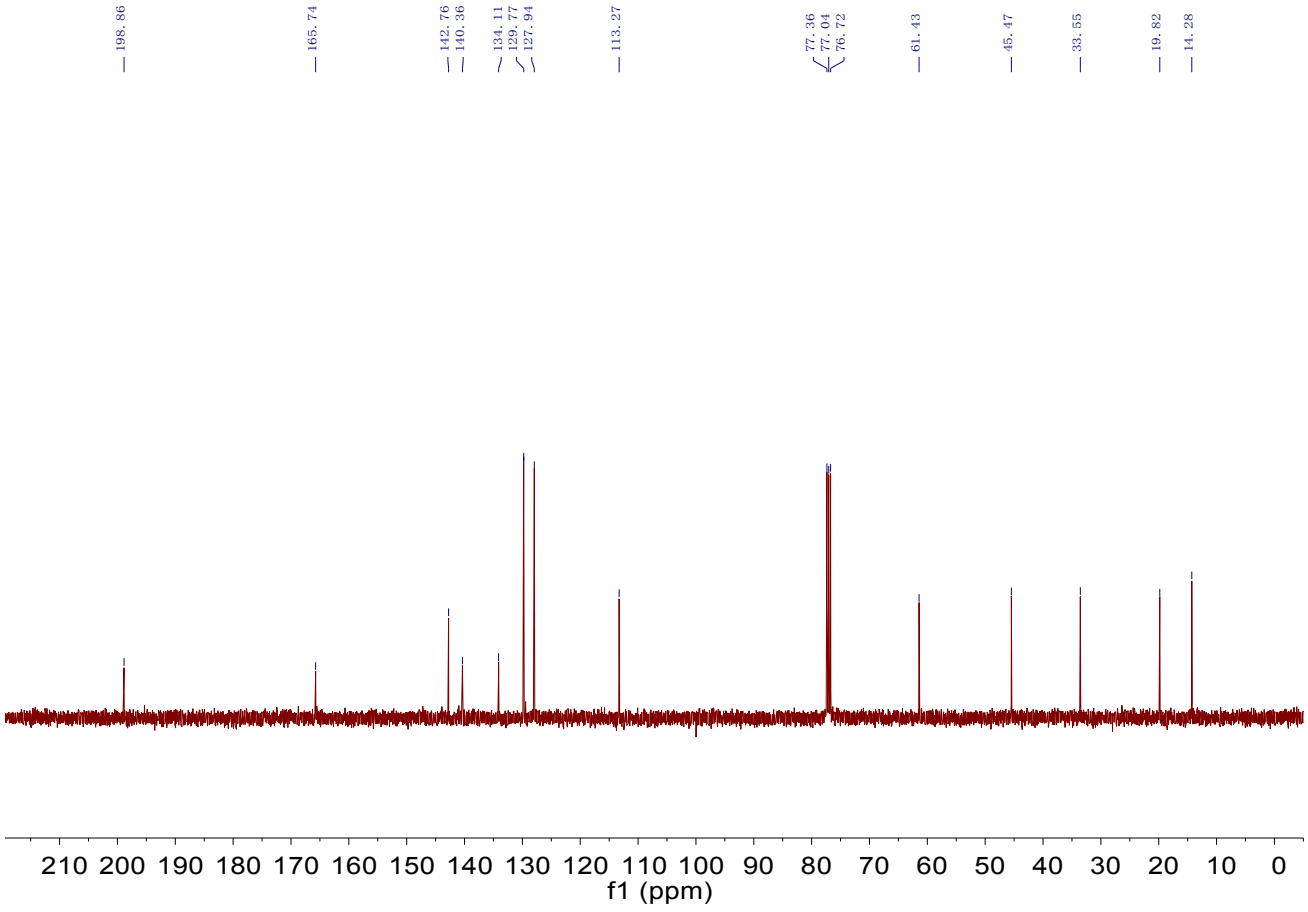

8.01
8.00
8.00
7.99
7.98
7.97
7.97
7.96
7.16
7.15
7.14
7.13
7.11
7.11
5.88
5.87
5.87
5.86
5.84
5.82
5.81
5.80
5.80
5.05
5.00
4.97
4.95
3.04
3.04
3.03
3.01
3.00
2.99
2.98
2.97
2.96
2.94
2.93
2.91
2.90
2.89
2.88
2.87
2.86
2.84
1.11
1.09
O
F
3e
2.19
2.21
1.00
2.13
3.18
3.12
f1 (ppm)

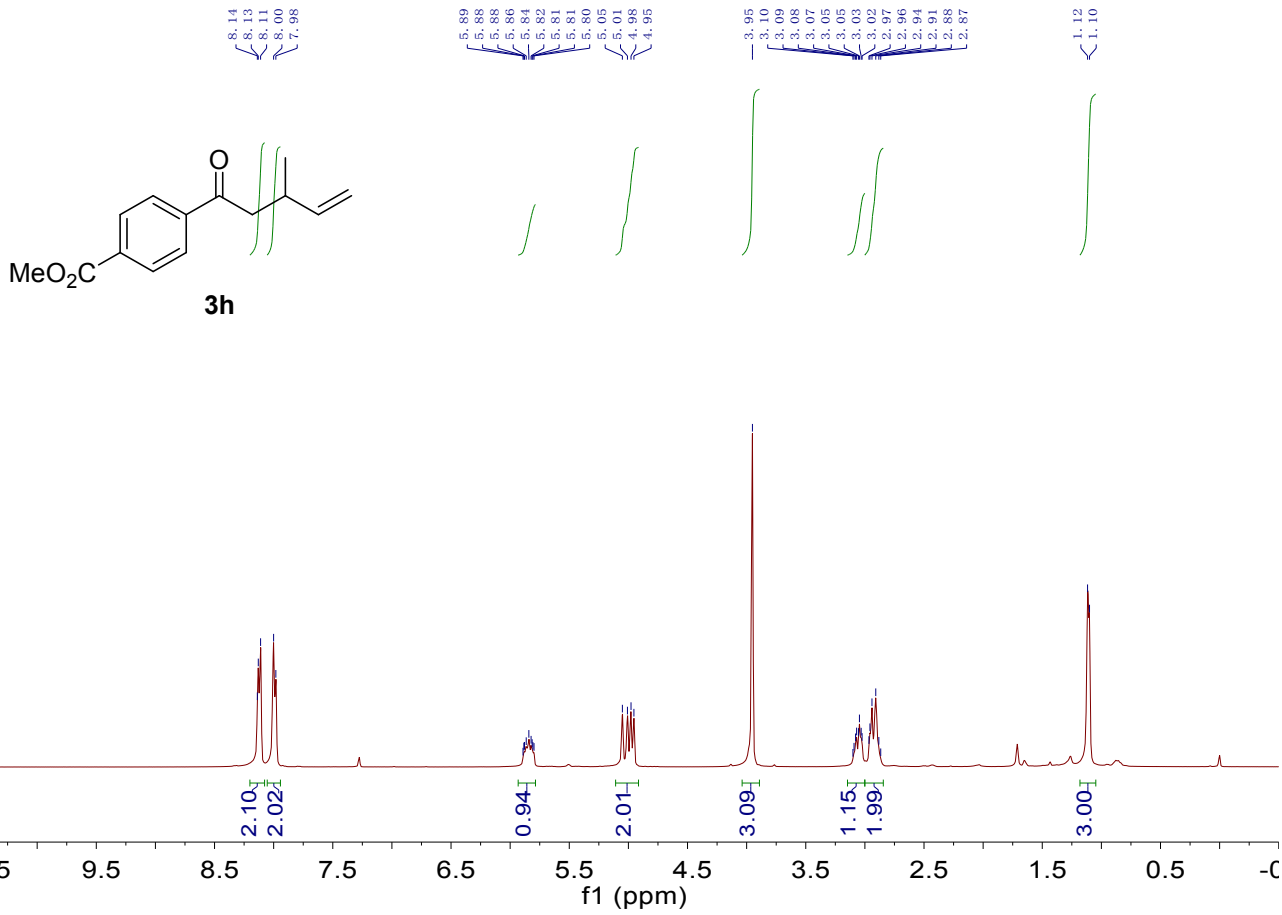

197.70
166.93
164.40
142.91
133.71
133.68
130.76
130.67
115.76
115.54
113.15
77.34
77.03
76.71
45.04
33.62
19.81
f1 (ppm)

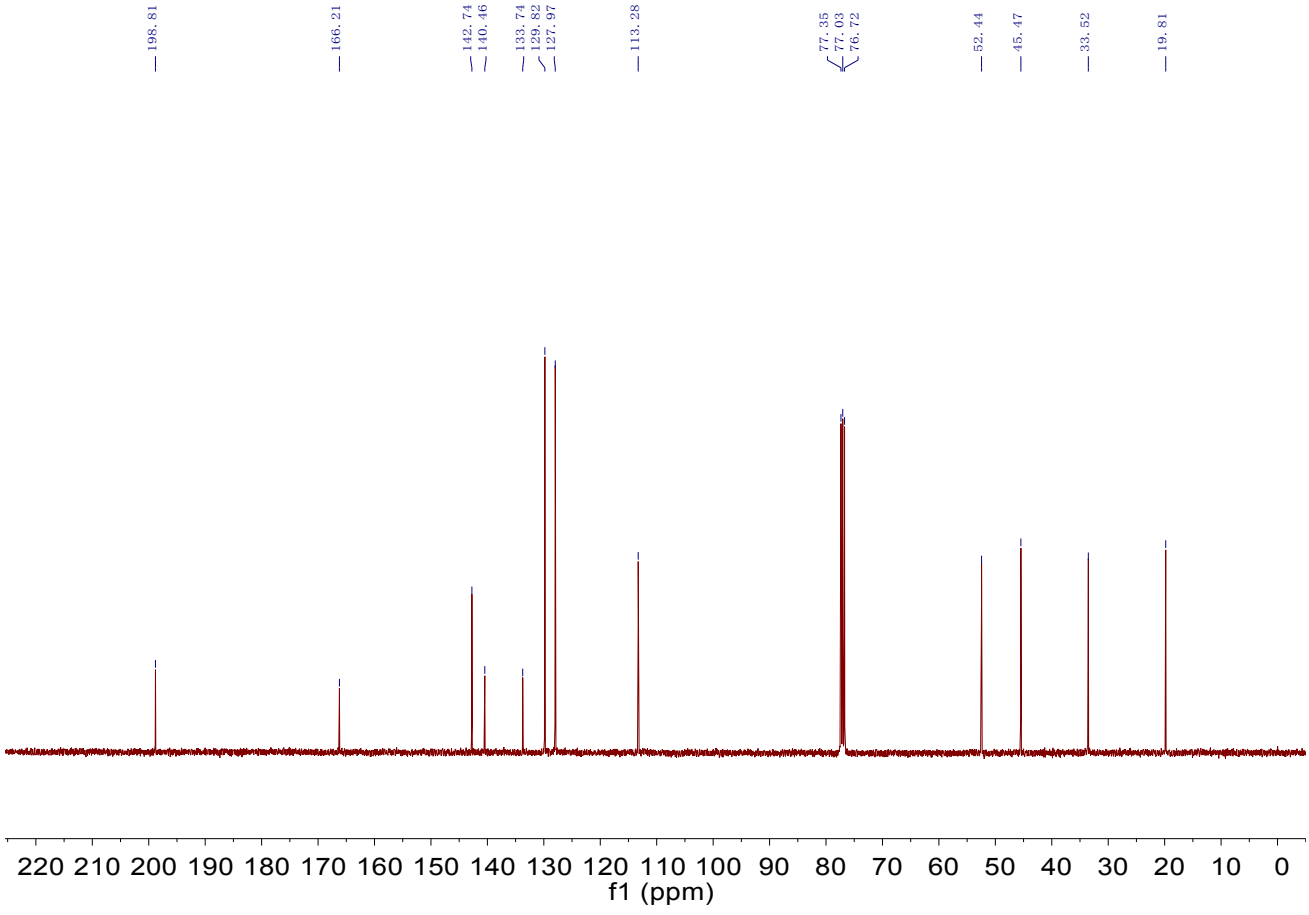

8.07
8.06
8.04
7.74
7.72
5.88
5.87
5.86
5.85
5.84
5.82
5.81
5.80
5.06
5.05
5.05
5.02
5.01
5.01
4.99
4.99
4.98
4.96
4.96
4.96
3.11
3.09
3.08
3.07
3.05
3.05
3.03
3.02
3.02
3.01
3.00
2.99
2.95
2.94
2.92
2.92
2.91
2.90
2.89
2.89
2.88
2.87
2.85
1.16
1.14
1.13
1.12
1.10
1.08
1.07
1.06
1.04
O
F3C
3f
2.20
2.16
1.00
2.07
3.02
3.28
f1 (ppm)

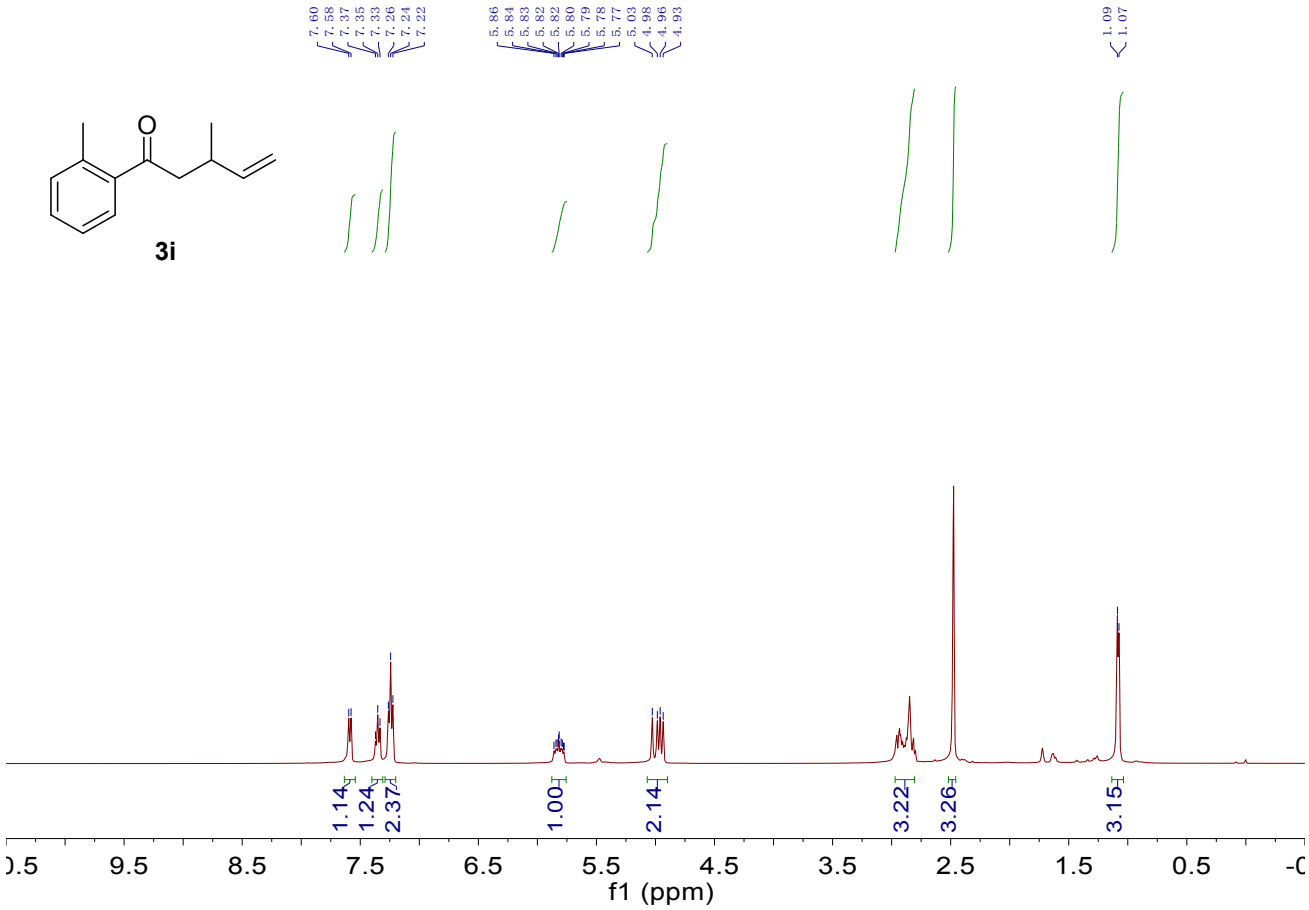

198.31
142.63
139.88
134.76
134.43
134.11
133.78
128.41
127.66
125.72
125.69
125.65
125.61
124.95
122.24
119.53
113.39
77.34
77.02
76.71
45.40
33.54
19.82
f1 (ppm)

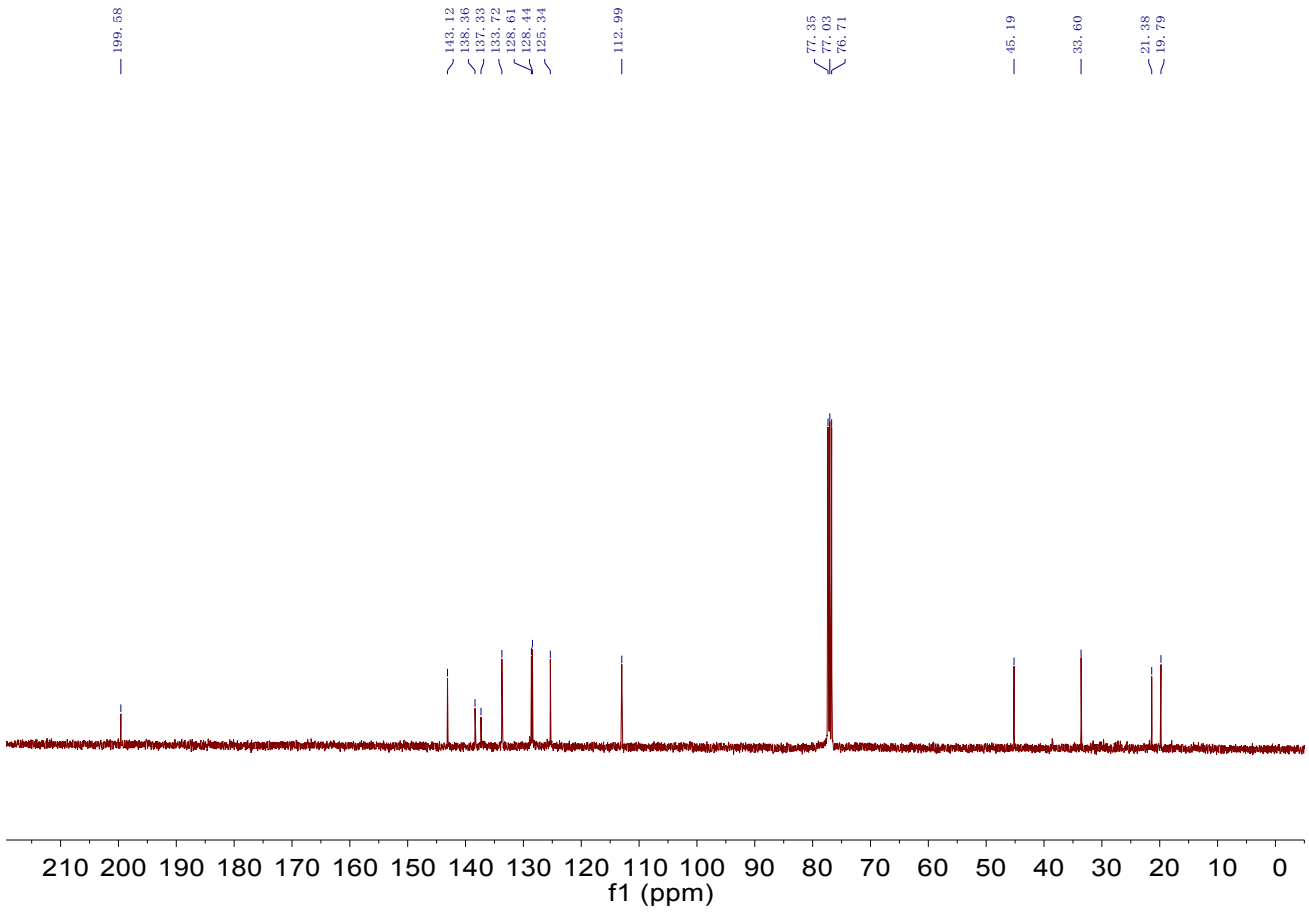

8.13
8.11
8.10
8.02
8.01
8.00
7.98
5.88
5.87
5.86
5.84
5.82
5.81
5.80
5.05
5.05
5.01
5.00
4.98
4.95
4.44
4.42
4.40
4.38
3.09
3.08
3.07
3.06
3.05
3.04
3.03
3.02
3.01
3.00
2.96
2.94
2.92
2.91
2.90
2.88
2.87
2.85
1.43
1.42
1.40
1.12
1.10
O
EtO2C
3g
2.28
2.24
1.01
2.18
2.29
3.09
3.29
3.06
f1 (ppm)

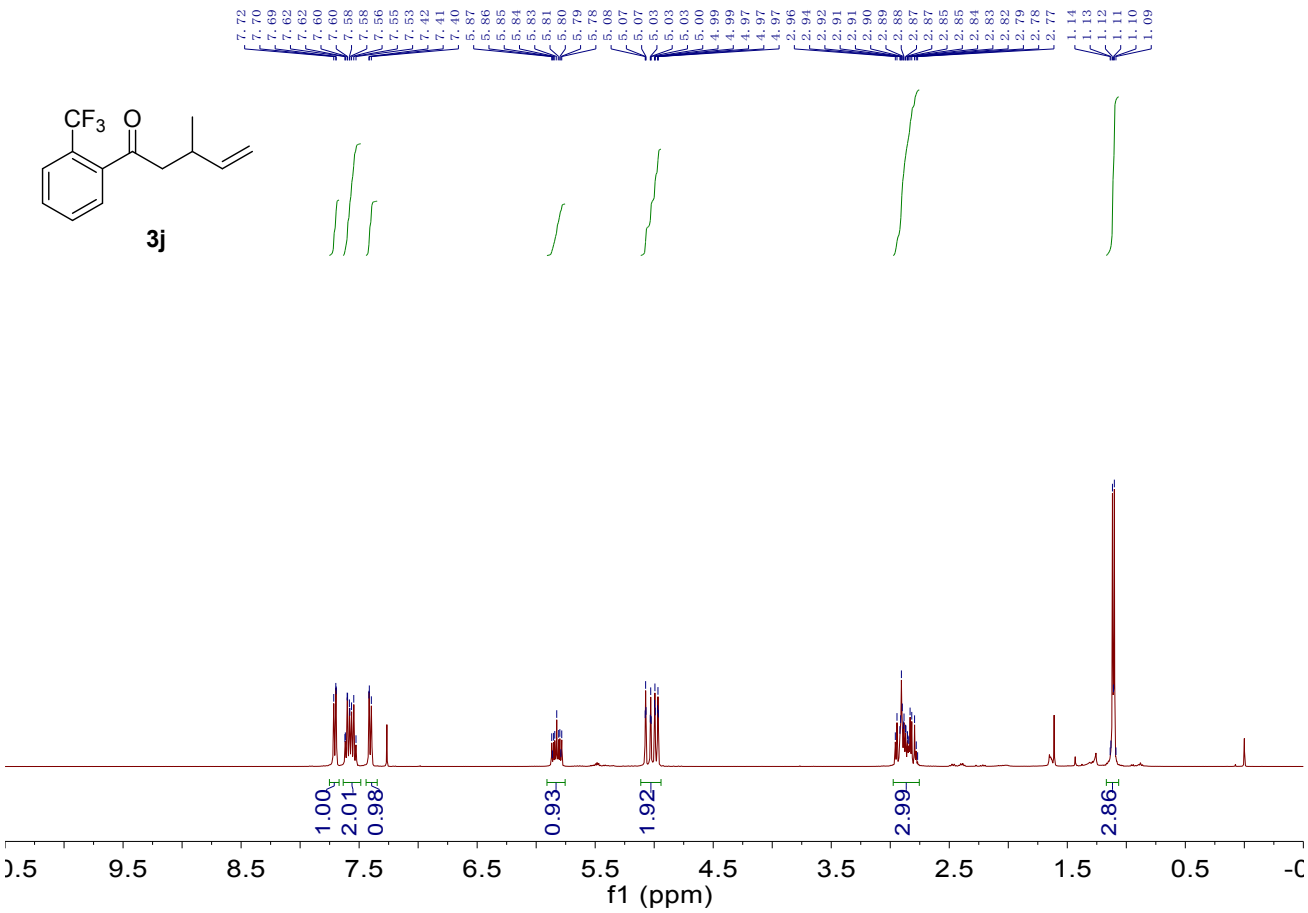

198.86
165.74
142.76
140.36
134.11
129.77
127.94
113.27
77.36
77.04
76.72
61.43
45.47
33.55
19.82
14.28
f1 (ppm)

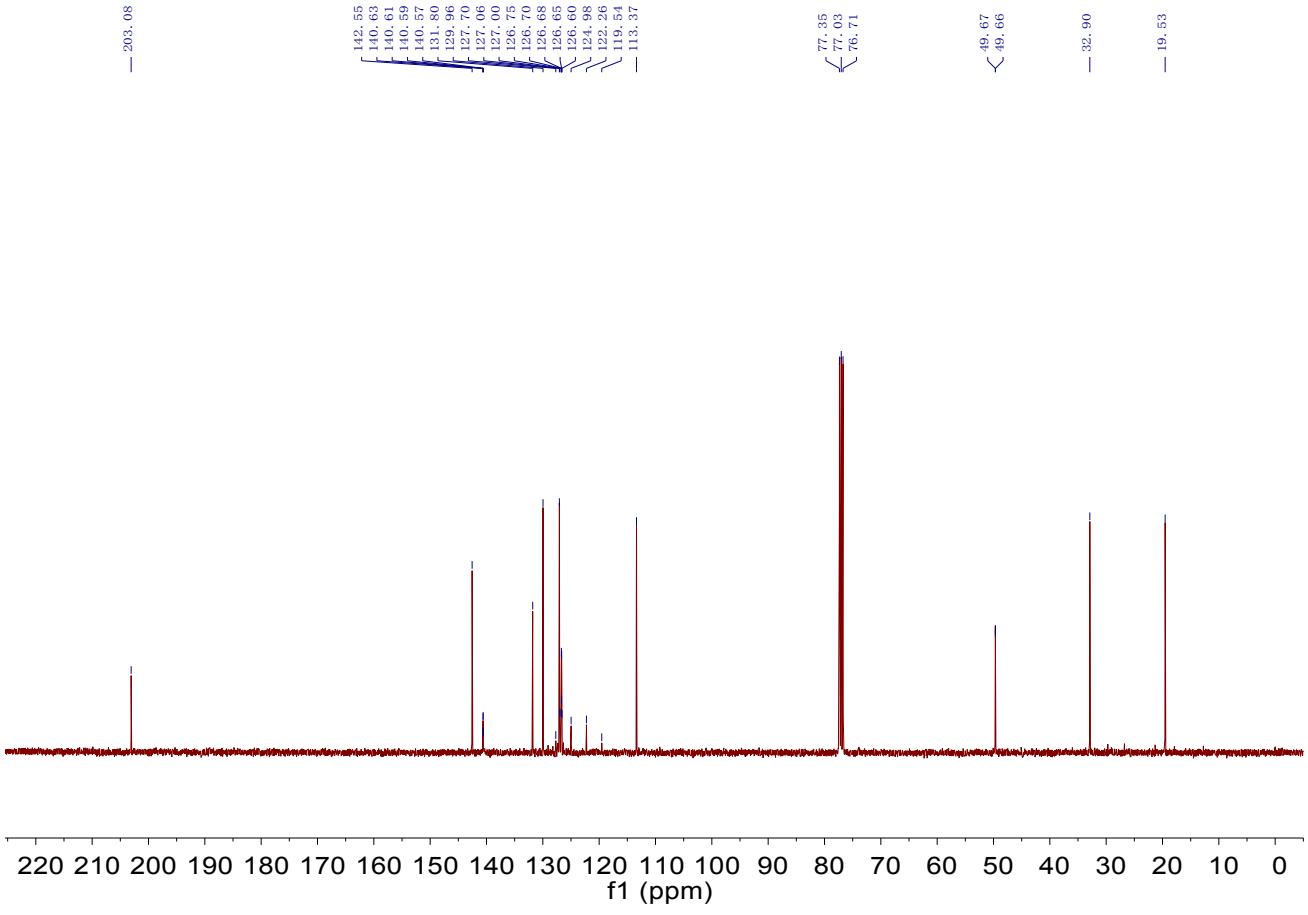

8.14
8.13
8.11
8.00
7.98
5.89
5.88
5.88
5.86
5.84
5.82
5.81
5.81
5.80
5.05
5.01
4.98
4.95
3.95
3.10
3.09
3.08
3.07
3.05
3.05
3.03
3.02
2.97
2.96
2.94
2.91
2.88
2.87
1.12
1.10
O
MeO2C
3h
2.10
2.02
0.94
2.01
3.09
1.15
1.99
3.00
f1 (ppm)

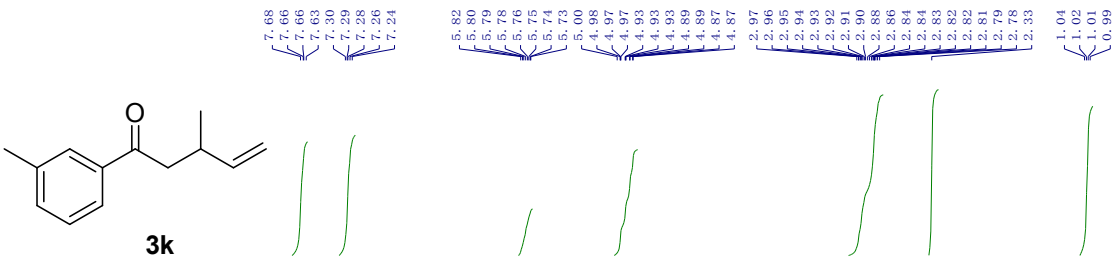

198.81
166.21
142.74
140.46
133.74
129.82
127.97
113.28
77.35
77.03
76.72
52.44
45.47
33.52
19.81
f1 (ppm)


7.60
7.58
7.37
7.35
7.33
7.26
7.24
7.22
5.86
5.84
5.83
5.82
5.82
5.80
5.79
5.78
5.77
5.03
4.98
4.96
4.93
1.09
1.07
O
3i
1.14
1.24
2.37
1.00
2.14
3.22
3.26
3.15
f1 (ppm)

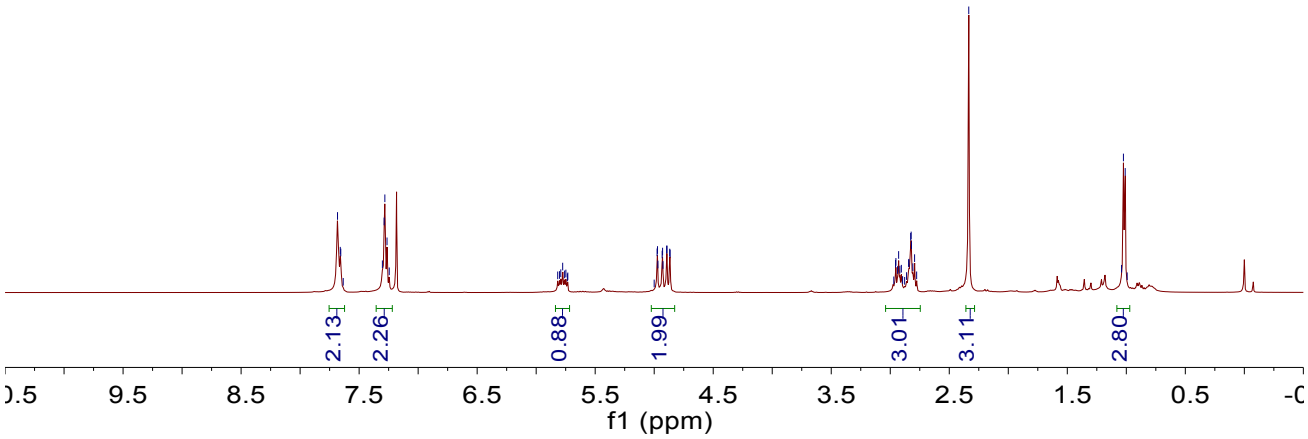

199.58
143.12
138.36
137.33
133.72
128.61
128.44
125.34
112.99
77.35
77.03
76.71
45.19
33.60
21.38
19.79
f1 (ppm)


CF3
O
3j
7.72 7.70 7.69 7.62 7.62 7.60 7.60 7.58 7.58 7.56 7.55 7.53 7.42 7.41 7.40
5.87 5.86 5.85 5.84 5.83 5.81 5.80 5.79 5.78
5.08 5.07 5.07 5.03 5.03 5.00 4.99 4.99 4.97 4.97 4.97
2.96 2.94 2.92 2.91 2.91 2.90 2.89 2.88 2.87 2.87 2.85 2.85 2.84 2.83 2.82 2.79 2.78 2.77
1.14 1.13 1.12 1.11 1.10 1.09
1.00 2.01 0.98 0.93 1.92 2.99 2.86
f1 (ppm)

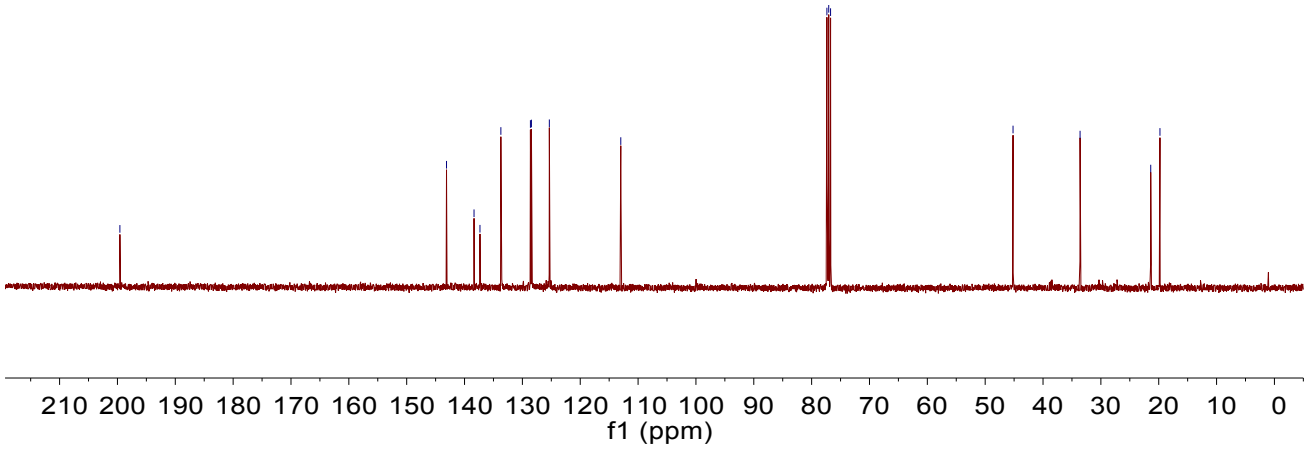

203.08
142.55 140.63 140.61 140.59 140.57 131.80 129.96 127.70 127.06 127.00 126.75 126.70 126.68 126.65 126.60 124.98 122.26 119.54 113.37
77.35 77.03 76.71
49.67 49.66
32.90
19.53
f1 (ppm)

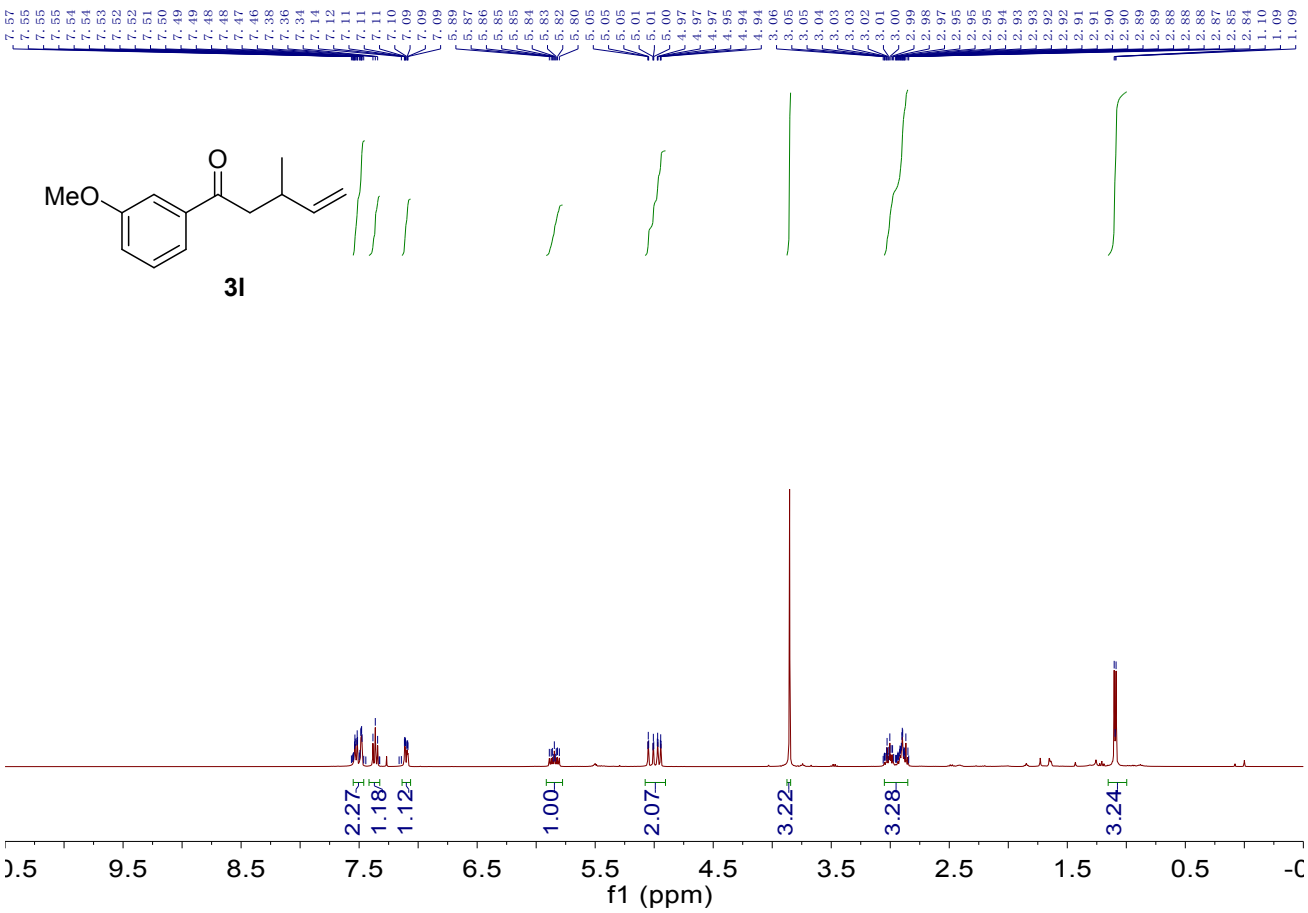

7.68
7.66
7.66
7.63
7.30
7.29
7.28
7.26
7.24
5.82
5.80
5.79
5.78
5.76
5.75
5.74
5.73
5.00
4.98
4.97
4.97
4.93
4.93
4.89
4.89
4.87
4.87
2.97
2.96
2.95
2.94
2.93
2.92
2.91
2.90
2.88
2.86
2.84
2.84
2.83
2.82
2.82
2.81
2.79
2.78
2.33
1.04
1.02
1.01
0.99
O

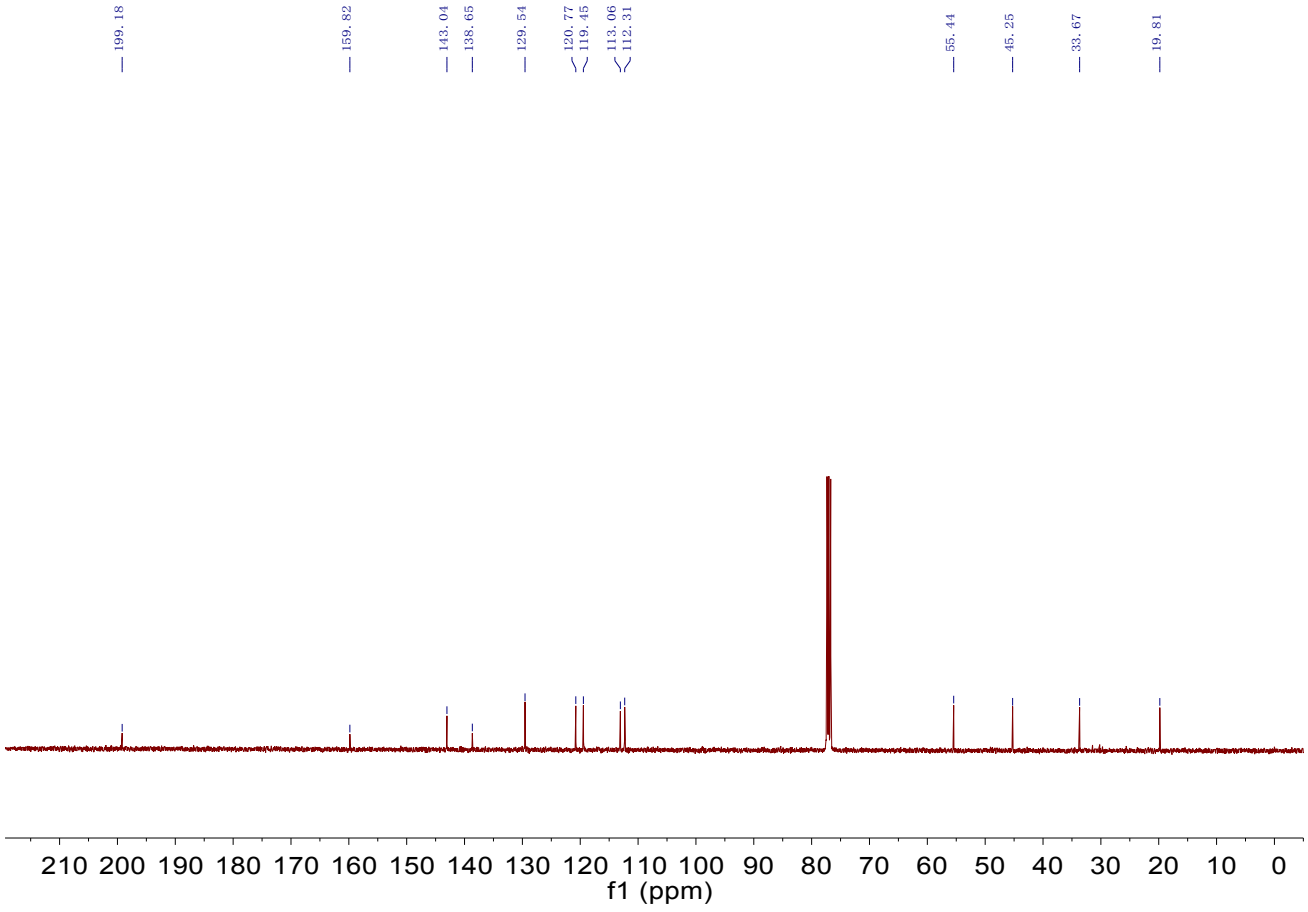
3k

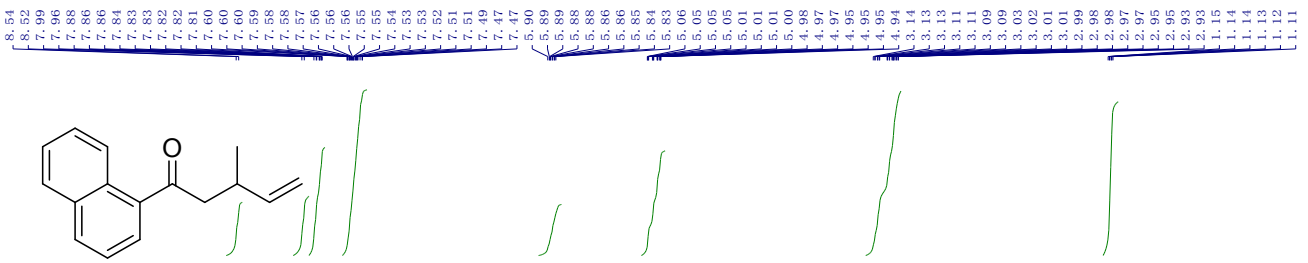

2.13
2.26
0.88
1.99
3.01
3.11
2.80
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)


199.58
143.11
138.36
137.33
133.72
128.61
128.44
125.34
112.99
77.36
77.04
76.73
45.18
33.60
21.38
19.79

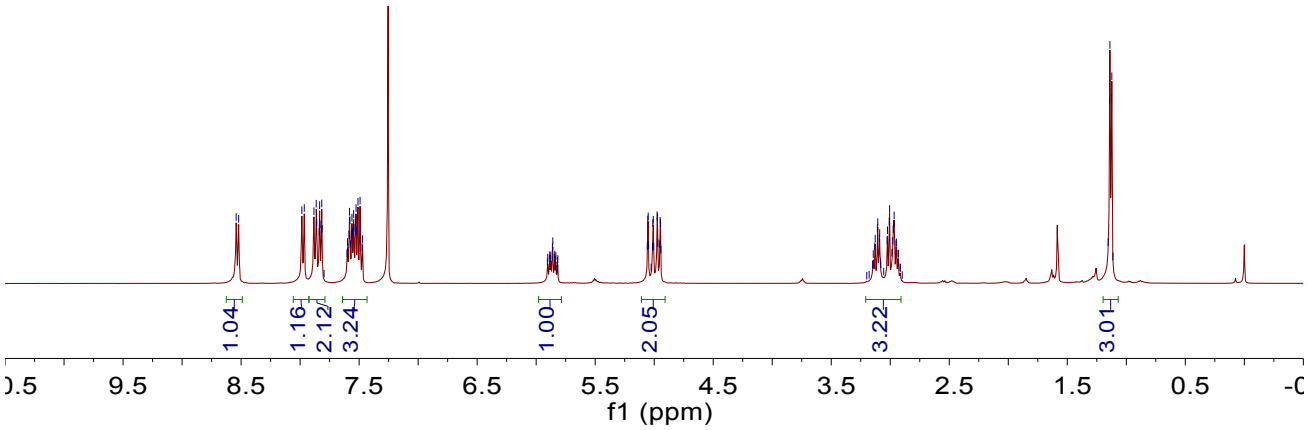

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

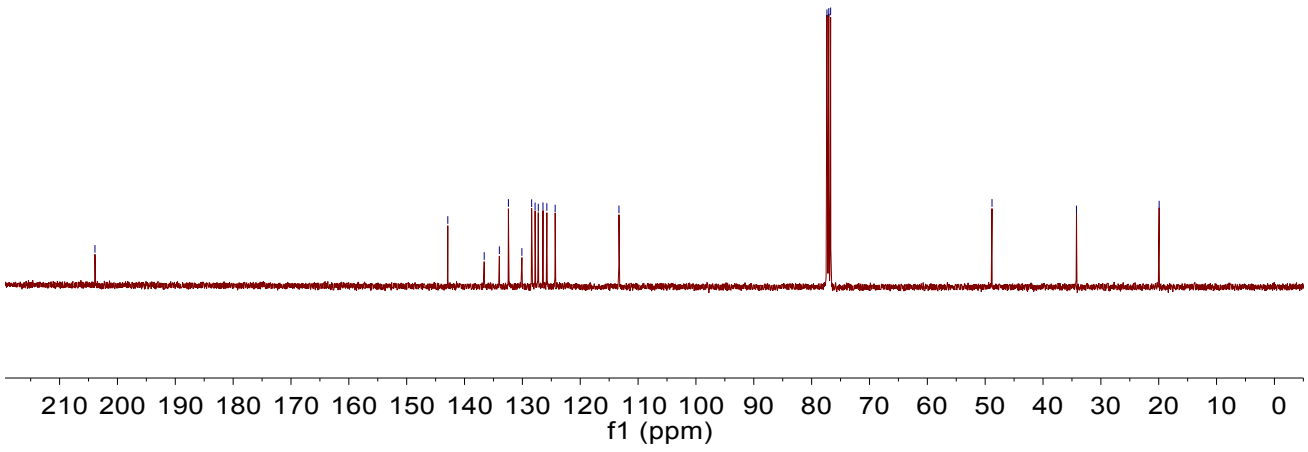

MeO
O
3l
2.27
1.18
1.12
1.00
2.07
3.22
3.28
3.24
f1 (ppm)

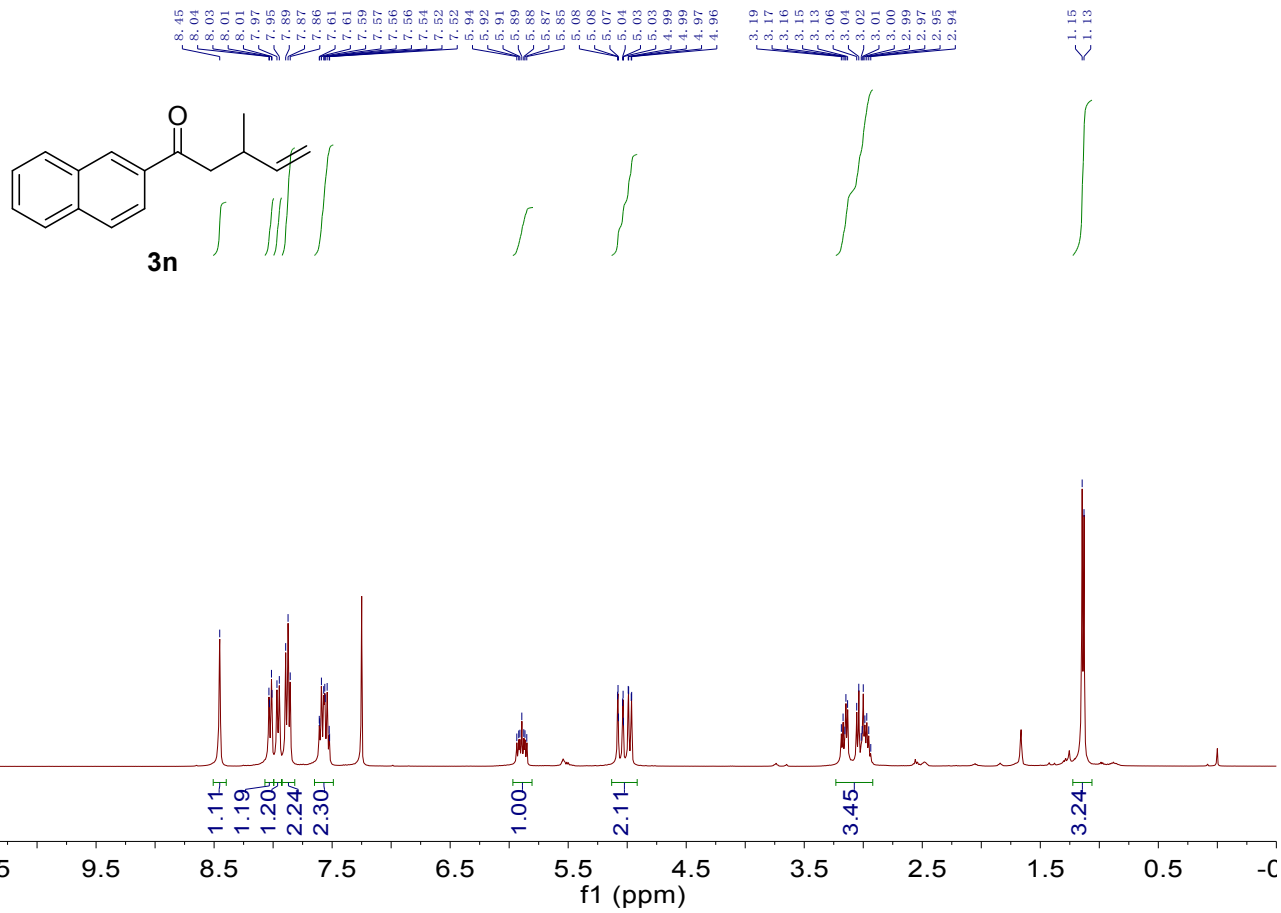

199.18
159.82
143.04
138.65
129.54
120.77
119.45
113.06
112.31
55.44
45.25
33.67
19.81
f1 (ppm)

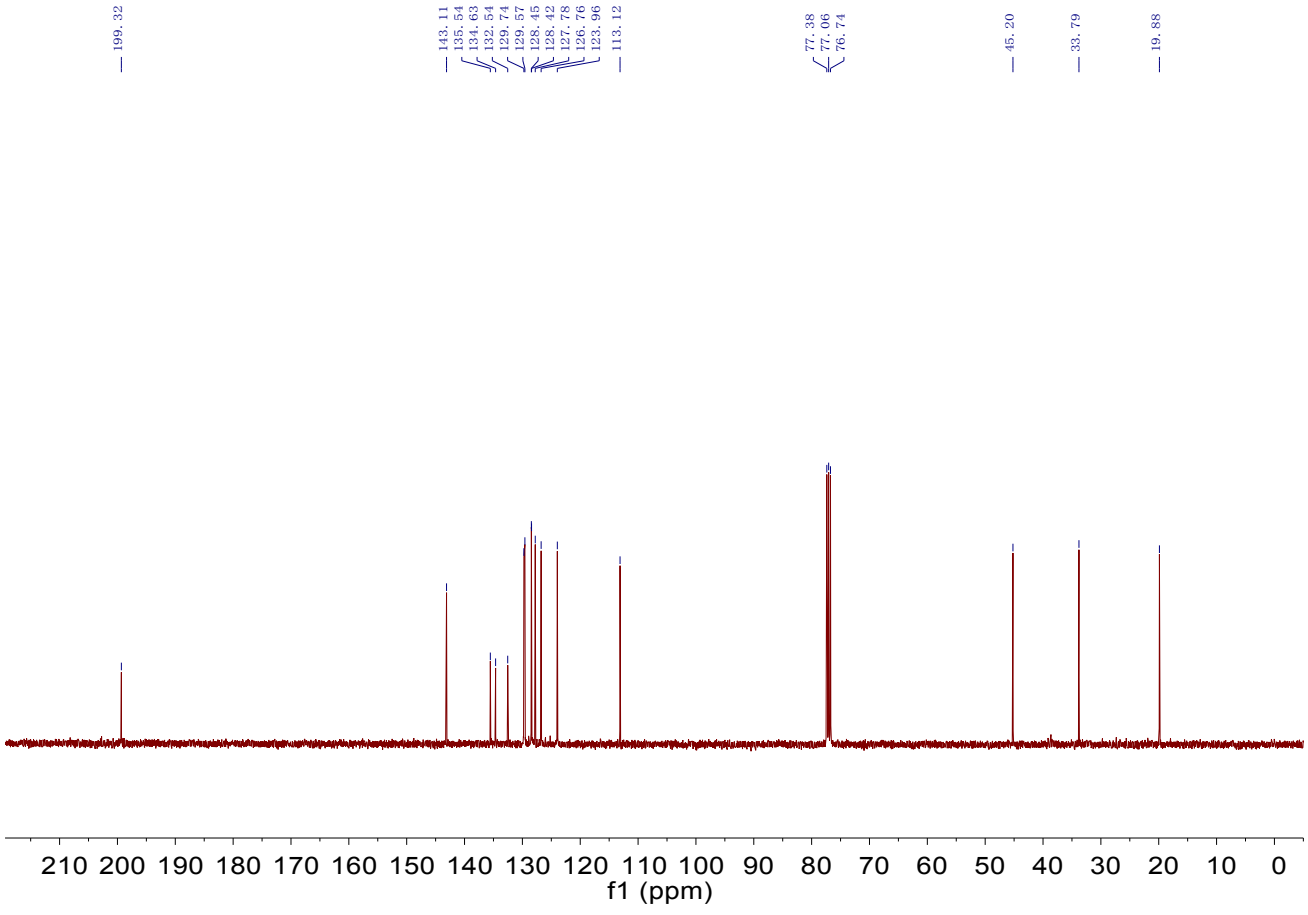


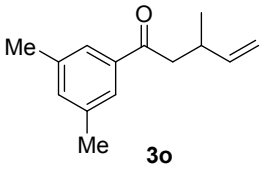
3m





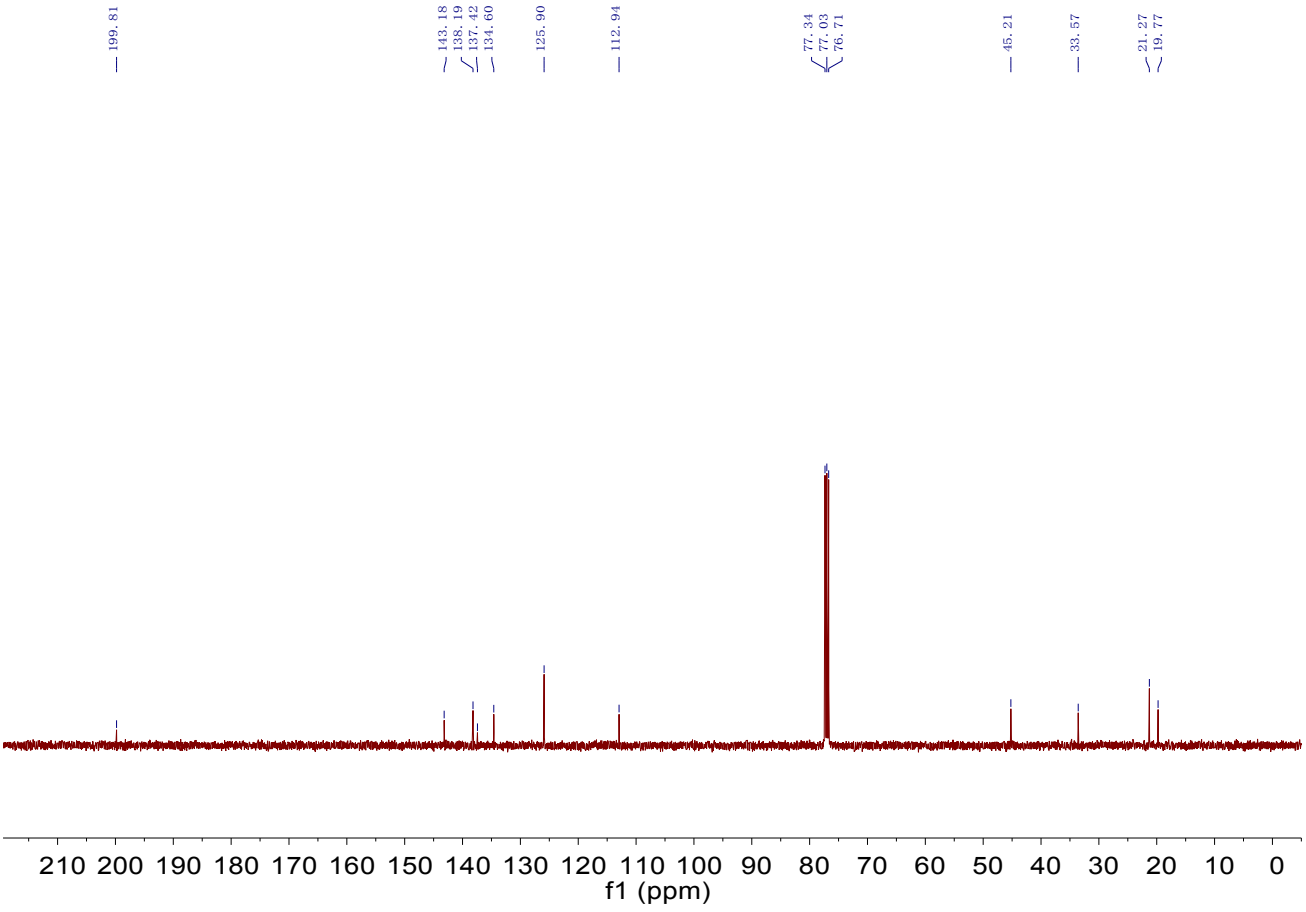

8.45
8.04
8.03
8.01
8.01
7.97
7.95
7.89
7.87
7.86
7.61
7.61
7.59
7.57
7.56
7.56
7.54
7.52
7.52
5.94
5.92
5.91
5.89
5.88
5.87
5.85
5.08
5.07
5.04
5.03
5.03
4.99
4.99
4.97
4.96
3.19
3.17
3.16
3.15
3.13
3.06
3.04
3.02
3.01
3.00
2.99
2.97
2.95
2.94
1.15
1.13
O
3n
1.11
1.19
1.20
2.24
2.30
1.00
2.11
3.45
3.24
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

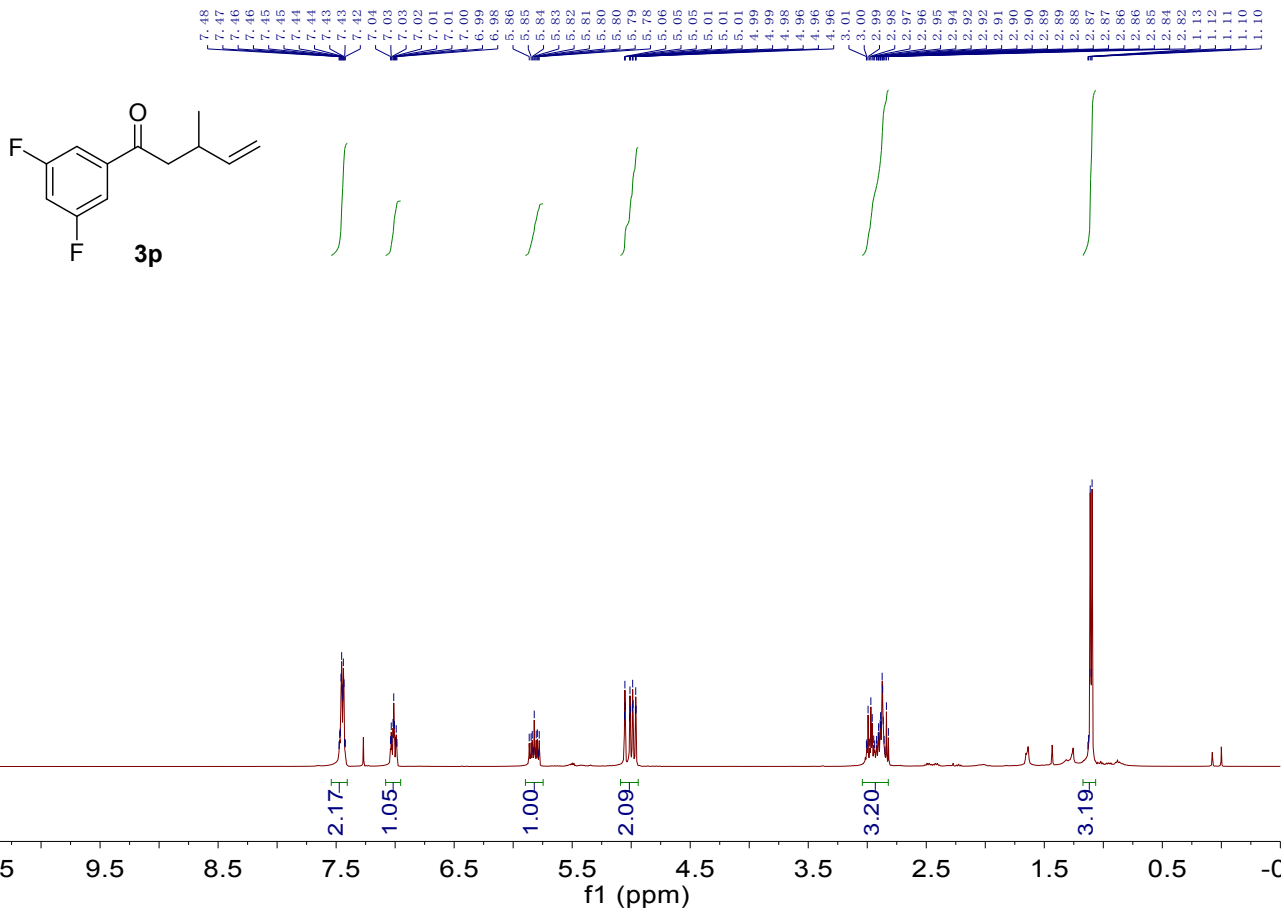

199.32
143.11
135.54
134.63
132.54
129.74
129.57
128.45
128.42
127.78
126.76
123.96
113.12
77.38
77.06
76.74
45.20
33.79
19.88
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

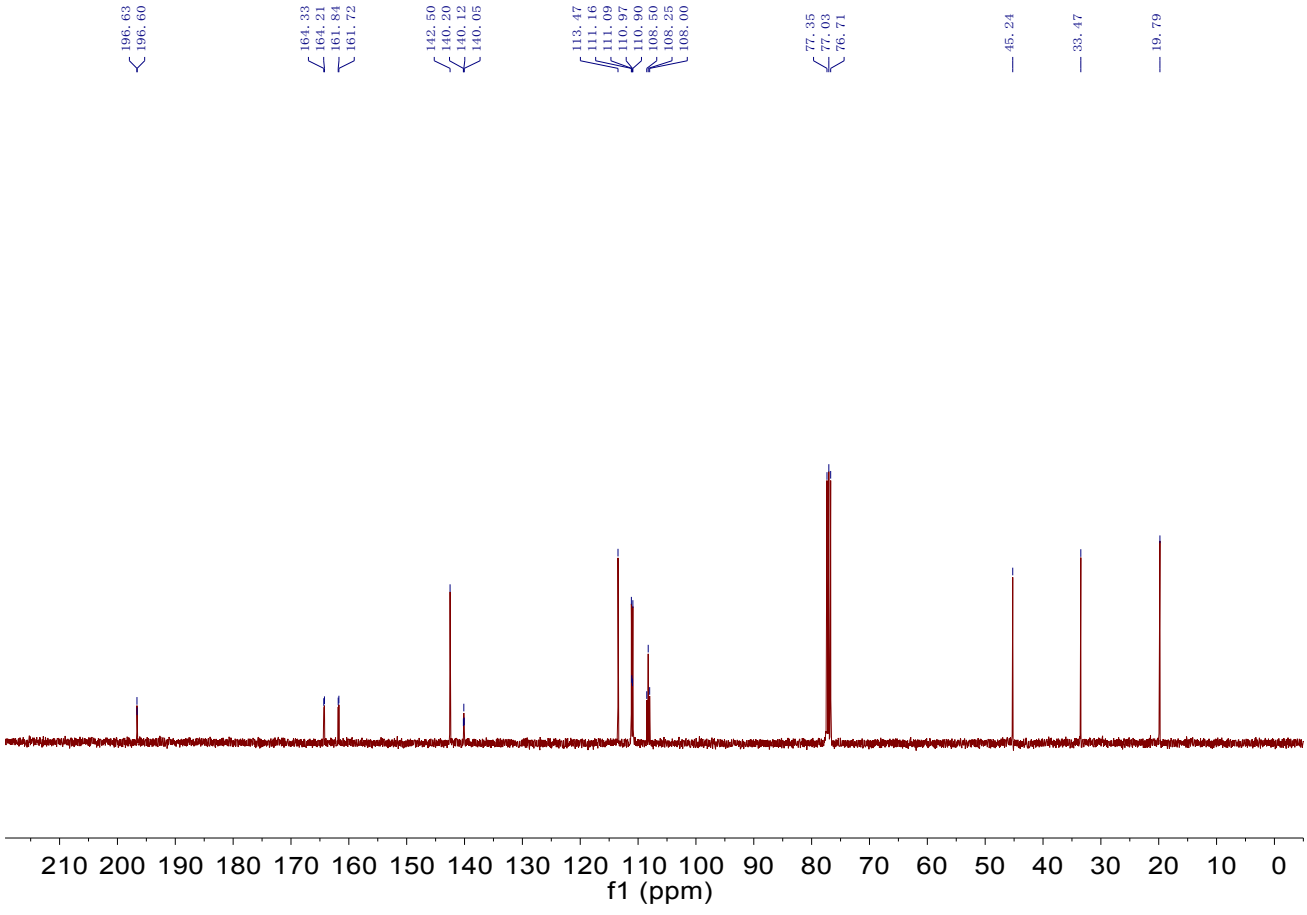

O
Me
Me

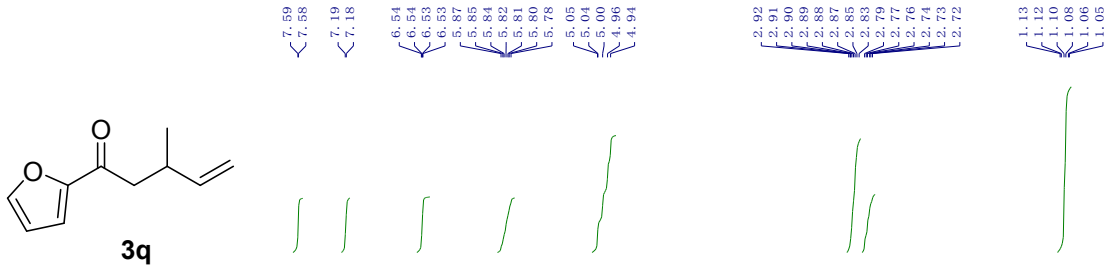
3o

7.56
7.55
7.19
5.89
5.88
5.88
5.87
5.86
5.85
5.84
5.84
5.83
5.81
5.05
5.05
5.02
5.01
5.01
5.00
4.97
4.96
4.94
4.94
4.94
3.03
3.02
3.01
3.00
2.99
2.98
2.98
2.97
2.96
2.93
2.92
2.90
2.90
2.89
2.89
2.88
2.86
2.84
2.39
2.37
1.10
1.08
2.24
0.97
1.00
2.20
3.19
6.17
3.26
f1 (ppm)

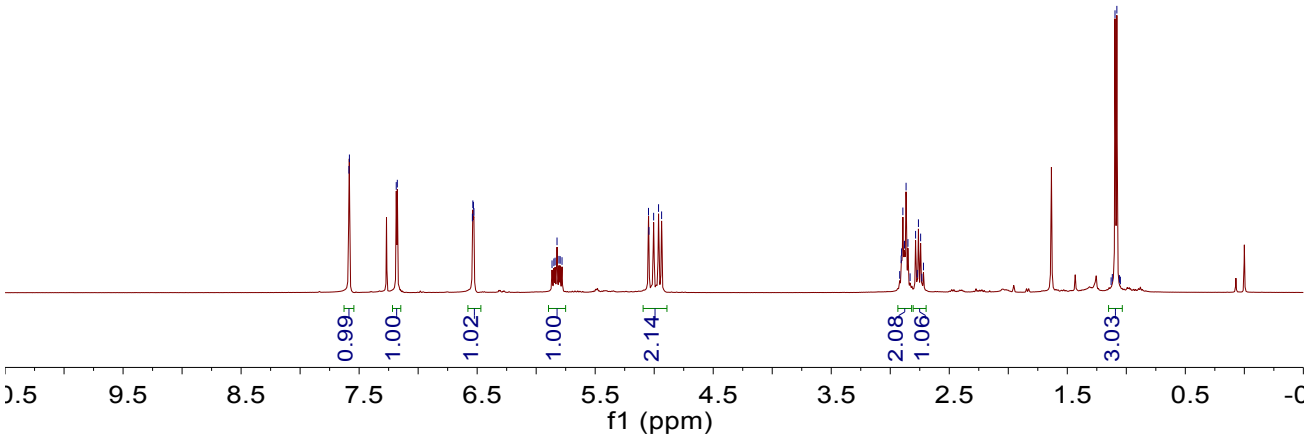

199.81
143.18
138.19
137.42
134.60
125.90
112.94
77.34
77.03
76.71
45.21
33.57
21.27
19.77
f1 (ppm)

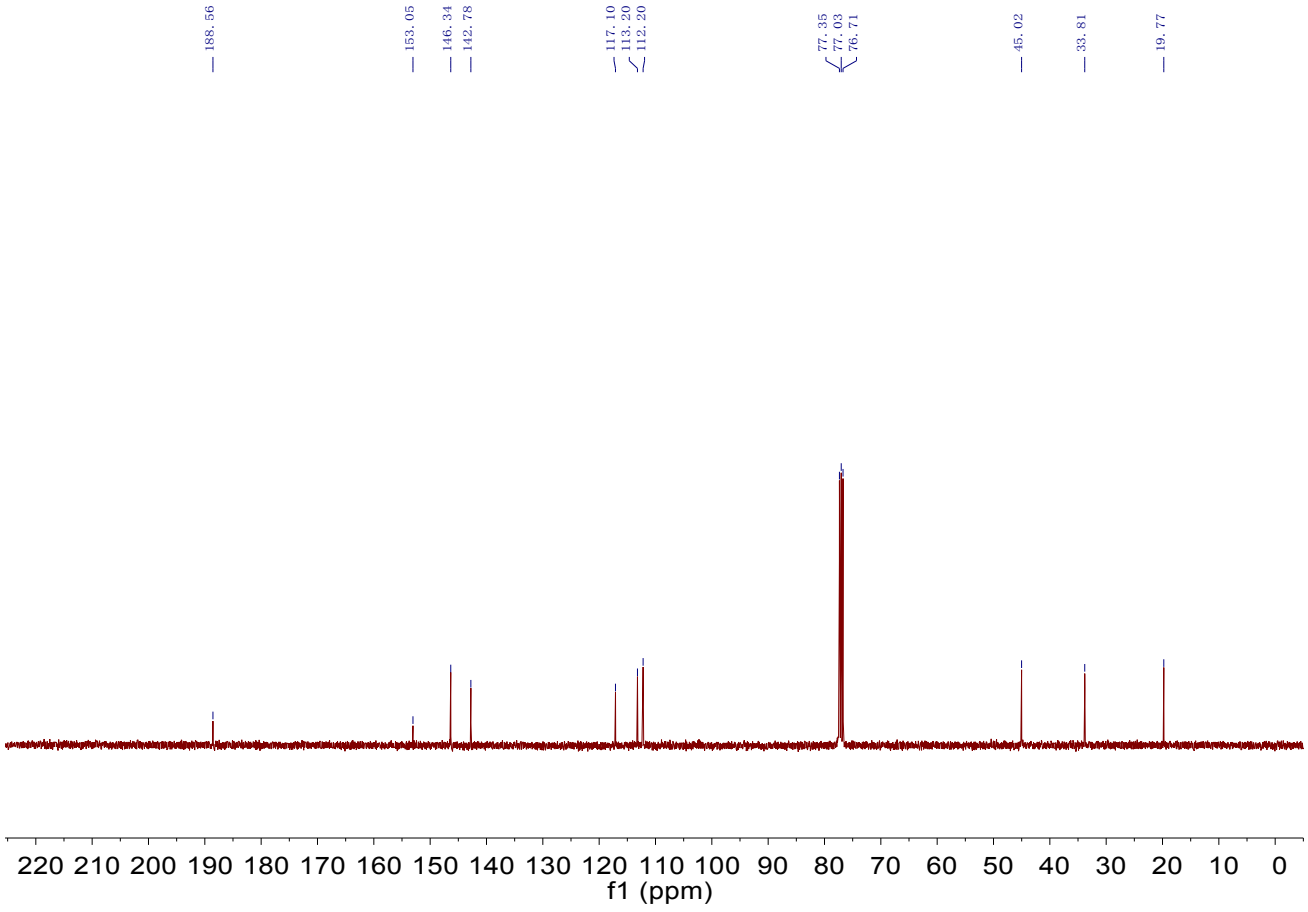

F
O
F
3p
2.17
1.05
1.00
2.09
3.20
3.19
f1 (ppm)

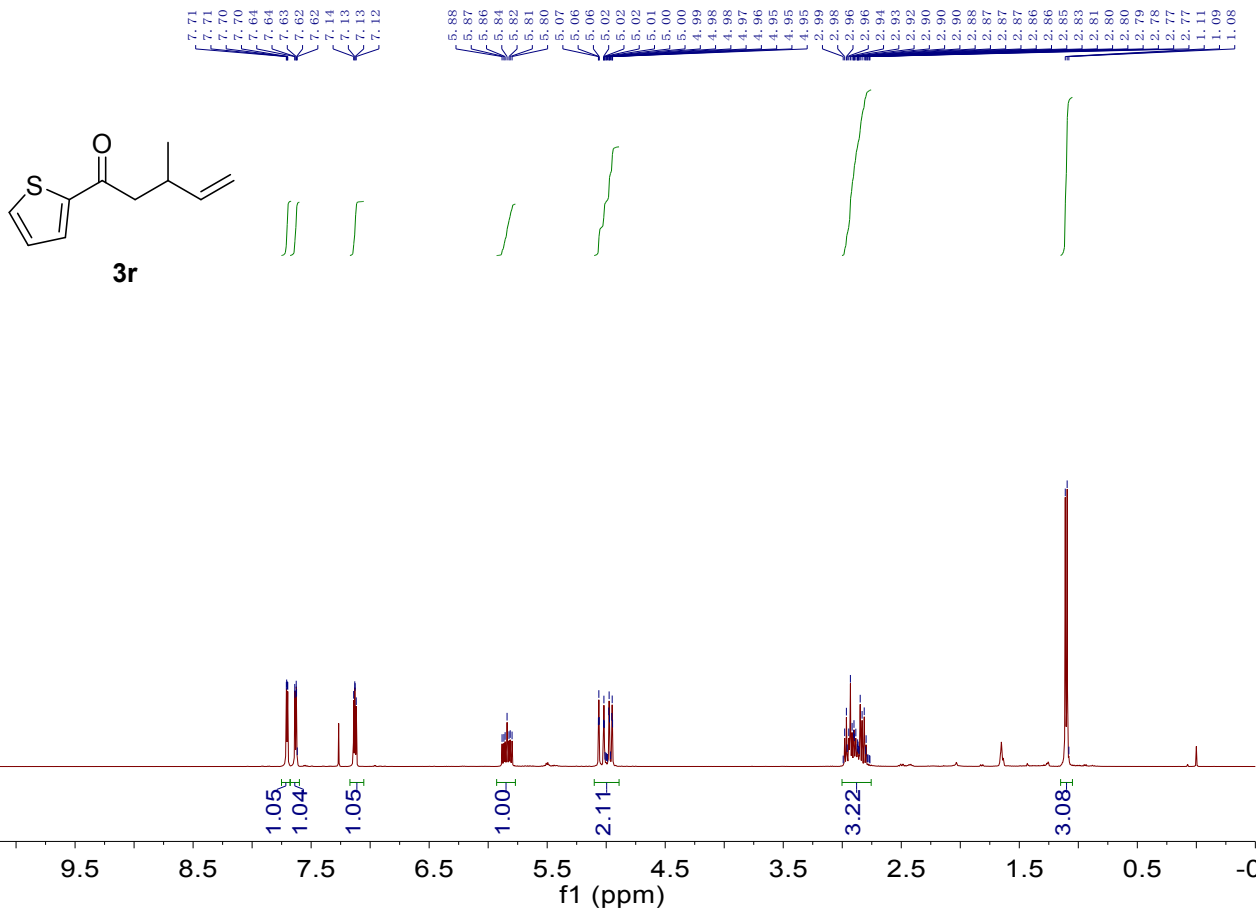

f1 (ppm)

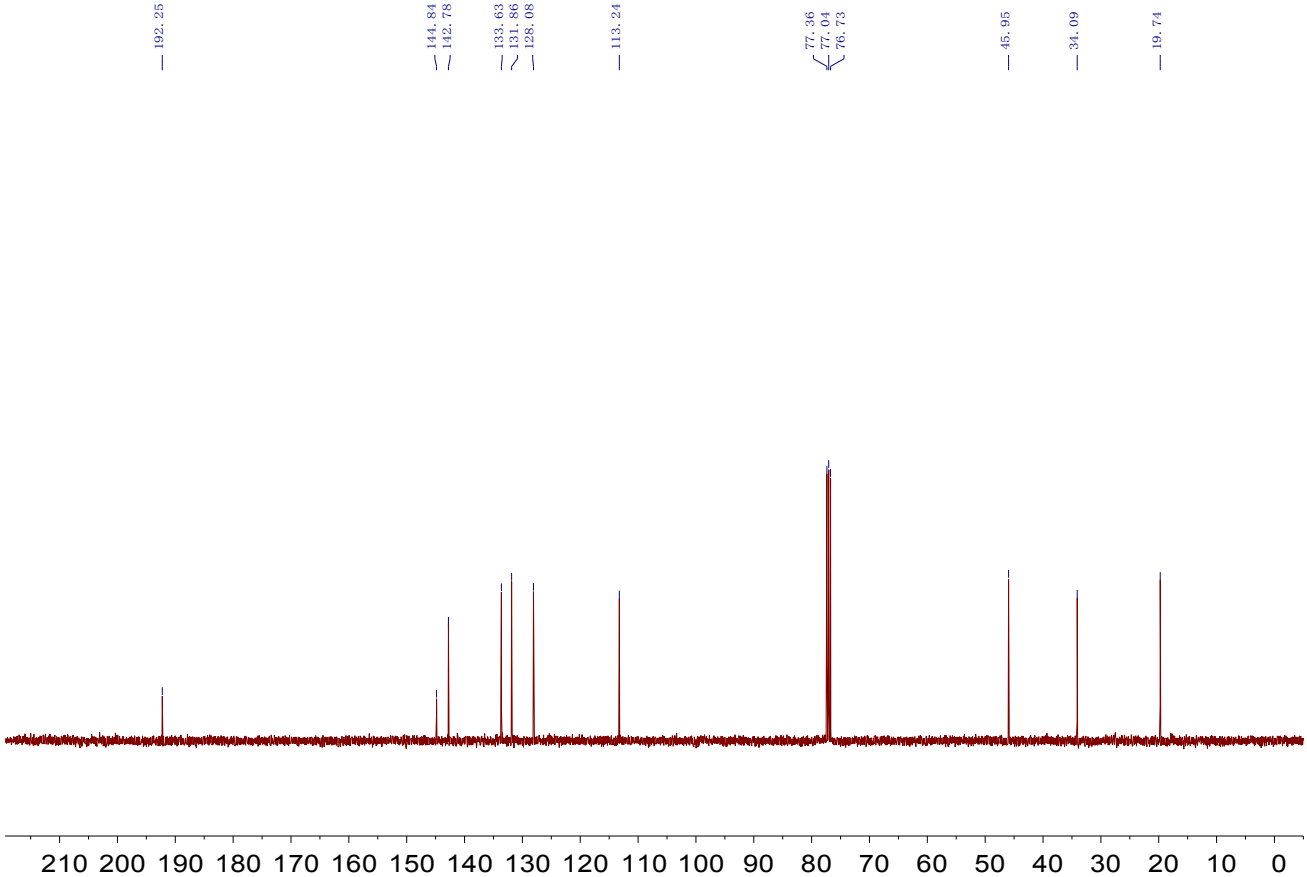

7.59
7.58
7.19
7.18
6.54
6.54
6.53
6.53
5.87
5.85
5.84
5.82
5.81
5.80
5.78
5.05
5.04
5.00
4.96
4.94
2.92
2.91
2.90
2.89
2.88
2.87
2.85
2.83
2.79
2.77
2.76
2.74
2.73
2.72
1.13
1.12
1.10
1.08
1.06
1.05
O
O

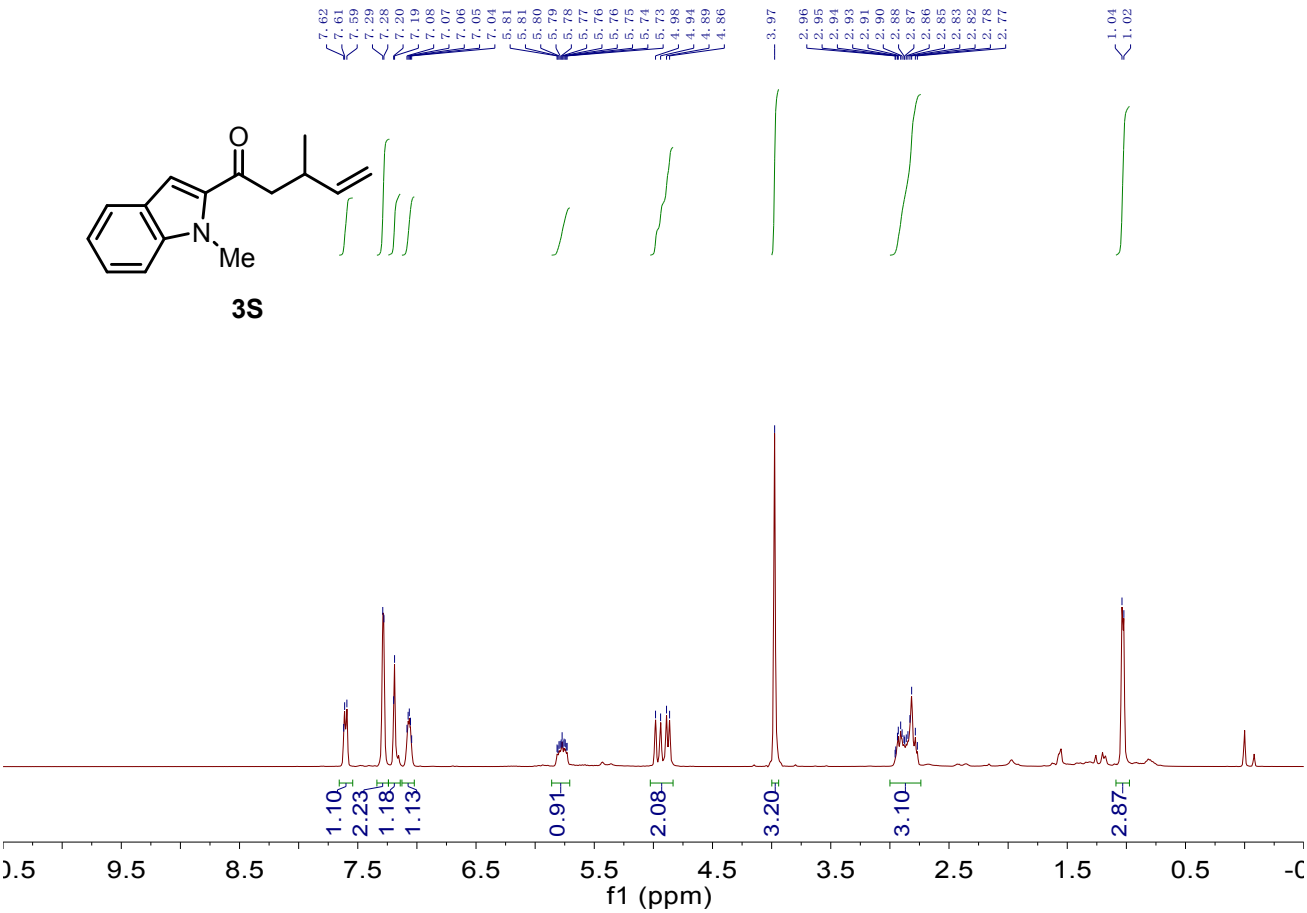
3q


0.99
1.00
1.02
1.00
2.14
2.08
1.06
3.03
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

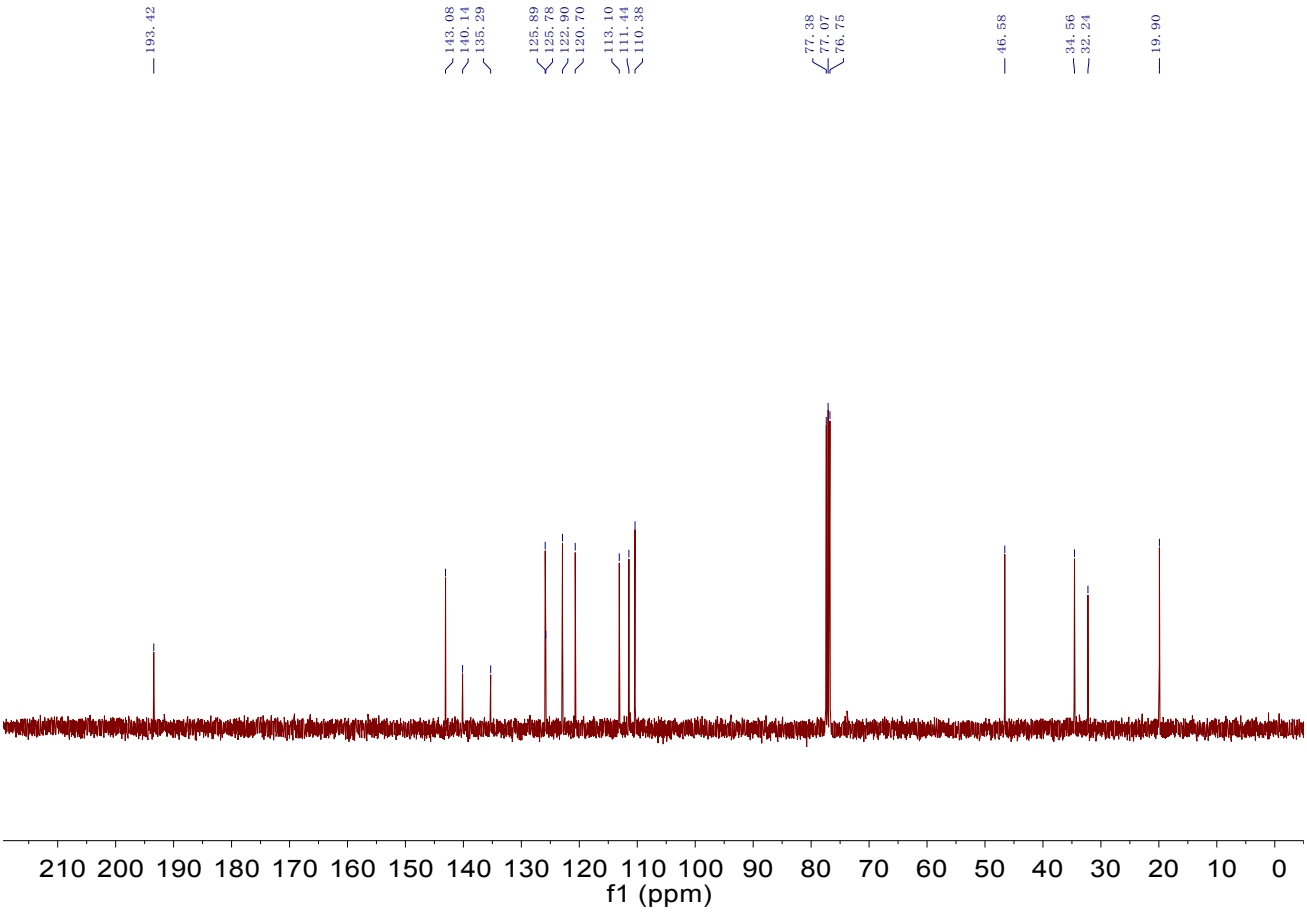

188.56
153.05
146.34
142.78
117.10
113.20
112.20
77.35
77.03
76.71
45.02
33.81
19.77
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

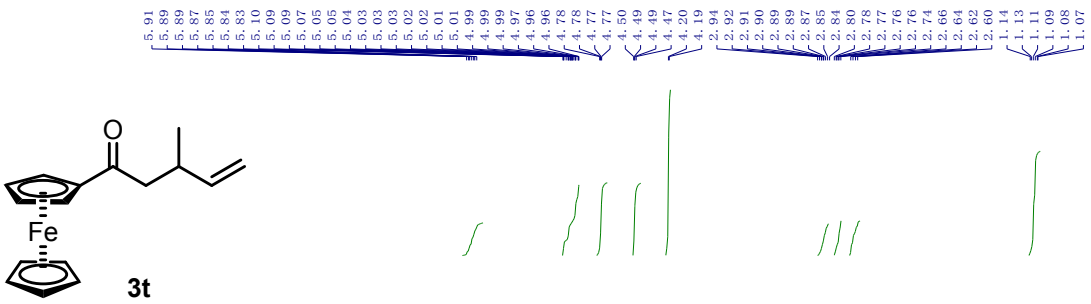

7.71
7.71
7.70
7.70
7.64
7.64
7.63
7.62
7.62
7.14
7.13
7.13
7.12
5.88
5.87
5.86
5.84
5.82
5.81
5.80
5.07
5.06
5.06
5.02
5.02
5.01
5.00
5.00
4.99
4.98
4.98
4.97
4.96
4.95
4.95
4.95
2.99
2.98
2.96
2.96
2.94
2.93
2.92
2.90
2.90
2.90
2.88
2.87
2.87
2.87
2.86
2.86
2.85
2.83
2.81
2.80
2.80
2.79
2.78
2.77
2.77
1.11
1.09
1.08
O
S
3r
1.05
1.04
1.05
1.00
2.11
3.22
3.08
f1 (ppm)


192.25
144.84
142.78
133.63
131.86
128.08
113.24
77.36
77.04
76.73
45.95
34.09
19.74
f1 (ppm)


7.62
7.61
7.59
7.29
7.28
7.20
7.19
7.08
7.07
7.06
7.05
7.04
5.81
5.81
5.80
5.79
5.78
5.77
5.76
5.76
5.75
5.74
5.73
4.98
4.94
4.89
4.86
3.97
2.96
2.95
2.94
2.93
2.91
2.90
2.88
2.87
2.86
2.85
2.83
2.82
2.78
2.77
1.04
1.02
O
N
Me
1.10
2.23
1.18
1.13
0.91
2.08
3.20
3.10
2.87
f1 (ppm)

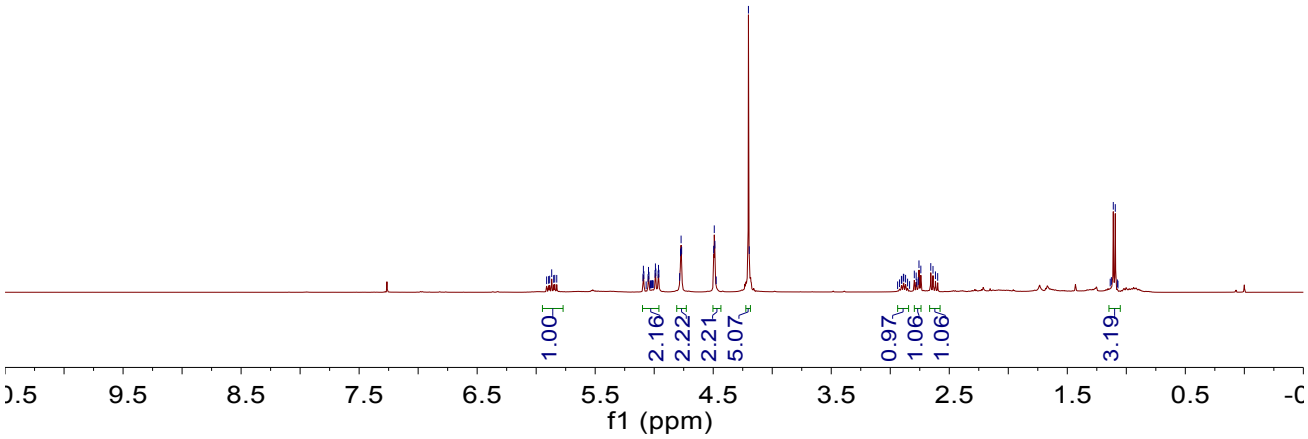
3S

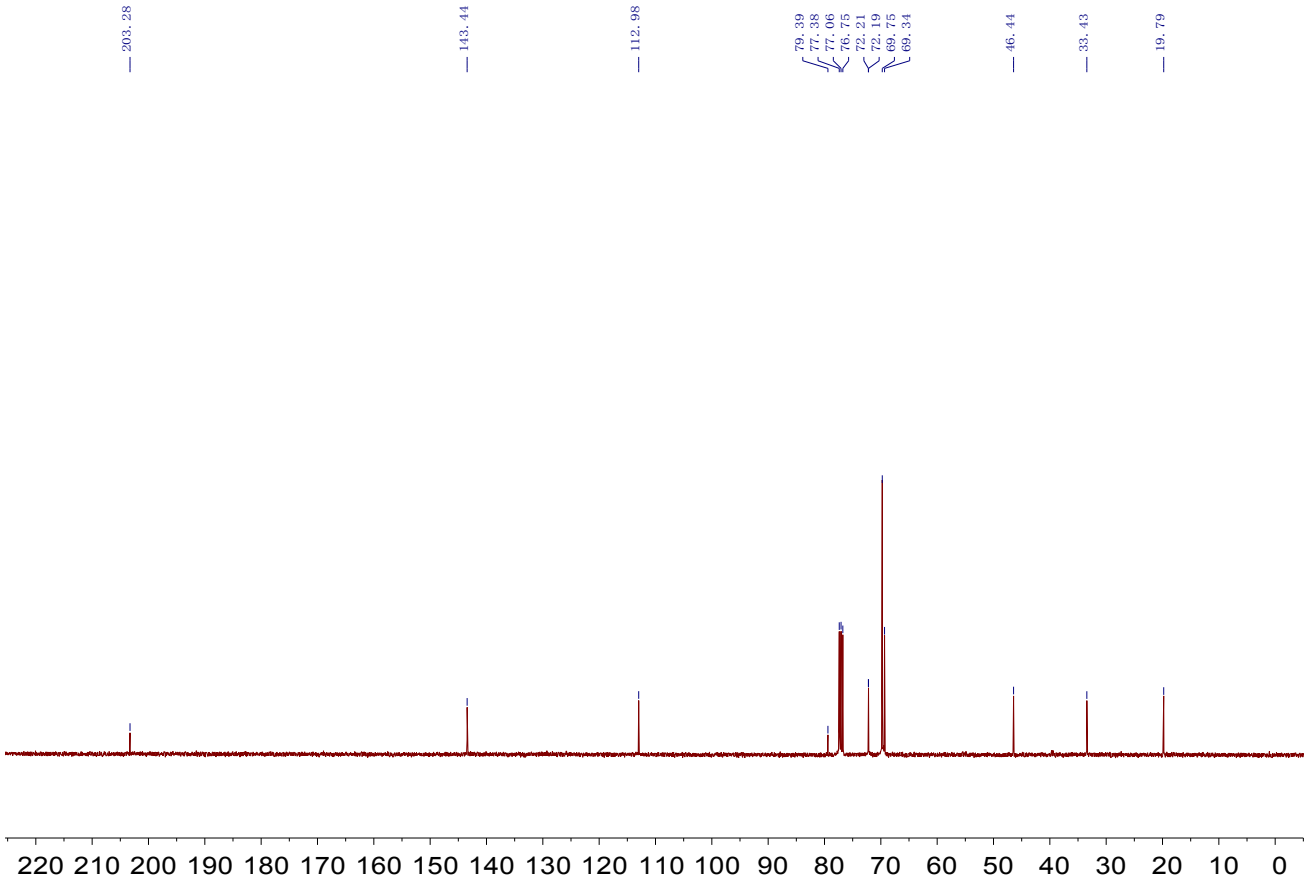

193.42
143.08
140.14
135.29
125.89
125.78
122.90
120.70
113.10
111.44
110.38
77.38
77.07
76.75
46.58
34.56
32.24
19.90
f1 (ppm)

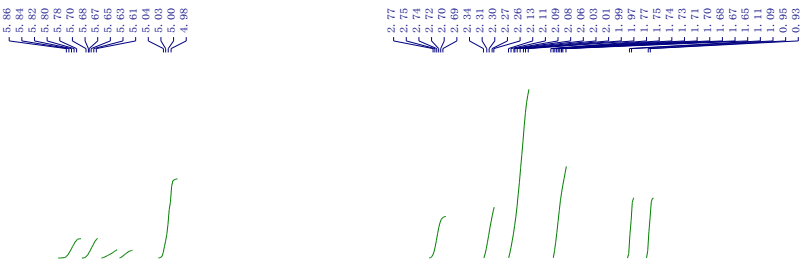

5.91
5.89
5.89
5.87
5.85
5.84
5.83
5.10
5.09
5.09
5.07
5.05
5.05
5.04
5.03
5.03
5.03
5.02
5.02
5.01
5.01
4.99
4.99
4.99
4.97
4.96
4.96
4.78
4.77
4.77
4.50
4.49
4.49
4.47
4.20
4.19
2.94
2.92
2.91
2.90
2.89
2.89
2.87
2.85
2.84
2.80
2.78
2.77
2.76
2.76
2.74
2.66
2.64
2.62
2.60
1.14
1.13
1.11
1.09
1.08
1.07

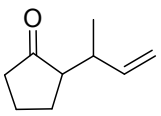
O
Fe

3t


1.00
2.16
2.22
2.21
5.07
0.97
1.06
1.06
3.19
f1 (ppm)

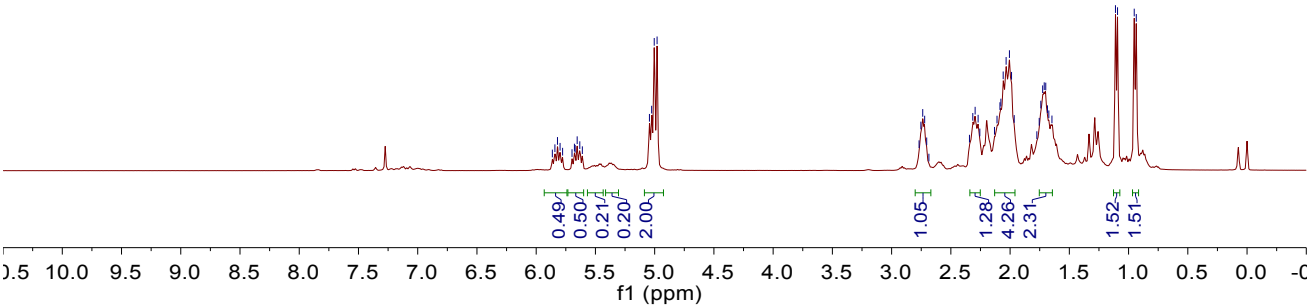

203.28
143.44
112.98
79.39
77.38
77.06
76.75
72.21
72.19
69.75
69.34
46.44
33.43
19.79
f1 (ppm)

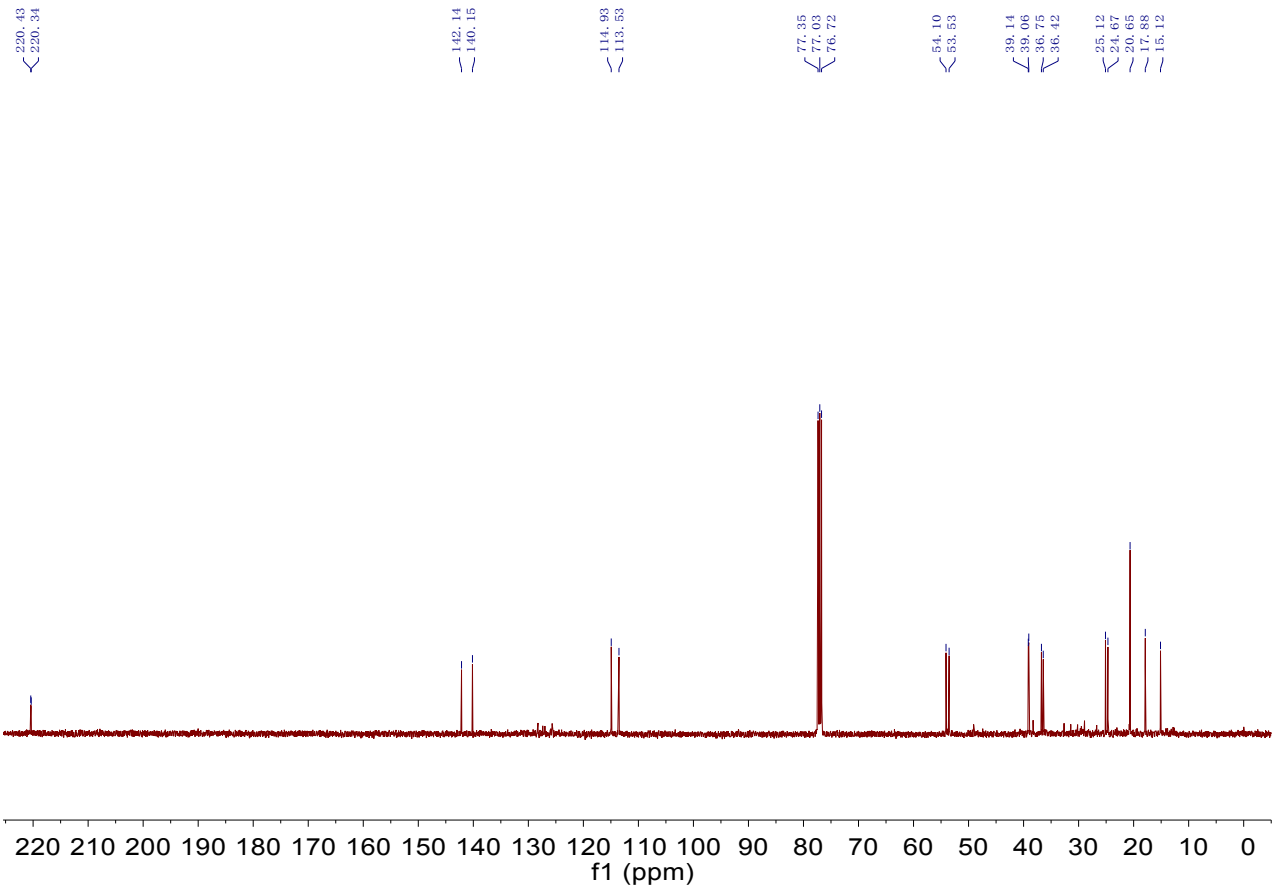


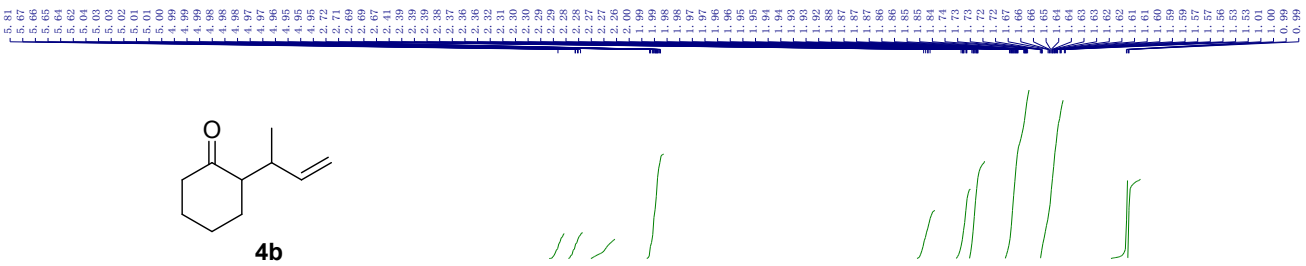


4a

contains 17% of the regioisomer (linear product)

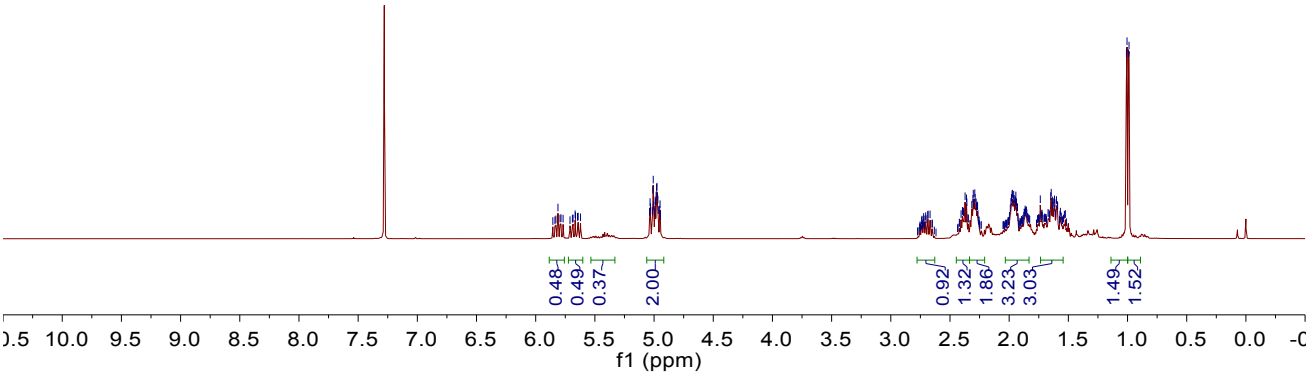


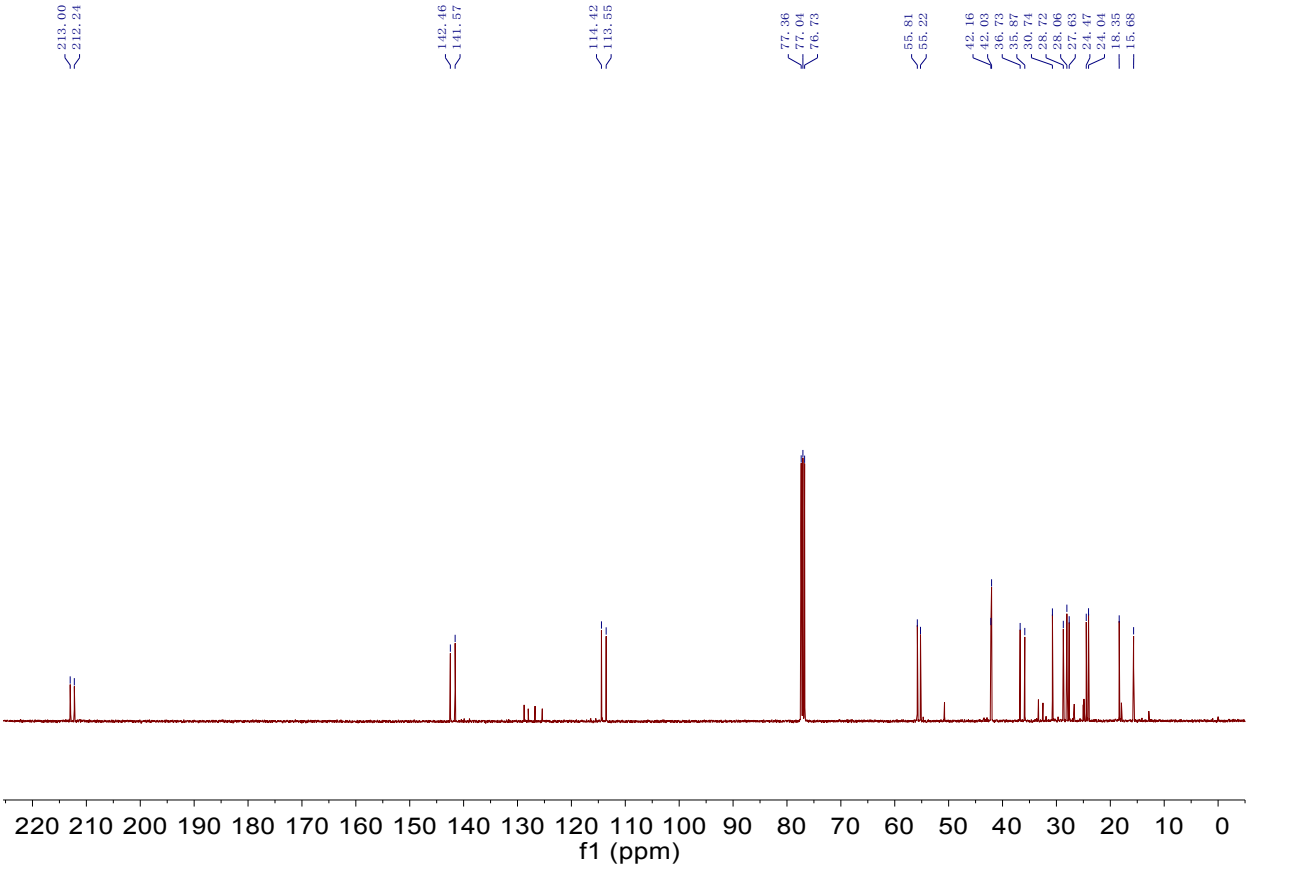


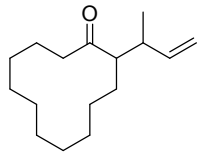


4b

contains 16% of the regioisomer (linear product)

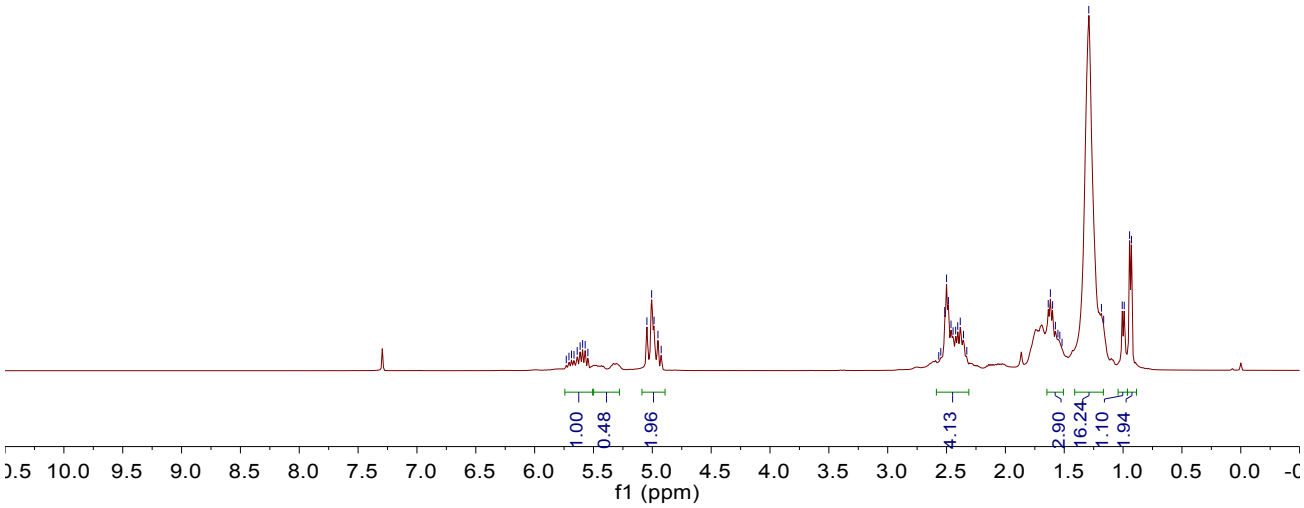


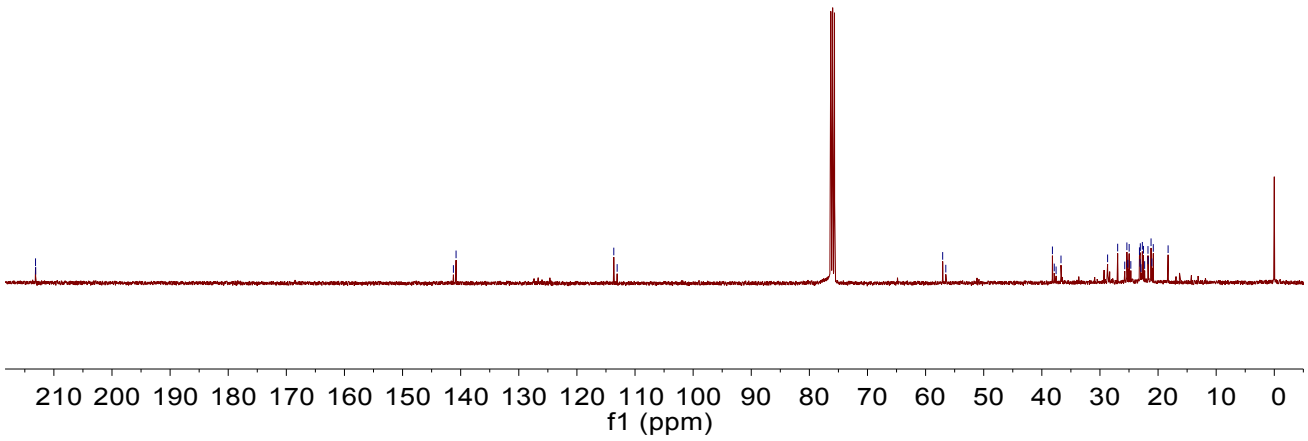


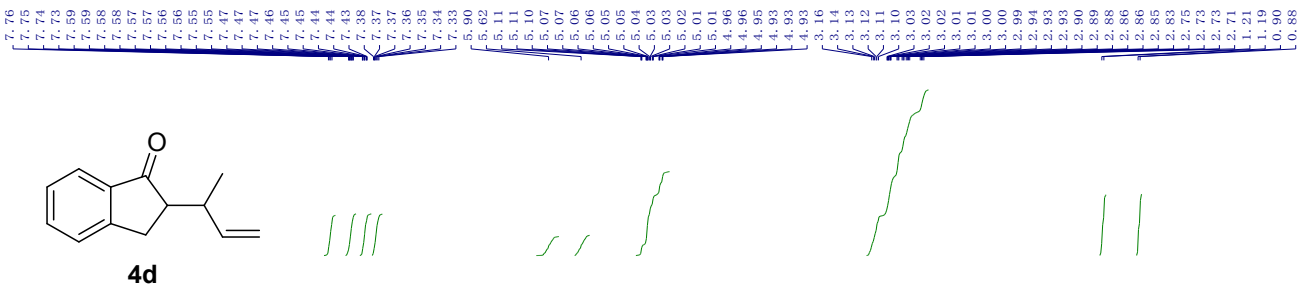


4c

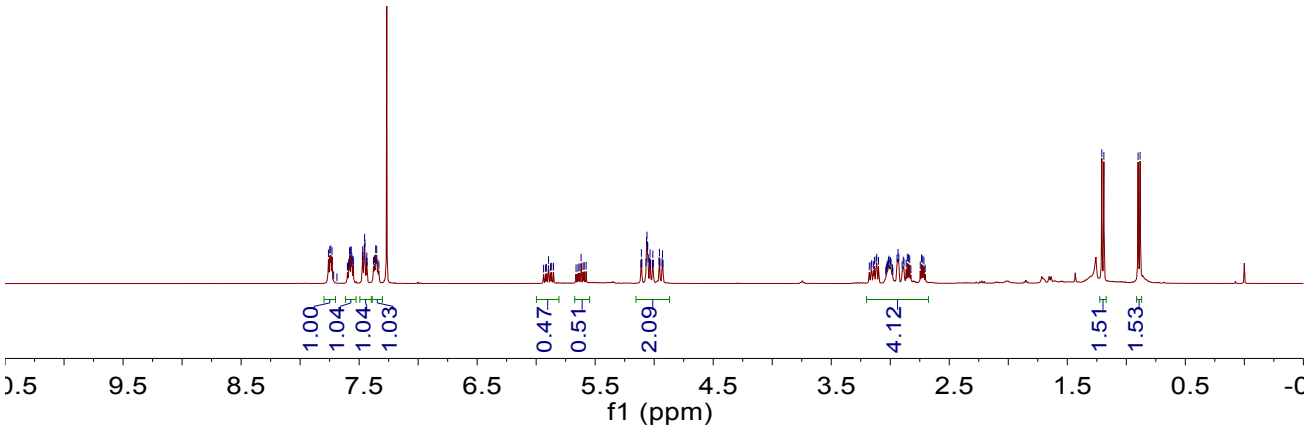
contains 20% of the regioisomer (linear product)

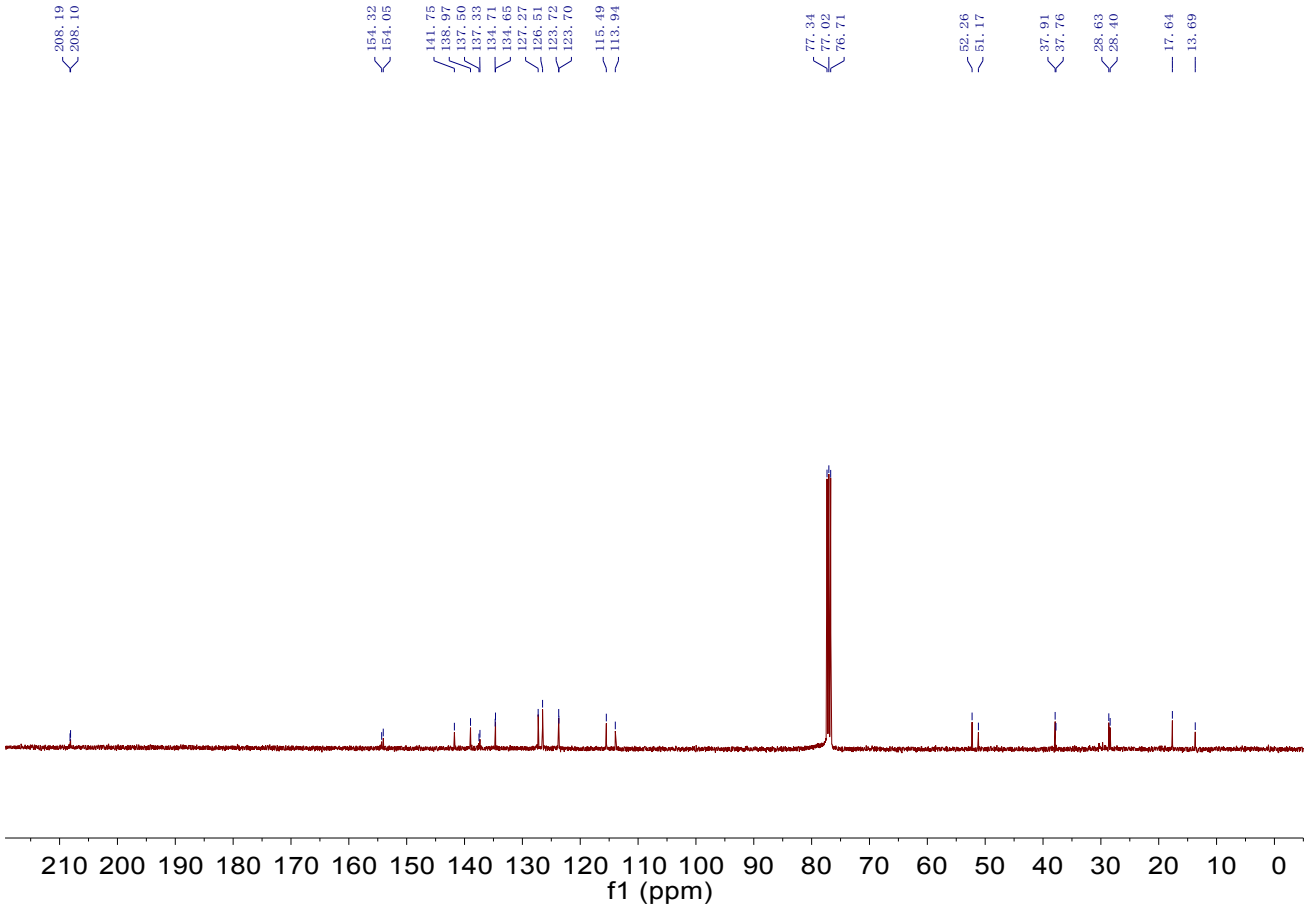


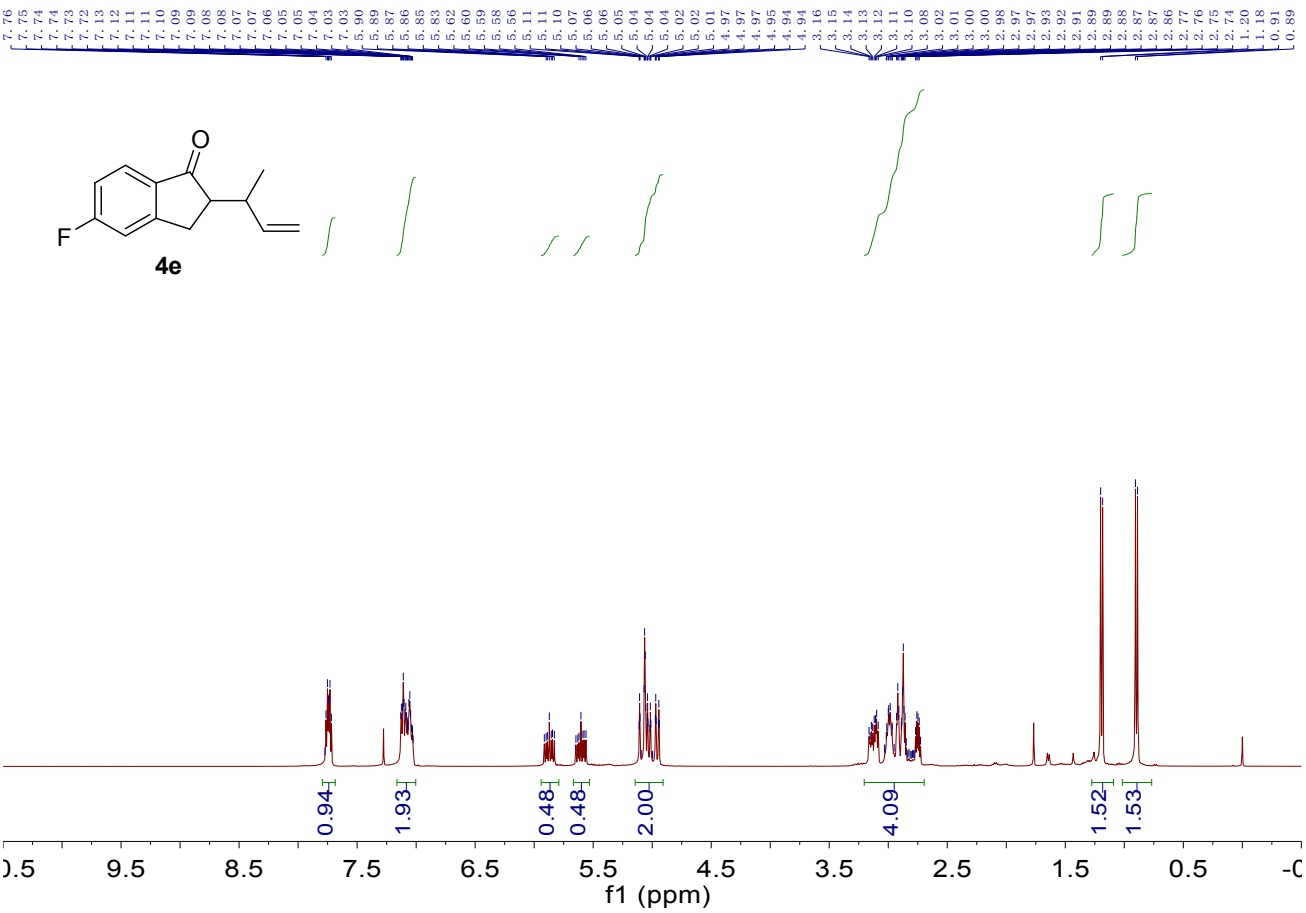


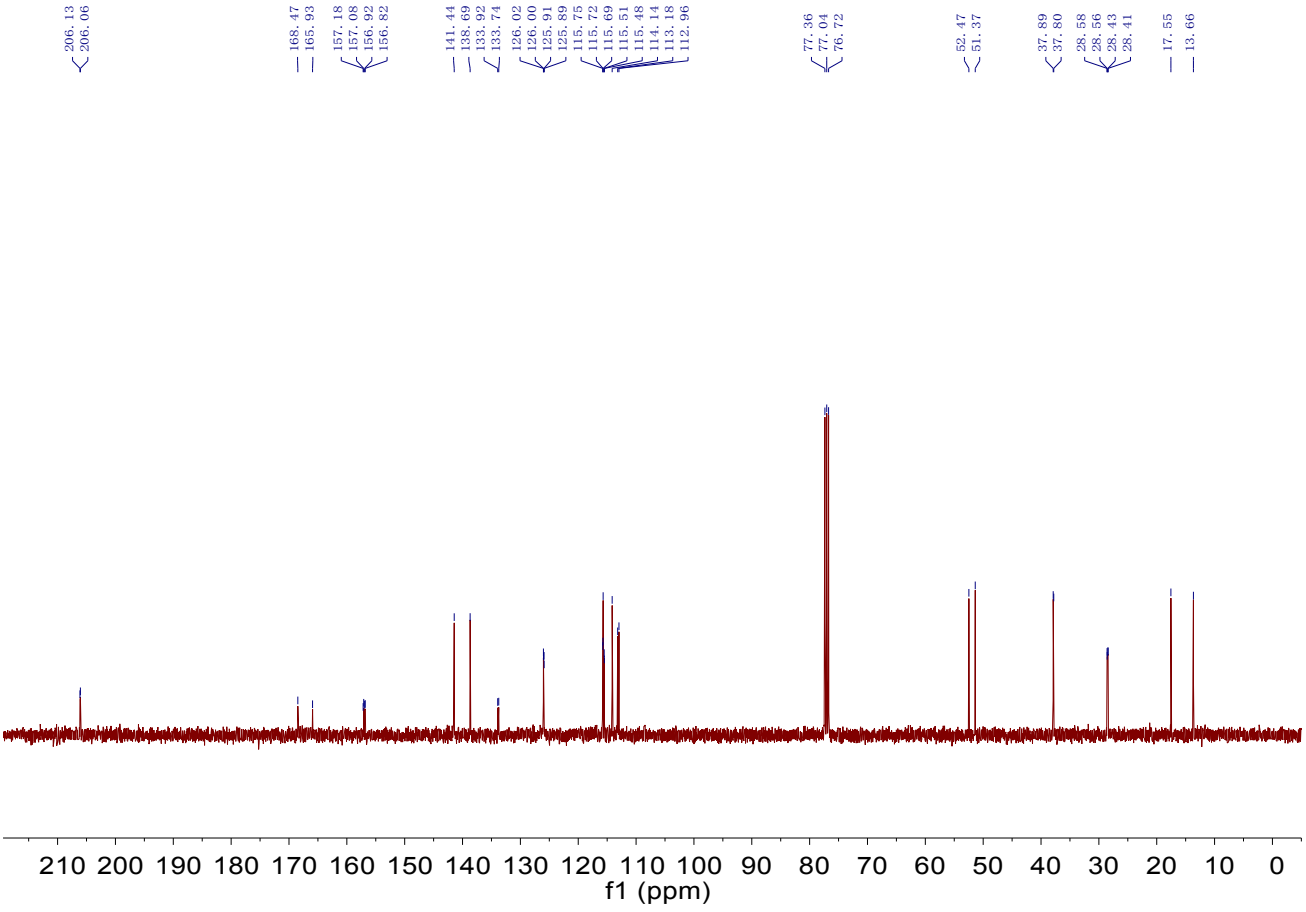


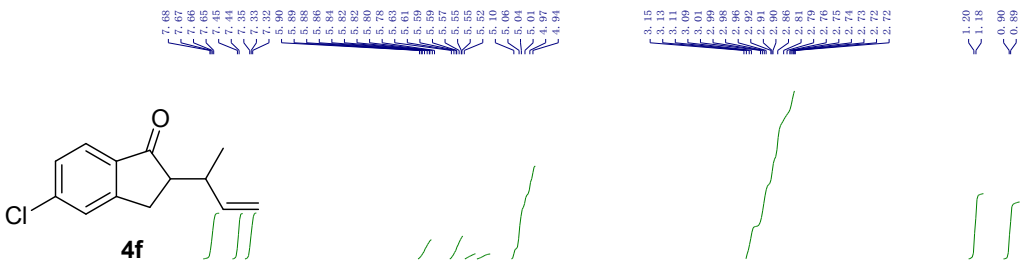
4d





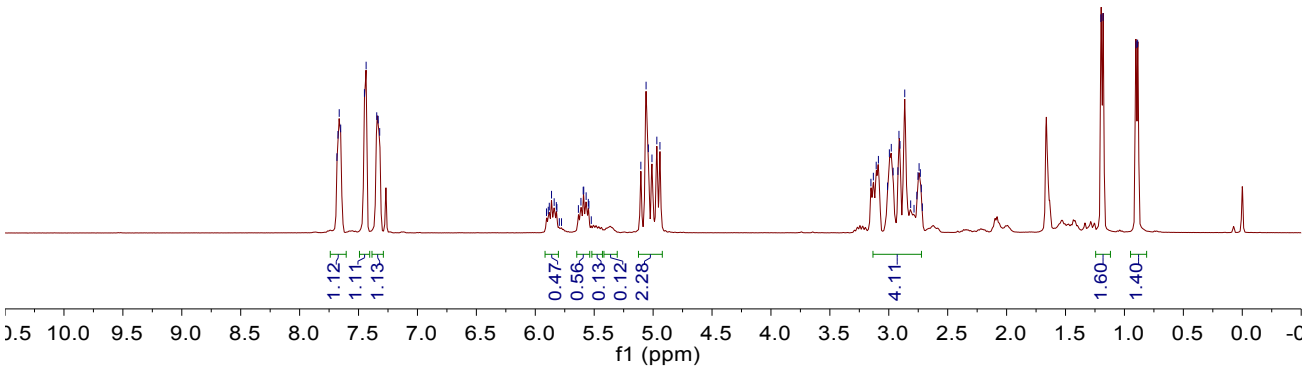

O
F
4e
0.94
1.93
0.48
0.48
2.00
4.09
1.52
1.53
f1 (ppm)

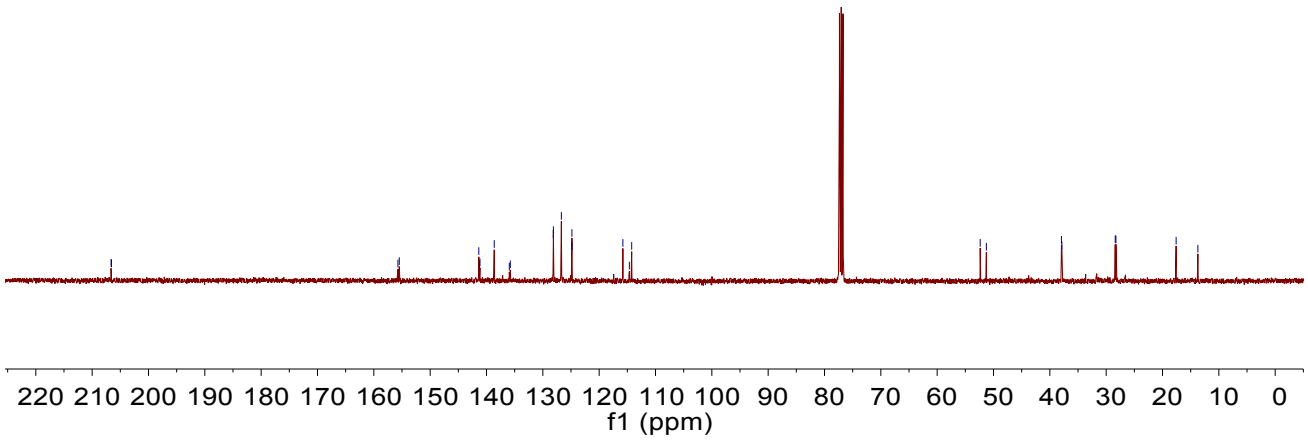

f1 (ppm)

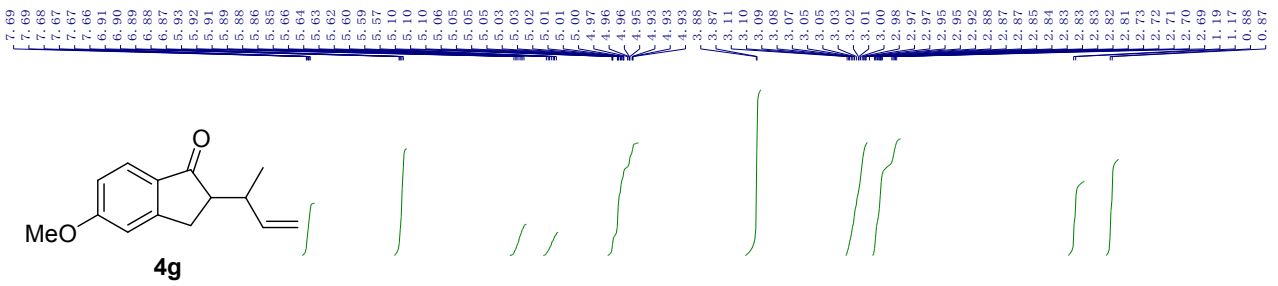


4f

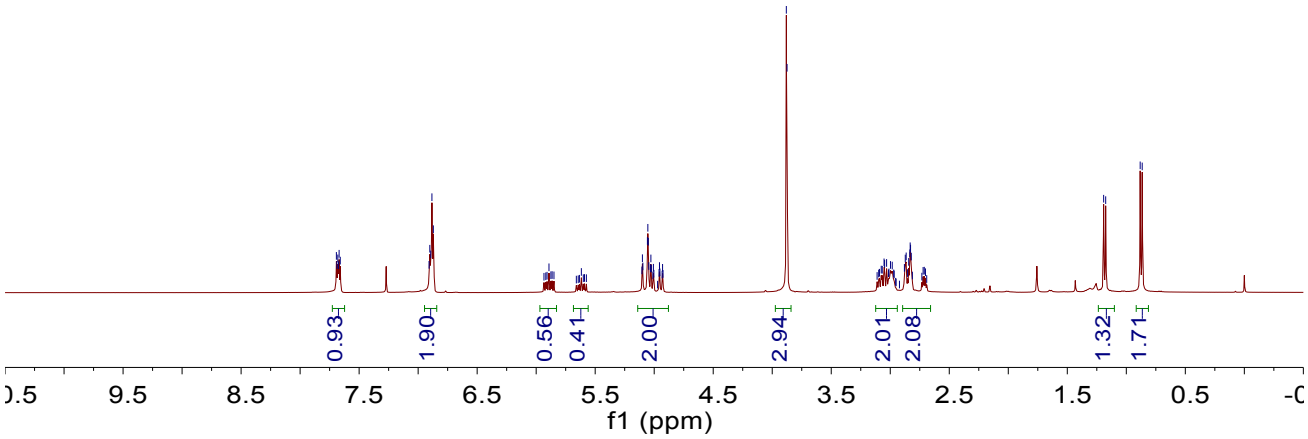
contains 11% of the regioisomer (linear product)

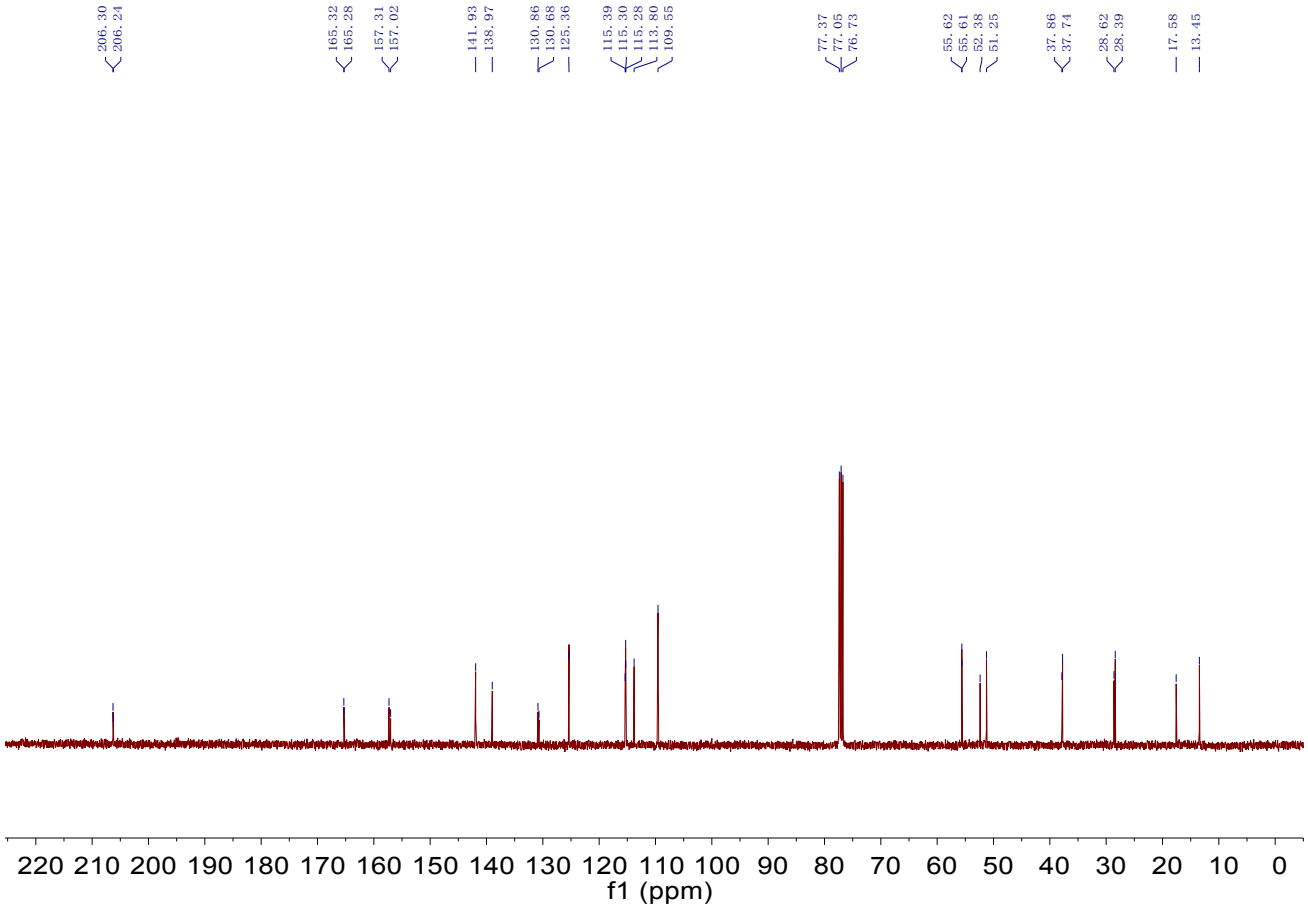


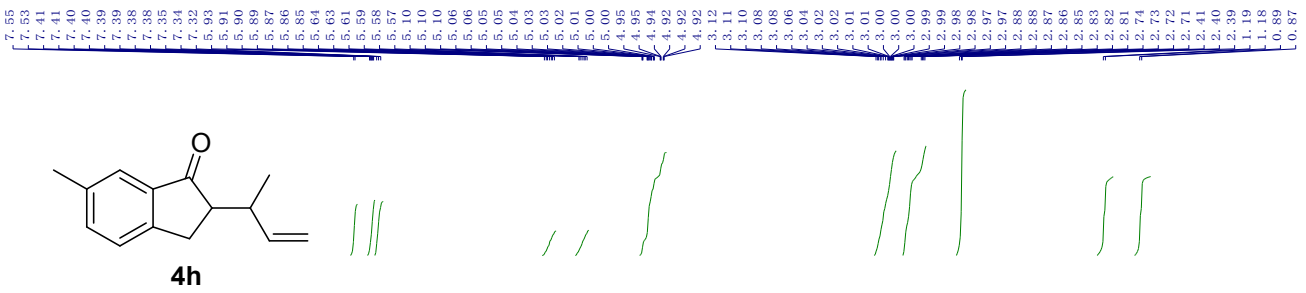




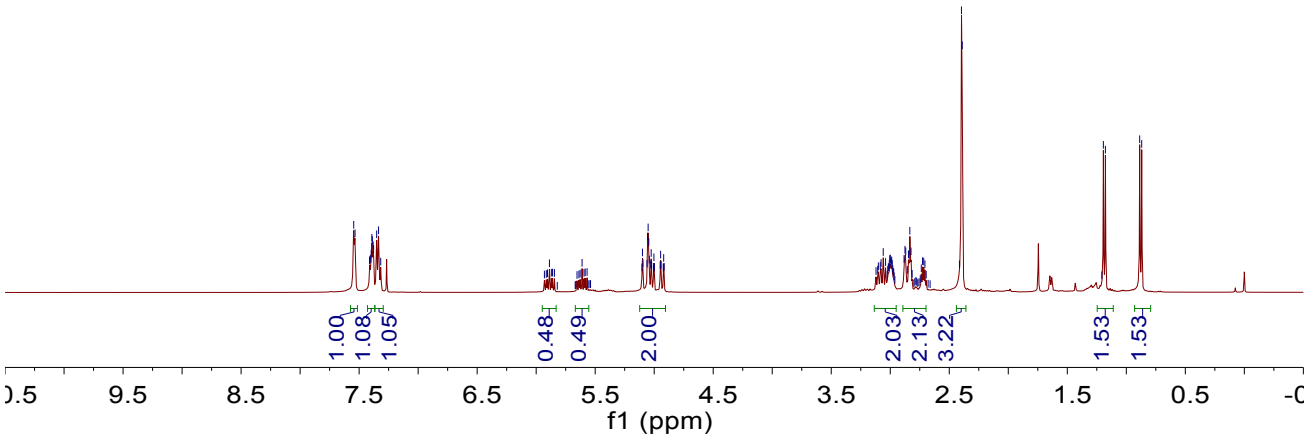
4g

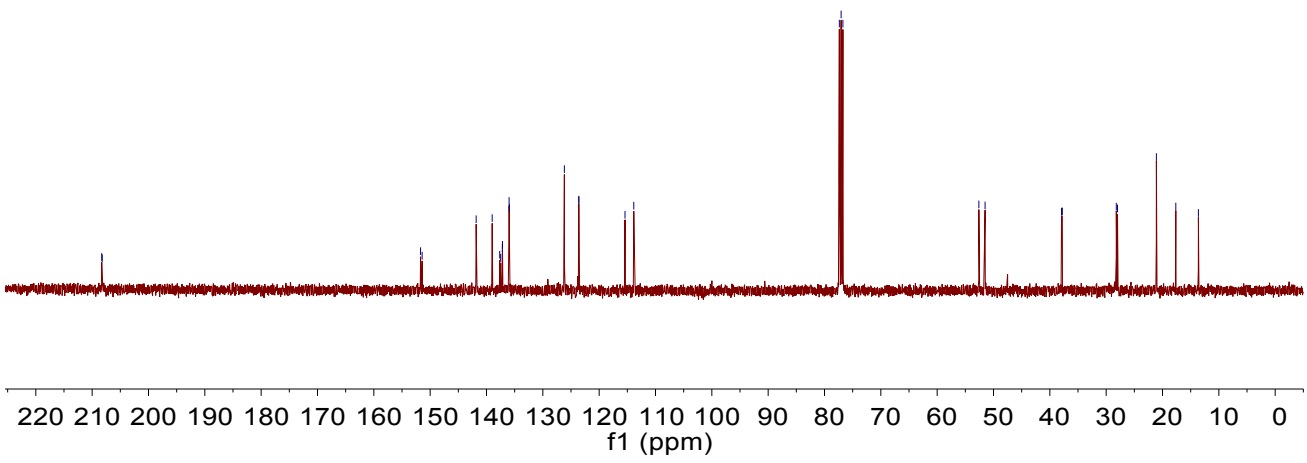


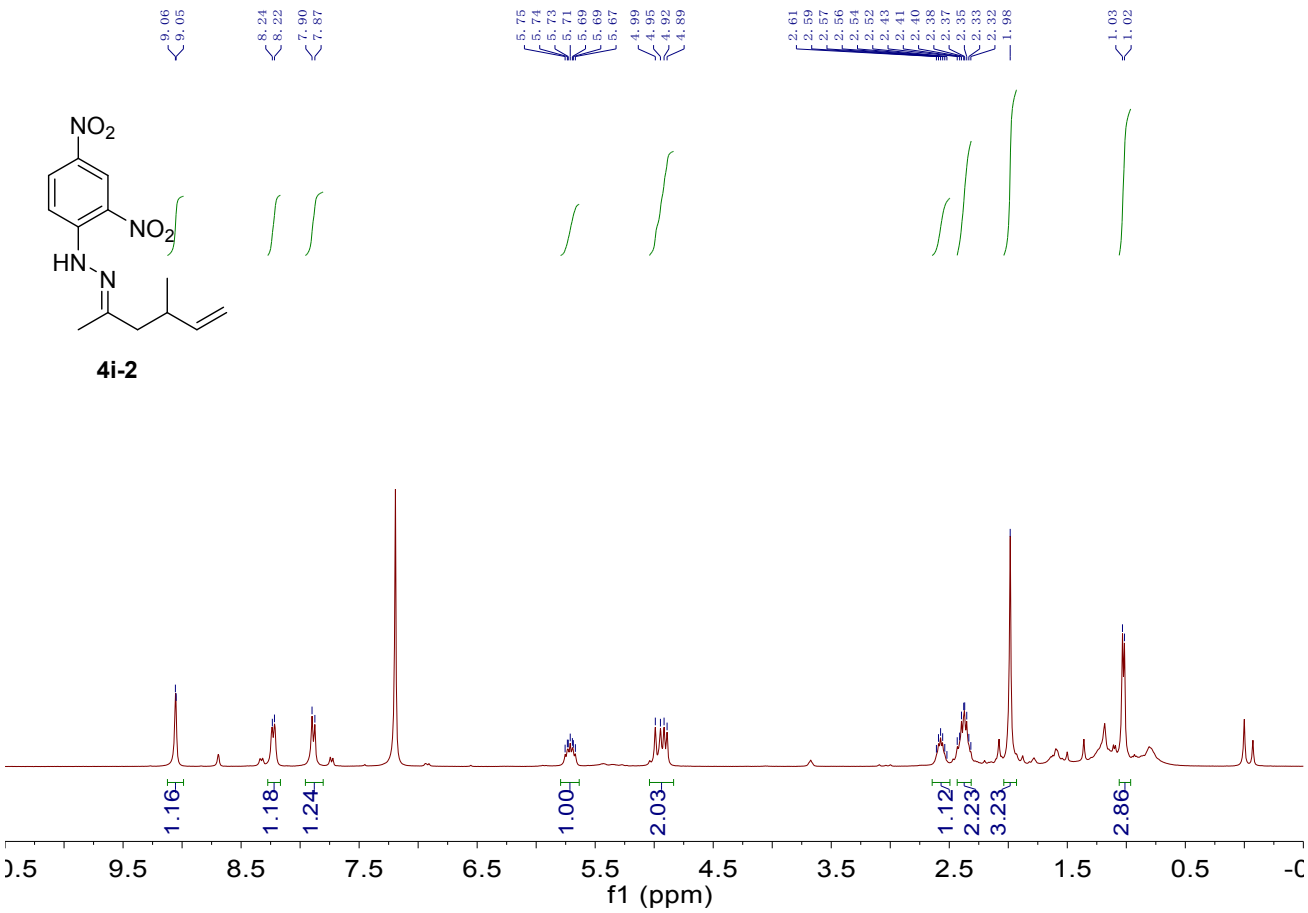


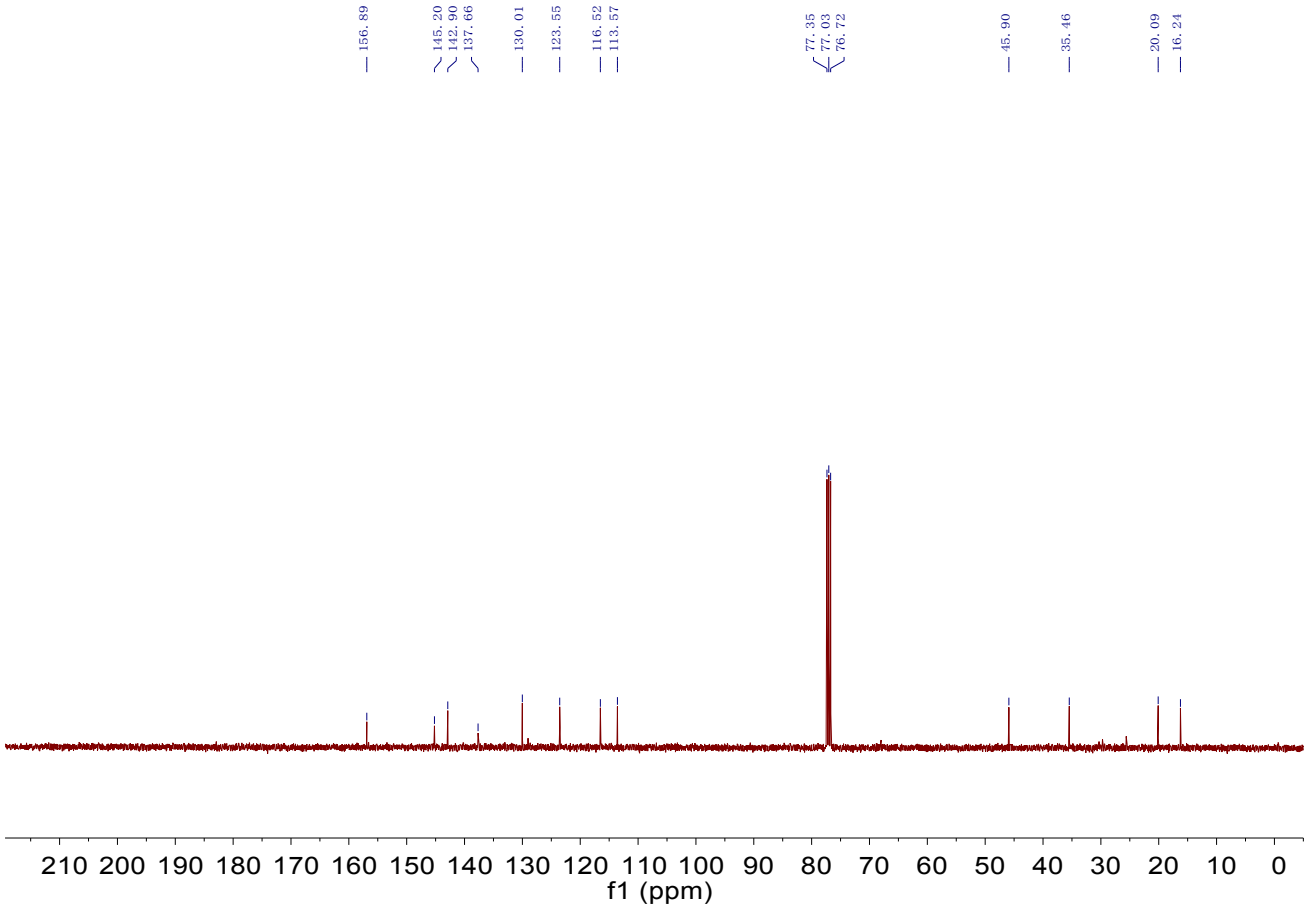


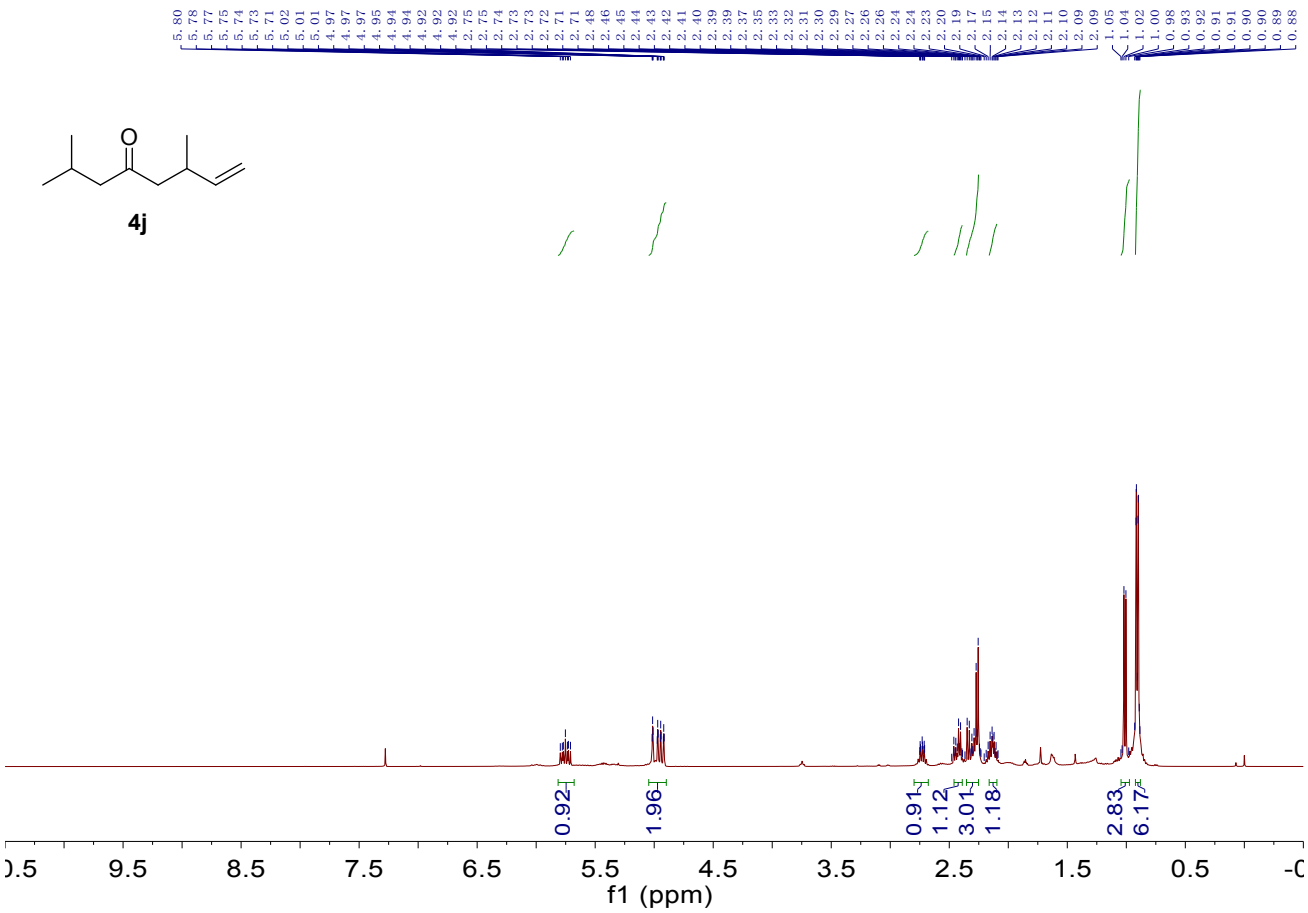
4h

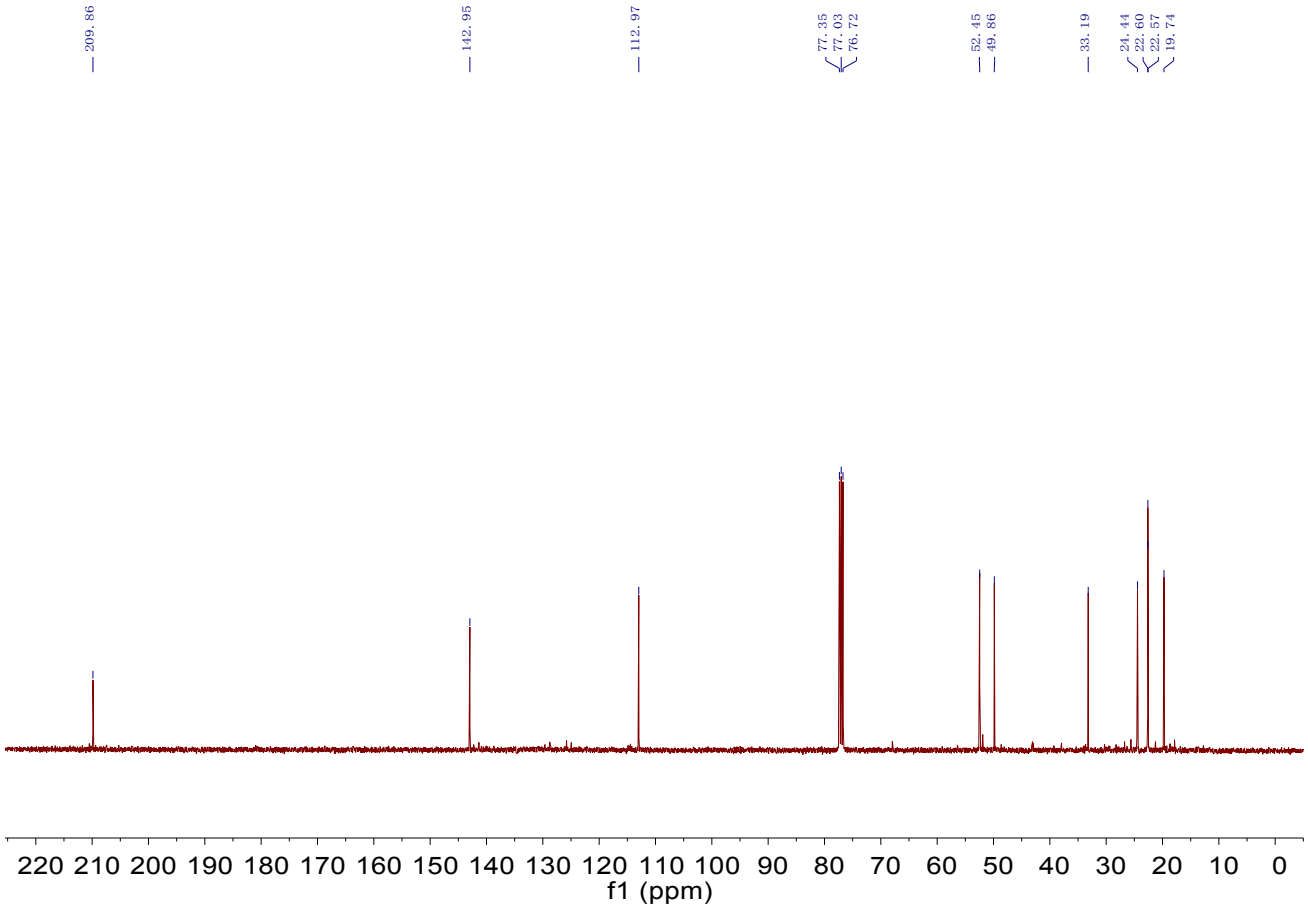


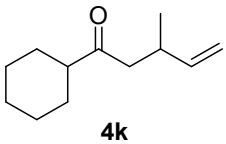



9.06
9.05
8.24
8.22
7.90
7.87
5.75
5.74
5.73
5.71
5.69
5.69
5.67
4.99
4.95
4.92
4.89
2.61
2.59
2.57
2.56
2.54
2.52
2.43
2.41
2.40
2.38
2.37
2.35
2.33
2.32
1.98
1.03
1.02
NO2
NO2
HN
N
4i-2
1.16
1.18
1.24
1.00
2.03
1.12
2.23
3.23
2.86
f1 (ppm)


156.89
145.20
142.90
137.66
130.01
123.55
116.52
113.57
77.35
77.03
76.72
45.90
35.46
20.09
16.24
f1 (ppm)

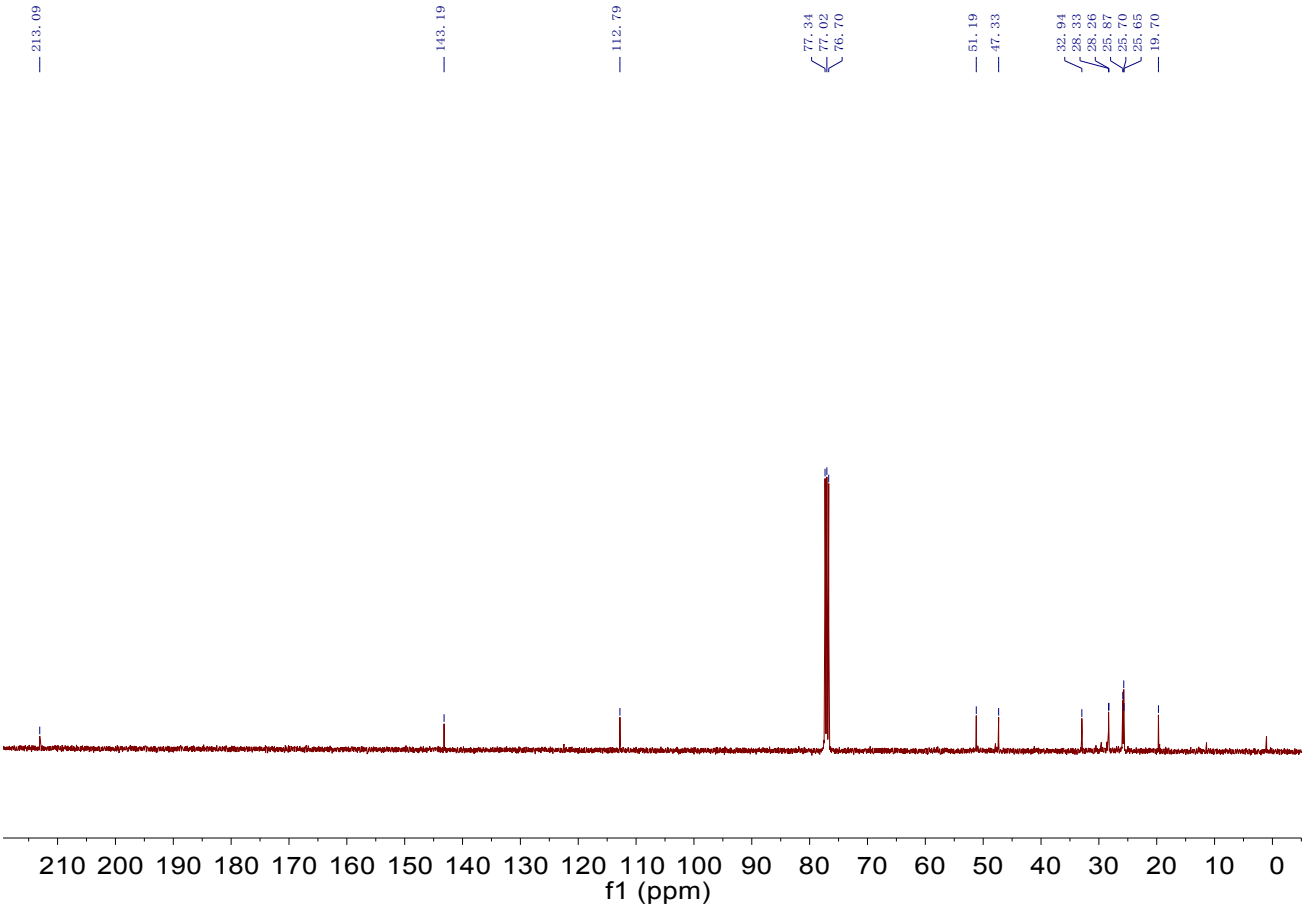

5.80 5.78 5.77 5.75 5.74 5.73 5.71 5.02 5.01 5.01 4.97 4.97 4.97 4.95 4.94 4.94 4.92 4.92 4.92 2.75 2.74 2.73 2.73 2.72 2.71 2.71 2.48 2.46 2.45 2.44 2.43 2.42 2.41 2.40 2.39 2.39 2.37 2.35 2.33 2.32 2.31 2.30 2.29 2.27 2.26 2.26 2.24 2.24 2.23 2.20 2.19 2.17 2.15 2.14 2.13 2.12 2.11 2.10 2.09 2.09 1.05 1.04 1.02 1.00 0.98 0.93 0.92 0.91 0.91 0.90 0.90 0.89 0.88
O
4j
0.92
1.96
0.91
1.12
3.01
1.18
2.83
6.17
f1 (ppm)

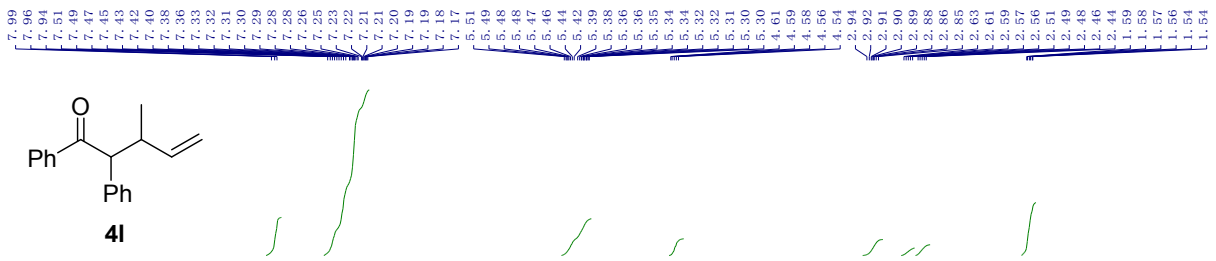

209.86
142.95
112.97
77.35
77.03
76.72
52.45
49.86
33.19
24.44
22.60
22.57
19.74
f1 (ppm)



4k

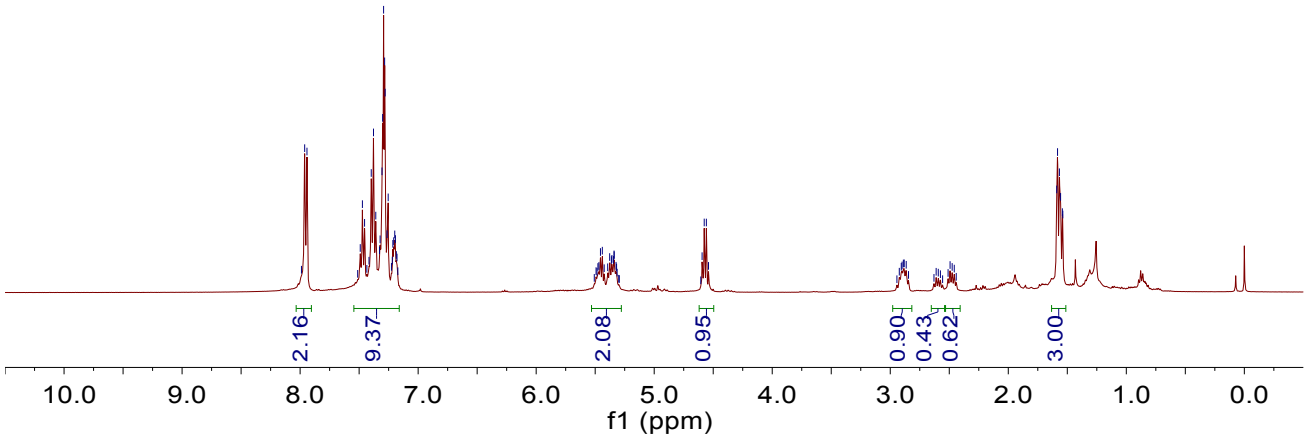
5.80
5.79
5.78
5.76
5.74
5.73
5.72
5.01
4.96
4.93
4.91
2.76
2.74
2.72
2.51
2.50
2.47
2.46
2.41
2.39
2.36
2.35
2.33
1.85
1.84
1.83
1.82
1.81
1.79
1.79
1.77
1.76
1.76
1.36
1.34
1.33
1.32
1.31
1.30
1.29
1.28
1.27
1.25
1.25
1.24
1.22
1.22
1.20
1.19
1.00
0.99
1.00
2.14
1.03
1.30
1.21
1.16
5.06
6.87
2.81
f1 (ppm)

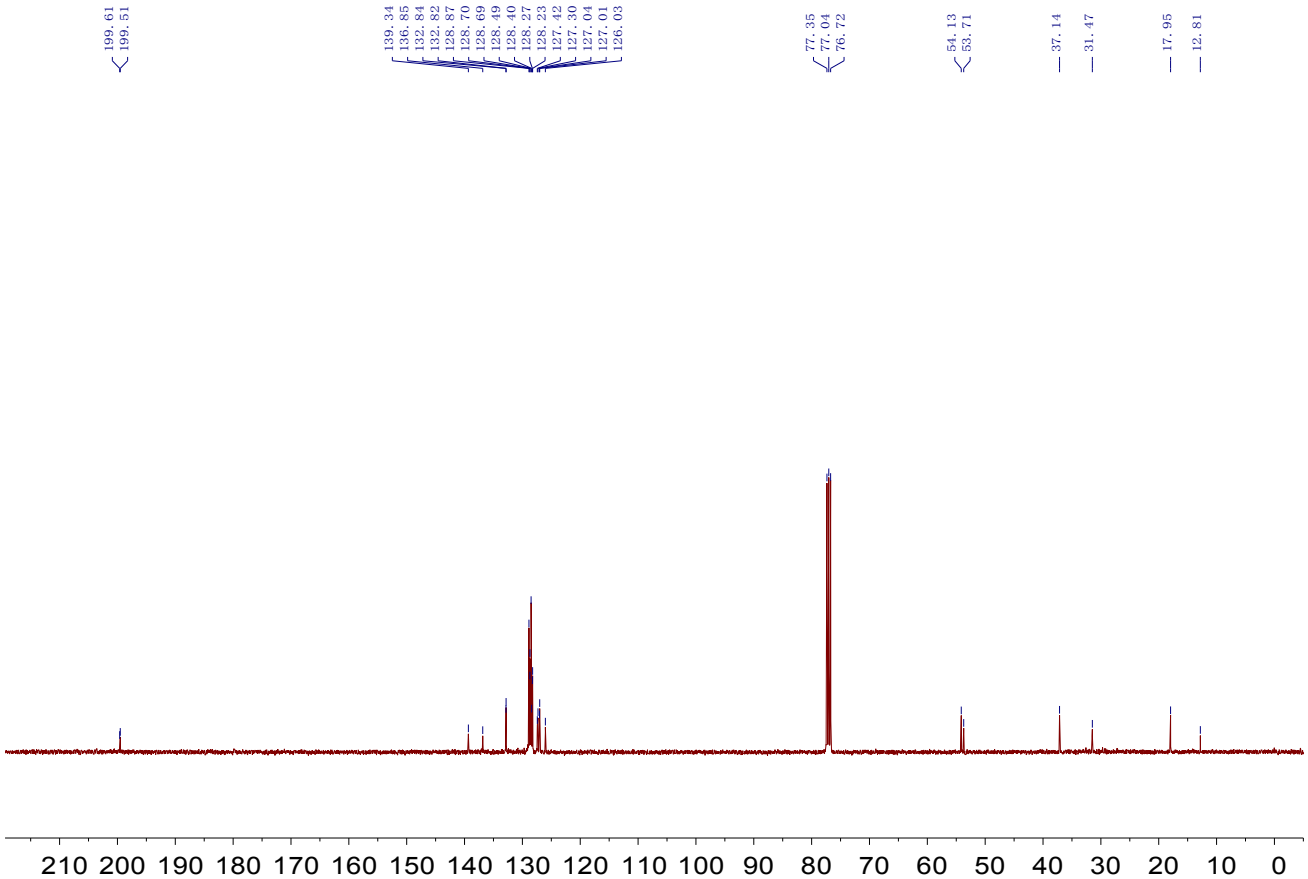

213.09
143.19
112.79
77.34
77.02
76.70
51.19
47.33
32.94
28.33
28.26
25.87
25.70
25.65
19.70
f1 (ppm)

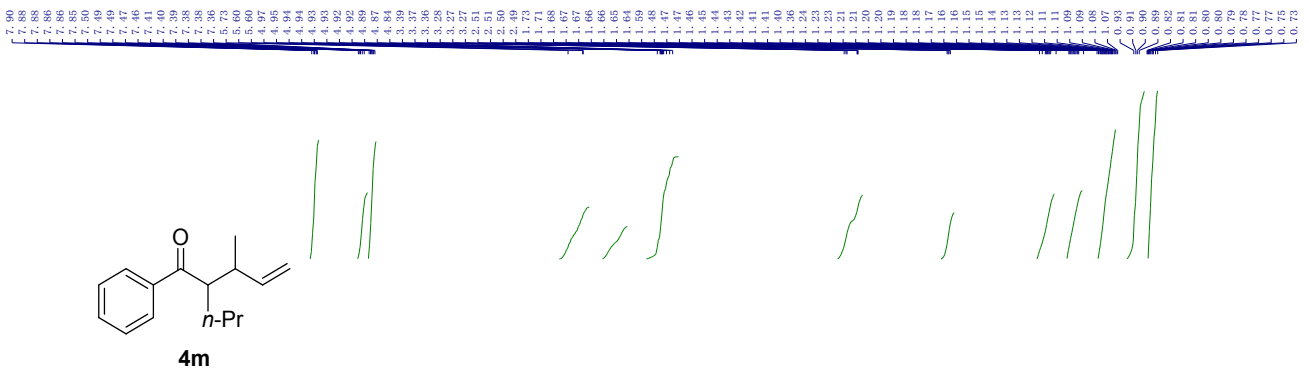


O
Ph
Ph

4l

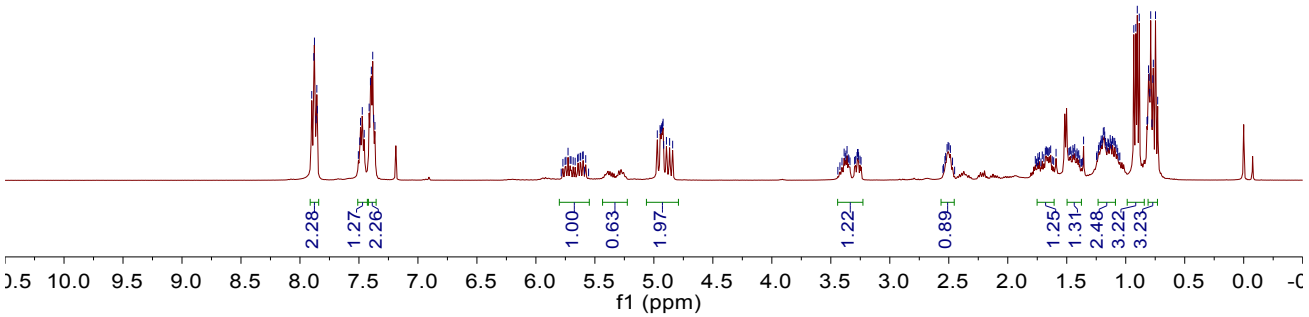

2.16
9.37
2.08
0.95
0.90
0.43
0.62
3.00
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

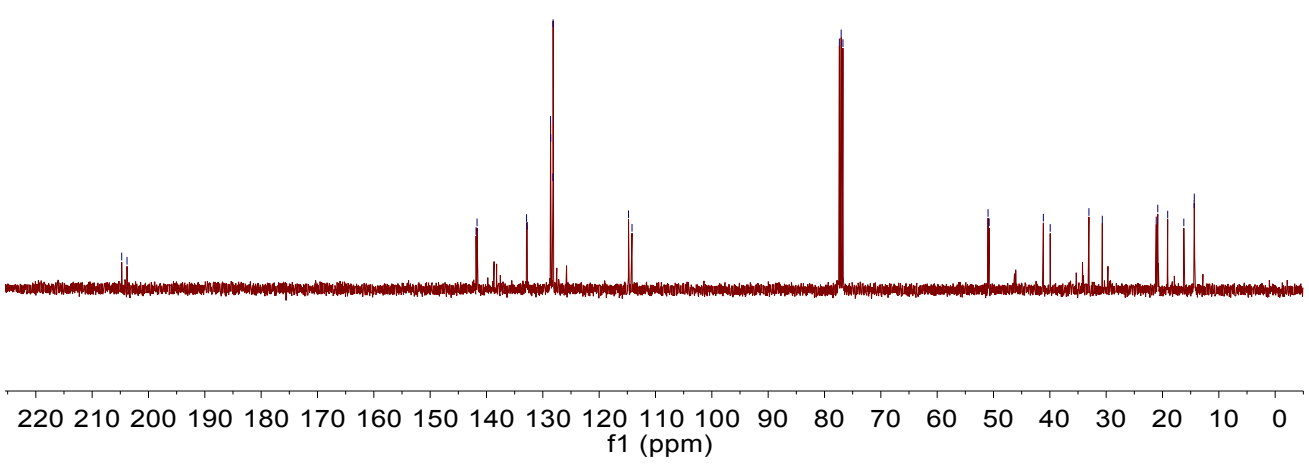

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

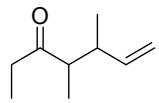


4m

contains 24% of the regioisomer (linear product)

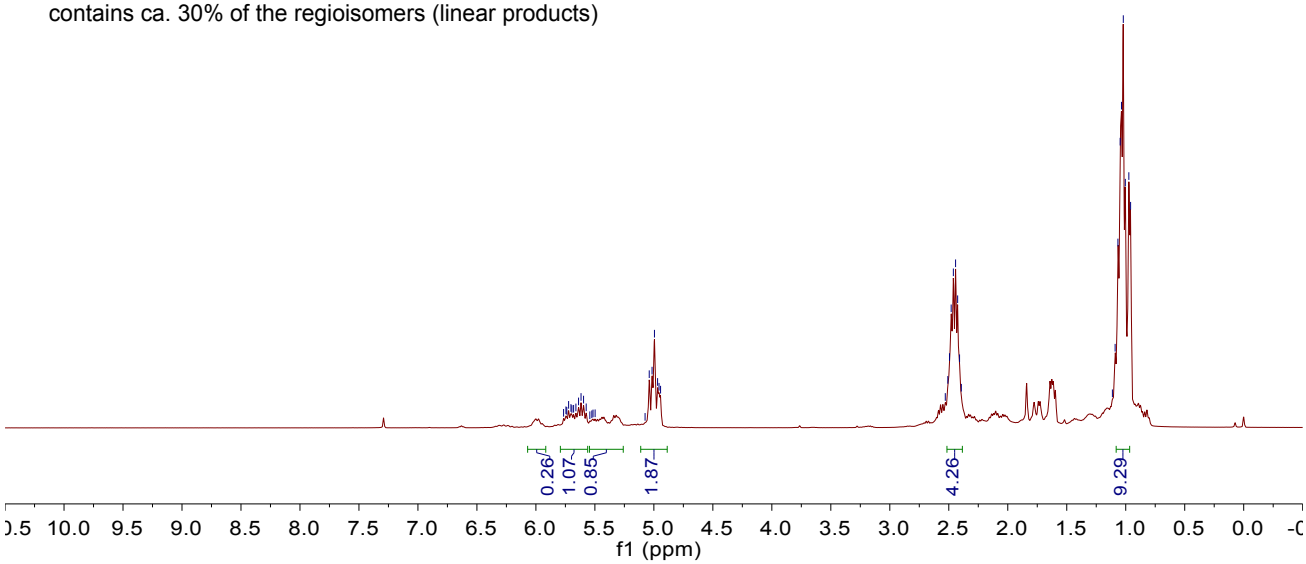


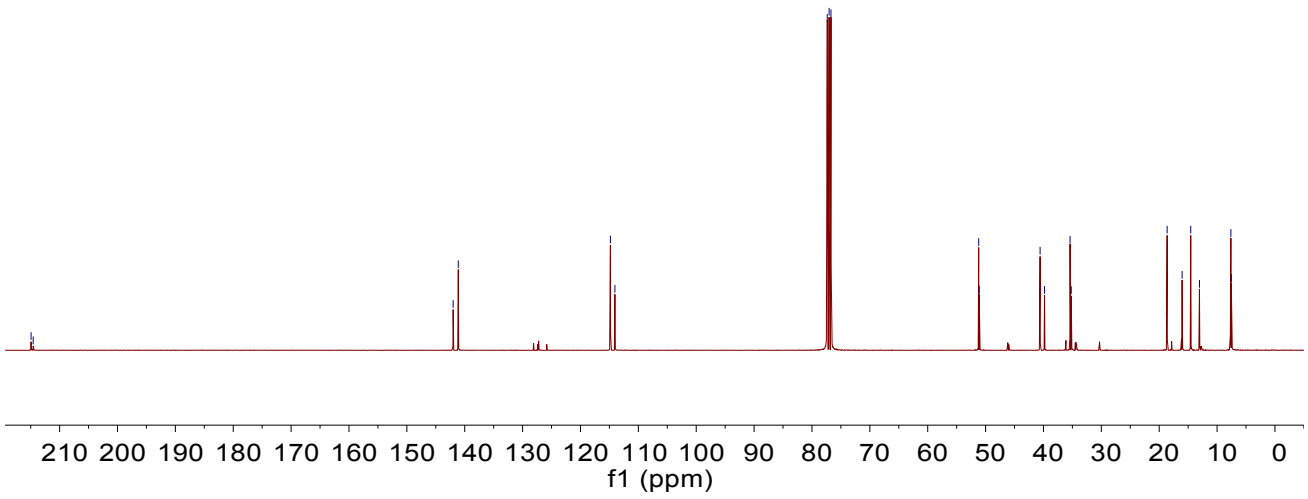


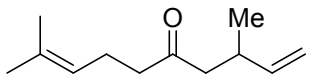


4n

contains ca. 30% of the regioisomers (linear products)

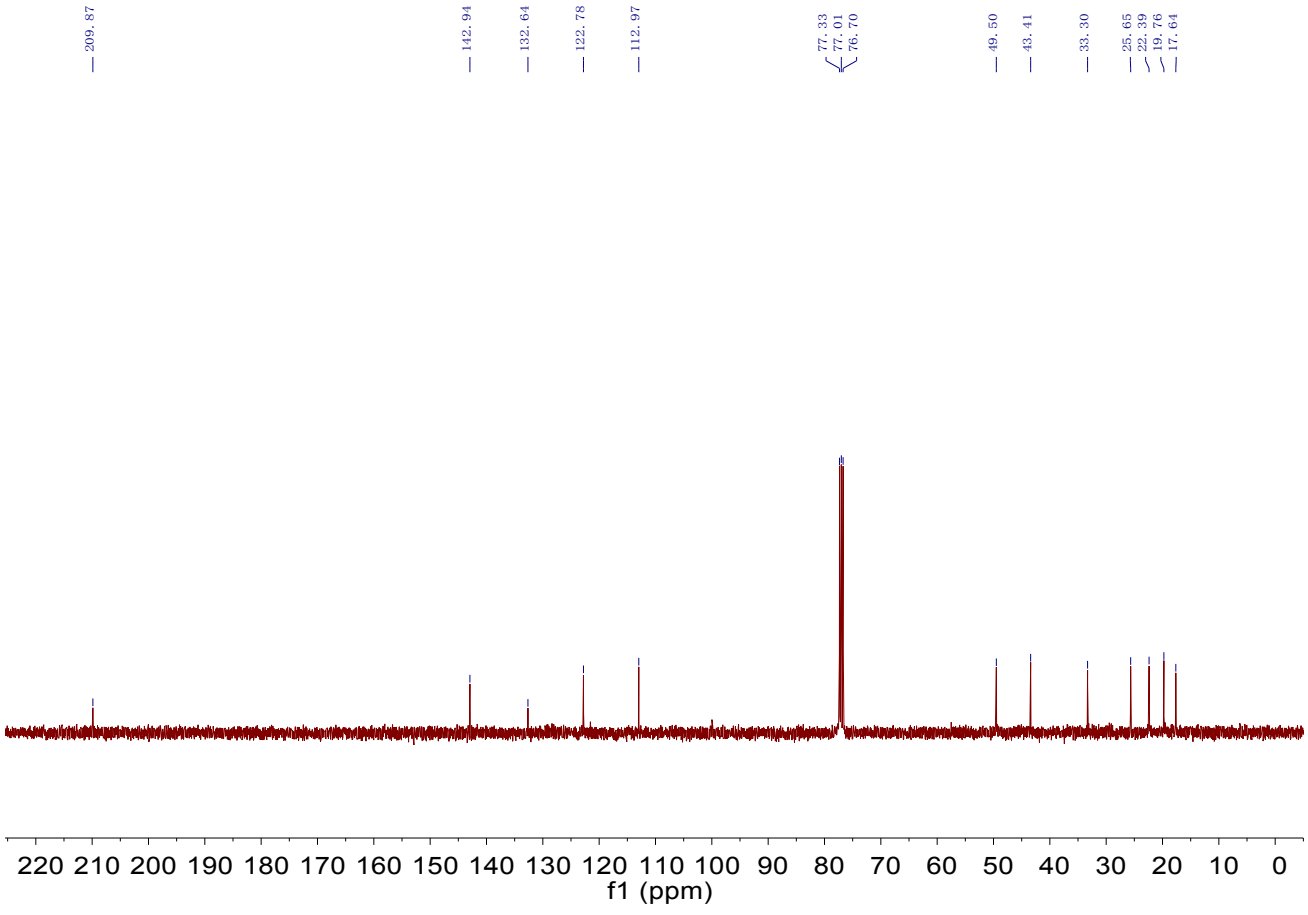


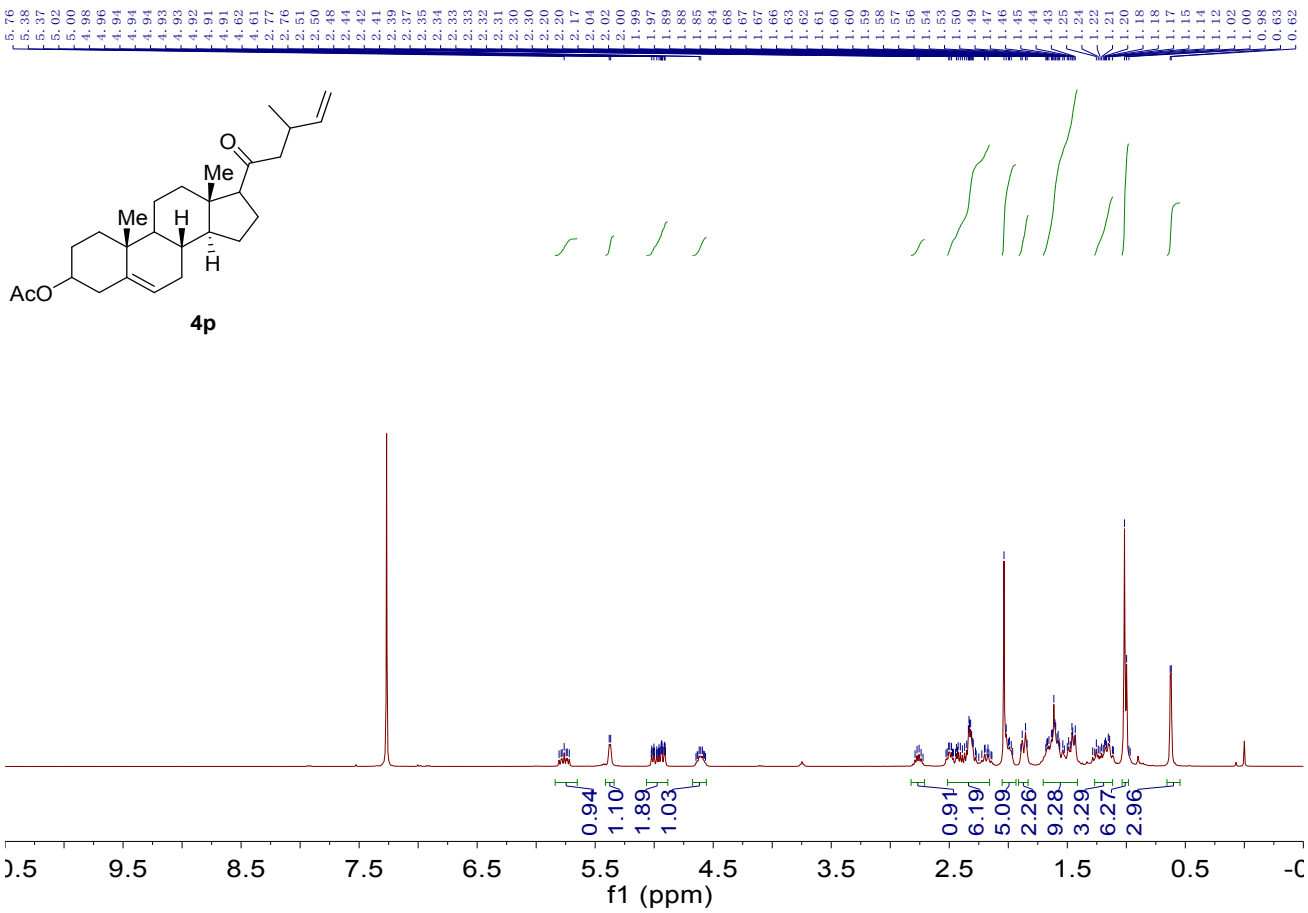


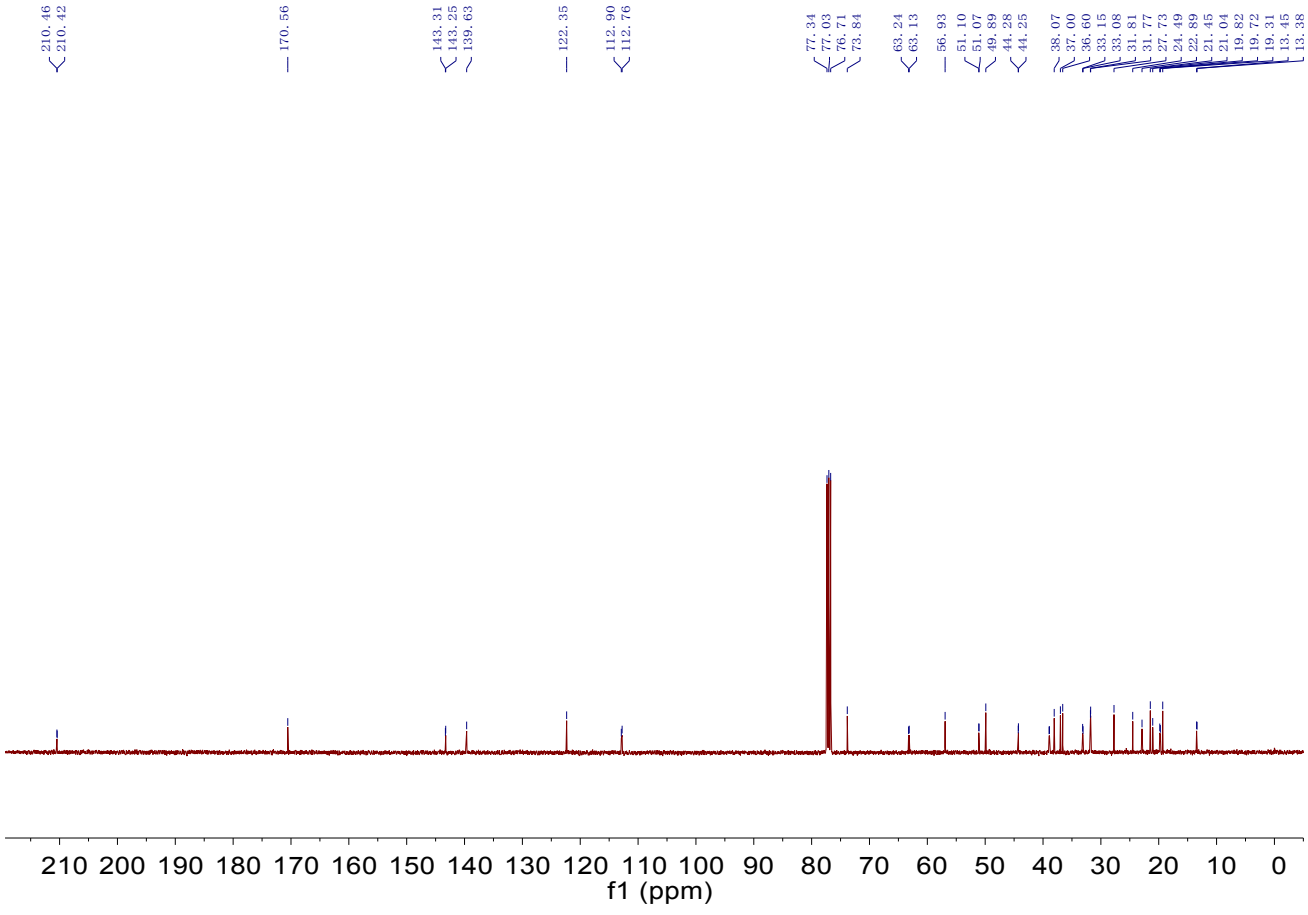

O
Me

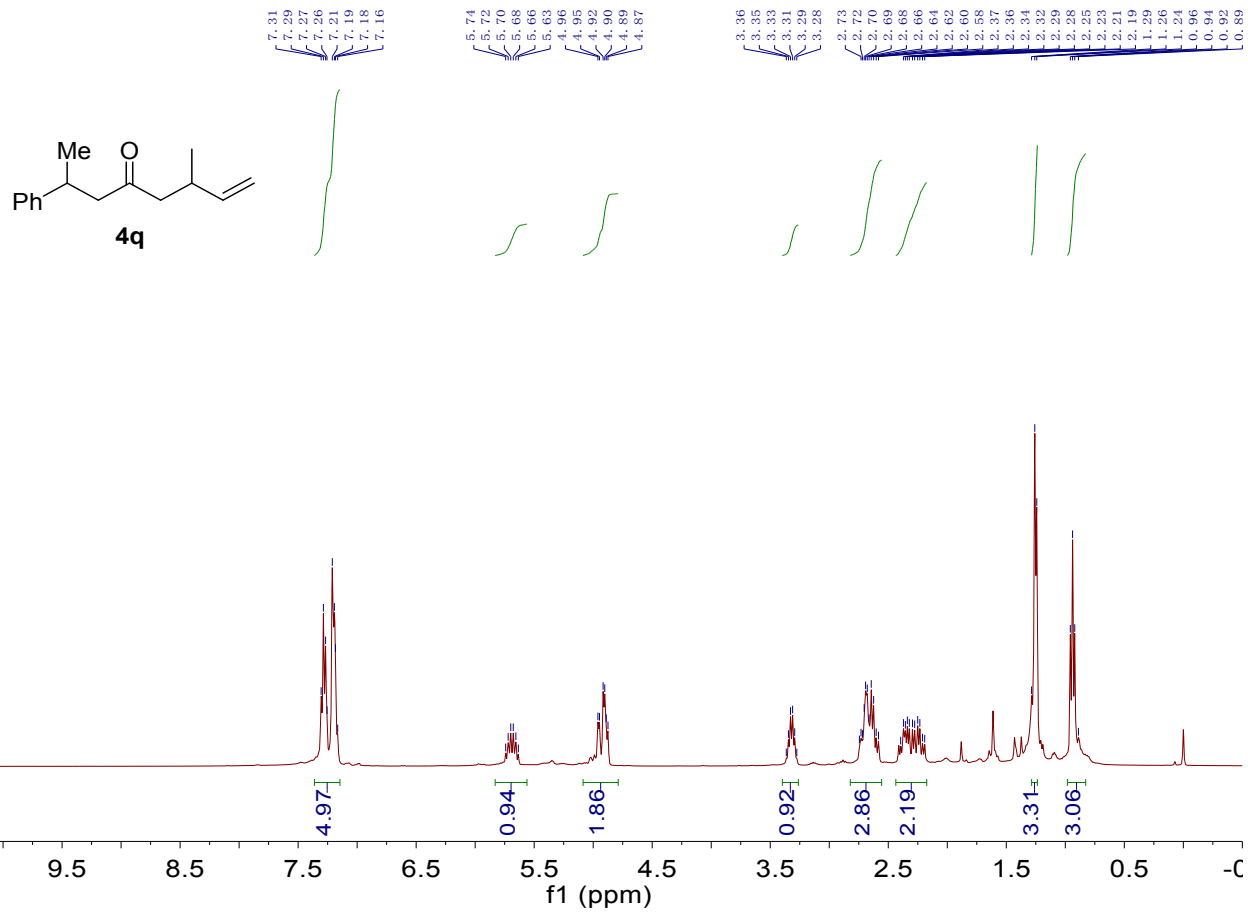
4o

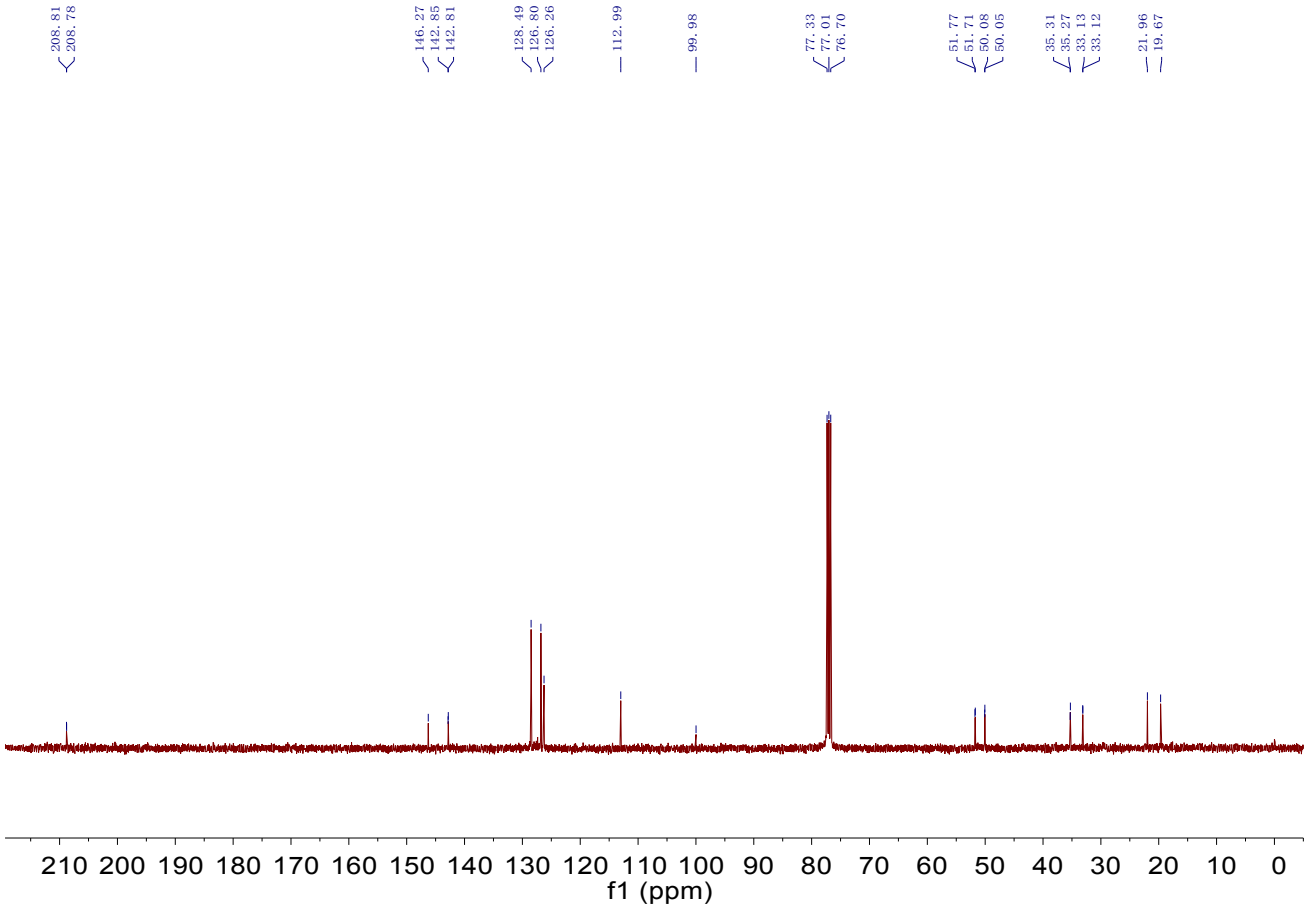
5.79
5.78
5.77
5.75
5.73
5.73
5.71
5.07
5.05
5.04
5.01
4.99
4.97
4.95
4.92
2.78
2.76
2.74
2.72
2.71
2.69
2.47
2.46
2.44
2.43
2.42
2.41
2.39
2.36
2.34
2.32
2.31
2.27
2.25
2.23
2.21
1.67
1.61
1.02
1.00
1.00
3.20
1.04
3.98
1.91
2.96
2.83
3.03
f1 (ppm)

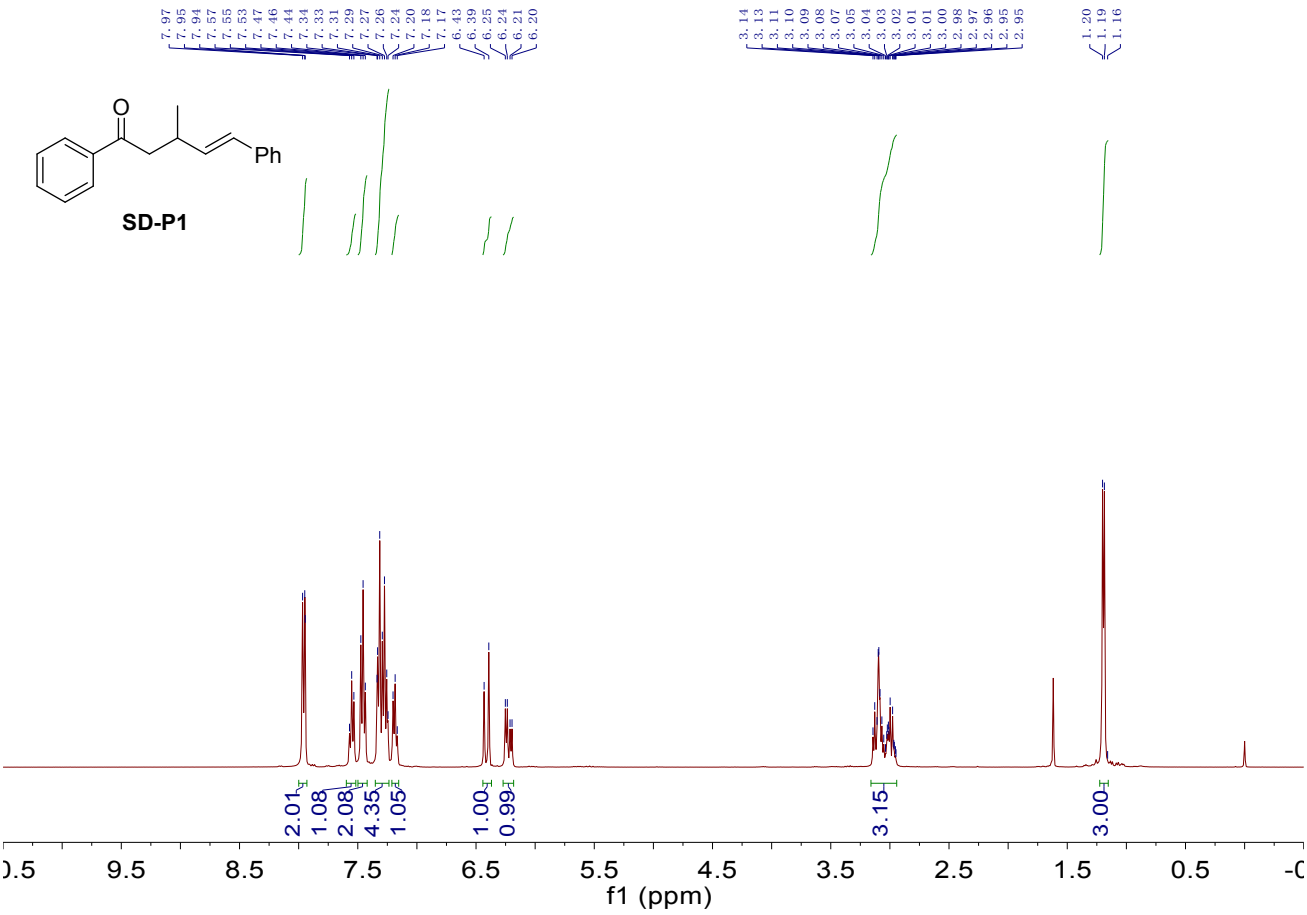

209.87
142.94
132.64
122.78
112.97
77.33
77.01
76.70
49.50
43.41
33.30
25.65
22.39
19.76
17.64
f1 (ppm)

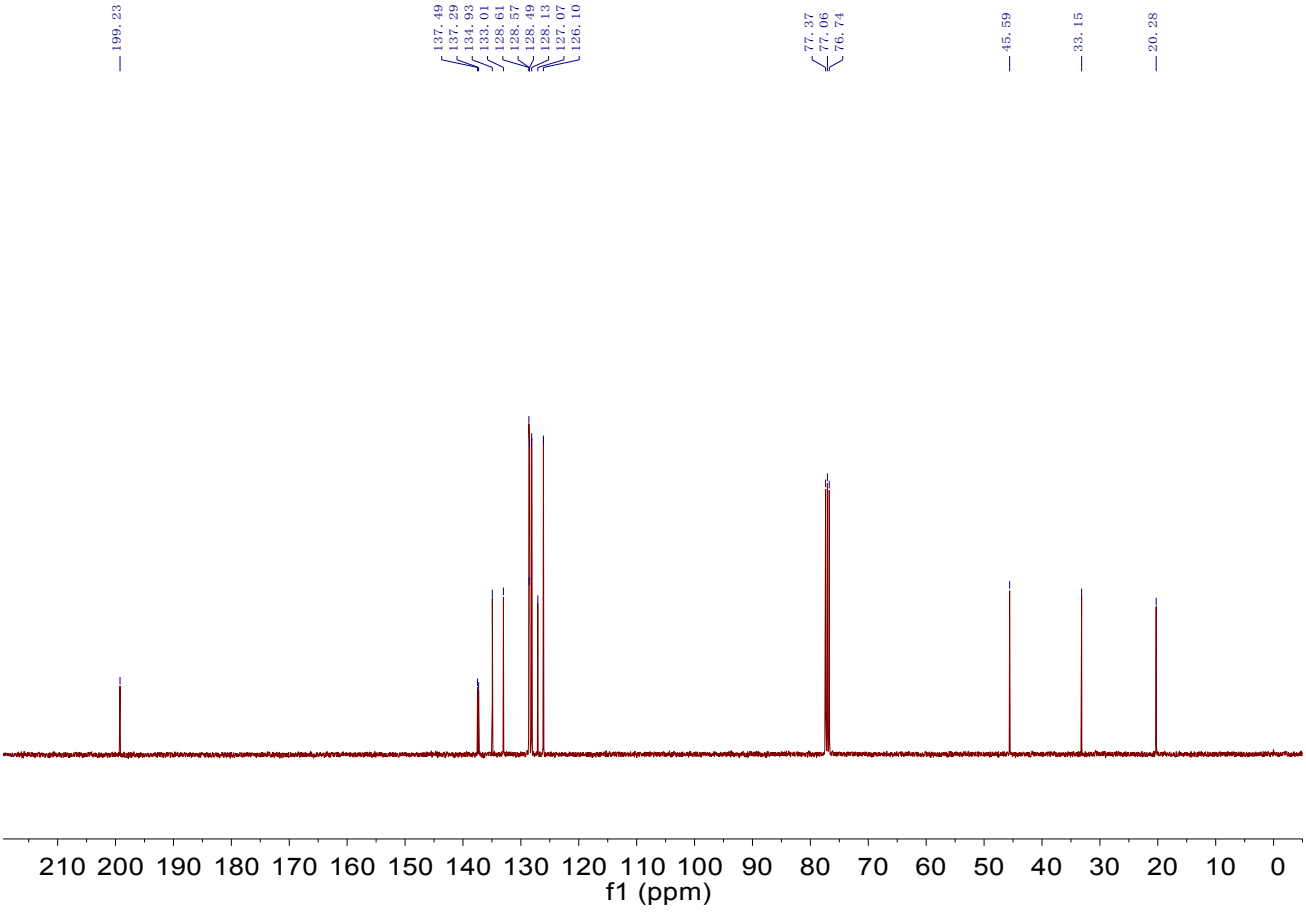

O
Me
Me
H
H
AcO
4p
0.94
1.10
1.89
1.03
0.91
6.19
5.09
2.26
9.28
3.29
6.27
2.96
f1 (ppm)

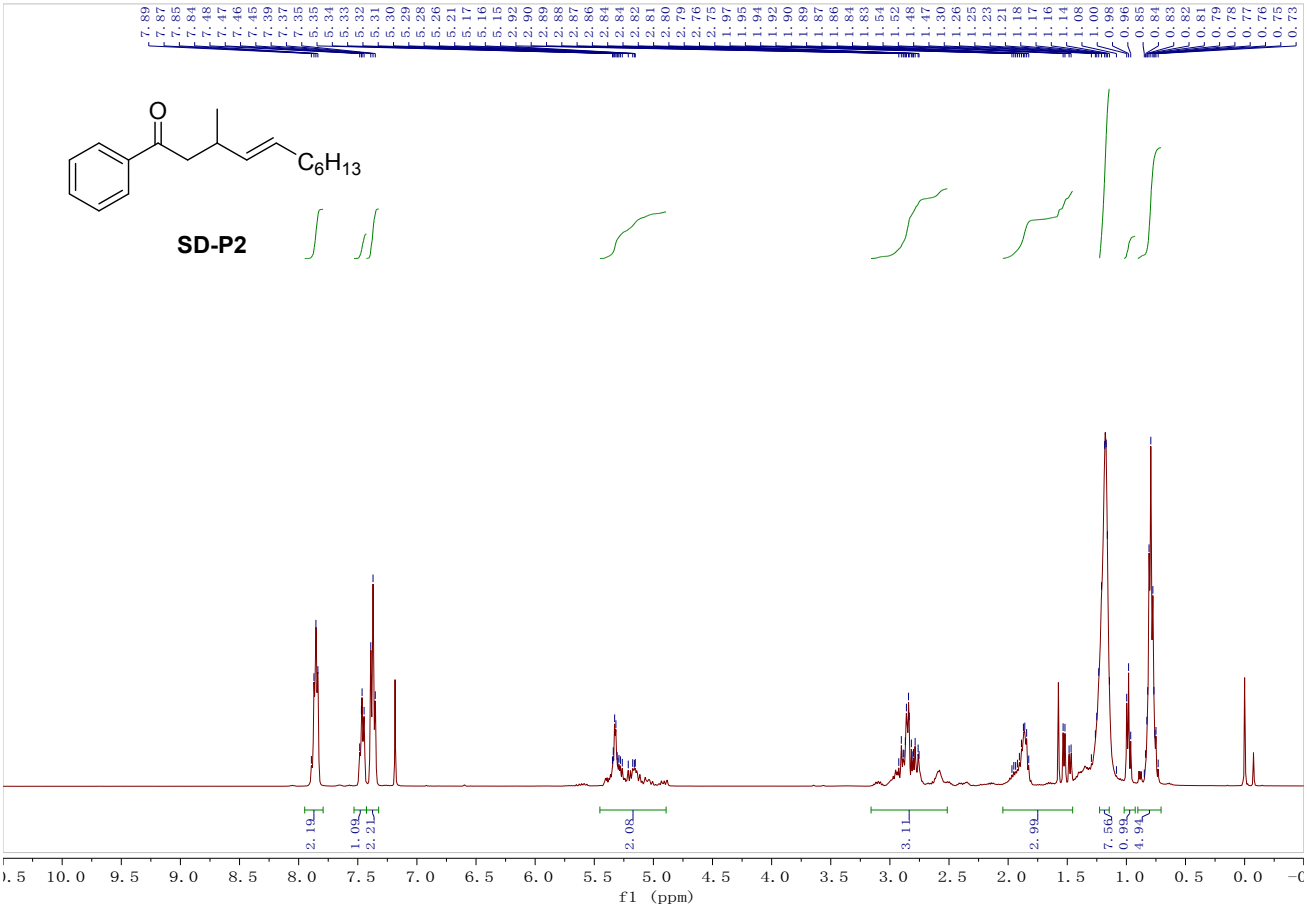

f1 (ppm)

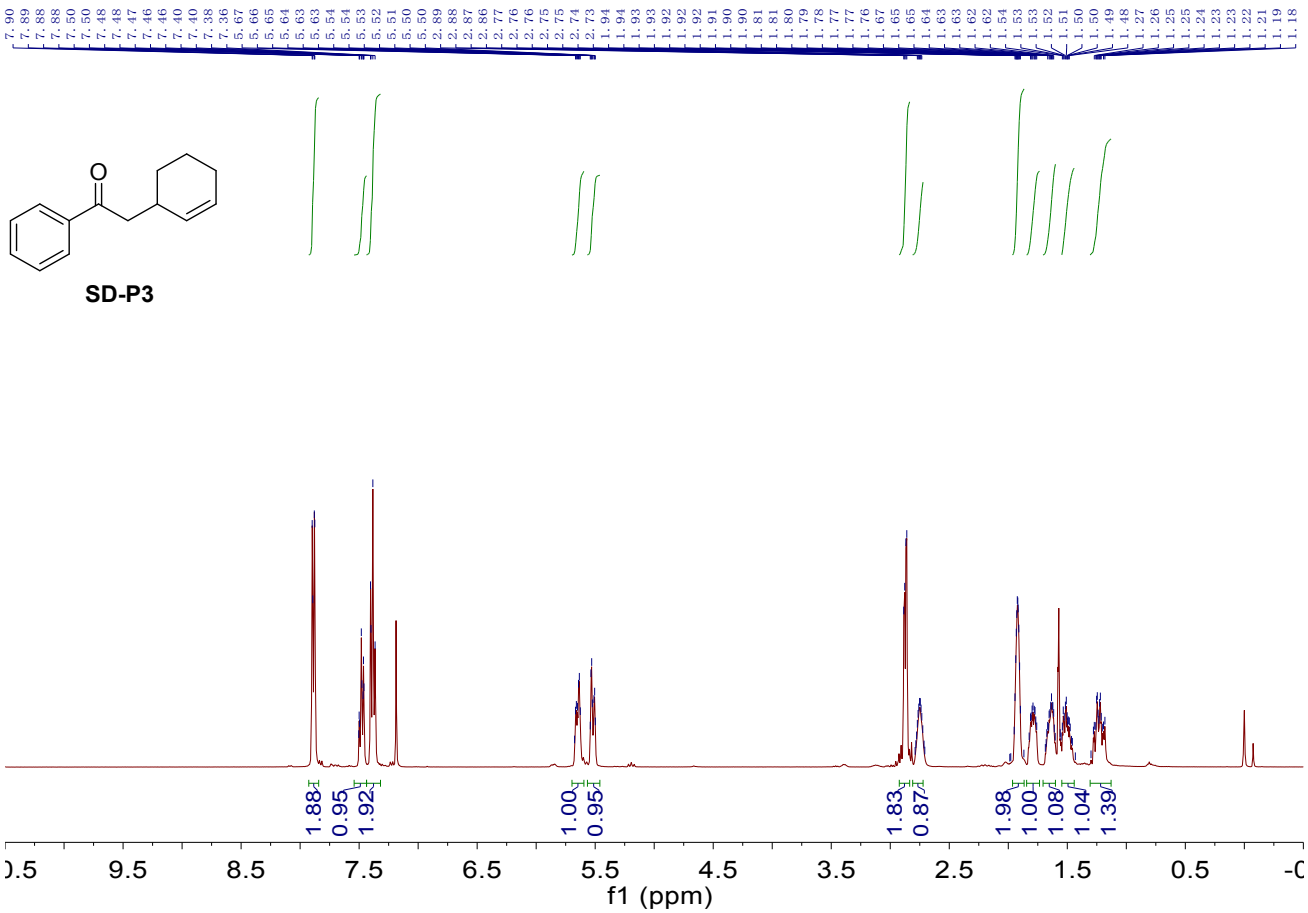

Me
O
Ph
4q
7.31
7.29
7.27
7.26
7.21
7.19
7.18
7.16
5.74
5.72
5.70
5.68
5.66
5.63
4.96
4.95
4.92
4.90
4.89
4.87
3.36
3.35
3.33
3.31
3.29
3.28
2.73
2.72
2.70
2.69
2.68
2.66
2.64
2.62
2.60
2.58
2.37
2.36
2.34
2.32
2.29
2.28
2.25
2.23
2.21
2.19
1.29
1.26
1.24
0.96
0.94
0.92
0.89
4.97
0.94
1.86
0.92
2.86
2.19
3.31
3.06
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

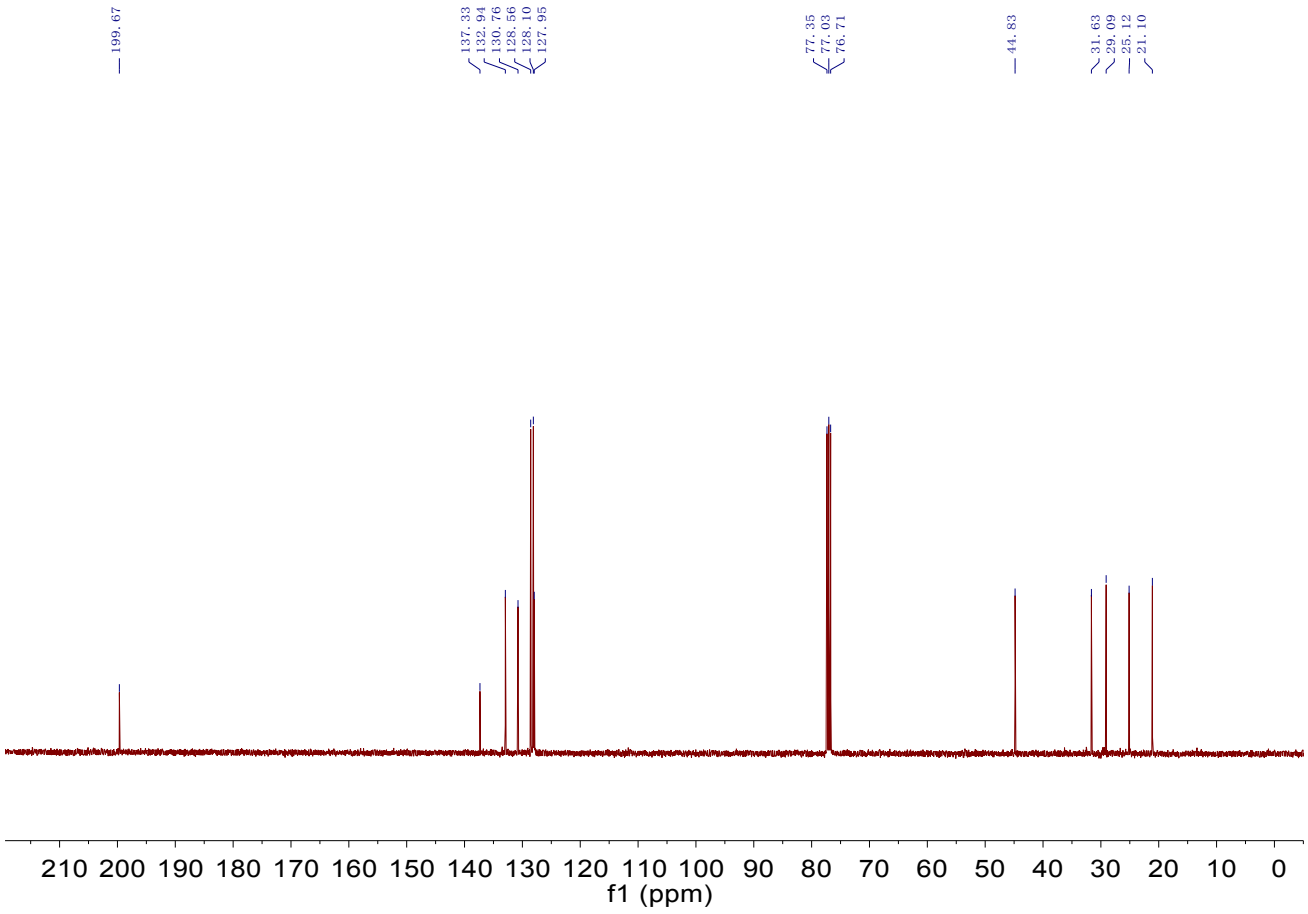

208.81
208.78
146.27
142.85
142.81
128.49
126.80
126.26
112.99
99.98
77.33
77.01
76.70
51.77
51.71
50.08
50.05
35.31
35.27
33.13
33.12
21.96
19.67
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

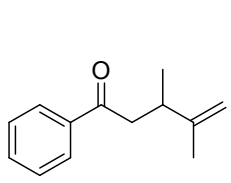

7.97
7.95
7.94
7.57
7.55
7.53
7.47
7.46
7.44
7.34
7.33
7.31
7.29
7.27
7.26
7.24
7.20
7.18
7.17
6.43
6.39
6.25
6.24
6.21
6.20
3.14
3.13
3.11
3.10
3.09
3.08
3.07
3.05
3.04
3.03
3.02
3.01
3.01
3.00
2.98
2.97
2.96
2.95
2.95
1.20
1.19
1.16
O
Ph
SD-P1
2.01
1.08
2.08
4.35
1.05
1.00
0.99
3.15
3.00
f1 (ppm)


199.23
137.49
137.29
134.93
133.01
128.61
128.57
128.49
128.13
127.07
126.10
77.37
77.06
76.74
45.59
33.15
20.28
f1 (ppm)


O
C6H13
SD-P2
f1 (ppm)

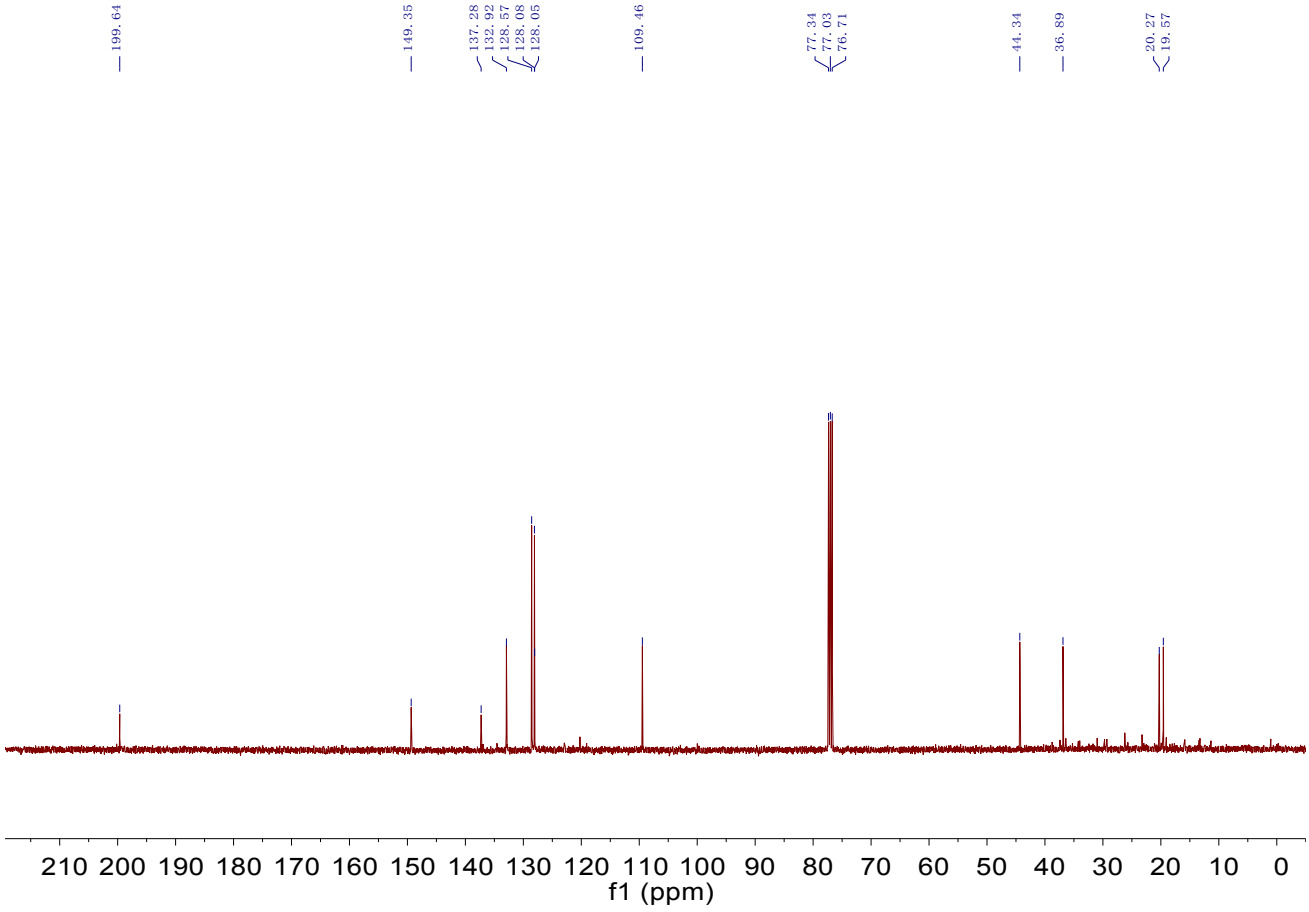

SD-P3
1.88
0.95
1.92
1.00
0.95
1.83
0.87
1.98
1.00
1.08
1.04
1.39
f1 (ppm)

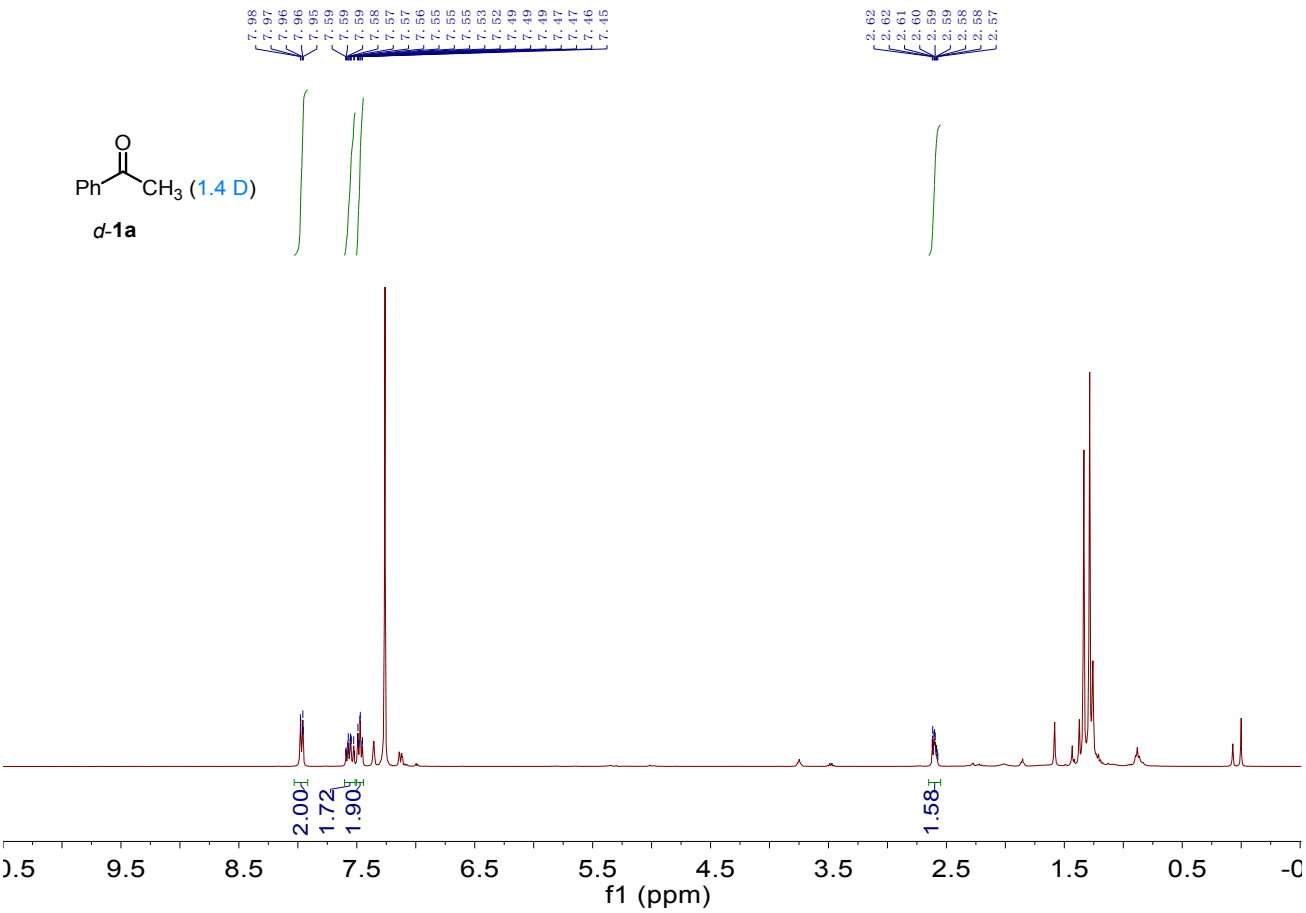

199.67
137.33
132.94
130.76
128.56
128.10
127.95
77.35
77.03
76.71
44.83
31.63
29.09
25.12
21.10
f1 (ppm)

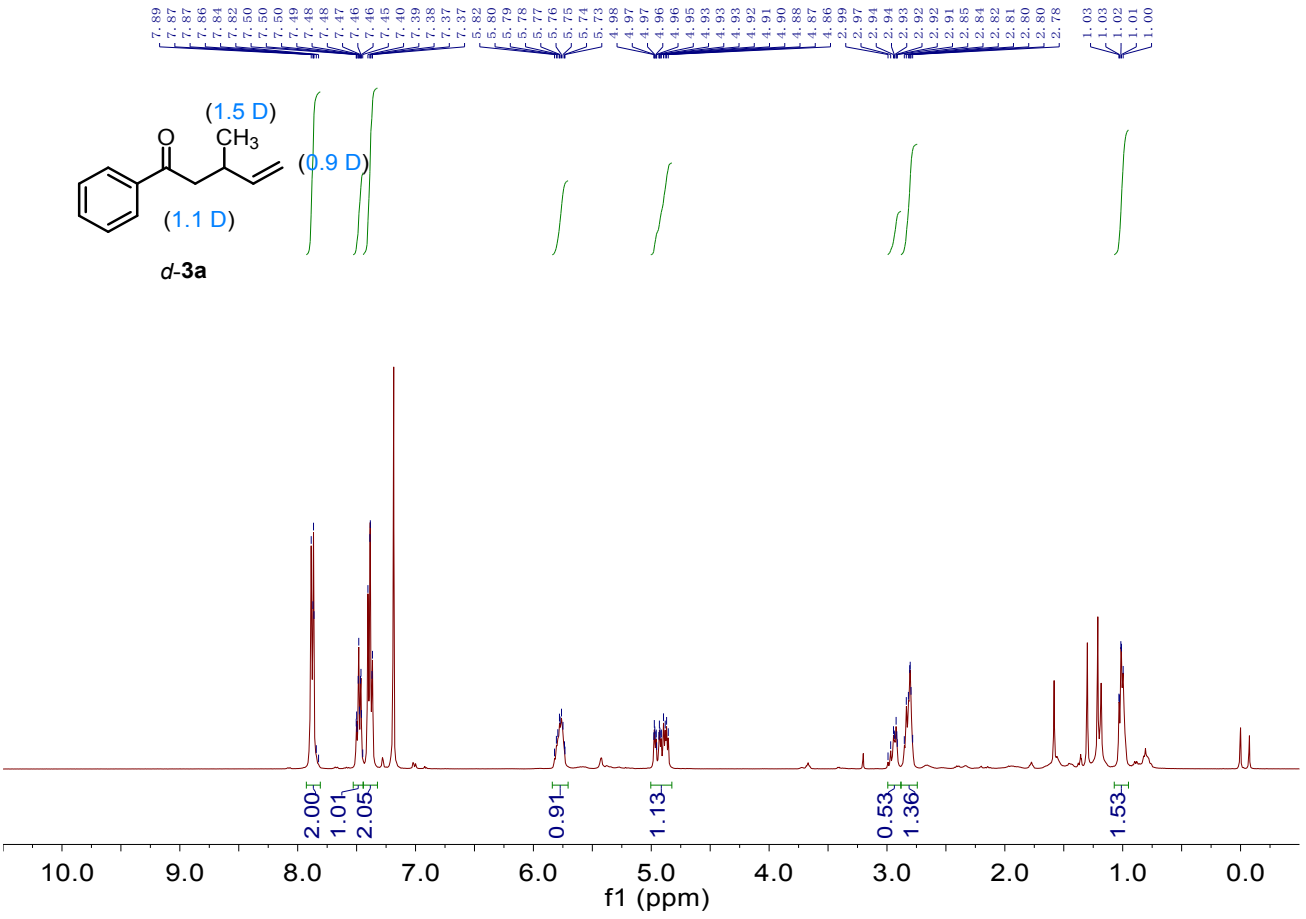


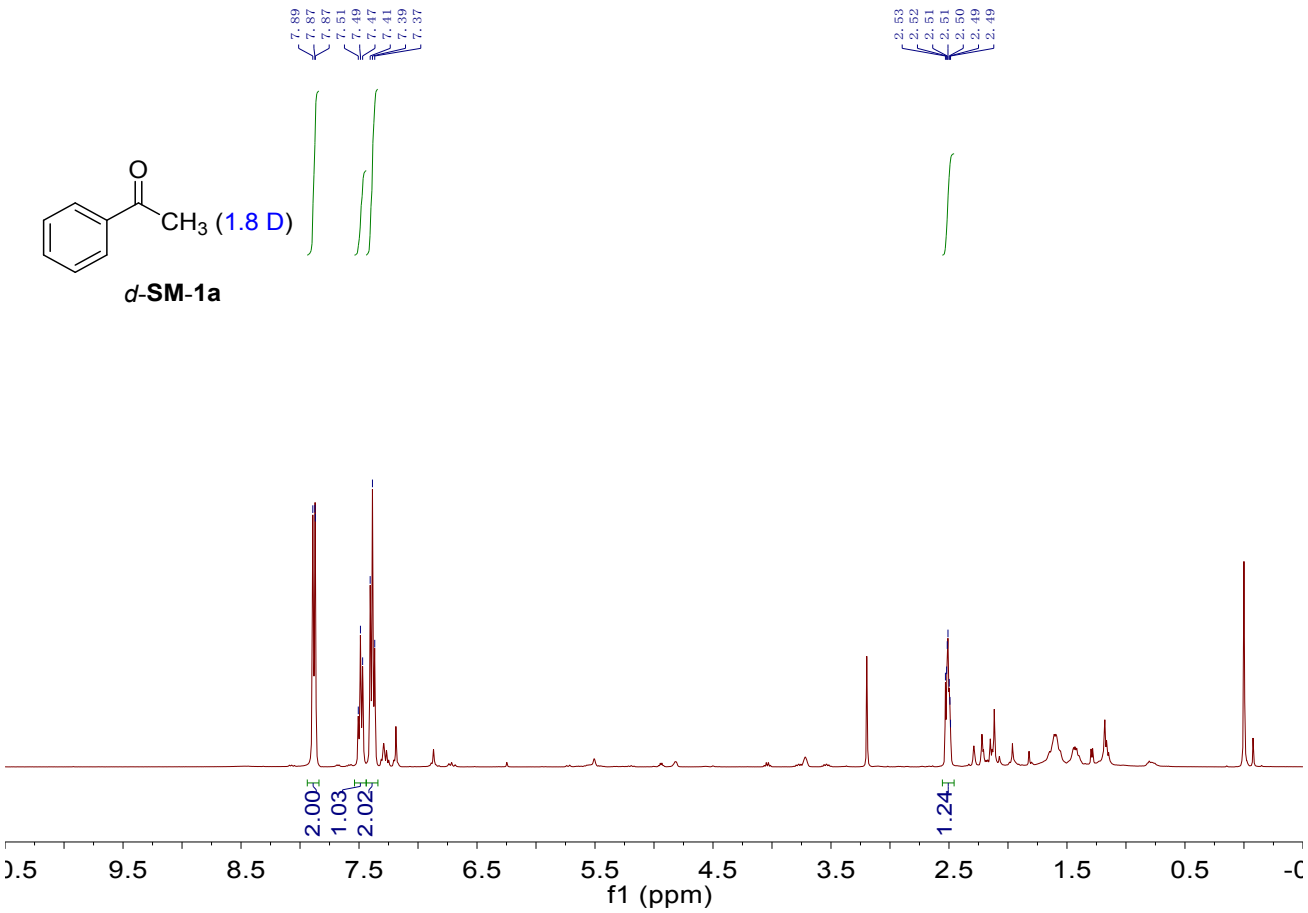
SD-P4

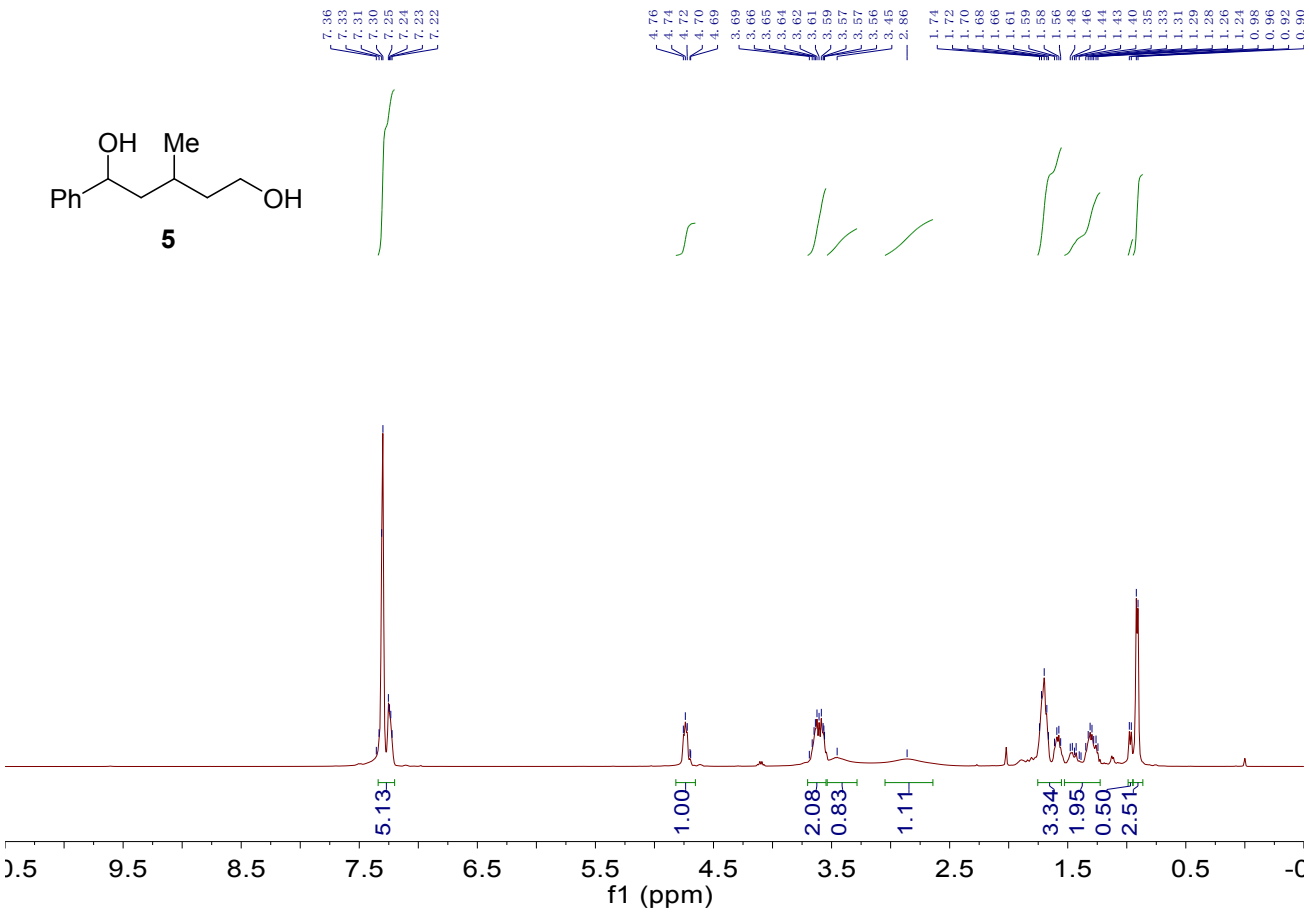
7.89
7.87
7.50
7.48
7.46
7.40
7.38
7.37
4.65
3.08
3.08
3.07
3.06
3.03
3.02
3.01
2.99
2.98
2.97
2.97
2.95
2.95
2.94
2.93
2.92
2.90
2.90
2.90
2.88
2.88
2.86
2.84
2.82
2.81
2.81
2.80
2.79
2.77
2.75
1.69
1.04
1.02
2.96
1.55
3.11
1.87
3.80
2.84
3.00
f1 (ppm)

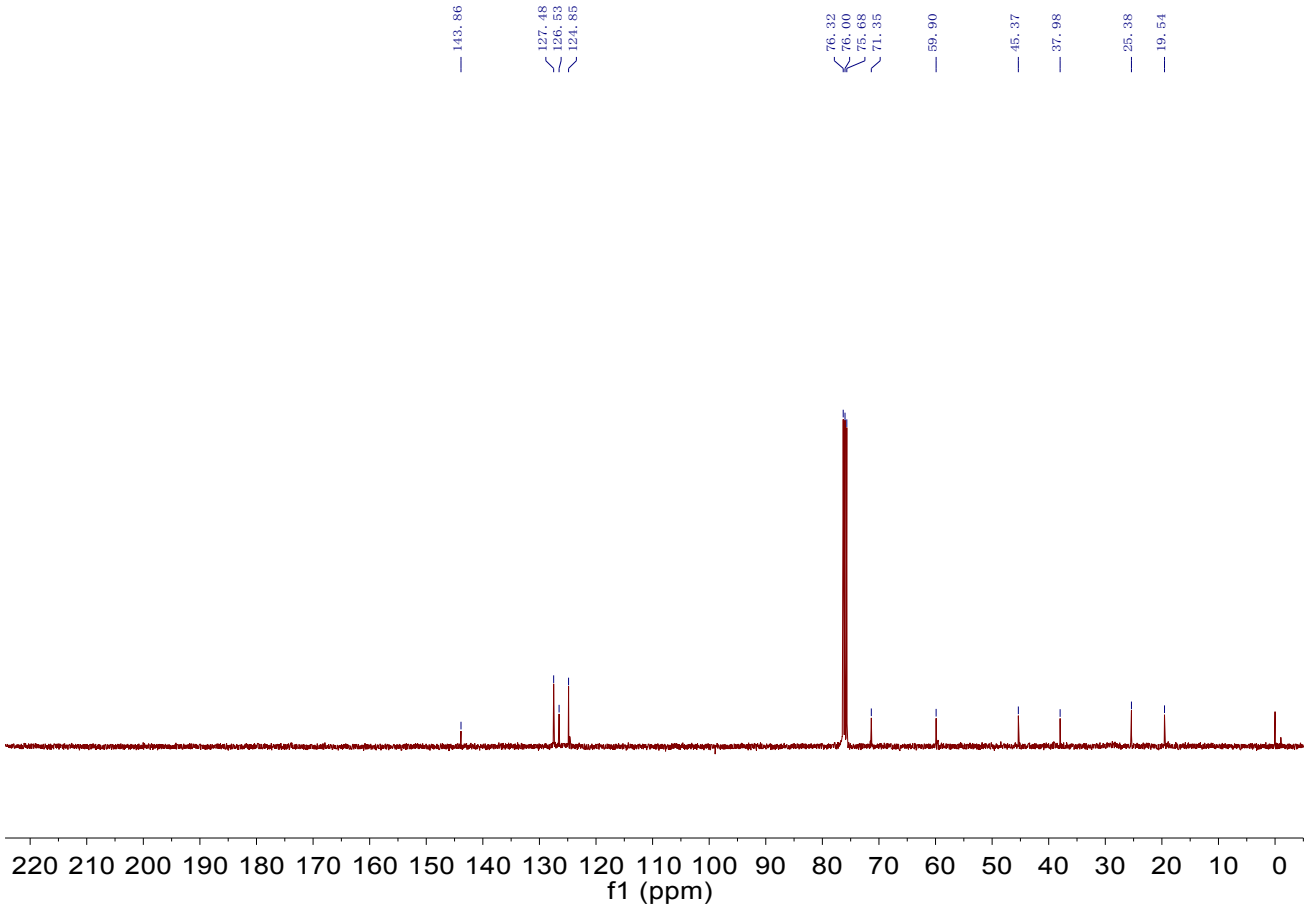

199.64
149.35
137.28
132.92
128.57
128.08
128.05
109.46
77.34
77.03
76.71
44.34
36.89
20.27
19.57
f1 (ppm)

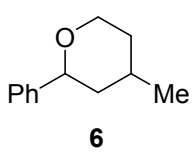

Ph
O
CH3 (1.4 D)
d-1a
2.00
1.72
1.90
1.58
f1 (ppm)


(1.5 D)
O
CH3
(0.9 D)
(1.1 D)
d-3a
2.00
1.01
2.05
0.91
1.13
0.53
1.36
1.53
f1 (ppm)


7.89
7.87
7.87
7.51
7.49
7.47
7.41
7.39
7.37
2.53
2.52
2.51
2.51
2.50
2.49
2.49
O
CH3 (1.8 D)
d-SM-1a
2.00
1.03
2.02
1.24
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

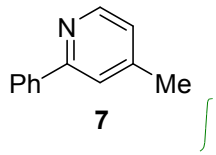

OH
Me
Ph
OH
5
7.36
7.33
7.31
7.30
7.25
7.24
7.23
7.22
4.76
4.74
4.72
4.70
4.69
3.69
3.66
3.65
3.64
3.62
3.61
3.59
3.57
3.57
3.56
3.45
2.86
1.74
1.72
1.70
1.68
1.66
1.61
1.59
1.58
1.56
1.48
1.46
1.44
1.43
1.40
1.35
1.33
1.31
1.29
1.28
1.26
1.24
0.98
0.96
0.92
0.90
5.13
1.00
2.08
0.83
1.11
3.34
1.95
0.50
2.51
f1 (ppm)


143.86
127.48
126.53
124.85
76.32
76.00
75.68
71.35
59.90
45.37
37.98
25.38
19.54
f1 (ppm)


O
Ph
Me

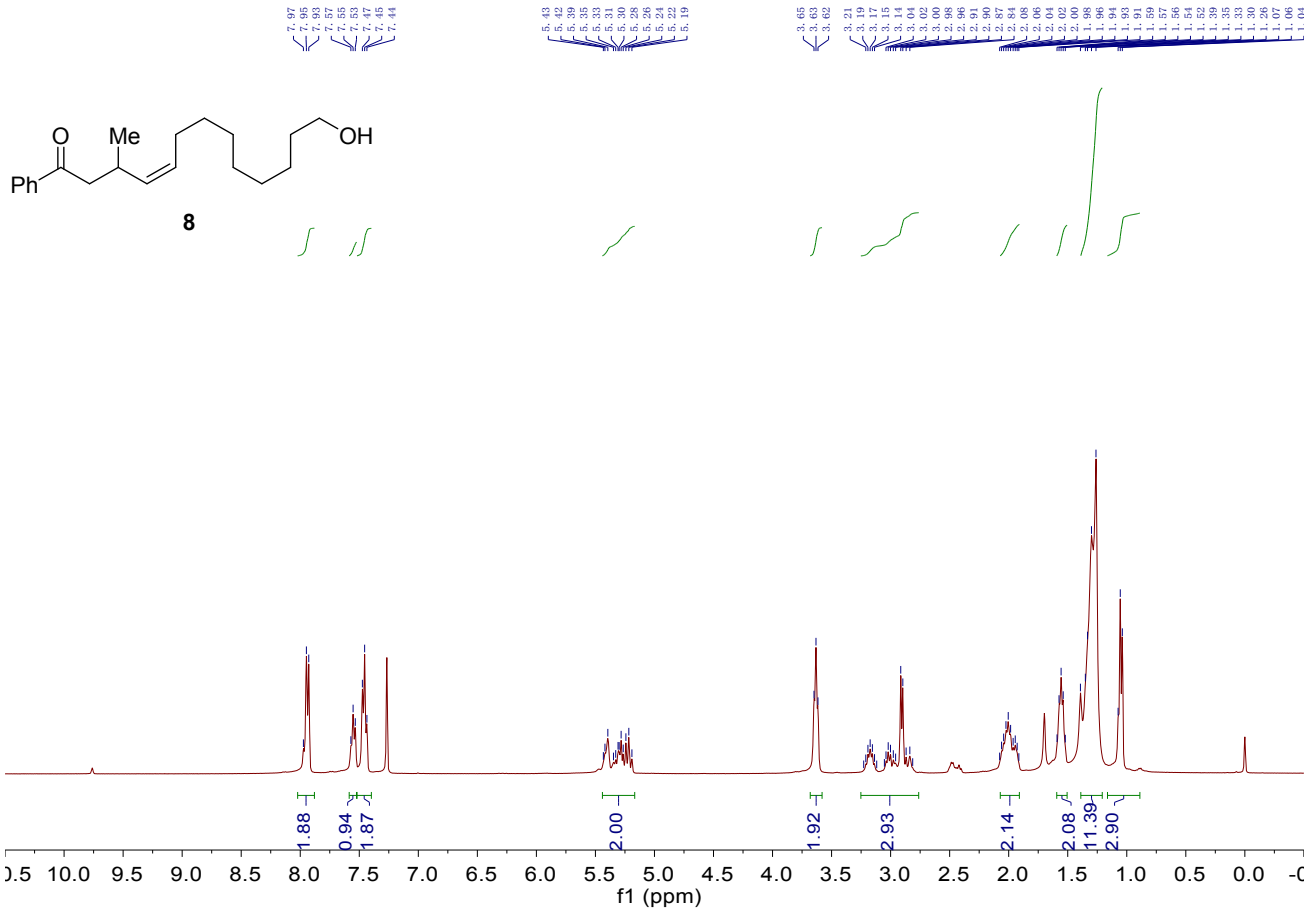
6

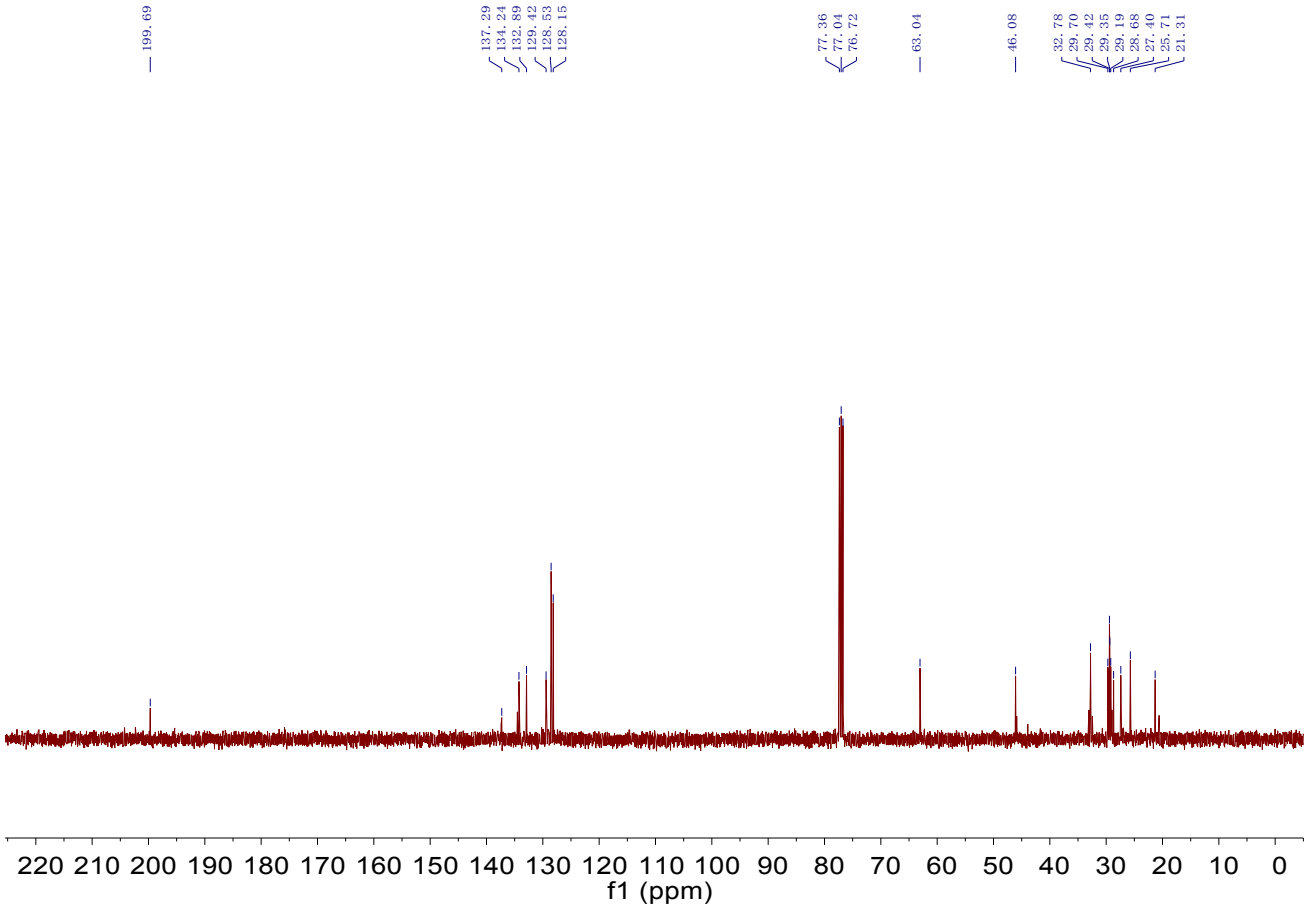
5.91
0.92
0.97
0.98
2.25
1.21
3.15
3.28
f1 (ppm)

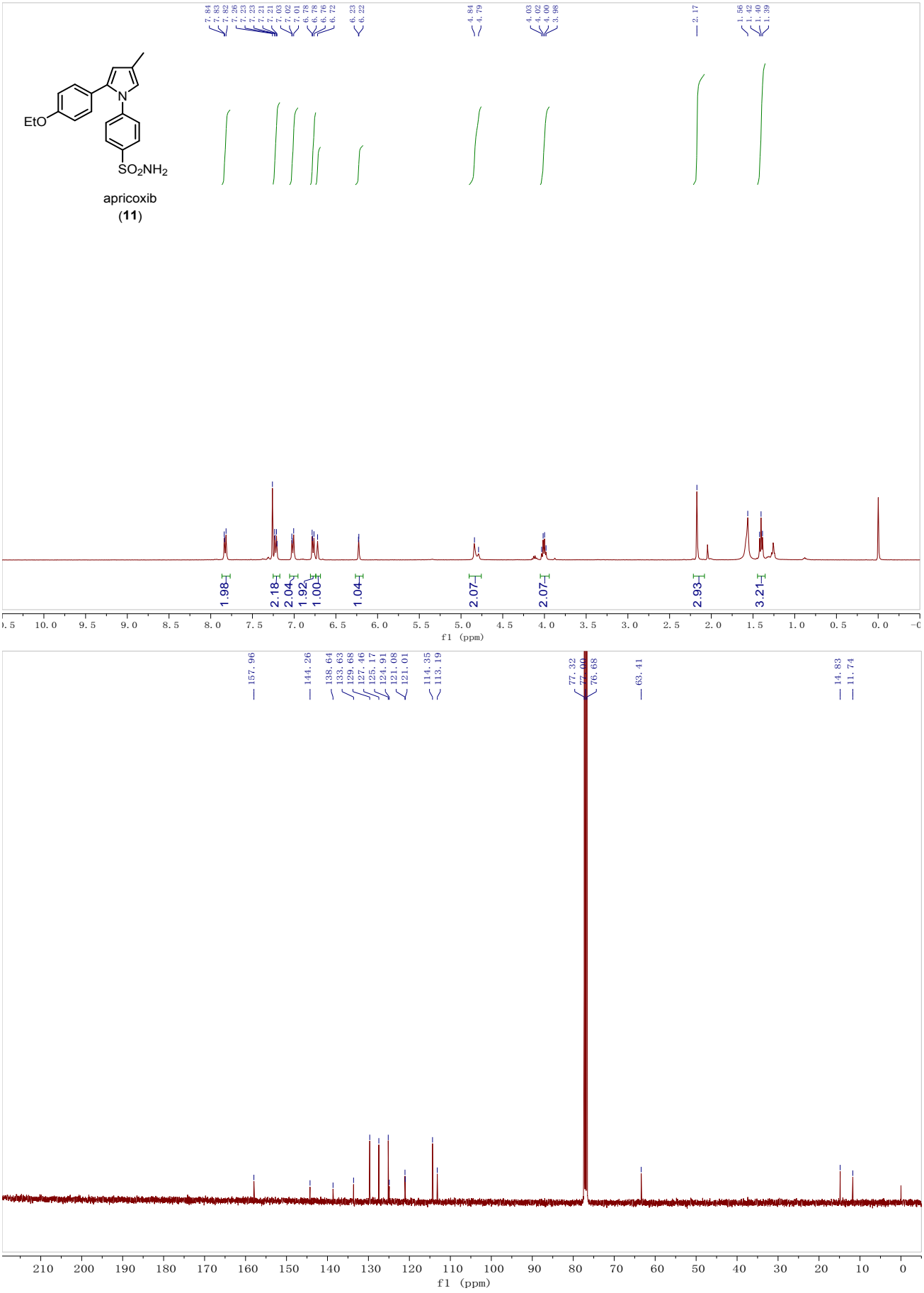

N
Ph
Me

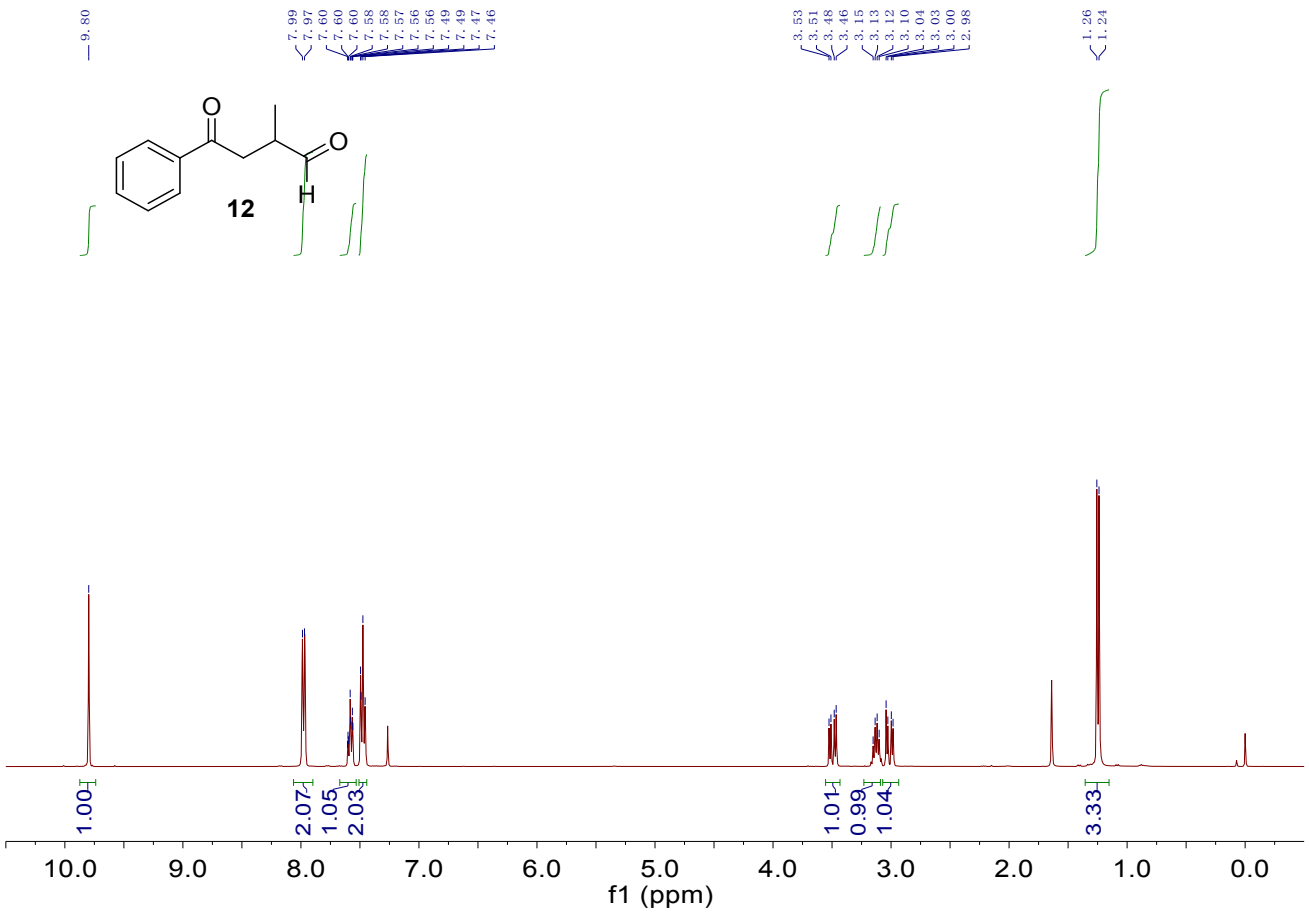
7

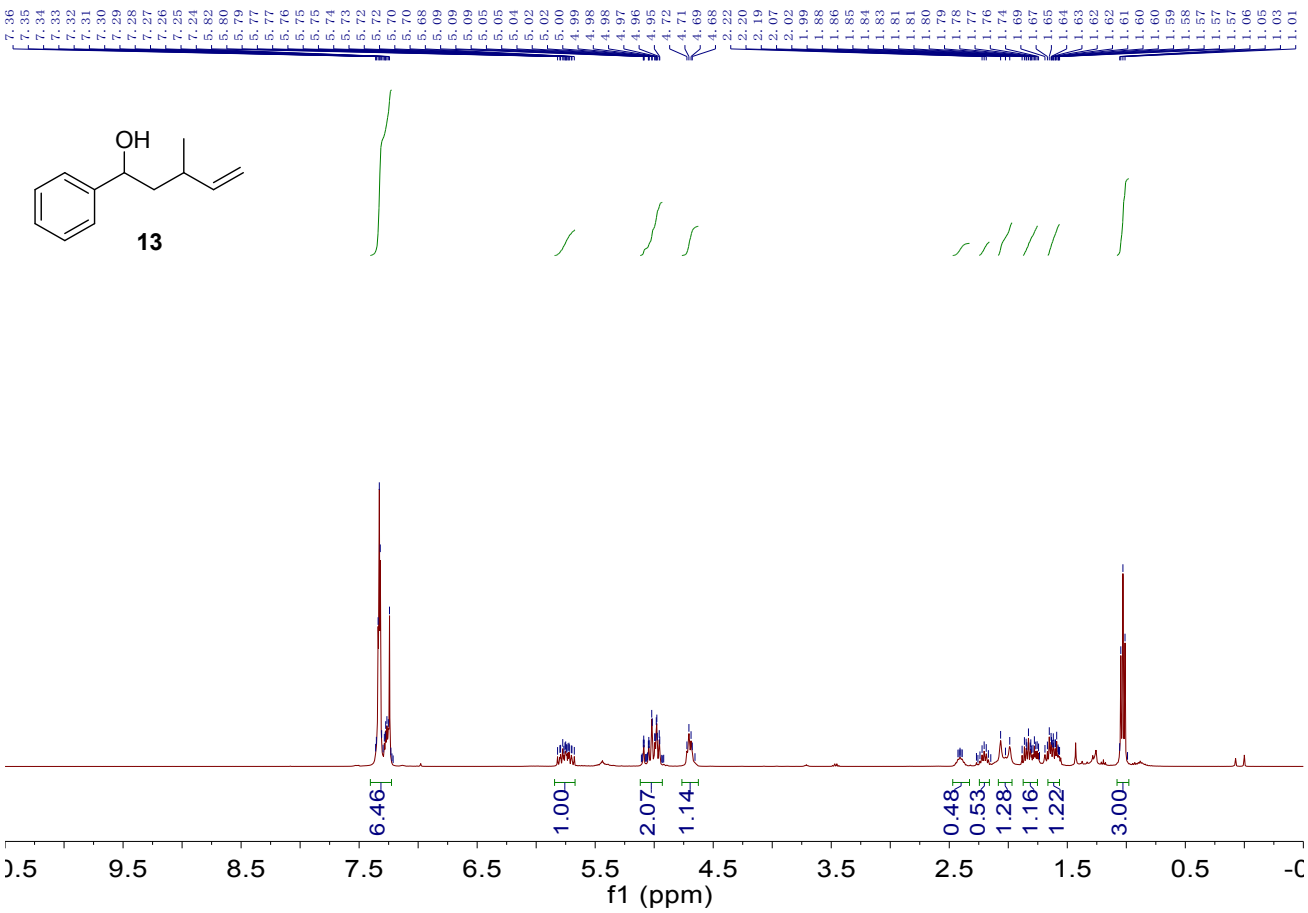
8.55
8.54
7.98
7.96
7.54
7.48
7.46
7.44
7.41
7.40
7.38
7.05
7.04
2.40
0.95
1.95
1.08
2.94
0.94
3.00
f1 (ppm)

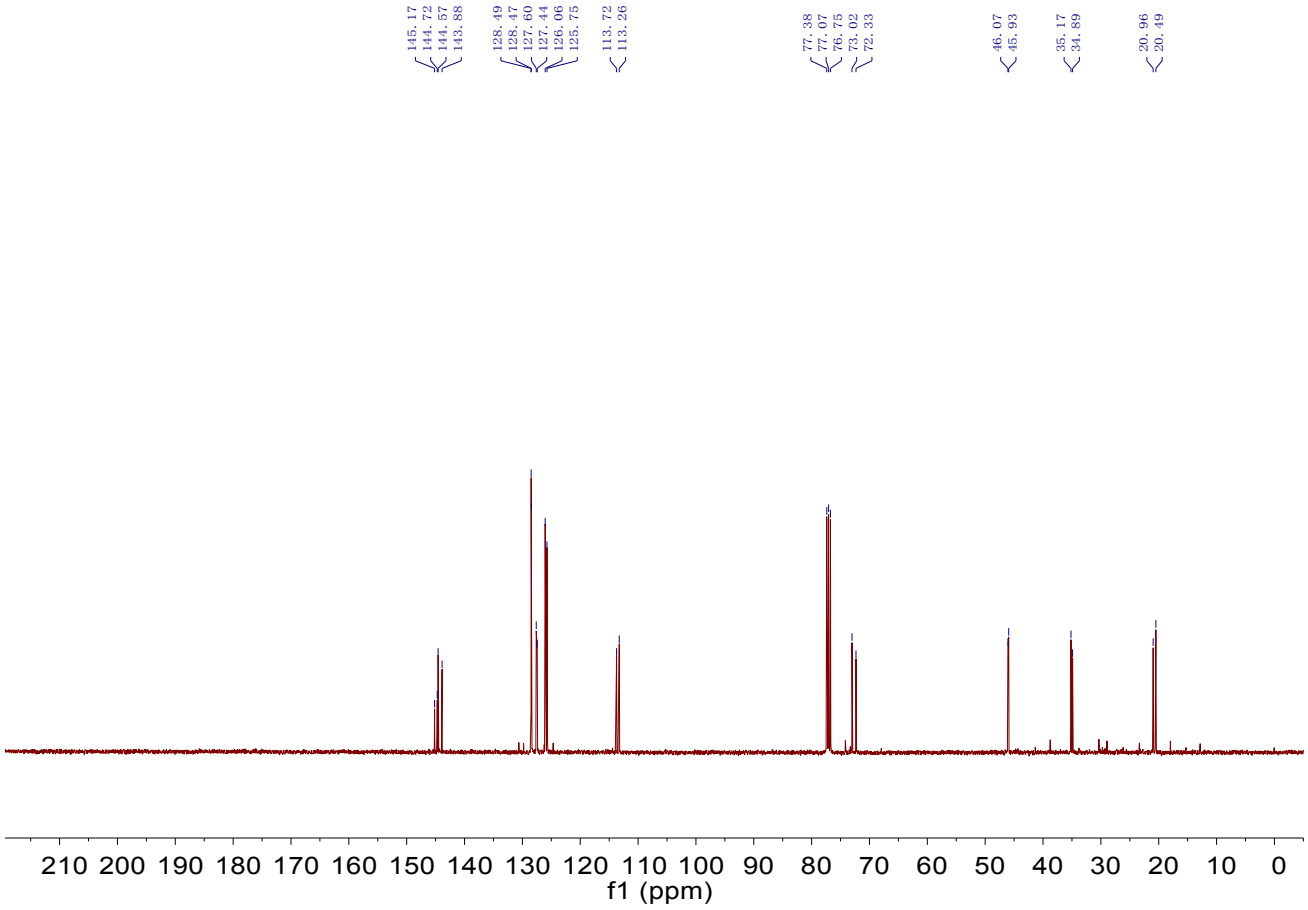

O
Me
OH
Ph
8
f1 (ppm)

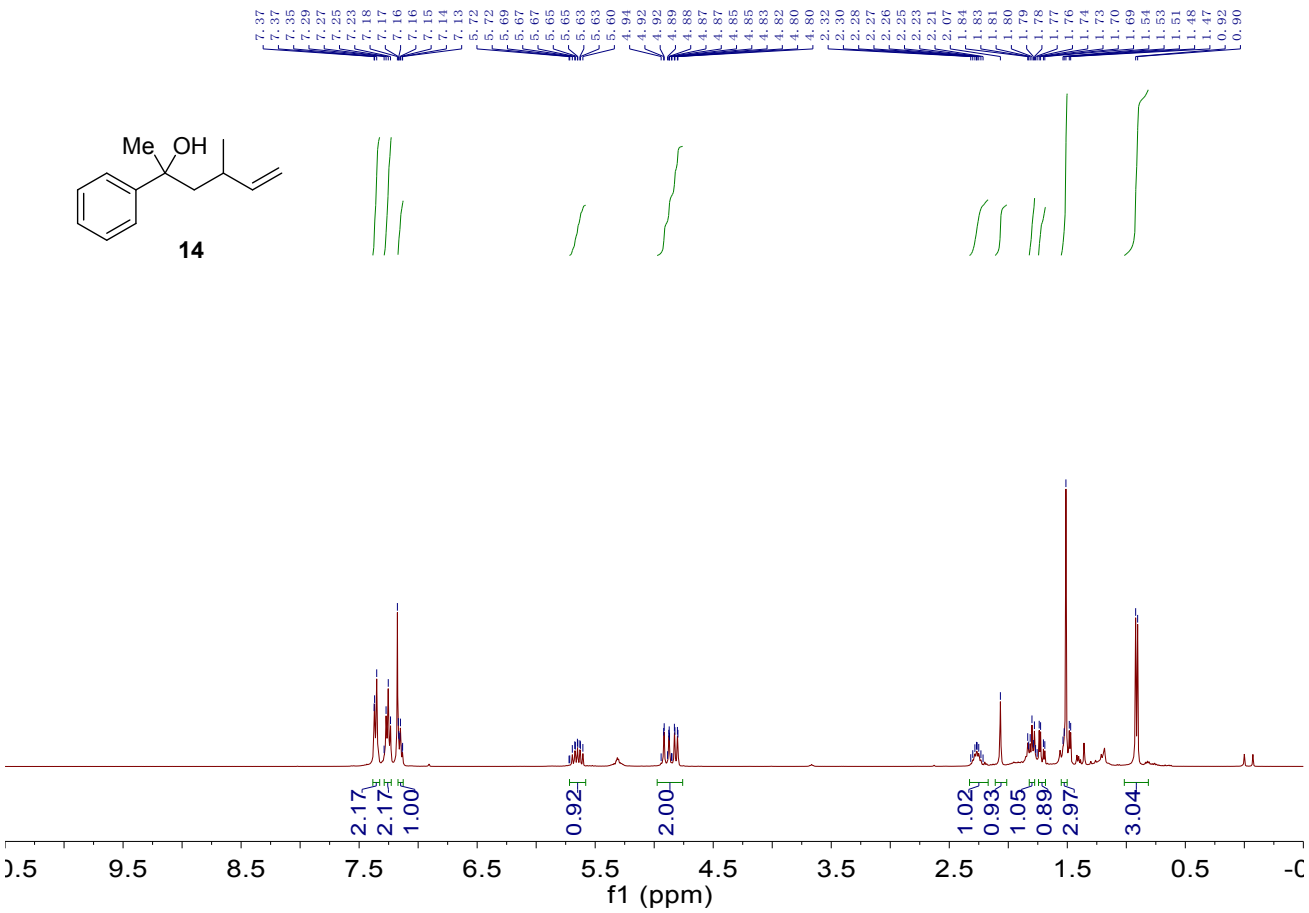

f1 (ppm)

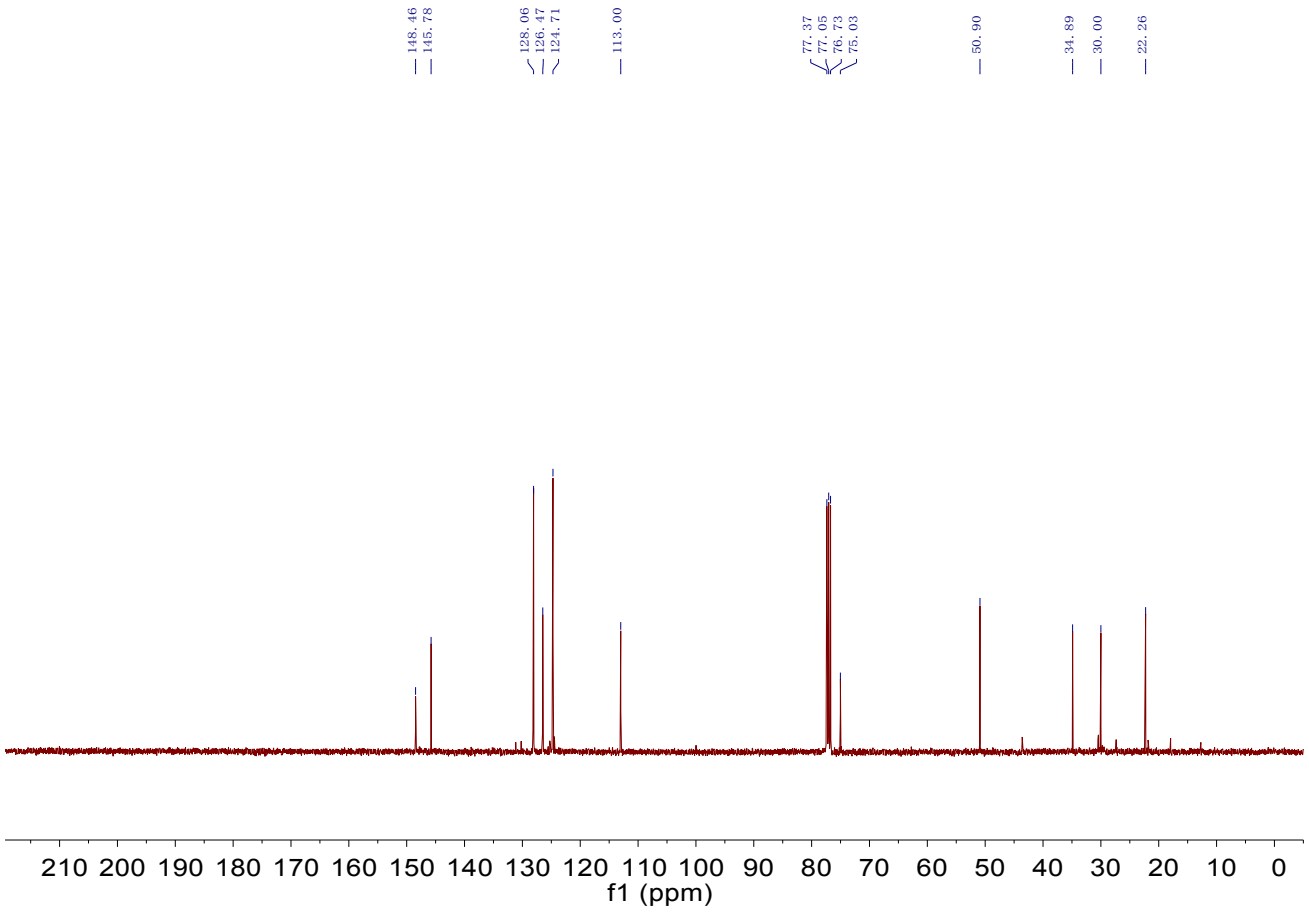

EtO
N
SO2NH2
apricoxib
(11)
f1 (ppm)
f1 (ppm)

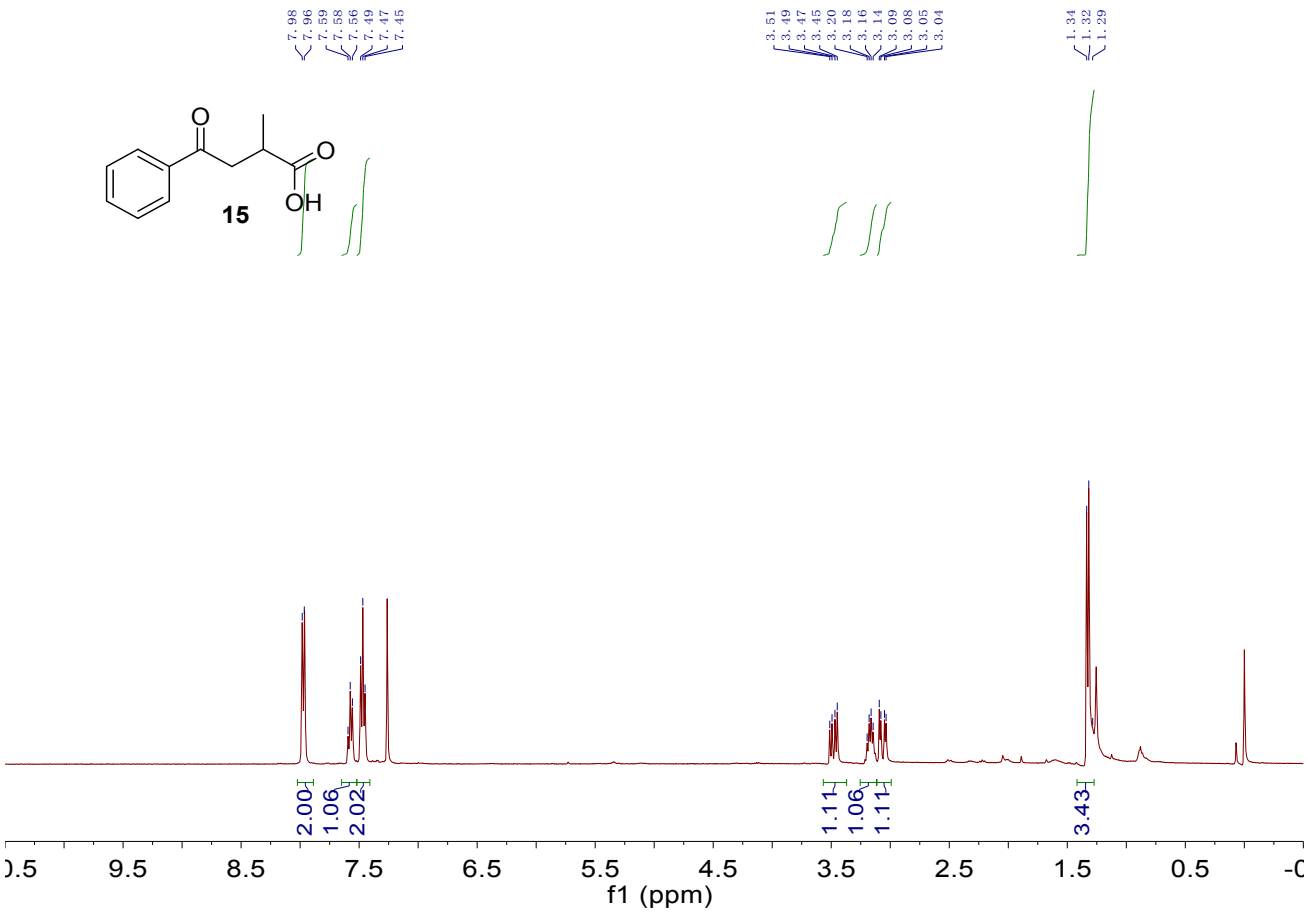

9.80
7.99
7.97
7.60
7.60
7.58
7.58
7.57
7.56
7.56
7.49
7.47
7.46
3.53
3.51
3.48
3.46
3.15
3.13
3.12
3.10
3.04
3.03
3.00
2.98
1.26
1.24
O
O
H
12
1.00
2.07
1.05
2.03
1.01
0.99
1.04
3.33
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

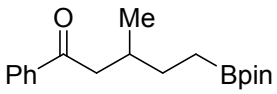

OH
13
6.46
1.00
2.07
1.14
0.48
0.53
1.28
1.16
1.22
3.00
f1 (ppm)


f1 (ppm)


Me
OH
14
f1 (ppm)

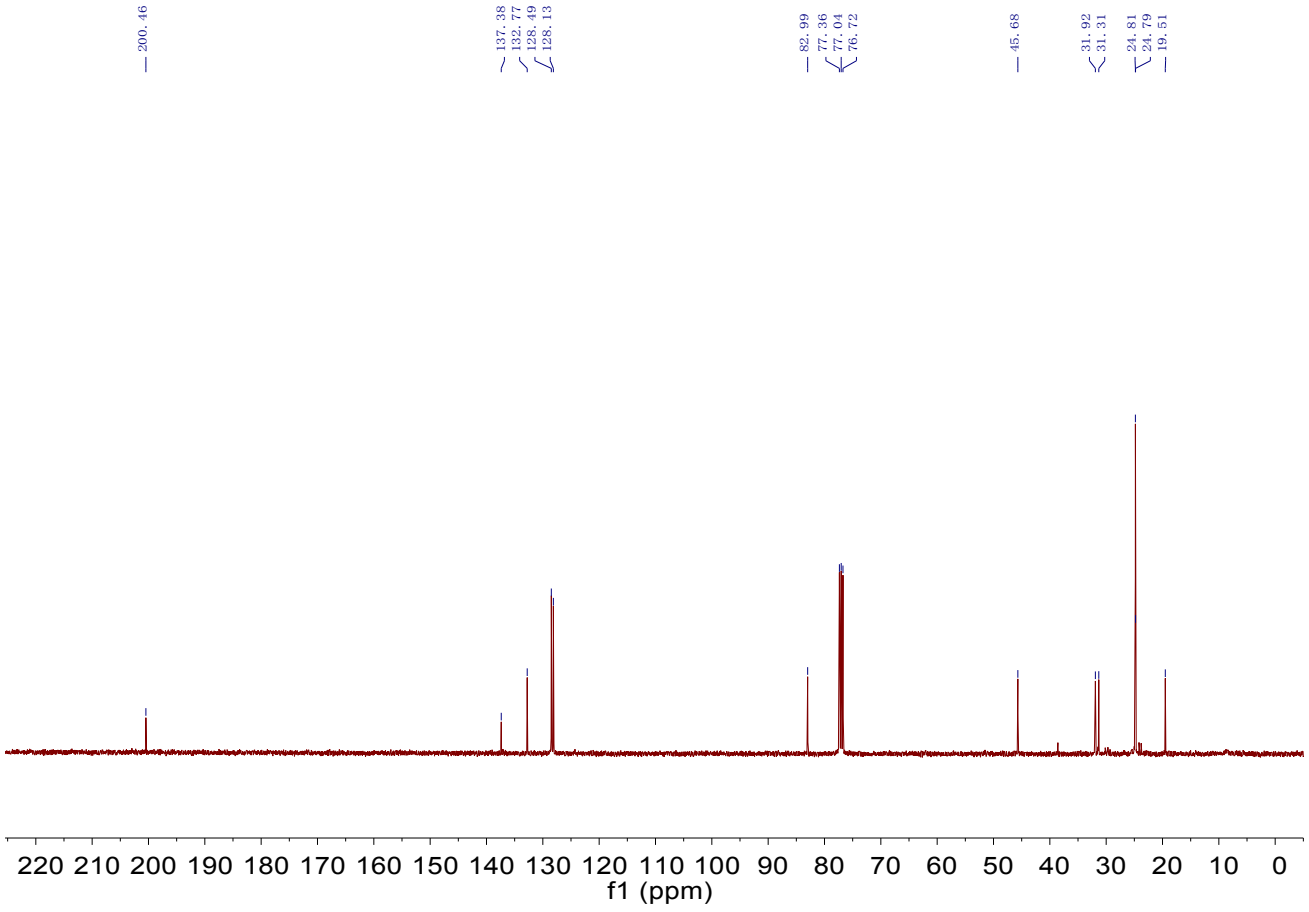

f1 (ppm)


7.98
7.96
7.59
7.58
7.56
7.49
7.47
7.45
3.51
3.49
3.47
3.45
3.20
3.18
3.16
3.14
3.09
3.08
3.05
3.04
1.34
1.32
1.29
O
O
OH
15
2.00
1.06
2.02
1.11
1.06
1.11
3.43
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

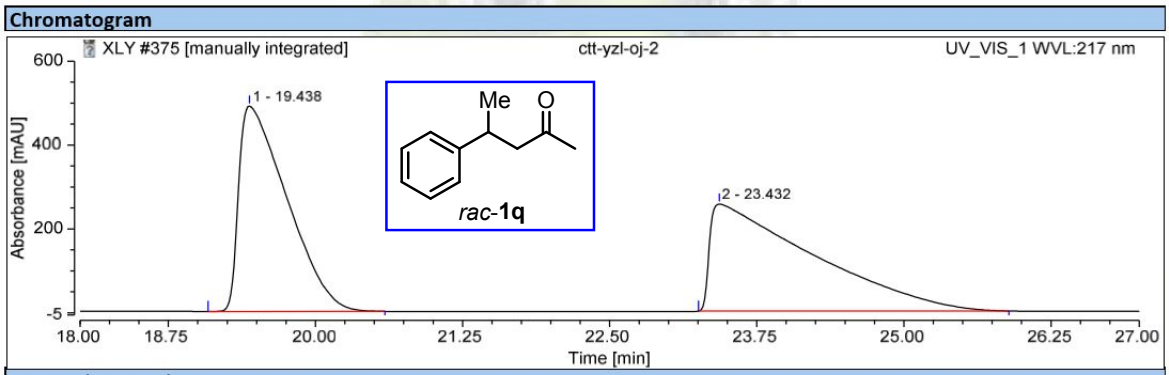

O
Me
Ph
Bpin

16

7.95
7.94
7.56
7.54
7.52
7.47
7.45
7.43
3.03
3.02
2.99
2.98
2.96
2.94
2.72
2.70
2.68
2.66
2.12
2.11
2.09
2.07
2.05
1.42
1.40
1.37
1.34
1.24
0.95
0.93
0.86
0.84
0.82
0.79
0.77
1.88
1.00
1.91
1.06
0.92
0.97
1.97
12.26
2.82
2.04
f1 (ppm)


200.46
137.38
132.77
128.49
128.13
82.99
77.36
77.04
76.72
45.68
31.92
31.31
24.81
24.79
19.51
f1 (ppm)

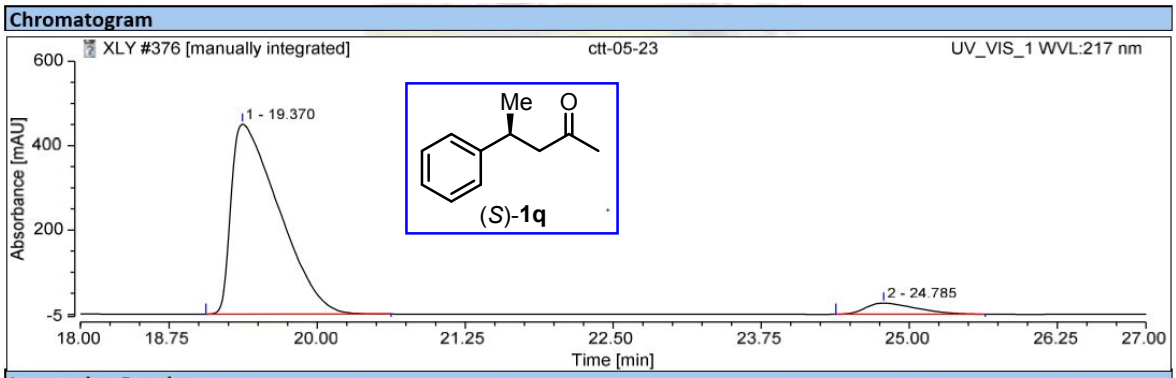
HPLC spectra of racemic **1q**:



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		19.438	231.866	489.382	47.34	65.74	n.a.
2		23.432	257.907	255.065	52.66	34.26	n.a.
Total:			**489.774**	**744.447**	**100.00**	**100.00**	

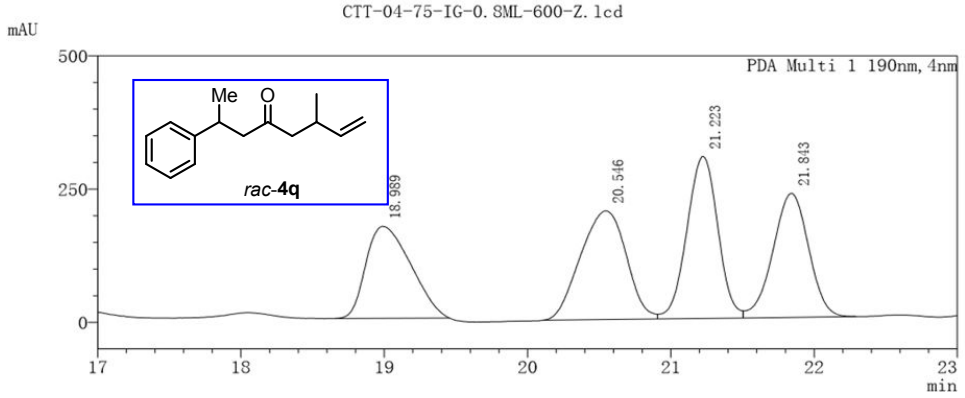
HPLC spectra of (*S*)-**1q**:



Integration Results

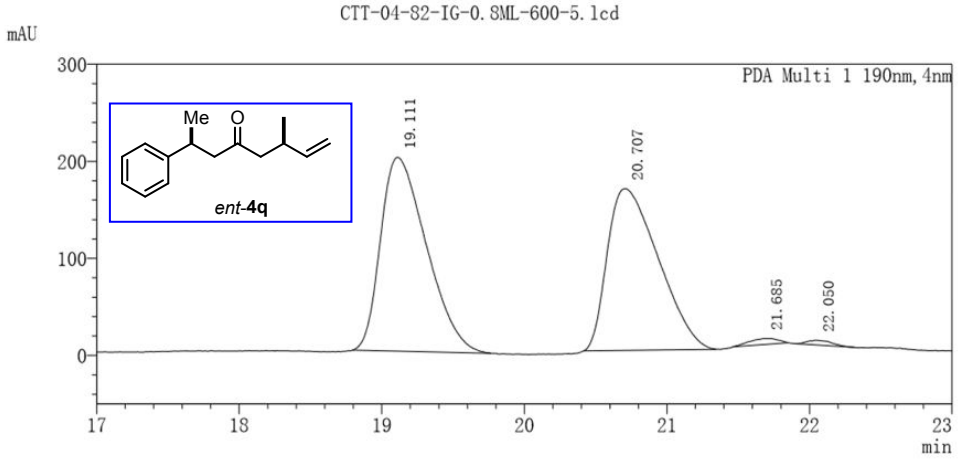
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		19.370	210.560	449.788	94.14	94.44	n.a.
2		24.785	13.110	26.487	5.86	5.56	n.a.
Total:			**223.670**	**476.275**	**100.00**	**100.00**	

HPLC spectra of racemic **4q**:



PDA Ch1 190 nm				
peak No.	time	peak area	peak height	area%
1	18.989	3745873	172822	22.177
2	20.546	4535376	204070	26.852
3	21.223	4570990	304320	27.062
4	21.843	4038338	232983	24.909
sum		16890577	914195	100

HPLC spectra of chiral *ent*-**4q**:



PDA Ch1 190 nm				
peak No.	time	peak area	peak height	area%
1	19.111	4465366	199716	50.993
2	20.707	4145710	166600	47.343
3	21.685	85889	6150	0.981
4	22.05	59821	4974	0.683
sum		8756787	377441	100