Facile Access to *anti*-1,2-Diol Derivatives via Ir-catalyzed Asymmetric Hydrogenation of α-Alkoxy β-Ketoesters

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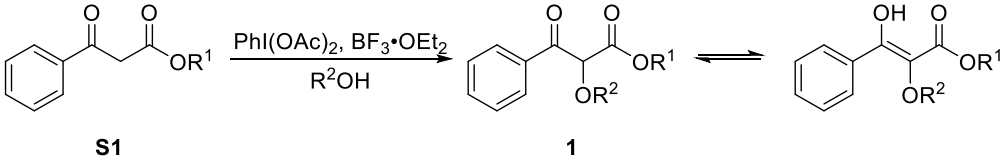
Contents

1. General Remarks

All reactions and manipulations which are sensitive to moisture or air were performed in an argon-filled glove box or using standard Schlenk techniques. Anhydrous MeOH ^{i}PrOH, MeCN, CH_2Cl_2, THF and EtOAc purchased from J&K were treated with bubbled argon before used. KO^{t}Bu, NaO^{t}Bu, KOMe, NaOMe, KOH, NaOH, Cs_2CO_3, K_2CO_3 and Na_2CO_3 were purchased from Sinopharm Chemical Reagent Co., Ltd. ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded with a Bruker ADVANCE III (400 MHz) spectrometer with $CDCl_3$ as the solvent. NMR chemical shifts are listed in ppm relative to $CHCl_3$ (7.26 ppm for ^{1}H, and 77.0 ppm for ^{13}C) or H_2O (4.79 ppm for ^{1}H). Data are reported as: multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant in hertz (Hz) and signal area integration in natural numbers. ^{13}C NMR analyses were run with decoupling. HPLC analyses were performed by Agilent 1290 UPLC using Daicel chiral column.

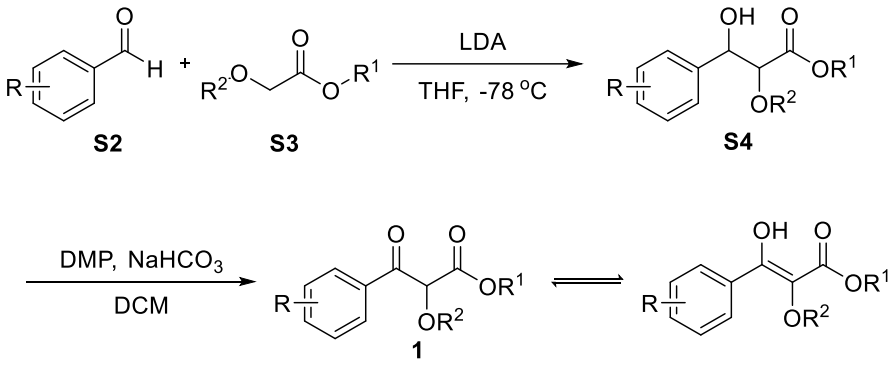
2. General Procedure for the Preparation of Substrate Compounds

Method A: [1]



To the solution of iodobenzene diacetate (1.1 equiv) in R^2OH (0.2 M) was added $BF_3{\cdot}OEt_2$ (1.1 equiv) under a nitrogen atmosphere. After the reaction mixture was stirred for 1 hour, the solution of *β*-ketoesters **S1** (a mixture of keto and enol forms; 1.0 equiv) in R^2OH (5 M) was dropwise added. The reaction mixture was stirred for 5 hours, quenched with saturated aqueous $NaHCO_3$, and evaporated in vacuo. The resulting mixture was extracted with EtOAc (× 3). The combined organic layers were dried over Na_2SO_4 and evaporated in vacuo. The residue was purified by flash column chromatography to give the corresponding *α*-methoxy-*β*-ketoesters **1**.

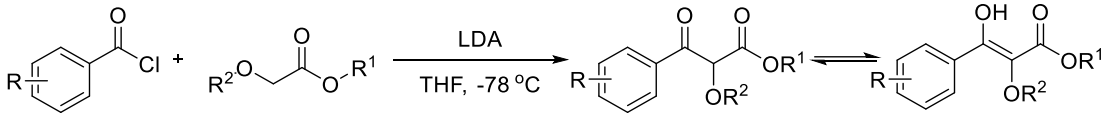
Method B:[2]



To a solution of **S3** (10 mmol) in anhydrous THF (10 mL) was added a solution of LDA in THF (2.0 M, 12.0 mL, 12 mmol) dropwise under Ar at -78 °C. After 15 min at -78 °C, **S2** (12 mmol, 1.2 equiv) was added dropwise. The reaction mixture was stirred for 5 hours, quenched with 1 M NH_4Cl, and evaporated in vacuo. The resulting mixture was extracted with EtOAc (× 3). The combined organic layers were dried over Na_2SO_4 and evaporated in vacuo. The residue was purified by flash column chromatography to give the alcohol **S4**.

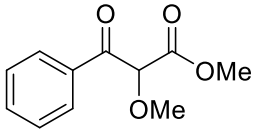
To a solution of the **S4** (5 mmol) in DCM, Dess-Martin periodinane (8 mmol) and $NaHCO_3$ (15 mmol) were added successively. The solution was allowed to stir at rt for 3 h. Then water was added, and the obtained suspension was stirred for another 1 h. After the reaction was finished, the reaction mixture was extracted with DCM (3 × 30 mL). The combined organic phase was dried with Na_2SO_4 and evaporated in vacuum. Purification of the residue by silica gel afforded the desired *α*-methoxy-*β*-ketoesters **1**.

Method C:



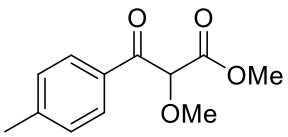
S5 **S3** **1**

To a solution of **S3** (10 mmol) in anhydrous THF (10 mL) was added a solution of LDA in THF (2.0 M, 12.0 mL, 12 mmol) dropwise under Ar at -78 °C. After 15 min at -78 °C, **S5** (12 mmol, 1.2 equiv) was added dropwise. The reaction mixture was stirred for 5 hours, quenched with 1 M NH_4Cl, and evaporated in vacuo. The resulting mixture was extracted with EtOAc (× 3). The combined organic layers were dried over Na_2SO_4 and evaporated in vacuo. The residue was purified by flash column chromatography to give the desired*α*-methoxy-*β*-ketoesters **1**.



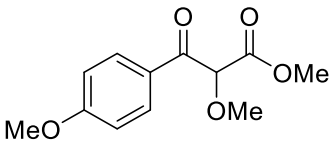
Methyl 2-methoxy-3-oxo-3-phenylpropanoate (**1a**)

Prepared according to Method A, pale yellow oil, 3.64 g, 87% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.65 – 7.57 (m, 1H), 7.48 (ddd, *J* = 8.6, 6.7, 1.2 Hz, 2H), 4.96 (s, 1H), 3.78 (s, 3H), 3.54 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.4, 167.9, 134.0, 134.0, 129.4, 128.7, 85.0, 58.7, 52.7. HRMS (ESI) m/z calcd. for $C_{11}H_{13}O_4$ $[M+H]^+$: 209.0808, found: 209.0810.



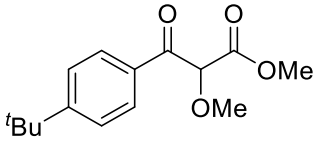
Methyl 2-methoxy-3-(4-methoxyphenyl)-3-oxopropanoate (**1b**)

Prepared according to Method B, pale yellow oil, 1.45 g, 64% yield over two steps.[1]H NMR (400 MHz, $CDCl_3$) δ 8.05 – 7.90 (m, 2H), 7.33 – 7.20 (m, 2H), 4.94 (s, 1H), 3.77 (s, 3H), 3.52 (s, 3H), 2.42 (s, 3H). [13]C NMR (101 MHz, $CDCl_3$) δ 191.9, 168.0, 145.1, 131.5, 129.5, 129.4, 85.0, 58.6, 52.7, 21.7. HRMS (ESI) m/z calcd. for $C_{12}H_{15}O_4$ $[M+H]^+$: 223.0965, found: 223.0965.



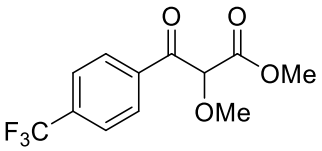
Methyl 2-methoxy-3-oxo-3-(p-tolyl)propanoate (**1c**)

Prepared according to Method B, white solid, 1.68 g, 71% yield over two steps. [1]H NMR (400 MHz, $CDCl_3$) δ 8.18 – 7.97 (m, 2H), 7.04 – 6.87 (m, 2H), 4.91 (s, 1H), 3.88 (s, 3H), 3.77 (s, 3H), 3.52 (s, 3H). [13]C NMR (101 MHz, $CDCl_3$) δ 190.8, 168.2, 164.2, 131.9, 127.0, 113.9, 85.2, 58.5, 55.5, 52.7. HRMS (ESI) m/z calcd. for $C_{12}H_{15}O_5$ $[M+H]^+$: 239.0914, found: 239.0914.



Methyl 3-(4-(tert-butyl)phenyl)-2-methoxy-3-oxopropanoate (**1d**)

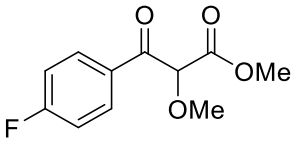
Prepared according to Method C, white soild, 1.25 g, 47% yield. [1]H NMR (400 MHz, $CDCl_3$) δ 8.07 – 7.96 (m, 2H), 7.56 – 7.41 (m, 2H), 4.95 (s, 1H), 3.78 (s, 3H), 3.53 (s, 3H), 1.34 (s, 9H). [13]C NMR (101 MHz, $CDCl_3$) δ 191.9, 168.1, 158.0, 131.4, 129.4, 125.7, 85.1, 58.6, 52.7, 35.2, 31.0. HRMS (ESI) m/z calcd. for $C_{15}H_{21}O_4$ $[M+H]^+$: 265.1434, found: 265.1434.



Methyl 3-(4-fluorophenyl)-2-methoxy-3-oxopropanoate (**1e**)

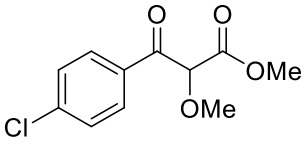
Prepared according to Method B, pale yellow oil, 2.07 g, 75% yield over two steps. [1]H NMR (400 MHz, $CDCl_3$) δ 8.19 (dt, *J* = 8.1, 0.8 Hz, 2H), 7.78 – 7.71 (m, 2H), 4.92 (s, 1H), 3.79 (s, 3H), 3.55 (s, 3H). [13]C NMR (101 MHz, $CDCl_3$) δ 191.6, 167.6, 136.5,

135.1 (q, J = 32.8 Hz), 129.8, 125.7 (q, J = 3.7 Hz), 123.4 (q, J = 272.7 Hz), 85.3, 58.9, 52.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.35. HRMS (ESI) m/z calcd. for $C_{12}H_{12}F_3O_4$ $[M+H]^+$: 277.0682, found: 277.0683.



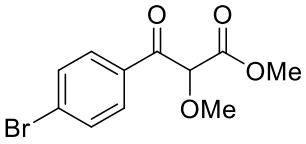
Methyl 3-(4-fluorophenyl)-2-methoxy-3-oxopropanoate (**1f**)

Prepared according to Method B, pale yellow oil, 1.77 g, 78% yield over two steps. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 – 8.07 (m, 2H), 7.21 – 7.07 (m, 2H), 4.89 (s, 1H), 3.78 (s, 3H), 3.53 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.8, 167.9, 166.2 (d, J = 256.9 Hz), 132.3 (d, J = 9.5 Hz), 130.3 (d, J = 3.0 Hz), 115.9 (d, J = 22.0 Hz), 85.4, 58.7, 52.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -102.93. HRMS (ESI) m/z calcd. for $C_{11}H_{12}FO_4$ $[M+H]^+$: 277.0714, found: 227.0715.



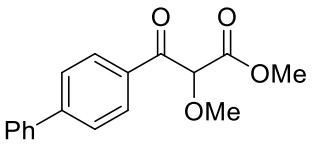
Methyl 3-(4-chlorophenyl)-2-methoxy-3-oxopropanoate (**1g**)

Prepared according to Method B, pale yellow oil, 1.48 g, 61% yield over two steps. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 8.6 Hz, 2H), 7.45 (d, J = 8.6 Hz, 2H), 4.88 (s, 1H), 3.78 (s, 3H), 3.53 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.3, 167.8, 140.7, 132.2, 130.9, 129.0, 85.3, 58.7, 52.8. HRMS (ESI) m/z calcd. for $C_{11}H_{12}ClO_4$ $[M+H]^+$: 243.0419, found: 243.0420.



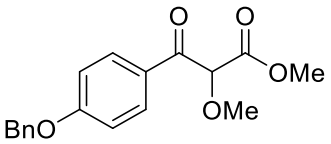
Methyl 3-(4-bromophenyl)-2-methoxy-3-oxopropanoate (**1h**)

Prepared according to Method B, pale yellow oil, 1.60 g, 56% yield over two steps. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 – 7.89 (m, 2H), 7.72 – 7.54 (m, 2H), 4.88 (s, 1H), 3.78 (s, 3H), 3.53 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.5, 167.7, 132.6, 132.0, 130.9, 129.5, 85.3, 58.8, 52.9. HRMS (ESI) m/z calcd. for $C_{11}H_{12}CBrO_4$ $[M+H]^+$: 286.9913, found: 286.9915.



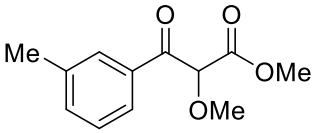
Methyl 3-(4-(benzyloxy)phenyl)-2-methoxy-3-oxopropanoate (**1i**)

Prepared according to Method C, pale yellow oil, 1.99 g, 70% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.19 – 8.13 (m, 2H), 7.73 – 7.67 (m, 2H), 7.65 – 7.60 (m, 2H), 7.52 – 7.44 (m, 2H), 7.44 – 7.38 (m, 1H), 4.98 (s, 1H), 3.80 (s, 3H), 3.56 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 192.0, 168.0, 146.7, 139.6, 132.6, 130.0, 129.0, 128.4, 127.3, 127.3, 85.2, 58.7, 52.8. HRMS (ESI) m/z calcd. for $C_{17}H_{17}O_4$ $[M+H]^+$: 285.1121, found: 285.1122.



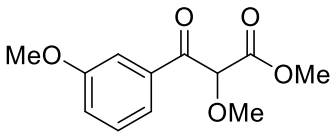
Methyl 3-([1,1'-biphenyl]-4-yl)-2-methoxy-3-oxopropanoate (**1j**)

Prepared according to Method B, pale yellow oil, 2.55 g, 81% yield over two steps. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.9 Hz, 2H), 7.48 – 7.30 (m, 5H), 7.01 (d, *J* = 8.9 Hz, 2H), 5.13 (s, 2H), 4.90 (s, 1H), 3.76 (s, 3H), 3.51 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.8, 168.2, 163.4, 136.00, 131.9, 128.7, 128.3, 127.5, 127.1, 114.7, 85.2, 70.2, 58.5, 52.7. HRMS (ESI) m/z calcd. for $C_{18}H_{19}O_5$ $[M+H]^+$: 315.1127, found: 315.1122.



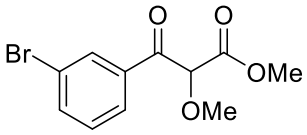
Methyl 2-methoxy-3-oxo-3-(m-tolyl)propanoate (**1k**)

Prepared according to Method B, pale yellow oil, 1.12 g, 50% yield over two steps. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.8 Hz, 2H), 7.42 (d, *J* = 7.6 Hz, 1H), 7.39 – 7.33 (m, 1H), 4.97 (s, 1H), 3.77 (s, 3H), 3.53 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 192.5, 168.0, 138.6, 134.9, 134.0, 129.7, 128.5, 126.6, 84.9, 58.6, 52.7, 21.3. HRMS (ESI) m/z calcd. for $C_{12}H_{15}O_4$ $[M+H]^+$: 223.0965, found: 223.0965.



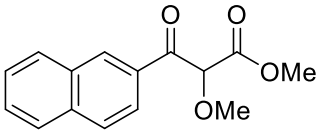
Methyl 2-methoxy-3-(3-methoxyphenyl)-3-oxopropanoate (**1l**)

Prepared according to Method B, pale yellow oil, 1.48 g, 62% yield over two steps. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.67 (ddd, *J* = 7.7, 1.6, 0.9 Hz, 1H), 7.58 (dd, *J* = 2.7, 1.6 Hz, 1H), 7.38 (t, *J* = 8.0 Hz, 1H), 7.15 (ddd, *J* = 8.3, 2.7, 0.9 Hz, 1H), 4.95 (s, 1H), 3.86 (s, 3H), 3.78 (s, 3H), 3.54 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 192.1, 167.9, 159.8, 135.2, 129.7, 122.1, 120.9, 113.1, 84.9, 58.7, 55.4, 52.8. HRMS (ESI) m/z calcd. for $C_{12}H_{15}O_5$ $[M+H]^+$: 239.0914, found: 239.0914.



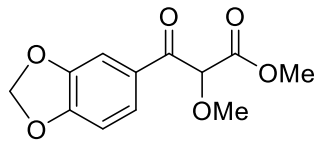
Methyl 3-(3-bromophenyl)-2-methoxy-3-oxopropanoate (**1m**)

Prepared according to Method B, pale yellow oil, 2.20 g, 77% yield over two steps. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.17 (t, *J* = 1.8 Hz, 1H), 8.00 (dt, *J* = 7.9, 1.3 Hz, 1H), 7.71 (ddd, *J* = 8.0, 2.0, 1.0 Hz, 1H), 7.34 (t, *J* = 7.9 Hz, 1H), 4.89 (s, 1H), 3.78 (s, 3H), 3.53 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 191.23, 167.64, 136.92, 135.65, 132.27, 130.27, 128.08, 123.00, 85.07, 58.85, 52.92. HRMS (ESI) m/z calcd. for $C_{11}H_{11}BrO_4$ $[M+H]^+$: 286.9913, found: 286.9914.



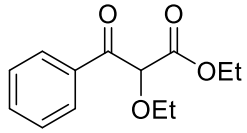
Methyl 2-methoxy-3-(naphthalen-2-yl)-3-oxopropanoate (**1n**)

Prepared according to Method C, pale yellow oil, 1.60 g, 62% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.69 – 8.66 (m, 1H), 8.07 (dd, *J* = 8.6, 1.8 Hz, 1H), 8.00 (dd, *J* = 8.5, 1.3 Hz, 1H), 7.93 – 7.83 (m, 2H), 7.62 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 7.56 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 5.07 (s, 1H), 3.78 (s, 3H), 3.58 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 192.4, 168.0, 136.0, 132.4, 131.9, 131.3, 130.0, 129.1, 128.6, 127.8, 126.9, 124.3, 85.2, 58.7, 52.8. HRMS (ESI) m/z calcd. for $C_{115}H_{15}O_4$ $[M+H]^+$: 259.0965, found: 259.0965.



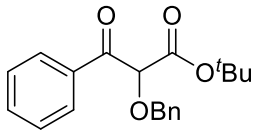
Methyl 3-(benzo[d][1,3]dioxol-5-yl)-2-methoxy-3-oxopropanoate (**1o**)

Prepared according to Method B, pale yellow oil, 1.14 g, 45% yield over two steps. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.53 (d, *J* = 1.8 Hz, 1H), 6.86 (d, *J* = 8.2 Hz, 1H), 6.06 (s, 2H), 4.88 (s, 1H), 3.78 (s, 3H), 3.52 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.4, 168.1, 152.6, 148.2, 128.6, 126.4, 108.9, 108.1, 102.0, 85.2, 58.6, 52.7. HRMS (ESI) m/z calcd. for $C_{15}H_{15}O_4$ $[M+H]^+$: 253.0707, found: 253.0707.



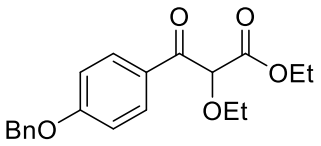
Ethyl 2-ethoxy-3-oxo-3-phenylpropanoate (**1p**)

Prepared according to Method A, pale yellow oil, 2.06 g, 87% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (dd, *J* = 8.4, 1.4 Hz, 2H), 7.70 – 7.54 (m, 1H), 7.47 (dd, *J* = 8.4, 7.1 Hz, 2H), 5.01 (s, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.83 – 3.71 (m, 1H), 3.71 – 3.59 (m, 1H), 1.27 (t, *J* = 7.0 Hz, 3H), 1.19 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.8, 167.8, 134.2, 133.8, 129.4, 128.6, 83.7, 66.9, 61.8, 15.1, 13.9. HRMS (ESI) m/z calcd. for $C_{15}H_{15}O_4$ $[M+H]^+$: 237.1121, found: 237.1122.



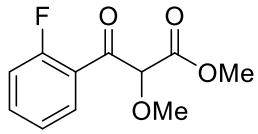
Tert-butyl 2-(benzyloxy)-3-oxo-3-phenylpropanoate (**1q**)

Prepared according to Method B, white solid, 2.54 g, 73% yield over two steps. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.2 Hz, 2H), 7.60 – 7.53 (m, 1H), 7.44 (dd, *J* = 8.4, 7.2 Hz, 2H), 7.38 – 7.28 (m, 5H), 4.94 (s, 1H), 4.72 (q, *J* = 11.7 Hz, 2H), 1.37 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 192.9, 166.6, 136.4, 134.4, 133.6, 129.3, 128.5, 128.5, 128.3, 128.2, 83.2, 82.5, 72.6, 27.8. HRMS (ESI) m/z calcd. for $C_{20}H_{22}NaO_4$ $[M+Na]^+$: 349.1410, found: 349.1410.



Ethyl 3-(4-(benzyloxy)phenyl)-2-ethoxy-3-oxopropanoate (**1r**)

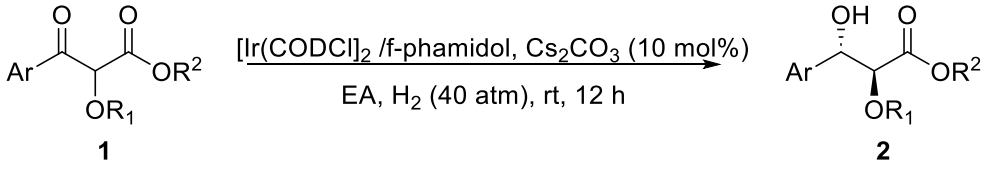
Prepared according to Method B, pale yellow oil, 2.26 g, 66% yield over two steps. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 – 8.04 (m, 2H), 7.52 – 7.27 (m, 5H), 7.01 (d, *J* = 9.0 Hz, 2H), 5.13 (s, 2H), 4.95 (s, 1H), 4.22 (qd, *J* = 7.1, 1.0 Hz, 2H), 3.78 – 3.67 (m, 1H), 3.67 – 3.52 (m, 1H), 1.27 (t, *J* = 7.0 Hz, 3H), 1.20 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 191.3, 168.0, 163.2, 136.0, 131.9, 128.7, 128.3, 127.5, 127.3, 114.6, 83.9, 70.2, 66.7, 61.8, 15.1, 14.0. HRMS (ESI) m/z calcd. for $C_{20}H_{23}O_5$ $[M+H]^+$: 343.1540, found: 343.1542.



Methyl 3-(2-fluorophenyl)-2-methoxy-3-oxopropanoate (**1s**)

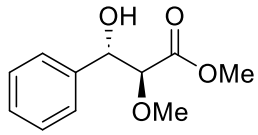
Prepared according to Method B, pale yellow oil, 1.44 g, 63% yield over two steps. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (td, *J* = 7.5, 1.9 Hz, 1H), 7.50 (dddd, *J* = 8.3, 7.2, 5.2, 1.9 Hz, 1H), 7.19 (td, *J* = 7.6, 1.1 Hz, 1H), 7.12 – 7.04 (m, 1H), 4.96 (s, 1H), 3.74 (s, 3H), 3.48 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.39 (d, *J* = 3.7 Hz), 166.54, 160.64 (d, *J* = 255.1 Hz), 134.39 (d, *J* = 9.3 Hz), 130.24 (d, *J* = 2.5 Hz), 123.69 (d, *J* = 3.4 Hz), 122.48 (d, *J* = 13.0 Hz), 115.49 (d, *J* = 23.4 Hz), 84.86 (d, *J* = 5.8 Hz), 58.44, 51.65. ^{19}F NMR (377 MHz, $CDCl_3$) δ -110.12. HRMS (ESI) m/z calcd. for $C_{11}H_{12}FO_4$ $[M+H]^+$: 227.0714, found: 227.0715.

2. General Procedure for Asymmetric Hydrogenation



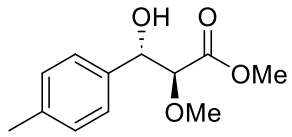
1 **2**

To a 4.0 mL vial equipped with α-methoxy-β-ketoester **1** (0.2 mmol, 1.0 eq.) was added the Ir/f-phamidol-precatalyst (1.5 mg, 2.0×10^{-3} mmol, 0.01 eq.), Cs_2CO_3 (6.6 mg, 0.02 mmol, 10 mol%.) and anhydrous EtOAc (1.0 mL) in an argon-filled glovebox. The autoclave was quickly purged with hydrogen gas for three times, and then pressurized to 40 bar H_2. The reaction solution was stirred at room temperature for 12 h, and then the pressure was released carefully. After slowly releasing the hydrogen pressure, the reaction mixture was passed through a short column of silica gel to get the pure product. The yield was determined by NMR analysis after the volatiles were removed under vacuum. The ee and dr values were determined by HPLC analysis on a chiral stationary phase.



Methyl (2*S*,3*S*)-3-hydroxy-2-methoxy-3-phenylpropanoate (**2a**)

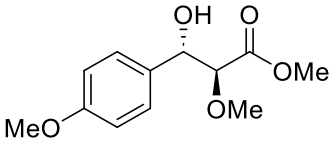
Colorless liquid, 46.1 mg, 99% yield, 99% ee, 97:3 dr; $[\alpha]^{20}_D$ = 2.2 (c = 1.0, $CHCl_3$); HPLC (Chiralpak IC column, hexane/isopropanol = 95/5; flow rate = 0.7 mL/min; UV detection at 210 nm; t_R=16.0 min (*anti*), t_R=18.6 min (*anti*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.27 (m, 5H), 5.02 – 4.94 (m, 1H), 3.99 (d, *J* = 5.8 Hz, 1H), 3.67 (s, 3H), 3.37 (s, 3H), 2.98 (d, *J* = 4.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.8, 138.3, 127.2, 127.1, 125.5, 83.4, 73.0, 57.9, 50.9. HRMS (ESI) m/z calcd. for $C_{11}H_{14}NaO_4$ $[M+Na]^+$: 233.0784, found: 233.0784.



Methyl (2*S*,3*S*)-3-hydroxy-2-methoxy-3-(p-tolyl)propanoate (**2b**)

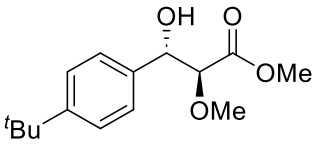
Colorless liquid, 49.2 mg, 99% yield, 98% ee, 95:5 dr; $[\alpha]^{20}_D$ = 3.5 (c = 1.0, $CHCl_3$); HPLC (Chiralpak IC column, hexane/isopropanol = 90/10; flow rate = 1.0 mL/min; UV detection at 230 nm; t_R=13.2 min (*anti*), t_R=16.9 min (*anti*), t_R=23.0 min (*syn*), t_R=28.3 min (*syn*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.0 Hz, 2H), 7.08 (d, *J* = 7.9 Hz, 2H), 4.87 (t, *J* = 5.3 Hz, 1H), 3.91 (d, *J* = 5.8 Hz, 1H), 3.62 (s, 3H), 3.30 (s, 3H), 2.78

(d, *J* = 5.1 Hz, 1H), 2.26 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 137.8, 136.4, 129.0, 126.4, 84.5, 73.9, 58.9, 51.9, 21.1. HRMS (ESI) m/z calcd. for $C_{12}H_{16}NaO_4$ $[M+Na]^+$: 247.0941, found: 247.0941.



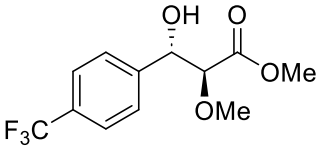
Methyl (2*S*,3*S*)-3-hydroxy-2-methoxy-3-(4-methoxyphenyl)propanoate (**2c**)

Colorless liquid, 56.4 mg, 99% yield, 98% ee, 99:1 dr; $[\alpha]^{20}_D$ = 1.7 (c = 1.0, $CHCl_3$); HPLC (Chiralpak IC column, hexane/isopropanol = 85/15; flow rate = 1.0 mL/min; UV detection at 230 nm; t_R=13.4 min (*anti*), t_R=17.2 min (*anti*), t_R=21.1 min (*syn*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (dd, *J* = 8.8, 2.1 Hz, 2H), 6.90 – 6.71 (m, 2H), 4.85 (t, *J* = 5.4 Hz, 1H), 3.90 (d, *J* = 5.9 Hz, 1H), 3.73 (s, 3H), 3.62 (s, 3H), 3.30 (s, 3H), 2.79 (d, *J* = 5.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 159.4, 131.6, 127.8, 113.7, 113.7, 84.5, 73.7, 58.9, 55.2, 51.9. HRMS (ESI) m/z calcd. for $C_{12}H_{16}NaO_5$ $[M+Na]^+$: 263.0890, found: 263.0890.



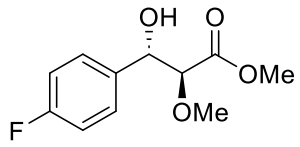
Methyl (2S,3S)-3-(4-(tert-butyl)phenyl)-3-hydroxy-2-methoxypropanoate (**2d**)

Colorless liquid, 56.7 mg, 99% yield, 93% ee, 96:4 dr; $[\alpha]^{20}_D$ = 1.5 (c = 1.0, $CHCl_3$); HPLC (Chiralpak IB column, hexane/isopropanol = 90/10; flow rate = 1.0 mL/min; UV detection at 210 nm; t_R=6.1 min (*anti*), t_R=6.6 min (*anti*), t_R=6.9 min (*syn*), t_R=7.4 min (*syn*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.5 Hz, 2H), 7.31 – 7.23 (m, 2H), 4.95 (t, *J* = 5.3 Hz, 1H), 4.00 (d, *J* = 5.9 Hz, 1H), 3.69 (s, 3H), 3.38 (s, 3H), 2.84 (d, *J* = 5.2 Hz, 1H), 1.31 (s, 10H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 151.0, 136.4, 126.3, 125.2, 125.1, 84.5, 84.5, 73.9, 73.8, 58.9, 51.9, 34.5, 31.3. HRMS (ESI) m/z calcd. for $C_{15}H_{22}NaO_4$ $[M+Na]^+$: 289.1410, found: 289.1410.



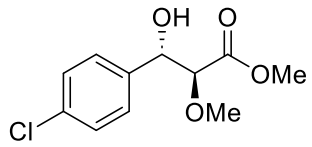
Methyl (2*S*,3*S*)-3-hydroxy-2-methoxy-3-(4-(trifluoromethyl)phenyl)propanoate (**2e**)

Colorless liquid, 59.8 mg, 99% yield, 96% ee, 95:5 dr; $[\alpha]^{20}_D$ = -2.4 (c = 1.0, $CHCl_3$); HPLC (Chiralpak IB column, hexane/isopropanol = 90/10; flow rate = 1.0 mL/min; UV detection at 230 nm; t_R=6.6 min (*anti*), t_R=7.4 min (*anti*), t_R=8.1 min (*syn*), t_R=8.8 min (*syn*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.1 Hz, 2H), 7.48 (d, *J* = 8.1 Hz, 2H), 5.03 (t, *J* = 4.8 Hz, 1H), 3.97 (d, *J* = 5.7 Hz, 1H), 3.68 (s, 3H), 3.38 (s, 3H), 3.25 (d, *J* = 4.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 143.4, 130.2 (q, *J* = 32.5 Hz), 126.9, 125.1 (q, *J* = 3.8 Hz), 124.0 (q, *J* = 272.1 Hz), 84.2, 73.4, 59.0, 52.0. ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.58. HRMS (ESI) m/z calcd. for $C_{12}H_{13}F_3NaO_4$ $[M+Na]^+$: 301.0658, found: 301.0659.



Methyl (2*S*,3*S*)-3-(4-fluorophenyl)-3-hydroxy-2-methoxypropanoate (**2f**)

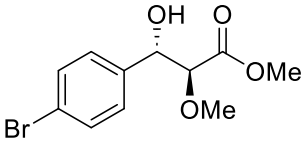
Colorless liquid, 50.0 mg, 99% yield, 97% ee, 95:5 dr; $[\alpha]^{20}_D$ = -1.8 (c = 1.0, $CHCl_3$); HPLC (Chiralpak IC column, hexane/isopropanol = 95/55; flow rate = 1.0 mL/min; UV detection at 210 nm; t_R=14.3 min (*anti*), t_R=15.3 min (*anti*), t_R=20.4 min (*syn*), t_R=29.7 min (*syn*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (dd, *J* = 8.6, 5.5 Hz, 2H), 7.03 (t, *J* = 8.7 Hz, 2H), 4.96 (t, *J* = 5.0 Hz, 1H), 3.95 (d, *J* = 5.7 Hz, 1H), 3.68 (s, 3H), 3.38 (s, 3H), 3.03 (d, *J* = 4.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.7, 161.5 (d, *J* = 246.3 Hz), 134.1 (d, *J* = 3.2 Hz), 127.3 (d, *J* = 8.3 Hz), 114.1 (d, *J* = 21.4 Hz), 83.3, 72.4, 57.9, 50.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.39 – -114.48 (m). HRMS (ESI) m/z calcd. for $C_{11}H_{13}FNaO_4$ $[M+Na]^+$: 251.0690, found: 251.0690.



Methyl (2S,3S)-3-(4-chlorophenyl)-3-hydroxy-2-methoxypropanoate (**2g**)

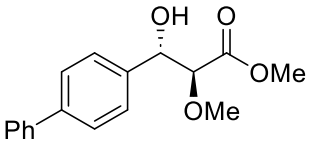
Colorless liquid, 52.7 mg, 99% yield, 96% ee, 94:6 dr; $[\alpha]^{20}_D$ = 3.1 (c = 1.0, $CHCl_3$); HPLC (Chiralpak IC column, hexane/isopropanol = 95/5; flow rate = 1.0 mL/min; UV detection at 230 nm; t_R=14.4 min (*anti*), t_R=15.4 min (*anti*), t_R=20.6 min (*syn*), t_R=30.1 min (*syn*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 4H), 4.98 – 4.91 (m, 1H), 3.94 (d, *J* = 5.7 Hz, 1H), 3.68 (s, 3H), 3.37 (s, 3H), 3.06 (s, 1H). ^{13}C NMR (101 MHz,

$CDCl_3$) δ 169.6, 136.9, 132.8, 127.4, 126.9, 83.2, 72.4, 58.0, 51.0. HRMS (ESI) m/z calcd. for $C_{11}H_{13}ClNaO_4$ $[M+Na]^+$: 267.0395, found: 267.0395.



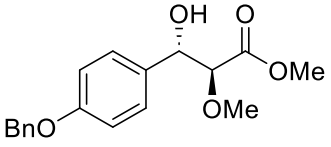
Methyl (2*S*,3*S*)-3-(4-bromophenyl)-3-hydroxy-2-methoxypropanoate (**2h**)

Colorless liquid, 61.7 mg, 99% yield, 98% ee, 96:4 dr; $[\alpha]^{20}_D$ = 1.6 (c = 1.0, $CHCl_3$); HPLC (Chiralpak IC column, hexane/isopropanol = 95/5; flow rate = 1.0 mL/min; UV detection at 210 nm; t_R=15.1 min (*anti*), t_R=16.3 min (*anti*), t_R=22.0 min (*syn*), t_R=29.3 min (*syn*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.43 (m, 2H), 7.26 – 7.20 (m, 2H), 4.94 (dd, *J* = 6.0, 2.8 Hz, 1H), 3.94 (d, *J* = 5.7 Hz, 1H), 3.68 (s, 3H), 3.38 (s, 3H), 3.06 (d, *J* = 3.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.6, 138.4, 131.3, 128.3, 122.0, 84.2, 73.4, 59.0, 52.0. HRMS (ESI) m/z calcd. for $C_{11}H_{13}BrNaO_4$ $[M+Na]^+$: 310.9889, found: 310.9889.



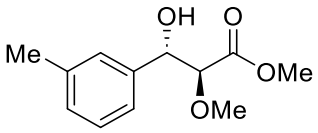
Methyl (2*S*,3*S*)-3-([1,1'-biphenyl]-4-yl)-3-hydroxy-2-methoxypropanoate (**2i**)

Colorless liquid, 61.4 mg, 99% yield, 99% ee, 95:5 dr; $[\alpha]^{20}_D$ = 7.5 (c = 1.0, $CHCl_3$); HPLC (Chiralpak IC column, hexane/isopropanol = 85/15; flow rate = 1.0 mL/min; UV detection at 210 nm; t_R=10.3 min (*anti*), t_R=12.3 min (*anti*), t_R=14.6 min (*syn*), t_R=19.2 min (*syn*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 – 7.45 (m, 4H), 7.42 – 7.31 (m, 4H), 7.31 – 7.23 (m, 1H), 4.95 (t, *J* = 5.3 Hz, 1H), 3.96 (d, *J* = 5.7 Hz, 1H), 3.62 (s, 3H), 3.33 (s, 3H), 2.91 (d, *J* = 5.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 140.9, 140.7, 138.4, 128.7, 127.3, 127.1, 127.0, 127.0, 84.5, 73.9, 59.0, 52.0. HRMS (ESI) m/z calcd. for $C_{17}H_{18}NaO_4$ $[M+Na]^+$: 309.1097, found: 309.1099.



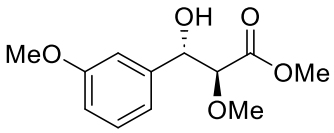
Methyl (2*S*,3*S*)-3-(4-(benzyloxy)phenyl)-3-hydroxy-2-methoxypropanoate (**2j**)

Colorless liquid, 67.5 mg, 99% yield, 99% ee, 99:1 dr; $[\alpha]^{20}_D$ = 3.0 (c = 1.0, $CHCl_3$); HPLC (Chiralpak IC column, hexane/isopropanol = 90/10; flow rate = 1.0 mL/min; UV detection at 210 nm; t_R=21.1 min (*anti*), t_R=29.1 min (*anti*), t_R=32.6 min (*syn*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.35 (m, 4H), 7.35 – 7.23 (m, 3H), 6.99 – 6.90 (m, 2H), 5.05 (s, 2H), 4.92 (t, *J* = 5.3 Hz, 1H), 3.96 (d, *J* = 5.8 Hz, 1H), 3.68 (s, 3H), 3.37 (s, 3H), 2.85 (d, *J* = 5.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 158.6, 136.9, 131.9, 128.6, 127.9, 127.9, 127.8, 127.5, 114.6, 84.5, 73.7, 70.0, 58.9, 51.9. HRMS (ESI) m/z calcd. for $C_{18}H_{20}NaO_4$ $[M+Na]^+$: 339.1203, found: 339.1204.



Methyl (2*S*,3*S*)-3-hydroxy-2-methoxy-3-(m-tolyl)propanoate (**2k**)

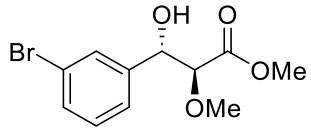
Colorless liquid, 49.1 mg, 99% yield, 96% ee, 95:5 dr; $[\alpha]^{20}_D$ = 0.8 (c = 1.0, $CHCl_3$); HPLC (Chiralpak IC column, hexane/isopropanol = 85/15; flow rate = 1.0 mL/min; UV detection at 210 nm; t_R=8.8 min (*anti*), t_R=10.5 min (*anti*), t_R=12.9 min (*syn*), t_R=18.9 min (*syn*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (t, *J* = 7.5 Hz, 1H), 7.19 – 7.06 (m, 3H), 4.94 (t, *J* = 5.2 Hz, 1H), 3.99 (d, *J* = 5.8 Hz, 1H), 3.68 (s, 3H), 3.38 (s, 3H), 2.84 (d, *J* = 5.0 Hz, 1H), 2.35 (d, *J* = 0.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.9, 138.3, 136.9, 127.9, 127.1, 126.2, 122.6, 83.5, 73.1, 57.8, 50.8, 20.4. HRMS (ESI) m/z calcd. for $C_{12}H_{16}NaO_4$ $[M+Na]^+$: 247.0941, found: 247.0942.



Methyl (2*S*,3*S*)-3-hydroxy-2-methoxy-3-(3-methoxyphenyl)propanoate (**2l**)

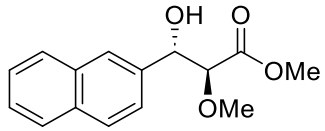
Colorless liquid, 52.2 mg, 99% yield, 97% ee, 95:5 dr; $[\alpha]^{20}_D$ = -2.7 (c = 1.0, $CHCl_3$); HPLC (Chiralpak IB column, hexane/isopropanol = 90/10; flow rate = 1.0 mL/min; UV detection at 210 nm; t_R=10.3 min (*anti*), t_R=11.2 min (*anti*), t_R=12.0 min (*syn*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (t, *J* = 8.0 Hz, 1H), 6.94 (dd, *J* = 7.5, 1.4 Hz, 2H), 6.88 – 6.80 (m, 1H), 4.95 (t, *J* = 4.9 Hz, 1H), 3.98 (d, *J* = 5.8 Hz, 1H), 3.80 (s, 3H), 3.69 (s, 3H), 3.37 (s, 3H), 2.94 (d, *J* = 4.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.8, 159.5,

141.1, 129.3, 118.8, 113.7, 112.0, 84.4, 74.0, 58.9, 55.2, 51.9. HRMS (ESI) m/z calcd. for $C_{12}H_{16}NaO_5$ $[M+Na]^+$: 263.0890, found: 263.0890.



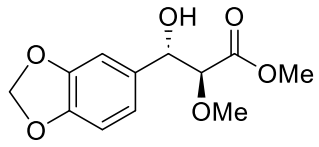
Methyl (2*S*,3*S*)-3-(3-bromophenyl)-3-hydroxy-2-methoxypropanoate (**2m**)

Colorless liquid, 60.7 mg, 99% yield, 95% ee, 95:5 dr; $[\alpha]^{20}_D$ = 1.2 (c = 1.0, $CHCl_3$); HPLC (Chiralpak IC column, hexane/isopropanol = 85/15; flow rate = 1.0 mL/min; UV detection at 230 nm; t_R=6.5 min (*anti*), t_R=7.9 min (*anti*), t_R=8.2 min (*syn*), t_R=10.0 min (*syn*).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (t, *J* = 1.9 Hz, 1H), 7.43 (ddd, *J* = 7.8, 2.0, 1.2 Hz, 1H), 7.31 – 7.25 (m, 1H), 7.21 (t, *J* = 7.8 Hz, 1H), 4.95 (t, *J* = 5.2 Hz, 1H), 3.95 (d, *J* = 5.7 Hz, 1H), 3.69 (s, 3H), 3.39 (s, 3H), 3.03 (d, *J* = 5.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 141.7, 131.1, 129.8, 129.7, 125.2, 122.4, 84.2, 73.4, 59.0, 52.1, 52.0. HRMS (ESI) m/z calcd. for $C_{11}H_{13}BrNaO_4$ $[M+Na]^+$: 310.9889, found: 310.9890.



Methyl (2*S*,3*S*)-3-hydroxy-2-methoxy-3-(naphthalen-2-yl)propanoate (**2n**)

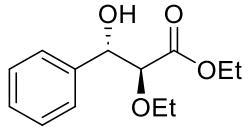
Colorless liquid, 56.3 mg, 99% yield, 99% ee, 94:6 dr; $[\alpha]^{20}_D$ = 13.3 (c = 1.0, $CHCl_3$); HPLC (Chiralpak IC column, hexane/isopropanol = 80/20; flow rate = 1.0 mL/min; UV detection at 260 nm; t_R=8.4 min (*anti*), t_R=9.9 min (*anti*), t_R=11.4 min (*syn*), t_R=15.4 min (*syn*).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 6.1, 3.3 Hz, 4H), 7.53 – 7.41 (m, 3H), 5.13 (d, *J* = 5.8 Hz, 1H), 4.07 (d, *J* = 5.8 Hz, 1H), 3.65 (s, 3H), 3.37 (s, 3H), 3.12 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.8, 135.8, 132.1, 132.0, 127.0, 126.9, 126.6, 125.0, 125.0, 124.7, 123.3, 83.4, 73.2, 57.9, 50.9. HRMS (ESI) m/z calcd. for $C_{15}H_{16}NaO_4$ $[M+Na]^+$: 283.0941, found: 283.0941.



Methyl (2*S*,3*S*)-3-(benzo[d][1,3]dioxol-5-yl)-3-hydroxy-2-methoxypropanoate (**2o**)

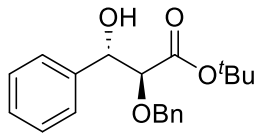
Colorless liquid, 55.2 mg, 99% yield, 98% ee, 99:1 dr; $[\alpha]^{20}_D$ = -5.0 (c = 1.0, $CHCl_3$);

HPLC (Chiralpak IA column, hexane/isopropanol = 95/5; flow rate = 1.0 mL/min; UV detection at 210 nm; t_R=35.2 min (*anti*), t_R=38.6 min (*anti*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.88 (d, *J* = 1.7 Hz, 1H), 6.83 – 6.72 (m, 2H), 5.95 (d, *J* = 0.8 Hz, 2H), 4.88 (d, *J* = 5.0 Hz, 1H), 3.94 (d, *J* = 5.9 Hz, 1H), 3.71 (s, 3H), 3.38 (s, 3H), 2.91 (d, *J* = 4.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.8, 147.6, 147.4, 133.4, 120.2, 108.0, 107.1, 101.0, 84.5, 73.9, 59.0, 52.0. HRMS (ESI) m/z calcd. for $C_{12}H_{14}NaO_4$ $[M+Na]^+$: 277.0683, found: 277.0683.



Ethyl (2*S*,3*S*)-2-ethoxy-3-hydroxy-3-phenylpropanoate (**2p**)

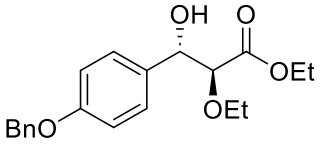
Colorless liquid, 51.6 mg, 99% yield, 99% ee, 97:3 dr; $[\alpha]^{20}_D$ = -1.1 (c = 1.0, $CHCl_3$); HPLC (Chiralpak IC column, hexane/isopropanol = 90/10; flow rate = 1.0 mL/min; UV detection at 210 nm; t_R=8.5 min (*anti*), t_R=9.1 min (*anti*), t_R=11.5 min (*syn*), t_R=14.7 min (*syn*). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 – 7.35 (m, 2H), 7.35 – 7.31 (m, 2H), 7.31 – 7.27 (m, 1H), 4.98 (t, *J* = 5.3 Hz, 1H), 4.11 (qd, *J* = 7.2, 1.9 Hz, 2H), 4.03 (d, *J* = 5.9 Hz, 1H), 3.65 (dq, *J* = 9.1, 7.0 Hz, 1H), 3.38 (dq, *J* = 9.3, 7.0 Hz, 1H), 3.03 (d, *J* = 4.8 Hz, 1H), 1.15 (dt, *J* = 14.5, 7.1 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.7, 138.5, 127.1, 126.9, 125.6, 81.6, 73.0, 65.8, 59.9, 13.9, 12.9. HRMS (ESI) m/z calcd. for $C_{13}H_{18}NaO_4$ $[M+Na]^+$: 261.1097, found: 261.1097.



Tert-butyl (2*S*,3*S*)-2-(benzyloxy)-3-hydroxy-3-phenylpropanoate (**2q**)

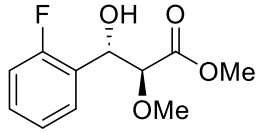
Colorless liquid, 69.6 mg, 99% yield, 96% ee, 99:1 dr; $[\alpha]^{20}_D$ = -11.6 (c = 1.0, $CHCl_3$); HPLC (Chiralpak IC column, hexane/isopropanol = 95/5; flow rate = 1.0 mL/min; UV detection at 210 nm; t_R=13.4 min (*anti*), t_R=15.4 min (*anti*), t_R=20.6 min (*syn*), t_R=23.4 min (*syn*). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.41 – 7.37 (m, 2H), 7.35 – 7.26 (m, 6H), 7.24 – 7.19 (m, 2H), 4.99 (t, *J* = 5.2 Hz, 1H), 4.69 (d, *J* = 11.5 Hz, 1H), 4.38 (d, *J* = 11.5 Hz, 1H), 4.04 (d, *J* = 5.8 Hz, 1H), 3.10 (d, *J* = 4.8 Hz, 1H), 1.35 (s, 9H). ^{13}C NMR

(151 MHz, $CDCl_3$) δ 169.6, 139.6, 137.1, 128.4, 128.1, 128.1, 127.9, 127.8, 126.9, 82.2, 82.0, 74.2, 72.8, 27.9. HRMS (ESI) m/z calcd. for $C_{20}H_{24}NaO_4$ $[M+Na]^+$: 351.1567, found: 351.1568.



Ethyl (2*S*,3*S*)-3-(4-(benzyloxy)phenyl)-2-ethoxy-3-hydroxypropanoate (**2r**)

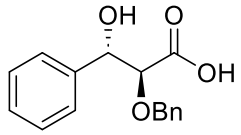
Colorless liquid, 63.0 mg, 99% yield, 99% ee, 99:1 dr; $[\alpha]^{20}_D$ = -1.3 (c = 1.0, $CHCl_3$); HPLC (Chiralpak IC column, hexane/isopropanol = 90/10; flow rate = 1.0 mL/min; UV detection at 210 nm; t_R=15.0 min (*anti*), t_R=16.9 min (*anti*), t_R=21.7 min (*syn*), t_R=22.9 min (*syn*). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42 (d, *J* = 7.1 Hz, 2H), 7.37 (t, *J* = 7.6 Hz, 2H), 7.30 (dd, *J* = 8.8, 2.4 Hz, 3H), 6.97 – 6.91 (m, 2H), 5.05 (s, 2H), 4.92 (t, *J* = 5.4 Hz, 1H), 4.12 (qd, *J* = 7.1, 1.8 Hz, 2H), 4.00 (d, *J* = 5.9 Hz, 1H), 3.65 (dq, *J* = 9.2, 7.0 Hz, 1H), 3.38 (dq, *J* = 9.2, 7.0 Hz, 1H), 2.95 (d, *J* = 5.0 Hz, 1H), 1.16 (td, *J* = 7.1, 4.2 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.8, 157.5, 135.9, 131.0, 127.5, 126.9, 126.4, 113.5, 81.7, 72.6, 68.9, 65.8, 59.9, 14.0, 13.0. HRMS (ESI) m/z calcd. for $C_{20}H_{24}NaO_5$ $[M+Na]^+$: 367.1516, found: 367.1517.



Methyl (2*S*,3*S*)-3-(2-fluorophenyl)-3-hydroxy-2-methoxypropanoate (**2s**)

Colorless liquid, 60.1 mg, 82% yield, 28% ee, 85:15 dr; $[\alpha]^{20}_D$ = 3.3 (c = 1.0, $CHCl_3$); HPLC (Chiralpak IC column, hexane/isopropanol = 95/5; flow rate = 1.0 mL/min; UV detection at 210 nm; t_R=18.0 min (*anti*), t_R=20.5 min (*anti*), t_R=25.7 min (*syn*), t_R=40.5 min (*syn*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (td, *J* = 7.6, 1.8 Hz, 1H), 7.20 (m, 1H), 7.07 (td, *J* = 7.5, 1.2 Hz, 1H), 6.96 (ddd, *J* = 10.6, 8.2, 1.2 Hz, 1H), 5.27 (d, *J* = 4.8 Hz, 1H), 4.06 (d, *J* = 4.7 Hz, 1H), 3.55 (s, 3H), 3.37 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.19, 158.90 (d, *J* = 245.7 Hz), 128.50 (d, *J* = 8.3 Hz), 126.95 (d, *J* = 4.1 Hz), 125.14 (d, *J* = 13.0 Hz), 123.10 (d, *J* = 3.4 Hz), 114.04 (d, *J* = 21.7 Hz), 82.14 (d, *J* = 1.7 Hz), 67.46 (d, *J* = 2.4 Hz), 57.68, 50.80. ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.87 –

-127.79 (m). HRMS (ESI) m/z calcd. for $C_{20}H_{24}NaO_5$ $[M+Na]^+$: 367.1516, found: 367.1517.

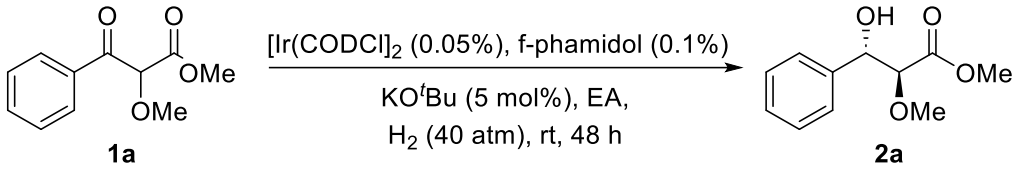


(2*S*,3*S*)-2-(Benzyloxy)-3-hydroxy-3-phenyl propanoic acid (**3**)[3]

Acid **3** was is obtained by the hydrolysis of ester **2r**. Colorless liquid, 32.1 mg. $[\alpha]^{20}_D$ = -16.8 (c = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 – 7.26 (m, 8H), 7.14 (dd, *J* = 6.6, 2.9 Hz, 2H), 5.00 (d, *J* = 6.2 Hz, 1H), 4.62 (d, *J* = 11.5 Hz, 1H), 4.38 (d, *J* = 11.5 Hz, 1H), 4.14 (d, *J* = 6.2 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 173.9, 138.9, 136.3, 128.5, 128.3, 128.2, 128.2, 126.9, 81.3, 74.2, 73.5.

3. Synthetic Applications

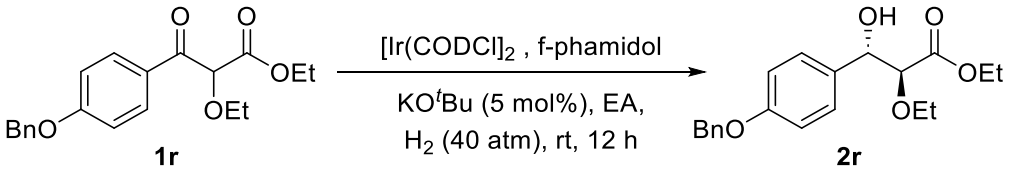
Scale-up synthesis of 2a



To a 2.5 mL vial was added the catalyst precursor $[Ir(COD)Cl]_2$ (3.4 mg, 0.005 mmol), f-phamidol (5.9 mg, 0.0105 mmol) and anhydrous EtOAc (1 mL) under argon atmosphere. The mixture was stirred for 1 h at room temperature to give a clear orange solution. An aliquot of the catalyst solution (200 uL, 0.001 mmol) was transferred into a 10.0 mL hydrogenation vessel, then Cs_2CO_3 (32.5 mg, 0.1 mmol), **1a** (416 mg, 2.0 mmol) and anhydrous EtOAc (5 mL) was added. The vessels were placed in an autoclave which was then charged with 40 atm of H_2 and stirred at 25-30 °C for 48 h. After slowly releasing the hydrogen pressure, the reaction mixture was passed through a short column of silica gel to get the pure product **2a** 413 mg, 98% yield, 98% ee, 96:4 dr.

The yield was determined by NMR analysis after the volatiles were removed under vacuum. The ee values were determined by HPLC analysis on a chiral stationary phase.

Scale-up synthesis of 2r

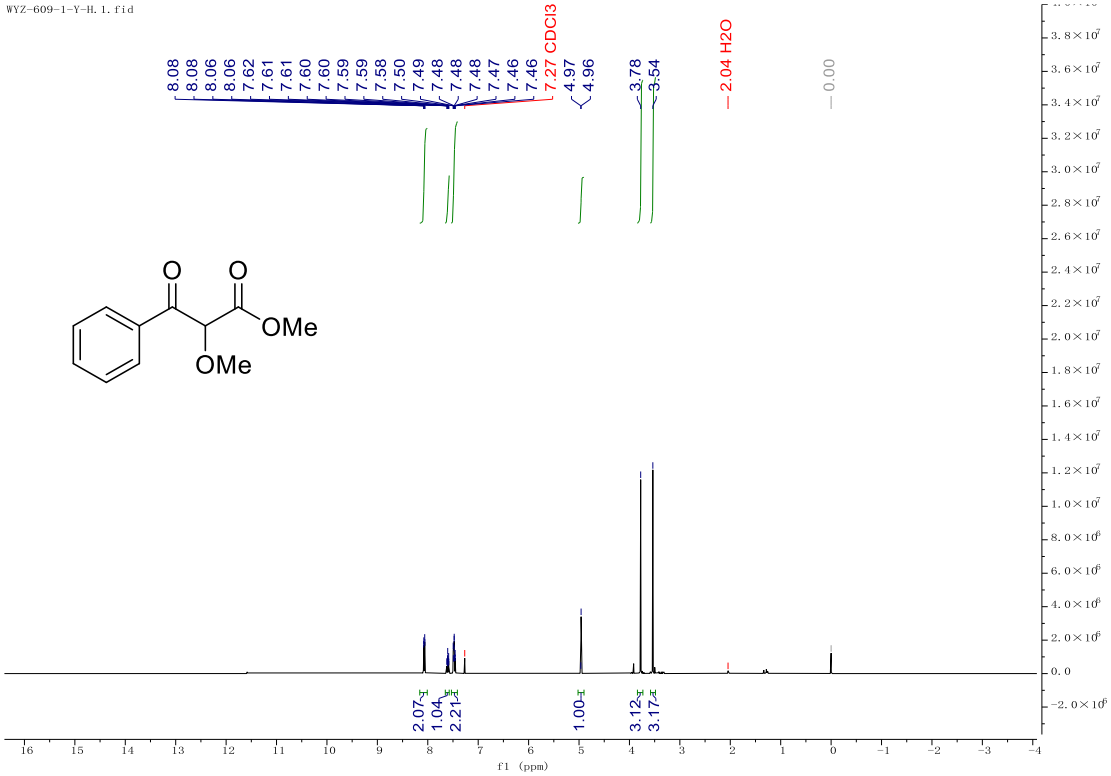


To a 20.0 mL vial equipped with α-methoxy-β-ketoesters **1r** (1.37 g, 4.0 mmol, 1.0 eq.) was added the Ir/f-phamidol-precatalyst (15.2 mg, 1.0×10^{-3} mmol, 0.005 eq.), Cs_2CO_3 (65.1 mg, 0.2 mmol, 5 mol%.) and anhydrous EtOAc (8.0 mL) in an argon-filled glovebox. The autoclave was quickly purged with hydrogen gas for three times, and then pressurized to 40 bar H_2. The reaction solution was stirred at room temperature for 48 h, and then the pressure was released carefully. After slowly releasing the hydrogen pressure, the reaction mixture was passed through a short column of silica gel to get the pure product **2r** (1.34 g, 99% yield, 99% ee, 99:1 dr).

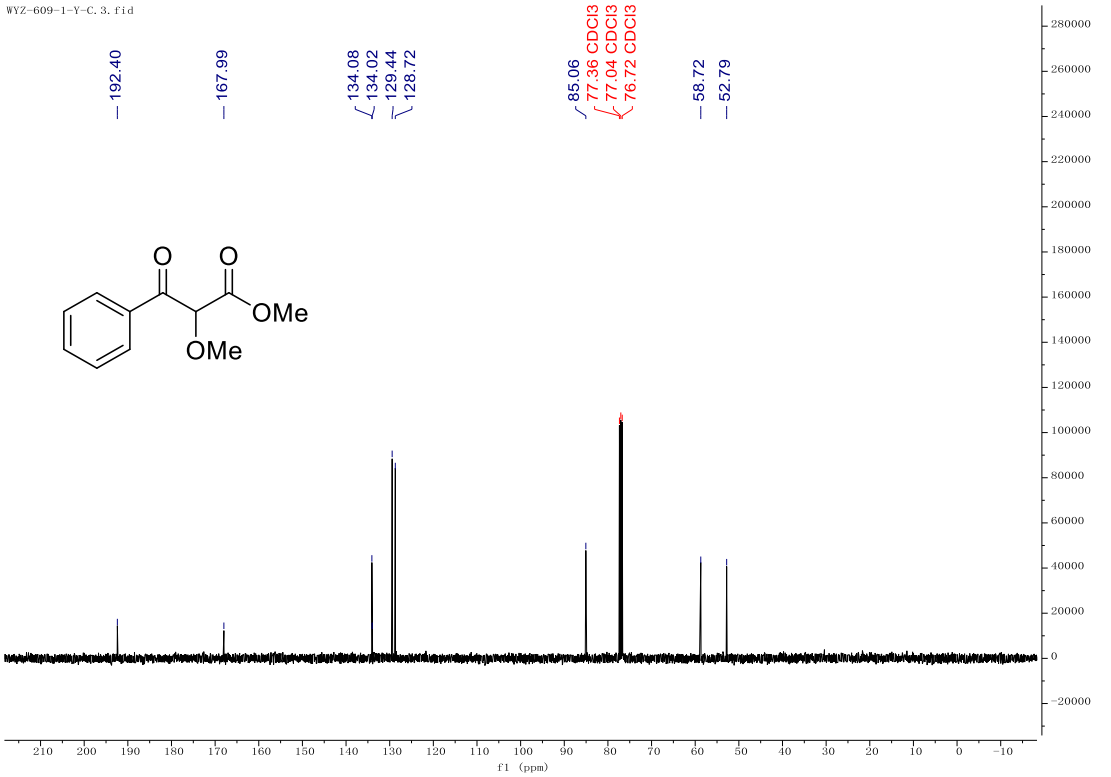
The yield was determined by NMR analysis after the volatiles were removed under vacuum. The ee and dr values were determined by HPLC analysis on a chiral stationary phase.

4. NMR Spectra

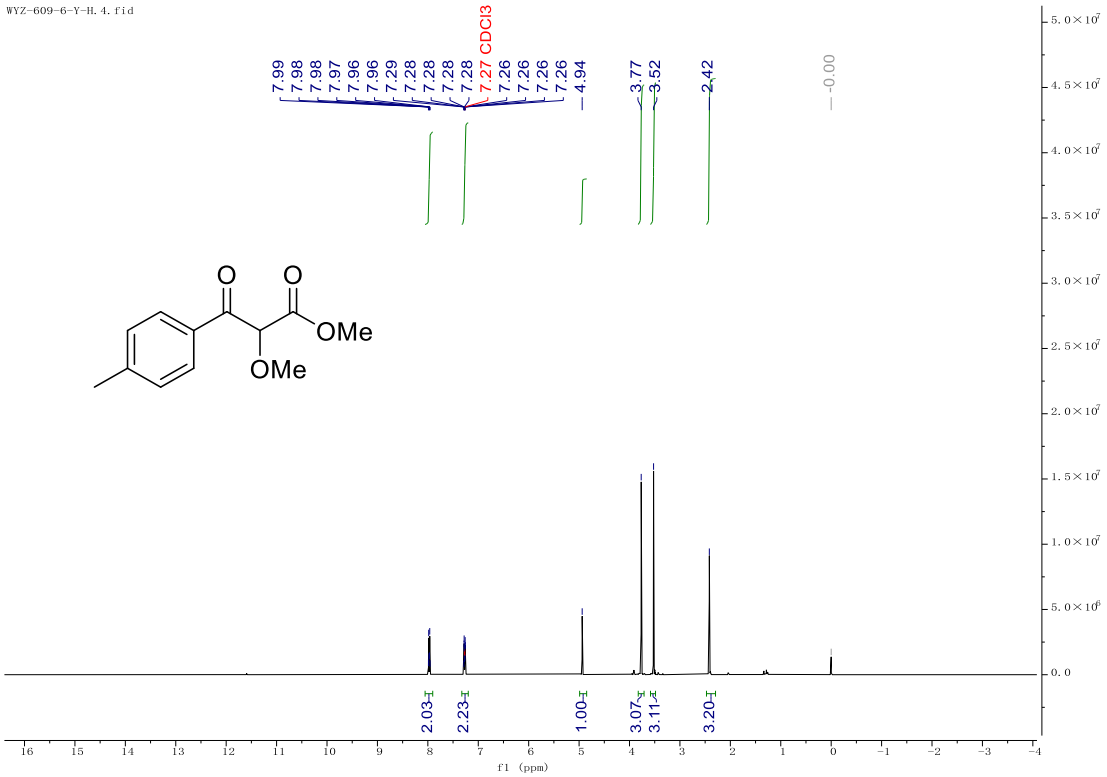
^{1}H NMR spectra (400 MHz, $CDCl_3$) of **1a**



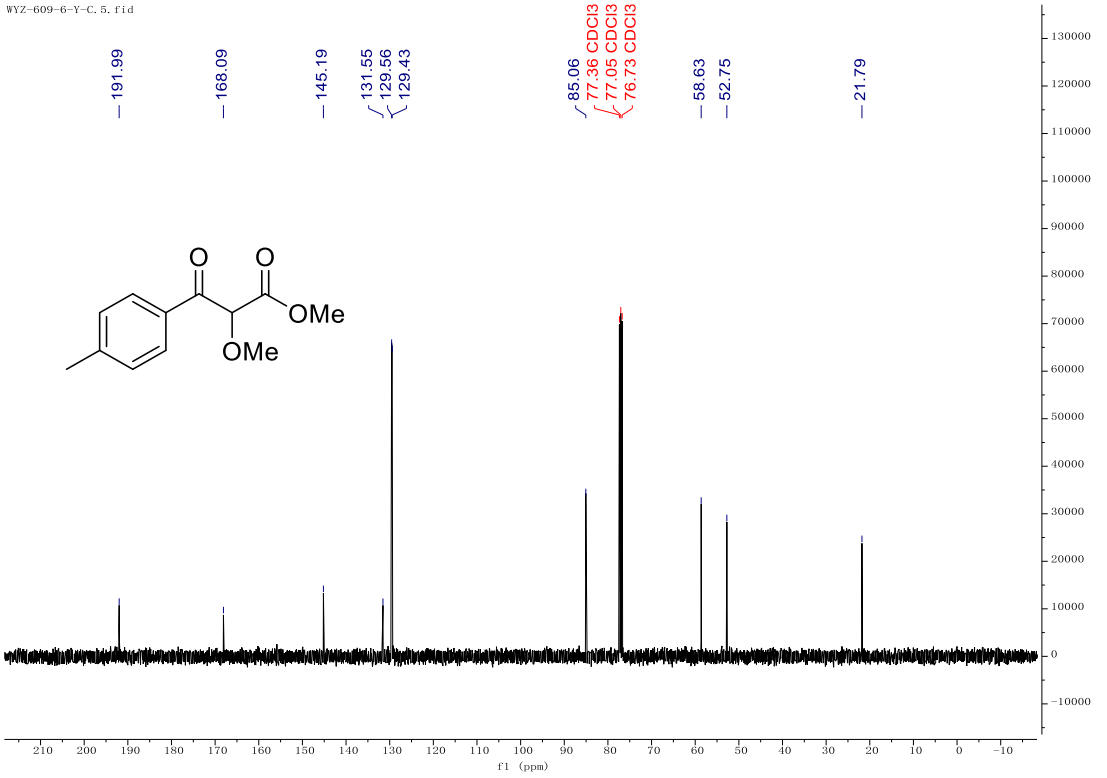
^{13}C NMR spectra (101 MHz, $CDCl_3$) of **1a**



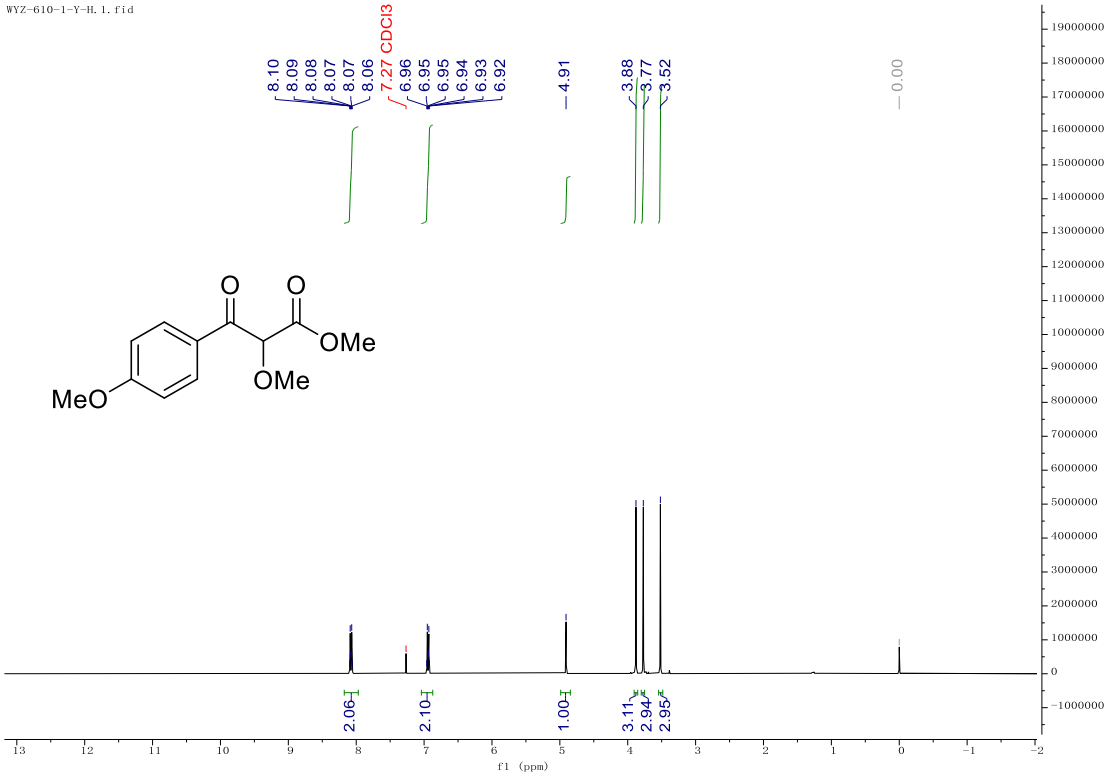
^{1}H NMR spectra (600 MHz, $CDCl_3$) of **1b**



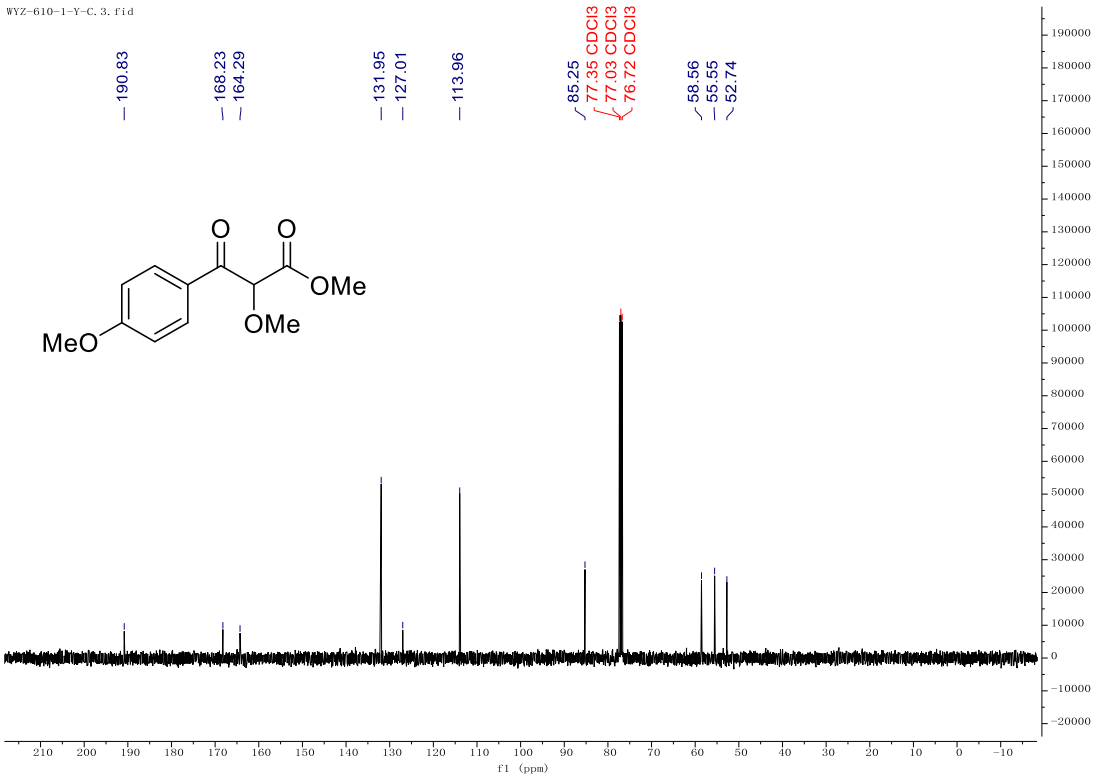
^{13}C NMR spectra (151 MHz, $CDCl_3$) of **1b**



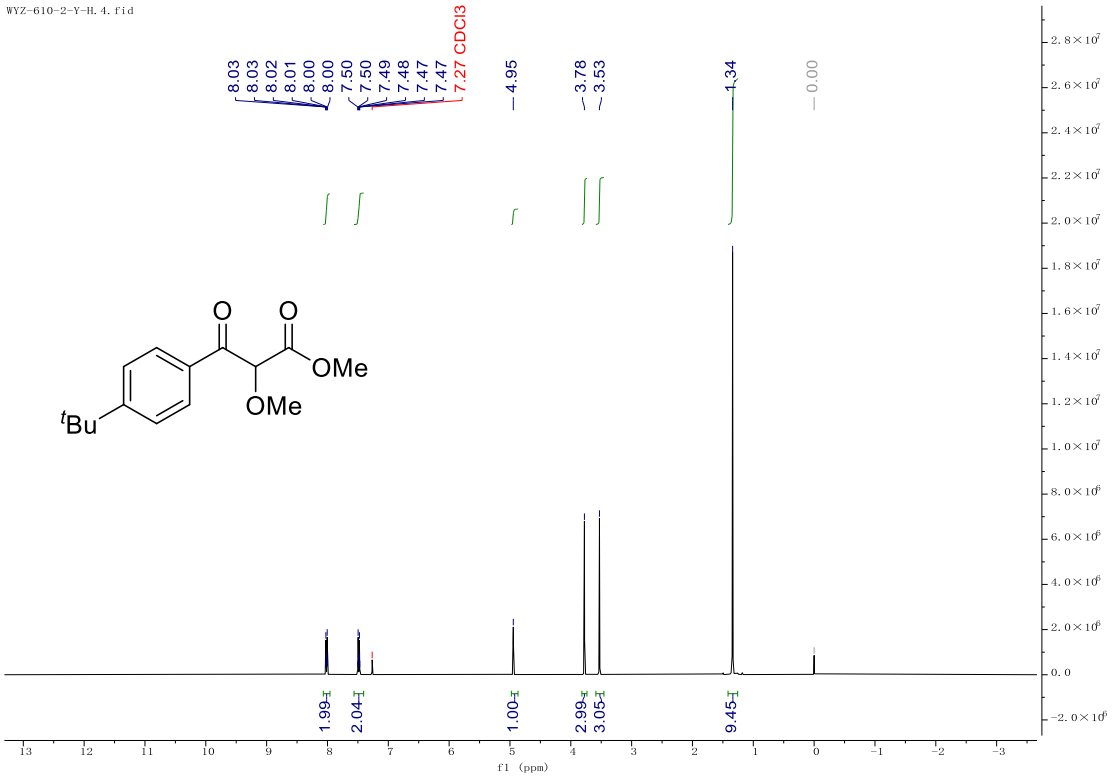
^{1}H NMR spectra (600 MHz, $CDCl_3$) of **1c**



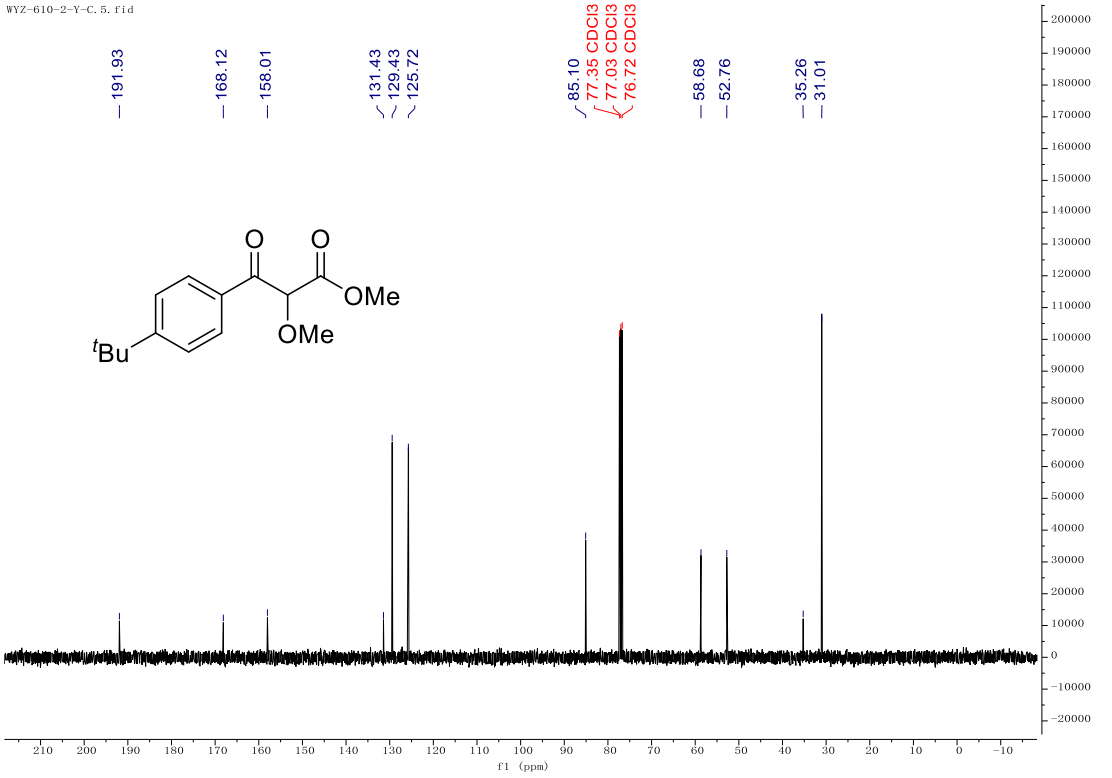
^{13}C NMR spectra (151 MHz, $CDCl_3$) of **1c**



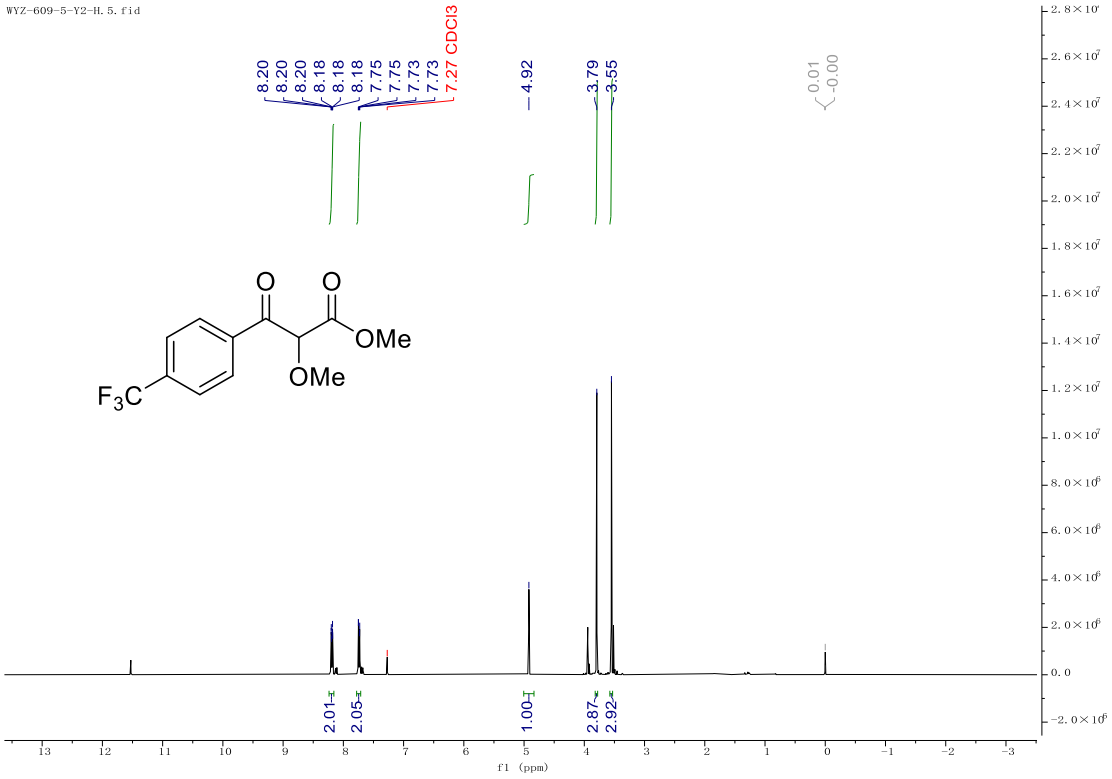
^{1}H NMR spectra (400 MHz, $CDCl_3$) of **1d**



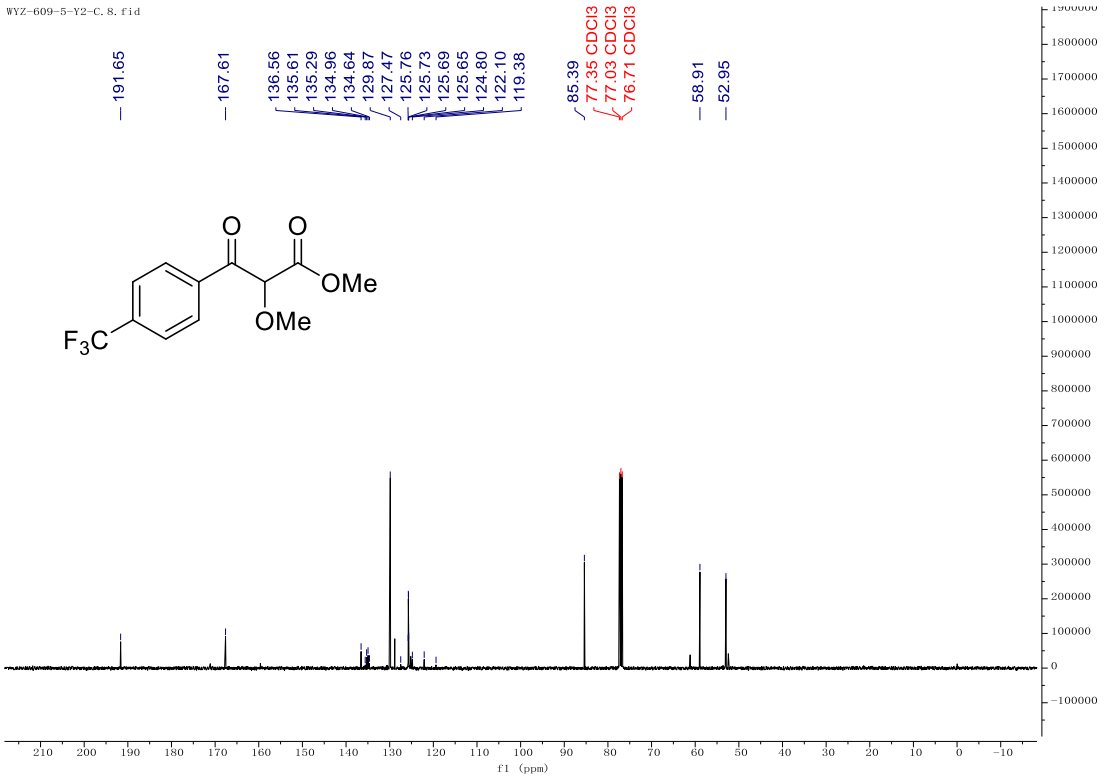
^{13}C NMR spectra (101 MHz, $CDCl_3$) of **1d**



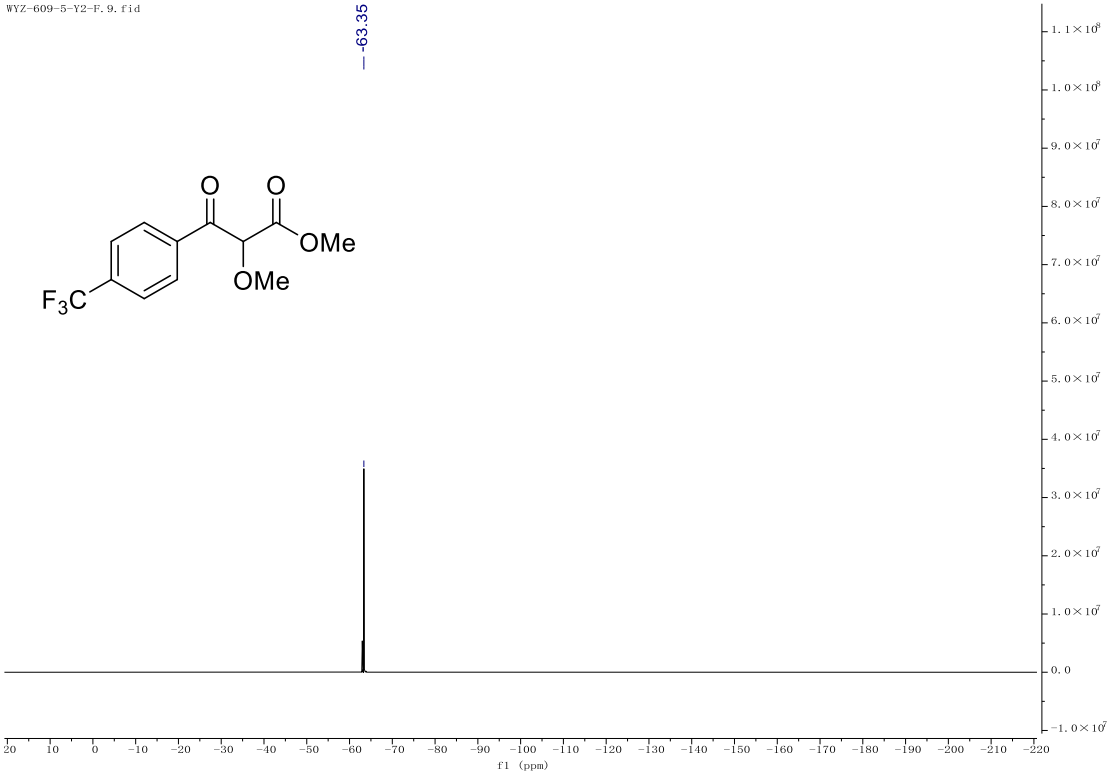
^{1}H NMR spectra (400 MHz, $CDCl_3$) of **1e**



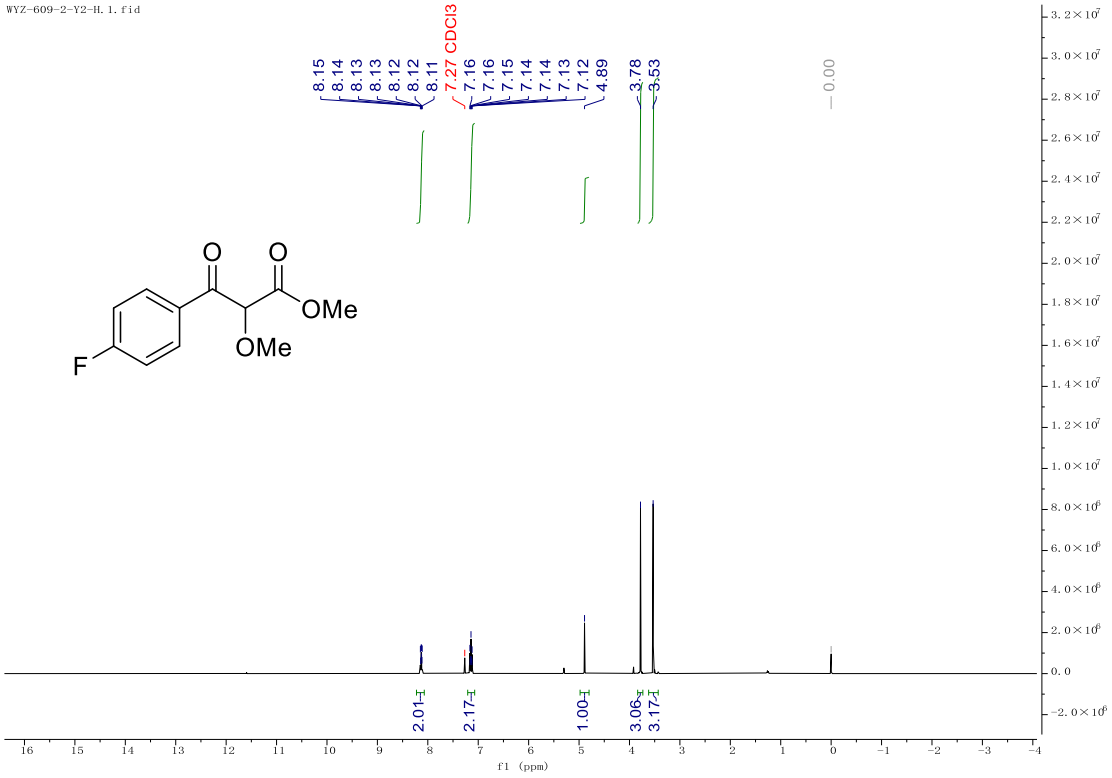
^{13}C NMR spectra (101 MHz, $CDCl_3$) of **1e**



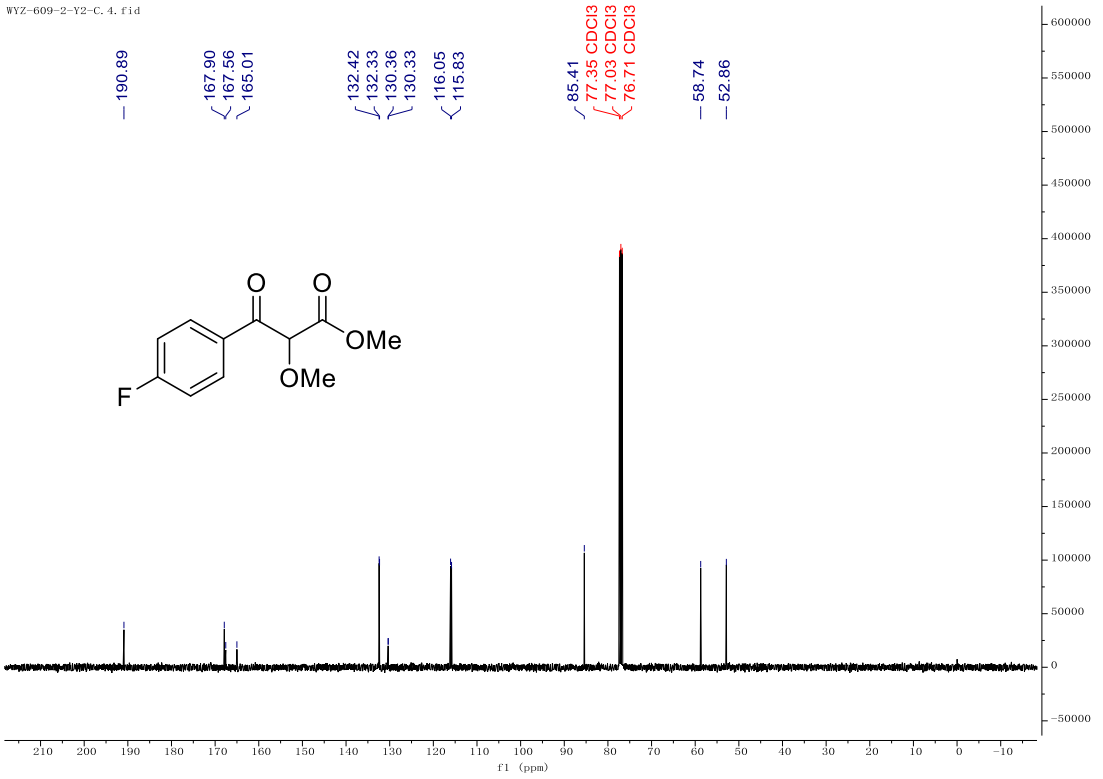
^{19}F NMR spectra (376 MHz, $CDCl_3$) of **1e**



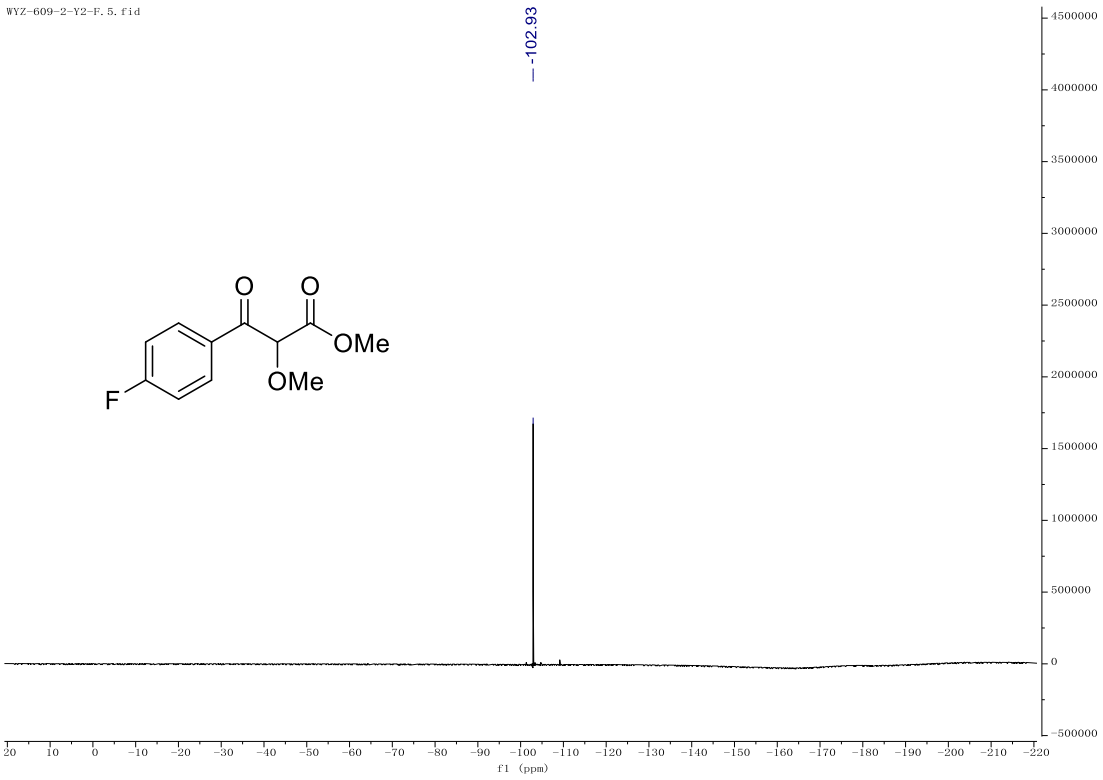
^{1}H NMR spectra (400 MHz, $CDCl_3$) of **1f**



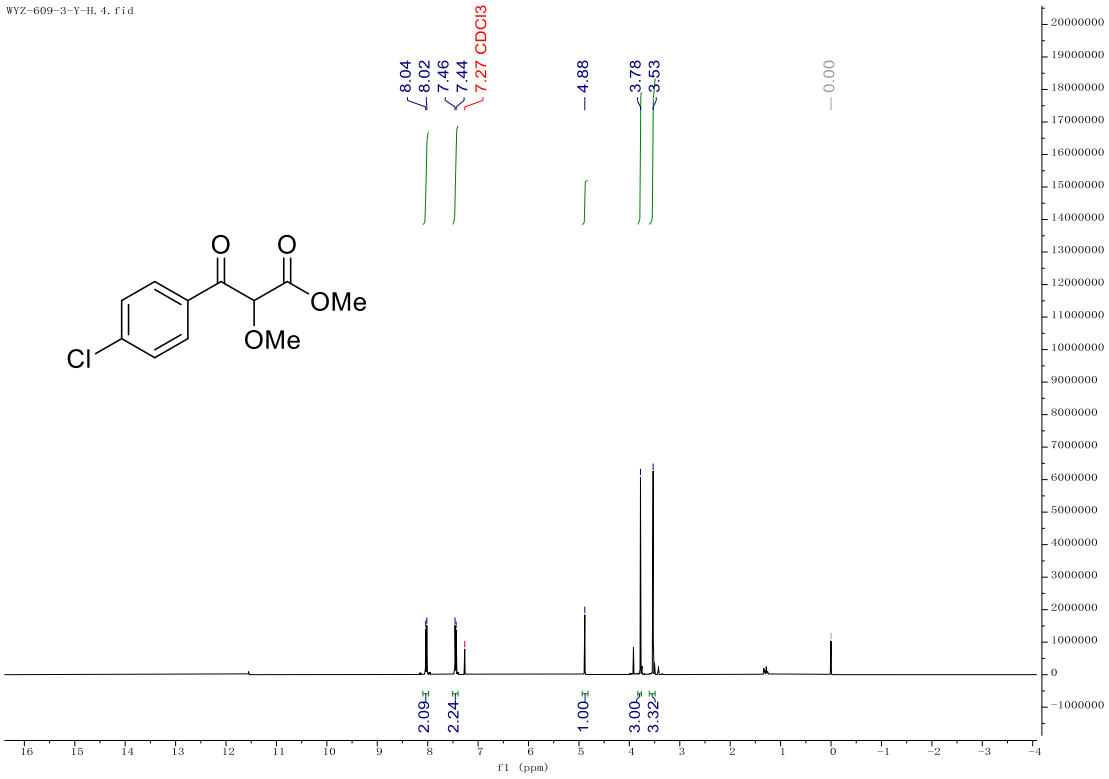
^{13}C NMR spectra (101 MHz, $CDCl_3$) of **1f**



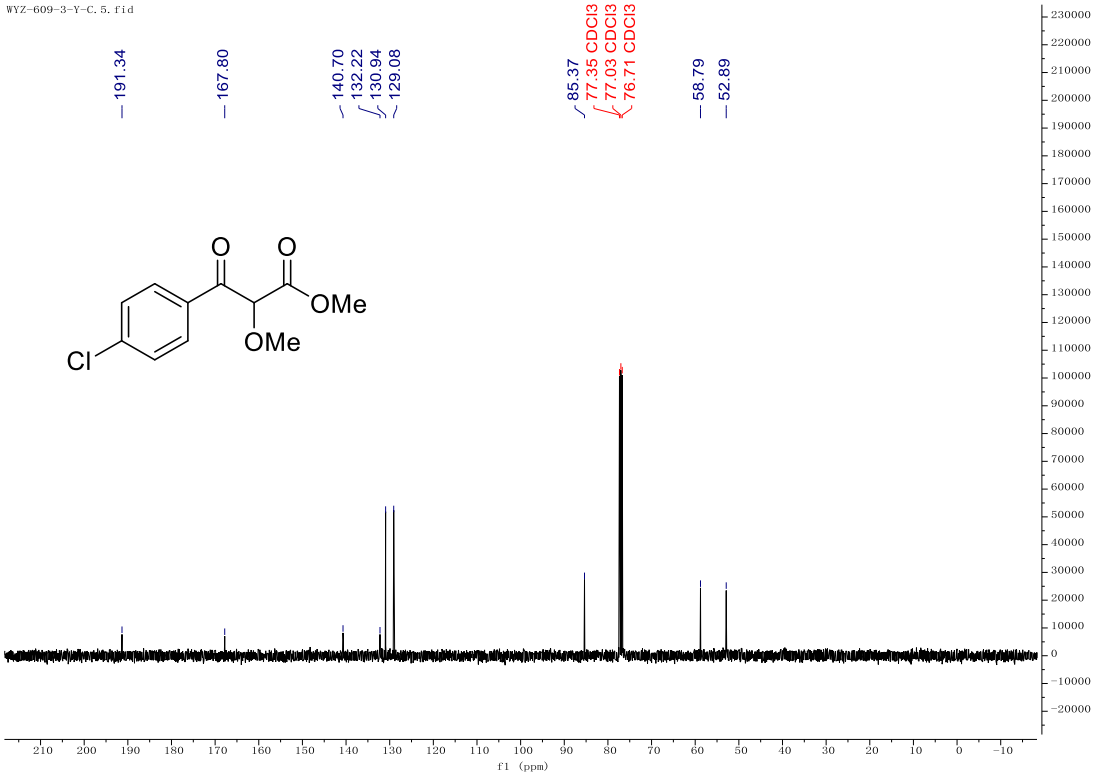
^{19}F NMR spectra (376 MHz, $CDCl_3$) of **1f**



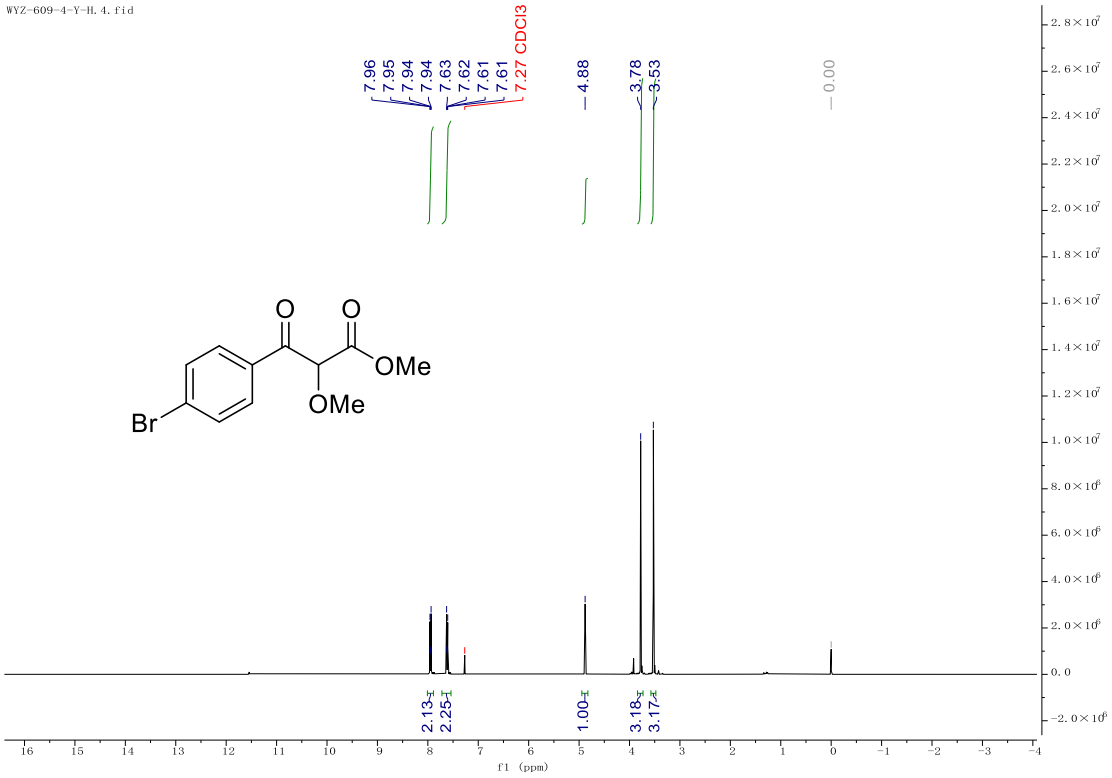
^{1}H NMR spectra (400 MHz, $CDCl_3$) of **1g**



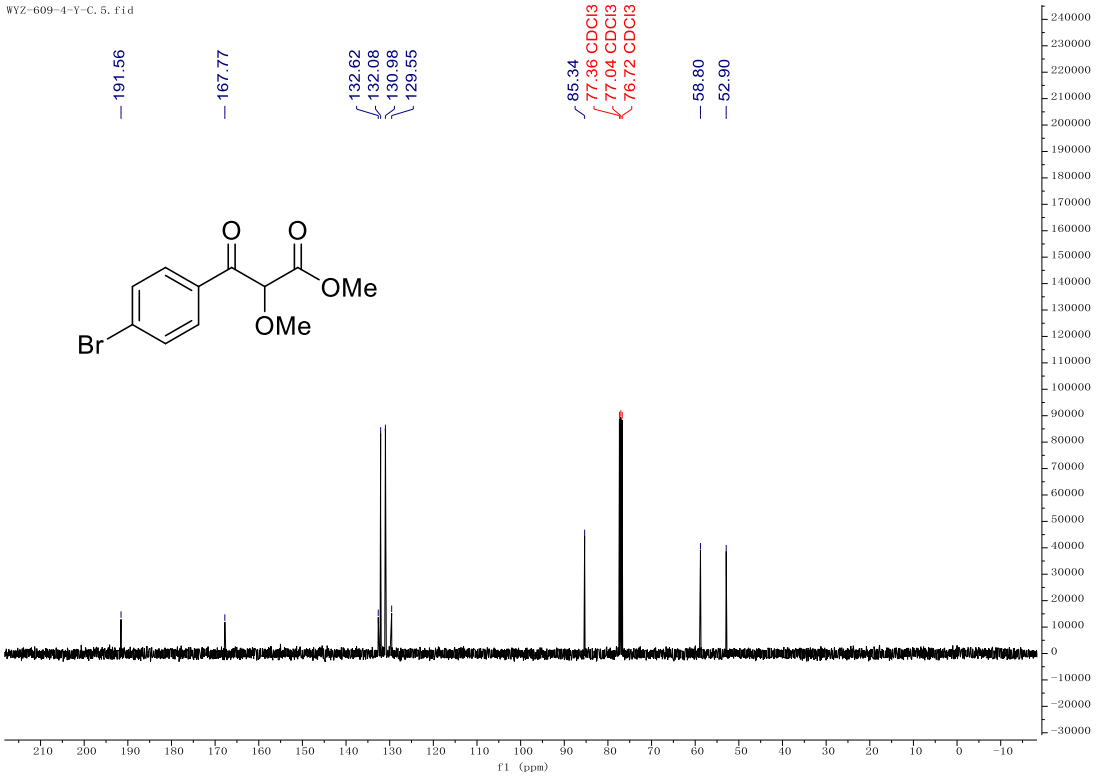
^{13}C NMR spectra (101 MHz, $CDCl_3$) of **1g**



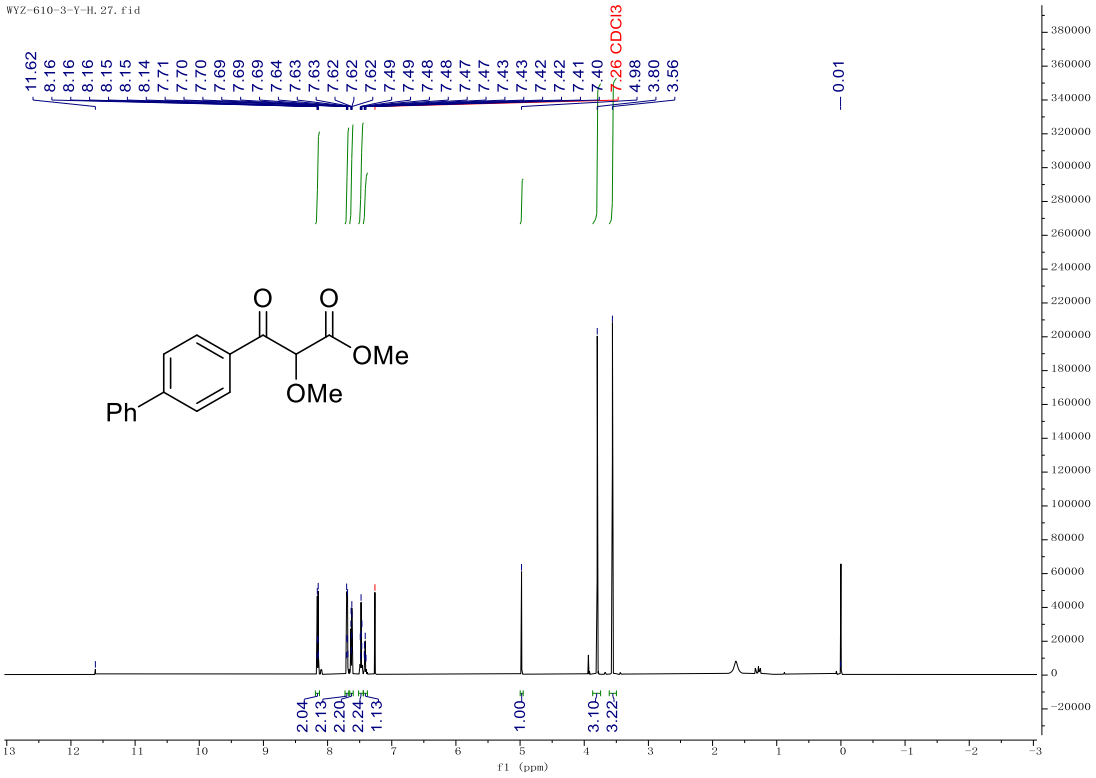
^{1}H NMR spectra (400 MHz, $CDCl_3$) of **1h**



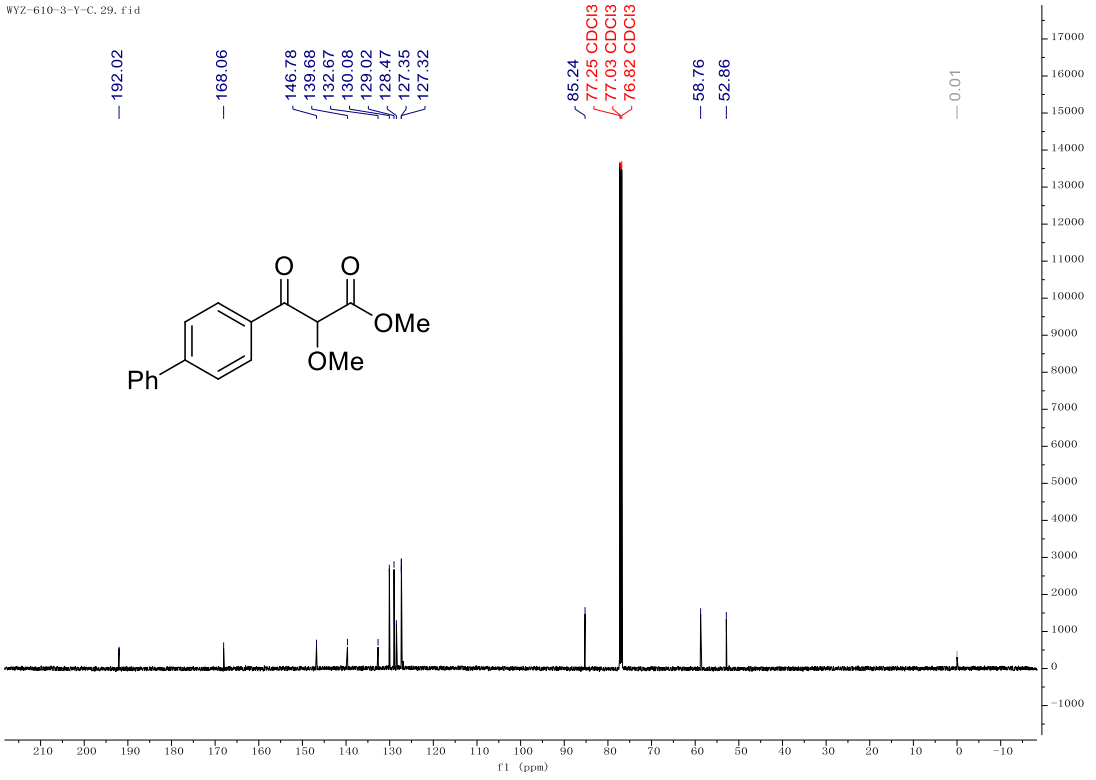
^{13}C NMR spectra (101 MHz, $CDCl_3$) of **1h**



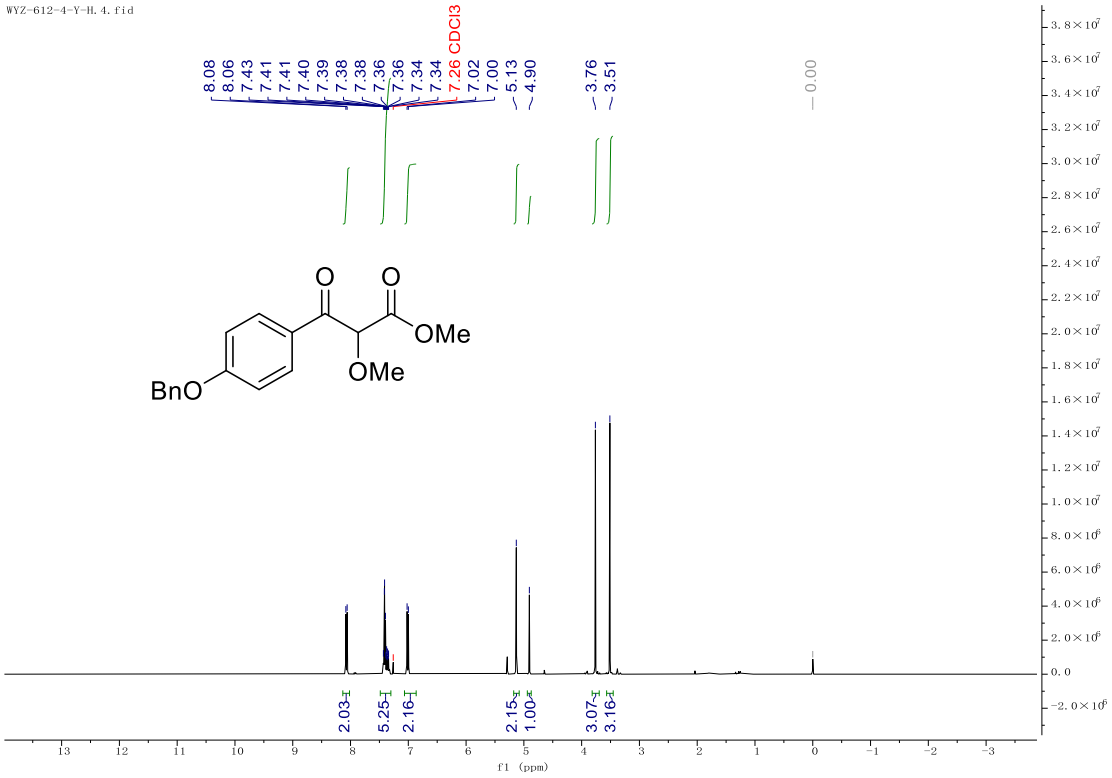
^{1}H NMR spectra (600 MHz, $CDCl_3$) of **1i**



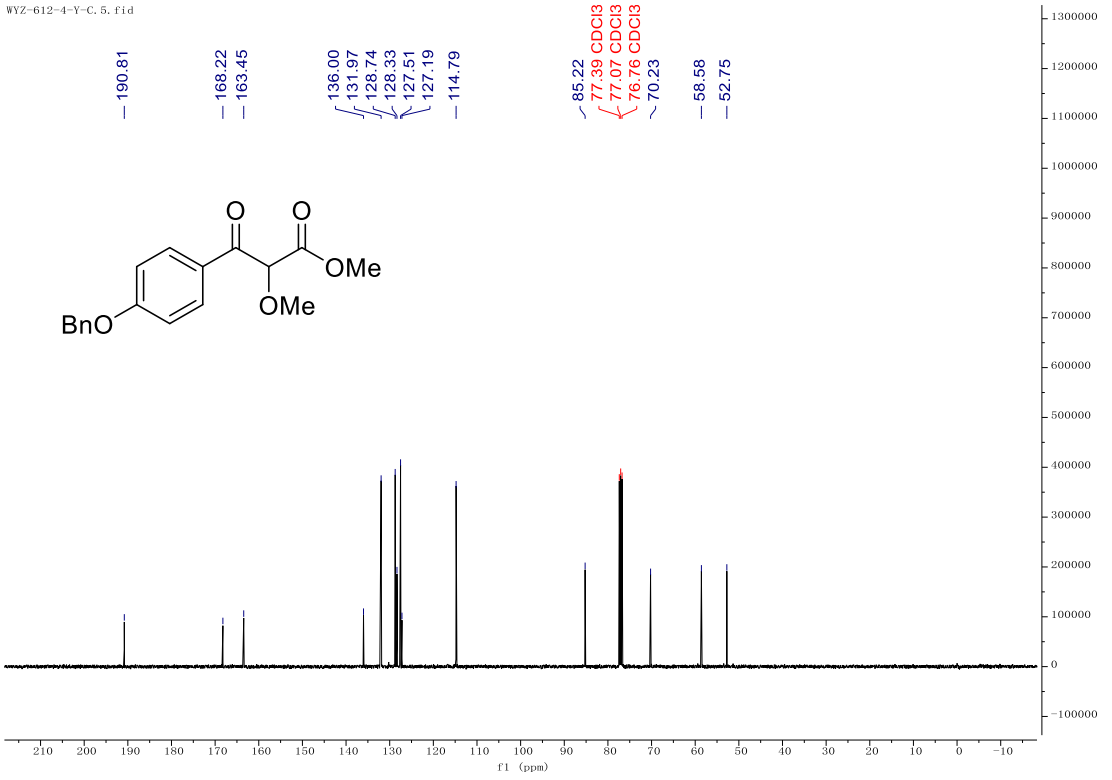
^{13}C NMR spectra (151 MHz, $CDCl_3$) of **1i**



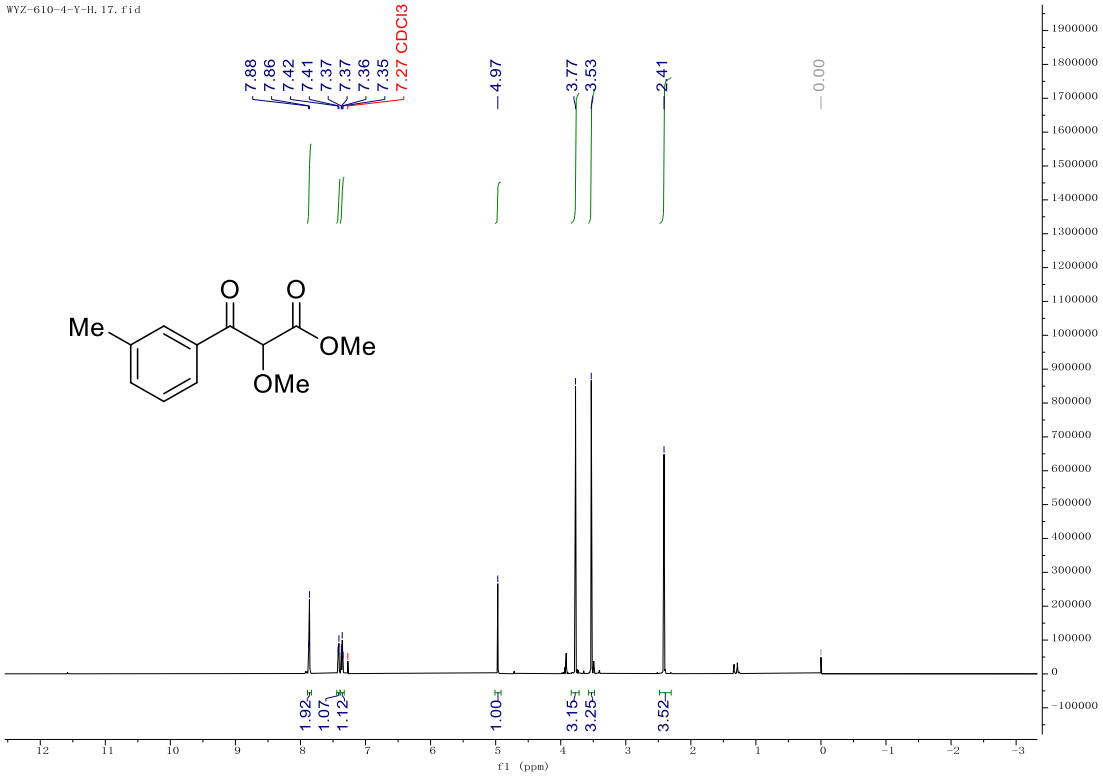
^{1}H NMR spectra (600 MHz, $CDCl_3$) of **1j**



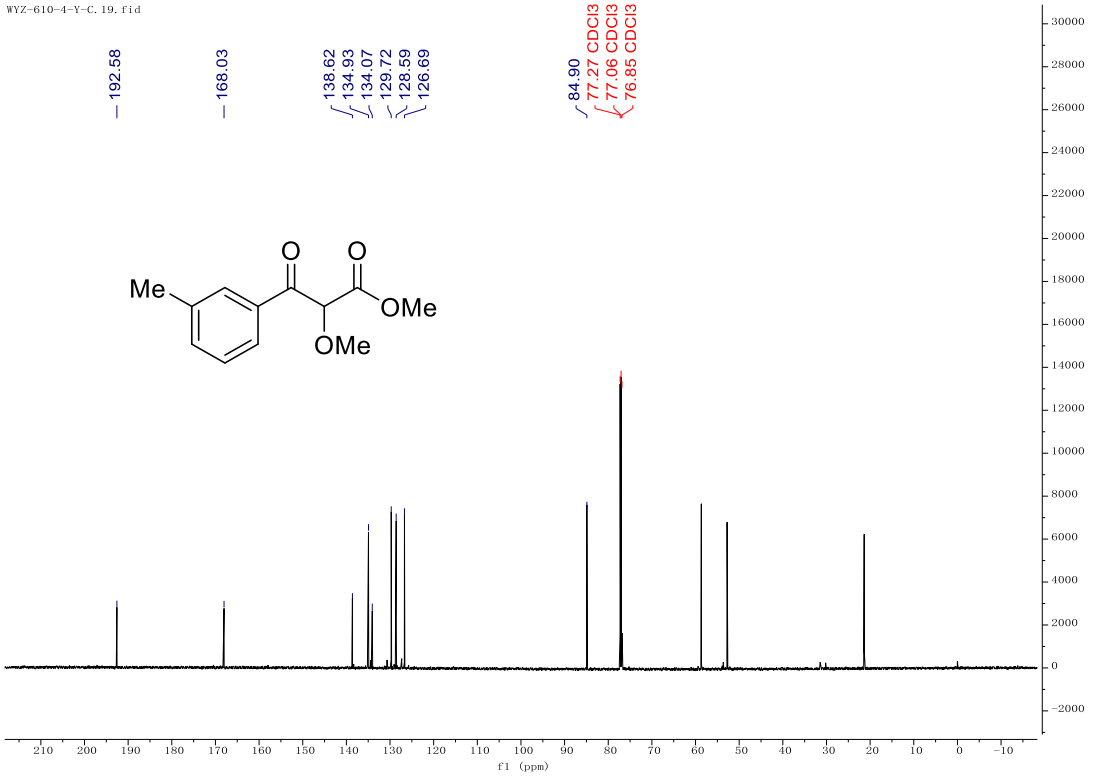
^{13}C NMR spectra (151 MHz, $CDCl_3$) of **1j**



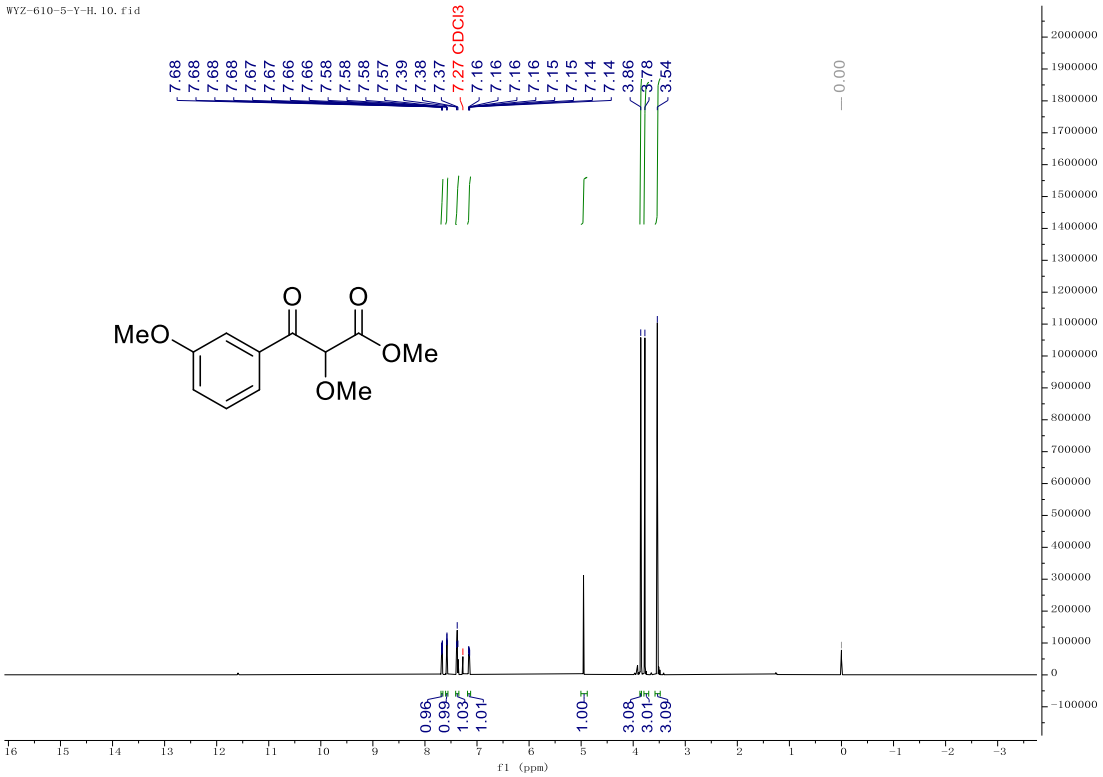
^{1}H NMR spectra (600 MHz, $CDCl_3$) of **1k**



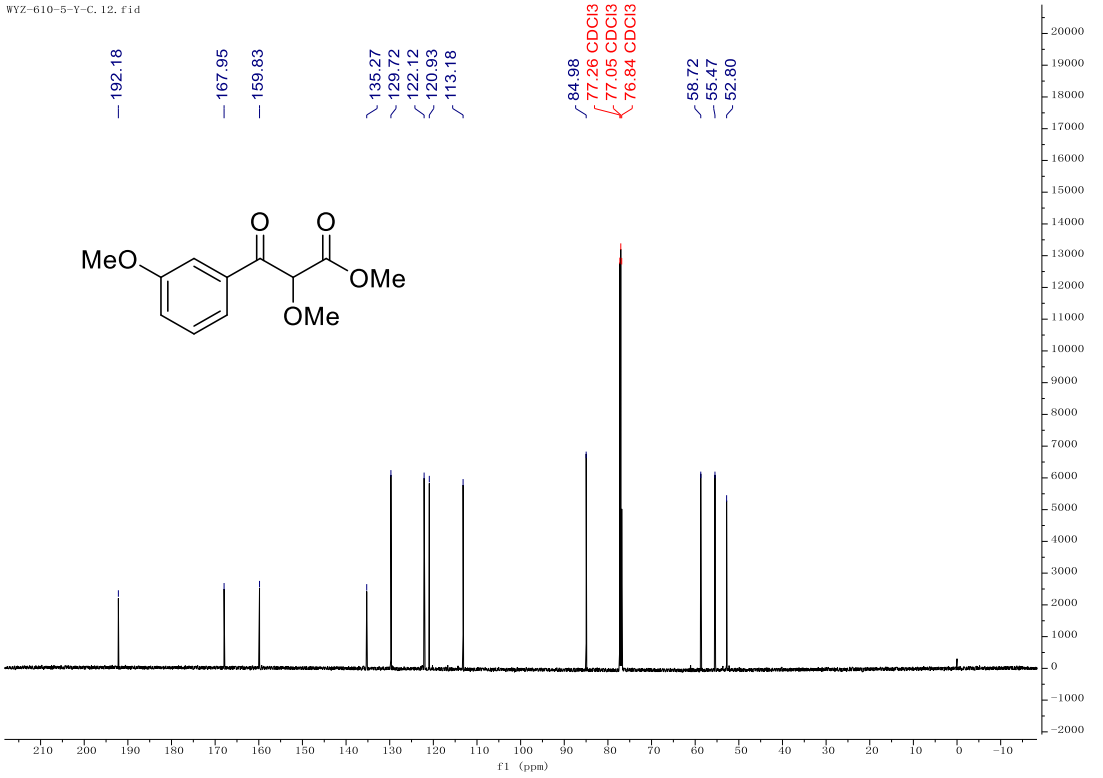
^{13}C NMR spectra (151 MHz, $CDCl_3$) of **1k**



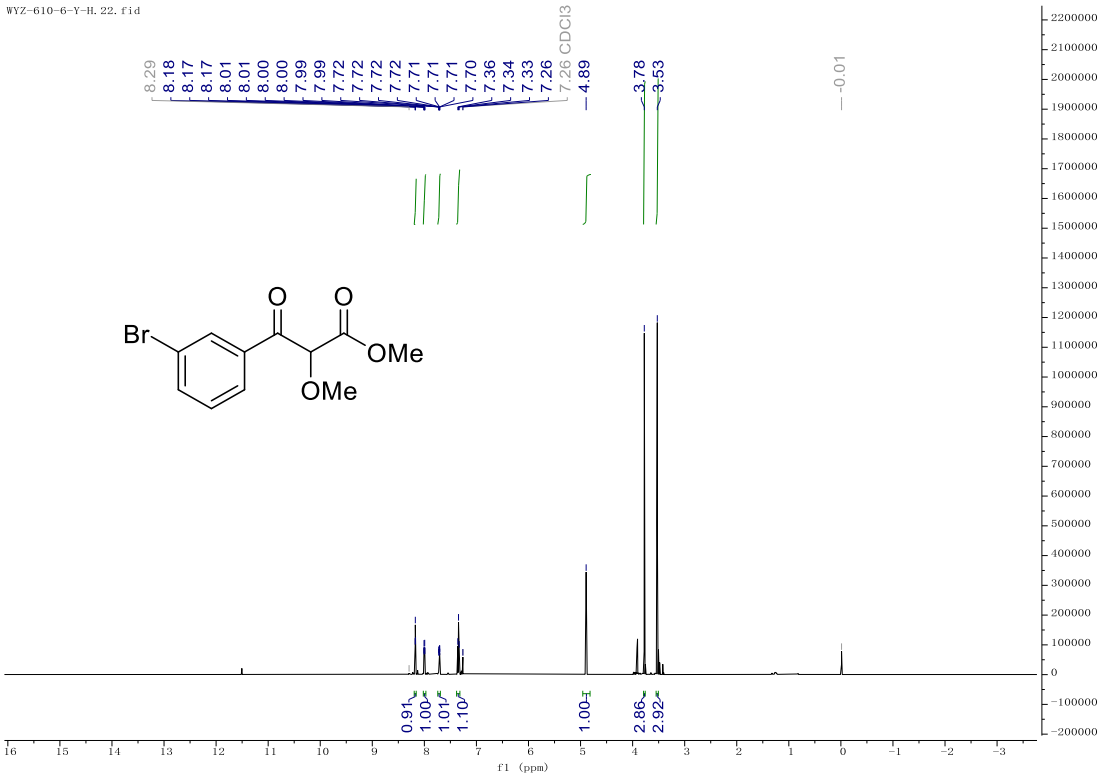
^{1}H NMR spectra (600 MHz, $CDCl_3$) of **1l**



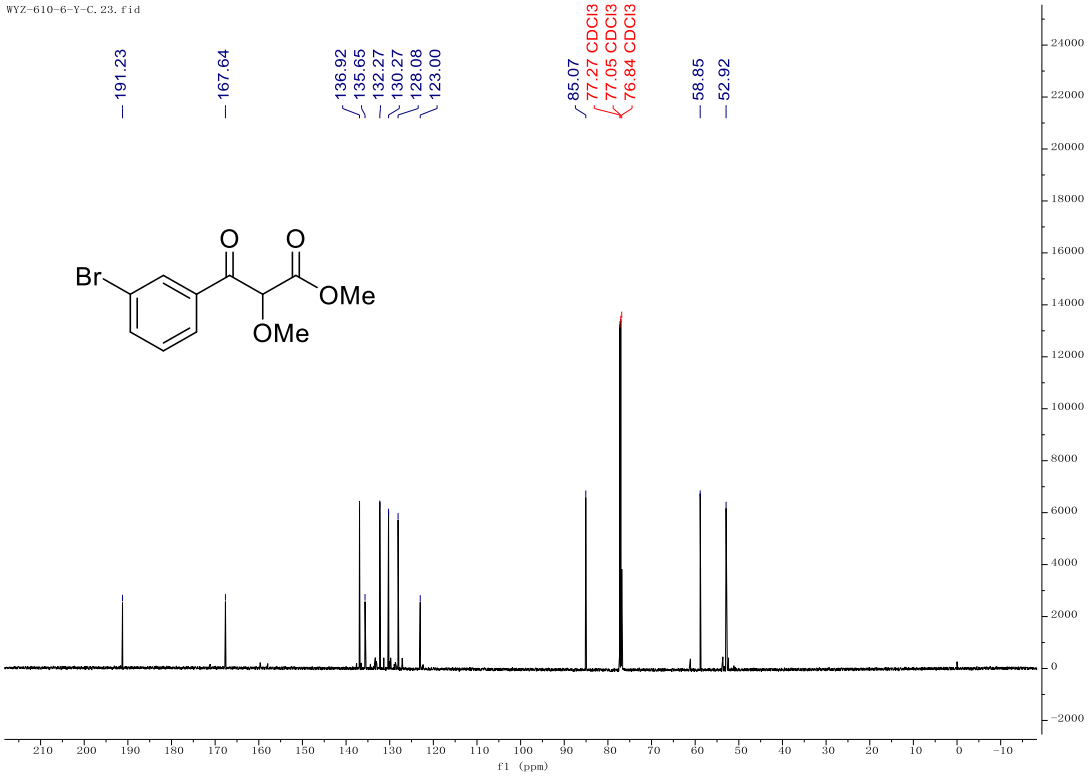
^{13}C NMR spectra (151 MHz, $CDCl_3$) of **1l**



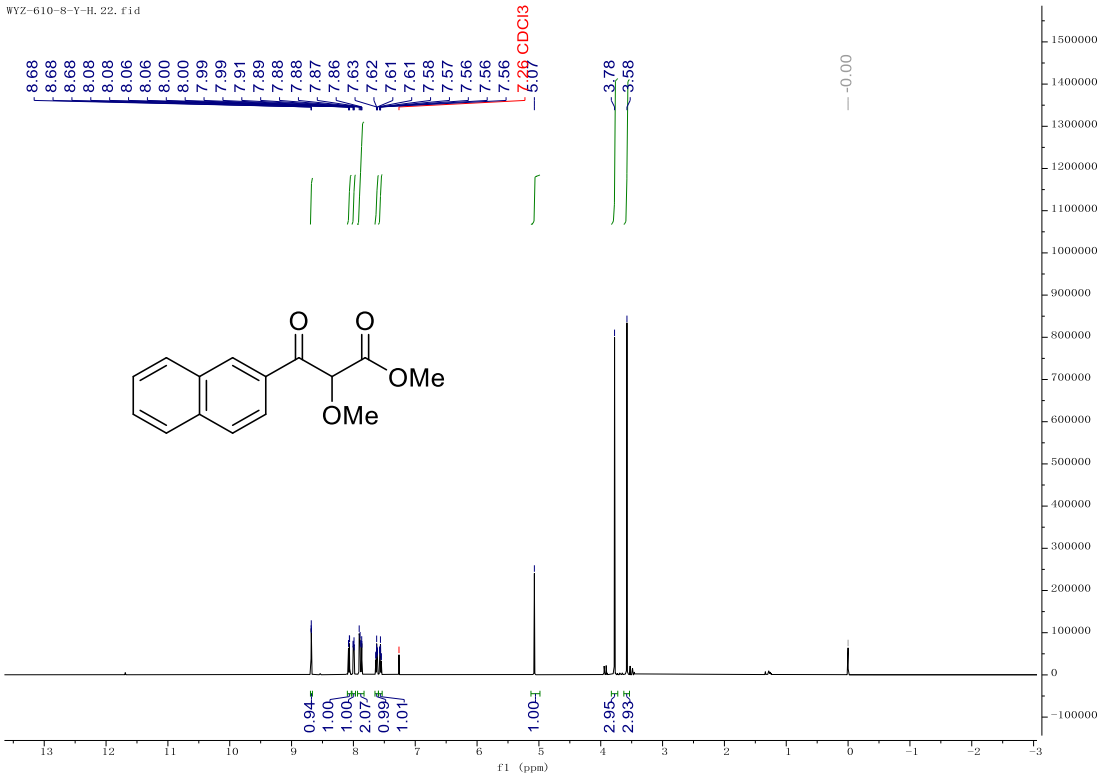
^{1}H NMR spectra (600 MHz, $CDCl_3$) of **1m**



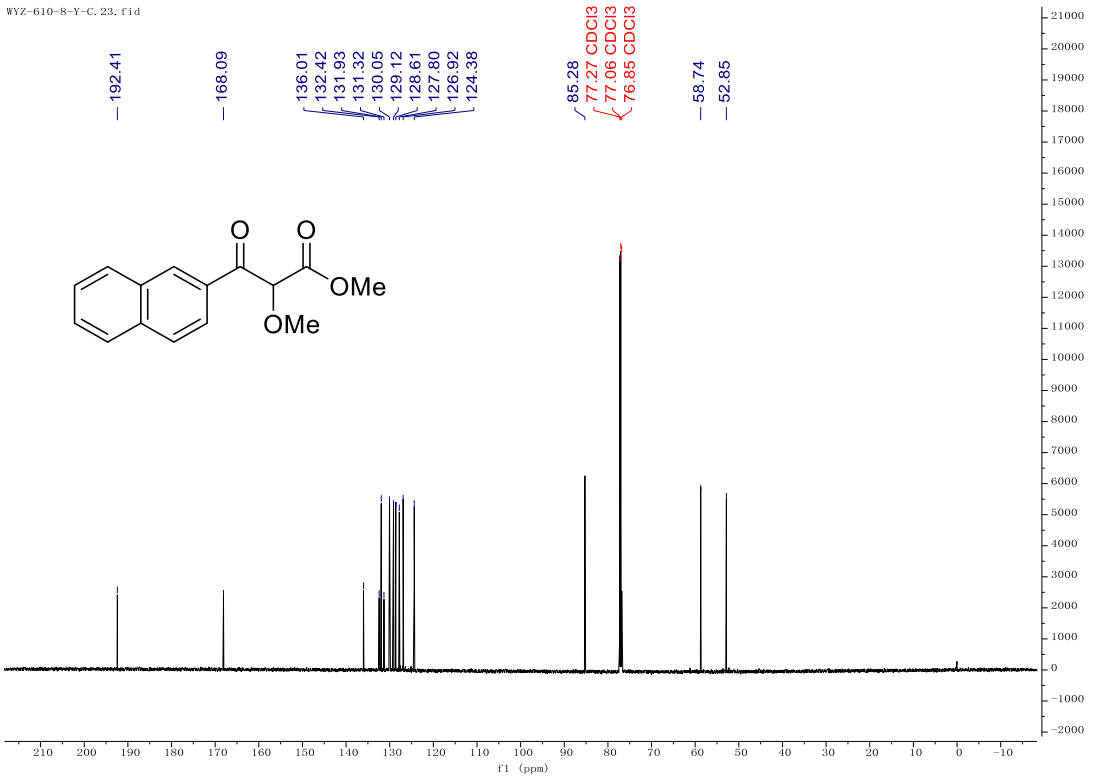
^{13}C NMR spectra (151 MHz, $CDCl_3$) of **1m**



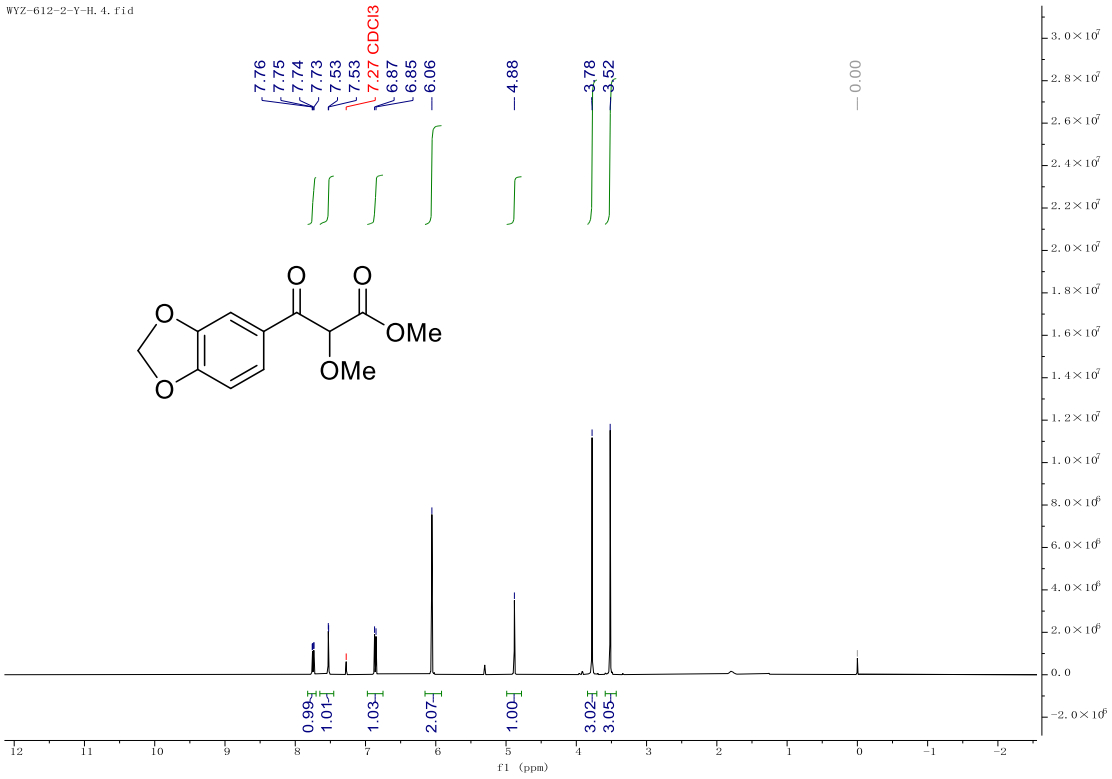
^{1}H NMR spectra (600 MHz, $CDCl_3$) of **1n**



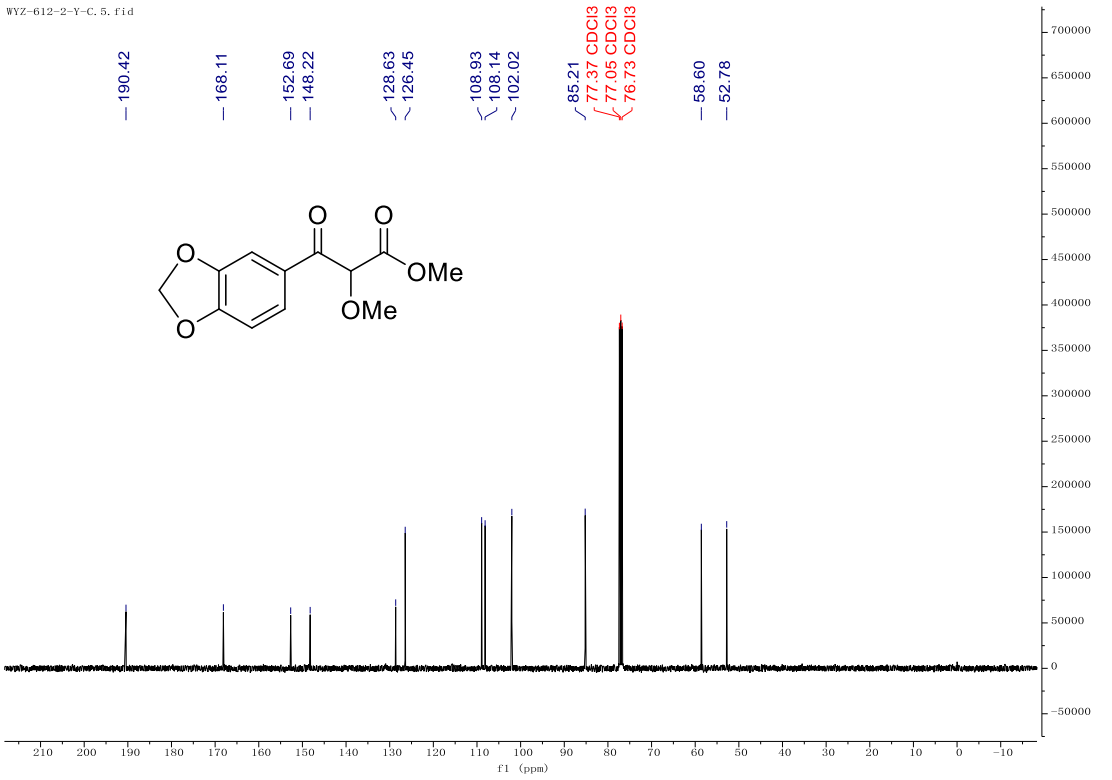
^{13}C NMR spectra (151 MHz, $CDCl_3$) of **1n**



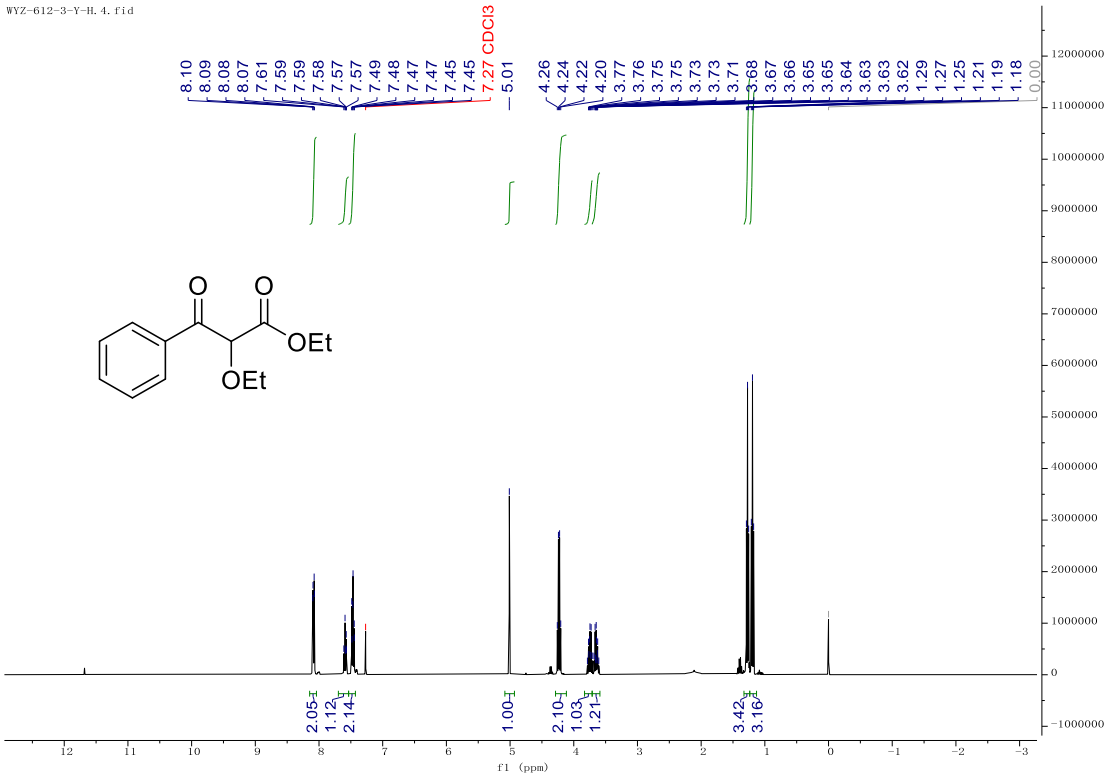
^{1}H NMR spectra (600 MHz, $CDCl_3$) of **1o**



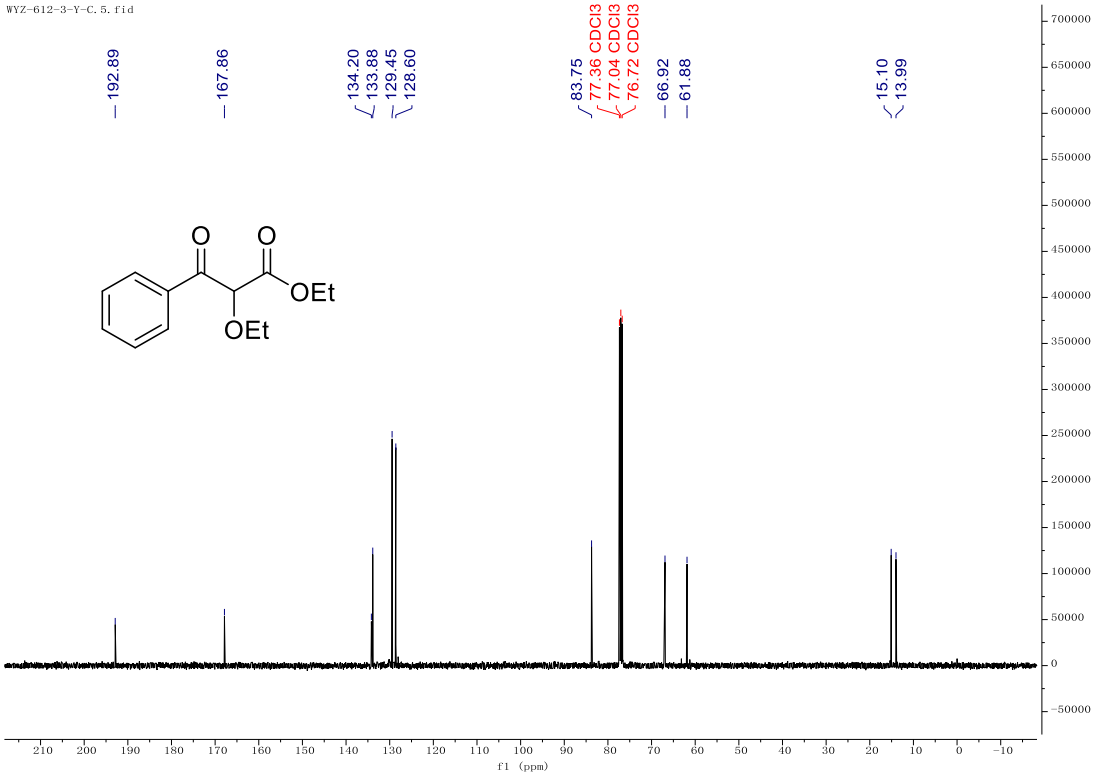
^{13}C NMR spectra (151 MHz, $CDCl_3$) of **1o**



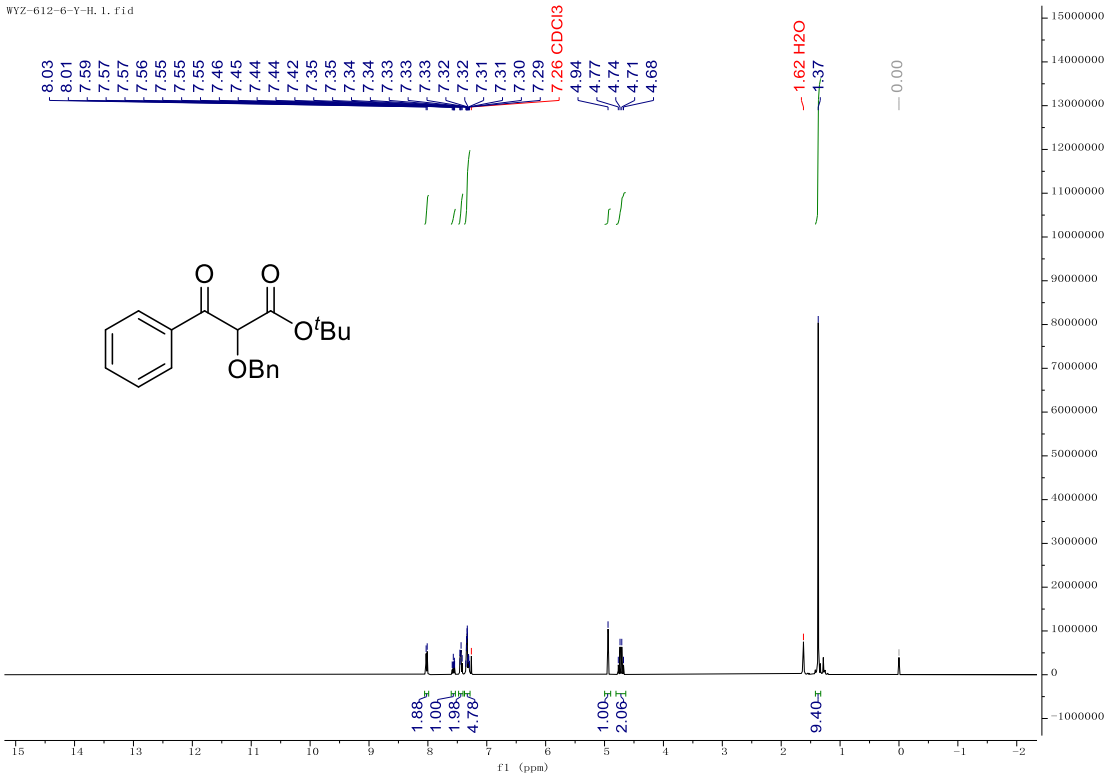
^{1}H NMR spectra (600 MHz, $CDCl_3$) of **1p**



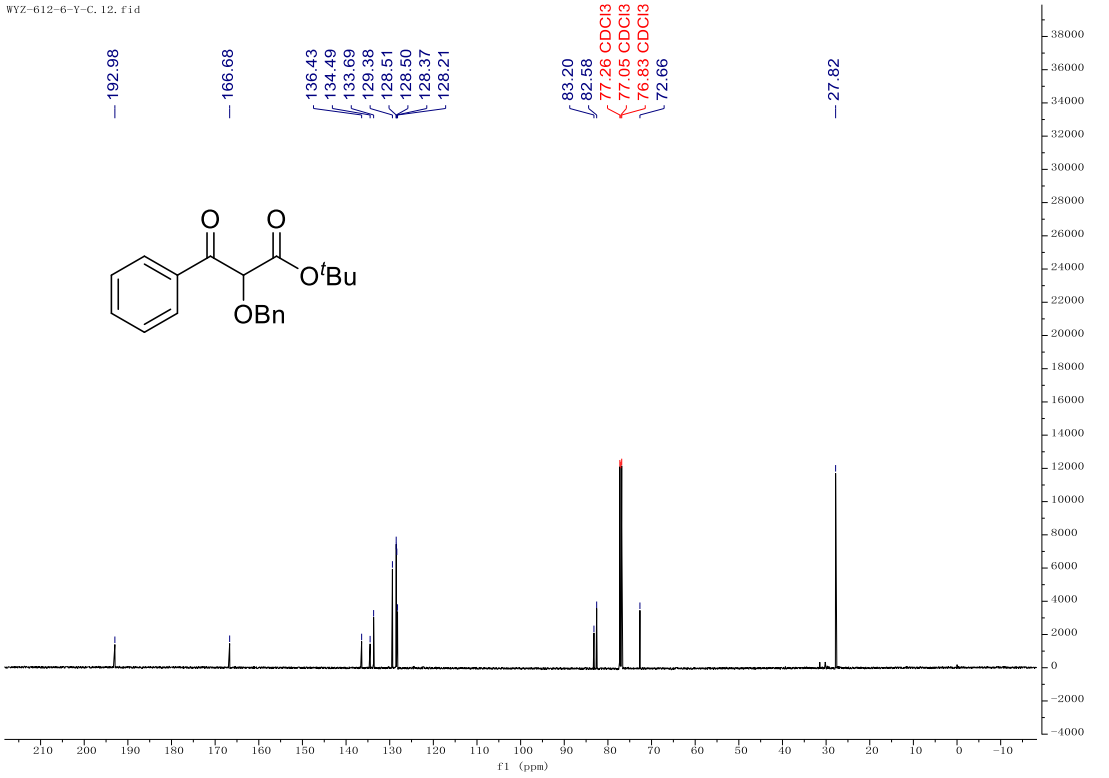
^{13}C NMR spectra (151 MHz, $CDCl_3$) of **1p**



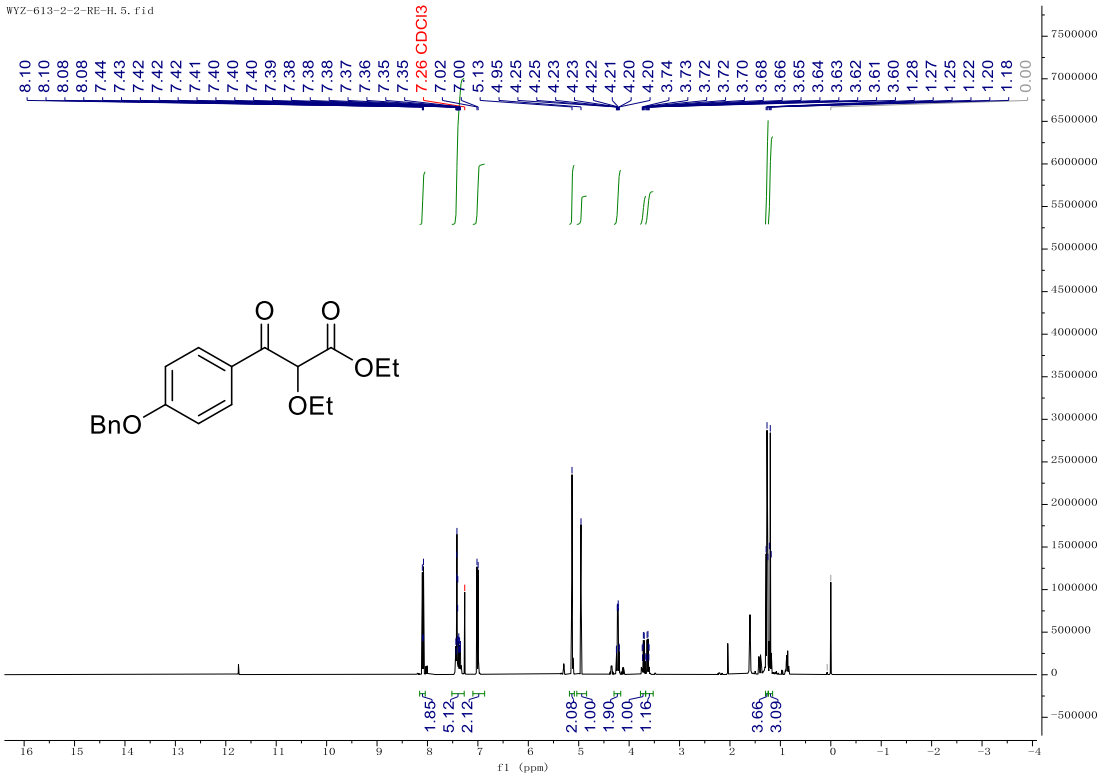
^{1}H NMR spectra (600 MHz, $CDCl_3$) of **1q**



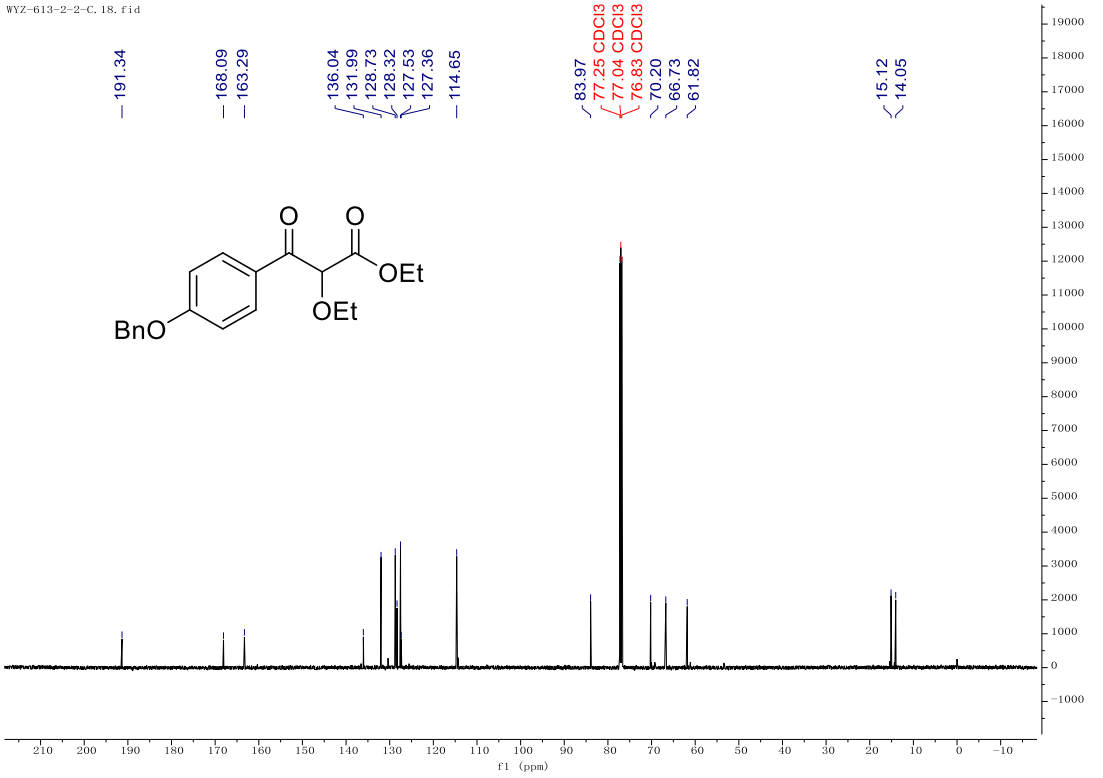
^{13}C NMR spectra (151 MHz, $CDCl_3$) of **1q**



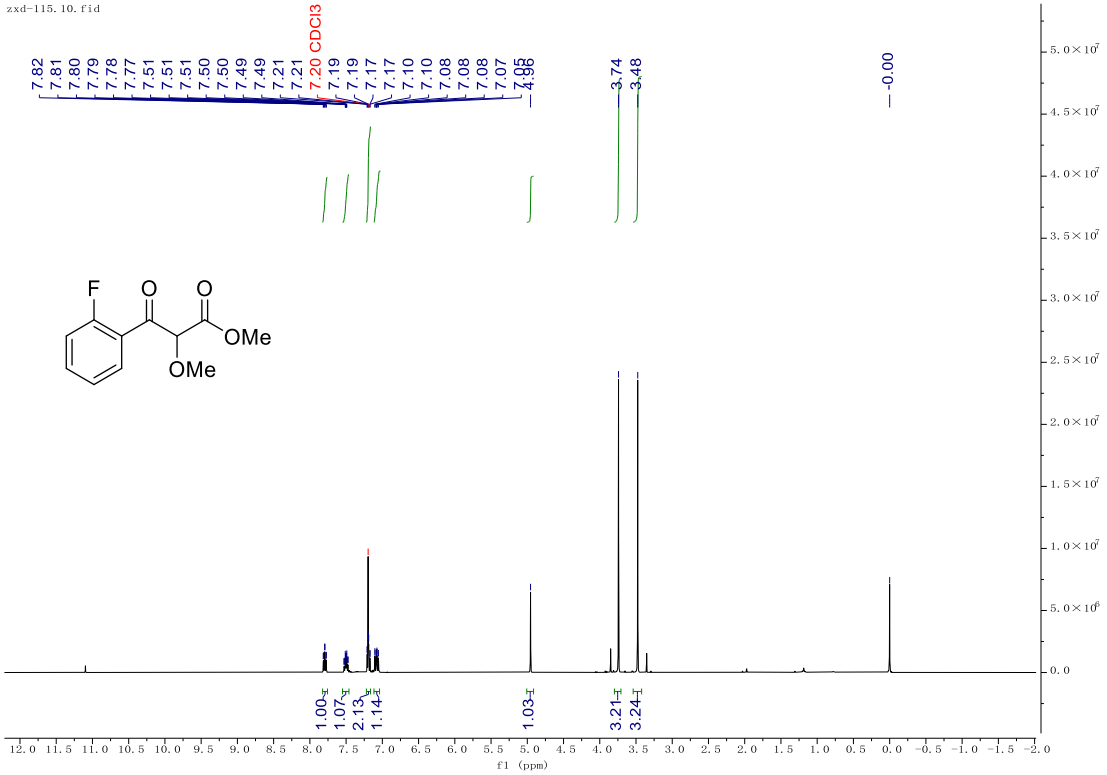
^{1}H NMR spectra (600 MHz, $CDCl_3$) of **1r**



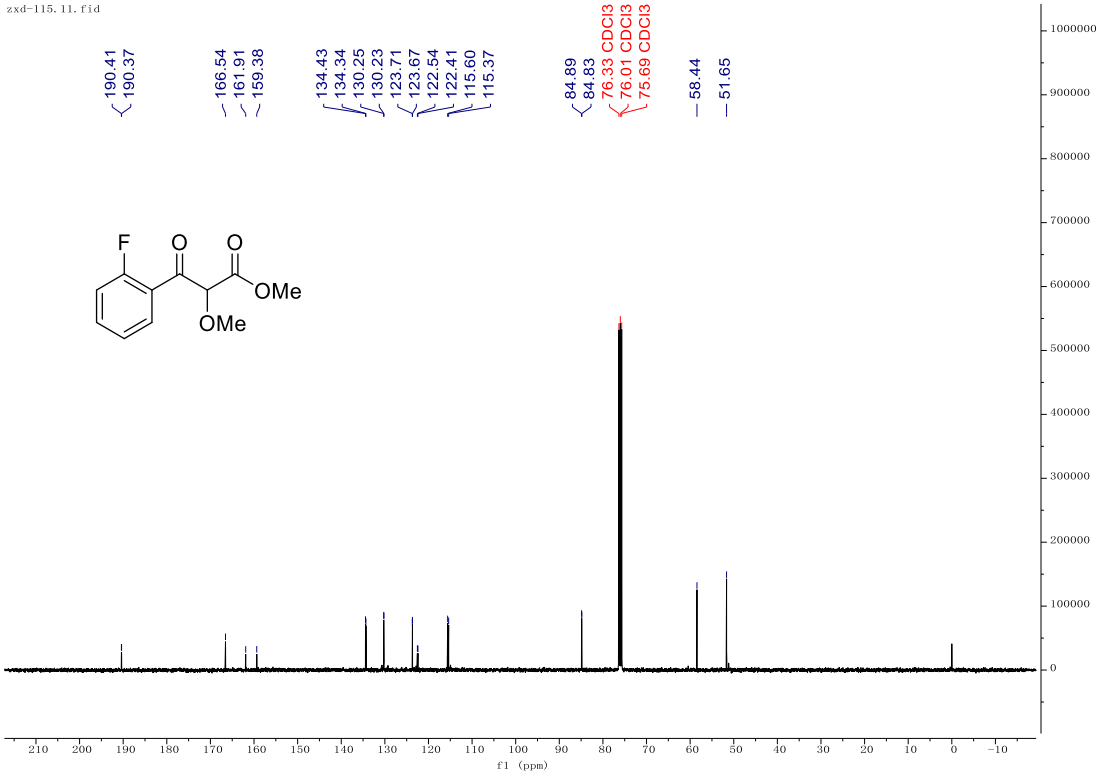
^{13}C NMR spectra (151 MHz, $CDCl_3$) of **1r**



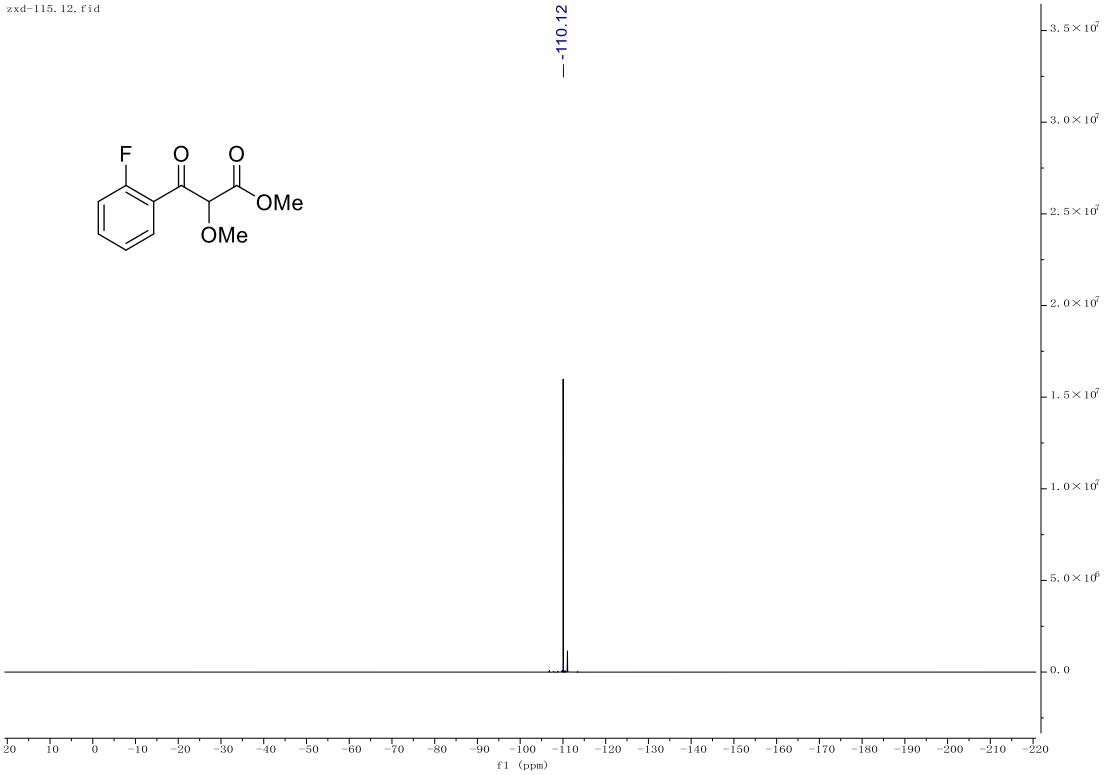
^{1}H NMR spectra (400 MHz, $CDCl_3$) of **1s**



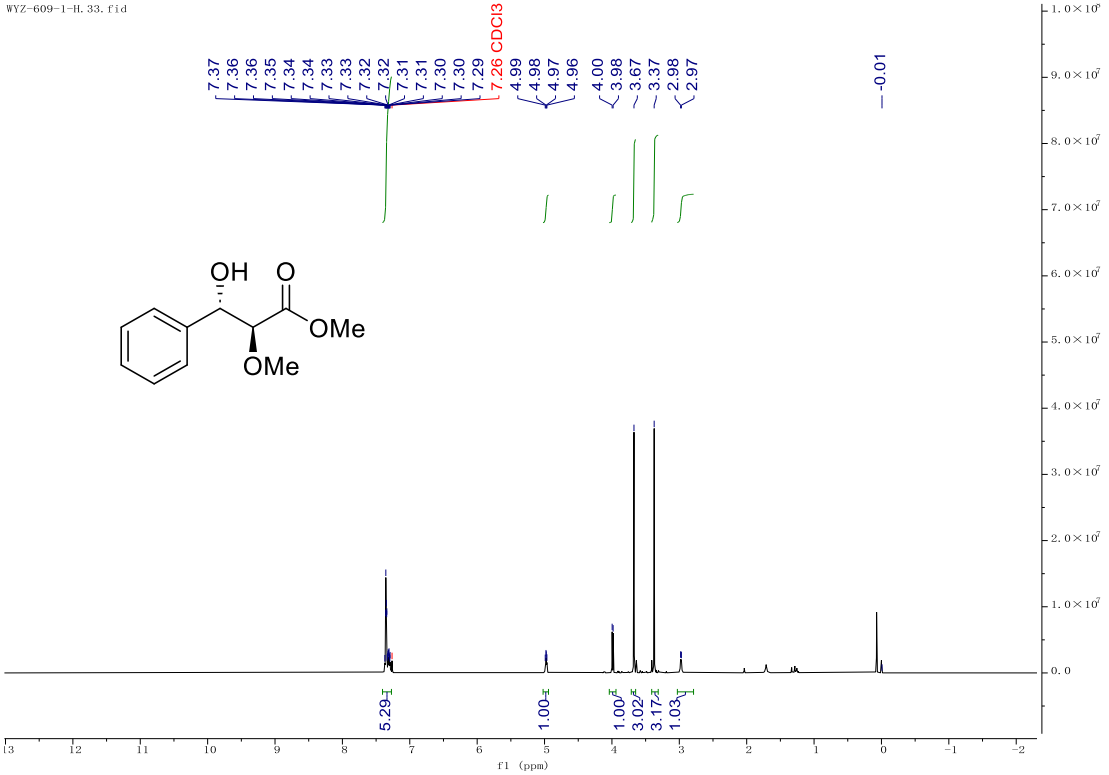
^{13}C NMR spectra (101 MHz, $CDCl_3$) of **1s**



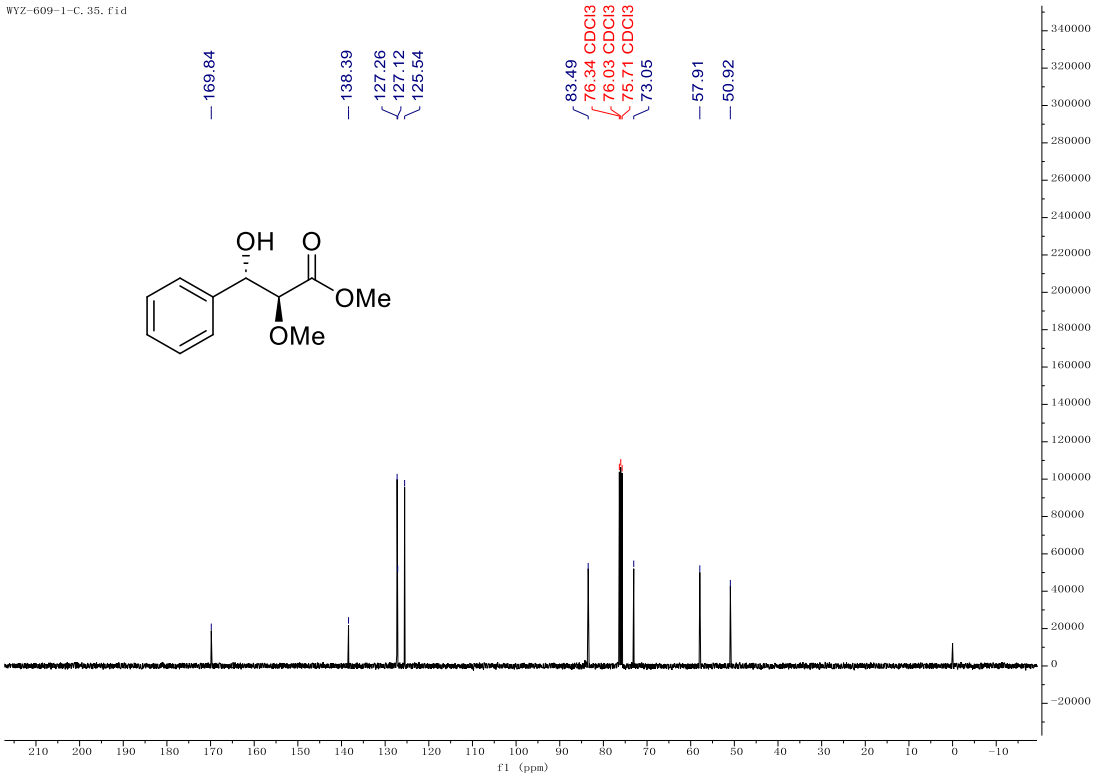
^{19}F NMR spectra (377 MHz, $CDCl_3$) of **1s**



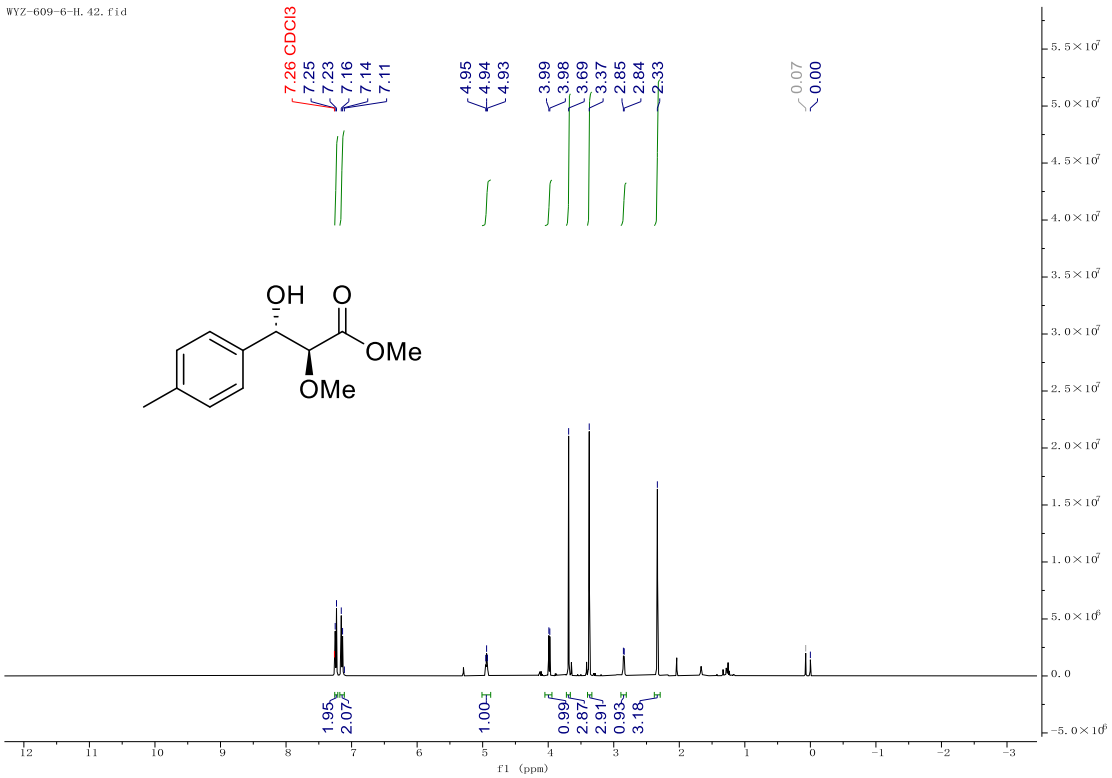
^{1}H NMR spectra (400 MHz, $CDCl_3$) of **2a**



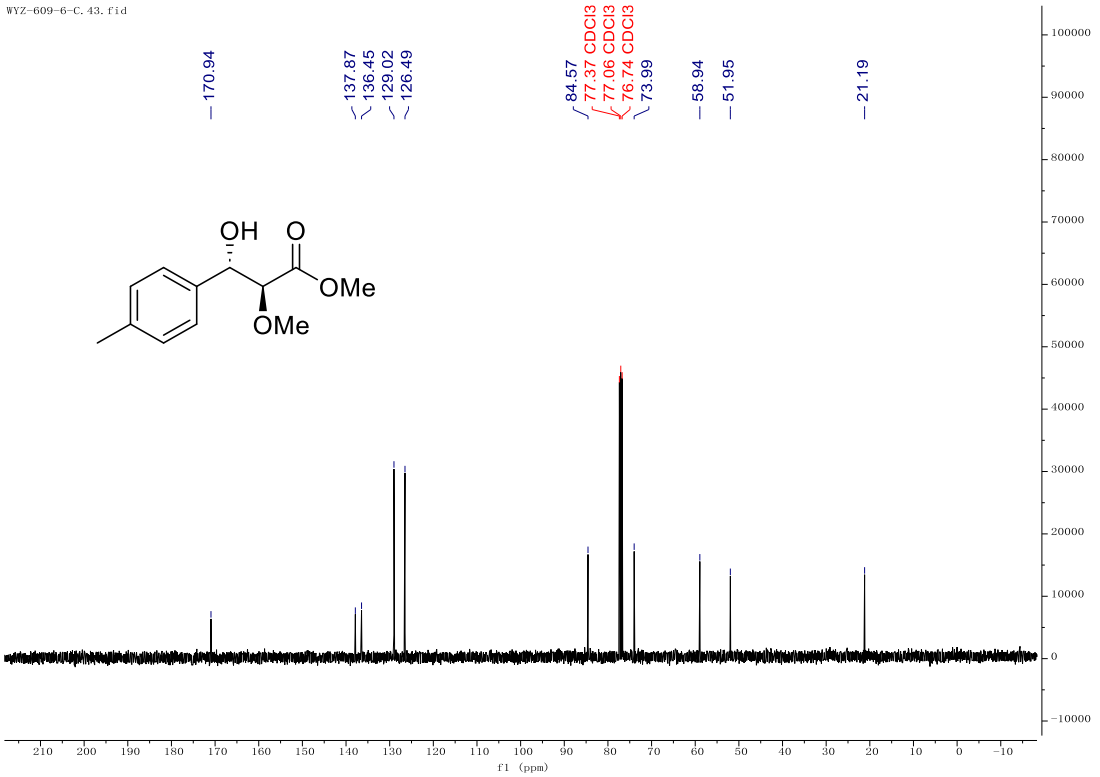
^{13}C NMR spectra (101 MHz, $CDCl_3$) of **2a**



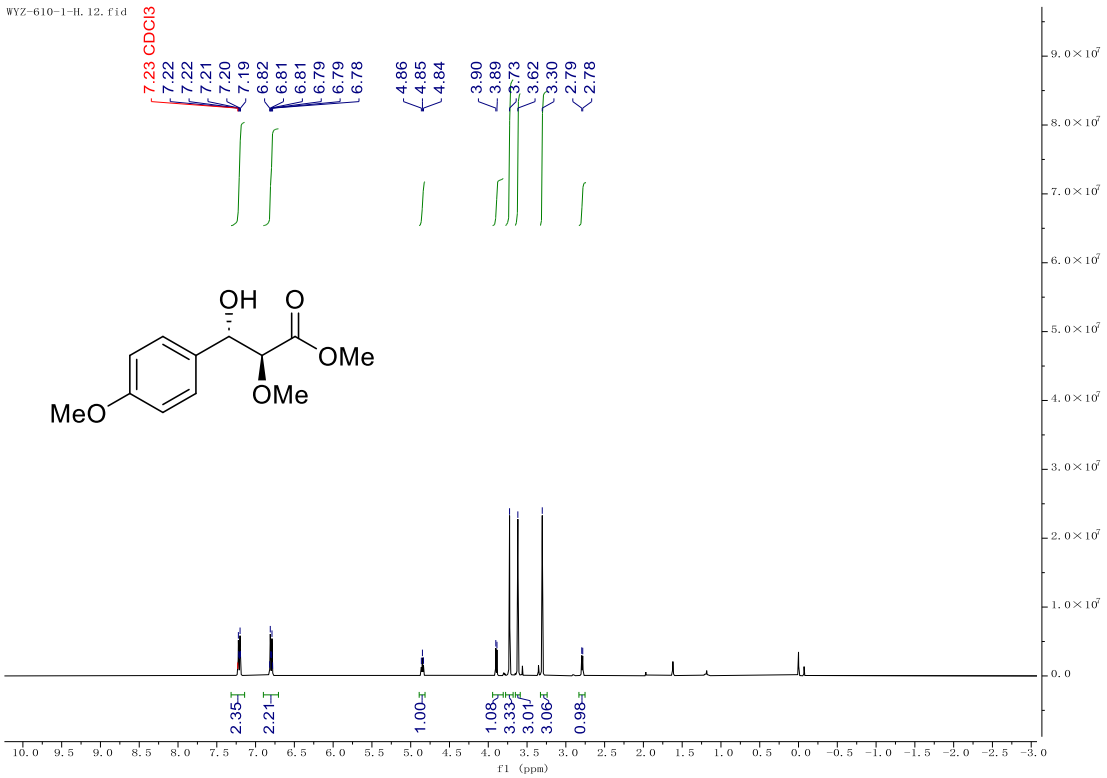
^{1}H NMR spectra (400 MHz, $CDCl_3$) of **2b**



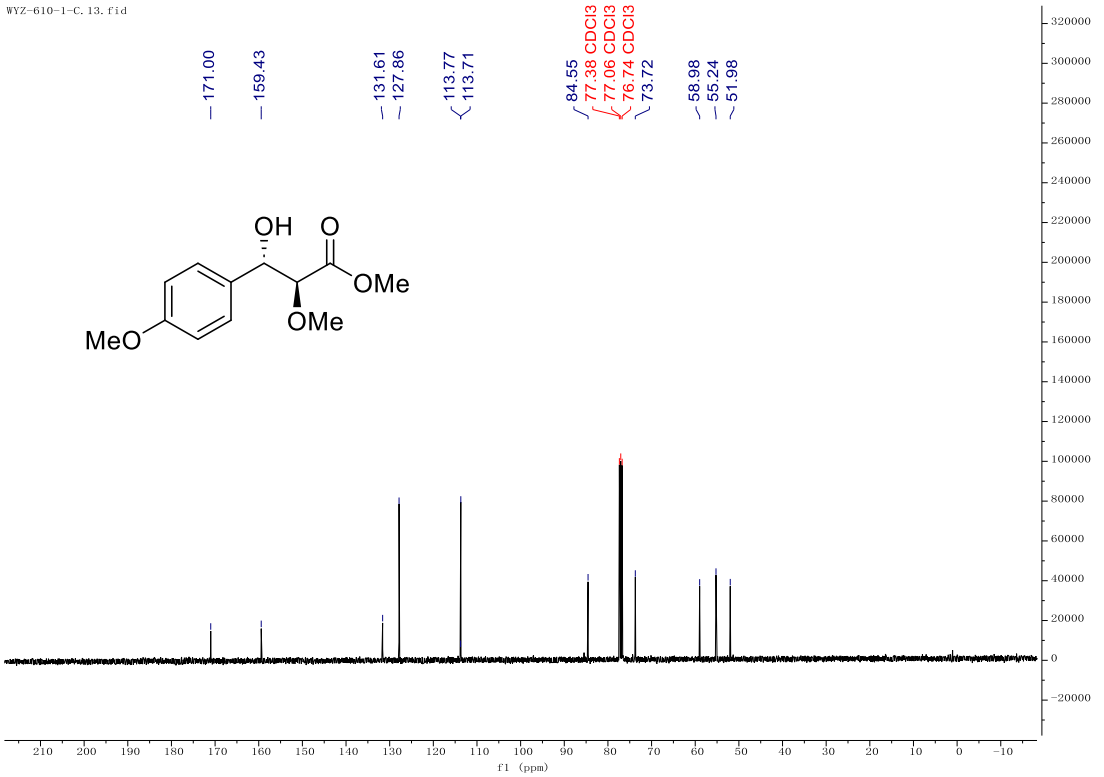
^{13}C NMR spectra (101 MHz, $CDCl_3$) of **2b**



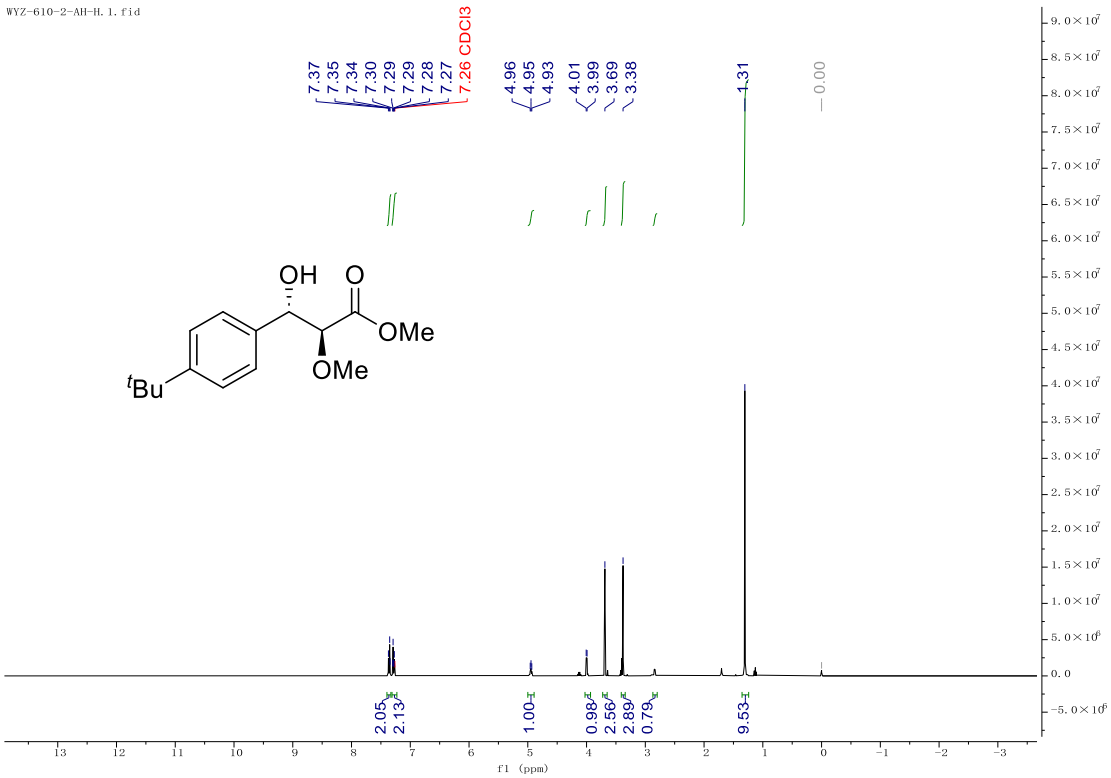
^{1}H NMR spectra (400 MHz, $CDCl_3$) of **2c**



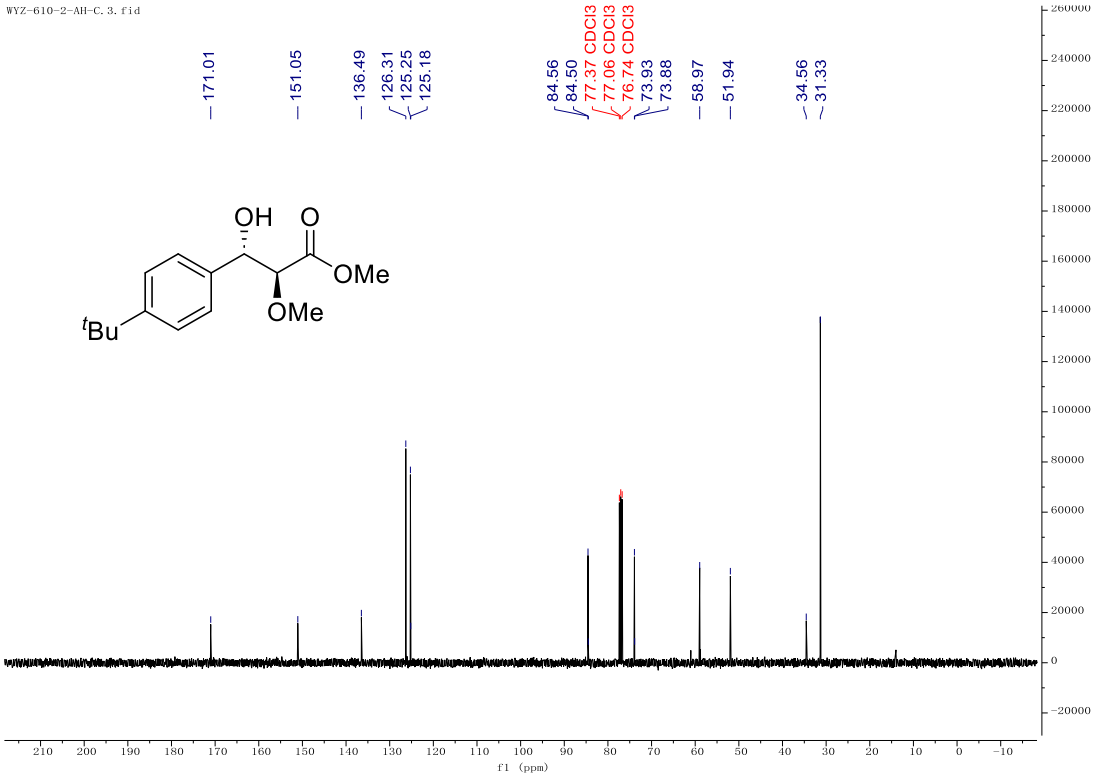
^{13}C NMR spectra (101 MHz, $CDCl_3$) of **2c**



^{1}H NMR spectra (400 MHz, $CDCl_3$) of **2d**



^{13}C NMR spectra (101 MHz, $CDCl_3$) of **2d**



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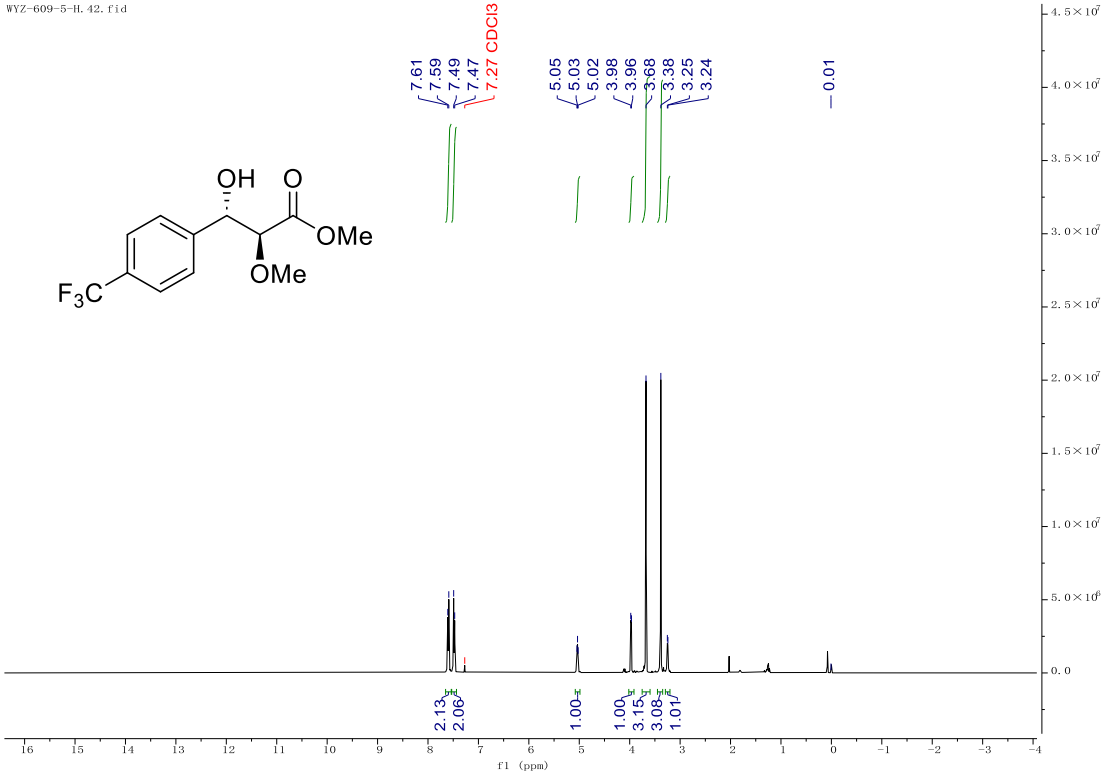
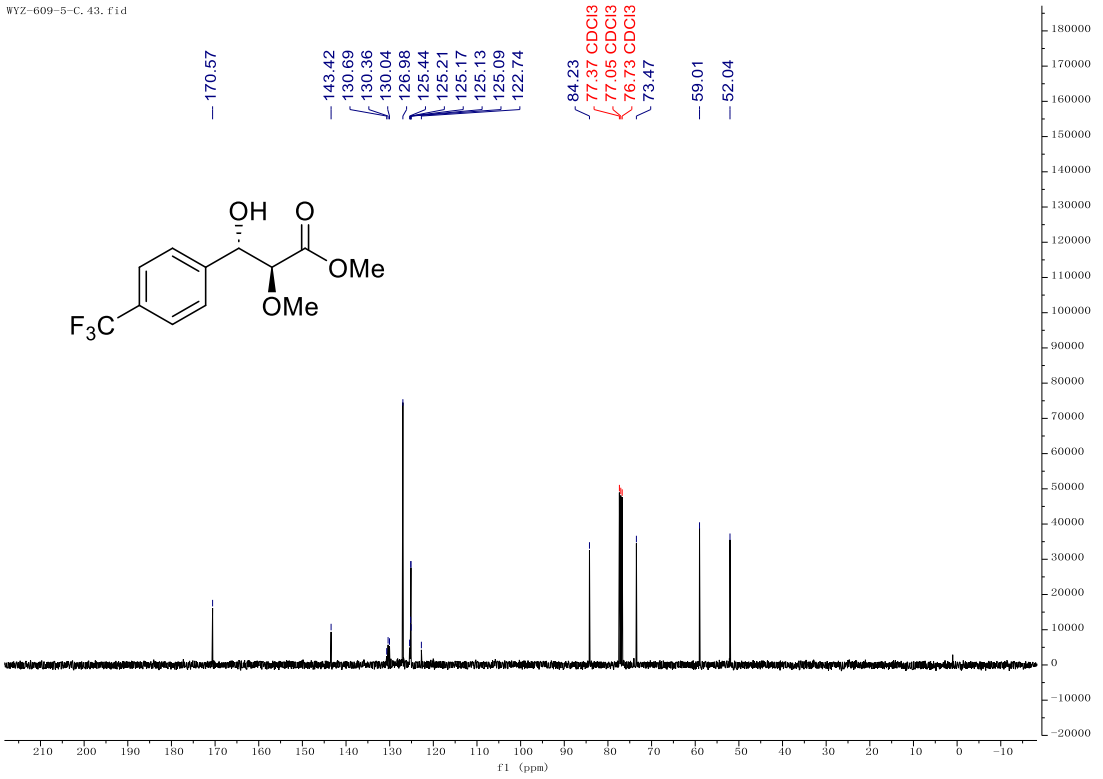
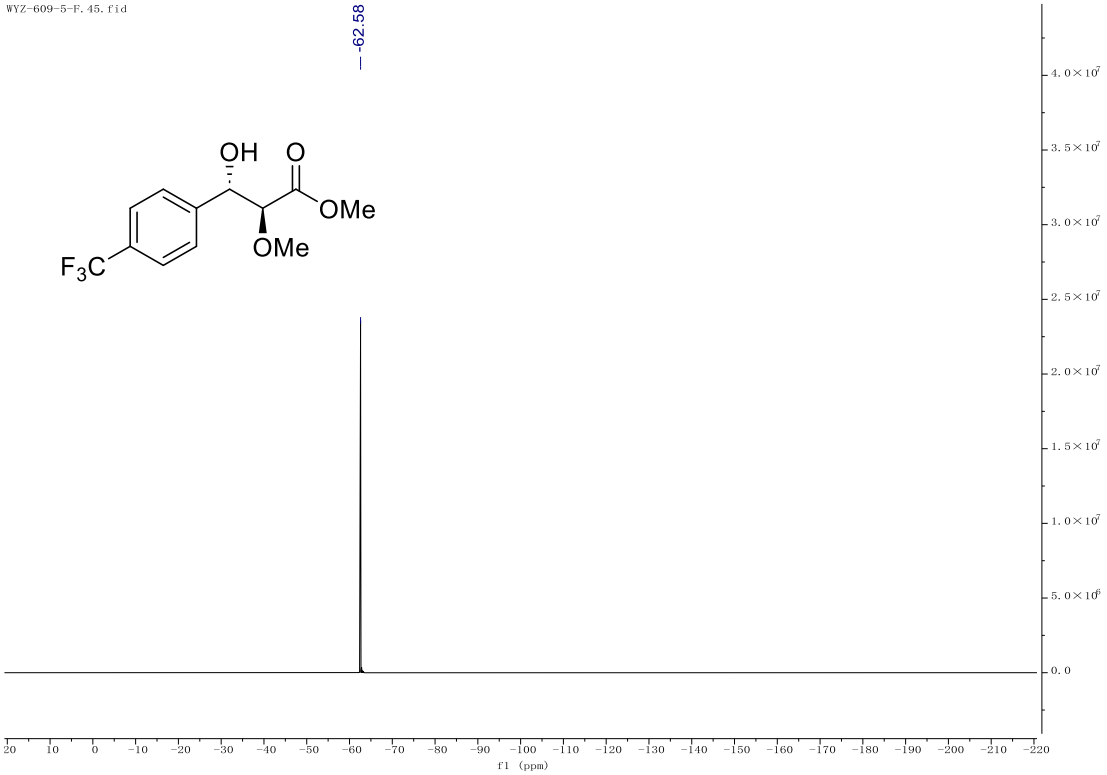


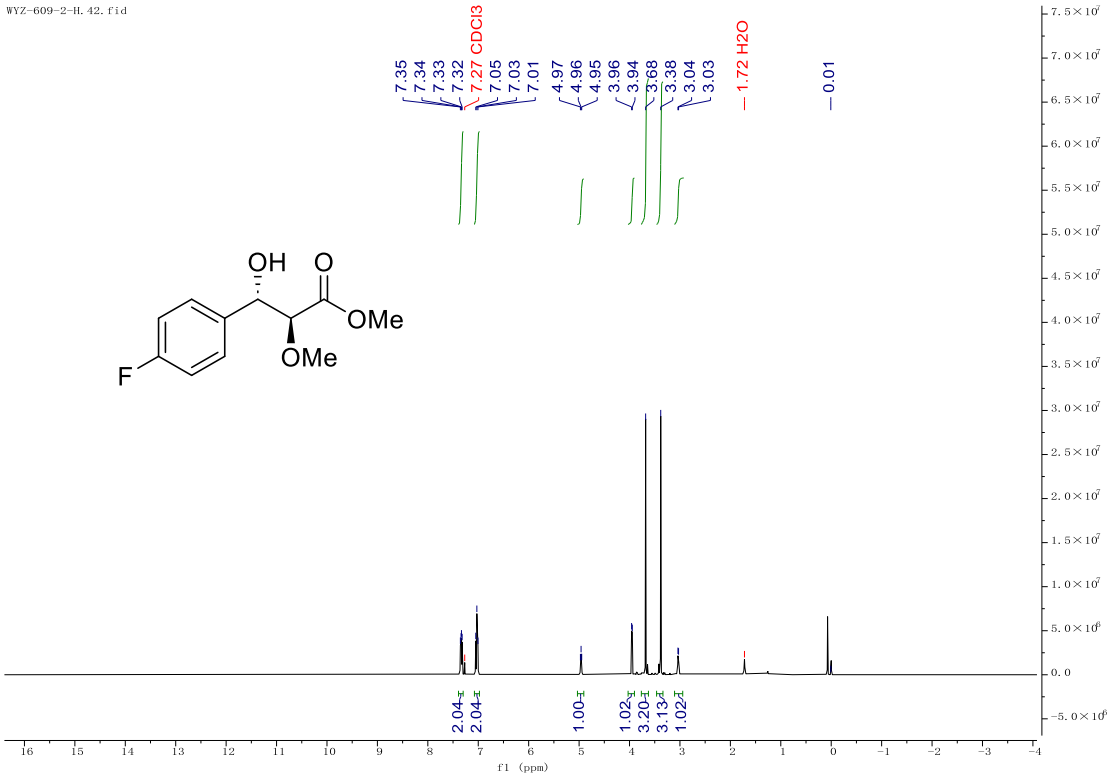
^{13}C NMR spectra (101 MHz, $CDCl_3$) of **2e**



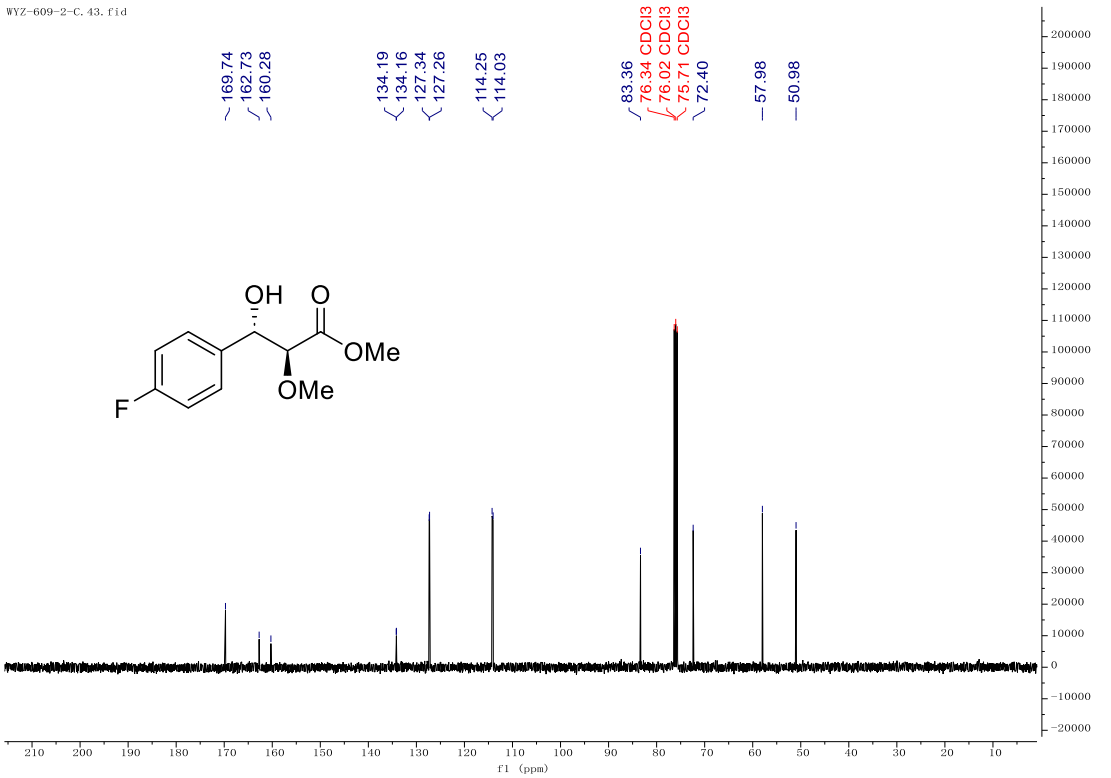
^{19}F NMR spectra (376 MHz, $CDCl_3$) of **2e**



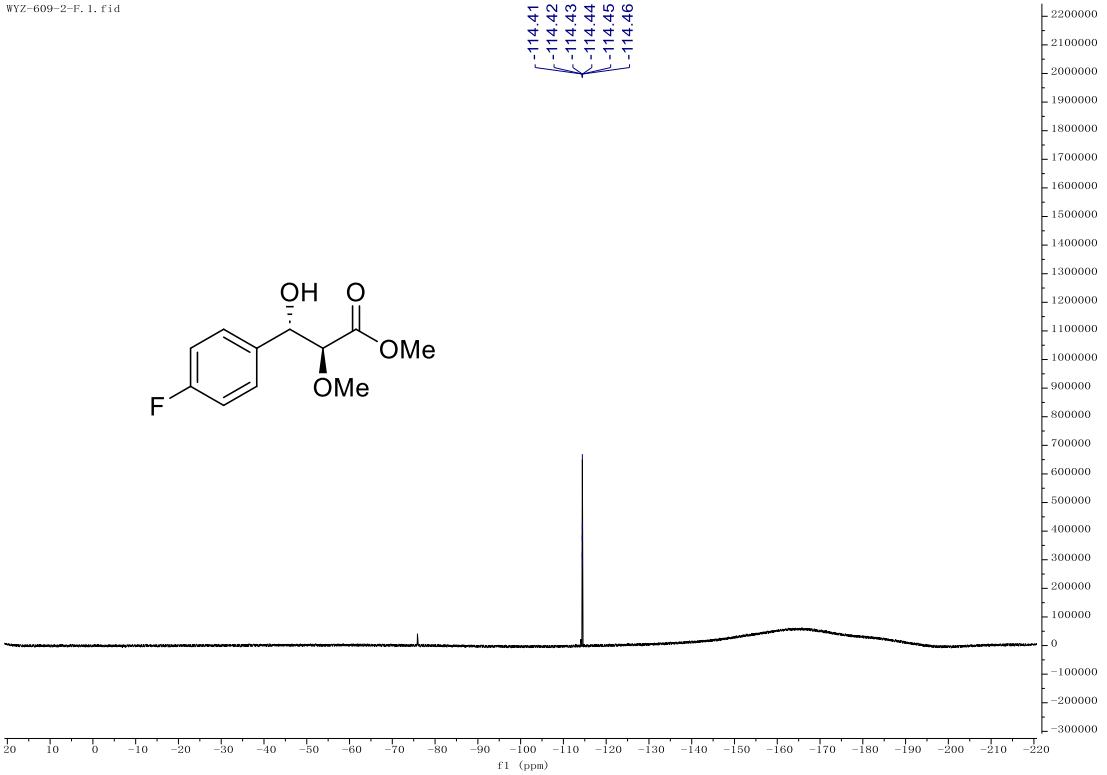
^{1}H NMR spectra (400 MHz, $CDCl_3$) of **2f**



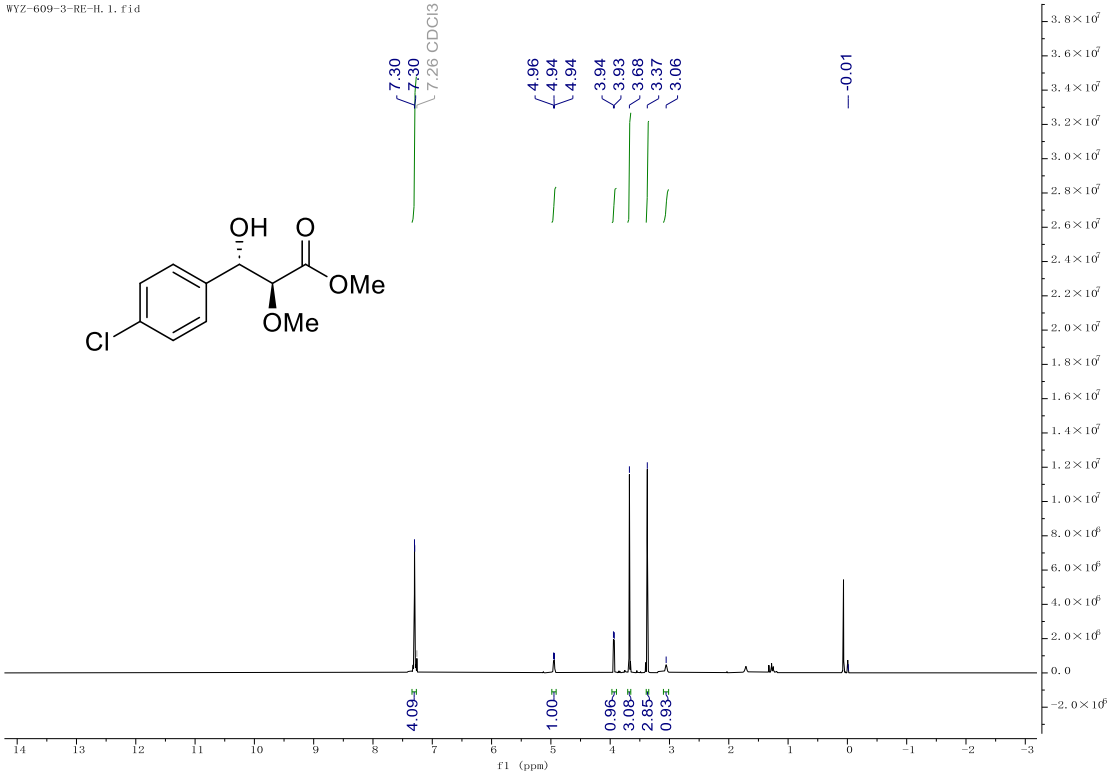
^{13}C NMR spectra (101 MHz, $CDCl_3$) of **2f**



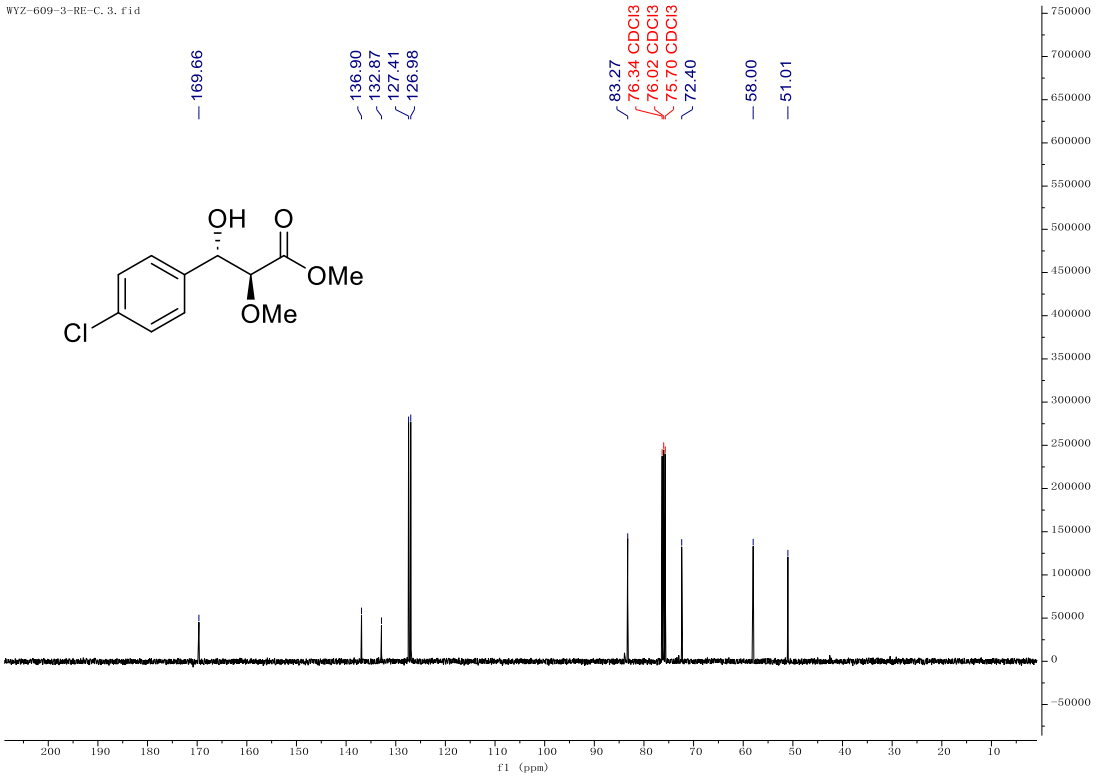
^{19}F NMR spectra (376 MHz, $CDCl_3$) of **2f**



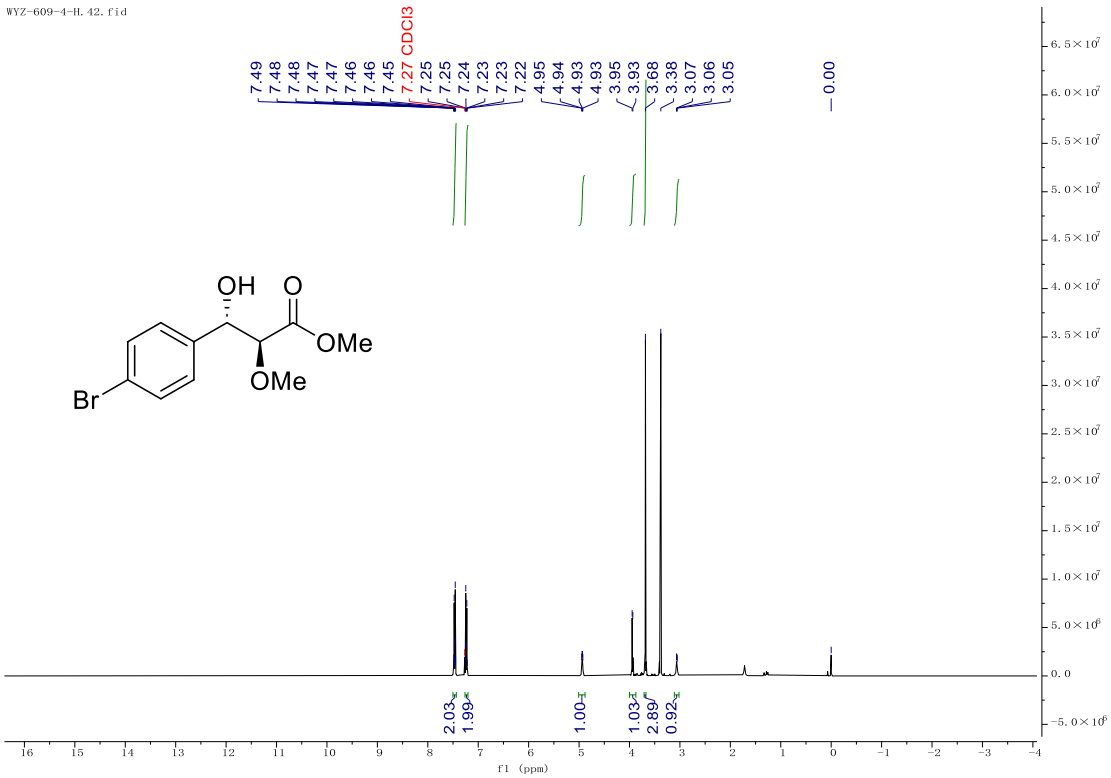
^{1}H NMR spectra (400 MHz, $CDCl_3$) of **2g**



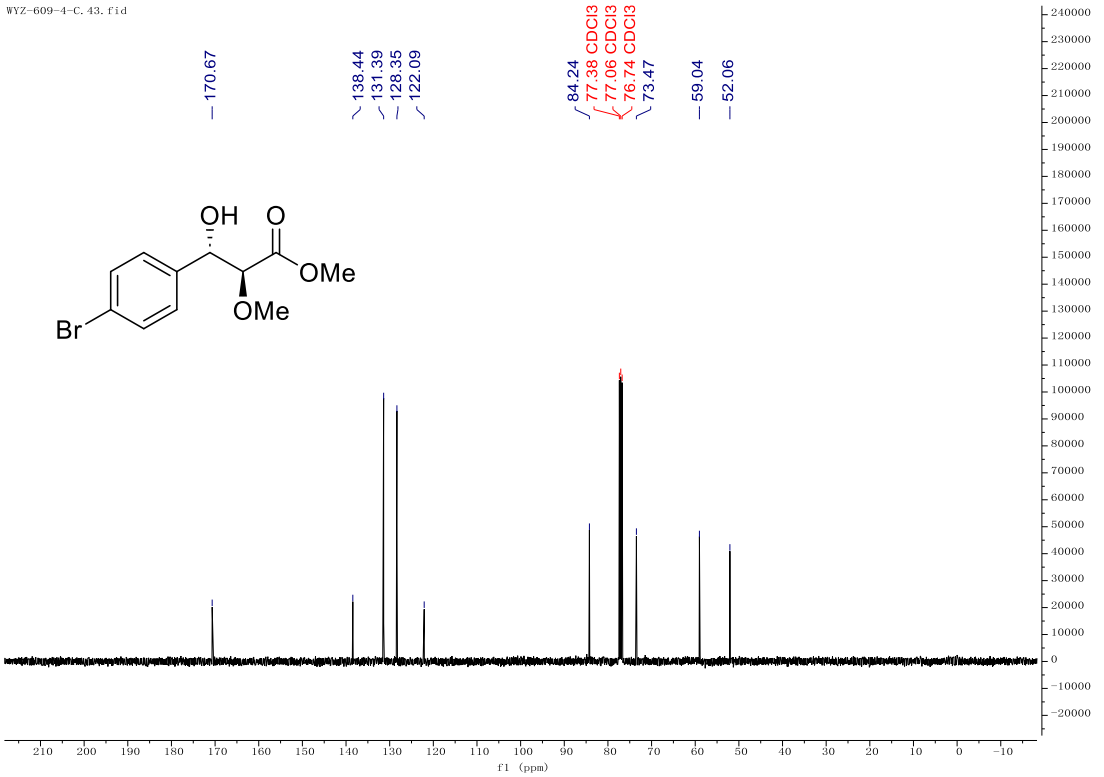
^{13}C NMR spectra (101 MHz, $CDCl_3$) of **2g**



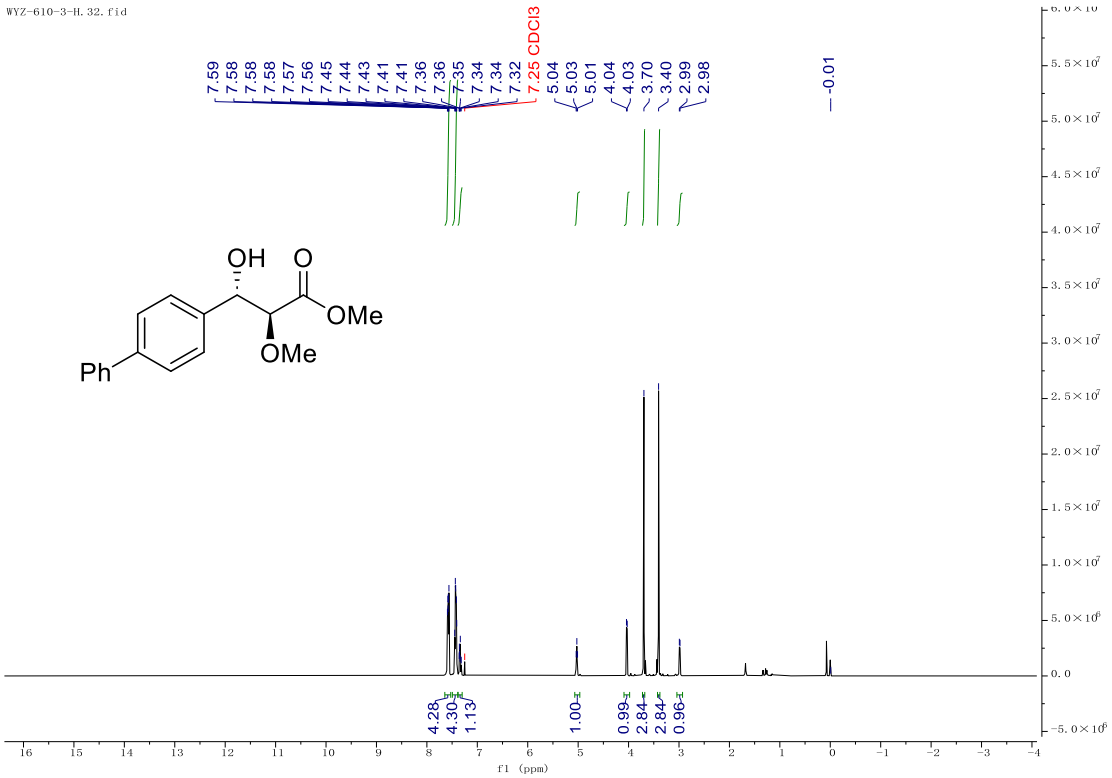
^{1}H NMR spectra (400 MHz, $CDCl_3$) of **2h**



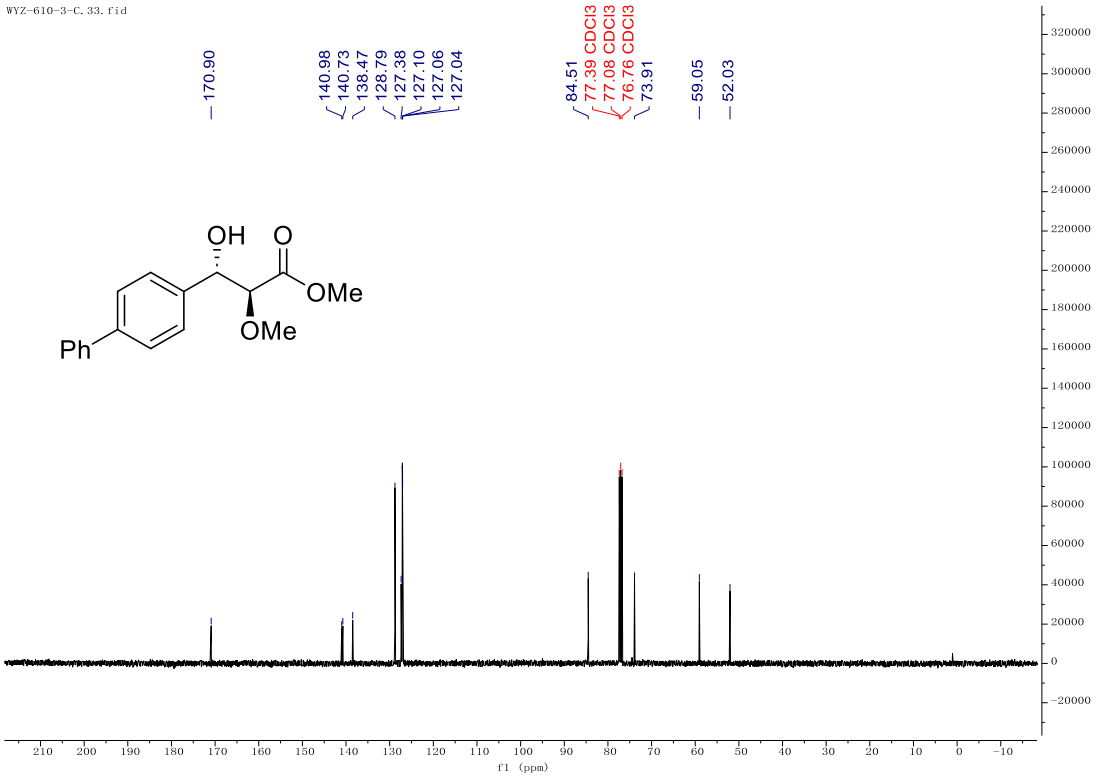
^{13}C NMR spectra (101 MHz, $CDCl_3$) of **2h**



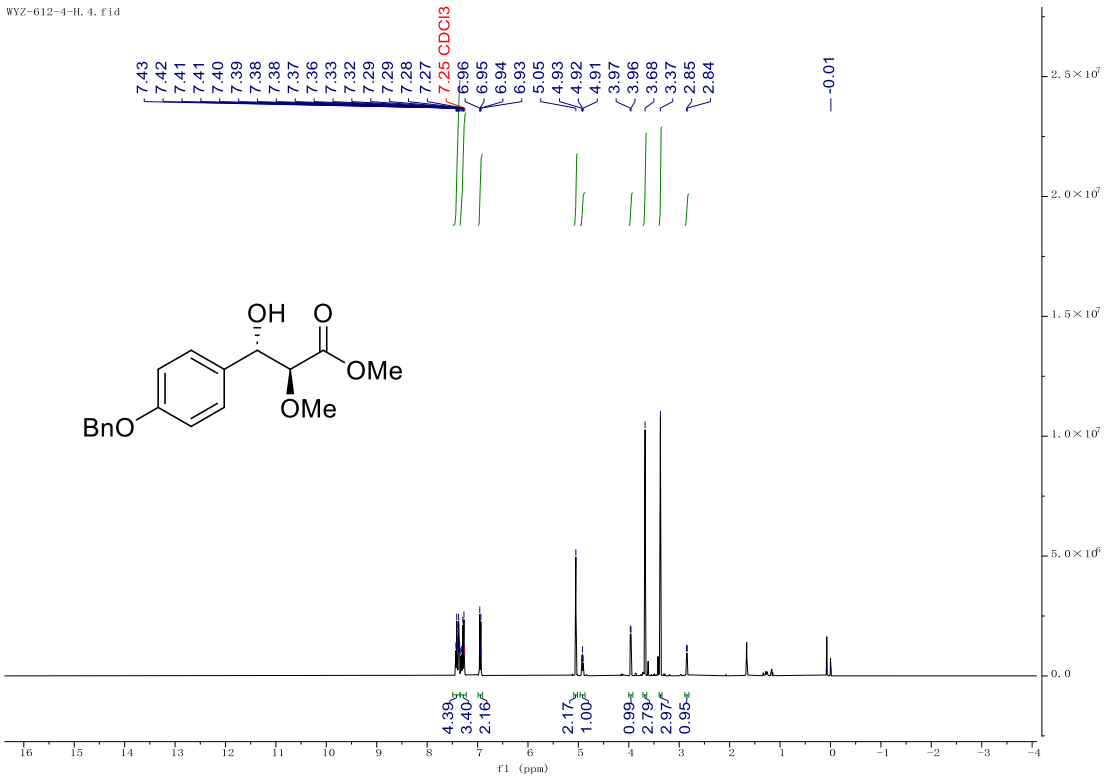
^{1}H NMR spectra (400 MHz, $CDCl_3$) of **2i**



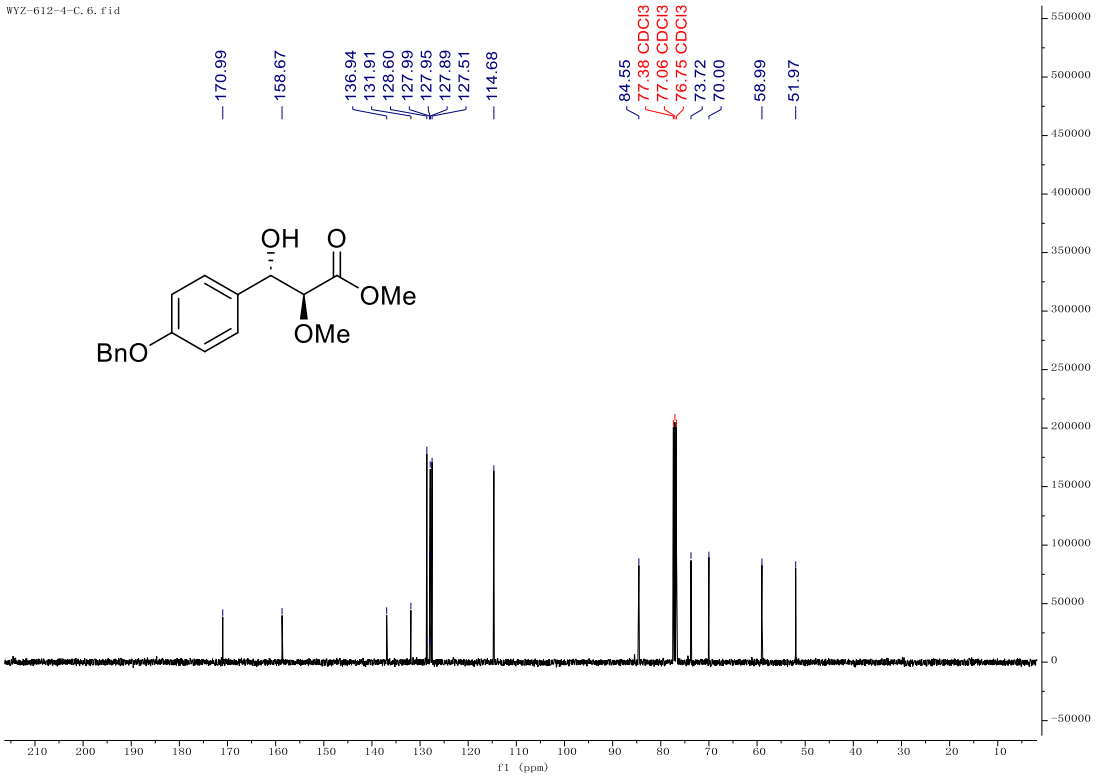
^{13}C NMR spectra (101 MHz, $CDCl_3$) of **2i**



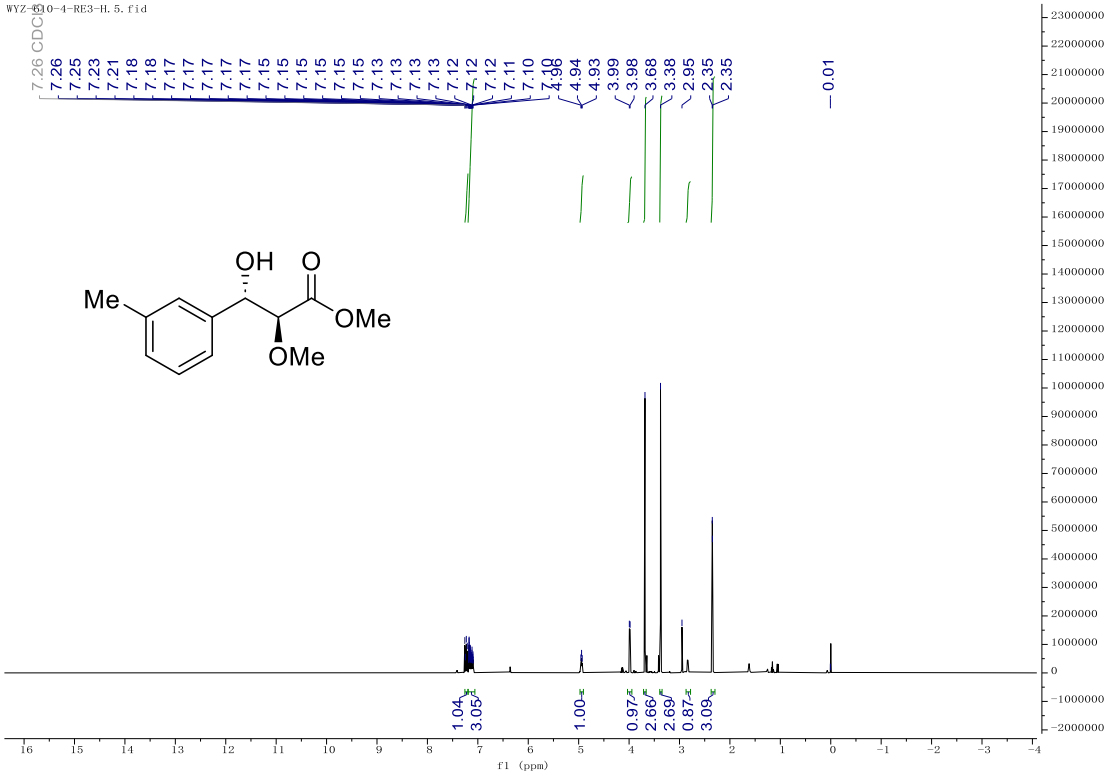
^{1}H NMR spectra (400 MHz, $CDCl_3$) of **2j**



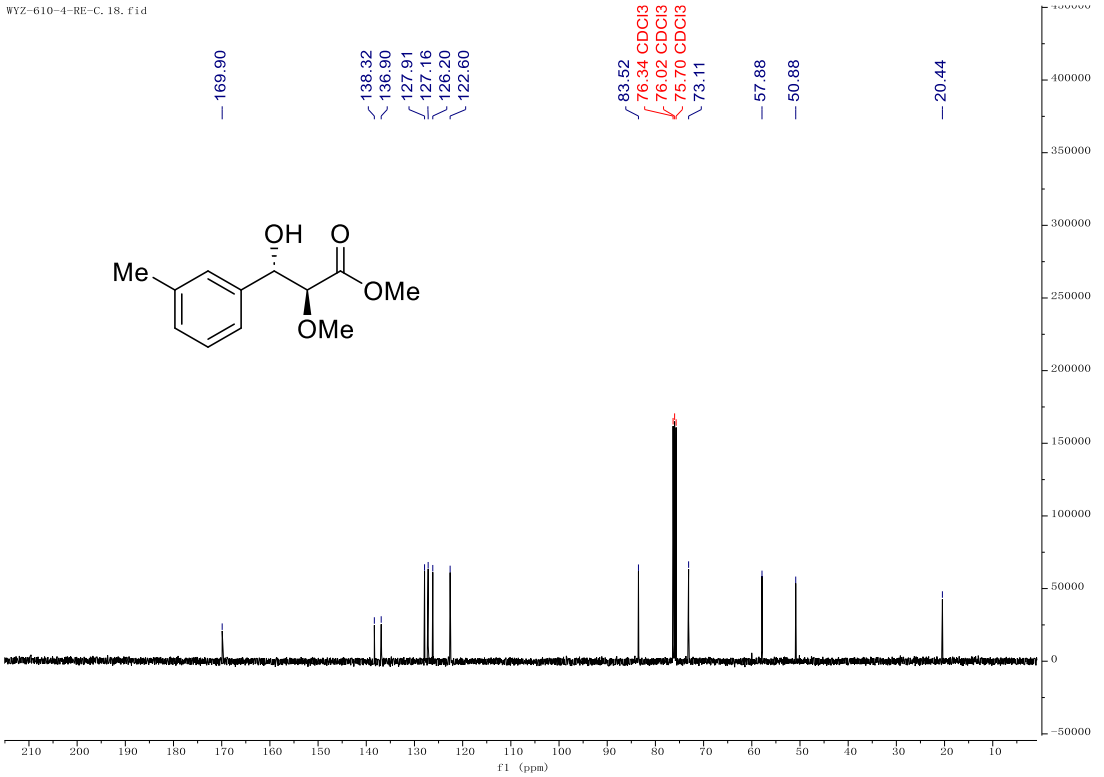
^{13}C NMR spectra (101 MHz, $CDCl_3$) of **2j**



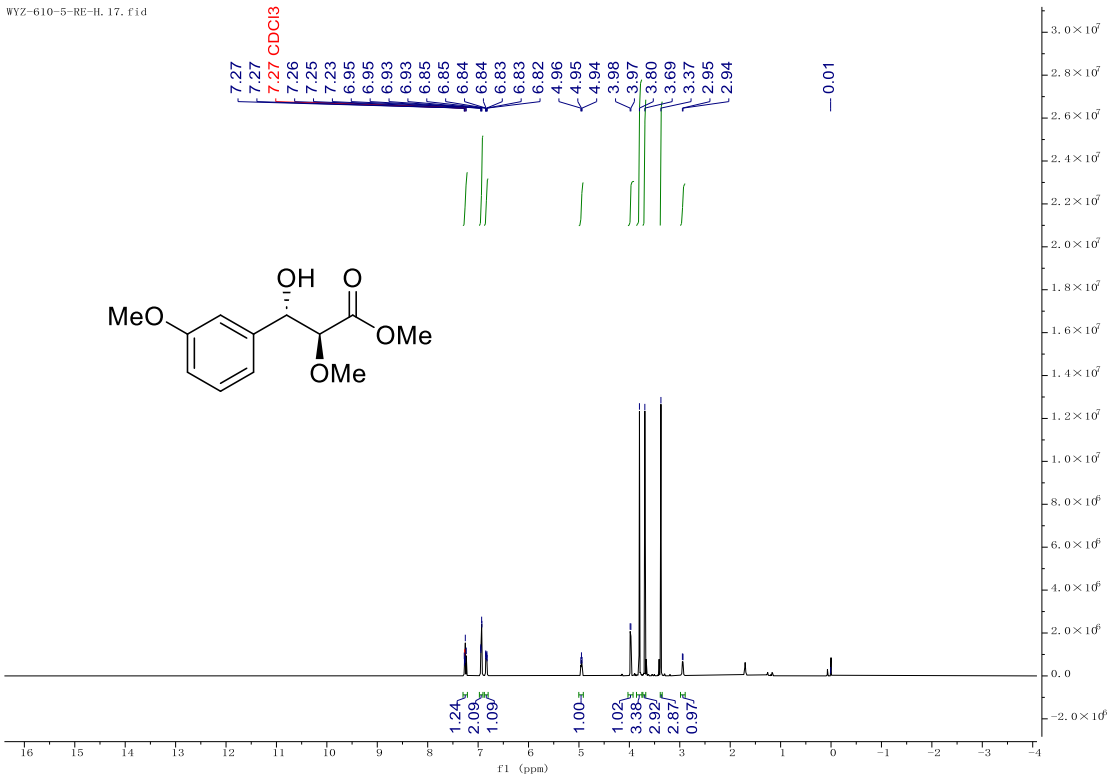
^{1}H NMR spectra (400 MHz, $CDCl_3$) of **2k**



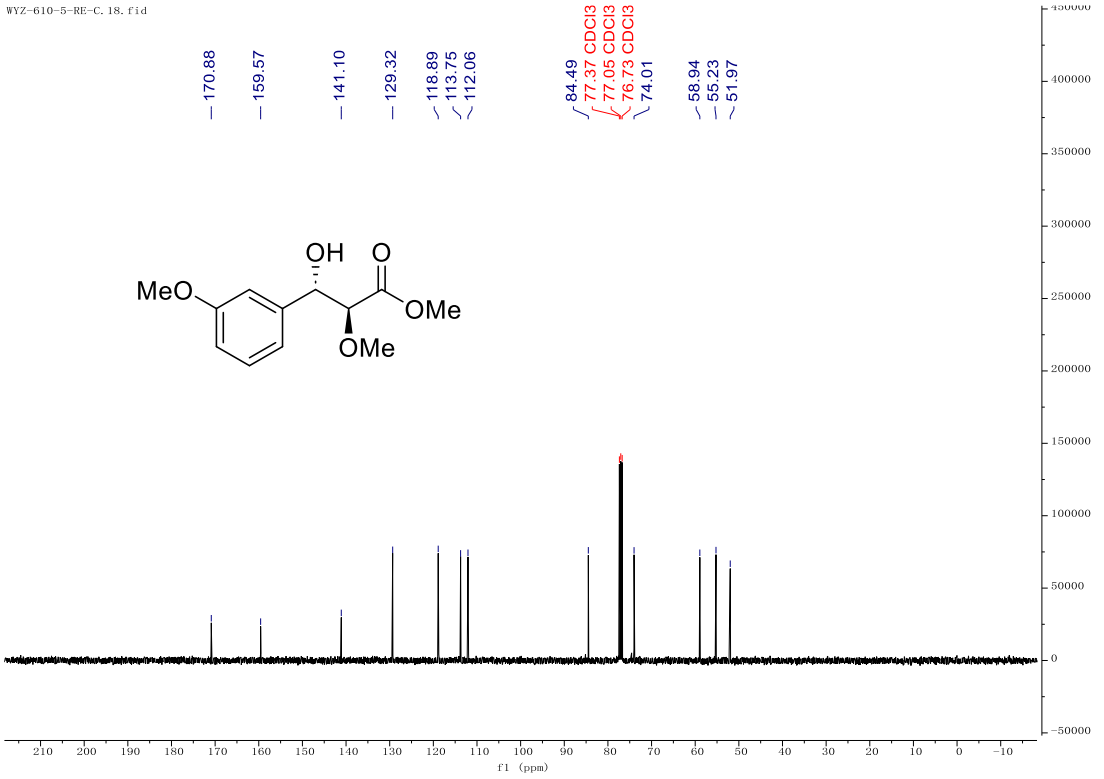
^{13}C NMR spectra (101 MHz, $CDCl_3$) of **2k**



^{1}H NMR spectra (400 MHz, $CDCl_3$) of **2l**



^{13}C NMR spectra (101 MHz, $CDCl_3$) of **2l**



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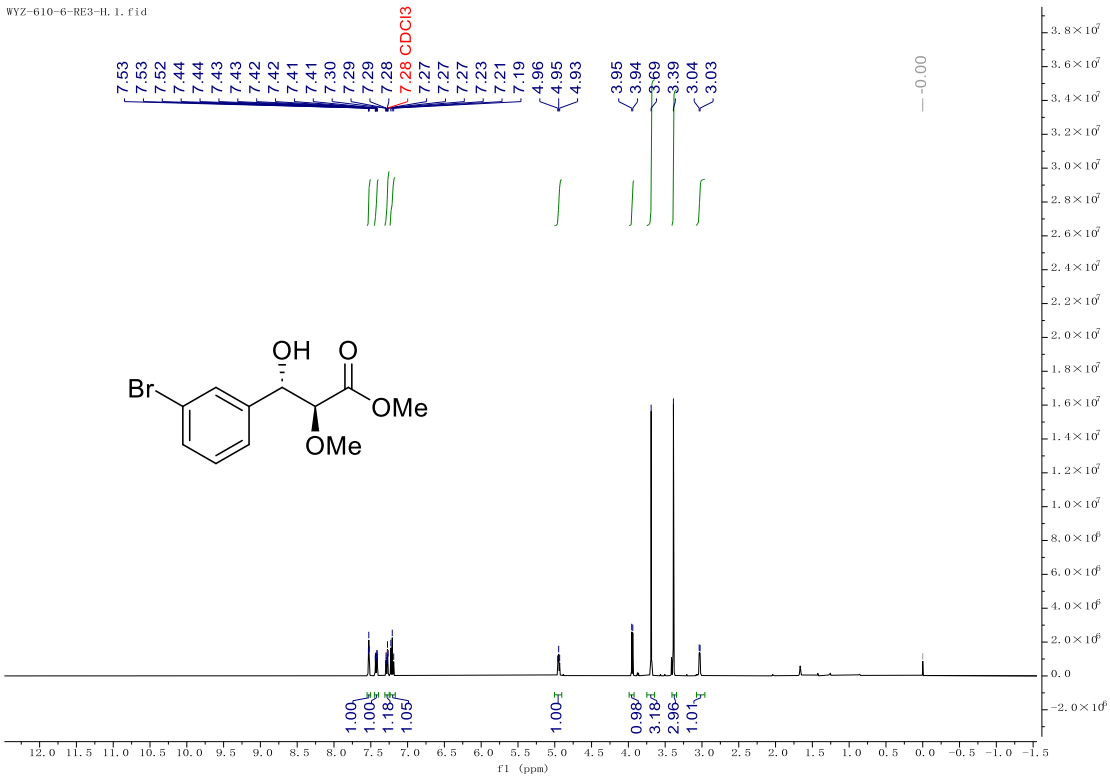
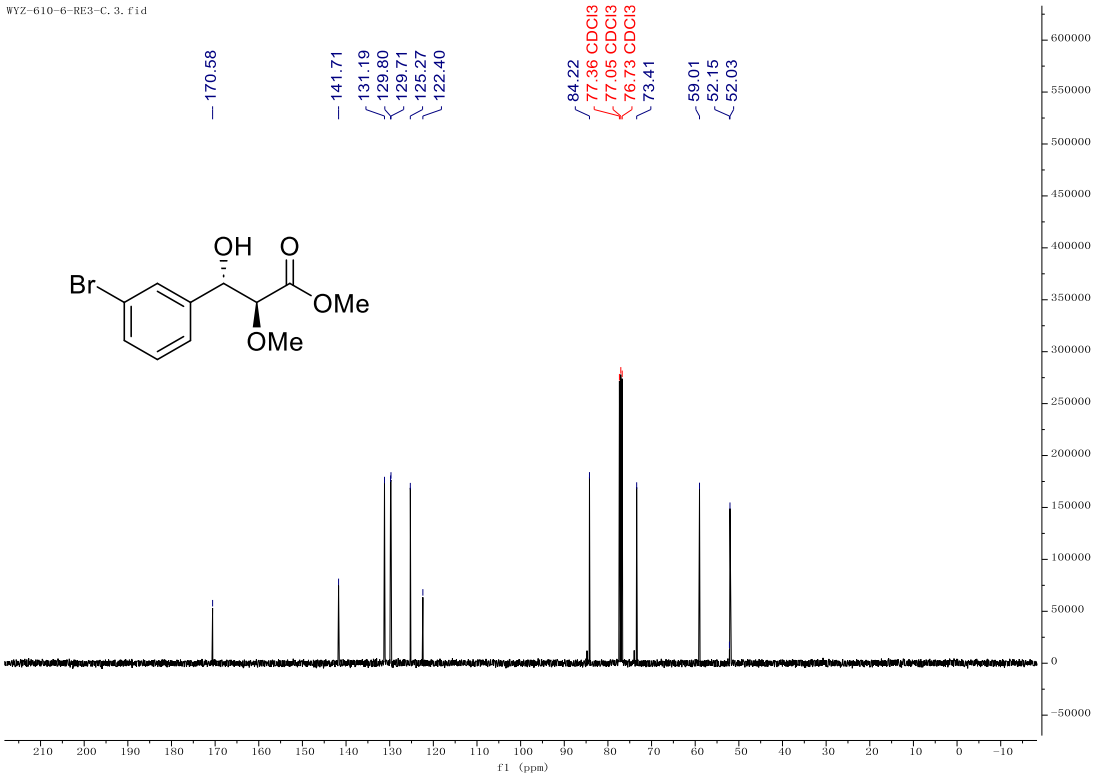
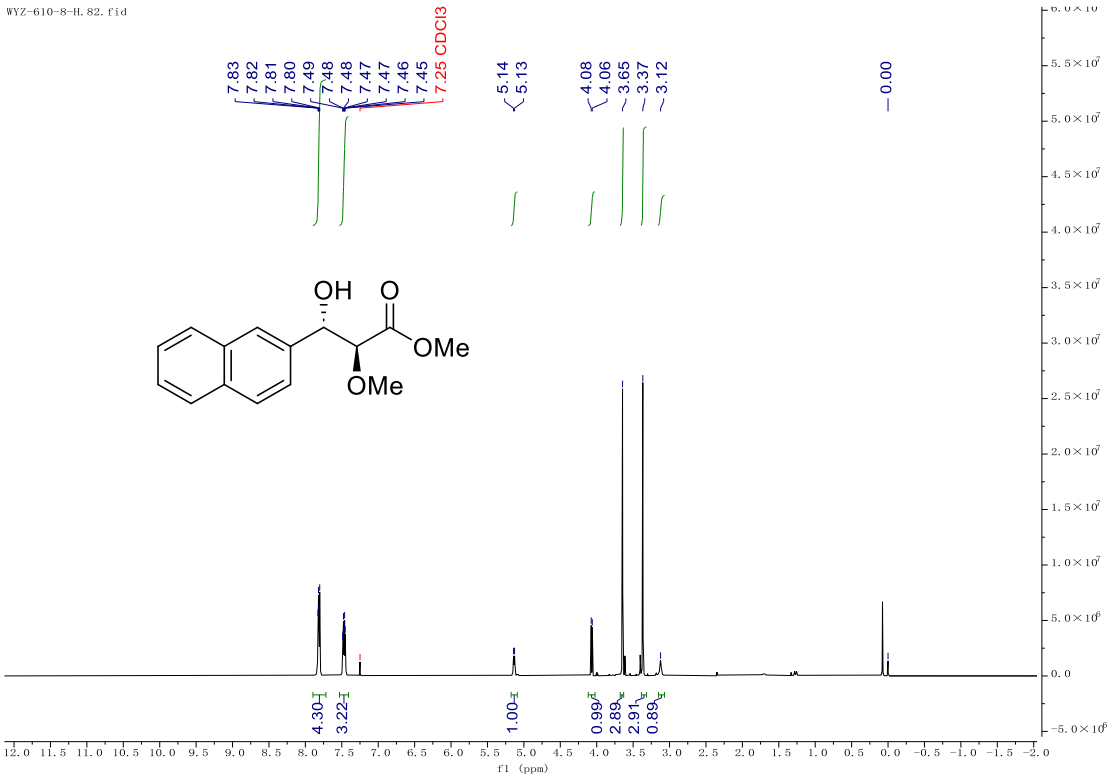


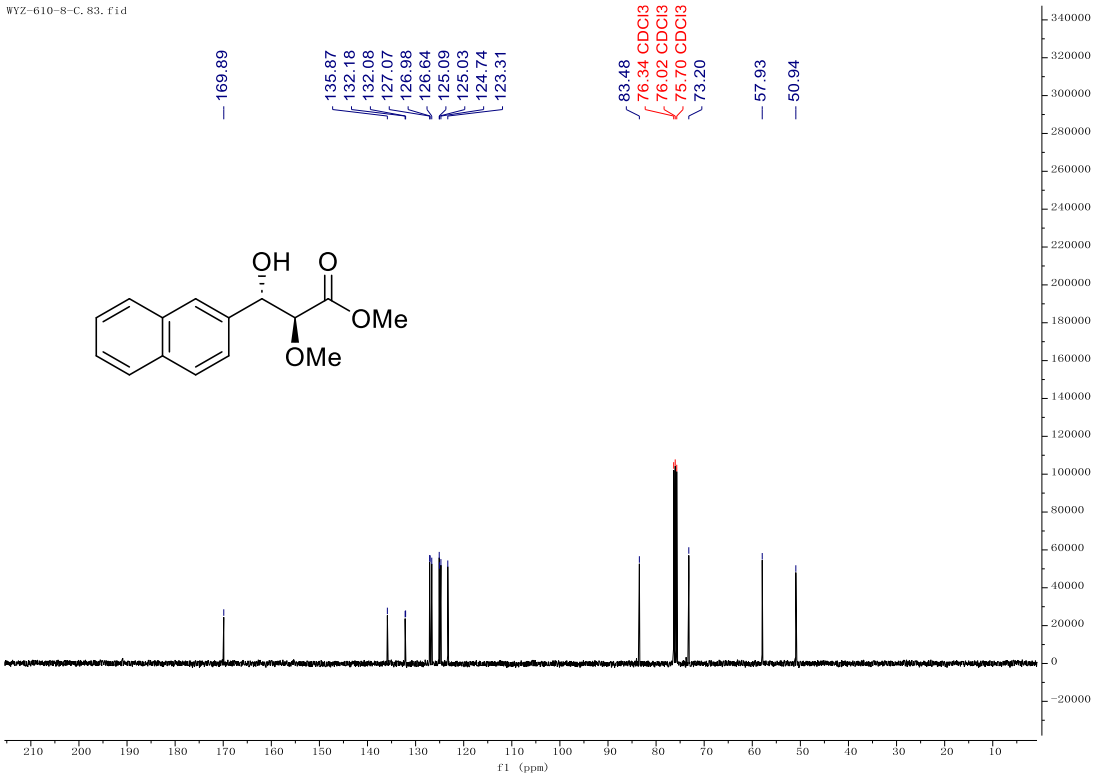
^{13}C NMR spectra (101 MHz, $CDCl_3$) of **2m**



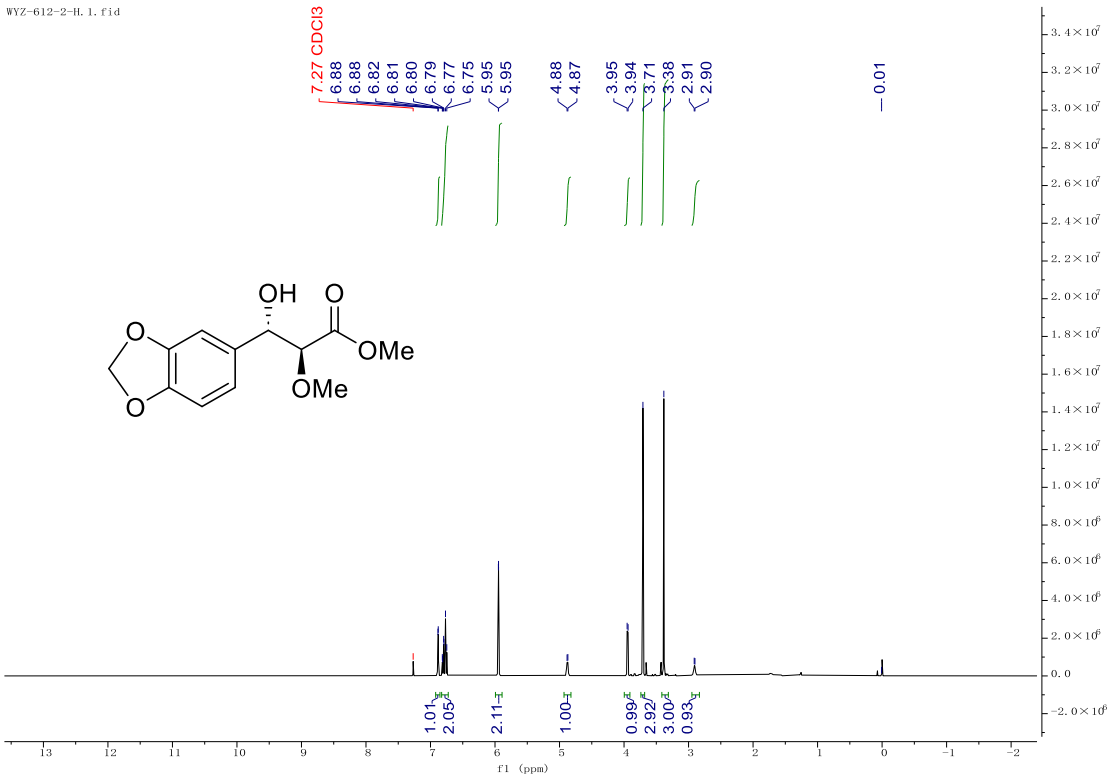
^{1}H NMR spectra (400 MHz, $CDCl_3$) of **2n**



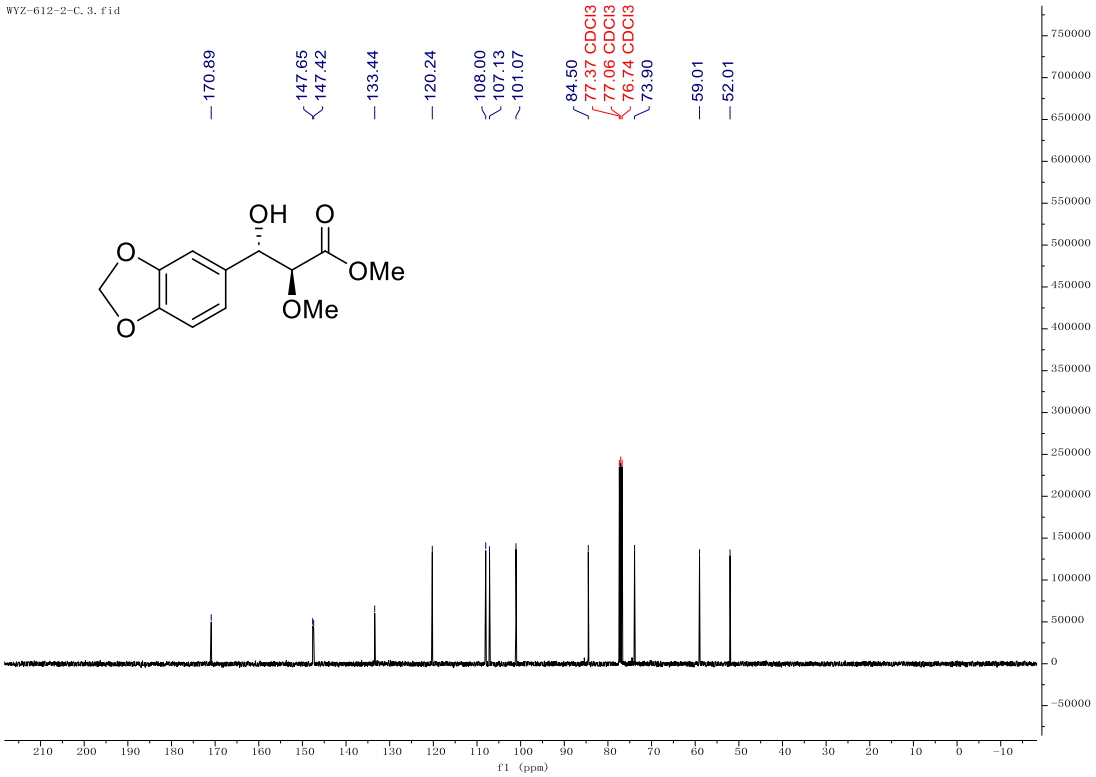
^{13}C NMR spectra (101 MHz, $CDCl_3$) of **2n**



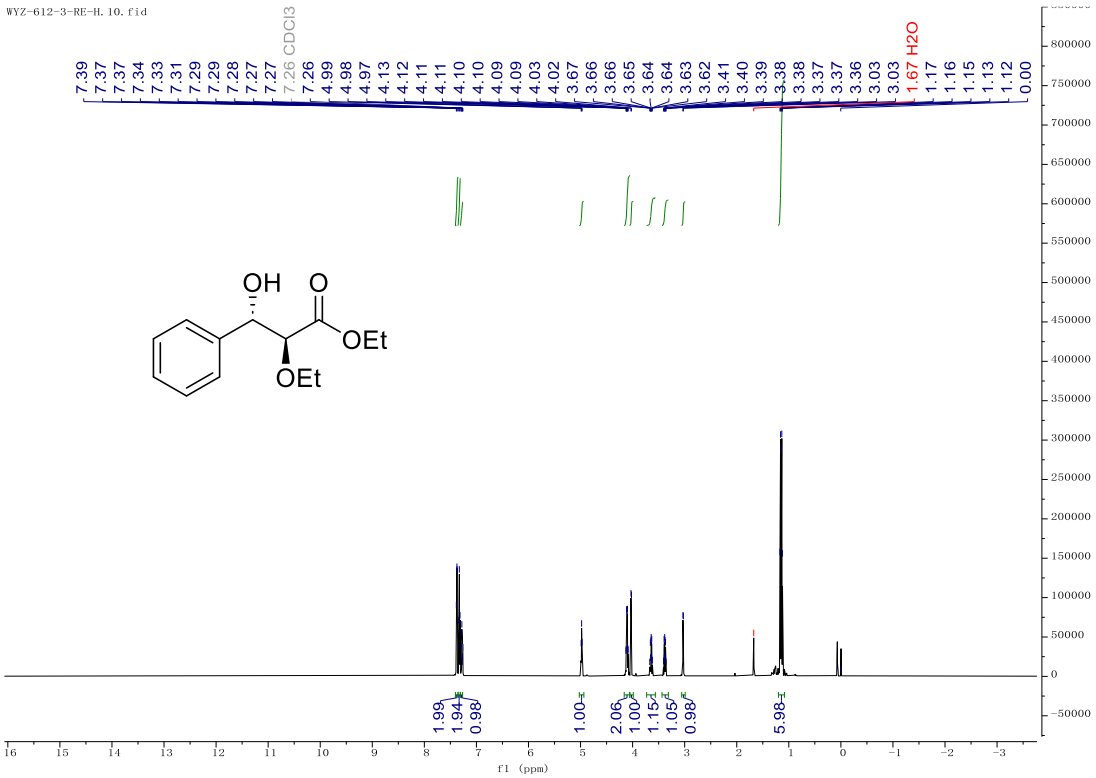
^{1}H NMR spectra (400 MHz, $CDCl_3$) of **2o**



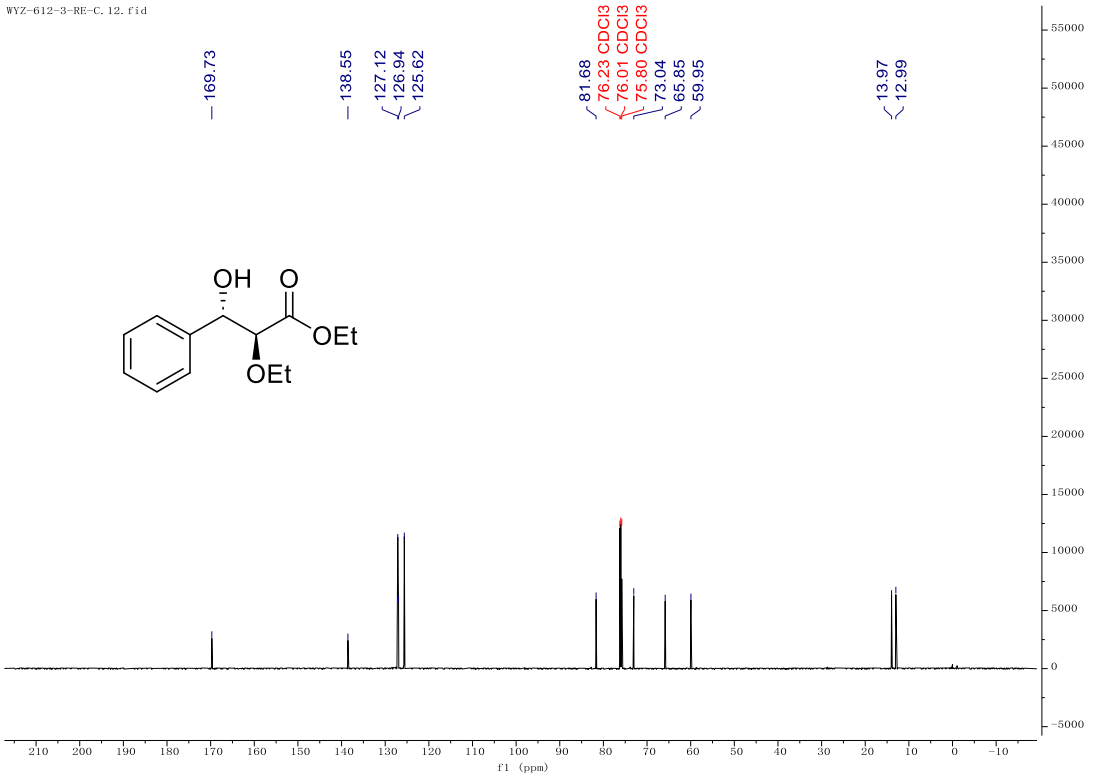
^{13}C NMR spectra (101 MHz, $CDCl_3$) of **2o**



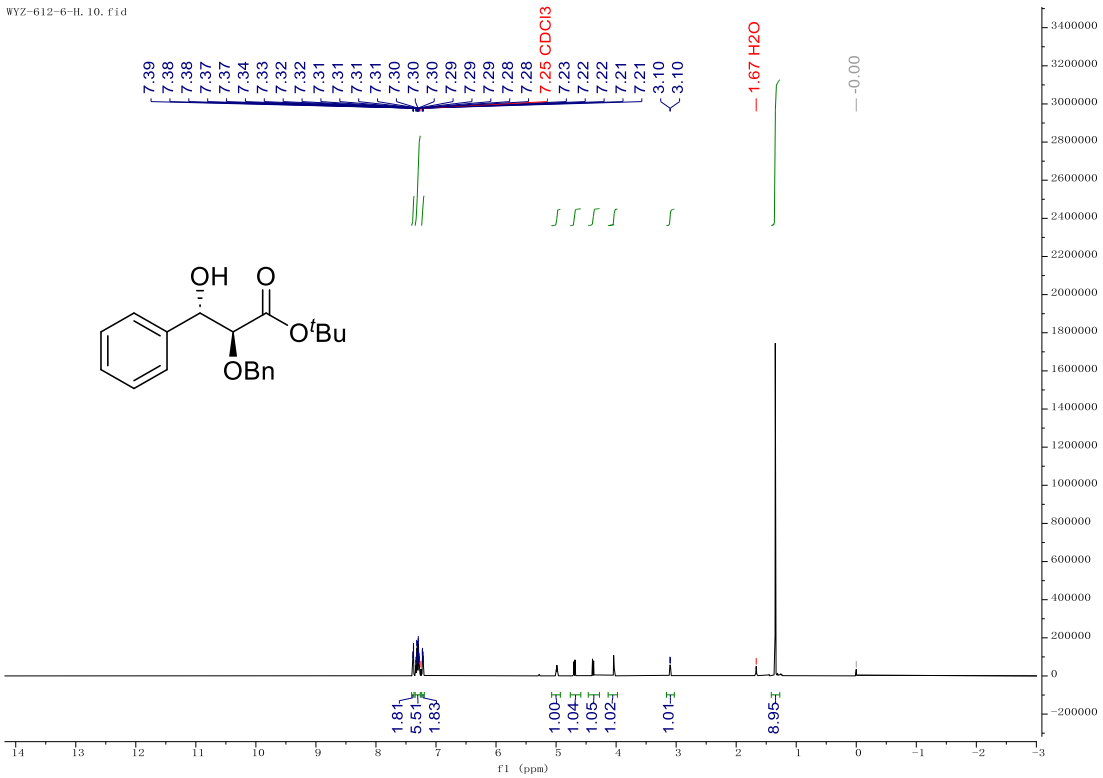
^{1}H NMR spectra (400 MHz, $CDCl_3$) of **2p**



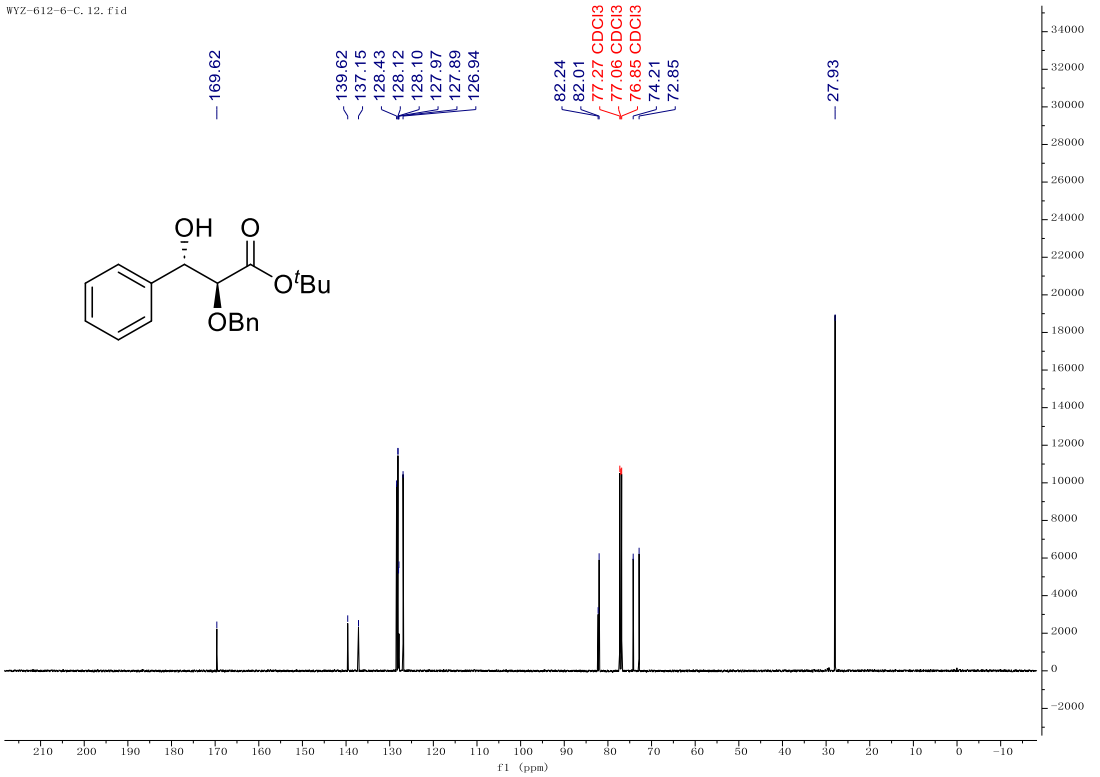
^{13}C NMR spectra (101 MHz, $CDCl_3$) of **2p**



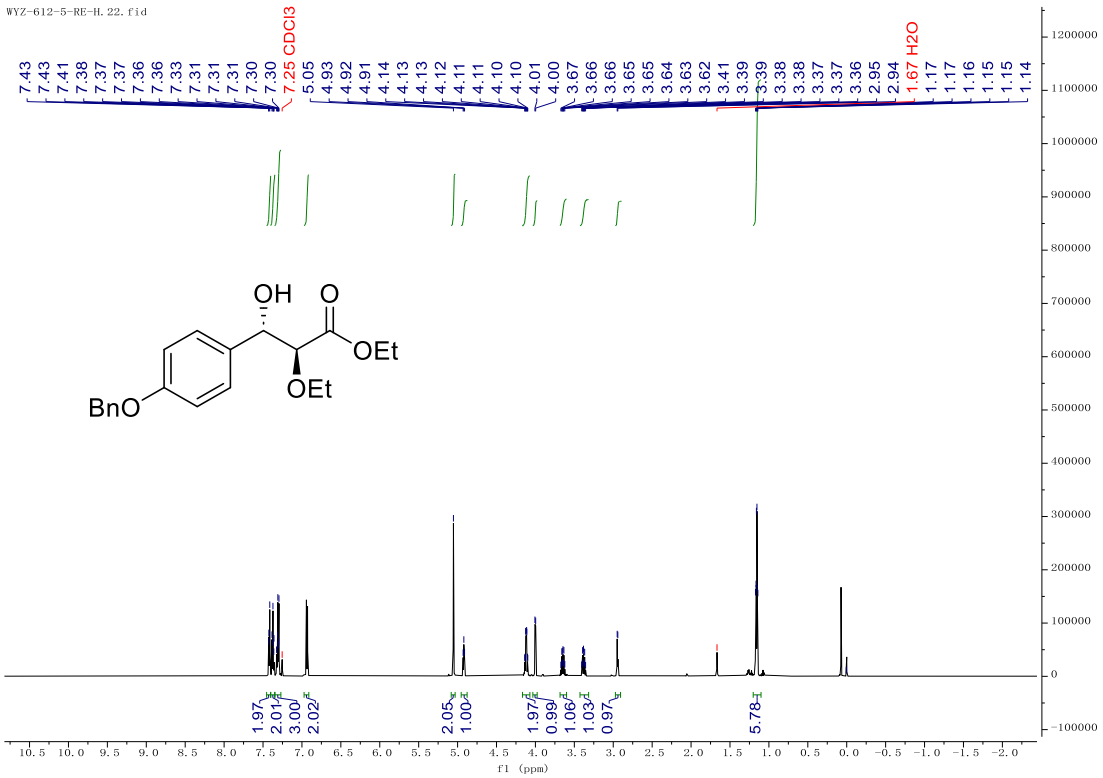
^{1}H NMR spectra (400 MHz, $CDCl_3$) of **2q**



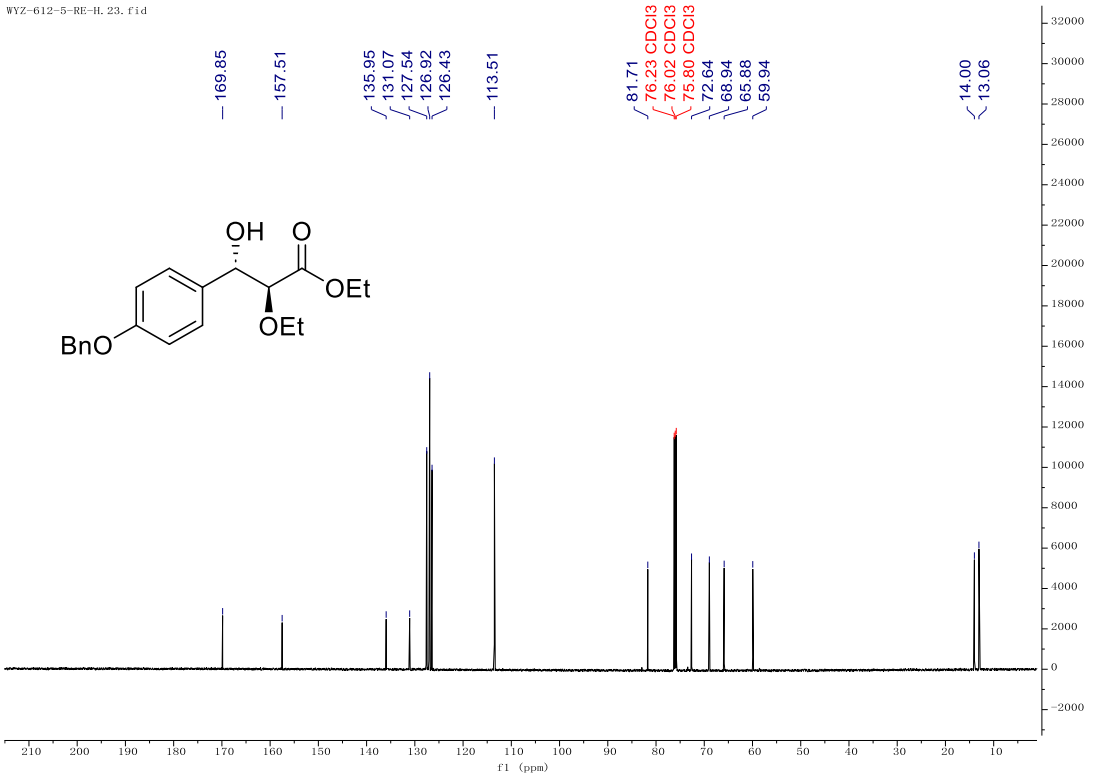
^{13}C NMR spectra (101 MHz, $CDCl_3$) of **2q**



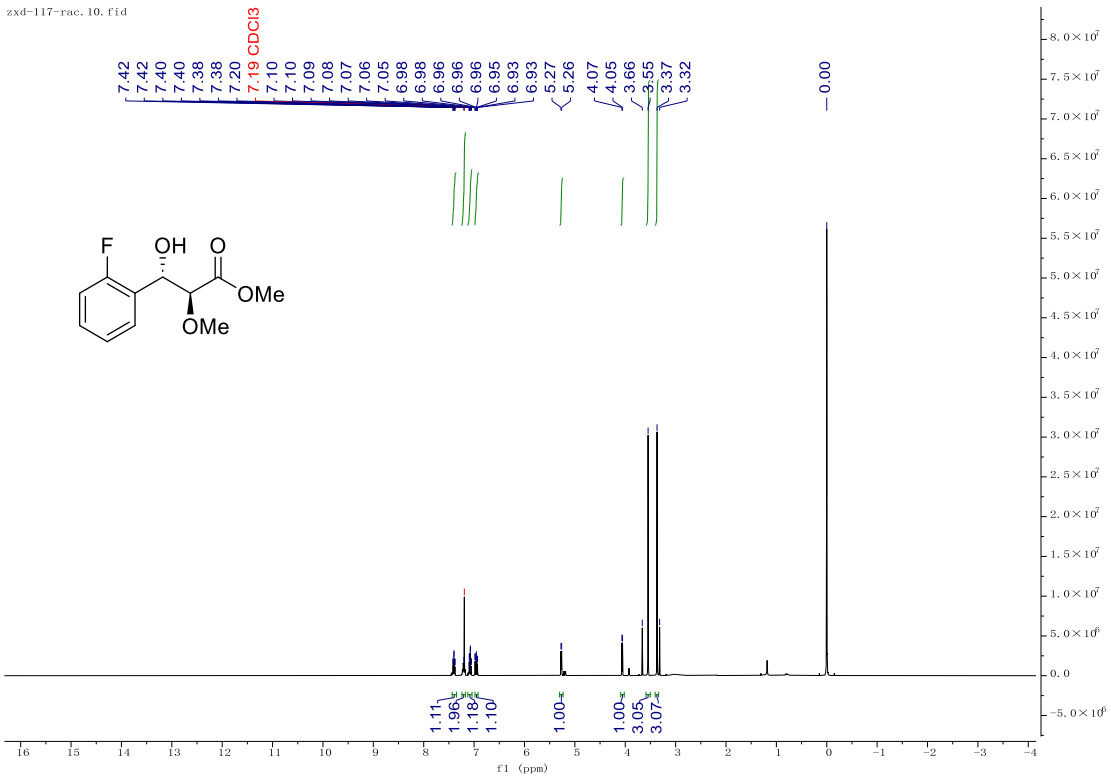
^{1}H NMR spectra (400 MHz, $CDCl_3$) of **2r**



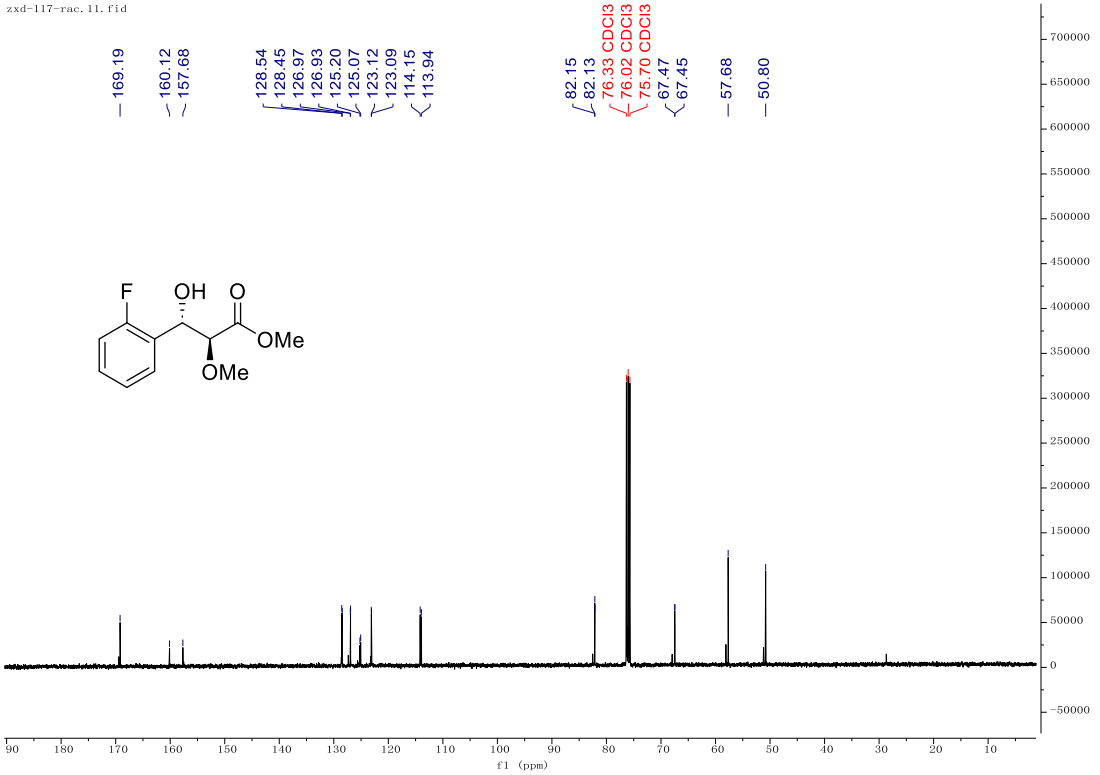
^{13}C NMR spectra (101 MHz, $CDCl_3$) of **2r**



^{1}H NMR spectra (400 MHz, $CDCl_3$) of **2s**

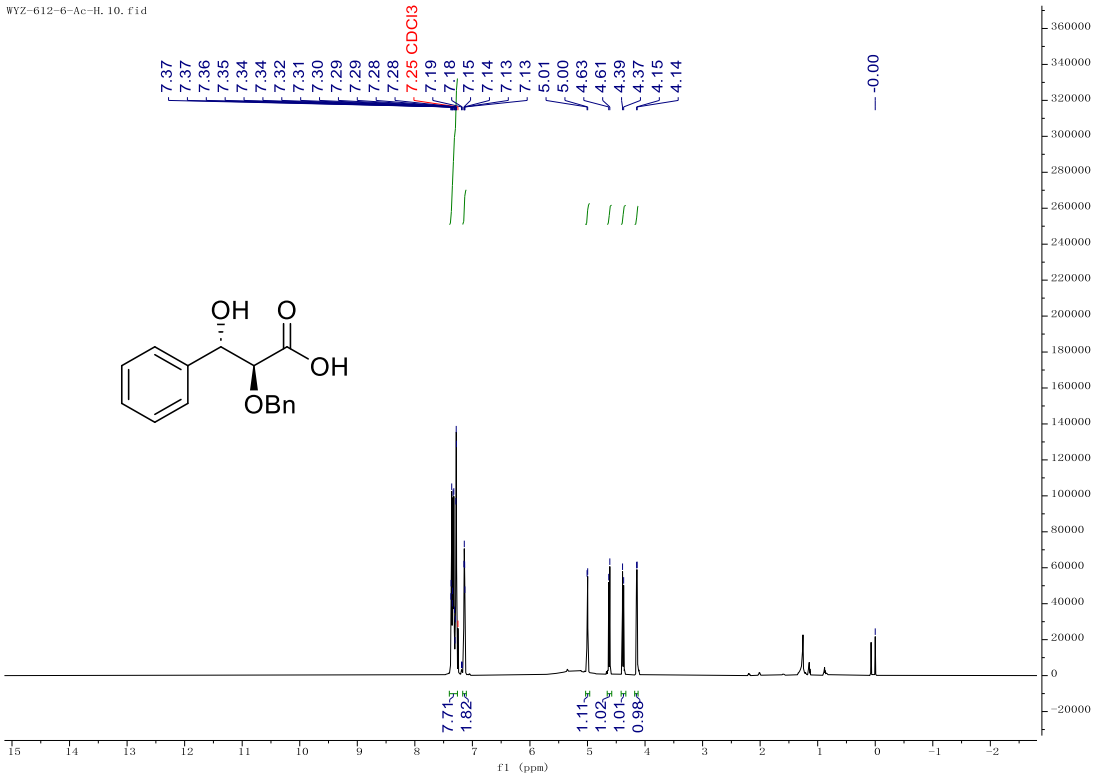


^{13}C NMR spectra (101 MHz, $CDCl_3$) of **2s**

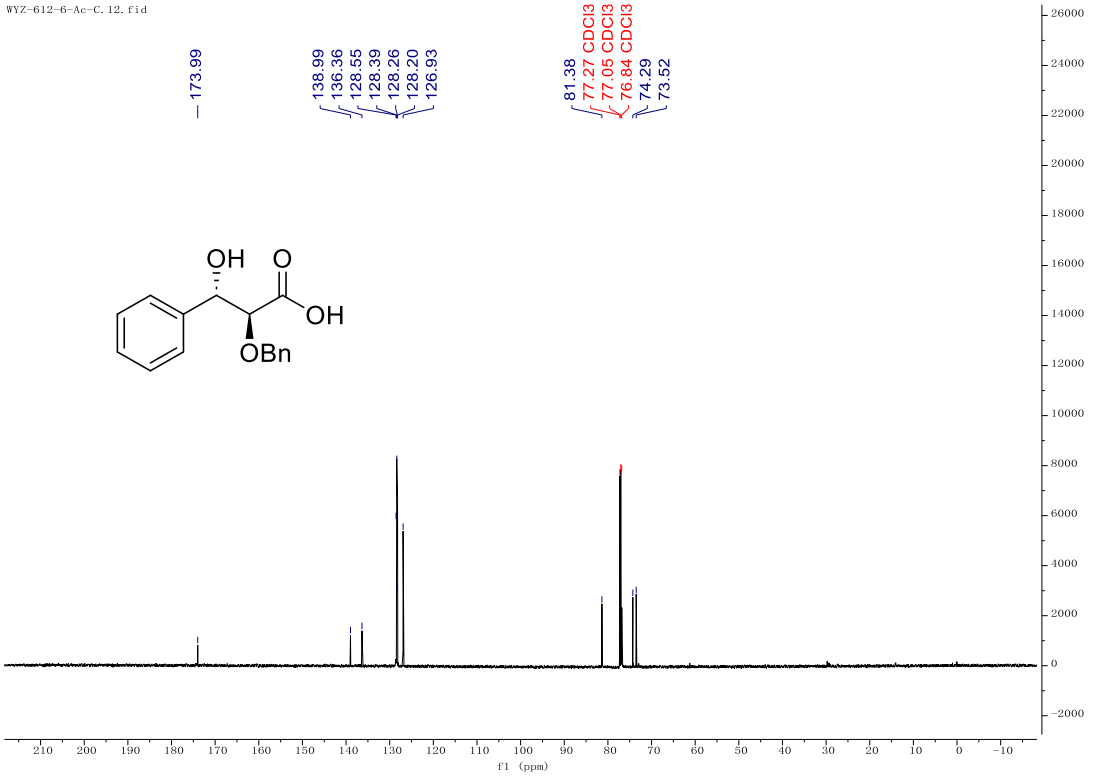


^{19}F NMR spectra (376 MHz, $CDCl_3$) of **2s**

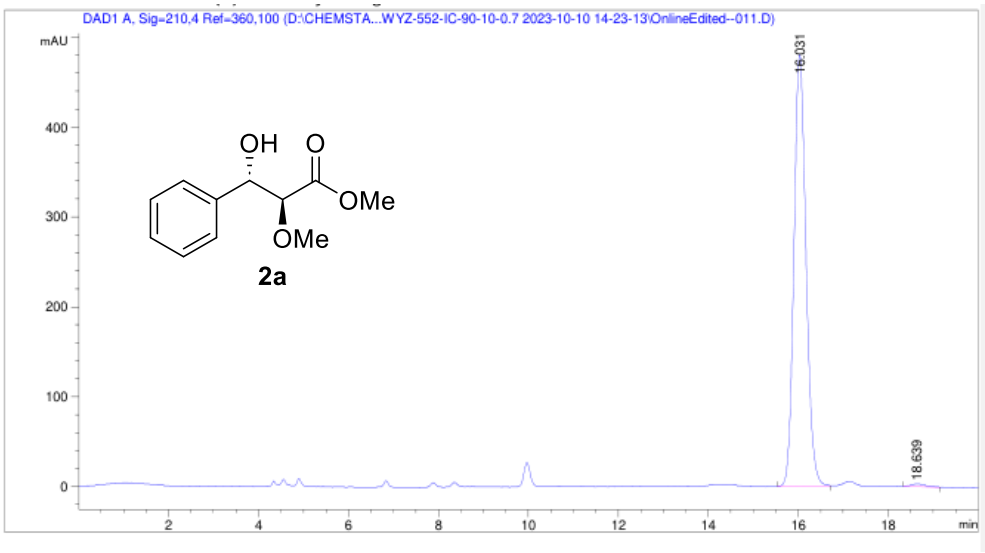
^{1}H NMR spectra (600 MHz, $CDCl_3$) of **3**



^{13}C NMR spectra (151 MHz, $CDCl_3$) of **3**

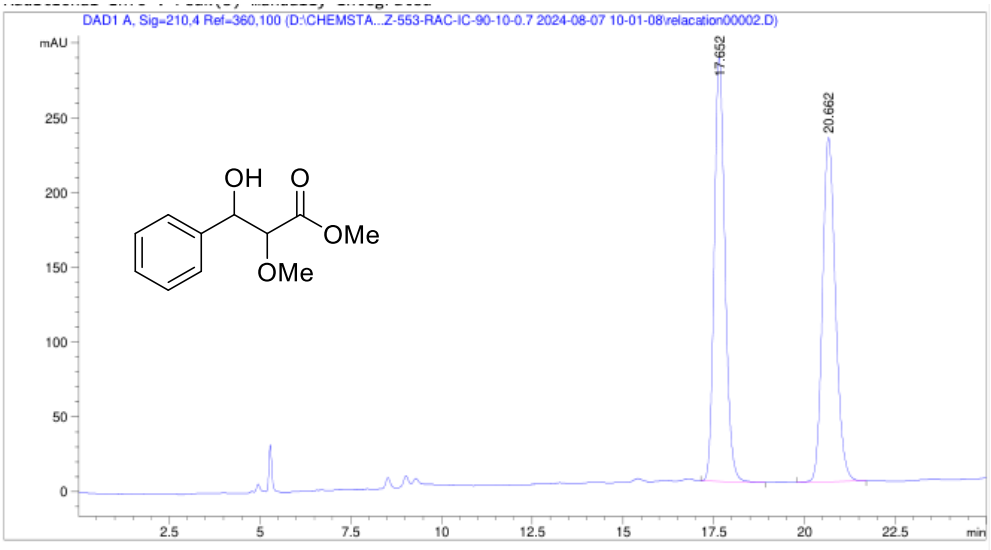


5. HPLC chromatograms



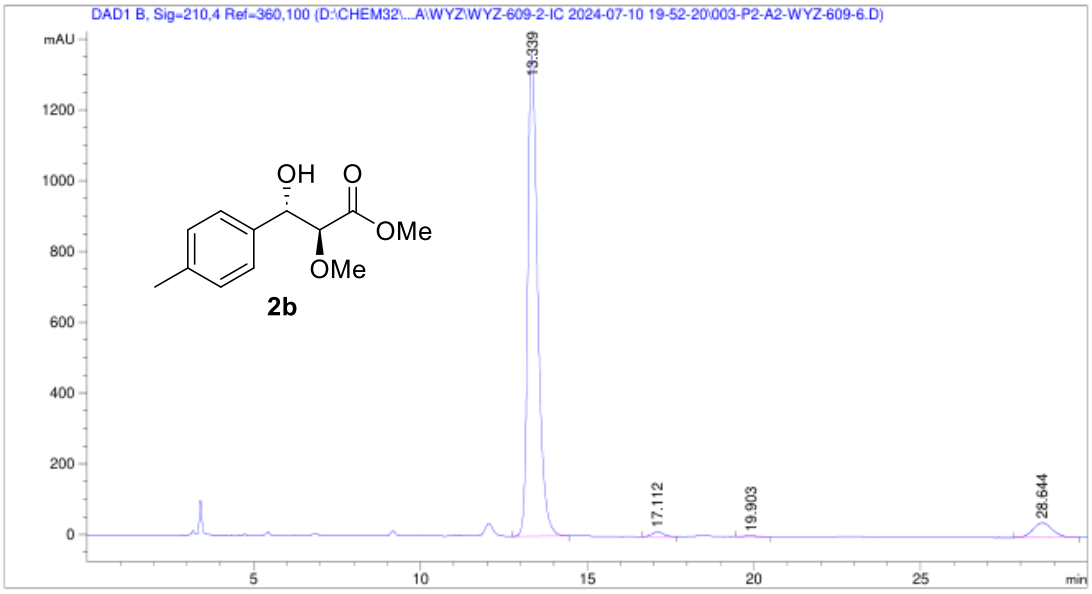
Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.031	BB	0.2862	8889.41211	479.74789	99.2935
2	18.639	BB	0.2583	63.25026	2.99597	0.7065
Totals :				8952.66236	482.74387	



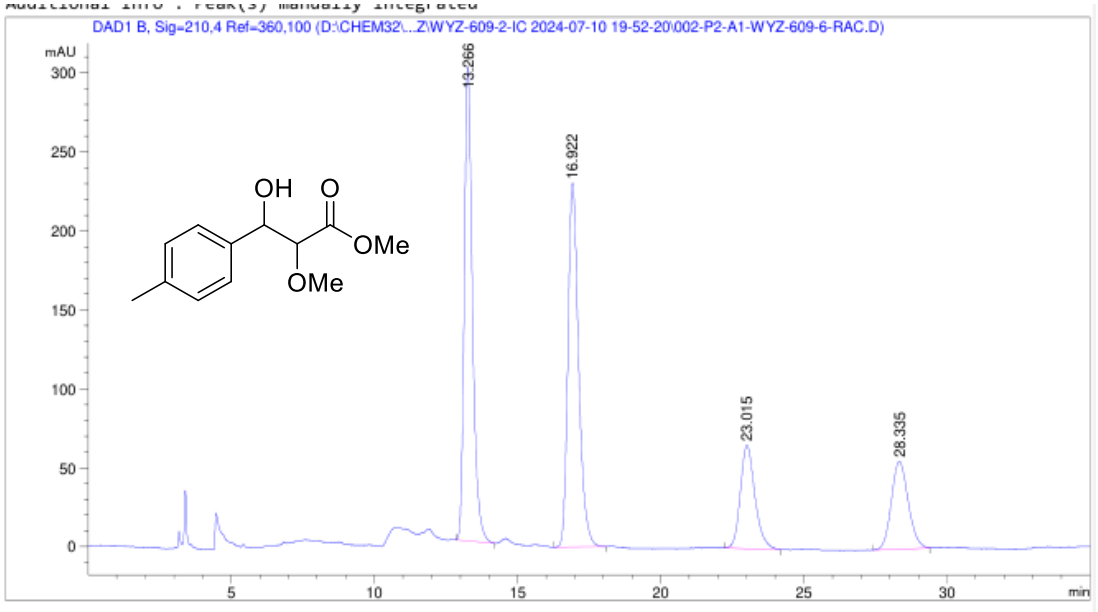
Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.652	BB	0.3150	5805.73535	283.41510	50.2096
2	20.662	BB	0.3858	5757.26904	230.16724	49.7904
Totals :				1.15630e4	513.58234	



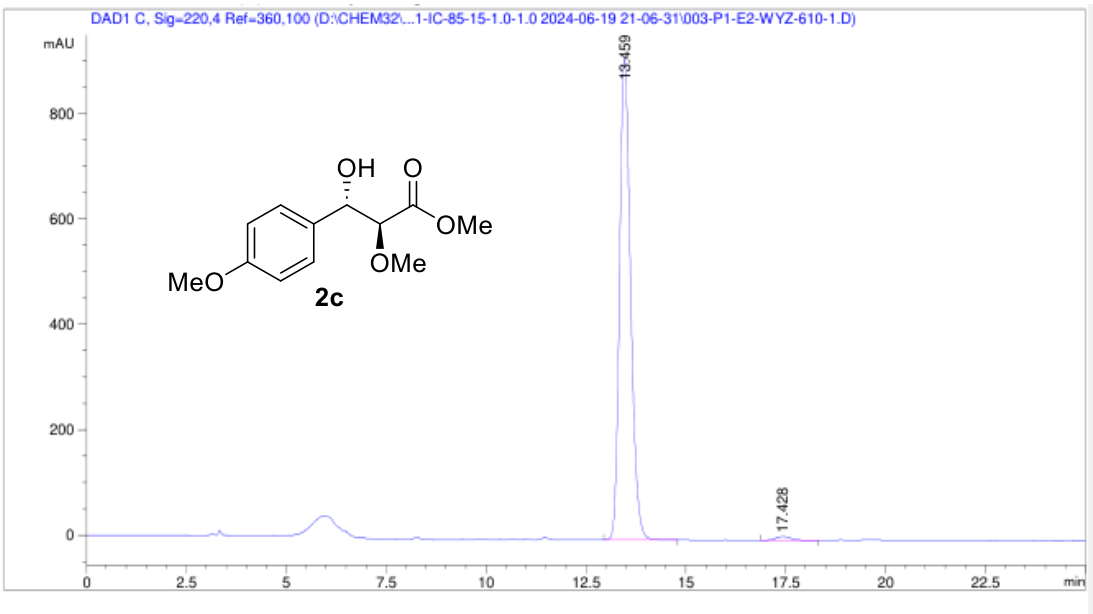
Signal 1: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.339	BB	0.3202	2.84382e4	1358.75134	93.2694
2	17.112	BB	0.3545	308.22278	13.09833	1.0109
3	19.903	BB	0.3619	61.99780	2.10352	0.2033
4	28.644	BB	0.5660	1681.96204	41.39870	5.5164
Totals :				3.04904e4	1415.35189	



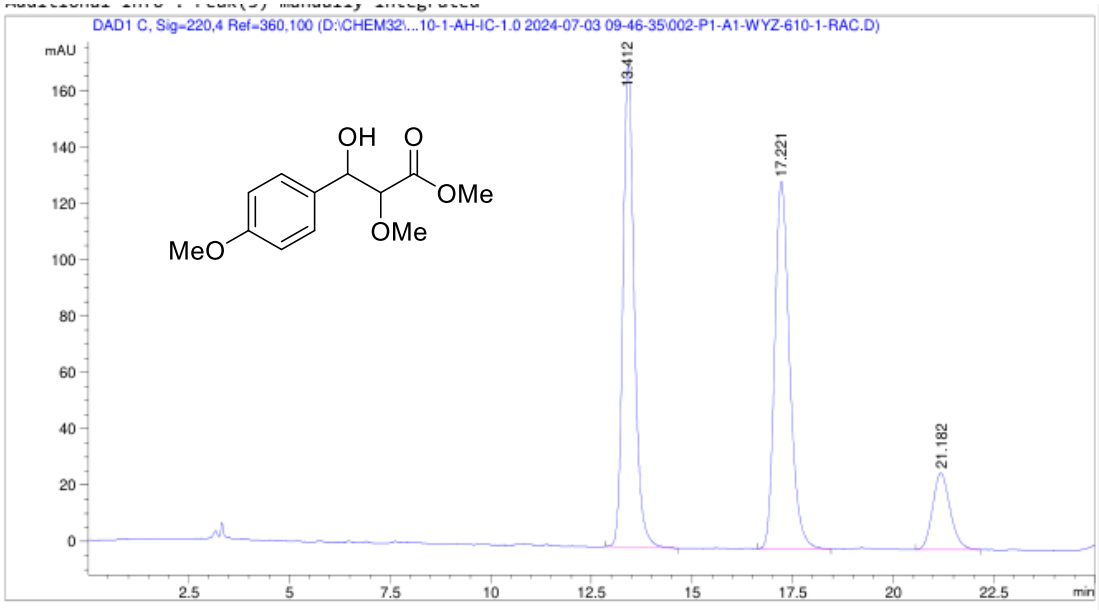
Signal 1: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.266	BB	0.3015	5953.34033	300.03384	36.1030
2	16.922	BB	0.3975	5953.59424	230.40375	36.1046
3	23.015	BB	0.5308	2316.46240	65.47560	14.0478
4	28.335	BB	0.5754	2266.46338	55.38942	13.7446
Totals :				1.64899e4	651.30261	



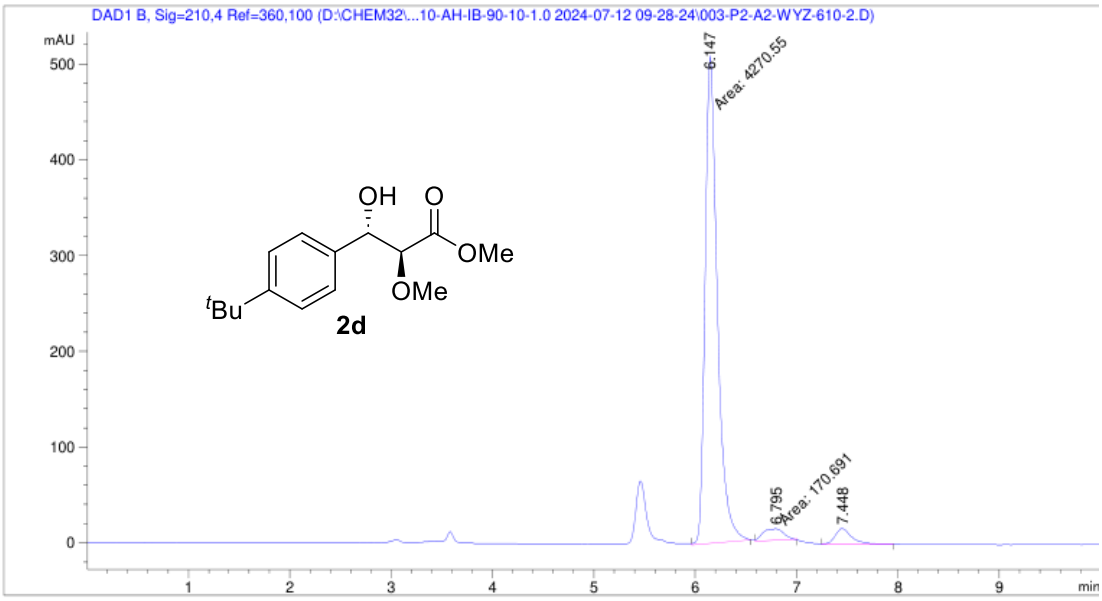
Signal 1: DAD1 C, Sig=220,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.459	BB	0.2959	1.75105e4	912.41620	98.9782
2	17.428	BB	0.3716	180.77164	7.08639	1.0218
Totals :				1.76912e4	919.50259	



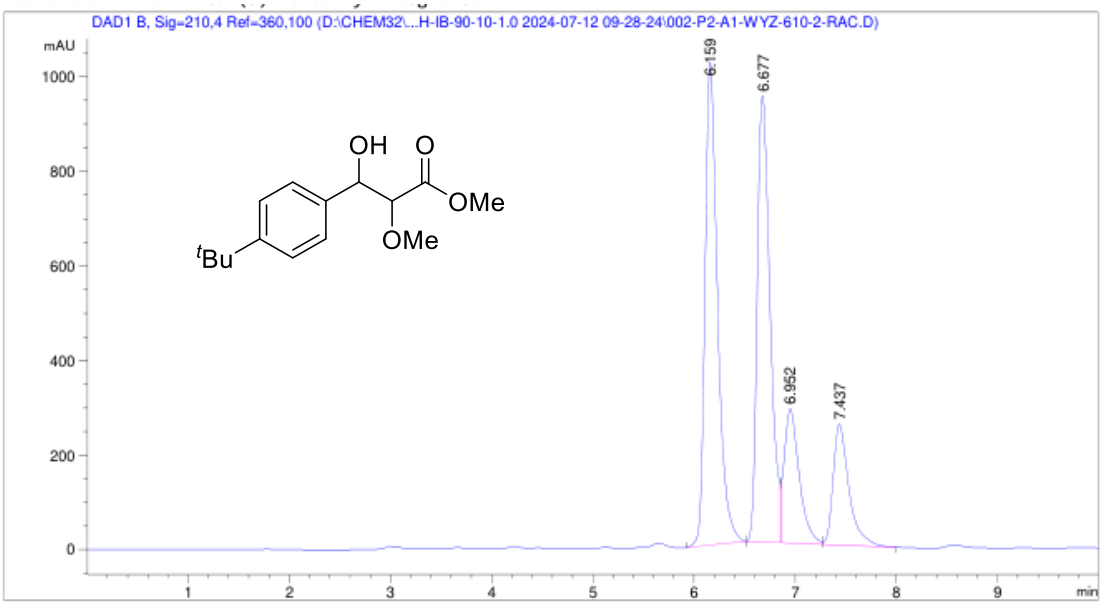
Signal 1: DAD1 C, Sig=220,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.412	BB	0.3008	3349.14258	170.77104	44.5706
2	17.221	BB	0.3904	3333.26465	130.31335	44.3593
3	21.182	BB	0.4625	831.83936	27.22568	11.0702
Totals :				7514.24658	328.31008	



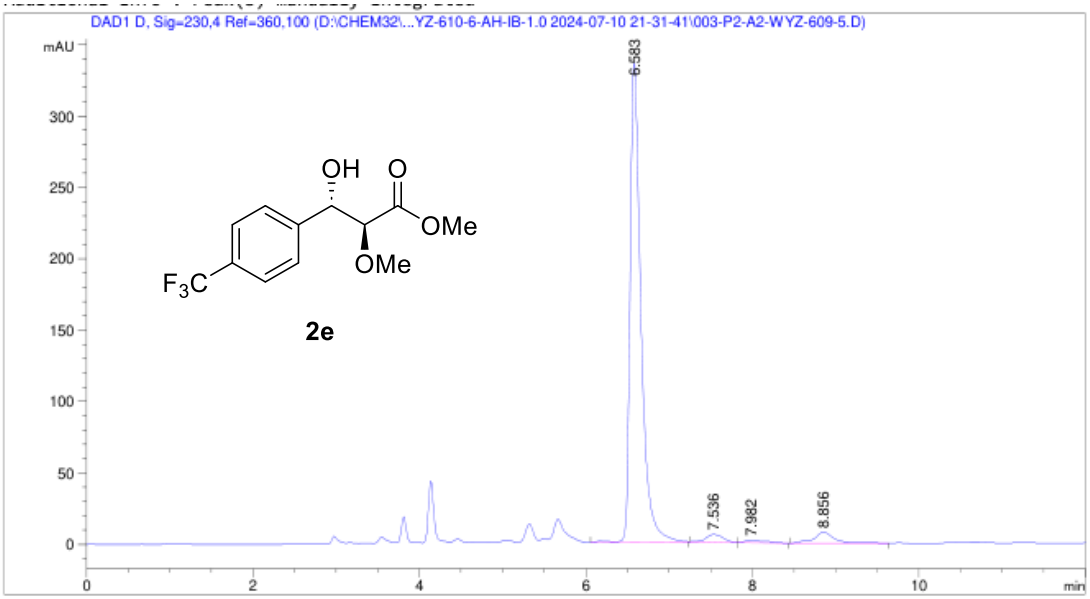
Signal 1: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.147	MM	0.1398	4270.54736	509.06567	92.3581
2	6.795	MM	0.2395	170.69121	11.87840	3.6915
3	7.448	VB	0.1686	182.66125	16.07520	3.9504
Totals :				4623.89983	537.01928	



Signal 1: DAD1 B, Sig=210,4 Ref=360,100

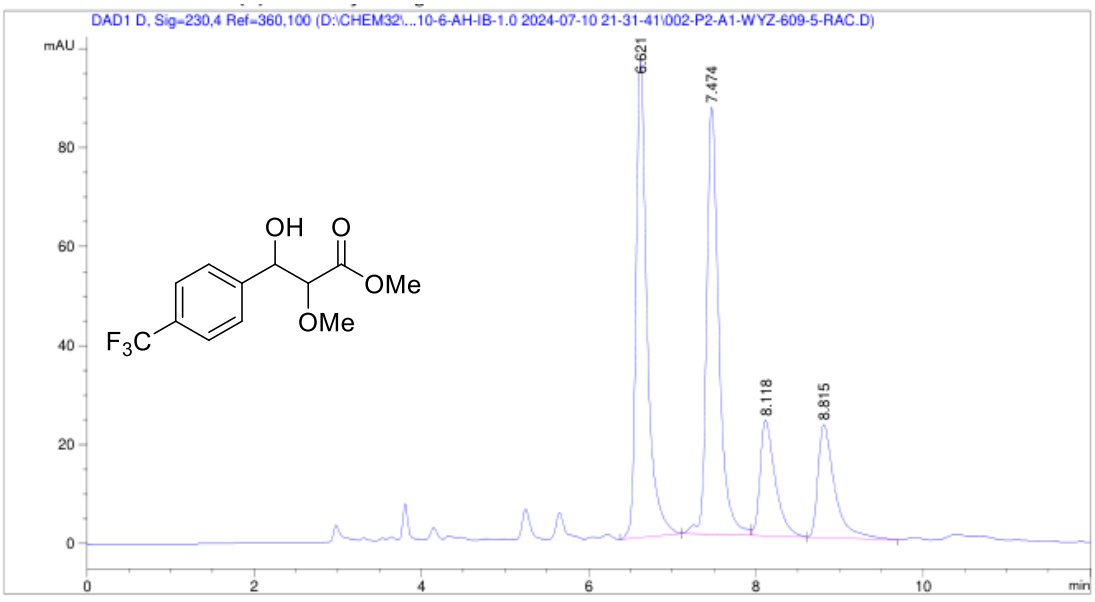
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.159	BB	0.1299	8750.66113	1021.74054	38.3219
2	6.677	BV	0.1349	8321.75781	943.38965	36.4436
3	6.952	VV	0.1564	2985.99048	284.60895	13.0766
4	7.437	VB	0.1626	2776.23169	255.78339	12.1580
Totals :				2.28346e4	2505.52252	



2e

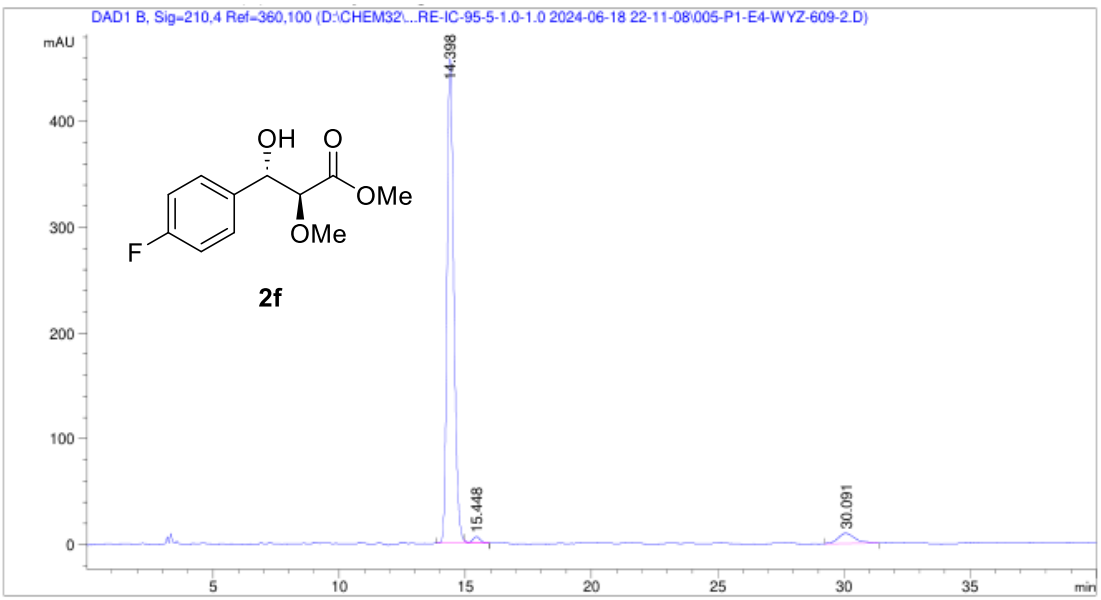
Signal 1: DAD1 D, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.583	VB R	0.1350	3021.57715	335.60306	92.6395
2	7.536	BB	0.2239	73.47603	5.23036	2.2527
3	7.982	BB	0.2267	30.48144	1.86451	0.9345
4	8.856	BB	0.2472	136.11501	7.81410	4.1732
Totals :				3261.64962	350.51203	



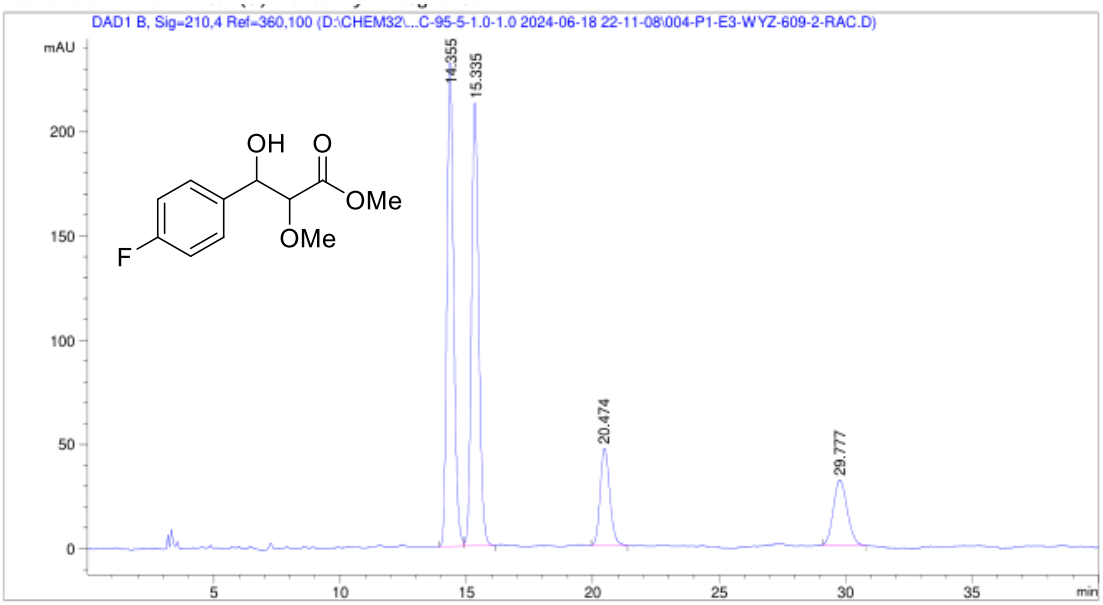
Signal 1: DAD1 D, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.621	BB	0.1367	881.05060	96.30665	37.1964
2	7.474	VV R	0.1511	876.71069	86.25386	37.0132
3	8.118	VB	0.1874	294.57959	23.31674	12.4366
4	8.815	BB	0.2059	316.30362	22.79578	13.3538
Totals :				2368.64450	228.67303	



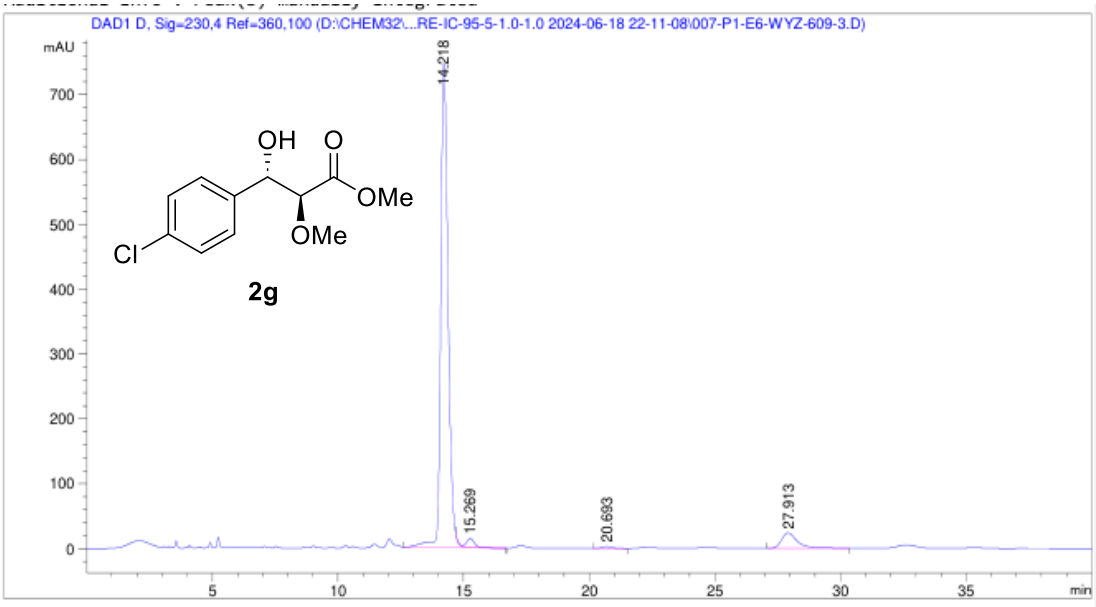
Signal 1: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.398	BV R	0.2884	8584.82227	458.58093	93.6617
2	15.448	VB E	0.2658	125.48026	6.10574	1.3690
3	30.091	BB	0.5930	455.47186	9.64349	4.9693
Totals :				9165.77438	474.33016	



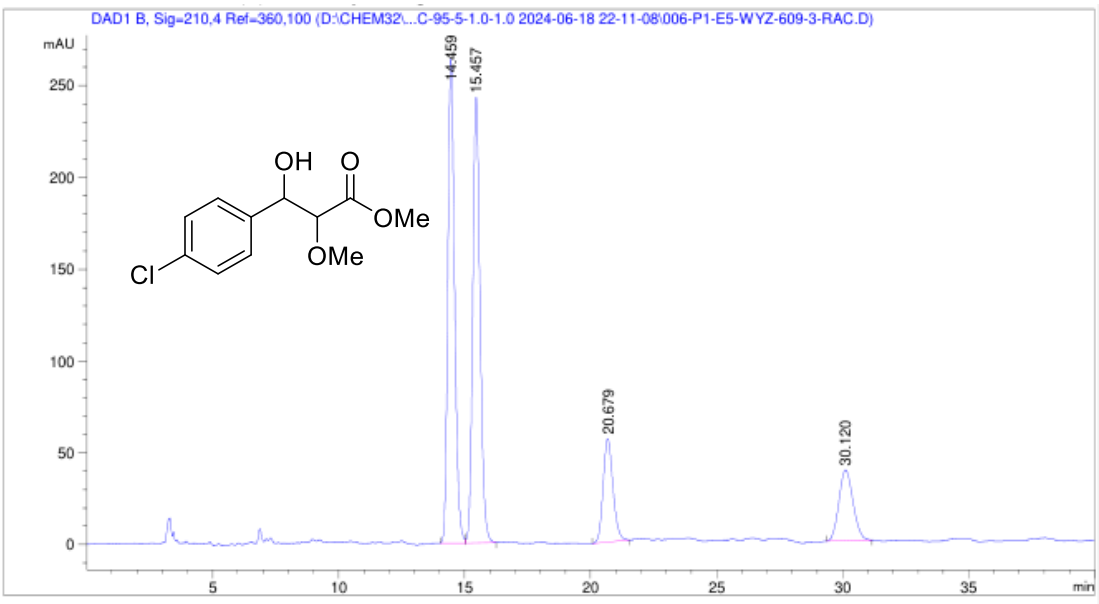
Signal 1: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.355	BV	0.2831	4274.63428	231.86563	39.0378
2	15.335	VB	0.3080	4261.93408	212.50787	38.9218
3	20.474	BB	0.4047	1223.21338	46.53404	11.1709
4	29.777	BB	0.5577	1190.21167	31.29240	10.8695
Totals :				1.09500e4	522.19994	



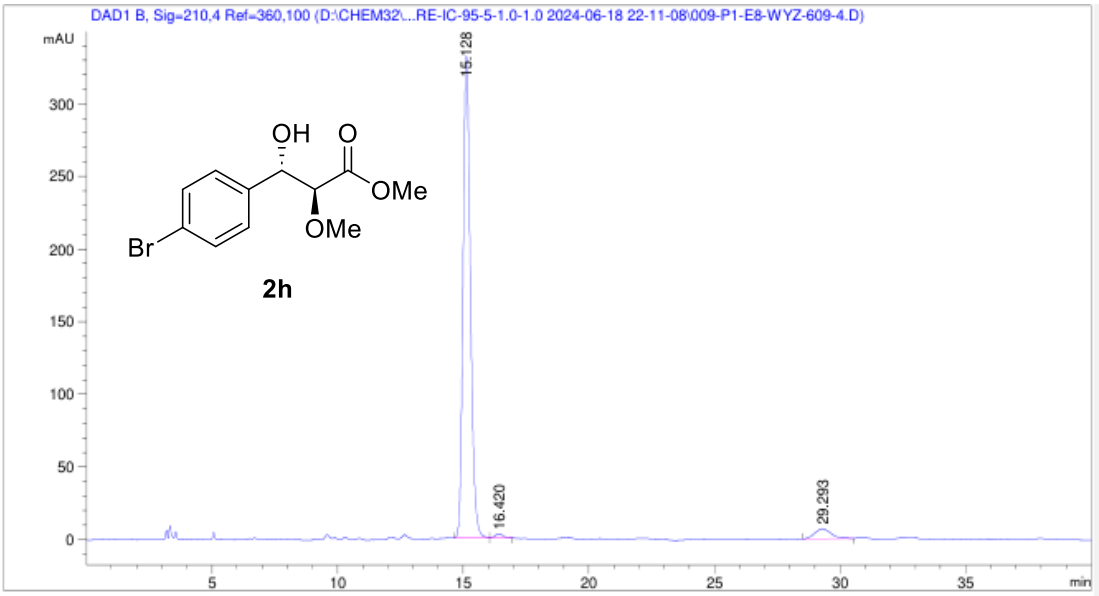
Signal 1: DAD1 D, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.218	BV R	0.3112	1.51705e4	746.14099	91.2174
2	15.269	VB E	0.3405	338.26062	14.81012	2.0339
3	20.693	BB	0.3563	80.31788	2.87205	0.4829
4	27.913	BB	0.6511	1042.07617	23.60020	6.2658
Totals :				1.66312e4	787.42336	



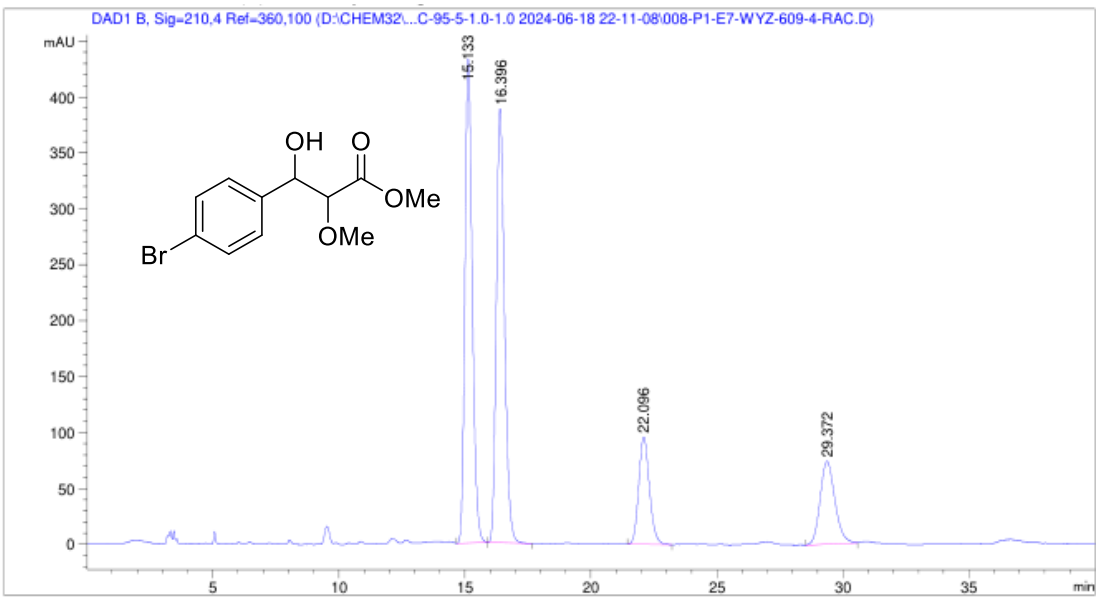
Signal 1: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.459	BV	0.2882	4926.91113	263.40848	38.2729
2	15.457	VB	0.3109	4924.94287	242.57971	38.2576
3	20.679	BB	0.4097	1525.49646	56.38049	11.8503
4	30.120	BB	0.5973	1495.76233	38.49614	11.6193
Totals :				1.28731e4	600.86482	



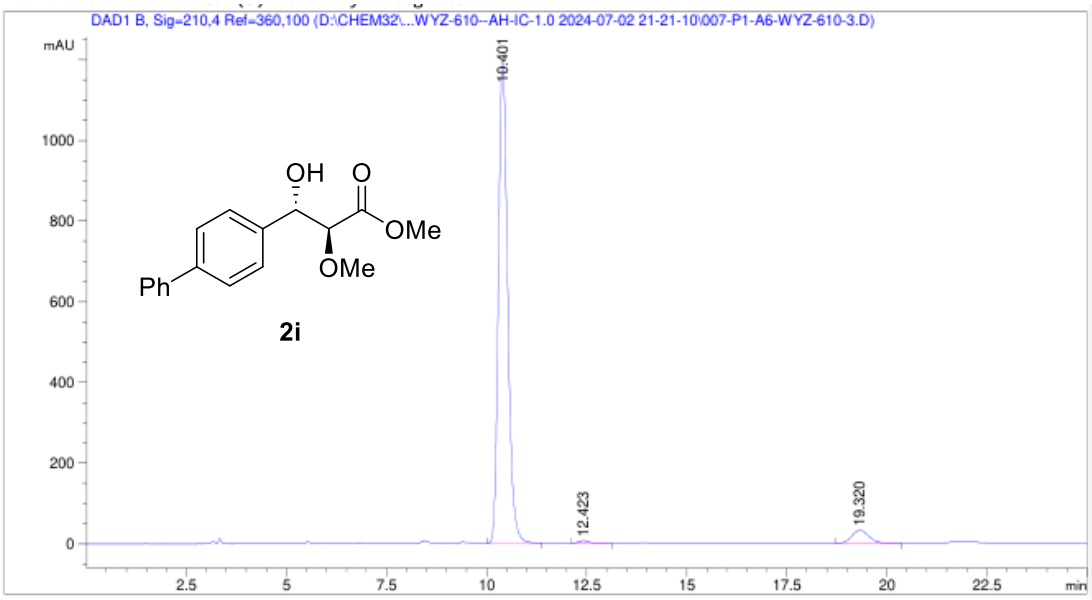
Signal 1: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.128	BB	0.3122	6720.53711	331.93326	94.8785
2	16.420	BB	0.2616	56.62384	2.73409	0.7994
3	29.293	BB	0.5478	306.14413	6.81873	4.3221
Totals :				7083.30508	341.48607	



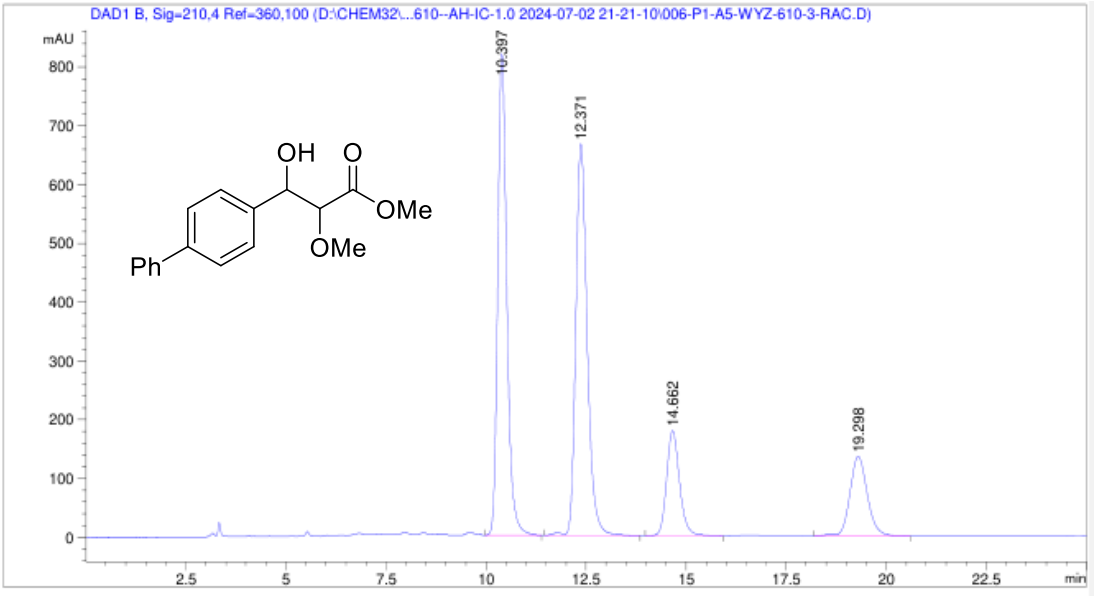
Signal 1: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.133	BB	0.3119	8747.77930	432.59357	37.4580
2	16.396	BB	0.3473	8752.95410	387.85748	37.4801
3	22.096	BB	0.4525	2856.55884	96.17087	12.2318
4	29.372	BB	0.6168	2996.28613	73.93647	12.8301
Totals :				2.33536e4	990.55839	



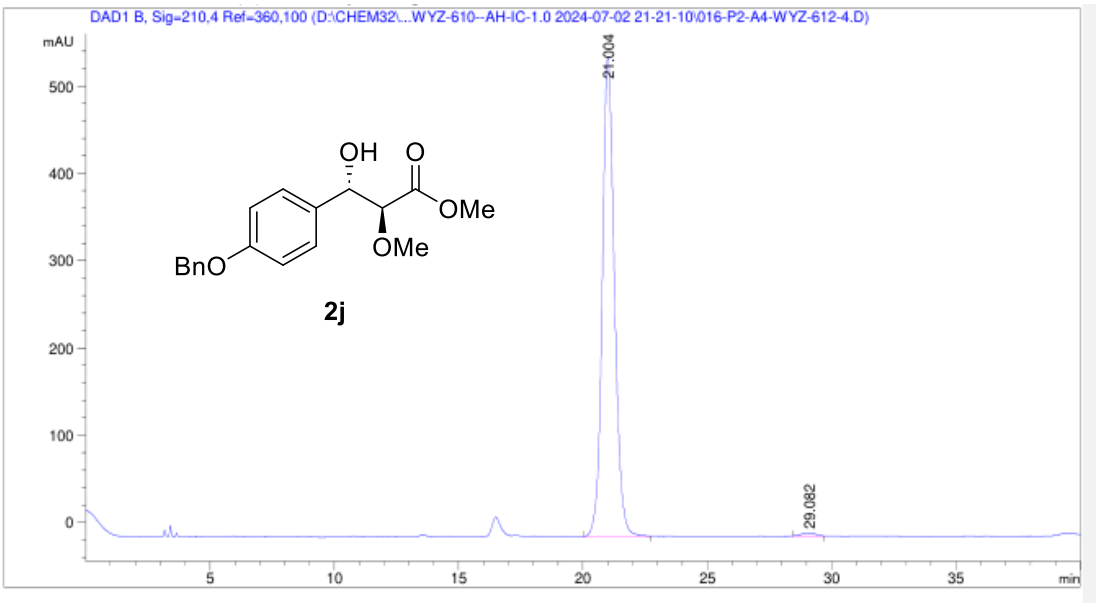
Signal 1: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.401	BB	0.2491	1.91682e4	1195.47449	94.5686
2	12.423	BB	0.2908	125.95611	6.36633	0.6214
3	19.320	BB	0.4486	974.94946	33.01235	4.8100
Totals :				2.02692e4	1234.85317	



Signal 1: DAD1 B, Sig=210,4 Ref=360,100

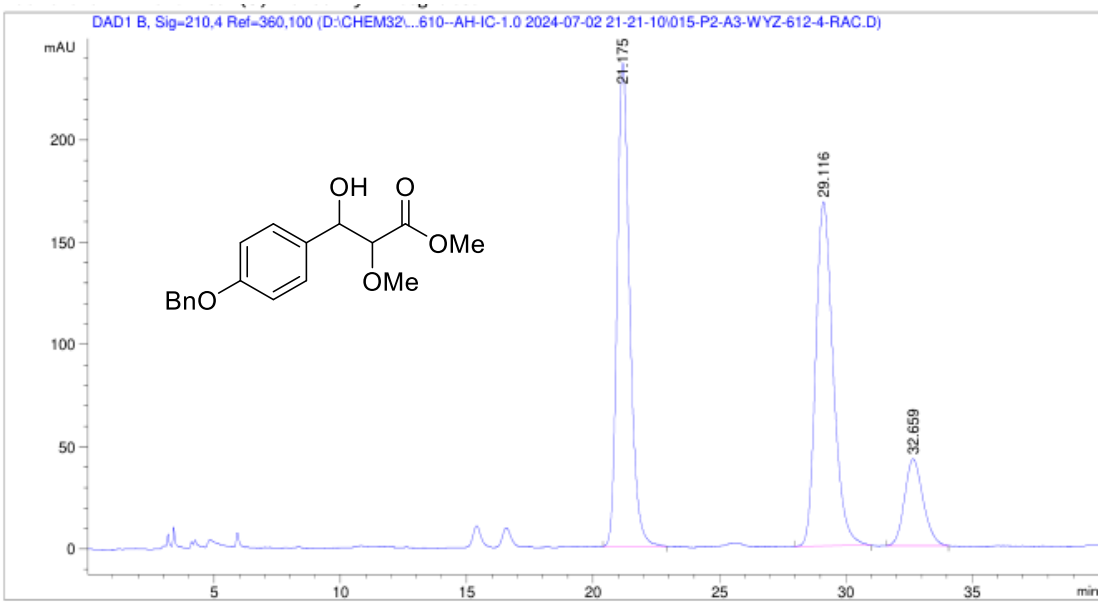
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.397	VB	0.2438	1.30365e4	818.50549	38.0331
2	12.371	VB R	0.3006	1.31218e4	666.50177	38.2819
3	14.662	BB	0.3454	4037.01221	178.83653	11.7777
4	19.298	BB	0.4634	4081.45190	135.51137	11.9073
Totals :				3.42768e4	1799.35516	



2j

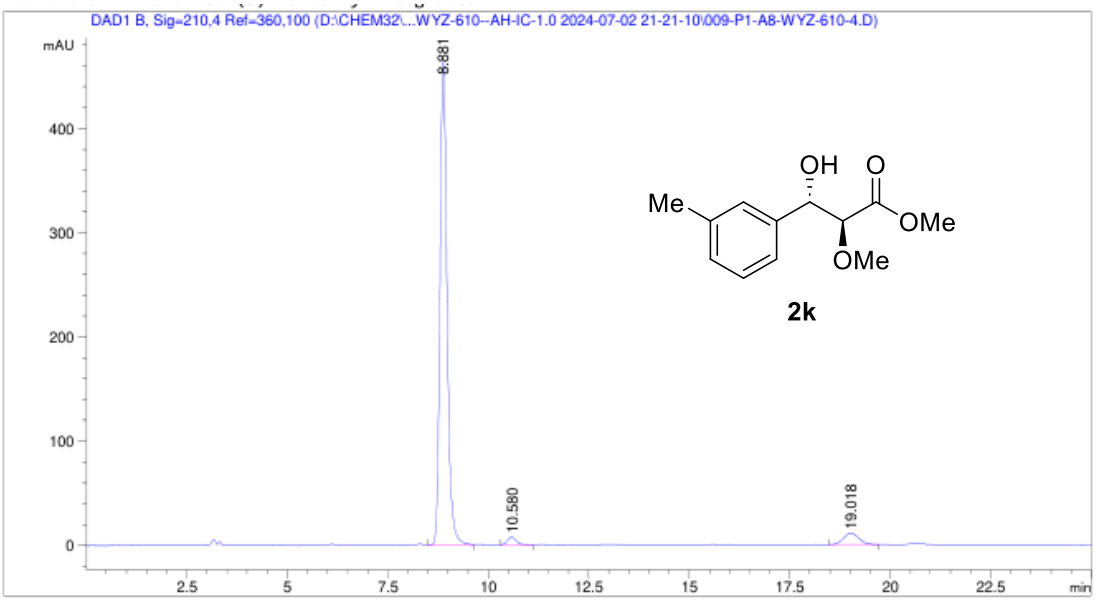
Signal 1: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.004	BB	0.5125	1.85438e4	548.33148	99.3074
2	29.082	BB	0.4577	129.33559	3.40099	0.6926
Totals :				1.86731e4	551.73247	



Signal 1: DAD1 B, Sig=210,4 Ref=360,100

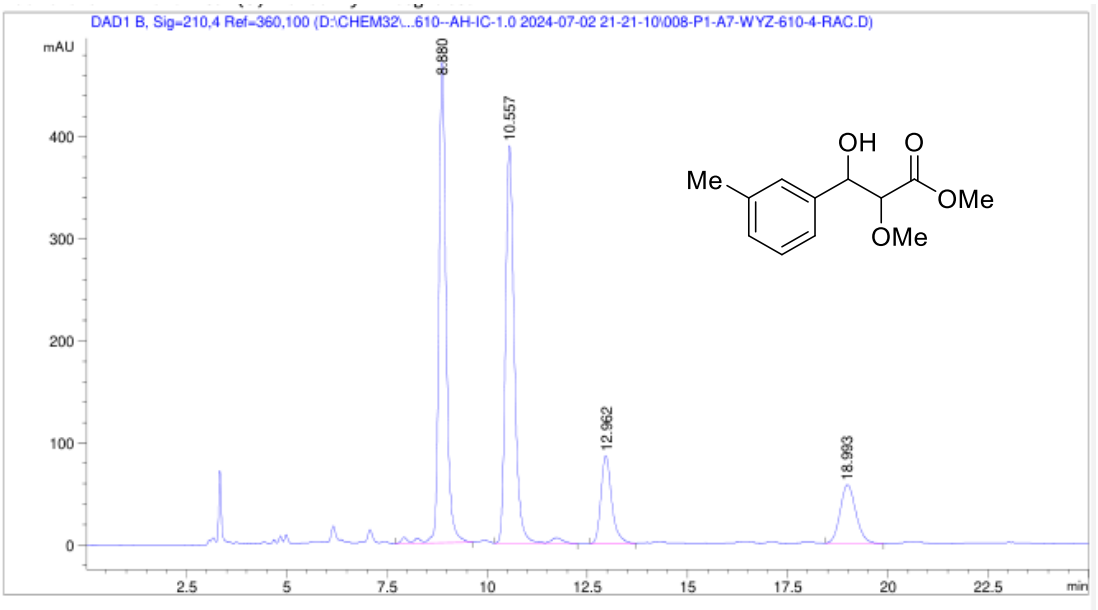
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.175	BB	0.5245	8123.31201	236.61098	44.1318
2	29.116	BB	0.7275	8100.80811	168.33057	44.0095
3	32.659	BB	0.6834	2182.81909	42.62933	11.8587
Totals :				1.84069e4	447.57087	



2k

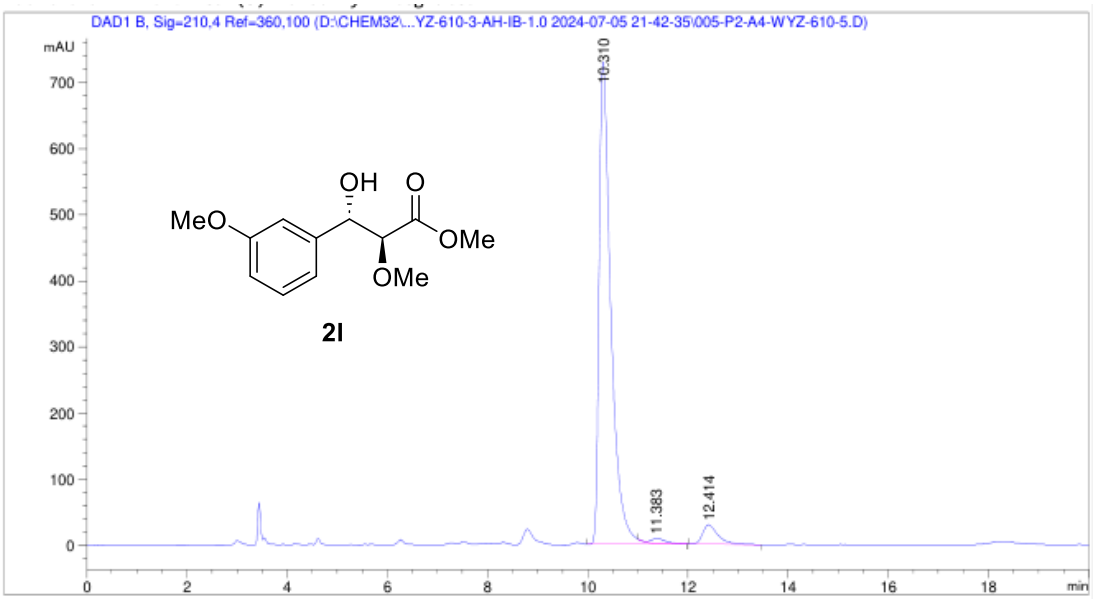
Signal 1: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.881	BB	0.1866	5666.74756	463.49976	93.3299
2	10.580	BB	0.2327	115.52114	7.37732	1.9026
3	19.018	BB	0.3292	289.46915	10.92203	4.7675
Totals :				6071.73785	481.79911	



Signal 1: DAD1 B, Sig=210,4 Ref=360,100

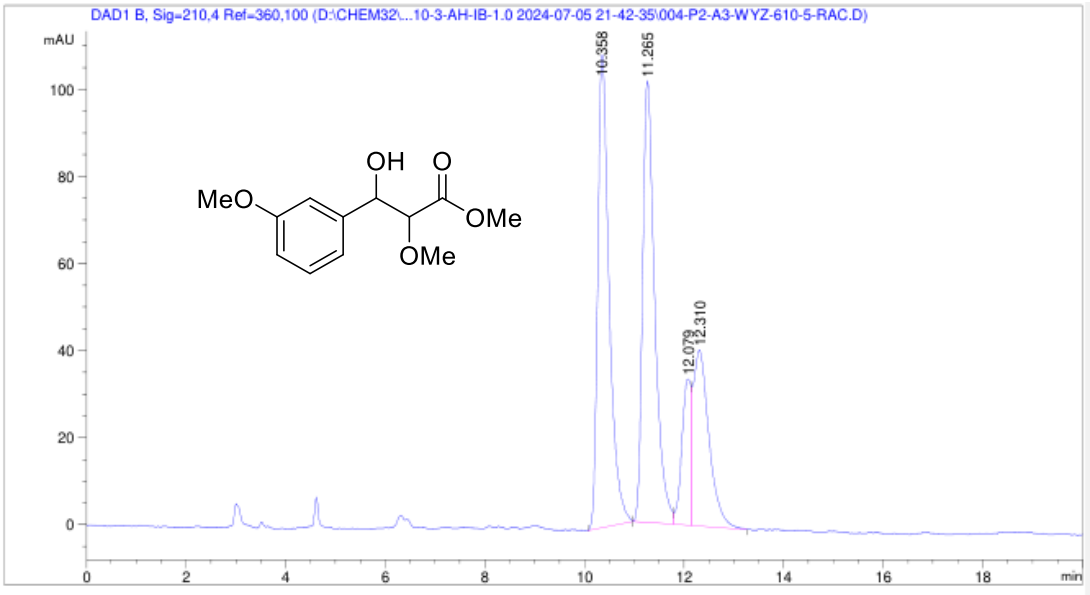
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.880	VB R	0.1899	6002.58887	471.12833	39.5051
2	10.557	BV R	0.2332	6020.23535	389.74423	39.6212
3	12.962	BB	0.2899	1607.50122	86.06207	10.5795
4	18.993	BB	0.4170	1564.14722	57.19684	10.2942
Totals :				1.51945e4	1004.13146	



2l

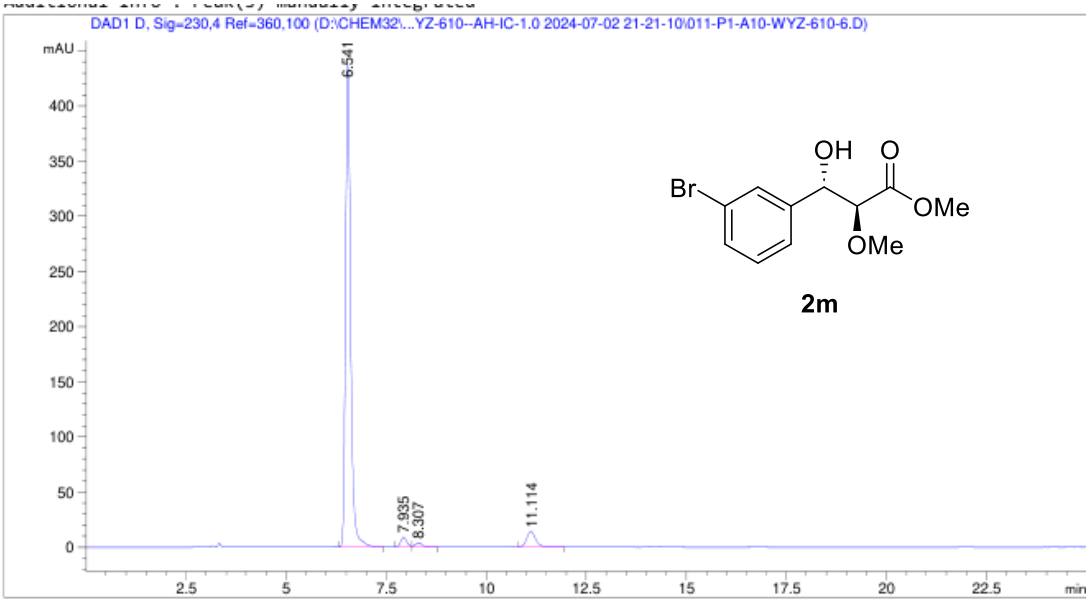
Signal 1: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.310	BV R	0.2398	1.18753e4	729.98511	93.8196
2	11.383	VB E	0.2905	159.22072	7.72479	1.2579
3	12.414	BB	0.3161	623.06519	29.30134	4.9225
Totals :				1.26576e4	767.01124	



Signal 1: DAD1 B, Sig=210,4 Ref=360,100

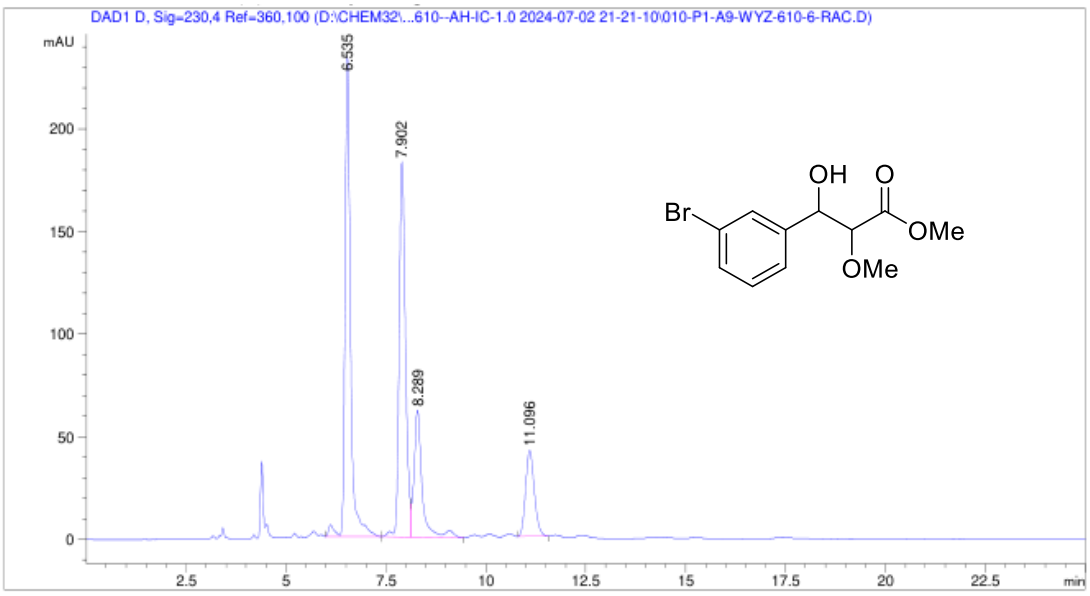
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.358	BB	0.2370	1721.51697	108.56081	36.2032
2	11.265	BV	0.2534	1714.04370	101.32056	36.0460
3	12.079	VV	0.1984	438.87424	33.59826	9.2294
4	12.310	VB	0.3142	880.71875	40.41536	18.5214
Totals :				4755.15366	283.89499	



2m

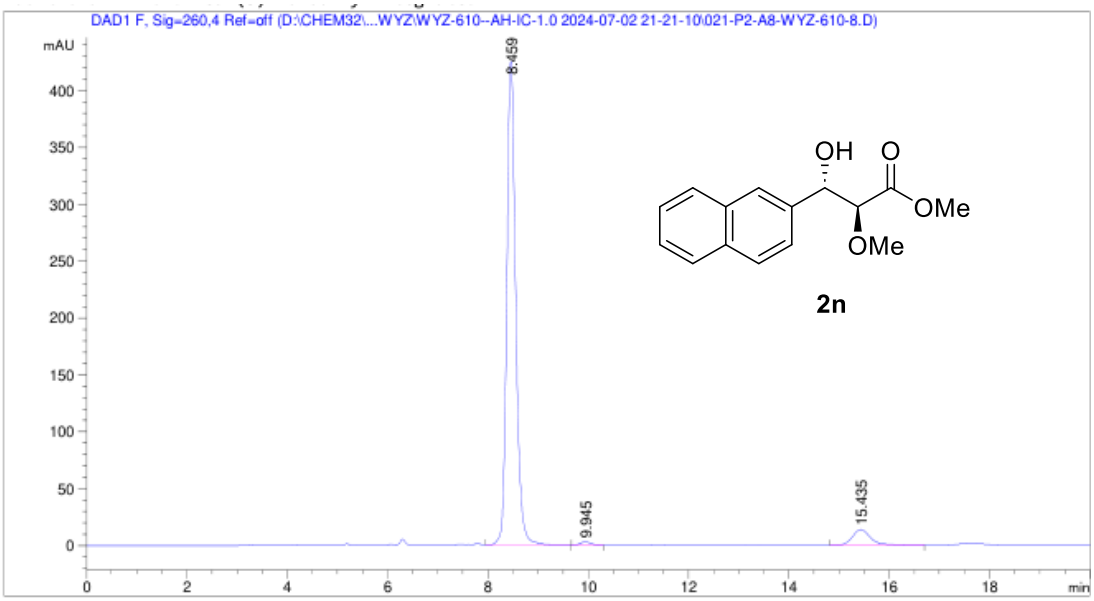
Signal 1: DAD1 D, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.541	BB	0.1320	3824.29590	437.23657	91.6606
2	7.935	BV	0.1622	89.11009	8.50681	2.1358
3	8.307	VB	0.1754	43.32380	3.79023	1.0384
4	11.114	BB	0.2395	215.50446	13.85028	5.1652
Totals :				4172.23425	463.38389	



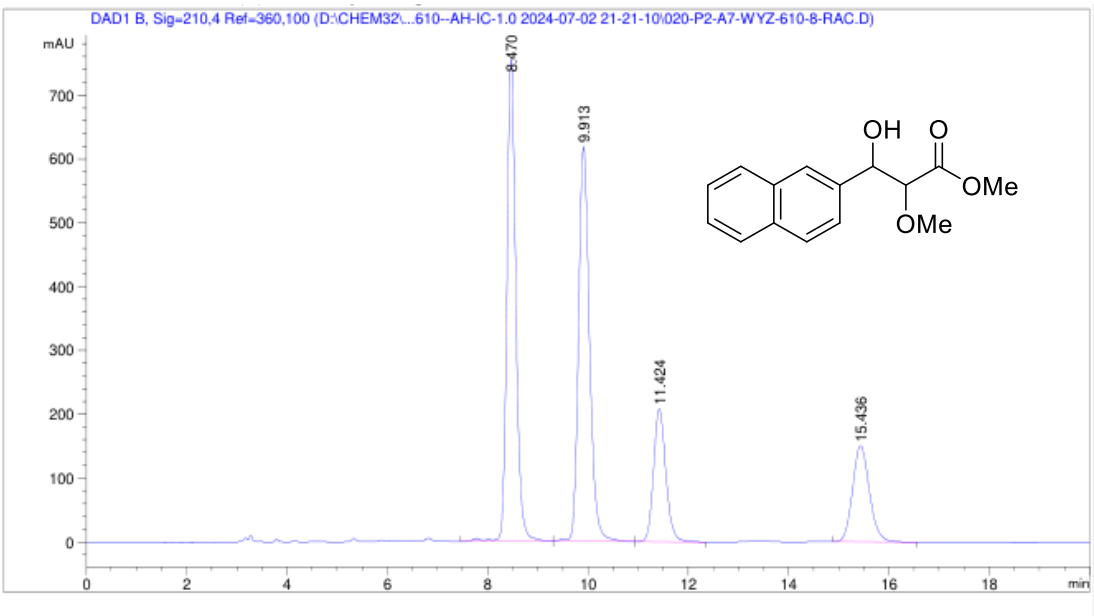
Signal 1: DAD1 D, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.535	VB R	0.1386	2229.97168	233.26588	38.6872
2	7.902	VV R	0.1700	2025.17786	182.51039	35.1343
3	8.289	VV R	0.1963	866.29425	61.77230	15.0291
4	11.096	VB	0.2367	642.65875	41.95615	11.1493
Totals :				5764.10254	519.50473	



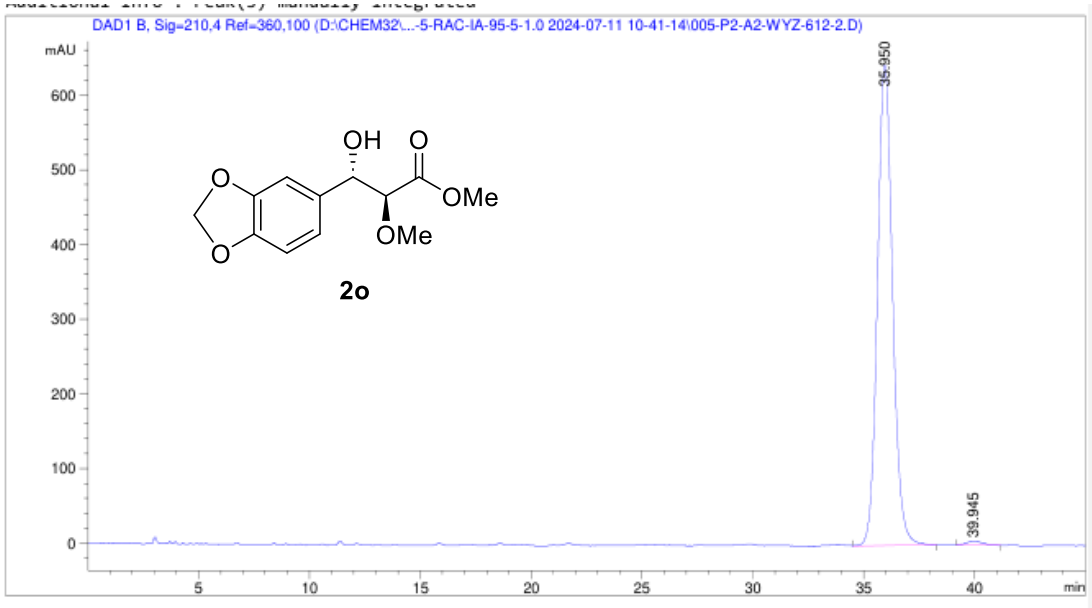
Signal 1: DAD1 F, Sig=260,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.459	BB	0.1885	5265.93359	425.24387	92.9839
2	9.945	BB	0.2224	41.22725	2.89021	0.7280
3	15.435	BB	0.3836	356.11420	13.95924	6.2881
Totals :				5663.27504	442.09332	



Signal 1: DAD1 B, Sig=210,4 Ref=360,100

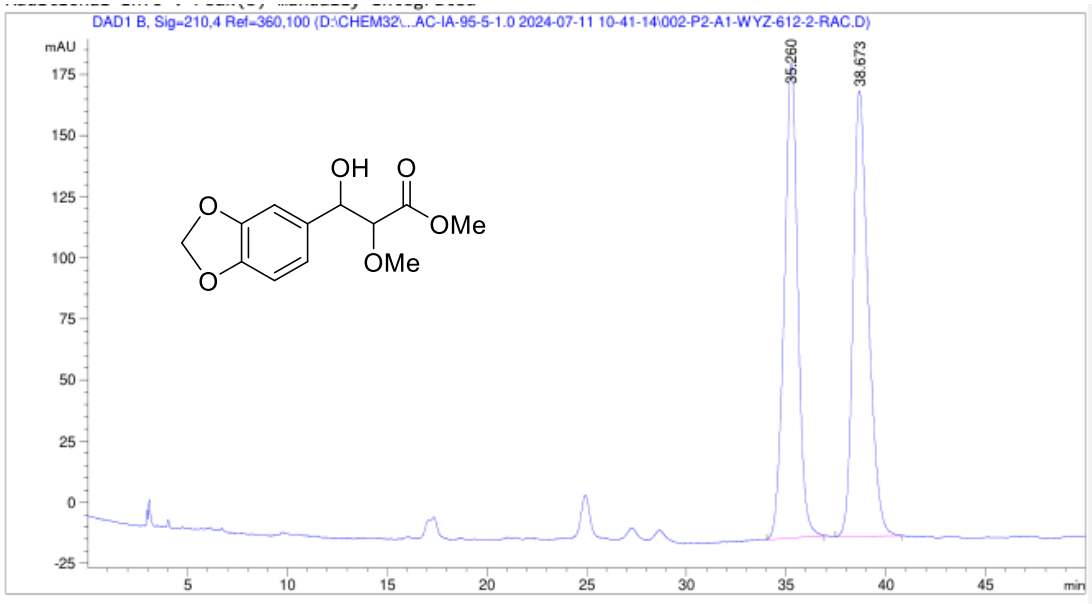
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.470	VB R	0.1902	9431.28223	755.77661	36.4263
2	9.913	VB R	0.2325	9375.48145	618.08258	36.2107
3	11.424	BB	0.2615	3559.81396	208.20245	13.7490
4	15.436	BB	0.3613	3524.85669	150.47789	13.6140
Totals :				2.58914e4	1732.53954	



2o

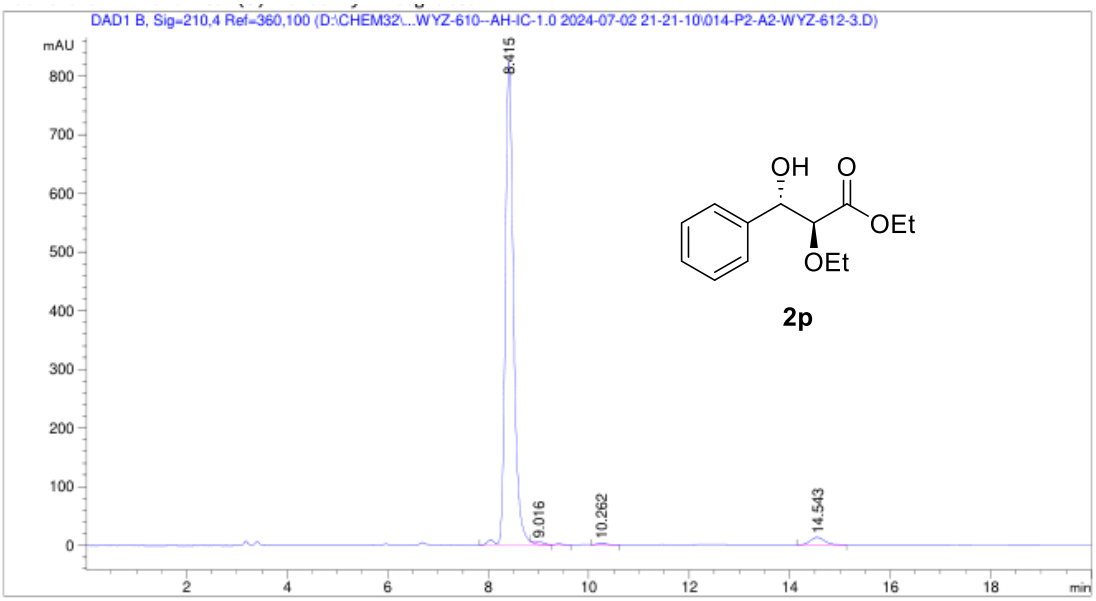
Signal 1: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	35.950	BB	0.7297	3.06216e4	642.94012	99.1065
2	39.945	BB	0.6250	276.08640	5.27128	0.8935
Totals :				3.08977e4	648.21140	



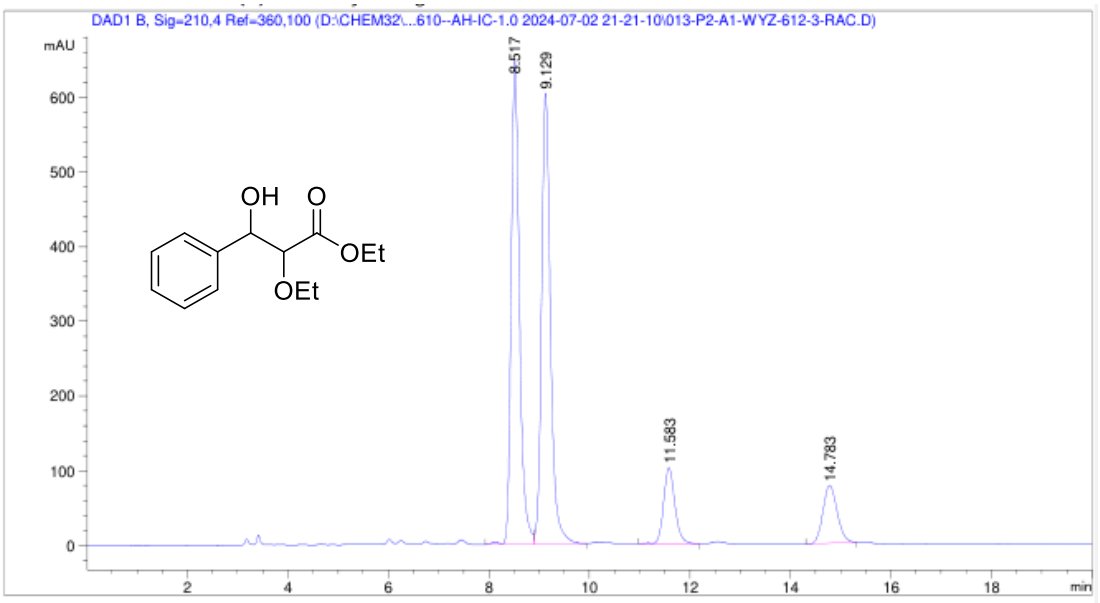
Signal 1: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	35.260	BB	0.6828	9140.53418	194.32420	48.5405
2	38.673	BB	0.7762	9690.20605	182.27994	51.4595
Totals :				1.88307e4	376.60414	



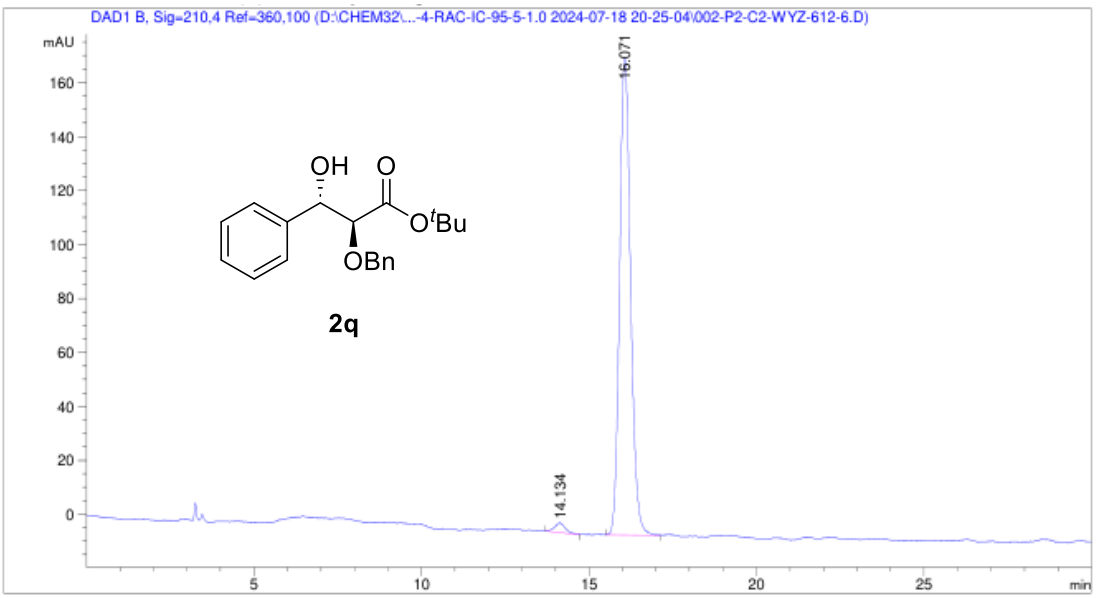
Signal 1: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.415	VV R	0.1751	9513.89941	824.71613	96.5541
2	9.016	VV E	0.1782	53.07420	4.17760	0.5386
3	10.262	BB	0.1819	37.23717	3.24401	0.3779
4	14.543	BB	0.3021	249.22514	12.74842	2.5293
Totals :				9853.43592	844.88616	



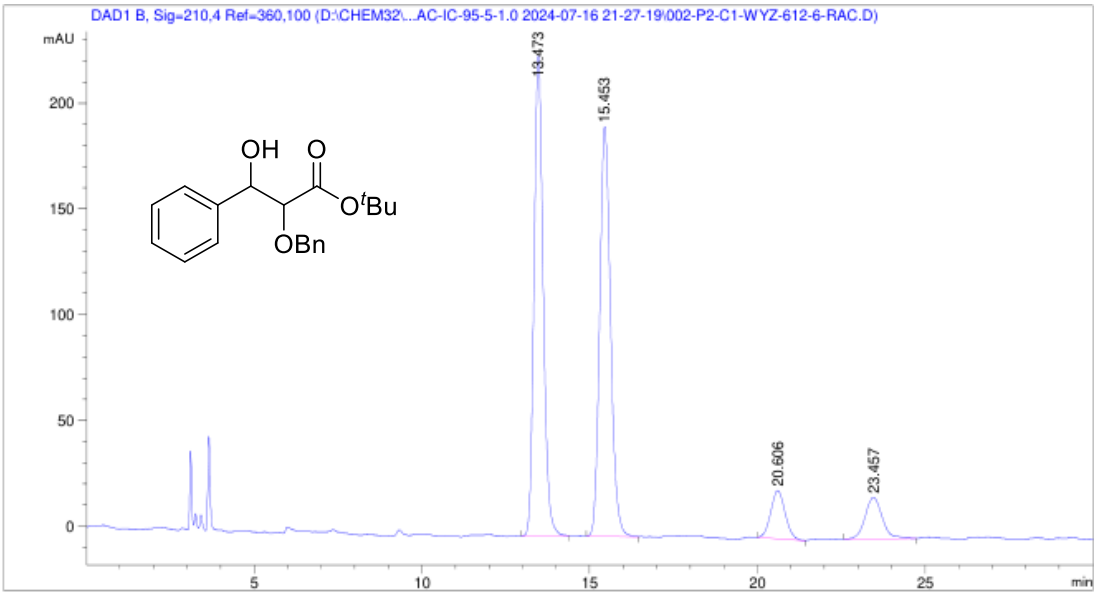
Signal 1: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.517	VV R	0.1743	7376.78271	647.78552	41.1009
2	9.129	VB	0.1880	7455.40771	603.84821	41.5390
3	11.583	VB R	0.2398	1599.76001	101.93784	8.9133
4	14.783	BB	0.3019	1516.01208	77.59644	8.4467
Totals :				1.79480e4	1431.16801	



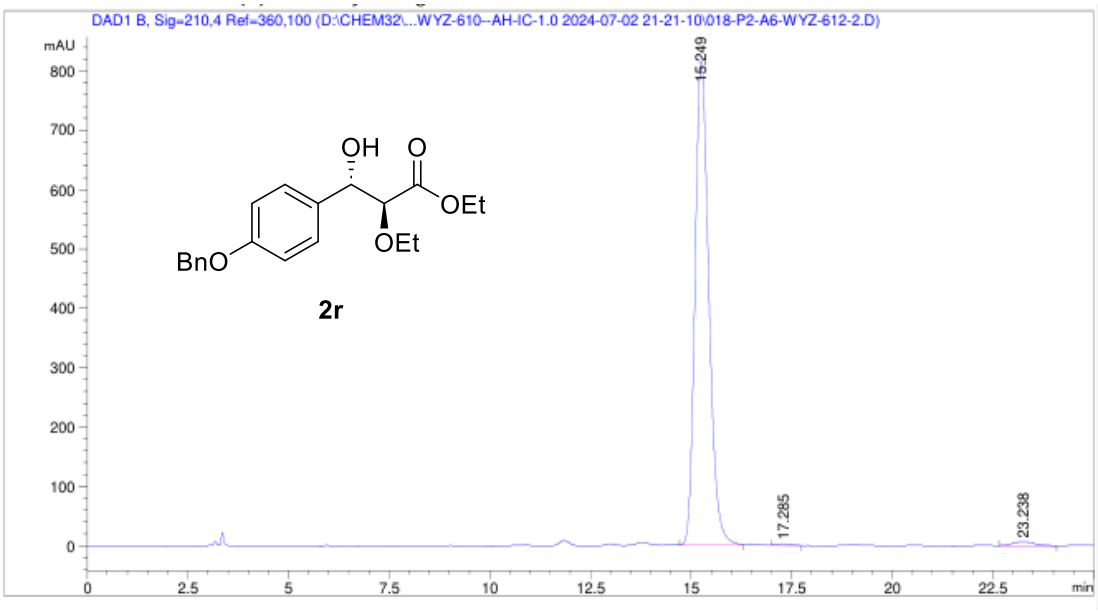
Signal 1: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.134	BB	0.2713	77.11781	3.52350	1.8833
2	16.071	BB	0.3512	4017.67896	176.71280	98.1167
Totals :				4094.79676	180.23629	



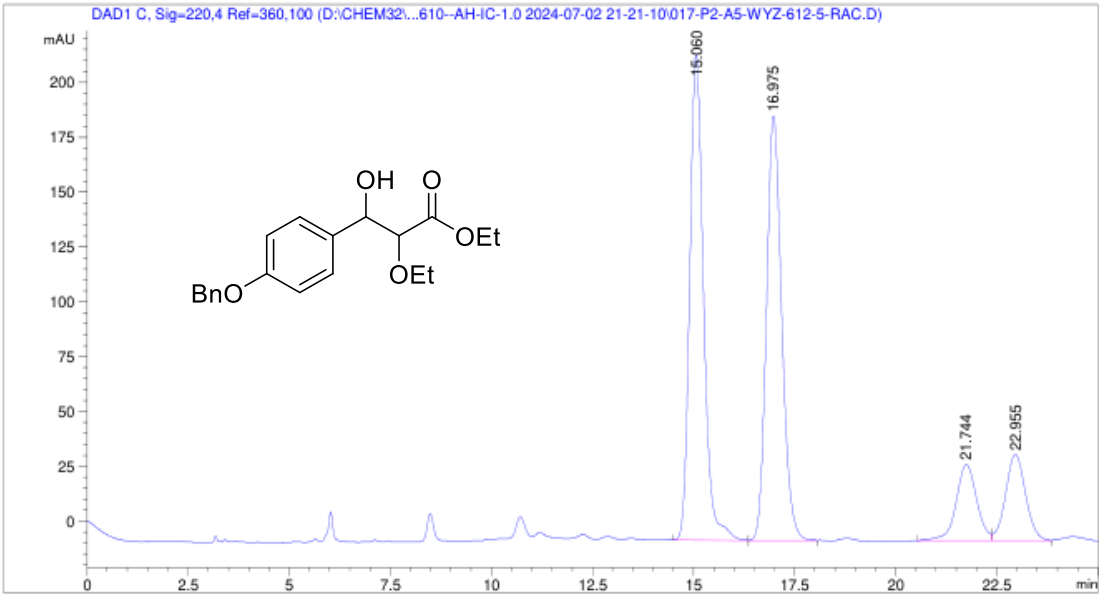
Signal 1: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.473	BB	0.2915	4314.28857	227.26022	42.9113
2	15.453	BB	0.3484	4361.80469	193.94235	43.3840
3	20.606	BB	0.4378	675.46204	22.78617	6.7184
4	23.457	BB	0.4815	702.40369	19.72126	6.9863
Totals :				1.00540e4	463.71001	



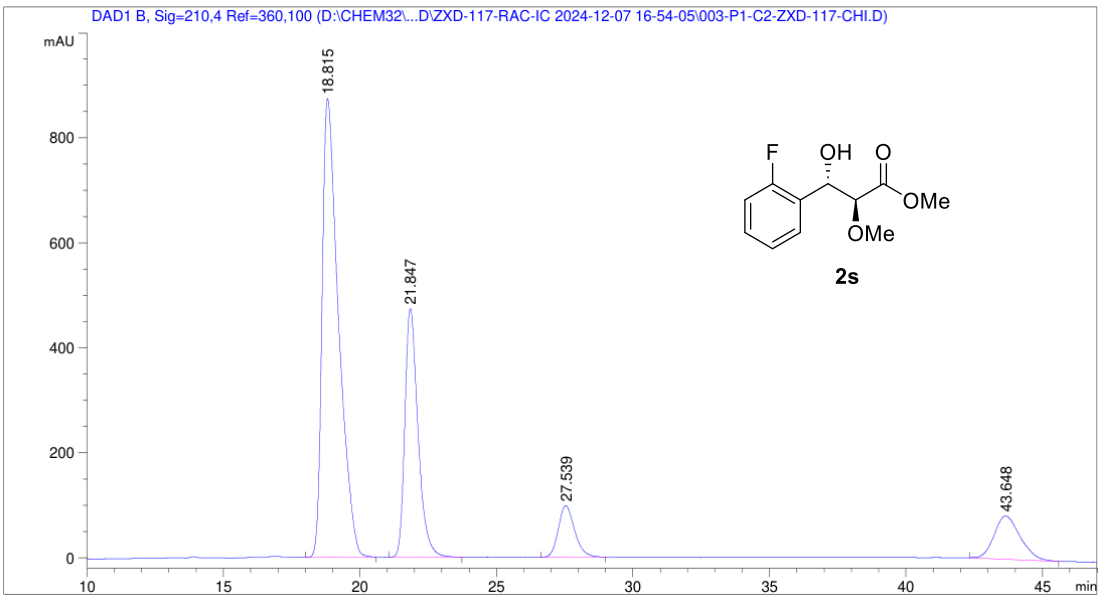
Signal 1: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.249	VB	0.3676	1.93983e4	815.23517	98.5667
2	17.285	BB	0.2959	50.03681	2.08570	0.2542
3	23.238	BB	0.4349	232.04288	6.37111	1.1791
Totals :				1.96803e4	823.69199	



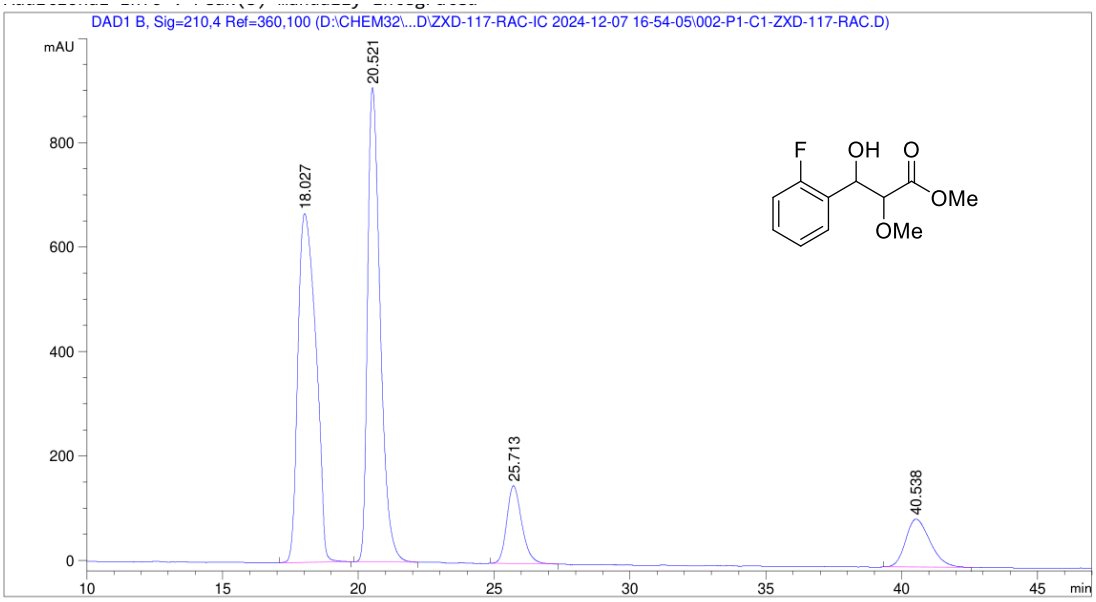
Signal 1: DAD1 C, Sig=220,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.060	BB	0.3611	5216.35840	221.22687	40.5664
2	16.975	BB	0.4020	5073.81934	193.43369	39.4580
3	21.744	BV	0.5252	1223.09570	34.70211	9.5117
4	22.955	VB	0.5087	1345.52673	39.17538	10.4639
Totals :				1.28588e4	488.53804	



Signal 1: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.815	BB	0.6154	3.66661e4	874.11792	59.0912
2	21.847	BB	0.5089	1.58811e4	474.00757	25.5940
3	27.539	BB	0.6183	4047.38672	97.89571	6.5228
4	43.648	BB	0.8192	5455.47949	82.31331	8.7921
Totals :				6.20500e4	1528.33450	



Signal 1: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.027	BB	0.7247	3.06419e4	668.61499	42.8527
2	20.521	BB	0.4984	2.93290e4	909.10474	41.0167
3	25.713	BB	0.5852	5771.36865	149.21532	8.0713
4	40.538	BB	0.8717	5762.84277	92.14124	8.0593
Totals :				7.15051e4	1819.07628	

6. References

[1] Miyata, R.; Shigeta, T.; Kumazawa, S.; Egi, M., Selective Syntheses of Coumarin and Benzofuran Derivatives Using Phenols and α-Methoxy-β-ketoesters. *SynOpen* **2023,** *07*, 8-16.

[2] Monnereau, L.; Cartigny, D.; Scalone, M.; Ayad, T.; Ratovelomanana-Vidal, V., Efficient Synthesis of Differentiated syn-1,2-Diol Derivatives by Asymmetric Transfer Hydrogenation–Dynamic Kinetic Resolution of α-Alkoxy-Substituted β-Ketoesters. *Chem. - Eur. J.* **2015,** *21*, 11799-11806.

[3] Gangar, M.; Ittuveetil, A.; Goyal, S.; Pal, A.; Harikrishnan, M.; Nair, V. A., Anti selective glycolate aldol reactions of (S)-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one: application towards the asymmetric synthesis of 8-4′-oxyneolignans. *RSC Adv.* **2016,** *6*, 102116-102126.