Reductive Coupling of Allenoates with Aldehydes Catalyzed by Halogenotin Hydride

Supporting Information

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1. Analysis

FTIR spectra were recorded as a thin film on a Nicolet IS5 spectrometer. All ^{1}H and ^{13}C NMR spectra were recorded with a JEOL JMTC-400/54/SS (400 and 100 MHz, respectively) in deuterio chloroform ($CDCl_3$) containing 0.03% (w/v) of tetramethylsilane as an internal standard. Yields were determined by ^{1}H NMR using 1,1,1,2-tetrachloroethane or 1,1,2,2-tetrachloroethane as an internal standard. Low- and high-resolution mass spectra were recorded on a JEOL JMS-700EI spectrometer. Flash column chromatography was performed by Yamazen YFLC-AI-580 using Hi-Flash Silica gel 2L Hi-Flash Column 20-3-mL/min eluted by Hexane/EtOAc with gradation mode changing from 9/1 to 3/7 depending on R_f values of each compound. Purification of products by recycling preparative HPLC was performed by Japan Analytical Industry Co., Ltd. LC-5060. Low-resolution mass spectra and High resolution mass spectra were obtained by Analytical Instrumentation Facility, Osaka University.

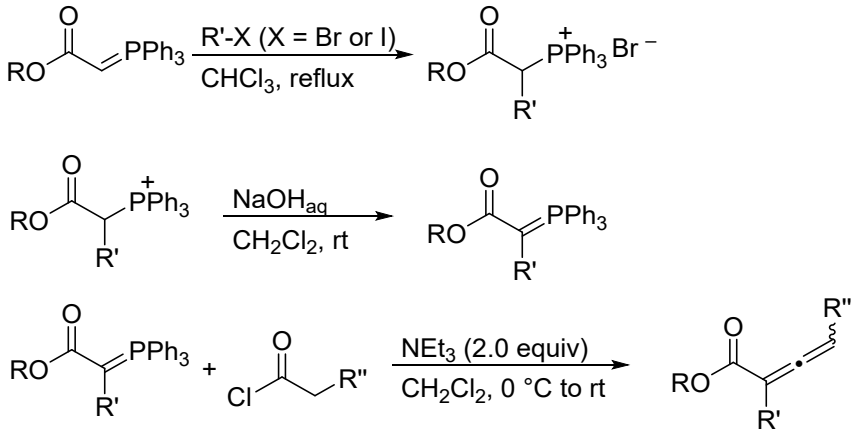
2. Materials

Solvent: Super-dehydrated tetrahydrofuran (THF) or toluene were purchased from commercial sources and used through GC MINI Solvent Dispensing System (Nikko Hansen & Co., LTD). Other dehydrated solvents such as cyclohexane, ethyl acetate (EtOAc), and cyclopentyl methyl ether (CPME) were bought from commercial sources.

Allenoate **1a-h**: All the allenoates except for **1a** were synthesized according to the previous reports and confirmed by ^{1}H NMR. Allenoate **1c** was newly prepared so the product information is reported in chapter 4. Allenoate **1a** was purchased from commercial sources.

Others: They were purchased from commercial sources and used without purification.

Representative Preparation of Allenoate 1:



Corresponding phosphonium ylide (1.0 equiv) and alkyl bromide or iodide (1.5 equiv) were dissolved in $CHCl_3$ (0.5 M) and the mixture was refluxed for 1-2 days. The solvent was removed under reduced pressure and the residue was used without purification.

The residue was dissolved in CH_2Cl_2 and 6 M NaOH aqueous solution. The generated mixture was

stirred vigorously at room temperature for 30 min. The aqueous media was extracted with CH_2Cl_2 twice and the collected organic layer was dried over $MgSO_4$. The organic solvent was removed *in vacuo*. The residue was used without purification.

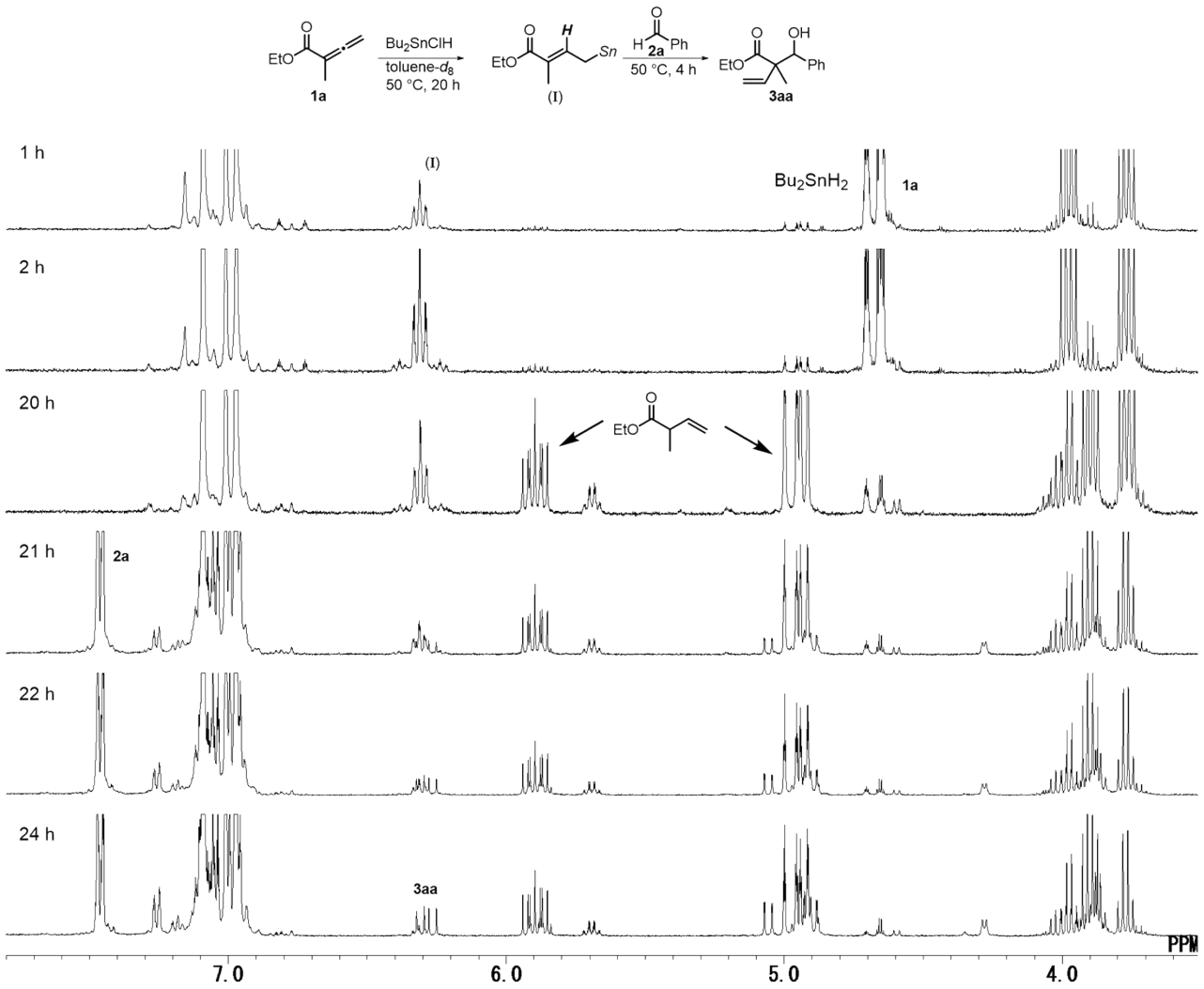
To the mixture of the residue and NEt_3 (2.0 equiv) in CH_2Cl_2 was added dropwise acid chloride (2.0 equiv) in CH_2Cl_2 at 0 °C. The resultant mixture was kept stirring for 48 h at room temperature. The precipitate was filtered off to give an organic layer, which was evaporated *in vacuo*. The residue was washed with pentane. The organic layer was purified by a silica-gel chromatography to give a pure allenoate **1**.

3. Experimental Procedures

All the reactions were performed in reaction glass vessels which were dried under reduced pressure with a heat-gun (ca. 600°C) for several minutes and filled with Ar. The temperature was set up and maintained with ChemiStation^{TM}.

Scheme 2:

To a mixture of Bu_2SnH_2 (0.0275 mmol) and Bu_2SnCl_2 in toluene-d_8 was added allenoate **1a** and the mixture was transferred into a sealed NMR tube. The tube was heated in an oil bath at 50 °C and ^{1}H NMR was taken each after 1 h, 2 h, and 20 h. After the addition of benzaldehyde (**2a**), ^{1}H NMR was taken each after 1 h, 2 h, and 4 h. The NMR chart is shown below.



After 20 h, the generation of allylic stannane (**I**) and ethyl 2-methylbut-3-enoate was observed. The enoate could be given by the protonation of the allylic stannane (**I**). The proton source could be H_2O coming from highly hydroscopic Bu_2SnH_2.

Table 1:

After stirring of a mixture of Bu_2SnCl_2 (0.025 mmol) and $Bu_2Sn(OMe)_2$ (0.025 mmol) in corresponding solvent (1 mL) for 10 min, Ph_2SiH_2 (0.55 mmol) was added and kept stirring for 10 min. Then allenoate **1a** (0.75 mmol), benzaldehyde (0.5 mmol), and MeOH (0.5 mmol) were successively added. The mixture was heated at 50 °C or 60 °C and stirred for 5 h. After the removal of the solvent *in vacuo*, a residue was dissolved in $CDCl_3$ with an internal standard and analyzed by ^1H NMR.

Table 2:

After stirring of a mixture of Bu_2SnCl_2 (0.025 mmol) and $Bu_2Sn(OMe)_2$ (0.025 mmol) in CPME (1 mL) for 10 min, Ph_2SiH_2 (0.55 mmol) was added and kept stirring for 10 min. Then allenoate **1a** (0.75 mmol), aldehyde **2a**-**2p** (0.5 mmol), and MeOH (0.5 mmol) were successively added. The mixture was

heated at 50 °C and stirred for 5 h or 24 h. After the removal of the solvent *in vacuo*, a residue was dissolved in $CDCl_3$ with an internal standard and analyzed by ^1H NMR. The residue was purified by a silica-gel chromatography with hexane/EtOAc eluent according to R_f value. Further purification was carried out by recrystallization or GPC.

Table 3:

After stirring of a mixture of Bu_2SnCl_2 (0.025 mmol) and $Bu_2Sn(OMe)_2$ (0.025 mmol) in CPME (1 mL) for 10 min, Ph_2SiH_2 (0.55 mmol) was added and kept stirring for 10 min. Then allenoate **1b-1g** (0.75 mmol), aldehyde **2i** (0.5 mmol), and MeOH (0.5 mmol) were successively added. The mixture was heated at 50 °C and stirred for 5 h or 24 h. After the removal of the solvent *in vacuo*, a residue was dissolved in $CDCl_3$ with an internal standard and analyzed by ^1H NMR. The residue was purified by a silica-gel chromatography with hexane/EtOAc eluent according to R_f value. Further purification was carried out by recrystallization or GPC.

Scheme 4:

After stirring of a mixture of Bu_2SnCl_2 (0.025 mmol) and $Bu_2Sn(OMe)_2$ (0.025 mmol) in CPME (1 mL) for 10 min, Ph_2SiH_2 (0.55 mmol) was added and kept stirring for 10 min. Then allenoate **1a** or **1h** (0.75 mmol), aldehyde **2a**, **2b**, **2f**, or **2q** (0.5 mmol), and MeOH (0.5 mmol) were successively added. The mixture was heated at 80 °C and stirred for 24 h. After the removal of the solvent *in vacuo*, a residue was dissolved in $CDCl_3$ with an internal standard and analyzed by ^1H NMR. The residue was purified by a silica-gel chromatography with hexane/EtOAc eluent according to R_f value. Further purification was carried out by recrystallization or GPC.

Scheme 6, epoxidation:

To a mixture of allylic alcohol **3ae**$_{syn}$ (0.4 mmol), $VO(acac)_2$ (0.02 mmol) in CH_2Cl_2 (3 mL) was added dropwise ^{t}BuOOH (0.6 mmol) at 0 °C and kept stirring for 48 h. The reaction was quenched with sat. $NaHCO_3$ aq and the aqueous media was extracted with Et_2O (2 x 10 mL). The collected organic layer was dried over Na_2SO_4. After the removal of the solvent in vacuo, a residue was dissolved in $CDCl_3$ with an internal standard and analyzed by ^1H NMR and found to contain epoxide **5ae** (60%, dr = 85:15). The residue was purified by a silica-gel chromatography with hexane/EtOAc eluent according to R_f value to give the pure major form of epoxide **5ae** (36%).

Scheme 6, lactonaization:

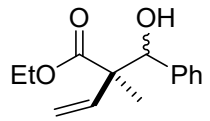
To a solution of 9-BBN (0.75 mmol) in THF (1.5 mL) was added lactone **4hf**$_{syn}$ slowly and the mixture was stirred for 24 h. After the addition of THF (1 mL) and MeOH (1 mL), sat. $NaHCO_3$ aq (2 mL) and 30% H_2O_2 aq (2 mL) were added slowly at 0 °C for 1 h. After the extraction with Et_2O (3 x 10 mL), the organic layer was dried over Na_2SO_4. Then the organic solvents were evaporated in vacuo to give a residue, which was used for the next reaction.

To a solution of the residue in CH_2Cl_2 was added $TsOH{\cdot}H_2O$ (0.05 mmol) and the mixture was stirred for 24 h at room temperature. The reaction was quenched with sat. $NaHCO_3$ aq and the aqueous media was extracted with Et_2O (3 x 10 mL). The collected organic layer was dried over Na_2SO_4. After the

removal of the solvents in vacuo, a residue was dissolved in CHCl3 and added slowly to Et_2O at 0 °C to give a pure product **6hf** (40%).

4. Product Data

Ethyl 2-(hydroxy(phenyl)methyl)-2-methylbut-3-enoate (3aa)



Major isomer (syn): Colorless oil.

R_f = 0.43 (hexane/EtOAc = 8:2).

IR (neat) 3489 cm^{-1} (OH), 1716 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.17 (3H, s), 1.26 (3H, t, J = 7.1 Hz), 3.16 (1H, d, J = 3.1 Hz), 4.18 (2H, q, J = 7.1 Hz), 5.01 (1H, d, J =2.9 Hz), 5.08 (1H, d, J = 17.6 Hz), 5.30 (1H, d, J = 10.9 Hz), 6.25 (1H, dd, J = 17.5, 10.7 Hz), 7.24-7.32 (5H, m).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 14.0, 16.7, 54.4, 61.2, 78.2, 116.9, 127.6, 127.7, 127.8, 137.2, 139.2, 175.3.

HRMS (CI) m/z: calcd. for $C_{14}H_{19}O_3$ 235.1329 ($[M+H]^+$), found 235.1328.

Minor isomer (anti): Colorless oil.

R_f = 0.40 (hexane/EtOAc = 8:2).

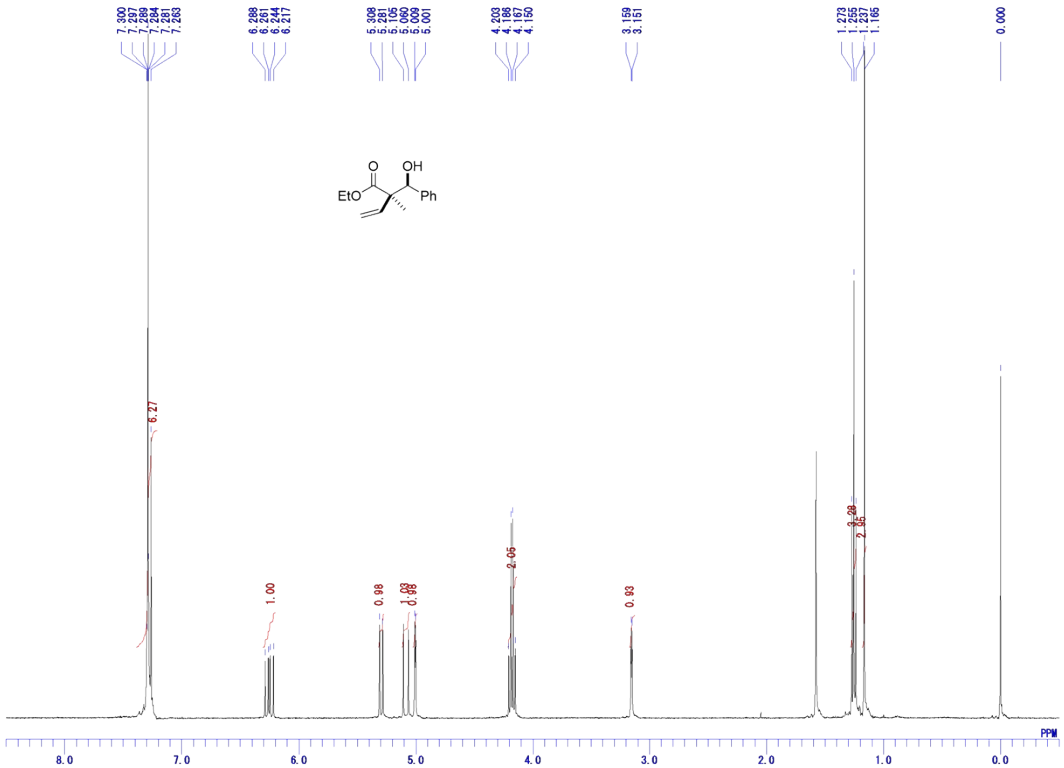
IR (neat) 3486 cm^{-1} (OH), 1717 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.24 (3H, s), 1.28 (3H, t, J = 7.1 Hz), 3.06 (1H, d, J = 5.1 Hz), 4.21 (2H, q, J = 7.1 Hz), 5.01-5.06 (2H, m), 5.18 (1H, d, J = 10.9 Hz), 5.94 (1H, dd, J = 17.5, 10.7 Hz), 7.25-7.33 (5H, m).

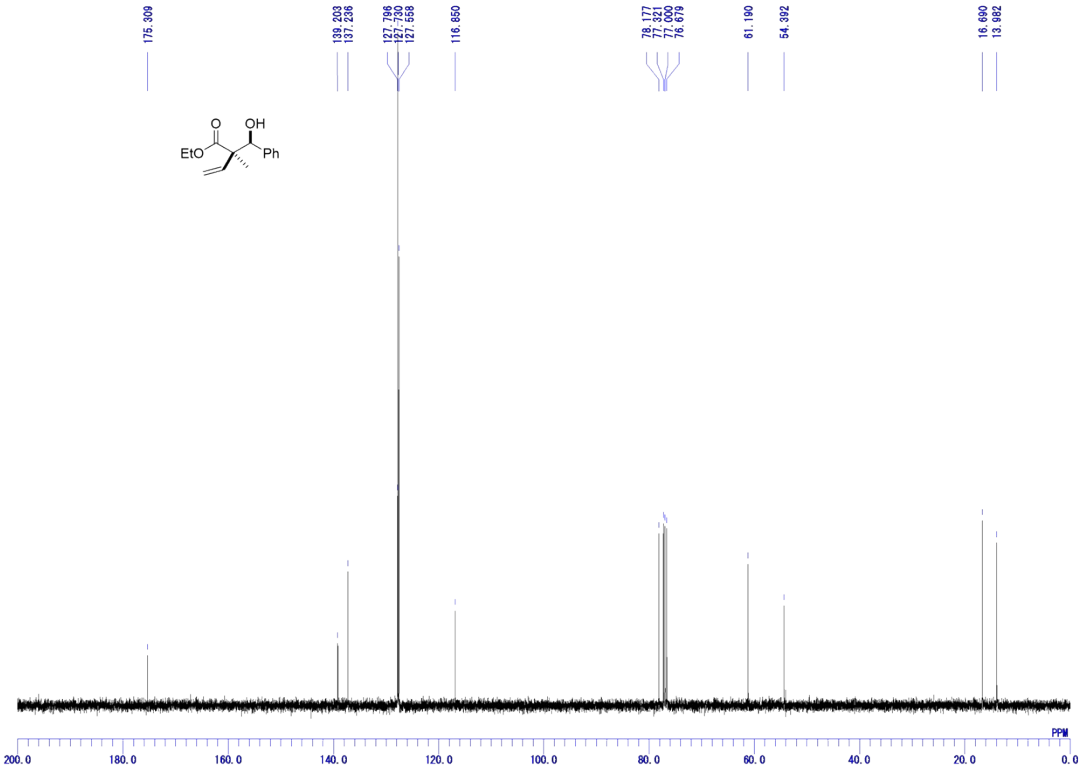
^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 14.0, 15.1, 54.8, 61.1, 77.9, 115.9, 127.4, 127.4, 127.5, 138.6, 139.6, 175.0.

HRMS (CI) m/z: calcd. for $C_{14}H_{19}O_3$ 235.1329 ($[M+H]^+$), found 235.1338.

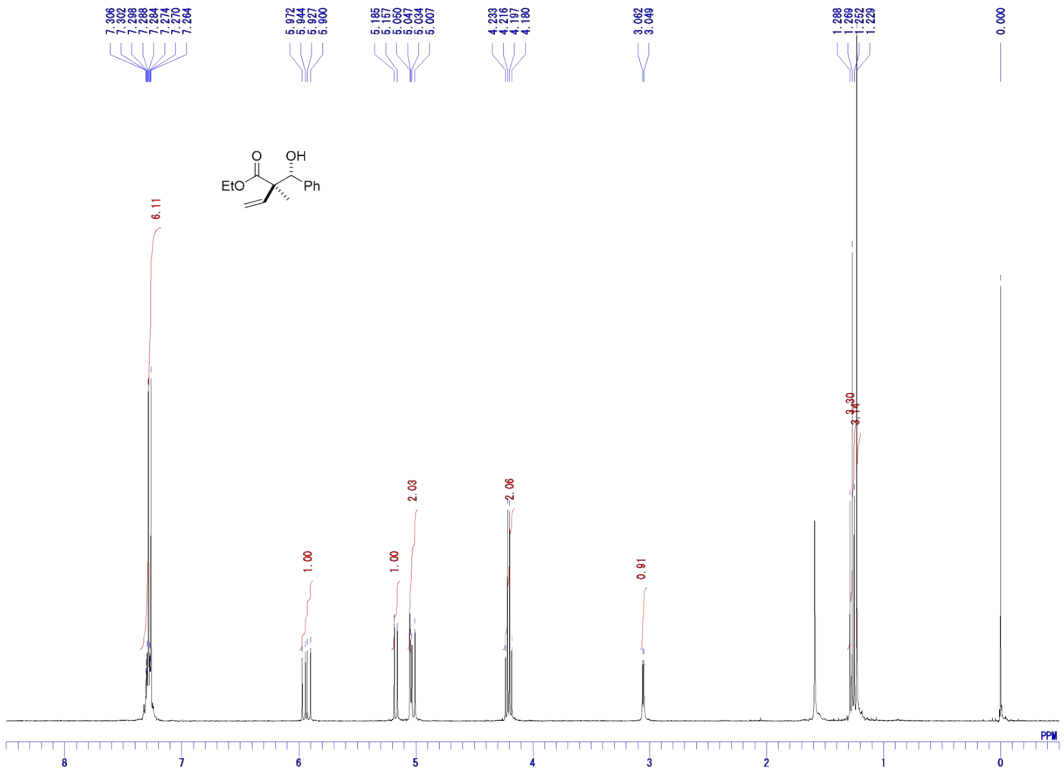
^{1}H NMR ($CDCl_3$, 400 MHz)



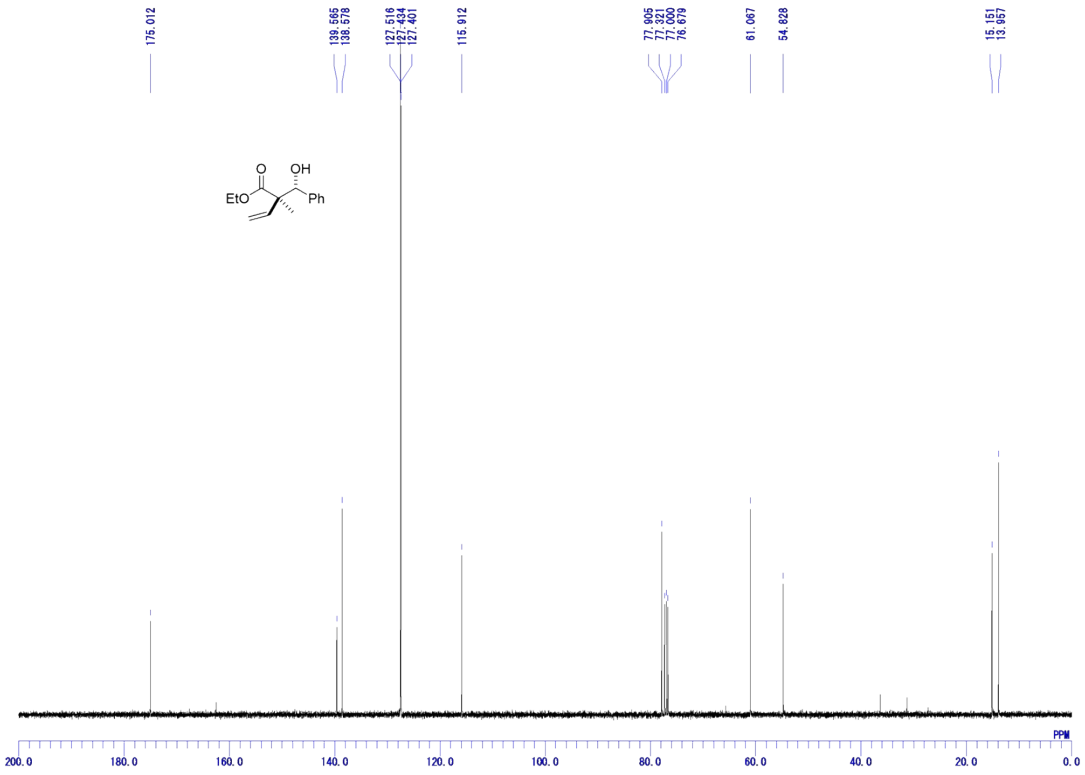
^{13}C NMR ($CDCl_3$, 100 MHz)



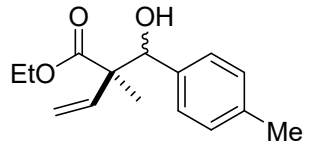
^{1}H NMR ($CDCl_3$, 400 MHz)



^{13}C NMR ($CDCl_3$, 100 MHz)



Ethyl 2-(hydroxy(p-tolyl)methyl)-2-methylbut-3-enoate (3ab)



Major isomer (syn): Colorless oil.

R_f = 0.53 (hexane/EtOAc = 8:2).

IR (neat) 3486 cm^{-1} (OH), 1716 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.16 (3H, s), 1.26 (3H, t, J = 7.1 Hz), 2.32 (3H, s), 3.05 (1H, d, J = 3.1 Hz), 4.17 (2H, q, J = 7.1 Hz), 4.97 (1H, d, J =2.9 Hz), 5.08 (1H, d, J = 17.9 Hz), 5.28 (1H, d, J = 10.9 Hz), 6.25 (1H, dd, J = 17.6, 10.9 Hz), 7.10 (2H, d, J =8.0 Hz), 7.17 (2H, d, J =8.2 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 13.9, 16.5, 20.9, 54.3, 61.0, 77.9, 116.4, 127.5, 128.1, 136.3, 137.1, 137.4, 175.2.

HRMS (CI) m/z: calcd. for $C_{15}H_{21}O_3$ 249.1485 ($[M+H]^+$), found 249.1496.

Minor isomer (anti): Colorless oil.

R_f = 0.45 (hexane/EtOAc = 8:2).

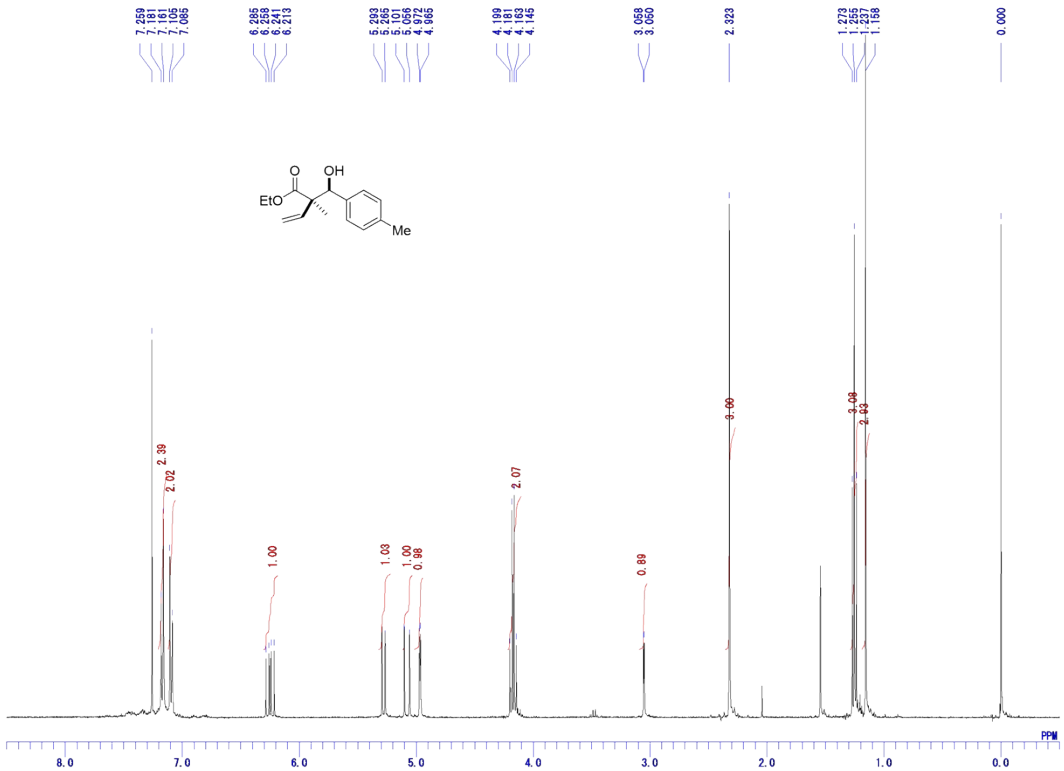
IR (neat) 3495 cm^{-1} (OH), 1717 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.22 (3H, s), 1.27 (3H, t, J = 7.1 Hz), 2.32 (3H, s), 2.95 (1H, d, J = 5.1 Hz), 4.20 (2H, q, J = 7.1 Hz), 4.99-5.05 (2H, m), 5.16 (1H, d, J = 10.9 Hz), 5.93 (1H, dd, J = 17.5, 10.7 Hz), 7.10 (2H, d, J =8.0 Hz), 7.16 (2H, d, J =8.2 Hz).

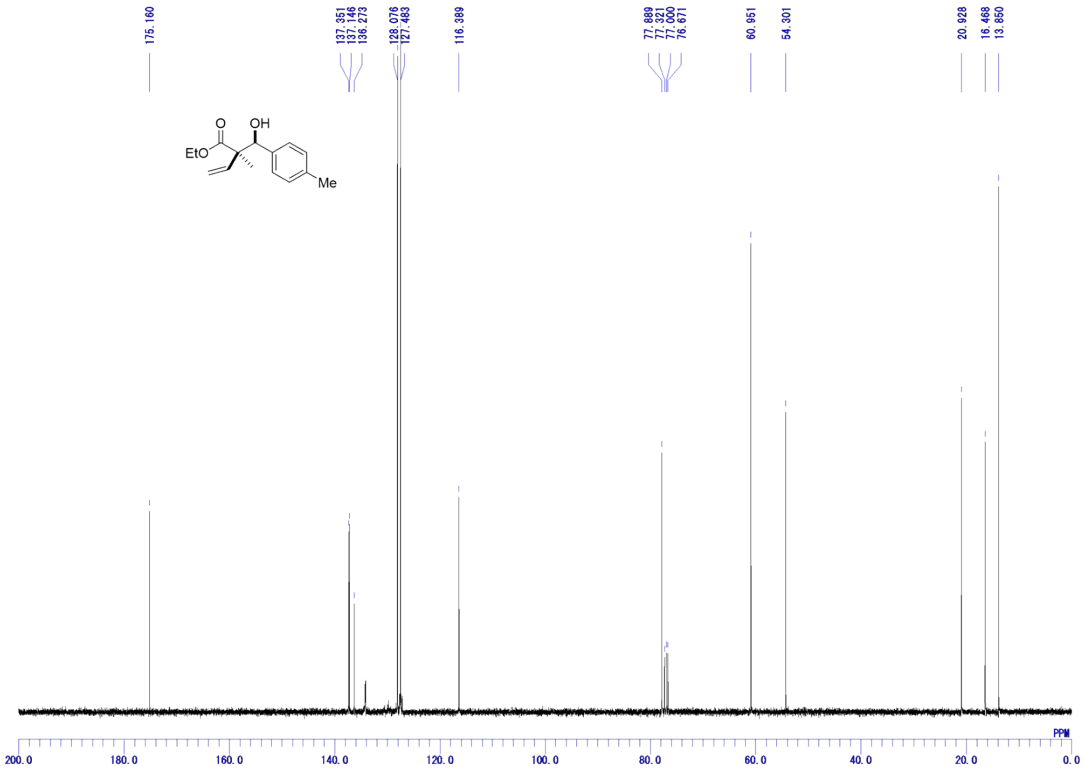
^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 14.0, 15.3, 21.0, 54.8, 61.1, 77.9, 115.8, 127.4, 128.2, 136.6, 137.2, 138.7, 175.1.

HRMS (CI) m/z: calcd. for $C_{15}H_{19}O_2$ 231.1380 ($[M-OH]^+$), found 231.1383.

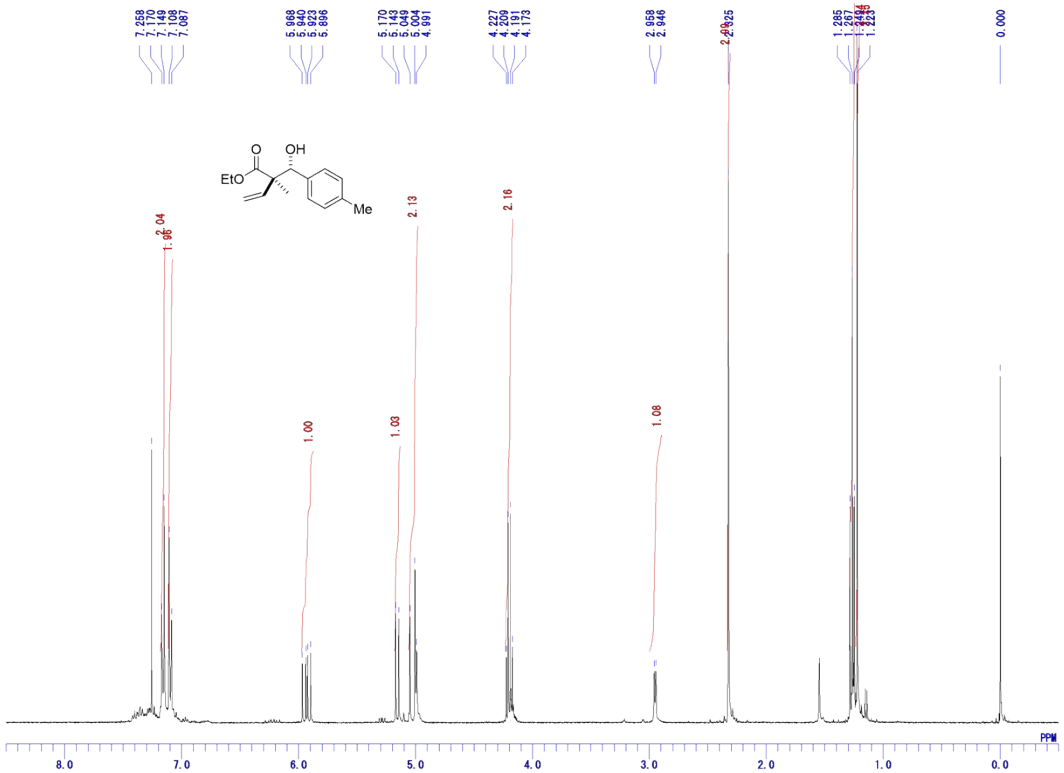
^{1}H NMR ($CDCl_3$, 400 MHz)



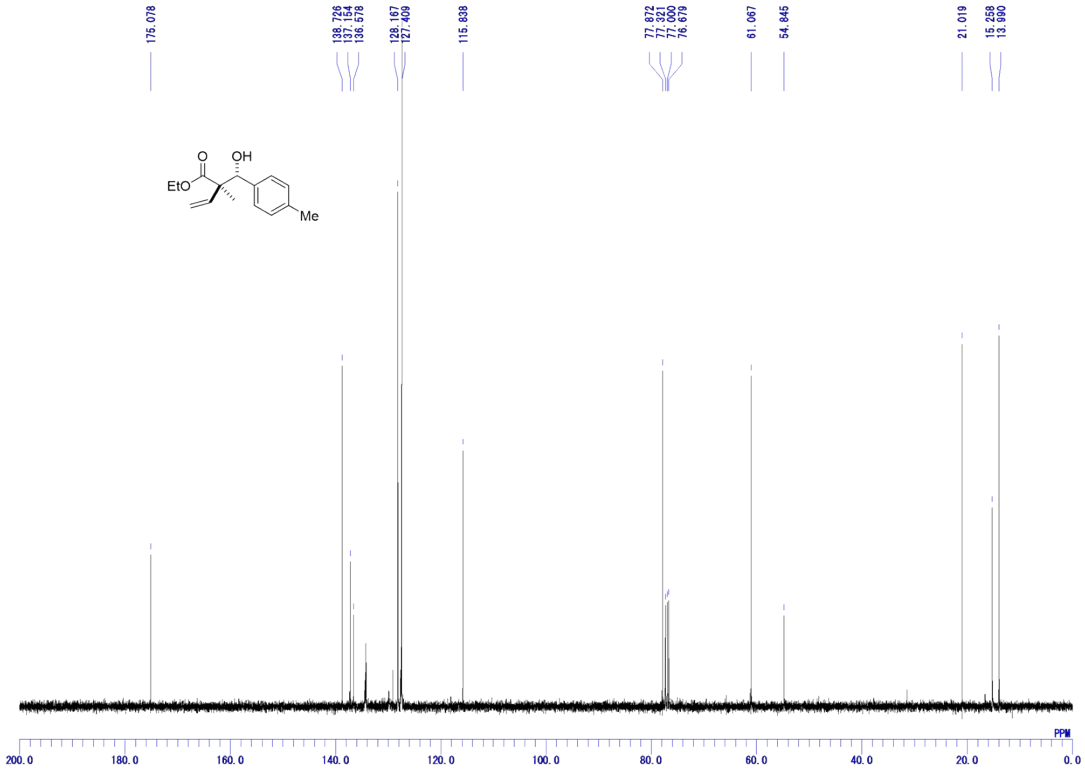
^{13}C NMR ($CDCl_3$, 100 MHz)



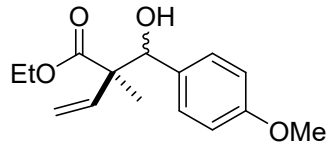
^{1}H NMR ($CDCl_3$, 400 MHz)



^{13}C NMR ($CDCl_3$, 100 MHz)



Ethyl 2-(hydroxy(4-methoxyphenyl)methyl)-2-methylbut-3-enoate (3ac)



Major isomer (syn): Colorless oil.

R_f = 0.33 (hexane/EtOAc = 8:2).

IR (neat) 3493 cm^{-1} (OH), 1716 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.15 (3H, s), 1.26 (3H, t, J = 7.1 Hz), 3.07 (1H, d, J = 2.9 Hz), 3.79 (3H, s), 4.17 (2H, q, J = 7.1 Hz), 4.96 (1H, d, J =2.9 Hz), 5.08 (1H, d, J = 17.6 Hz), 5.28 (1H, d, J = 10.9 Hz), 6.25 (1H, dd, J = 17.6, 10.9 Hz), 6.83 (2H, d, J =8.7 Hz), 7.21 (2H, d, J =8.5 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 14.0, 16.6, 54.5, 55.1, 61.1, 77.8, 112.9, 116.7, 128.8, 131.4, 137.3, 159.1, 175.3.

HRMS (CI) m/z: calcd. for $C_{15}H_{21}O_4$ 265.1434 ($[M+H]^+$), found 265.1433.

Minor isomer (anti): Colorless oil.

R_f = 0.26 (hexane/EtOAc = 8:2).

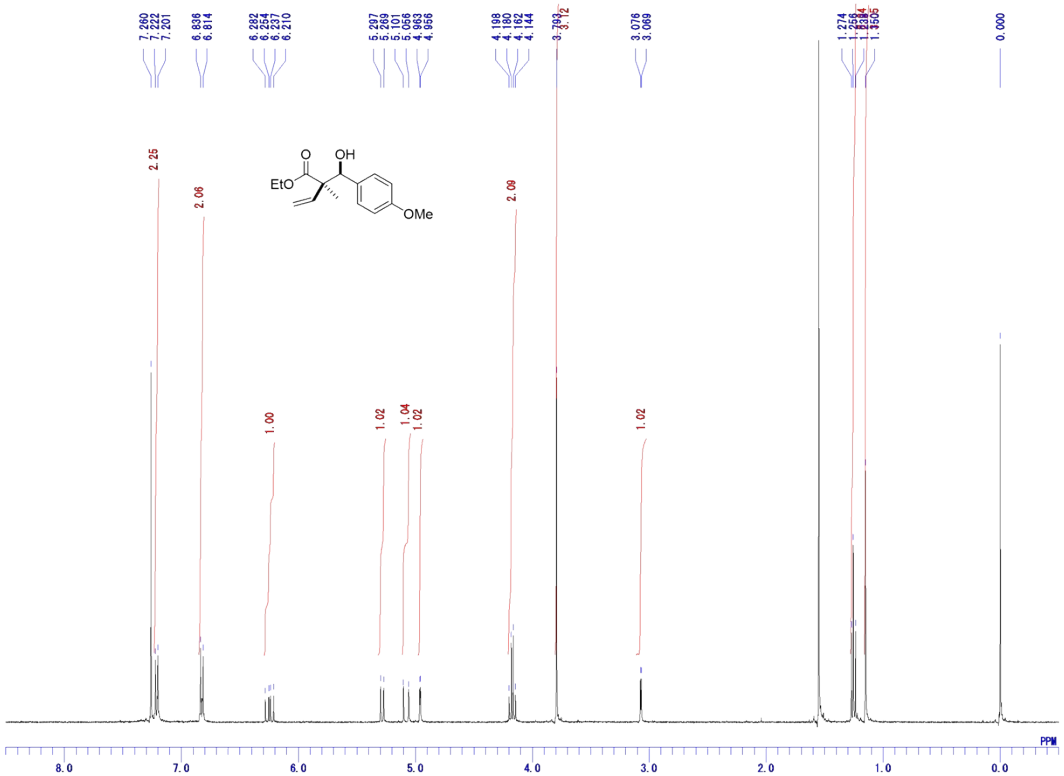
IR (neat) 3449 cm^{-1} (OH), 1704 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.22 (3H, s), 1.27 (3H, t, J = 7.1 Hz), 2.98 (1H, d, J = 5.1 Hz), 3.80 (3H, s), 4.20 (2H, q, J = 7.1 Hz), 4.99-5.05 (2H, m), 5.16 (1H, d, J = 10.9 Hz), 5.92 (1H, dd, J = 17.5, 10.7 Hz), 6.83 (2H, d, J =8.9 Hz), 7.20 (2H, d, J =8.5 Hz).

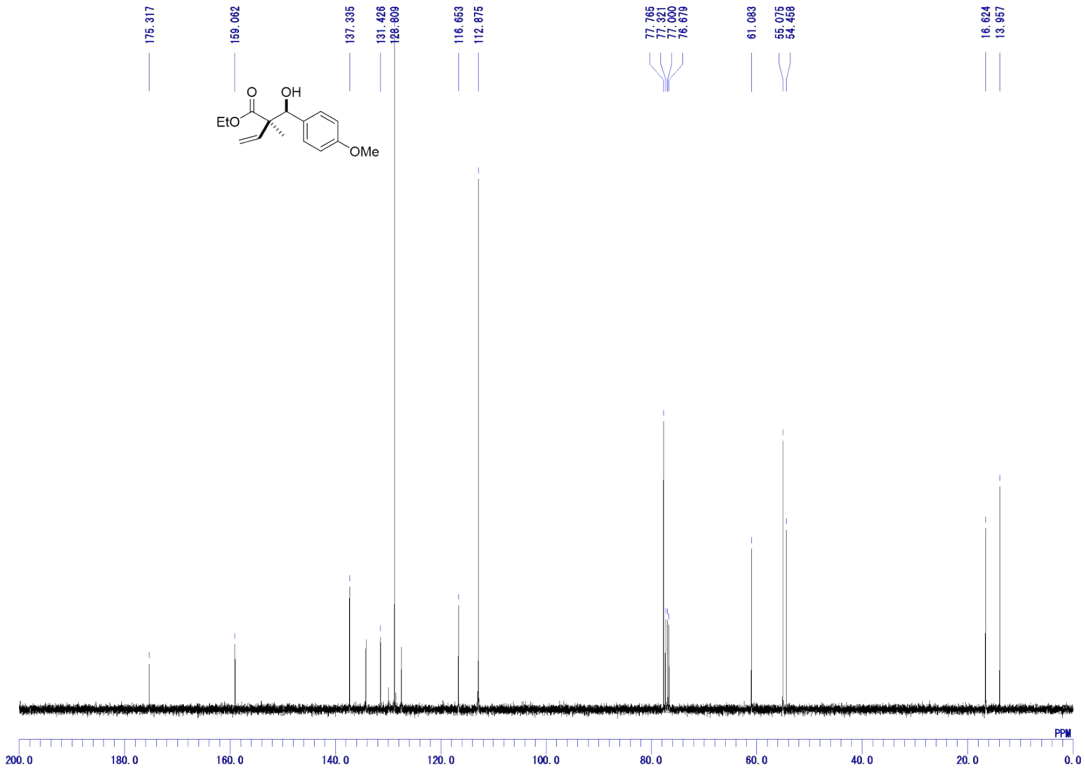
^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 14.0, 15.4, 54.9, 55.2, 61.1, 77.7, 112.9, 115.9, 128.0, 131.7, 138.8, 159.0, 175.2.

HRMS (CI) m/z: calcd. for $C_{15}H_{21}O_4$ 265.1434 ($[M+H]^+$), found 265.1444.

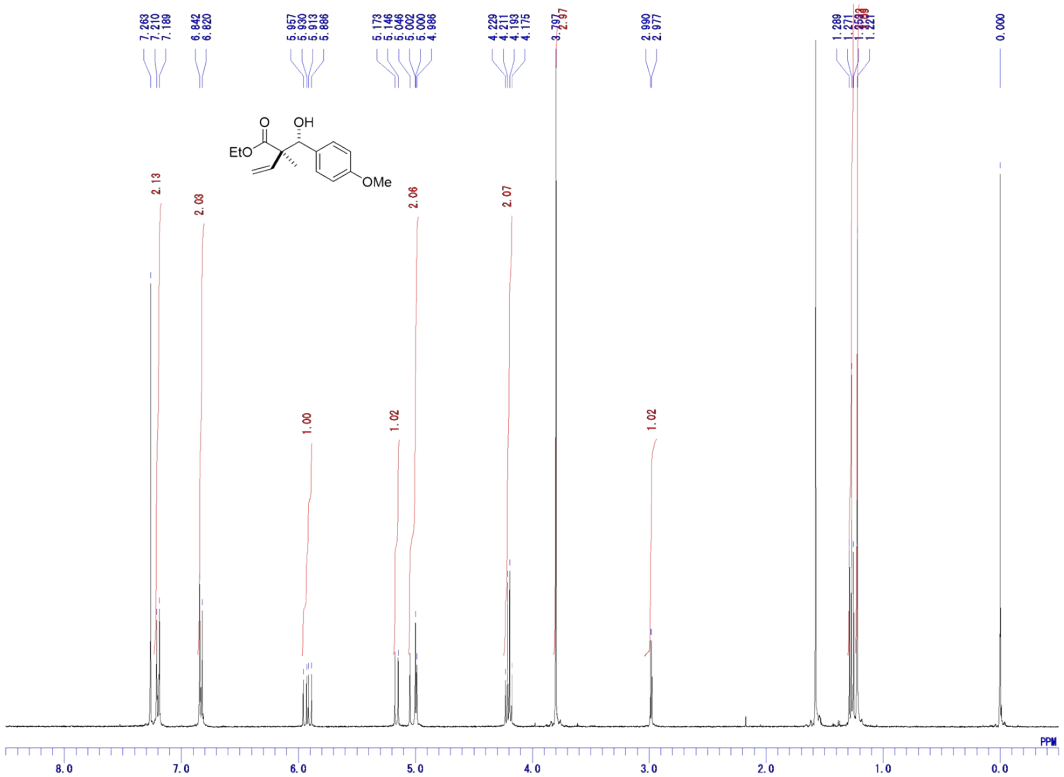
^{1}H NMR ($CDCl_3$, 400 MHz)



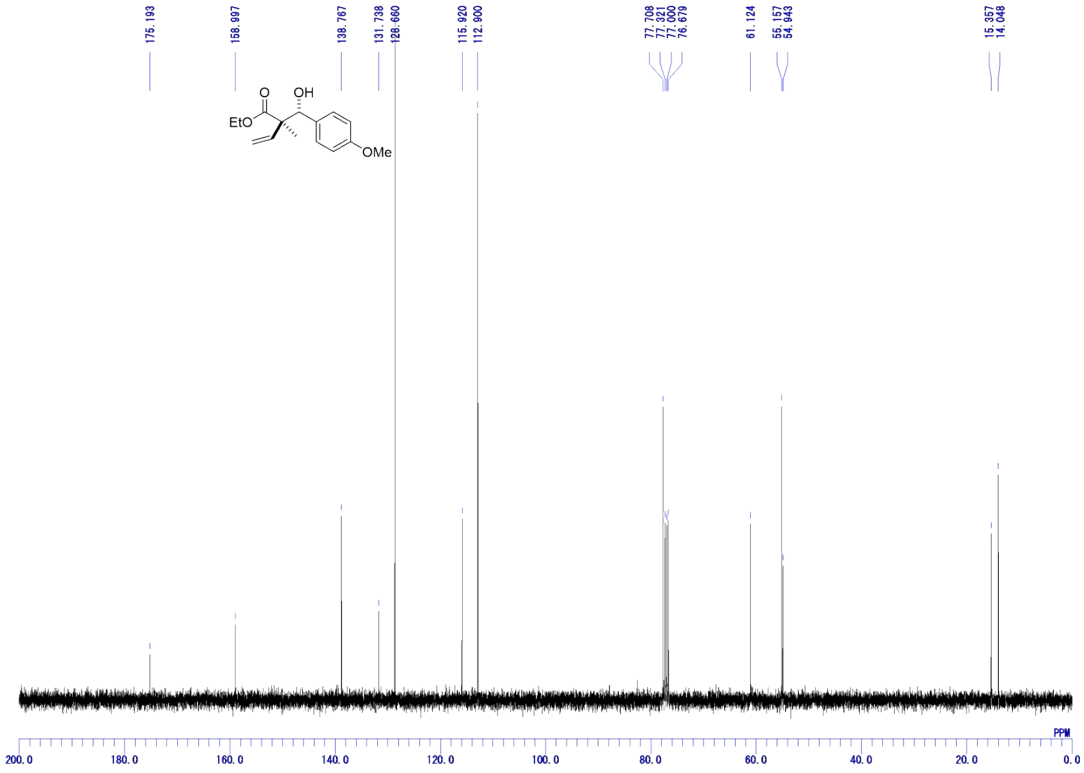
^{13}C NMR ($CDCl_3$, 100 MHz)



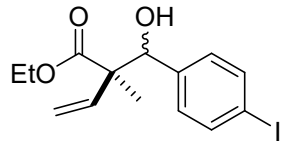
^{1}H NMR ($CDCl_3$, 400 MHz)



^{13}C NMR ($CDCl_3$, 100 MHz)



Ethyl 2-(hydroxy(4-iodophenyl)methyl)-2-methylbut-3-enoate (3ad)



<u>Major isomer</u> (syn): Colorless oil.

R_f = 0.48 (hexane/EtOAc = 8:2).

IR (neat) 3495 cm^{-1} (OH), 1714 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.14 (3H, s), 1.26 (3H, t, J = 7.1 Hz), 3.22 (1H, d, J = 3.1 Hz), 4.17 (2H, q, J = 7.1 Hz), 4.95 (1H, d, J =2.9 Hz), 5.08 (1H, d, J = 17.9 Hz), 5.30 (1H, d, J = 10.9 Hz), 6.19 (1H, dd, J = 17.5, 10.7 Hz), 7.04 (2H, d, J =8.5 Hz), 7.62 (2H, d, J =8.5 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 13.9, 16.5, 54.0, 61.1, 77.4, 93.4, 116.9, 129.6, 136.4, 136.7, 138.9, 175.0.

HRMS (CI) m/z: calcd. for $C_{14}H_{18}IO_3$ 361.0295 ($[M+H]^+$), found 361.0298.

<u>Minor isomer</u> (anti): White solid.

Mp: 92-94 ℃

R_f = 0.45 (hexane/EtOAc = 8:2).

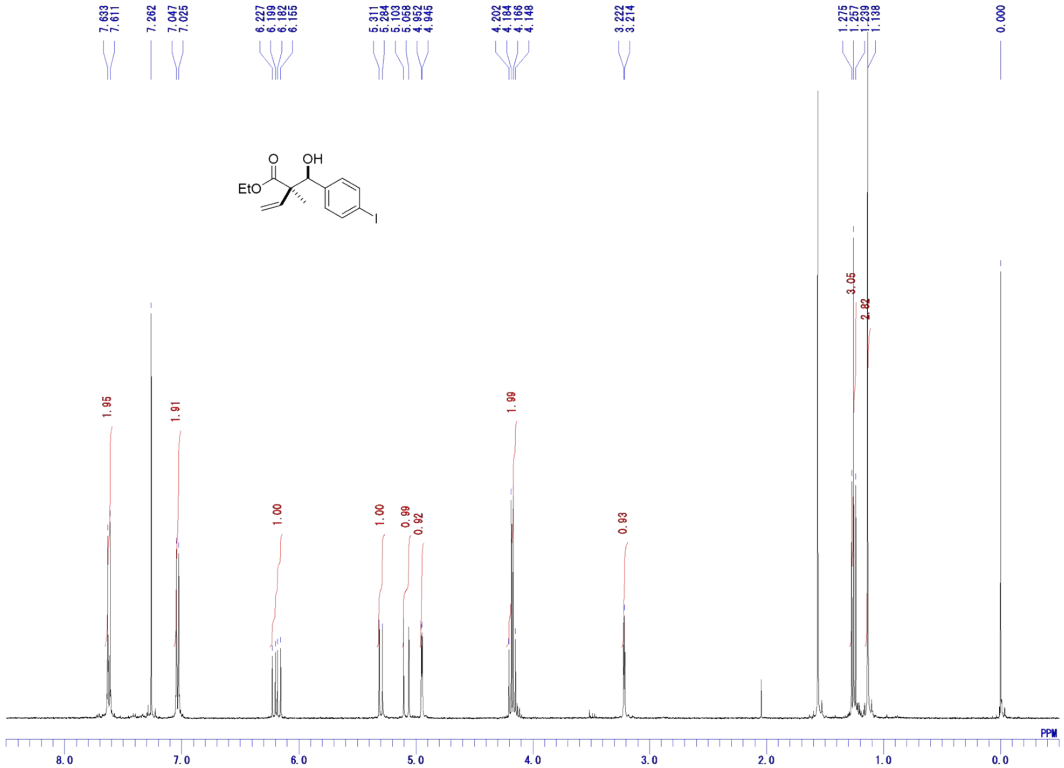
IR (neat) 3503 cm^{-1} (OH), 1708 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.19 (3H, s), 1.27 (3H, t, J = 7.1 Hz), 3.09 (1H, d, J = 5.1 Hz), 3.80 (3H, s), 4.20 (2H, q, J = 7.1 Hz), 4.99-5.05 (2H, m), 5.18 (1H, d, J = 10.9 Hz), 5.87 (1H, dd, J = 17.5, 10.7 Hz), 7.03 (2H, d, J =8.5 Hz), 7.62 (2H, d, J =8.5 Hz).

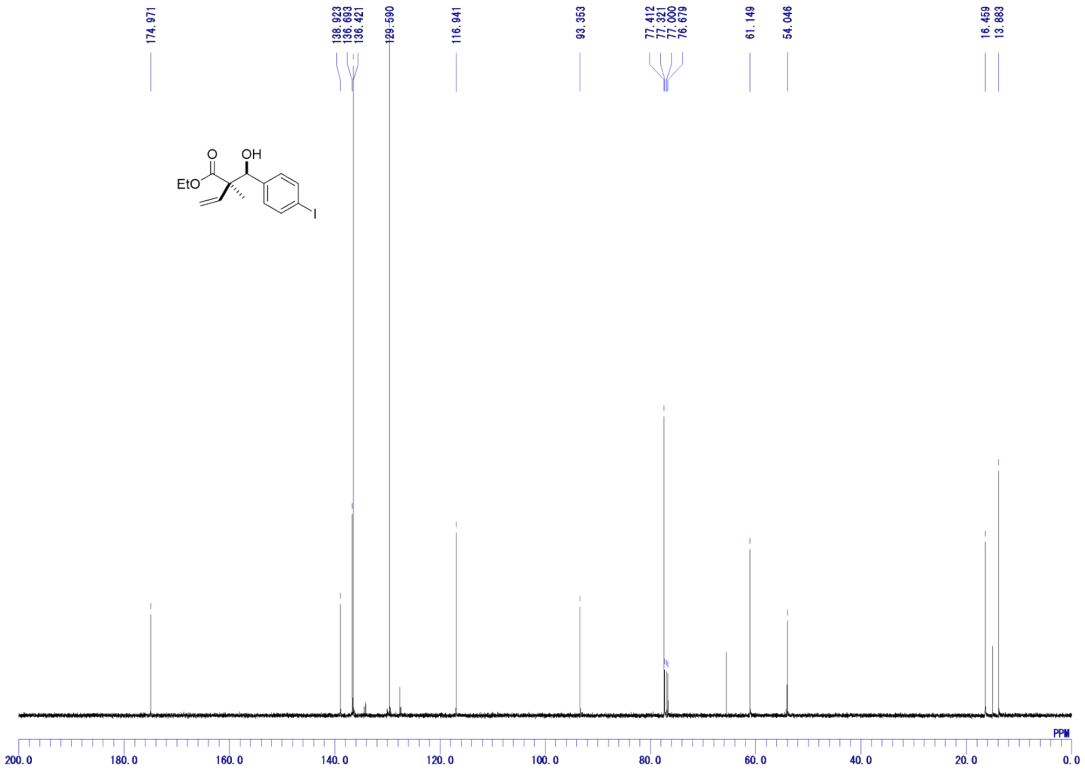
^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 14.0, 14.9, 54.7, 61.3, 77.3, 93.2, 116.4, 129.5, 136.5, 138.2, 139.2, 175.0.

HRMS (CI) m/z: calcd. for $C_{14}H_{18}IO_3$ 361.0295 ($[M+H]^+$), found 361.0294.

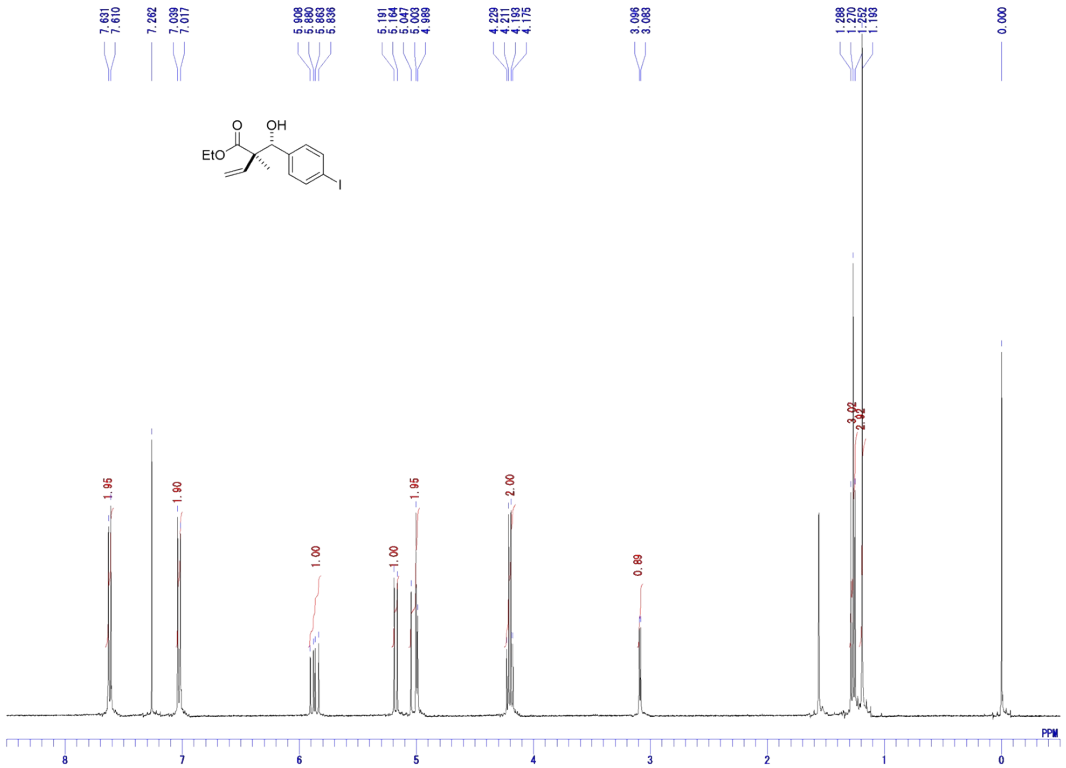
^{1}H NMR ($CDCl_3$, 400 MHz)



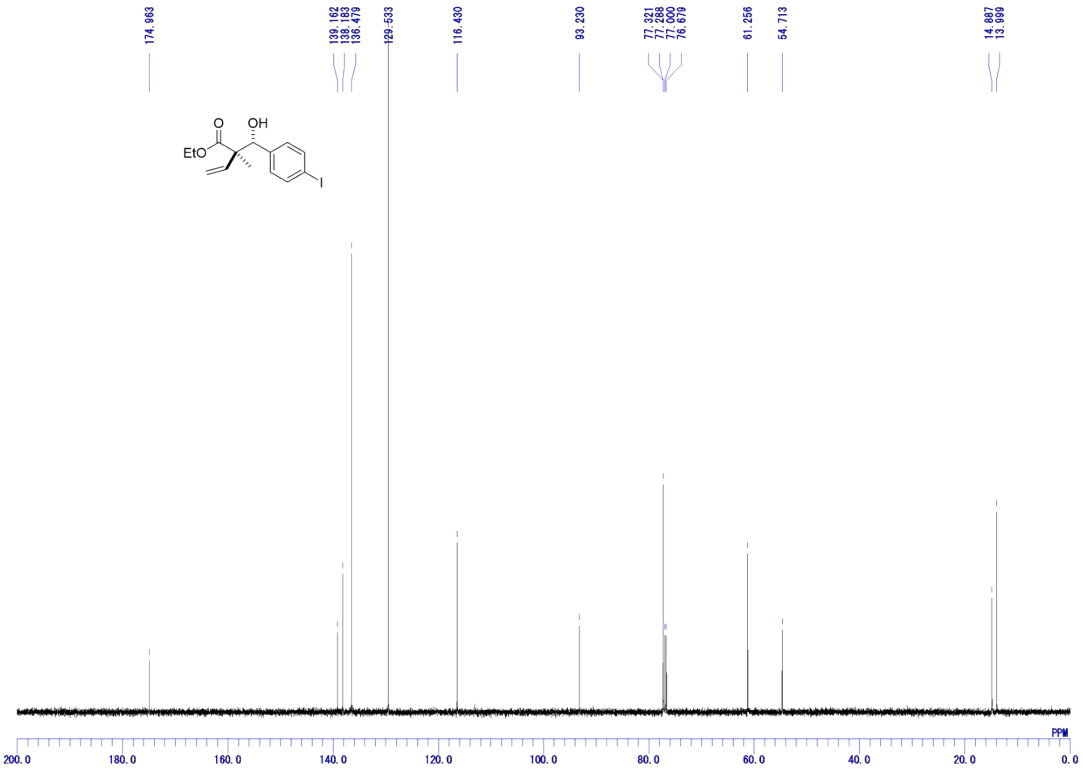
^{13}C NMR ($CDCl_3$, 100 MHz)



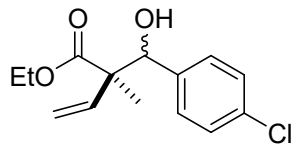
^{1}H NMR ($CDCl_3$, 400 MHz)



^{13}C NMR ($CDCl_3$, 100 MHz)



Ethyl 2-((4-chlorophenyl)(hydroxy)methyl)-2-methylbut-3-enoate (3ae)



<u>Major isomer</u> (syn): Colorless oil.

R_f = 0.60 (hexane/EtOAc = 8:2).

IR (neat) 3485 cm^{-1} (OH), 1715 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.14 (3H, s), 1.26 (3H, t, J = 7.1 Hz), 3.23 (1H, d, J = 2.9 Hz), 4.18 (2H, q, J = 7.1 Hz), 4.98 (1H, d, J =2.9 Hz), 5.08 (1H, d, J = 17.6 Hz), 5.30 (1H, d, J = 10.6 Hz), 6.20 (1H, dd, J = 17.6, 10.6 Hz), 7.21-7.28 (4H, m).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 13.8, 16.4, 54.1, 61.1, 77.3, 116.9, 127.5, 129.0, 133.3, 136.8, 137.8, 175.0.

HRMS (CI) m/z: calcd. for $C_{14}H_{17}ClO_3Na$ 291.0764 ($[M+Na]^+$), found 291.0761.

<u>Minor isomer</u> (anti): Colorless oil.

R_f = 0.59 (hexane/EtOAc = 8:2).

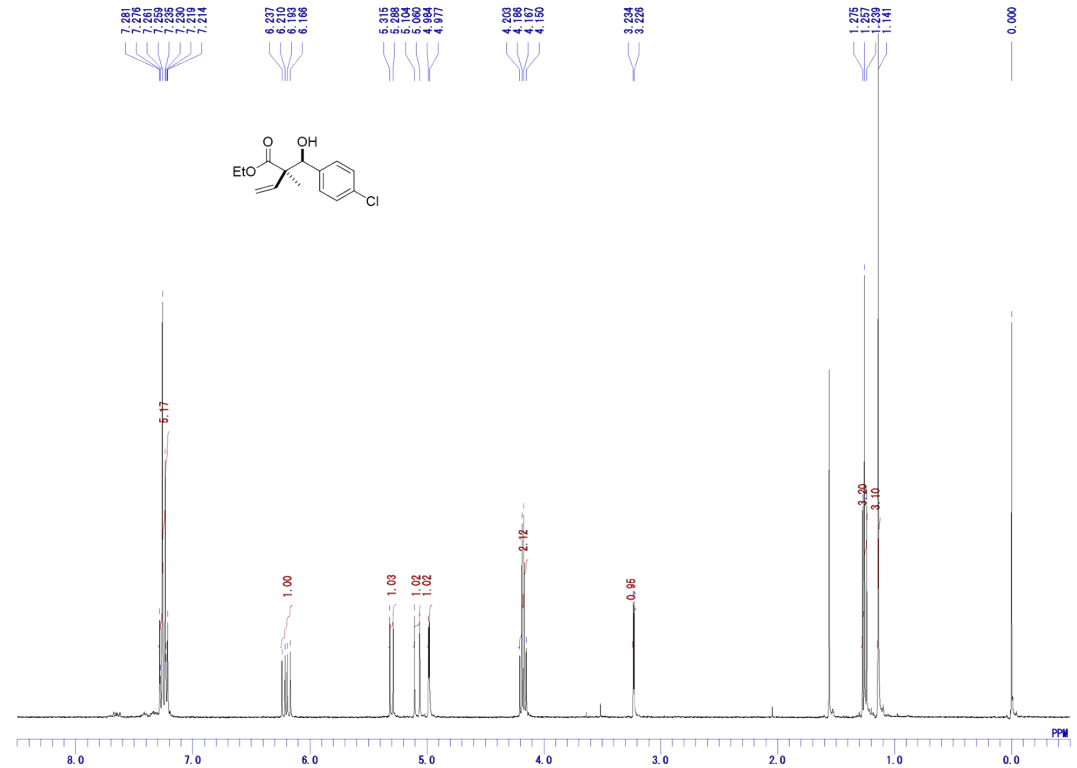
IR (neat) 3494 cm^{-1} (OH), 1715 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.20 (3H, s), 1.27 (3H, t, J = 7.1 Hz), 3.11 (1H, d, J = 4.8 Hz), 4.20 (2H, q, J = 7.1 Hz), 5.00-5.05 (2H, m), 5.18 (1H, d, J = 10.6 Hz), 5.88 (1H, dd, J = 17.5, 10.7 Hz), 7.21-7.28 (4H, m).

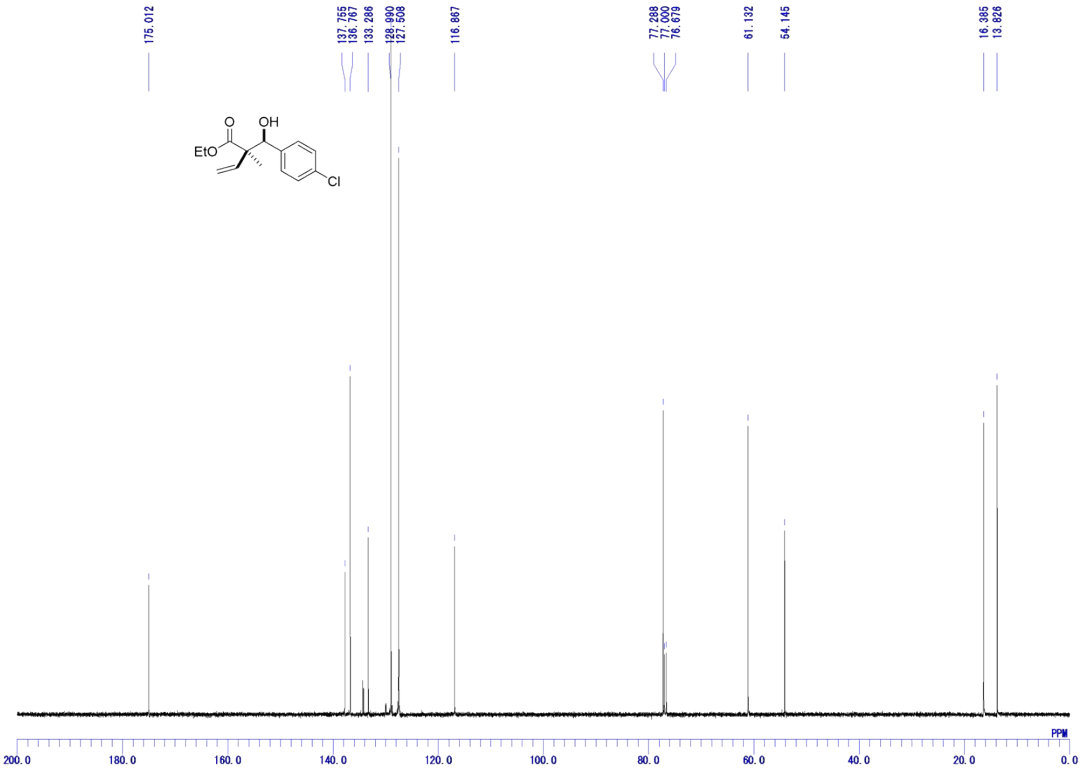
^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 14.0, 14.9, 54.8, 61.3, 77.2, 116.4, 127.6, 128.9, 133.3, 138.0, 138.2, 175.0.

HRMS (CI) m/z: calcd. for $C_{14}H_{18}ClO_3$ 269.0939 ($[M+H]^+$), found 269.0951.

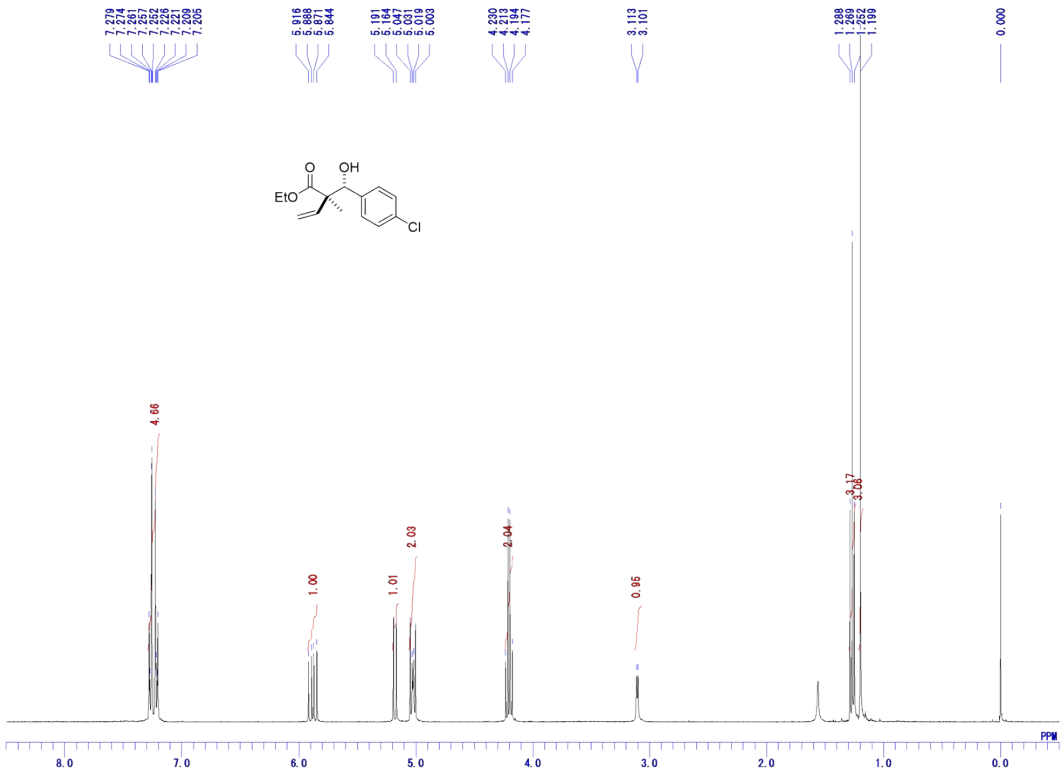
^{1}H NMR ($CDCl_3$, 400 MHz)



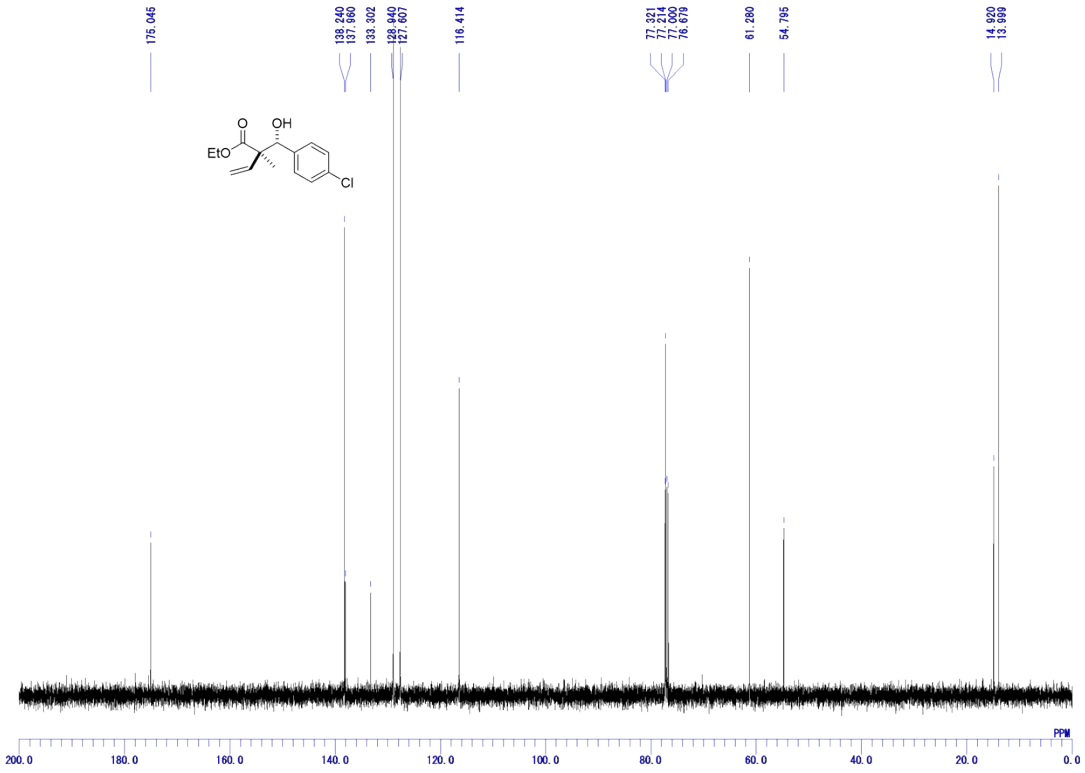
^{13}C NMR ($CDCl_3$, 100 MHz)



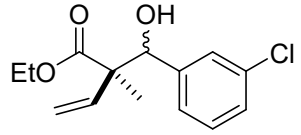
^{1}H NMR ($CDCl_3$, 400 MHz)



^{13}C NMR ($CDCl_3$, 100 MHz)



Ethyl 2-((3-chlorophenyl)(hydroxy)methyl)-2-methylbut-3-enoate (3af)



Major isomer (syn): Colorless oil.

R_f = 0.45 (hexane/EtOAc = 8:2).

IR (neat) 3491 cm^{-1} (OH), 1717 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.16 (3H, s), 1.26 (3H, t, J = 7.1 Hz), 3.22 (1H, d, J = 2.9 Hz), 4.18 (2H, q, J = 7.2 Hz), 4.97 (1H, d, J =3.1 Hz), 5.10 (1H, d, J = 17.4 Hz), 5.32 (1H, d, J = 10.9 Hz), 6.20 (1H, dd, J = 17.6, 10.9 Hz), 7.16-7.30 (4H, m).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 13.9, 16.4, 54.3, 61.3, 77.4, 117.2, 125.9, 127.8, 127.9, 128.8, 133.5, 136.9, 141.3, 175.0.

HRMS (CI) m/z: calcd. for $C_{16}H_{23}O_3$ 269.0939 ($[M+H]^+$), found 269.0952.

Minor isomer (anti): Colorless oil.

R_f = 0.40 (hexane/EtOAc = 8:2).

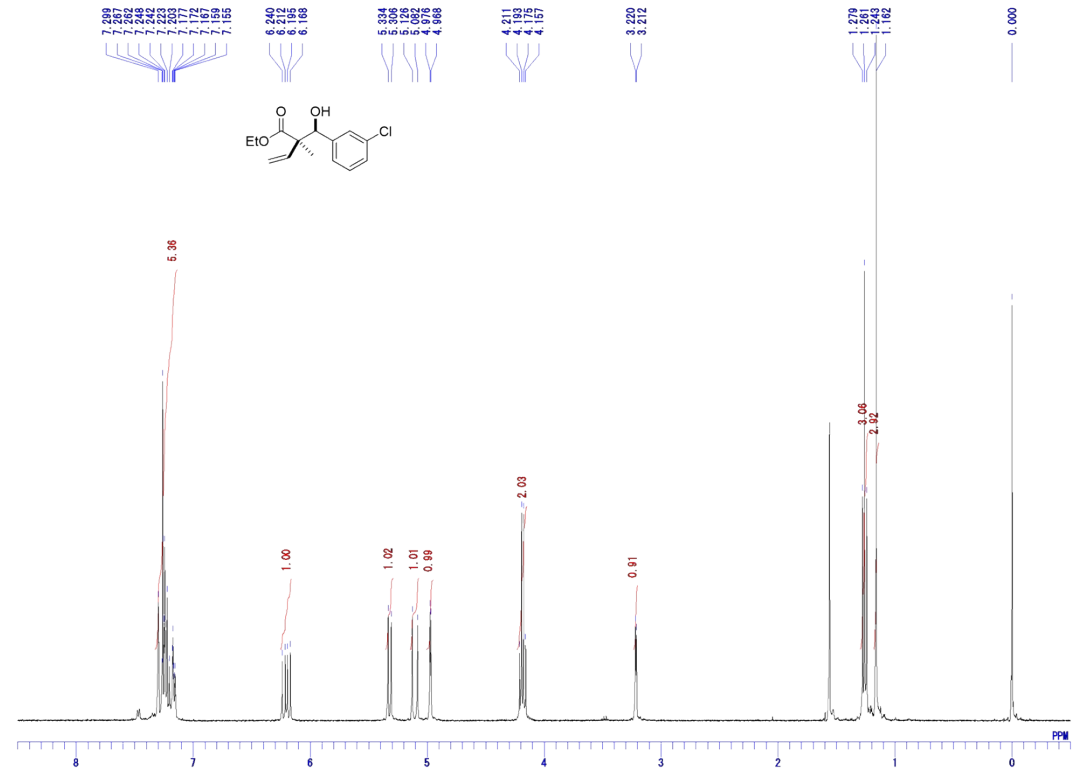
IR (neat) 3478 cm^{-1} (OH), 1715 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.22 (3H, s), 1.27 (3H, t, J = 7.1 Hz), 3.14 (1H, d, J = 5.1 Hz), 4.21 (2H, q, J = 7.2 Hz), 5.01-5.07 (2H, m), 5.20 (1H, d, J = 10.6 Hz), 5.90 (1H, dd, J = 17.5, 10.7 Hz), 7.14-7.30 (4H, m).

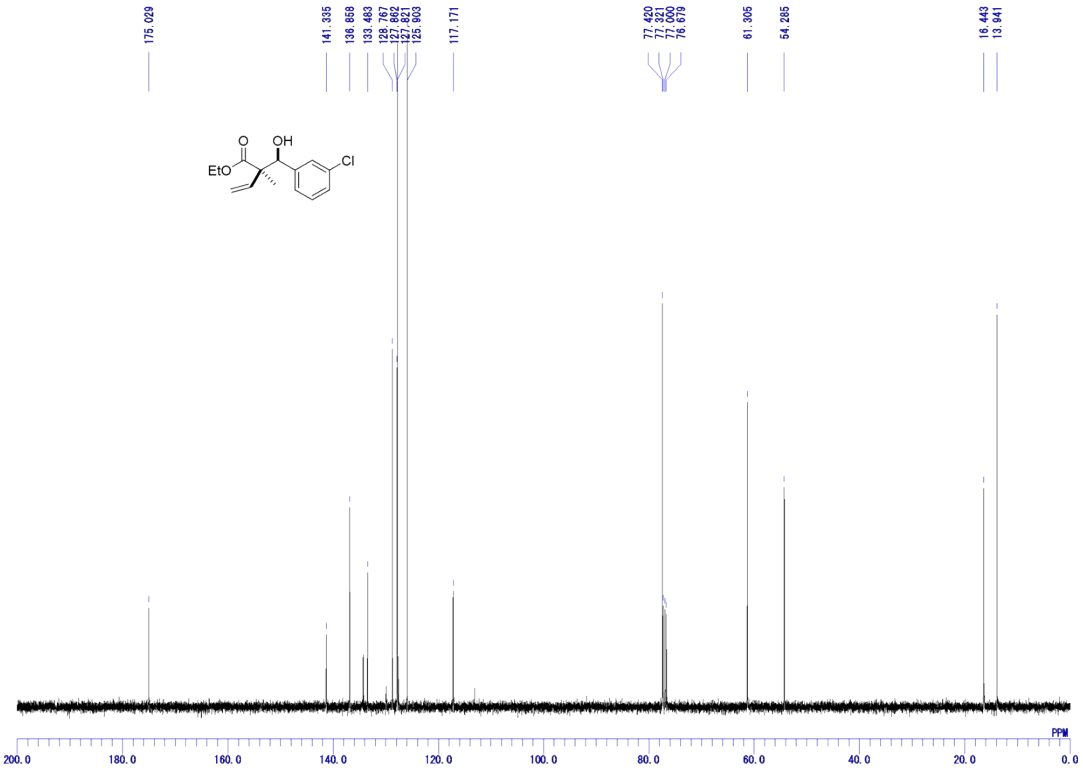
^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 14.0, 15.0, 54.8, 61.3, 77.2, 116.4, 125.8, 127.6, 127.7, 128.7, 133.5, 138.2, 141.6, 174.9.

HRMS (CI) m/z: calcd. for $C_{16}H_{23}O_3$ 269.0939 ($[M+H]^+$), found 269.0942.

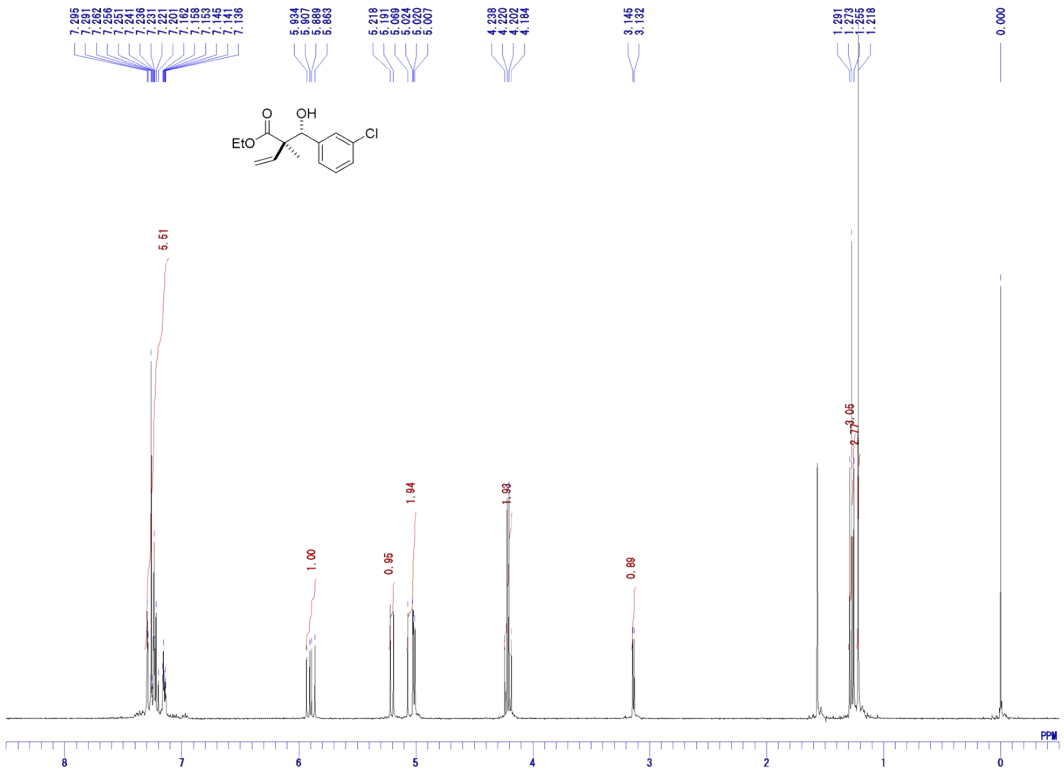
^{1}H NMR ($CDCl_3$, 400 MHz)



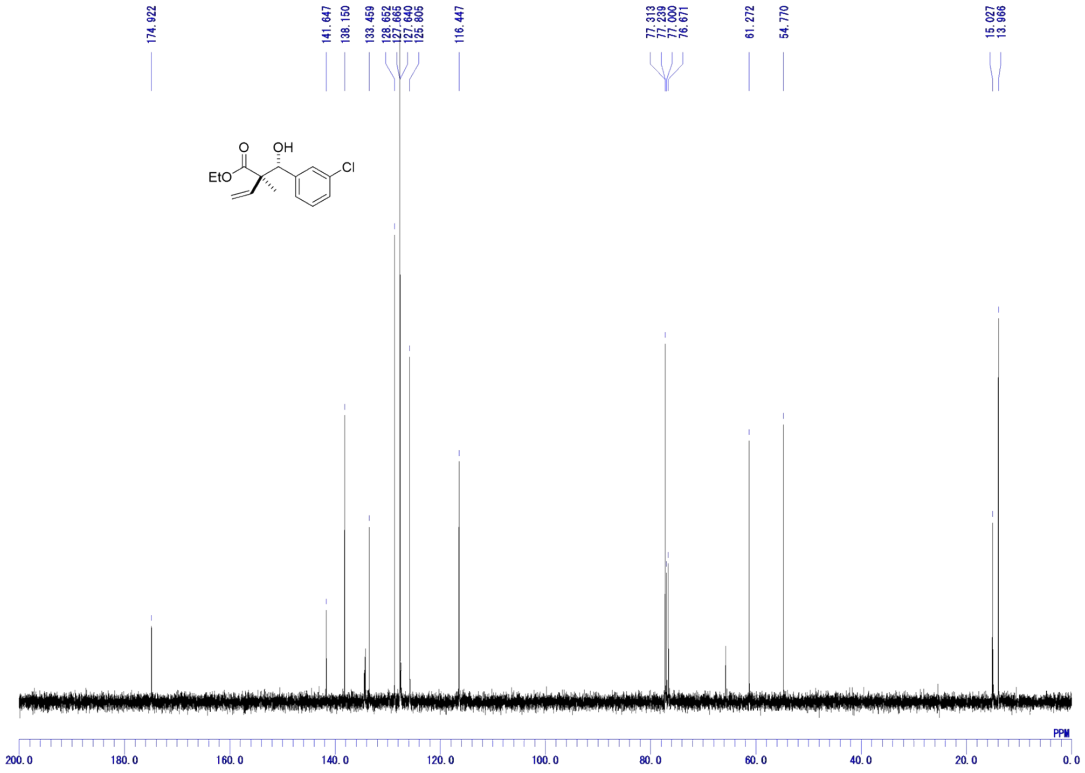
^{13}C NMR ($CDCl_3$, 100 MHz)



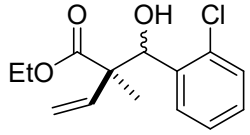
^{1}H NMR ($CDCl_3$, 400 MHz)



^{13}C NMR ($CDCl_3$, 100 MHz)



Ethyl 2-((2-chlorophenyl)(hydroxy)methyl)-2-methylbut-3-enoate (3ag)



Major isomer (syn): Colorless oil.

R_f = 0.50 (hexane/EtOAc = 8:2).

IR (neat) 3485 cm^{-1} (OH), 1706 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.21 (3H, s), 1.29 (3H, t, J = 7.1 Hz), 3.65 (1H, d, J = 3.4 Hz), 4.23 (2H, q, J = 7.2 Hz), 5.02 (1H, d, J =17.6 Hz), 5.31 (1H, d, J = 10.9 Hz), 5.63 (1H, d, J = 3.1 Hz), 6.28 (1H, dd, J = 17.5, 10.7 Hz), 7.18-7.25 (2H, m), 7.32 (1H, dd, J = 7.5, 1.7 Hz), 7.48 (1H, dd, J = 7.2, 2.2 Hz),

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 13.8, 17.2, 54.3, 61.2, 73.1, 117.0, 125.9, 128.6, 128.7, 130.1, 133.2, 135.5, 136.9, 175.8.

HRMS (CI) m/z: calcd. for $C_{14}H_{17}ClO_3Na$ 291.0758 ($[M+Na]^+$), found 291.0769.

Minor isomer (anti): Colorless oil.

R_f = 0.45 (hexane/EtOAc = 8:2).

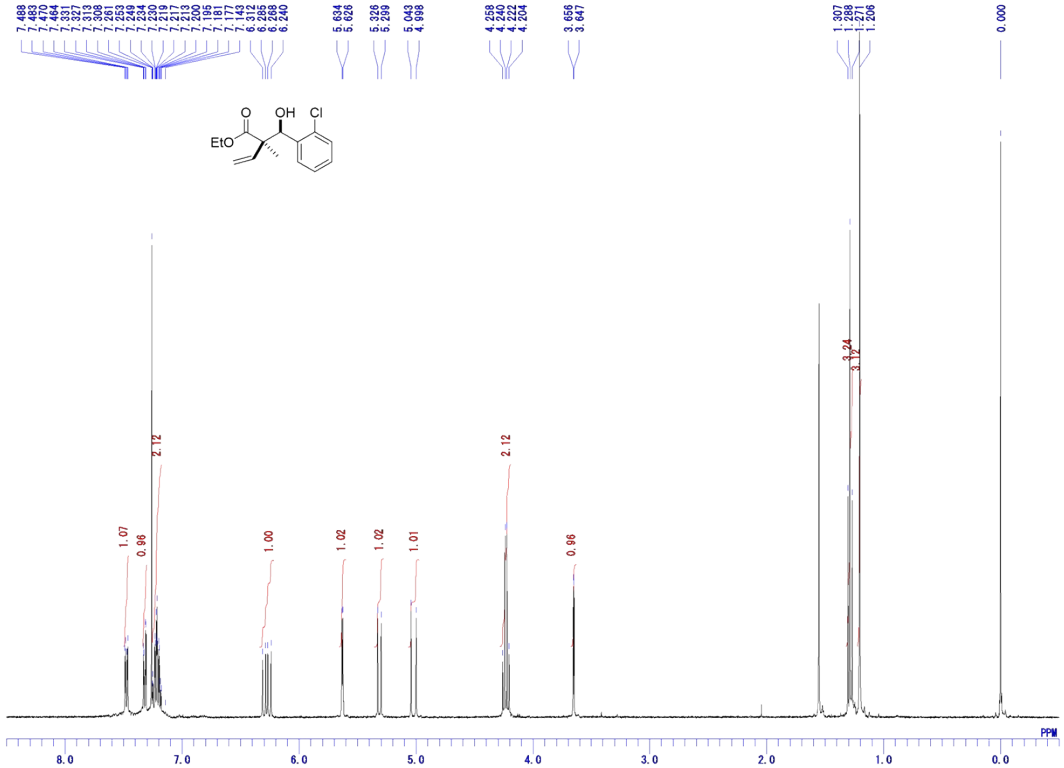
IR (neat) 3484 cm^{-1} (OH), 1716 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.27-1.30 (6H, m), 3.41 (1H, d, J = 5.3 Hz), 4.23 (2H, q, J = 7.1 Hz), 4.99 (1H, dd, J =17.4, 0.7 Hz), 5.11 (1H, dd, J = 10.7, 0.6 Hz), 5.61 (1H, d, J = 5.6 Hz), 6.14 (1H, dd, J = 17.5, 10.7 Hz), 7.18-7.28 (4H, m), 7.31 (1H, dd, J = 7.7, 1.4 Hz), 7.50 (1H, dd, J = 7.7, 1.7 Hz),

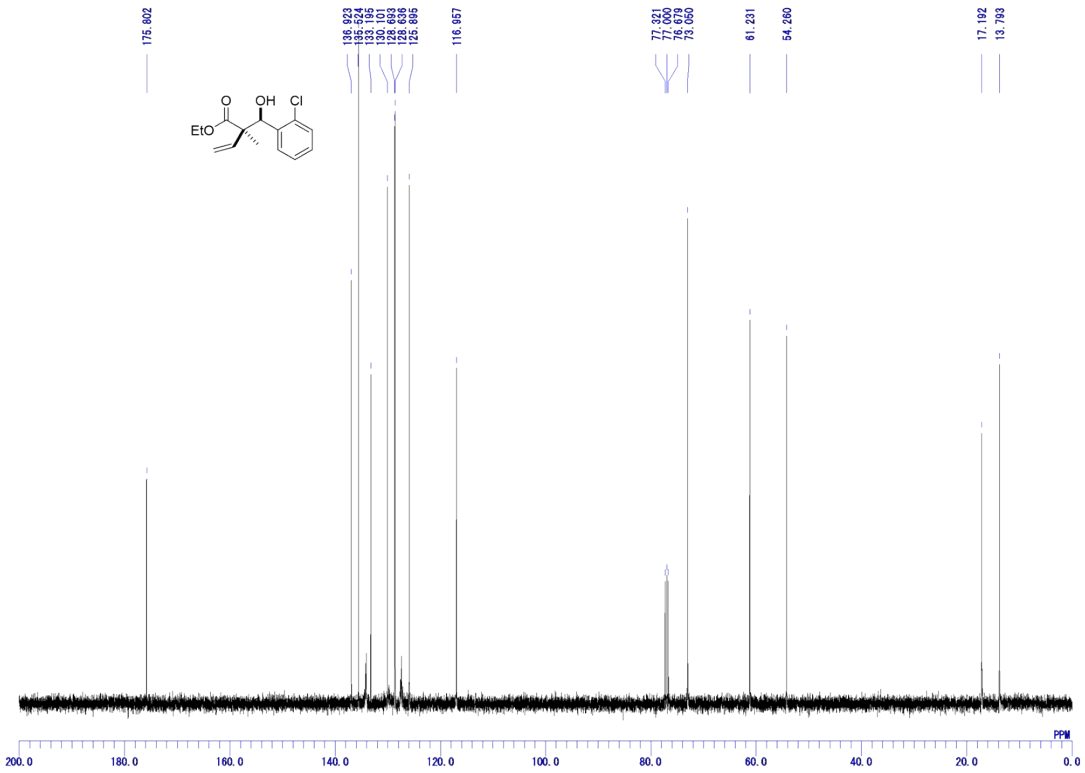
^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 14.0, 14.8, 55.3, 61.3, 73.1, 115.6, 126.3, 128.7, 129.2, 129.2, 133.4, 137.6, 137.9, 175.2.

HRMS (CI) m/z: calcd. for $C_{14}H_{17}ClO_3Na$ 291.0758 ($[M+Na]^+$), found 291.0761.

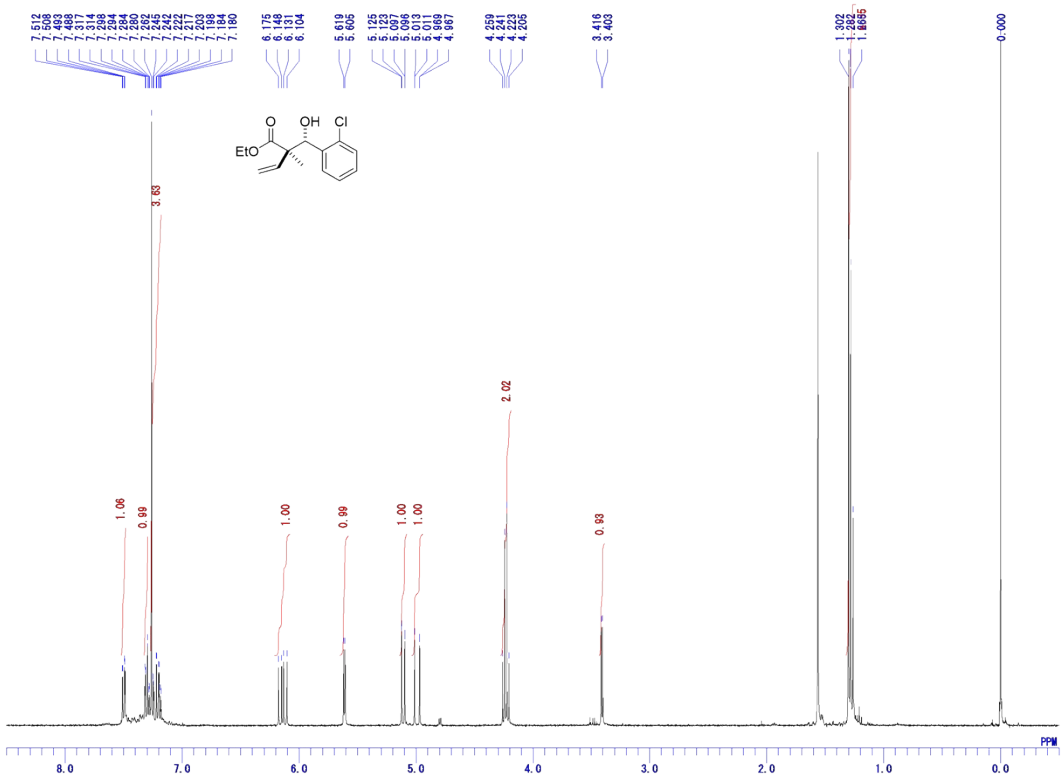
^{1}H NMR ($CDCl_3$, 400 MHz)



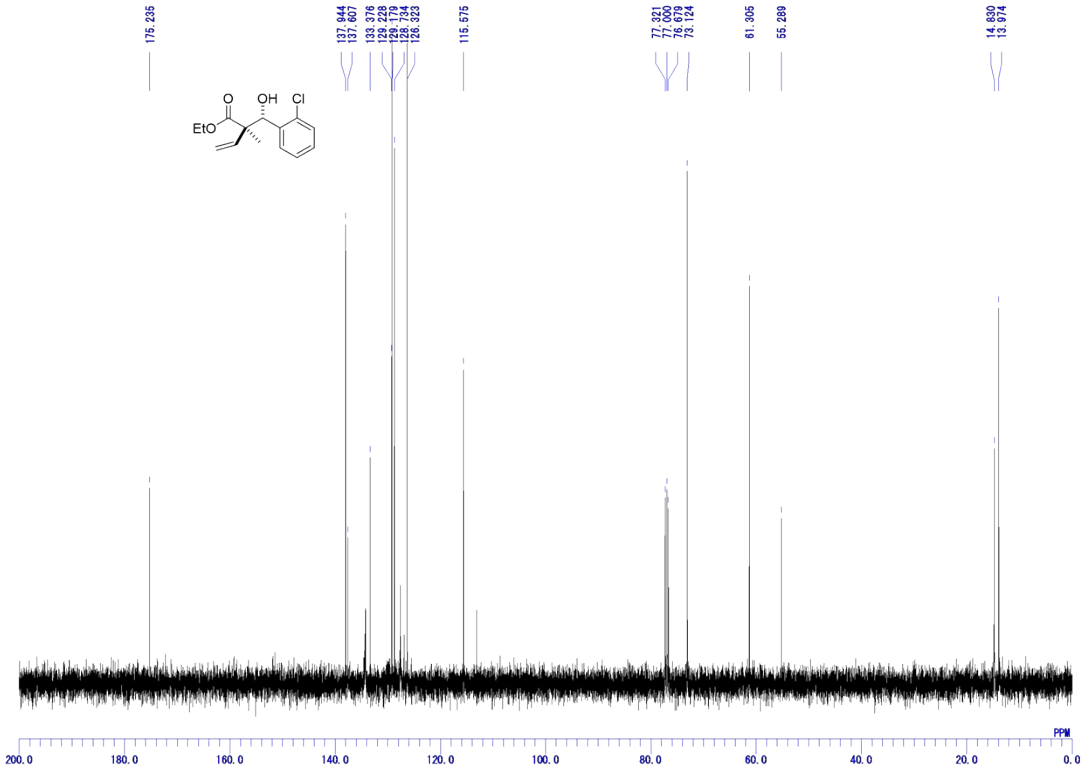
^{13}C NMR ($CDCl_3$, 100 MHz)



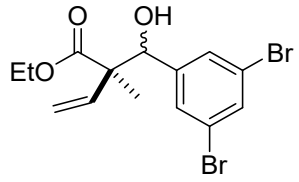
^{1}H NMR ($CDCl_3$, 400 MHz)



^{13}C NMR ($CDCl_3$, 100 MHz)



Ethyl 2-((3,5-dibromophenyl)(hydroxy)methyl)-2-methylbut-3-enoate (3ah)



Major isomer (syn): White solid.

Mp: 89-91℃

R_f = 0.55 (hexane/EtOAc = 8:2).

IR (neat) 3460 cm^{-1} (OH), 1694 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.16 (3H, s), 1.27 (3H, t, J = 7.1 Hz), 3.22 (1H, d, J = 2.9 Hz), 4.19 (2H, q, J = 7.1 Hz), 4.92 (1H, d, J = 2.9 Hz), 5.13 (1H, d, J = 17.6 Hz), 5.35 (1H, d, J = 10.6 Hz), 6.16 (1H, dd, J = 17.6, 10.9 Hz), 7.38 (2H, d, J = 1.9 Hz), 7.57 (1H, t, J = 1.7 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 14.0, 16.3, 54.3, 61.5, 76.8, 117.7, 122.1, 129.5, 133.3, 136.5, 143.2, 174.8.

HRMS (CI) m/z: calcd. for $C_{14}H_{17}Br_2O_3$ 390.9539 ($[M+H]^+$), found 390.9538.

Minor isomer (anti): Colorless oil.

R_f = 0.45 (hexane/EtOAc = 8:2).

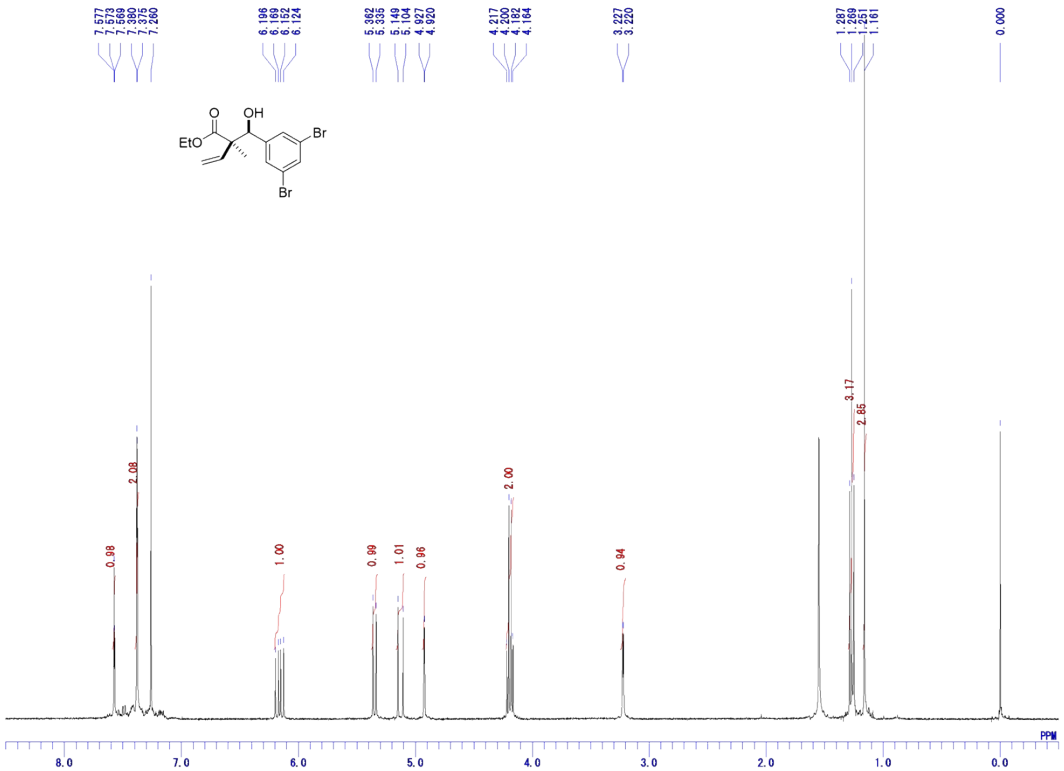
IR (neat) 3448 cm^{-1} (OH), 1693 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.21 (3H, s), 1.28 (3H, t, J = 7.1 Hz), 3.20 (1H, d, J = 5.3 Hz), 4.22 (2H, q, J = 7.0 Hz), 4.98 (1H, d, J = 5.3 Hz), 5.07 (1H, d, J = 17.6 Hz), 5.25 (1H, d, J = 10.9 Hz), 5.87 (1H, dd, J = 17.5, 10.7 Hz), 7.37 (2H, d, J = 1.9 Hz), 7.57 (1H, t, J = 1.7 Hz).

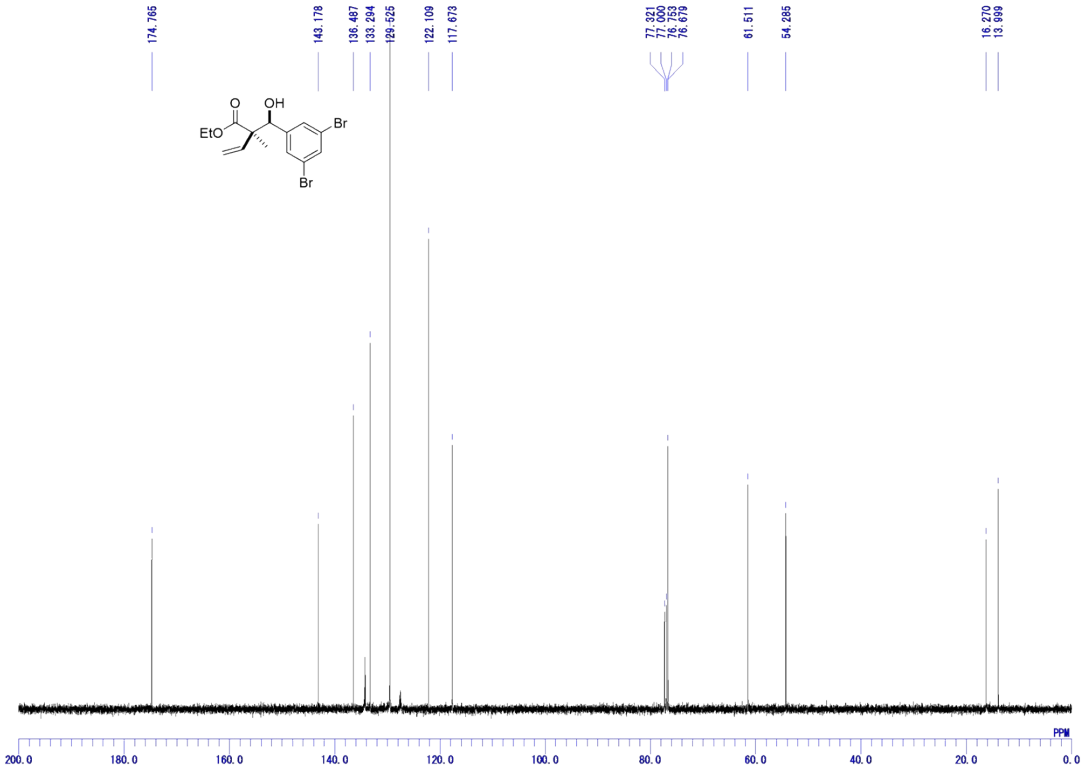
^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 14.1, 15.1, 54.8, 61.6, 76.7, 117.1, 122.1, 129.5, 133.2, 137.8, 143.4, 174.9.

HRMS (CI) m/z: calcd. for $C_{14}H_{17}Br_2O_3$ 390.9539 ($[M+H]^+$), found 390.9544.

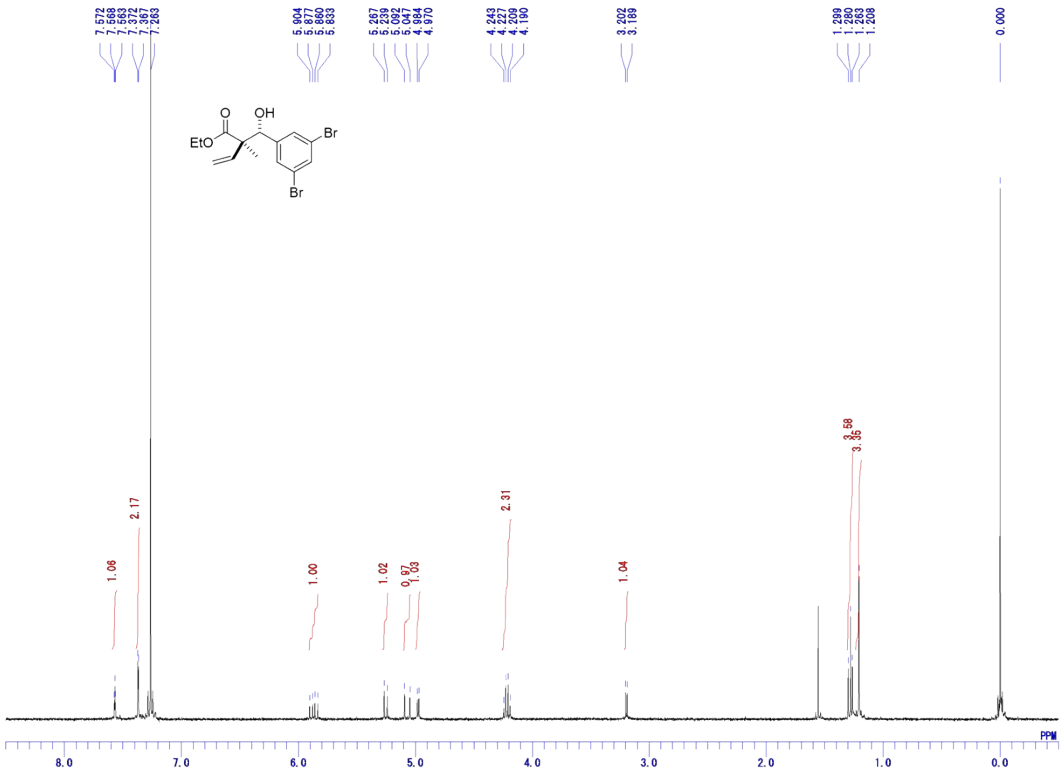
^{1}H NMR ($CDCl_3$, 400 MHz)



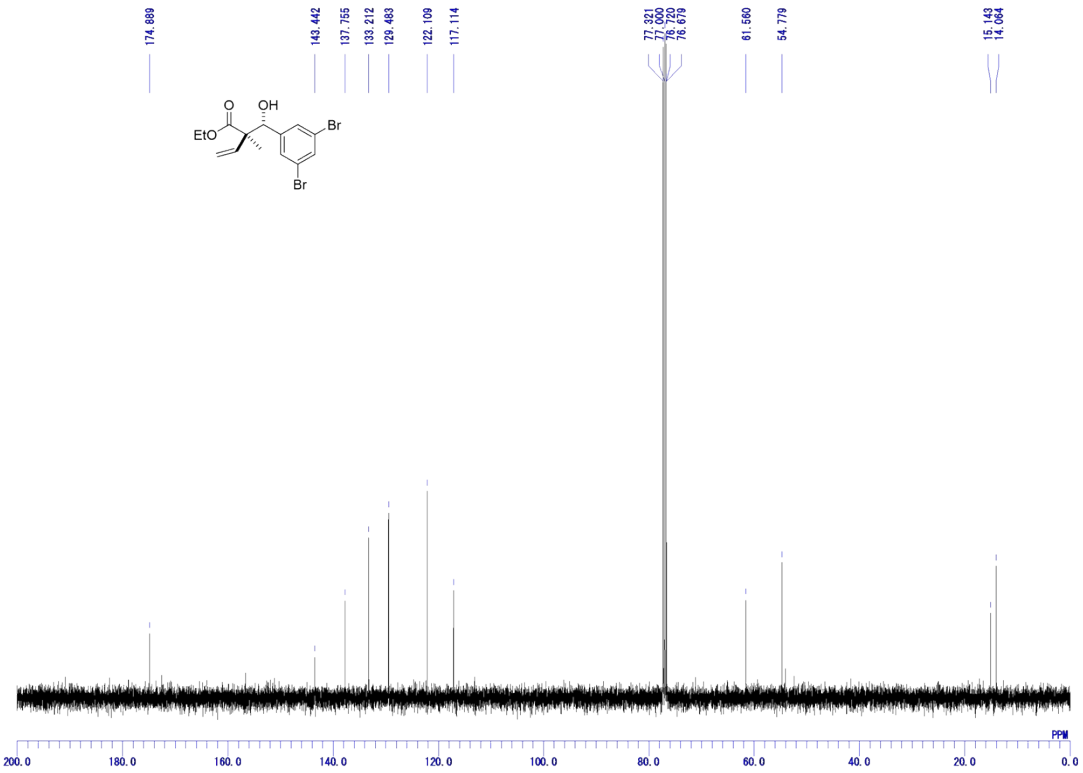
^{13}C NMR ($CDCl_3$, 100 MHz)



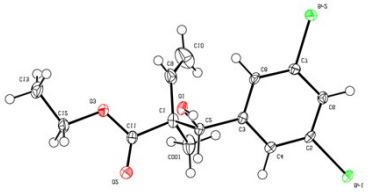
^{1}H NMR ($CDCl_3$, 400 MHz)



^{13}C NMR ($CDCl_3$, 100 MHz)



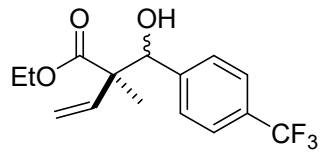
X-ray structure



CCDC: 2158597

Empirical formula	$C_{14}H_{16}O_3Br_2$
Formula weight	392.09
Temperature/K	123
Crystal system	triclinic
Space group	P-1
a/Å	8.81840(10)
b/Å	8.9121(2)
c/Å	11.45210(10)
α/°	93.2370(10)
β/°	108.2430(10)
γ/°	115.398(2)
Volume/Å^3	752.85(2)
Z	2
ρ_{calc}g/cm^3	1.730
μ/mm^{-1}	6.849
F(000)	388.0
Crystal size/mm^3	0.248 × 0.185 × 0.178
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	8.338 to 147.97
Index ranges	$-10 \leq h \leq 10$, $-10 \leq k \leq 11$, $-12 \leq l \leq 14$
Reflections collected	7529
Independent reflections	2963 [R_{int} = 0.0319, R_{sigma} = 0.0299]
Data/restraints/parameters	2963/0/175
Goodness-of-fit on F^2	1.088
Final R indexes [I>=2σ (I)]	R_1 = 0.0322, wR_2 = 0.0821
Final R indexes [all data]	R_1 = 0.0338, wR_2 = 0.0832
Largest diff. peak/hole / e Å^{-3}	0.80/-1.56

Ethyl 2-(hydroxy(4-(trifluoromethyl)phenyl)methyl)-2-methylbut-3-enoate (3ai)



Major isomer (syn): Colorless oil.

R_f = 0.48 (hexane/EtOAc = 8:2).

IR (neat) 3495 cm^{-1} (OH), 1716 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.16 (3H, s), 1.26 (3H, t, J = 7.1 Hz), 3.32 (1H, d, J = 3.1 Hz), 4.19 (2H, q, J = 7.1 Hz), 5.05-5.07 (2H, m), 5.32 (1H, d, J = 10.9 Hz), 6.21 (1H, dd, J = 17.6, 10.9 Hz), 7.42 (2H, d, J =8.2 Hz), 7.56 (2H, d, J =8.2 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 13.9, 16.6, 54.2, 61.4, 77.5, 117.4, 124.1 (q, J_{CF} = 273.2 Hz), 124.4 (q, J_{CF} = 3.8 Hz), 128.1, 129.9 (q, J_{CF} = 32.5 Hz), 136.6, 143.3, 175.1.

^{19}F{^{1}H} NMR ($CDCl_3$, 376 MHz) δ -62.46 (3F, s).

HRMS (CI) m/z: calcd. for $C_{15}H_{18}F_3O_3$ 303.1203 ($[M+H]^+$), found 303.1204.

Minor isomer (anti): Colorless oil.

Mp: 88-89℃

R_f = 0.43 (hexane/EtOAc = 8:2).

IR (neat) 3496 cm^{-1} (OH), 1708 cm^{-1} (C=O).

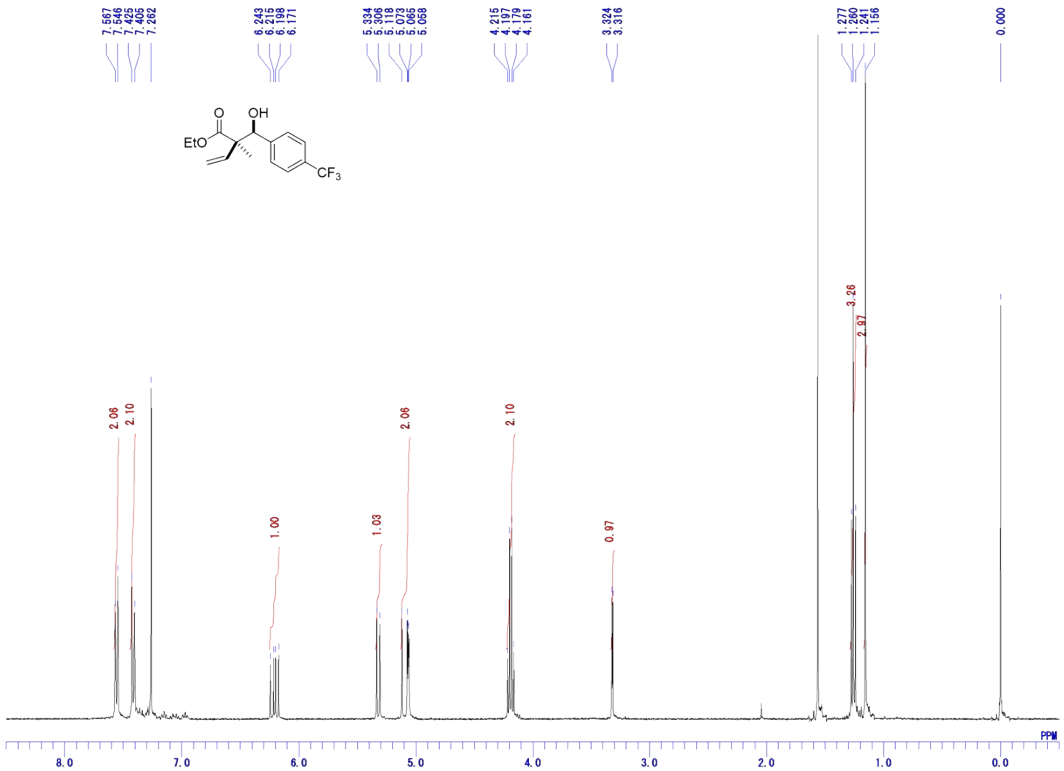
^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.21 (3H, s), 1.28 (3H, t, J = 7.1 Hz), 3.20 (1H, d, J = 4.8 Hz), 4.22 (2H, q, J = 7.2 Hz), 5.04 (1H, d, J = 17.4 Hz), 5.12 (1H, d, J = 4.8 Hz), 5.20 (1H, d, J = 10.6 Hz), 5.89 (1H, dd, J = 17.5, 10.7 Hz), 7.41 (2H, d, J =8.0 Hz), 7.56 (2H, d, J =8.5 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 14.0, 14.8, 54.8, 61.4, 77.3, 116.7, 124.1 (q, J_{CF} = 274.1 Hz), 124.4 (q, J_{CF} = 3.8 Hz), 128.0, 129.7 (q, J_{CF} = 32.8 Hz), 138.0, 143.5, 175.0.

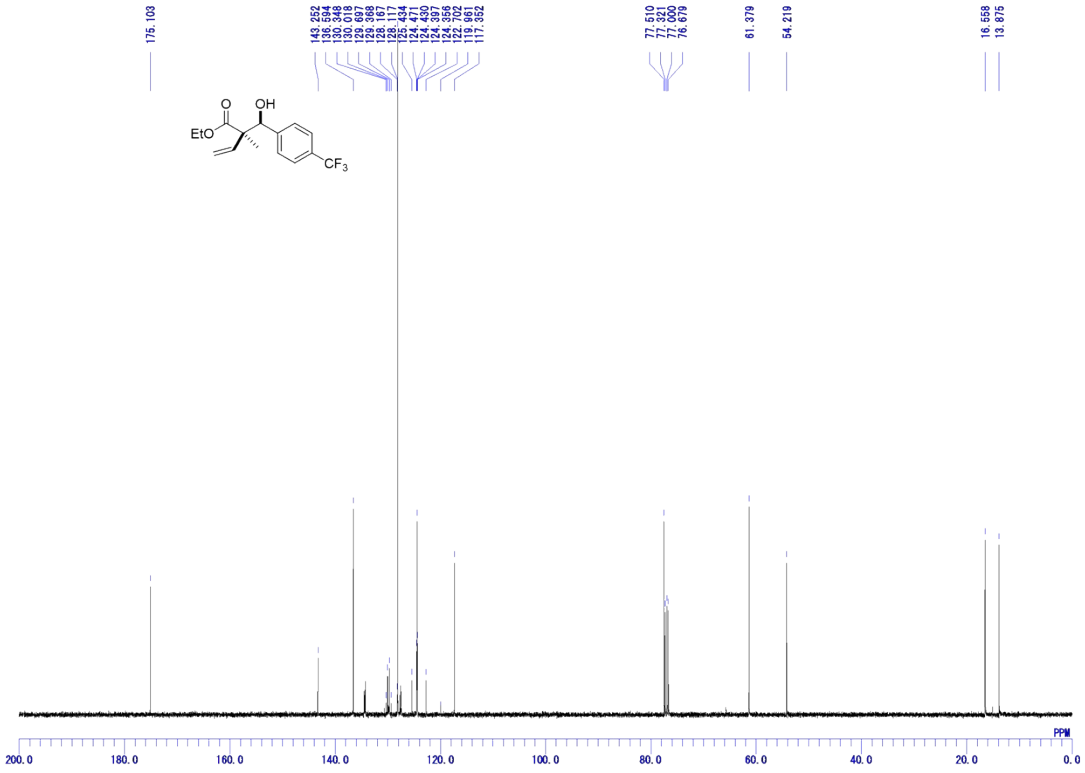
^{19}F{^{1}H} NMR ($CDCl_3$, 376 MHz) δ -62.44 (3F, s).

HRMS (CI) m/z: calcd. for $C_{15}H_{18}F_3O_3$ 303.1203 ($[M+H]^+$), found 303.1210.

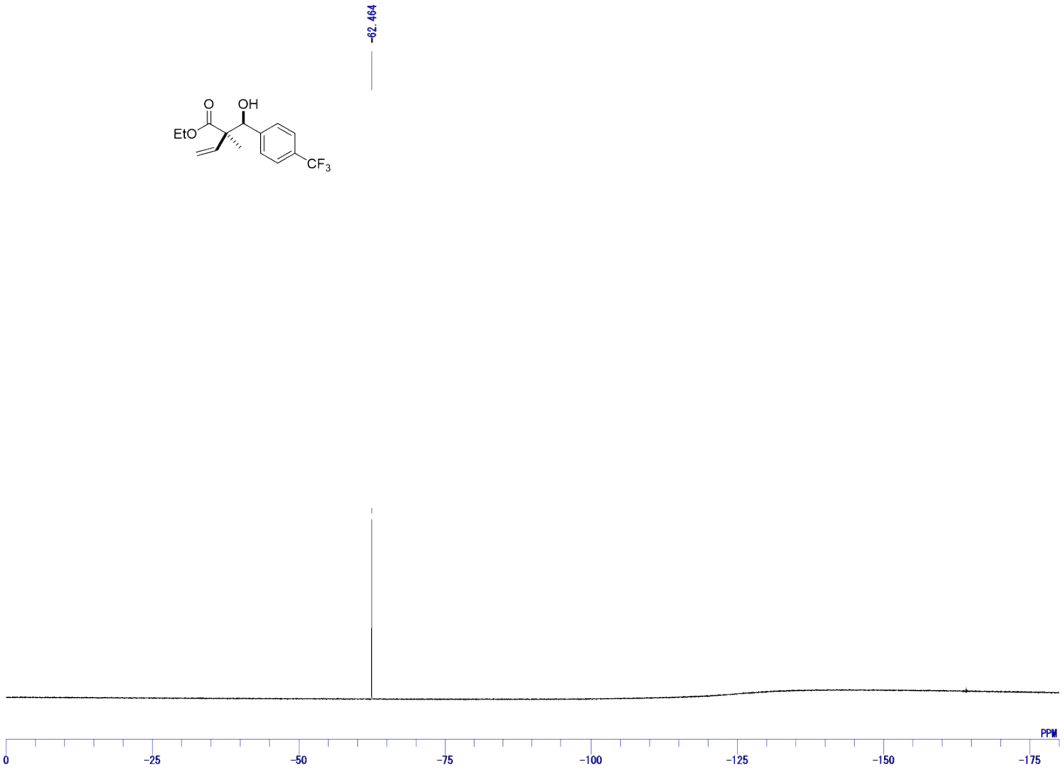
^{1}H NMR ($CDCl_3$, 400 MHz)



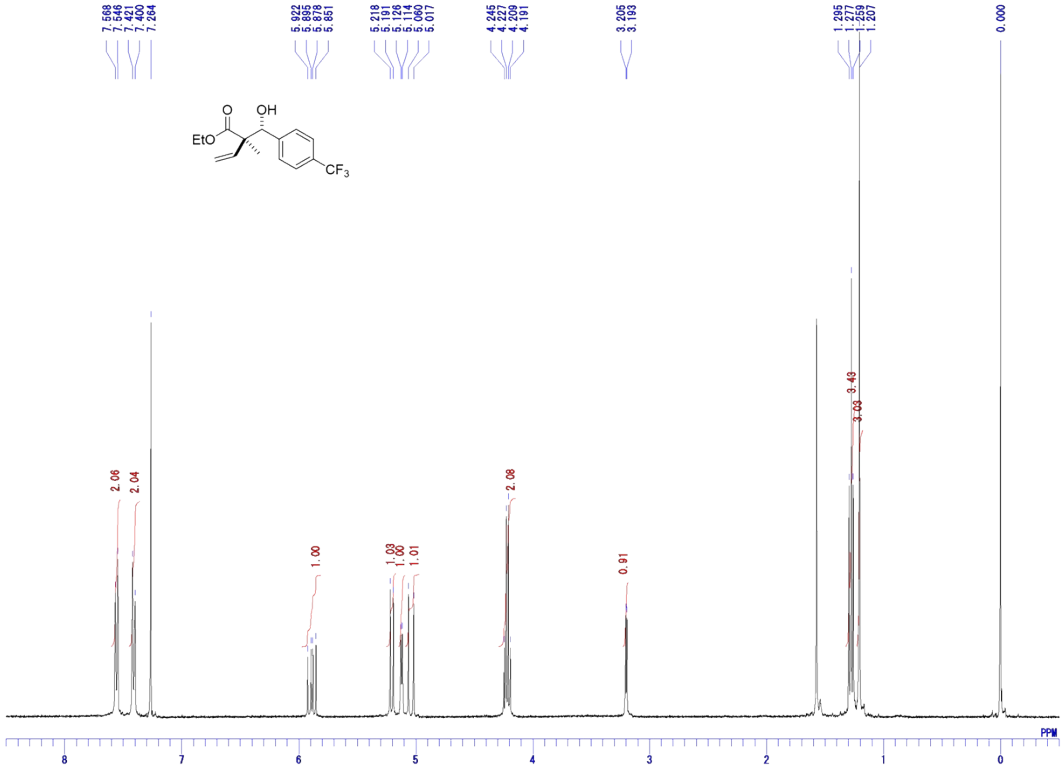
^{13}C NMR ($CDCl_3$, 100 MHz)



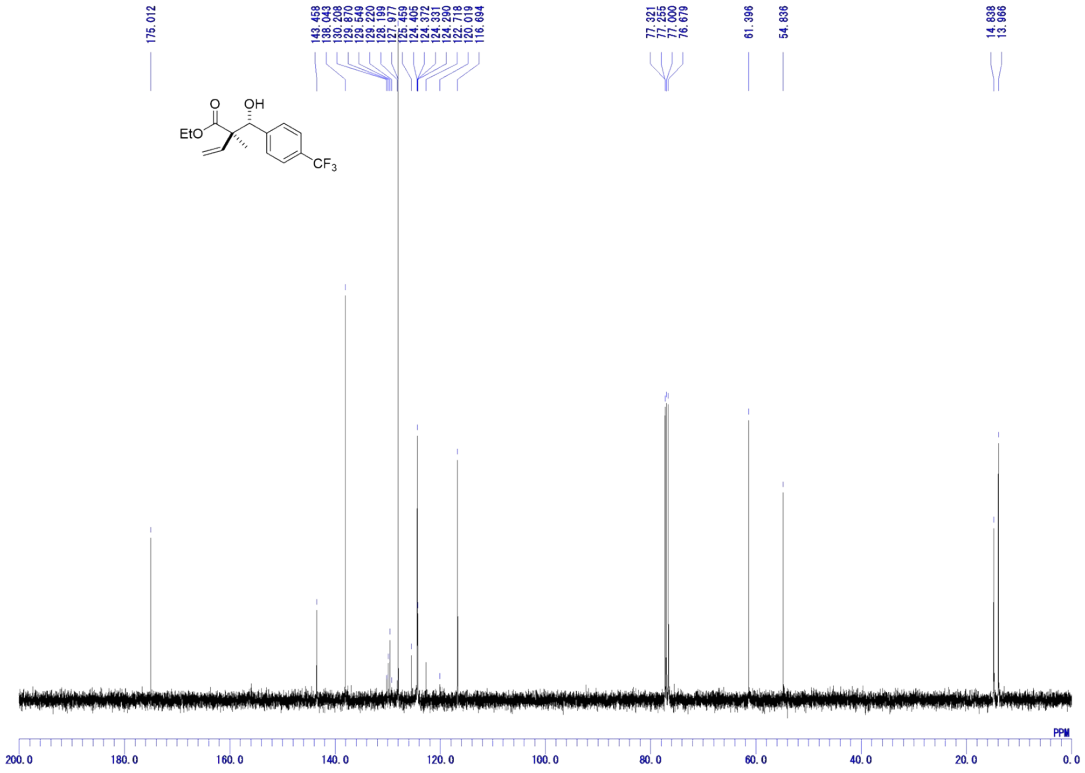
$^{19}F\{^{1}H\}$ NMR ($CDCl_3$, 376 MHz)



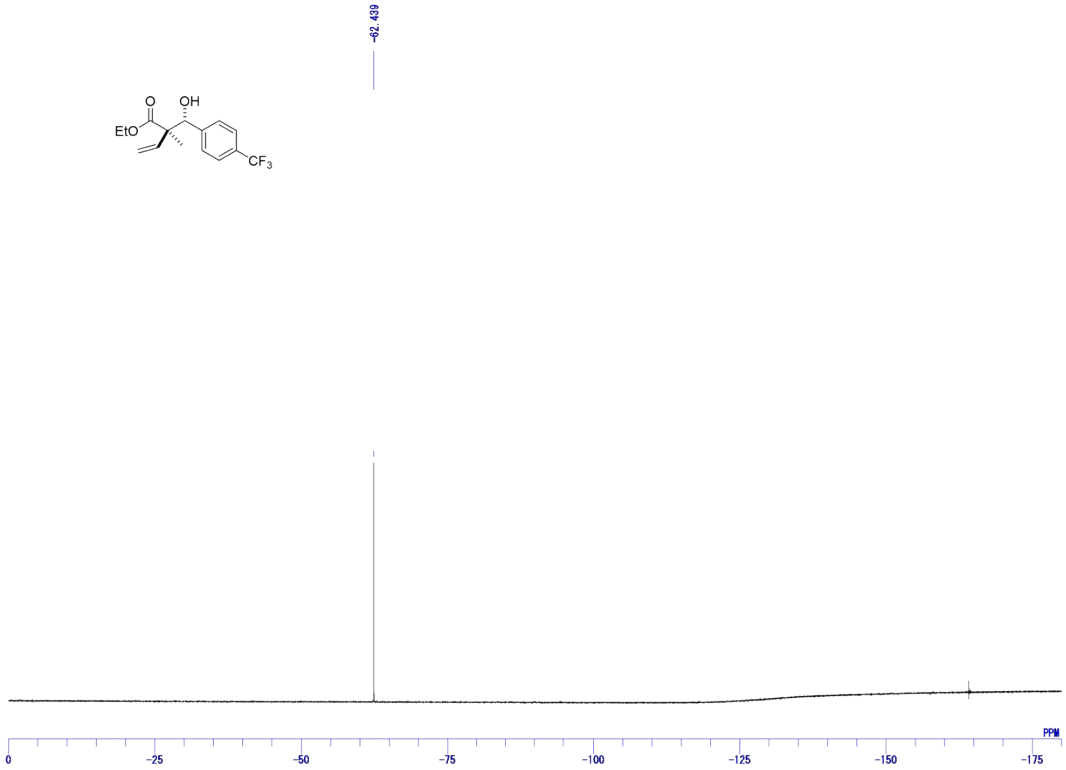
^{1}H NMR ($CDCl_3$, 400 MHz)



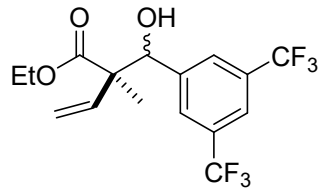
^{13}C NMR ($CDCl_3$, 100 MHz)



$^{19}F\{^{1}H\}$ NMR ($CDCl_3$, 376 MHz)



Ethyl 2-((3,5-bis(trifluoromethyl)phenyl)(hydroxy)methyl)-2-methylbut-3-enoate (3aj)



<u>Major isomer</u> (syn): Colorless oil.

R_f = 0.58 (hexane/EtOAc = 8:2).

IR (neat) 3468 cm^{-1} (OH), 1716 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.14 (3H, s), 1.27 (3H, t, J = 7.1 Hz), 3.40 (1H, d, J = 2.9 Hz), 4.19 (2H, q, J = 7.2 Hz), 5.09-5.15 (2H, m), 5.37 (1H, d, J = 10.6 Hz), 6.19 (1H, dd, J = 17.5, 10.7 Hz), 7.76 (2H, s), 7.80 (1H, s).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 13.9, 16.1, 54.3, 61.7, 77.0, 118.2, 121.7-121.8 (m), 123.3 (q, J_{CF} = 272.8 Hz), 128.0 (d), 130.8 (q, J_{CF} = 33.6 Hz), 136.2, 141.8 (d), 174.8.

^{19}F{^{1}H} NMR ($CDCl_3$, 376 MHz) δ -62.81 (3F, s).

HRMS (CI) m/z: calcd. for $C_{16}H_{17}F_6O_3$ 371.1076 ($[M+H]^+$), found 371.1088.

<u>Minor isomer</u> (anti): Colorless oil.

R_f = 0.55 (hexane/EtOAc = 8:2).

IR (neat) 3458 cm^{-1} (OH), 1714 cm^{-1} (C=O).

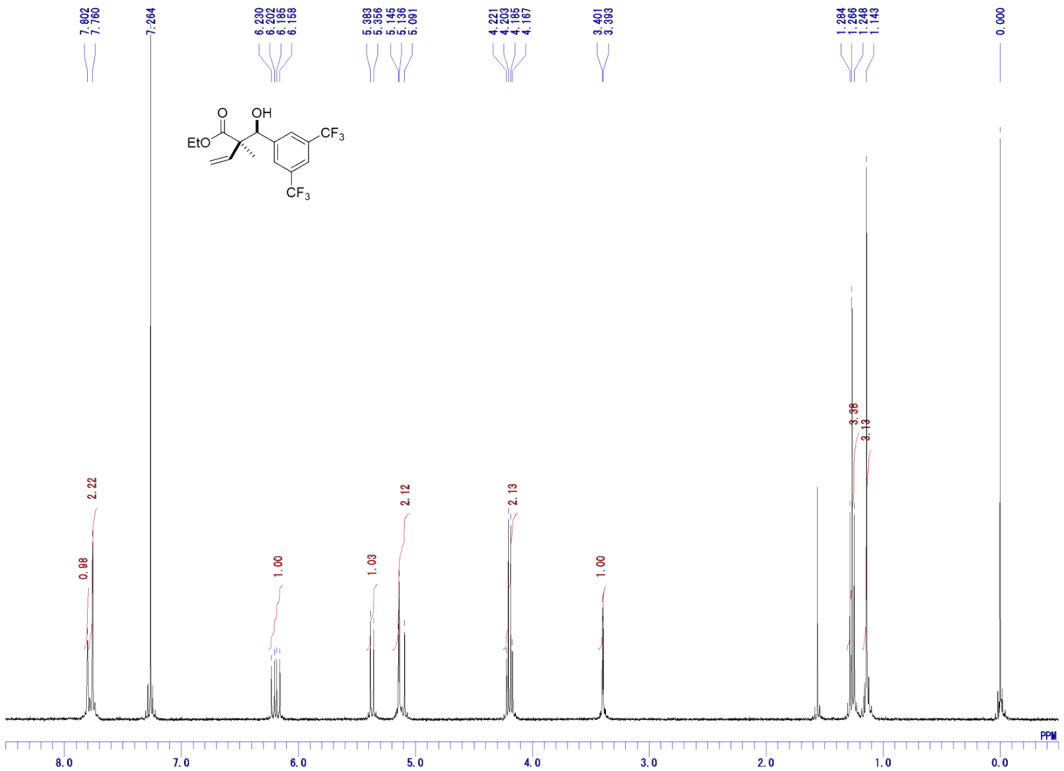
^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.18 (3H, s), 1.28 (3H, t, J = 7.1 Hz), 3.39 (1H, d, J = 4.6 Hz), 4.23 (2H, q, J = 7.2 Hz), 5.04 (1H, d, J = 17.4 Hz), 5.20 (1H, d, J = 4.6 Hz), 5.26 (1H, d, J = 10.6 Hz), 5.88 (1H, dd, J = 17.4, 10.6 Hz), 7.75 (2H, s), 7.79 (1H, s).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 13.9, 14.5, 54.8, 61.7, 76.6, 117.5, 121.4-121.6 (m), 123.3 (q, J_{CF} = 272.8 Hz), 127.9 (d), 130.7 (q, J_{CF} = 33.3 Hz), 137.4, 142.0, 174.9.

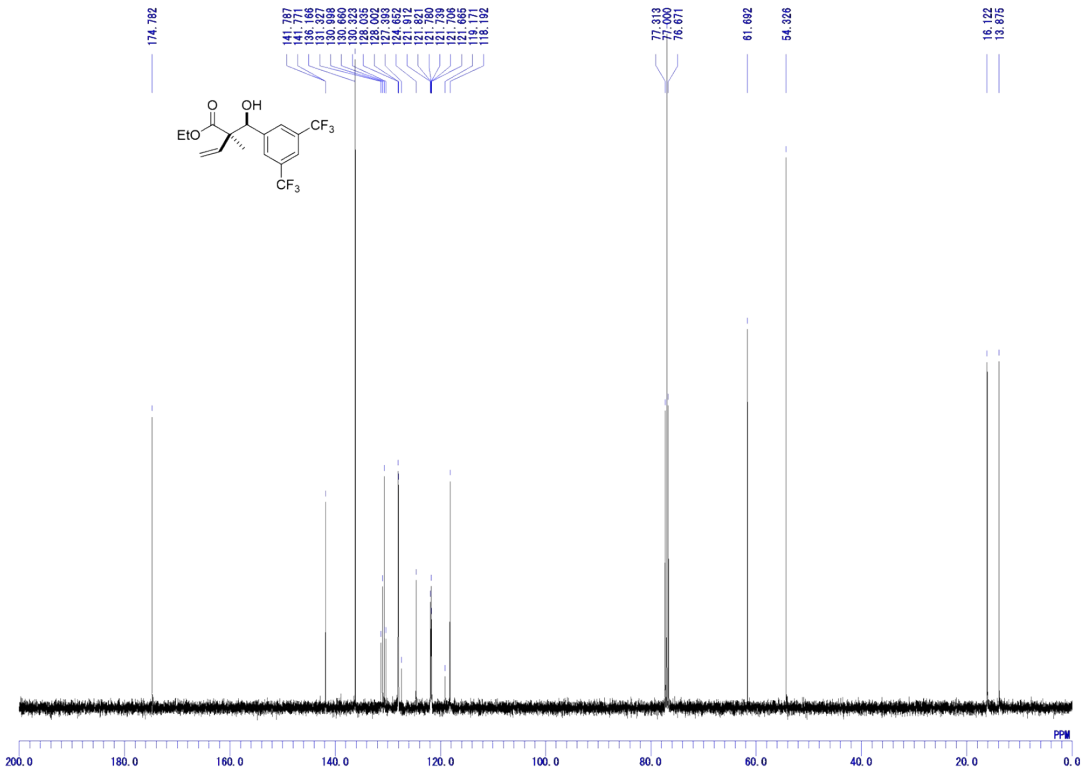
^{19}F{^{1}H} NMR ($CDCl_3$, 376 MHz) δ -62.81 (3F, s).

HRMS (CI) m/z: calcd. for $C_{16}H_{17}F_6O_3$ 371.1076 ($[M+H]^+$), found 371.1083.

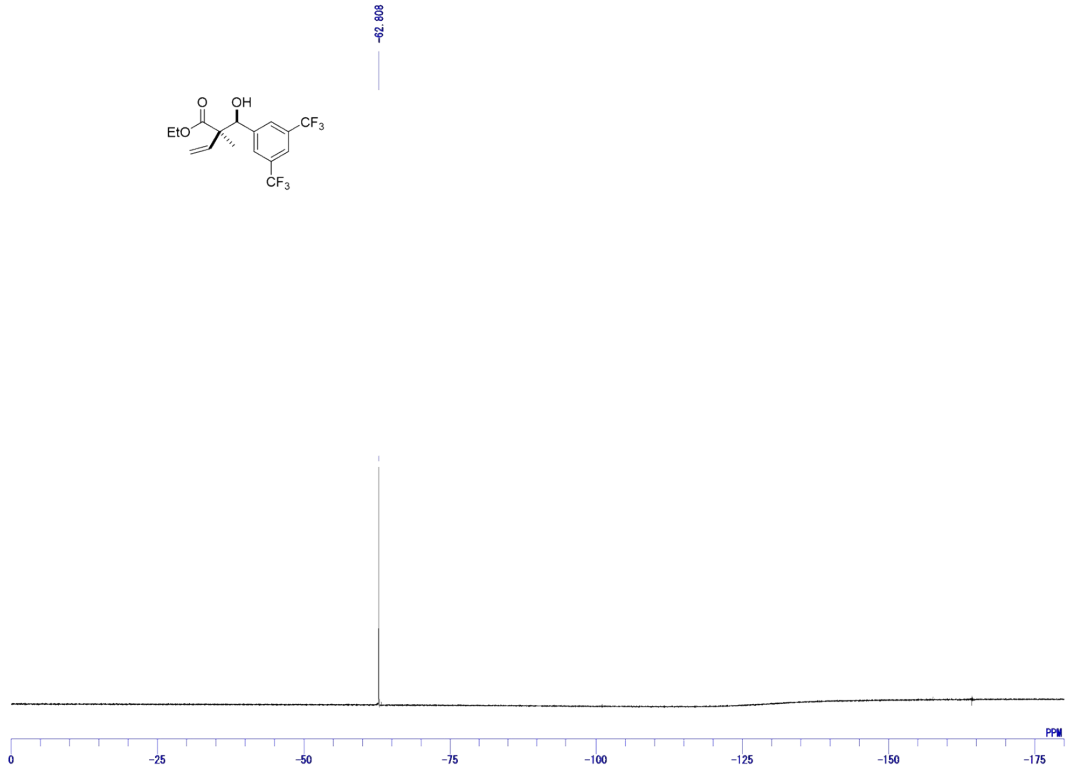
^{1}H NMR ($CDCl_3$, 400 MHz)



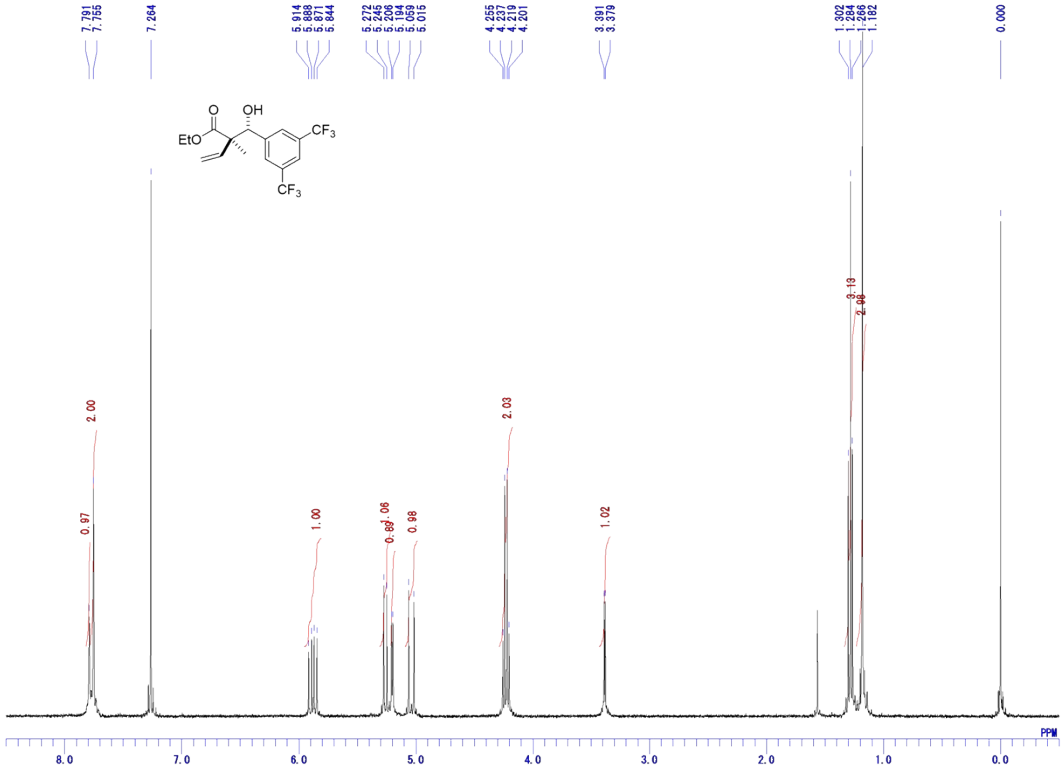
^{13}C NMR ($CDCl_3$, 100 MHz)



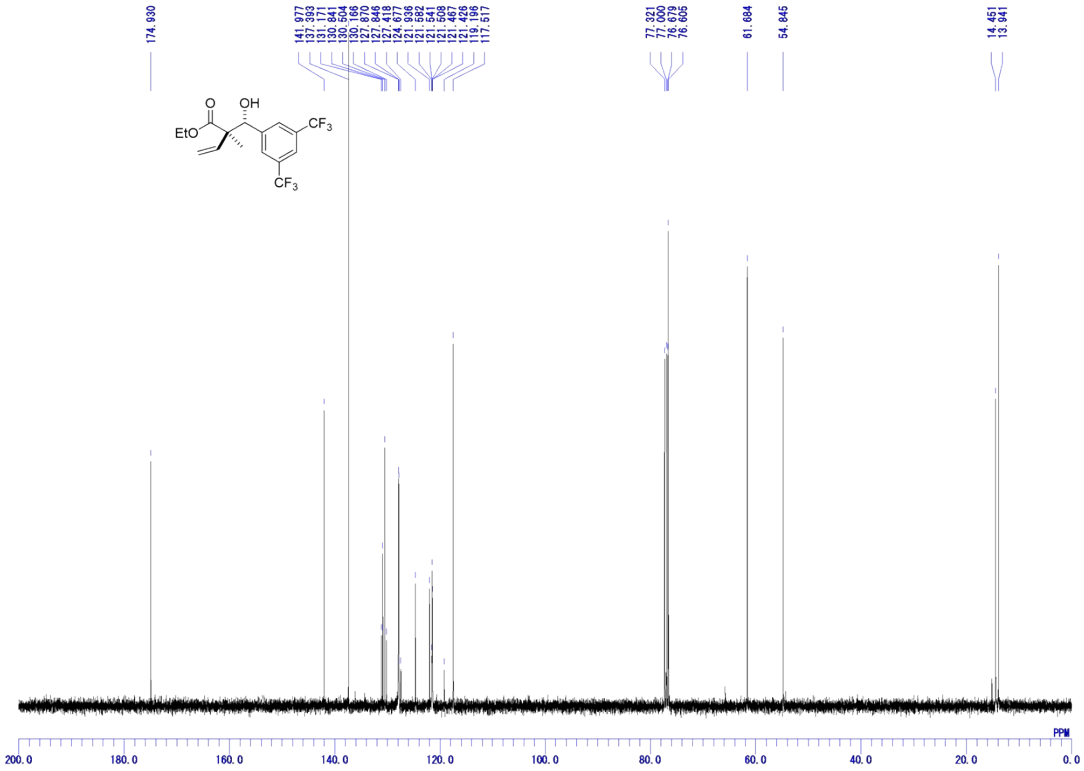
$^{19}F\{^{1}H\}$ NMR ($CDCl_3$, 376 MHz)



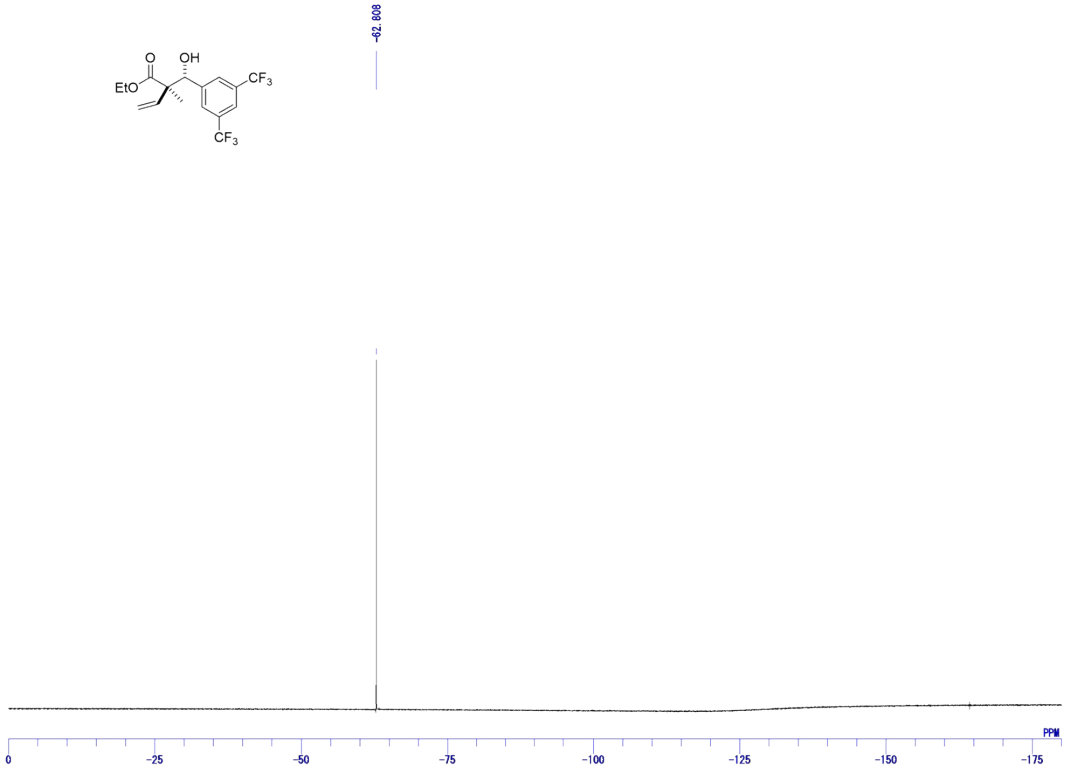
^{1}H NMR ($CDCl_3$, 400 MHz)



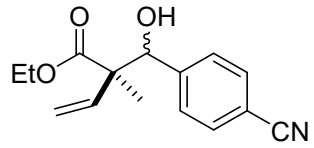
^{13}C NMR ($CDCl_3$, 100 MHz)



$^{19}F\{^{1}H\}$ NMR ($CDCl_3$, 376 MHz)



Ethyl 2-((4-cyanophenyl)(hydroxy)methyl)-2-methylbut-3-enoate (3ak)



Major isomer (syn): Colorless oil.

R_f = 0.33 (hexane/EtOAc = 8:2).

IR (neat) 3483 cm^{-1} (OH), 1716 cm^{-1} (C=O), 2229 cm^{-1} (CN).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.14 (3H, s), 1.26 (3H, t, J = 7.1 Hz), 3.36 (1H, s), 4.19 (2H, q, J = 7.1 Hz), 5.05 (1H, s), 5.09 (1H, d, J = 17.6 Hz), 5.32 (1H, d, J = 10.6 Hz), 6.17 (1H, dd, J = 17.6, 10.9 Hz), 7.41 (2H, d, J = 8.2 Hz), 7.59 (2H, d, J = 8.5 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 13.8, 16.3, 54.0, 61.2, 77.1, 111.1, 117.2, 118.5, 128.4, 131.1, 136.3, 144.7, 174.7.

HRMS (CI) m/z: calcd. for $C_{15}H_{18}NO_3$ 260.1281 ($[M+H]^+$), found 260.1282.

Minor isomer (anti): Colorless oil.

Isolated as mixture of diastereomers

R_f = 0.28 (hexane/EtOAc = 8:2).

IR (neat) 3484 cm^{-1} (OH), 1717 cm^{-1} (C=O), 2229 cm^{-1} (CN).

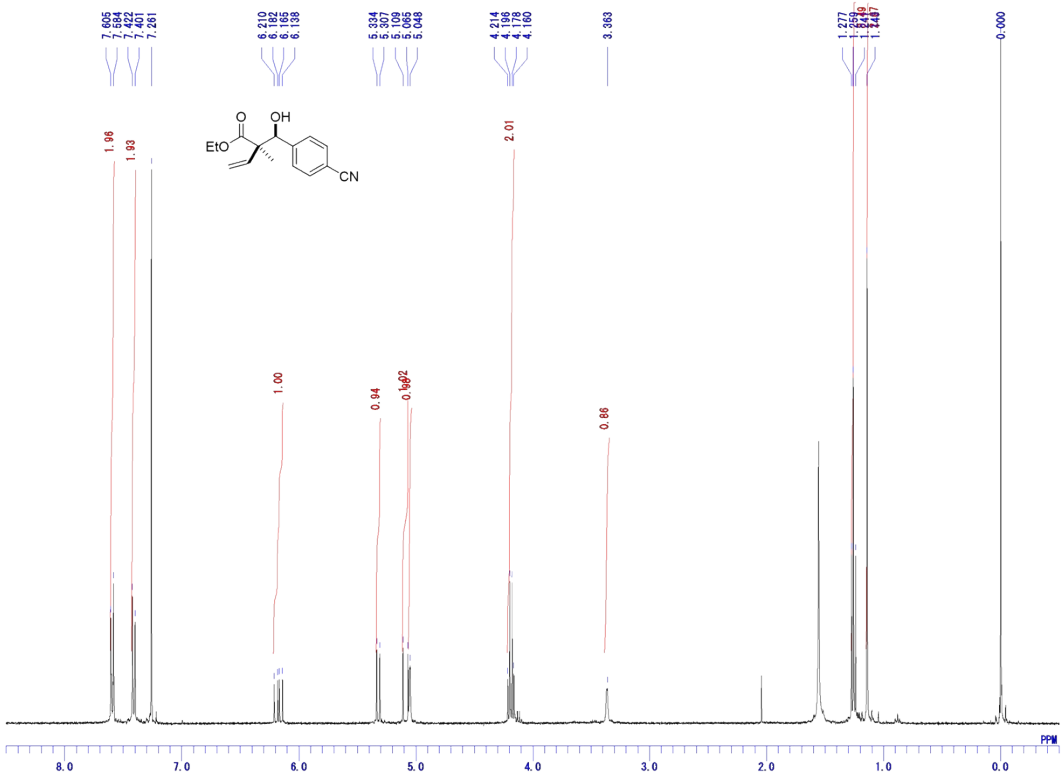
^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.14 (3H, s, major), 1.19 (3H, s, minor)*, 1.23-1.30 (3H, m, major+minor)*, 3.27 (1H, d, J = 4.8 Hz, minor)*, 3.39 (1H, d, J = 3.1 Hz, major), 4.16-4.24 (2H, m, major+minor)*, 5.01-5.07 (1H, m, major+minor)*, 5.12 (1H, d, J = 4.8 Hz, major+minor)*, 5.21 (1H, d, J = 10.9 Hz, minor) *, 5.32 (1H, d, J = 11.1 Hz, major), 5.86 (1H, dd, J = 17.5, 10.7 Hz, minor)*, 6.18 (1H, dd, J = 17.5, 10.7 Hz, major), 7.41 (2H, d, J = 8.0 Hz, major+minor)*, 7.59 (2H, d, J = 8.5 Hz, major+minor)*.

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 14.0, 14.0*, 14.7*, 16.6, 54.2, 54.8*, 61.5*, 61.5, 77.1*, 77.4, 111.4*, 111.6, 117.0*, 117.8, 118.7, 118.7*, 128.4*, 128.6, 131.2*, 131.4, 136.3, 137.8*, 144.5, 144.7*, 174.9*, 175.0.

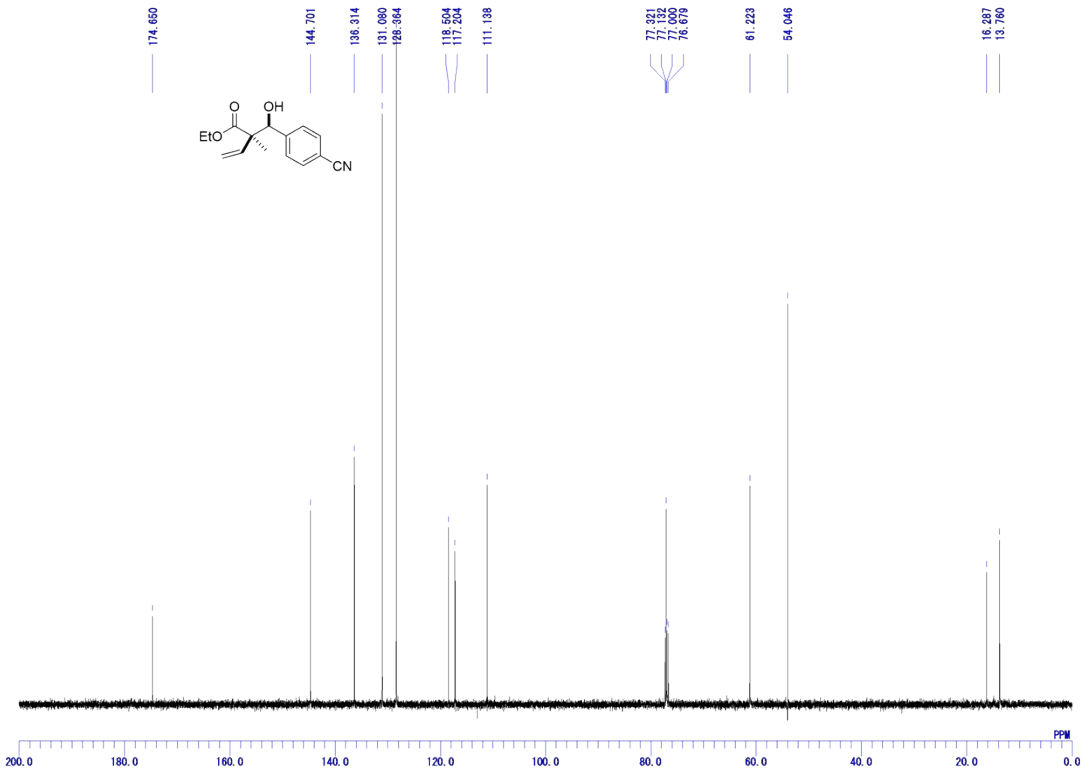
* Mark corresponds to minor isomer.

HRMS (CI) m/z: calcd. for $C_{15}H_{18}NO_3$ 260.1281 ($[M+H]^+$), found 260.1281.

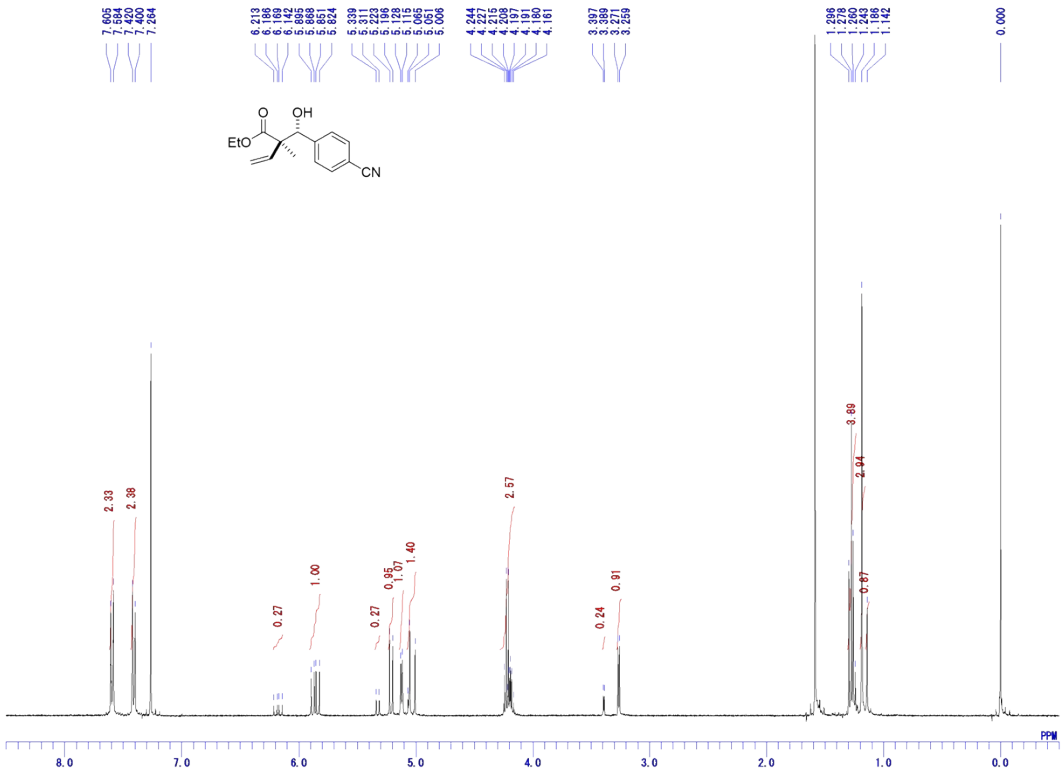
^{1}H NMR ($CDCl_3$, 400 MHz)



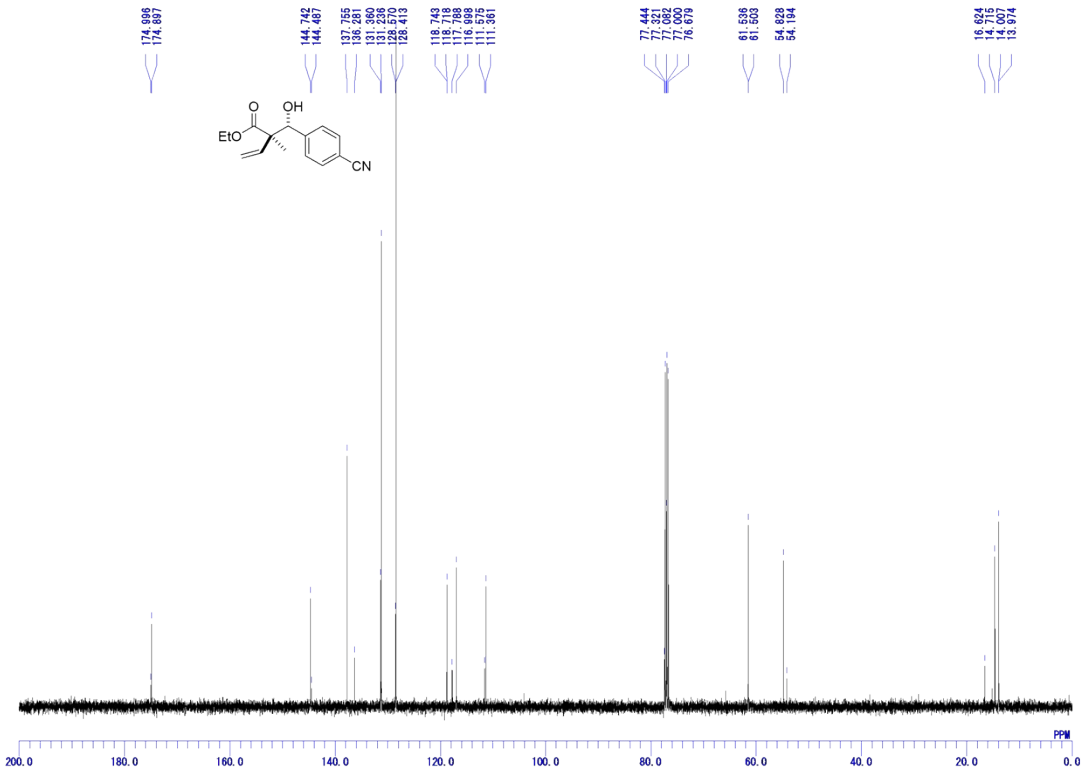
^{13}C NMR ($CDCl_3$, 100 MHz)



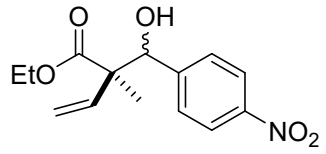
^{1}H NMR ($CDCl_3$, 400 MHz)



^{13}C NMR ($CDCl_3$, 100 MHz)



Ethyl 2-(hydroxy(4-nitrophenyl)methyl)-2-methylbut-3-enoate (3al)



Major isomer (syn): Yellow oil.

R_f = 0.35 (hexane/EtOAc = 8:2).

IR (neat) 3507 cm^{-1} (OH), 1715 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.16 (3H, s), 1.27 (3H, t, J = 7.2 Hz), 3.42 (1H, d, J = 3.1 Hz), 4.20 (2H, q, J = 7.2 Hz), 5.07-5.12 (2H, m), 5.33 (1H, d, J = 10.6 Hz), 6.19 (1H, dd, J = 17.5, 10.7 Hz), 7.48 (2H, d, J = 8.7 Hz), 8.16 (2H, d, J = 8.9 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 13.9, 16.5 (d), 54.1, 61.5, 77.1 (d), 117.7, 122.6, 128.6, 136.2, 146.6, 147.3, 174.8.

HRMS (CI) m/z: calcd. for $C_{14}H_{18}NO_5$ 280.1179 ($[M+H]^+$), found 280.1184.

Minor isomer (anti): Yellow oil.

Isolated as mixture of diastereomers

R_f = 0.28 (hexane/EtOAc = 8:2).

IR (neat) 3480 cm^{-1} (OH), 1708 cm^{-1} (C=O).

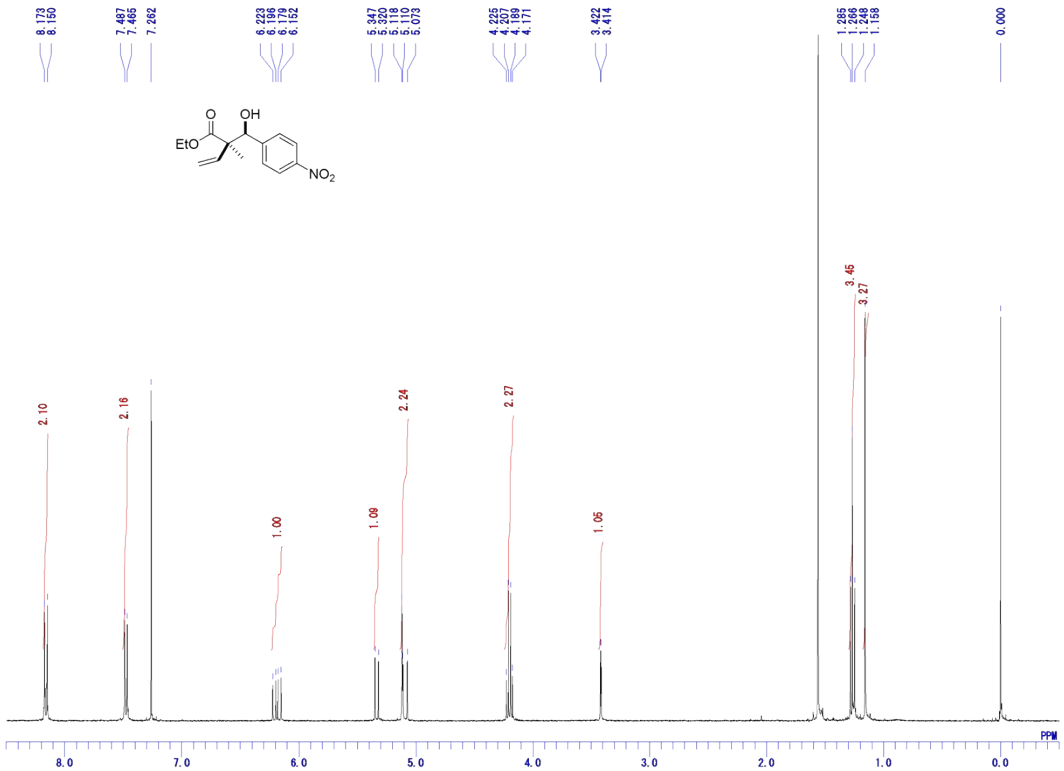
^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.20 (3H, s), 1.28 (3H, t, J = 7.1 Hz), 3.30 (1H, d, J = 4.8 Hz), 4.23 (2H, q, J = 7.2 Hz), 5.04 (1H, d, J = 17.6 Hz), 5.18 (1H, d, J = 4.8 Hz), 5.22 (1H, d, J = 10.6 Hz), 5.87 (1H, dd, J = 17.4, 10.6 Hz), 7.47 (2H, d, J = 8.2 Hz), 8.16 (2H, d, J = 8.9 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 14.0, 14.7 (d), 54.9, 61.6, 77.0 (d), 117.2, 122.6, 128.6, 136.7, 146.7, 147.4, 174.9.

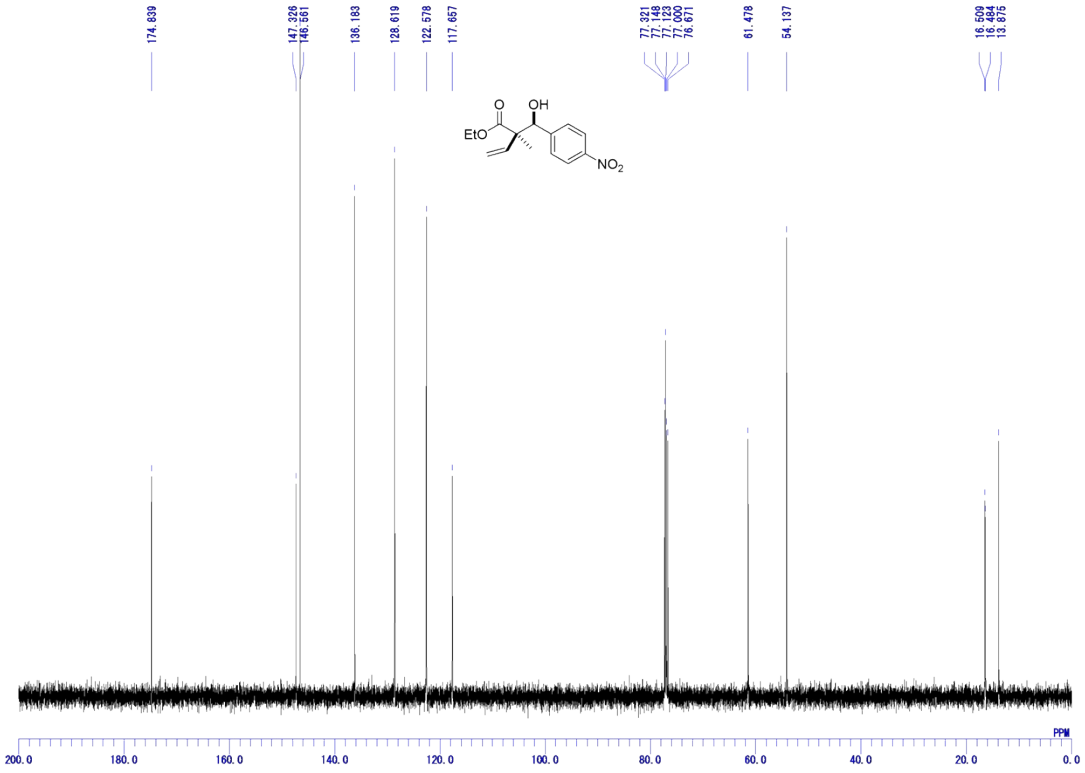
* Mark corresponds to minor isomer.

HRMS (CI) m/z: calcd. for $C_{14}H_{18}NO_5$ 280.1179 ($[M+H]^+$), found 280.1188.

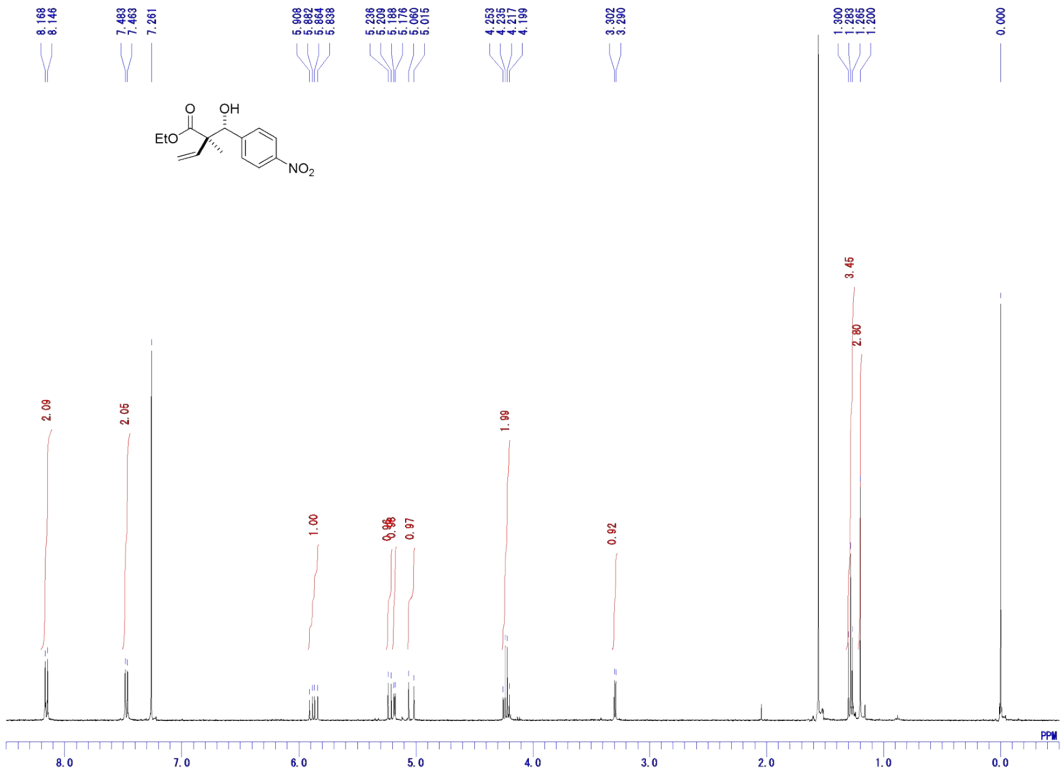
^{1}H NMR ($CDCl_3$, 400 MHz)



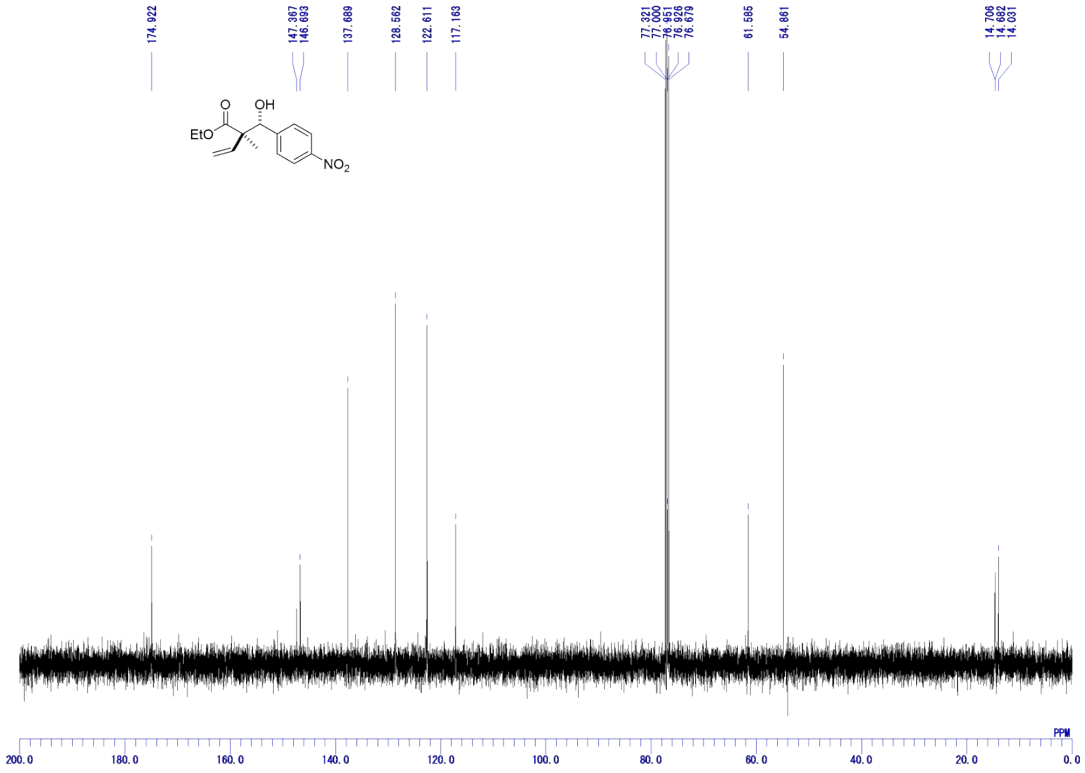
^{13}C NMR ($CDCl_3$, 100 MHz)



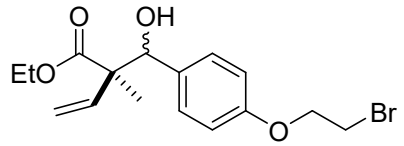
^{1}H NMR ($CDCl_3$, 400 MHz)



^{13}C NMR ($CDCl_3$, 100 MHz)



Ethyl 2-(hydroxy(4-methoxyphenyl)methyl)-2-methylbut-3-enoate (3am)



<u>Major isomer</u> (syn): Colorless oil.

R_f = 0.43 (hexane/EtOAc = 8:2).

IR (neat) 3508 cm^{-1} (OH), 1715 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.15 (3H, s), 1.26 (3H, t, J = 7.1 Hz), 3.11 (1H, d, J = 3.1 Hz), 3.63 (2H, t, J = 6.3 Hz), 4.17 (2H, q, J = 7.2 Hz), 4.28, (2H, t, J = 6.3 Hz), 4.96 (1H, d, J =2.9 Hz), 5.08 (1H, dd, J = 17.5, 0.8 Hz), 5.29 (1H, dd, J = 10.9, 0.7 Hz), 6.23 (1H, dd, J = 17.6, 10.9 Hz), 6.84 (2H, d, J =8.7 Hz), 7.22 (2H, d, J =8.5 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 13.9, 16.6, 29.1, 54.4, 61.1, 67.7, 77.6, 113.7, 116.8, 128.9, 132.2, 137.2, 157.5, 175.2.

HRMS (CI) m/z: calcd. for $C_{15}H_{21}O_4$ 356.0623 ($[M]^+$), found 356.0626.

<u>Minor isomer</u> (anti): White solid.

Mp: 96-98°C

R_f = 0.40 (hexane/EtOAc = 8:2).

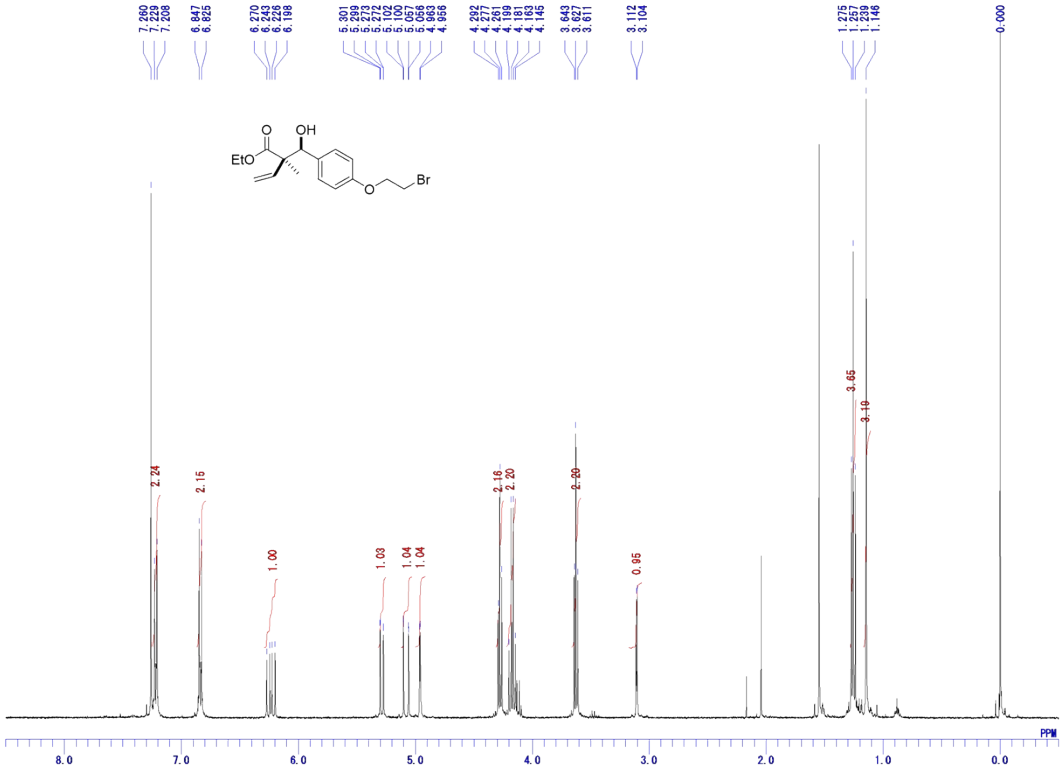
IR (neat) 3451 cm^{-1} (OH), 1699 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.21 (3H, s), 1.27 (3H, t, J = 7.1 Hz), 3.01 (1H, d, J = 5.1 Hz), 3.64 (2H, t, J = 6.3 Hz), 4.20 (2H, q, J = 7.1 Hz), 4.28, (2H, t, J = 6.3 Hz), 4.99-5.04 (2H, m), 5.16 (1H, d, J = 10.9 Hz), 5.91 (1H, dd, J = 17.5, 10.7 Hz), 6.84 (2H, d, J =8.7 Hz), 7.21 (2H, d, J =8.7 Hz).

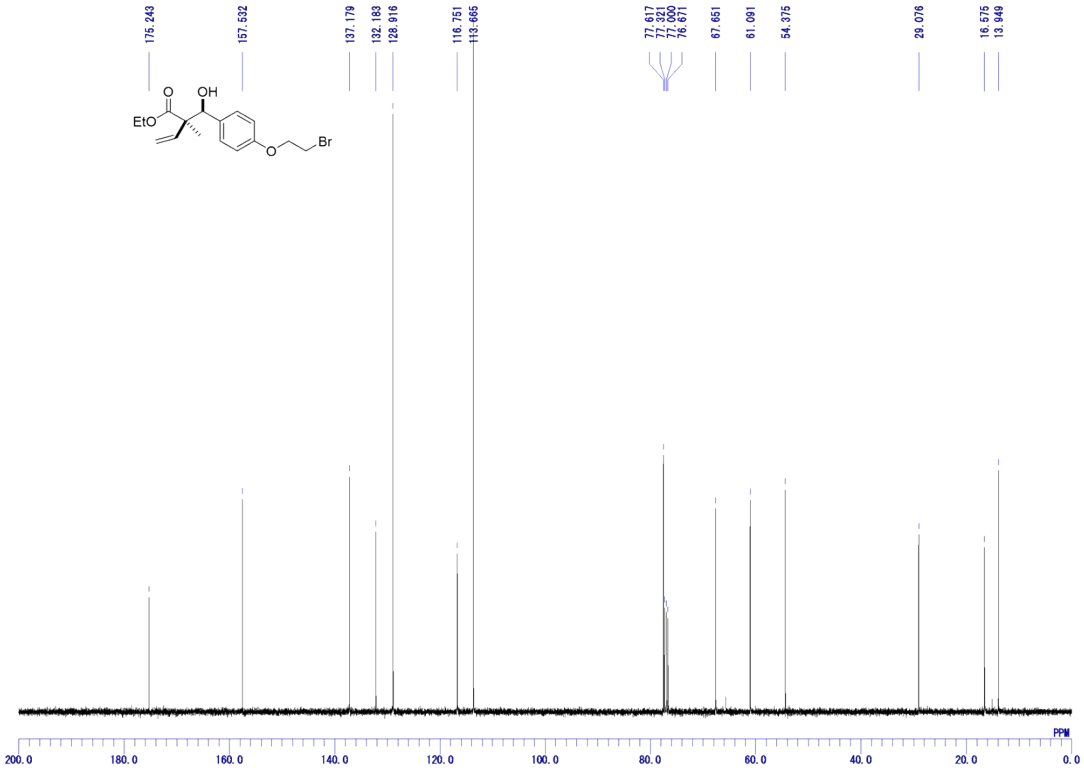
^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 14.0, 15.2, 29.1, 54.9, 61.1, 67.7, 77.5, 113.7, 116.0, 128.8, 132.5, 138.6, 157.4, 175.1.

HRMS (CI) m/z: calcd. for $C_{15}H_{21}O_4$ 356.0623 ($[M]^+$), found 356.06238

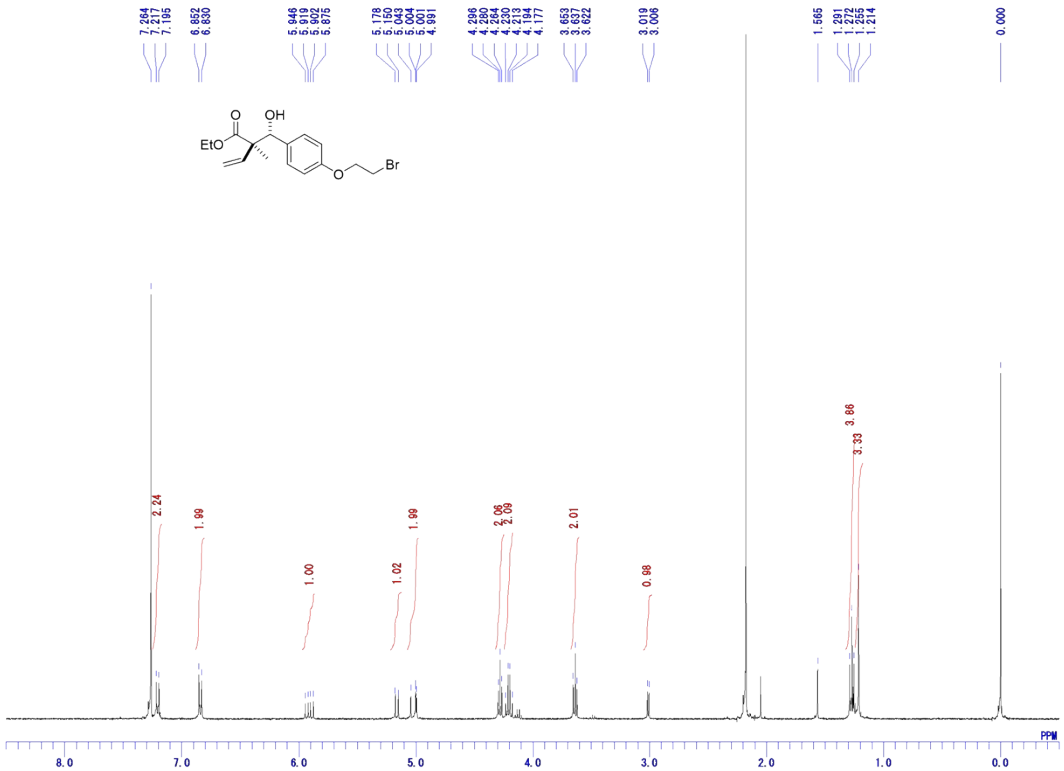
^{1}H NMR ($CDCl_3$, 400 MHz)



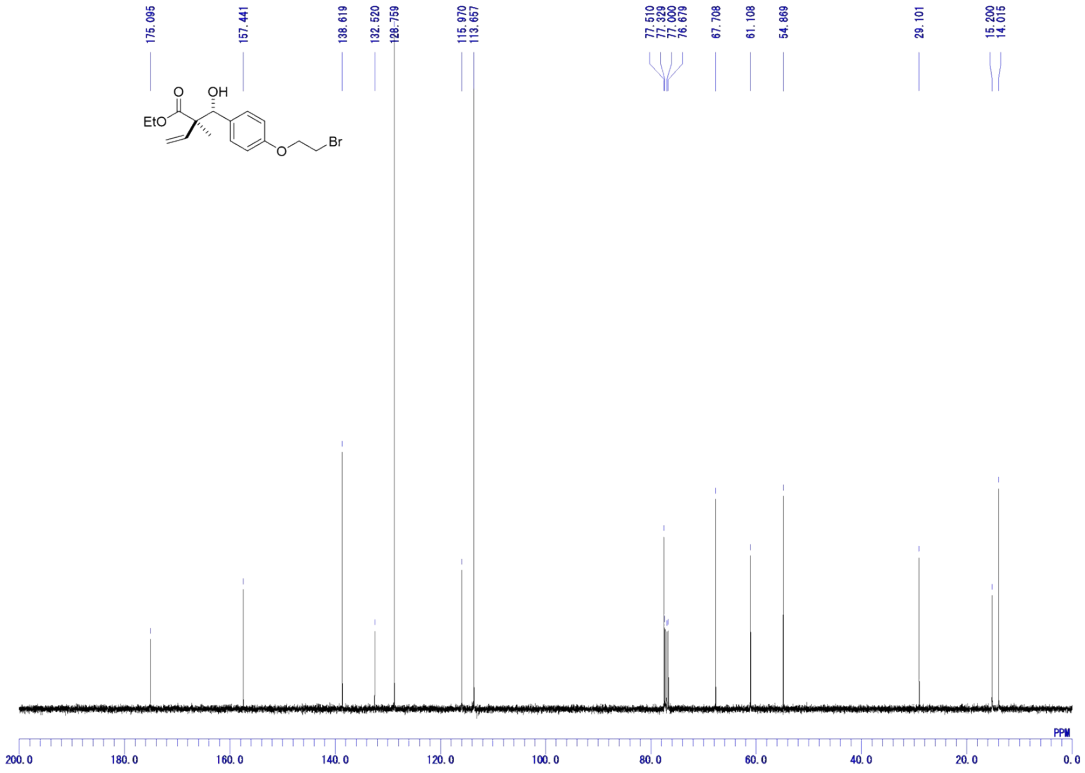
^{13}C NMR ($CDCl_3$, 100 MHz)



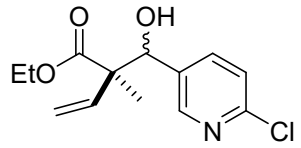
^{1}H NMR ($CDCl_3$, 400 MHz)



^{13}C NMR ($CDCl_3$, 100 MHz)



Ethyl 2-((6-chloropyridin-3-yl)(hydroxy)methyl)-2-methylbut-3-enoate (3an)



Major isomer (syn): Pale yellow oil.

R_f = 0.28 (hexane/EtOAc = 8:2).

IR (neat) 3434 cm^{-1} (OH), 1716 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.15 (3H, s), 1.27 (3H, t, J = 7.1 Hz), 3.43 (1H, d, J = 3.1 Hz), 4.20 (2H, q, J = 7.2 Hz), 5.03 (1H, d, J = 2.9 Hz), 5.09 (1H, d, J = 17.6 Hz), 5.34 (1H, d, J = 10.6 Hz), 6.17 (1H, dd, J = 17.6, 10.9 Hz), 7.28 (2H, s), 7.63 (1H, dd, J = 8.2, 2.4 Hz), 8.28 (1H, d, J = 2.4 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 13.9, 16.7, 54.1, 61.6, 75.4, 117.9, 123.3, 133.9, 135.9, 138.4, 148.9, 150.7, 174.9.

HRMS (CI) m/z: calcd. for $C_{13}H_{17}ClNO_3$ 270.0891 ($[M+H]^+$), found 270.0891.

Minor isomer (anti): Pale yellow oil.

Isolated as mixture of diastereomers

R_f = 0.25 (hexane/EtOAc = 8:2).

IR (neat) 3334 cm^{-1} (OH), 1717 cm^{-1} (C=O).

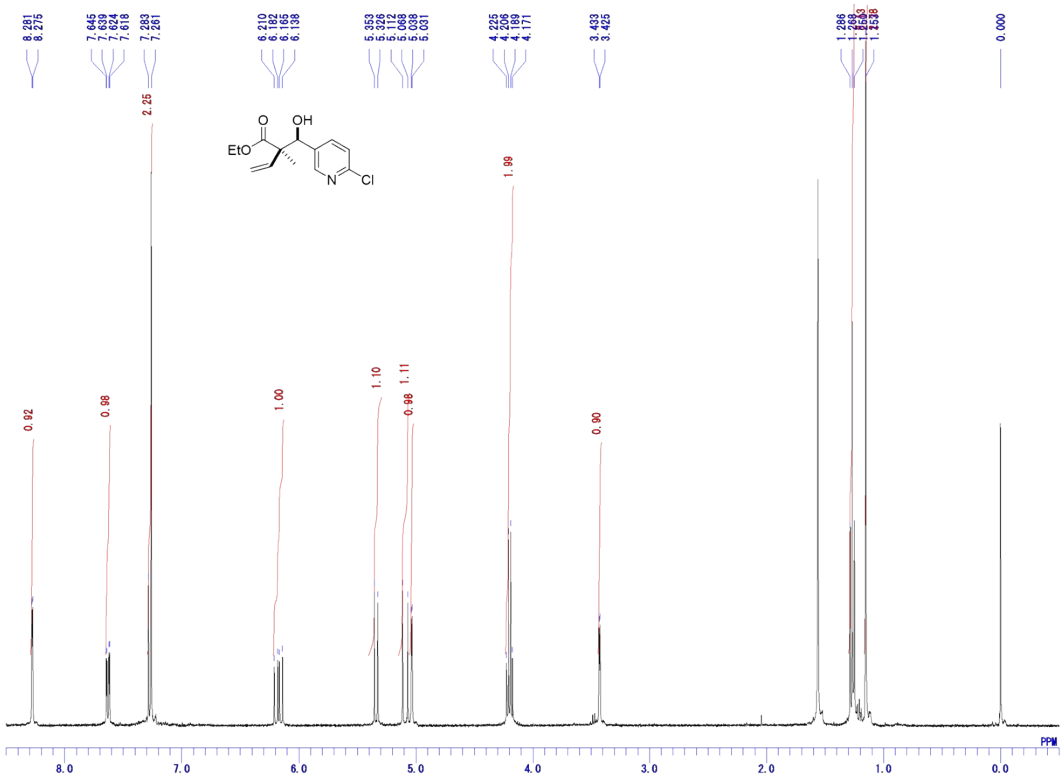
^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.15 (3H, s, major), 1.20 (3H, s, minor)*, 1.25-1.30 (3H, m, major+minor)*, 3.35 (1H, d, J = 4.8 Hz, minor)*, 3.49 (1H, d, J = 3.1 Hz, major), 4.17-4.25 (2H, m, major+minor)*, 5.02-5.06 (1H, m, major+minor)*, 5.11 (1H, d, J = 4.3 Hz, major+minor)*, 5.23 (1H, d, J = 10.6 Hz, minor) *, 5.34 (1H, d, J = 10.9 Hz, major), 5.84 (1H, dd, J = 17.5, 10.7 Hz, minor)*, 6.18 (1H, dd, J = 17.6, 10.9 Hz, major), 7.29 (2H, s, major+minor)*, 7.63 (1H, dd, J = 8.2, 2.4 Hz, major+minor)*, 8.27 (1H, d, J = 2.4 Hz, major+minor)*.

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 14.0*, 14.5*, 16.7, 54.1, 54.7*, 61.6, 61.6*, 75.0*, 75.4, 117.4*, 118.1, 123.2*, 123.3, 133.9, 135.9, 137.5*, 138.1*, 138.4, 148.9*, 149.0, 150.6*, 174.9*, 175.0.

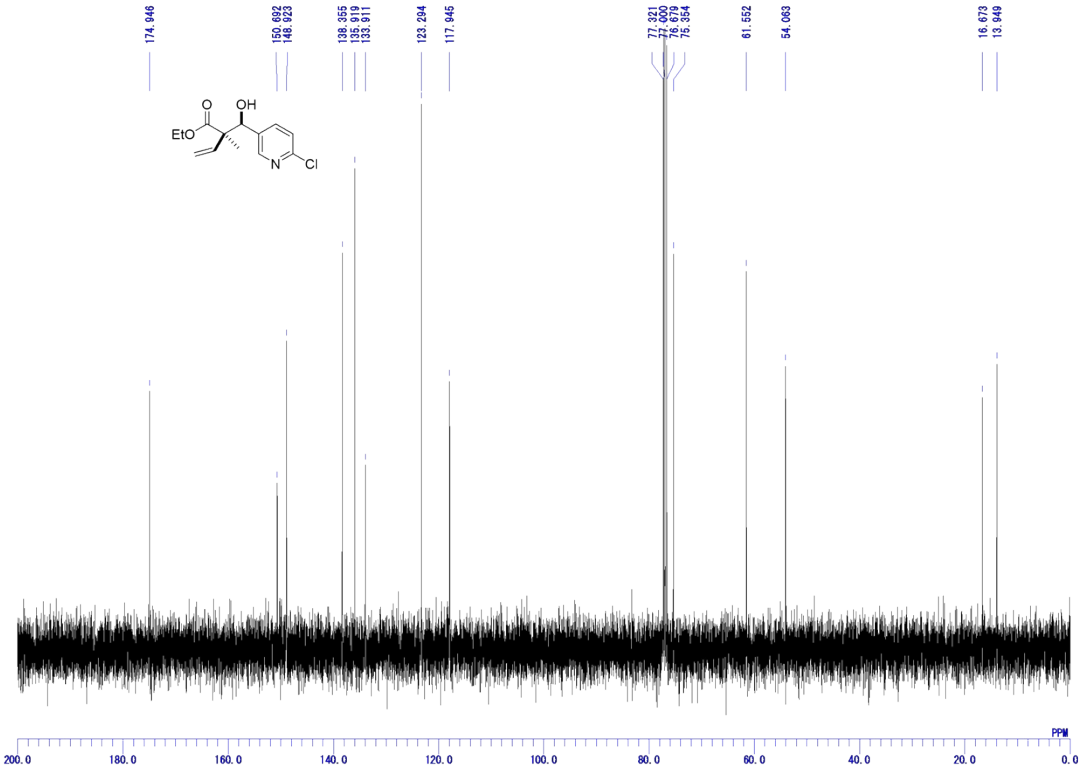
* Mark corresponds to minor isomer.

HRMS (CI) m/z: calcd. for $C_{13}H_{17}ClNO_3$ 270.0891 ($[M+H]^+$), found 270.0892.

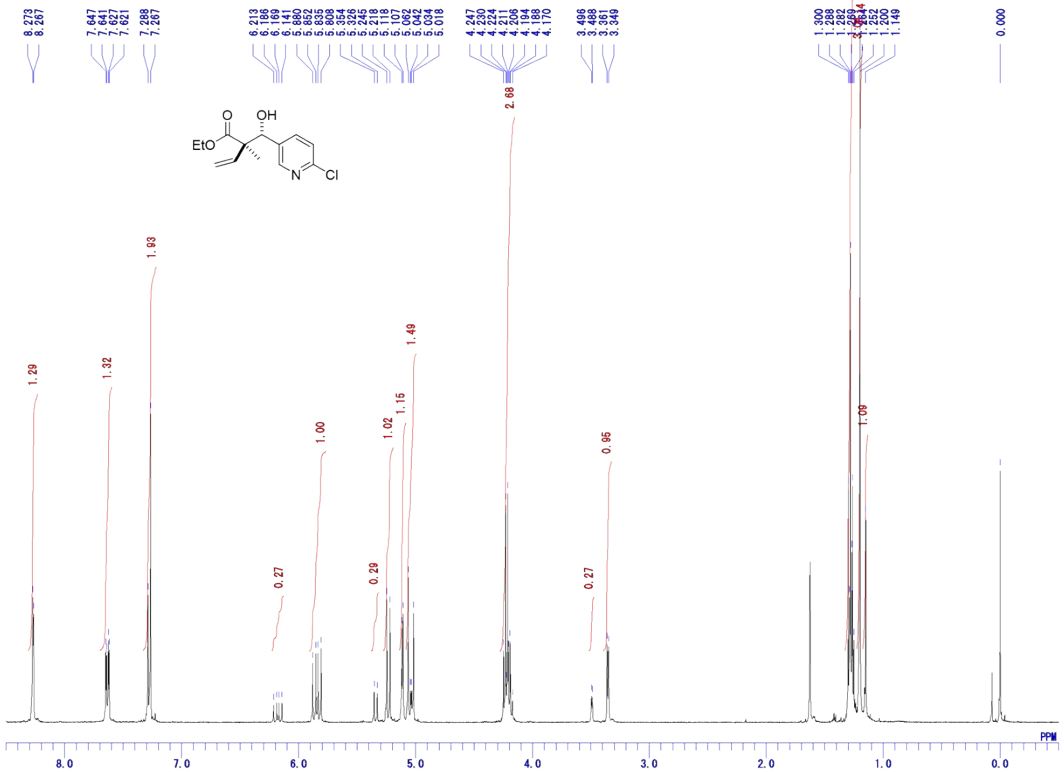
^{1}H NMR ($CDCl_3$, 400 MHz)



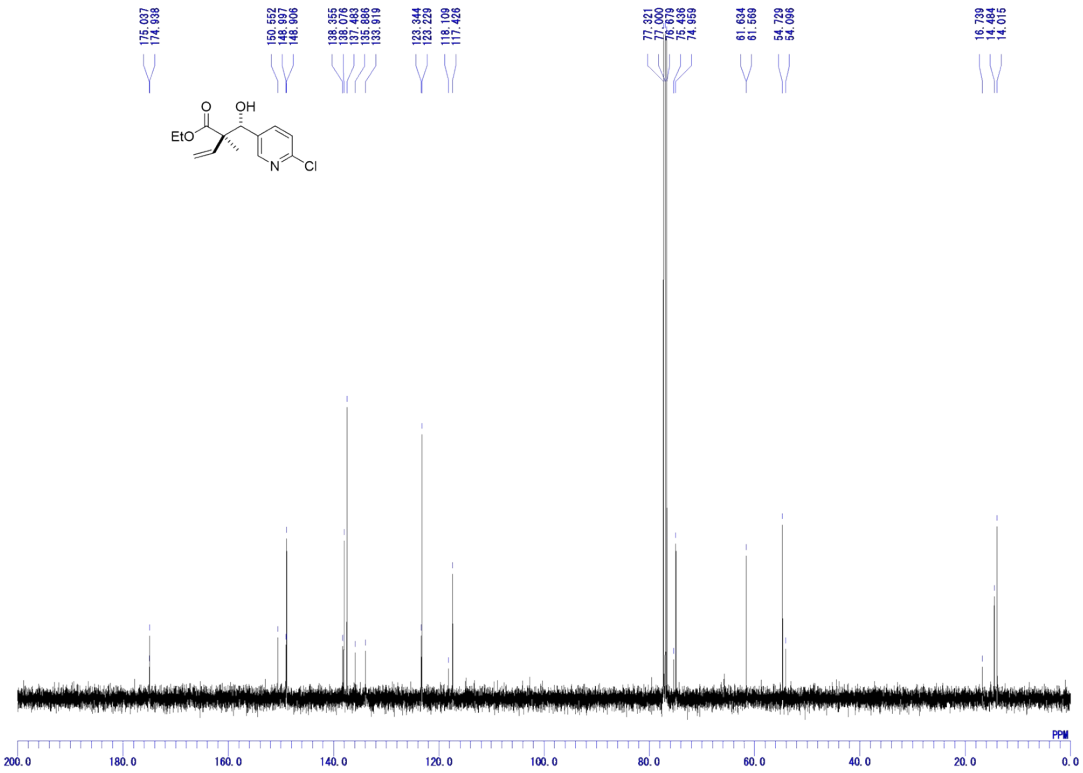
^{13}C NMR ($CDCl_3$, 100 MHz)



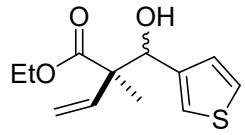
^{1}H NMR ($CDCl_3$, 400 MHz)



^{13}C NMR ($CDCl_3$, 100 MHz)



Ethyl 2-(hydroxy(thiophen-3-yl)methyl)-2-methylbut-3-enoate (3ao)



<u>Major isomer</u> (syn): Colorless oil.

R_f = 0.40 (hexane/EtOAc = 8:2).

IR (neat) 3485 cm^{-1} (OH), 1716 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.20 (3H, s), 1.26 (3H, t, J = 7.1 Hz), 3.07 (1H, s), 4.18 (2H, q, J = 7.2 Hz), 5.11 (1H, s), 5.15 (1H, d, J = 17.6 Hz), 5.30 (1H, d, J = 10.9 Hz), 6.22 (1H, dd, J = 17.6, 10.6 Hz), 7.02 (1H, dt, J = 5.0, 0.5 Hz), 7.17 (1H, dt, J = 3.0, 0.7 Hz), 7.23 (1H, dd, J = 5.0, 3.0 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 13.6, 15.9, 54.0, 60.7, 74.3, 116.1, 122.2, 124.3, 126.7, 137.5, 140.9, 174.7.

HRMS (EI) m/z: calcd. for $C_{12}H_{16}O_3S$ 240.0820 ($[M]^+$), found 240.0818.

<u>Minor isomer</u> (anti): Colorless oil.

Isolated as mixture of diastereomers

R_f = 0.33 (hexane/EtOAc = 8:2).

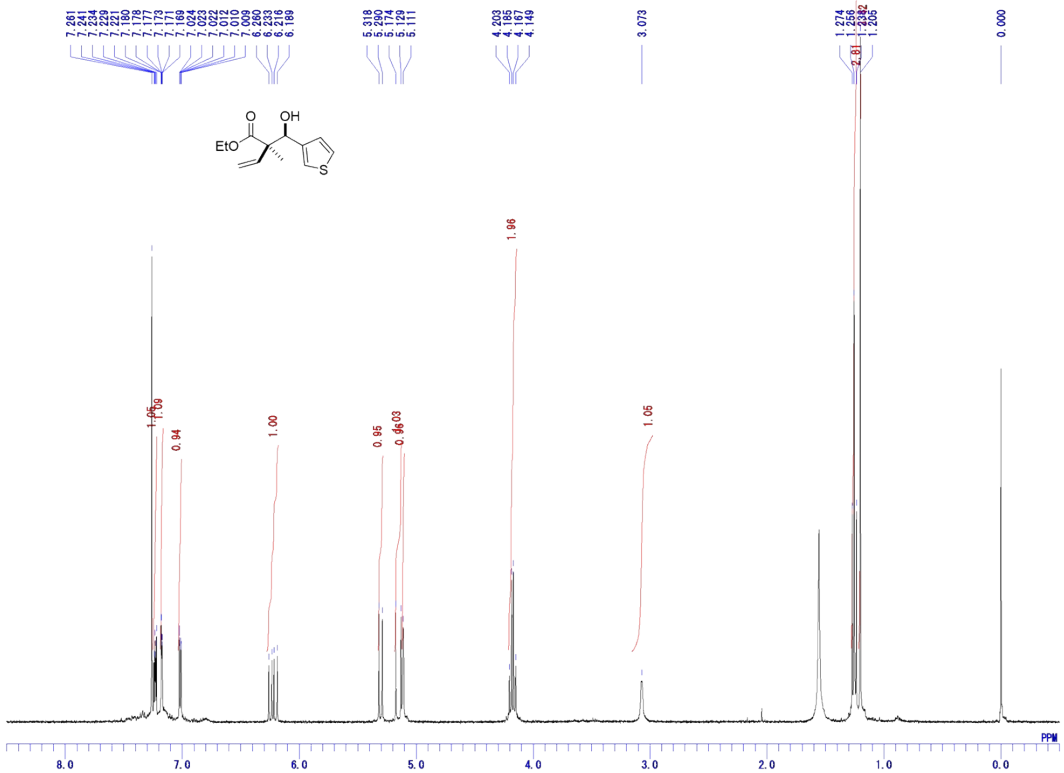
IR (neat) 3482 cm^{-1} (OH), 1709 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.25-1.29 (6H, m), 3.08 (1H, d, J = 5.8 Hz), 4.20 (2H, q, J = 7.1 Hz), 5.08-5.12 (2H, m), 5.21 (1H, d, J = 10.7, 0.6 Hz), 5.95 (1H, dd, J = 17.5, 10.7 Hz), 7.00 (1H, dd, J = 5.1, 1.2 Hz), 7.15-7.16 (1H, m), 7.23 (1H, dd, J = 5.1, 3.1 Hz).

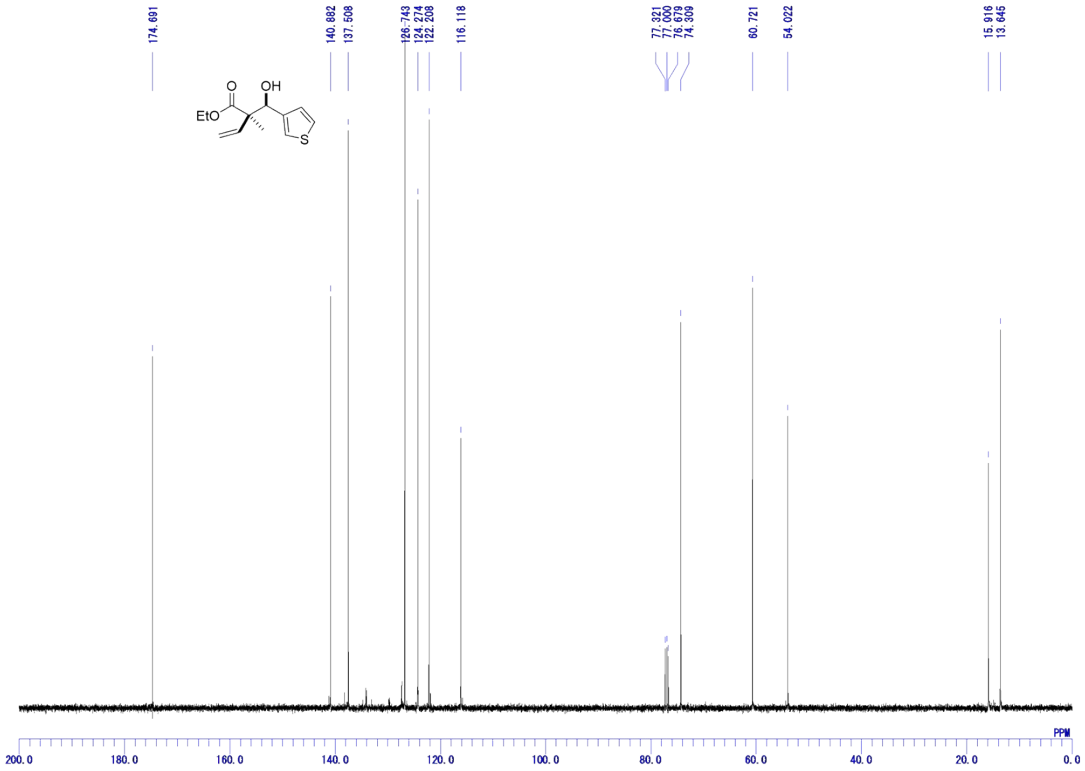
^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 14.0, 15.8, 54.6, 61.2, 74.9, 116.2, 122.3, 124.7, 126.9, 138.5, 141.3, 175.1.

HRMS (CI) m/z: calcd. for $C_{12}H_{16}O_3S$ 240.0820 ($[M]^+$), found 240.0819.

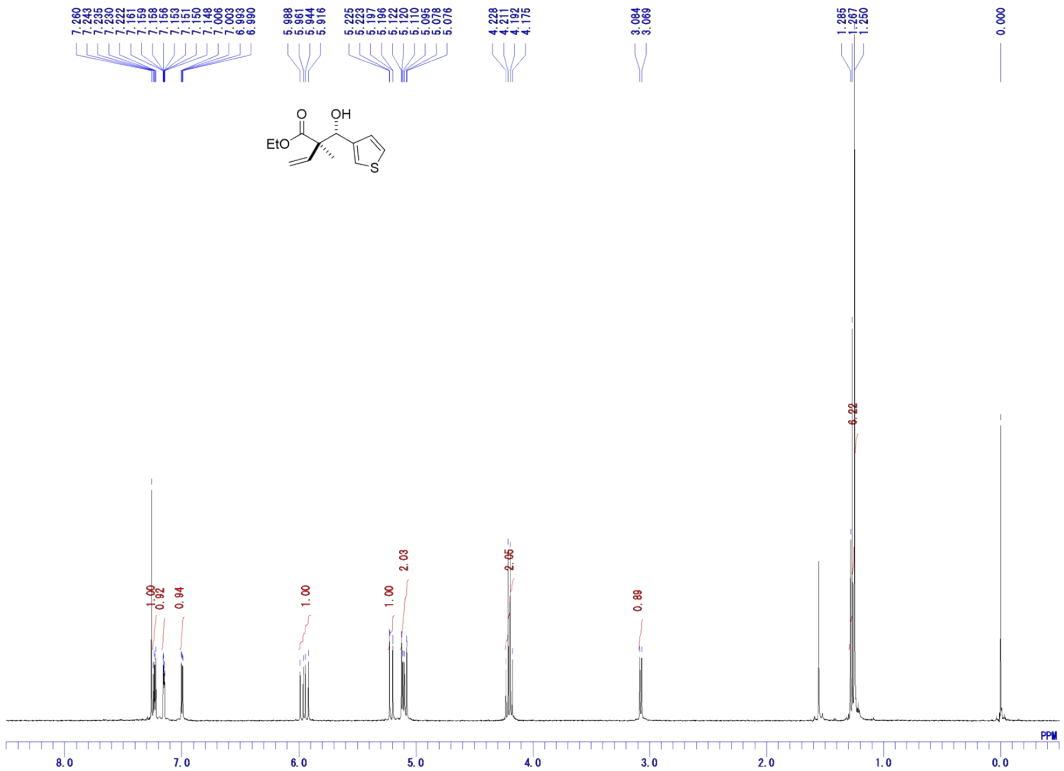
^{1}H NMR ($CDCl_3$, 400 MHz)



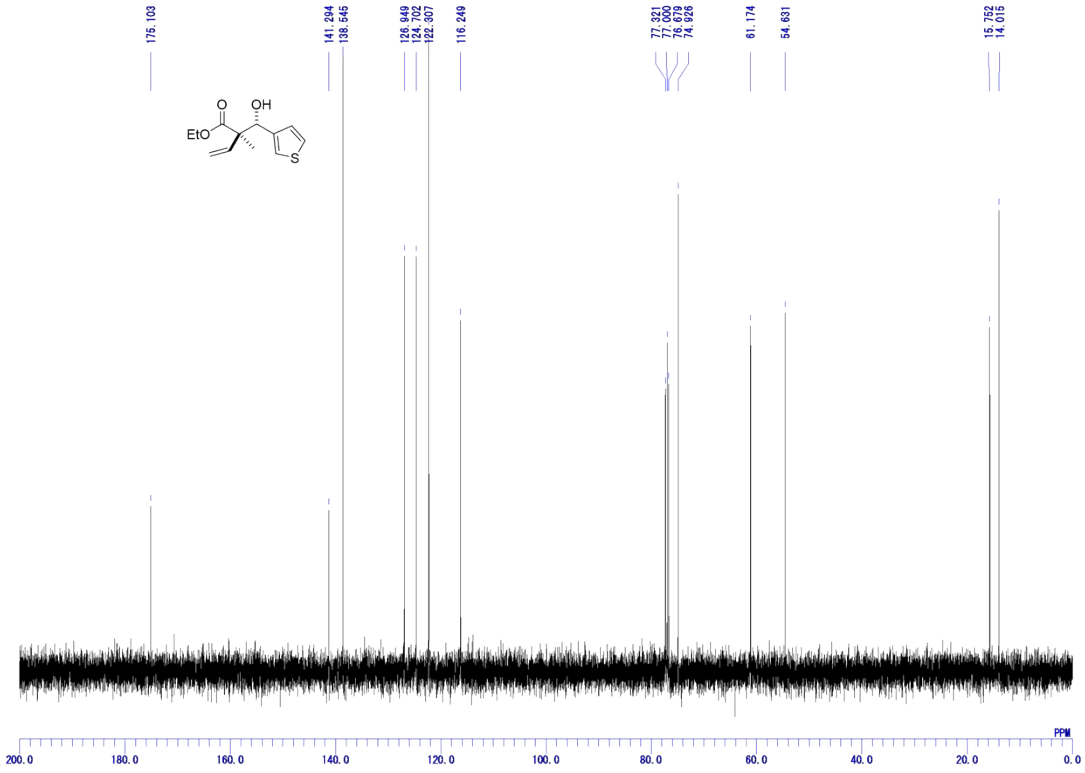
^{13}C NMR ($CDCl_3$, 100 MHz)



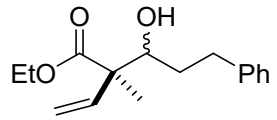
^{1}H NMR ($CDCl_3$, 400 MHz)



^{13}C NMR ($CDCl_3$, 100 MHz)



Ethyl 3-hydroxy-2-methyl-5-phenyl-2-vinylpentanoate (3ap)



<u>Major isomer</u> (syn): Colorless oil.

R_f = 0.48 (hexane/EtOAc = 8:2).

IR (neat) 3509 cm^{-1} (OH), 1715 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.23 (3H, t, J = 7.1 Hz), 1.26 (3H, s), 1.64-1.69 (2H, m), 2.55 (1H, d, J = 4.6 Hz), 2.64 (1H, m), 2.89-2.96 (1H, m), 3.80 (1H, m), 4.14 (2H, q, J = 7.1 Hz), 5.18 (1H, dd, J = 17.5, 0.8 Hz), 5.27 (1H, dd, J = 10.9, 0.7 Hz), 6.10 (1H, dd, J = 17.5, 10.7 Hz), 7.16-7.30 (5H, m)

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 14.0, 16.2, 32.7, 33.5, 53.8, 61.0, 74.9, 116.3, 125.7, 128.3, 128.4, 138.1, 142.0, 175.3

HRMS (CI) m/z: calcd. for $C_{16}H_{23}O_3$ 263.1642 ($[M+H]^+$), found 263.1644.

<u>Minor isomer</u> (anti): Colorless oil.

R_f = 0.45 (hexane/EtOAc = 8:2).

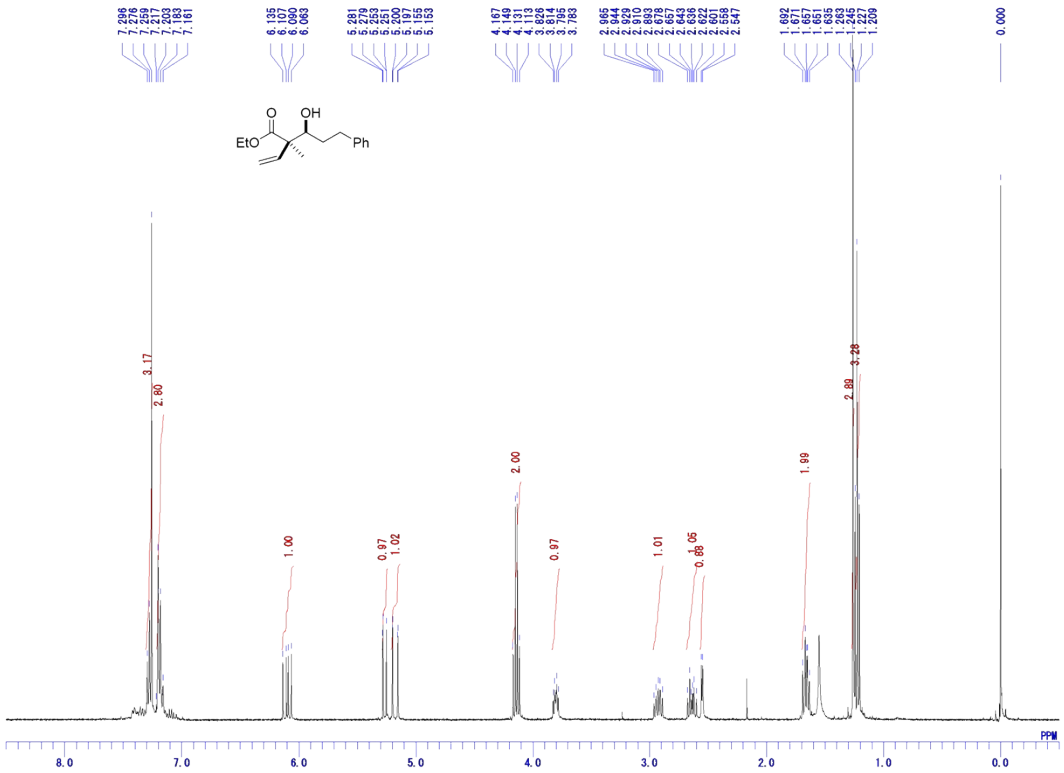
IR (neat) 3506 cm^{-1} (OH), 1716 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.25 (3H, t, J = 7.1 Hz), 1.29 (3H, s), 1.52-1.62 (1H, m), 1.73 (1H, m), 2.50 (1H, d, J = 6.8 Hz), 2.63 (1H, m), 2.97-2.90 (1H, m), 3.85-3.89 (1H, m), 4.16 (2H, q, J = 7.1 Hz), 5.14 (1H, d, J = 17.4 Hz), 5.20 (1H, d, J = 10.9 Hz), 5.88 (1H, dd, J = 17.5, 10.7 Hz), 7.16-7.30 (5H, m).

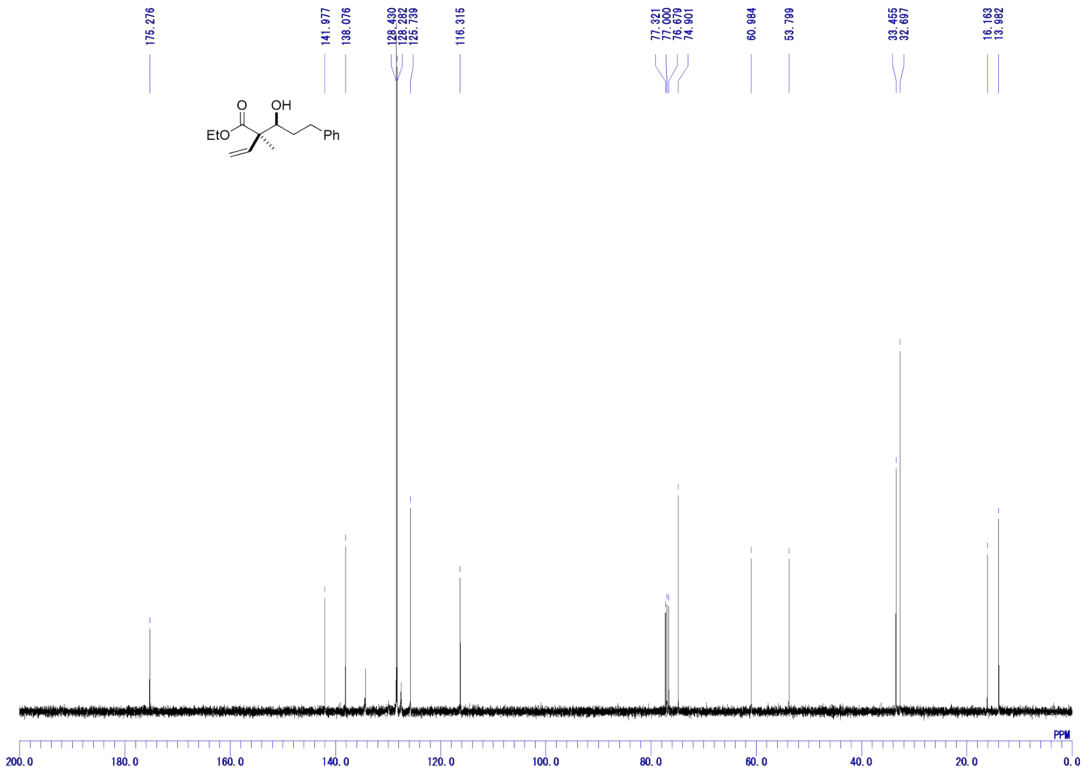
^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 14.0, 15.0, 32.8, 33.3, 54.1, 61.0, 75.0, 116.0, 125.7, 128.3, 128.4, 138.5, 142.0, 175.4.

HRMS (CI) m/z: calcd. for $C_{16}H_{23}O_3$ 263.1642 ($[M+H]^+$), found 263.1643.

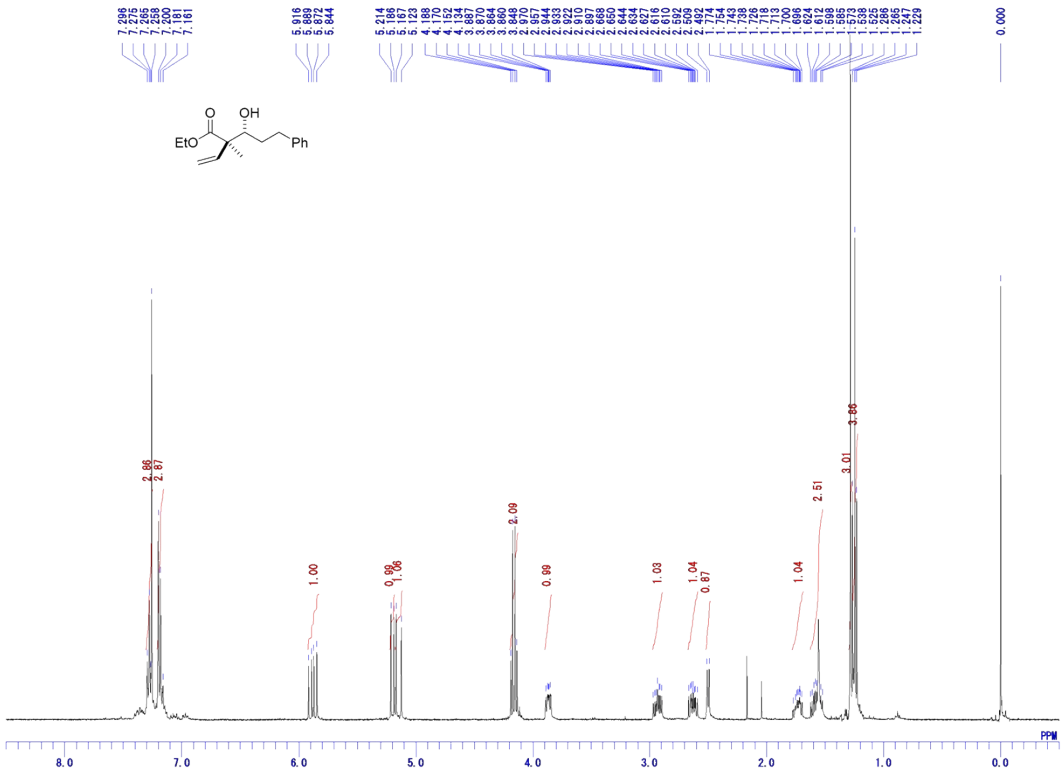
^{1}H NMR ($CDCl_3$, 400 MHz)



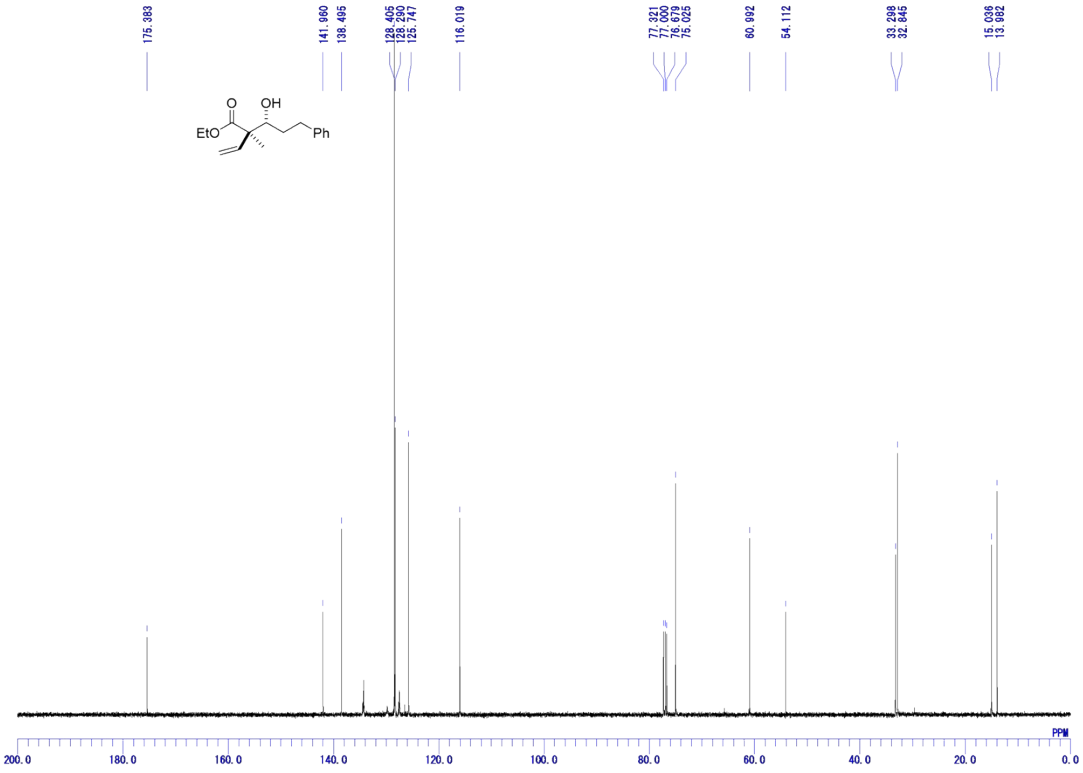
^{13}C NMR ($CDCl_3$, 100 MHz)



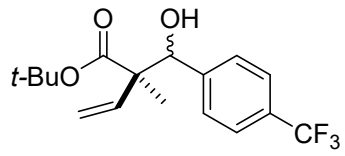
^{1}H NMR ($CDCl_3$, 400 MHz)



^{13}C NMR ($CDCl_3$, 100 MHz)



***tert*-Butyl 2-(hydroxy(4-(trifluoromethyl)phenyl)methyl)-2-methylbut-3-enoate (3bi)**



Major isomer (syn): Colorless oil.

Mp: 103-105°C

R_f = 0.53 (hexane/EtOAc = 8:2).

IR (neat) 3446 cm^{-1} (OH), 1687 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.11 (3H, s), 1.46 (9H, s), 3.53 (2H, d, J = 2.9 Hz), 5.01 (1H, d, J = 2.9 Hz), 5.08 (1H, dd, J = 17.6, 0.7 Hz), 5.29 (1H, dd, J = 10.9, 0.7 Hz), 6.15 (1H, dd, J = 17.6, 10.9 Hz), 7.43 (2H, d, J = 8.2 Hz), 7.55 (2H, d, J = 8.2 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 15.4, 27.9, 55.1, 77.6 (d), 82.1, 117.2, 124.1 (q, J_{CF} = 270.4 Hz), 124.4 (d, J_{CF} = 4.1 Hz), 128.3, 130.0, 136.9, 143.4, 174.5.

^{19}F{^{1}H} NMR ($CDCl_3$, 376 MHz) δ -62.41 (3F, s).

HRMS (CI) m/z: calcd. for $C_{17}H_{22}F_3O_3$ 331.1516 ($[M+H]^+$), found 331.1514.

Minor isomer (anti): Colorless oil.

Mp: 108-110°C

R_f = 0.50 (hexane/EtOAc = 8:2).

IR (neat) 3450 cm^{-1} (OH), 1689 cm^{-1} (C=O).

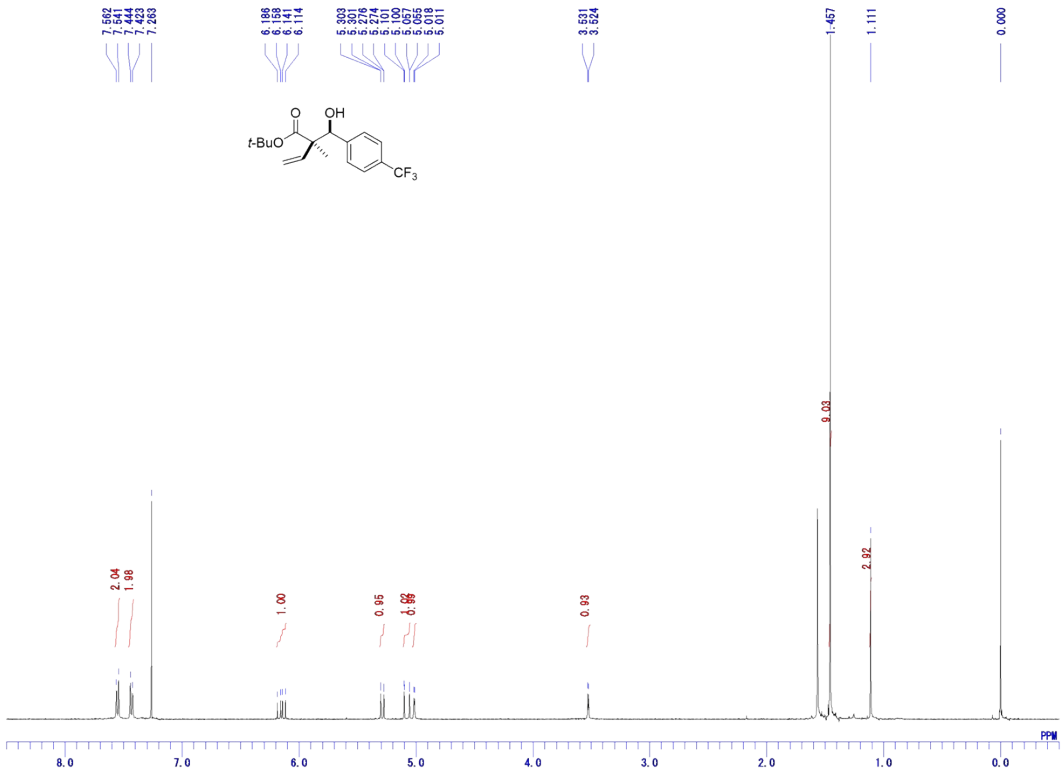
^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.14 (3H, s), 1.47 (9H, s), 3.41 (2H, d, J = 5.1 Hz), 5.02-5.06 (1H, m), 5.18 (1H, d, J = 10.6 Hz), 5.87 (1H, dd, J = 17.5, 10.7 Hz), 7.41 (2H, d, J = 8.2 Hz), 7.55 (2H, d, J = 8.2 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 17.1, 27.9, 54.5, 77.6 (d), 82.0, 116.3, 122.8, 124.4 (q, J_{CF} = 3.8 Hz), 128.1, 129.7 (d, J_{CF} = 32.0 Hz), 138.7, 143.7, 174.4.

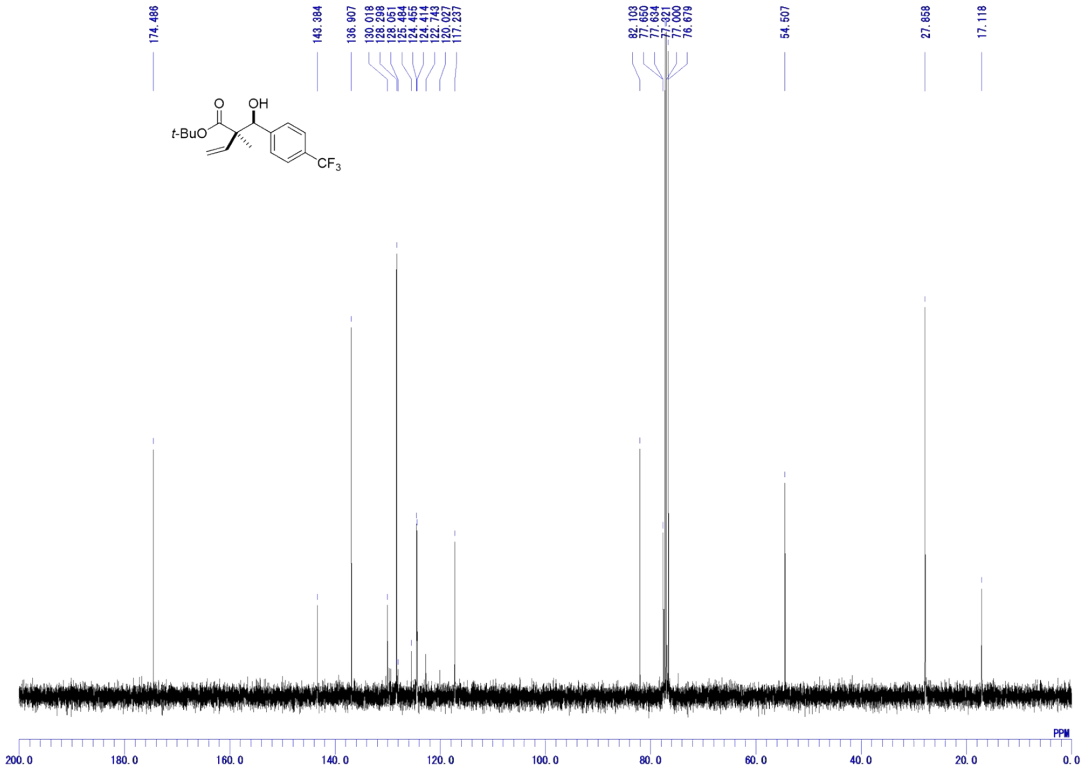
^{19}F{^{1}H} NMR ($CDCl_3$, 376 MHz) δ -62.44 (3F, s).

HRMS (CI) m/z: calcd. for $C_{17}H_{22}F_3O_3$ 331.1516 ($[M+H]^+$), found 331.1528.

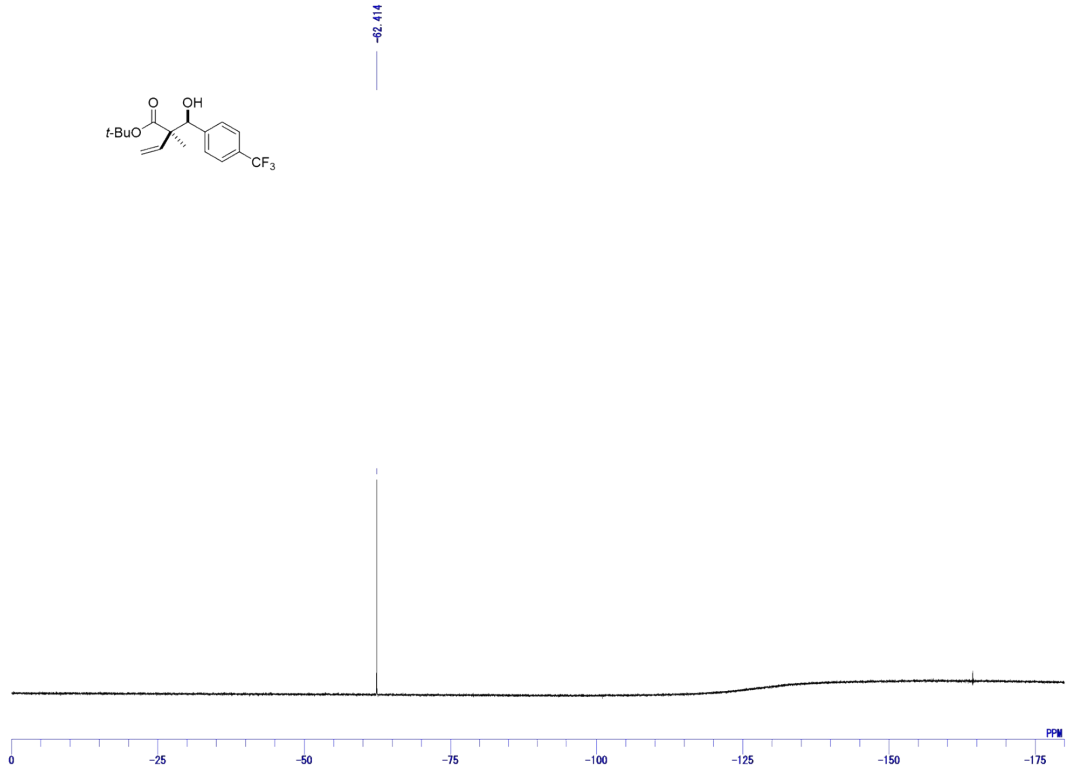
^{1}H NMR ($CDCl_3$, 400 MHz)



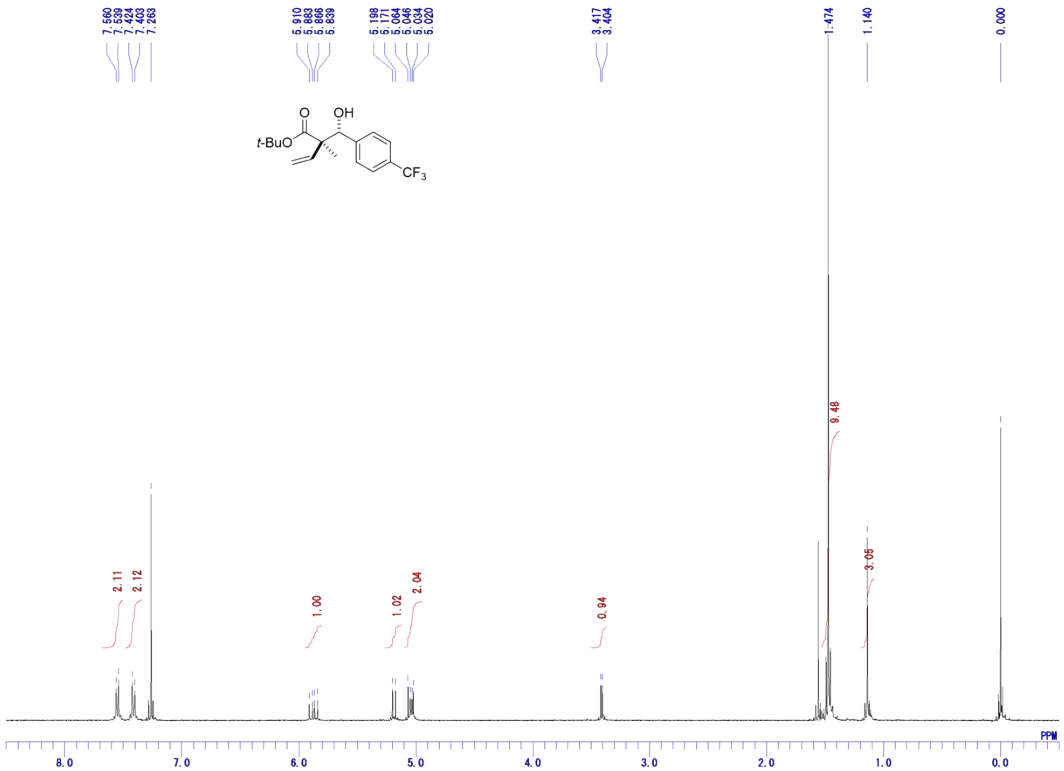
^{13}C NMR ($CDCl_3$, 100 MHz)



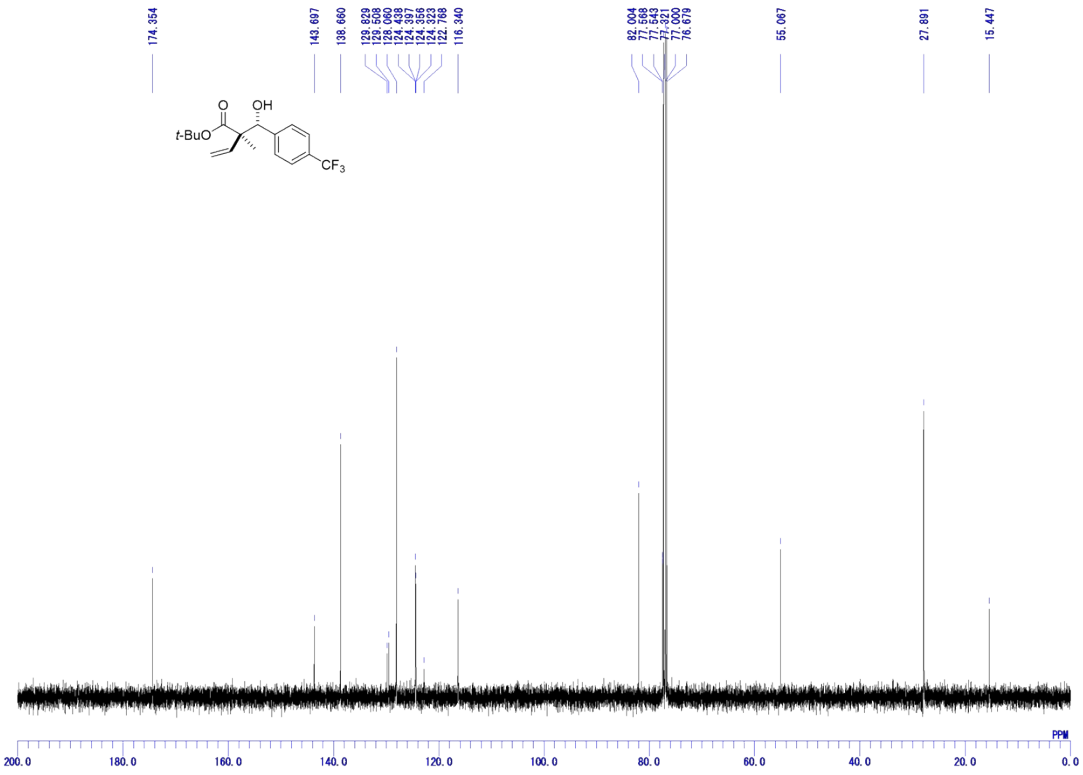
$^{19}F\{^{1}H\}$ NMR ($CDCl_3$, 376 MHz)



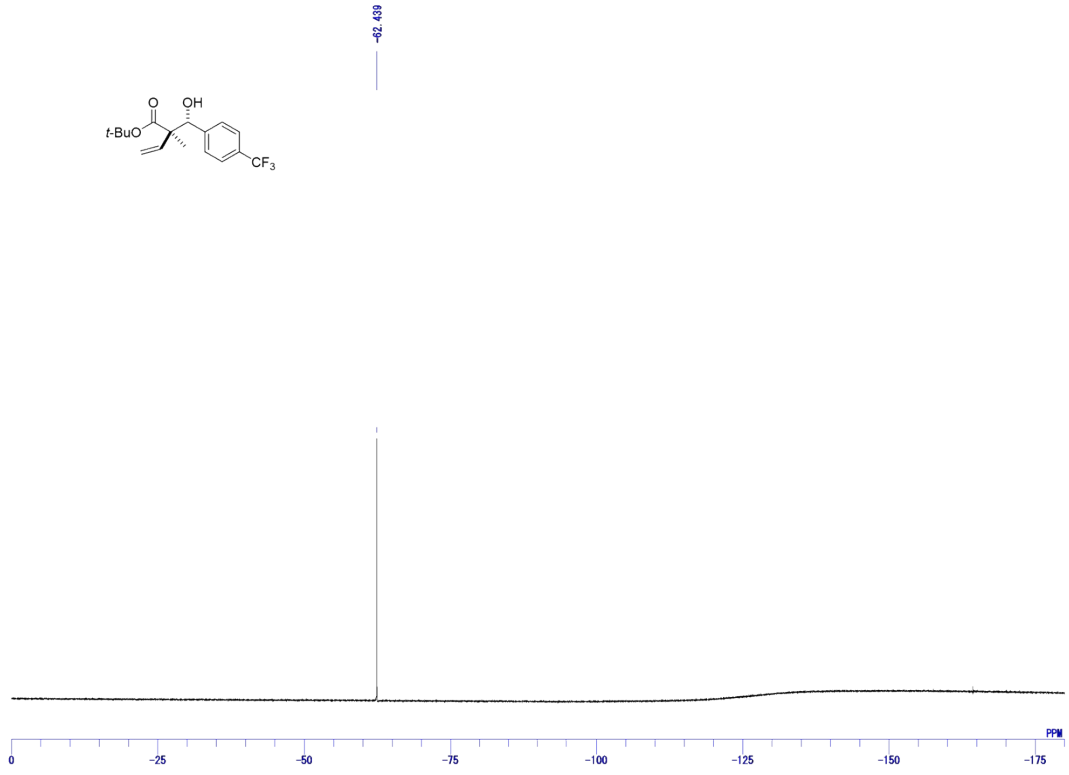
^{1}H NMR ($CDCl_3$, 400 MHz)



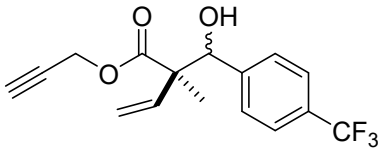
^{13}C NMR ($CDCl_3$, 100 MHz)



$^{19}F\{^{1}H\}$ NMR ($CDCl_3$, 376 MHz)



Prop-2-yn-1-yl 2-(hydroxy(4-(trifluoromethyl)phenyl)methyl)-2-methylbut-3-enoate (3ci)



Major isomer (syn): Colorless oil.

R_f = 0.35 (hexane/EtOAc = 8:2).

IR (neat) 3494 cm^{-1} (OH), 1726 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.19 (3H, s), 2.51 (1H, t, J = 2.4 Hz), 3.01 (1H, d, J = 3.1 Hz), 4.69-4.78 (2H, m), 5.11-5.15 (2H, m), 5.36 (1H, d, J = 10.9 Hz), 6.23 (1H, dd, J = 17.5, 10.7 Hz), 7.43 (2H, d, J = 8.5 Hz), 7.56 (2H, d, J = 8.2 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 16.3 (q), 52.7 (t), 54.5, 75.4, 77.0, 77.4, 118.1, 124.1 (d, J_{CF} = 272.0 Hz), 124.6 (d, J_{CF} = 4.1 Hz), 128.1, 130.1 (d, J_{CF} = 32.8 Hz), 136.1, 142.9, 174.1.

^{19}F{^{1}H} NMR ($CDCl_3$, 376 MHz) δ -62.46 (3F, s).

HRMS (CI) m/z: calcd. for $C_{16}H_{16}F_3O_3$ 313.1046 ($[M+H]^+$), found 313.1052.

Minor isomer (anti): Colorless oil.

R_f = 0.33 (hexane/EtOAc = 8:2).

IR (neat) 3485 cm^{-1} (OH), 1727 cm^{-1} (C=O).

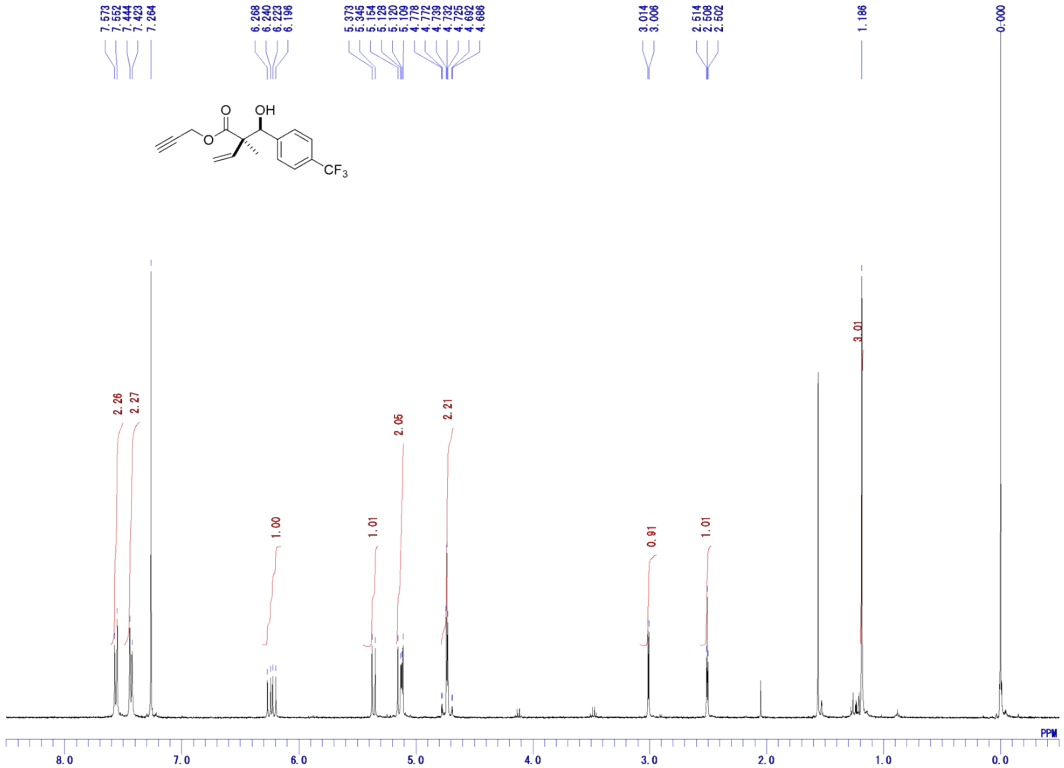
^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.24 (3H, s), 2.51 (1H, t, J = 2.4 Hz), 2.90 (1H, d, J = 4.8 Hz), 4.72-4.82 (2H, m), 5.07 (1H, d, J = 17.4 Hz), 5.19 (1H, d, J = 4.8 Hz), 5.23 (1H, d, J = 10.9 Hz), 5.88 (1H, dd, J = 17.5, 10.7 Hz), 7.42 (2H, d, J = 8.7 Hz), 7.56 (2H, d, J = 8.2 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 14.6 (q), 52.7 (t), 55.1, 75.3, 77.1 (d), 77.2, 117.3, 124.1 (d, J_{CF} = 272.0 Hz), 124.5, 128.0, 129.9 (d, J_{CF} = 32.8 Hz), 137.4, 143.1, 174.0.

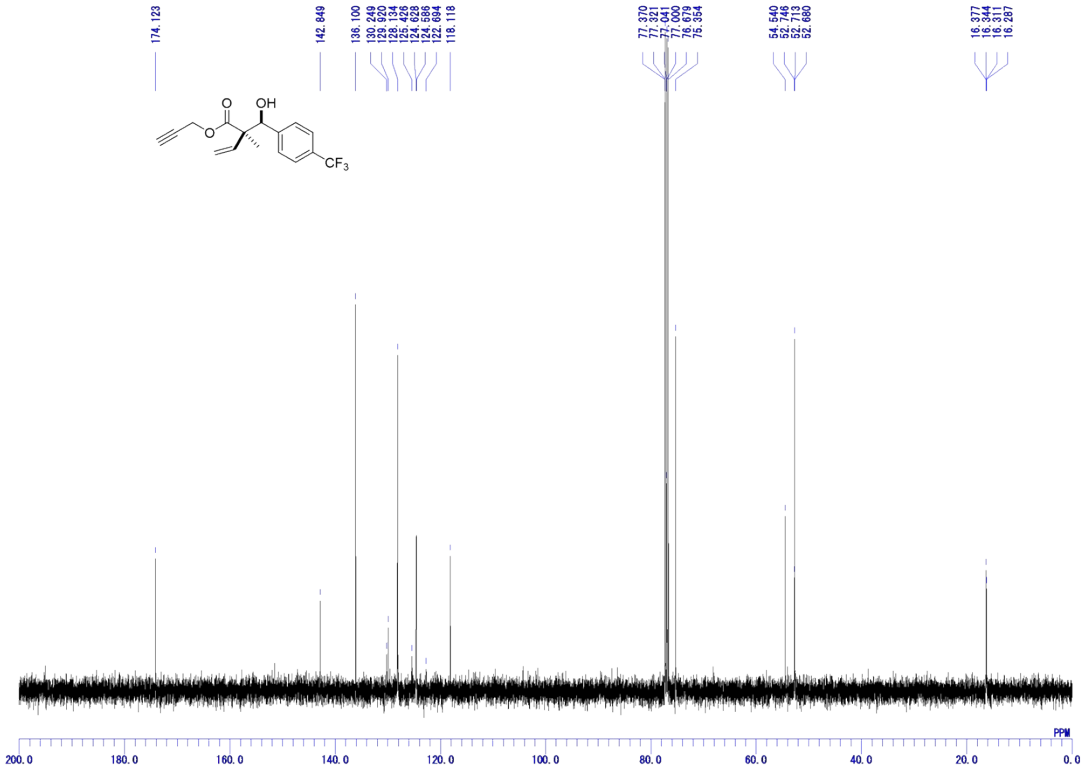
^{19}F{^{1}H} NMR ($CDCl_3$, 376 MHz) δ -62.49 (3F, s).

HRMS (CI) m/z: calcd. for $C_{16}H_{16}F_3O_3$ 313.1046 ($[M+H]^+$), found 313.1049.

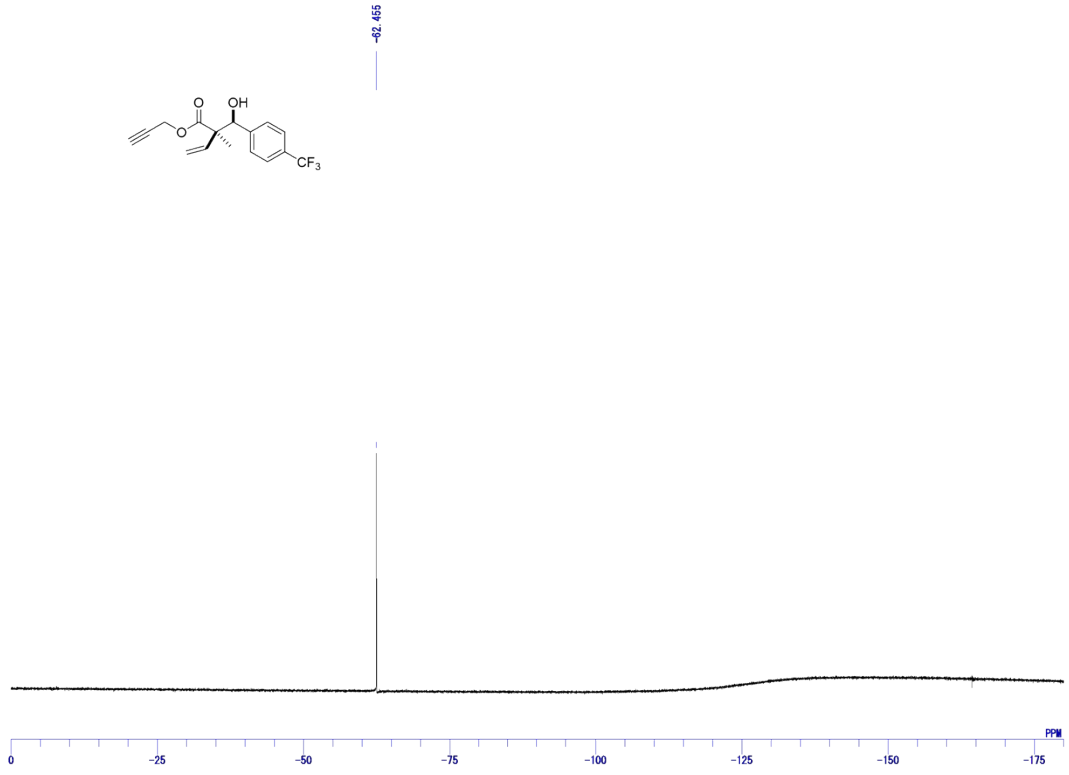
^{1}H NMR ($CDCl_3$, 400 MHz)



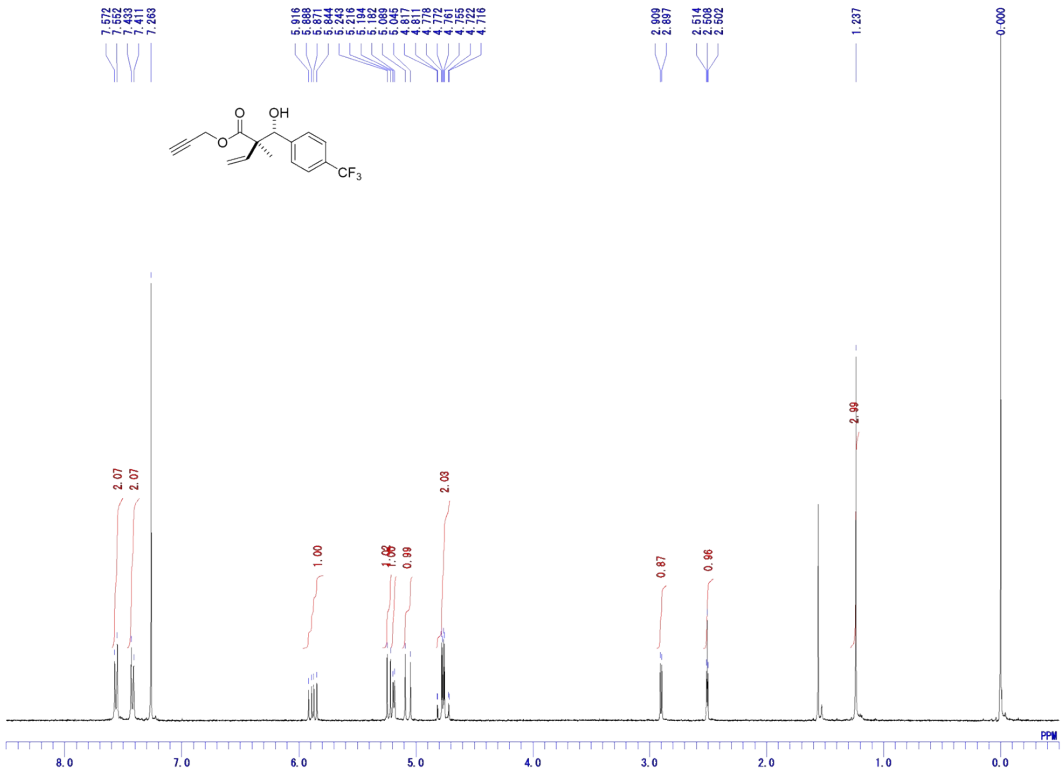
^{13}C NMR ($CDCl_3$, 100 MHz)



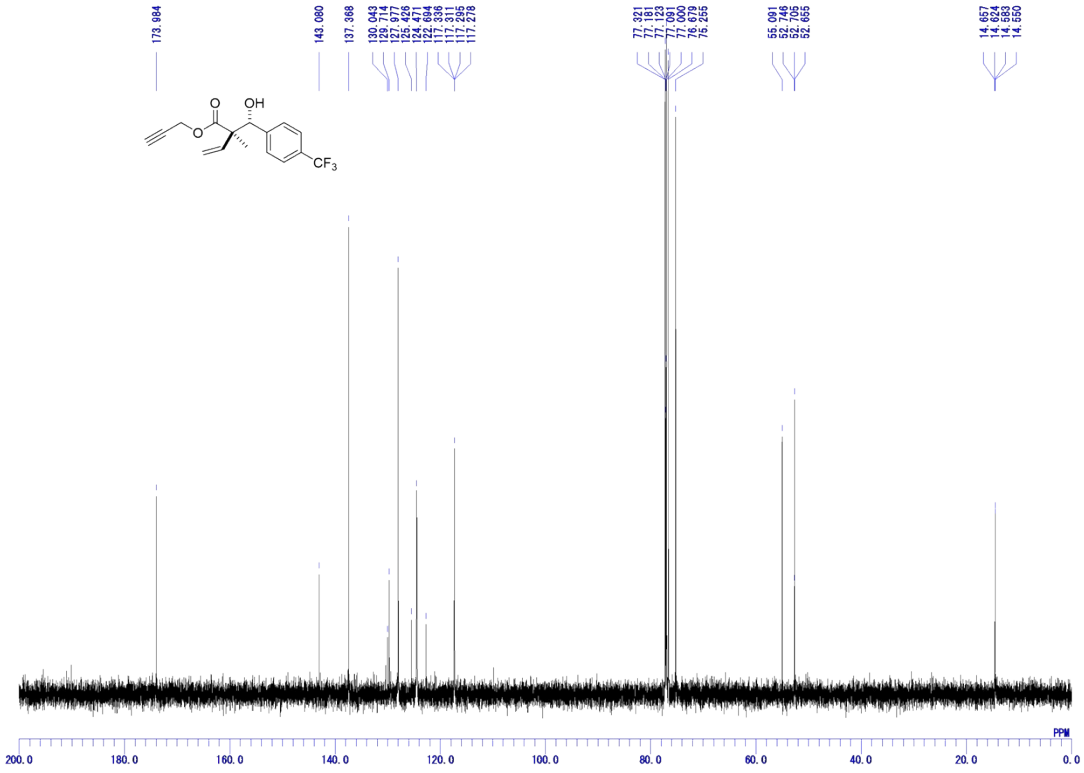
$^{19}F\{^{1}H\}$ NMR ($CDCl_3$, 376 MHz)



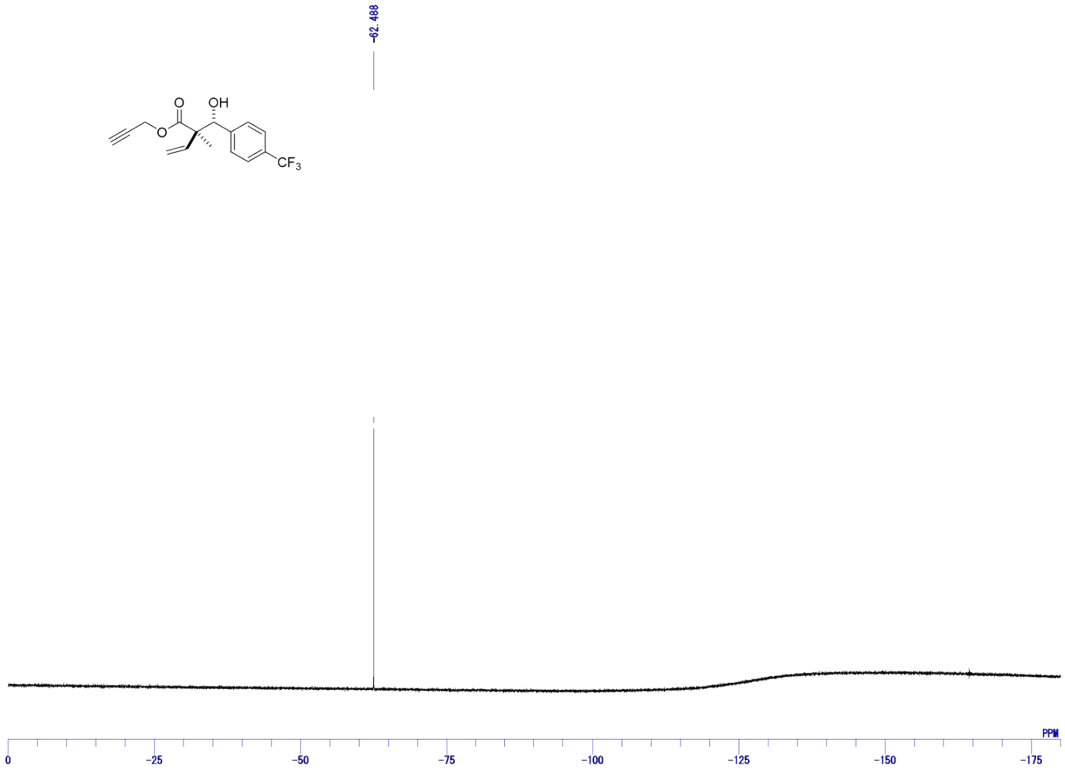
^{1}H NMR ($CDCl_3$, 400 MHz)



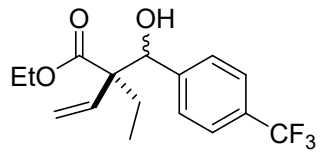
^{13}C NMR ($CDCl_3$, 100 MHz)



$^{19}F\{^{1}H\}$ NMR ($CDCl_3$, 376 MHz)



Ethyl 2-ethyl-2-(hydroxy(4-(trifluoromethyl)phenyl)methyl)but-3-enoate (3di)



Major isomer (syn): Colorless oil.

R_f = 0.50 (hexane/EtOAc = 8:2).

IR (neat) 3486 cm^{-1} (OH), 1717 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.90 (3H, t, J = 7.4 Hz), 1.29 (3H, t, J = 7.1 Hz), 1.67 (2H, q, J = 7.5 Hz), 3.43 (1H, d, J = 4.6 Hz), 4.25 (2H, dq, J = 7.1, 1.2 Hz), 4.96 (1H, dd, J = 18.0, 0.8 Hz), 5.08 (1H, d, J = 4.8 Hz), 5.32 (1H, dd, J = 11.1, 0.7 Hz), 6.00 (1H, dd, J = 18.1, 11.1 Hz), 7.40 (2H, d, J = 8.2 Hz), 7.55 (2H, d, J = 8.2 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 8.89, 14.1 (d), 25.5, 58.4, 61.3, 77.3, 117.6, 124.1 (q, J_{CF} = 272.0 Hz), 124.3 (q, J_{CF} = 4.1 Hz), 128.3, 129.8 (q, J_{CF} = 32.5 Hz), 134.2, 143.5, 175.1.

^{19}F{^{1}H} NMR ($CDCl_3$, 376 MHz) δ -62.47 (3F, s).

HRMS (CI) m/z: calcd. for $C_{16}H_{20}F_3O_3$ 317.1359 ($[M+H]^+$), found 317.1362.

Minor isomer (anti): Colorless oil.

R_f = 0.55 (hexane/EtOAc = 8:2).

IR (neat) 3479 cm^{-1} (OH), 1713 cm^{-1} (C=O).

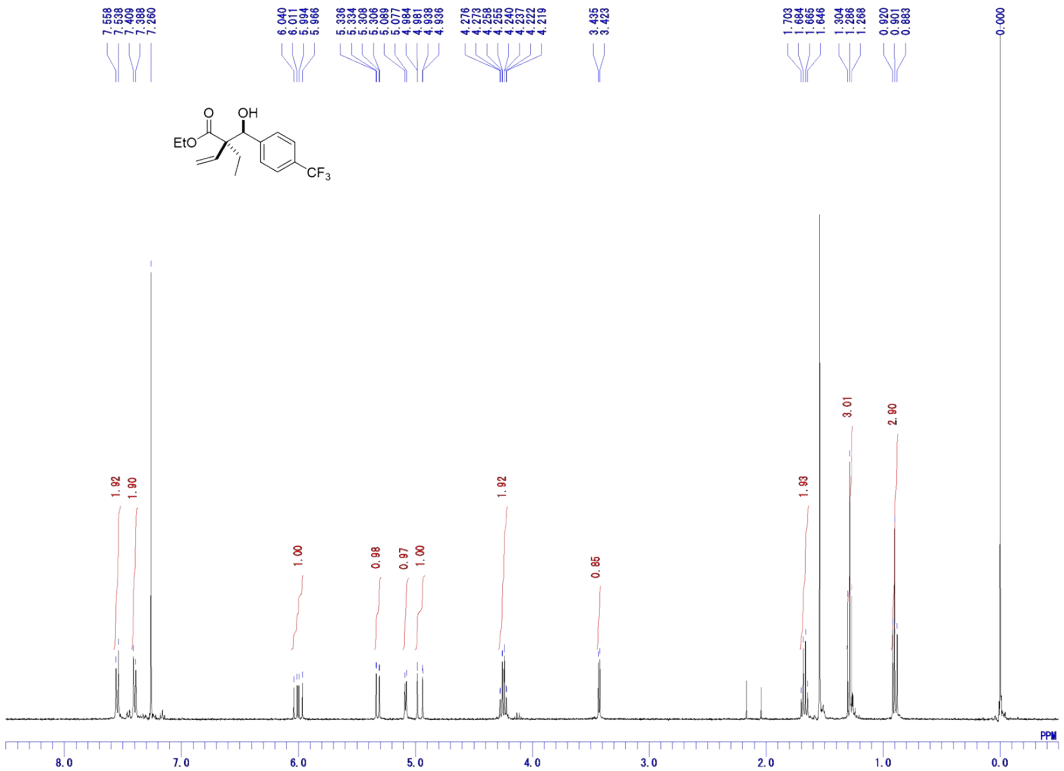
^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.91 (3H, t, J = 7.4 Hz), 1.23 (3H, t, J = 7.1 Hz), 1.76-1.97 (2H, m), 3.17 (1H, d, J = 6.0 Hz), 4.13-4.21 (2H, m), 4.99 (1H, d, J = 6.0 Hz), 5.18 (1H, dd, J = 17.9, 0.7 Hz), 5.40 (1H, dd, J = 11.1, 0.7 Hz), 5.82 (1H, dd, J = 17.9, 11.1 Hz), 7.38 (2H, d, J = 8.5 Hz), 7.55 (2H, d, J = 8.0 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 9.26, 14.0 (t), 25.3, 58.9, 61.1, 77.6 (d), 117.7, 124.1 (q, J_{CF} = 272.0 Hz), 124.5 (q, J_{CF} = 4.1 Hz), 127.9, 129.8 (q, J_{CF} = 32.2 Hz), 135.2, 144.1, 173.9.

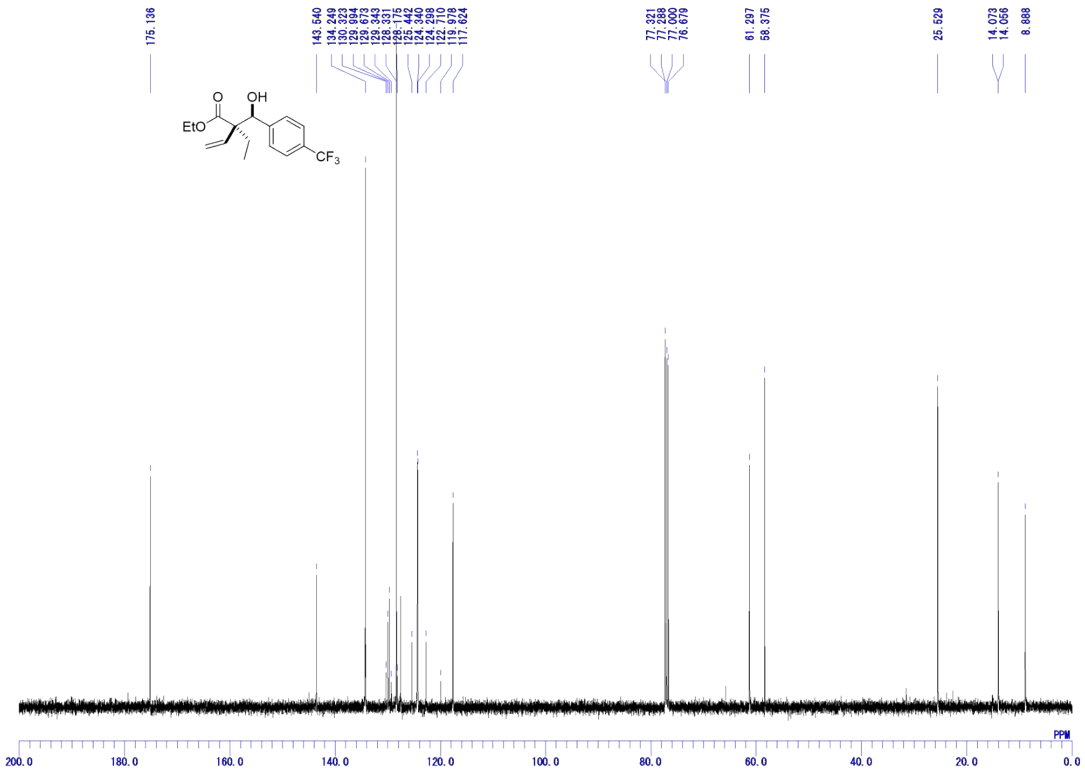
^{19}F{^{1}H} NMR ($CDCl_3$, 376 MHz) δ -62.46 (3F, s).

HRMS (CI) m/z: calcd. for $C_{16}H_{20}F_3O_3$ 317.1359 ($[M+H]^+$), found 317.1360.

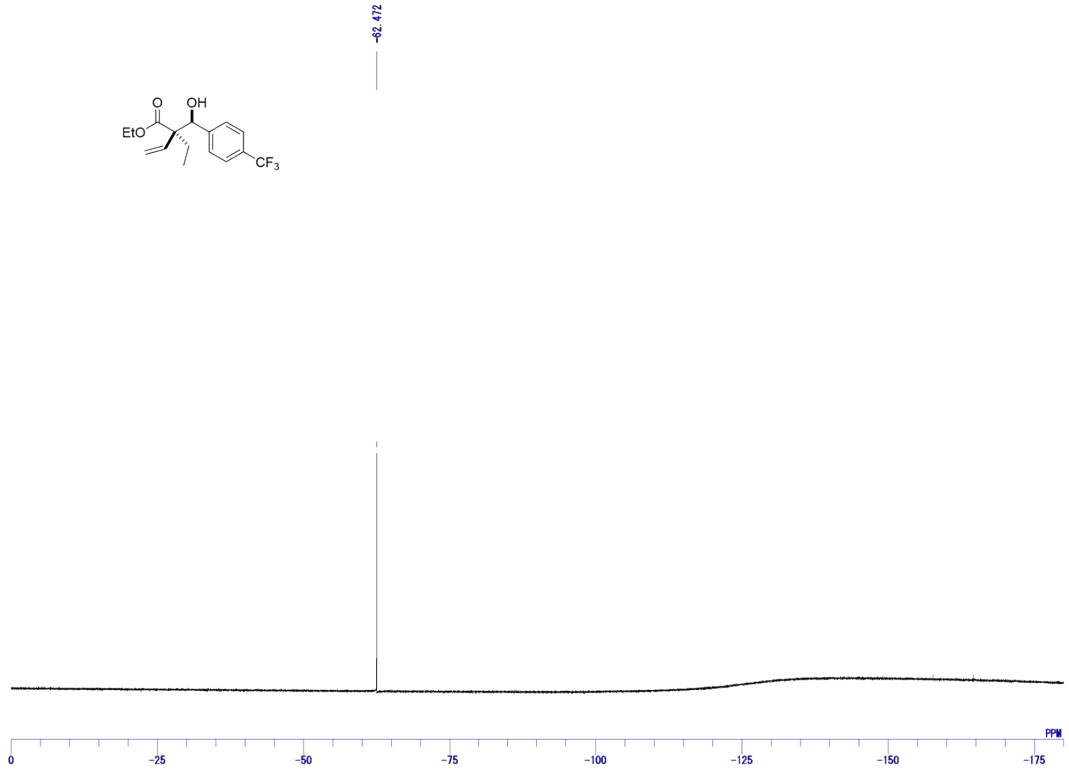
^{1}H NMR ($CDCl_3$, 400 MHz)



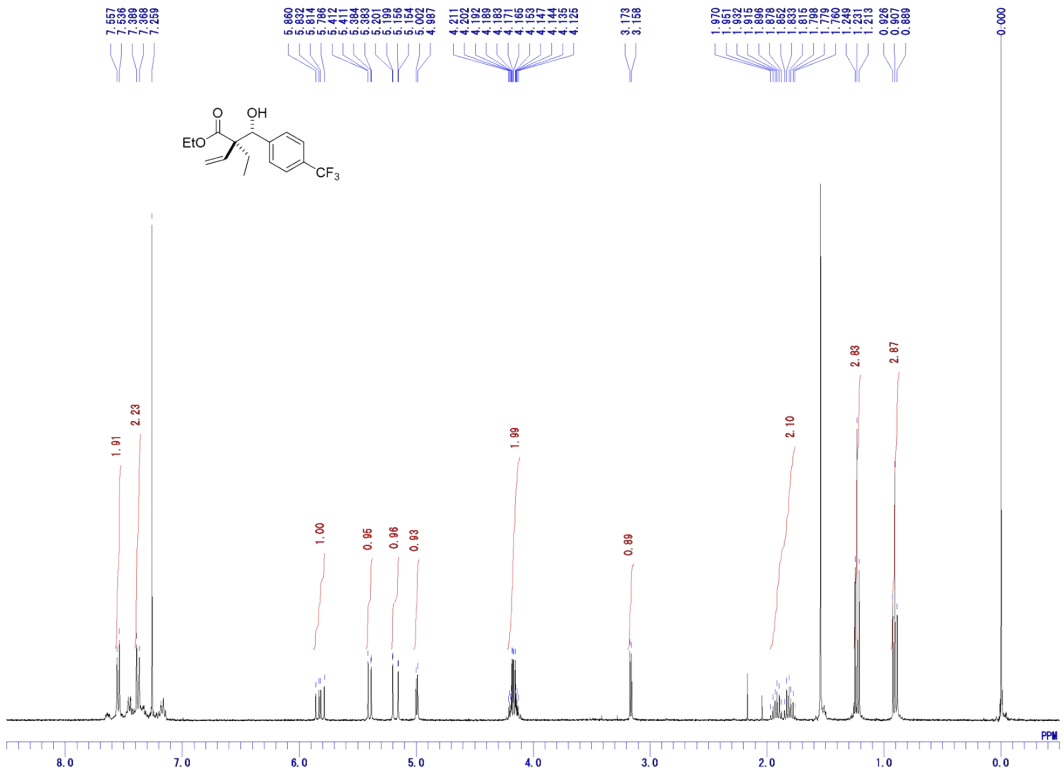
^{13}C NMR ($CDCl_3$, 100 MHz)



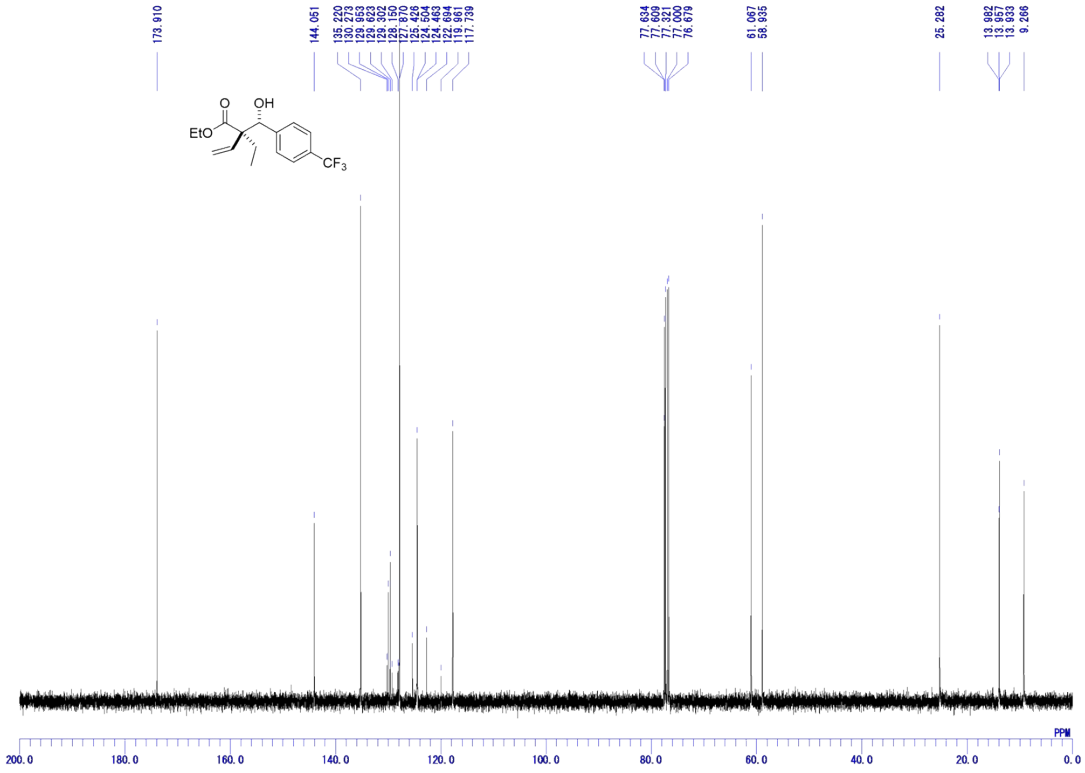
$^{19}F\{^{1}H\}$ NMR ($CDCl_3$, 376 MHz)



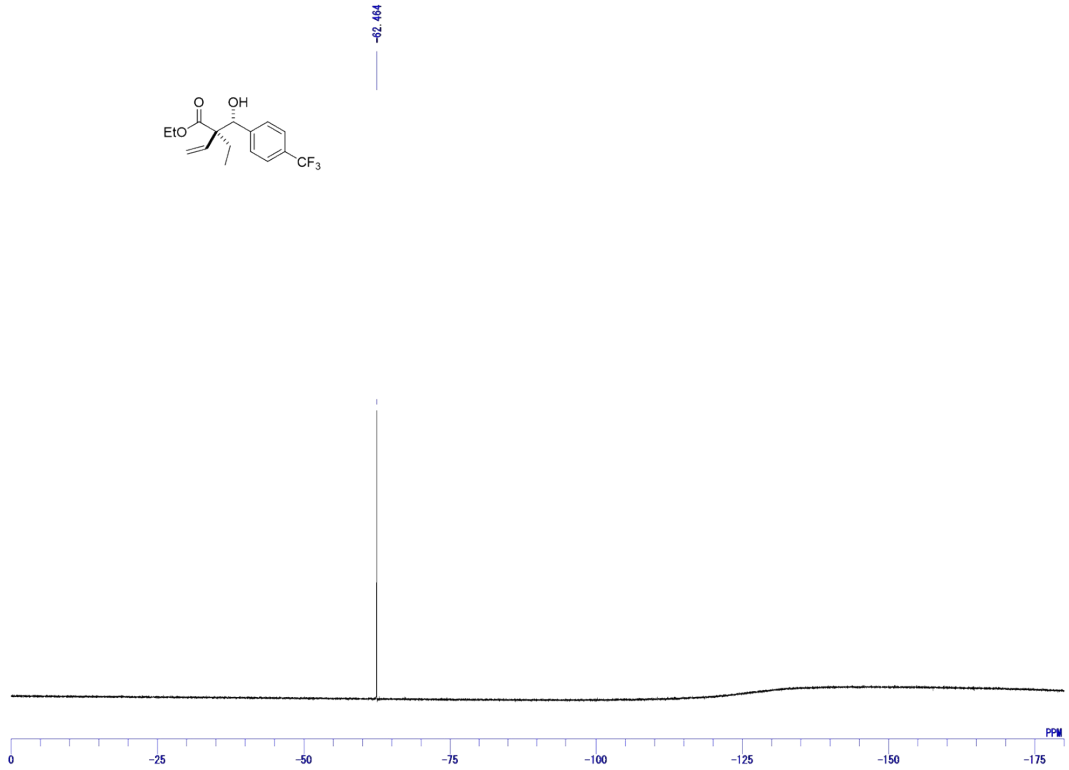
^{1}H NMR ($CDCl_3$, 400 MHz)



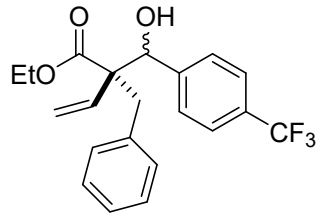
^{13}C NMR ($CDCl_3$, 100 MHz)



$^{19}F\{^{1}H\}$ NMR ($CDCl_3$, 376 MHz)



Ethyl 2-benzyl-2-(hydroxy(4-(trifluoromethyl)phenyl)methyl)but-3-enoate (3ei)



Major isomer (syn): Colorless oil.

R_f = 0.53 (hexane/EtOAc = 8:2).

IR (neat) 3484 cm^{-1} (OH), 1717 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.10 (3H, t, J = 7.1 Hz), 3.16 (2H, d, J = 4.1 Hz), 3.78 (1H, d, J = 6.5 Hz), 4.03-4.16 (2H, m), 5.06 (1H, d, J = 6.3 Hz), 5.17 (1H, d, J = 18.1 Hz), 5.41 (1H, d, J = 11.3 Hz), 6.05 (1H, dd, J = 17.9, 11.3 Hz), 7.11-7.25 (5H, m), 7.39 (2H, d, J = 8.0 Hz), 7.55 (2H, d, J = 8.2 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 13.6, 39.3, 58.5, 61.3, 78.0, 118.6, 124.0 (q, J_{CF} = 272.0 Hz), 124.3 (q, J_{CF} = 3.8 Hz), 126.5, 127.9, 128.6, 129.8 (q, J_{CF} = 32.2 Hz), 129.9, 134.7, 136.5, 143.7 (d), 174.5.

^{19}F{^{1}H} NMR ($CDCl_3$, 376 MHz) δ -62.48 (3F, s).

HRMS (CI) m/z: calcd. for $C_{21}H_{22}F_3O_3$ 379.1516 ($[M+H]^+$), found 379.1519.

Minor isomer (anti): Colorless oil.

R_f = 0.55 (hexane/EtOAc = 8:2).

IR (neat) 3502 cm^{-1} (OH), 1721 cm^{-1} (C=O).

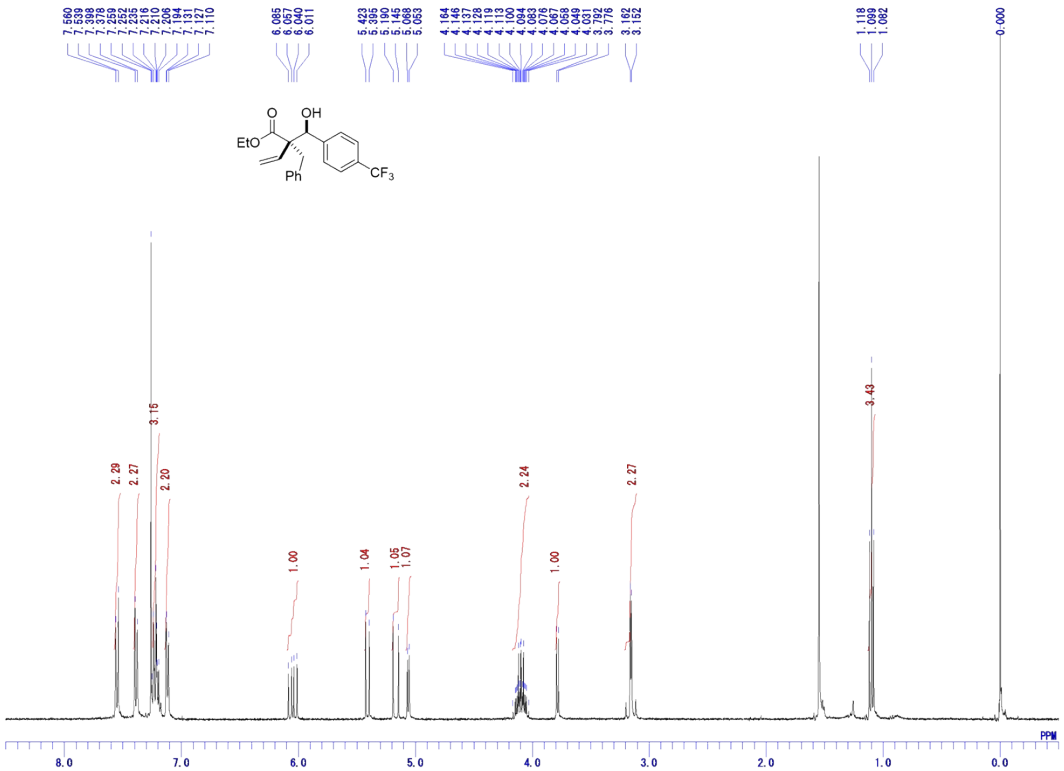
^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.05 (3H, t, J = 7.1 Hz), 3.03 (1H, d, J = 6.0 Hz), 3.15 (1H, d, J = 14.0 Hz), 3.42 (1H, d, J = 14.0 Hz), 3.94-4.04 (2H, m), 5.12 (1H, d, J = 6.0 Hz), 5.37 (1H, d, J = 17.9 Hz), 5.49 (1H, d, J = 11.3 Hz), 5.94 (1H, dd, J = 18.0, 11.2 Hz), 7.14-7.25 (5H, m), 7.43 (2H, d, J = 8.2 Hz), 7.56 (2H, d, J = 8.5 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 13.7, 38.9, 59.3, 61.1, 76.7, 118.8, 124.0 (d, J_{CF} = 271.2 Hz), 124.6 (q, J_{CF} = 3.8 Hz), 126.5, 127.9, 128.4, 130.0 (q, J_{CF} = 32.5 Hz), 130.2, 135.2, 136.9, 143.9, 173.1.

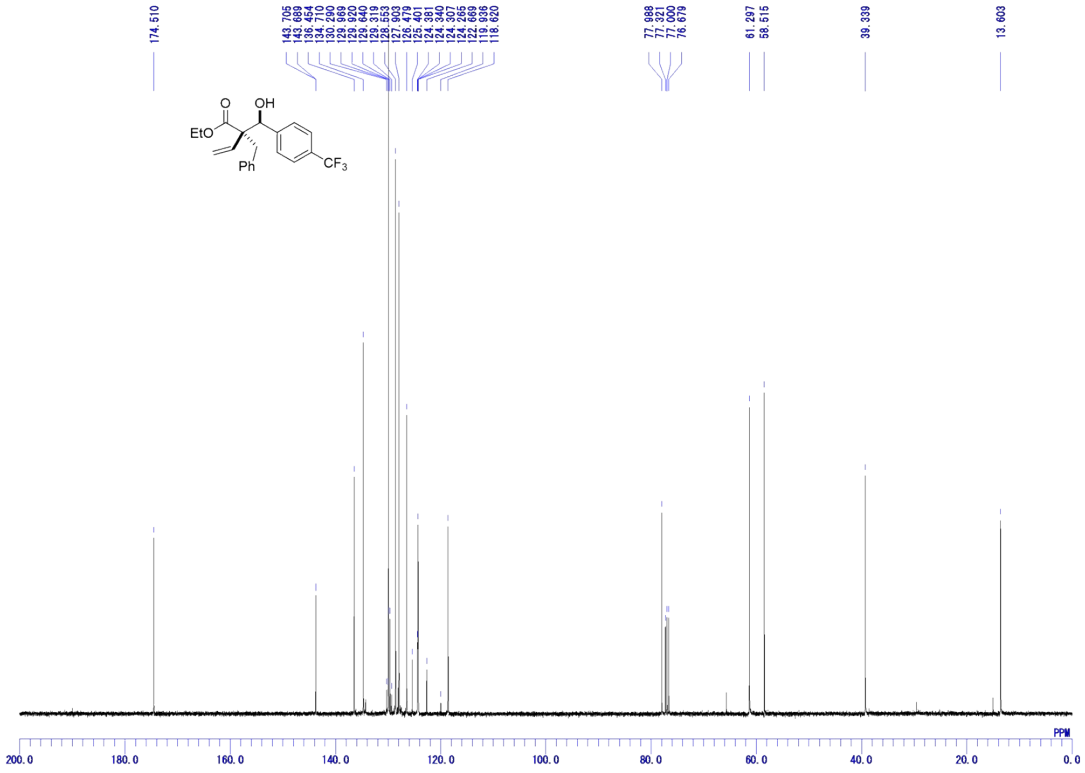
^{19}F{^{1}H} NMR ($CDCl_3$, 376 MHz) δ -62.49 (3F, s).

HRMS (CI) m/z: calcd. for $C_{21}H_{22}F_3O_3$ 379.1516 ($[M+H]^+$), found 379.1524.

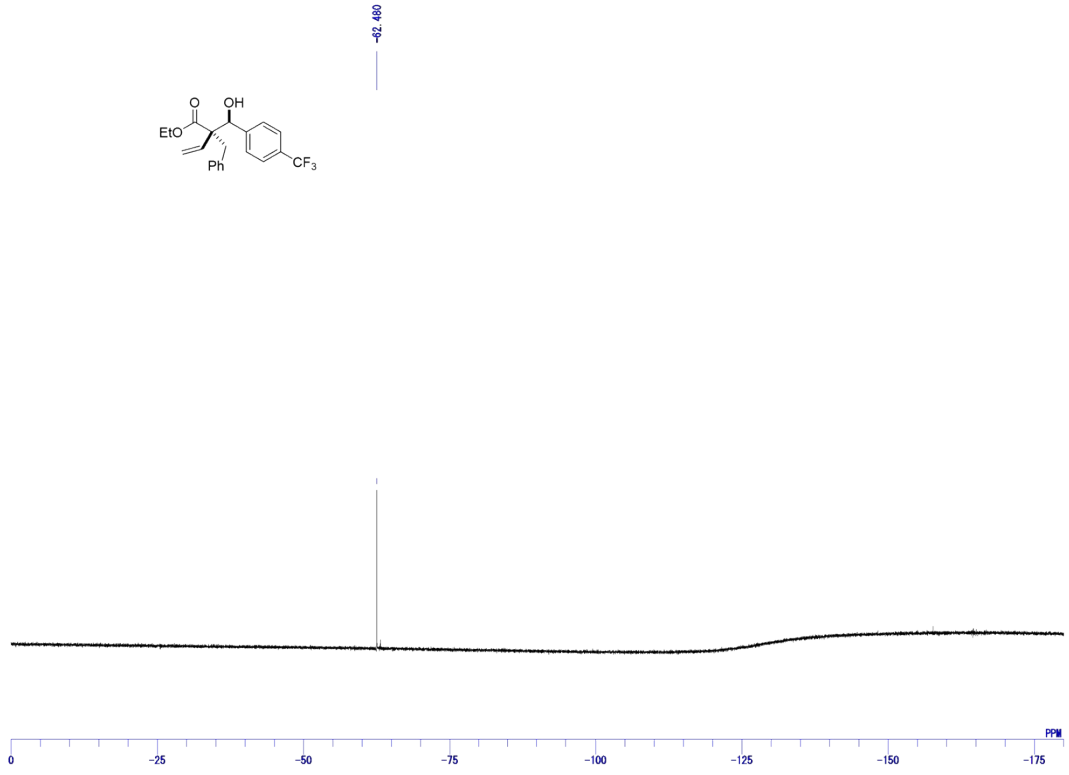
^{1}H NMR ($CDCl_3$, 400 MHz)



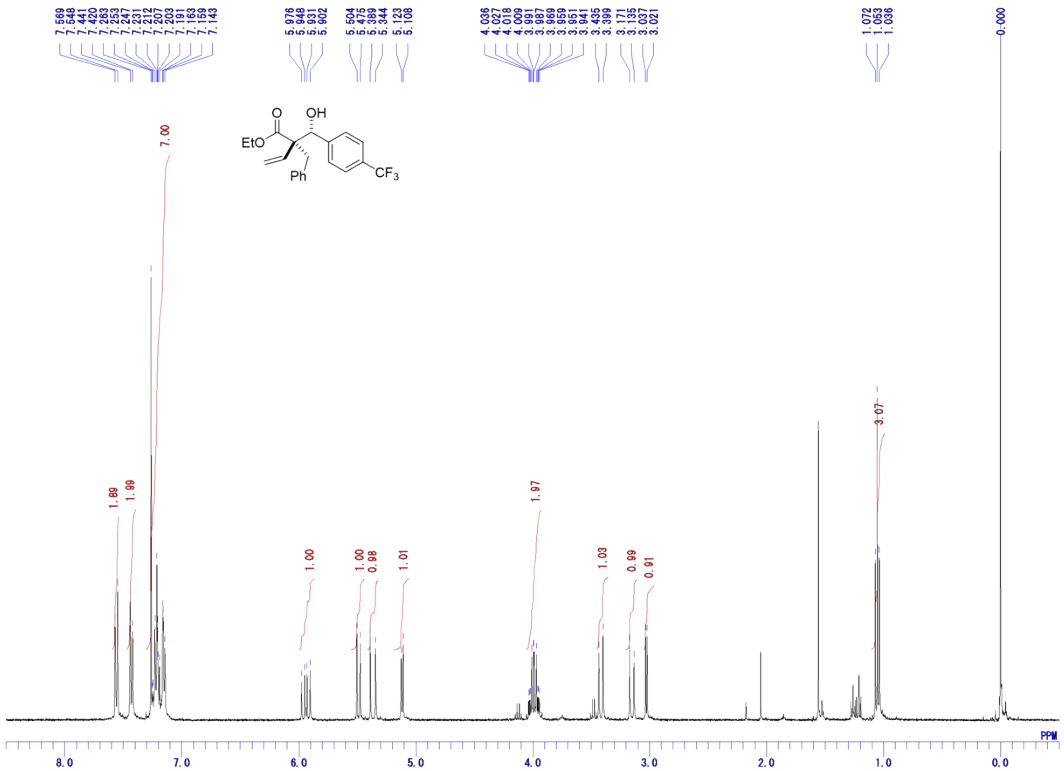
^{13}C NMR ($CDCl_3$, 100 MHz)



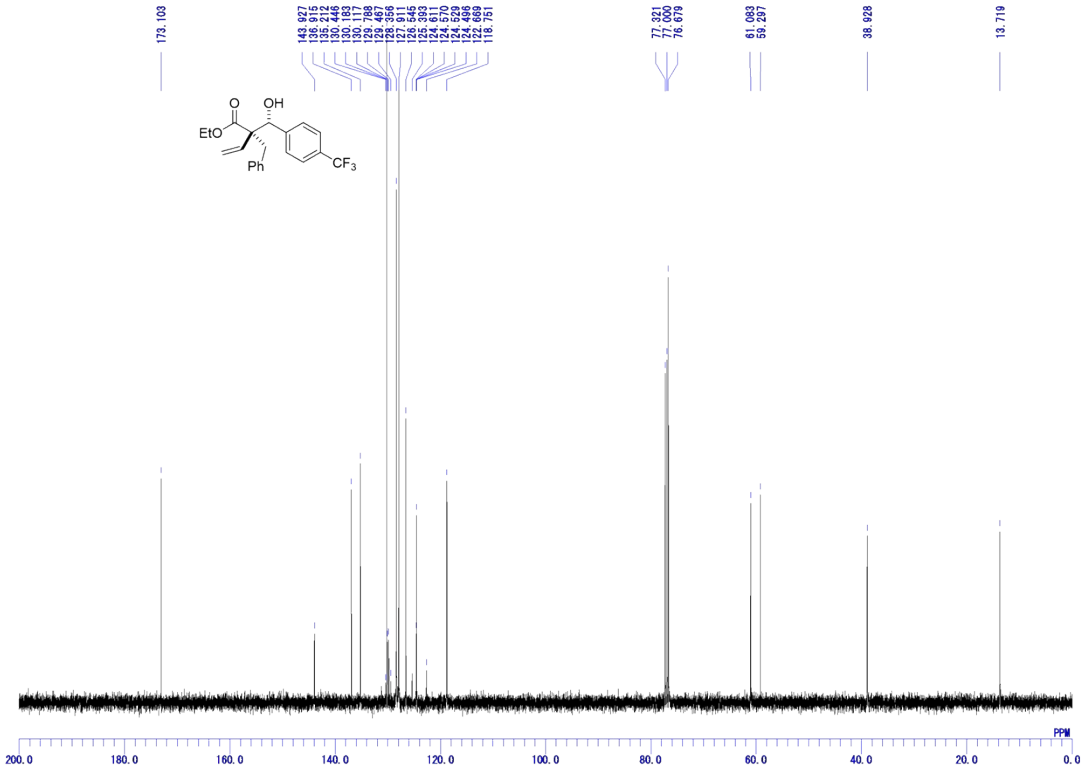
$^{19}F\{^{1}H\}$ NMR ($CDCl_3$, 376 MHz)



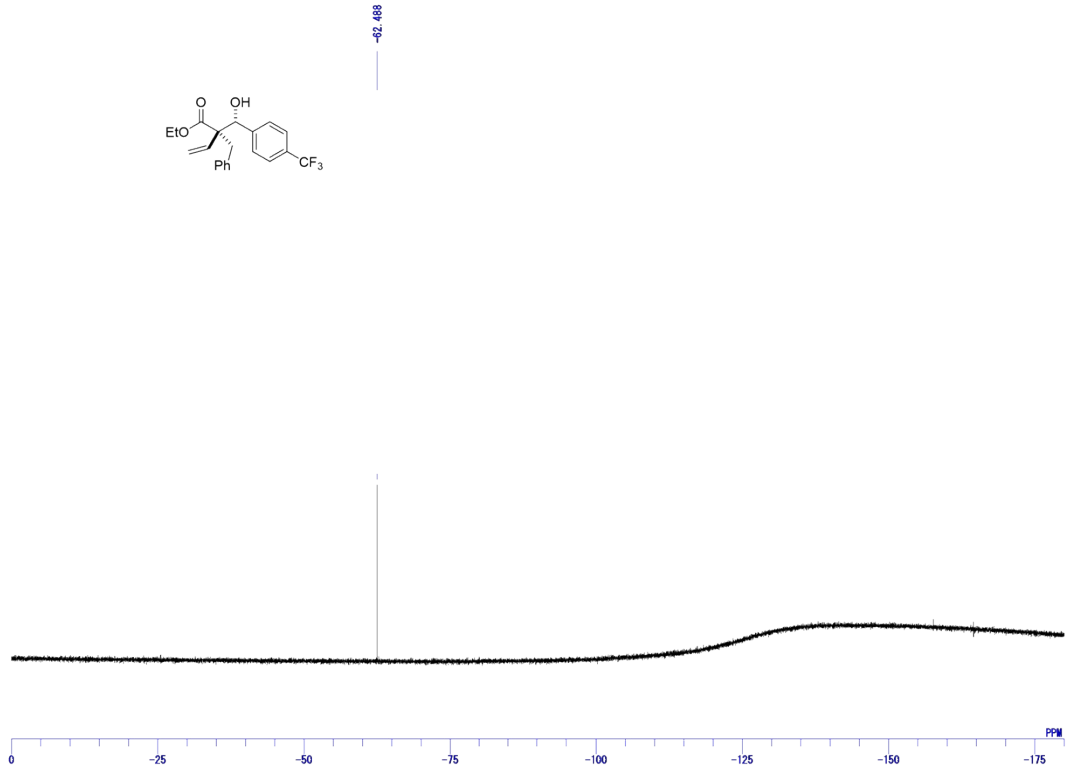
^{1}H NMR ($CDCl_3$, 400 MHz)



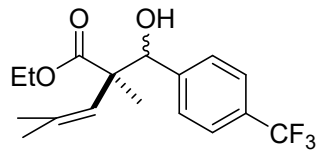
^{13}C NMR ($CDCl_3$, 100 MHz)



$^{19}F\{^{1}H\}$ NMR ($CDCl_3$, 376 MHz)



Ethyl 2-(hydroxy(4-(trifluoromethyl)phenyl)methyl)-2,4-dimethylpent-3-enoate (3fi)



Major isomer: Colorless oil.

R_f = 0.58 (hexane/EtOAc = 8:2).

IR (neat) 3514 cm^{-1} (OH), 1698 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.22 (3H, s), 1.27 (3H, t, J = 4.1 Hz), 1.53 (3H, d, J = 1.0 Hz), 1.76 (3H, d, J = 1.2 Hz), 3.55 (1H, d, J = 3.6 Hz), 4.13-4.27 (2H, m), 5.01-5.02 (2H, m), 7.45 (2H, d, J = 8.2 Hz), 7.56 (2H, d, J = 8.2 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 13.8, 18.9, 21.5, 27.1, 52.0, 61.1, 78.0, 124.0, 124.1 (q, J_{CF} = 272.0 Hz), 124.2 (q, J_{CF} = 3.6 Hz), 128.3, 129.6 (q, J_{CF} = 32.5 Hz), 136.3, 143.6 (d), 176.8.

^{19}F{^{1}H} NMR ($CDCl_3$, 376 MHz) δ -62.41 (3F, s).

HRMS (CI) m/z: calcd. for $C_{17}H_{22}F_3O_3$ 331.1516 ($[M+H]^+$), found 331.1515.

Minor isomer: Colorless oil.

R_f = 0.55 (hexane/EtOAc = 8:2).

IR (neat) 3473 cm^{-1} (OH), 1703 cm^{-1} (C=O).

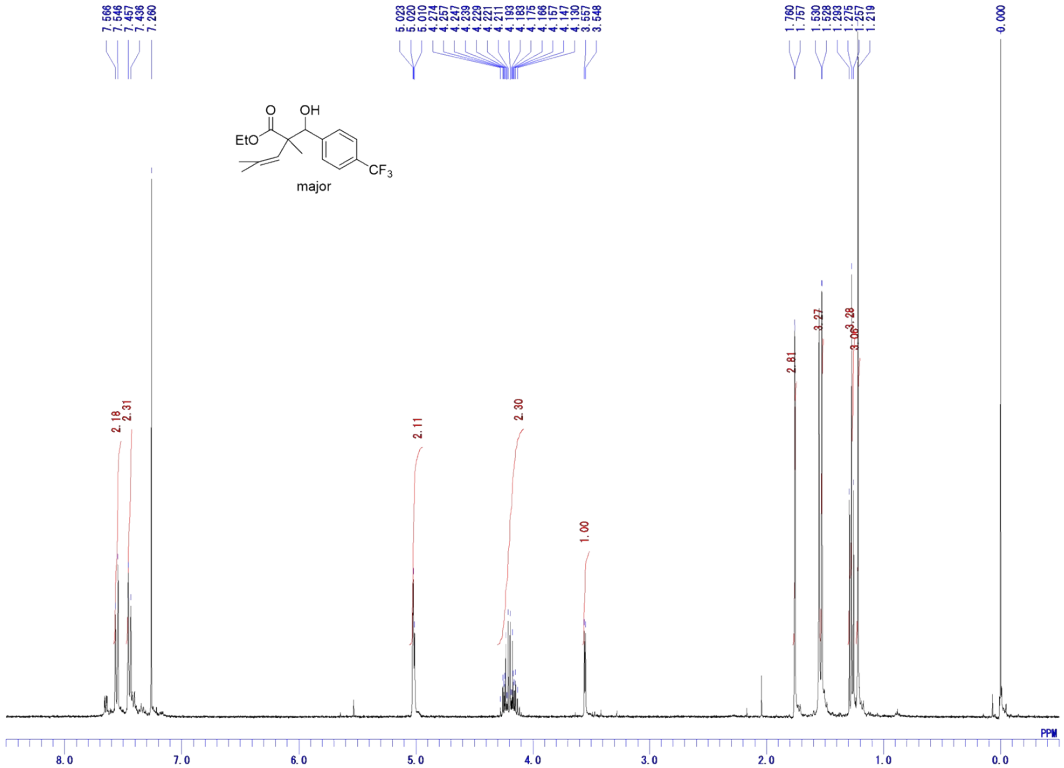
^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.22 (3H, s), 1.28 (3H, t, J = 7.1 Hz), 1.63 (3H, d, J = 1.2 Hz), 1.72 (3H, d, J = 1.4 Hz), 4.20-4.26 (3H, m), 4.76 (1H, t, J = 1.3 Hz), 5.14 (1H, d, J = 3.1 Hz), 7.38 (2H, d, J = 8.0 Hz), 7.54 (2H, d, J = 8.2 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 14.1, 18.8, 19.2, 26.7, 52.0, 61.1, 78.0, 124.2 (q, J_{CF} = 3.8 Hz), 124.2 (q, J_{CF} = 272.0 Hz), 126.6 (d), 128.4, 129.5 (q, J_{CF} = 32.2 Hz), 135.5, 143.5, 178.4.

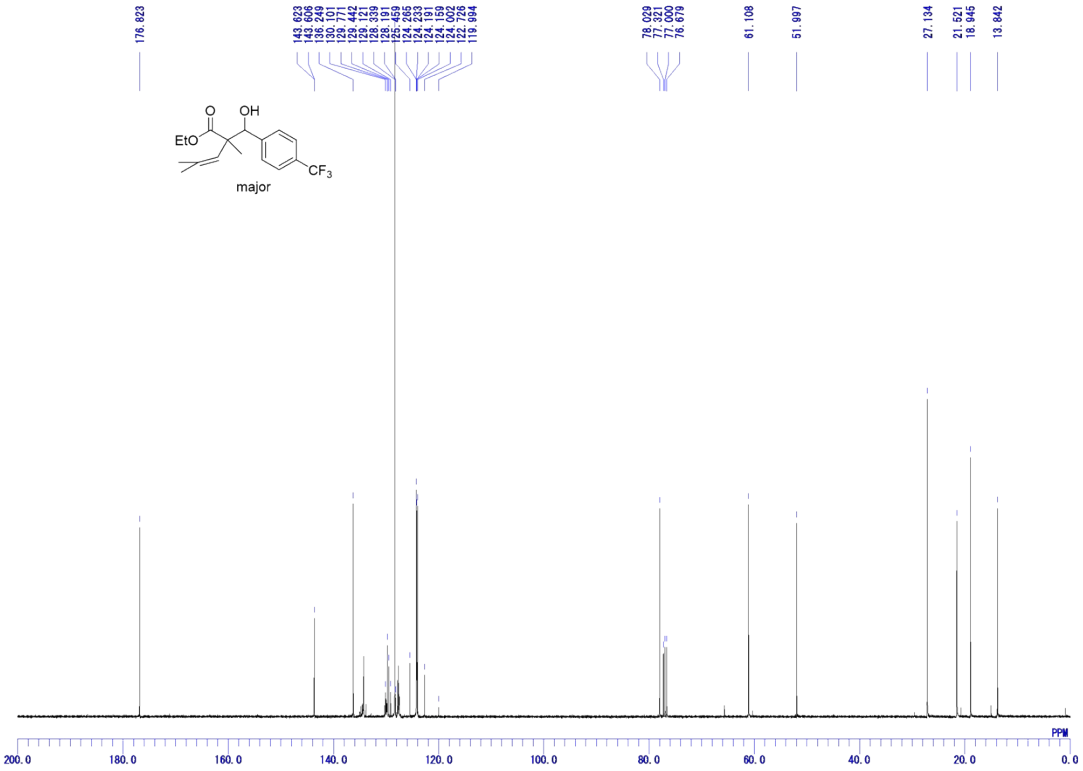
^{19}F{^{1}H} NMR ($CDCl_3$, 376 MHz) δ -62.37 (3F, s).

HRMS (CI) m/z: calcd. for $C_{17}H_{22}F_3O_3$ 331.1516 ($[M+H]^+$), found 331.1517.

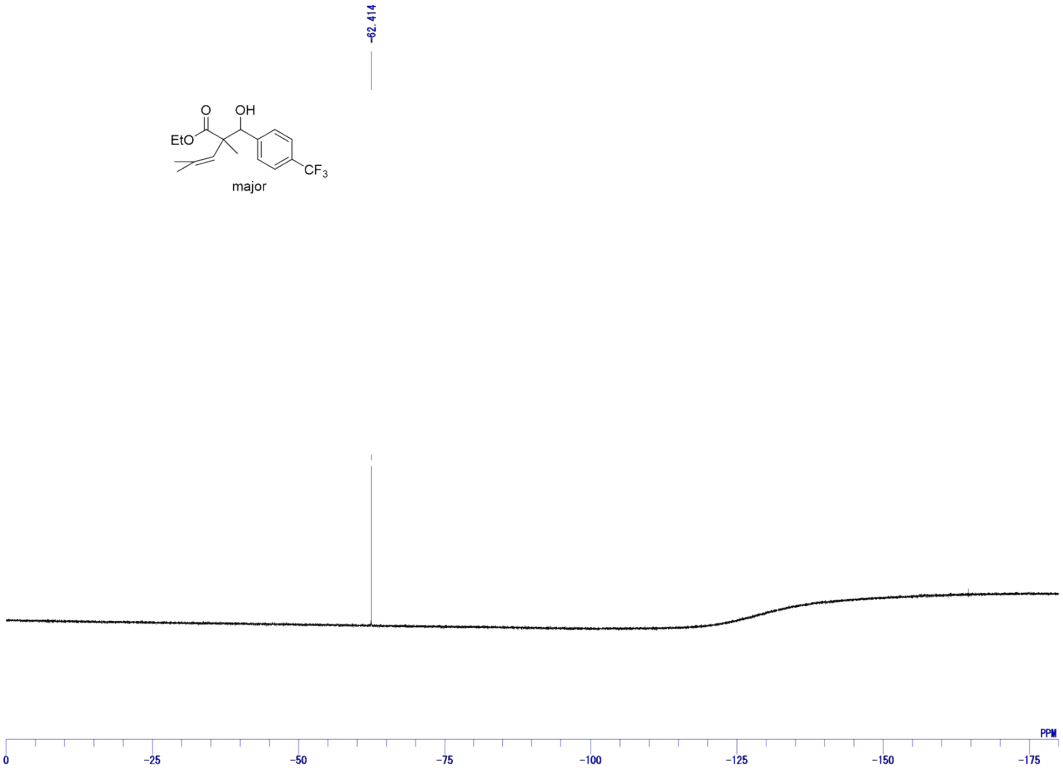
^{1}H NMR ($CDCl_3$, 400 MHz)



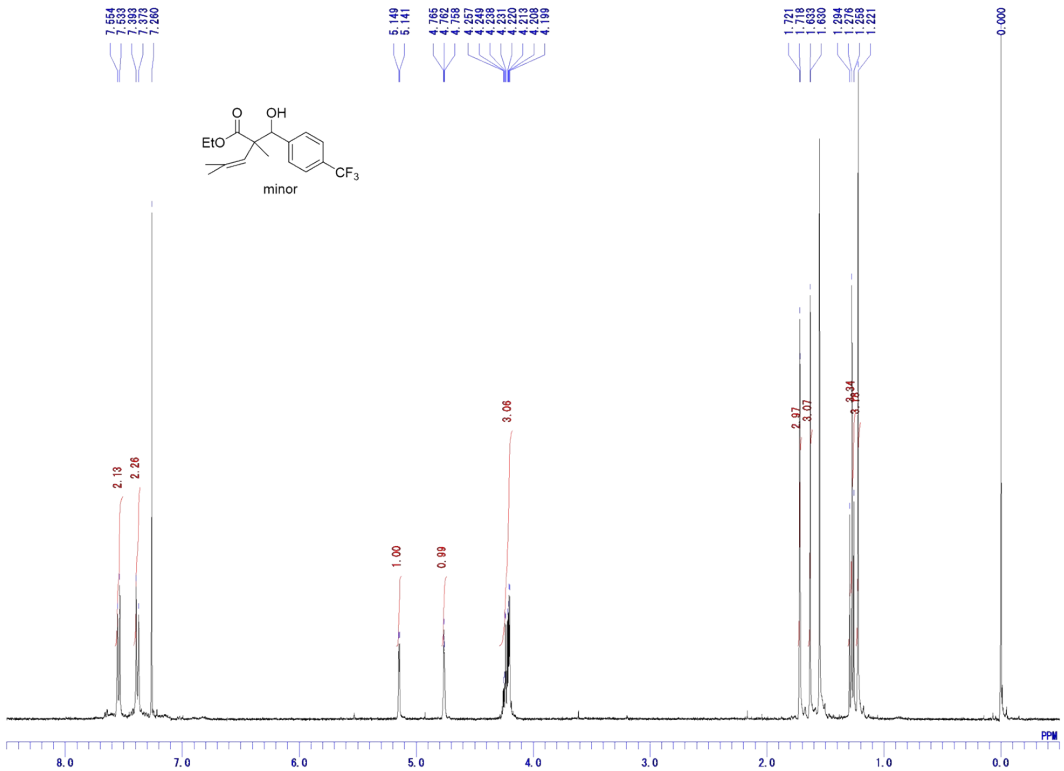
^{13}C NMR ($CDCl_3$, 100 MHz)



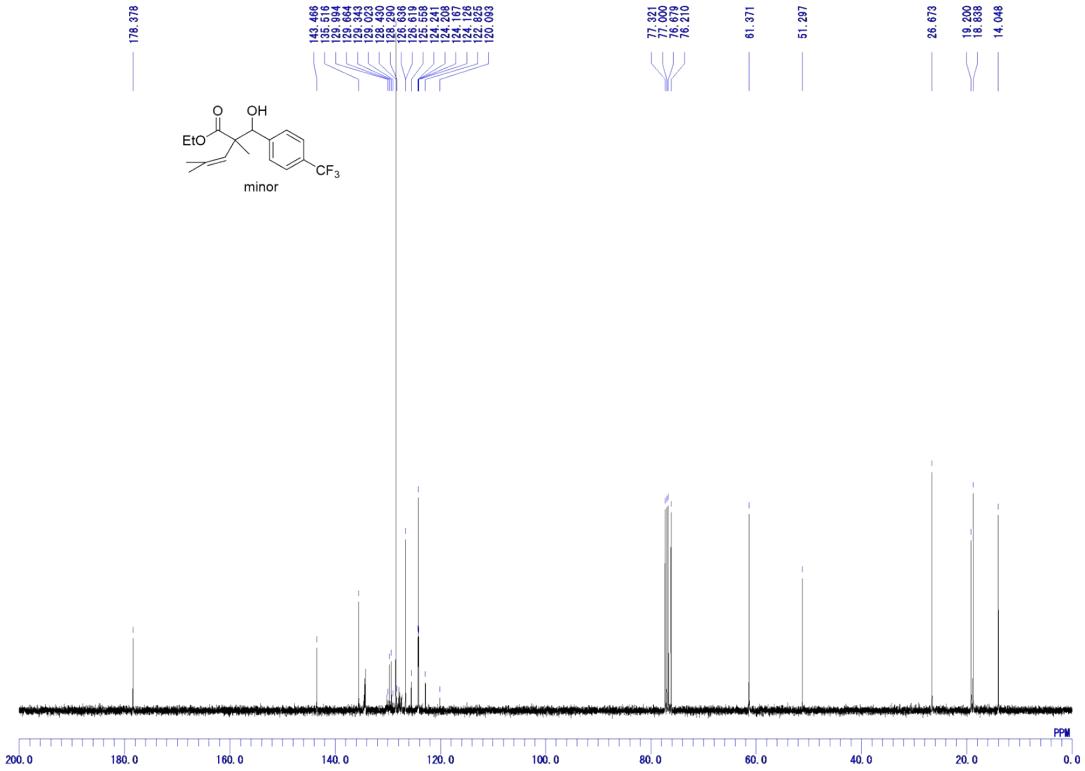
$^{19}F\{^{1}H\}$ NMR ($CDCl_3$, 376 MHz)



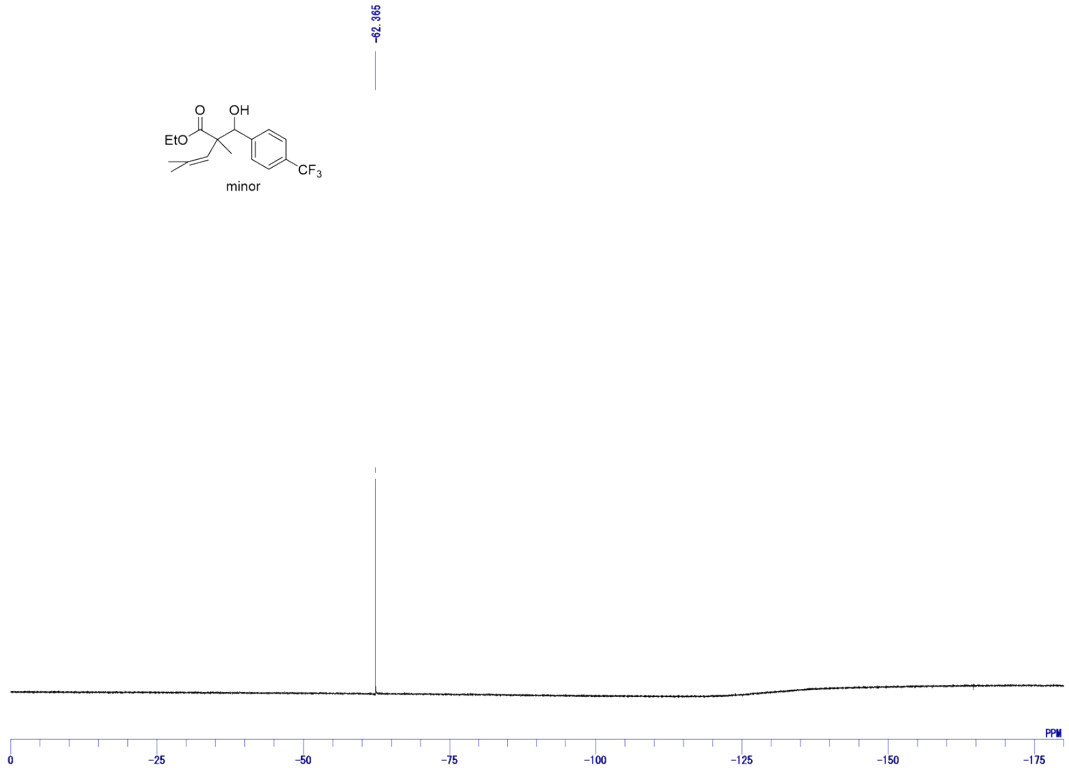
^{1}H NMR ($CDCl_3$, 400 MHz)



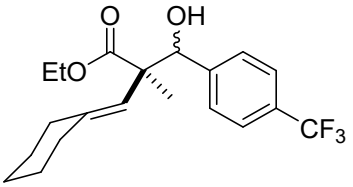
^{13}C NMR ($CDCl_3$, 100 MHz)



$^{19}F\{^{1}H\}$ NMR ($CDCl_3$, 376 MHz)



Ethyl 2-(cyclohexylidenemethyl)-3-hydroxy-2-methyl-3-(4-(trifluoromethyl)phenyl)propanoate (3gi)



Major isomer: Colorless oil.

R_f = 0.58 (hexane/EtOAc = 8:2).

IR (neat) 3488 cm^{-1} (OH), 1696 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.21 (3H, s), 1.28 (3H, t, J = 7.2 Hz), 1.48-1.59 (6H, m), 1.93-2.14 (4H, m) 3.49 (1H, d, J = 3.6 Hz), 4.10-4.27 (2H, m), 4.87 (1H, s), 5.03 (1H, d, J = 3.6 Hz), 7.46 (2H, d, J = 8.0 Hz), 7.55 (2H, d, J = 8.2 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 13.9 (q), 22.7 (q), 26.3, 27.1, 28.4, 30.3, 38.1, 51.4, 61.2 (t), 77.9, 120.7 (d), 124.1 (q, J_{CF} = 272.0 Hz), 124.3 (d, J_{CF} = 3.3 Hz), 128.5, 129.7 (q, J_{CF} = 32.2 Hz), 143.5 (d), 144.1, 177.4.

^{19}F{^{1}H} NMR ($CDCl_3$, 376 MHz) δ -62.41 (3F, s).

HRMS (CI) m/z: calcd. for $C_{20}H_{26}F_3O_3$ 371.1829 ($[M+H]^+$), found 371.1832.

Minor isomer: Colorless oil.

R_f = 0.55 (hexane/EtOAc = 8:2).

IR (neat) 3473 cm^{-1} (OH), 1704 cm^{-1} (C=O).

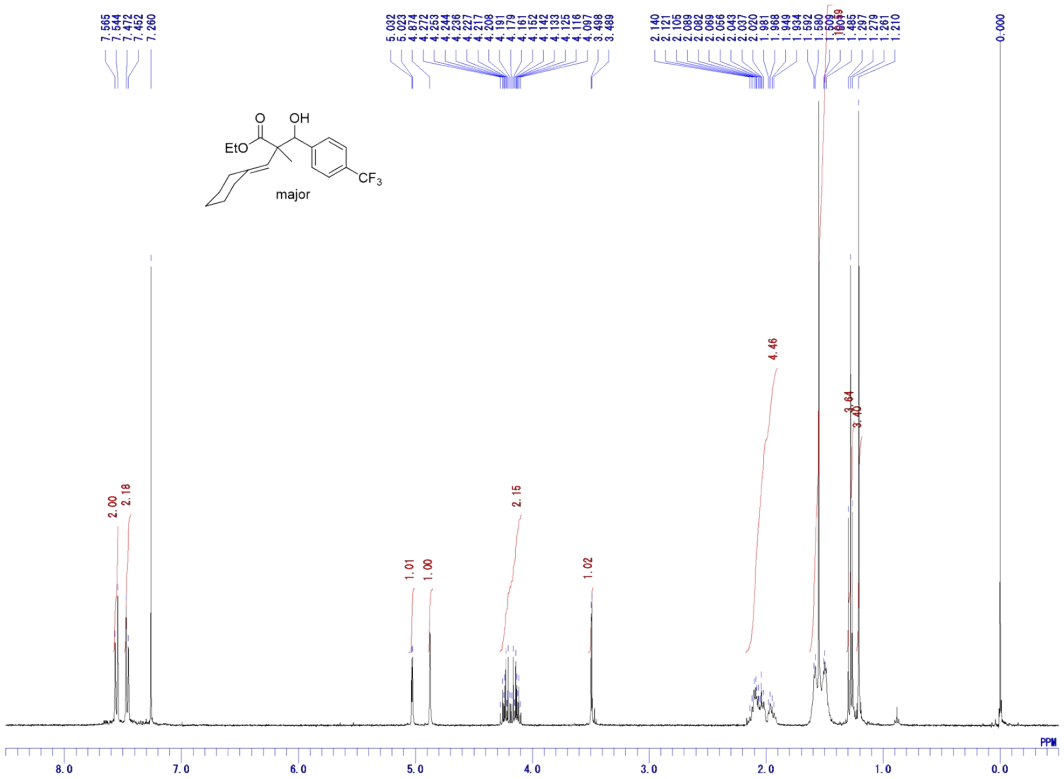
^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.23 (3H, s), 1.28 (3H, t, J = 7.1 Hz), 1.52-1.61 (6H, m), 2.06-2.11 (4H, m) 4.13-4.28 (2H, m), 4.37 (1H, d, J = 3.1 Hz), 4.67 (1H, s), 5.12 (1H, d, J = 2.9 Hz), 7.44 (2H, d, J = 8.5 Hz), 7.54 (2H, d, J = 8.2 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 14.0 (q), 19.4 (q), 26.2, 26.9, 28.0, 29.8, 37.5, 50.6, 61.3 (t), 76.5 (d), 123.5 (d), 123.9-124.2 (m), 124.2 (q, J_{CF} = 271.2 Hz), 128.3-128.7 (m), 129.4 (q, J_{CF} = 32.2 Hz), 142.9, 143.3, 178.9.

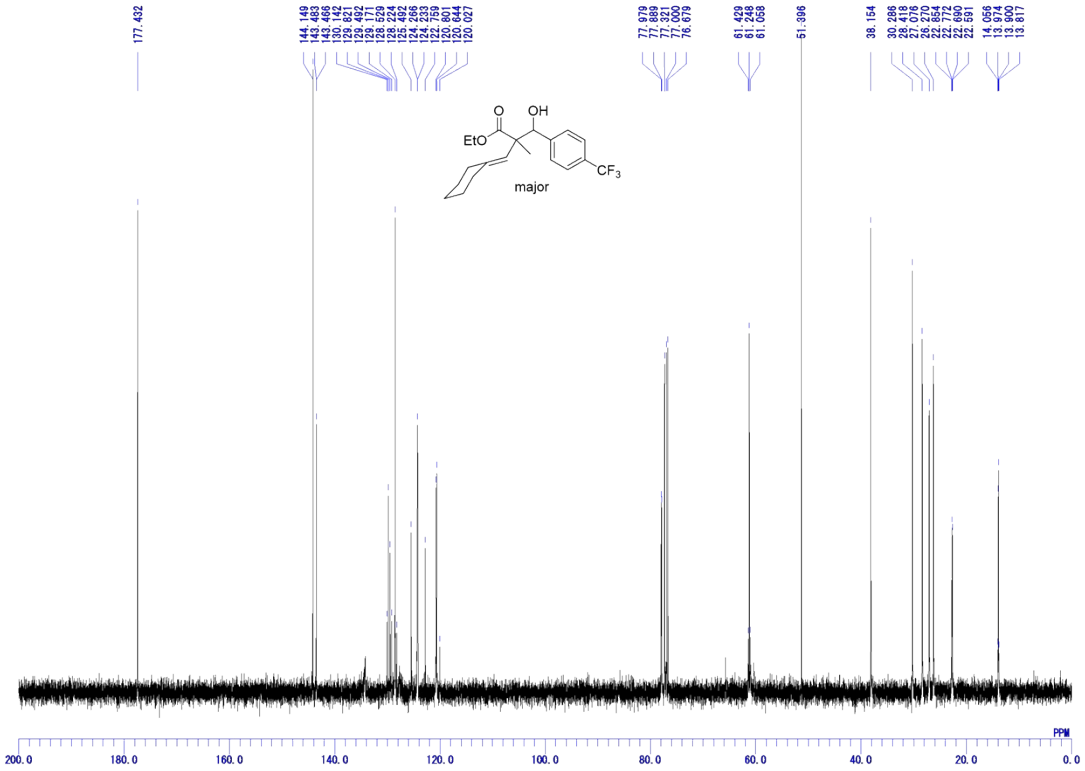
^{19}F{^{1}H} NMR ($CDCl_3$, 376 MHz) δ -62.36 (3F, s).

HRMS (CI) m/z: calcd. for $C_{20}H_{26}F_3O_3$ 371.1829 ($[M+H]^+$), found 371.1829.

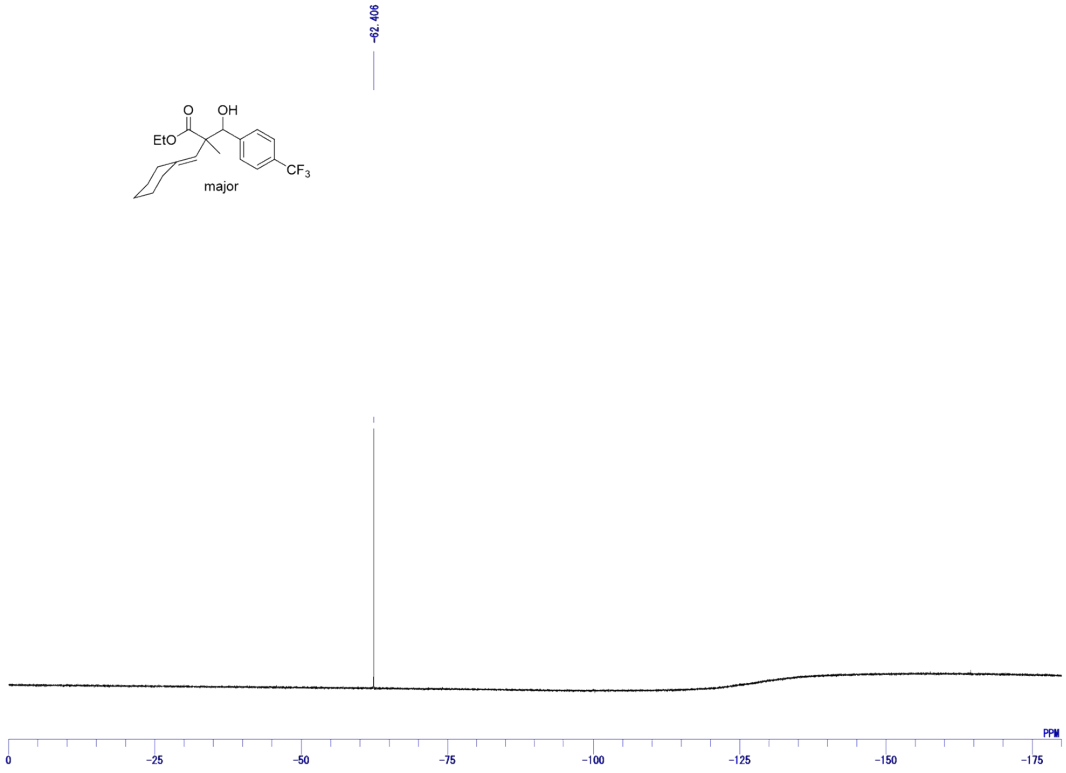
^{1}H NMR ($CDCl_3$, 400 MHz)



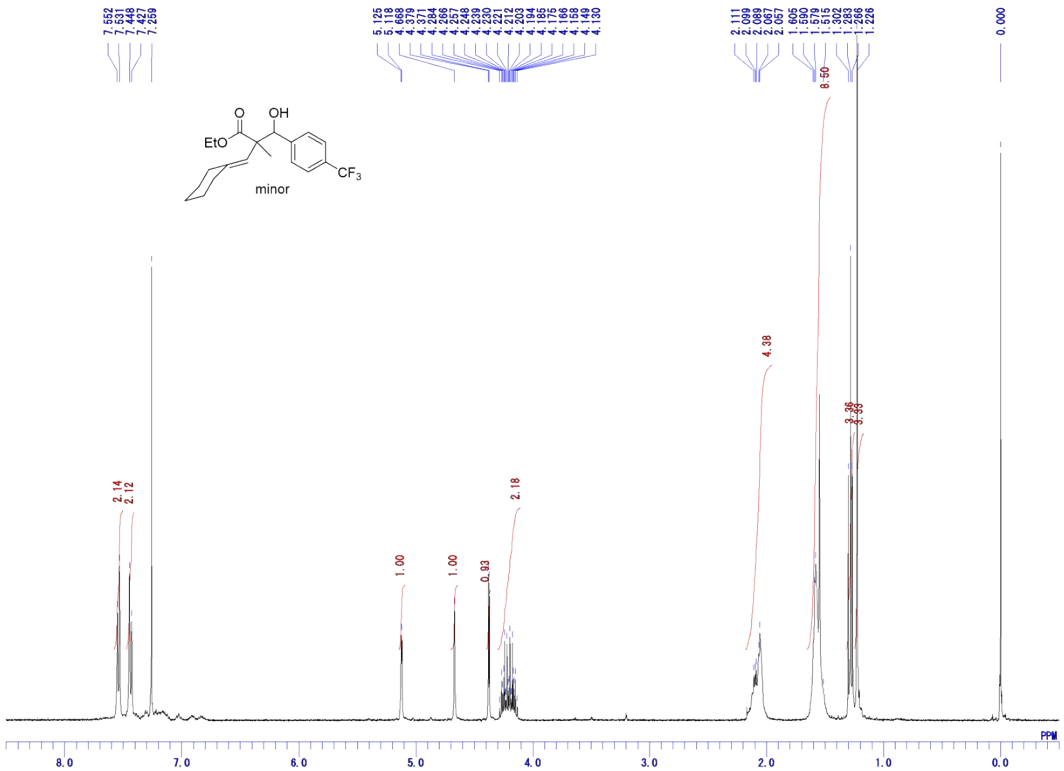
^{13}C NMR ($CDCl_3$, 100 MHz)



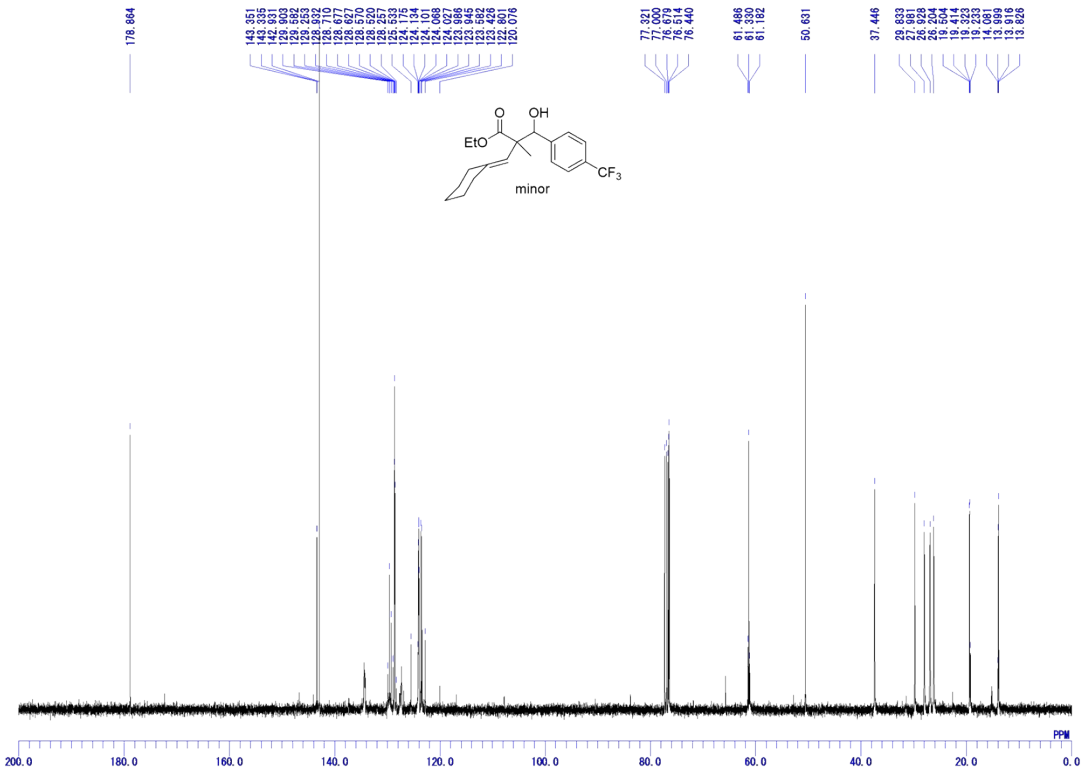
$^{19}F\{^{1}H\}$ NMR ($CDCl_3$, 376 MHz)



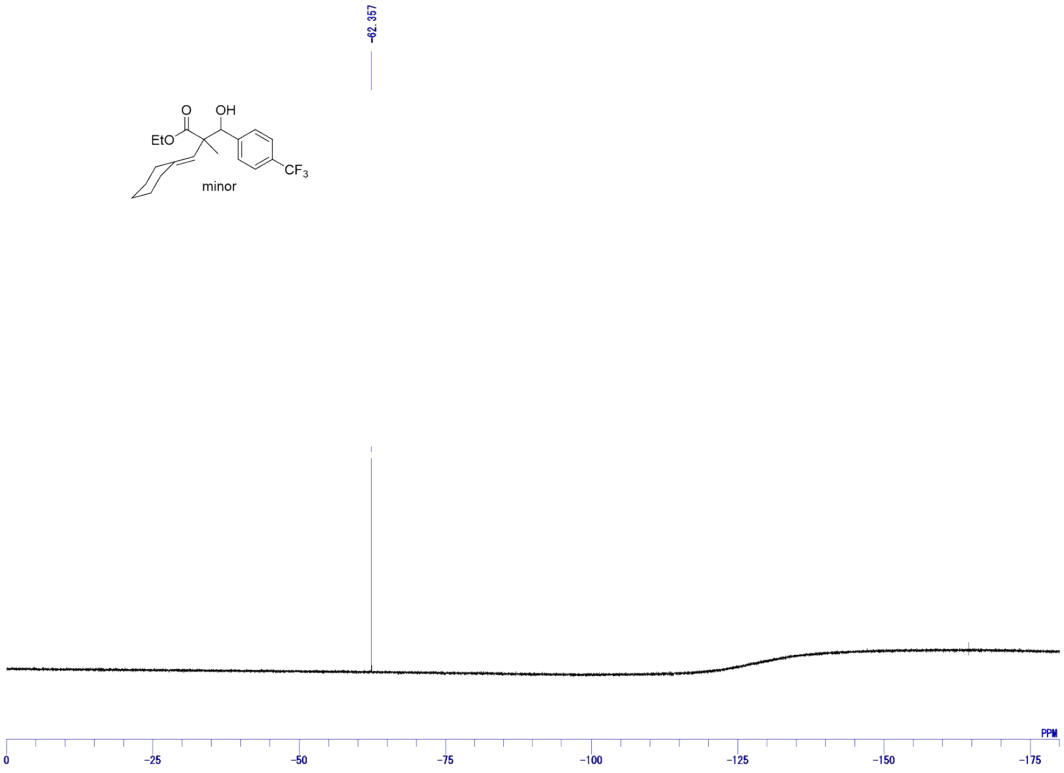
^{1}H NMR ($CDCl_3$, 400 MHz)



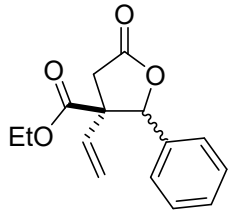
^{13}C NMR ($CDCl_3$, 100 MHz)



$^{19}F\{^{1}H\}$ NMR ($CDCl_3$, 376 MHz)



Ethyl 5-oxo-2-phenyl-3-vinyltetrahydrofuran-3-carboxylate (4ha)



Major isomer (syn): Colorless oil.

R_f = 0.35 (hexane/EtOAc = 8:2).

IR (neat) 1724 cm^{-1} (C=O), 1789 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.92 (3H, t, J = 7.2 Hz), 2.89 (1H, d, J = 17.1 Hz), 3.25 (1H, d, J = 17.1 Hz), 3.67-3.86 (2H, m), 5.34-5.43 (3H, m), 6.38 (1H, dd, J = 17.6, 10.9 Hz), 7.27-7.29 (2H, m), 7.34-7.38 (3H, m).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 13.4, 36.1, 58.3, 61.7, 87.0, 116.5, 125.7, 128.4, 129.0, 134.5, 135.1, 169.9, 174.1.

HRMS (CI) m/z: calcd. for $C_{15}H_{17}O_4$ 261.1121 ($[M+H]^+$), found 261.1126.

Minor isomer (anti): Colorless oil.

R_f = 0.40 (hexane/EtOAc = 8:2).

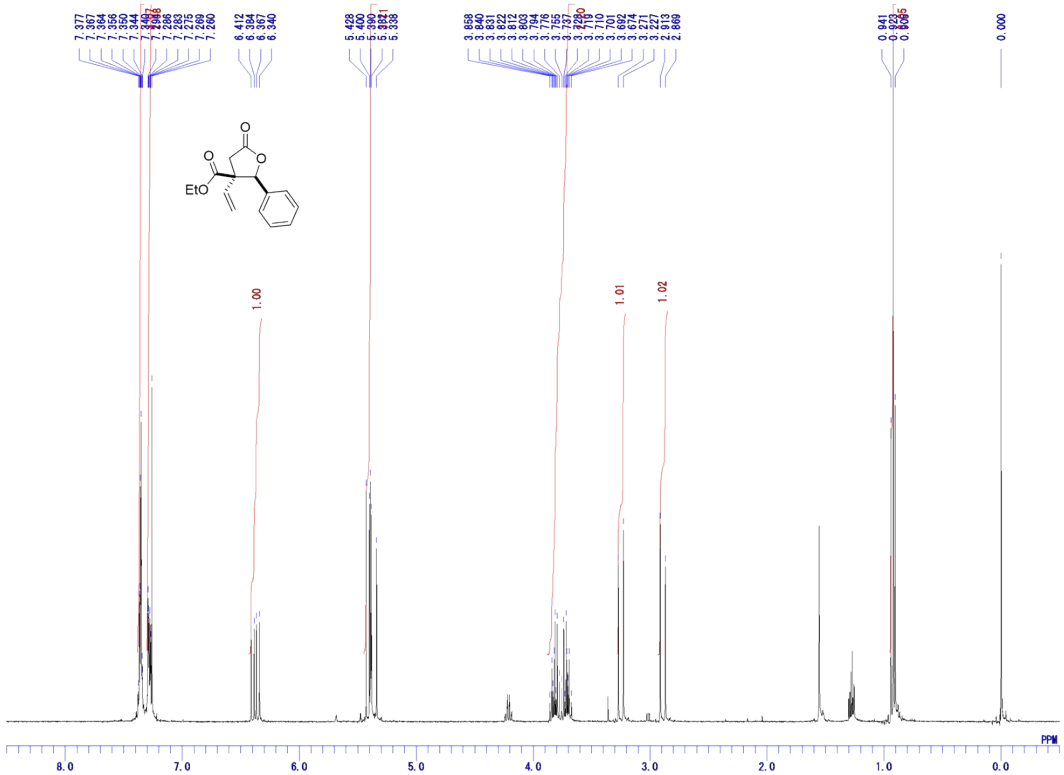
IR (neat) 1724 cm^{-1} (C=O), 1790 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.32 (3H, t, J = 7.2 Hz), 2.95 (1H, d, J = 17.1 Hz), 3.31 (1H, d, J = 17.4 Hz), 4.25-4.33 (2H, m), 5.10-5.19 (2H, m), 5.48 (1H, dd, J = 17.6, 10.6 Hz), 5.90 (1H, s), 7.22-7.25 (2H, m), 7.34-7.37 (3H, m).

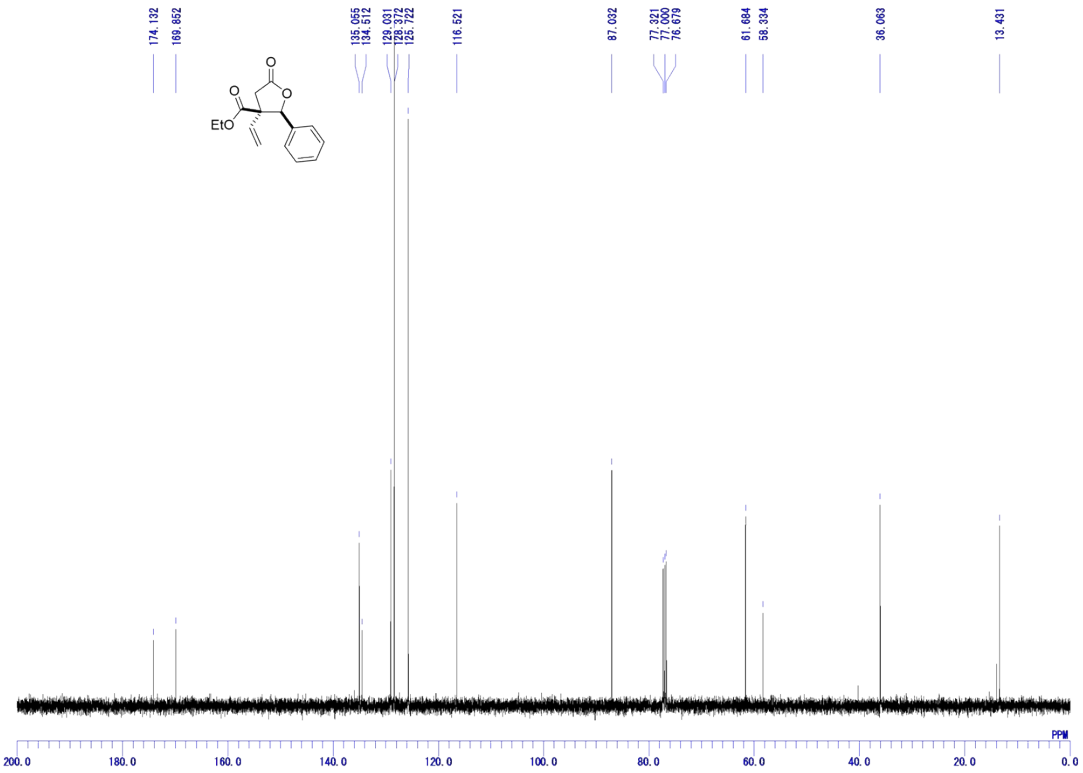
^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 13.9, 35.9, 57.2, 62.3, 85.1, 117.2, 126.4, 128.2, 128.7, 133.1, 134.1, 171.2, 173.9.

HRMS (CI) m/z: calcd. for $C_{15}H_{17}O_4$ 261.1121 ($[M+H]^+$), found 261.1125.

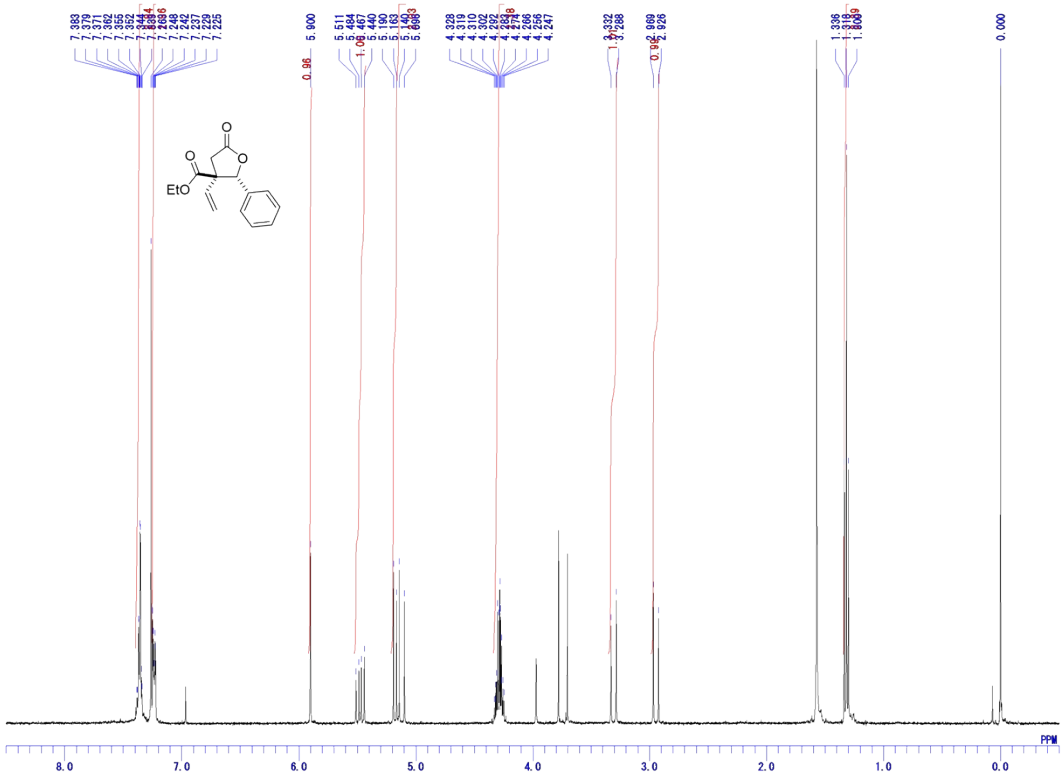
^{1}H NMR ($CDCl_3$, 400 MHz)



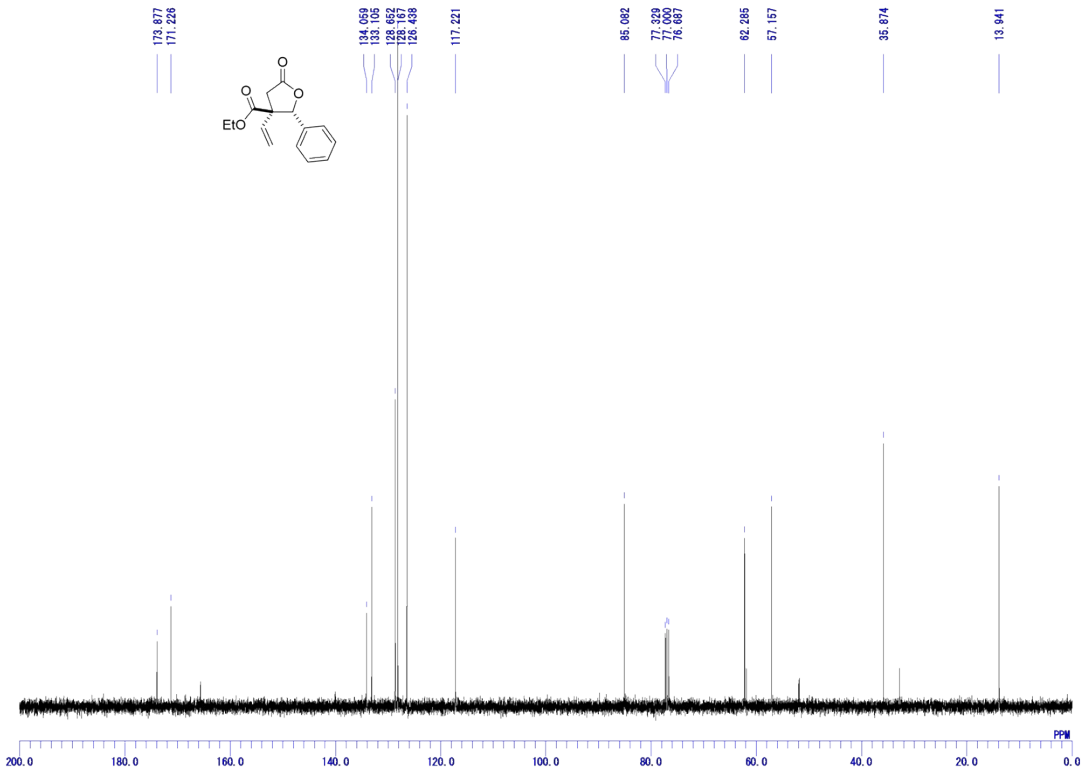
^{13}C NMR ($CDCl_3$, 100 MHz)



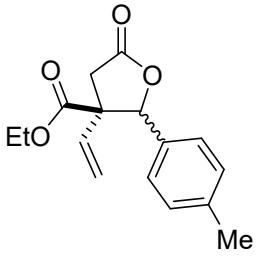
^{1}H NMR ($CDCl_3$, 400 MHz)



^{13}C NMR ($CDCl_3$, 100 MHz)



Ethyl 5-oxo-2-(p-tolyl)-3-vinyltetrahydrofuran-3-carboxylate (4hb)



<u>Major isomer</u> (syn): Colorless oil.

R_f = 0.35 (hexane/EtOAc = 8:2).

IR (neat) 1727 cm^{-1} (C=O), 1787 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.96 (3H, t, J = 7.1 Hz), 2.34 (3H, s), 2.89 (1H, d, J = 17.1 Hz), 3.24 (1H, d, J = 17.1 Hz), 3.71-3.88 (2H, m), 5.32-5.42 (3H, m), 6.36 (1H, dd, J = 17.6, 10.9 Hz), 7.16 (4H, s).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 13.3, 21.0, 35.9, 58.2, 61.5, 86.9, 116.3, 125.5, 128.9, 131.4, 135.0, 138.7, 169.8, 174.1.

HRMS (CI) m/z: calcd. for $C_{16}H_{19}O_4$ 275.1278 ($[M+H]^+$), found 275.1279.

<u>Minor isomer</u> (anti): Colorless oil.

R_f = 0.38 (hexane/EtOAc = 8:2).

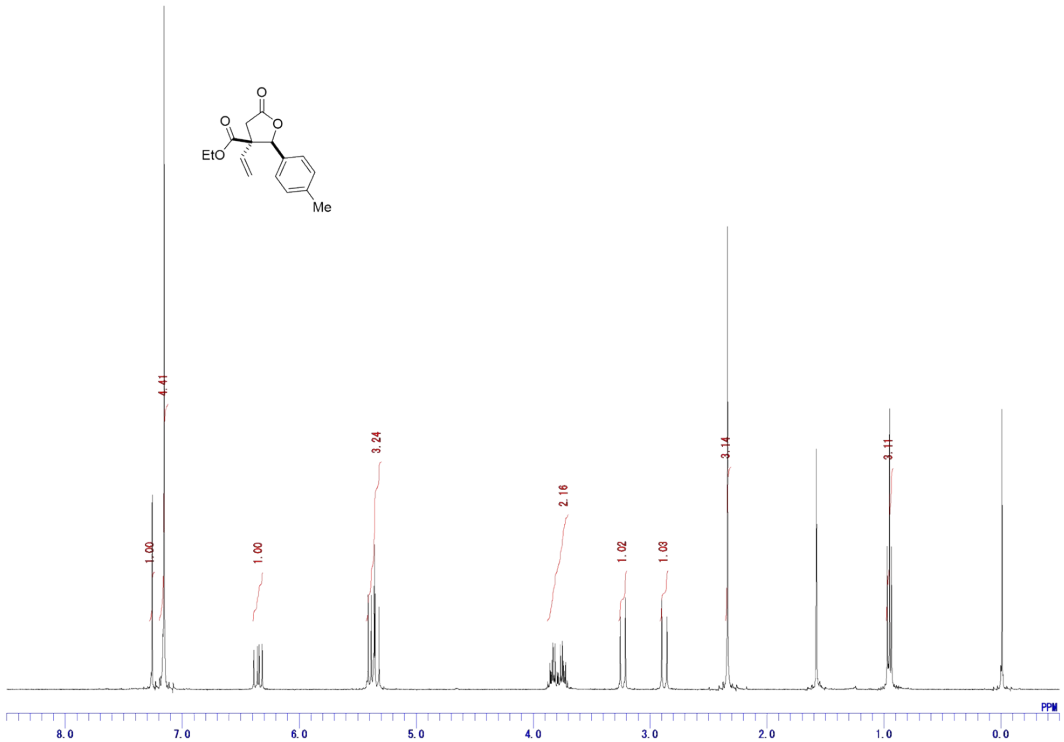
IR (neat) 1723 cm^{-1} (C=O), 1789 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.31 (3H, t, J = 7.1 Hz), 2.36 (3H, s), 2.94 (1H, d, J = 17.4 Hz), 3.30 (1H, d, J = 17.4 Hz), 4.24-4.32 (2H, m), 5.11 (1H, d, J = 17.6 Hz), 5.18 (1H, d, J = 10.6 Hz), 5.49 (1H, dd, J = 17.5, 10.7 Hz), 5.86 (1H, s), 7.11 (2H, d, J = 8.2 Hz), 7.17 (2H, d, J = 8.2 Hz).

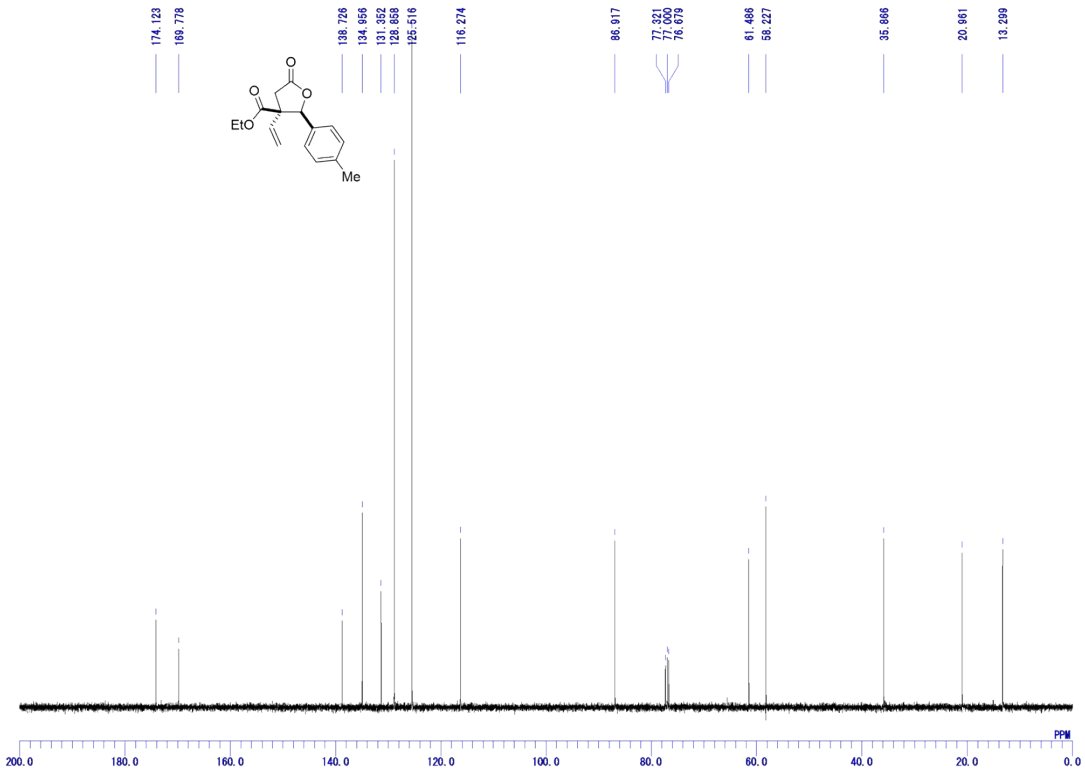
^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 14.0, 21.1, 35.9, 57.2, 62.3, 85.2, 117.1, 126.4, 128.9, 131.0, 133.2, 138.5, 171.3, 174.0.

HRMS (CI) m/z: calcd. for $C_{16}H_{19}O_4$ 275.1278 ($[M+H]^+$), found 275.1289.

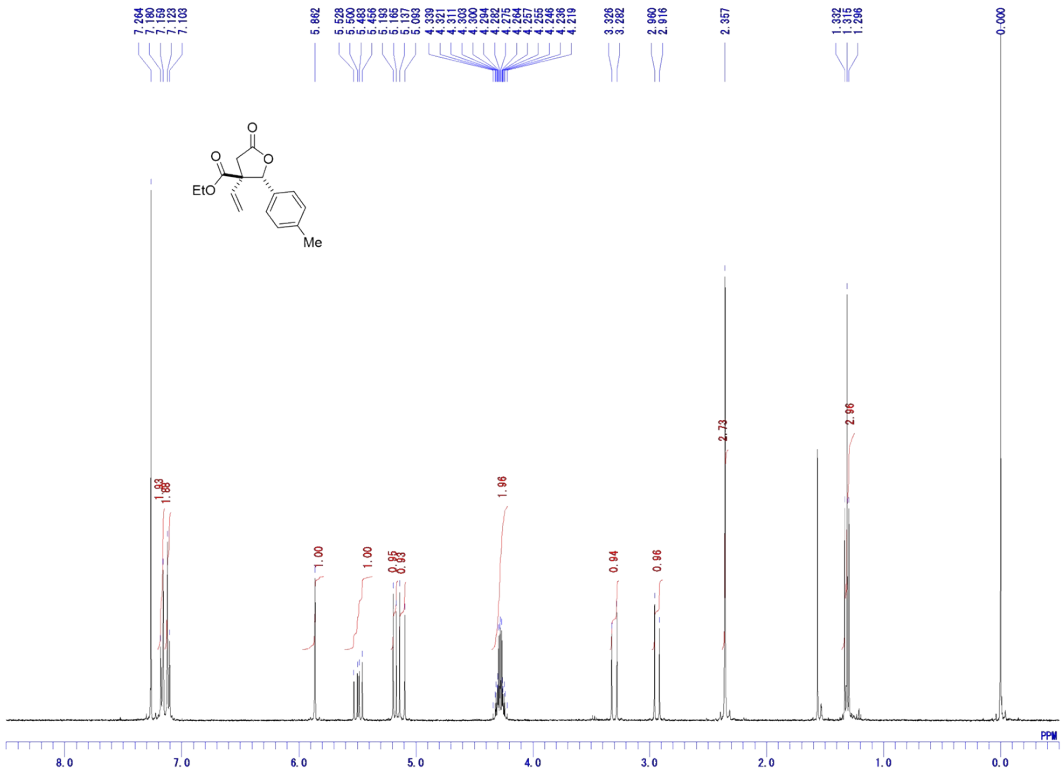
^{1}H NMR ($CDCl_3$, 400 MHz)



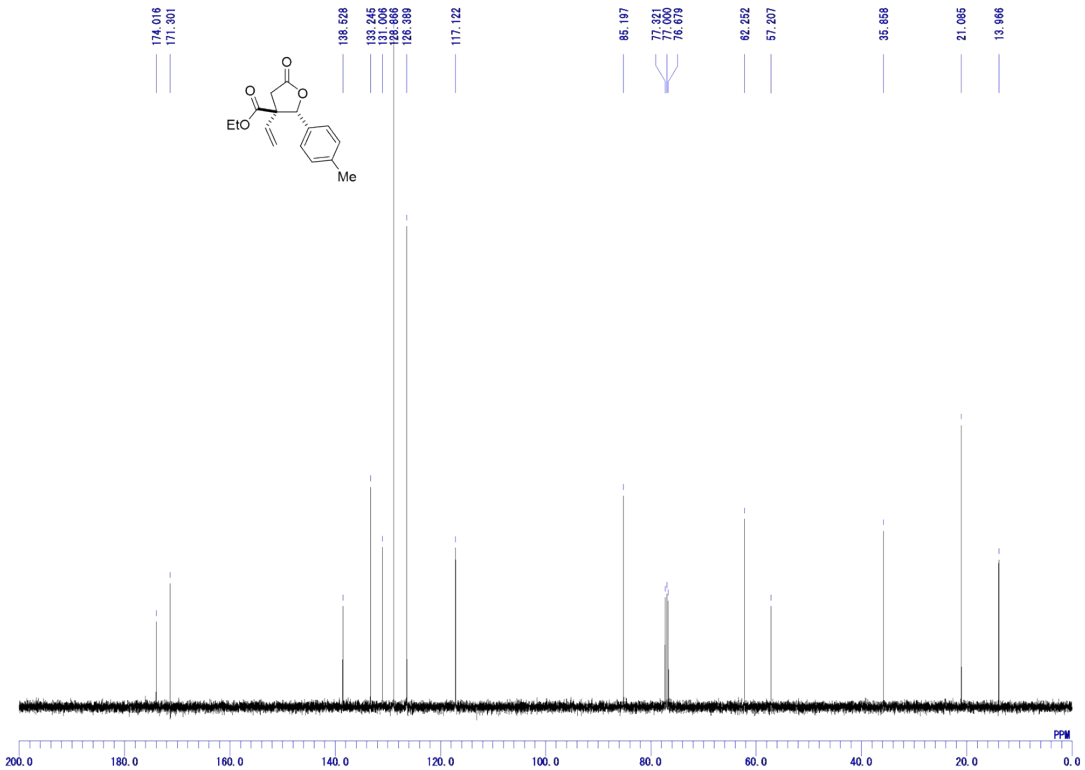
^{13}C NMR ($CDCl_3$, 100 MHz)



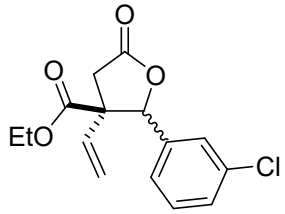
^{1}H NMR ($CDCl_3$, 400 MHz)



^{13}C NMR ($CDCl_3$, 100 MHz)



Ethyl 2-(3-chlorophenyl)-5-oxo-3-vinyltetrahydrofuran-3-carboxylate (4hf)



Major isomer (syn): Colorless oil.

R_f = 0.33 (hexane/EtOAc = 8:2).

IR (neat) 1724 cm^{-1} (C=O), 1791 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.99 (3H, t, J = 7.1 Hz), 2.91 (1H, d, J = 17.1 Hz), 3.21 (1H, d, J = 17.1 Hz), 3.76-3.92 (2H, m), 5.35 (1H, s), 5.38 (1H, d, J = 17.4 Hz), 5.45 (1H, d, J = 10.9 Hz), 6.36 (1H, dd, J = 17.6, 10.9 Hz), 7.19-7.17 (1H, m), 7.28-7.36 (3H, m).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 13.4, 36.1, 58.1, 61.7, 85.9, 116.9, 123.8, 125.8, 129.0, 129.6, 134.3, 134.3, 136.5, 169.6, 173.5.

HRMS (CI) m/z: calcd. for $C_{15}H_{16}ClO_4$ 295.0732 ($[M+H]^+$), found 295.0731.

Minor isomer (anti): Colorless oil.

R_f = 0.40 (hexane/EtOAc = 8:2).

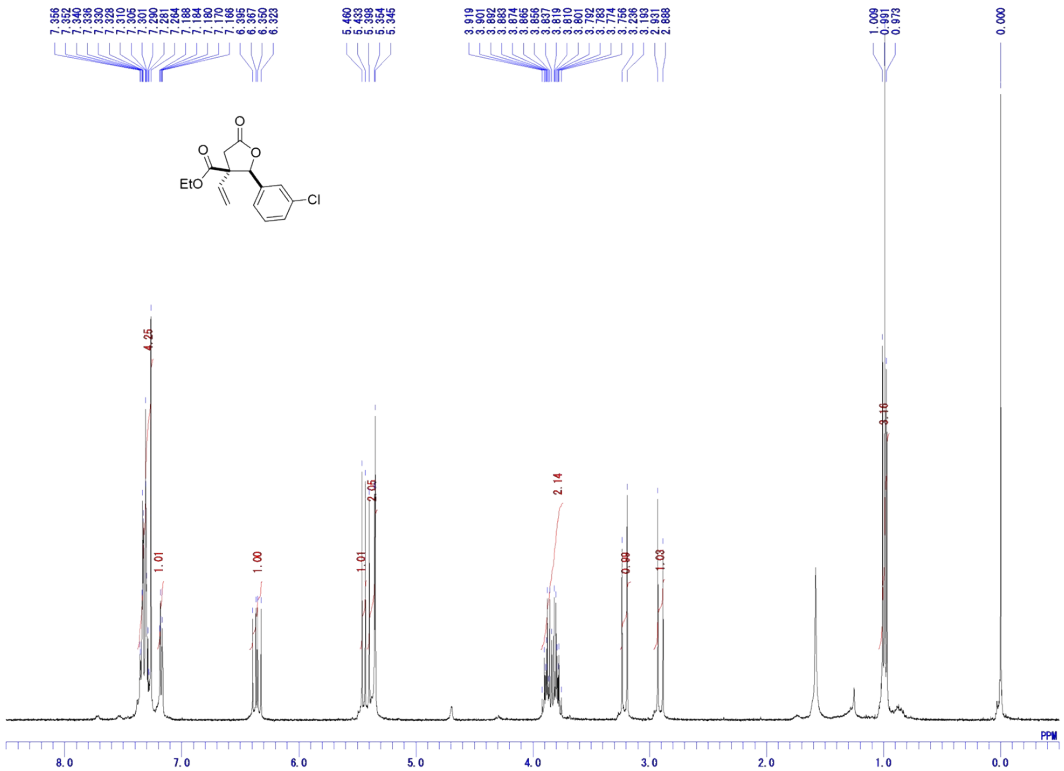
IR (neat) 1728 cm^{-1} (C=O), 1790 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.33 (3H, t, J = 7.1 Hz), 2.96 (1H, d, J = 17.4 Hz), 3.30 (1H, d, J = 17.4 Hz), 4.23-4.36 (2H, m), 5.15 (1H, d, J = 17.6 Hz), 5.23 (1H, d, J = 10.6 Hz), 5.46 (1H, dd, J = 17.5, 10.7 Hz), 5.85 (1H, s), 7.13-7.16 (1H, m), 7.28-7.35 (3H, m).

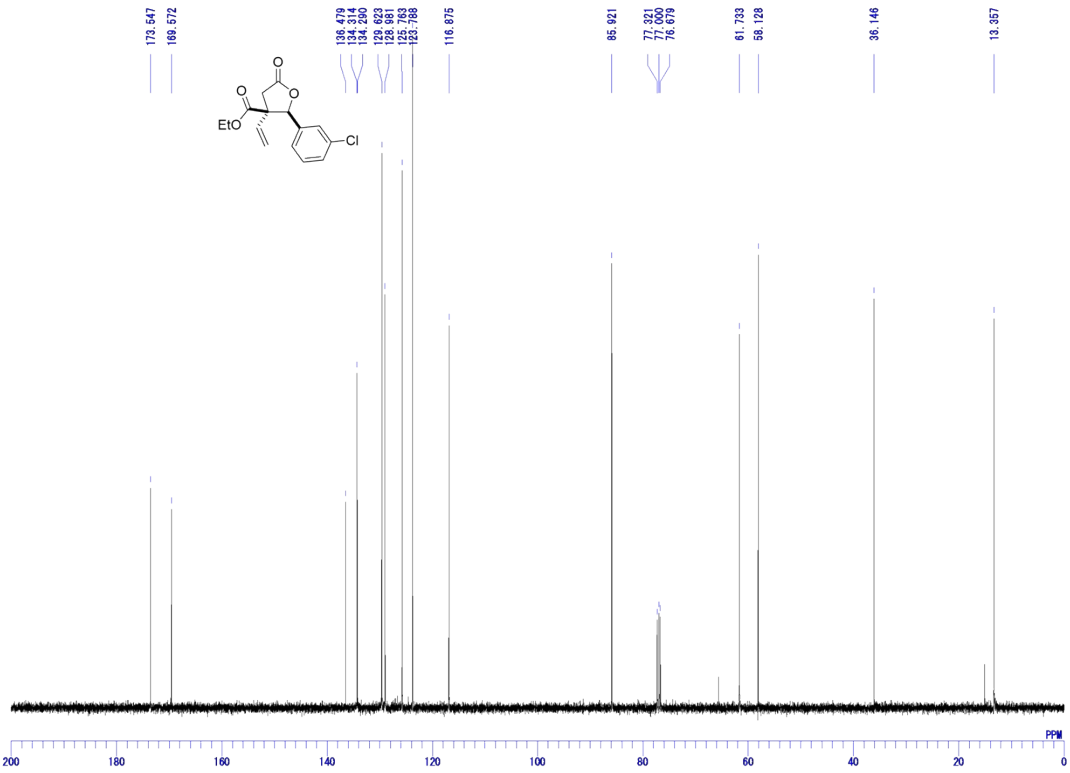
^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 13.9, 36.0, 57.0, 62.4, 84.0, 117.7, 124.7, 126.7, 128.8, 129.5, 132.7, 134.2, 136.2, 171.0, 173.4.

HRMS (CI) m/z: calcd. for $C_{15}H_{16}ClO_4$ 295.0732 ($[M+H]^+$), found 295.0739.

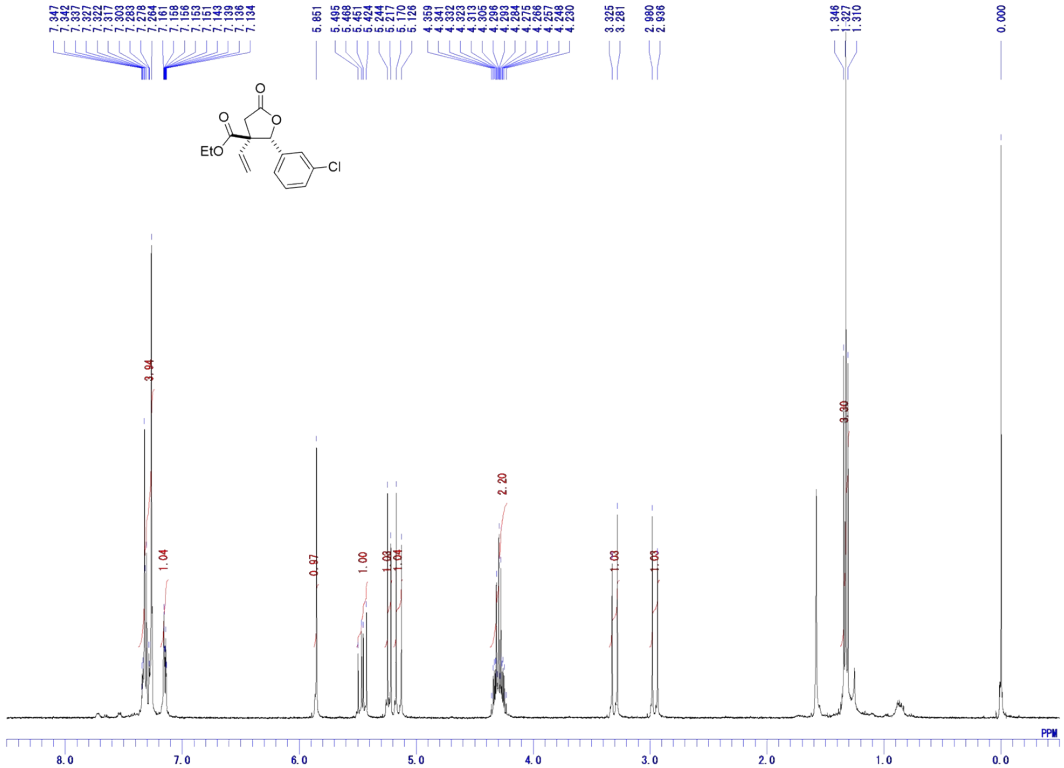
^{1}H NMR ($CDCl_3$, 400 MHz)



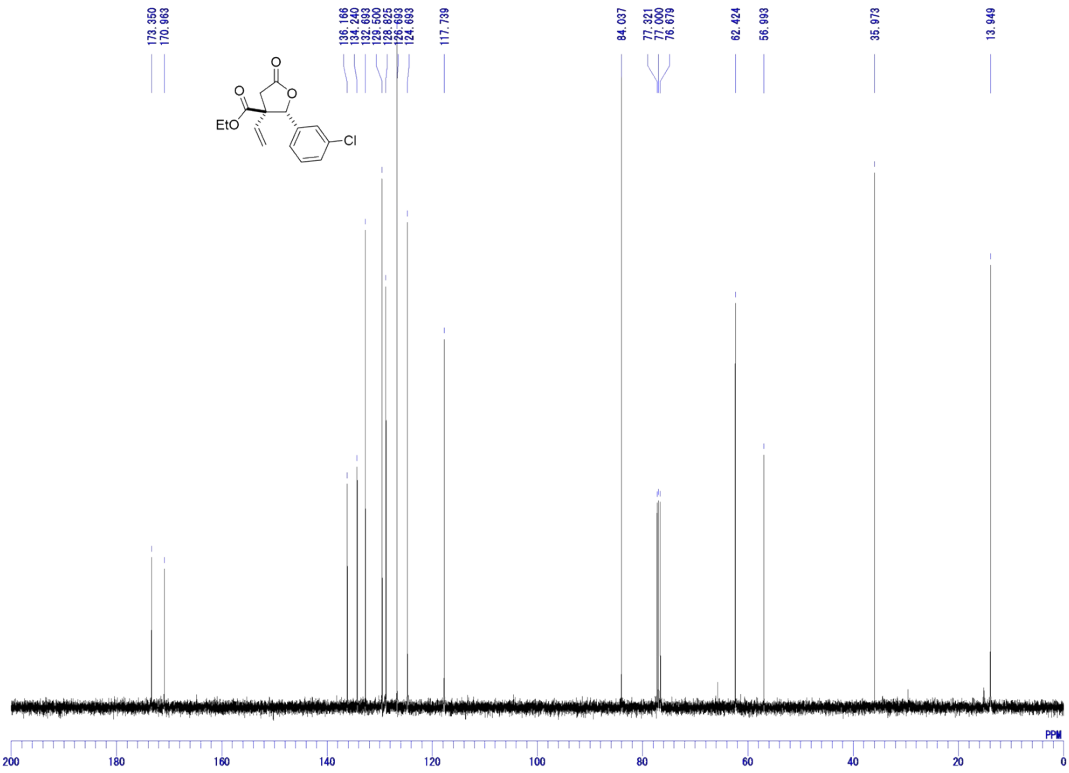
^{13}C NMR ($CDCl_3$, 100 MHz)



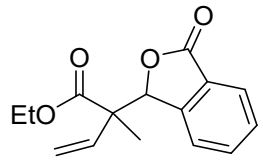
^{1}H NMR ($CDCl_3$, 400 MHz)



^{13}C NMR ($CDCl_3$, 100 MHz)



Ethyl 2-(3-chlorophenyl)-5-oxo-3-vinyltetrahydrofuran-3-carboxylate (4aq)



Major isomer: Colorless oil.

R_f = 0.38 (hexane/EtOAc = 8:2).

IR (neat) 1725 cm^{-1} (C=O), 1763 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.10 (3H, s), 1.29 (3H, t, J = 7.1 Hz), 4.27 (2H, dq, J = 7.2, 1.7 Hz), 5.24 (1H, d, J = 17.6 Hz), 5.31 (1H, d, J = 10.6 Hz), 5.91 (1H, s), 6.14 (1H, dd, J = 17.5, 10.7 Hz), 7.37 (1H, dd, J = 7.5, 0.7 Hz), 7.54 (1H, t, J = 7.5 Hz), 7.64 (1H, td, J = 7.5, 1.0 Hz), 7.91 (1H, d, J = 7.7 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 14.0, 14.7, 52.3, 61.7, 83.3, 119.0, 123.1, 125.7, 127.0, 129.5, 133.7, 135.2, 146.5, 170.0, 172.4.

HRMS (CI) m/z: calcd. for $C_{15}H_{16}ClO_4$ 261.1121 ($[M+H]^+$), found 261.1125.

Minor isomer: Colorless oil.

R_f = 0.35 (hexane/EtOAc = 8:2).

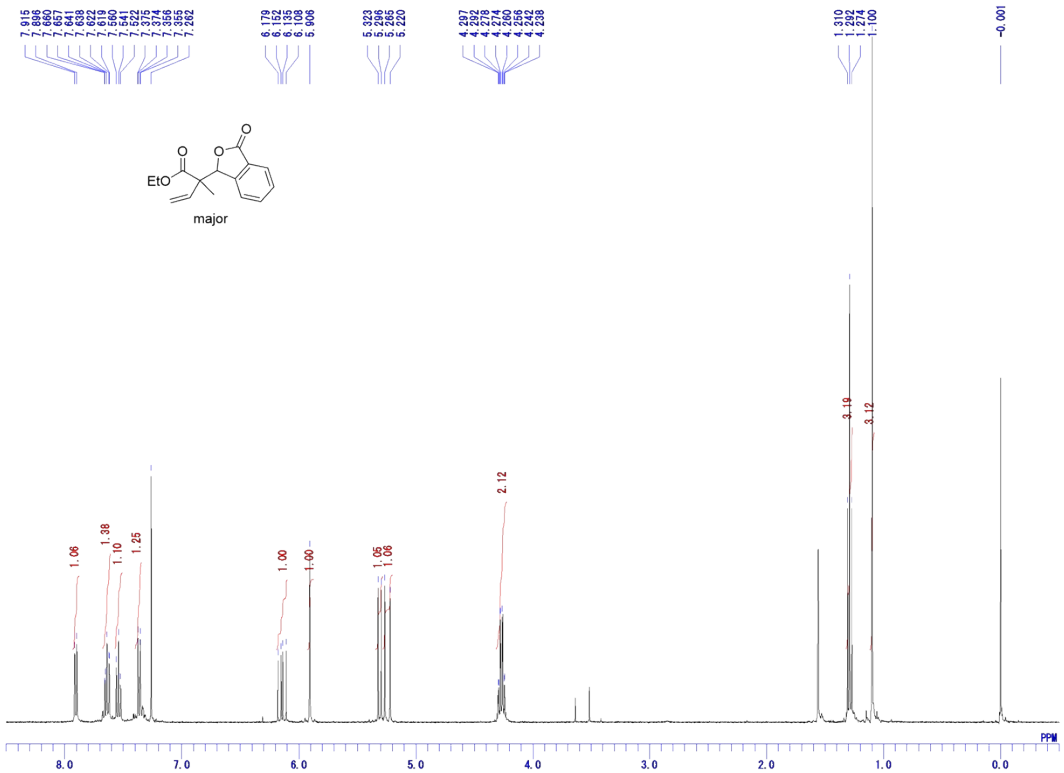
IR (neat) 1731 cm^{-1} (C=O), 1765 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.14 (3H, s), 1.32 (3H, t, J = 7.1 Hz), 4.28 (2H, q, J = 7.1 Hz), 5.32 (1H, d, J = 17.4 Hz), 5.32 (1H, d, J = 10.9 Hz), 5.91-5.98 (2H, m), 7.45 (1H, d, J = 7.7 Hz), 7.54 (1H, t, J = 7.4 Hz), 7.62 (1H, t, J = 7.5 Hz), 7.90 (1H, d, J = 7.5 Hz).

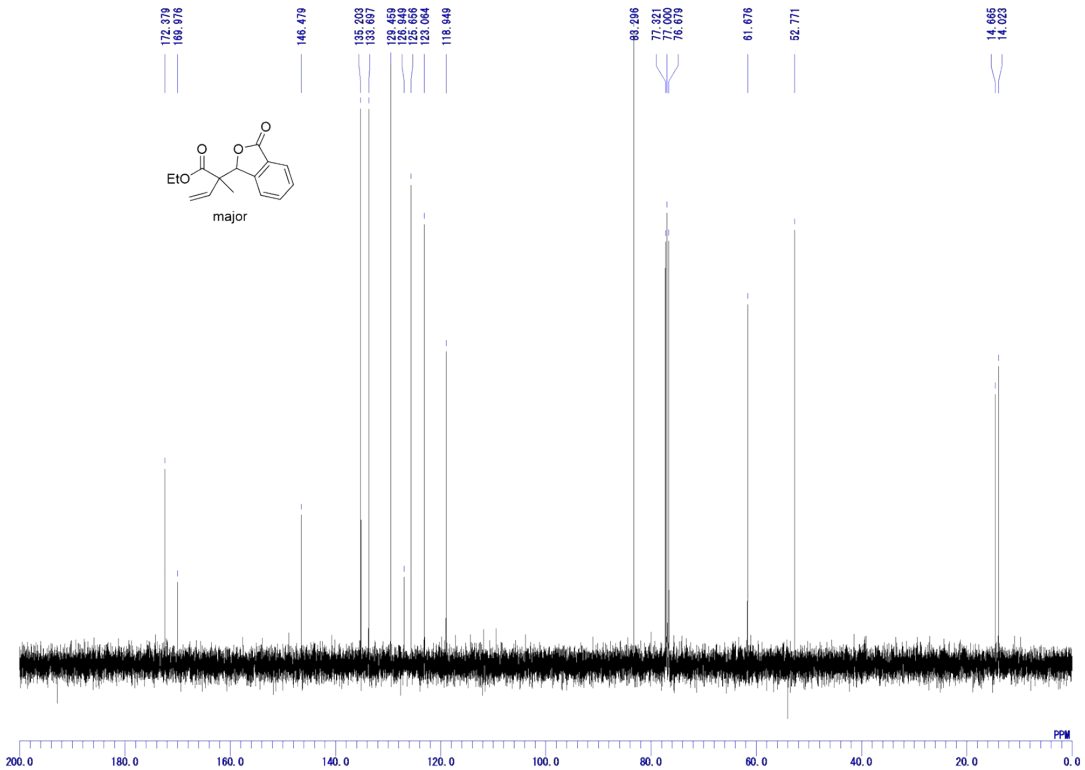
^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 13.8, 15.2, 52.7, 61.4, 83.7, 116.9, 122.7, 125.5, 126.8, 129.3, 134.0, 137.2, 146.6, 169.9, 172.2.

HRMS (CI) m/z: calcd. for $C_{15}H_{16}ClO_4$ 261.1121 ($[M+H]^+$), found 261.1121.

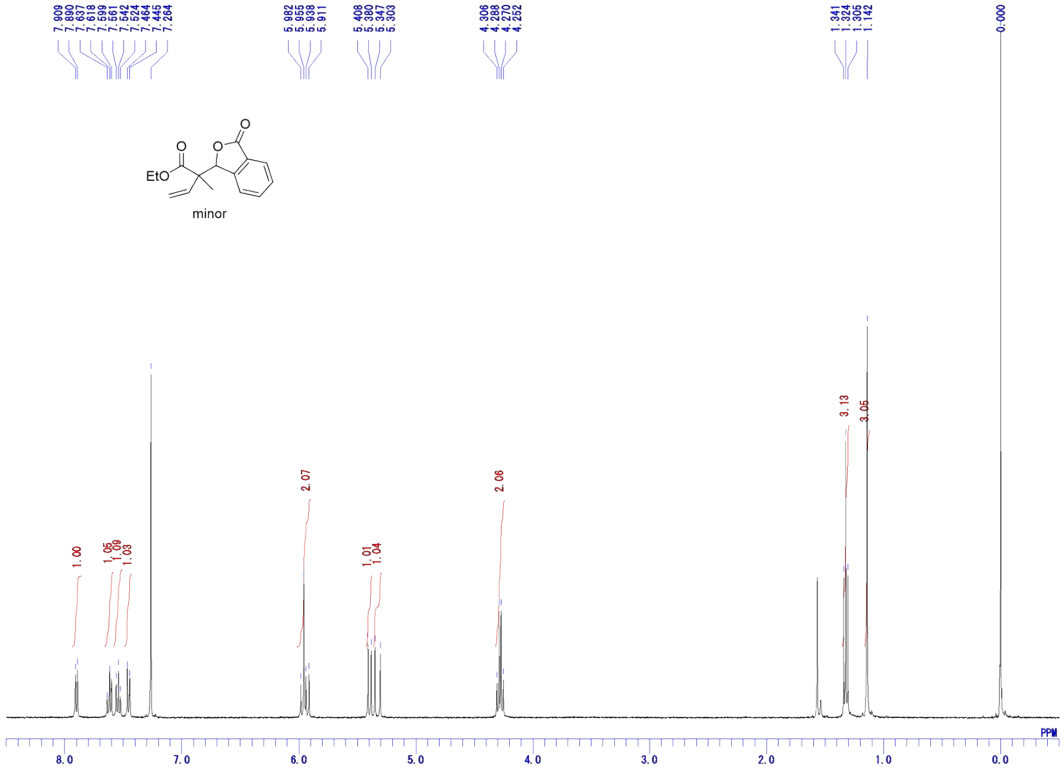
^{1}H NMR ($CDCl_3$, 400 MHz)



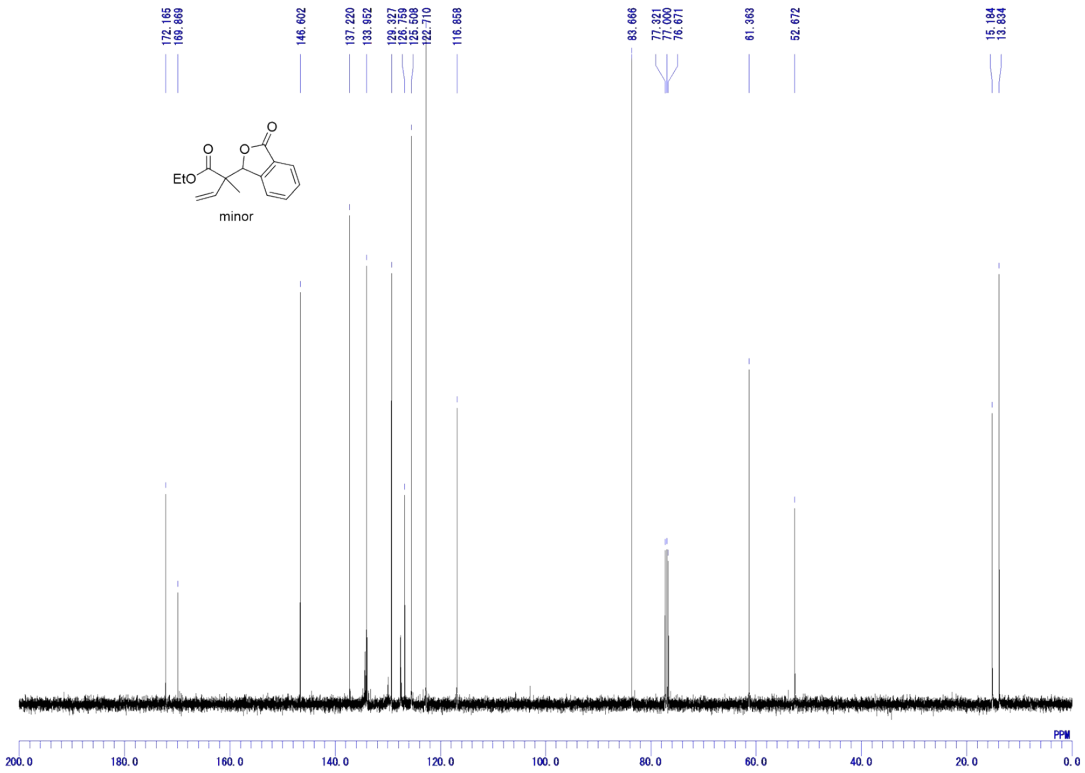
^{13}C NMR ($CDCl_3$, 100 MHz)



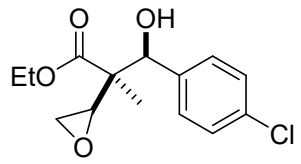
^{1}H NMR ($CDCl_3$, 400 MHz)



^{13}C NMR ($CDCl_3$, 100 MHz)



Ethyl 3-(4-chlorophenyl)-3-hydroxy-2-methyl-2-(oxiran-2-yl)propanoate (5ae)



Major isomer: White solid.

Mp: 96-98°C

R_f = 0.33 (hexane/EtOAc = 8:2).

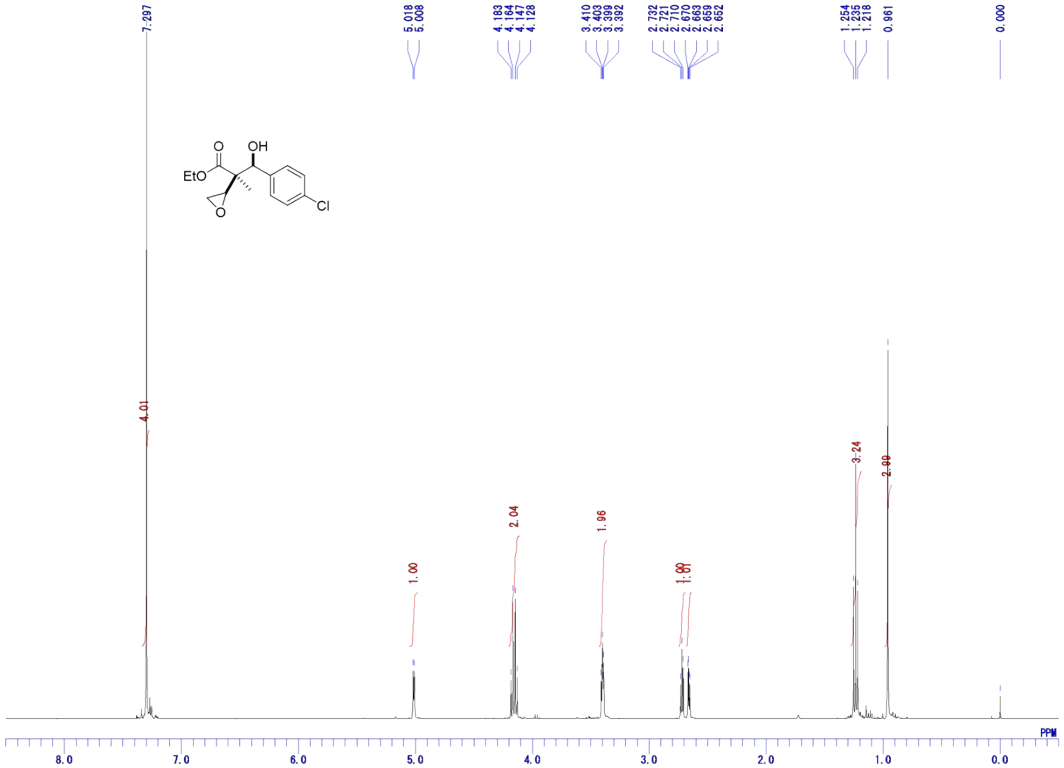
IR (neat) 3385 cm^{-1} (OH), 1722 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.96 (3H, s), 1.24 (3H, t, J = 7.1 Hz), 2.66 (1H, dd, J = 4.5, 2.8 Hz), 2.72 (1H, t, J = 4.3 Hz), 3.40 (1H, dd, J = 4.2, 2.8 Hz), 4.16 (2H, q, J = 7.2 Hz), 5.01 (1H, d, J = 3.9 Hz), 7.30 (4H, s).

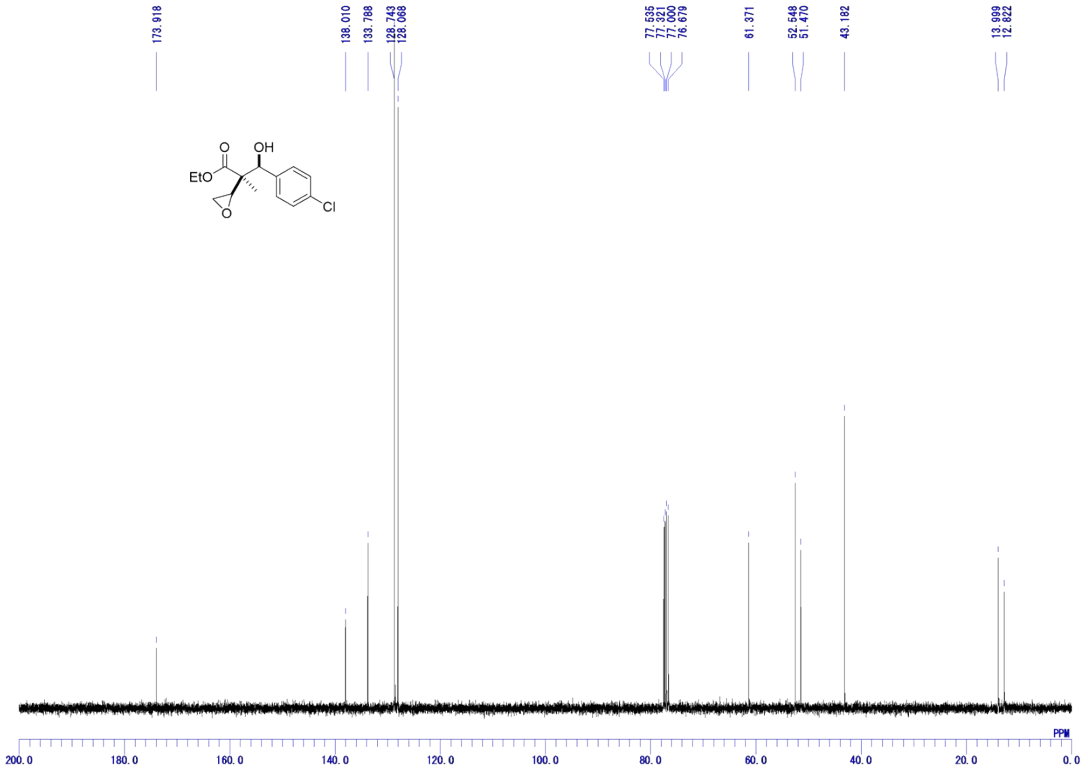
^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 12.8, 14.0, 43.2, 51.5, 52.6, 61.4, 77.5, 128.1, 128.7, 133.8, 138.0, 173.9.

HRMS (CI) m/z: calcd. for $C_{14}H_{18}ClO_4$ 285.0888 ($[M+H]^+$), found 285.0896.

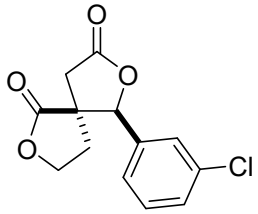
^{1}H NMR ($CDCl_3$, 400 MHz)



^{13}C NMR ($CDCl_3$, 100 MHz)



6-(3-chlorophenyl)-2,7-dioxaspiro[4.4]nonane-1,8-dione (6hf)



White solid.

Mp: 146-148°C

R_f = 0.20 (hexane/EtOAc = 5:5).

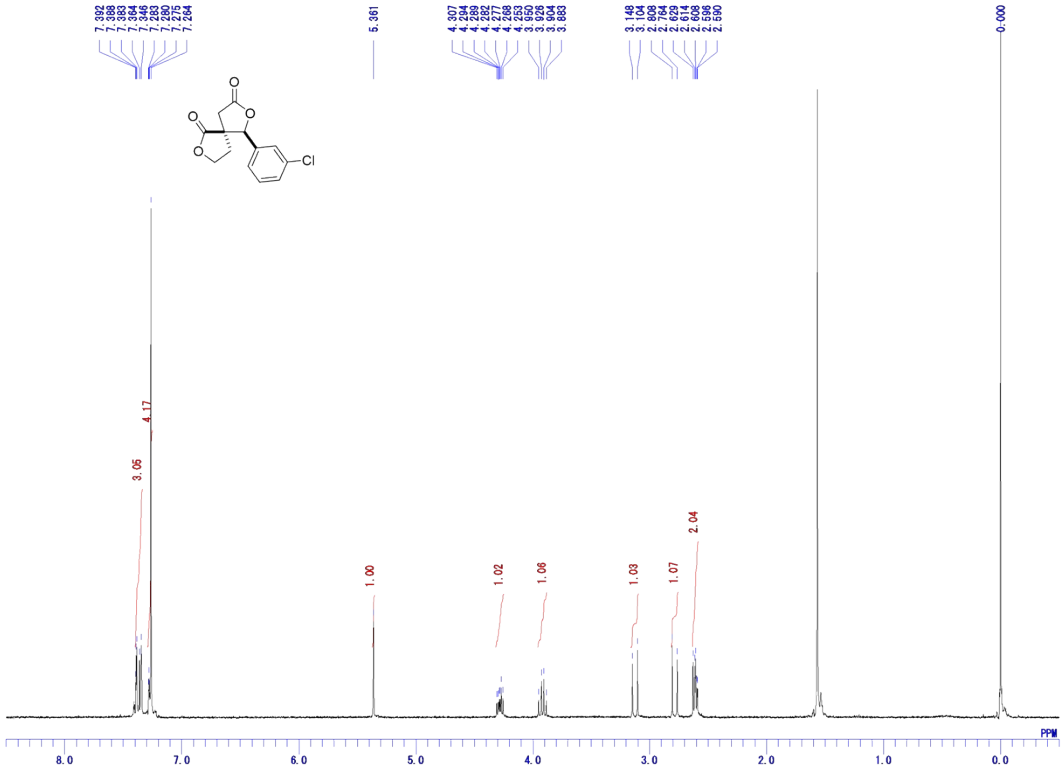
IR (neat) 1755 cm^{-1} (C=O), 1790 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.59-2.63 (2H, m), 2.79 (1H, d, J = 17.4 Hz), 3.13 (1H, d, J = 17.4 Hz), 3.92 (2H, q, J = 8.9 Hz), 4.25-4.31 (1H, m), 5.36 (1H, s), 7.28 (1H, m), 7.35-7.39 (3H, m).

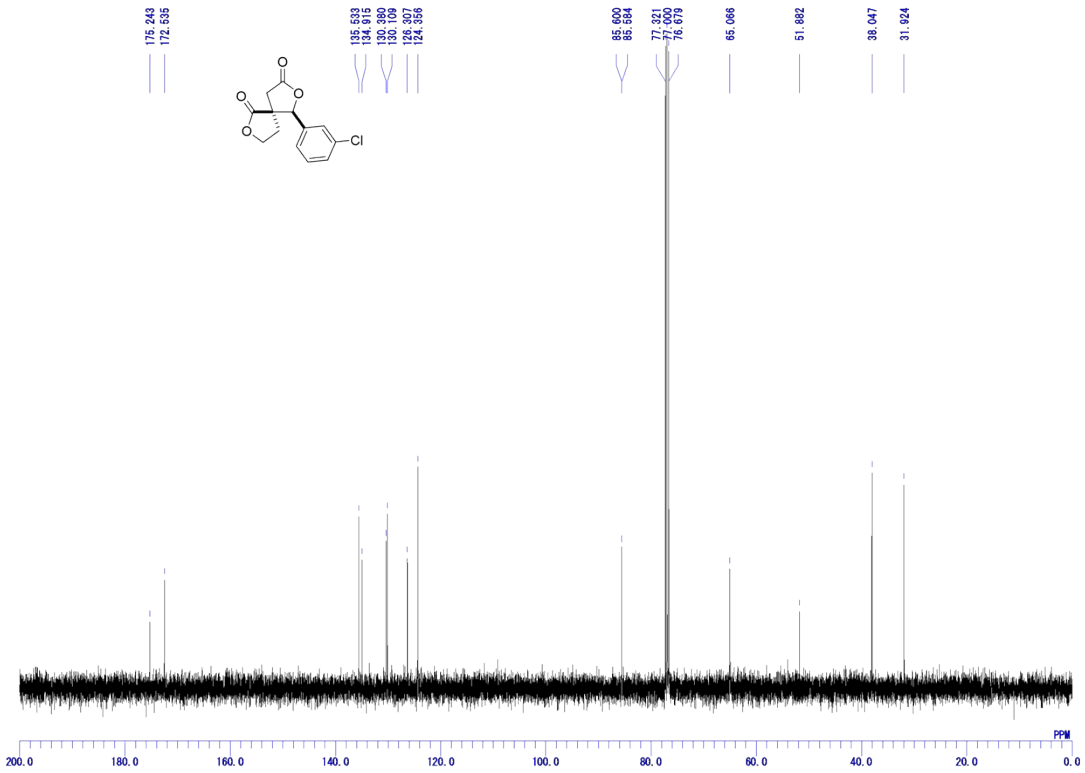
^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 31.9, 38.0, 51.9, 65.1, 85.6 (d), 124.4, 126.3, 130.1, 130.4, 134.9, 135.5, 172.5, 175.2.

HRMS (CI) m/z: calcd. for $C_{13}H_{12}ClO_4$ 267.0419 ($[M+H]^+$), found 267.0422.

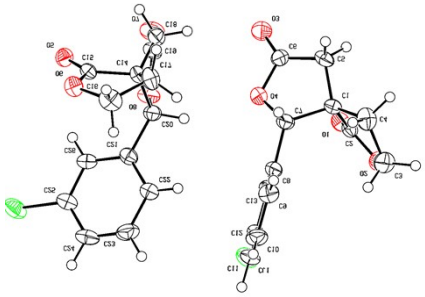
^{1}H NMR ($CDCl_3$, 400 MHz)



^{13}C NMR ($CDCl_3$, 100 MHz)



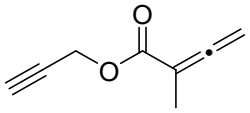
X-ray structure



CCDC: 2159477

Empirical formula	$C_{13}H_{11}ClO_4$
Formula weight	266.67
Temperature/K	173
Crystal system	triclinic
Space group	P-1
a/Å	6.3452(4)
b/Å	10.1024(6)
c/Å	19.4282(10)
α/°	84.271(4)
β/°	88.200(5)
γ/°	75.258(5)
Volume/Å^3	1198.35(12)
Z	4
ρ_{calc}g/cm^3	1.478
μ/mm^{-1}	2.881
F(000)	552.0
Crystal size/mm^3	0.068 × 0.059 × 0.048
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	9.092 to 149.046
Index ranges	$-6 \leq h \leq 7$, $-12 \leq k \leq 12$, $-23 \leq l \leq 24$
Reflections collected	12650
Independent reflections	4737 [R_{int} = 0.0420, R_{sigma} = 0.0437]
Data/restraints/parameters	4737/0/328
Goodness-of-fit on F^2	1.120
Final R indexes [I>=2σ (I)]	R_1 = 0.1282, wR_2 = 0.3923
Final R indexes [all data]	R_1 = 0.1337, wR_2 = 0.3947
Largest diff. peak/hole / e Å^{-3}	1.58/-0.59

Ethyl 5-oxo-2-phenyl-3-vinyltetrahydrofuran-3-carboxylate (1c)



Colorless oil.

R_f = 0.63 (hexane/EtOAc = 8:2).

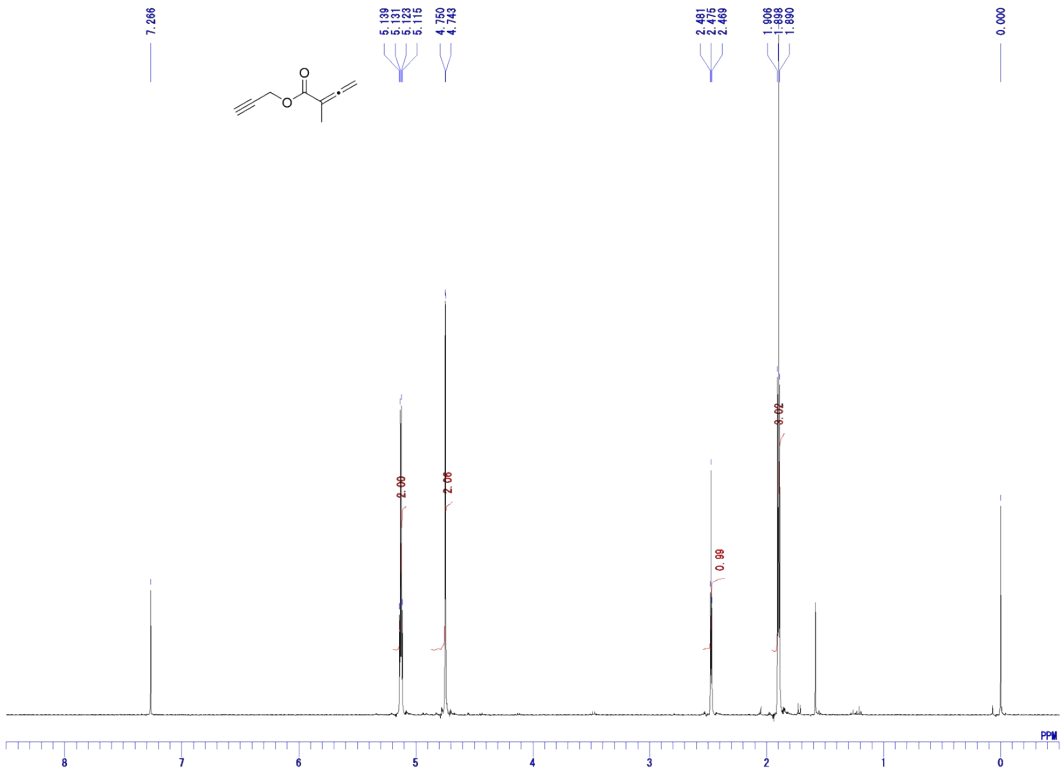
IR (neat) 1710 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.90 (3H, t, J = 3.1 Hz), 2.47 (1H, t, J = 2.4 Hz), 4.75 (2H, d, J = 2.7 Hz), 5.13 (2H, q, J = 3.1 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 14.5, 52.3, 74.7, 76.7, 78.2, 94.7, 166.6, 214.3.

HRMS (CI) m/z: calcd. for $C_8H_9O_2$ 137.0597 ($[M+H]^+$), found 137.0603.

^{1}H NMR ($CDCl_3$, 400 MHz)



^{13}C NMR ($CDCl_3$, 100 MHz)