**Supporting Information for**

# Highly Efficient Synthesis of Chiral Aromatic Ketones *via* Rh-Catalyzed Asymmetric Hydrogenation of $\beta,\beta$-disubstituted enones

**Tao Zhang,[a,†] Jun Jiang,[b,†] Lin Yao,[c] Huiling Geng,[a,*] Xumu Zhang[d,*]**

[a] *School of Chemistry & Pharmacy, Northwest A&F University, Yangling, Shaanxi 712100, China. E-mail: genghuiling@nwsuaf.edu.cn*

[b] *College of Chemistry and Molecular Sciences, Wuhan University, Wuhan, Hubei 430072, China*

[c] *School of Chemistry & Pharmacy, The Fourth Military Medical University, Xi'an, Shaanxi 710032, China*

[d] *Department of chemistry, South University of Science and Technology, Shenzhen, Guangzhou 518055, China. E-mail: zhangxm@sustc.edu.cn*

## Contents

1. General Information.....S2

2. General procedure for the synthesis of substrates. .....S2

2.1 Procedure for the synthesis of $\beta$-substituted $\alpha,\beta$-unsaturated esters **1**. .....S2

2.2 Procedure for the synthesis of intermediates **2**. .....S3

2.3 Procedure for the synthesis of substrates **3**. .....S3

3. NMR and ESI-MS Data of compounds **3** .....S3

4. General procedure for the asymmetric hydrogenation of **3**. .....S7

5. NMR, optical rotation and ESI-MS Data of product **4** .....S7

6. Reference…….S20

7. NMR spectra of compounds **3** and **4** .....S20

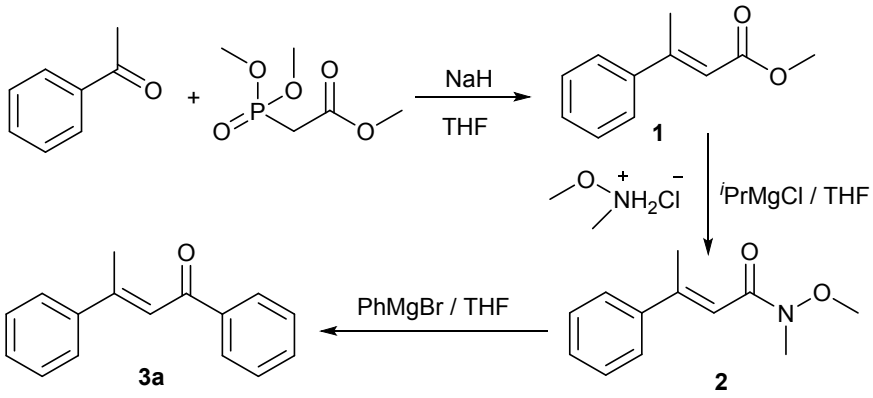
# 1. General Information.

All reactions dealing with air or moisture sensitive compounds were carried out in a dry reaction vessel under nitrogen protection or in the nitrogen-filled glove box. Unless otherwise noted, all reagents and solvents were purchased from commercial suppliers without further purification. THF was dried with sodium chips and indicated by benzophenone. Anhydrous solvents were purchased from Sigma-Aldrich and transferred by syringe. All products were puried by chromatography using silica gel from SORBTECH (40-63 $\mu$m). Thin layer chromatography was carried out using silica gel plates from Merk ($GF_{254}$). $[Rh(NBD)Cl]_2$ and other metal precursors were purchased from Heraeus.

$^1H$ NMR and $^{13}C$ NMR spectra were recorded on a Bruker Avance (400 MHz) spectrometer with $CDCl_3$ as the solvent and tetramethylsilane (TMS) as the internal standard. Chemical shifts were reported upfield to TMS (0.00 ppm) for $^1H$ NMR and relative to $CDCl_3$ (77.0 ppm) for $^{13}C$ NMR. All data was presented as: multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant in hertz (Hz) and signal area integration in natural numbers. $^{13}C$ NMR analyses were run with decoupling. Enantiomeric excess values were determined with Agilent 1100 Series HPLC instrument. Optical rotations were measured using a 1 mL cell with a1 dm path length on a Jasco P-2000 polarimeter at 589 nm.

# 2. General procedure for the synthesis of substrates.

All substrates **3a-3q** were prepared through Horner-Wadsworth-Emmons reaction using aromatic ketones as starting material according to the reported procedure.[1]




## 2.1 Procedure for the synthesis of $\beta,\beta$-disubstituted-$\alpha$, $\beta$-unsaturated esters 1.

To a suspension of sodium hydride (60% dispersion in mineral oil, 40 mmol) in dry THF (100 mL), trimethyl phosphonoacetate (24 mmol) was added dropwise at 0 ºC under argon atmosphere. After 30 min, appropriate ketones (20 mmol) was added dropwise to the reaction system at the same temperature. The reaction mixture was then warmed to reflux and vigorously stirred for 8 h. After the mixture was cooled to room temperature in an ice bath, saturated aqueous solution of ammonium chloride (20 mL) was added dropwise to quench the reaction. The aqueous phase was extracted with diethyl ether (2 × 50 mL) and the combined organic phase was washed with brine (50 mL), dried over sodium sulfate. After removing the solvent by rotary evaporation, the product mixture was achieved and purified as a colorless oil by column-chromatography using the mixture of hexane and ethyl acetate as the eluent ($V_{hexane}$: $V_{EtOAc}$= 95:5).

### 2.2 Procedure for the synthesis of intermediates 2.

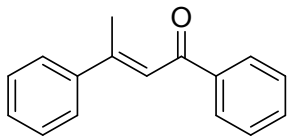
To a solution of the (*E*)-ester **1** (15 mmol) and *N*,*O*-dimethylhydroxyamine hydrochloride (2.93 g, 30 mmol) in THF (30 mL), a THF solution of *i*-PrMgCl (32.5 mL, 2M in THF) was slowly added at –5 °C. The resulting mixture was then stirred for 30 min and treated with saturated aqueous solution of $NH_4Cl$ (20 mL). The mixture solution was extracted with ethyl acetate (3 × 30 mL), washed with brine (30 mL) and dried over $Na_2SO_4$. After concentration of the combined organic phase, the residue was purified by silica-gel column chromatography ($V_{hexane}$:$V_{EtOAc}$ = 10:1~2:1) to obtain the *N*-methoxy amide.

### 2.3 Procedure for the synthesis of substrates 3.

At the temperature of –5～0 °C, a THF solution (20 mL) of PhMgBr (15 mmol) was slowly added to the solution of *N*-methoxy amide (2.05 g, 10 mmol) in THF (20 mL) in 30min. The resulting solution was stirred at –5 °C for 30 min and treated with saturated aqueous solution of $NH_4Cl$ (20 mL). The mixture was extracted with ethyl acetate (3 × 30 mL), washed with brine (30 mL) and dried over $Na_2SO_4$. After concentration of the organic phase, the residue was purified by silica-gel column chromatography ($V_{hexane}$: $V_{EtOAc}$ = 50:1 as eluent) to afford (*E*)-enones.

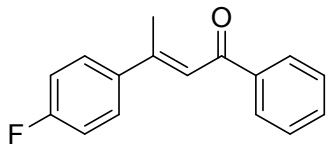
## 3. NMR and ESI-MS Data of compounds 3.

(*E*)-1, 3-diphenylbut-2-en-1-one **3a**



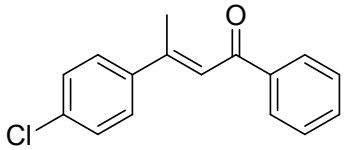

Light yellow oil; 51% yield; $^1$H NMR (400 MHz, $CDCl_3$): δ 8.05-7.95 (m, 2H), 7.65-7.55 (m, 3H), 7.55-7.40 (m, 5H) 7.18 (s, 1H), 2.61 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 191.85, 155.05, 142.83, 139.42, 132.54, 129.13, 128.63, 128.56, 128.30, 126.51, 122.15, 18.90; ESI–MS: calculated for $C_{16}H_{15}O^+$ ($[M+H]^+$) 223.11, found 223.33.

(*E*)-3-(4-fluorophenyl)-1-phenylbut-2-en-1-one **3b**




Light yellow oil; 55 % yield; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.15-7.95 (m, 2H), 7.75-7.45 (m, 6H), 7.15-7.08 (m, 2H), 2.60 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 191.65, 164.57, 162.09, 153.67, 139.32, 138.76 (d, *J* = 3.3 Hz), 132.60, 128.43 (d, *J* = 31.6 Hz), 128.33 (d, *J* = 8.3 Hz), 121.99 (d, *J* = 1.0 Hz), 115.56 (d, *J* = 21.6 Hz), 18.86; ESI–MS: calculated for $C_{16}H_{14}FO^+$ ($[M+H]^+$) 241.10, found 241.22.

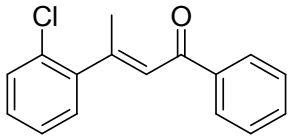
(*E*)-3-(4-chlorophenyl)-1-phenylbut-2-en-1-one **3c**




Light yellow oil; 40 % yield; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.95-7.83(m, 2H), 7.50-7.32 (m, 5H), 7.28-7.22 (m, 2H), 7.02 (s, 1H), 2.44 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 191.64, 153.35,

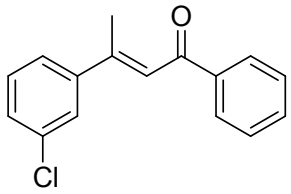
141.10, 139.21, 135.11, 132.67, 128.81, 128.61, 128.29, 127.81, 122.39, 18.71; ESI–MS: calculated for $C_{16}H_{14}ClO^+$ ([M+H]$^+$) 257.07 and 259.07, found 257.09 and 259.06.

(*E*)-3-(2-chlorophenyl)-1-phenylbut-2-en-1-one **3d**



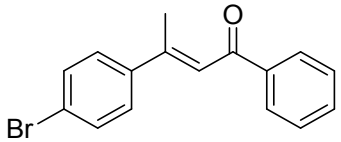

Light yellow oil; 45 % yield; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.03-8.01 (m, 2H), 7.60-7.45 (m, 6H), 7.32-7.29 (m, 1H), 6.89 (s, 1H), 2.52 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 191.71, 154.17, 143.08, 138.86, 132.74, 131.46, 129.99, 129.08, 128.59, 128.42, 128.34, 126.88, 125.36, 20.91; ESI–MS: calculated for $C_{16}H_{14}ClO^+$ ([M+H]$^+$) 257.07 and 259.07, found 257.22 and 259.15.

(*E*)-3-(3-chlorophenyl)-1-phenylbut-2-en-1-one **3e**



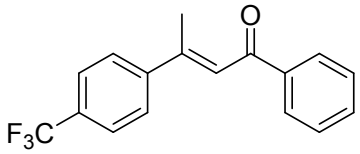

Light yellow oil; 55 % yield; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.00-7.97 (m, 2H), 7.56-7.42 (m, 5H), 7.37-7.34 (m, 2H), 7.13 (s, 1H), 2.55 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 191.70, 153.06, 144.62, 139.07, 134.64, 132.75, 129.88, 129.01, 128.62, 128.32, 126.64, 124.65, 123.00, 18.76. ESI–MS: calculated for $C_{16}H_{14}ClO^+$ ([M+H]$^+$) 257.07 and 259.07, found 257.11 and 259.07.

(*E*)-3-(4-bromophenyl)-1-phenylbut-2-en-1-one **3f**



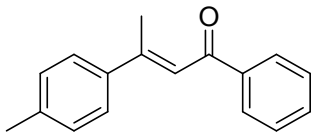

Light yellow oil; 35 % yield; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.95-7.85 (m, 2H), 7.48-7.42 (m, 3H), 7.40-7.30 (m, 4H), 7.03 (s, 1H), 2.45 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 191.67, 153.38, 141.60, 139.19, 132.68, 131.78, 128.61, 128.29, 128.08, 123.35, 122.45, 18.68; ESI–MS: calculated for $C_{16}H_{14}BrO^+$ ([M+H]$^+$) 301.02 and 303.02, found 301.16 and 303.12.

(*E*)-1-phenyl-3-(4-(trifluoromethyl)phenyl)but-2-en-1-one **3g**



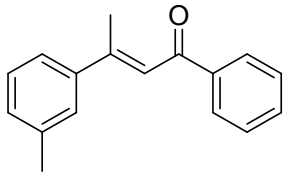

Light yellow oil; 51 % yield; 1H NMR (400 MHz, CDCl3) δ 7.95-7.78 (m, 2H), 7.60-7.50 (m, 3H) 7.48-7.25 (m, 4H), 7.05 (s, 1H), 2.47 (s, 3H); 13C NMR (100 MHz, CDCl3) δ 191.65, 152.85, 146.33, 138.94, 132.84, 130.87 (q, *J* = 32.7 Hz), 128.65, 128.65, 128.33, 126.83, 125.58 (q, *J* = 3.7 Hz), 123.74, 18.76; ESI–MS: calculated for C17H14F3O+ ([M+H]+) 291.10, found 291.08.

(*E*)-1-phenyl-3-(*p*-tolyl)but-2-en-1-one **3h**



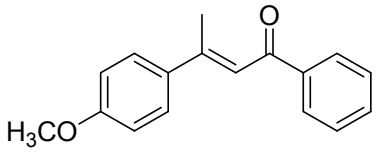
Light yellow oil; 54 % yield; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.05-7.95 (m, 2H), 7.60-7.44 (m, 5H), 7.27-7.20 (m, 2H), 7.16 (s, 1H), 2.59 (s, 3H), 2.39 (s, 3H). $^{13}$C NMR(100 MHz, $CDCl_3$) δ 191.85, 155.12, 139.85, 139.58, 139.36, 132.42, 129.32, 128.52, 128.25, 126.43, 121.32, 21.23, 18.78; ESI–MS: calculated for $C_{17}H_{17}O^+$ ([M+H]$^+$) 237.13, found 237.17.

(*E*)-1-phenyl-3-(*m*-tolyl)but-2-en-1-one **3i**



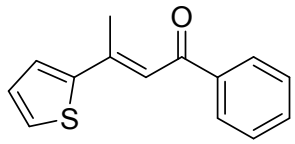

Light yellow oil; 43 % yield; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.89-7.88 (m, 2H), 7.44-7.33 (m, 4H), 7.26-7.17 (m, 3H), 7.05 (s, 1H), 2.48 (s, 3H), 2.29 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 191.85, 155.36, 142.88, 139.51, 138.25, 132.50, 129.93, 128.56, 128.30, 127.21, 123.68, 121.96, 21.53, 18.97; ESI–MS: calculated for $C_{17}H_{17}O^+$ ([M+H]$^+$) 237.13, found 237.29.

(*E*)-3-(4-methoxyphenyl)-1-phenylbut-2-en-1-one **3j**



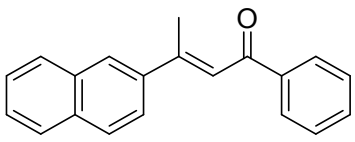

Light yellow oil; 41 % yield; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.00-7.97 (m, 2H), 7.57-7.54 (m, 2H), 7.48-7.45 (m, 2H), 7.16 (s, 1H), 6.95-6.93 (m, 2H), 3.85 (s, 3H), 2.60 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 191.76, 160.66, 154.79, 139.75, 134.92, 132.34, 128.50, 128.21, 127.92, 120.39, 114.00, 55.39, 18.65; ESI–MS: calculated for $C_{17}H_{17}O_2^+$ ([M+H]$^+$) 253.12, found 253.19.

(*E*)-1-phenyl-3-(thiophen-2-yl)but-2-en-1-one **3k**



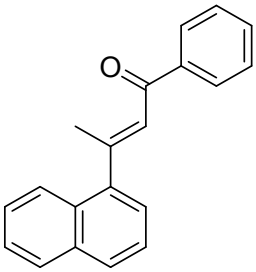

Light yellow oil; 47 % yield; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.00-7.97 (m, 2H), 7.57-7.44 (m, 4H), 7.39-7.34 (m, 2H), 7.12-7.10 (m, 1H), 2.67 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 191.24, 147.66, 146.30, 139.60, 132.46, 128.55, 128.20, 128.14, 127.30, 119.05, 18.29; ESI–MS: calculated for $C_{14}H_{13}OS^+$ ([M+H]$^+$) 229.06, found 229.27.

(*E*)-3-(naphthalen-2-yl)-1-phenylbut-2-en-1-one **3l**



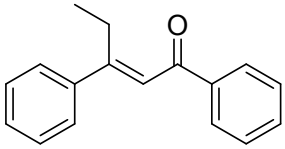

Light yellow oil; 57 % yield; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.04-8.02 (m, 2H), 7.91-7.85 (m, 3H), 7.72-7.69 (m, 1H), 7.55-7.50 (m, 5H), 7.25 (s, 1H), 2.71 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 191.89, 154.78, 139.93, 139.48, 133.60, 133.23, 132.56, 128.58, 128.55, 128.32, 128.29, 127.64, 126.79, 126.59, 126.17, 124.09, 122.53, 18.88; ESI–MS: calculated for $C_{20}H_{17}O^+$ ([M+H]$^+$) 273.12, found 273.32.

(*E*)-3-(naphthalen-1-yl)-1-phenylbut-2-en-1-one **3m**



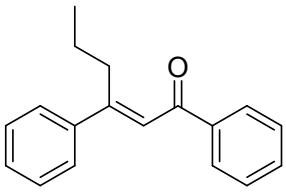
Light yellow oil; 50 % yield; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.00-7.98 (m, 3H), 7.84-7.82 (m, 2H), 7.53-7.44 (m, 6H), 7.38-7.37 (m, 1H), 7.05 (s, 1H), 2.68 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 191.41, 156.75, 142.65, 139.11, 133.83, 132.65, 130.28, 128.60, 128.56, 128.35, 128.25, 126.42, 126.07, 125.42, 125.31, 125.11, 124.35, 22.48; ESI–MS: calculated for $C_{20}H_{17}O^+$ ([M+H]$^+$) 273.12, found 273.24.

(*E*)-1, 3-diphenylpent-2-en-1-one **3n**



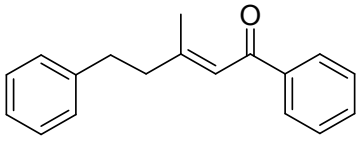
Light yellow oil; 51 % yield; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.99-7.97 (m, 2H), 7.54-7.52 (m, 3H), 7.47-7.39 (m, 5H), 7.04 (s, 1H), 3.10-3.05 (q, $J$ = 1.2 Hz, 2H), 1.15-1.11 (t, $J$ = 1.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 199.23, 144.69, 137.33, 132.88, 128.52, 128.40, 128.06, 127.65, 126.26, 45.62, 43.05, 29.22, 12.07; ESI–MS: calculated for $C_{17}H_{17}O^+$ ([M+H]$^+$) 237.12, found 237.23.

(*E*)-1,3-diphenylhex-2-en-1-one **3o**



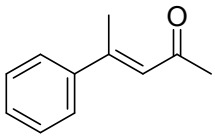
Light yellow oil; 43 % yield; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.00-7.97 (m, 2H), 7.54-7.51 (m, 3H), 7.49-7.39 (m, 5H), 7.05 (s, 1H), 3.06-3.02 (t, $J$ = 1.3 Hz, 2H ), 1.54-1.49 (m, $J$ = 1.3 Hz, 2H), 0.97-0.93 (t, $J$ = 1.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 191.58, 159.96, 142.03, 139.40, 132.50, 128.90, 128.61, 128.52, 128.31, 126.83, 122.66, 33.60, 22.40, 14.15; ESI–MS: calculated for $C_{18}H_{19}O^+$ ([M+H]$^+$) 251.14, found 251.35.

(*E*)-3-methyl-1, 5-diphenylpent-2-en-1-one **3p**



Light yellow oil; 45 % yield; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.92-7.90 (m, 2H), 7.54-7.43 (m, 3H), 7.28-7.15 (m, 4H), 6.76 (s, 1H), 2.95-2.83 (ddtt, $J$ = 1.3 Hz, 4H), 2.00 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 191.82, 157.95, 141.04, 139.19, 132.30, 128.53, 128.43, 128.39, 128.22, 126.13, 121.62, 42.99, 33.98, 19.71; ESI–MS: calculated for $C_{18}H_{19}O^+$ ([M+H]$^+$) 251.14, found 251.44.

(*E*)-4-phenylpent-3-en-2-one **3q**



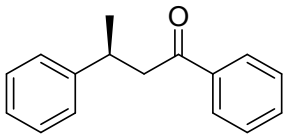
Light yellow oil; 55 % yield; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.49-7.47 (m, 2H), 7.38-7.37 (m, 3H), 6.51(s, 1H), 2.54 (s, 3H), 2.29 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 198.86, 153.86, 142.56, 129.08, 128.55, 126.48, 124.56, 32.21, 18.35. ESI–MS: calculated for $C_{11}H_{13}O^+$ ([M+H]$^+$) 161.09, found 161.44.

## 4. General procedure for the asymmetric hydrogenation of 3.

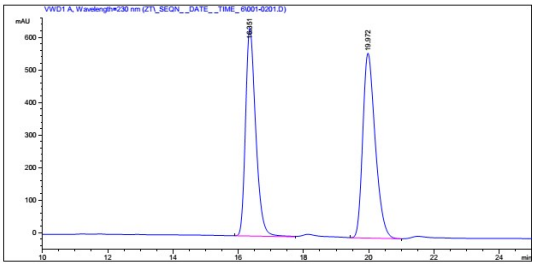
In a nitrogen-filled glovebox, appropriate $[Rh(NBD)Cl]_2$ (4.6 mg, 0.01 mmol) and ligand (2.1 eq.) was dissolved in 4.0 ml anhydrous solvent and stirred at room temperature for 30 min. A specified volume of the resulting solution (0.4 ml, 1% Rh catalyst) was transferred by syringe to a Score-Break ampule charged with substrate **3** solution (0.2 mmol in 1.2 ml). The ampule was placed into an autoclave, which was then charged with 60 atm of $H_2$. The autoclave was stirred at desired temperature for the indicated period of time. After release of hydrogen gas, the resulting mixture passed through a silica plug to remove metal complex and was concentrated under reduced pressure. The crude product was analyzed by $^1$H NMR to determine the conversion. The enantiomeric excess was directly determined by HPLC analysis. The absolute configurations were assigned according to the literature and their analogues.

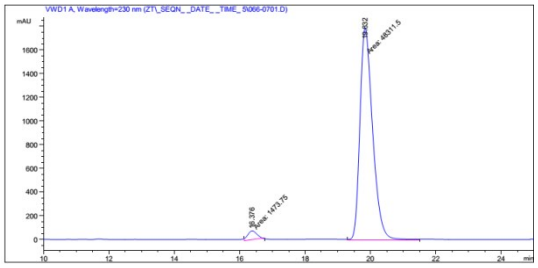
## 5. NMR, optical rotation and ESI-MS Data of product 4.

(*S*)-1,3-diphenylbutan-1-one **4a**



Light yellow oil; yield: 99%; 94% *ee*. $[\alpha]_D^{22}$ = +4.6° (c = 1.0, $CHCl_3$) (lit. +0.57°, c = 1.0, $CHCl_3$) [1]. The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 99:1; flow rate = 0.5 mL/min; UV detection at 230 nm; $t_R$ = 16.3 min (minor), $t_R$ = 19.8 min (major). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.93-7.91 (m, 2H), 7.56-7.42 (m, 3H), 7.32-7.17 (m, 5H), 3.53-3.46 (m, 1H), 3.33-3.15 (m, 2H), 1.34 (d, *J* = 6.9 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 199.07, 146.59, 137.29, 132.92, 128.55, 128.53, 128.07, 126.85, 126.27, 47.05, 35.62, 21.85; ESI–MS: calculated for $C_{16}H_{17}O^+$ ([M+H]$^+$) 225.12, found 225.83.

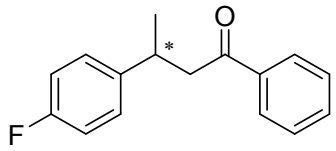




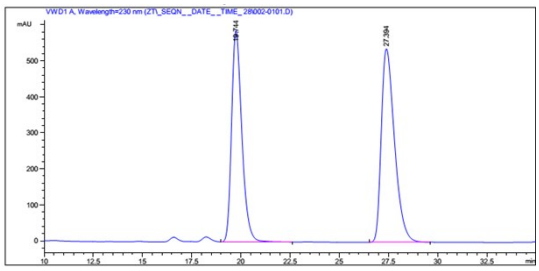
Signal 1: VWD1 A, Wavelength=230 nm

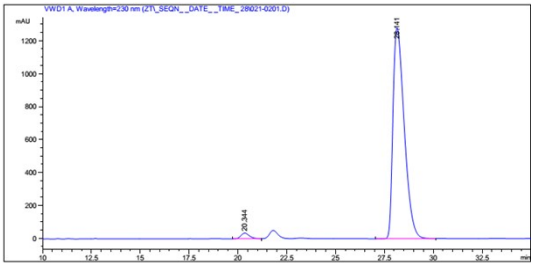
| Peak # | RetTime [min] | Type | Width [min] | Area mAU *s | Height [mAU ] | Area % |
|---|---|---|---|---|---|---|
| 1 | 16.376 | MM | 0.3233 | 1473.74536 | 75.98515 | 2.9602 |
| 2 | 19.832 | MM | 0.4504 | 4.83115e4 | 1787.53967 | 97.0398 |
| Totals : | | | | 4.97852e4 | 1863.52482 | |

(+)-3-(4-fluorophenyl)-1-phenylbutan-1-one **4b**



Light yellow oil; yield: 99%; 96% *ee*. $[\alpha]_D^{22}$ = + 4.7 ° (c = 1.0, $CHCl_3$). The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane:isopropanol = 99.5:0.5; flow rate = 0.5 mL/min; UV detection at 230 nm; $t_R$ = 20.3 min (minor), 28.1 min (major). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.92-7.90 (m, 2H), 7.54-7.42 (m, 3H), 7.24-7.20 (m, 2H), 6.99-6.95 (m, 2H), 3.53-3.48 (m, 1H), 3.29-3.13 (m, 2H), 1.32 (d, *J* = 7.0 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$)δ 198.85, 162.59, 160.16, 142.16 (d, *J* = 3.2 Hz), 137.20, 133.01, 128.30 (d, *J* = 55.2 Hz), 128.24 (d, *J*= 7.8 Hz), 115.22 (d, *J*= 21.1 Hz), 47.09, 34.92, 22.09; ESI–MS: calculated for $C_{16}H_{16}FO^+$ ([M+H]$^+$) 243.11, found 243.14.

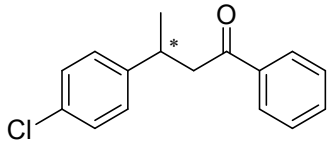




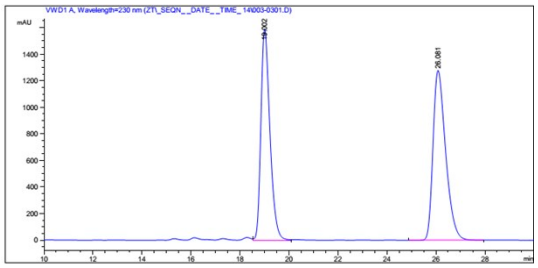
Signal 1: VWD1 A, Wavelength=230 nm

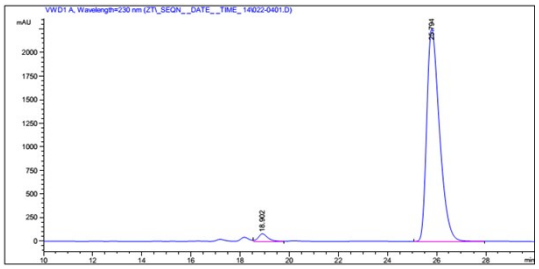
| Peak # | RetTime [min] | Type | Width [min] | Area mAU *s | Height [mAU ] | Area % |
|---|---|---|---|---|---|---|
| 1 | 20.344 | BV | 0.4645 | 1043.17590 | 34.39869 | 1.9940 |
| 2 | 28.141 | BB | 0.6245 | 5.12728e4 | 1280.13989 | 98.0060 |
| Totals : | | | | 5.23159e4 | 1314.53858 | |

(+)-3-(4-chlorophenyl)-1-phenylbutan-1-one **4c**




Light yellow oil; yield: 99%; 95% *ee*. $[\alpha]_D^{22}$ = + 2.8 ° (c = 1.0, $CHCl_3$) (lit. +1.76°, c = 1.3, $CHCl_3$)[2]. The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 99:1; flow rate = 0.5 mL/min; UV detection at 230 nm; $t_R$ = 18.9 min (minor), 25.8 min (major). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.92-7.90 (m, 2H), 7.55-7.42 (m, 3H), 7.27-7.19 (m, 4H), 3.52-3.45 (m, 1H), 3.29-3.14 (m, 2H), 1.32 (d, *J* = 6.9 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 198.66, 145.00, 137.14, 133.05, 131.90, 128.61, 128.60, 128.26, 128.02, 46.83, 34.99, 21.93; ESI–MS: calculated for $C_{16}H_{16}ClO^+$ ([M+H]$^+$) 259.08 and 261.08, found 259.20 and 261.20.

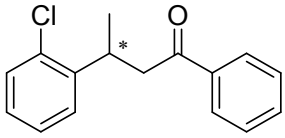




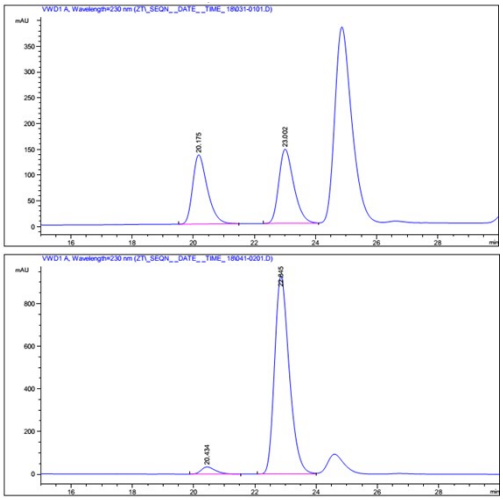
Signal 1: VWD1 A, Wavelength=230 nm

| Peak # | RetTime [min] | Type | Width [min] | Area mAU *s | Height [mAU ] | Area % |
|---|---|---|---|---|---|---|
| 1 | 18.902 | VV | 0.3974 | 2164.51807 | 81.06301 | 2.5962 |
| 2 | 25.794 | BB | 0.5511 | 8.12089e4 | 2255.32153 | 97.4038 |
| Totals : | | | | 8.33734e4 | 2336.38454 | |

(+)-3-(2-chlorophenyl)-1-phenylbutan-1-one **4d**



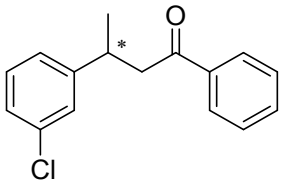

Light yellow oil; Yield: 89%, 93% *ee*; $[\alpha]_D^{22}$ =+9.9 ° (c = 1.0, $CHCl_3$); The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane:isopropanol = 99.5:0.5; flow rate = 0.5 mL/min; UV detection at 230 nm; $t_R$ = 20.4 min (minor), 22.8 min (major); $^1$H NMR (400 MHz, $CDCl_3$) δ 8.00-7.95 (m, 2H), 7.57-7.23 (m, 6H), 7.16-7.12 (m, 1H), 4.02-3.97 (m, 1H), 3.39-3.10 (m, 2H), 1.33 (d, *J* = 6.9 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 198.59, 143.56, 137.06, 133.52, 133.02, 129.80, 128.58, 128.12, 127.38, 127.32, 127.06, 45.62, 31.88, 20.15; ESI–MS: calculated for $C_{16}H_{16}ClO^+$ ([M+H]$^+$) 259.08 and 261.08, found 259.89 and 261.74.



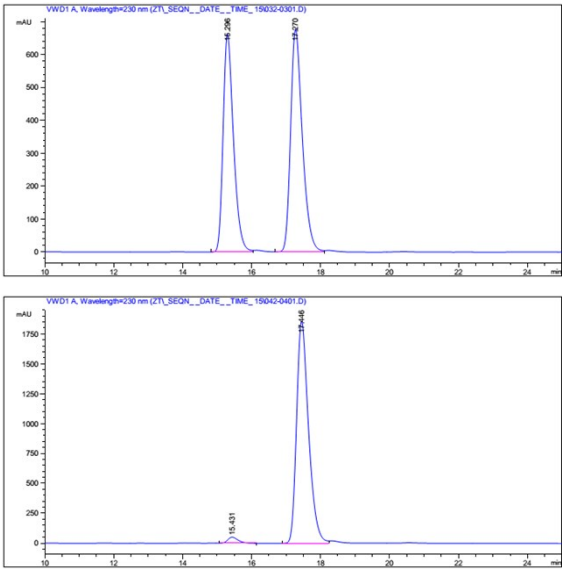
Signal 1: VWD1 A, Wavelength=230 nm

| Peak # | RetTime [min] | Type | Width [min] | Area mAU *s | Height [mAU ] | Area % |
|---|---|---|---|---|---|---|
| 1 | 20.434 | BB | 0.4881 | 1089.24805 | 33.66535 | 3.3954 |
| 2 | 22.845 | BV | 0.5103 | 3.09909e4 | 928.44543 | 96.6046 |
| Totals : | | | | 3.20802e4 | 962.11078 | |

(+)-3-(3-chlorophenyl)-1-phenylbutan-1-one **4e**



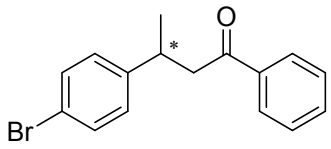
Light yellow oil; Yield: 99%, 95 %*ee*; $[\alpha]_D^{22}$ = +4.7 ° (c = 1.0, $CHCl_3$); The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 99:1; flow rate = 0.5 mL/min; UV detection at 230 nm; $t_R$ = 15.4 min (minor), 17.4 min (major); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.86-7.84 (m, 2H), 7.47-7.35 (m, 3H), 7.18-7.07 (m, 4H), 3.45-3.38 (m, 1H), 3.23-3.07 (m, 2H), 1.25 (d, *J* = 6.9 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 198.52, 148.68, 137.12, 134.30, 133.08, 129.78, 128.61, 128.04, 127.05, 126.46, 125.24, 46.69, 35.28, 21.80; ESI–MS: calculated for $C_{16}H_{16}ClO^+$ ([M+H]$^+$) 259.08 and 261.08, found 258.86 and 260.90.



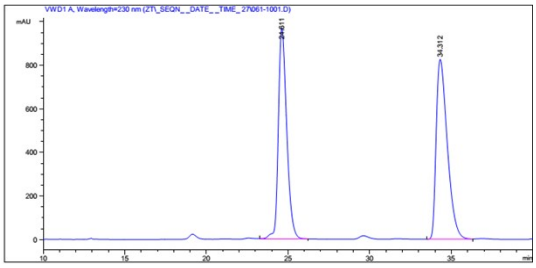
Signal 1: VWD1 A, Wavelength=230 nm

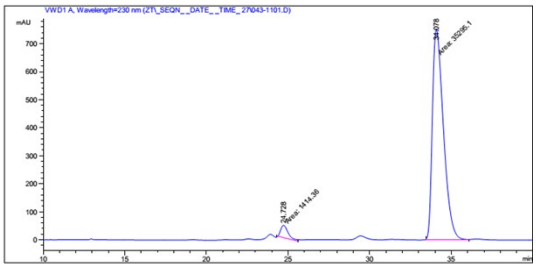
| Peak # | RetTime [min] | Type | Width [min] | Area mAU *s | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 15.431 | VB | 0.3130 | 1058.00366 | 51.06998 | 2.3100 |
| 2 | 17.446 | BV | 0.3638 | 4.47430e4 | 1858.80078 | 97.6900 |
| Totals : | | | | 4.58010e4 | 1909.87076 | |

(+)-3-(4-bromophenyl)-1-phenylbutan-1-one **4f**




Light yellow oil; Yield: 94%, 92% *ee*; $[\alpha]_D^{22}$ =+4.8 ° (c = 1.0, $CHCl_3$); The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 95.5:0.5; flow rate = 0.5 mL/min; UV detection at 230 nm; $t_R$ = 24.7 min (minor), 34.0 min (major); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.92-7.90 (m, 2H), 7.55-7.40 (m, 5H), 7.16-7.13 (m, 2H), 3.51-3.46 (m, 1H), 3.29-3.14 (m, 2H), 1.32 (d, *J* = 7.0 Hz, 3H);$^{13}$C NMR (100 MHz, $CDCl_3$)δ 198.63, 145.56, 137.15, 133.08, 131.60, 128.70, 128.62, 128.04, 119.95, 46.78, 35.07, 21.91; ESI–MS: calculated for $C_{16}H_{16}BrO^+$ ([M+H]$^+$) 303.03 and 305.03, found 303.11 and 305.10.

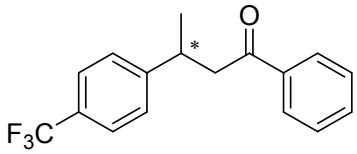




Signal 1: VWD1 A, Wavelength=230 nm

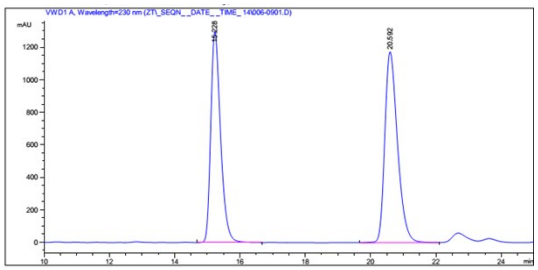
| Peak # | RetTime [min] | Type | Width [min] | Area mAU *s | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 24.728 | MM | 0.5351 | 1414.36365 | 44.05515 | 3.8529 |
| 2 | 34.078 | MM | 0.7822 | 3.52951e4 | 752.07782 | 96.1471 |
| Totals : | | | | 3.67094e4 | 796.13297 | |

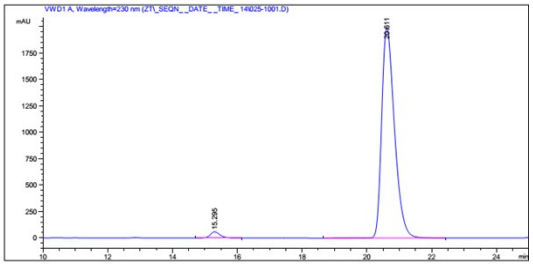
(+)-1-phenyl-3-(4-(trifluoromethyl)phenyl)butan-1-one **4g**




Light yellow oil; yield: 97%; 96% *ee*. $[\alpha]_D^{22}$ = +8.3 ° (c = 1.0, $CHCl_3$). The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 99:1; flow rate = 0.5 mL/min; UV detection at 230 nm; $t_R$ = 15.2 min (minor), 20.6 min (major). $^1$H NMR (400

MHz, $CDCl_3$) δ 7.92-7.90 (m, 2H), 7.57-7.54 (m, 2H), 7.46-7.37 (m, 5H), 3.62-3.56 (m, 1H), 3.34-3.15 (m, 2H), 1.36 (d, *J* = 7.0 Hz, 3H);$^{13}$C NMR (100 MHz, $CDCl_3$) δ 198.41, 150.63, 137.08, 133.17, 128.66, 128.66,128.66 (q, *J* = 33.0 Hz), 128.04, 127.30, 125.51 (q, *J* = 3.8 Hz), 46.58, 35.38, 21.86; ESI–MS: calculated for $C_{17}H_{16}F_3O^+$ ([M+H]$^+$) 293.11, found 293.16.

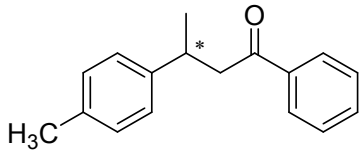




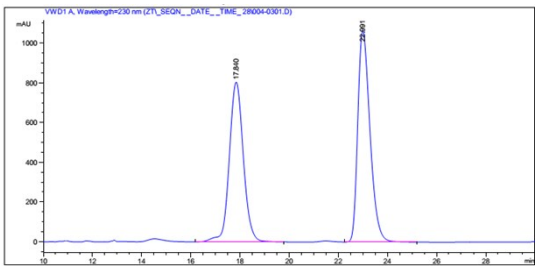
Signal 1: VWD1 A, Wavelength=230 nm

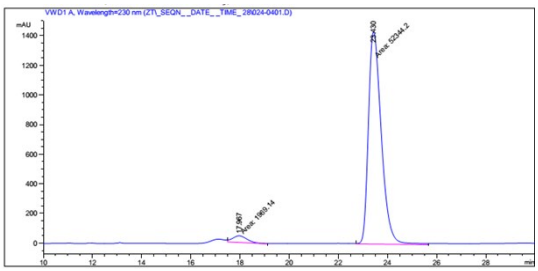
| Peak # | RetTime [min] | Type | Width [min] | Area mAU *s | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 15.295 | VB | 0.3179 | 1254.73682 | 59.37255 | 2.2439 |
| 2 | 20.611 | BB | 0.4241 | 5.46622e4 | 1988.33435 | 97.7561 |
| Totals : | | | | 5.59170e4 | 2047.70690 | |

(+)-1-phenyl-3-(*p*-tolyl)butan-1-one **4h**



Light yellow oil; yield: 98%; 91% *ee*. $[\alpha]_D^{22}$ = +3.3 ° (c = 1.0, $CHCl_3$). The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane:isopropanol = 99.5:0.5; flow rate = 0.5 mL/min; UV detection at 230 nm; $t_R$ = 17.9 min (minor), 23.4 min (major). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.94-7.91 (m, 2H), 7.56-7.42 (m, 3H), 7.18-7.10 (m, 4H), 3.49-3.44 (m, 1H), 3.30-3.13 (m, 2H), 2.31 (s, 3H), 1.32 (d, *J* = 6.9 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 199.18, 143.60, 137.29, 135.75, 132.92, 129.21, 128.55, 128.09, 126.71, 47.16, 35.22, 21.96, 20.97; ESI–MS: calculated for $C_{17}H_{19}O^+$ ([M+H]$^+$) 239.14, found 239.36.

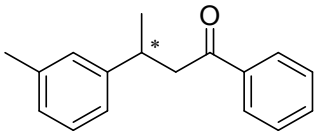




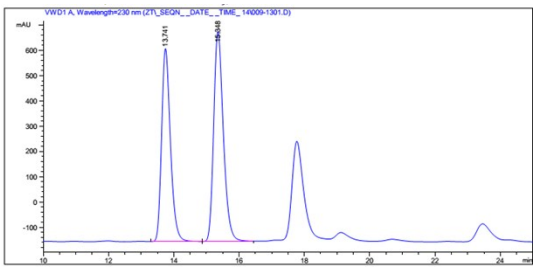
Signal 1: VWD1 A, Wavelength=230 nm

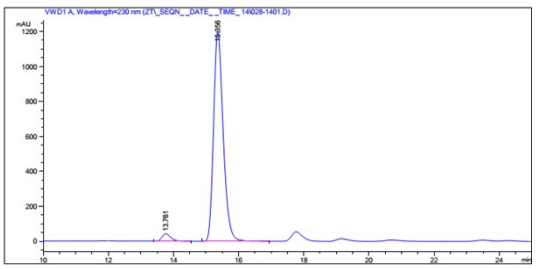
| Peak # | RetTime [min] | Type | Width [min] | Area mAU *s | Height [mAU ] | Area % |
|---|---|---|---|---|---|---|
| 1 | 17.967 | MM | 0.7139 | 1969.14478 | 45.97083 | 3.6255 |
| 2 | 23.430 | MM | 0.6077 | 5.23442e4 | 1435.65588 | 96.3745 |
| Totals : | | | | 5.43134e4 | 1481.62671 | |

(-)-1-phenyl-3-(*m*-tolyl)butan-1-one **4i**



Light yellow oil; yield: 95%; 94% *ee*. $[\alpha]_D^{22} = -1.4$ ° (c = 0.5, $CHCl_3$). The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane:isopropanol = 99:1; flow rate = 0.5 mL/min; UV detection at 230 nm; $t_R$ = 13.7 min (minor), 15.3 min (major). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.94-7.92 (m, 2H), 7.54-7.42 (m, 3H), 7.21-7.00 (m, 4H), 3.49-3.44 (m, 1H), 3.31-3.14 (m, 2H), 2.33(s, 3H), 1.32 (d, *J* = 6.9 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 199.14, 146.59, 138.05, 137.33, 132.90, 128.54, 128.42, 128.08, 127.68, 127.02, 123.80, 47.08, 35.55, 21.85, 21.46; ESI–MS: calculated for $C_{17}H_{19}O^+$ ([M+H]$^+$) 239.14, found 239.22.

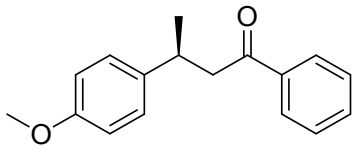




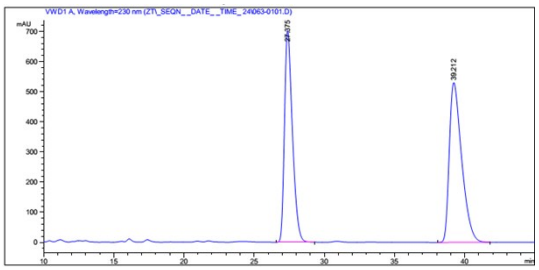
Signal 1: VWD1 A, Wavelength=230 nm

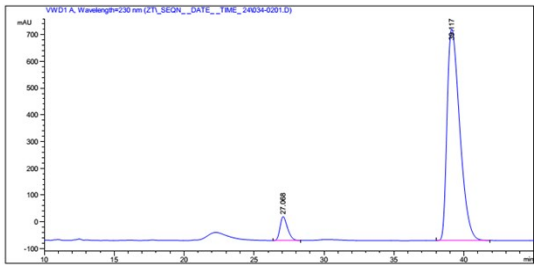
| Peak # | RetTime [min] | Type | Width [min] | Area mAU *s | Height [mAU ] | Area % |
|---|---|---|---|---|---|---|
| 1 | 13.761 | VB | 0.2855 | 804.29840 | 42.93528 | 3.1646 |
| 2 | 15.356 | BB | 0.3111 | 2.46111e4 | 1204.70996 | 96.8354 |
| Totals : | | | | 2.54154e4 | 1247.64524 | |

(*S*)-3-(4-methoxyphenyl)-1-phenylbutan-1-one **4j**



Light yellow oil; yield: 64%; 88% *ee*. $[\alpha]_D^{22}$ = +3.6° (c = 1.0, $CHCl_3$). (lit. +21.64°, c = 5.09, $CCl_4$) [4]. The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 99:1; flow rate = 0.5 mL/min; UV detection at 230 nm; $t_R$ = 27.0 min (minor), 39.1 min (major). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.93-7.91 (m, 2H), 7.54-7.42 (m, 3H), 7.20-7.18 (m, 2H), 6.85-6.83 (m, 2H), 3.78 (s, 3H), 3.49-3.43 (m, 1H), 3.39-3.12 (m, 2H), 1.31 (d, *J* = 6.9 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 199.24, 158.02, 138.70, 137.29, 132.93, 128.56, 128.09, 127.75, 113.92, 55.26, 47.31, 34.86, 22.08; ESI–MS: calculated for $C_{17}H_{19}O_2^+$ ([M+H]$^+$) 255.13, found 255.08.

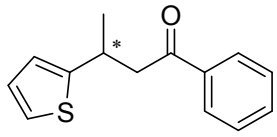




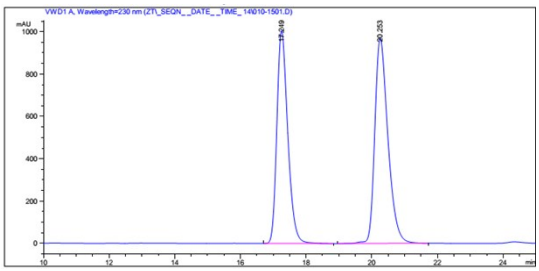
Signal 1: VWD1 A, Wavelength=230 nm

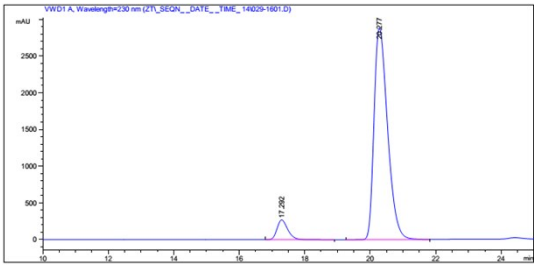
| Peak # | RetTime [min] | Type | Width [min] | Area mAU *s | Height [mAU ] | Area % |
|---|---|---|---|---|---|---|
| 1 | 27.068 | BB | 0.5608 | 3306.63452 | 89.46017 | 6.2369 |
| 2 | 39.117 | BB | 0.9826 | 4.97106e4 | 790.54340 | 93.7631 |
| Totals : | | | | 5.30173e4 | 880.00357 | |

(+)-1-phenyl-3-(thiophen-2-yl)butan-1-one **4k**



Light yellow oil; yield: 97%; 86% *ee*. $[\alpha]_D^{22}$ = +5.2 ° (c = 1.0, $CHCl_3$). The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane:isopropanol = 99:1; flow rate = 0.5 mL/min; UV detection at 230 nm; $t_R$ = 17.2 min (minor), 20.2 min (major). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.95-7.93 (m, 2H), 7.57-7.43 (m, 3H), 7.13-7.11 (m, 1H), 6.92-6.86 (m, 2H), 3.87-3.82 (m, 1H), 3.40-3.17 (m, 2H), 1.42 (d, *J* = 6.9 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 198.47, 150.65, 137.16, 133.06, 128.60, 128.07, 126.61, 122.89, 122.78, 47.90, 31.06, 22.78; ESI–MS: calculated for $C_{14}H_{15}OS^+$ ([M+H]$^+$) 231.08, found 230.98.

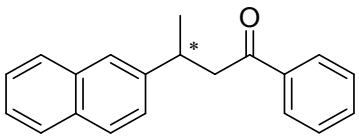




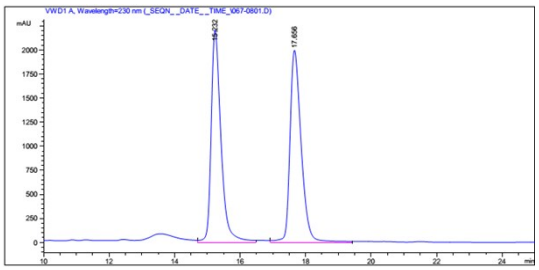
Signal 1: VWD1 A, Wavelength=230 nm

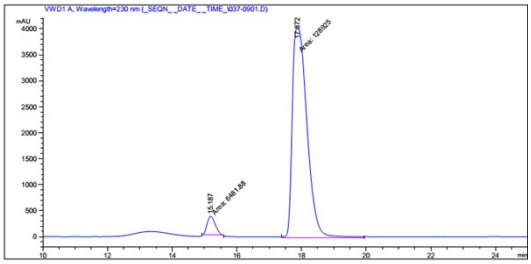
| Peak # | RetTime [min] | Type | Width [min] | Area mAU *s | Height [mAU ] | Area % |
|---|---|---|---|---|---|---|
| 1 | 17.292 | BB | 0.3488 | 6159.67188 | 270.36603 | 6.9073 |
| 2 | 20.277 | BB | 0.4435 | 8.30162e4 | 2884.94360 | 93.0927 |
| Totals : | | | | 8.91759e4 | 3155.30963 | |

(-)-3-(naphthalen-2-yl)-1-phenylbutan-1-one **4l**



Light yellow oil; yield: 80 %; 90 % *ee*. $[\alpha]_D^{22} = -3.9$ ° (c = 0.5, $CHCl_3$) (lit. –4.54°, c = 0.44, $CHCl_3$)[2]. The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 97:3; flow rate = 0.5 mL/min; UV detection at 230 nm; $t_R$ = 15.2 min (minor), 17.8 min (major). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.95-7.93 (m, 2H), 7.80-7.69 (m, 4H), 7.54-7.41 (m, 6H), 3.71-3.66 (m, 1H), 3.42-3.24 (m, 2H), 1.42 (d, *J* = 6.9 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 199.00, 144.06, 137.29, 133.66, 132.98, 132.32, 128.63, 128.20, 128.10, 127.65, 127.60, 125.98, 125.72 , 125.34, 124.97, 46.98, 35.71, 21.89; ESI–MS: calculated for $C_{20}H_{19}O^+$ ([M+H]$^+$) 275.14, found 275.11.

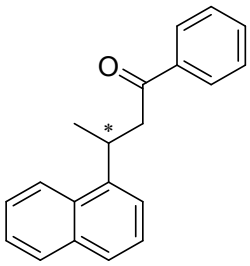




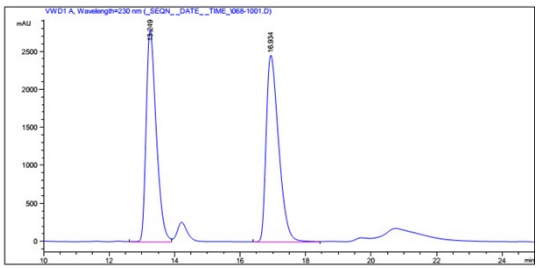
Signal 1: VWD1 A, Wavelength=230 nm

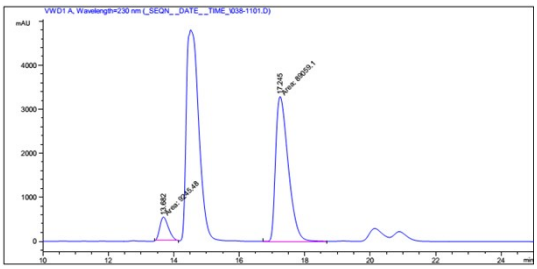
| Peak # | RetTime [min] | Type | Width [min] | Area mAU *s | Height [mAU ] | Area % |
|---|---|---|---|---|---|---|
| 1 | 15.187 | MM | 0.2957 | 6481.87598 | 365.28055 | 4.7870 |
| 2 | 17.872 | MM | 0.5310 | 1.28925e5 | 4046.60278 | 95.2130 |
| Totals : | | | | 1.35407e5 | 4411.88333 | |

(+)-3-(naphthalen-1-yl)-1-phenylbutan-1-one **4m**



Light yellow oil; yield: 44 %; 81 % *ee*. $[\alpha]_D^{22}$ = +10.3 ° (c = 1.0, $CHCl_3$). The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 98: 2; flow rate = 0.5 mL/min; UV detection at 230 nm; $t_R$ = 13.6 min (minor), 17.2 min (major). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.20-8.17 (m, 1H), 7.97-7.85 (m, 3H), 7.74-7.72 (m, 1H), 7.57-7.42 (m, 7H), 4.44-4.39 (m, 1H), 3.43-3.30 (m, 2H), 1.48 (d, *J* = 6.8 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 199.09, 142.67, 137.29, 134.05, 133.05, 131.17, 128.99, 128.60, 128.09, 126.83, 126.10, 125.52, 123.18, 122.55, 46.75, 29.66, 21.08; ESI–MS: calculated for $C_{20}H_{19}O^+$ ([M+H]$^+$) 275.14, found 275.21.

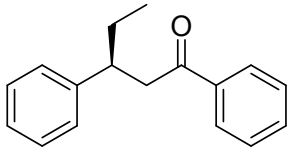




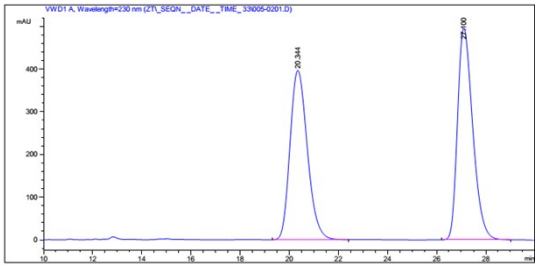
Signal 1: VWD1 A, Wavelength=230 nm

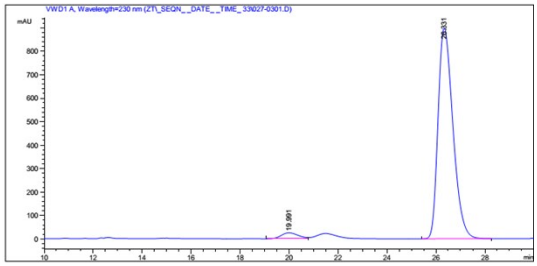
| Peak # | RetTime [min] | Type | Width [min] | Area mAU *s | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 13.682 | MM | 0.2960 | 9245.47559 | 520.58569 | 9.4049 |
| 2 | 17.245 | MM | 0.4502 | 8.90591e4 | 3297.12402 | 90.5951 |
| Totals : | | | | 9.83046e4 | 3817.70972 | |

(*S*)-1,3-diphenylpentan-1-one **4n**



Light yellow oil; yield: 99%; 94% *ee*. $[\alpha]_D^{22}$ = +4.4 ° (c = 1.0, $CHCl_3$) (lit. +2.49°, c = 1.1, $CHCl_3$) [1]. The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 99.5:0.5; flow rate = 0.5 mL/min; UV detection at 230 nm; $t_R$ = 19.9 min (minor), 26.3 min (major). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.91-7.88 (m, 2H), 7.53-7.40 (m, 3H), 7.30-7.16 (m, 5H), 3.28-3.22 (m, 3H), 1.82-1.61 (m, 2H), 0.80 (t, *J* = 7.3 Hz, 3H);$^{13}$C NMR (100 MHz, $CDCl_3$) δ 199.23, 144.69, 137.33, 132.88, 128.52, 128.40, 128.06, 127.65, 126.26, 45.62, 43.05, 29.22, 12.07; ESI–MS: calculated for $C_{17}H_{19}O^+$ ($[M+H]^+$) 239.14, found 239.40.

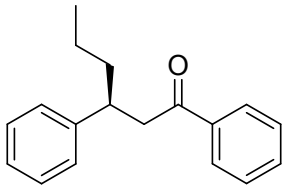



Signal 1: VWD1 A, Wavelength=230 nm

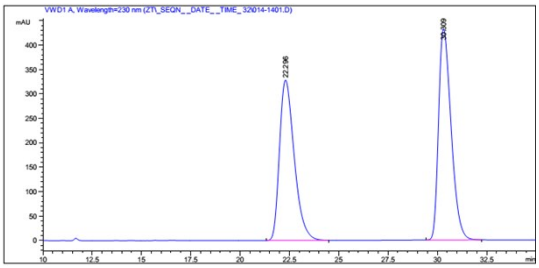
| Peak # | RetTime [min] | Type | Width [min] | Area mAU *s | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 19.991 | BV | 0.7612 | 1234.20642 | 25.37203 | 3.1580 |
| 2 | 26.331 | BB | 0.6574 | 3.78479e4 | 898.55573 | 96.8420 |
| Totals : | | | | 3.90821e4 | 923.92776 | |

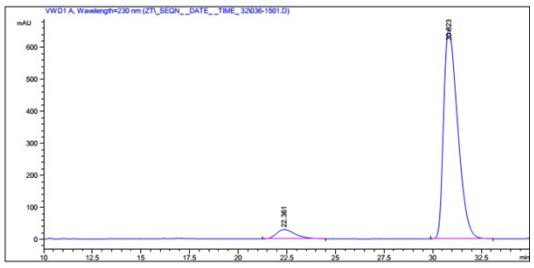
(*S*)-1,3-diphenylhexan-1-one **4o**



Light yellow oil; yield: 99%; 89% *ee*. $[\alpha]_D^{22}$ = +5.6 ° (c = 1.0, $CHCl_3$). (lit. +4.7°, c = 1.0, EtOH) [3]. The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane:

isopropanol = 99.5:0.5; flow rate = 0.5 mL/min; UV detection at 230 nm; $t_R$ = 22.3 min (minor), 30.8 min (major). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.90-7.88 (m, 2H), 7.54-7.51 (m, 1H), 7.44-7.40 (m, 2H), 7.29-7.15 (m, 5H), 3.38-3.19 (m, 3H), 1.73-1.58 (m, 2H), 1.23-1.16 (m, 2H), 0.85 (t, *J* = 7.3 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 199.21, 144.99, 137.33, 132.88, 128.52, 128.41, 128.05, 127.58, 126.24, 45.97, 41.10, 38.59, 20.63, 13.99; ESI–MS: calculated for $C_{18}H_{21}O^+$ ($[M+H]^+$) 253.15, found 253.15.

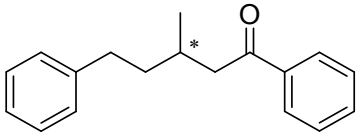




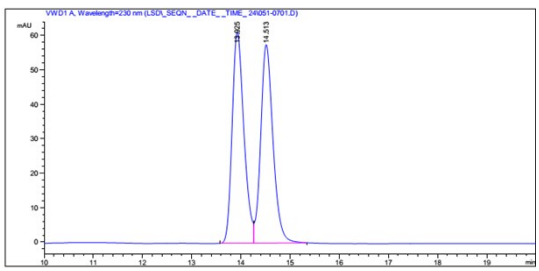
Signal 1: VWD1 A, Wavelength=230 nm

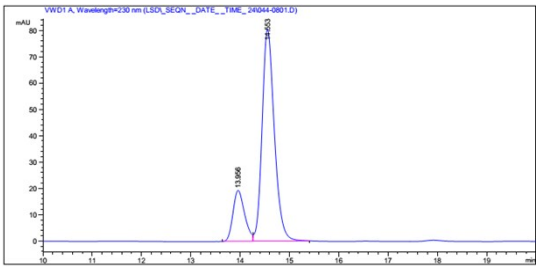
| Peak # | RetTime [min] | Type | Width [min] | Area mAU *s | Height [mAU ] | Area % |
|---|---|---|---|---|---|---|
| 1 | 22.361 | BB | 1.0319 | 1988.24121 | 29.13862 | 5.6922 |
| 2 | 30.823 | BB | 0.7880 | 3.29408e4 | 654.59064 | 94.3078 |
| Totals : | | | | 3.49290e4 | 683.72926 | |

(+)-3-methyl-1, 5-diphenylpentan-1-one **4p**



Light yellow oil; yield: 99%; 63% *ee*. $[\alpha]_D^{22}$ = +1.6 ° (c = 0.5, $CHCl_3$) (lit. +7.1°, c = 1.1, $CHCl_3$) [1]. The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 99:1; flow rate = 0.5 mL/min; UV detection at 230 nm; $t_R$ = 13.9 min (minor), 14.5 min (major). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.93-7.91 (m, 2H), 7.54-7.42 (m, 3H), 7.28-7.16 (m, 5H), 3.02-2.62 (m, 4H), 2.29-2.22 (m, 1H), 1.78-1.55 (m, 2H), 1.03 (d, *J* = 6.7 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 200.13, 142.43, 137.48, 132.85, 128.55, 128.34, 128.32, 128.09, 125.72, 45.87, 38.88, 33.45, 29.63, 19.96; ESI–MS: calculated for $C_{18}H_{21}O^+$ ($[M+H]^+$) 253.15, found 253.25.

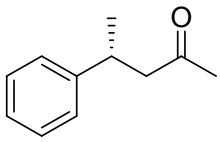




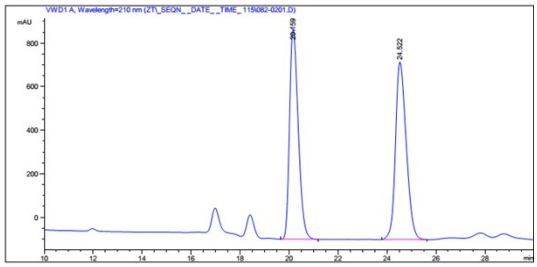
Signal 1: VWD1 A, Wavelength=230 nm

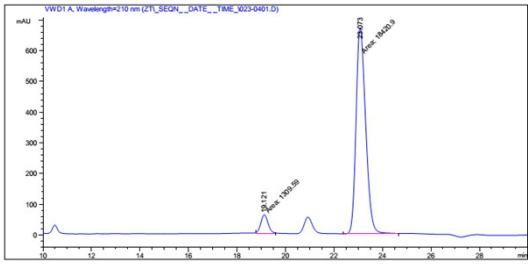
| Peak # | RetTime [min] | Type | Width [min] | Area mAU *s | Height [mAU ] | Area % |
|---|---|---|---|---|---|---|
| 1 | 13.956 | BV | 0.2512 | 318.27734 | 19.38582 | 18.6066 |
| 2 | 14.553 | VB | 0.2642 | 1392.28345 | 80.57129 | 81.3934 |
| Totals : | | | | 1710.56079 | 99.95711 | |

(*R*)-4-phenylpentan-2-one **4q**



Light yellow oil; yield: 96%; 87% *ee*. $[\alpha]_D^{22}$ = −5.8 ° (c = 0.5, $CHCl_3$) (lit. -40.0°, c = 2.13, $CHCl_3$) [2]. The enantiomeric excess was determined by HPLC on Chiralpak AS-H column, hexane: isopropanol = 99:1; flow rate = 0.5 mL/min; UV detection at 210 nm; $t_R$ = 19.1 min (minor), 23.0min (major). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.31-7.17 (m, 5H), 3.33-3.26 (m, 1H), 2.79-2.63 (m, 2H), 2.06 (s, 3H), 1.27 (d, *J* = 7.0 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 207.78, 146.18, 128.54, 126.76, 126.31, 52.02, 35.48, 30.54, 21.99; ESI–MS: calculated for $C_{11}H_{15}O^+$ ([M+H]$^+$) 163.11, found163.24.





Signal 1: VWD1 A, Wavelength=210 nm

| Peak # | RetTime [min] | Type | Width [min] | Area mAU *s | Height [mAU ] | Area % |
|---|---|---|---|---|---|---|
| 1 | 19.121 | MM | 0.3535 | 1309.58838 | 61.74215 | 6.6374 |
| 2 | 23.073 | MM | 0.4578 | 1.84209e4 | 670.63953 | 93.3626 |
| Totals : | | | | 1.97305e4 | 732.38168 | |

## 6. Reference

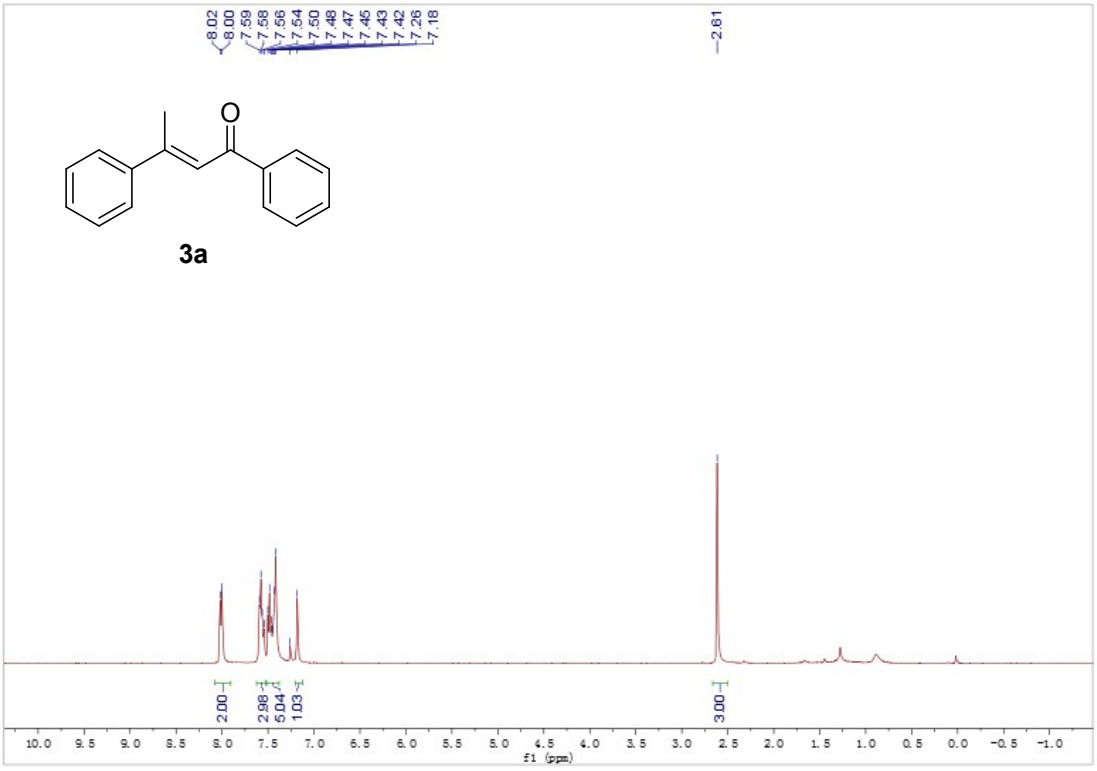
(1) S. M. Lu, C. A. Bolm, *Chem. Eur. J.*, 2008, **14**, 7513-7516.

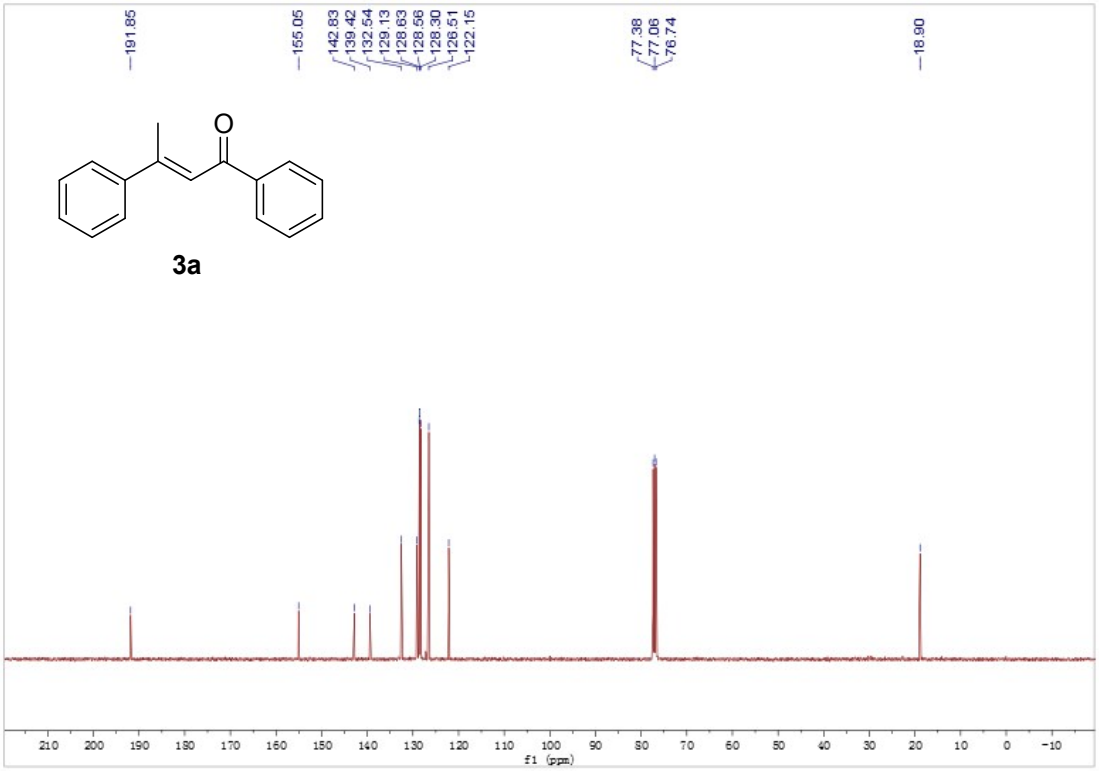
(2) K. Endo, D. Hamada, S. Yakeishi, T. Shibata, *Angew. Chem. Int. Ed.*, 2013, **52**, 606-610.

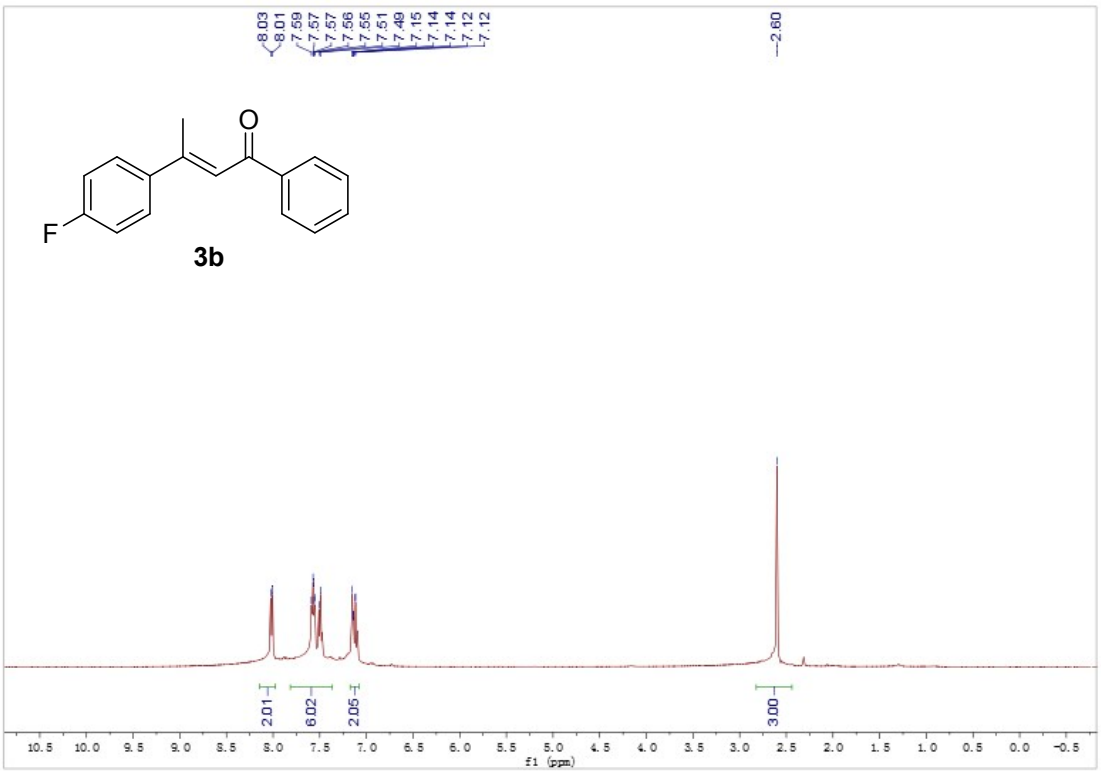
(3) T. Yasukawa, H. Miyamura, S. Kobayashi, *J. Am. Chem. Soc.*, 2012, **134**, 16963-16966.

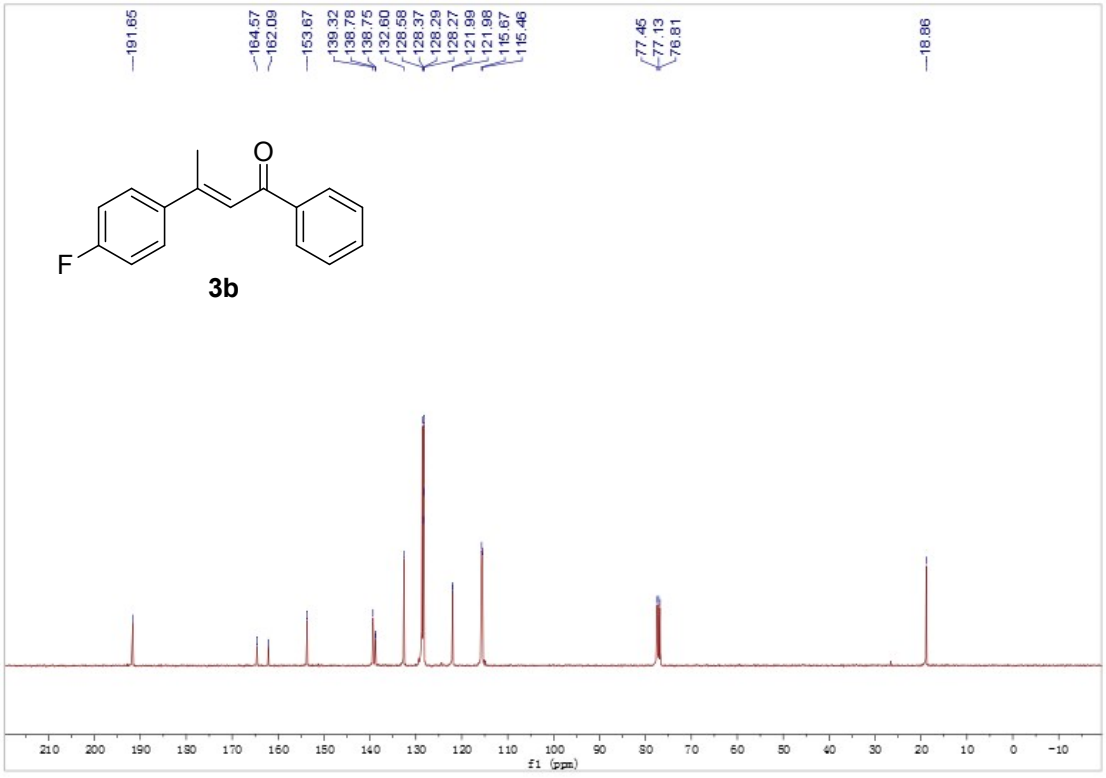
(4) W. D. Ollis, M. Rey, I. O. Sutherland. J. Chem. Soc., Perkin Trans. 1, 1983, **5,** 1009-1027.

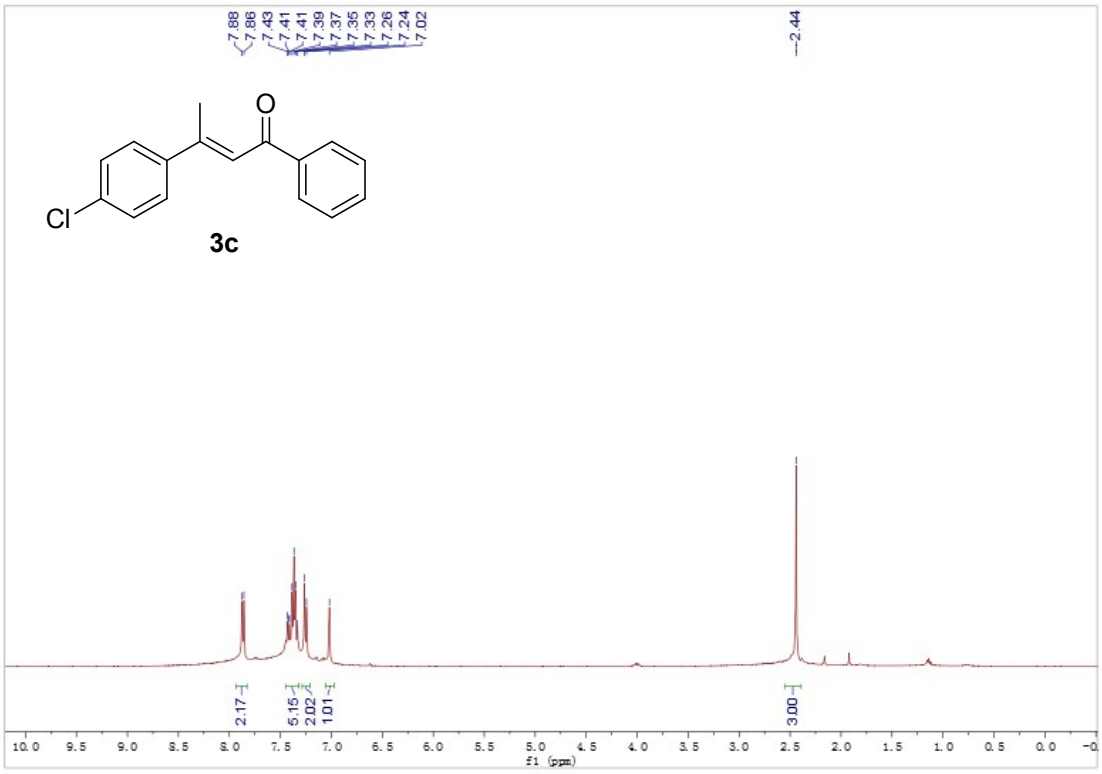
## 7. NMR spectrum of compounds 3 and 4.

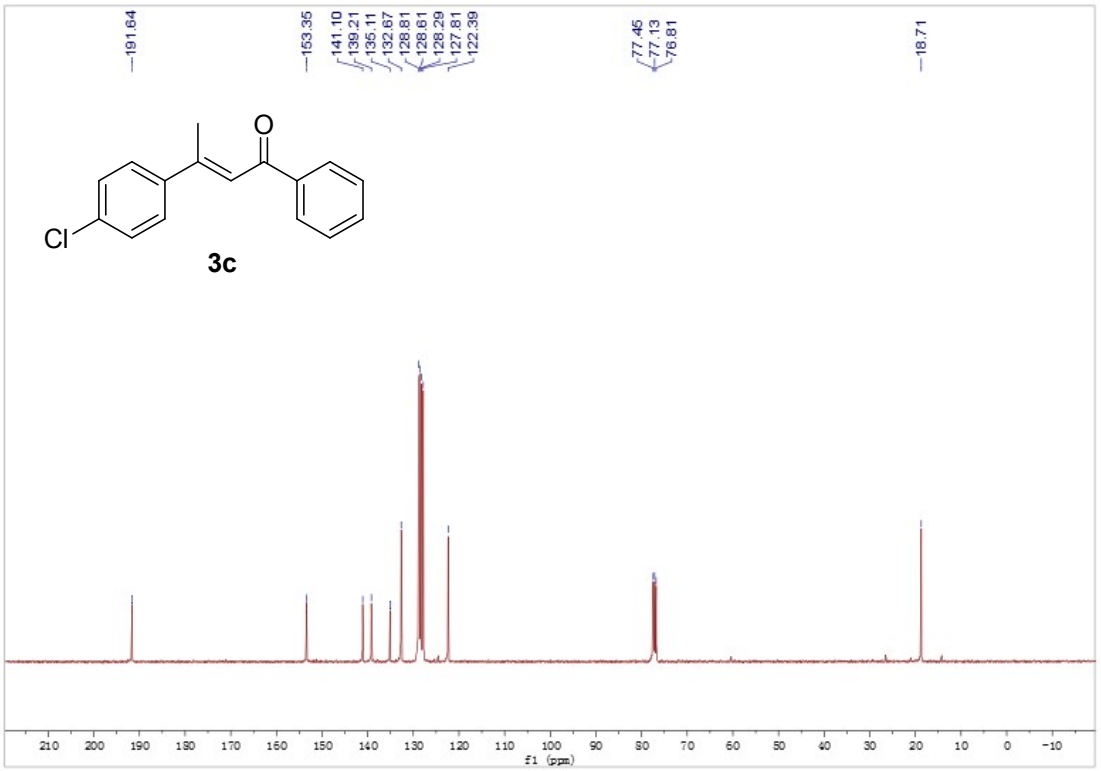


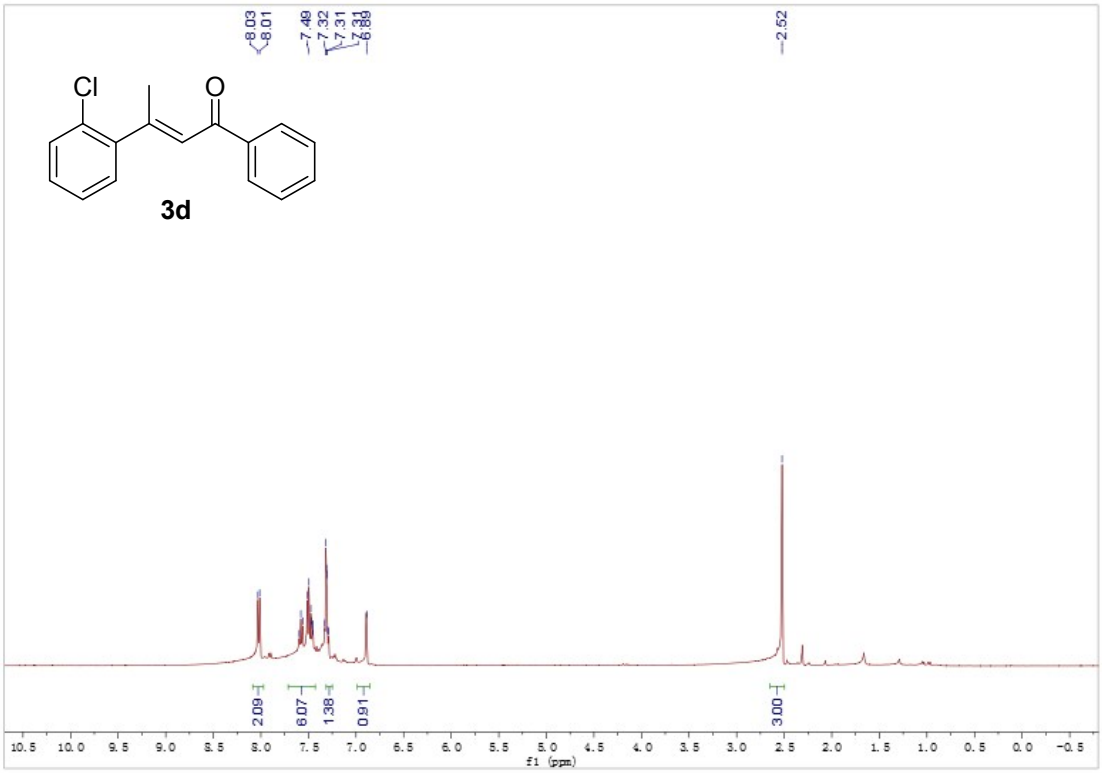



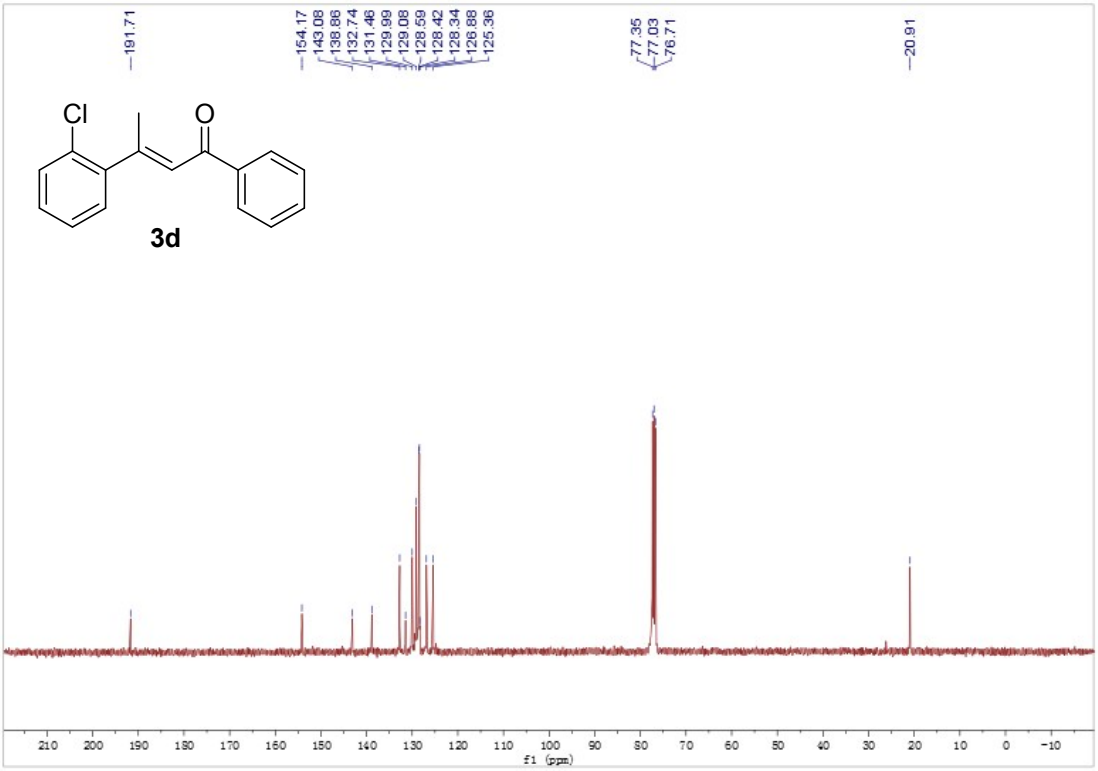

8.03
8.01
7.59
7.57
7.57
7.57
7.56
7.55
7.51
7.49
7.15
7.14
7.14
7.12
7.12
2.60
O
F
3b
2.01
6.02
2.05
3.00
f1 (ppm)

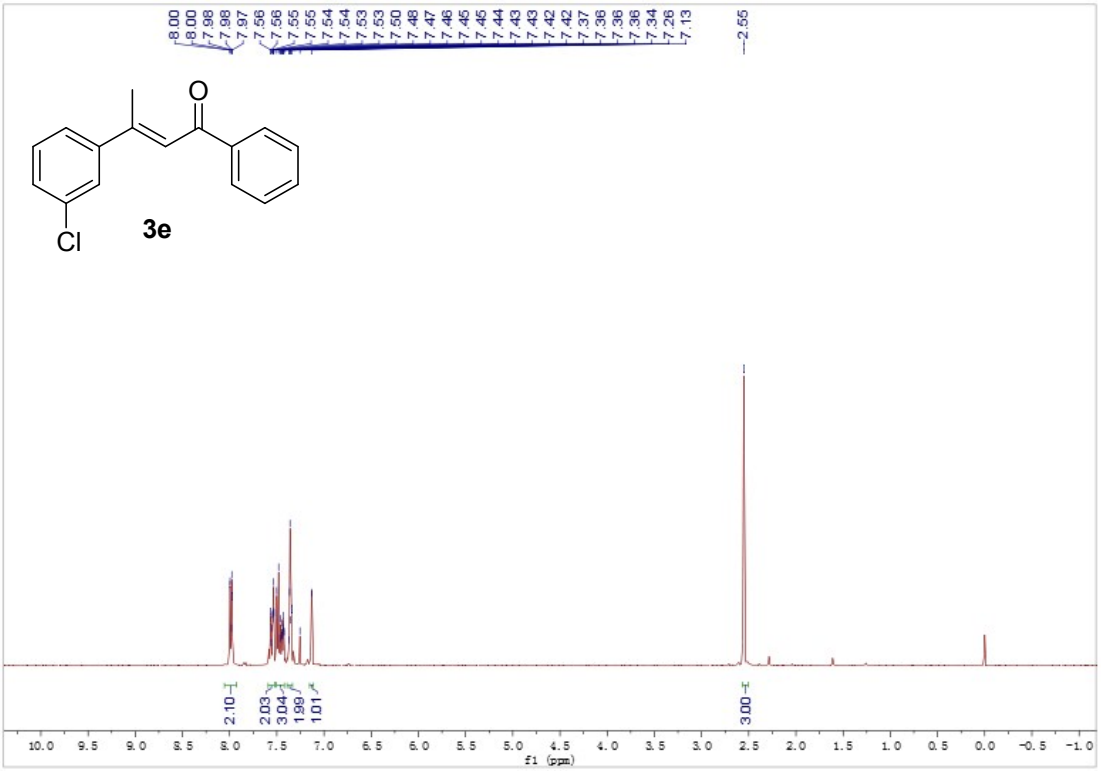

191.65
164.57
162.09
153.67
139.32
138.78
138.75
132.60
128.58
128.37
128.29
128.27
121.99
121.98
115.67
115.46
77.45
77.13
76.81
18.86
O
F
3b
f1 (ppm)

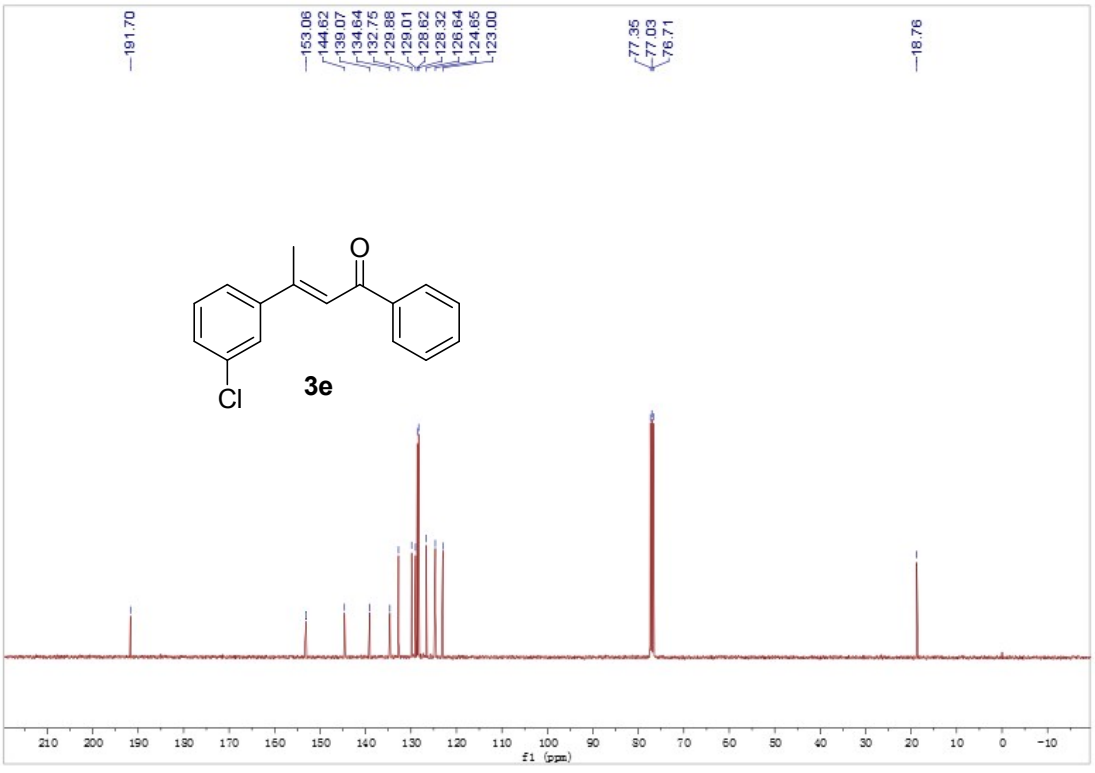

7.88
7.86
7.43
7.41
7.41
7.39
7.37
7.35
7.33
7.26
7.24
7.02
2.44
O
Cl
3c
2.17
5.15
2.02
1.01
3.00
f1 (ppm)

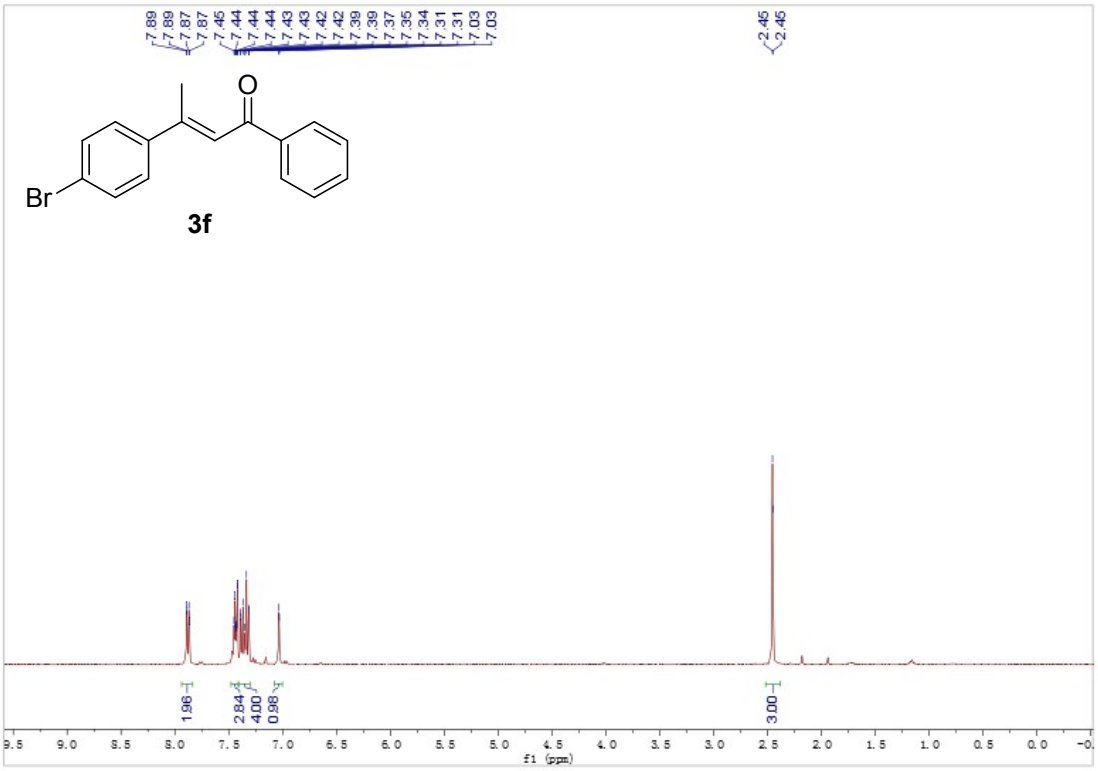

191.64
153.35
141.10
139.21
135.11
132.67
128.81
128.61
128.29
127.81
122.39
77.45
77.13
76.81
18.71
O
Cl
3c
f1 (ppm)

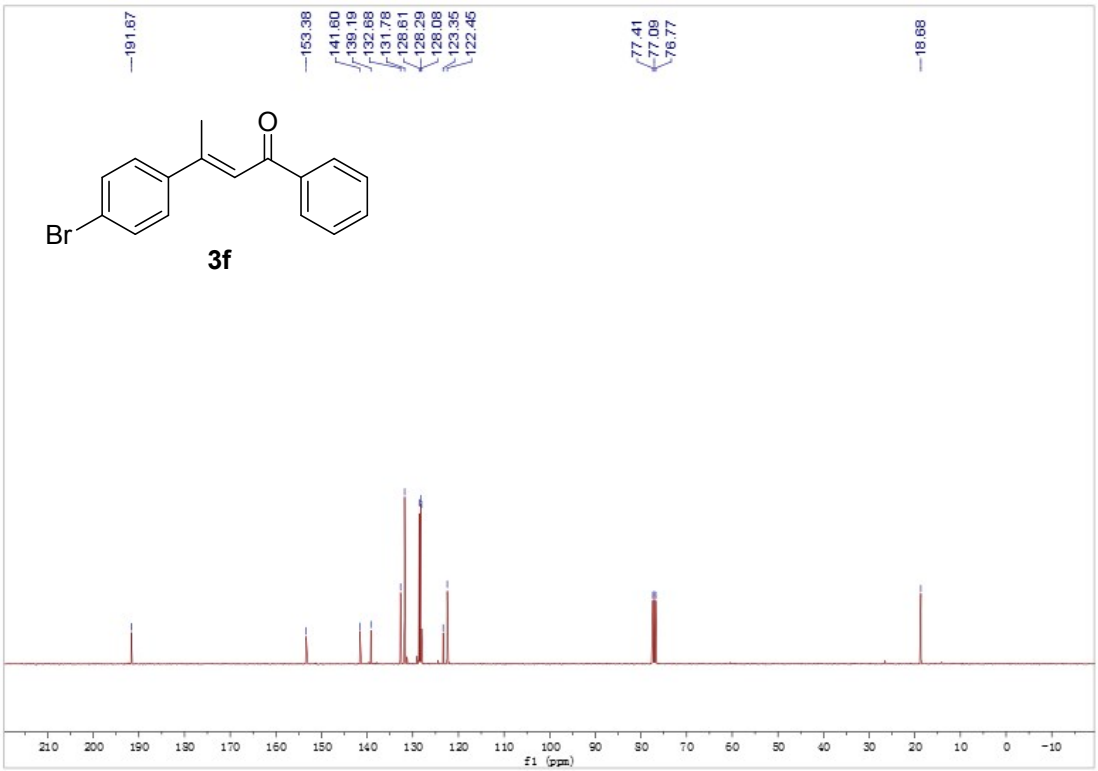

8.03
8.01
7.49
7.32
7.31
7.31
6.89
2.52
Cl
O
3d
2.09
6.07
1.38
0.91
3.00
f1 (ppm)

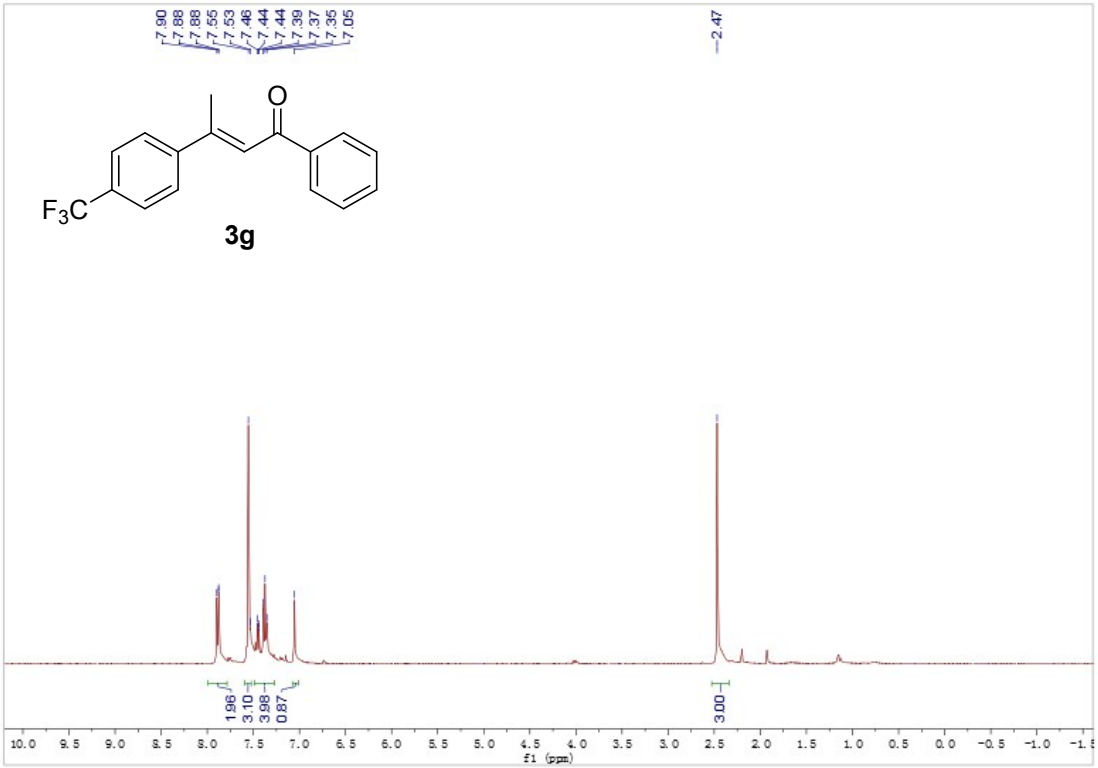

191.71
154.17
143.08
138.86
132.74
131.46
129.99
129.08
128.59
128.42
128.34
126.88
125.36
77.35
77.03
76.71
20.91
Cl
O
3d
f1 (ppm)

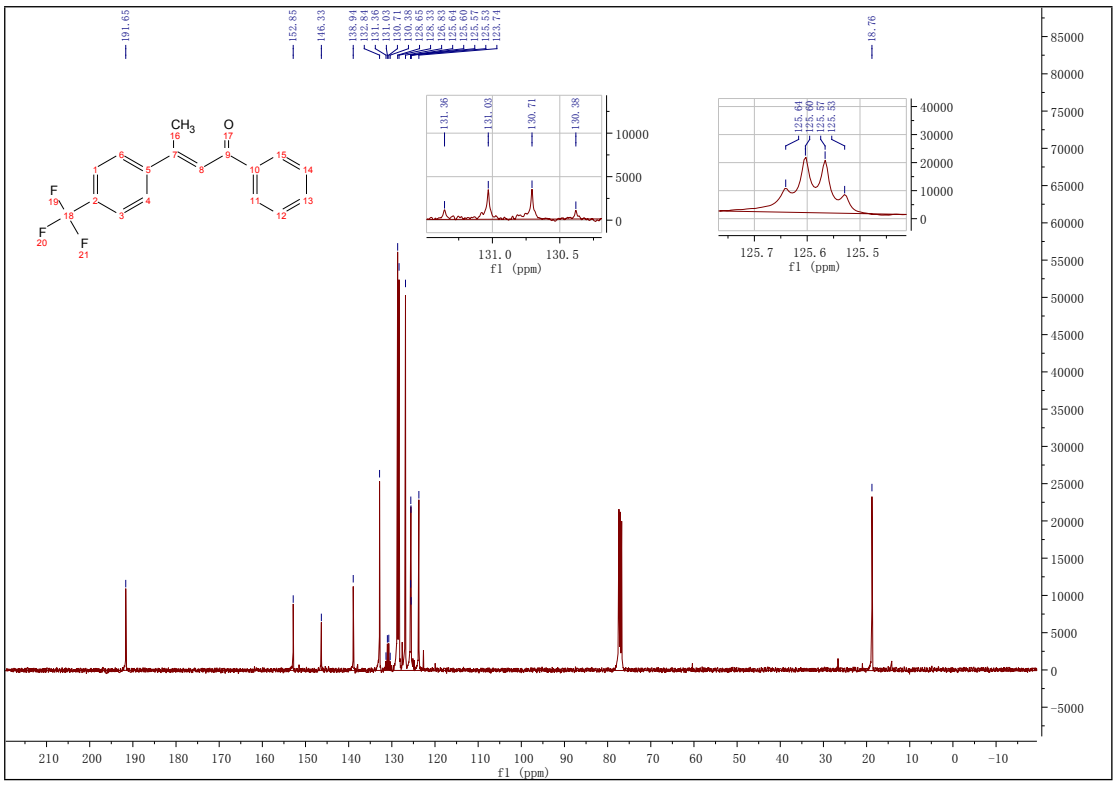

8.00
8.00
7.98
7.98
7.97
7.56
7.56
7.55
7.55
7.54
7.54
7.53
7.53
7.50
7.48
7.47
7.46
7.45
7.45
7.44
7.43
7.43
7.42
7.42
7.37
7.36
7.36
7.36
7.34
7.26
7.13
2.55
O
Cl
3e
2.10
2.03
3.04
1.99
1.01
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

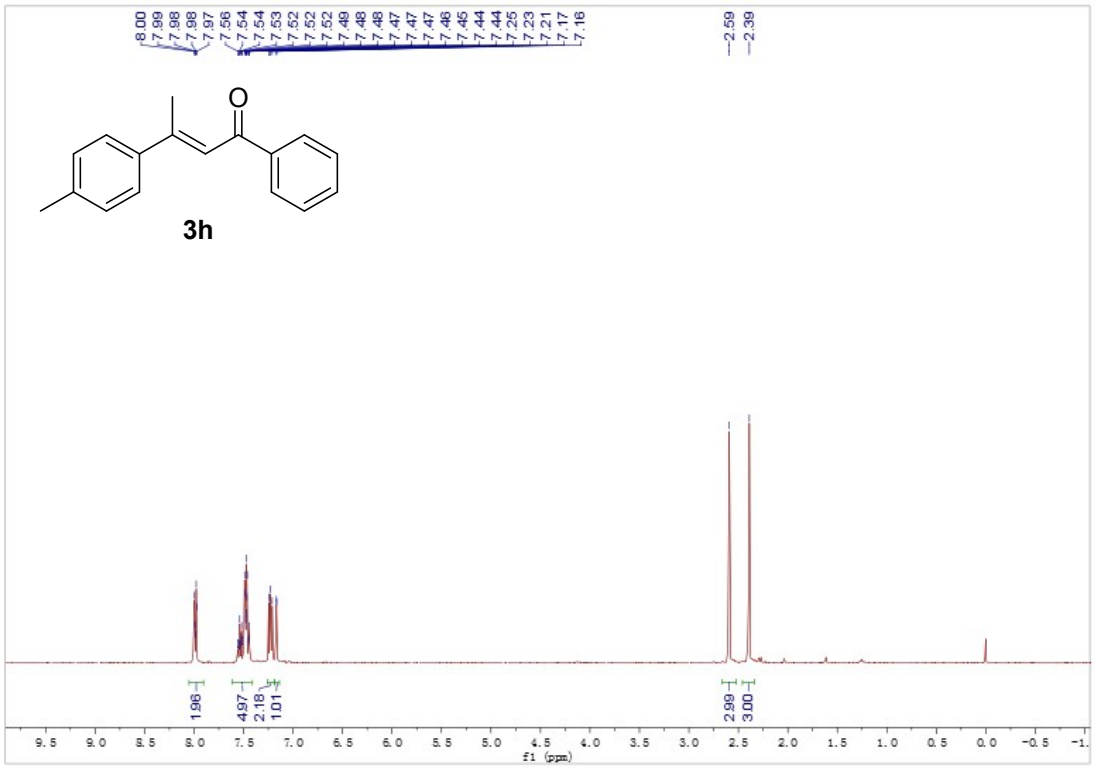

191.70
153.06
144.62
139.07
134.64
132.75
129.88
129.01
128.62
128.32
126.84
124.65
123.00
77.35
77.03
76.71
18.78
O
Cl
3e
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

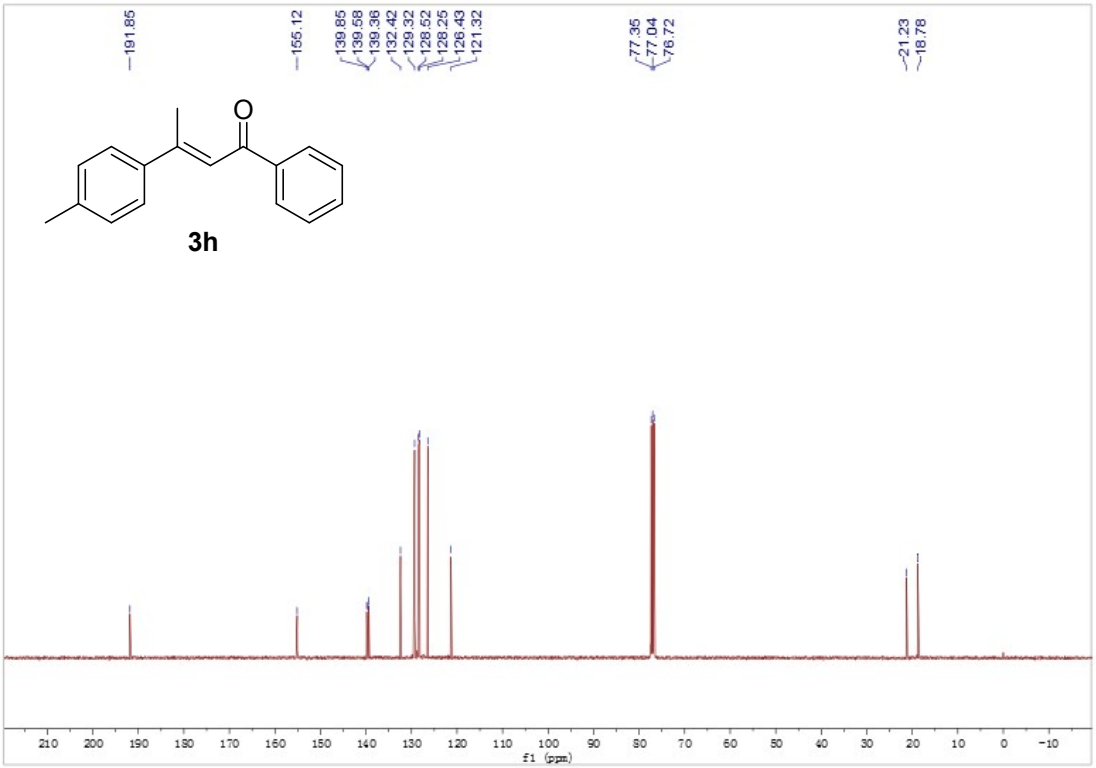

7.89
7.89
7.87
7.87
7.45
7.44
7.44
7.44
7.43
7.43
7.42
7.42
7.39
7.39
7.37
7.35
7.34
7.31
7.31
7.03
7.03
2.45
2.45
O
Br
3f
1.96
2.84
4.00
0.98
3.00
f1 (ppm)

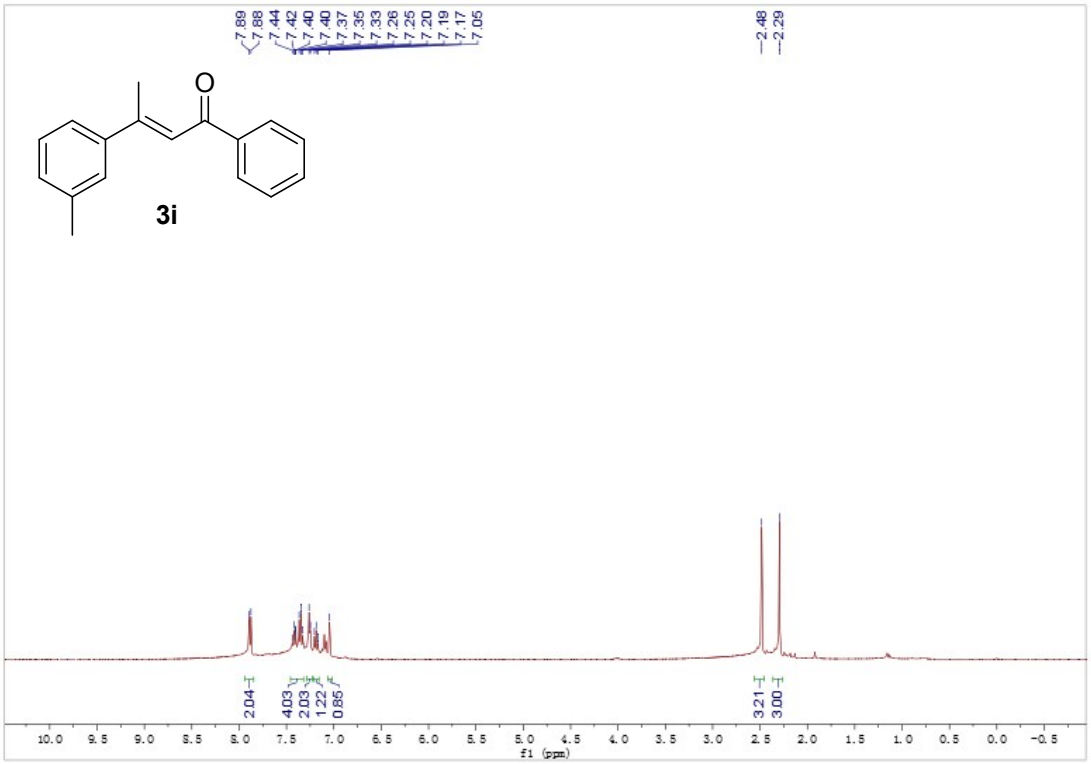

191.67
153.38
141.60
139.19
132.68
131.78
128.61
128.29
128.08
123.35
122.45
77.41
77.09
76.77
18.68
O
Br
3f
f1 (ppm)

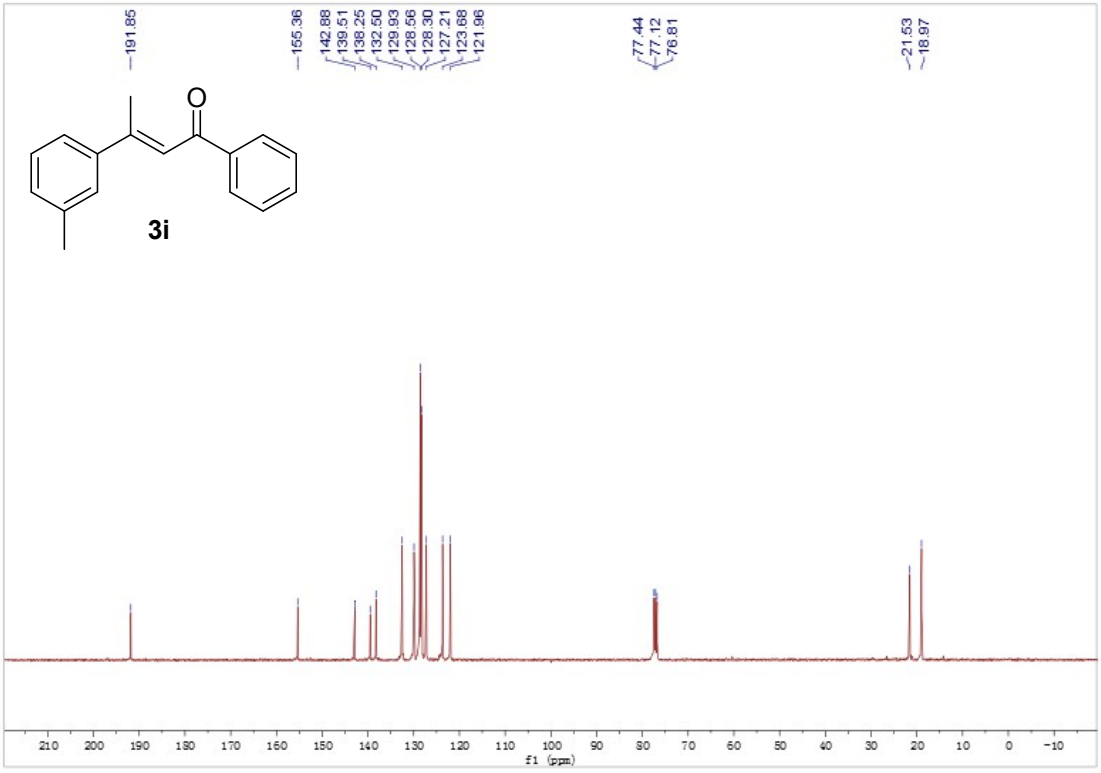

7.90
7.88
7.88
7.55
7.53
7.46
7.44
7.44
7.39
7.37
7.35
7.05
2.47
O
F3C
3g
1.96
3.10
3.98
0.87
3.00
f1 (ppm)

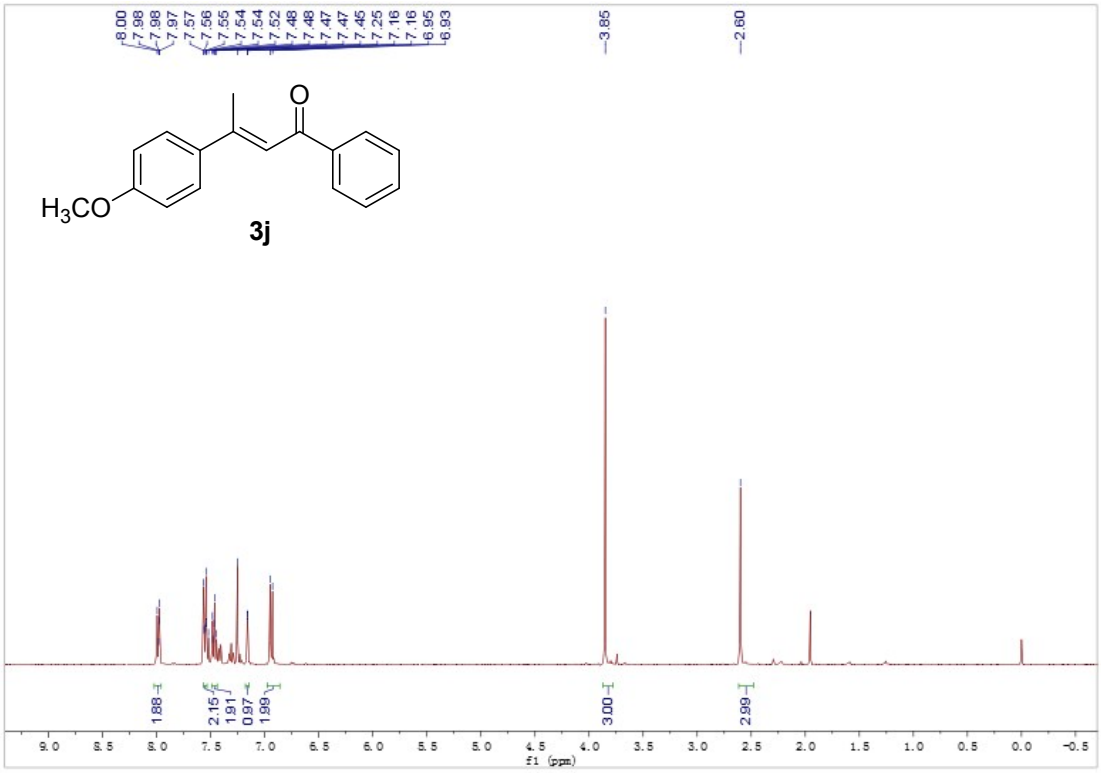

191.65
152.85
146.33
138.94
132.84
131.36
131.03
130.71
130.38
128.65
128.33
126.83
125.64
125.60
125.57
125.53
123.74
18.76
CH3
O
F
F
F
131.36
131.03
130.71
130.38
125.64
125.60
125.57
125.53
f1 (ppm)
f1 (ppm)

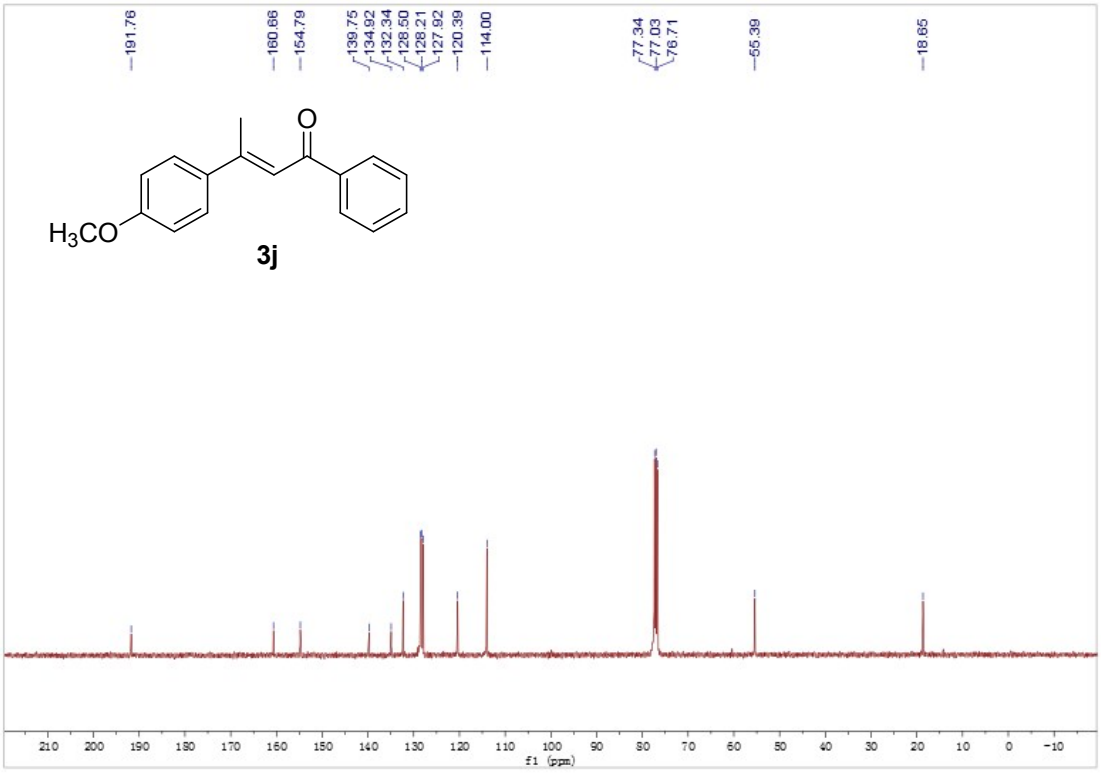

8.00
7.99
7.98
7.98
7.97
7.56
7.54
7.54
7.53
7.52
7.52
7.52
7.49
7.48
7.48
7.47
7.47
7.47
7.46
7.45
7.44
7.44
7.25
7.23
7.21
7.17
7.16
2.59
2.39
O
3h
1.96
4.97
2.18
1.01
2.99
3.00
f1 (ppm)

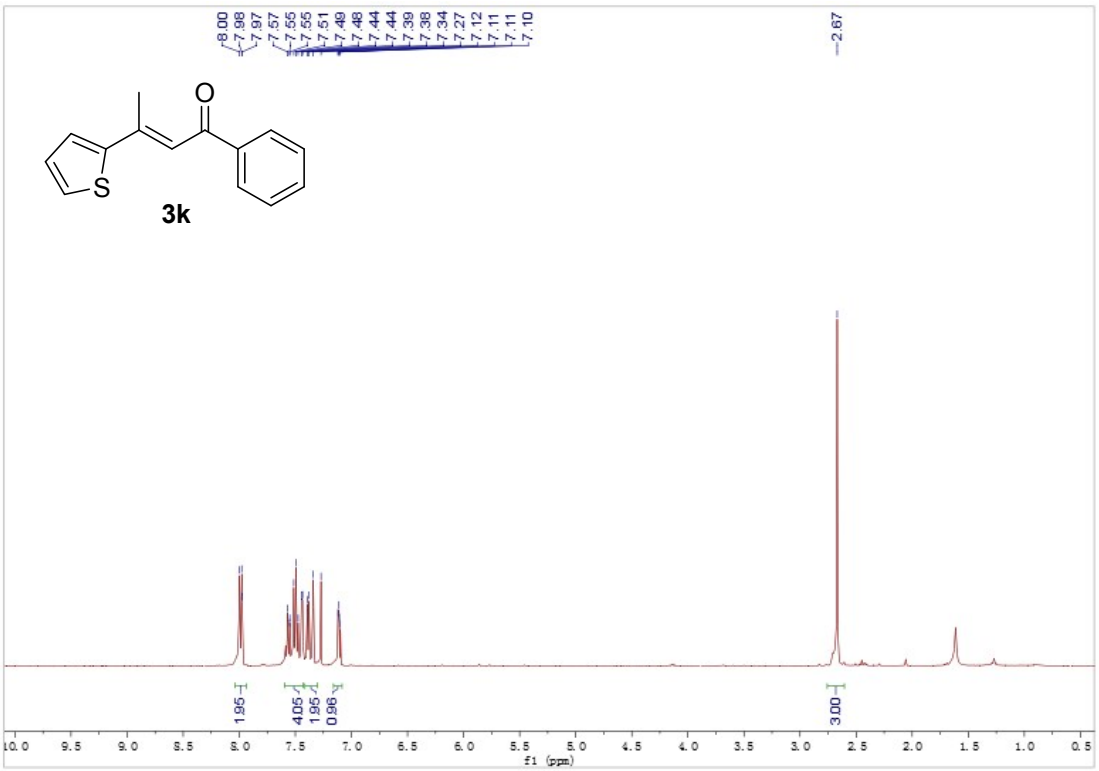

191.85
155.12
139.85
139.58
139.36
132.42
129.32
128.52
128.25
126.43
121.32
77.35
77.04
76.72
21.23
18.78
O
3h
f1 (ppm)

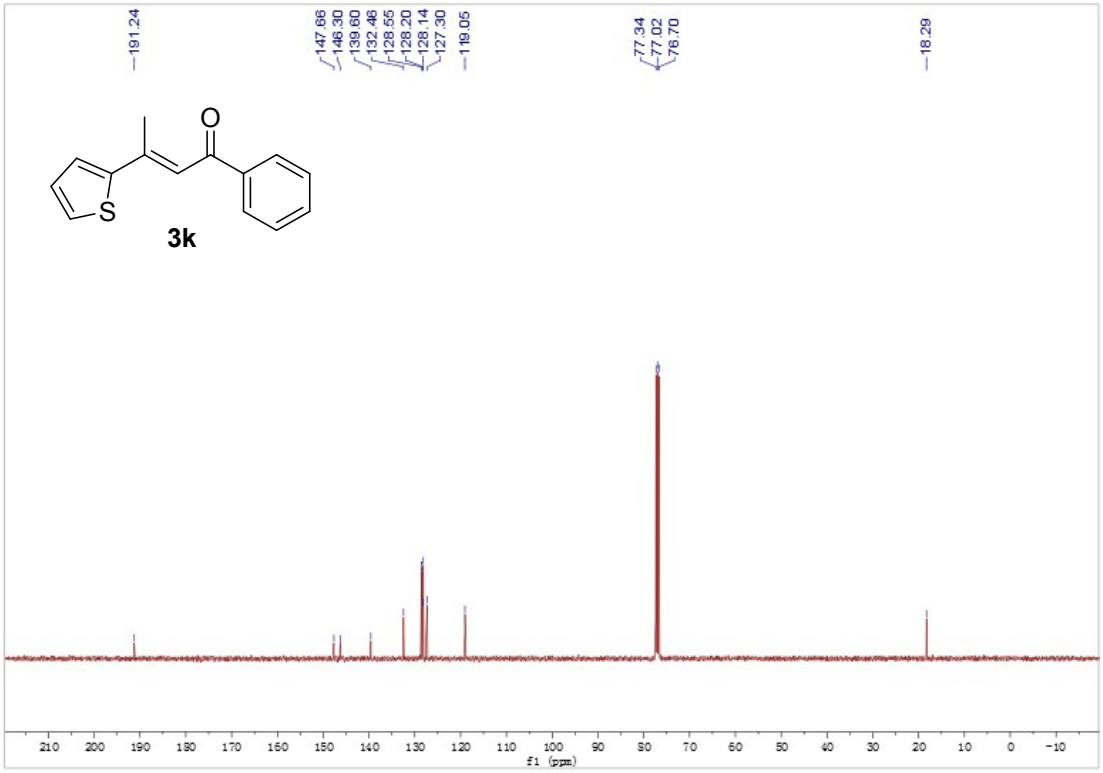

7.89
7.88
7.44
7.42
7.40
7.40
7.40
7.37
7.35
7.33
7.26
7.25
7.20
7.19
7.17
7.05
2.48
2.29
O
3i
2.04
4.03
2.03
1.22
0.85
3.21
3.00
f1 (ppm)

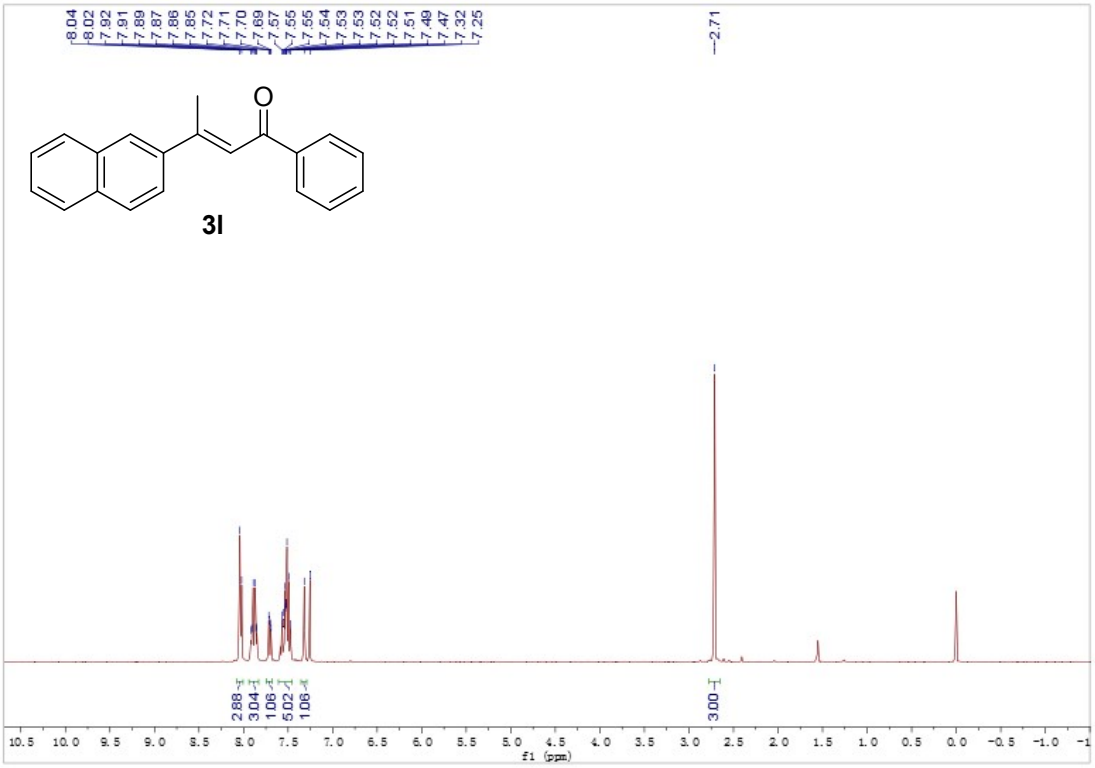

191.85
155.36
142.88
139.51
138.25
132.50
129.93
128.56
128.30
127.21
123.68
121.96
77.44
77.12
76.81
21.53
18.97
O
3i
f1 (ppm)

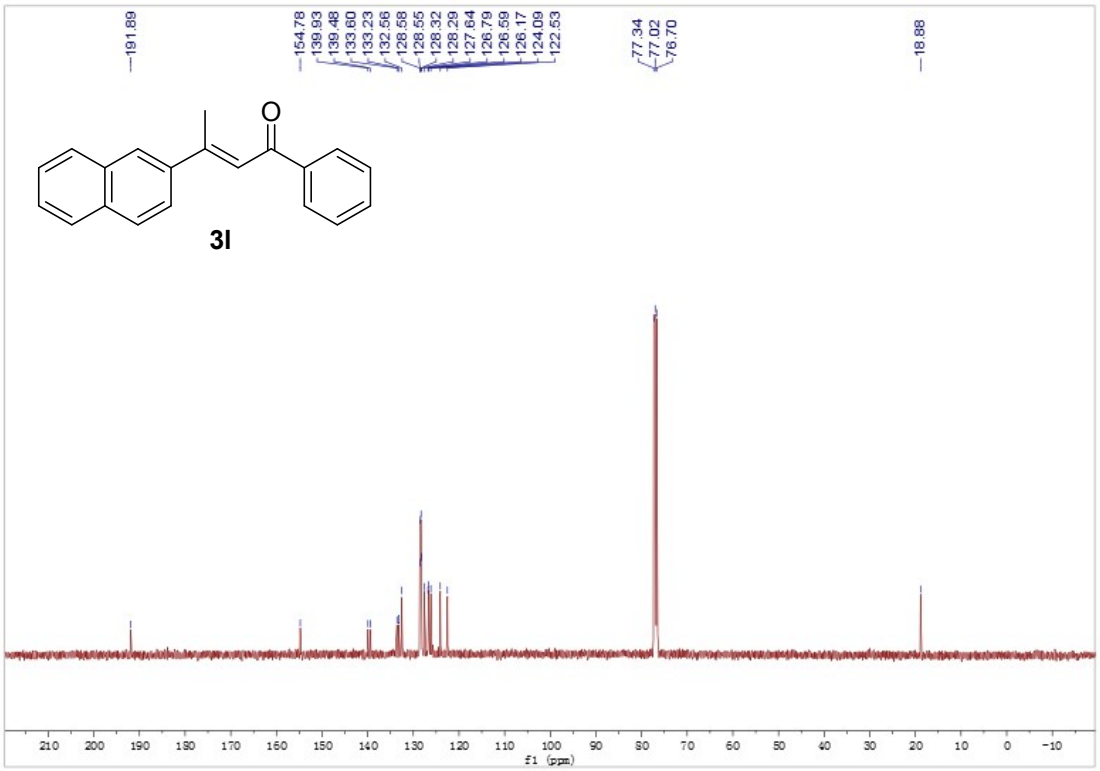

8.00
7.98
7.98
7.97
7.57
7.56
7.55
7.54
7.54
7.52
7.48
7.48
7.47
7.47
7.45
7.25
7.16
6.95
6.93
3.85
2.60
O
H3CO
3j
1.88
2.15
1.91
0.97
1.99
3.00
2.99
f1 (ppm)

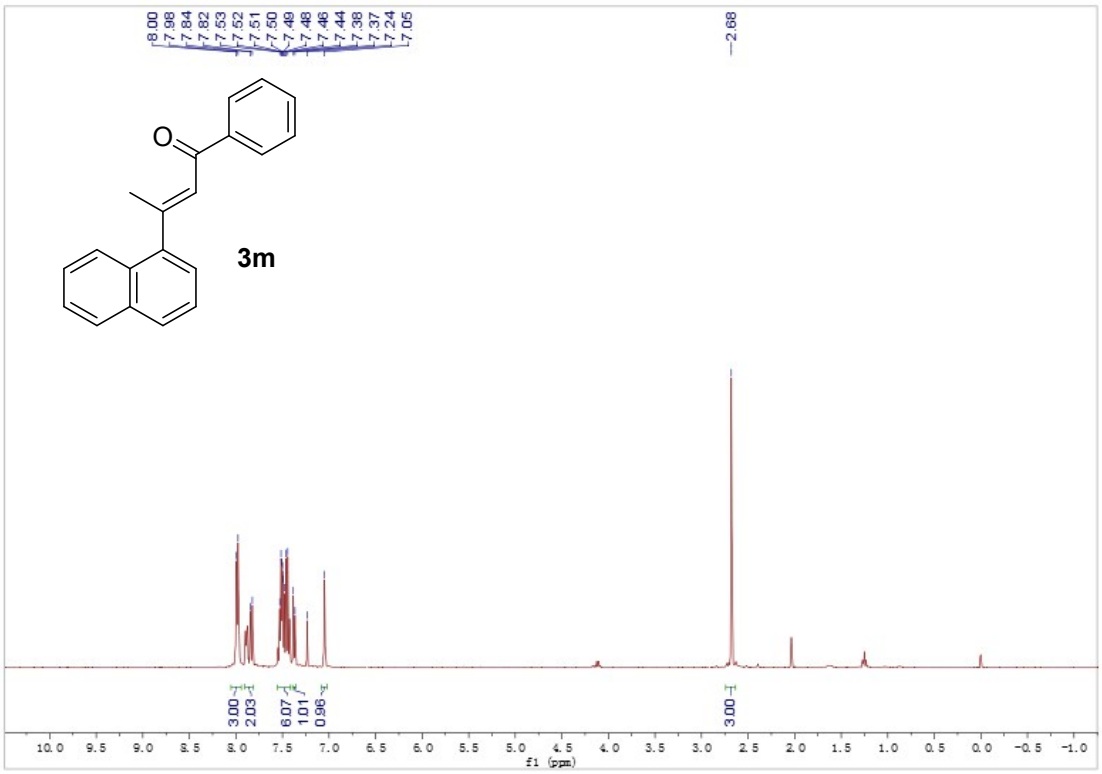

191.76
160.66
154.79
139.75
134.92
132.34
128.50
128.21
127.92
120.39
114.00
77.34
77.03
76.71
55.39
18.65
O
H3CO
3j
f1 (ppm)

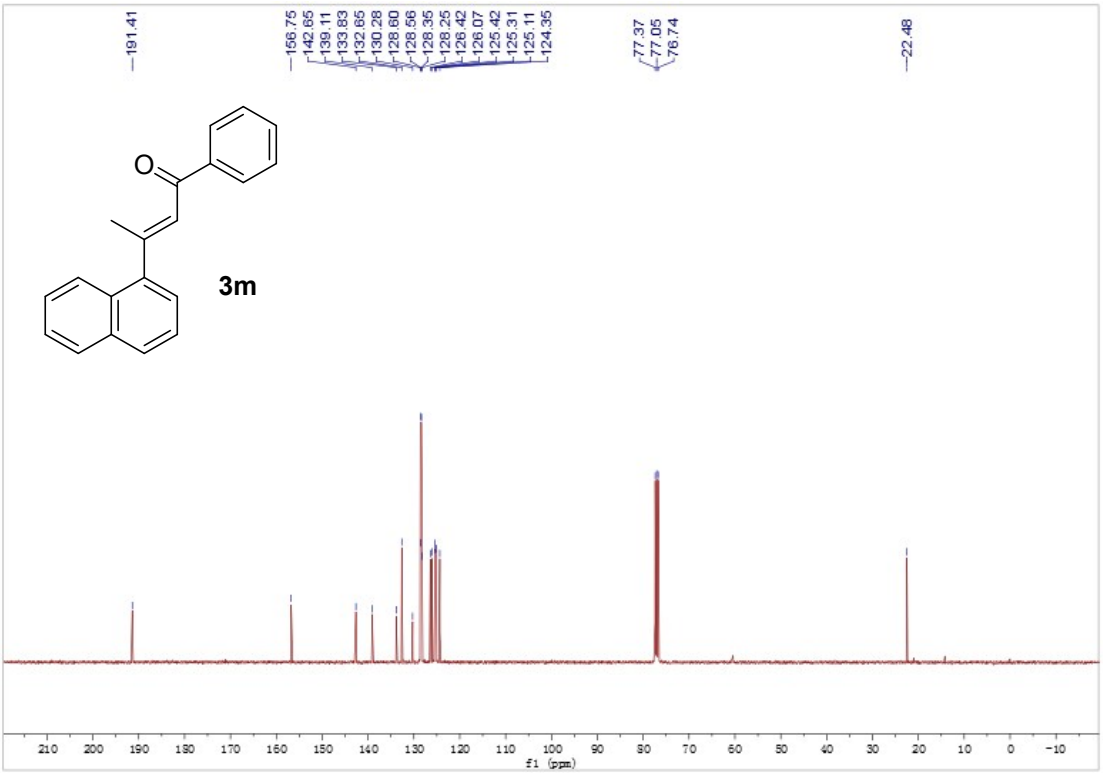

8.00
7.98
7.97
7.57
7.55
7.55
7.51
7.49
7.48
7.44
7.44
7.39
7.38
7.34
7.27
7.12
7.11
7.11
7.10
2.67
O
S
3k
1.95
4.05
1.95
0.96
3.00
f1 (ppm)

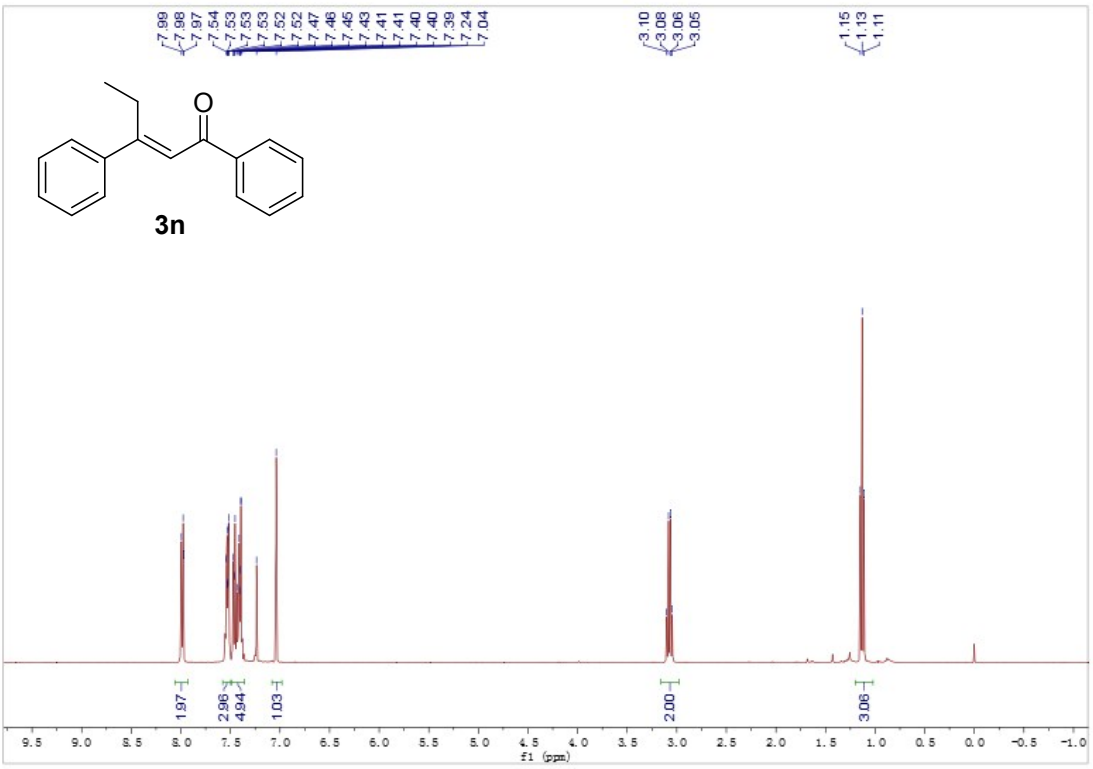

191.24
147.66
146.30
139.60
132.46
128.55
128.20
128.14
127.30
119.05
77.34
77.02
76.70
18.29
O
S
3k
f1 (ppm)

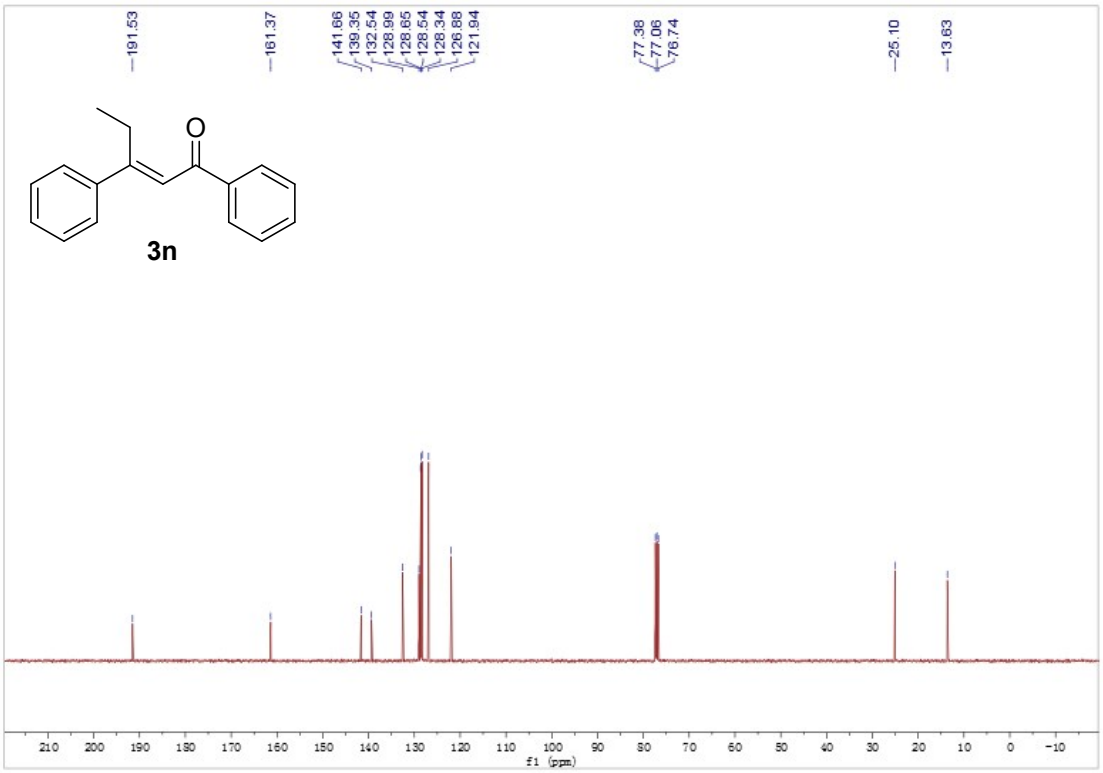

8.04
8.02
7.92
7.91
7.89
7.87
7.86
7.85
7.72
7.71
7.70
7.69
7.57
7.55
7.55
7.54
7.53
7.53
7.52
7.52
7.51
7.49
7.47
7.32
7.25
2.71
O
3l
2.88
3.04
1.06
5.02
1.06
3.00
f1 (ppm)

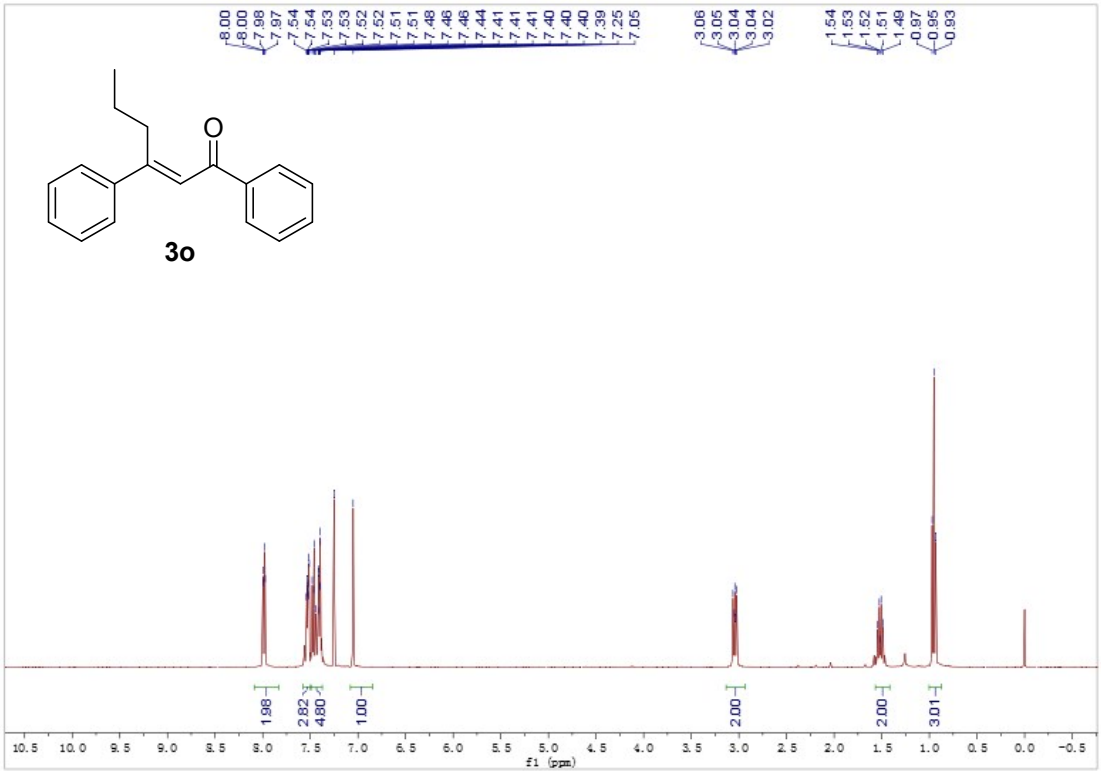

191.89
154.78
139.93
139.48
133.60
133.23
132.56
128.58
128.55
128.32
128.29
127.64
126.79
126.59
126.17
124.09
122.53
77.34
77.02
76.70
18.88
O
3l
f1 (ppm)

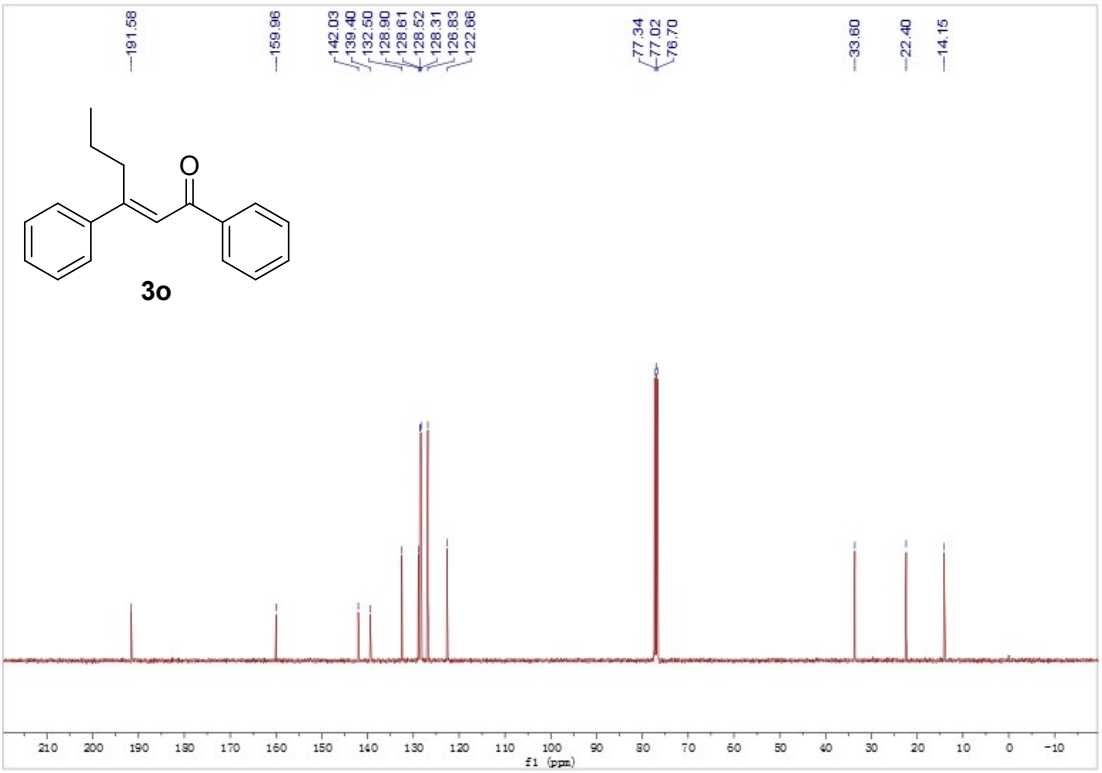

8.00
7.98
7.84
7.82
7.53
7.52
7.51
7.50
7.49
7.48
7.46
7.44
7.38
7.37
7.24
7.05
2.68
O
3m
3.00
2.03
6.07
1.01
0.96
3.00
f1 (ppm)

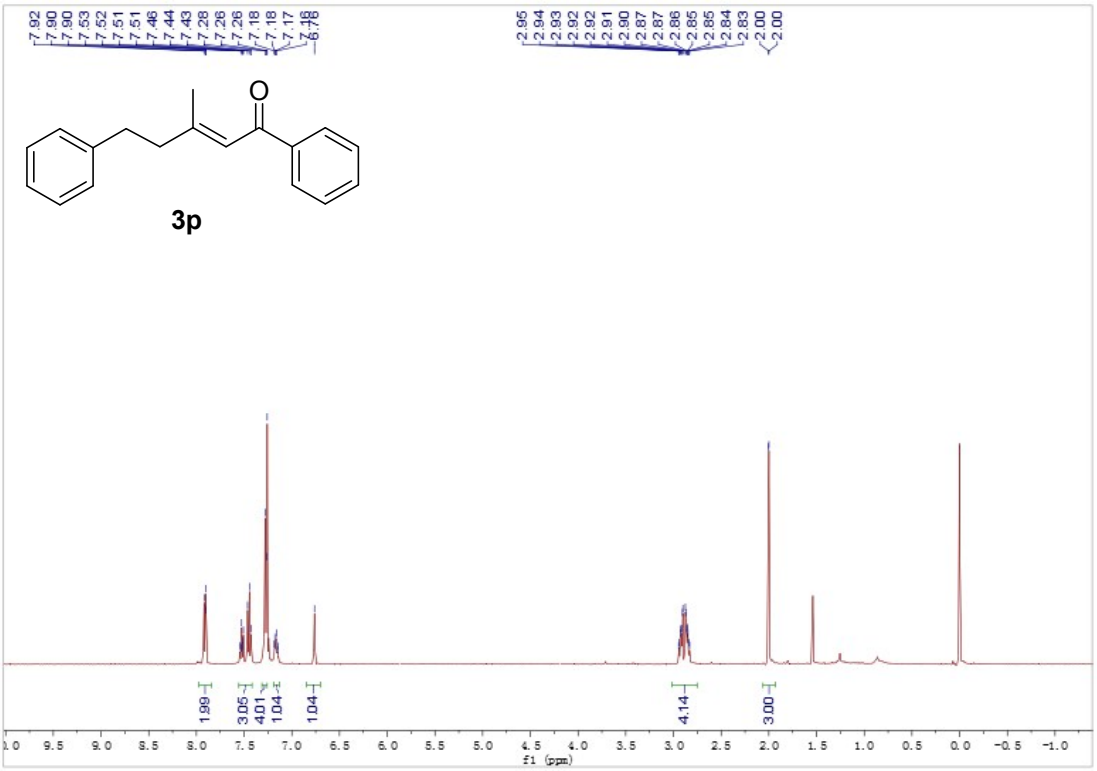

191.41
156.75
142.65
139.11
133.83
132.65
130.28
128.60
128.56
128.35
128.25
126.42
126.07
125.42
125.31
125.11
124.35
77.37
77.05
76.74
22.48
O
3m
f1 (ppm)

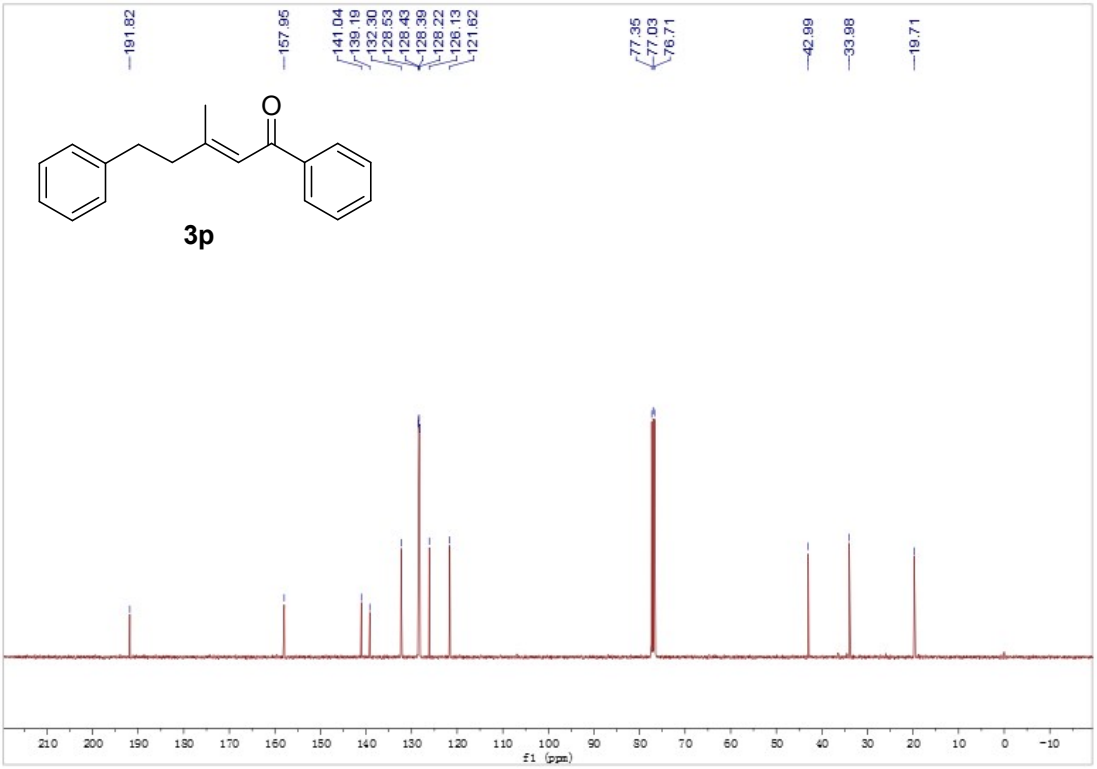

7.99
7.98
7.97
7.54
7.53
7.53
7.53
7.52
7.52
7.47
7.46
7.45
7.43
7.41
7.41
7.40
7.40
7.39
7.24
7.04
3.10
3.08
3.06
3.05
1.15
1.13
1.11
O
3n
1.97
2.96
4.94
1.03
2.00
3.06
f1 (ppm)

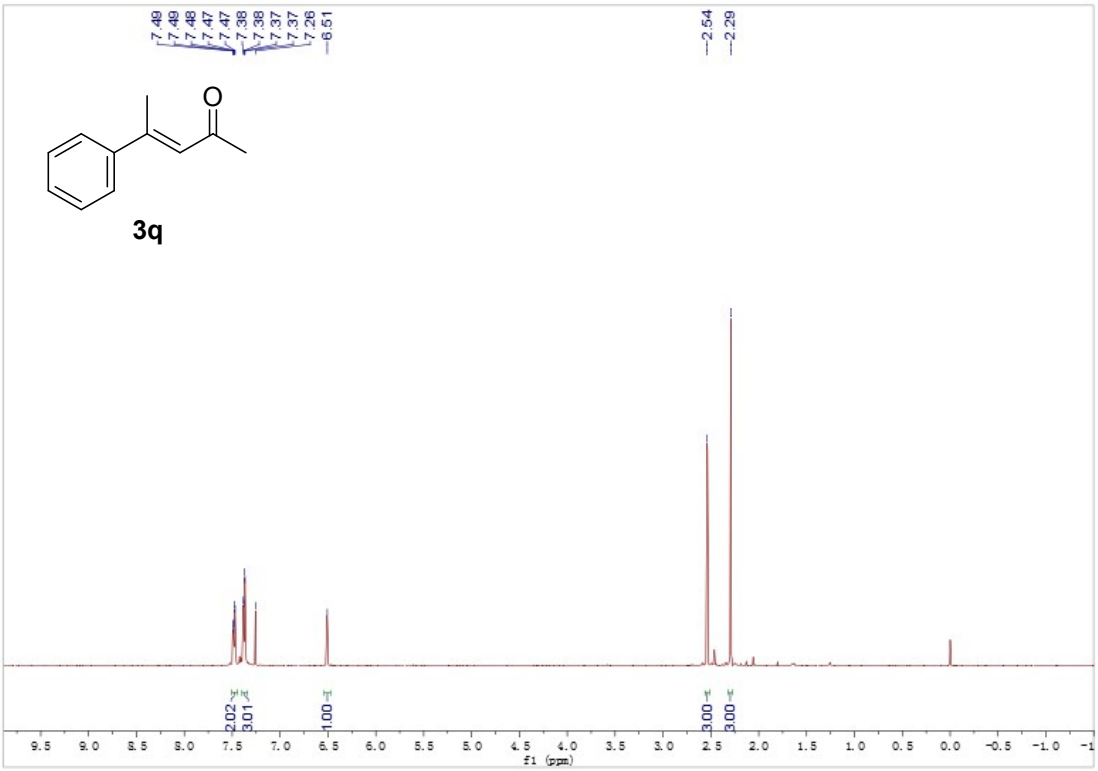

191.53
161.37
141.66
139.35
132.54
128.99
128.65
128.54
128.34
126.88
121.94
77.38
77.06
76.74
25.10
13.63
O
3n
f1 (ppm)

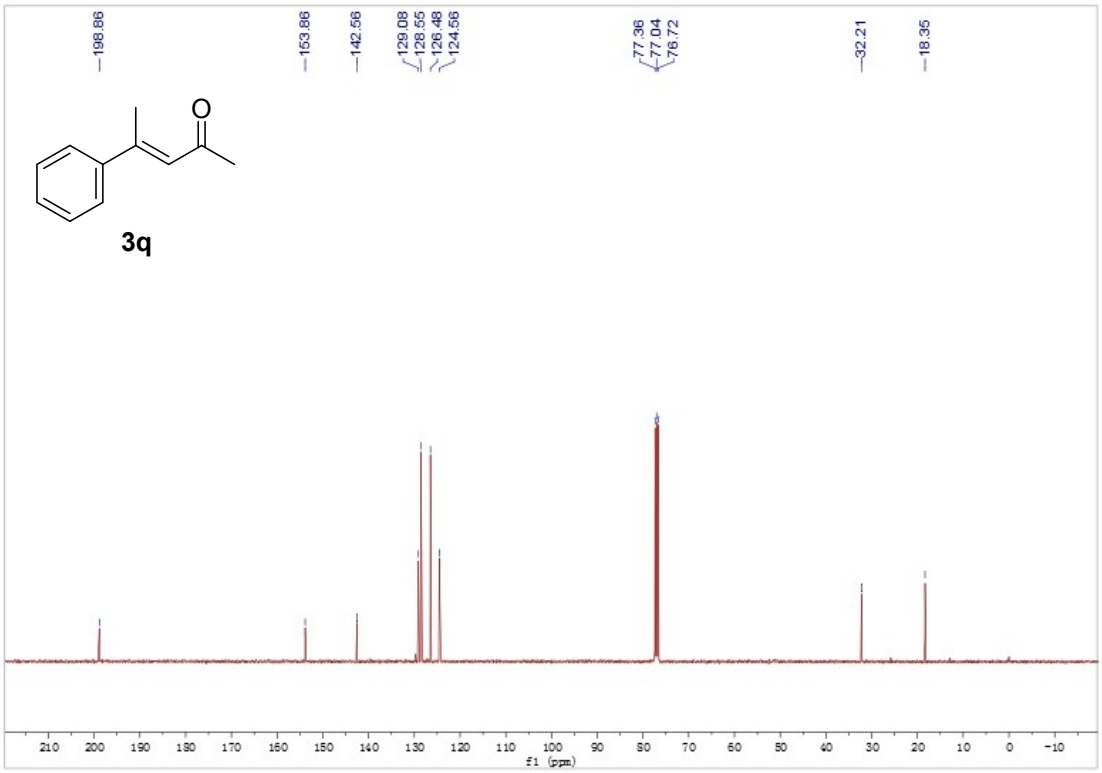

8.00
8.00
7.98
7.97
7.54
7.54
7.53
7.53
7.52
7.52
7.51
7.51
7.48
7.46
7.46
7.44
7.41
7.41
7.41
7.40
7.40
7.40
7.39
7.25
7.05
3.06
3.05
3.04
3.04
3.02
1.54
1.53
1.52
1.51
1.49
0.97
0.95
0.93
O
3o
1.98
2.82
4.80
1.00
2.00
2.00
3.01
f1 (ppm)

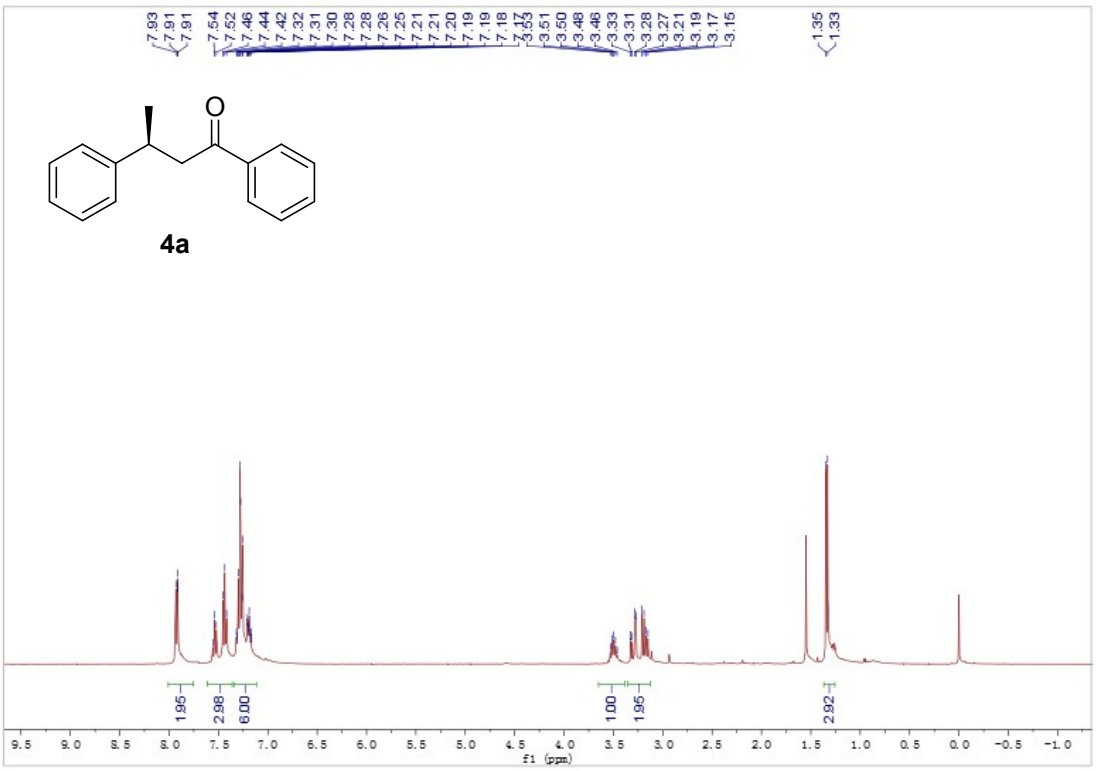

191.58
159.96
142.03
139.40
132.50
128.90
128.61
128.52
128.31
126.83
122.66
77.34
77.02
76.70
33.60
22.40
14.15
O
3o
f1 (ppm)

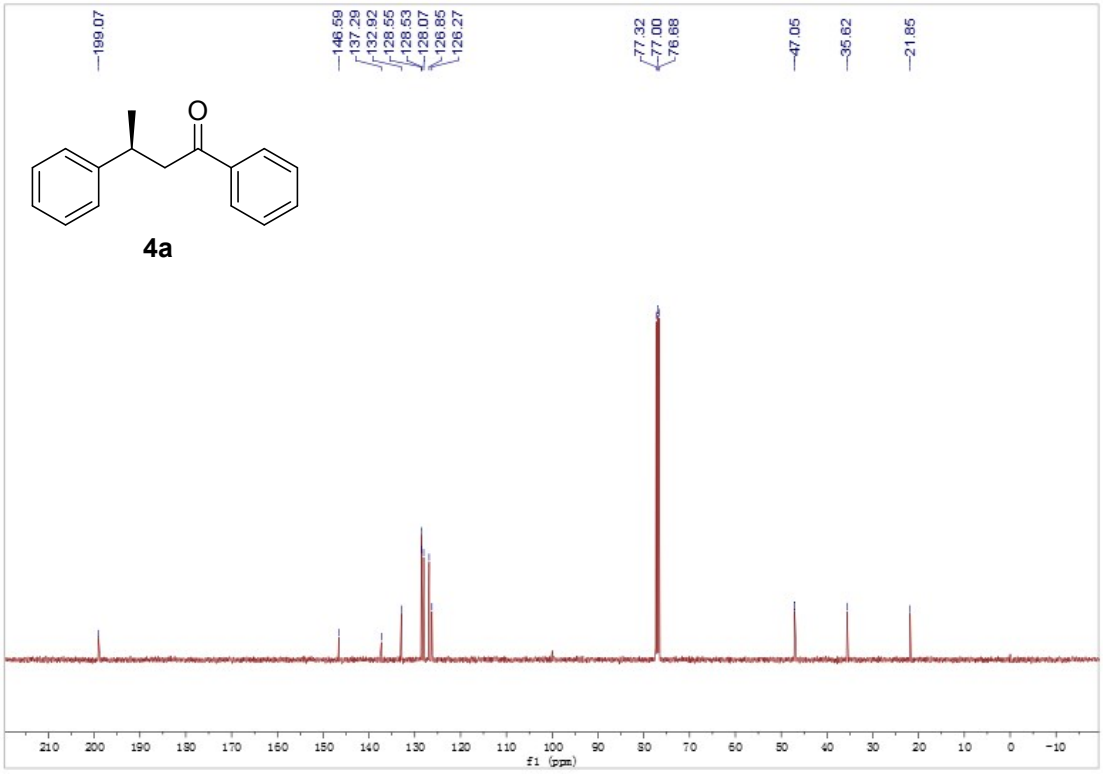

7.92
7.90
7.90
7.53
7.52
7.51
7.51
7.46
7.44
7.43
7.28
7.26
7.18
7.18
7.17
2.96
2.94
2.93
2.92
2.92
2.91
2.90
2.87
2.86
2.85
2.85
2.84
2.83
2.00
2.00
O
3p
1.99
3.05
4.01
1.04
1.04
4.14
3.00
f1 (ppm)

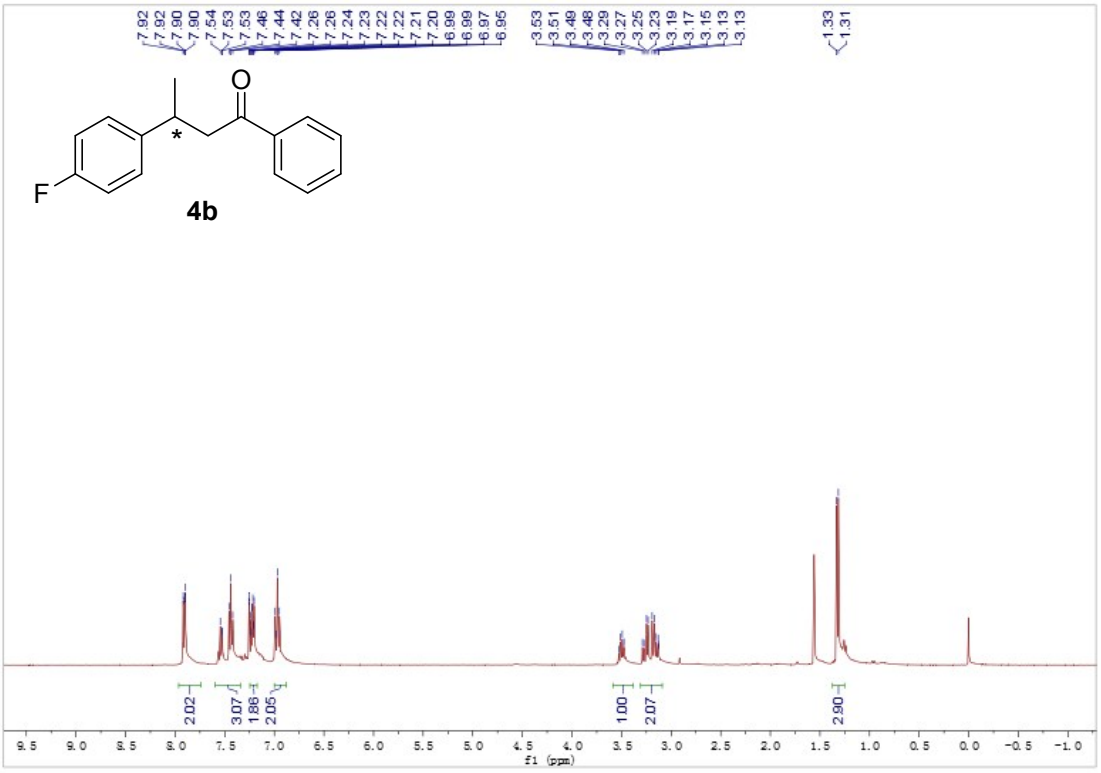

191.82
157.95
141.04
139.19
132.30
128.53
128.43
128.39
128.22
126.13
121.62
77.35
77.03
76.71
42.99
33.98
19.71
O
3p
f1 (ppm)

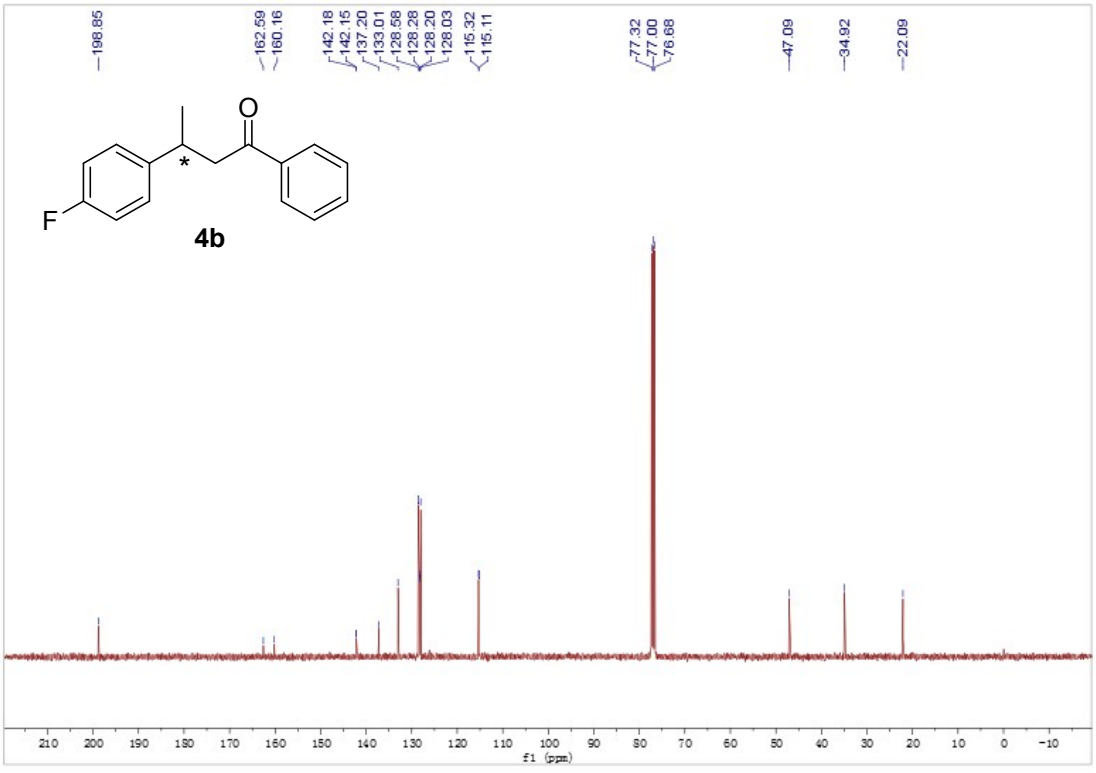

7.49
7.49
7.48
7.47
7.47
7.38
7.38
7.37
7.37
7.26
6.51
2.54
2.29
O
3q
2.02
3.01
1.00
3.00
3.00
f1 (ppm)

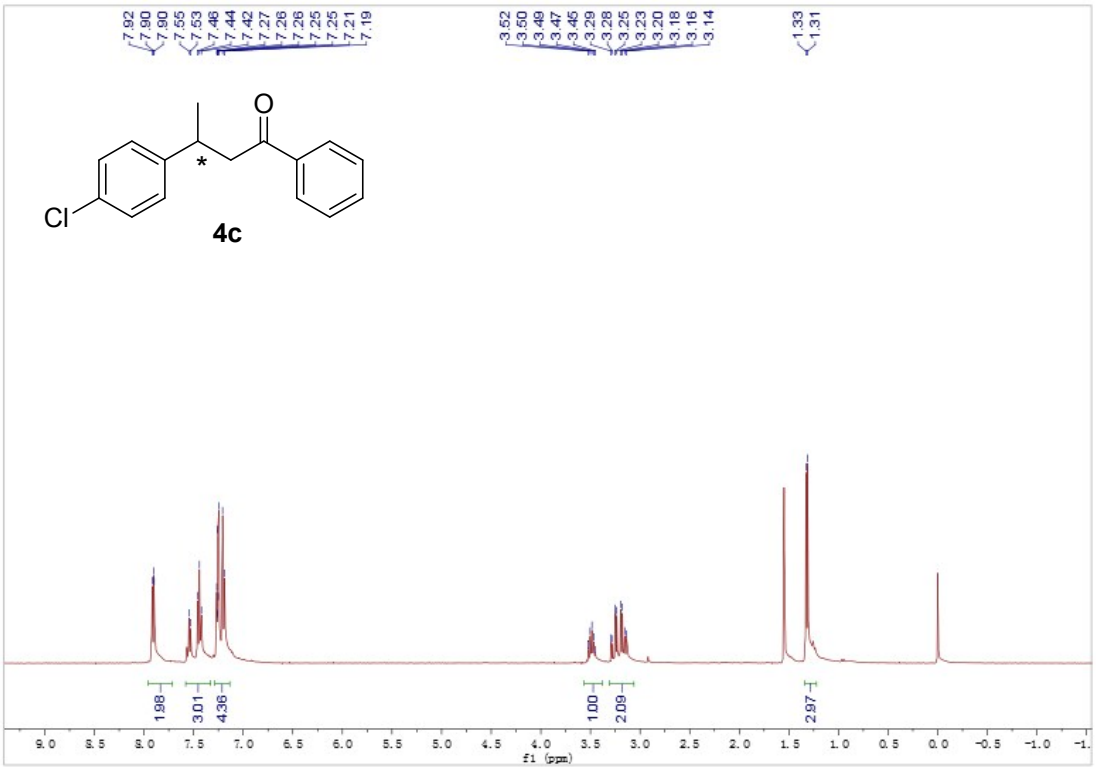

198.86
153.86
142.56
129.08
128.55
126.48
124.56
77.36
77.04
76.72
32.21
18.35
O
3q
f1 (ppm)

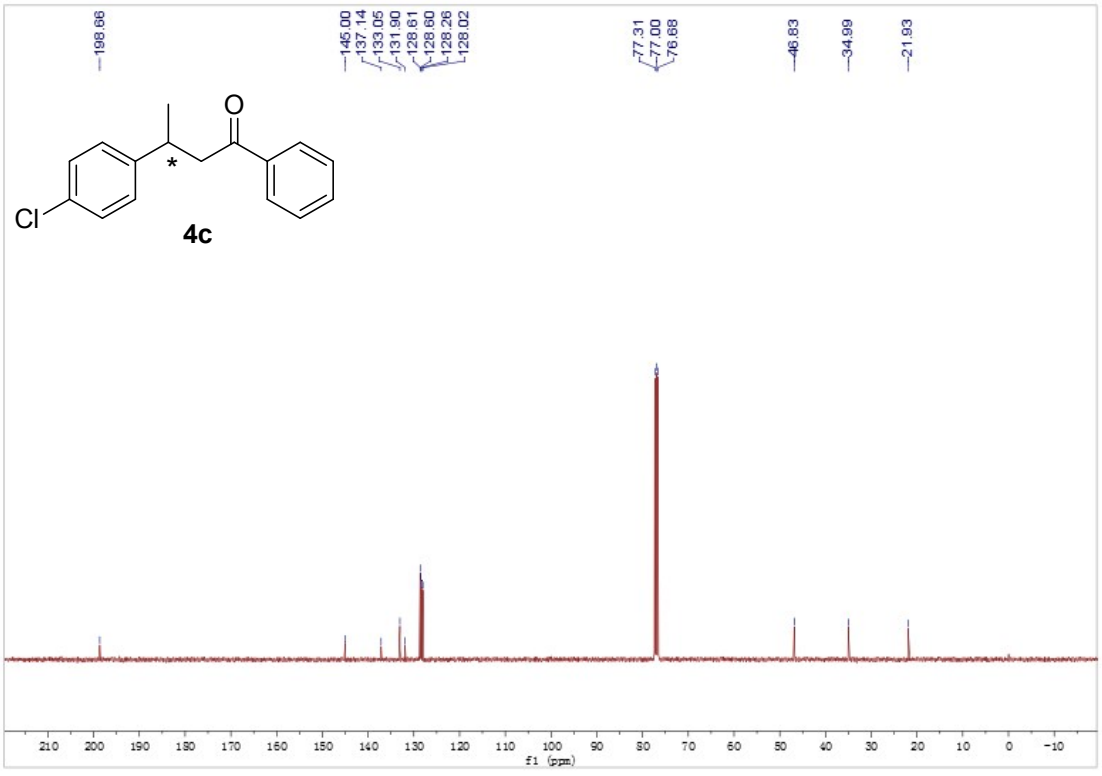

7.93
7.91
7.91
7.54
7.52
7.46
7.44
7.42
7.32
7.31
7.30
7.28
7.28
7.26
7.25
7.21
7.21
7.20
7.19
7.19
7.18
7.17
3.53
3.51
3.50
3.48
3.46
3.33
3.31
3.28
3.27
3.21
3.19
3.17
3.15
1.35
1.33
O
4a
1.95
2.98
6.00
1.00
1.95
2.92
f1 (ppm)

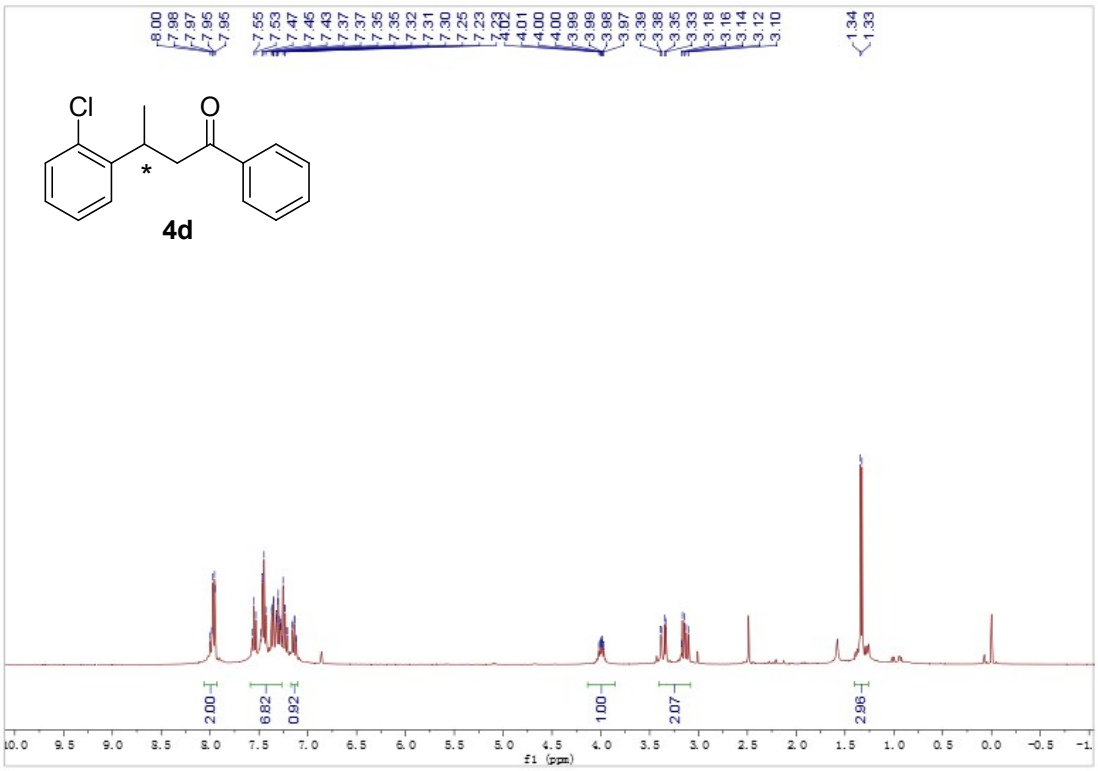

199.07
146.59
137.29
132.92
128.55
128.53
128.07
126.85
126.27
77.32
77.00
76.68
47.05
35.62
21.85
O
4a
f1 (ppm)

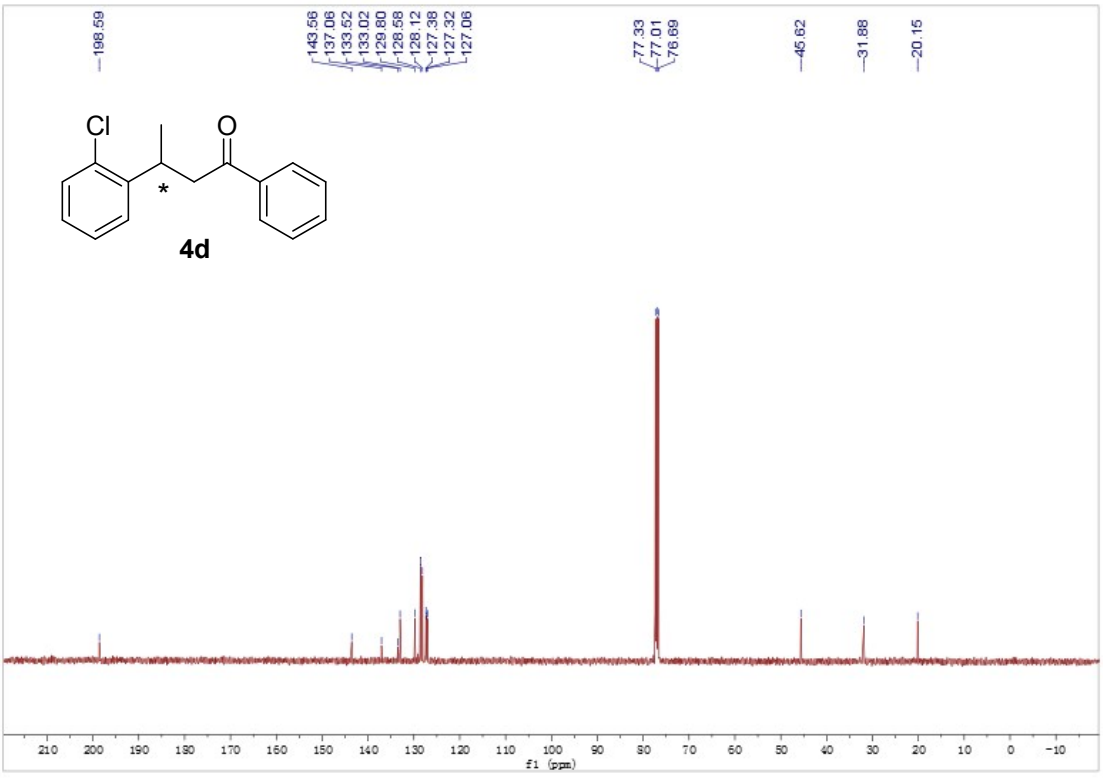

7.92
7.92
7.90
7.90
7.54
7.53
7.53
7.46
7.44
7.42
7.26
7.26
7.24
7.23
7.22
7.22
7.21
7.20
6.99
6.99
6.97
6.95
3.53
3.51
3.49
3.48
3.29
3.27
3.25
3.23
3.19
3.17
3.15
3.13
3.13
1.33
1.31
O
*
F
4b
2.02
3.07
1.86
2.05
1.00
2.07
2.90
f1 (ppm)

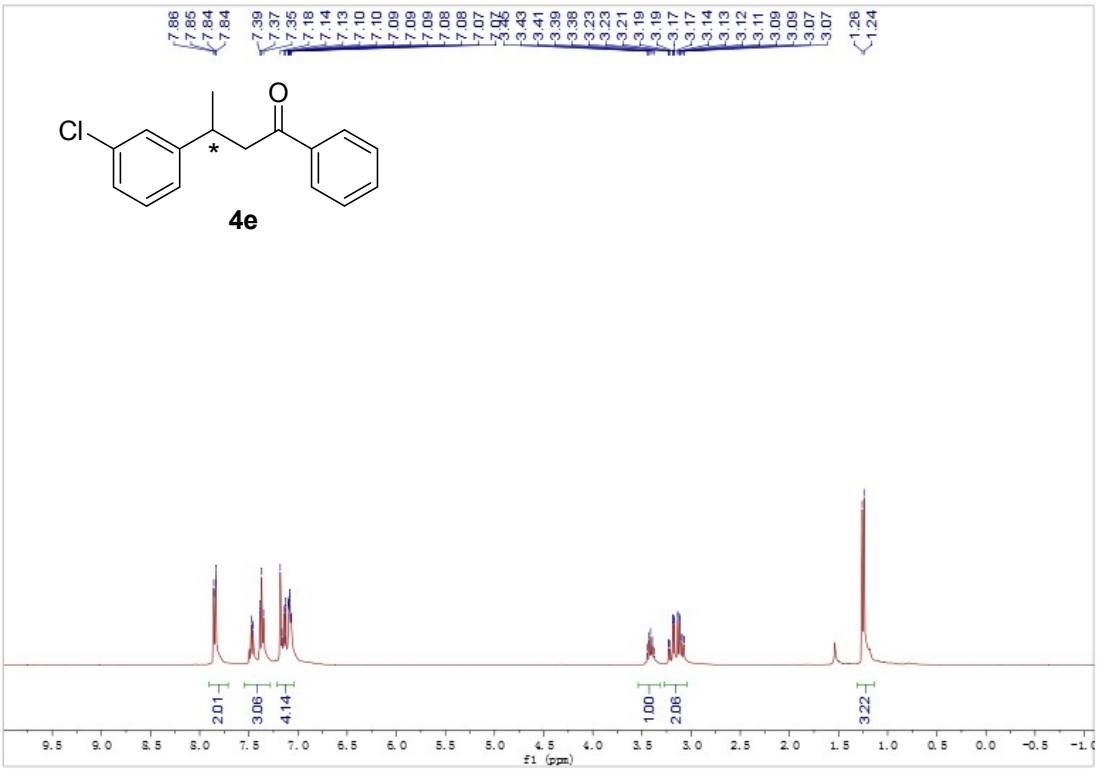

198.85
162.59
160.16
142.18
142.15
137.20
133.01
128.58
128.28
128.20
128.03
115.32
115.11
77.32
77.00
76.68
47.09
34.92
22.09
O
*
F
4b
f1 (ppm)

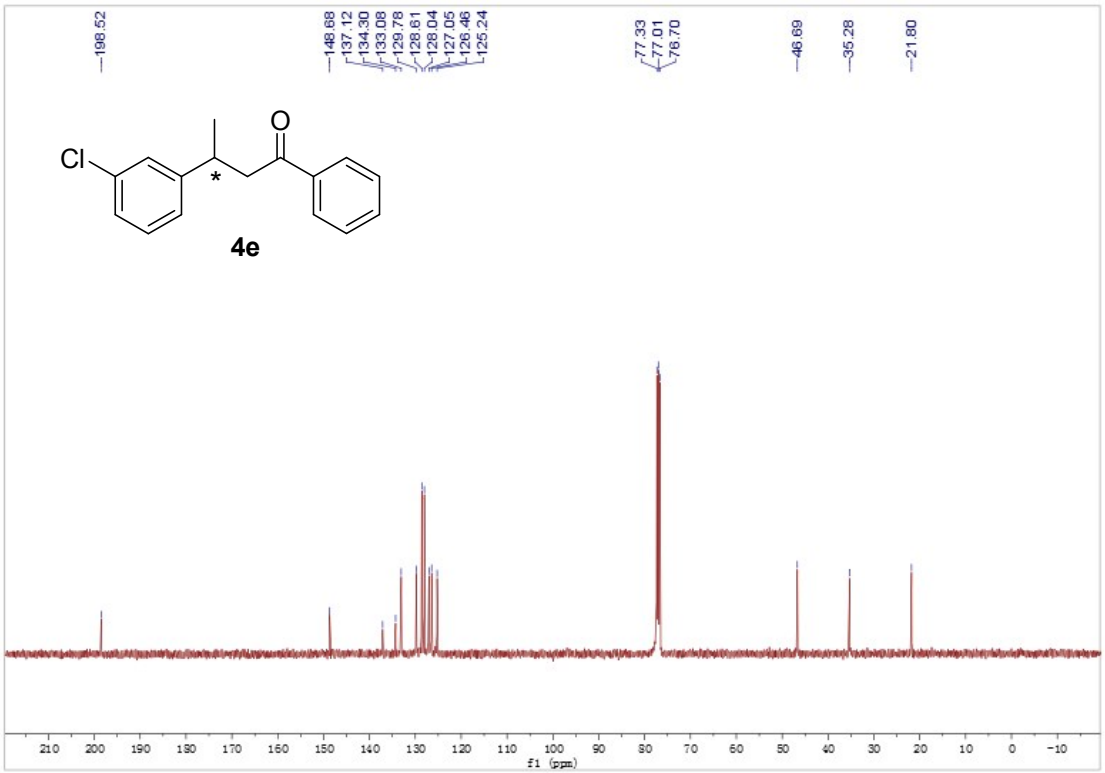

7.92
7.90
7.90
7.55
7.53
7.46
7.44
7.42
7.27
7.26
7.26
7.25
7.25
7.21
7.19
3.52
3.50
3.49
3.47
3.45
3.29
3.28
3.25
3.23
3.20
3.18
3.16
3.14
1.33
1.31
O
*
Cl
4c
1.98
3.01
4.36
1.00
2.09
2.97
f1 (ppm)

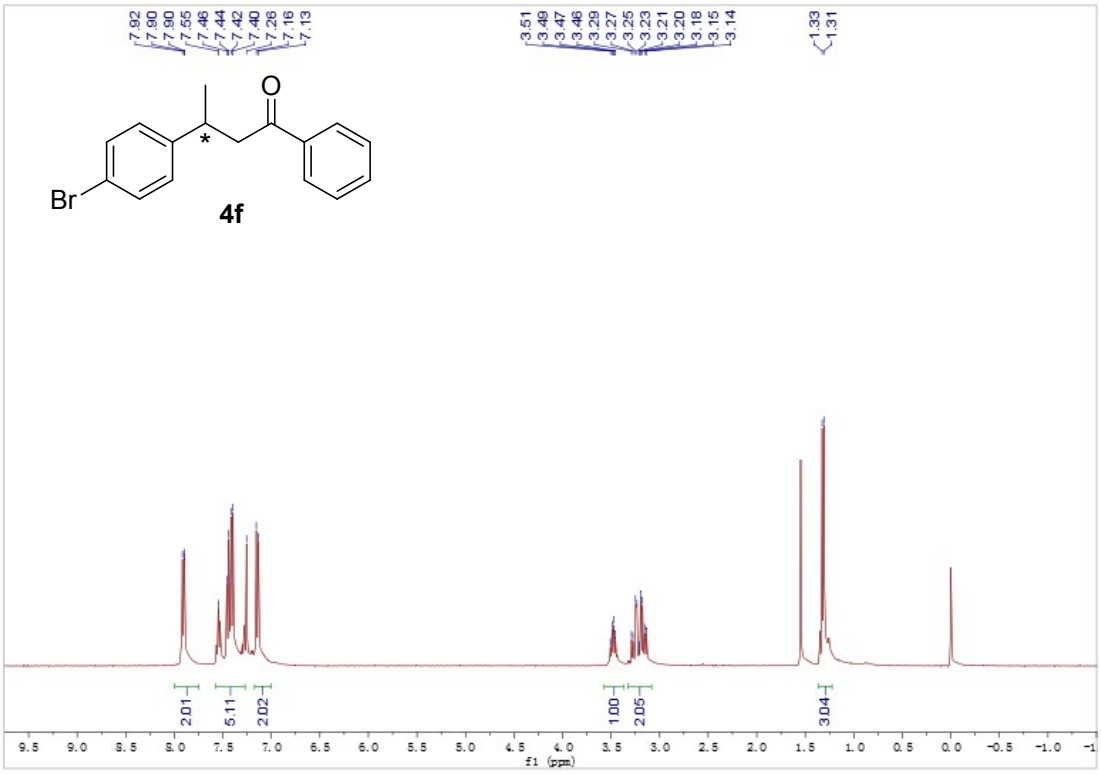

198.66
145.00
137.14
133.05
131.90
128.61
128.60
128.28
128.02
77.31
77.00
76.68
46.83
34.99
21.93
O
*
Cl
4c
f1 (ppm)

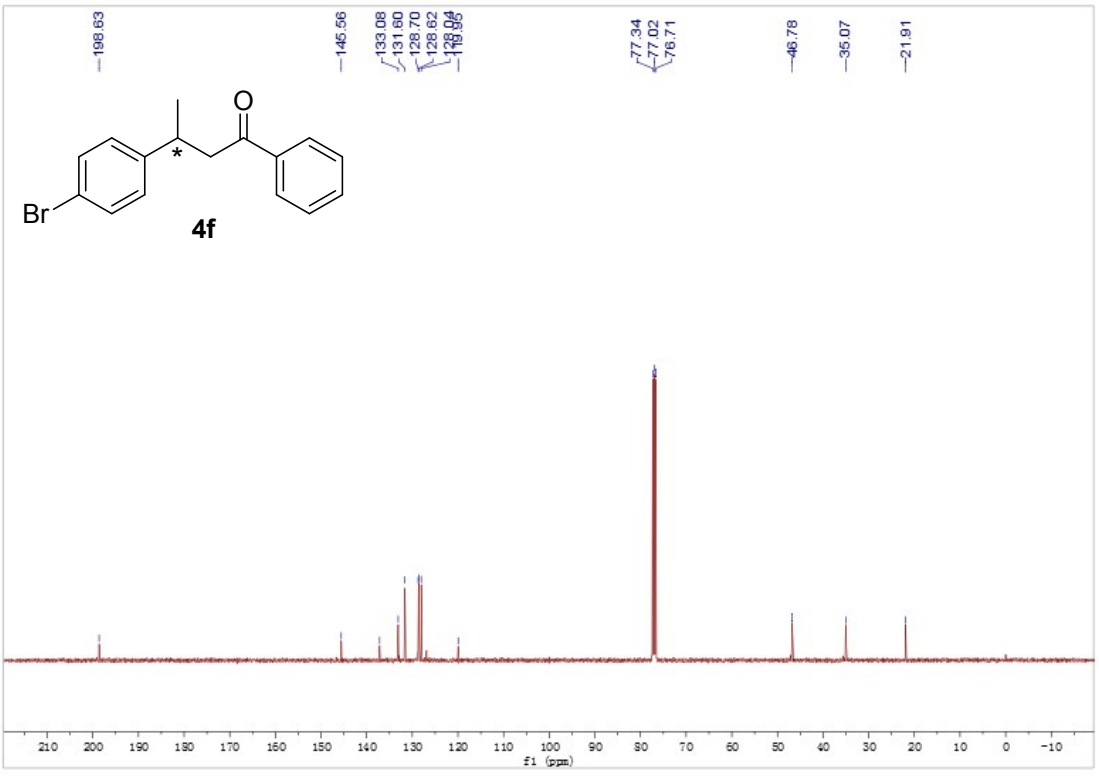

8.00
7.98
7.97
7.96
7.95
7.55
7.53
7.47
7.45
7.43
7.37
7.37
7.35
7.35
7.32
7.31
7.30
7.25
7.23
4.02
4.01
4.00
4.00
3.99
3.99
3.98
3.97
3.39
3.38
3.35
3.33
3.18
3.16
3.14
3.12
3.10
1.34
1.33
Cl
O
*
4d
2.00
6.82
0.92
1.00
2.07
2.96
f1 (ppm)

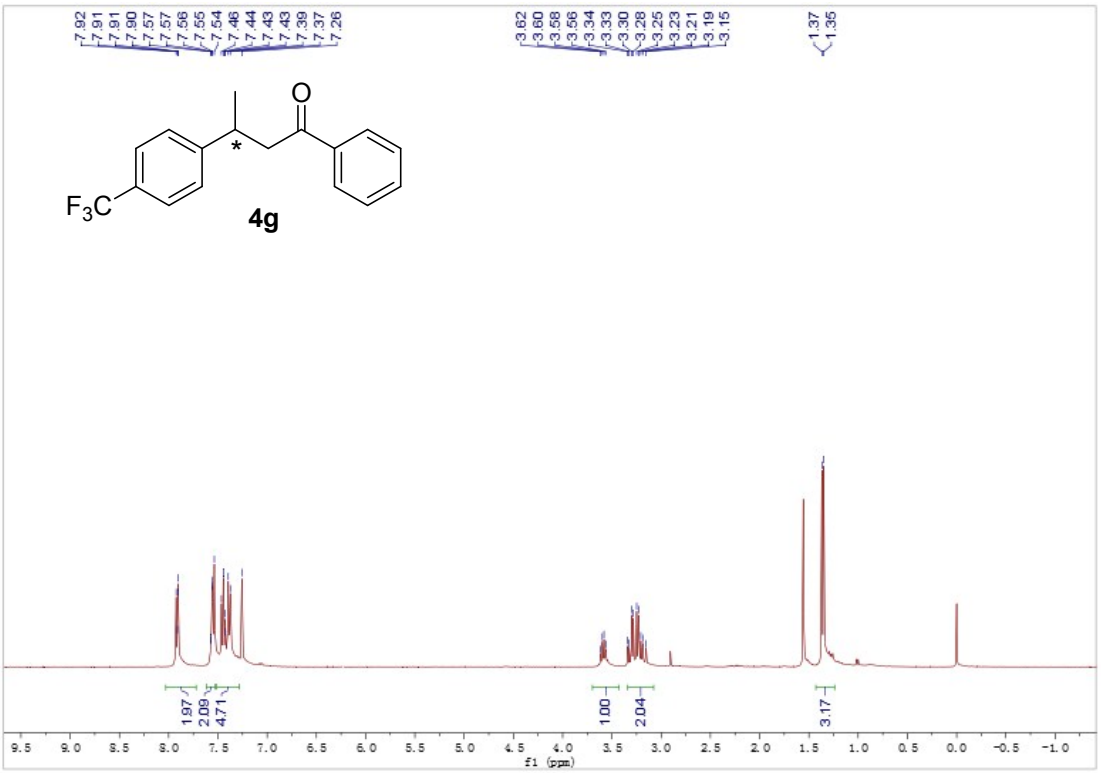

198.59
143.56
137.06
133.52
133.02
129.80
128.58
128.12
127.38
127.32
127.06
77.33
77.01
76.69
45.62
31.88
20.15
Cl
O
*
4d
f1 (ppm)

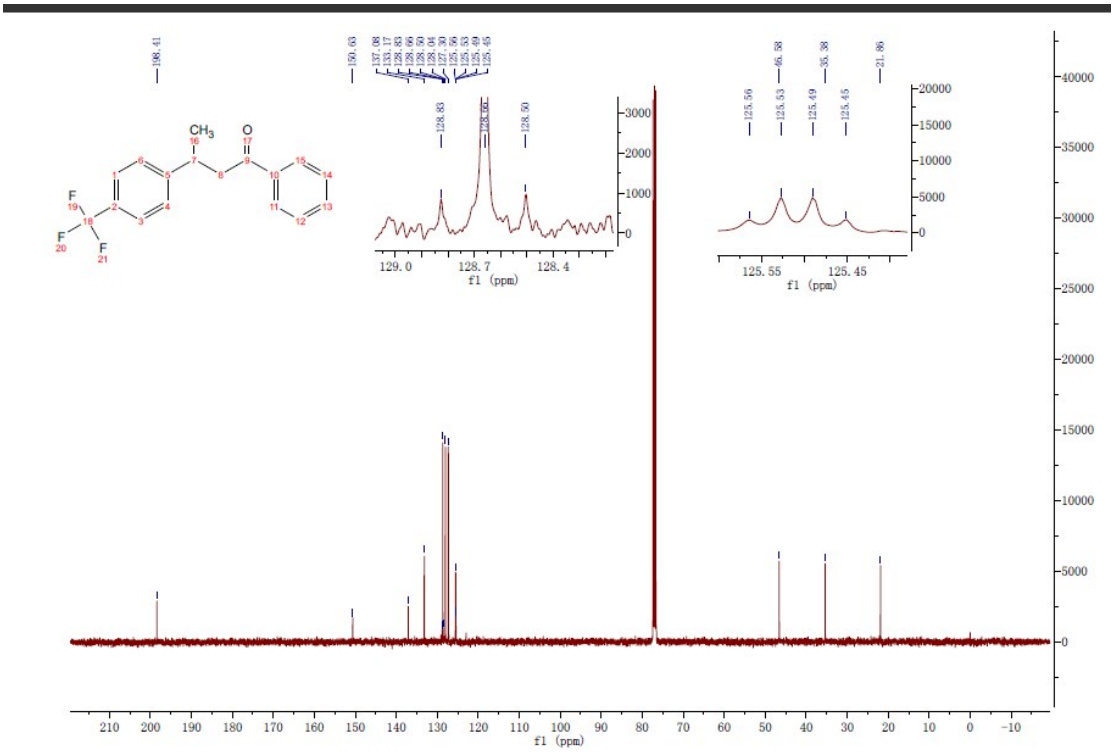

7.86
7.85
7.84
7.84
7.39
7.37
7.35
7.18
7.14
7.13
7.10
7.10
7.09
7.09
7.09
7.08
7.08
7.07
7.07
3.45
3.43
3.41
3.39
3.38
3.23
3.23
3.21
3.19
3.19
3.17
3.17
3.14
3.13
3.12
3.11
3.09
3.09
3.07
3.07
1.26
1.24
Cl
O
*
4e
2.01
3.06
4.14
1.00
2.06
3.22
f1 (ppm)

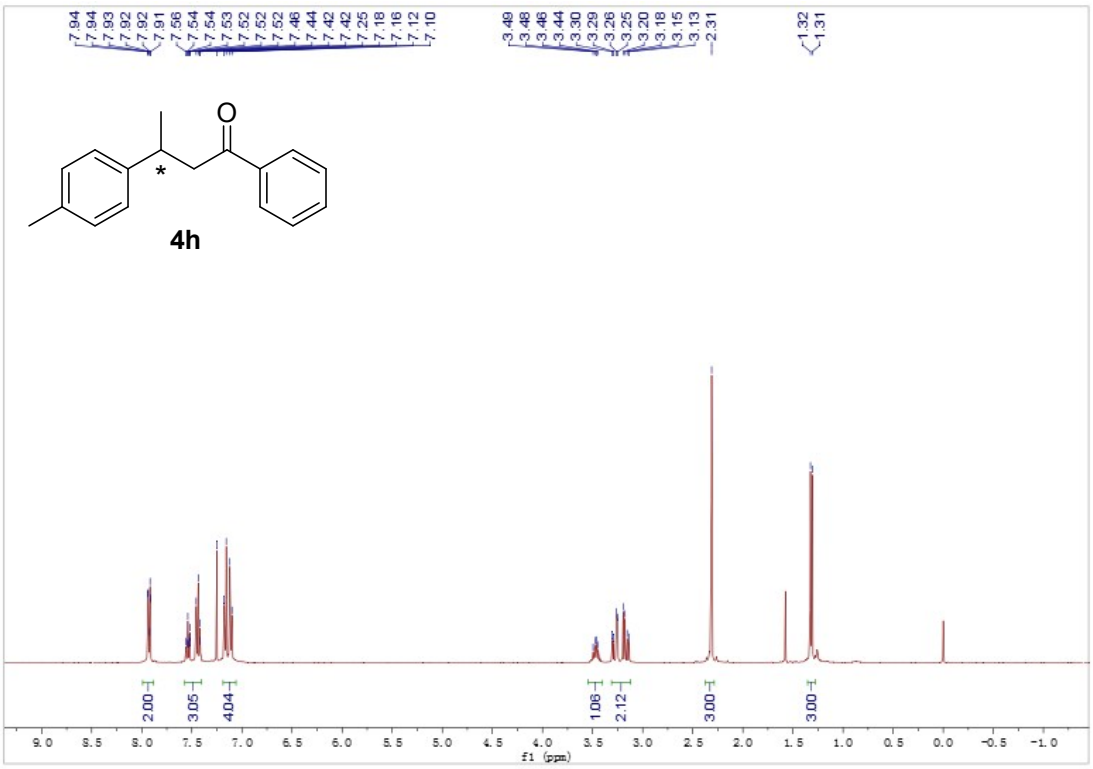

198.52
148.88
137.12
134.30
133.08
129.78
128.61
128.04
127.05
126.46
125.24
77.33
77.01
76.70
46.69
35.28
21.80
Cl
O
*
4e
f1 (ppm)

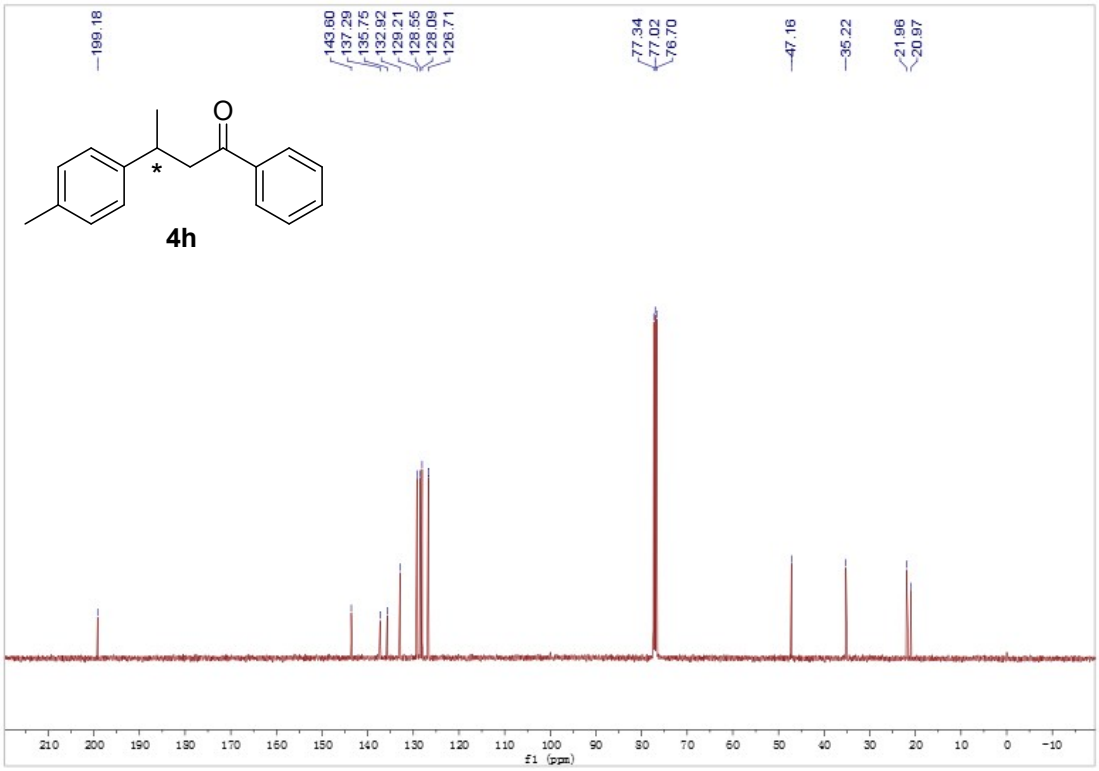

7.92
7.90
7.90
7.55
7.46
7.44
7.42
7.40
7.26
7.16
7.13
3.51
3.49
3.47
3.46
3.29
3.27
3.25
3.23
3.21
3.20
3.18
3.15
3.14
1.33
1.31
O
*
Br
4f
2.01
5.11
2.02
1.00
2.05
3.04
f1 (ppm)

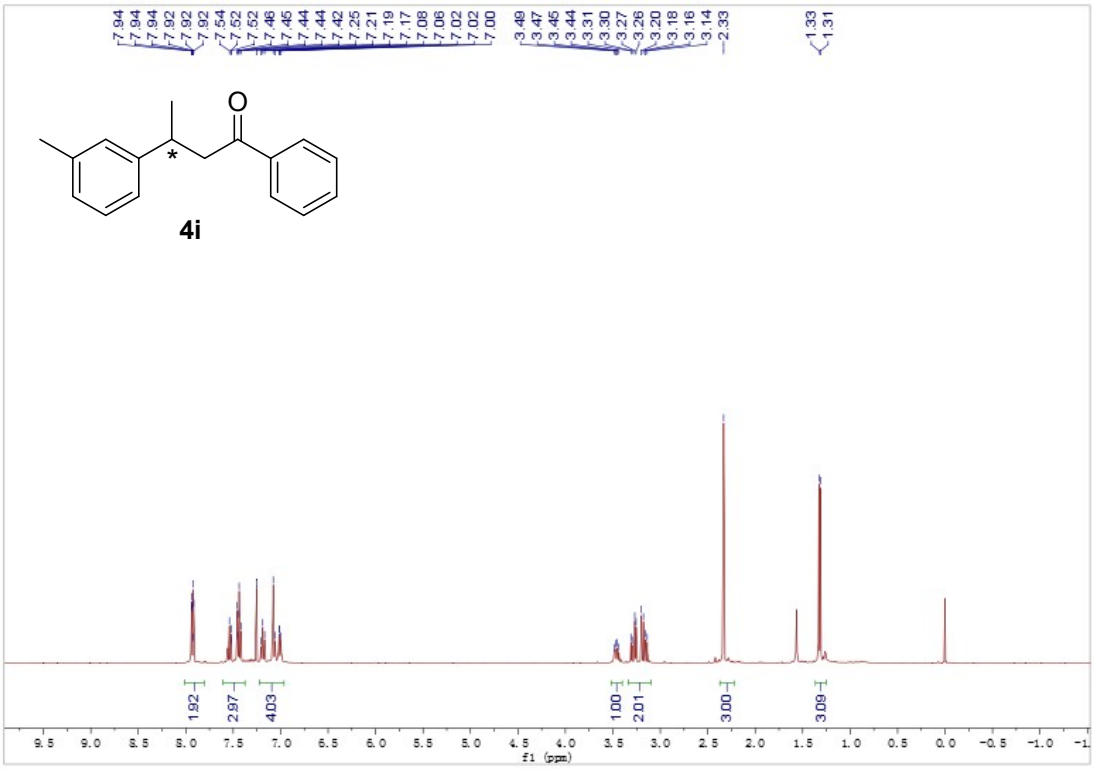

198.63
145.56
133.08
131.60
128.70
128.62
128.04
77.34
77.02
76.71
46.78
35.07
21.91
O
*
Br
4f
f1 (ppm)

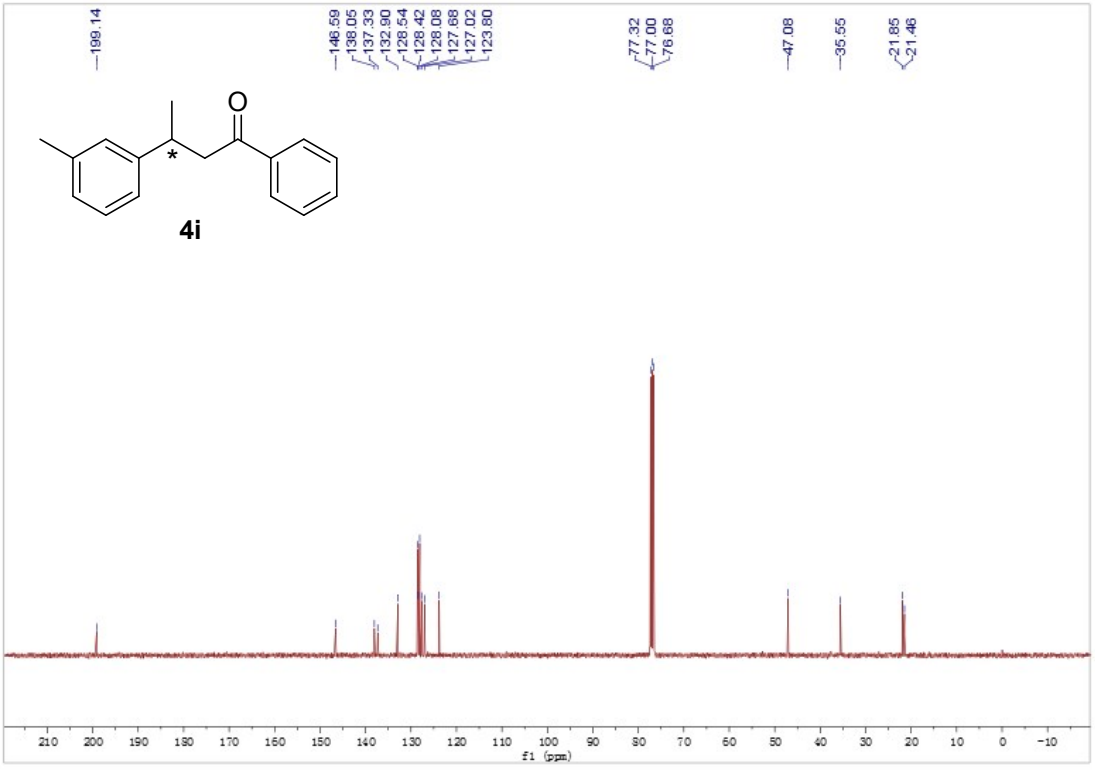

7.92
7.91
7.91
7.90
7.57
7.57
7.56
7.55
7.54
7.46
7.44
7.43
7.43
7.39
7.37
7.26
3.62
3.60
3.58
3.56
3.34
3.33
3.30
3.28
3.25
3.23
3.21
3.19
3.15
1.37
1.35
O
*
F3C
4g
1.97
2.09
4.71
1.00
2.04
3.17
f1 (ppm)

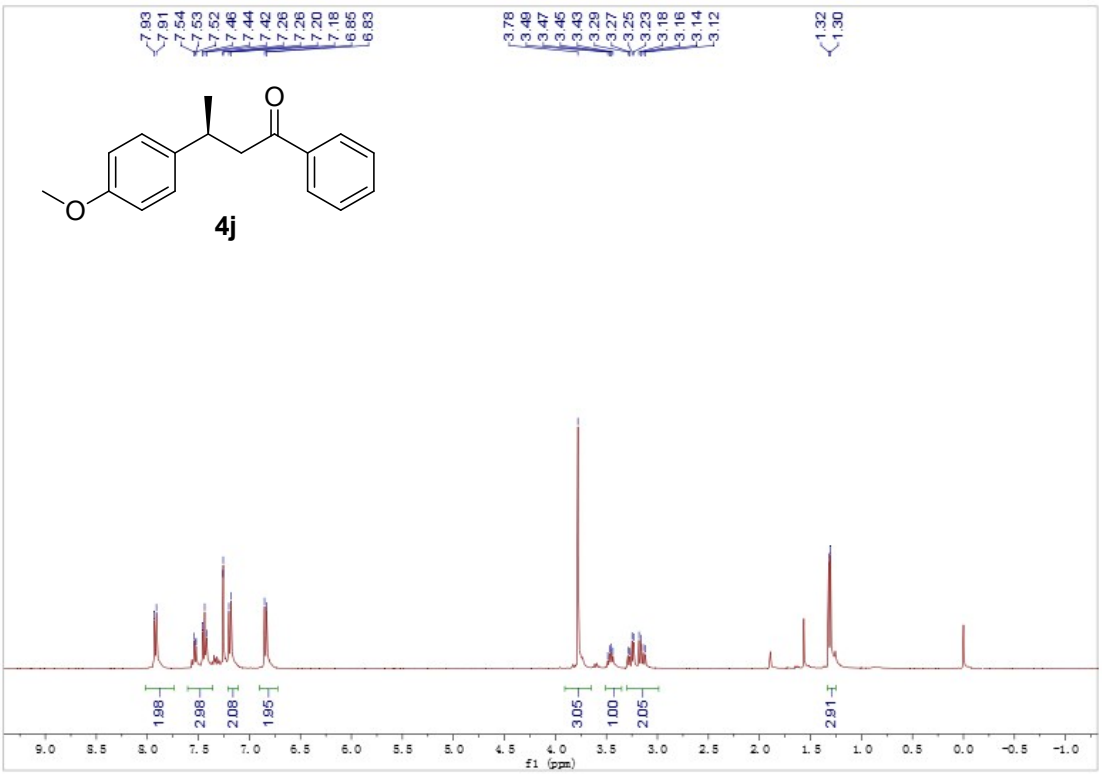

196.41
150.63
137.08
133.17
128.83
128.66
128.50
128.04
127.30
125.56
125.53
125.49
125.45
128.83
128.66
128.50
129.0
128.7
128.4
f1 (ppm)
66.58
65.38
21.86
125.56
125.53
125.49
125.45
125.55
125.45
f1 (ppm)
CH3
O
F
F
F
f1 (ppm)

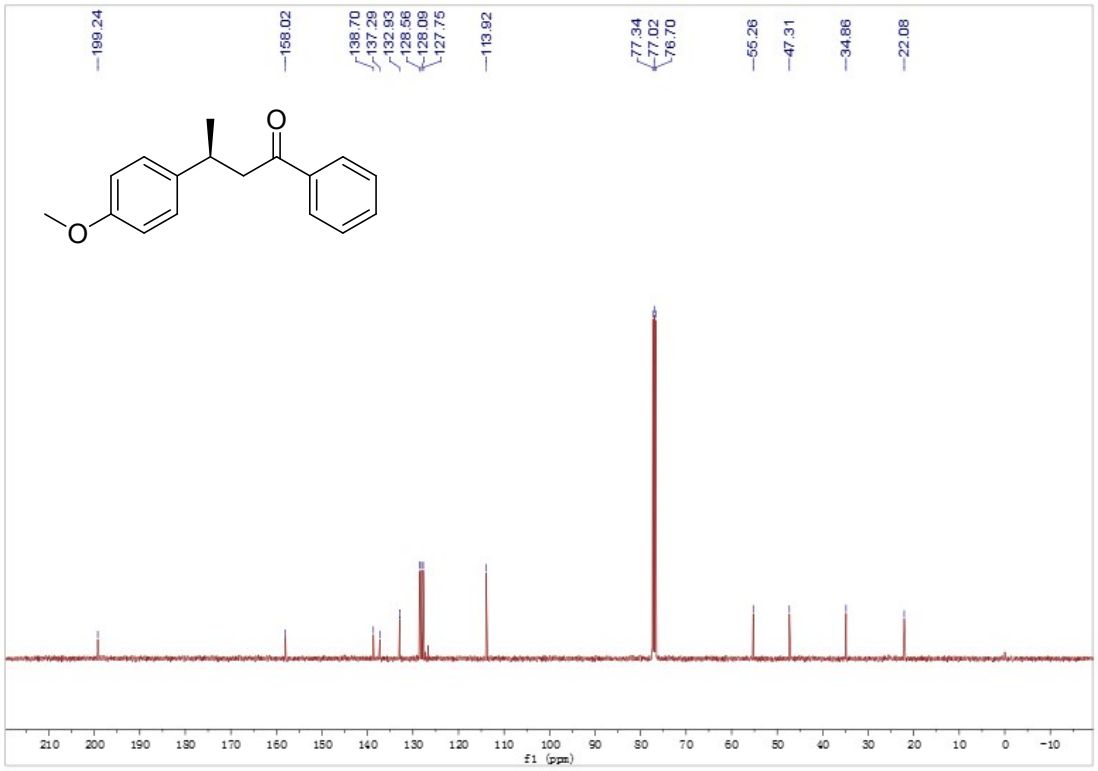

7.94
7.94
7.93
7.92
7.92
7.91
7.56
7.54
7.54
7.53
7.52
7.52
7.52
7.46
7.44
7.42
7.42
7.25
7.18
7.16
7.12
7.10
3.49
3.48
3.46
3.44
3.30
3.29
3.26
3.25
3.20
3.18
3.15
3.13
2.31
1.32
1.31
O
*
4h
2.00
3.05
4.04
1.06
2.12
3.00
3.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

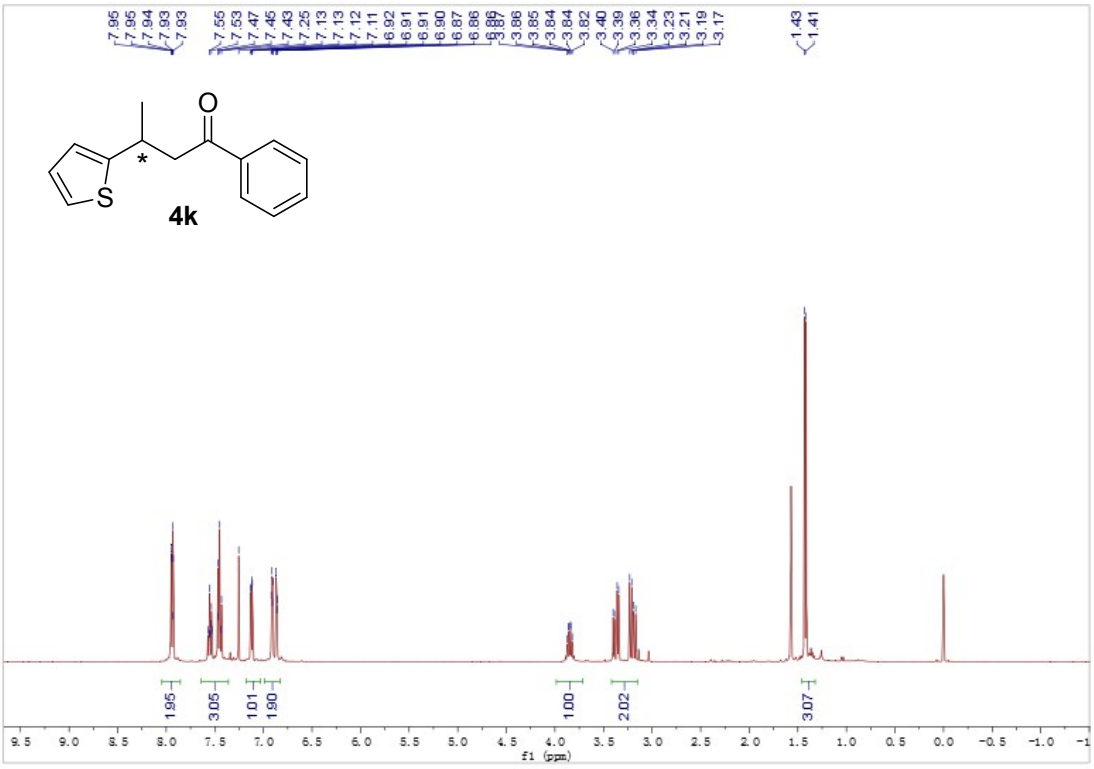

199.18
143.60
137.29
135.75
132.92
129.21
128.55
128.09
126.71
77.34
77.02
76.70
47.16
35.22
21.96
20.97
O
*
4h
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

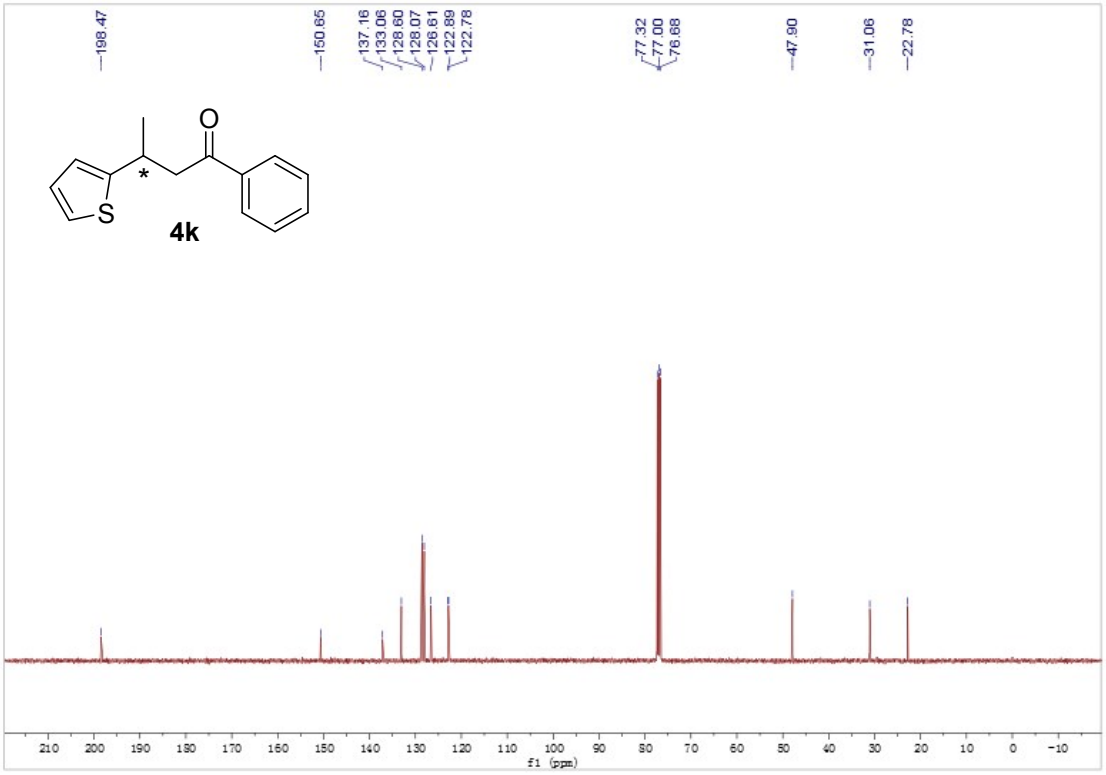

7.94
7.94
7.94
7.92
7.92
7.54
7.52
7.52
7.46
7.45
7.44
7.44
7.42
7.25
7.21
7.19
7.17
7.08
7.06
7.02
7.02
7.00
3.49
3.47
3.45
3.44
3.31
3.30
3.27
3.26
3.20
3.18
3.16
3.14
2.33
1.33
1.31
O
*
4i
1.92
2.97
4.03
1.00
2.01
3.00
3.09
f1 (ppm)

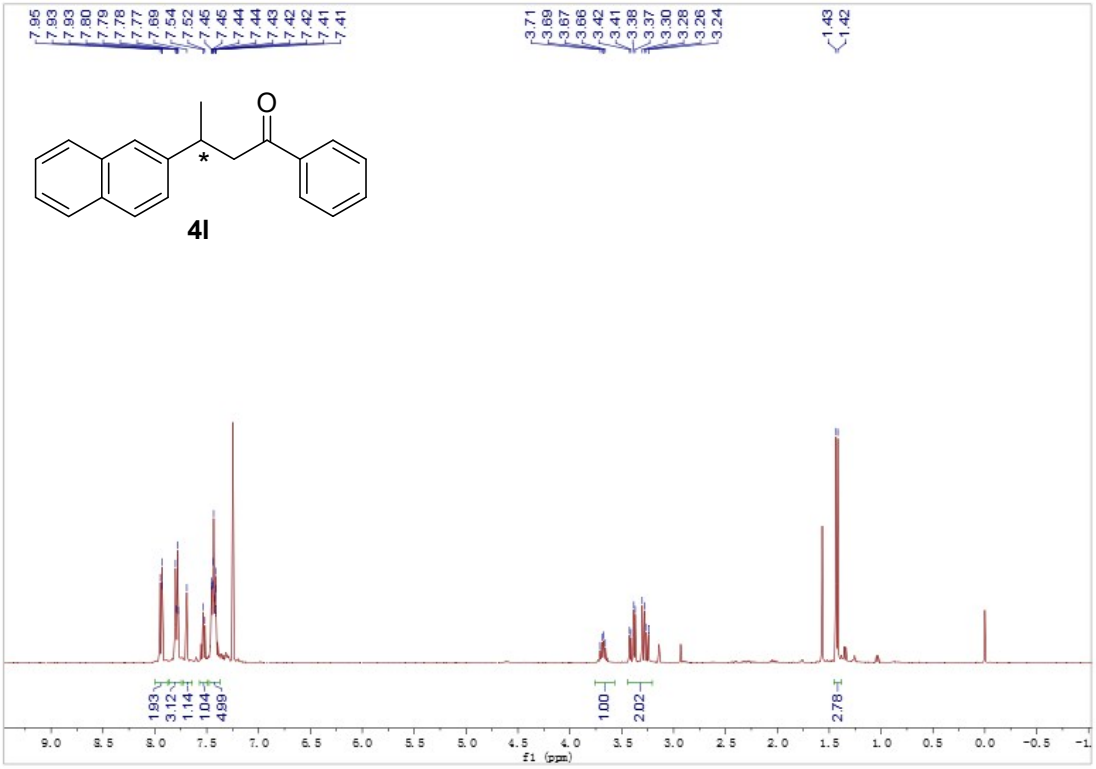

199.14
146.59
138.05
137.33
132.90
128.54
128.42
128.08
127.88
127.02
123.80
77.32
77.00
76.68
47.08
35.55
21.85
21.46
O
*
4i
f1 (ppm)

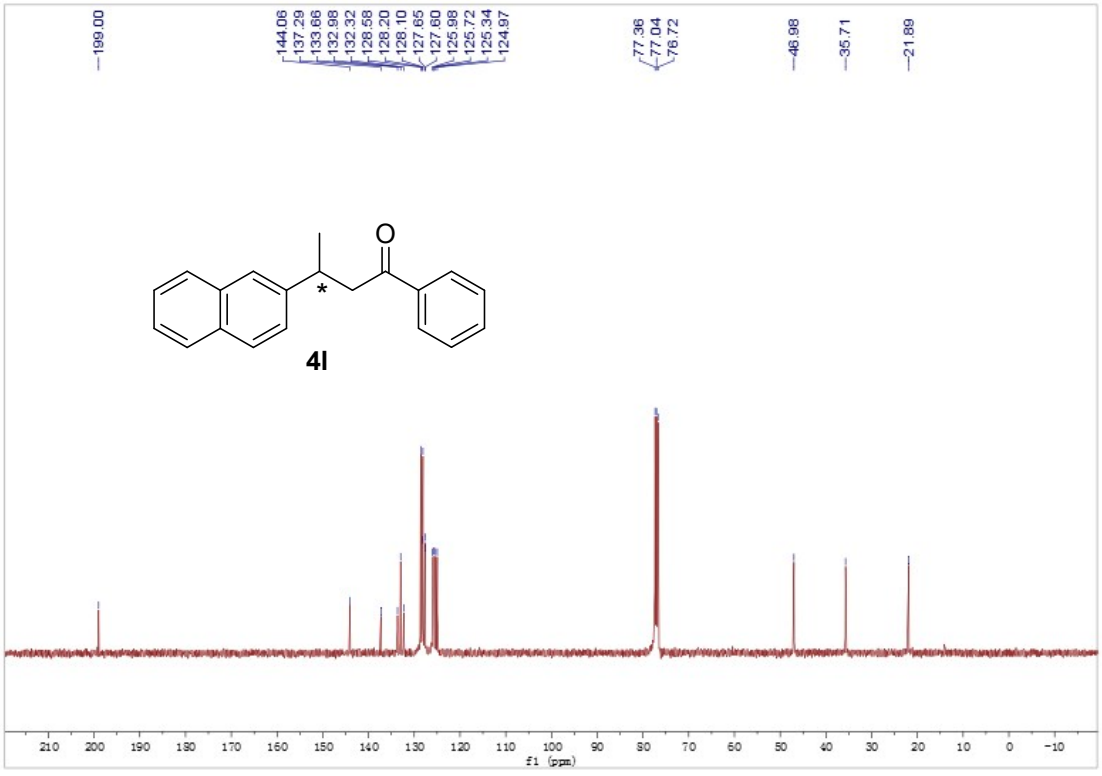

7.93
7.91
7.54
7.53
7.52
7.46
7.44
7.42
7.26
7.26
7.20
7.18
6.85
6.83
3.78
3.49
3.47
3.45
3.43
3.29
3.27
3.25
3.23
3.18
3.16
3.14
3.12
1.32
1.30
O
O
4j
1.98
2.98
2.08
1.95
3.05
1.00
2.05
2.91
f1 (ppm)

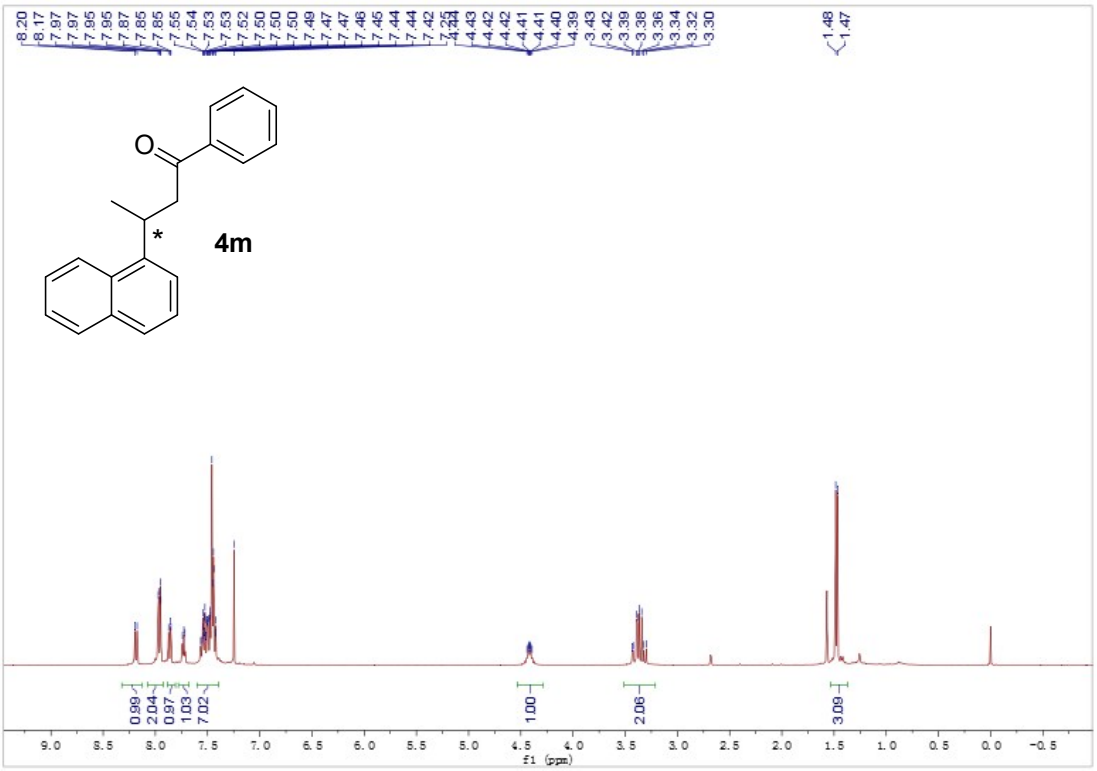

199.24
158.02
138.70
137.29
132.93
128.56
128.09
127.75
113.92
77.34
77.02
76.70
55.26
47.31
34.86
22.08
O
O
f1 (ppm)

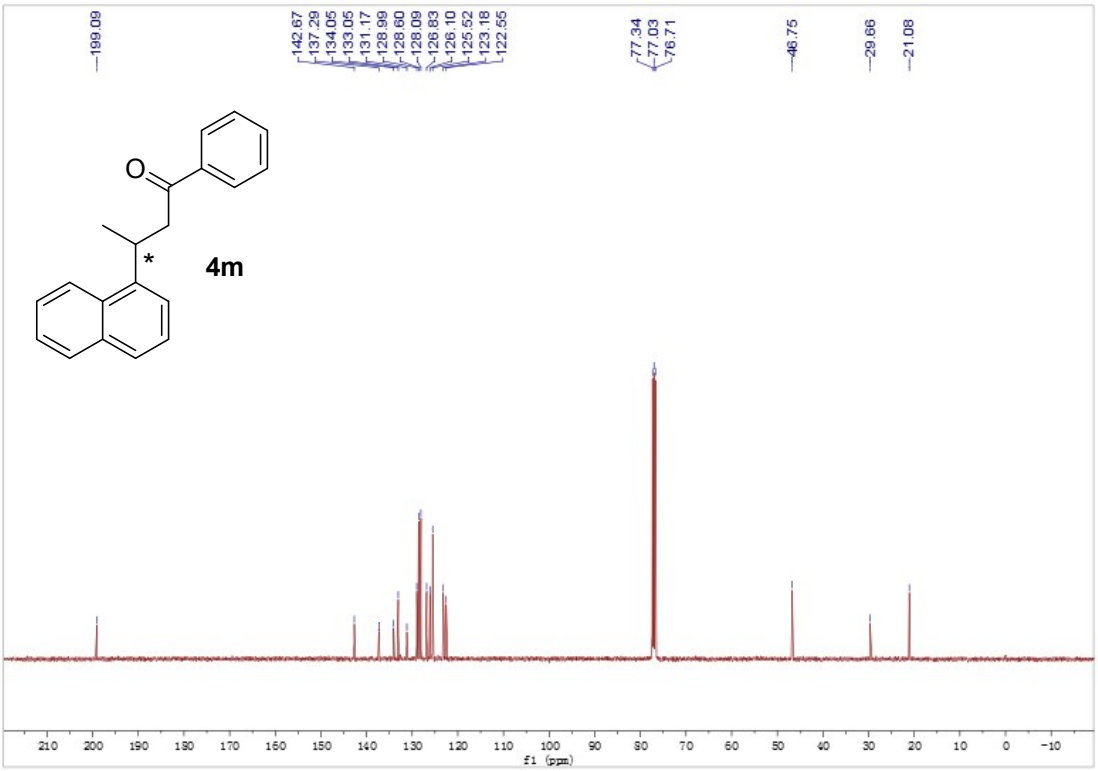

7.95
7.95
7.94
7.93
7.93
7.55
7.53
7.47
7.45
7.43
7.25
7.13
7.13
7.12
7.11
6.92
6.91
6.91
6.90
6.87
6.86
3.87
3.86
3.85
3.84
3.84
3.82
3.40
3.39
3.36
3.34
3.23
3.21
3.19
3.17
1.43
1.41
O
*
S
4k
1.95
3.05
1.01
1.90
1.00
2.02
3.07
f1 (ppm)

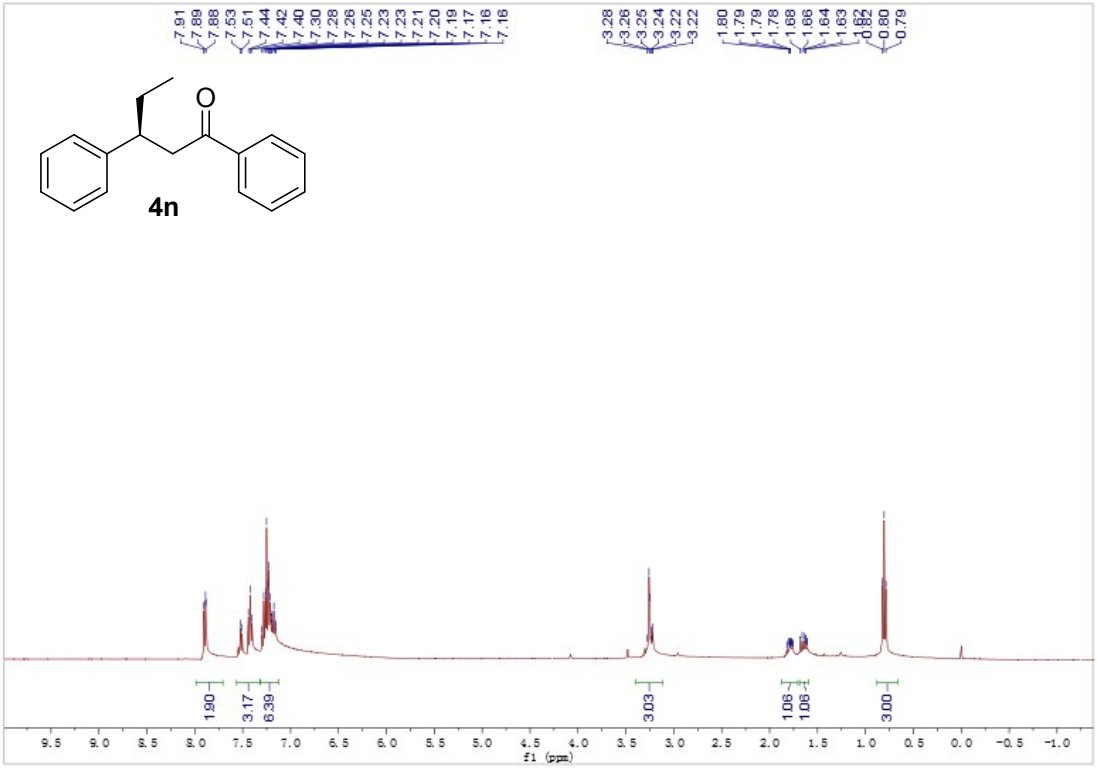

198.47
150.65
137.16
133.06
128.60
128.07
126.61
122.89
122.78
77.32
77.00
76.68
47.90
31.06
22.78
O
*
S
4k
f1 (ppm)

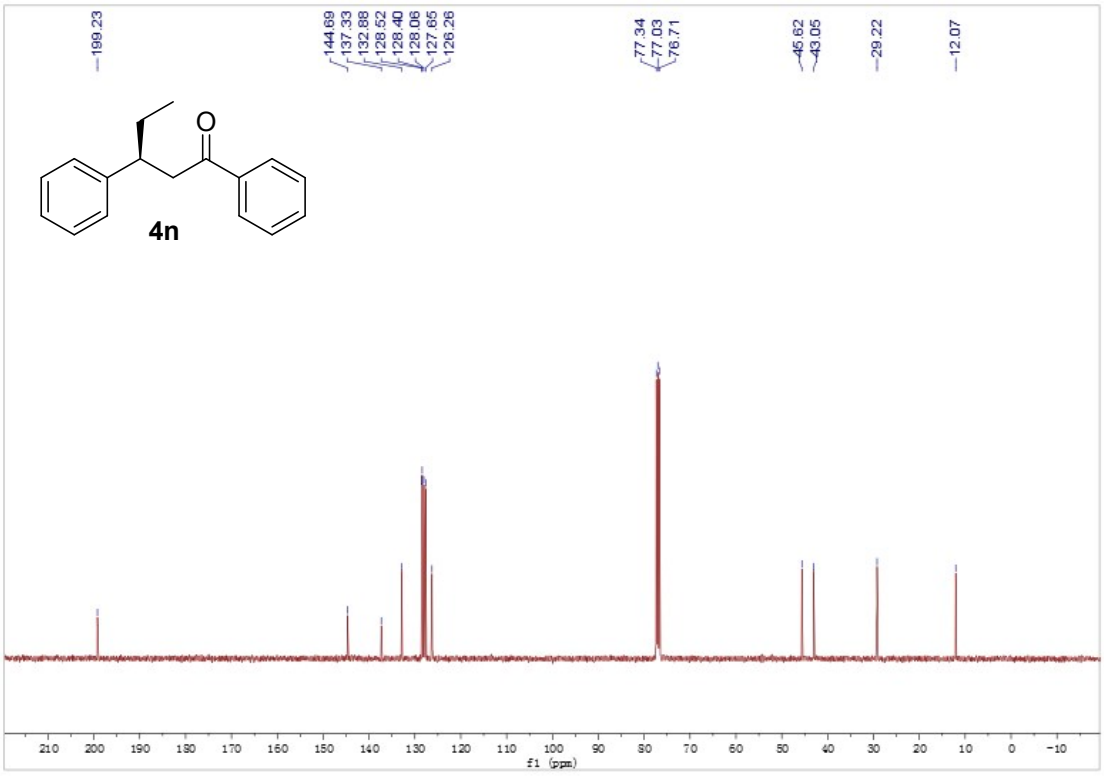

7.95
7.93
7.93
7.80
7.79
7.78
7.77
7.69
7.54
7.52
7.45
7.45
7.44
7.44
7.43
7.42
7.42
7.41
7.41
3.71
3.69
3.67
3.66
3.42
3.41
3.38
3.37
3.30
3.28
3.26
3.24
1.43
1.42
O
*
4l
1.93
3.12
1.14
1.04
4.99
1.00
2.02
2.78
f1 (ppm)

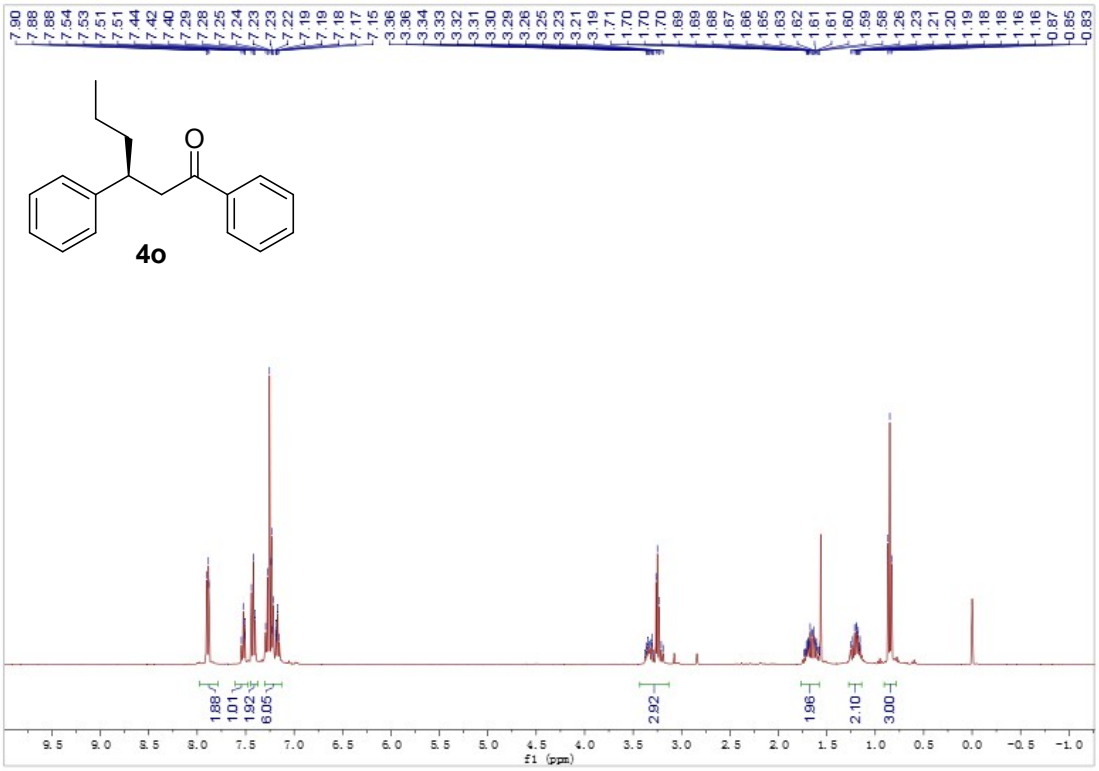

199.00
144.06
137.29
133.66
132.98
132.32
128.58
128.20
128.10
127.65
127.60
125.98
125.72
125.34
124.97
77.36
77.04
76.72
46.98
35.71
21.89
O
*
4l
f1 (ppm)

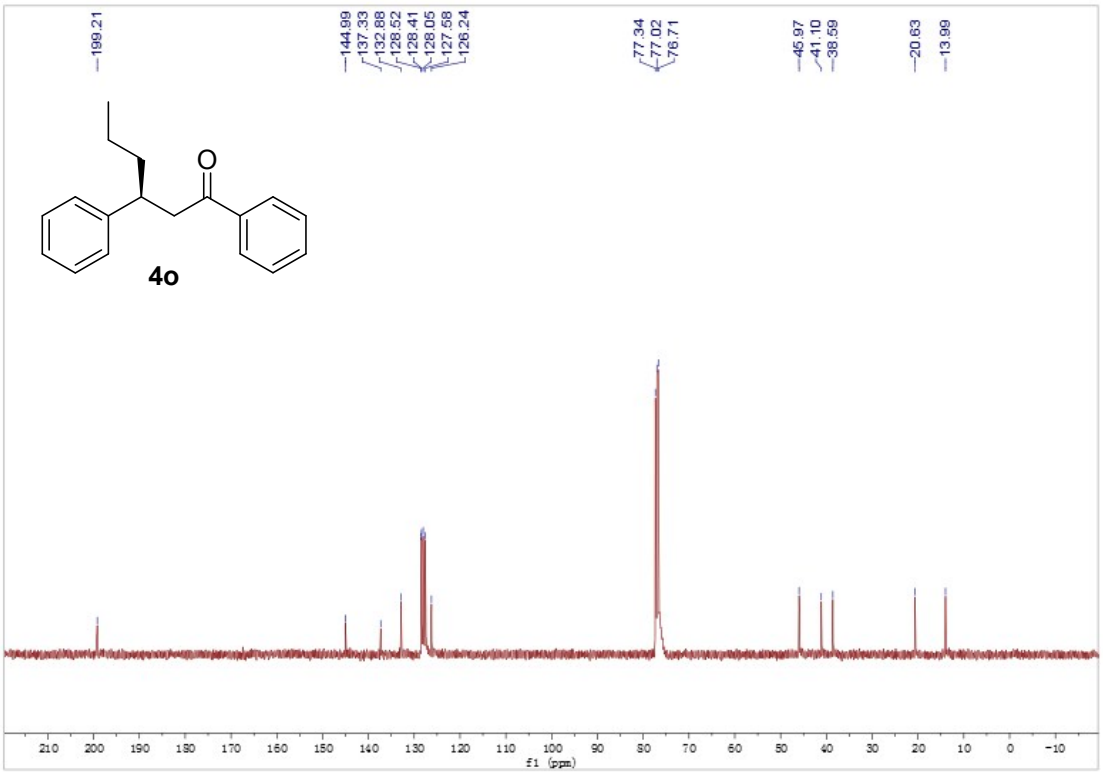

4m

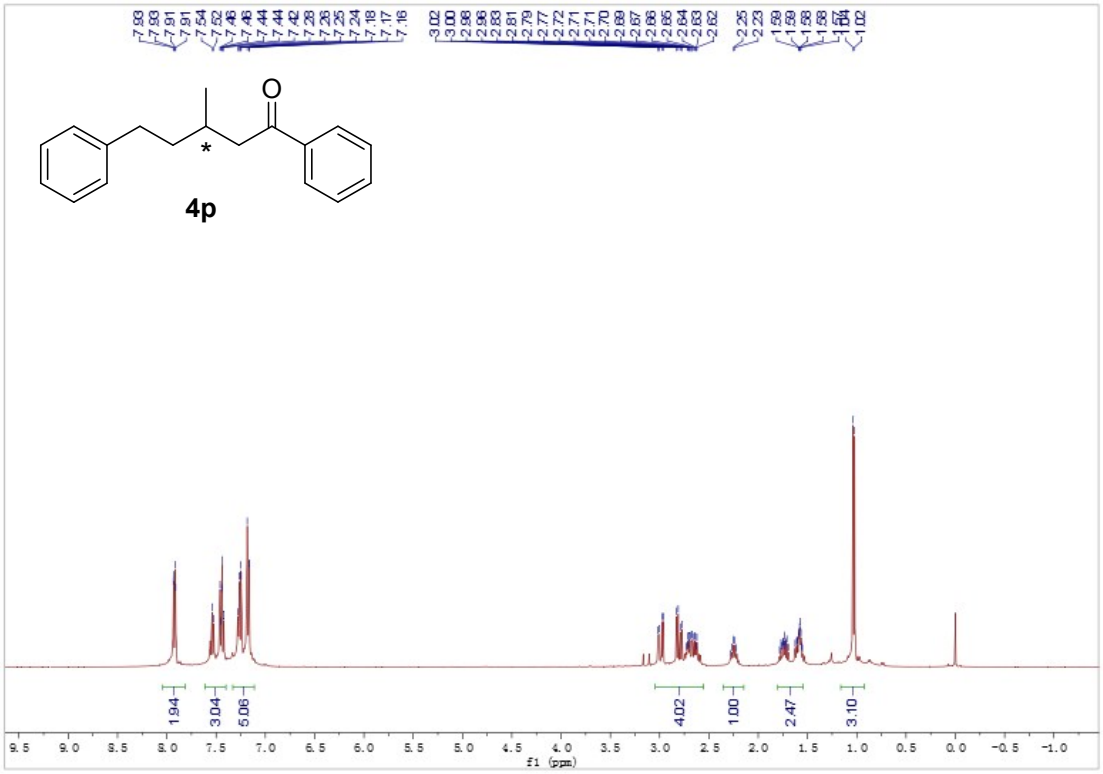

4m

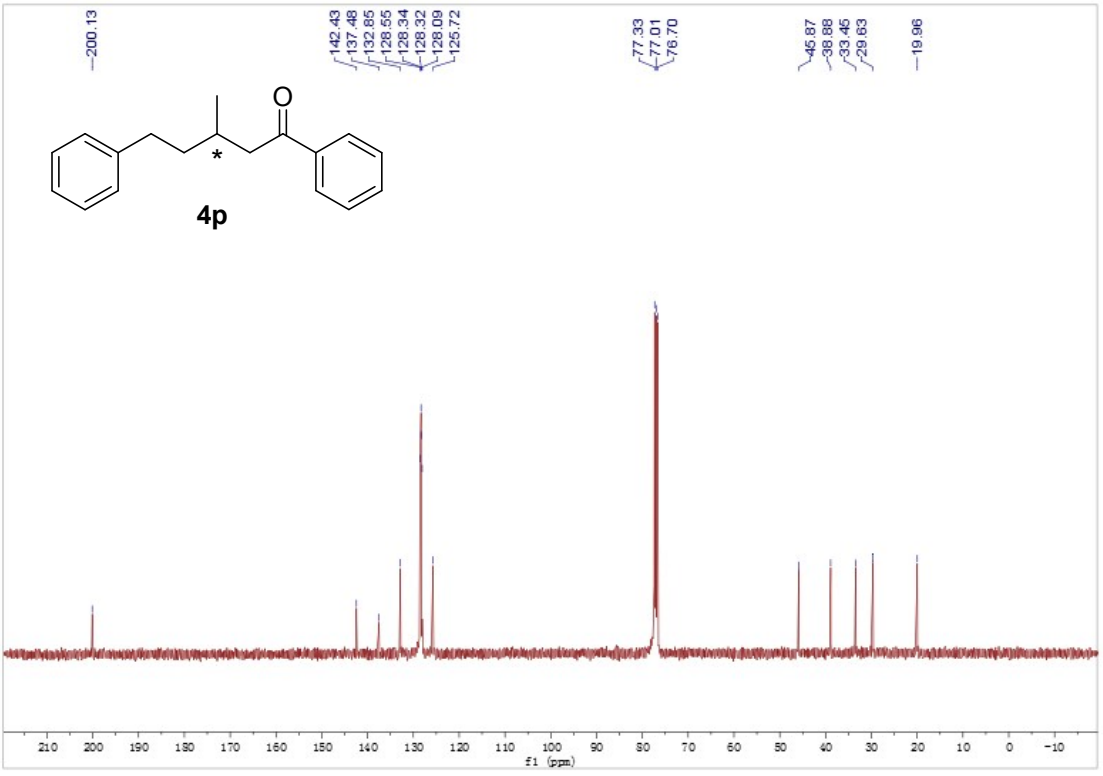

7.91
7.89
7.88
7.53
7.51
7.44
7.42
7.40
7.30
7.28
7.26
7.25
7.23
7.21
7.20
7.19
7.17
7.16
7.16
3.28
3.26
3.25
3.24
3.22
3.22
1.80
1.79
1.79
1.78
1.68
1.66
1.64
1.63
1.62
0.82
0.80
0.79
O
4n
1.90
3.17
6.39
3.03
1.06
1.06
3.00
f1 (ppm)

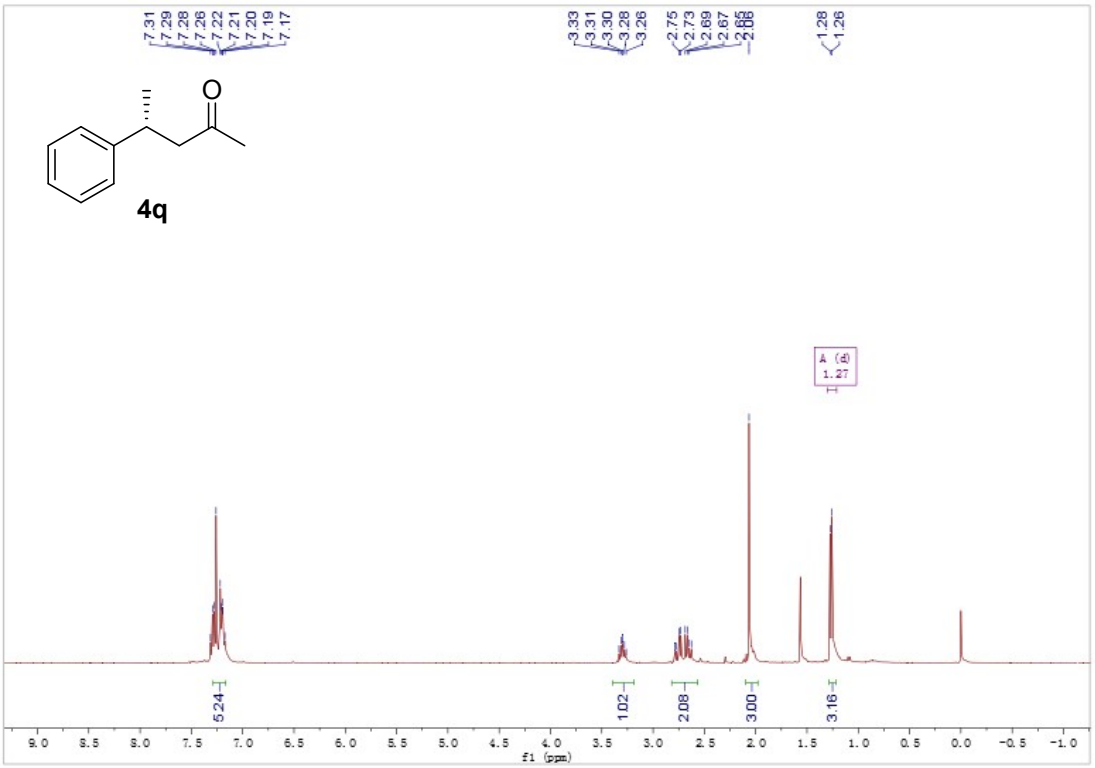

199.23
144.69
137.33
132.88
128.52
128.40
128.06
127.65
126.26
77.34
77.03
76.71
45.62
43.05
29.22
12.07
O
4n
f1 (ppm)

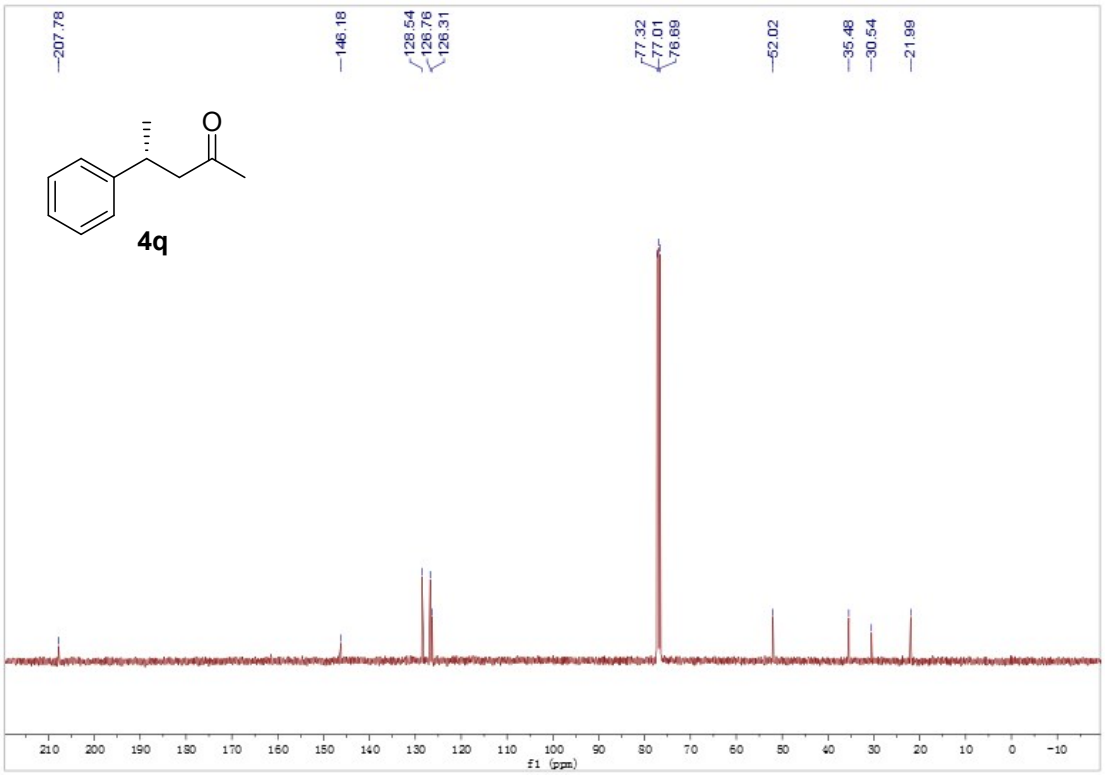

O
4o
1.88
1.01
1.92
6.05
2.92
1.96
2.10
3.00
f1 (ppm)


199.21
144.99
137.33
132.88
128.52
128.41
128.05
127.58
126.24
77.34
77.02
76.71
45.97
41.10
38.59
20.63
13.99
O
4o
f1 (ppm)


4p
1.94
3.04
5.06
4.02
1.00
2.47
3.10
f1 (ppm)


4p
200.13
142.43
137.48
132.85
128.55
128.34
128.32
128.09
125.72
77.33
77.01
76.70
45.87
38.88
33.45
29.63
19.96
f1 (ppm)


7.31
7.29
7.28
7.26
7.22
7.21
7.20
7.19
7.17
3.33
3.31
3.30
3.28
3.26
2.75
2.73
2.69
2.67
2.65
2.63
1.28
1.26
O
4q
A (d)
1.27
5.24
1.02
2.08
3.00
3.16
f1 (ppm)


207.78
146.18
128.54
126.76
126.31
77.32
77.01
76.69
62.02
35.48
30.54
21.99
O
4q
f1 (ppm)