Electronic Supplementary Information

Palladium-Catalyzed Three-Component Reaction for Synthesis 3,3-Disubstituted Allylic Alcohols with Region- and Stereoselective

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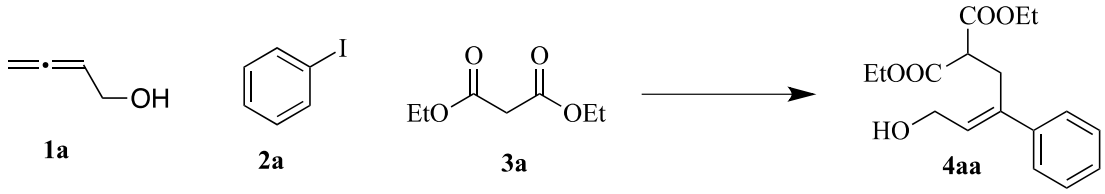
1. General Information

Unless otherwise noted, all reagents and solvents were obtained from commercial sources and used without further purification. Solvents were dried using standard methods and distilled before use. Reactions were monitored by thin-layer chromatography (TLC) on silica plates (F-254) and visualized under UV light. All ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker ARX-400, 400 MHz spectrometers with TMS as an internal standard. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; m, multiplet; q, quartet. The coupling constants, *J*, are reported in hertz (Hz). HRMS analysis was performed on a Q-TOF mass analyzer using the ESI ionization method. Column chromatography was run on silica gel (200-300 mesh) from Qingdao Ocean Chemicals (Qingdao, Shandong, China).

2. General Procedure and Product Characterization

2.1 The Optimal Experimental Conditions

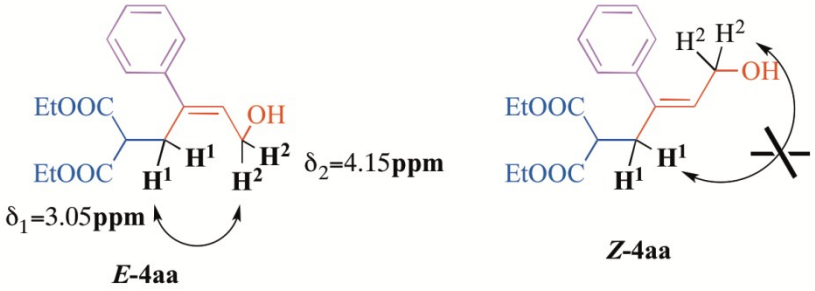


1a **2a** **3a** **4aa**

Representative procedure for the synthesis of diethyl (*E*)-2-(4-hydroxy-2-phenylbut-2-en-1-yl)malonate (**4aa**) products: allenic alcohol **1a** (70 mg, 0.10 mmol), iodobenzene **2a** (244mg, 0.12 mmol, 1.2 equiv.) and diethyl malonate **3a** (191 mg, 0.12 mmol, 1.2 equiv.) were consecutively added to a sealed tube charged with a mixture of K_2CO_3 (413 mg, 0.30 mmol, 3.0 equiv.), $[Pd(PPh_3)_4]$ (57 mg, 0.005 mmol, 5 mol%) in THF(3 mL), under an atmosphere of nitrogen. The reaction mixture was stirred at 80°C for 10 h. After the reaction was complete, water (10 mL) was added, and the solution was extracted with dichloromethane. The organic phase was separated, washed with brine, dried ($MgSO_4$), filtered, and concentrated in vacuo to give the crude product, which was purified by column chromatography on silica gel with a mixture of dichloromethane/methanol (60:1, v/v) to afford the desired product **4aa**.

2.2 The Structural Confirmation of the representative compound 4aa

The chemical structures of the target compounds were confirmed by ^{1}H NMR, ^{13}C NMR, and MS spectra. The representative compound **4aa** was found to have the molecular formula determined by mass spectroscopy. ^{1}H NMR spectroscopy showed that all the protons of **4aa** resonated with the expected chemical shifts (**Figure 2SA**), the exchangeable signal observed at δ = 4.79 was assigned to –OH (**Figure 2SB**). The results of ^{13}C NMR experiment further confirmed its chemical structure. In addition, the configuration of alkene double bond was investigated by NOESY NMR. As shown in (**Figure 1SB**), an evident NOE signal was observed between protons of H^1 (vinyl-C**H$_2$**-C, δ_1 = 3.05 ppm) and H^2 (C-C**H$_2$**-OH, δ_2 = 4.15 ppm), which existed only in the *E* isomer due to the appropriate intramolecular H-H distance (**Figure 1SA**). Thus, all the related compounds were assigned the same *E*-configuration by analogy unambiguously.


EtOOC
EtOOC
OH
H1
H2
H1
H2
δ2=4.15ppm
δ1=3.05ppm
E-4aa
H2 H2
OH
EtOOC
EtOOC
H1
H1
Z-4aa

A

Figure 1SA

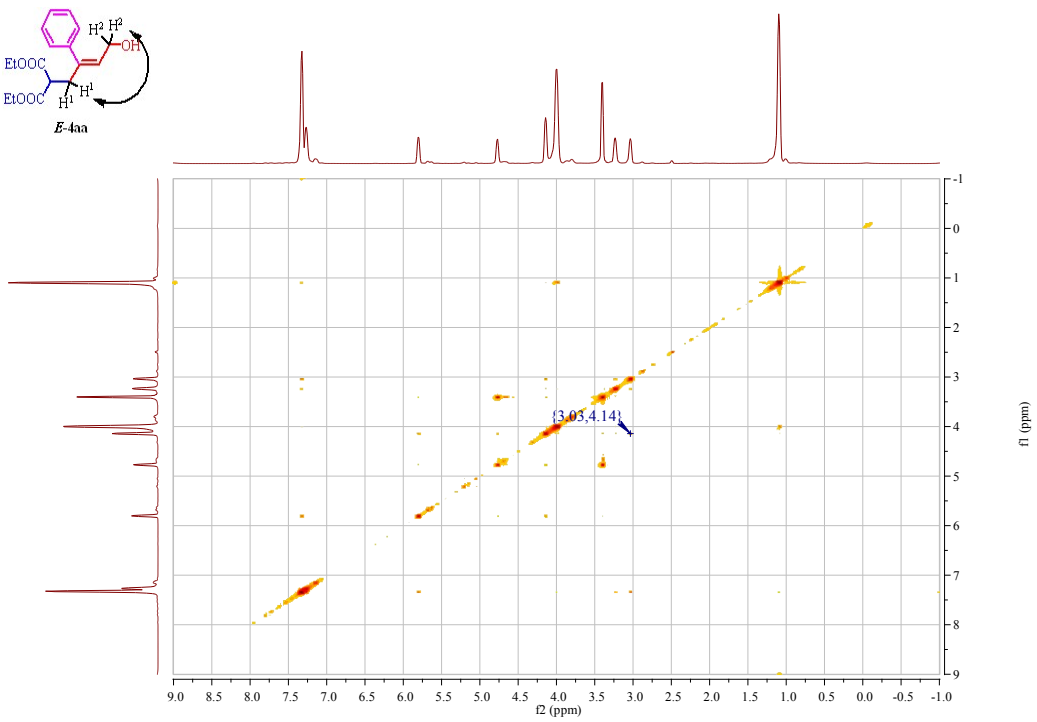


Figure 1SB

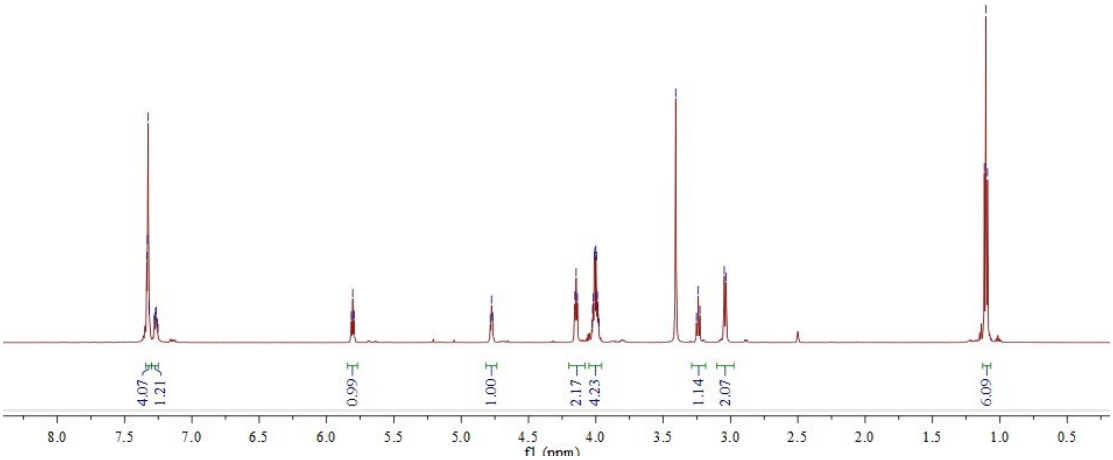


Figure 2SA

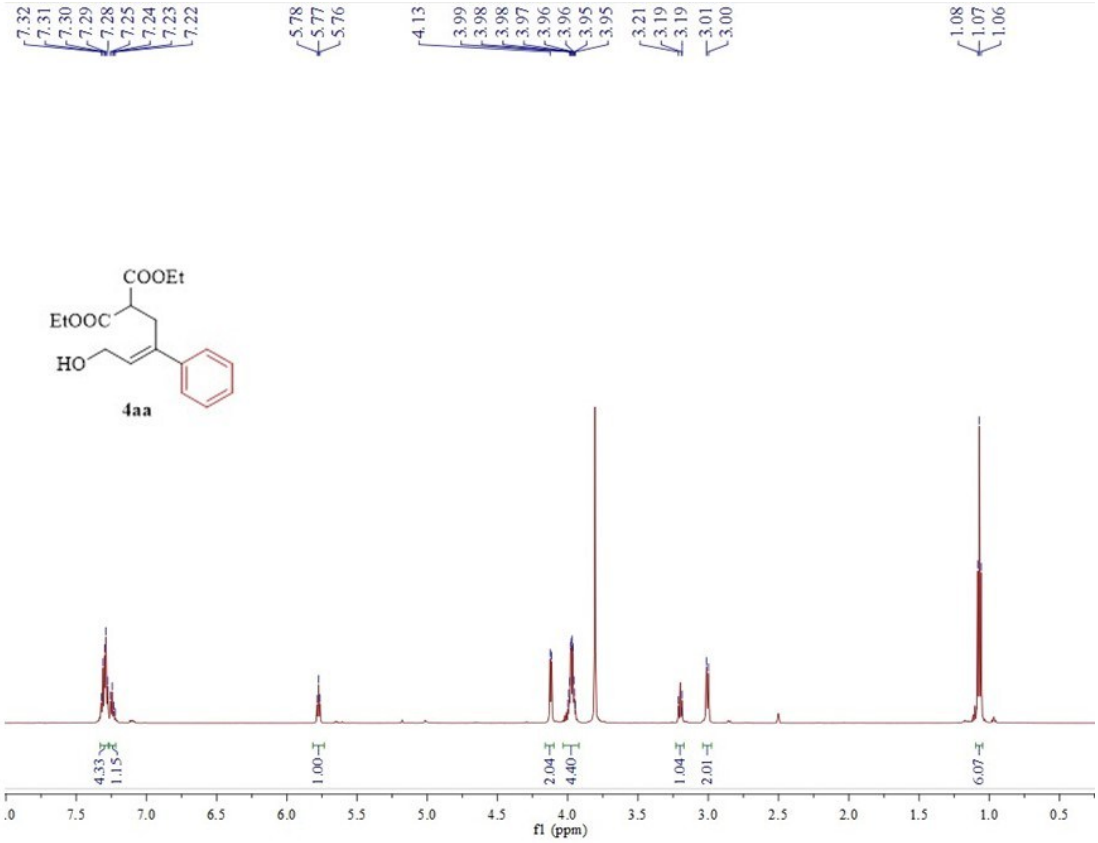
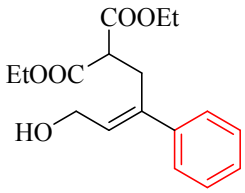


Figure 2SB

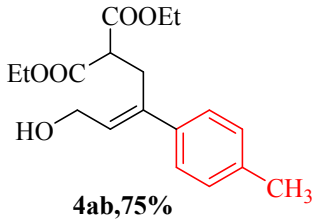
2.3 Product Characterization



4aa,74%

diethyl (*E*)-2-(4-hydroxy-2-phenylbut-2-en-1-yl)malonate (4aa)

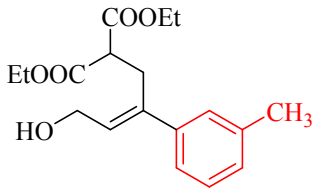
Yield: 74% (colorless oil). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.37 – 7.31 (m, 4H), 7.30 – 7.25 (m, 1H), 5.81 (t, J = 6.2 Hz, 1H), 4.79 (t, J = 5.2 Hz, 1H), 4.15 (t, J = 5.6 Hz, 2H), 4.04 – 3.98 (m, 4H), 3.25 (t, J = 7.8 Hz, 1H), 3.05 (d, J = 7.8 Hz, 2H), 1.12 (t, J = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.74, 141.08, 136.34, 132.62, 128.84, 127.75, 126.72, 61.44, 58.37, 50.72, 28.77, 14.22. HRMS (ESI-Q-TOF, m/z) calcd for $C_{17}H_{22}O_5$ $[M + Na]^+$: 325.0836, found $[M + Na]^+$: 325.0874.



4ab,75%

diethyl (*E*)-2-(4-hydroxy-2-(p-tolyl)but-2-en-1-yl)malonate (4ab)

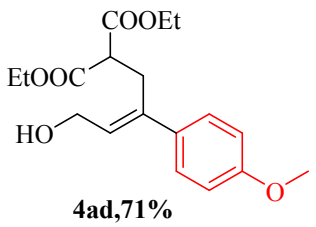
Yield: 75% (colorless oil). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.22 (d, J = 8.1 Hz, 2H), 7.15 (d, J = 8.0 Hz, 2H), 5.78 (t, J = 6.3 Hz, 1H), 4.13 (d, J = 6.3 Hz, 2H), 4.04 – 3.99 (m, 4H), 3.23 (t, J = 7.8 Hz, 1H), 3.01 (d, J = 7.8 Hz, 2H), 2.30 (s, 3H), 1.12 (t, J = 7.1 Hz, 6H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 168.67, 137.99, 136.92, 136.00, 131.70, 129.37, 126.48, 61.35, 58.25, 50.58, 28.62, 20.99, 14.17. HRMS (ESI-Q-TOF, m/z) calcd for $C_{18}H_{24}O_5$ [M + Na]$^+$:343.1521, found [M + Na]$^+$: 343.1553.



4ac,42%

diethyl (*E*)-2-(4-hydroxy-2-(*m*-tolyl)but-2-en-1-yl)malonate (4ac)

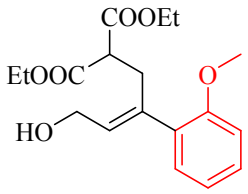
Yield: 42% (colorless oil). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.23 (t, J = 7.5 Hz, 1H), 7.11 (dd, J = 14.2, 7.0 Hz, 3H), 5.78 (t, J = 6.2 Hz, 1H), 4.13 (d, J = 6.3 Hz, 2H), 4.04 – 3.99 (m, 4H), 3.24 (t, J = 7.8 Hz, 1H), 3.01 (d, J = 7.8 Hz, 2H), 2.31 (s, 3H), 1.12 (t, J = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.76, 141.07, 137.91, 136.37, 132.39, 128.72, 128.42, 127.40, 123.81, 61.44, 58.34, 50.72, 28.78, 21.50, 14.25. HRMS (ESI-Q-TOF, m/z) calcd for $C_{18}H_{24}O_5$ [M + Na]$^+$:343.1521, found [M + Na]$^+$:343.1556.



4ad,71%

diethyl (*E*)-2-(4-hydroxy-2-(4-methoxyphenyl)but-2-en-1-yl)malonate (4ad)

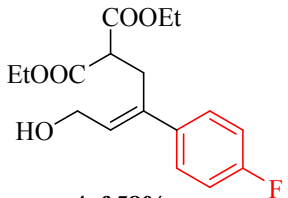
Yield: 71% (colorless oil). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.26 (d, J = 8.7 Hz, 2H), 6.90 (d, J = 8.7 Hz, 2H), 5.72 (t, J = 6.3 Hz, 1H), 4.68 (t, J = 5.2 Hz, 1H), 4.10 (t, J = 5.8 Hz, 2H), 4.06 – 3.98 (m, 4H), 3.23 (t, J = 7.8 Hz, 1H), 2.99 (d, J = 7.8 Hz, 2H), 1.12 (t, J = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, DMSO) δ 168.77, 159.09, 135.80, 133.28, 131.02, 127.84, 114.25, 61.43, 58.33, 55.53, 50.74, 28.76, 14.27. HRMS (ESI-Q-TOF, m/z) calcd for $C_{18}H_{24}O_6$ [M + Na]$^+$:359.1471, found [M + Na]$^+$: 343.1431.



4ae,53%

diethyl (*E*)-2-(4-hydroxy-2-(2-methoxyphenyl)but-2-en-1-yl)malonate (4ae)

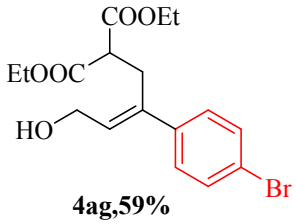
Yield: 53% (colorless oil). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.27 (ddd, J = 8.2, 7.2, 1.9 Hz, 1H), 7.00 – 6.88 (m, 3H), 5.48 (t, J = 6.2 Hz, 1H), 4.11 (d, J = 6.2 Hz, 2H), 4.02 – 3.96 (m, 4H), 3.76 (s, 3H), 3.11 (t, J = 7.7 Hz, 1H), 2.96 (d, J = 7.7 Hz, 2H), 1.11 (t, J = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.84, 156.83, 136.13, 133.56, 130.87, 130.75, 129.22, 120.81, 111.44, 61.36, 57.99, 55.71, 50.83, 29.64, 14.25. HRMS (ESI-Q-TOF, m/z) calcd for $C_{18}H_{24}O_6$ [M + Na]$^+$:359.1471, found [M + Na]$^+$: 359.1428.



4af,58%

diethyl (*E*)-2-(2-(4-fluorophenyl)-4-hydroxybut-2-en-1-yl)malonate (4af)

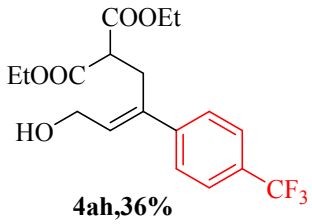
Yield: 58% (colorless oil). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.37 (dd, J = 8.2, 5.7 Hz, 2H), 7.16 (t, J = 8.7 Hz, 2H), 5.77 (t, J = 6.1 Hz, 1H), 4.75 (t, J = 5.1 Hz, 1H), 4.12 (t, J = 5.6 Hz, 2H), 4.04 – 3.99 (m, 4H), 3.24 (t, J = 7.8 Hz, 1H), 3.02 (d, J = 7.8 Hz, 2H), 1.12 (t, J = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, DMSO) δ 168.70, 161.99 (d, $J_{C\text{-}F}$=245.4 Hz), 137.53 (d, $J_{C\text{-}F}$=3.0 Hz), 135.42, 132.77, 128.76 (d, $J_{C\text{-}F}$=8.1 Hz), 115.57 (d, $J_{C\text{-}F}$=21.2 Hz), 61.45, 58.31, 50.67, 40.21, 28.86, 14.24. HRMS (ESI-Q-TOF, m/z) calcd for $C_{17}H_{21}FO_5$ [M + Na]$^+$:347.1271, found [M + Na]$^+$: 347.1292.



4ag,59%

diethyl (*E*)-2-(2-(4-bromophenyl)-4-hydroxybut-2-en-1-yl)malonate (4ag)

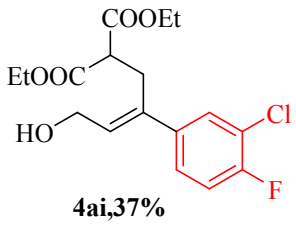
Yield: 59% (colorless oil). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.53 (d, J = 8.4 Hz, 2H), 7.29 (d, J = 8.4 Hz, 2H), 5.82 (t, J = 6.2 Hz, 1H), 4.77 (t, J = 5.2 Hz, 1H), 4.12 (t, J = 5.6 Hz, 2H), 4.04 – 3.99 (m, 4H), 3.24 (t, J = 7.9 Hz, 1H), 3.01 (d, J = 7.9 Hz, 2H), 1.12 (t, J = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.67, 140.32, 135.27, 133.42, 131.74, 128.93, 120.93, 61.48, 58.33, 50.63, 28.57, 14.26. HRMS (ESI-Q-TOF, m/z) calcd for $C_{17}H_{21}BrO_5$ [M + Na]$^+$:407.0470, found [M + Na]$^+$:407.0452.



4ah,36%

diethyl (*E*)-2-(4-hydroxy-2-(4-(trifluoromethyl)phenyl)but-2-en-1-yl)malonate (4ah)

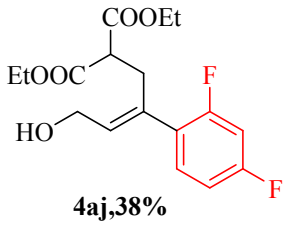
Yield: 36% (colorless oil). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.70 (d, J = 8.1 Hz, 2H), 7.56 (d, J = 8.1 Hz, 2H), 5.92 (t, J = 6.1 Hz, 1H), 4.84 (t, J = 5.1 Hz, 1H), 4.17 (t, J = 5.5 Hz, 2H), 4.03 – 3.98 (m, 4H), 3.27 (t, J = 7.9 Hz, 1H), 3.07 (d, J = 7.9 Hz, 2H), 1.11 (t, J = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.63, 145.30, 135.24, 134.95, 128.15(q, $J_{C\text{-}F}$=31.3 Hz), 127.59, 125.72 (d, $J_{C\text{-}F}$=4.0 Hz), 61.48, 58.36, 50.62, 28.57, 14.21. HRMS (ESI-Q-TOF, m/z) calcd for $C_{18}H_{21}F_3O_5$ [M + Na]$^+$:397.1239, found [M + Na]$^+$:397.1235.



4ai,37%

diethyl (*E*)-2-(2-(3-chloro-4-fluorophenyl)-4-hydroxybut-2-en-1-yl)malonate (4ai)

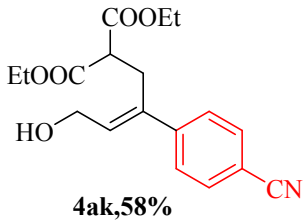
Yield: 37% (colorless oil). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.53 (dd, J = 7.2, 1.9 Hz, 1H), 7.41 – 7.27 (m, 2H), 5.82 (t, J = 6.2 Hz, 1H), 4.79 (d, J = 5.0 Hz, 1H), 4.16 – 4.07 (m, 2H), 4.04 – 3.99 (m, 4H), 3.26 (t, J = 7.9 Hz, 1H), 3.01 (d, J = 7.9 Hz, 2H), 1.12 (t, J = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.67, 156.96(d, J_{C-F}=247.4 Hz), 139.15, 134.53, 134.01, 128.87, 127.59(d, J_{C-F}=7.0 Hz), 119.85(d, J_{C-F}=18.1 Hz), 117.20 (d, J_{C-F}=21.2 Hz), 61.48, 58.27, 50.62, 28.72, 14.23. HRMS (ESI-Q-TOF, m/z) calcd for $C_{17}H_{20}ClFO_5$ [M + Na]$^+$:381.0881, found [M + Na]$^+$:381.0889.



4aj,38%

diethyl (*E*)-2-(2-(2,4-difluorophenyl)-4-hydroxybut-2-en-1-yl)malonate (4aj)

Yield: 38% (colorless oil). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.49 – 7.33 (m, 2H), 7.20–7.14(m, 1H), 5.84 (t, J = 6.1 Hz, 1H), 4.78 (br, 1H), 4.15 – 4.10 (m, 2H), 4.05 – 3.99 (m, 4H), 3.27 (t, J = 7.9 Hz, 1H), 3.01 (d, J = 7.9 Hz, 2H), 1.12 (t, J = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.67, 150.93(dd, J_{C-F}=12.1 Hz, J_{C-F}=53.5 Hz), 148.22(dd, J_{C-F}=13.1 Hz, J_{C-F}=54.5 Hz), 138.87(q, J_{C-F}=2.0 Hz), 134.58, 133.88, 123.68(q, J_{C-F}=3.0 Hz), 117.78(d, J_{C-F}=17.1 Hz), 115.84(d, J_{C-F}=18.1 Hz), 61.47, 58.28, 50.60, 28.65, 14.24. HRMS (ESI-Q-TOF, m/z) calcd for $C_{17}H_{20}F_2O_5$ [M + Na]$^+$:365.1176, found [M + Na]$^+$:365.1188.

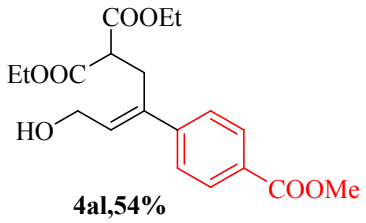


4ak,58%

diethyl (*E*)-2-(2-(4-cyanophenyl)-4-hydroxybut-2-en-1-yl)malonate (4ak)

Yield: 58% (colorless oil). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.81 (d, J = 8.4 Hz, 2H), 7.55 (d, J = 8.5 Hz, 2H), 5.95 (t, J = 6.1 Hz, 1H), 4.85 (s, 1H), 4.16 (d, J = 6.1 Hz, 2H), 4.03 – 3.98 (m, 4H), 3.26 (t, J = 7.9 Hz, 1H), 3.06 (d, J = 8.0 Hz, 2H), 1.11 (t, J = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.60, 145.90, 135.64, 135.13, 132.81, 127.70, 119.25, 110.30, 61.51, 58.39, 50.61, 28.34, 14.24.

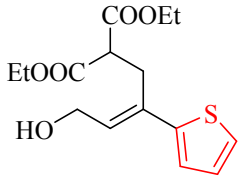
HRMS (ESI-Q-TOF, m/z) calcd for $C_{18}H_{21}NO_5$ [M + Na]$^+$:354.1371, found [M + Na]$^+$:354.1383.



4al,54%

diethyl (*E*)-2-(4-hydroxy-2-(4-(methoxycarbonyl)phenyl)but-2-en-1-yl)malonate (4al)

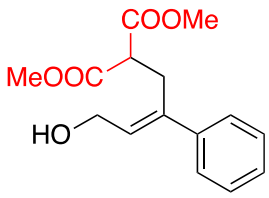
Yield: 54% (colorless oil). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.93 (d, J = 8.3 Hz, 2H), 7.49 (d, J = 8.4 Hz, 2H), 5.94 (t, J = 6.1 Hz, 1H), 4.82 (s, 1H), 4.14- 4.18(m, 2H), 4.03 – 3.98 (m, 4H), 3.86 (s, 3H), 3.26 (t, J = 7.9 Hz, 1H), 3.06 (d, J = 7.9 Hz, 2H), 1.11 (t, J = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.64, 166.44, 145.85, 135.45, 134.82, 129.78, 128.82, 127.02, 61.48, 58.39, 52.54, 50.66, 28.46, 14.23. HRMS (ESI-Q-TOF, m/z) calcd for $C_{19}H_{24}O_7$ [M + Na]$^+$:387.1421, found [M + Na]$^+$:387.1439.



4an,46%

diethyl (*E*)-2-(4-hydroxy-2-(thiophen-2-yl)but-2-en-1-yl)malonate (4an)

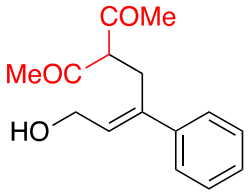
Yield: 46% (colorless oil). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.40 (d, J = 5.8 Hz, 1H), 7.09 (d, J = 2.9 Hz, 1H), 7.02 (dd, J = 5.1, 3.6 Hz, 1H), 5.97 (t, J = 6.4 Hz, 1H), 4.77 (t, J = 5.3 Hz, 2H), 4.14 – 3.99 (m, 6H), 3.51 (t, J = 7.8 Hz, 1H), 2.99 (d, J = 7.8 Hz, 2H), 1.13 (t, J = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.77, 144.65, 131.15, 130.01, 128.20, 125.18, 124.19, 61.57, 57.99, 50.99, 29.03, 14.28. HRMS (ESI-Q-TOF, m/z) calcd for $C_{15}H_{20}O_5S$ [M + Na]$^+$:335.0929, found [M + Na]$^+$:335.0918.



5aa, 74%

dimethyl (E)-2-(4-hydroxy-2-phenylbut-2-en-1-yl)malonate (5aa)

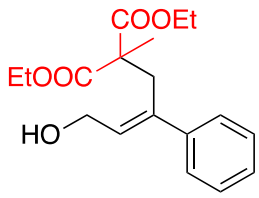
Yield: 74% (colorless oil).^{1}H NMR (400 MHz, DMSO-d_6) δ 7.38 – 7.27 (m, 5H), 5.80 (t, J = 6.3 Hz, 1H), 4.13 (d, J = 6.3 Hz, 2H), 3.55 (s, 6H), 3.30 (t, J = 7.9 Hz, 1H), 3.05 (d, J = 7.9 Hz, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.16, 141.03, 136.26, 132.70, 128.88, 127.79, 126.71, 58.30, 52.74, 50.55, 28.88. HRMS (ESI-Q-TOF, m/z) calcd for $C_{15}H_{18}O_5$ [M + Na]$^+$:301.1052, found [M + Na]$^+$:301.1038.



5ab, 62%

(*E*)-3-(4-hydroxy-2-phenylbut-2-en-1-yl)pentane-2,4-dione (5ab)

Yield: 62% (colorless oil).^{1}H NMR (400 MHz, DMSO-d_6) δ 7.40 – 7.28 (m, 5H), 5.76 (t, J = 6.2 Hz, 1H), 4.72 (s, 1H), 4.12 (d, J = 6.2 Hz, 2H), 3.72 (t, J = 7.3 Hz, 1H), 2.94 (d, J = 7.3 Hz, 2H), 2.05 (s, 6H). ^{13}C NMR (101 MHz, DMSO) δ 204.42, 141.32, 137.01, 132.15, 129.00, 127.81, 126.74, 65.00, 58.44, 30.58, 28.01. HRMS (ESI-Q-TOF, m/z) calcd for $C_{15}H_{18}O_3$ [M + Na]$^+$:269.1154, found [M + Na]$^+$:269.1168.

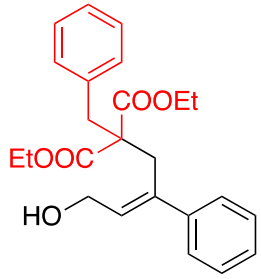


5ac, 51%

diethyl (*E*)-2-(4-hydroxy-2-phenylbut-2-en-1-yl)-2-methylmalonate (5ac)

Yield: 51% (colorless oil). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.32 – 7.21 (m, 5H), 5.72 (t, J = 6.5 Hz, 1H), 4.78 (s, 1H), 4.12 – 4.08 (m, 2H), 3.83 (dq, J = 10.8, 7.1 Hz, 2H), 3.85 – 3.80 (m,2H), 3.70 –

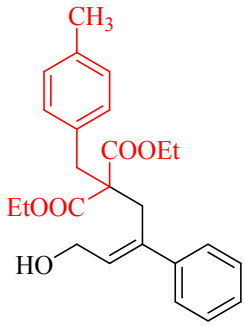
3.66 (m,2H), 3.12 (s, 2H), 1.14 (s, 3H), 1.05 (t, J = 7.1 Hz, 6H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 171.34, 142.85, 135.94, 135.10, 128.23, 127.38, 127.25, 61.10, 58.57, 52.98, 34.48, 19.72, 13.97. HRMS (ESI-Q-TOF, m/z) calcd for $C_{18}H_{24}O_5$ [M + Na]$^+$:343.1521, found [M + Na]$^+$:343.1530.



5ad, 50%

diethyl (*E*)-2-benzyl-2-(4-hydroxy-2-phenylbut-2-en-1-yl)malonate (5ad)

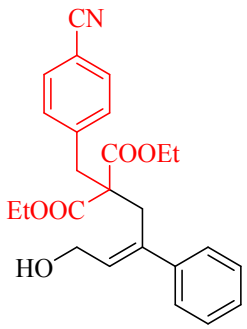
Yield: 50% (colorless oil). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.43 – 7.15 (m, 8H), 7.04 (d, J = 6.5 Hz, 2H), 5.63 (t, J = 6.5 Hz, 1H), 3.96 (d, J = 6.5 Hz, 2H), 3.81-3.64 (m, 4H), 3.14 (s, 2H), 2.95 (s, 2H), 1.00 (t, J = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.49, 143.24, 136.69, 136.24, 135.64, 130.24, 128.41, 128.33, 127.55, 127.43, 127.09, 61.14, 58.50, 33.93, 13.93. HRMS (ESI-Q-TOF, m/z) calcd for $C_{24}H_{28}O_5$ [M + Na]$^+$:419.1834, found [M + Na]$^+$:419.1850.



5ae,36%

diethyl (*E*)-2-(4-hydroxy-2-phenylbut-2-en-1-yl)-2-(4-methylbenzyl)malonate (5ae)

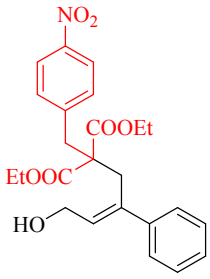
Yield: 36% (colorless oil). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.34 – 7.24 (m, 5H), 7.04 (d, J = 7.8 Hz, 2H), 6.92 (d, J = 8.0 Hz, 2H), 5.63 (t, J = 6.5 Hz, 1H), 3.97 (d, J = 6.5 Hz, 2H), 3.80 – 3.67 (m, 4H), 3.12 (s, 2H), 2.90 (s, 2H), 2.25 (s, 3H), 1.02 (t, J = 7.1 Hz, 6H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 170.43, 143.17, 136.22, 136.01, 135.48, 133.36, 130.03, 128.90, 128.23, 127.47, 127.33, 61.03, 58.43, 38.90, 33.63, 20.97, 13.87. HRMS (ESI-Q-TOF, m/z) calcd for $C_{25}H_{30}O_5$ [M + Na]$^+$:433.1991, found [M + Na]$^+$:433.2007.



5af,44%

diethyl (*E*)-2-(4-cyanobenzyl)-2-(4-hydroxy-2-phenylbut-2-en-1-yl)malonate (5af)

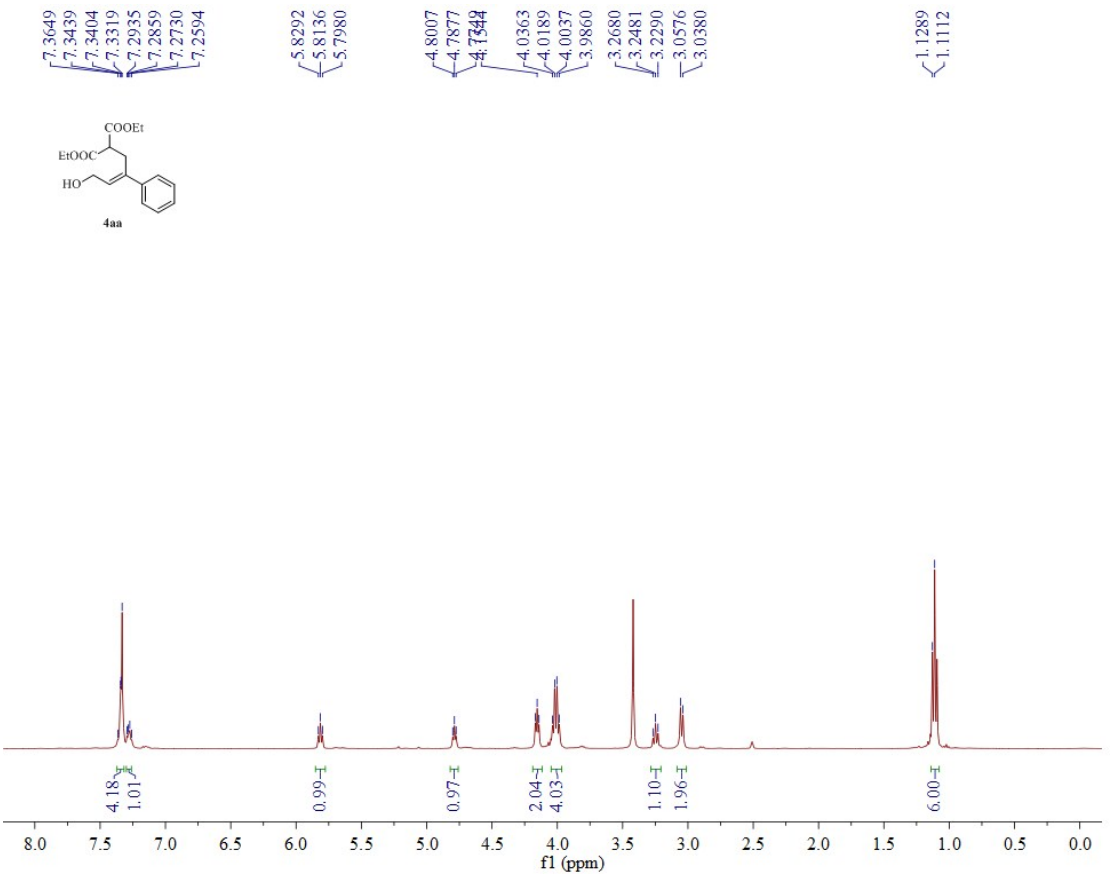
Yield: 44% (colorless oil). ^{1}H NMR (600 MHz, DMSO) δ 7.72 (d, J = 8.2 Hz, 2H), 7.35 – 7.21 (m, 7H), 5.67 (t, J = 6.5 Hz, 1H), 4.00 (d, J = 6.5 Hz, 2H), 3.81 – 3.61 (m, 4H), 3.19 (s, 2H), 3.03 (s, 2H), 0.98 (t, J = 7.1 Hz, 6H).^{13}C NMR (151 MHz, DMSO-d_6) δ 170.11, 142.92, 142.89, 135.85, 135.69, 132.16, 131.37, 131.32, 128.29, 127.46, 119.18, 109.89, 61.25, 58.39, 39.29, 34.29, 13.79. HRMS (ESI-Q-TOF, m/z) calcd for $C_{25}H_{30}O_5$ $[M + Na]^+$:444.1787, found $[M + Na]^+$:444.1751.



5ag, 48%

diethyl (*E*)-2-(4-hydroxy-2-phenylbut-2-en-1-yl)-2-(4-nitrobenzyl)malonate (5ag)

Yield: 48% (colorless oil).1H NMR (600 MHz, DMSO) δ 8.12 (d, J = 8.8 Hz, 2H), 7.35 –7.25 (m, 7H), 5.69 (t, J = 6.5 Hz, 1H), 4.03 (d, J = 6.5 Hz, 2H), 3.79 – 3.64 (m, 4H), 3.21 (s, 2H), 3.08 (s, 2H), 0.98 (t, J = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.15, 146.81, 145.25, 142.99, 135.94, 135.82, 131.71, 128.40, 127.57, 123.39, 61.40, 58.48, 39.11, 34.45, 13.88. HRMS (ESI-Q-TOF, m/z) calcd for $C_{25}H_{30}O_5$ $[M + Na]^+$:464.1685, found $[M + Na]^+$:464.1677.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4.0363
4.0189
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3.0380
1.1289
1.1112
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EtOOC
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0.97
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4.03
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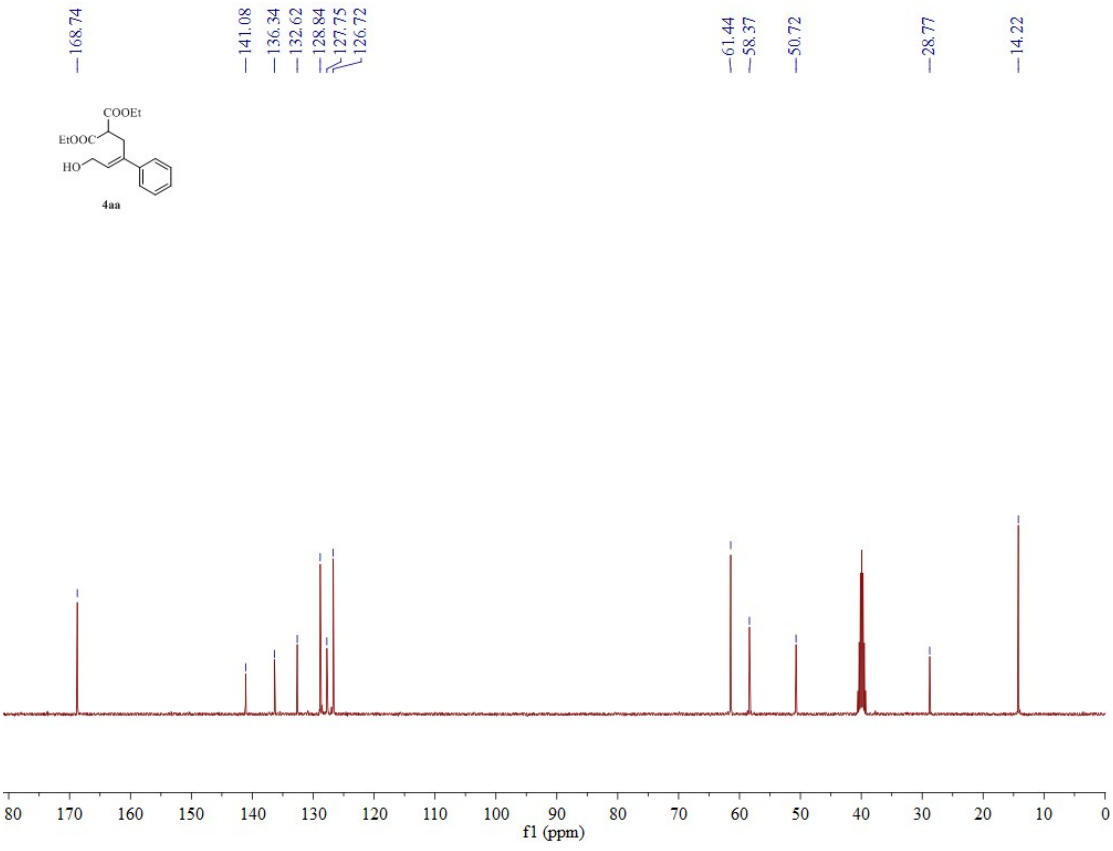
6.00
f1 (ppm)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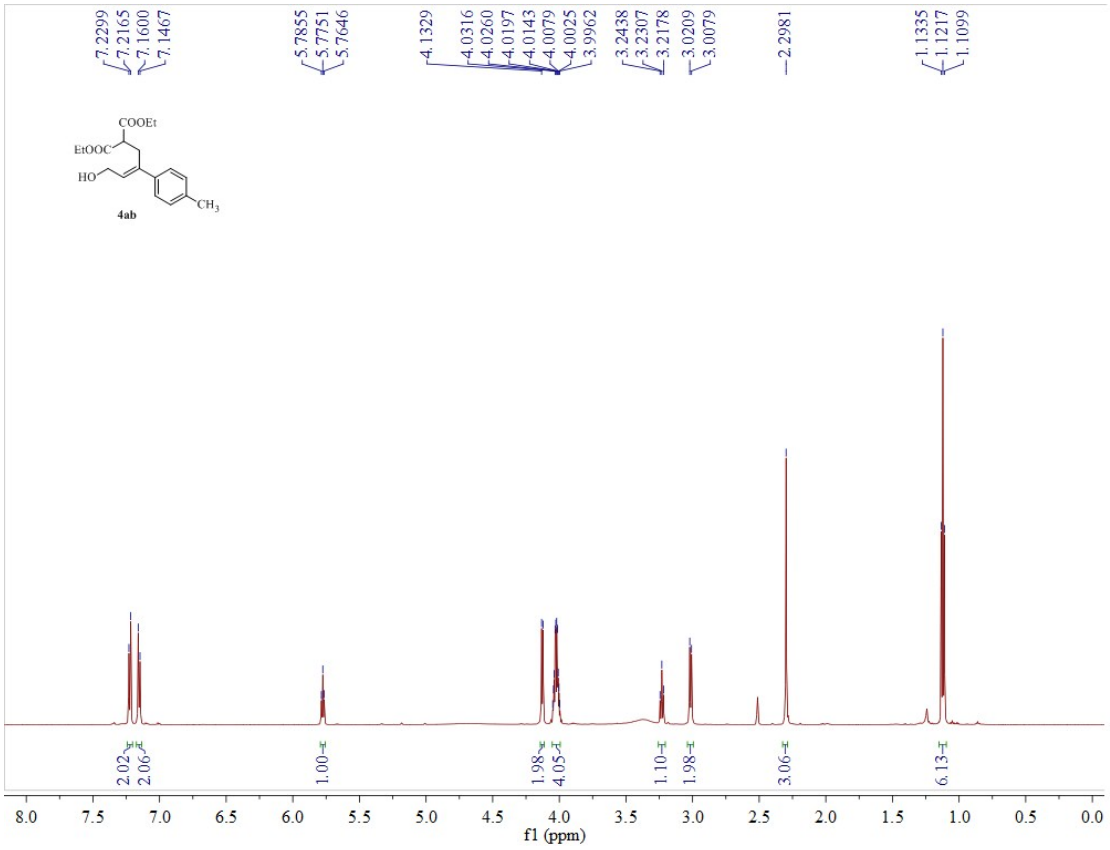
f1 (ppm)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1.1099
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1.98
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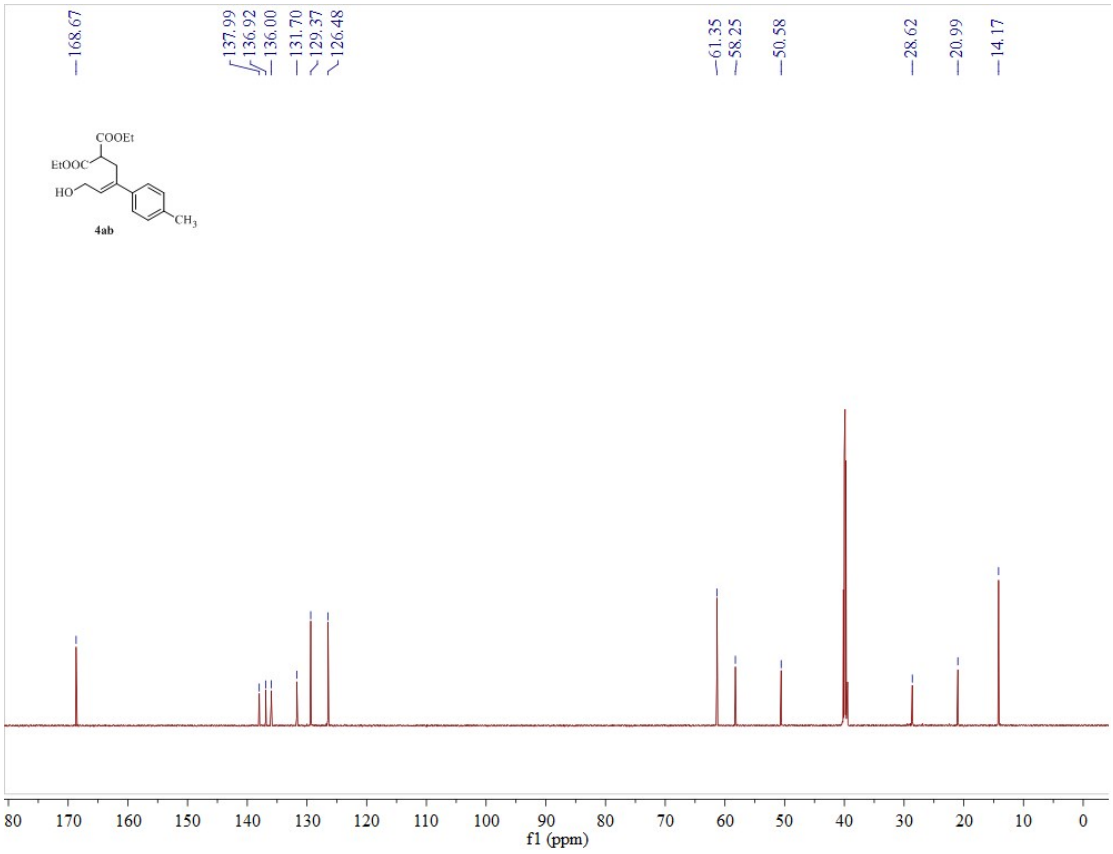
f1 (ppm)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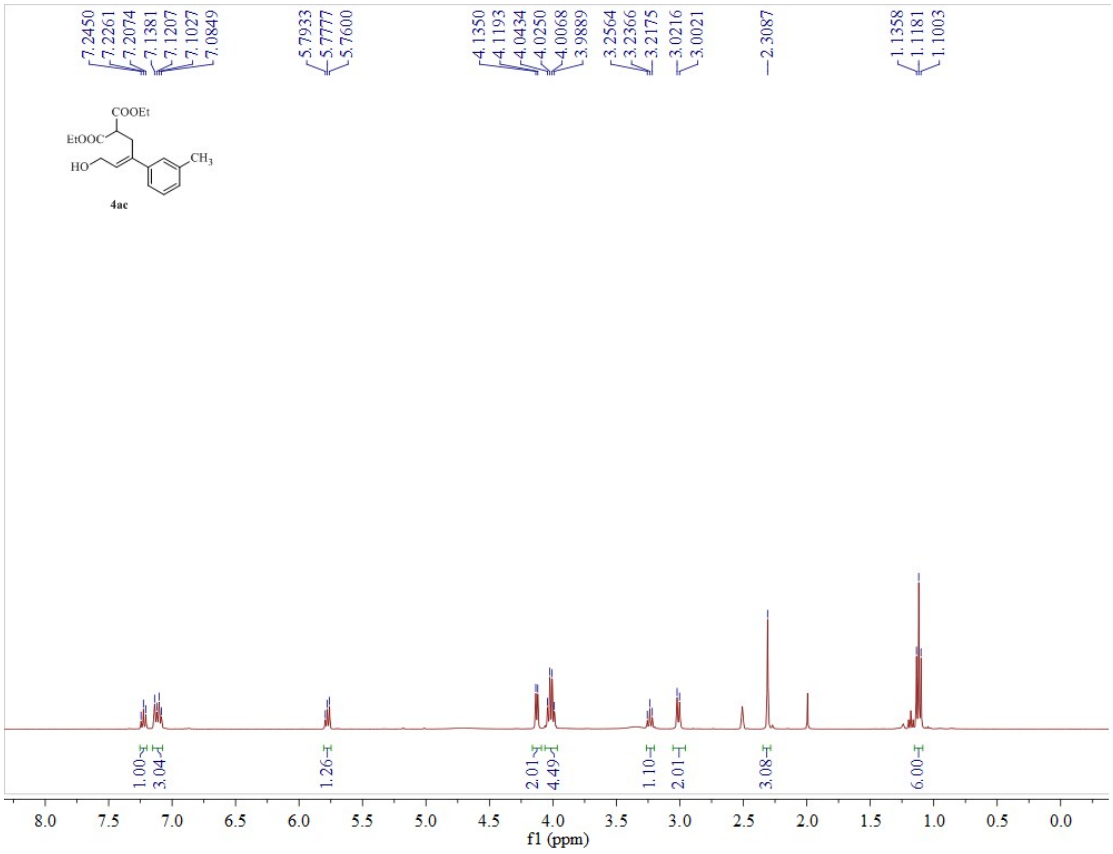
HO
CH3
4ab
f1 (ppm)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4.0068
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3.2366
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EtOOC
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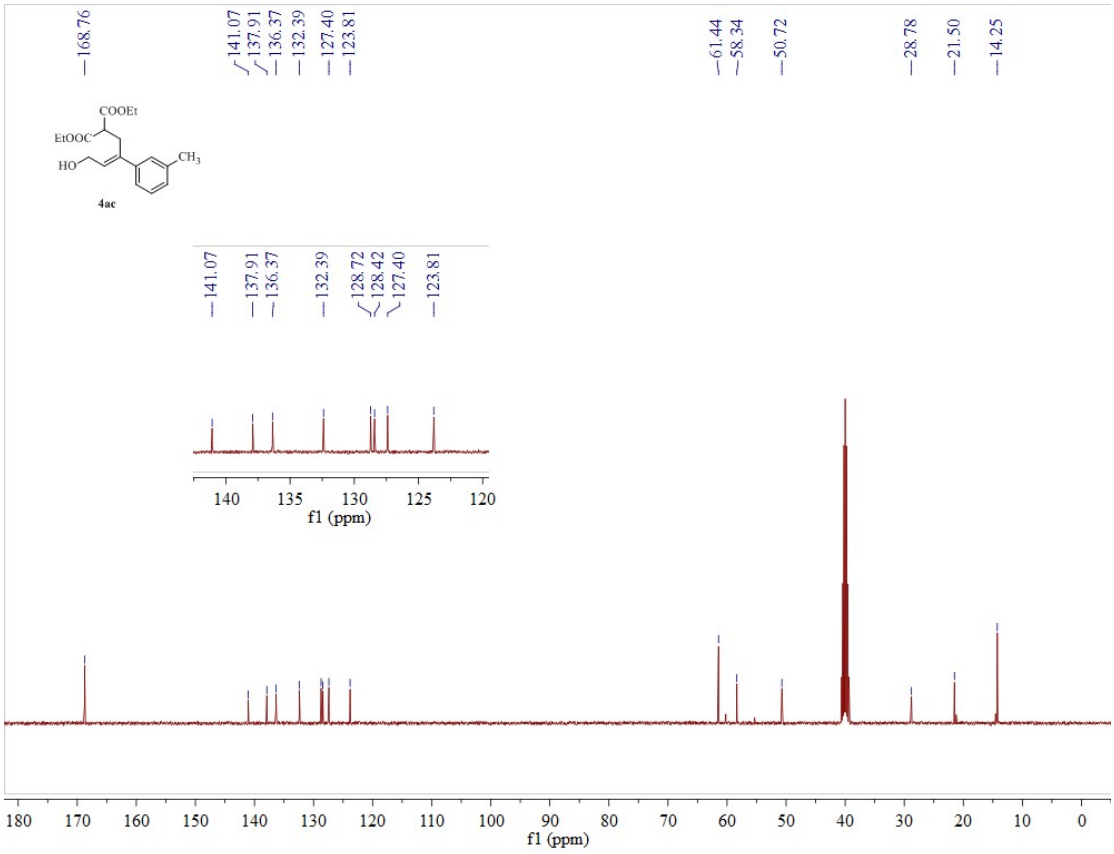
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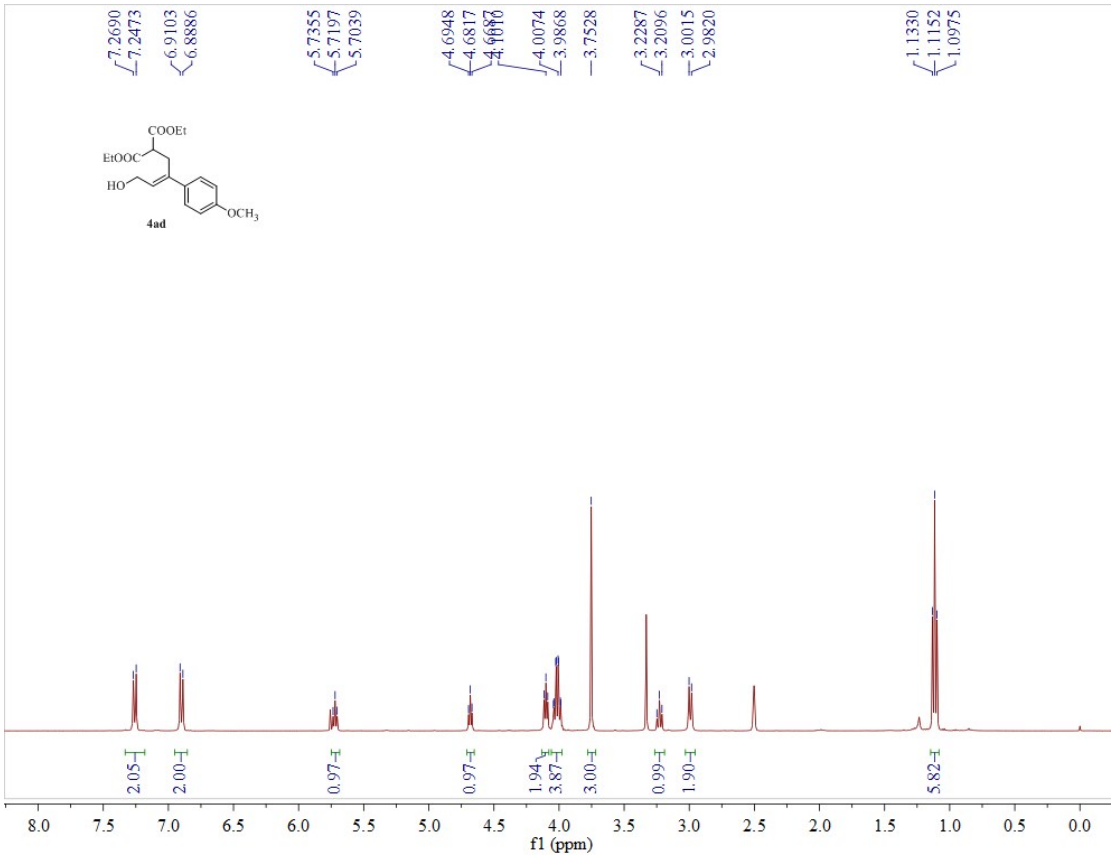
123.81
f1 (ppm)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EtOOC
HO
OCH3
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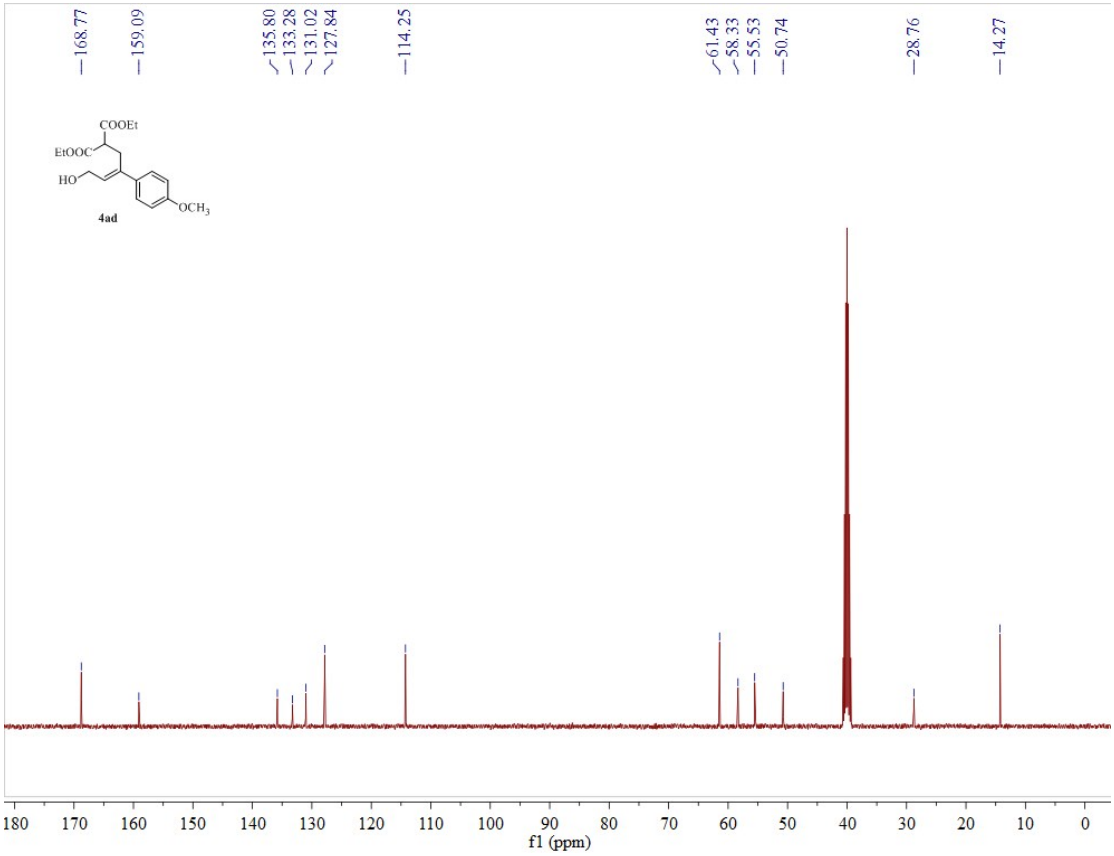
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EtOOC
HO
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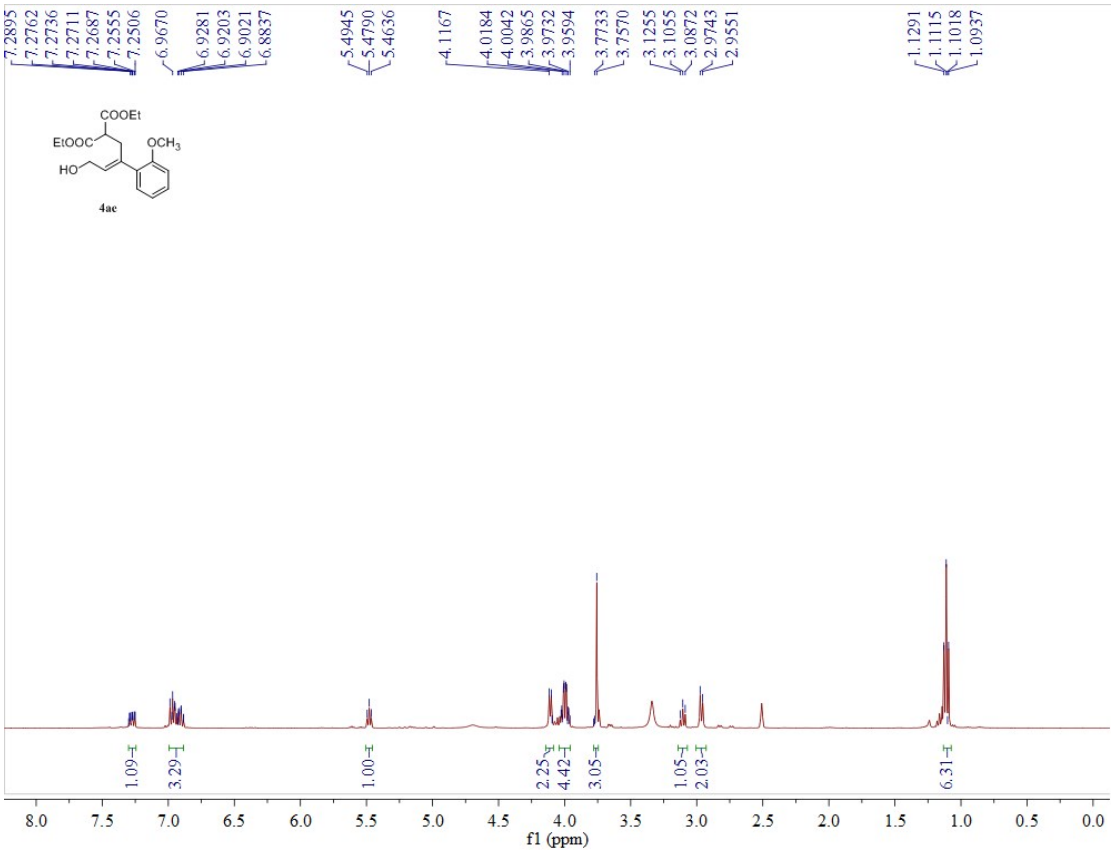
4ad
f1 (ppm)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1.05
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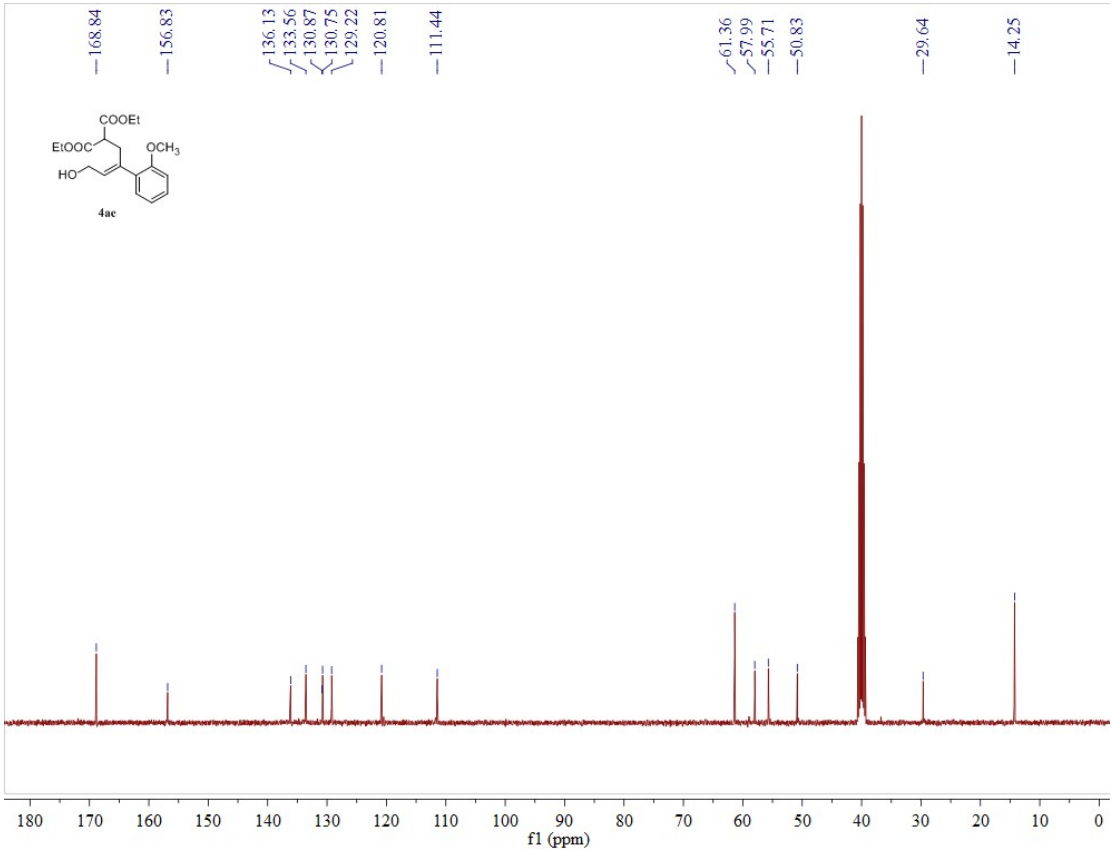
f1 (ppm)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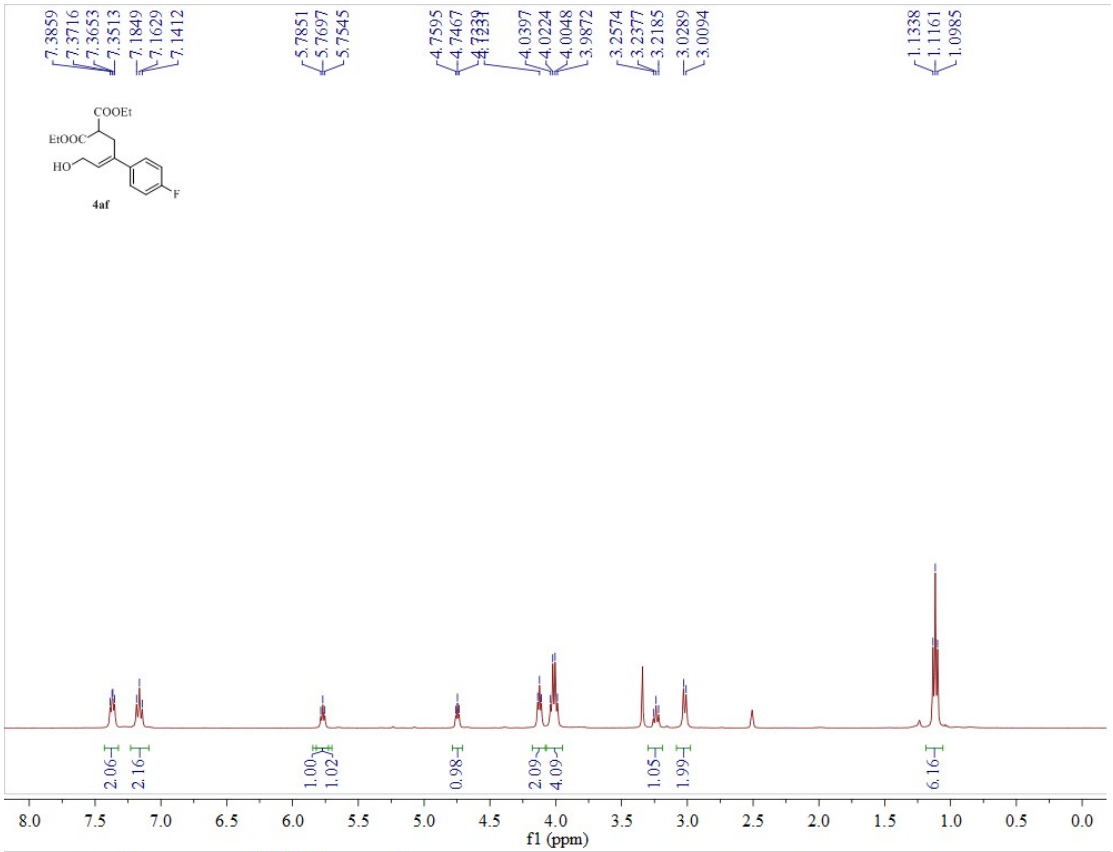
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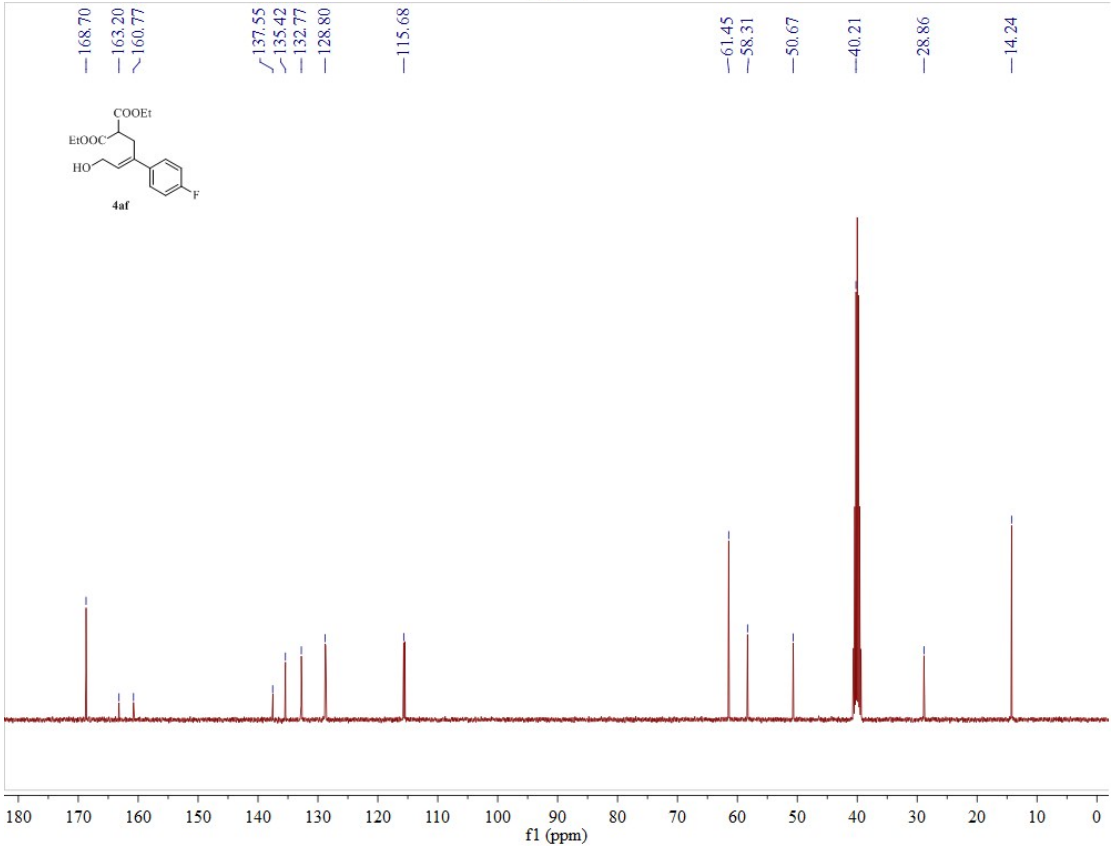
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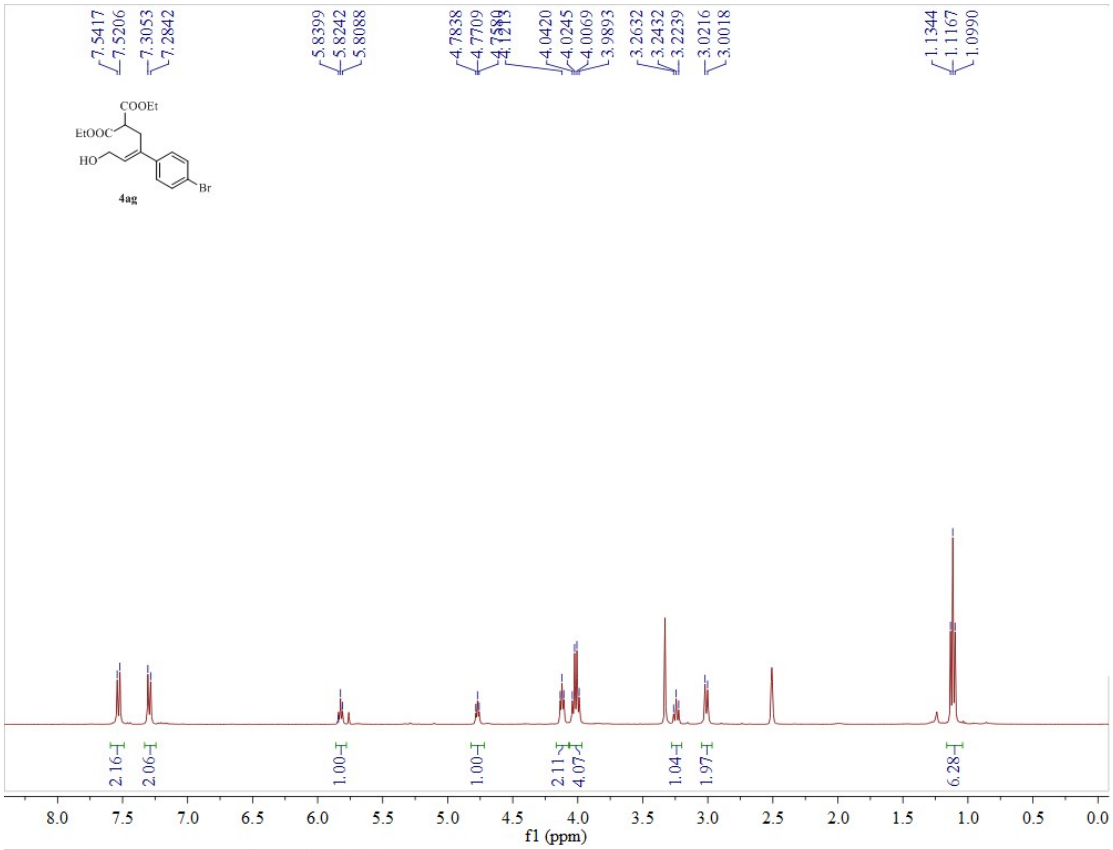
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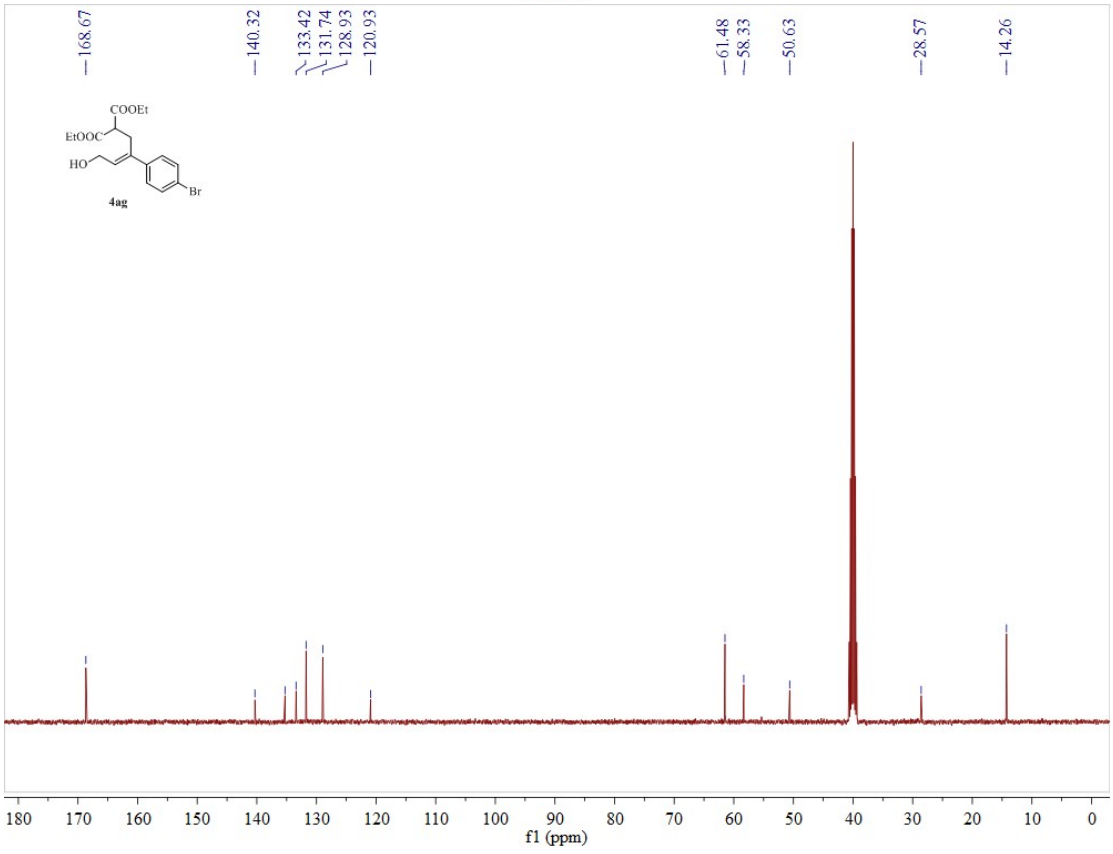
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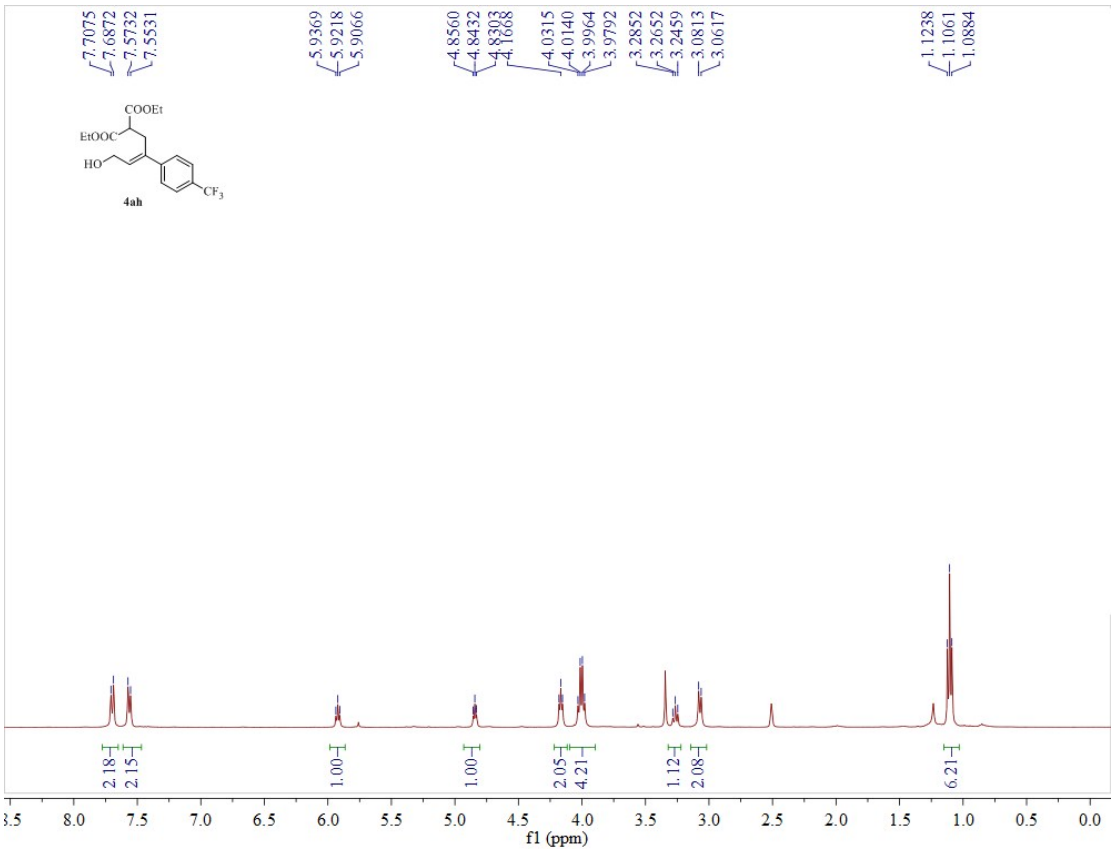
f1 (ppm)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EtOOC
HO
CF3
4ah
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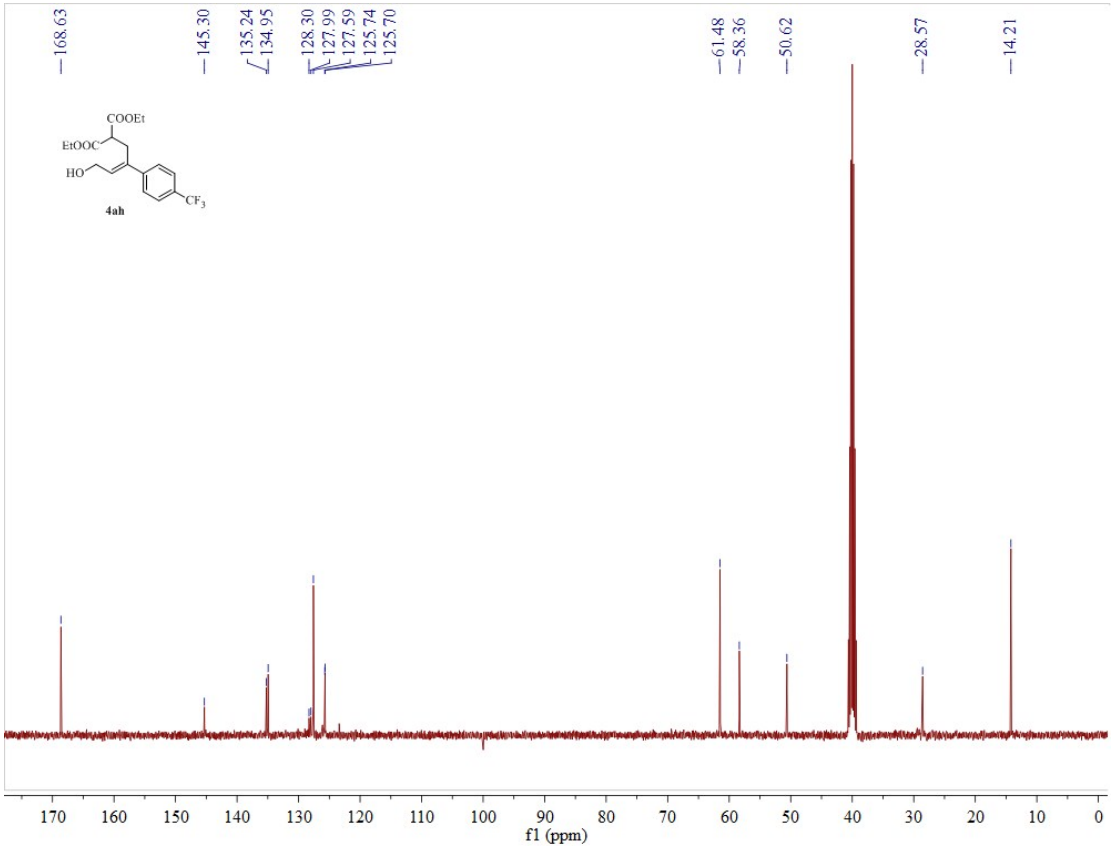
2.15
1.00
1.00
2.05
4.21
1.12
2.08
6.21
f1 (ppm)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145.30
135.24
134.95
128.30
127.99
127.59
125.74
125.70
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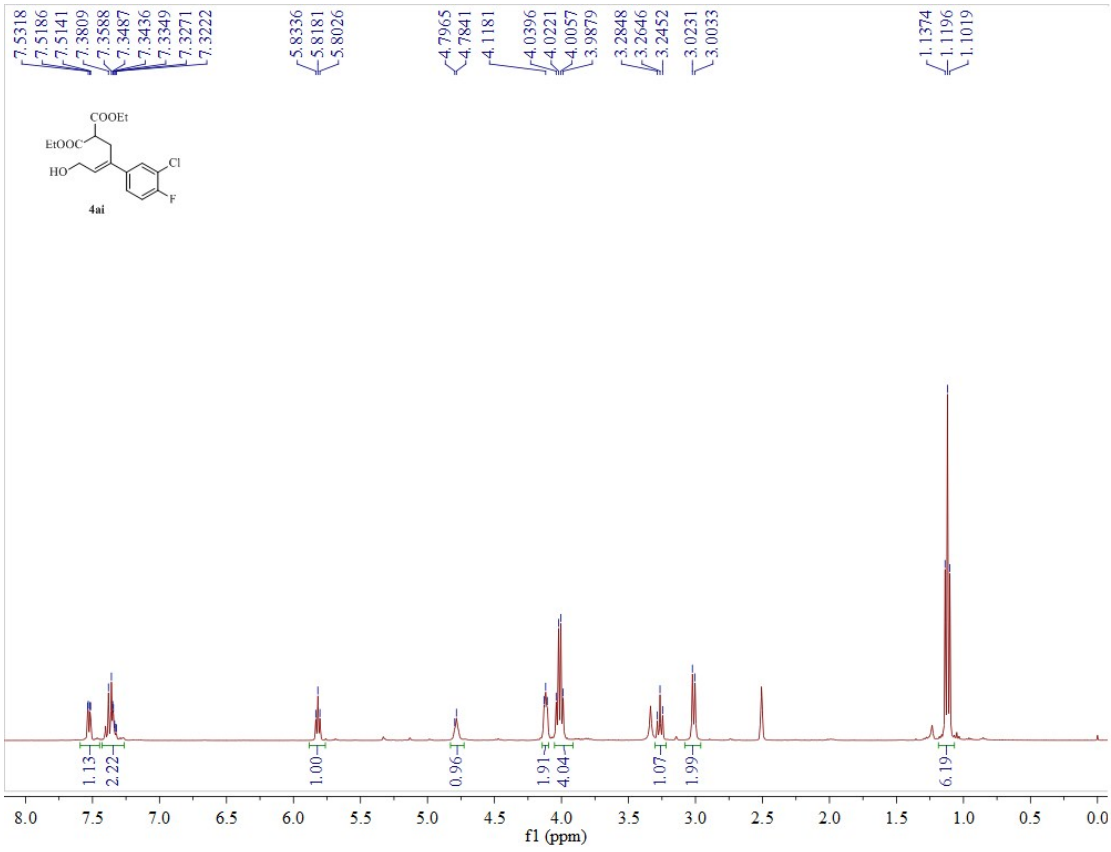
58.36
50.62
28.57
14.21
COOEt
EtOOC
HO
CF3
4ah
f1 (ppm)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7.5141
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7.3588
7.3487
7.3436
7.3349
7.3271
7.3222
5.8336
5.8181
5.8026
4.7965
4.7841
4.1181
4.0396
4.0221
4.0057
3.9879
3.2848
3.2646
3.2452
3.0231
3.0033
1.1374
1.1196
1.1019
COOEt
EtOOC
HO
Cl
F
4ai
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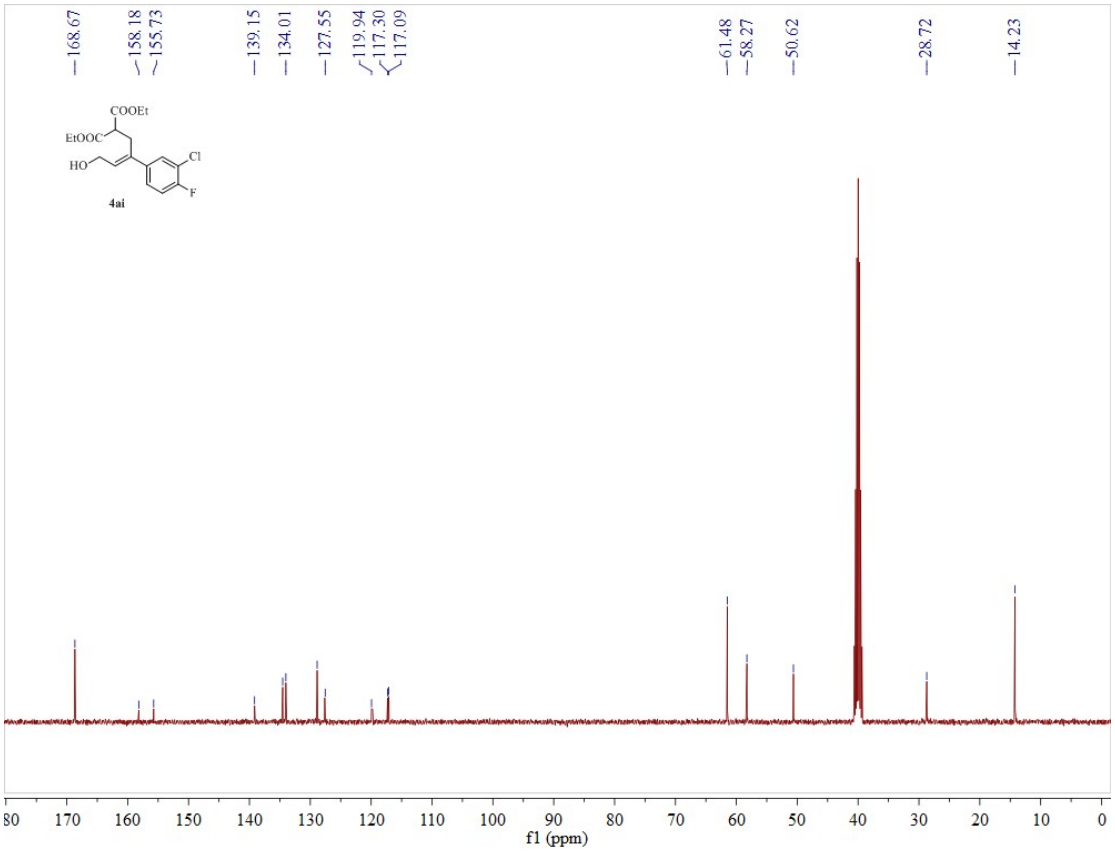
2.22
1.00
0.96
1.91
4.04
1.07
1.99
6.19
f1 (ppm)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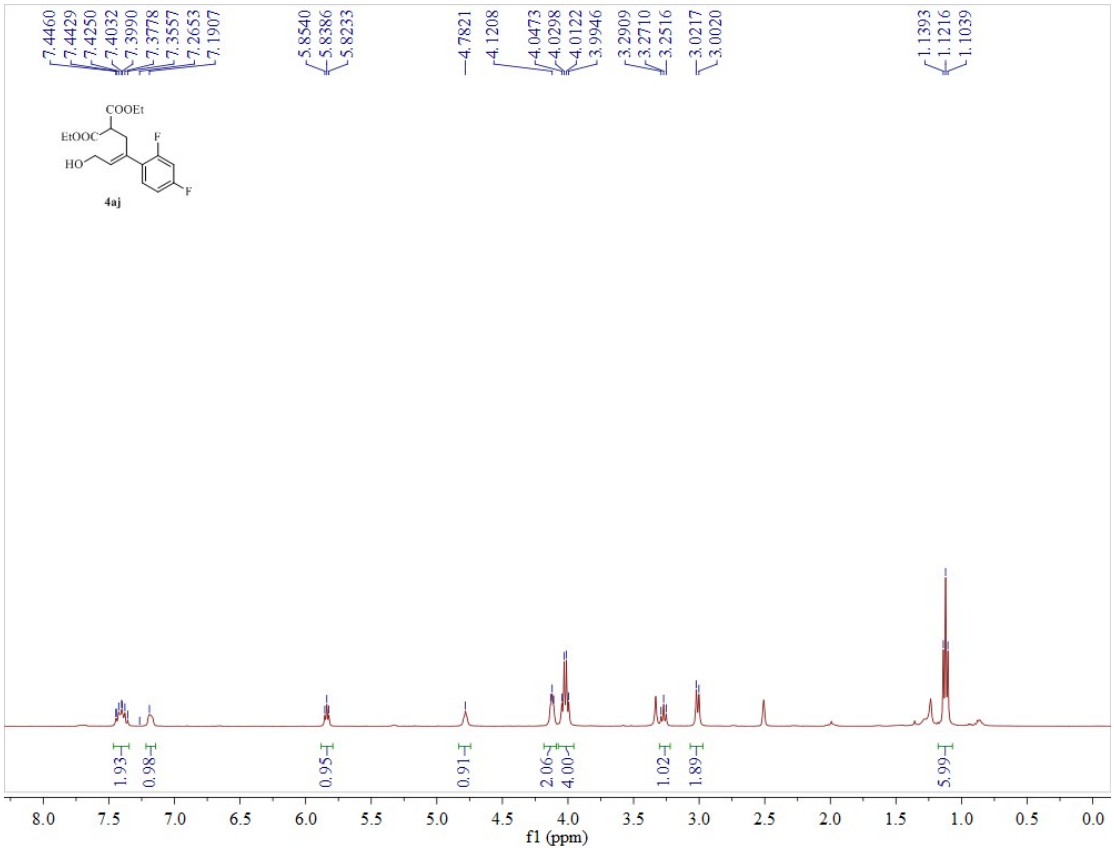
139.15
134.01
127.55
119.94
117.30
117.09
61.48
58.27
50.62
28.72
14.23
COOEt
EtOOC
HO
Cl
F
4ai
f1 (ppm)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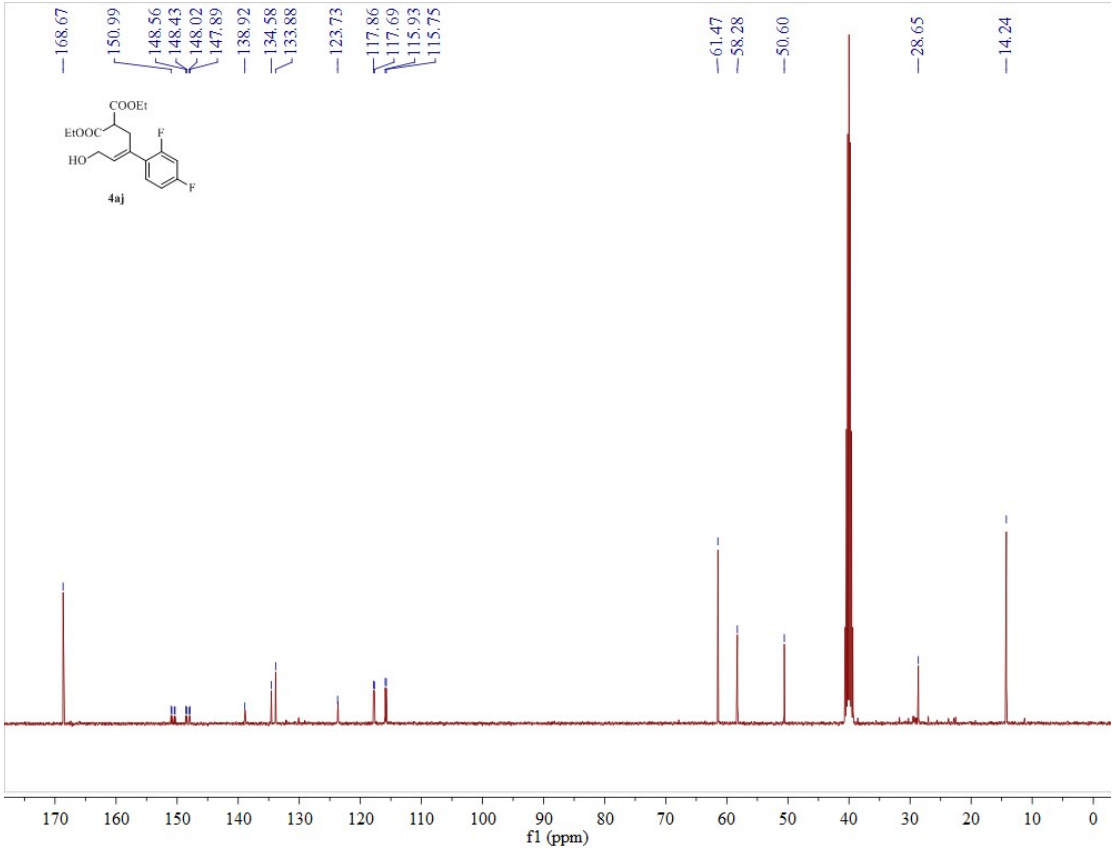
7.4250
7.4032
7.3990
7.3778
7.3557
7.2653
7.1907
5.8540
5.8386
5.8233
4.7821
4.1208
4.0473
4.0298
4.0122
3.9946
3.2909
3.2710
3.2516
3.0217
3.0020
1.1393
1.1216
1.1039
COOEt
EtOOC
HO
F
F
4aj
1.93
0.98
0.95
0.91
2.06
4.00
1.02
1.89
5.99
f1 (ppm)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148.02
147.89
138.92
134.58
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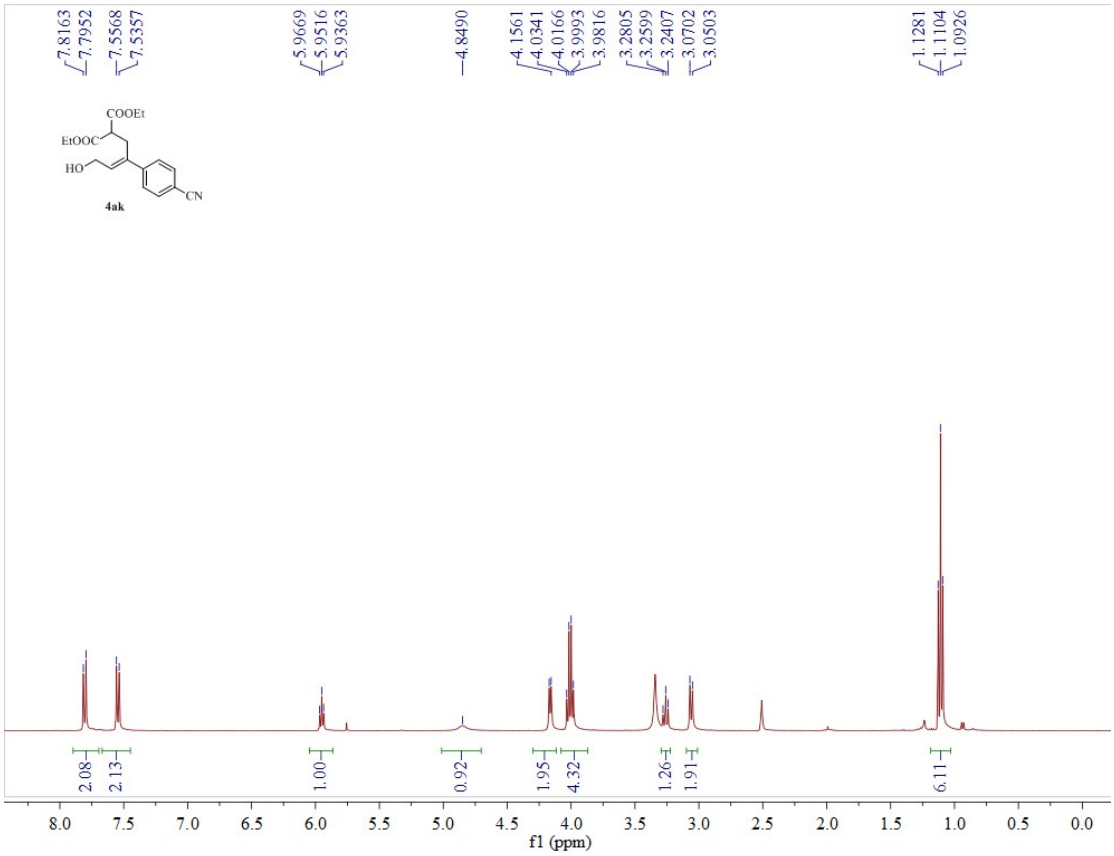
123.73
117.86
117.69
115.93
115.75
61.47
58.28
50.60
28.65
14.24
COOEt
EtOOC
HO
F
F
4aj
f1 (ppm)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5.9363
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4.1561
4.0341
4.0166
3.9993
3.9816
3.2805
3.2599
3.2407
3.0702
3.0503
1.1281
1.1104
1.0926
COOEt
EtOOC
HO
CN
4ak
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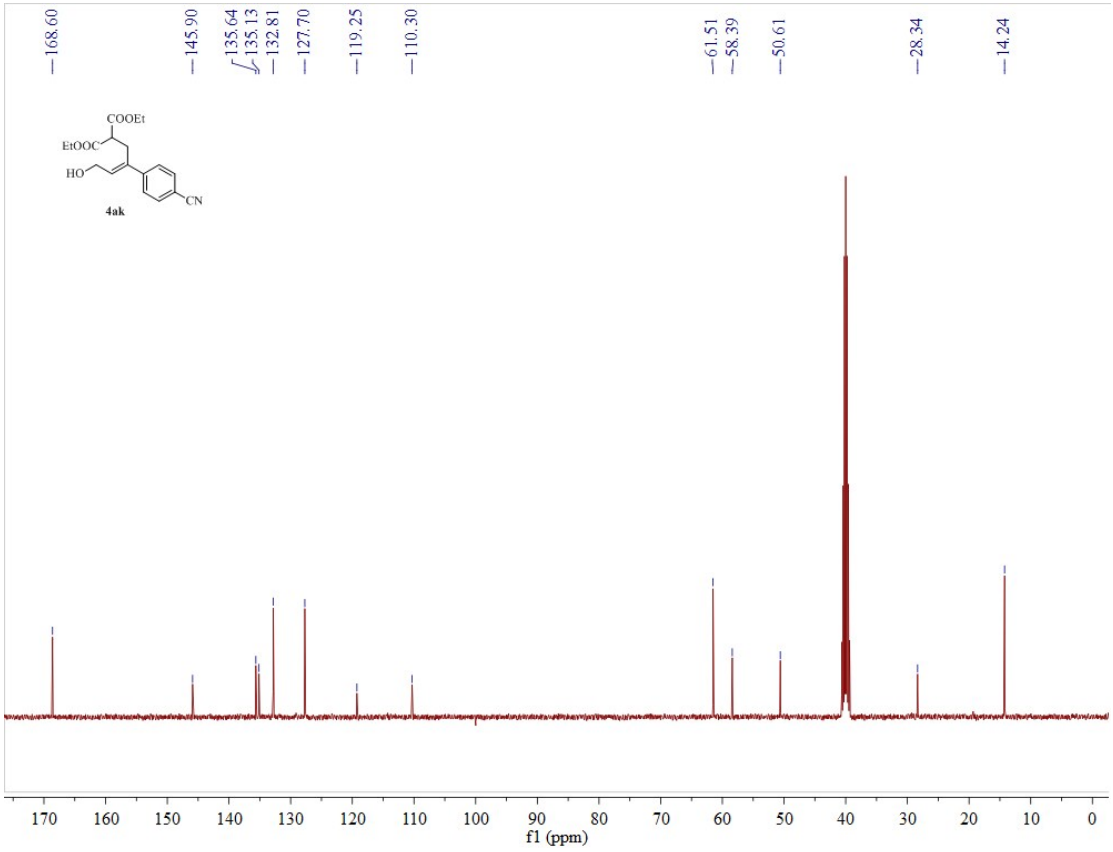
2.13
1.00
0.92
1.95
4.32
1.26
1.91
6.11
f1 (ppm)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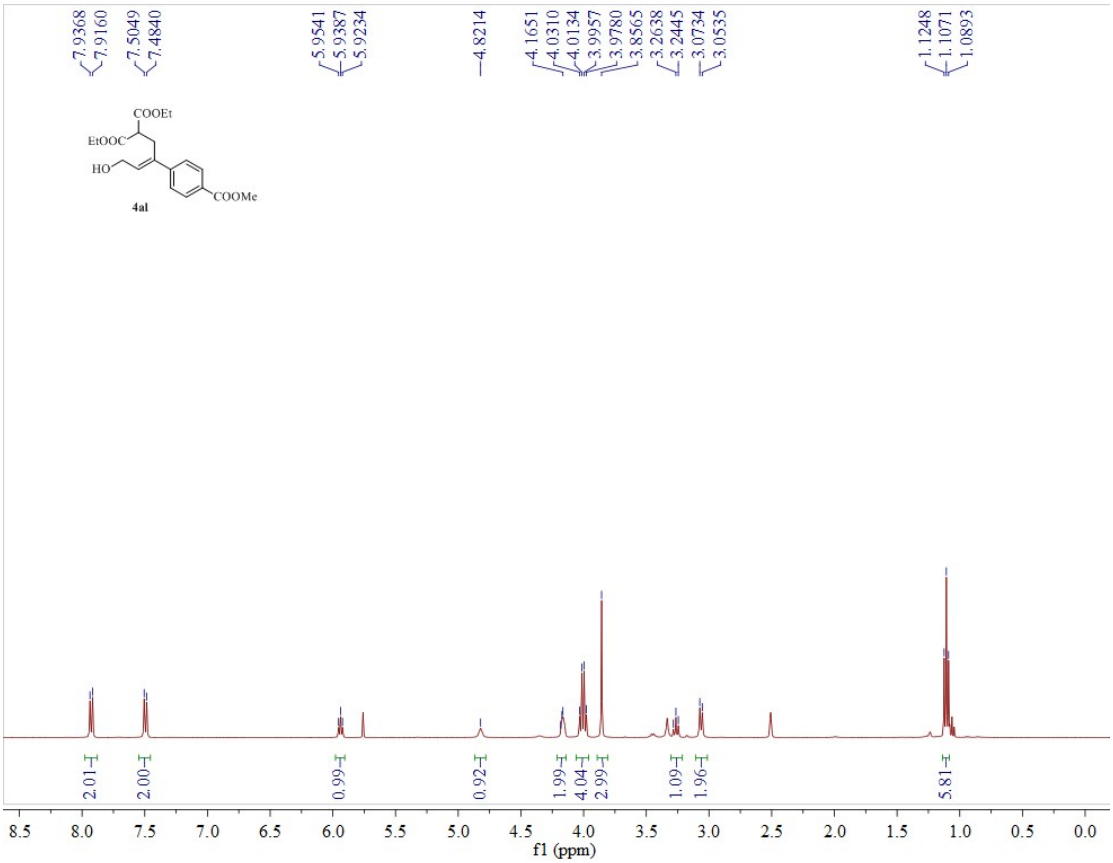
135.13
132.81
127.70
119.25
110.30
61.51
58.39
50.61
28.34
14.24
COOEt
EtOOC
HO
CN
4ak
f1 (ppm)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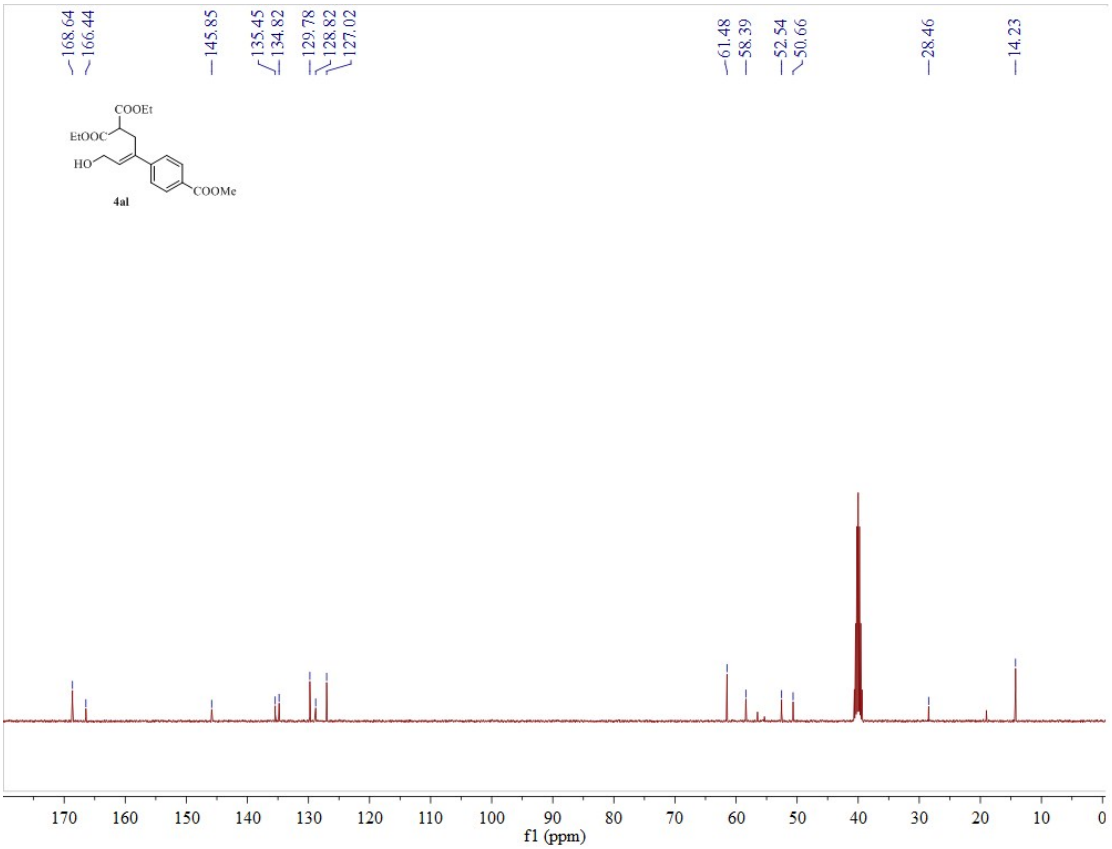
7.4840
5.9541
5.9387
5.9234
4.8214
4.1651
4.0310
4.0134
3.9957
3.9780
3.8565
3.2638
3.2445
3.0734
3.0535
1.1248
1.1071
1.0893
COOEt
EtOOC
HO
COOMe
4al
2.01
2.00
0.99
0.92
1.99
4.04
2.99
1.09
1.96
5.81
f1 (ppm)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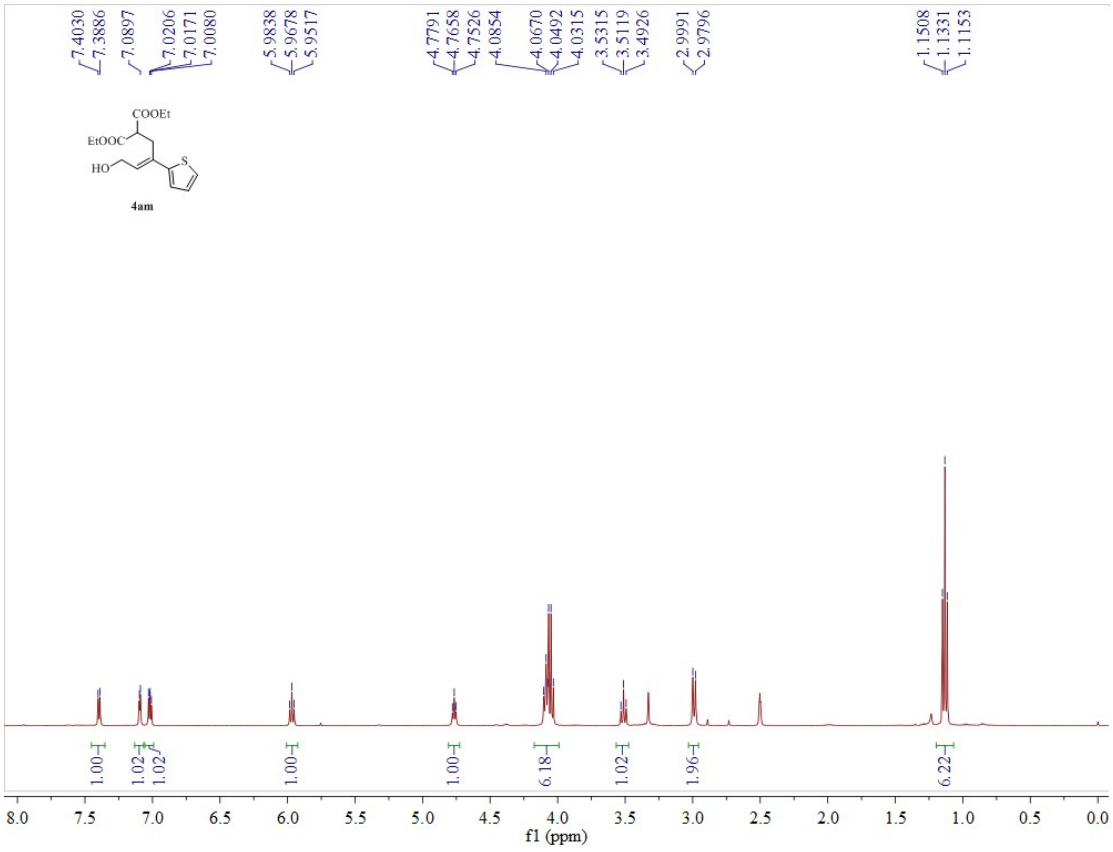
166.44
145.85
135.45
134.82
129.78
128.82
127.02
61.48
58.39
52.54
50.66
28.46
14.23
COOEt
EtOOC
HO
COOMe
4al
f1 (ppm)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7.0171
7.0080
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5.9678
5.9517
4.7791
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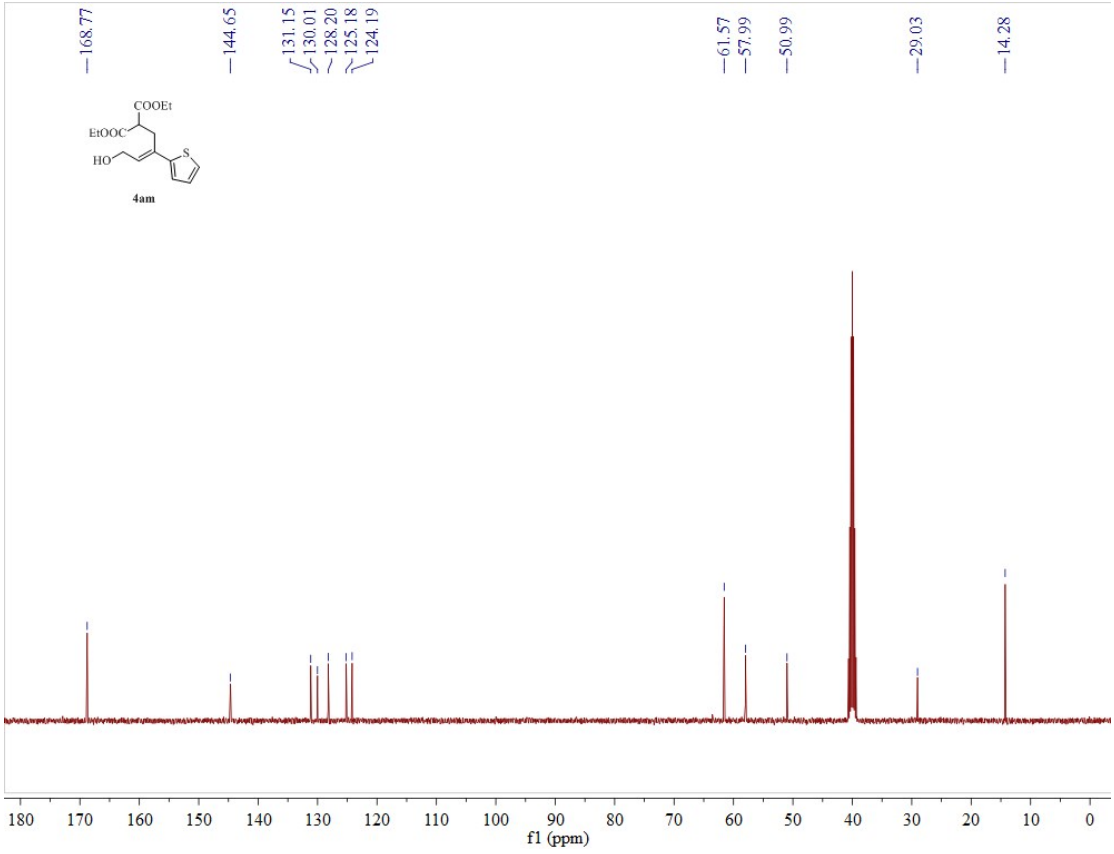
4.7526
4.0854
4.0670
4.0492
4.0315
3.5315
3.5119
3.4926
2.9991
2.9796
1.1508
1.1331
1.1153
COOEt
EtOOC
HO
S
4am
1.00
1.02
1.02
1.00
1.00
6.18
1.02
1.96
6.22
f1 (ppm)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130.01
128.20
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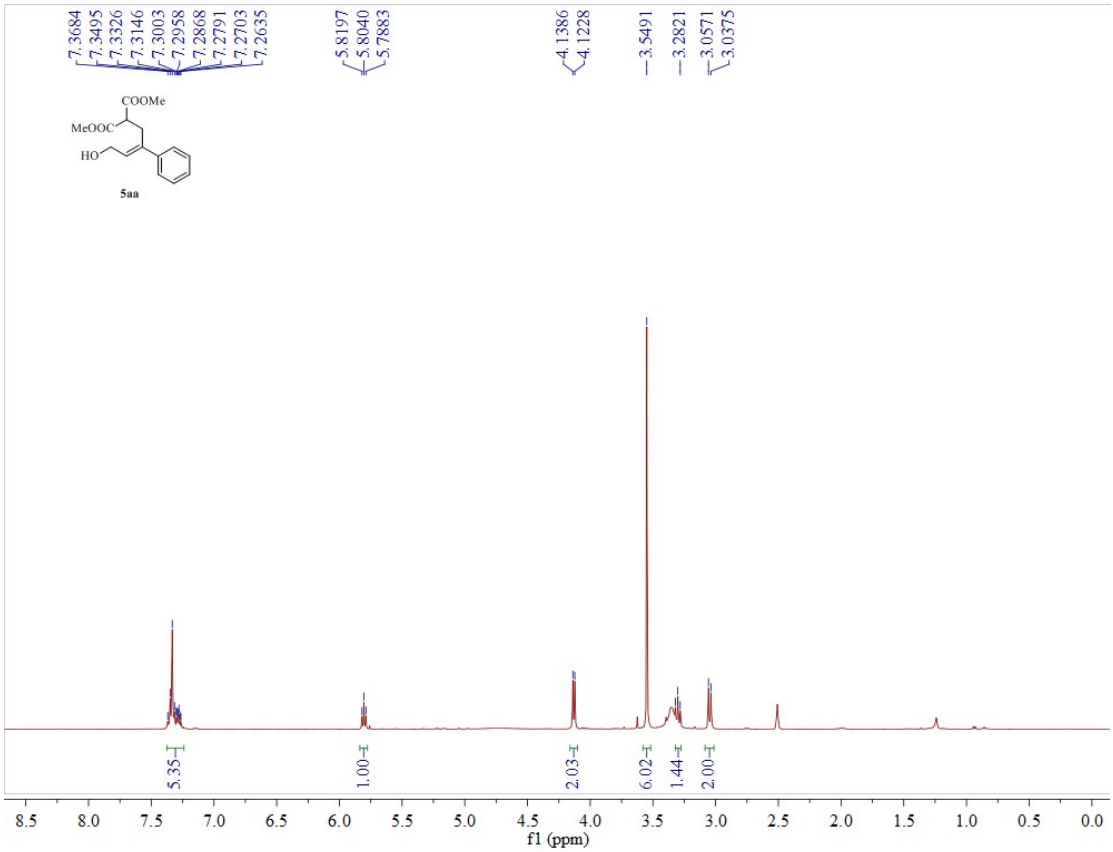
61.57
57.99
50.99
29.03
14.28
COOEt
EtOOC
HO
S
4am
f1 (ppm)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7.2703
7.2635
5.8197
5.8040
5.7883
4.1386
4.1228
3.5491
3.2821
3.0571
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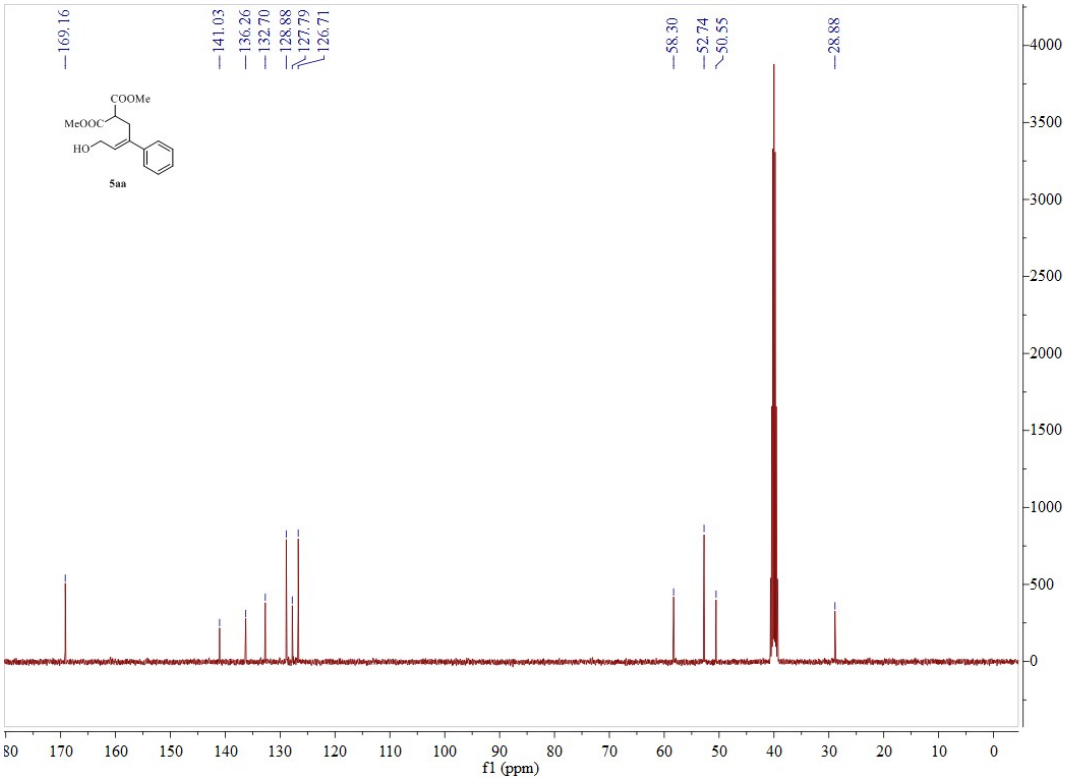
COOMe
MeOOC
HO
5aa
5.35
1.00
2.03
6.02
1.44
2.00
f1 (ppm)


169.16
141.03
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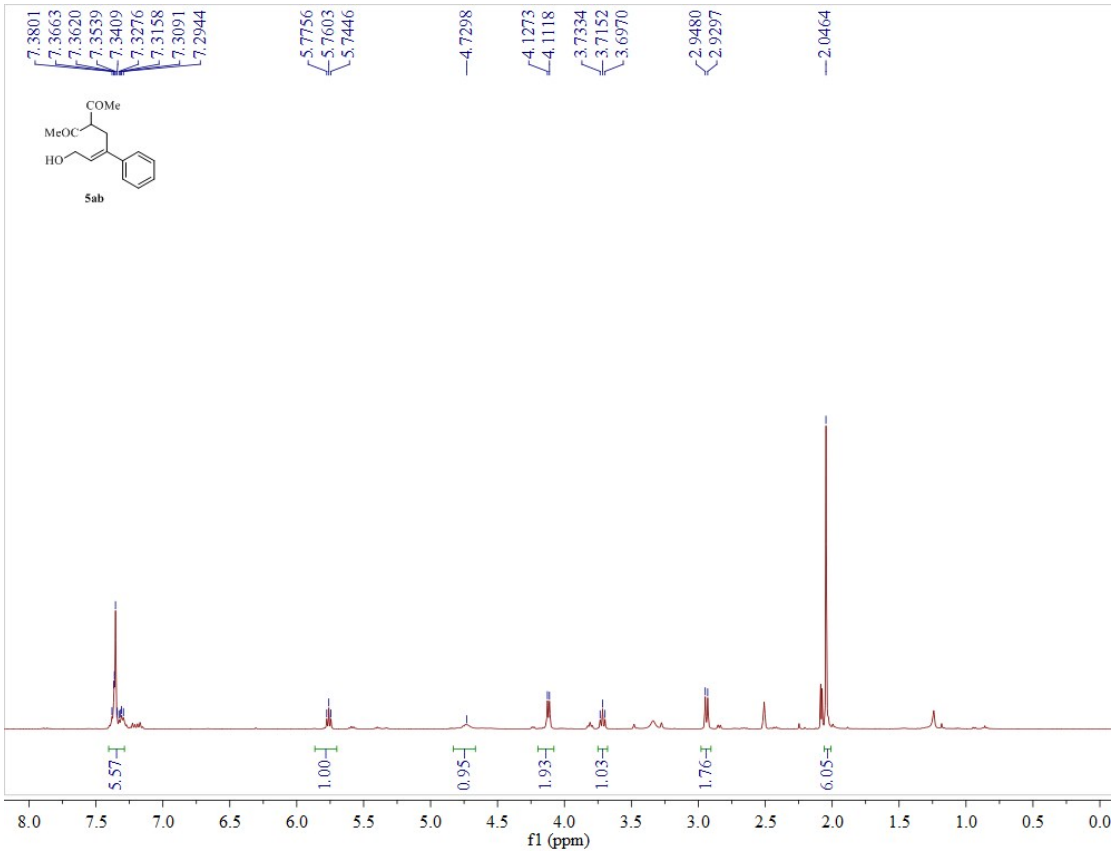
58.30
52.74
50.55
28.88
COOMe
MeOOC
HO
5aa
f1 (ppm)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7.3158
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7.2944
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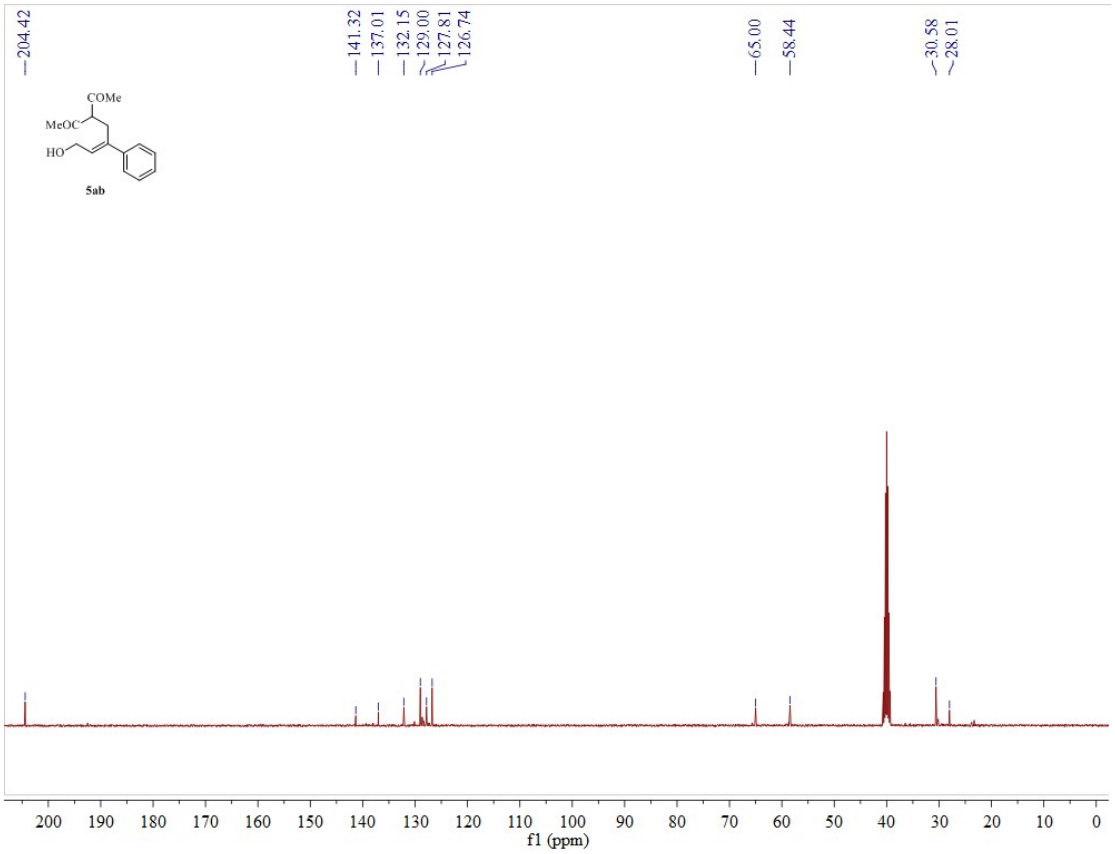
5.7603
5.7446
4.7298
4.1273
4.1118
3.7334
3.7152
3.6970
2.9480
2.9297
2.0464
COMe
MeOC
HO
5ab
5.57
1.00
0.95
1.93
1.03
1.76
6.05
f1 (ppm)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141.32
137.01
132.15
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65.00
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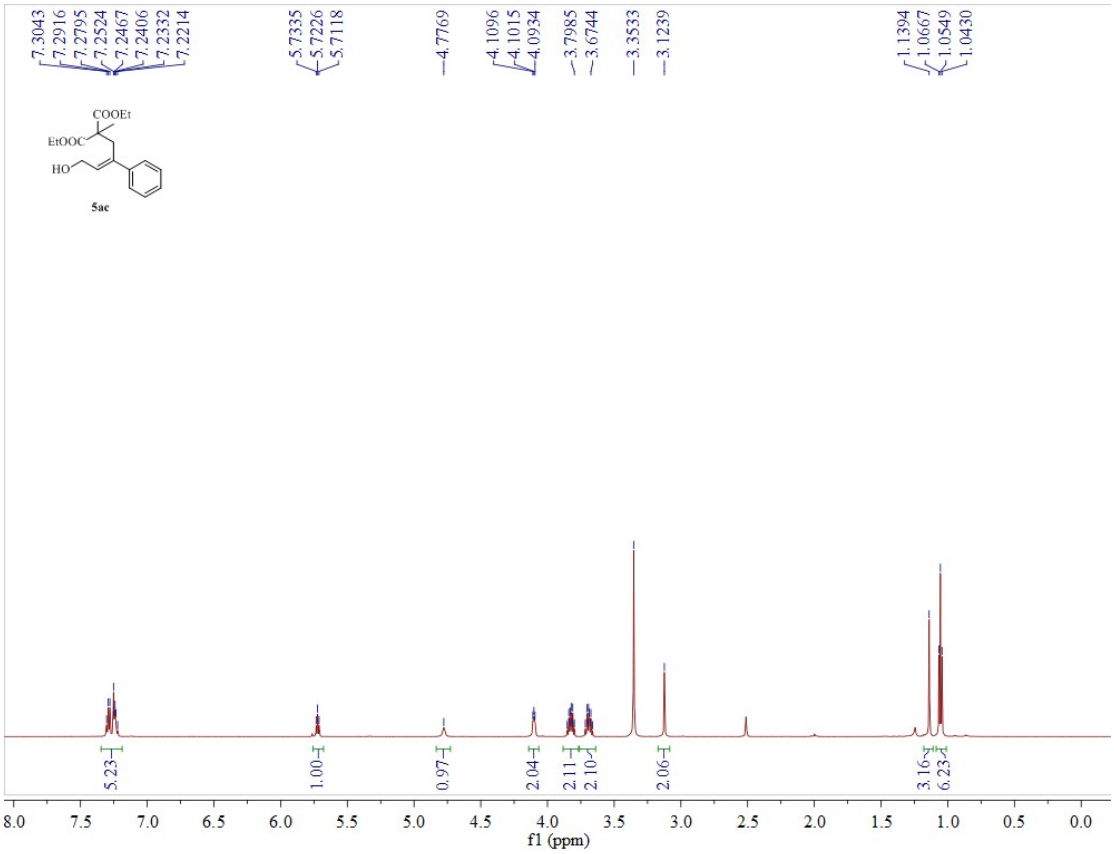
30.58
28.01
COMe
MeOC
HO
5ab
f1 (ppm)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7.2214
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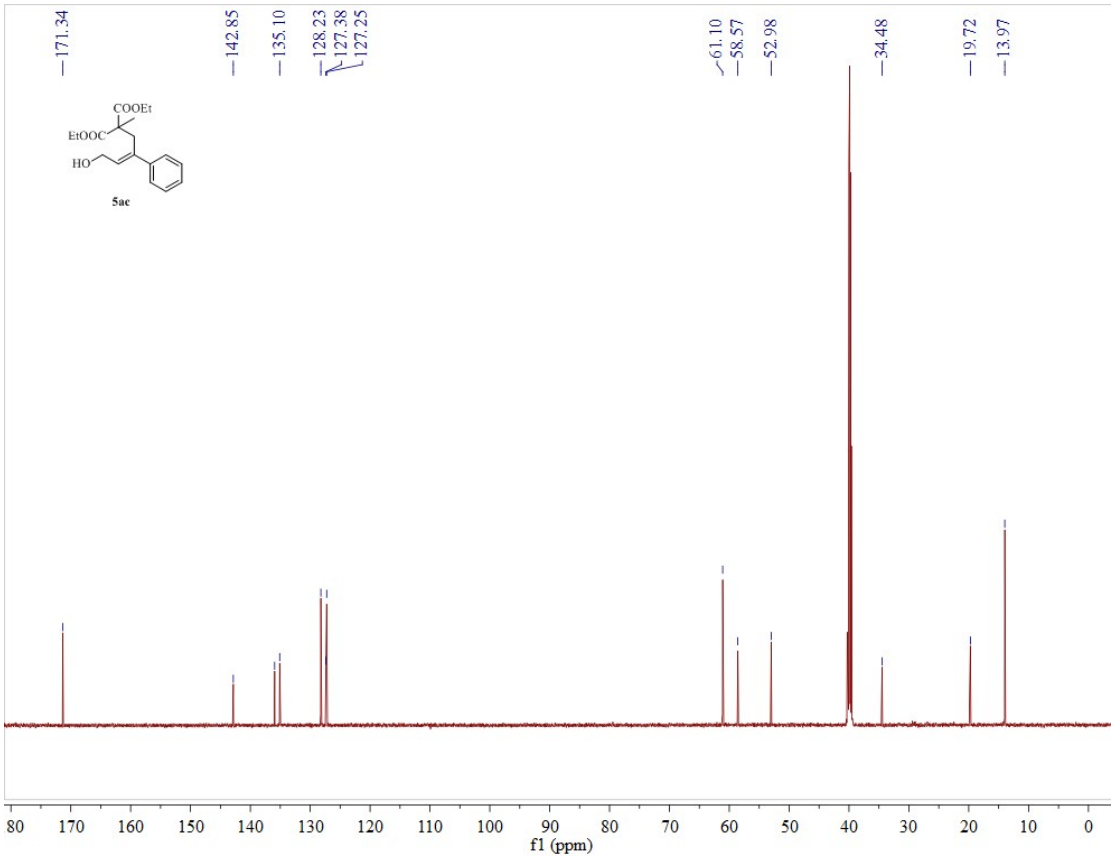
5.7226
5.7118
4.7769
4.1096
4.1015
4.0934
3.7985
3.6744
3.3533
3.1239
1.1394
1.0667
1.0549
1.0430
COOEt
EtOOC
HO
5ac
5.23
1.00
0.97
2.04
2.11
2.10
2.06
3.16
6.23
f1 (ppm)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127.38
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58.57
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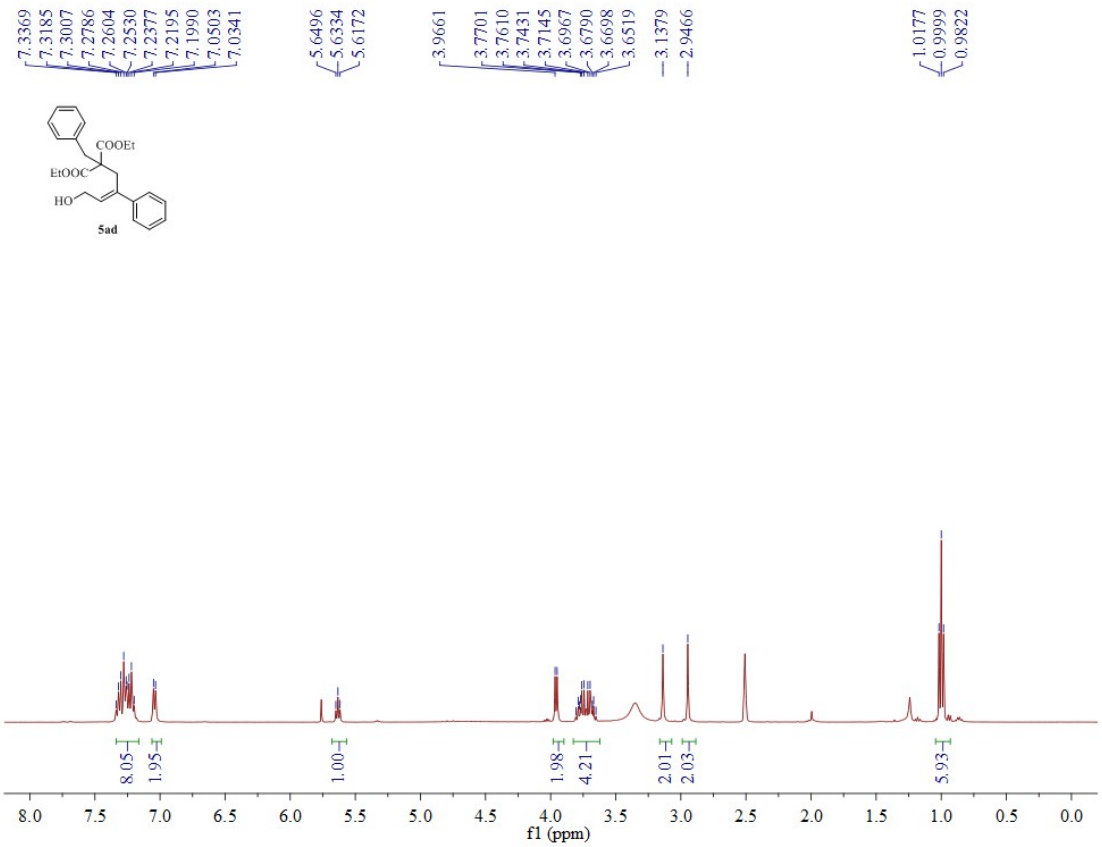
34.48
19.72
13.97
COOEt
EtOOC
HO
5ac
f1 (ppm)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7.1990
7.0503
7.0341
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5.6334
5.6172
3.9661
3.7701
3.7610
3.7431
3.7145
3.6967
3.6790
3.6698
3.6519
3.1379
2.9466
1.0177
0.9999
0.9822
COOEt
EtOOC
HO
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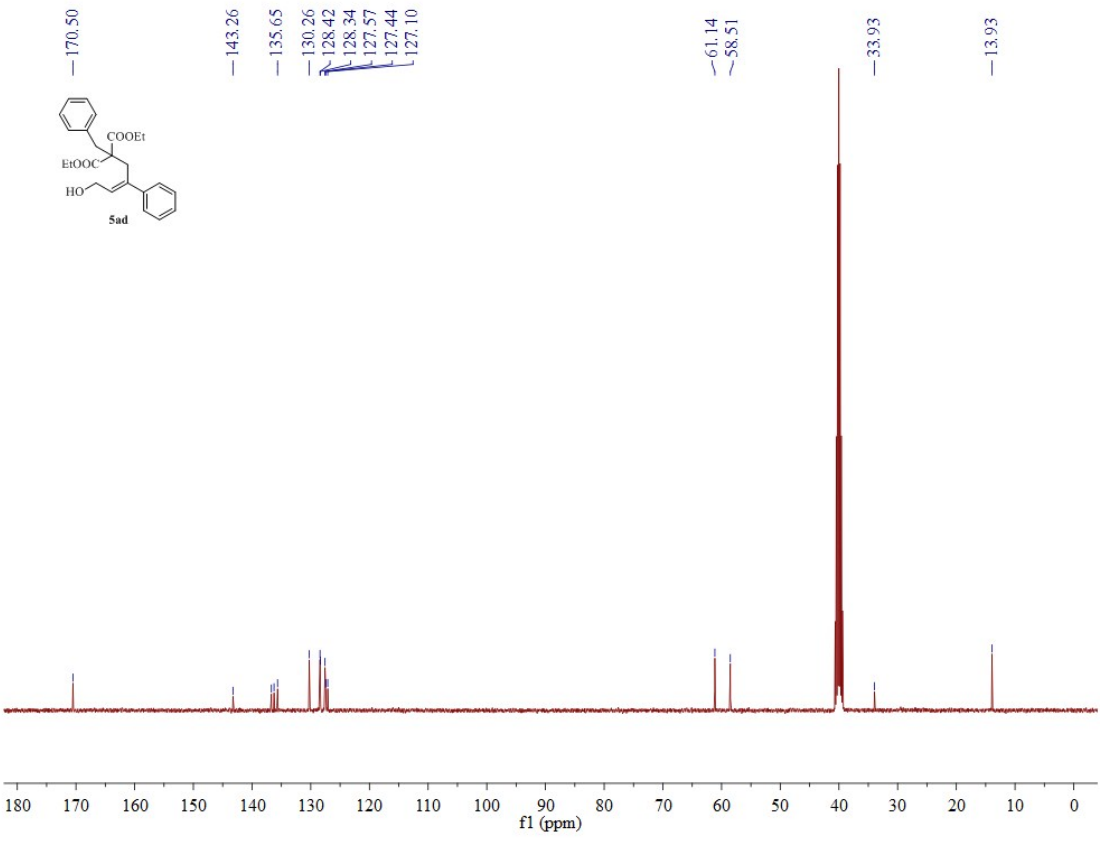
1.95
1.00
1.98
4.21
2.01
2.03
5.93
f1 (ppm)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128.34
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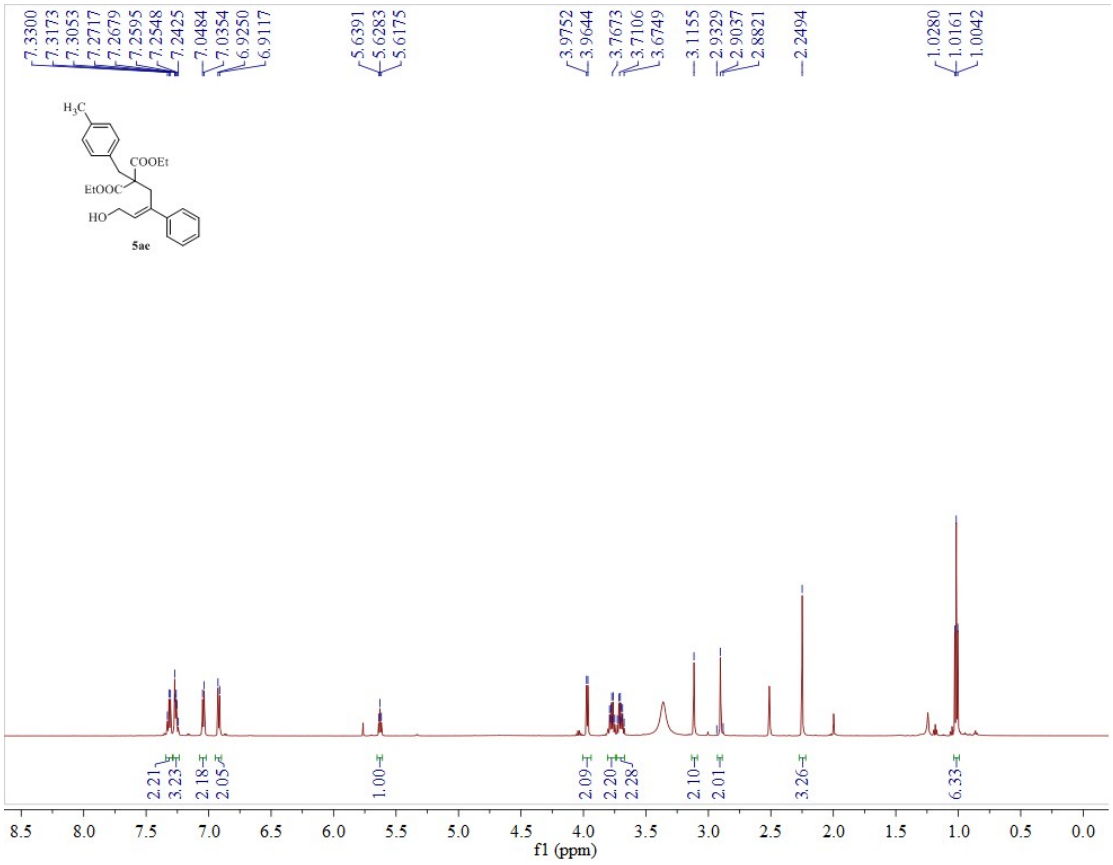
127.10
61.14
58.51
33.93
13.93
COOEt
EtOOC
HO
5ad
f1 (ppm)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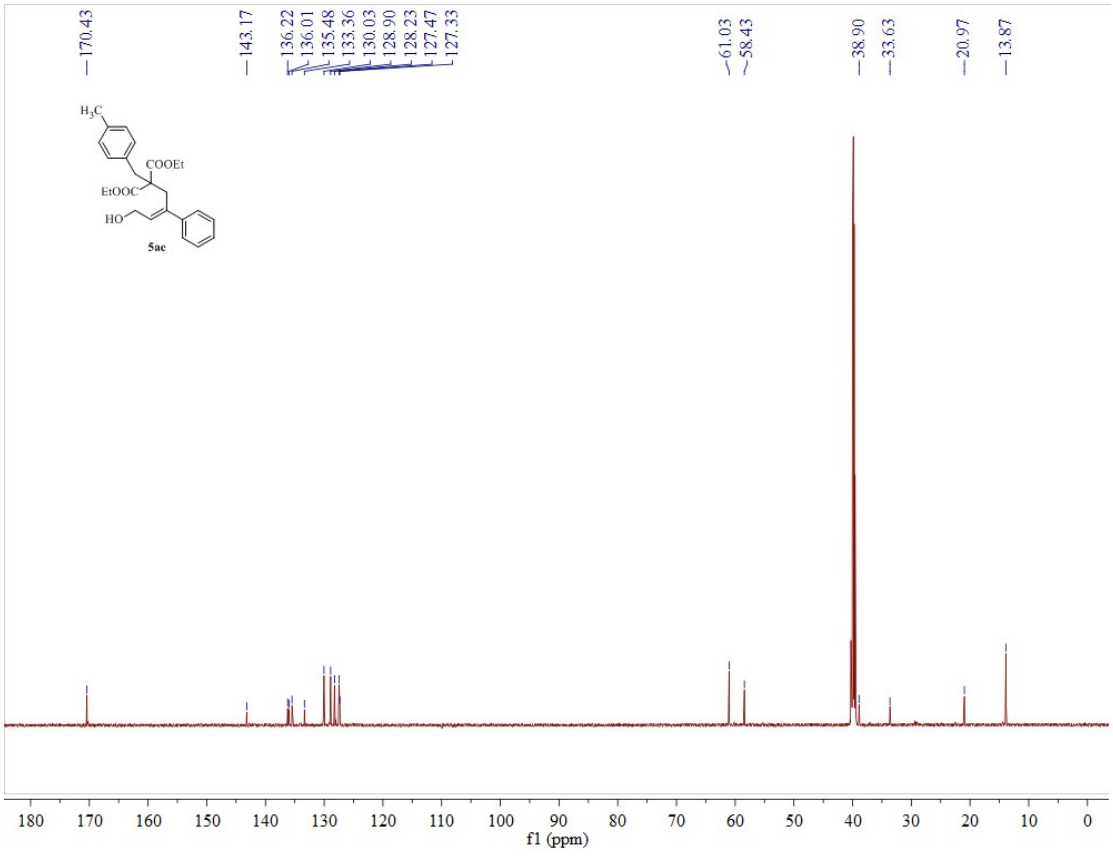
7.0484
7.0354
6.9250
6.9117
5.6391
5.6283
5.6175
3.9752
3.9644
3.7673
3.7106
3.6749
3.1155
2.9329
2.9037
2.8821
2.2494
1.0280
1.0161
1.0042
COOEt
EtOOC
HO
5ae
2.21
3.23
2.18
2.05
1.00
2.09
2.20
2.28
2.10
2.01
3.26
6.33
f1 (ppm)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133.36
130.03
128.90
128.23
127.47
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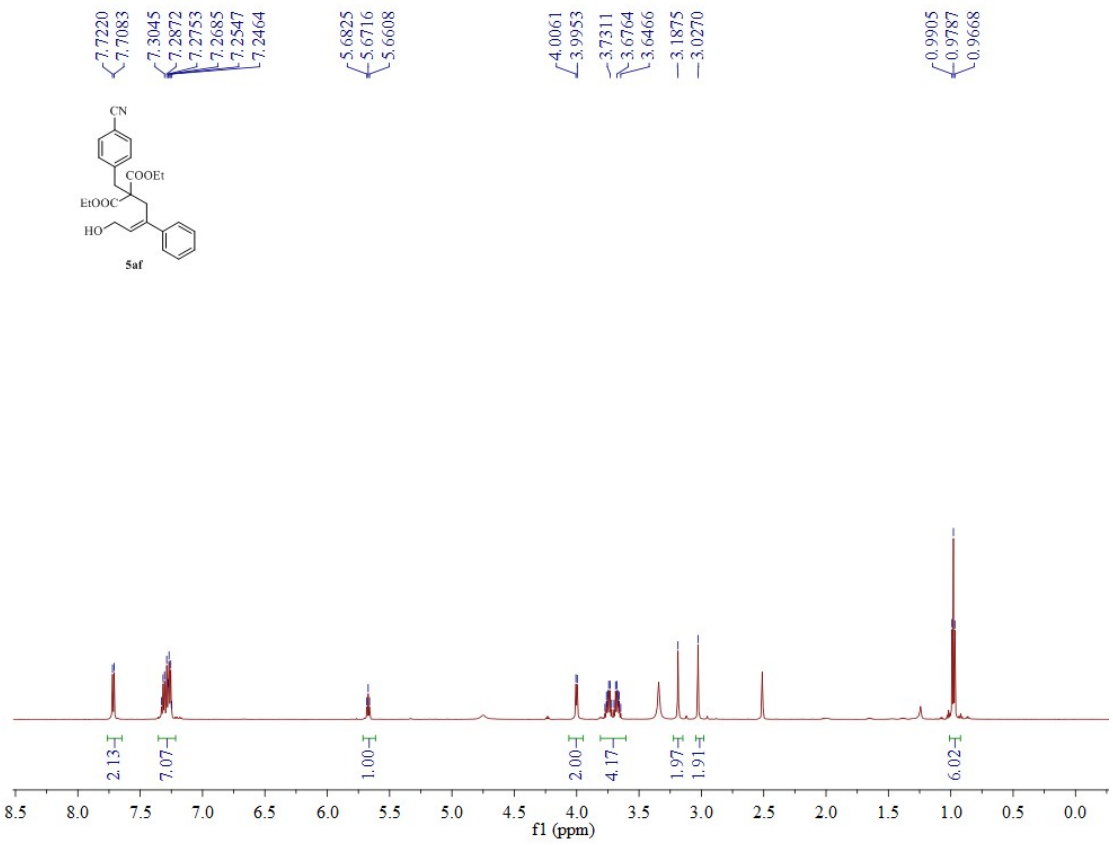
58.43
38.90
33.63
20.97
13.87
COOEt
EtOOC
HO
5ae
f1 (ppm)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7.2547
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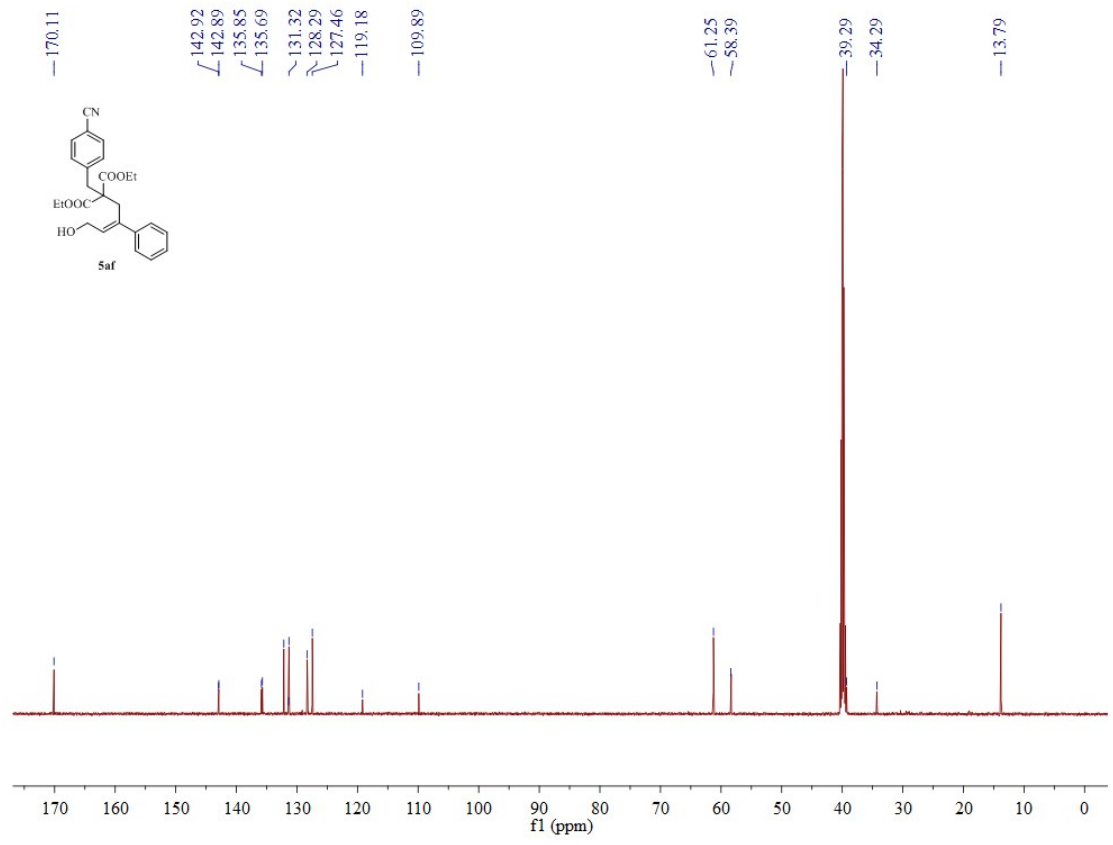
5.6608
4.0061
3.9953
3.7311
3.6764
3.6466
3.1875
3.0270
0.9905
0.9787
0.9668
CN
COOEt
EtOOC
HO
5af
2.13
7.07
1.00
2.00
4.17
1.97
1.91
6.02
f1 (ppm)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135.69
131.32
128.29
127.46
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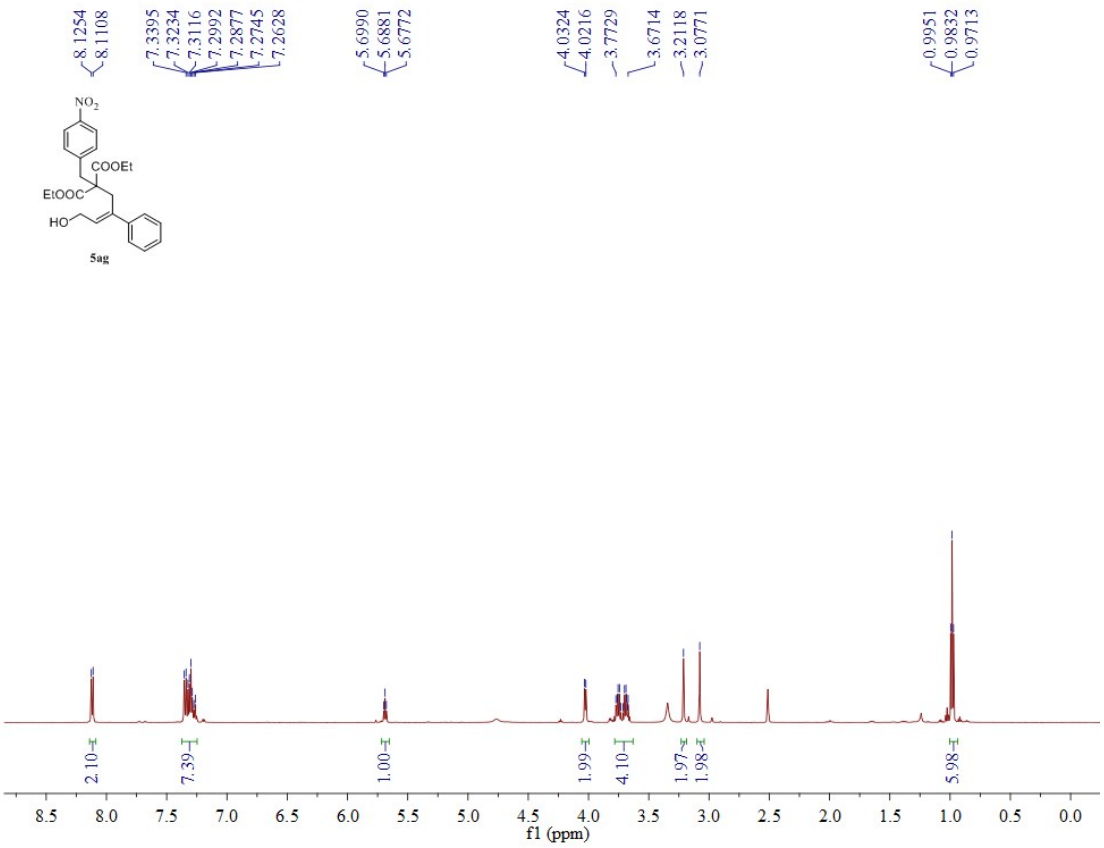
39.29
34.29
13.79
CN
COOEt
EtOOC
HO
5af
f1 (ppm)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7.2628
5.6990
5.6881
5.6772
4.0324
4.0216
3.7729
3.6714
3.2118
3.0771
0.9951
0.9832
0.9713
NO2
COOEt
EtOOC
HO
5ag
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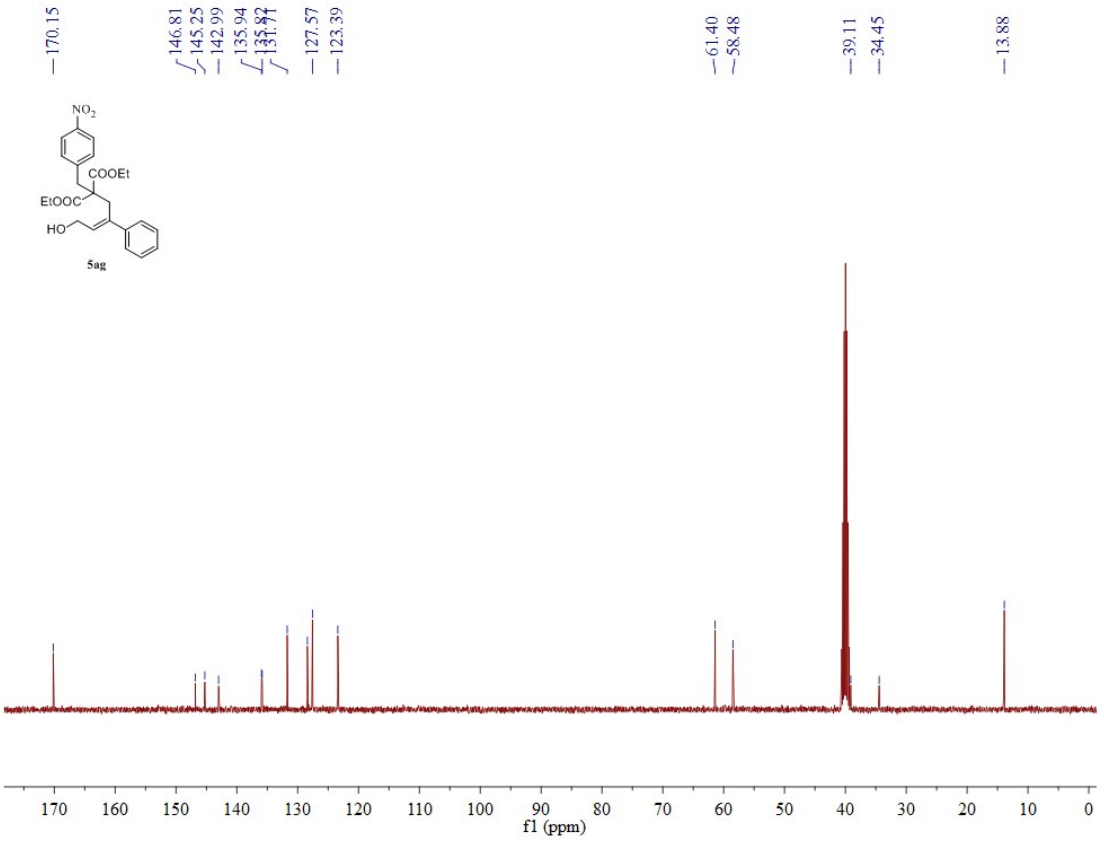
7.39
1.00
1.99
4.10
1.97
1.98
5.98
f1 (ppm)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135.94
127.57
123.39
61.40
58.48
39.11
34.45
13.88
NO2
COOEt
EtOOC
HO
5ag
f1 (ppm)