Direct Asymmetric Reductive Amination of α-Keto Acetals: A Platform for Synthesizing Diverse α-Functionalized Amines

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Supporting Information

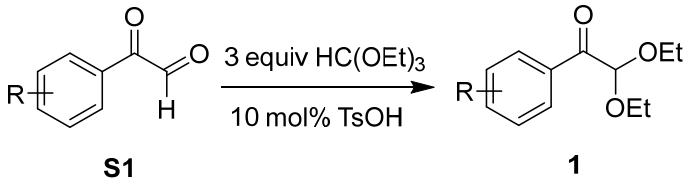
Contents

I. General Information

Unless otherwise mentioned, all experiments were carried out under an atmosphere of argon in a glovebox or using standard Schlenk techniques. Solvents were dried with standard procedures and degassed with N_2. Flash column chromatography was performed using Tsingdao silica gel (60, particle size 300-400 mesh). NMR spectra were recorded on a Bruker DPX 400 spectrometer at 400 MHz for ^{1}H NMR, 101 MHz for ^{13}C NMR or 126 MHz for ^{13}C NMR in $CDCl_3$ or CD_3OD with tetramethylsilane (TMS) as internal standard. Chemical shifts are reported in ppm and coupling constants are given in Hz. Chemical shifts were reported relative to TMS (0.00 ppm) for ^{1}H NMR and relative to $CDCl_3$ (77.16 ppm) or CD_3OD (49.00 ppm) for ^{13}C NMR. Enantiomeric excesses were determined by chiral HPLC analysis on Agilent Technologies 1260 Infinity II instrument or UPLC analysis on Agilent Technologies 1290 Infinity II instrument using a chiral stationary phase in comparison with the authentic racemates. High resolution mass spectra (HRMS) were obtained on Thermo Scientific Q Exactive hybrid quadrupole-Orbitrap mass spectrometer at the Department of Chemistry, Southern University of Science and Technology. PE refers to petroleum ether, HEX refers to hexane, EA refers to ethyl acetate, TFE refers to 2,2,2-trifluoroethanol, and MTBE refers to methyl *tert*-butyl ether.

II. General Procedures for the Synthesis of Substrates

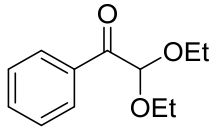
General Procedure:



S1 **1**

To a suspension of arylglyoxal or its monohydrate[1] (10.0 mmol) and PTS (*p*-toluenesulfonic acid, 0.1 equiv) in CH_2Cl_2 (40 mL) at room temperature was added $HC(OEt)_3$ (4.44 g, 30.0 mmol). The mixture was stirred for 2 h at 35 ℃. The reaction was quenched by 30 mL saturated $NaHCO_3$ solution and extracted by CH_2Cl_2 (3 x 30 mL). The combined organic phase was dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. The residue was subjected to column chromatography on silica gel (eluent: HEX/EA = 100/2) to afford desired keto acetals.

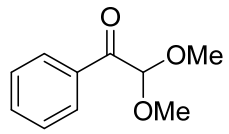
Characterization data of substrate



Chemical Formula: $C_{12}H_{16}O_3$
Exact Mass: 208.1099

2,2-Diethoxy-1-phenylethan-1-one (1aa)

Substrate **1aa** is commercially available. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.18 – 8.14 (m, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 2H), 5.28 (s, 1H), 3.76 (dq, *J* = 9.6, 7.1 Hz, 2H), 3.66 (dq, *J* = 9.6, 7.0 Hz, 2H), 1.25 (t, *J* = 7.0 Hz, 6H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 194.2, 133.9, 133.6, 129.8, 128.5, 102.5, 63.3, 15.3.

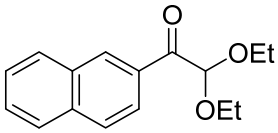


Chemical Formula: $C_{10}H_{12}O_3$
Exact Mass: 180.0786

2,2-Dimethoxy-1-phenylethan-1-one (1ab)

Substrate **1ab** was synthesized according to a reported procedure. [1]

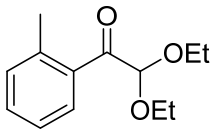
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.15 – 8.08 (m, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 5.23 (s, 1H), 3.48 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 193.5, 133.9, 133.8, 129.6, 128.6, 103.4, 54.7.



Chemical Formula: $C_{16}H_{18}O_3$
Exact Mass: 258.1256

2,2-Diethoxy-1-(naphthalen-2-yl)ethan-1-one (1b)

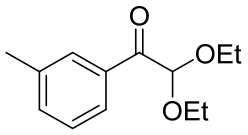
Substrate **1b** was synthesized according to **General procedure**. Light yellow oil, 5.0 mmol scale, 0.57 g, 2.2 mmol, 44% yield, R_f = 0.5 (Hex/EA = 95/5), obtained by purification with flash column chromatography on silica gel (eluent: Hex/EA = 1/0.02). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.78 (s, 1H), 8.15 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.99 (d, *J* = 8.1 Hz, 1H), 7.90 – 7.85 (m, 2H), 7.62 – 7.58 (m, 1H), 7.56 – 7.52 (m, 1H), 5.41 (s, 1H), 3.81 (dq, *J* = 9.6, 7.1 Hz, 2H), 3.71 (dq, *J* = 9.6, 7.0 Hz, 2H), 1.27 (t, *J* = 7.1 Hz, 6H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 194.2, 136.0, 132.6, 132.2, 131.2, 130.1, 128.8, 128.2, 127.9, 126.7, 125.1, 102.7, 63.4, 15.4. The NMR data is consistent with that reported.[2]



Chemical Formula: $C_{13}H_{18}O_3$
Exact Mass: 222.1256

2,2-Diethoxy-1-(*o*-tolyl)ethan-1-one (1c)

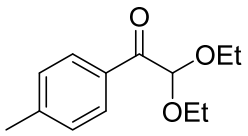
Substrate **1c** was synthesized according to **General procedure**. Colorless oil, 10 mmol scale, 1.4 g, 6.3 mmol, 63% yield, R_f = 0.5 (Hex/EA = 95/5), obtained by purification with flash column chromatography on silica gel (eluent: Hex/EA = 1/0.02). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.02 – 7.95 (m, 1H), 7.42 – 7.35 (m, 1H), 7.29 – 7.21 (m, 2H), 5.21 (s, 1H), 3.81 – 3.60 (m, 4H), 2.52 (s, 3H), 1.23 (t, *J* = 7.1 Hz, 6H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 197.5, 139.9, 134.4, 132.0, 131.9, 130.2, 125.4, 102.5, 63.2, 21.5, 15.3. The NMR data is consistent with that reported.[3]



Chemical Formula: $C_{13}H_{18}O_3$
Exact Mass: 222.1256

2,2-Diethoxy-1-(*m*-tolyl)ethan-1-one (1d)

Substrate **1d** was synthesized according to **General procedure**. Light yellow oil, 10 mmol scale, 1.34 g, 6.04 mmol, 60% yield, R_f = 0.5 (Hex/EA = 95/5), obtained by purification with flash column chromatography on silica gel (eluent: Hex/EA = 1/0.02). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.04 – 7.91 (m, 2H), 7.40 – 7.31 (m, 2H), 5.30 (s, 1H), 3.75 (p, *J* = 7.4 Hz, 2H), 3.66 (p, *J* = 7.5 Hz, 2H), 2.41 (s, 3H), 1.25 (t, *J* = 7.0 Hz, 6H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 194.3, 138.3, 134.4, 134.0, 130.2, 128.4, 127.1, 102.2, 63.2, 21.5, 15.4. The NMR data is consistent with that reported.[3]

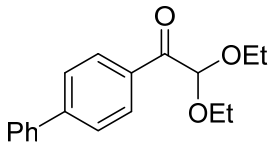


Chemical Formula: $C_{13}H_{18}O_3$
Exact Mass: 222.1256

2,2-Diethoxy-1-(*p*-tolyl)ethan-1-one (1e)

Substrate **1e** was synthesized according to **General procedure**. Colorless oil, 1.4 mmol scale, 0.24 g, 1.1 mmol, 76% yield, R_f = 0.5 (Hex/EA = 95/5), obtained by purification

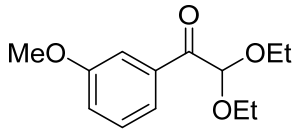
with flash column chromatography on silica gel (eluent: Hex/EA = 1/0.02). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.06 (d, *J* = 8.3 Hz, 2H), 7.25 (d, *J* = 8.1 Hz, 2H), 5.26 (s, 1H), 3.80 – 3.60 (m, 4H), 2.41 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 6H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 193.8, 144.5, 131.4, 130.0, 129.2, 102.5, 63.2, 21.9, 15.3. The NMR data is consistent with that reported.[2]



Chemical Formula: $C_{18}H_{20}O_3$
Exact Mass: 284.1412

1-([1,1'-Biphenyl]-4-yl)-2,2-diethoxyethan-1-one (1f)

Substrate **1f** was synthesized according to **General procedure**. Colorless oil, 18.5 mmol scale, 4.10 g, 14.4 mmol, 78% yield, R_f = 0.5 (Hex/EA = 95/5), obtained by purification with flash column chromatography on silica gel (eluent: Hex/EA = 1/0.02). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.25 (d, *J* = 8.5 Hz, 2H), 7.70 – 7.60 (m, 4H), 7.51 – 7.43 (m, 2H), 7.43 – 7.37 (m, 1H), 5.29 (s, 1H), 3.79 (dq, *J* = 9.5, 7.1 Hz, 2H), 3.68 (dq, *J* = 9.6, 7.0 Hz, 2H), 1.27 (t, *J* = 7.1 Hz, 6H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 193.8, 146.2, 140.1, 132.6, 130.5, 129.0, 128.4, 127.4, 127.1, 102.8, 63.40, 15.4. HRMS (ESI), m/z: $[M+Na]^+$ Calcd for $C_{18}H_{20}O_3Na^+$: 307.1305; Found: 307.1304.

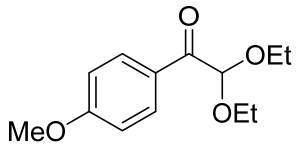


Chemical Formula: $C_{13}H_{18}O_4$
Exact Mass: 238.1205

2,2-Diethoxy-1-(3-methoxyphenyl)ethan-1-one (1g)

Substrate **1g** was synthesized according to **General procedure**. Light yellow oil, 9.1 mmol scale, 1.94 g, 8.15 mmol, 90% yield, R_f = 0.5 (Hex/EA = 95/5), obtained by purification with flash column chromatography on silica gel (eluent: Hex/EA = 1/0.02).

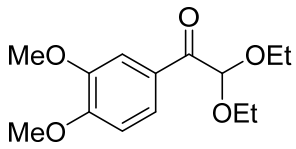
^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.78 (d, *J* = 7.7 Hz, 1H), 7.66 (s, 1H), 7.35-7.37 (t, *J* = 7.9 Hz, 1H), 7.12 (dd, *J* = 8.2, 2.0 Hz, 1H), 5.28 (s, 1H), 3.85 (s, 3H), 3.79 – 3.72 (m, 2H), 3.71 – 3.62 (m, 2H), 1.25 (t, *J* = 7.1 Hz, 6H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 193.9, 159.7, 135.2, 129.5, 122.6, 120.3, 113.8, 102.3, 63.2, 55.5, 15.3. The NMR data is consistent with that reported.[3]



Chemical Formula: $C_{13}H_{18}O_4$
Exact Mass: 238.1205

2,2-Diethoxy-1-(4-methoxyphenyl)ethan-1-one (1h)

Substrate **1h** was synthesized according to **General procedure**. Light yellow oil, 9.1 mmol scale, 1.99 g, 8.36 mmol, 92% yield, R_f = 0.5 (Hex/EA = 95/5), obtained by purification with flash column chromatography on silica gel (eluent: Hex/EA = 1/0.02). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.16 (d, *J* = 8.9 Hz, 2H), 6.93 (d, *J* = 8.9 Hz, 2H), 5.23 (s, 1H), 3.87 (s, 3H), 3.75 (dq, *J* = 9.6, 7.1 Hz, 2H), 3.64 (dq, *J* = 9.6, 7.0 Hz, 2H), 1.24 (t, *J* = 7.0 Hz, 6H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 192.8, 163.9, 132.3, 126.9, 113.7, 102.8, 63.2, 55.6, 15.3. The NMR data is consistent with that reported.[2]

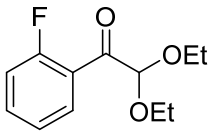


Chemical Formula: $C_{14}H_{20}O_5$
Exact Mass: 268.1311

1-(3,4-Dimethoxyphenyl)-2,2-diethoxyethan-1-one (1i)

Substrate **1i** was synthesized according to **General procedure**. Light yellow oil, 5 mmol scale, 1.1 g, 4.1 mmol, 82% yield, R_f = 0.5 (Hex/EA = 95/5), obtained by purification with flash column chromatography on silica gel (eluent: Hex/EA = 1/0.02). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.92 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.67 (d, *J* = 2.0 Hz, 1H), 6.90 (d, *J* = 8.5 Hz, 1H), 5.25 (s, 1H), 3.95 (s, 3H), 3.94 (s, 3H), 3.79 – 3.73

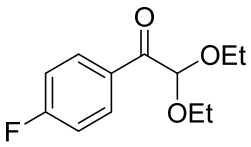
(m, 2H), 3.69 – 3.63 (m, 2H), 1.25 (t, J = 7.1 Hz, 6H). $^{13}C\{^{1}H\}$ NMR (151 MHz, Chloroform-*d*) δ 192.8, 153.8, 148.9, 126.9, 125.0, 111.7, 110.1, 102.7, 63.3, 56.2, 56.1, 15.4. The NMR data is consistent with that reported.[2]



Chemical Formula: $C_{12}H_{15}FO_3$
Exact Mass: 226.1005

2,2-Diethoxy-1-(2-fluorophenyl)ethan-1-one (1j)

Substrate **1j** was synthesized according to **General procedure**. Colorless oil, 15.5 mmol scale, 2.91 g, 12.9 mmol, 83% yield, R_f = 0.5 (Hex/EA = 95/5), obtained by purification with flash column chromatography on silica gel (eluent: Hex/EA = 1/0.02). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.93 – 7.84 (m, 1H), 7.57 – 7.48 (m, 1H), 7.26 – 7.20 (m, 1H), 7.16 – 7.09 (m, 1H), 5.39 (d, J = 2.3 Hz, 1H), 3.80 – 3.63 (m, 4H), 1.24 (t, J = 7.1 Hz, 6H). $^{13}C\{^{1}H\}$ NMR (101 MHz, Chloroform-*d*) δ 193.5 (d, J = 4.3 Hz), 161.7 (d, J = 255.4 Hz), 134.8 (d, J = 9.1 Hz), 131.4 (d, J = 2.9 Hz), 124.5 (d, J = 3.3 Hz), 124.2 (d, J = 13.7 Hz), 116.5 (d, J = 23.3 Hz), 101.8 (d, J = 5.8 Hz), 63.2, 15.3. HRMS (ESI), m/z: $[M+Na]^+$ Calcd for $C_{12}H_{15}FO_3Na^+$: 249.0897; Found: 249.0897.

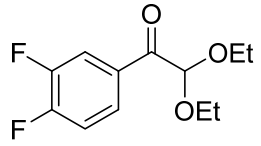


Chemical Formula: $C_{12}H_{15}FO_3$
Exact Mass: 226.1005

2,2-Diethoxy-1-(4-fluorophenyl)ethan-1-one (1k)

Substrate **1k** was synthesized according to **General procedure**. Light yellow oil, 3.8 mmol scale, 0.66 g, 2.9 mmol, 77% yield, R_f = 0.5 (Hex/EA = 95/5), obtained by purification with flash column chromatography on silica gel (eluent: Hex/EA = 1/0.02).^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.22 (dd, J = 8.7, 5.6 Hz, 2H), 7.12 (t, J = 8.6 Hz, 2H), 5.18 (s, 1H), 3.82 – 3.74 (m, 2H), 3.69 – 3.60 (m, 2H), 1.25 (t, J = 7.1

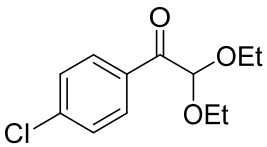
Hz, 6H). $^{13}C\{^{1}H\}$ NMR (151 MHz, Chloroform-*d*) δ 192.8, 166.1 (d, *J* = 255.5 Hz), 132.8 (d, *J* = 9.3 Hz), 130.1 (d, *J* = 3.1 Hz), 115.6 (d, *J* = 21.7 Hz), 103.3, 63.7, 15.3. The NMR data is consistent with that reported.[4]



Chemical Formula: $C_{12}H_{14}F_2O_3$
Exact Mass: 244.0911

1-(3,4-Difluorophenyl)-2,2-diethoxyethan-1-one (1l)

Substrate **1l** was synthesized according to **General procedure**. Colorless oil, 16.6 mmol scale, 2.55 g, 10.4 mmol, 63% yield, R_f = 0.5 (Hex/EA = 95/5), obtained by purification with flash column chromatography on silica gel (eluent: Hex/EA = 1/0.02). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.04 (ddd, *J* = 11.1, 7.9, 2.1 Hz, 1H), 8.01 – 7.96 (m, 1H), 7.23 (ddd, *J* = 9.8, 8.6, 7.6 Hz, 1H), 5.11 (s, 1H), 3.79 (dq, *J* = 9.6, 7.1 Hz, 2H), 3.63 (dq, *J* = 9.6, 7.0 Hz, 2H), 1.25 (t, *J* = 7.1 Hz, 6H). $^{13}C\{^{1}H\}$ NMR (151 MHz, Chloroform-*d*) δ 191.9, 154.0 (dd, *J* = 257.6, 13.0 Hz), 150.2 (dd, *J* = 249.6, 13.0 Hz), 130.6 (t, *J* = 4.3 Hz), 127.3 (dd, *J* = 7.4, 3.6 Hz), 119.5 (d, *J* = 19.2 Hz), 117.4 (d, *J* = 17.6 Hz), 103.8, 64.0, 15.3. HRMS (ESI), m/z: $[M+H]^+$ Calcd for $C_{12}H_{14}F_2O_3Na^+$: 267.0803; Found: 267.0802.

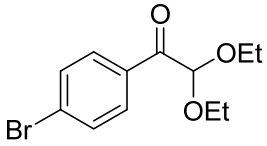


Chemical Formula: $C_{12}H_{15}ClO_3$
Exact Mass: 242.0710

1-(4-Chlorophenyl)-2,2-diethoxyethan-1-one (1m)

Substrate **1m** was synthesized according to **General procedure**. Colorless oil, 12 mmol scale, 1.68 g, 6.94 mmol, 58% yield, R_f = 0.5 (Hex/EA = 95/5), obtained by purification with flash column chromatography on silica gel (eluent: Hex/EA = 1/0.02). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.12 (d, *J* = 8.7 Hz, 2H), 7.42 (d, *J* = 8.7 Hz, 2H), 5.17 (s,

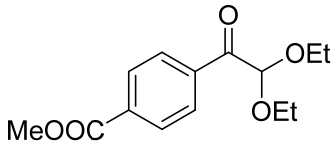
1H), 3.77 (dq, *J* = 9.5, 7.1 Hz, 2H), 3.64 (dq, *J* = 9.5, 7.0 Hz, 2H), 1.24 (t, *J* = 7.1 Hz, 6H). $^{13}C\{^{1}H\}$ NMR (151 MHz, Chloroform-*d*) δ 193.2, 140.0, 132.0, 131.5, 128.8, 103.3, 63.7, 15.3. The NMR data is consistent with that reported.[2]



Chemical Formula: $C_{12}H_{15}BrO_3$
Exact Mass: 286.0205

1-(4-Bromophenyl)-2,2-diethoxyethan-1-one (1n)

Substrate **1n** was synthesized according to **General procedure**. Colorless oil, 5 mmol scale, 1.20 g, 4.20 mmol, 84% yield, R_f = 0.5 (Hex/EA = 95/5), obtained by purification with flash column chromatography on silica gel (eluent: Hex/EA = 1/0.02). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.04 (d, *J* = 8.4 Hz, 2H), 7.59 (d, *J* = 8.5 Hz, 2H), 5.17 (s, 1H), 3.77 (dq, *J* = 9.4, 7.1 Hz, 2H), 3.64 (dq, *J* = 9.4, 7.0 Hz, 2H), 1.24 (t, *J* = 7.1 Hz, 6H). $^{13}C\{^{1}H\}$ NMR (151 MHz, Chloroform-*d*) δ 193.4, 132.4, 131.8, 131.5, 128.9, 103.2, 63.7, 15.3. The NMR data is consistent with that reported.[2]

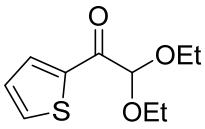


Chemical Formula: $C_{14}H_{18}O_5$
Exact Mass: 266.1154

Methyl 4-(2,2-diethoxyacetyl)benzoate (1o)

Substrate **1o** was synthesized according to **General procedure**. Light yellow oil, 8.3 mmol scale, 1.34 g, 5.04 mmol, 61% yield, R_f = 0.5 (Hex/EA = 95/5), obtained by purification with flash column chromatography on silica gel (eluent: Hex/EA = 1/0.02). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.22 (d, *J* = 8.5 Hz, 2H), 8.10 (d, *J* = 8.5 Hz, 2H), 5.23 (s, 1H), 3.95 (s, 3H), 3.78 (dq, *J* = 9.5, 7.1 Hz, 2H), 3.66 (dq, *J* = 9.6, 7.1 Hz, 2H), 1.25 (t, *J* = 7.1 Hz, 6H). $^{13}C\{^{1}H\}$ NMR (101 MHz, Chloroform-*d*) δ 193.8, 166.4, 137.1,

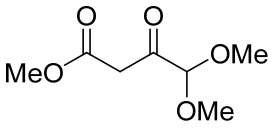
134.1, 129.9, 129.6, 103.0, 63.7, 52.5, 15.3. The NMR data is consistent with that reported.[4]



Chemical Formula: $C_{10}H_{14}O_3S$
Exact Mass: 214.0664

2,2-Diethoxy-1-(thiophen-2-yl)ethan-1-one (1p)

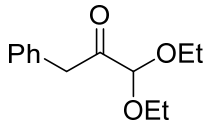
Substrate **1p** was synthesized according to **General procedure**. Light yellow oil, 6.7 mmol scale, 0.97 g, 4.5 mmol, 68% yield, R_f = 0.6 (Hex/EA = 95/5), obtained by purification with flash column chromatography on silica gel (eluent: Hex/EA = 1/0.02). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.07 (dd, *J* = 3.9, 1.2 Hz, 1H), 7.67 (dd, *J* = 4.9, 1.2 Hz, 1H), 7.14 (dd, *J* = 4.9, 3.8 Hz, 1H), 5.13 (s, 1H), 3.78 (dq, *J* = 9.5, 7.0 Hz, 2H), 3.67 (dq, *J* = 9.5, 7.0 Hz, 2H), 1.28 (t, *J* = 7.1 Hz, 6H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 187.9, 139.8, 134.9, 134.7, 128.1, 102.4, 63.3, 15.3. HRMS (ESI), m/z: $[M+Na]^+$ Calcd for $C_{10}H_{14}O_3SNa^+$: 237.0556; Found: 237.0555.



Chemical Formula: $C_7H_{12}O_5$
Exact Mass: 176.0685

Methyl 4,4-dimethoxy-3-oxobutanoate (1q)

Substrate **1q** is commercially available. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 11.8 (s, 0.19 H), 5.44 (s, 0.18 H), 5.84 (s, 0.18 H), 4.58 (s, 1H), 3.77 (s, 0.55H), 3.74 (s, 3H), 3.60 (s, 2H), 3.43 (s, 6H), 3.38 (s, 1.17H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 198.2, 167.6, 103.7, 99.6, 90.6, 55.1, 53.5, 52.5, 51.6, 44.3.

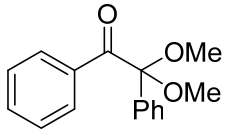


Chemical Formula: $C_{13}H_{18}O_3$
Exact Mass: 222.1256

1,1-Diethoxy-3-phenylpropan-2-one (1r)

Substrate **1r** was synthesized according to a reported procedure. [5]

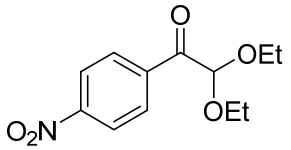
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35 – 7.18 (m, 6H), 4.63 (s, 1H), 3.89 (s, 2H), 3.70 (dq, *J* = 9.5, 7.1 Hz, 2H), 3.55 (dq, *J* = 9.5, 7.1 Hz, 2H), 1.25 (t, *J* = 7.1 Hz, 6H). The NMR data is consistent with that reported.[5]



Chemical Formula: $C_{16}H_{16}O_3$
Exact Mass: 256.1099

2,2-Dimethoxy-1,2-diphenylethan-1-one (1s)

Substrate **1s** is commercially available. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.09 – 8.01 (m, 2H), 7.64 – 7.59 (m, 2H), 7.46 – 7.40 (m, 1H), 7.37 – 7.27 (m, 5H), 3.22 (s, 6H).^{13}C{H^1} NMR (101 MHz, Chloroform-*d*) δ 195.3, 137.0, 134.4, 133.0, 130.1, 129.1, 128.7, 128.27, 127.1, 103.7, 50.2.



Chemical Formula: $C_{12}H_{15}NO_5$
Exact Mass: 253.0950

2,2-Diethoxy-1-(4-nitrophenyl)ethan-1-one (1t)

Substrate **1t** was synthesized according to **General procedure**. Light yellow oil, 19.7 mmol scale, 1.04 g, 4.11 mmol, 22% yield, R_f = 0.5 (Hex/EA = 95/5), obtained by purification with flash column chromatography on silica gel (eluent: Hex/EA = 1/0.02). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 – 8.24 (m, 4H), 5.15 (s, 1H), 3.89 – 3.77 (m,

2H), 3.72 – 3.60 (m, 2H), 1.26 (t, J = 7.0 Hz, 6H). $^{13}C\{^{1}H\}$ NMR (101 MHz, Chloroform-*d*) δ 192.9, 150.5, 138.2, 131.2, 123.5, 104.0, 64.3, 15.3. The NMR data is consistent with that reported.[4]

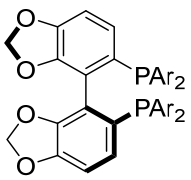
III. General Procedures for Direct Asymmetric Reductive Amination of α-Keto Acetals

3.1 General Procedure for direct asymmetric reductive amination of α-keto acetals

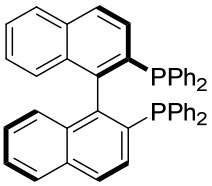
The catalyst $Ru(OAc)_2$(**L**) was synthesized according to reported procedures.[6]

In a glovebox, $Ru(OAc)_2$(**L**) (0.002 mmol), substrate (0.2 mmol), ammonium salt (30.8 mg, 0.4 mmol) and TFE (1.0 ml) were successively added to a 5 mL vial equipped with a magnetic stirring bar. The mixture was then transferred to a stain-less autoclave and purged by three cycles of pressurization/venting with H_2. The required H_2 pressure (50 atm) was then installed, and the autoclave was placed in an oil bath preheated to 90 ℃. The autoclave was cooled down to room temperature after 20 h and the pressure was slowly released in the hood. The reaction was quenched by saturated $NaHCO_3$ solution (2 mL) and extracted with DCM (3 mL x 3). The combined organic phase was dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. The residue was subjected to column chromatography on silica gel (eluent: DCM/MeOH/Et_3N = 1/0.01/0.002) to afford desired products.

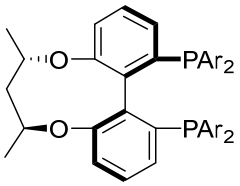
To facilitate the measurement of enantiomeric excess, the chiral primary amines obtained were all derived into their acylamides or benzylamides. Procedure: primary amine (0.2 mmol) was dissolved in dichloromethane (1 mL), followed by addition of triethylamine (80 μL) and acetic anhydride (40 μL) or BzCl (40 μL) at 0 °C. After stirred at room temperature for 2 h, saturated $NaHCO_3$ solution (1 mL) was added to quench the reaction. The organic phase was separated, dried, and evaporated under reduced pressure. The corresponding acetamides obtained were used for HPLC test to evaluate the ee value. For primary amine products **2ab**, **2c**, **2j** and **2q**, the yields and characterizations were determined after acetylation or benzoylation due to difficulty of purification.



L1a *(S)*-SEGPHOS Ar = Ph
L1b Ar = 4-MeO-3,5-^{t}Bu$_2$C$_6$H$_2$
L1c Ar = 3,5-Me$_2$C$_6$H$_3$



L2 *(R)*-BINAP

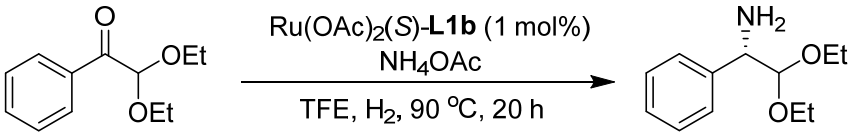


L3 *(R)*-DTBM-C$_3$*-TunePhos
R = 4-MeO-3,5-^{t}Bu$_2$C$_6$H$_2$

3.2 Determination of products' absolute configuration

The absolute configuration of **2aa** was established by converting it to a known amino alcohol. For the details, please see **4.4 Reduction to amino alcohol**.

3.3 Evaluation of hydrogen pressure

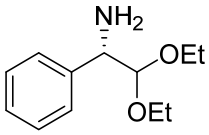


1aa **2aa**

entry	solvent	P/bar	yield	ee
1	TFE	50	87%	97%
2	TFE	40	85%	95%
3	TFE	30	88%	95%
4	TFE	2	0	-

Reaction conditions: **1** (0.1 mmol), Ru(OAc)$_2$(*S*)-**L1b** (0.001 mmol), NH$_4$OAc (0.2 mmol), TFE (0.5 mL), H$_2$, 90 °C, 20 h.

3.44Characterization data of products

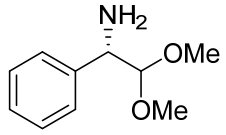


Chemical Formula: $C_{12}H_{19}NO_2$
Exact Mass: 209.1416

(*S*)-2-Bromo-5,6-dihydro-[1,1'-biphenyl]-3(4H)-ol (2aa)

Light yellow oil, 36.4 mg, 0.174 mmol, 87% yield (41.8 mg **1aa** used), 97% ee, $[\alpha]^{27}_D$ = +9.6 (c=0.5, $CHCl_3$), R_f = 0.3 (DCM/MeOH = 95/5), obtained by purification with flash column chromatography on silica gel (eluent: DCM/MeOH/Et_3N = 1/0.01/0.002).

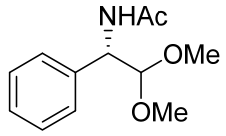
^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.41 (d, *J* = 7.3 Hz, 2H), 7.32 (t, *J* = 7.5 Hz, 2H), 7.27 – 7.24 (m, 1H), 4.38 (d, *J* = 6.1 Hz, 1H), 4.00 (d, *J* = 6.1 Hz, 1H), 3.80 – 3.73 (m, 1H), 3.58 – 3.52 (m, 1H), 3.52 – 3.45 (m, 1H), 3.26 – 3.18 (m, 1H), 1.22 (t, *J* = 7.0 Hz, 3H), 1.02 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 141.6, 128.2, 127.9, 127.4, 107.1, 64.2, 63.9, 58.9, 15.4, 15.2. The ee value were determined after acylation. HPLC: Chiracel OD-3 Column (250 mm); detected at 210 nm; *n*-hexane / *i*-propanol = 90/10; flow = 0.8 mL/min; Retention time: 6.9 min (major), 8.5 min (minor). HRMS (ESI), m/z: $[M+H]^+$ Calcd for $C_{12}H_{20}NO_2^+$: 210.1489; Found: 210.1493.



Chemical Formula: $C_{10}H_{15}NO_2$
Exact Mass: 181.1103

(*S*)-2,2-Dimethoxy-1-phenylethan-1-amine (2ab)

Because of difficulty of purification, the yield and characterization of **2c** is determined after acetylation to **2ab-Ac**.

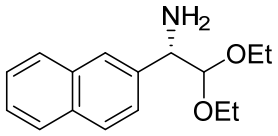


Chemical Formula: $C_{12}H_{17}NO_3$
Exact Mass: 223.1208

(*S*)-N-(2,2-Dimethoxy-1-phenylethyl)acetamide (2ab-Ac)

White solid, 40.6 mg, 0.182 mmol, 91% overall yield after acetylation (36.2 mg **1ab** used), 94% ee, $[\alpha]^{27}_{D}$ = +38.6 (c=0.5, $CHCl_3$), R_f = 0.4 (Hex/EA = 65/35), obtained by purification with flash column chromatography on silica gel (eluent: Hex/EA = 1/0.2). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.34 – 7.30 (m, 4H), 7.28 – 7.24 (m, 1H), 6.44 – 6.27 (m, 1H), 5.18 (dd, *J* = 8.4, 3.2 Hz, 1H), 4.42 (d, *J* = 3.2 Hz, 1H), 3.43 (s, 3H), 3.37 (s, 3H), 2.03 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 169.8, 138.6, 128.5, 127.7, 127.5, 106.5, 56.2, 55.8, 54.7, 23.5. HPLC: Chiracel OD-H Column (250 mm);

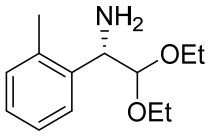
detected at 210 nm; *n*-hexane / *i*-propanol = 95/5; flow = 0.8 mL/min; Retention time: 20.0 min (major), 25.1 min (minor). HRMS (ESI), m/z: $[M+Na]^+$ Calcd for $C_{12}H_{17}NO_3Na^+$: 246.1101; Found: 246.1100.



Chemical Formula: $C_{16}H_{21}NO_2$
Exact Mass: 259.1572

(*S*)-2,2-Diethoxy-1-(naphthalen-2-yl)ethan-1-amine (2b)

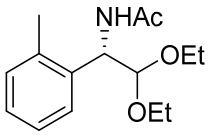
Light yellow oil, 47.1 mg, 0.182 mmol, 91% yield (51.8 mg **1b** used), 98% ee, $[\alpha]^{24}_D$ = +7.6 (c=0.5, $CHCl_3$), R_f = 0.3 (DCM/MeOH = 95/5), obtained by purification with flash column chromatography on silica gel (eluent: DCM/MeOH/Et_3N = 1/0.01/0.002). ^1H NMR (600 MHz, Chloroform-*d*) δ 7.89 – 7.87 (m, 1H), 7.84 – 7.81 (m, 2H), 7.80 (d, *J* = 8.7 Hz, 1H), 7.56 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.47 – 7.43 (m, 2H), 4.48 (d, *J* = 6.2 Hz, 1H), 4.18 (d, *J* = 6.1 Hz, 1H), 3.84 – 3.73 (m, 1H), 3.59 – 3.48 (m, 2H), 3.26 – 3.18 (m, 1H), 1.23 (t, *J* = 7.0 Hz, 3H), 1.00 (t, *J* = 7.0 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, Chloroform-*d*) δ 139.2, 133.4, 133.1, 128.1, 127.8, 127.7, 126.6, 126.3, 126.0, 125.8, 107.1, 64.3, 64.0, 59.0, 15.5, 15.3. The ee value were determined after acylation. HPLC: Chiracel ODH Column (250 mm); detected at 210 nm; *n*-hexane / *i*-propanol = 95/5; flow = 0.8 mL/min; Retention time: 16.8 min (minor), 25.8 min (major). HRMS (ESI), m/z: $[M+Na]^+$ Calcd for $C_{16}H_{22}NO_2^+$: 260.1645; Found: 260.1644.



Chemical Formula: $C_{13}H_{21}NO_2$
Exact Mass: 223.1572

(*S*)-2,2-Diethoxy-1-(*o*-tolyl)ethan-1-amine (2c)

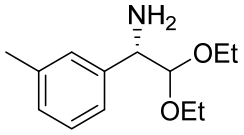
Because of difficulty of purification, the yield and characterization of **2c** is determined after acetylation to **2c-Ac**.



Chemical Formula: $C_{15}H_{23}NO_3$
Exact Mass: 265.1678

(*S*)-N-(2,2-Diethoxy-1-(*o*-tolyl)ethyl)acetamide (2c-Ac)

White solid, 27.0 mg, 0.102 mmol, 52% overall yield after acetylation (44.4 mg **1c** used), 78 % ee, $[\alpha]^{27}_D$ = +6.1 (c=0.5, $CHCl_3$), R_f = 0.3 (Hex/EA = 65/35), obtained by purification with flash column chromatography on silica gel (eluent: Hex/EA = 1/0.2). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.34 – 7.27 (m, 1H), 7.23 – 7.11 (m, 3H), 6.39 (d, *J* = 8.1 Hz, 1H), 5.39 (dd, *J* = 8.1, 2.7 Hz, 1H), 4.47 (d, *J* = 2.8 Hz, 1H), 3.73 (dq, *J* = 9.0, 7.1 Hz, 1H), 3.66 (dq, *J* = 8.8, 7.1 Hz, 1H), 3.58 (dq, *J* = 9.0, 7.1 Hz, 1H), 3.37 (dq, *J* = 9.2, 7.1 Hz, 1H), 2.45 (s, 3H), 2.02 (s, 3H), 1.21 (t, *J* = 7.0 Hz, 3H), 1.14 (t, *J* = 7.1 Hz, 3H). ^{13}C{H^1} NMR (151 MHz, Chloroform-*d*) δ 169.6, 137.4, 136.1, 130.4, 127.4, 126.9, 126.0, 103.6, 64.5, 63.7, 51.6, 23.6, 19.7, 15.3, 15.2. HPLC: Chiracel OD-3 Column (250 mm); detected at 210 nm; *n*-hexane / *i*-propanol = 95/5; flow = 0.8 mL/min; Retention time: 9.4 min (major), 10.9 min (minor). HRMS (ESI), m/z: $[M+Na]^+$ Calcd for $C_{15}H_{23}NO_3Na^+$: 288.1570; Found: 288.1568.

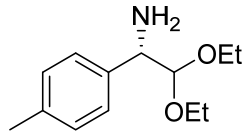


Chemical Formula: $C_{13}H_{21}NO_2$
Exact Mass: 223.1572

(*S*)-2,2-Diethoxy-1-(*m*-tolyl)ethan-1-amine (2d)

Light yellow oil, 27.1 mg, 0.122 mmol, 61% yield (44.5 mg **1d** used), >99% ee, $[\alpha]^{22}_D$ = +6.4 (c=0.5, $CHCl_3$), R_f = 0.3 (DCM/MeOH = 95/5), obtained by purification with flash column chromatography on silica gel (eluent: DCM/MeOH/Et_3N = 1/0.01/0.002). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.25 – 7.17 (m, 3H), 7.10 – 7.04 (m, 1H), 4.39 (d, *J* = 6.1 Hz, 1H), 3.96 (d, *J* = 6.1 Hz, 1H), 3.84 – 3.71 (m, 1H), 3.61 – 3.44 (m, 2H),

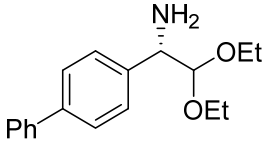
3.29 – 3.18 (m, 1H), 2.35 (s, 3H), 1.22 (t, *J* = 7.0 Hz, 3H), 1.03 (t, *J* = 7.0 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, Chloroform-*d*) δ 141.5, 137.8, 128.6, 128.2, 128.1, 125.0, 107.1, 64.1, 63.9, 58.8, 21.6, 15.4, 15.2. The ee value were determined after acylation. HPLC: Chiracel ODH Column (250 mm); detected at 210 nm; *n*-hexane / *i*-propanol = 95/5; flow = 0.8 mL/min; Retention time: 9.8 min (minor), 11.5 min (major). HRMS (ESI), m/z: $[M+H]^+$ Calcd for $C_{13}H_{22}NO_2^+$: 224.1645; Found: 224.1643.



Chemical Formula: $C_{13}H_{21}NO_2$
Exact Mass: 223.1572

(*S*)-2,2-Diethoxy-1-(*p*-tolyl)ethan-1-amine (2e)

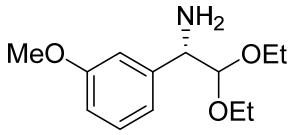
Light yellow oil, 34.3 mg, 0.154 mmol, 77% yield (44.6 mg **1e** used), 97 % ee, $[\alpha]^{21}_D$ = +11.8 (c=0.5, $CHCl_3$), R_f = 0.3 (DCM/MeOH = 95/5), obtained by purification with flash column chromatography on silica gel (eluent: DCM/MeOH/Et_3N = 1/0.01/0.002). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.28 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 7.9 Hz, 2H), 4.37 (d, *J* = 6.1 Hz, 1H), 3.96 (d, *J* = 6.1 Hz, 1H), 3.81 – 3.71 (m, 1H), 3.59 – 3.44 (m, 2H), 3.28 – 3.18 (m, 1H), 2.33 (s, 3H), 1.22 (t, *J* = 7.0 Hz, 3H), 1.03 (t, *J* = 7.0 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, Chloroform-*d*) δ 138.5, 137.0, 128.9, 127.7, 107.1, 64.1, 63.9, 58.6, 21.2, 15.4, 15.3. The ee value were determined after acylation. HPLC: Chiracel OD-3 Column (250 mm); detected at 210 nm; *n*-hexane / *i*-propanol = 95/5; flow = 1.0 mL/min; Retention time: 8.9 min (major), 10.6 min (minor). HRMS (ESI), m/z: $[M+H]^+$ Calcd for $C_{13}H_{22}NO_2^+$: 224.1645; Found: 224.1642.



Chemical Formula: $C_{18}H_{23}NO_2$
Exact Mass: 285.1729

(*S*)-1-([1,1'-Biphenyl]-4-yl)-2,2-diethoxyethan-1-amine (2f)

Light yellow oil, 49.6 mg, 0.174 mmol, 87% yield (57.0 mg **1f** used), 94% ee, $[\alpha]^{26}_D$ = +21.3 (c=0.5, $CHCl_3$), R_f = 0.3 (DCM/MeOH = 95/5), obtained by purification with flash column chromatography on silica gel (eluent: DCM/MeOH/Et_3N = 1/0.01/0.002). ^1H NMR (600 MHz, Chloroform-*d*) δ 7.59 (d, *J* = 8.0 Hz, 2H), 7.56 (d, *J* = 7.9 Hz, 2H), 7.48 (d, *J* = 7.9 Hz, 2H), 7.42 (t, *J* = 7.5 Hz, 2H), 7.33 (t, *J* = 7.1 Hz, 1H), 4.45 (d, *J* = 6.0 Hz, 1H), 4.05 (d, *J* = 6.0 Hz, 1H), 3.83 – 3.74 (m, 1H), 3.63 – 3.48 (m, 2H), 3.33 – 3.23 (m, 1H), 1.23 (t, *J* = 7.0 Hz, 3H), 1.05 (t, *J* = 7.0 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, Chloroform-*d*) δ 141.0, 140.4, 140.3, 128.9, 128.3, 127.3, 127.1, 127.0, 106.8, 64.2, 64.0, 58.5, 15.4, 15.3. The ee value were determined after acylation. HPLC: Chiracel OD-3 Column (250 mm); detected at 210 nm; *n*-hexane / *i*-propanol = 95/5; flow = 1.0 mL/min; Retention time: 11.4 min (major), 12.8 min (minor). HRMS (ESI), m/z: $[M+H]^+$ Calcd for $C_{18}H_{24}NO_2^+$: 286.1802; Found: 286.1806.

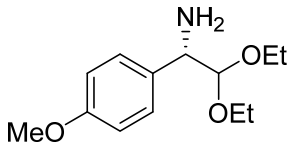


Chemical Formula: $C_{13}H_{21}NO_3$
Exact Mass: 239.1521

(*S*)-2,2-Diethoxy-1-(3-methoxyphenyl)ethan-1-amine (2g)

Light yellow oil, 42.6 mg, 0.178 mmol, 89% yield (47.8 mg **1g** used), 95% ee, $[\alpha]^{26}_D$ = +5.1 (c=0.5, $CHCl_3$), R_f = 0.3 (DCM/MeOH = 95/5), obtained by purification with flash column chromatography on silica gel (eluent: DCM/MeOH/Et_3N = 1/0.01/0.002). ^1H NMR (400 MHz, Chloroform-*d*) δ 7.23 (t, *J* = 8.1 Hz, 1H), 7.02 – 6.96 (m, 2H), 6.84 – 6.79 (m, 1H), 4.38 (d, *J* = 6.0 Hz, 1H), 3.98 (d, *J* = 6.1 Hz, 1H), 3.83 – 3.72 (m, 4H), 3.61 – 3.44 (m, 2H), 3.29 – 3.19 (m, 1H), 1.22 (t, *J* = 7.1 Hz, 3H), 1.04 (t, *J* = 7.0 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, Chloroform-*d*) δ 159.6, 143.3, 129.2, 120.3, 113.3, 113.1, 107.0, 64.3, 64.0, 58.9, 55.3, 15.4, 15.3. The ee value were determined after acylation. HPLC: Chiracel AD-3 Column (250 mm); detected at 210 nm; *n*-hexane / *i*-propanol = 95/5; flow = 0.8 mL/min; Retention time: 16.2 min (minor), 20.2 min

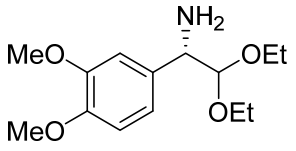
(major). HRMS (ESI), m/z: $[M+H]^+$ Calcd for $C_{13}H_{22}NO_3^+$: 240.1594; Found: 240.1592.



Chemical Formula: $C_{13}H_{21}NO_3$
Exact Mass: 239.1521

(*S*)-2,2-Diethoxy-1-(4-methoxyphenyl)ethan-1-amine (2h)

Light yellow oil, 34.9 mg, 0.146 mmol, 73% yield (47.8 mg **1h** used), 92% ee, $[\alpha]^{22}_D$ = +12.0 (c=0.5, CH_2Cl_2), R_f = 0.3 (DCM/MeOH = 95/5), obtained by purification with flash column chromatography on silica gel (eluent: DCM/MeOH/Et_3N = 1/0.01/0.002). ^1H NMR (600 MHz, Chloroform-d) δ 7.32 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 4.34 (d, *J* = 6.2 Hz, 1H), 3.95 (d, *J* = 6.1 Hz, 1H), 3.80 (s, 3H), 3.78 – 3.73 (m, 1H), 3.58 – 3.44 (m, 2H), 3.27 – 3.18 (m, 1H), 1.22 (t, *J* = 7.0 Hz, 3H), 1.03 (t, *J* = 7.0 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, Chloroform-d) δ 158.9, 133.7, 128.9, 113.6, 107.2, 64.2, 63.9, 58.2, 55.3, 15.4, 15.3. The ee value were determined after acylation. HPLC: Chiracel ODH Column (250 mm); detected at 210 nm; *n*-hexane / *i*-propanol = 95/5; flow = 0.8 mL/min; Retention time: 9.6 min (major). HRMS (ESI), m/z: $[M+H]^+$ Calcd for $C_{13}H_{22}NO_3^+$: 240.1594; Found: 240.1590.

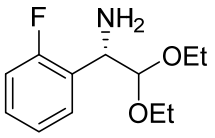


Chemical Formula: $C_{14}H_{23}NO_4$
Exact Mass: 269.1627

(*S*)-1-(3,4-Dimethoxyphenyl)-2,2-diethoxyethan-1-amine (2i)

Light yellow oil, 42.0 mg, 0.156 mmol, 78% yield (53.8 mg **1i** used), 85% ee, $[\alpha]^{23}_D$ = +4.3 (c=0.5, $CHCl_3$), R_f = 0.3 (DCM/MeOH = 95/5), obtained by purification with flash column chromatography on silica gel (eluent: DCM/MeOH/Et_3N = 1/0.01/0.002). ^1H NMR (600 MHz, Chloroform-*d*) δ 7.00 (d, *J* = 1.9 Hz, 1H), 6.95 (dd, *J* = 8.2, 1.9 Hz,

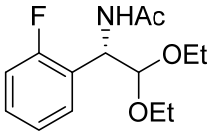
1H), 6.83 (d, *J* = 8.2 Hz, 1H), 4.35 (d, *J* = 6.2 Hz, 1H), 3.95 (d, *J* = 6.2 Hz, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 3.80 – 3.74 (m, 1H), 3.57 – 3.46 (m, 2H), 3.26 – 3.17 (m, 1H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.04 (t, *J* = 7.0 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (151 MHz, Chloroform-*d*) δ 148.8, 148.4, 134.0, 120.0, 111.0, 110.9, 107.1, 64.4, 64.3, 63.9, 58.6, 56.0, 15.4, 15.3. The ee value were determined after acylation. HPLC: Chiracel OJ-3 Column (250 mm); detected at 210 nm; *n*-hexane / *i*-propanol = 90/10; flow = 0.8 mL/min; Retention time: 10.6 min (minor), 13.9 min (major). HRMS (ESI), m/z: $[M+H]^+$ Calcd for $C_{14}H_{24}NO_4^+$: 270.1700; Found: 270.1969.



Chemical Formula: $C_{12}H_{18}FNO_2$
Exact Mass: 227.1322

(*S*)-2,2-Diethoxy-1-(2-fluorophenyl)ethan-1-amine (2j)

Because of difficulty of purification, the yield and characterization of **2j** is determined after acetylation to **2j-Ac**.

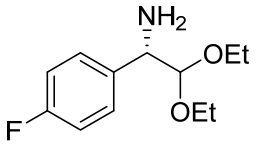


Chemical Formula: $C_{14}H_{20}FNO_3$
Exact Mass: 269.1427

(*S*)-N-(2,2-Diethoxy-1-(2-fluorophenyl)ethyl)acetamide (2j-Ac)

Light yellow oil, 41.2 mg, 0.153 mmol, 77% overall yield after acetylation (45.3 mg **1j** used), 99% ee, $[\alpha]^{27}_D$ = +9.6 (c=0.5, $CHCl_3$), R_f = 0.2 (Hex/EA = 1/0.2), obtained by purification with flash column chromatography on silica gel (eluent: Hex/EA = 80/20). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.30-7.28 (td, *J* = 7.6, 1.7 Hz, 1H), 7.26 – 7.21 (m, 1H), 7.13 – 7.07 (m, 1H), 7.06 – 6.98 (m, 1H), 6.39 (d, 1H), 5.46 (dd, *J* = 8.4, 2.9 Hz, 1H), 4.59 (d, *J* = 3.0 Hz, 1H), 3.74 – 3.64 (m, 2H), 3.64 – 3.57 (m, 1H), 3.42 – 3.35 (m, 1H), 2.06 (s, 3H), 1.21 (t, *J* = 7.0 Hz, 3H), 1.09 (t, *J* = 7.1 Hz, 3H). $^{13}C\{^{1}H\}$ NMR

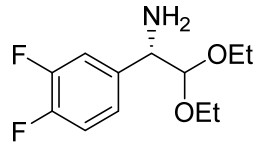
(151 MHz, Chloroform-*d*) δ 169.8, 160.6 (d, *J* = 245.6 Hz), 129.1, 129.1 (d, *J* = 3.4 Hz), 125.8 (d, *J* = 13.4 Hz), 124.1 (d, *J* = 3.6 Hz), 115.4 (d, *J* = 21.9 Hz), 102.8 (d, *J* = 1.8 Hz), 64.2, 63.7, 50.4, 23.5, 15.2, 15.1. HPLC: Chiracel OD-3 Column (250 mm); detected at 210 nm; *n*-hexane / *i*-propanol = 95/5; flow = 0.8 mL/min; Retention time: 10.3 min (minor), 10.6 min (major). HRMS (ESI), m/z: $[M+Na]^+$ Calcd for $C_{14}H_{20}FNO_3Na^+$: 292.1319; Found: 292.1318.



Chemical Formula: $C_{12}H_{18}FNO_2$
Exact Mass: 227.1322

(*S*)-2,2-Diethoxy-1-(4-fluorophenyl)ethan-1-amine (2k)

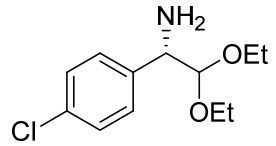
Light yellow oil, 28.6 mg, 0.126 mmol, 63% yield (45.4 mg **1k** used), 98% ee, $[\alpha]^{23}_D$ = +7.0 (c=0.5, $CHCl_3$), R_f = 0.3 (DCM/MeOH = 95/5), obtained by purification with flash column chromatography on silica gel (eluent: DCM/MeOH/Et_3N = 1/0.01/0.002). ^1H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.35 (m, 2H), 7.03 – 6.98 (m, 2H), 4.34 (d, *J* = 6.1 Hz, 1H), 3.99 (d, *J* = 6.1 Hz, 1H), 3.81 – 3.70 (m, 1H), 3.62 – 3.44 (m, 2H), 3.28 – 3.16 (m, 1H), 1.22 (t, *J* = 7.0 Hz, 3H), 1.03 (t, *J* = 7.0 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, Chloroform-*d*) δ 162.3 (d, *J* = 245.0 Hz), 137.2 (d, *J* = 3.0), 129.4 (d, *J* = 7.9 Hz), 115.0 (d, *J* = 21.2 Hz), 107.0, 64.4, 64.0, 58.2, 15.4, 15.2. The ee value were determined after acylation. HPLC: Chiracel AD-3 Column (250 mm); detected at 210 nm; *n*-hexane / *i*-propanol = 95/5; flow = 0.8 mL/min; Retention time: 14.4 min (minor), 16.3 min (major). HRMS (ESI), m/z: $[M+H]^+$ Calcd for $C_{12}H_{19}FNO_2^+$: 228.1394; Found: 228.1392.



Chemical Formula: $C_{12}H_{17}F_2NO_2$
Exact Mass: 245.1227

(*S*)-1-(3,4-Difluorophenyl)-2,2-diethoxyethan-1-amine (2l)

Light yellow oil, 29.9 mg, 0.122 mmol, 61% yield (49.0 mg **1l** used), 98% ee, $[\alpha]^{25}_{D}$ = +3.2 (c=0.5, $CHCl_3$), R_f = 0.3 (DCM/MeOH = 95/5), obtained by purification with flash column chromatography on silica gel (eluent: DCM/MeOH/Et_3N = 1/0.01/0.002). ^1H NMR (600 MHz, Chloroform-*d*) δ 7.31 (ddd, *J* = 11.5, 7.7, 2.1 Hz, 1H), 7.17 – 7.14 (m, 1H), 7.13 – 7.07 (m, 1H), 4.40 (d, *J* = 5.9 Hz, 1H), 4.01 (d, *J* = 5.9 Hz, 1H), 3.79 – 3.72 (m, 1H), 3.64 – 3.57 (m, 1H), 3.52 (dq, *J* = 9.3, 7.0 Hz, 1H), 3.33 – 3.25 (m, 1H), 1.22 (t, *J* = 7.0 Hz, 3H), 1.06 (t, *J* = 7.0 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, Chloroform-*d*) δ 150.2 (dd, *J* = 247.6, 13.8 Hz), 149.9 (dd, *J* = 247.6 12.8 Hz)137.2, 124.2 (dd, *J* = 6.2, 3.5 Hz), 117.0 (d, *J* = 10.7), 116.9 (d, *J* = 9.9), 105.8, 64.6, 64.2, 57.9, 15.4, 15.2. The ee value were determined after acylation. HPLC: Chiracel OD-3 Column (250 mm); detected at 210 nm; *n*-hexane / *i*-propanol = 95/5; flow = 0.8 mL/min; Retention time: 10.1 min (minor), 10.7 min (major). HRMS (ESI), m/z: $[M+H]^+$ Calcd for $C_{12}H_{18}F_2NO_2^+$: 246.1300; Found: 246.1296.

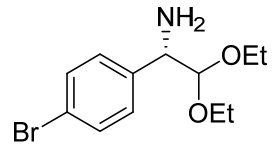


Chemical Formula: $C_{12}H_{18}ClNO_2$
Exact Mass: 243.1026

(*S*)-1-(4-Chlorophenyl)-2,2-diethoxyethan-1-amine (2m)

Light yellow oil, 39.8 mg, 0.164 mmol, 79% yield (50.2 mg **1m** used), >99% ee, $[\alpha]^{26}_{D}$ = +8.2 (c=0.5, $CHCl_3$), R_f = 0.3 (DCM/MeOH = 95/5), obtained by purification with flash column chromatography on silica gel (eluent: DCM/MeOH/Et_3N = 1/0.01/0.002). ^1H NMR (600 MHz, Chloroform-*d*) δ 7.36 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.5 Hz, 2H), 4.37 (d, *J* = 6.0 Hz, 1H), 4.00 (d, *J* = 6.0 Hz, 1H), 3.79 – 3.73 (m, 1H), 3.60 – 3.54 (m, 1H), 3.53 – 3.47 (m, 1H), 3.28 – 3.22 (m, 1H), 1.21 (t, *J* = 7.0 Hz, 3H), 1.04 (t, *J* = 7.0 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, Chloroform-*d*) δ 139.6, 133.3, 129.4, 128.4, 106.5, 64.5, 64.1, 58.3, 15.4, 15.2. The ee value were determined after acylation. HPLC: Chiracel OJ-3 Column (250 mm); detected at 210 nm; *n*-hexane / *i*-propanol = 95/5;

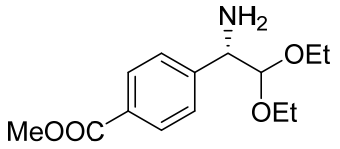
flow = 0.8 mL/min; Retention time: 15.7 min (major). HRMS (ESI), m/z: $[M+H]^+$ Calcd for $C_{12}H_{19}ClNO_2^+$: 244.1099; Found: 244.1096.



Chemical Formula: $C_{12}H_{18}BrNO_2$
Exact Mass: 287.0521

(*S*)-1-(4-Bromophenyl)-2,2-diethoxyethan-1-amine (2n)

Light yellow oil, 43.2mg, 0.150 mmol, 74% yield (58.4 mg **1n** used), 95% ee, $[\alpha]^{21}_D$ = +9.4 (c=0.5, $CHCl_3$), R_f = 0.3 (DCM/MeOH = 95/5), obtained by purification with flash column chromatography on silica gel (eluent: DCM/MeOH/Et_3N = 1/0.01/0.002). ^1H NMR (400 MHz, Chloroform-*d*) δ 7.57 (d, *J* = 8.5 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 2H), 4.46 (d, *J* = 6.0 Hz, 1H), 4.09 (d, *J* = 6.1 Hz, 1H), 3.93 – 3.84 (m, 1H), 3.74 – 3.57 (m, 2H), 3.41 – 3.31 (m, 1H), 1.34 (t, *J* = 7.0 Hz, 3H), 1.17 (t, *J* = 7.0 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, Chloroform-*d*) δ 140.7, 131.3, 129.7, 121.3, 106.8, 64.4, 64.0, 58.4, 15.4, 15.2. The ee value were determined after acylation. HPLC: Chiracel AD-3 Column (250 mm); detected at 210 nm; *n*-hexane / *i*-propanol = 95/5; flow = 0.8 mL/min; Retention time: 14.8 min (minor), 16.7 min (major). HRMS (ESI), m/z: $[M+H]^+$ Calcd for $C_{12}H_{19}BrNO_2^+$: 288.0594; Found: 288.0598.

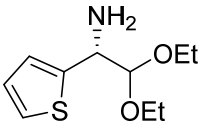


Chemical Formula: $C_{14}H_{21}NO_4$
Exact Mass: 267.1471

(*S*)-Methyl-4-(1-amino-2,2-diethoxyethyl)benzoate (2o)

Light yellow oil, 37.4 mg, 0.140 mmol, 70% yield (53.4 mg **1o** used), 96% ee, $[\alpha]^{22}_D$ = +2.6 (c=0.5, $CHCl_3$), R_f = 0.3 (DCM/MeOH = 95/5), obtained by purification with flash column chromatography on silica gel (eluent: DCM/MeOH/Et_3N = 1/0.01/0.002). ^1H NMR (600 MHz, Chloroform-*d*) δ 8.00 (d, *J* = 8.4 Hz, 2H), 7.49 (d, *J* = 8.1 Hz, 2H),

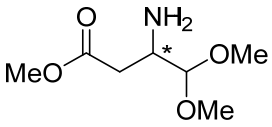
4.38 (d, *J* = 6.0 Hz, 1H), 4.07 (d, *J* = 5.9 Hz, 1H), 3.91 (s, 3H), 3.79 – 3.71 (m, 1H), 3.60 – 3.54 (m, 1H), 3.52 – 3.45 (m, 1H), 3.26 – 3.19 (m, 1H), 1.21 (t, *J* = 7.0 Hz, 3H), 1.02 (t, *J* = 7.0 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (151 MHz, Chloroform-*d*) δ 167.2, 146.9, 129.5, 129.3, 128.0, 106.7, 64.5, 64.0, 58.8, 52.2, 15.4, 15.2. The ee value were determined after acylation. HPLC: Chiracel AD-3 Column (250 mm); detected at 210 nm; *n*-hexane / *i*-propanol = 90/10; flow = 0.8 mL/min; Retention time: 12.0 min (major), 14.9 min (minor). HRMS (ESI), m/z: $[M+H]^+$ Calcd for $C_{14}H_{22}NO_4^+$: 268.1543; Found: 268.1539.



Chemical Formula: $C_{10}H_{17}NO_2S$
Exact Mass: 215.0980

(*R*)-2,2-Diethoxy-1-(thiophen-2-yl)ethan-1-amine (2p)

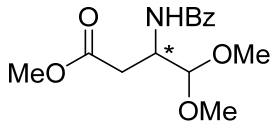
Light yellow oil, 36.3 mg, 0.169 mmol, 85% yield (42.8 mg **1p** used), 62% ee, $[\alpha]^{22}_D$ = +2.6 (c=0.5, $CHCl_3$), R_f = 0.3 (DCM/MeOH = 95/5), obtained by purification with flash column chromatography on silica gel (eluent: DCM/MeOH/Et_3N = 1/0.01/0.002). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.22 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.04 (d, *J* = 3.4 Hz, 1H), 6.97 (dd, *J* = 5.1, 3.5 Hz, 1H), 4.39 (d, *J* = 5.9 Hz, 1H), 4.33 – 4.25 (m, 1H), 3.84 – 3.74 (m, 1H), 3.69 – 3.50 (m, 2H), 3.41 – 3.29 (m, 1H), 1.24 (t, *J* = 7.0 Hz, 3H), 1.12 (t, *J* = 7.0 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, Chloroform-*d*) δ 145.4, 126.6, 124.9, 124.5, 106.6, 64.4, 64.0, 55.1, 15.4, 15.3. The ee value were determined after acylation. UPLC: Chiracel OD-3 Column (250 mm); detected at 210 nm; *n*-hexane / *i*-propanol = 95/5; flow = 0.5 mL/min; Retention time: 3.9 min (major), 4.4 min (minor). HRMS (ESI), m/z: $[M+H]^+$ Calcd for $C_{10}H_{18}NO_2S^+$: 216.1053; Found: 216.1056.



Chemical Formula: $C_7H_{15}NO_4$
Exact Mass: 177.1001

Methyl 3-amino-4,4-dimethoxybutanoate (**2q**)

For direct asymmetric reductive amination of **2q**, MeOH was used as solvent instead of TFE. Because of difficulty of purification, the yield and characterization of **2q** is determined after benzoylation to **2q-Bz**.



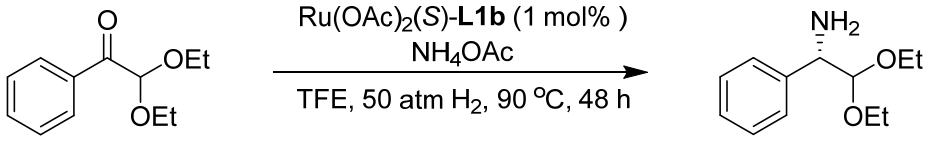
Chemical Formula: $C_{14}H_{19}NO_5$
Exact Mass: 281.1263

Methyl 3-benzamido-4,4-dimethoxybutanoate (2q-Bz)

White solid, 46.6 mg, 0.166 mmol, 83% yield (35.4 mg **1q** used), 98% ee, $[\alpha]^{24}_D$ = -2.3 (c=1.0, $CHCl_3$), R_f = 0.5 (Hex/EA = 80/20), obtained by purification with flash column chromatography on silica gel (eluent: Hex/EA = 1/0.1). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.82 – 7.78 (m, 2H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.04 – 6.92 (m, 1H), 4.71 – 4.64 (m, 1H), 4.50 (d, *J* = 3.9 Hz, 1H), 3.70 (s, 3H), 3.46 (s, 3H), 3.43 (s, 3H), 2.70 (qd, *J* = 15.7, 5.8 Hz, 2H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 172.7, 167.1, 134.4, 131.8, 128.7, 127.2, 104.8, 56.2, 55.6, 52.0, 48.2, 33.6. HPLC: Chiracel AD-3 Column (250 mm); detected at 230 nm; *n*-hexane / *i*-propanol = 90/10; flow = 0.8 mL/min; Retention time: 17.2 min (minor), 19.9 min (major). HRMS (ESI), m/z: $[M+Na]^+$ Calcd for $C_{14}H_{19}NO_5Na^+$: 304.1155; Found: 304.1153.

IV. Product Transformations

4.1 Gram-scale reaction:

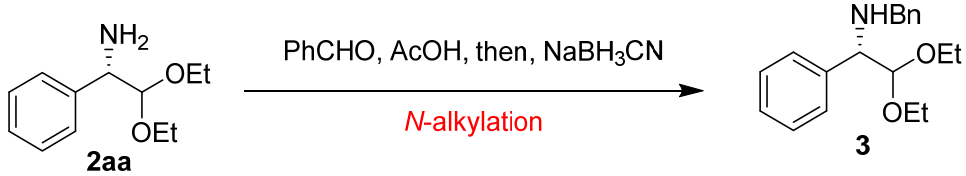


1aa
1.01 g, 4.9 mmol

2aa
80% yield, 96% ee

In a glovebox, $Ru(OAc)_2$(*S*-**L1b**) (70 mg, 0.050 mmol), **1aa** (1.01 g, 4.9 mmol), ammonium salt (0.77 g, 10 mmol) and TFE (20 ml) were successively added to a 50 mL reaction tube equipped with a magnetic stirring bar. The mixture was then transferred to a stain-less autoclave and purged by three cycles of pressurization/venting with H_2. The required H_2 pressure (50 atm) was then installed, and the autoclave was placed in an oil bath preheated to 90 ℃. The autoclave was cooled down to room temperature after 48 h and the pressure was slowly released in the hood. The reaction was quenched by saturated $NaHCO_3$ solution (20 mL) and extracted with DCM (30 mL x 3). The combined organic phase was dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. The residue was subjected to column chromatography on silica gel (eluent: DCM/MeOH/Et_3N = 1/0.01/0.002) to afford desired products 0.81 g, 80% yield, 96% ee.

4.2 N-Alkylation:

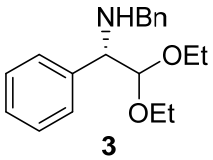


2aa

3

AcOH (0.3 mmol，18 μL) was added to the solution of **2aa** (0.2 mmol, 40.8 mg) and PhCHO (0.3 mmol, 31.8 mg) in 3 mL MeOH, and the mixture was stirred for 3 h at room temperature. Then, $NaBH_3CN$ (0.6 mmol, 38 mg) was added, and the reaction was stirred at 40 ℃ for 15 h. Upon completion of reaction, the reaction was quenched by 3 mL of saturated NH_4Cl/H_2O solution, followed by extraction with EA (10 mL x 3 times). The organic layer was combined, dried over anhydrous Na_2SO_4, filtered and

then evaporated under reduced pressure. The residue was subjected to flash column chromatography on silica gel (eluent: Hex/EA = 1/0.1) to afford **3** as a yellow solid.



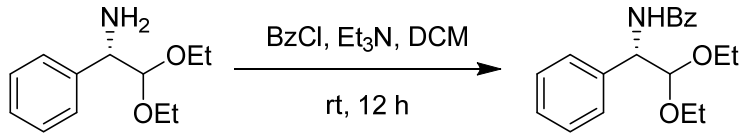
3

Chemical Formula: $C_{19}H_{25}NO_2$
Exact Mass: 299.1885

(*S*)-N-Benzyl-2,2-diethoxy-1-phenylethan-1-amine (3)

Yellow solid, 46.6 mg, 0.156 mmol, 78% yield, 95% ee, $[\alpha]^{22}_D$ = +35.0 (c=0.5, $CHCl_3$), R_f = 0.3 (Hex/EA = 95/5). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.48 – 7.41 (m, 2H), 7.36 – 7.20 (m, 8H), 4.42 (d, *J* = 7.0 Hz, 1H), 3.79 – 3.60 (m, 3H), 3.53 – 3.42 (m, 3H), 3.12 – 3.03 (m, 1H), 1.21 (t, *J* = 7.1 Hz, 3H), 0.93 (t, *J* = 7.0 Hz, 3H). HPLC: Chiracel AD-3 Column (250 mm); detected at 210 nm; *n*-hexane / *i*-propanol = 95/5; flow = 0.8 mL/min; Retention time: 5.5 min (major), 6.6 min (minor). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 140.7, 139.8, 129.0, 128.4, 128.3, 128.2, 127.5, 126.9, 106.5, 65.3, 64.5, 63.0, 51.1, 15.4, 15.1. HRMS (ESI), m/z: $[M+H]^+$ Calcd for $C_{19}H_{26}NO_2^+$: 300.1958, Found: 300.1957.

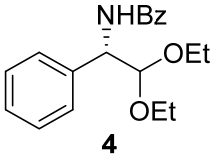
4.3 N-Benzoylation:



2aa **4**

Primary amine **2aa** (41.8 mg, 0.2 mmol) was dissolved in dichloromethane (1 mL), followed by addition of triethylamine (80 μL) and BzCl (40 μL) at 0 °C. After stirred at room temperature for 2 h, saturated $NaHCO_3$ solution (3 mL) was added to quench the reaction, followed by extraction with DCM (5 mL x 3 times). The organic phase was combined, dried over anhydrous Na_2SO_4, filtered, and then evaporated under

reduced pressure. The residue was subjected to flash column chromatography on silica gel (eluent: Hex/EA = 1/0.1 to afford **4** as a white solid.



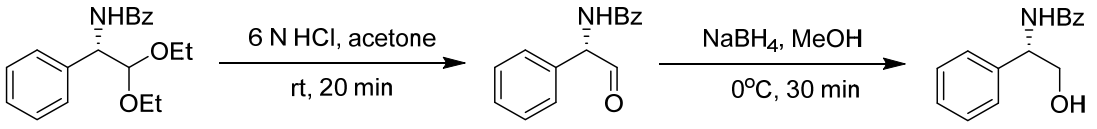
4

Chemical Formula: $C_{19}H_{23}NO_3$
Exact Mass: 313.1678

(*S*)-N-(2,2-Diethoxy-1-phenylethyl)benzamide (4)

White solid, 58.8 mg, 0.188 mmol, 94% yield, 97% ee, $[\alpha]^{22}_D$ = -34.1 (c=0.5, $CHCl_3$), R_f = 0.5 (Hex/EA = 80/20). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.84 – 7.79 (m, 2H), 7.54 – 7.50 (m, 1H), 7.48 – 7.42 (m, 4H), 7.35 – 7.29 (m, 2H), 7.28 – 7.22 (m, 1H), 5.24 (d, *J* = 6.2 Hz, 1H), 4.80 (d, *J* = 6.2 Hz, 1H), 3.76 – 3.61 (m, 2H), 3.56 (dq, *J* = 9.4, 7.0 Hz, 1H), 3.41 (dq, *J* = 9.4, 7.0 Hz, 1H), 3.31 (p, *J* = 1.7 Hz, 1H), 1.15 (t, *J* = 7.1 Hz, 3H), 1.06 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Methanol-d_4) δ 169.9, 140.5, 135.9, 132.7, 129.6, 129.2, 129.0, 128.4, 128.4, 105.0, 64.8, 63.5, 57.6, 15.6, 15.4. HPLC: Chiracel AS-3 Column (250 mm); detected at 230 nm; *n*-hexane / *i*-propanol = 90/10; flow = 0.8 mL/min; Retention time: 9.2 min (major), 14.2 min (minor). HRMS (ESI), m/z: $[M+Na]^+$ Calcd for $C_{19}H_{23}NO_3Na^+$: 336.1570, Found: 336.1568.

4.4 Reduction to amino alcohol:

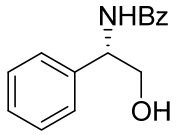


4 **S2** **5**

Compound **4** (31.3 mg, 0.1 mmol) was dissolved in 0.5 mL acetone at room temperature, then 0.5 mL of 6 mol/L HCl was added. The reaction was stirred at room temperature for 20 min and monitored by TLC. Upon completion of reaction, 3 mL H_2O was added, followed by extraction with EA (3 x 5 mL). The organic phase was combined, dried over anhydrous Na_2SO_4, filtered, and then evaporated under reduced

pressure to obtained crude aldehyde **S2**, which could be used in the next step without further purification.

The crude **S2** (*ca*. 0.1 mmol) obtained in the last step was dissolve in 1 mL MeOH, then $NaBH_4$ (5.5 mg) was added at 0 °C and stirred for 30 min. Upon completion of reaction, 3 mL saturated NH_4Cl solution was added to quench the reaction, followed by extraction with EA (3 x 5 mL). The residue was subjected to flash column chromatography on silica gel (eluent: Hex/EA = 1/0.1) to afford **5** as white solid.

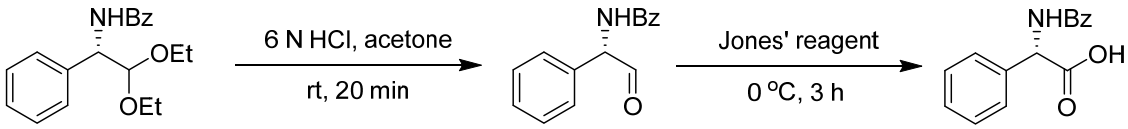


Chemical Formula: $C_{15}H_{15}NO_2$
Exact Mass: 241.1103

(*S*)-N-(2-Hydroxy-1-phenylethyl)benzamide (5)

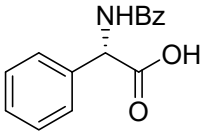
White solid, 23.5 mg, 0.0975 mmol, 98% yield over two steps, 97% ee, $[\alpha]^{23}_D$ = -16.6 (c=0.5, MeOH), R_f = 0.5 (Hex/EA = 90/10). ^{1}H NMR (600 MHz, Methanol-d_4) δ 7.88 – 7.84 (m, 2H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.41 (d, *J* = 7.6 Hz, 2H), 7.33 (t, *J* = 7.5 Hz, 2H), 7.25 (t, *J* = 7.4 Hz, 1H), 5.20 (t, *J* = 6.6 Hz, 1H), 3.86 (d, *J* = 6.6 Hz, 2H). ^{13}C{^{1}H} NMR (151 MHz, Methanol-d_4) δ 170.4, 141.4, 135.9, 132.7, 129.5, 129.5, 128.4, 128.4, 128.0, 66.1, 57.8. HRMS (ESI), m/z: $[M+H]^+$ Calcd for $C_{15}H_{16}NO_2^+$: 242.1176, Found: 242.1174. HPLC: Chiracel OJ-3 Column (250 mm); detected at 210 nm; *n*-hexane / *i*-propanol = 90/10; flow = 0.8 mL/min; Retention time: 14.9 min (major), 16.8 min (minor). The absolute configuration of **5** was determined by comparing its sign of the optical rotation with that reported in the literature.[7] The absolute configuration of **2aa**, **2ab**, **2c**-**2p** was thus determined by similarity with **5**.

4.5 Oxidation to amino acid:



4 **S2** **6**

Jones's reagent was added to crude **S2** (0.2 mmol, see **4.4** for preparation) in 1.5 mL acetone over 0.5 h at 0 °C. The reaction was then stirred for 3 h at this temperature. Several drops of *i*-PrOH were added to quench the reaction and then concentrated. Water (4 mL) was then added, and the organic layers were extracted by DCM (3x 4 mL). The organic phase was combined, dried over anhydrous Na_2SO_4, filtered, and then evaporated under reduced pressure. The residue was subjected to flash column chromatography on silica gel (eluent: DCM/MeOH = 1/0.03) to afford **6** as white solid.

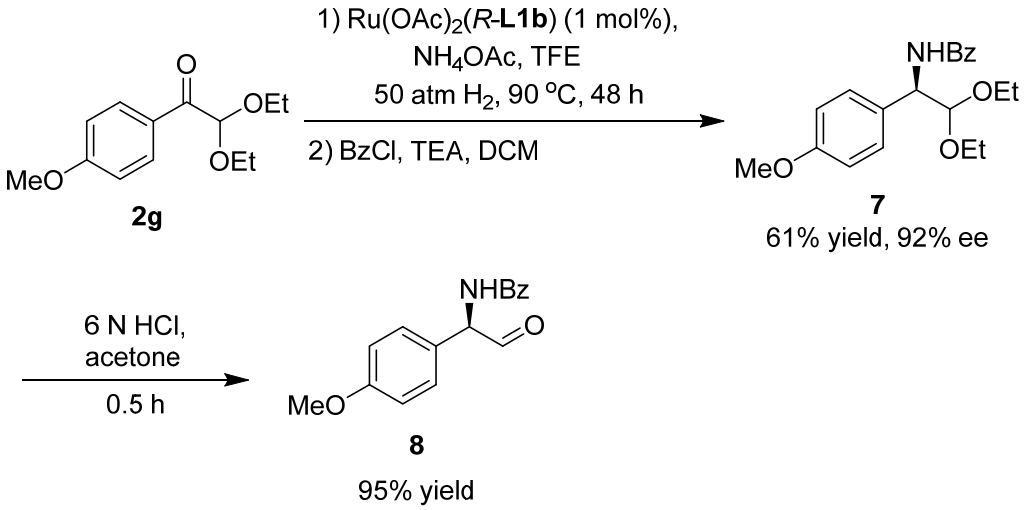


Chemical Formula: $C_{15}H_{13}NO_3$
Exact Mass: 255.0895

(*S*)-2-Benzamido-2-phenylacetic acid (6)

White solid, 37.7 mg, 0.148 mmol, 74% yield over 2 steps, 91% ee, $[\alpha]^{23}_D$ = +48.0 (c=0.5, MeOH) ,R_f = 0.2 (DCM/MeOH = 95/5). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.92 – 7.82 (m, 2H), 7.56 – 7.43 (m, 5H), 7.33 – 7.19 (m, 3H), 5.44 (s, 1H). ^{13}C NMR (151 MHz, Methanol-d_4) δ 176.0, 168.9, 140.7, 135.5, 132.8, 129.6, 129.4, 128.5, 128.3, 60.4. HPLC: Chiral-NZ(2) Column (250 mm); detected at 230 nm; *n*-hexane / (EtOH+0.1% TEA) = 50/50; flow = 0.5 mL/min; Retention time: 7.8 min (minor), 8.7 min (major). HRMS (ESI), m/z: $[M-H]^-$ Calcd for $C_{15}H_{12}NO_3^-$: 254.0823, Found: 254.0819. The absolute configuration of **6** was established by comparison of its sign of the optical rotation with that reported in the literature.[8]

4.6 Formal synthesis of (-)-Cytoxazone

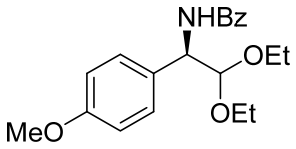


In a glovebox, Ru(OAc)$_2$(*R*-**L1b**) (54 mg, 0.040 mmol), **2g** (0. 87 g, 3.7 mmol), ammonium salt (0.62 g, 8.1 mmol) and TFE (15 ml) were successively added to a 50 mL reaction tube equipped with a magnetic stirring bar. The mixture was then transferred to a stain-less autoclave and purged by three cycles of pressurization/venting with H_2. The required H_2 pressure (50 atm) was then installed, and the autoclave was placed in an oil bath preheated to 90 ℃. The autoclave was cooled down to room temperature after 48 h and the pressure was slowly released in the hood. The reaction was quenched by saturated $NaHCO_3$ solution (20 mL) and extracted with DCM (30 mL x 3). The combined organic phase was dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. The residue was subjected to the next step without purification.

Primary amine obtained in the last step was dissolved in dichloromethane (20 mL) followed by addition of triethylamine (1.6 mL) and BzCl (3.2 mL) at 0 °C. After stirred at room temperature for 2 h, saturated $NaHCO_3$ solution (20 mL) was added to quench the reaction. The organic phase was separated, dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. The residue was subjected to flash column chromatography on silica gel (eluent: Hex/EA = 1/0.2) to afford **7** as white solid (0.76 g, 61% yield over 2 steps).

Compound **7** (34.3 mg, 0.1 mmol) was dissolved in 0.5 mL acetone at room temperature, then 6 mol/L HCl (0.5 mL) was added. The reaction was stirred at room temperature for 20 min and monitored by TLC. Upon completion of reaction, H_2O (3

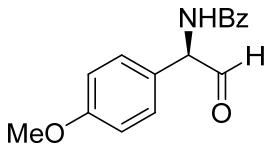
mL) was added and the organic layers were extracted with EA (3 x 5 mL). The organic phase was combined, dried over anhydrous Na_2SO_4, filtered and then evaporated under reduced pressure. The residue was subjected to flash column chromatography on silica gel (eluent: Hex/EA = 1/0.15) to afford **7** as a white solid (25.7 mg, 95% yield).



Chemical Formula: $C_{20}H_{25}NO_4$
Exact Mass: 343.1784

(*R*)-N-(2,2-Diethoxy-1-(4-methoxyphenyl)ethyl)benzamide (7)

White solid, 0.76 g, 2.2 mmol, 61% yield over 2 steps, 92% ee, $[\alpha]^{23}_D$ = +39.7 (c=0.5, $CHCl_3$), R_f = 0.6 (Hex/EA = 80/20). ^{1}H NMR (600 MHz, Methanol-d_4) δ 7.84 – 7.78 (m, 2H), 7.55 – 7.51 (m, 1H), 7.48 – 7.44 (m, 2H), 7.37 – 7.34 (m, 2H), 6.92 – 6.85 (m, 2H), 5.19 (d, *J* = 6.2 Hz, 1H), 4.76 (d, *J* = 6.2 Hz, 1H), 3.77 (s, 3H), 3.74 – 3.63 (m, 2H), 3.56 (dq, *J* = 9.4, 7.0 Hz, 1H), 3.42 (dq, *J* = 9.5, 7.0 Hz, 1H), 3.31 (p, *J* = 1.6 Hz, 2H), 1.16 (t, *J* = 7.0 Hz, 3H), 1.07 (t, *J* = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, Methanol-d_4) δ 169.8, 160.5, 136.0, 132.7, 132.5, 130.1, 129.6, 128.4, 114.6, 105.1, 64.8 63.6, 57.0, 55.7, 15.6, 15.4. HRMS (ESI), m/z: $[M+Na]^+$ Calcd for $C_{20}H_{25}NO_4Na^+$: 366.1676, Found: 366.1675. HPLC: Chiracel OJ-3 Column (250 mm); detected at 210 nm; *n*-hexane / *i*-propanol = 95/5; flow = 0.8 mL/min; Retention time: 20.4 min (major), 29.3 min (minor).



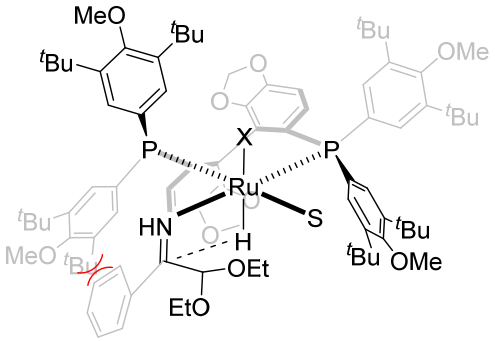
Chemical Formula: $C_{16}H_{15}NO_3$
Exact Mass: 269.1052

(*R*)-N-(1-(4-Methoxyphenyl)-2-oxoethyl)benzamide (8)

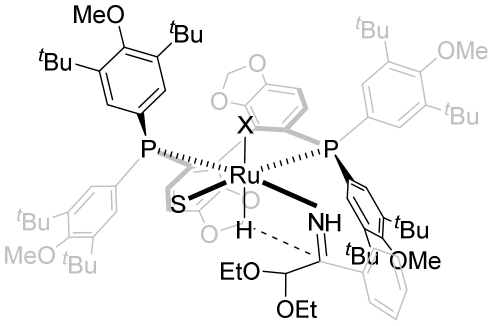
Pale yellow solid, 25.7 mg, 0.0956 mmol, 95% yield. $[\alpha]^{27}_D$ = -1.8 (c=0.5, $CHCl_3$), R_f = 0.4 (Hex/EA = 80/20). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.62 (s, 1H), 7.87 – 7.81

(m, 2H), 7.55 – 7.40 (m, 4H), 7.29 (d, *J* = 8.7 Hz, 2H), 6.94 (d, *J* = 8.8 Hz, 2H), 5.71 (d, *J* = 5.8 Hz, 1H), 3.80 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, Chloroform-*d*) δ 195.0, 166.9, 160.2, 133.7, 132.1, 129.7, 128.8, 127.3, 125.1, 115.0, 63.4, 55.5. HRMS (ESI), m/z: $[M+H]^+$ Calcd for $C_{16}H_{16}NO_3^+$: 270.1125, Found: 270.1124. The NMR data is consistent with that reported.[9]

V. Proposed enantioinduction models



(*R*)-product, disfavored

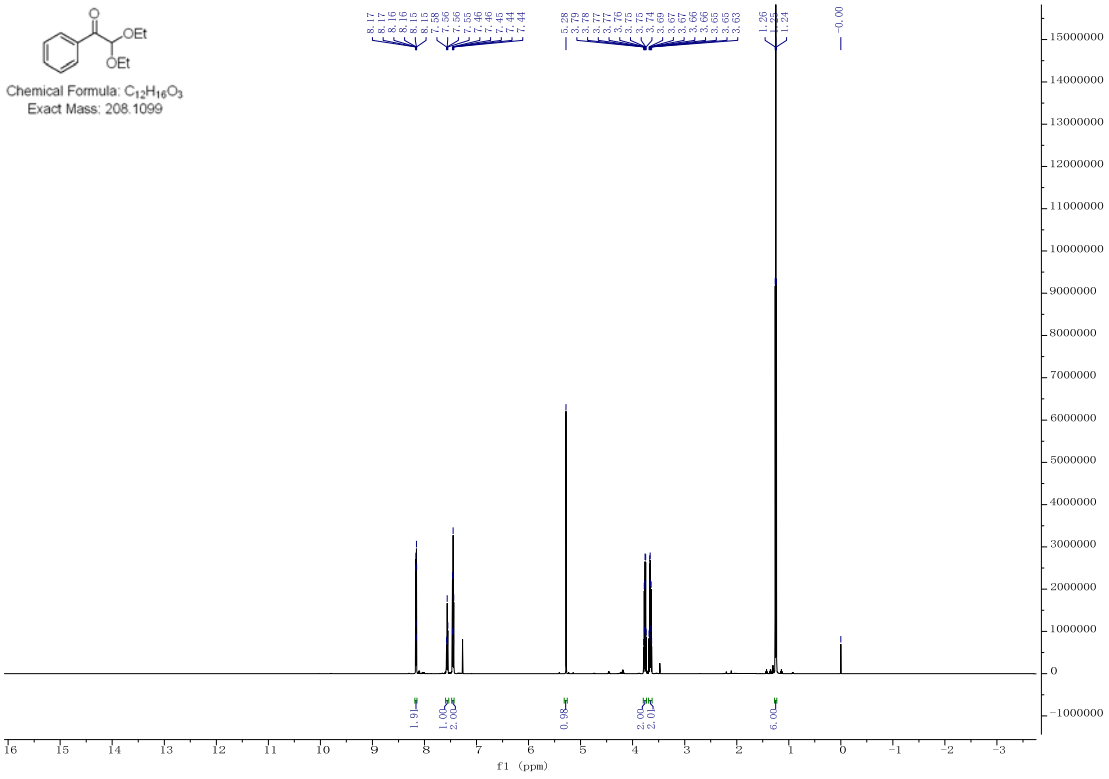


(*S*)-product, favored

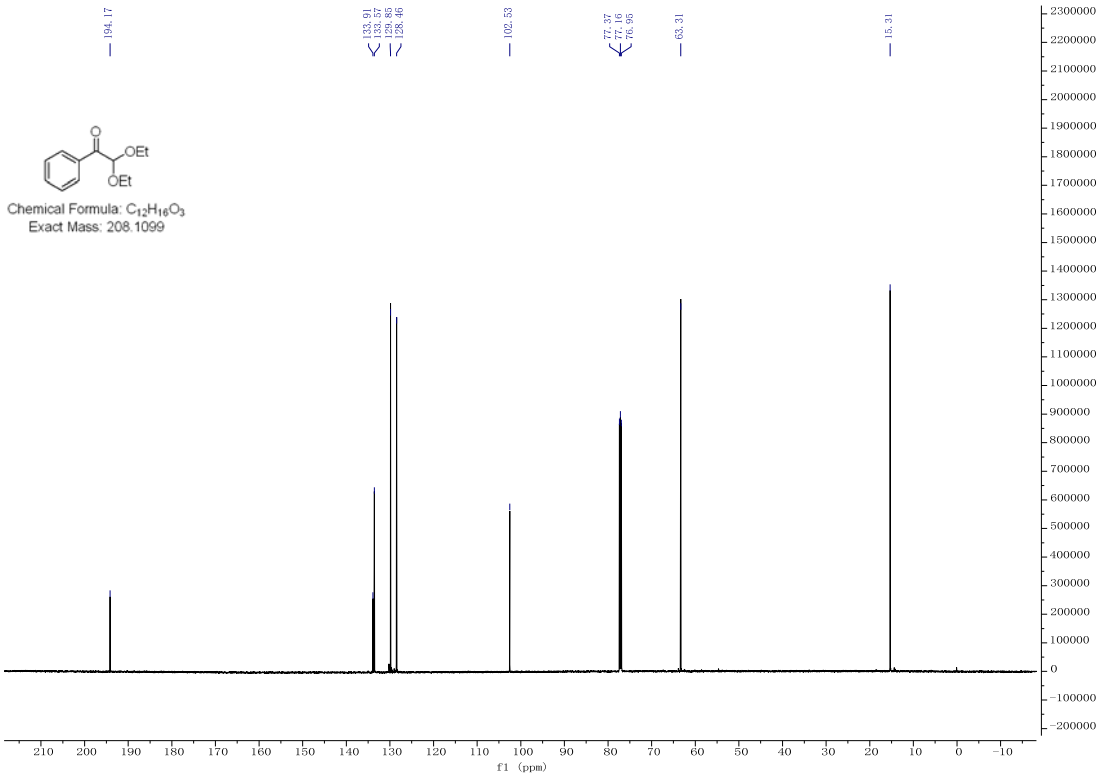
A pair of enantioinduction models for this reaction are tentatively proposed to explain the observed high enantiocontrol. As depicted in the figure, (*S*)-product favored transition state can avoid the steric repulsion between the aryl group on substrate and the DTBM group on P atom, while this steric hindrance repulsion is envisaged in the case of (*R*)-product favored transition state. The energy difference between two transition states led to *S* product as the major product.

VI. NMR spectra

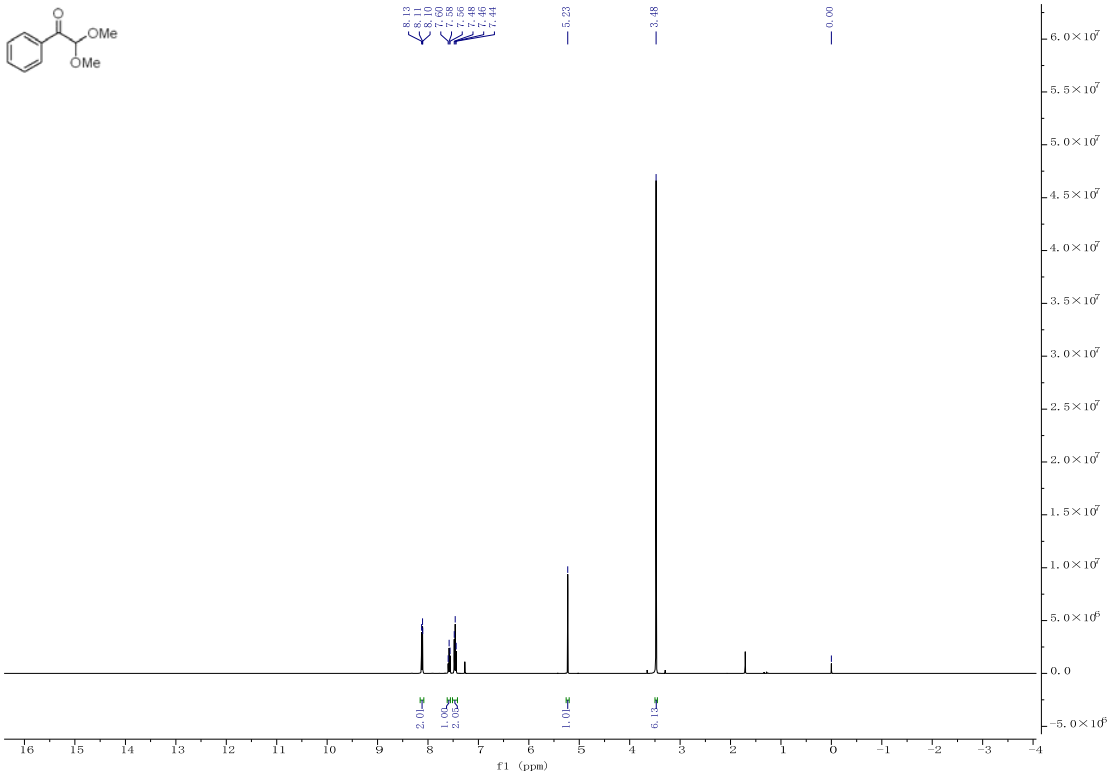
^{1}H NMR (600 MHz, Chloroform-d) of compound **1aa**



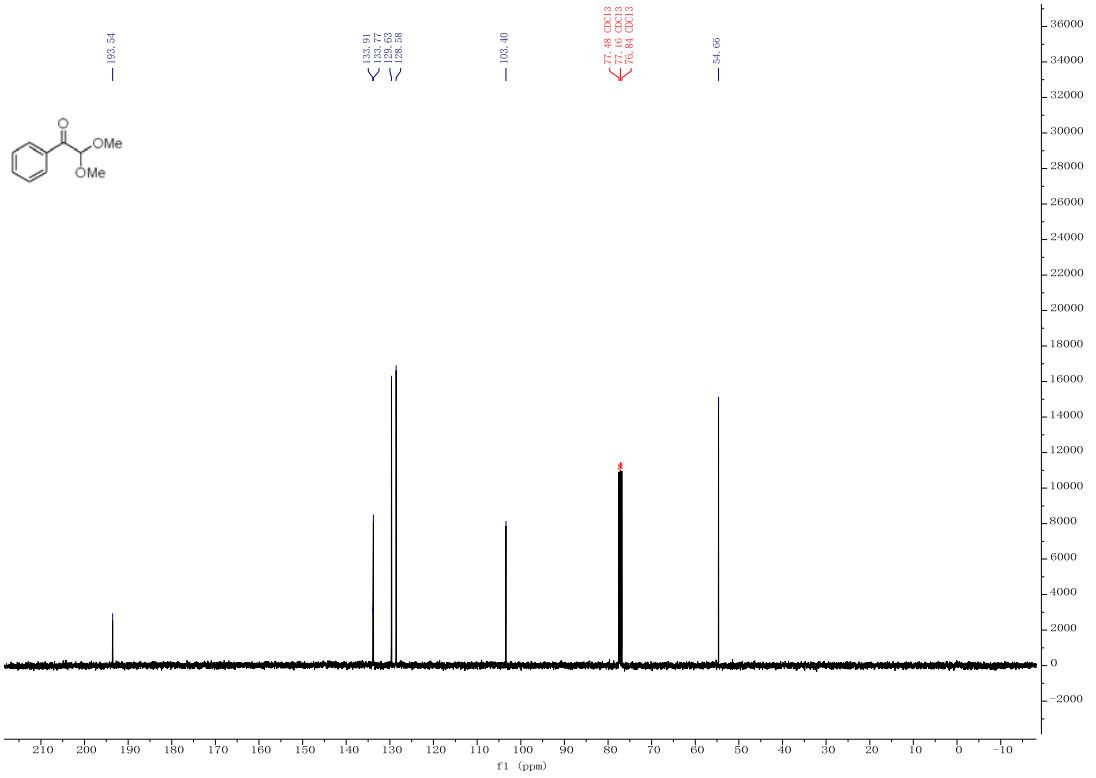
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **1aa**



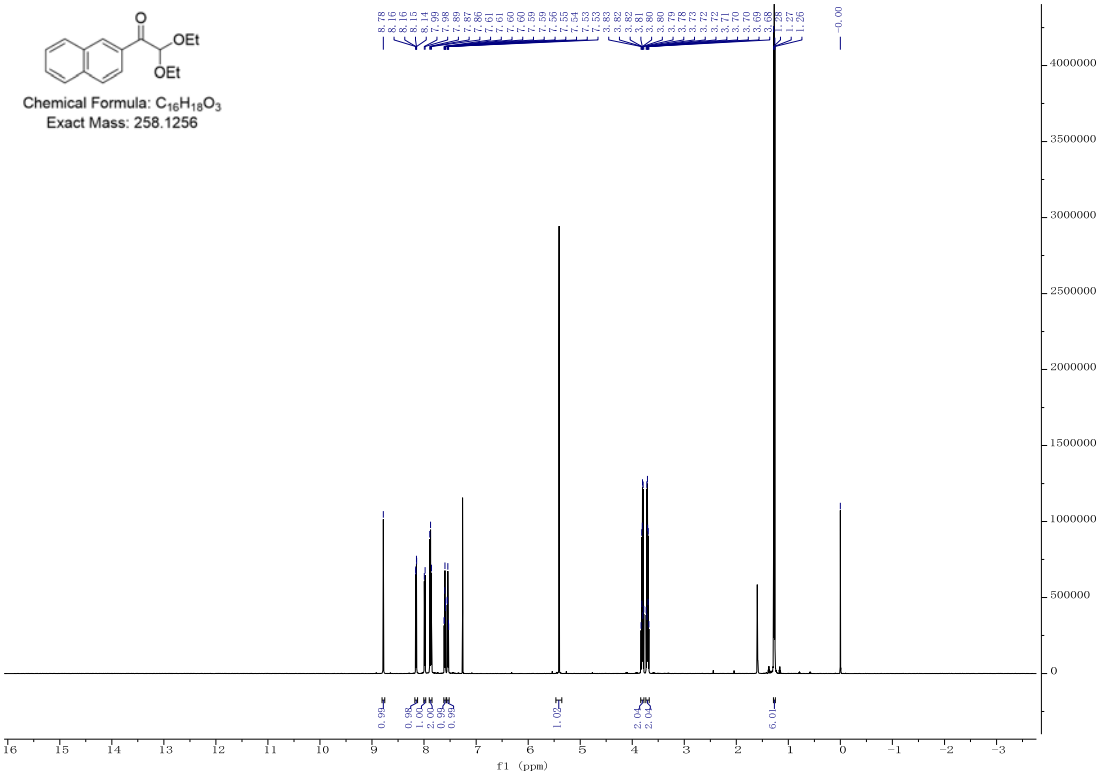
^{1}H NMR (400 MHz, Chloroform-d) of compound **1ab**



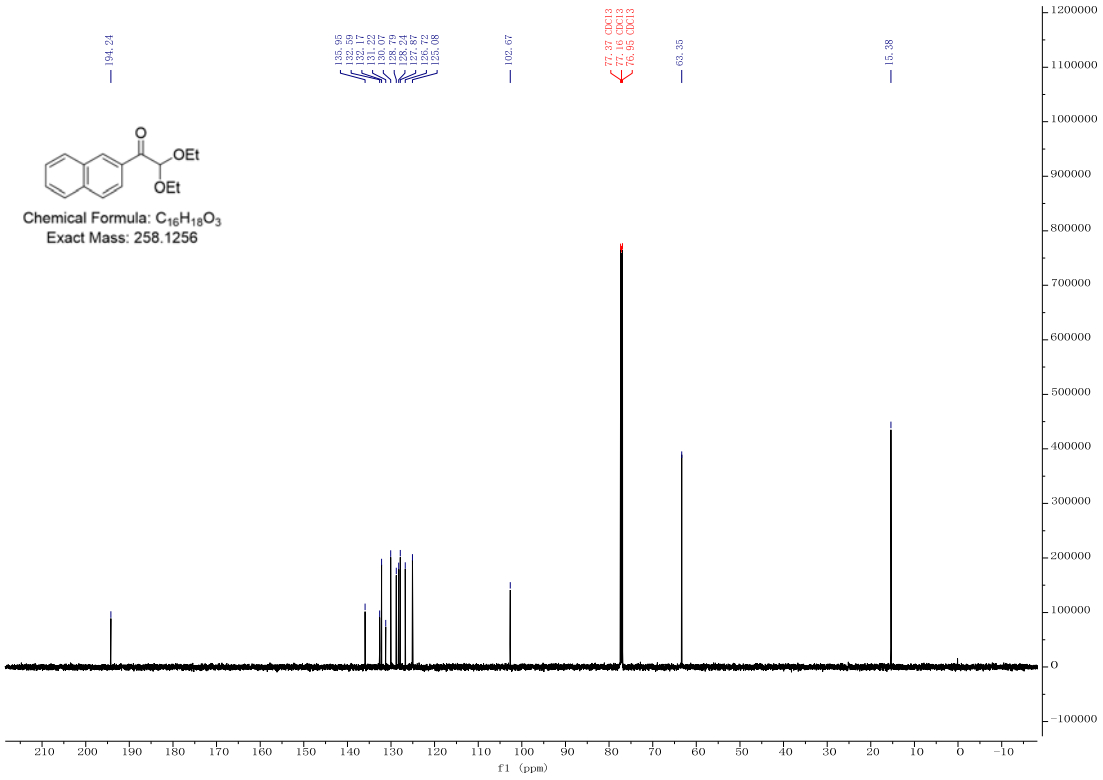
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **1ab**



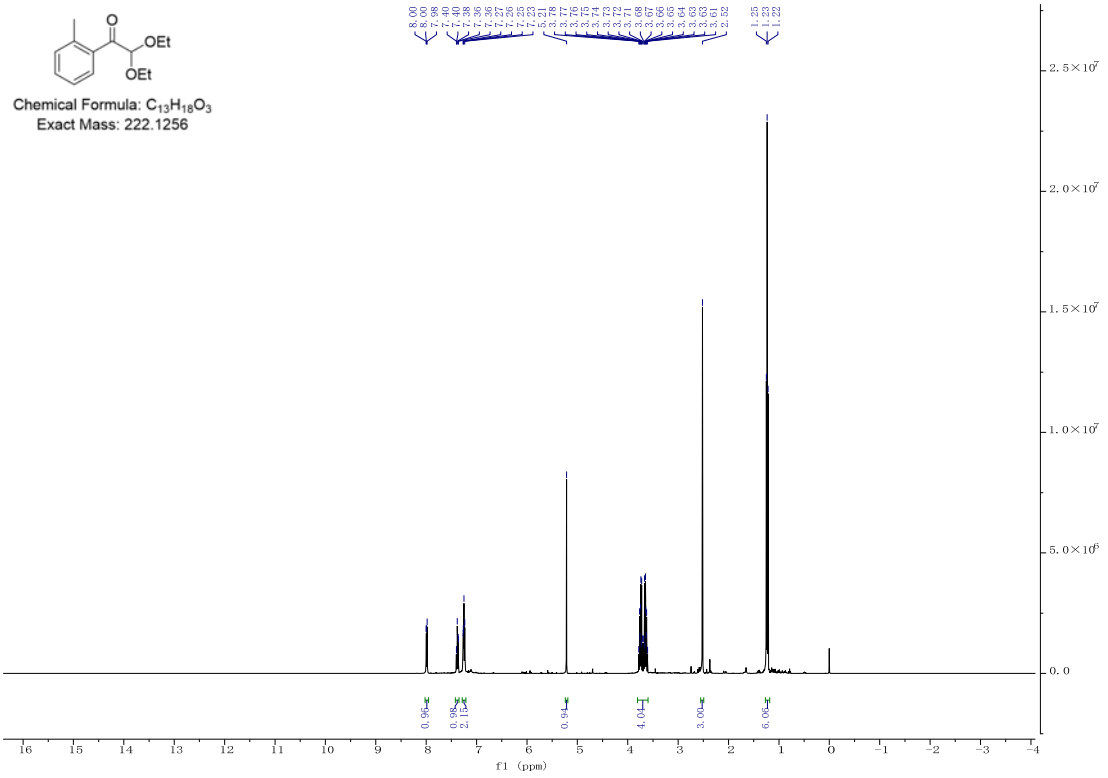
^{1}H NMR (600 MHz, Chloroform-d) of compound **1b**



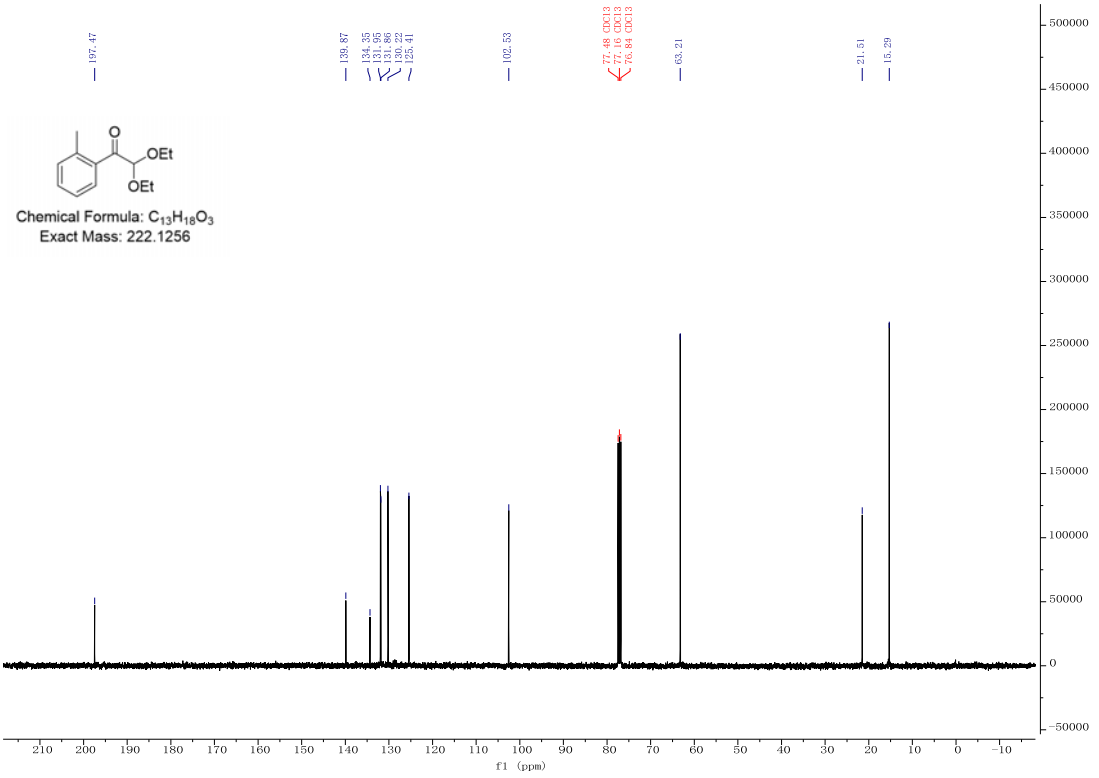
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **1b**



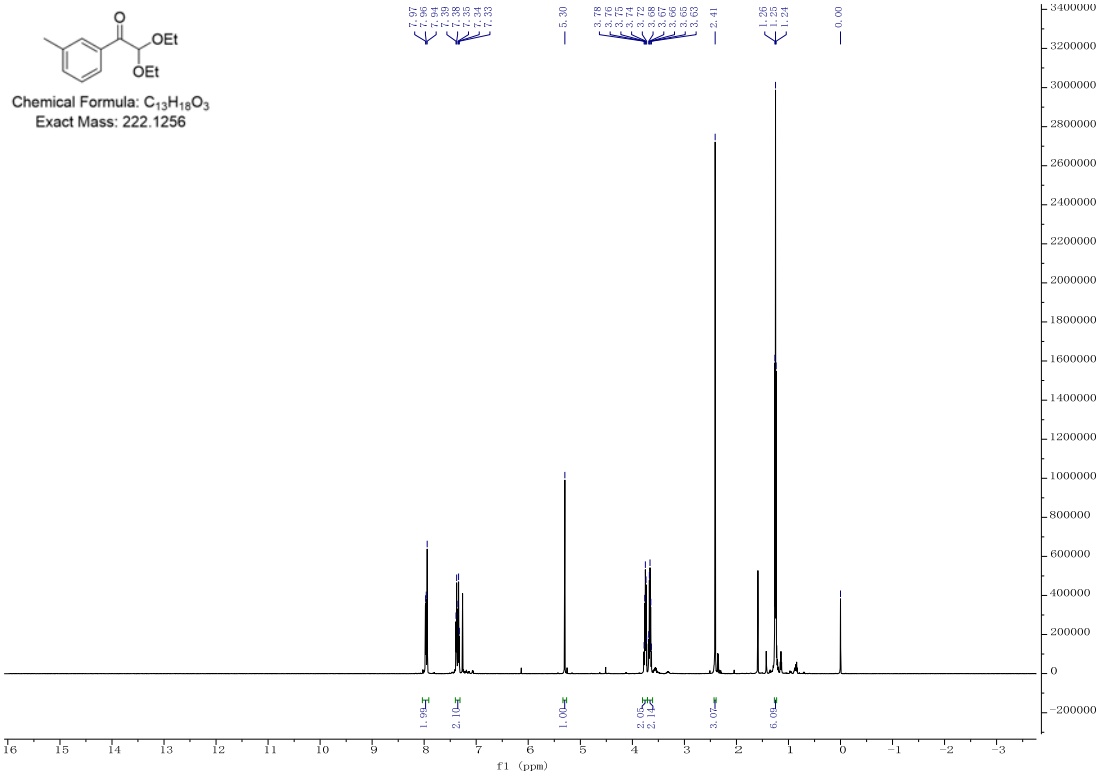
^{1}H NMR (400 MHz, Chloroform-d) of compound **1c**



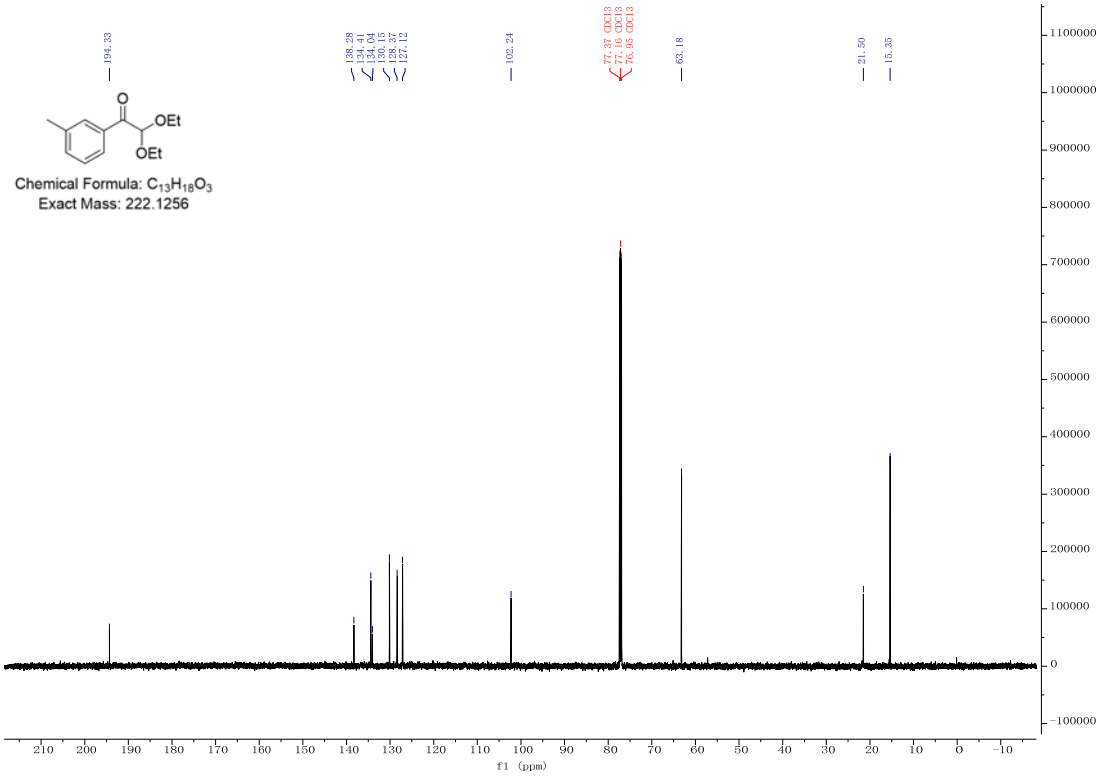
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **1c**



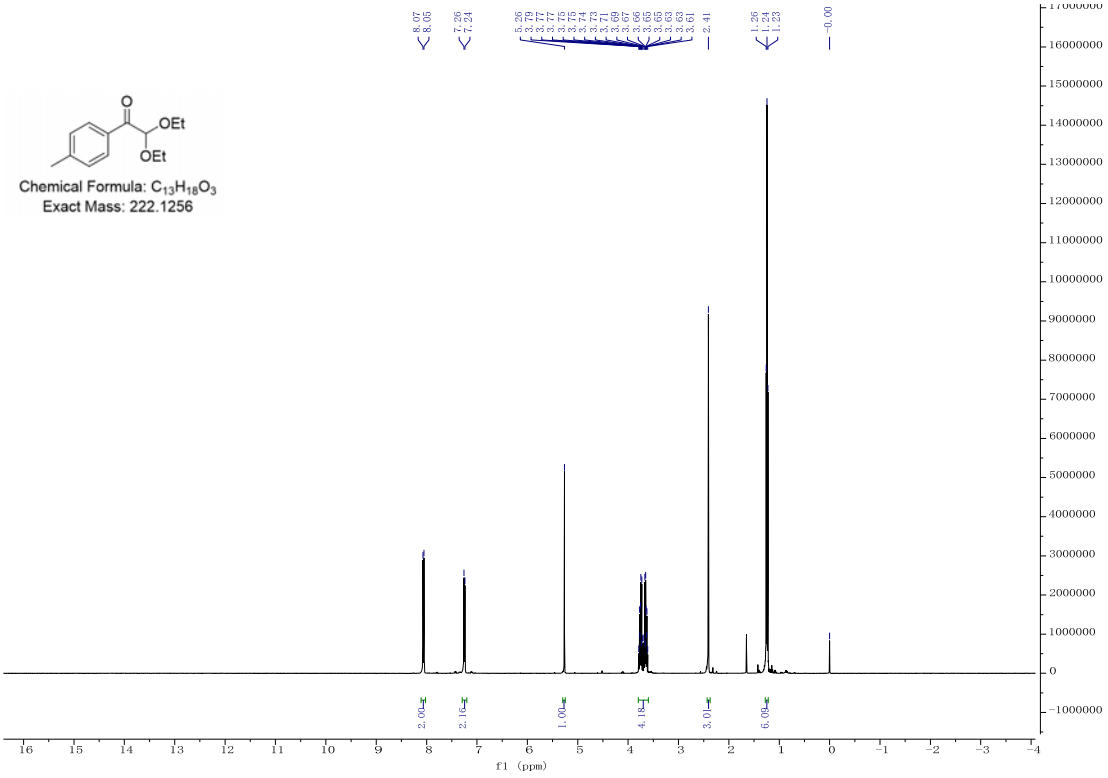
^{1}H NMR (600 MHz, Chloroform-d) of compound **1d**



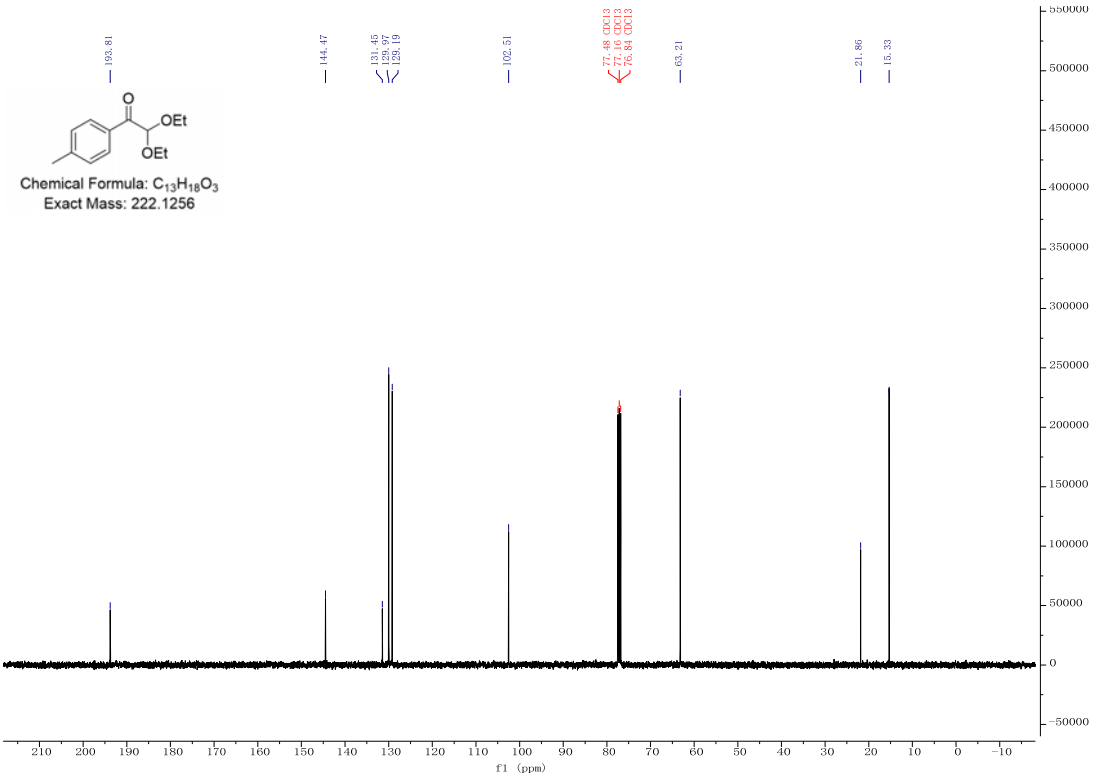
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **1d**



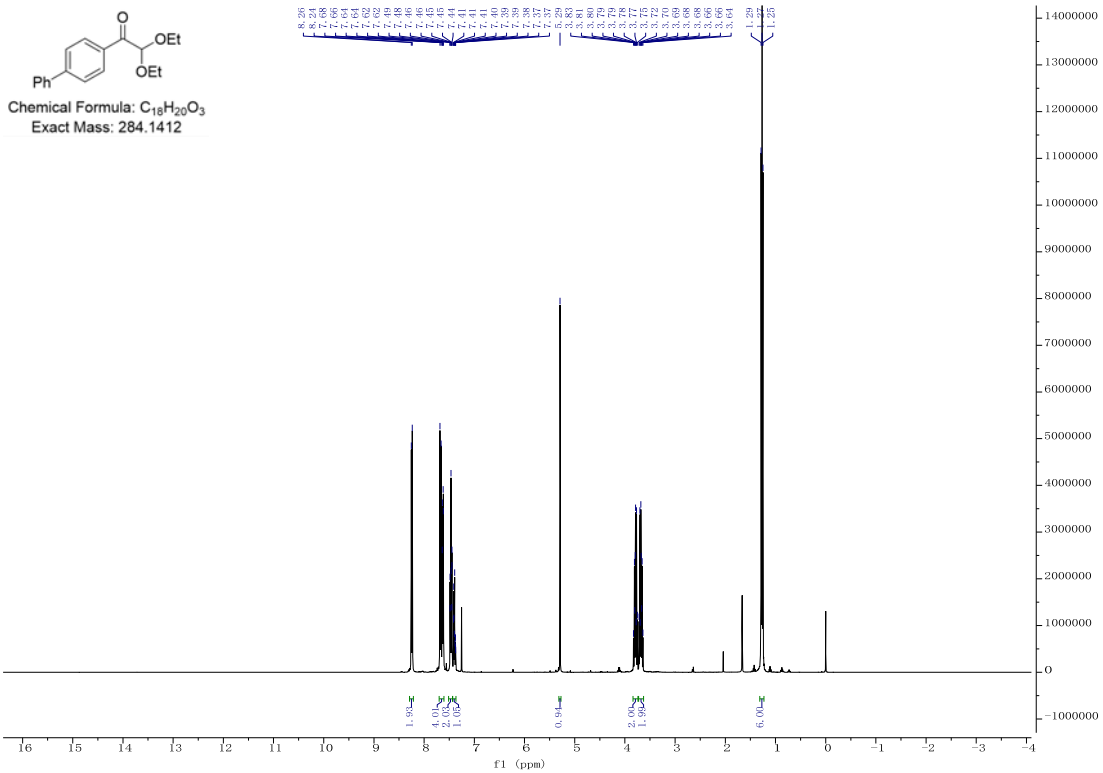
^{1}H NMR (400 MHz, Chloroform-d) of compound **1e**



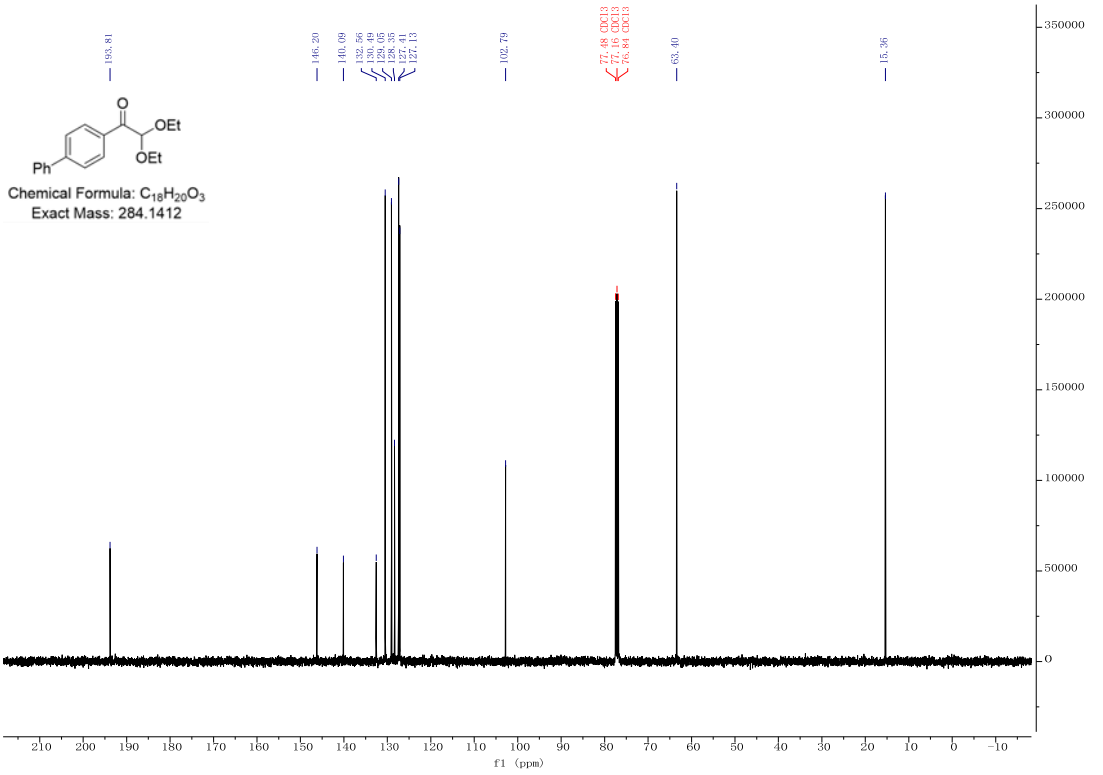
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **1e**



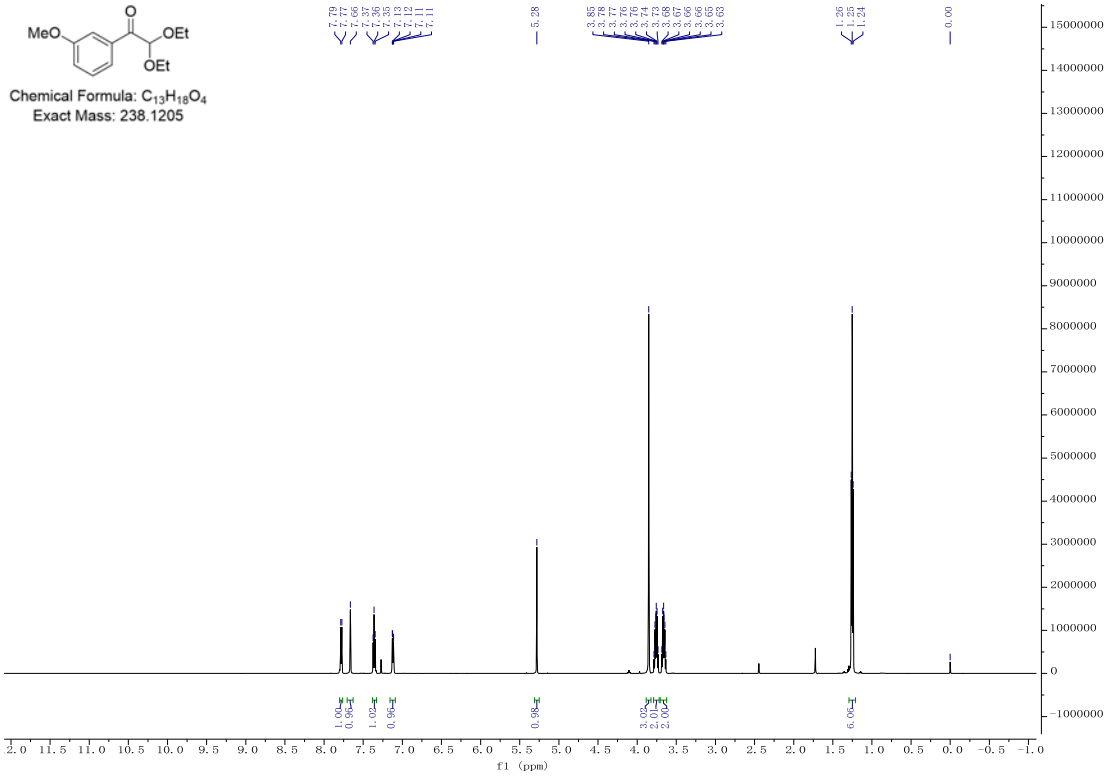
^{1}H NMR (400 MHz, Chloroform-d) of compound **1f**



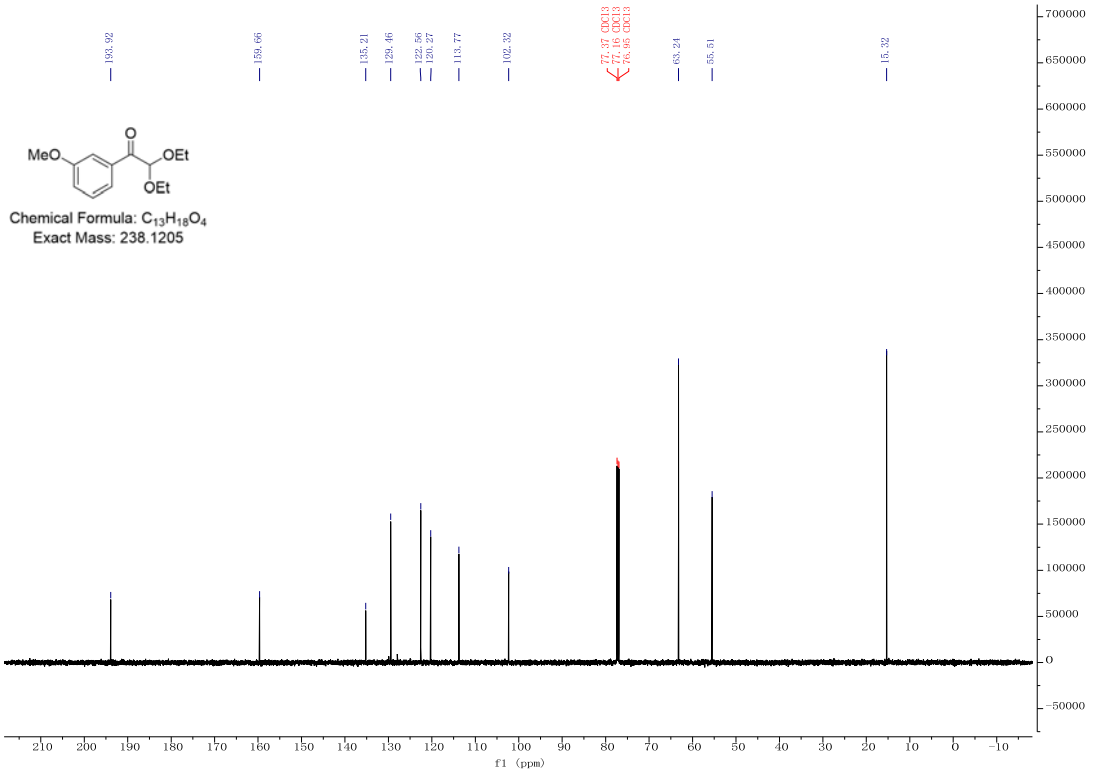
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **1f**



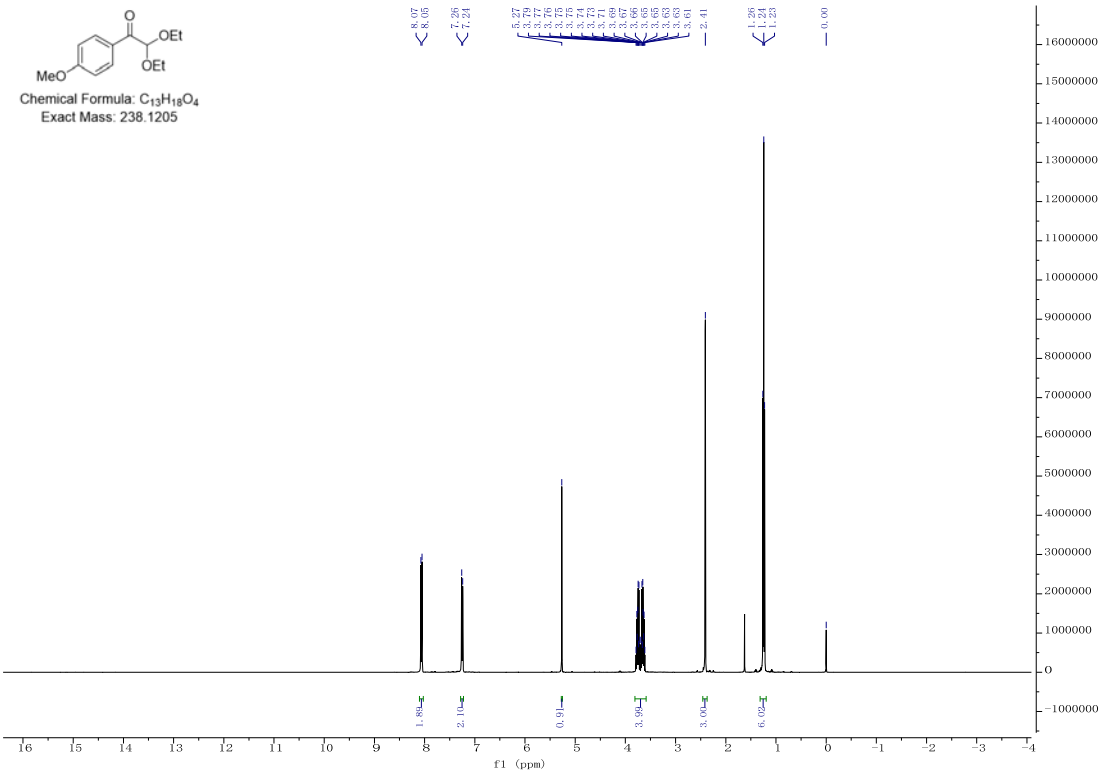
^{1}H NMR (600 MHz, Chloroform-d) of compound **1g**



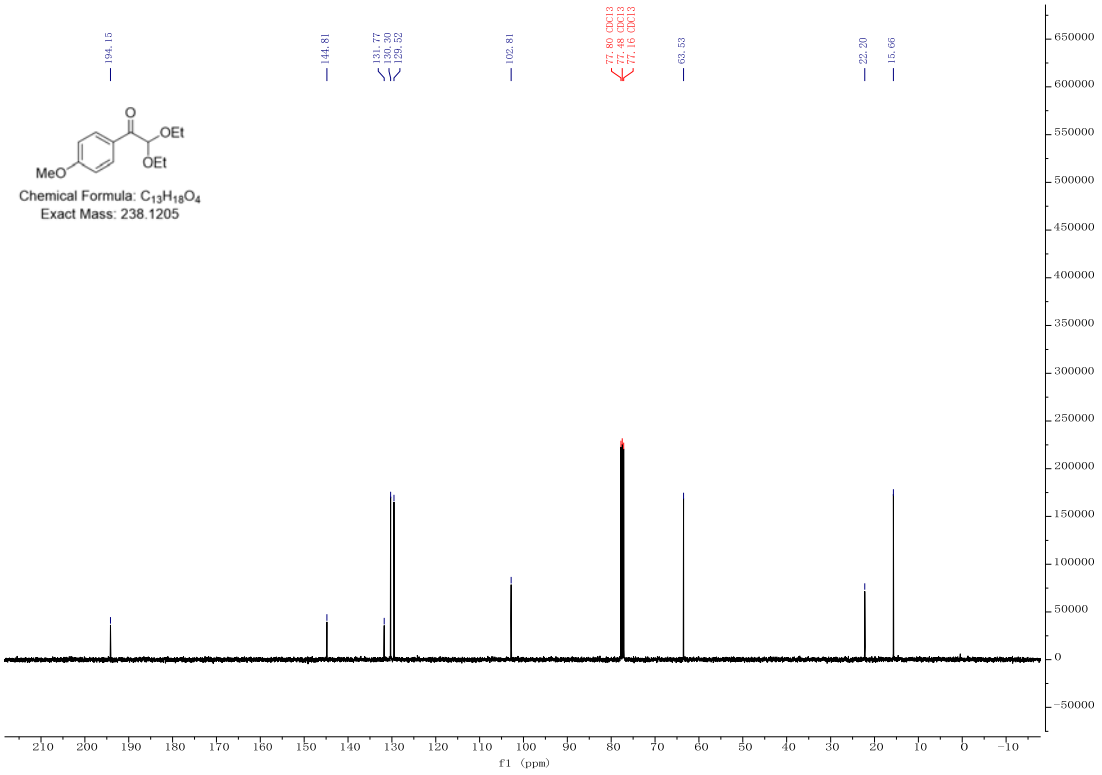
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **1g**



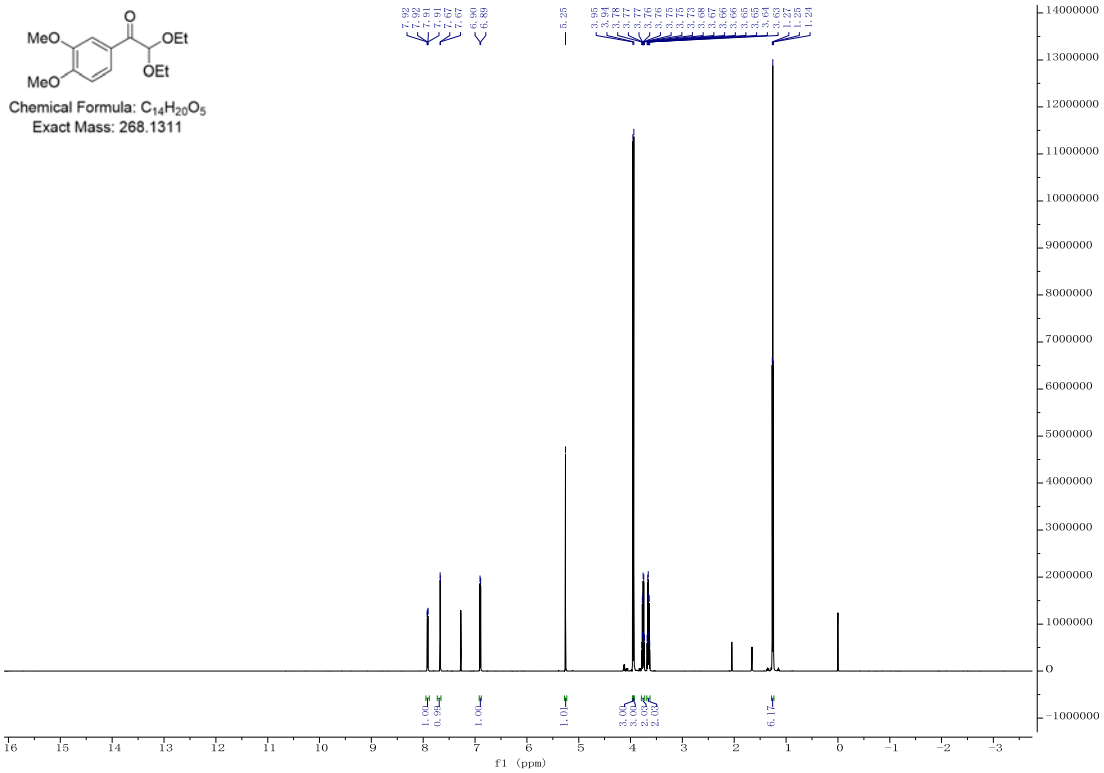
^{1}H NMR (400 MHz, Chloroform-d) of compound **1h**



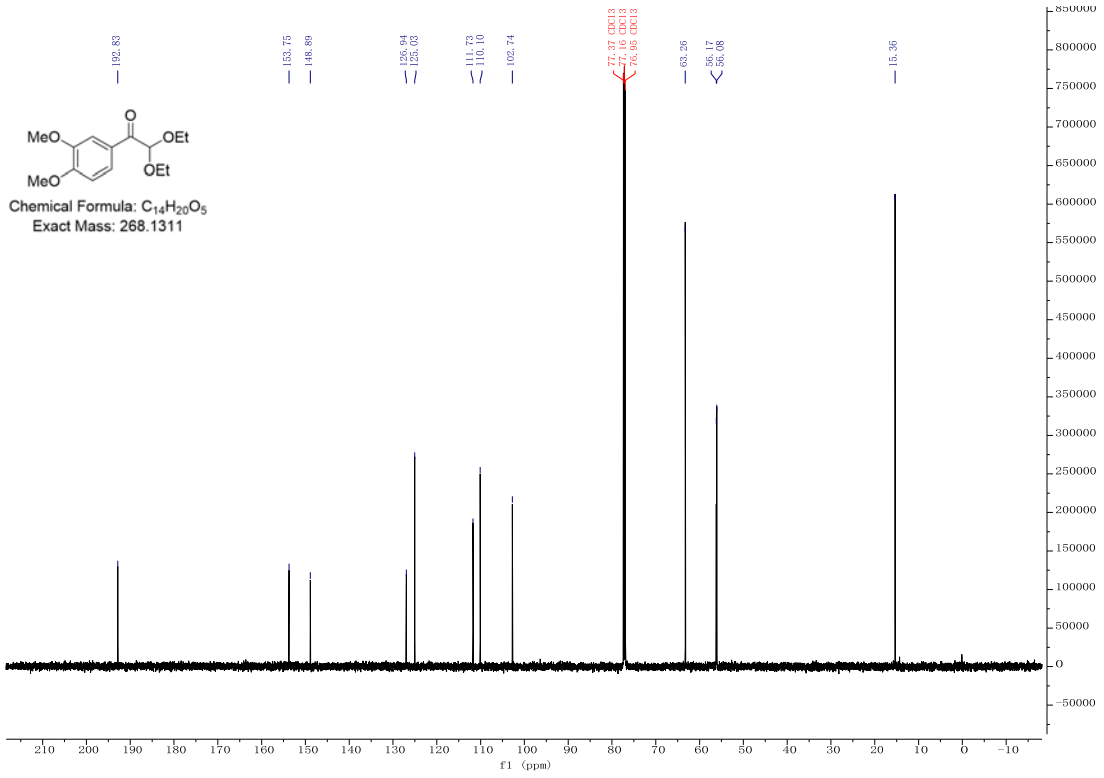
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **1h**



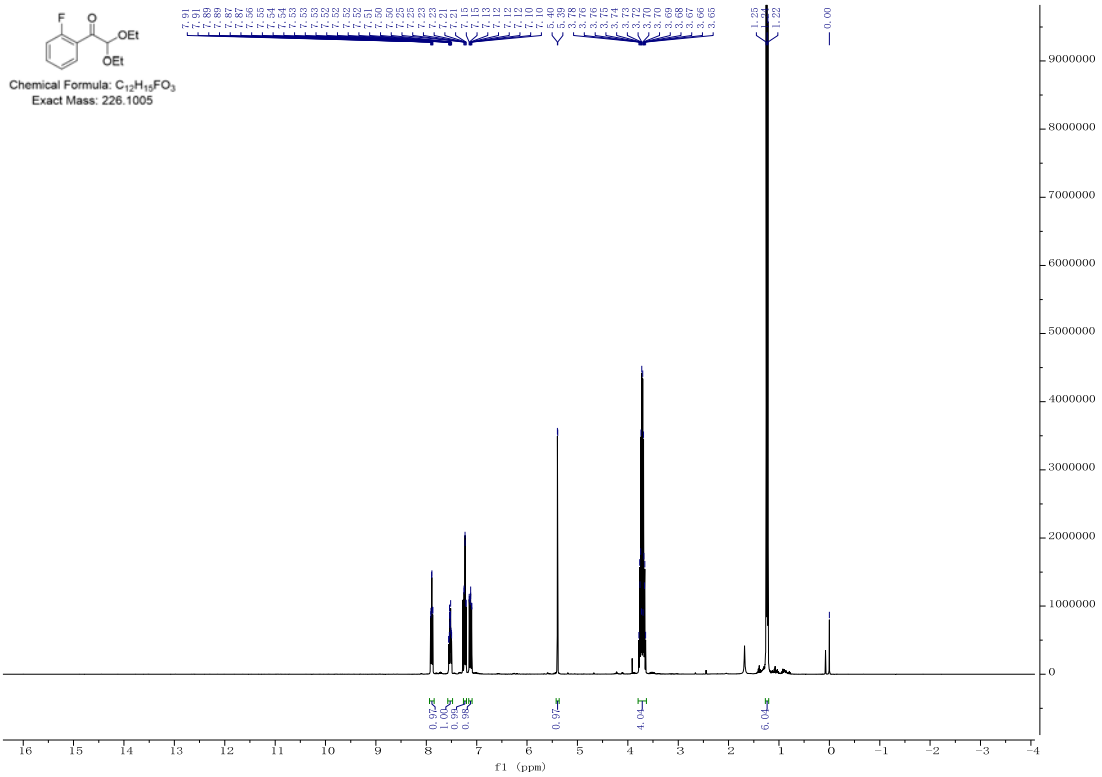
^{1}H NMR (600 MHz, Chloroform-d) of compound **1i**



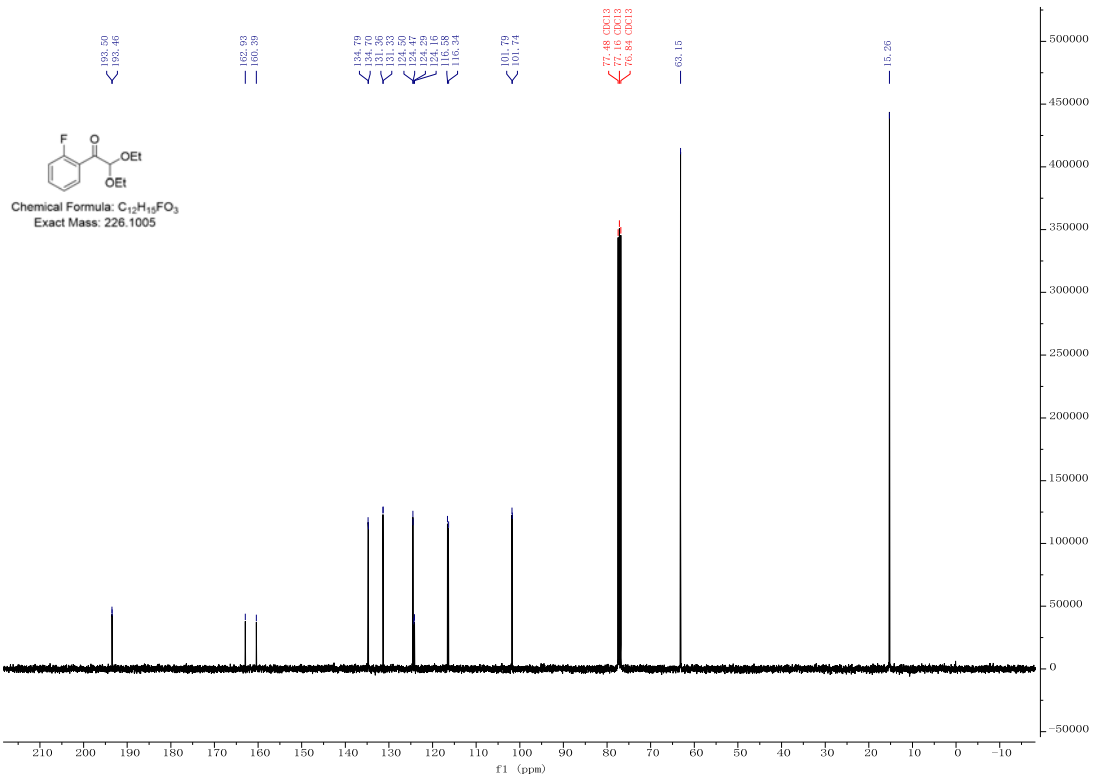
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **1i**



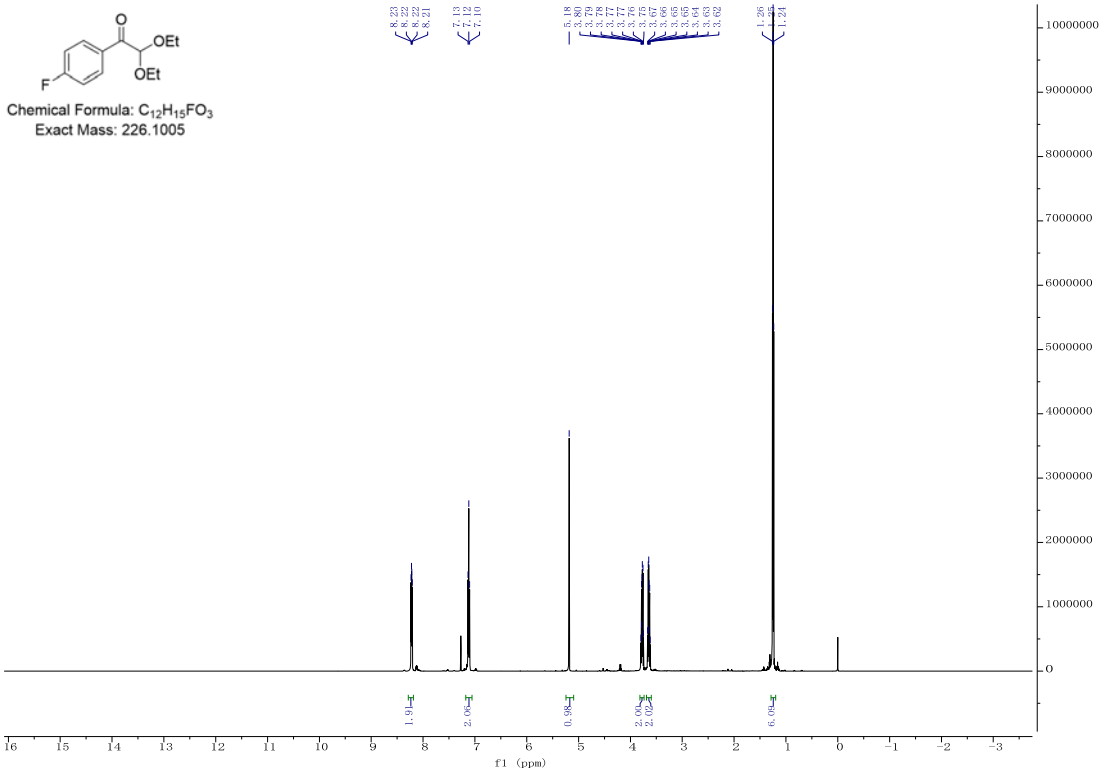
^{1}H NMR (400 MHz, Chloroform-d) of compound **1j**



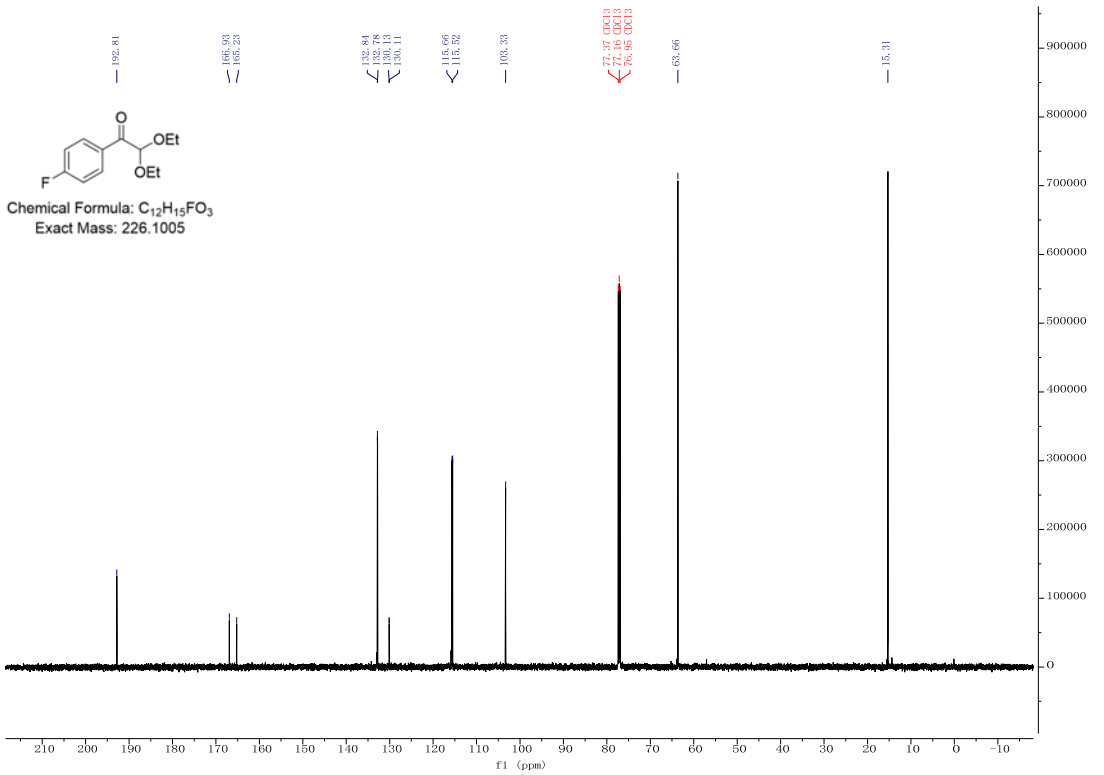
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **1j**



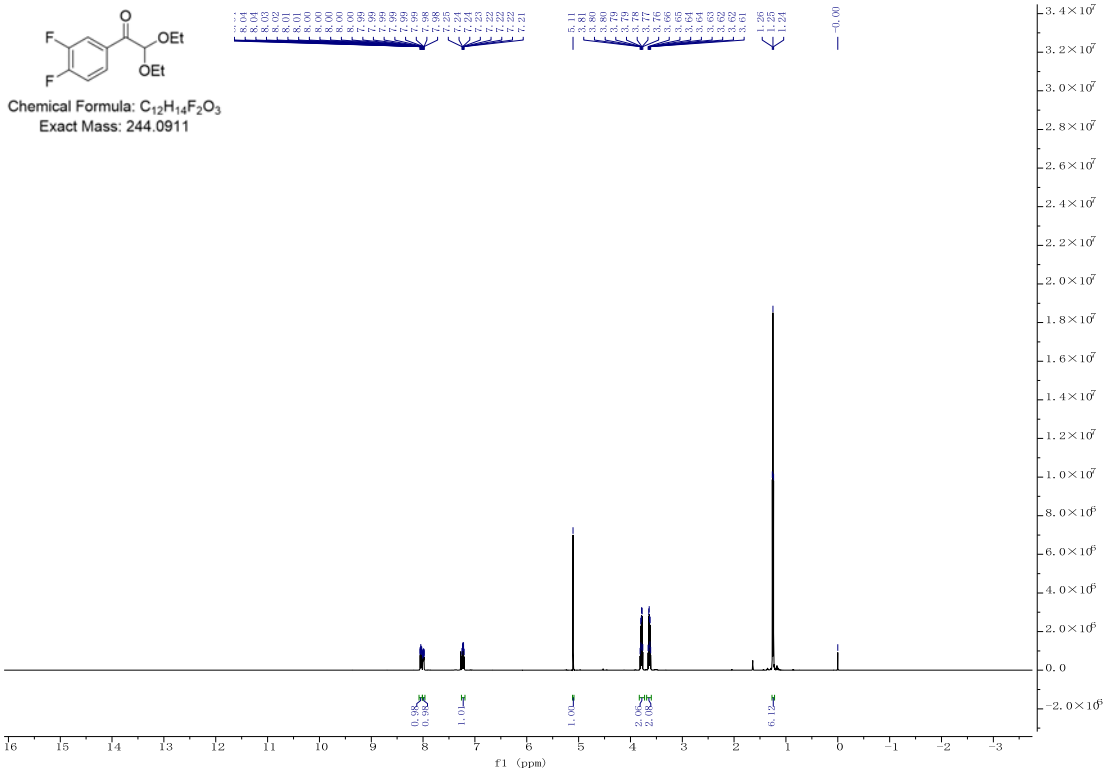
^{1}H NMR (600 MHz, Chloroform-d) of compound **1k**



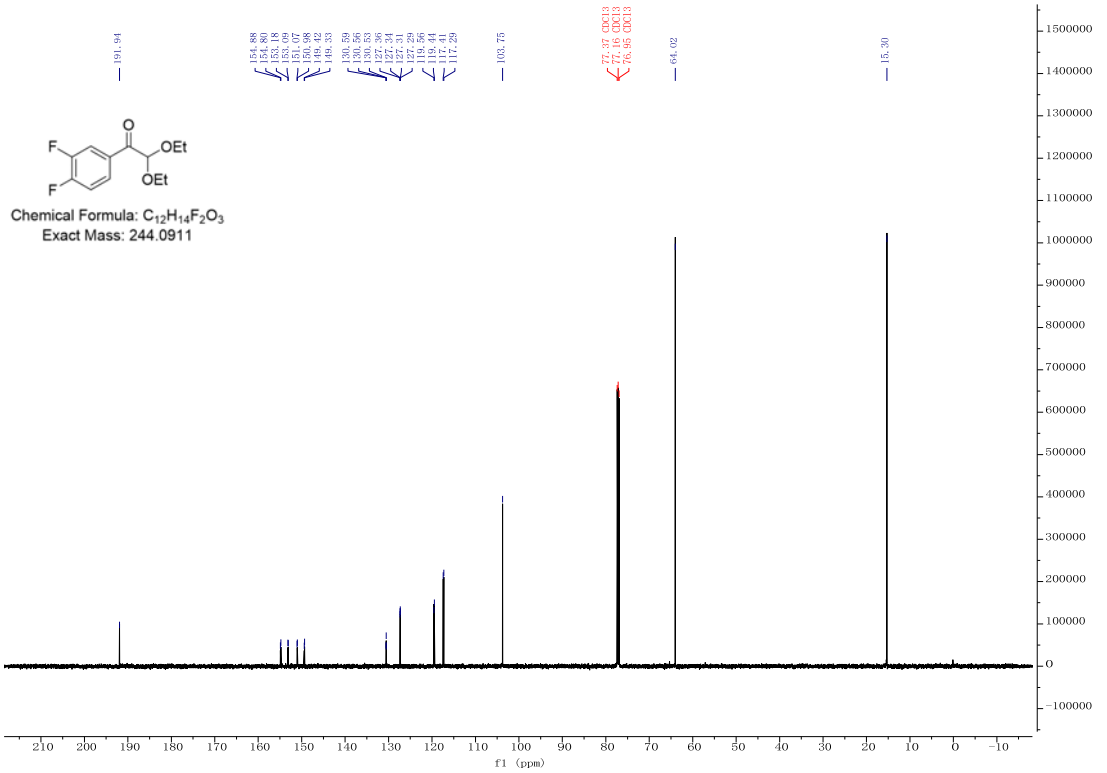
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **1k**



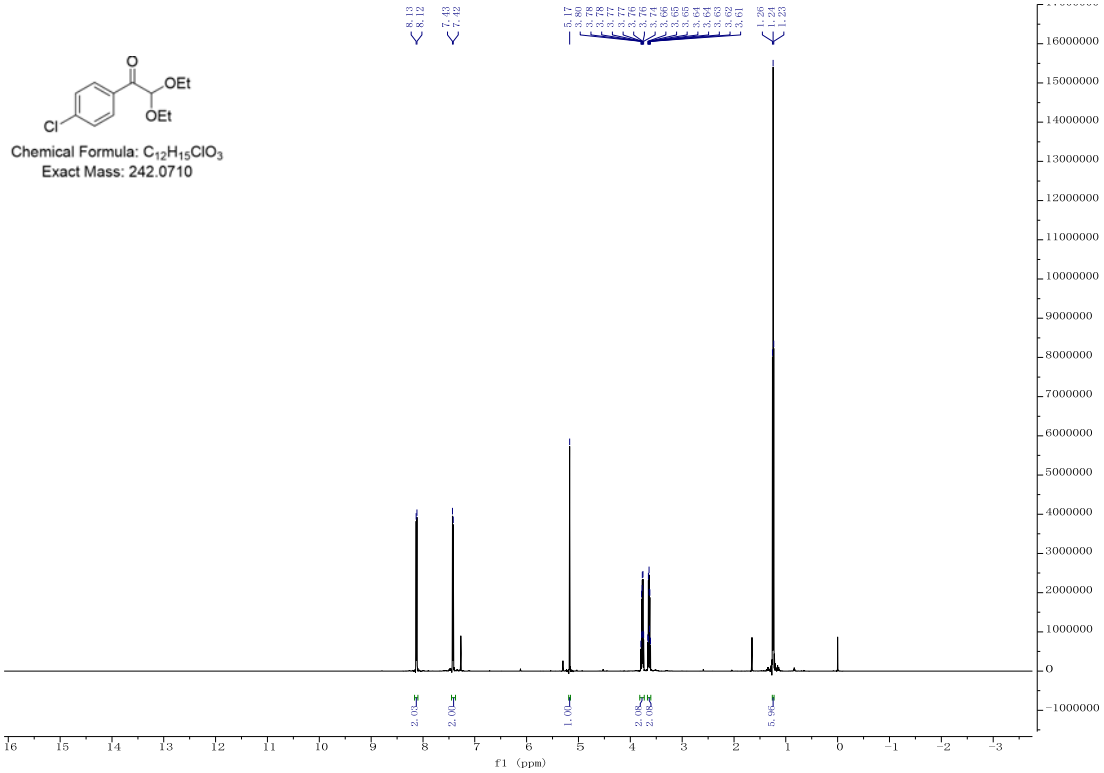
^{1}H NMR (600 MHz, Chloroform-d) of compound **1l**



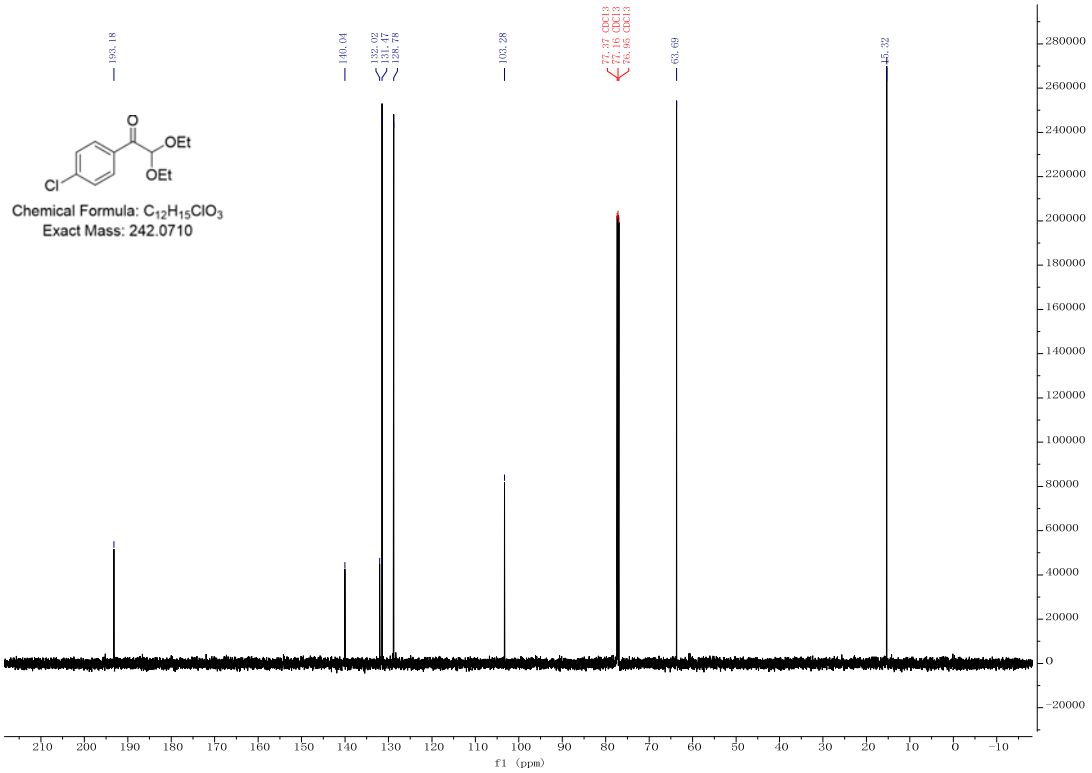
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **1l**



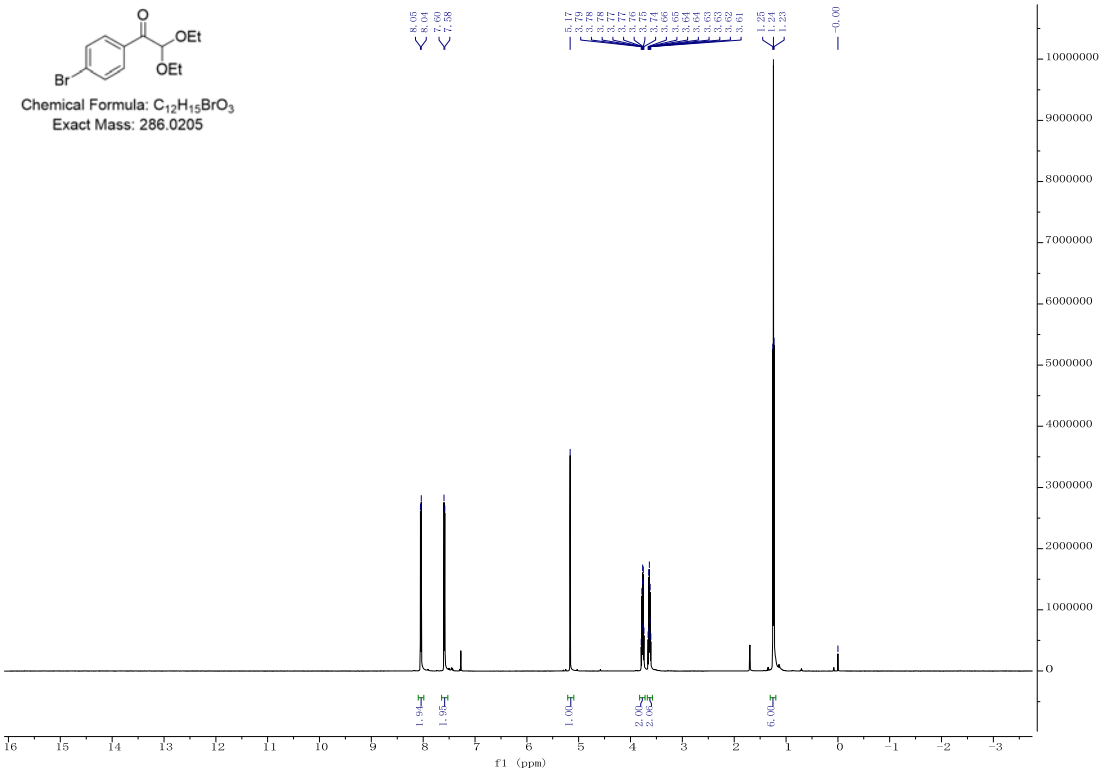
^{1}H NMR (600 MHz, Chloroform-d) of compound **1m**



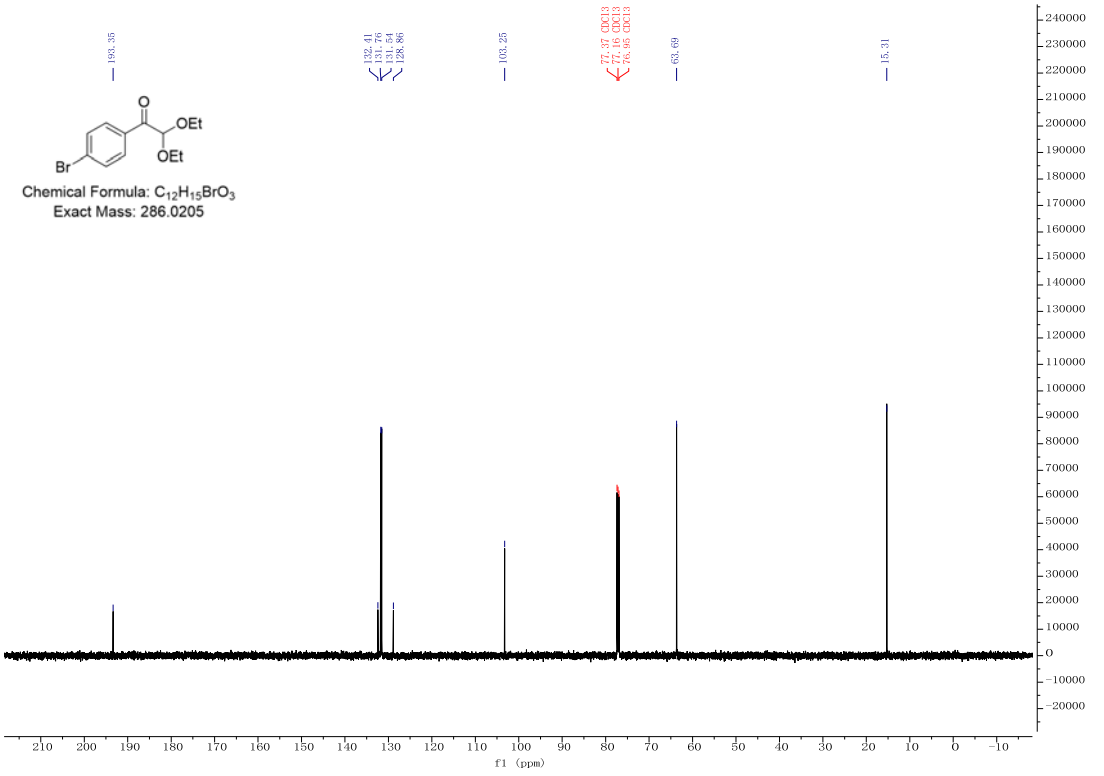
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **1m**



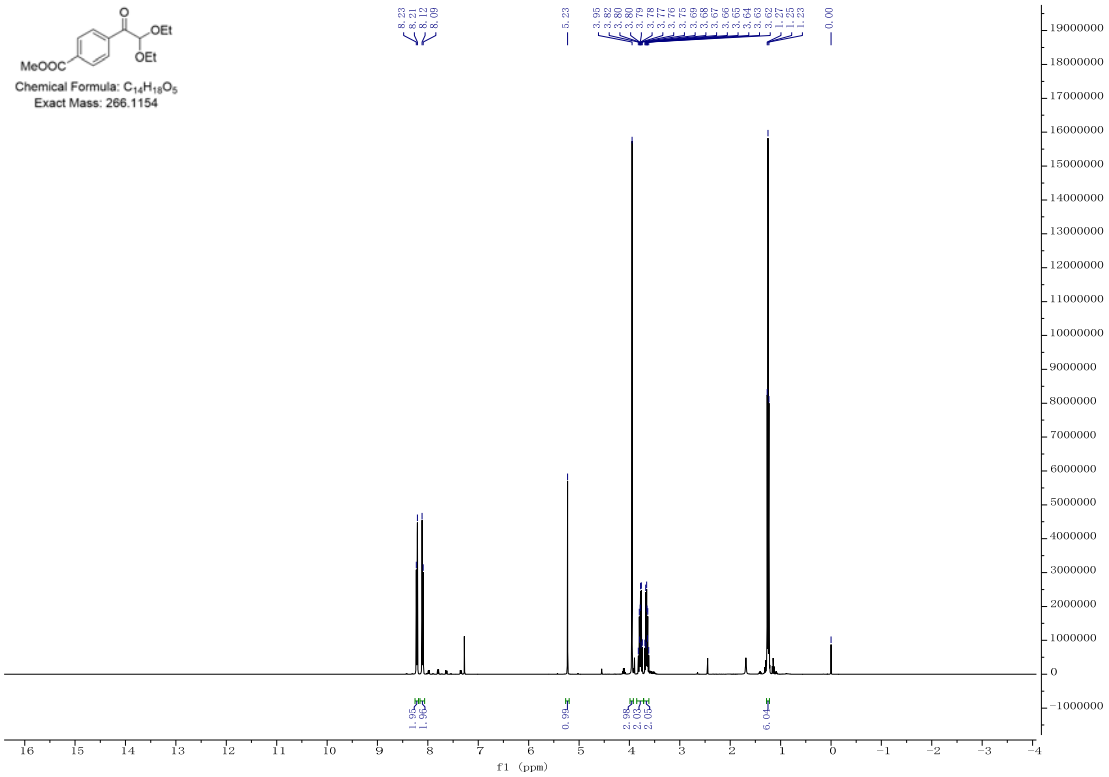
^{1}H NMR (600 MHz, Chloroform-d) of compound **1n**



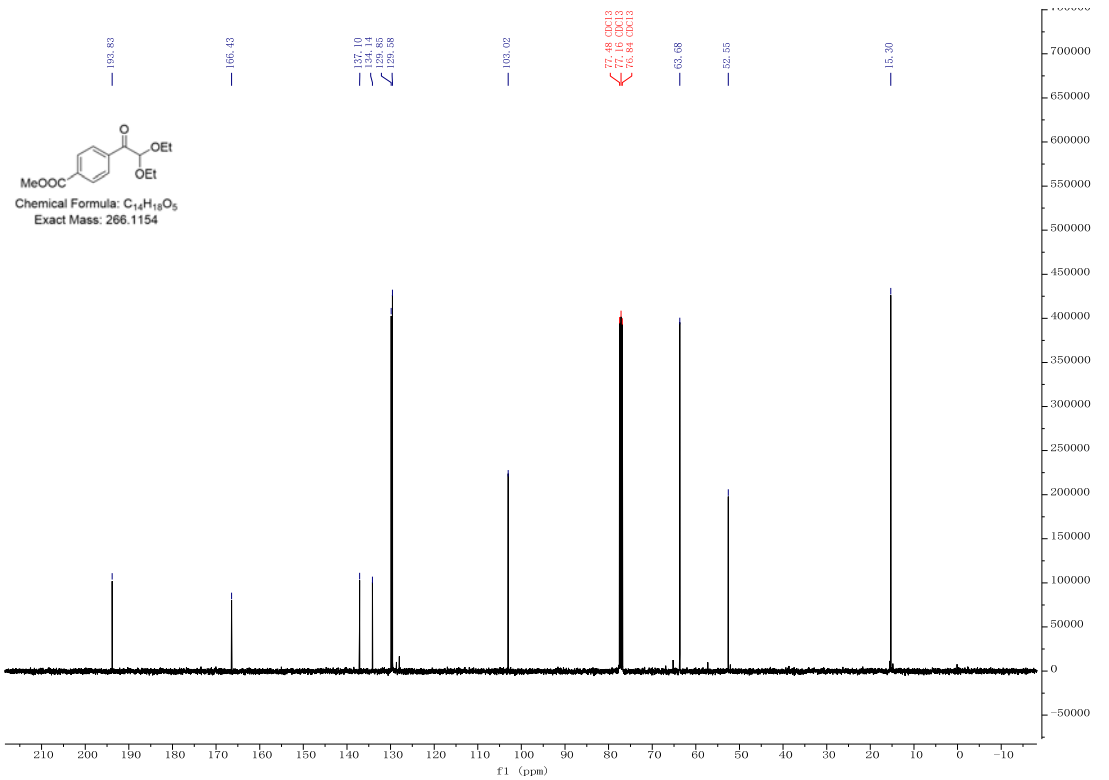
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **1n**



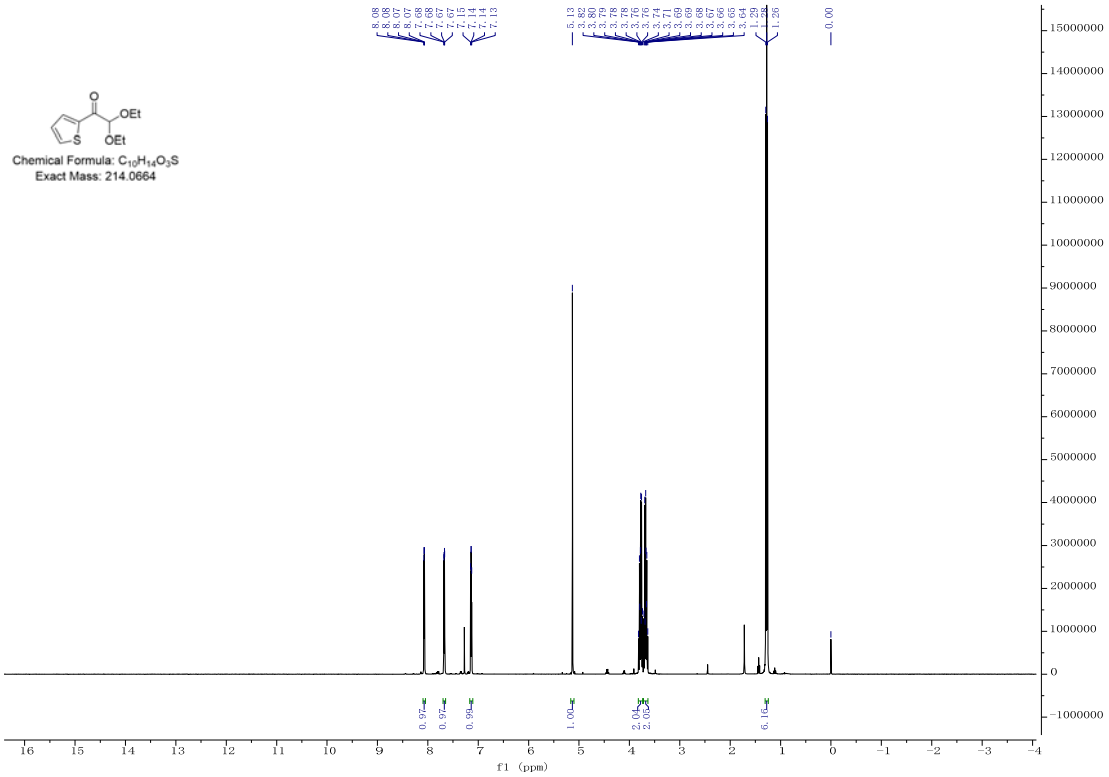
^{1}H NMR (400 MHz, Chloroform-d) of compound **1o**



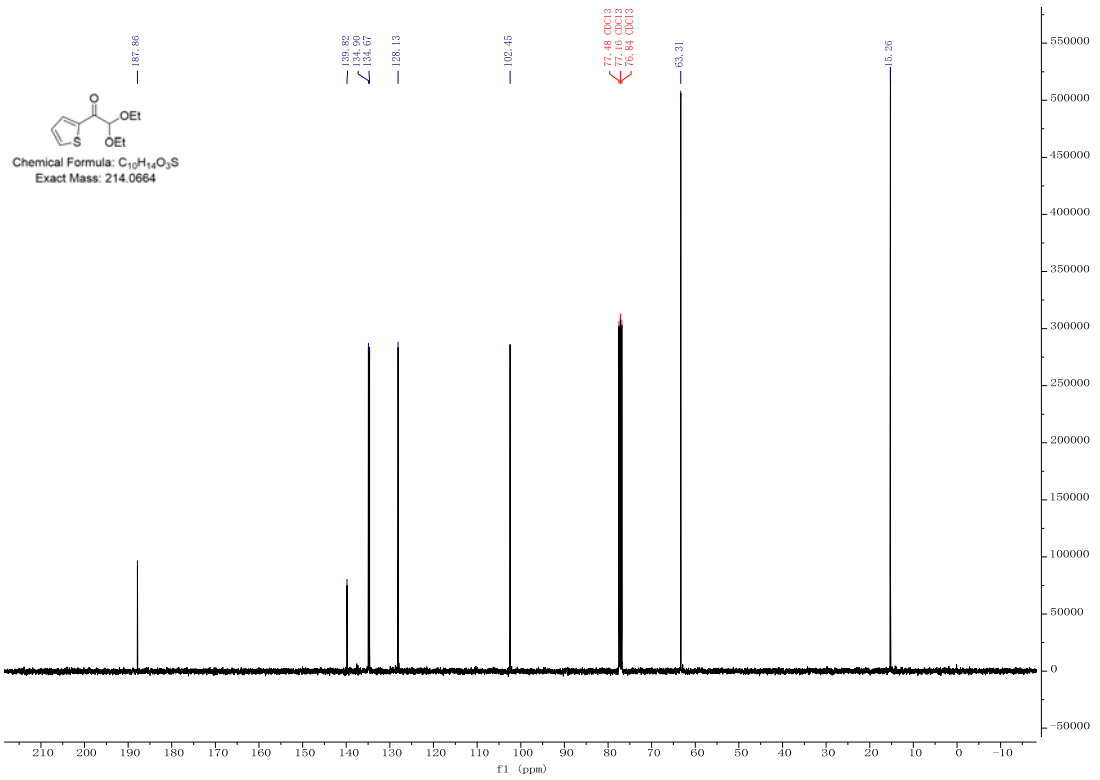
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **1o**



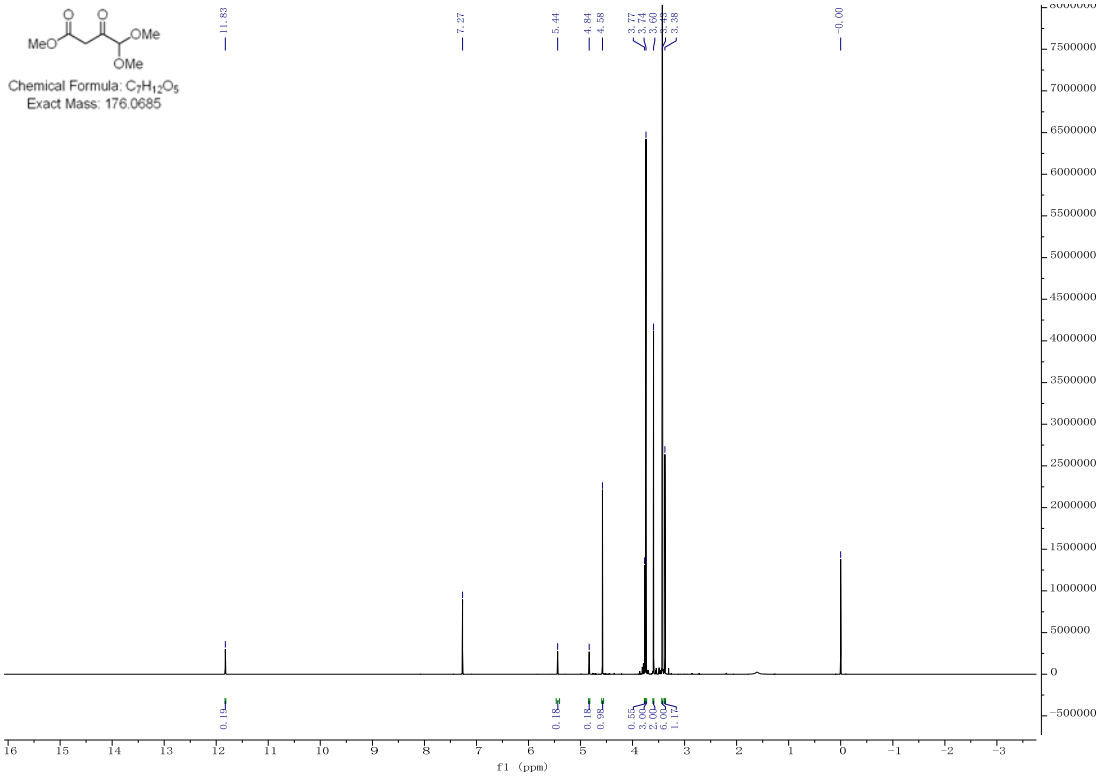
^{1}H NMR (400 MHz, Chloroform-d) of compound **1p**



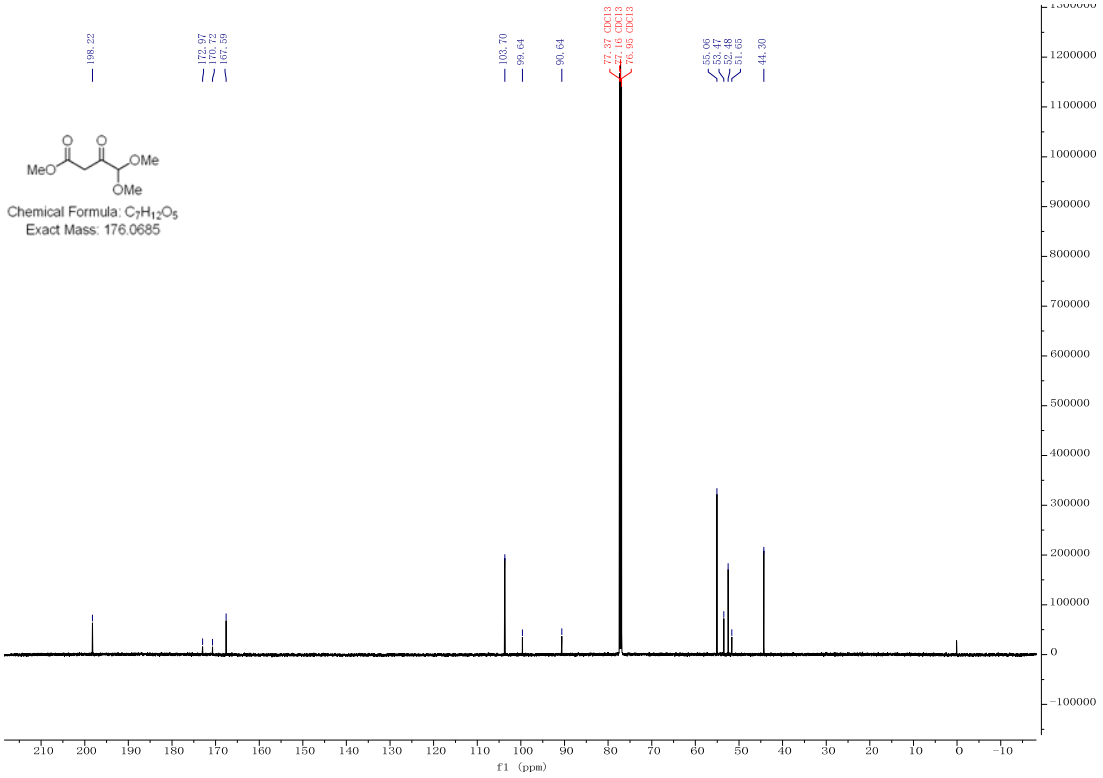
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **1p**



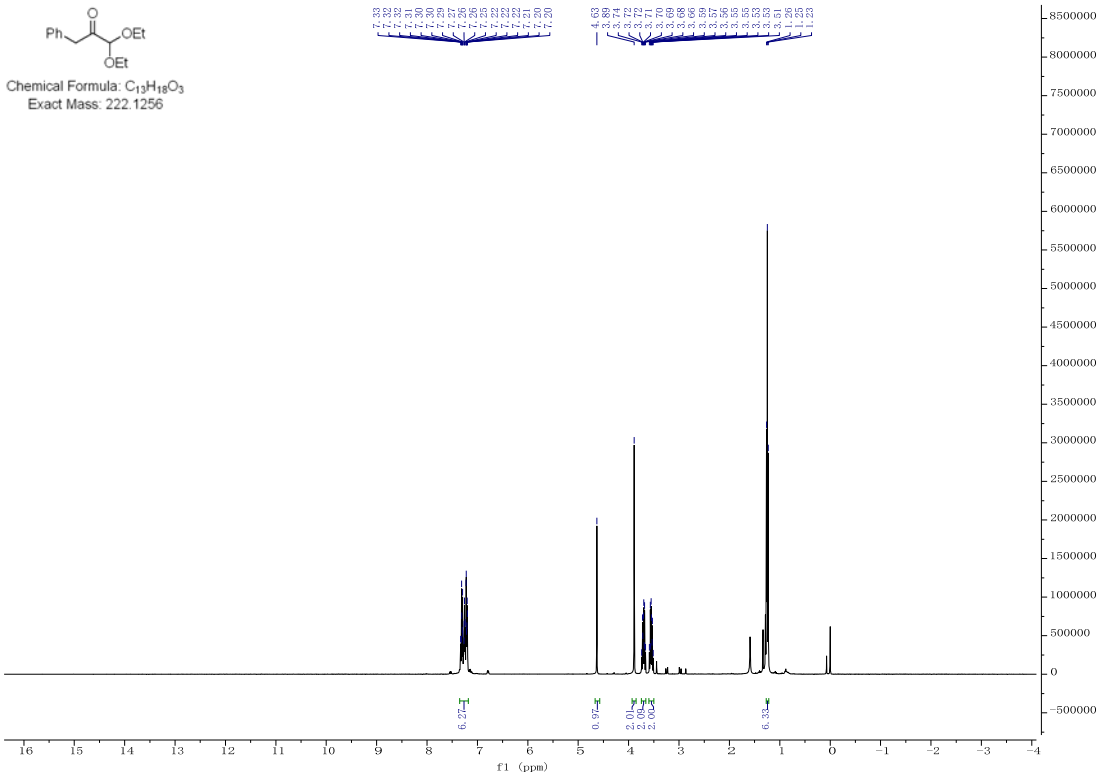
^{1}H NMR (600 MHz, Chloroform-d) of compound **1q**



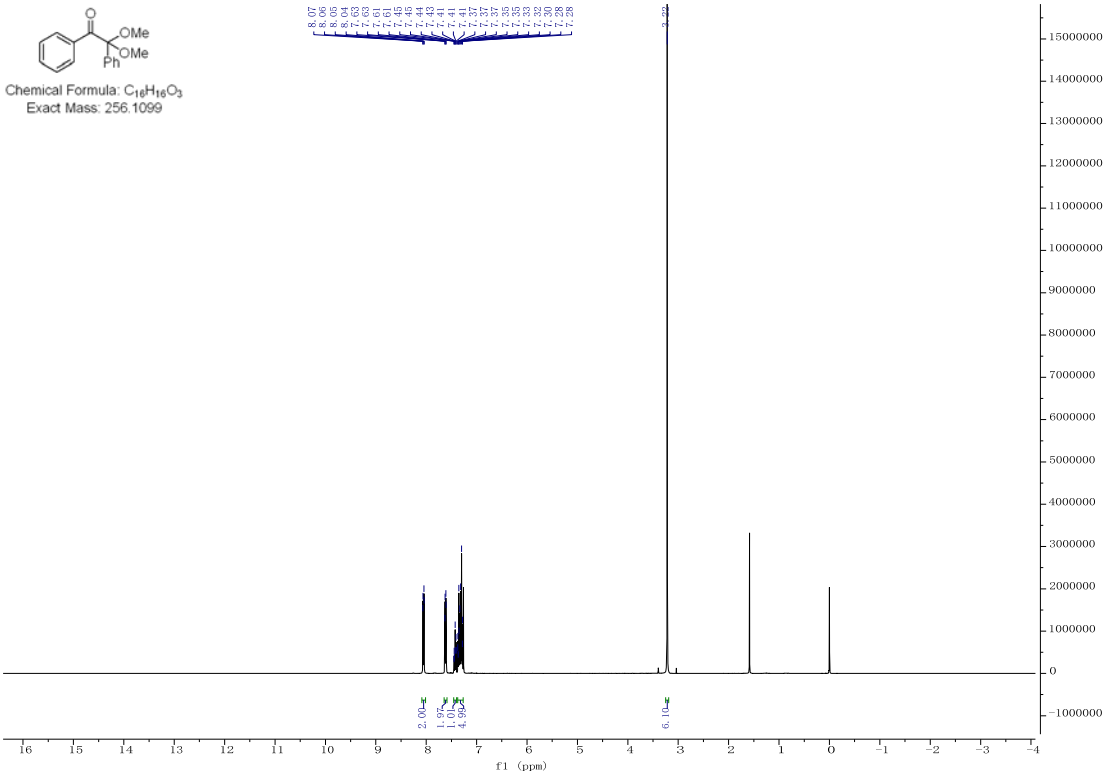
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **1q**



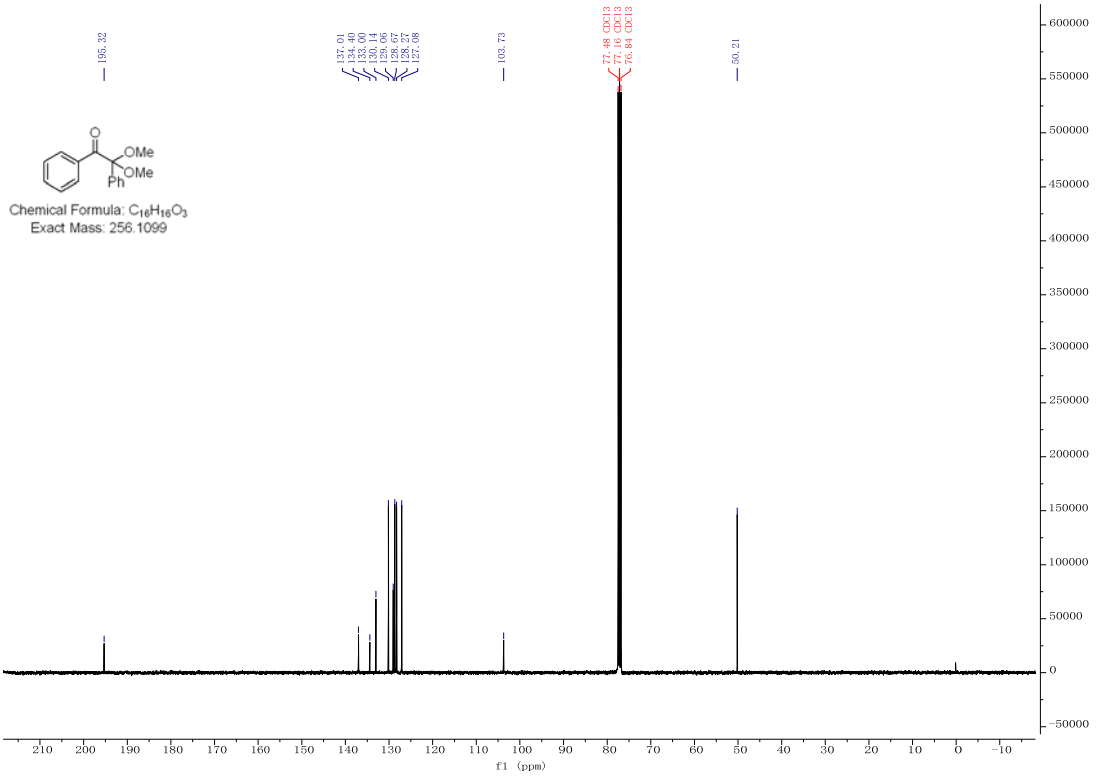
^{1}H NMR (400 MHz, Chloroform-d) of compound **1r**



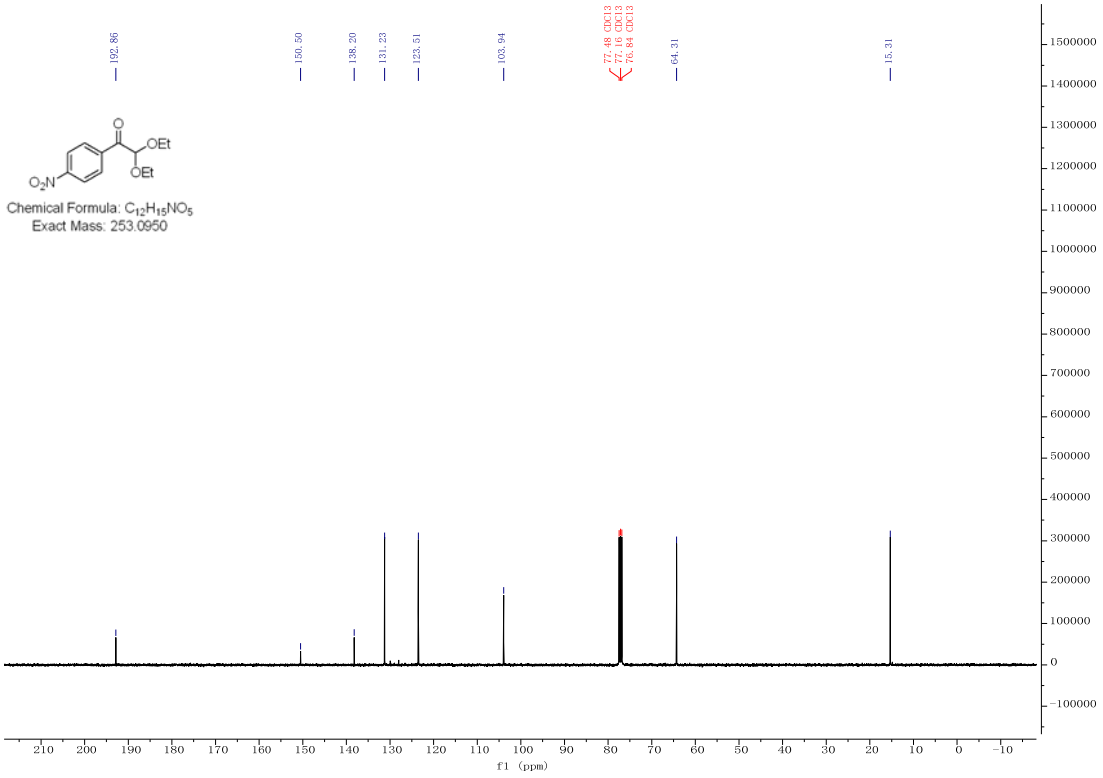
^{1}H NMR (400 MHz, Chloroform-d) of compound **1s**



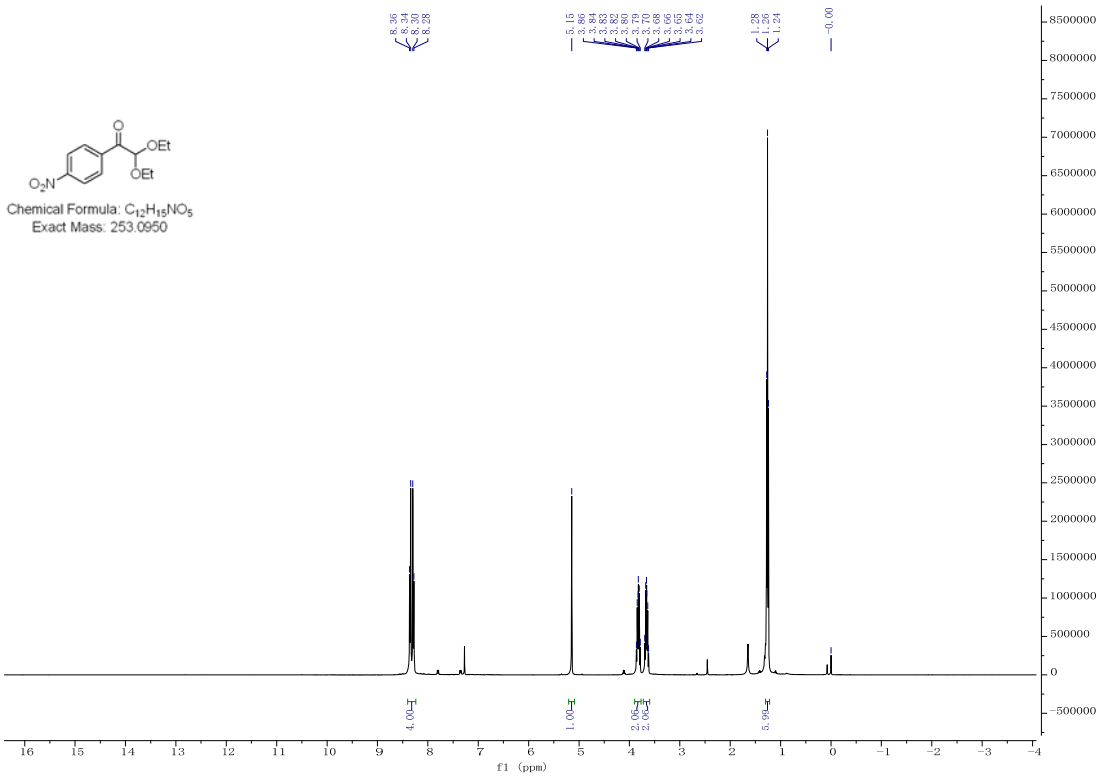
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **1s**



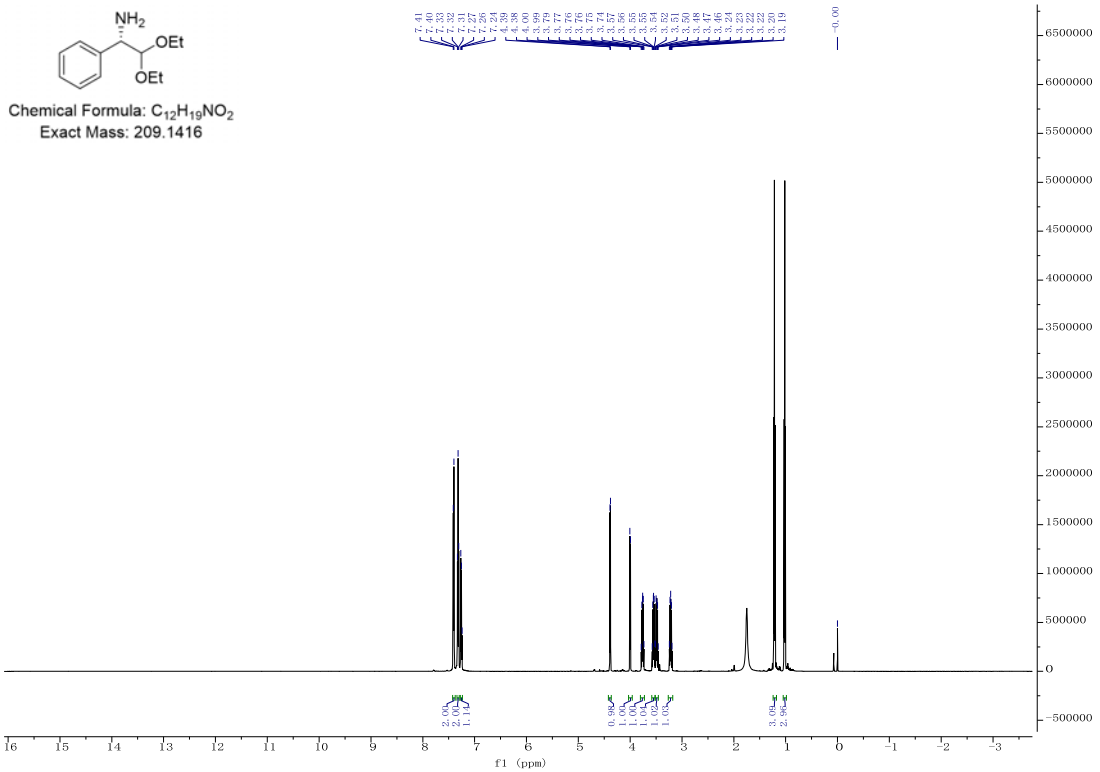
^{1}H NMR (400 MHz, Chloroform-d) of compound **1t**



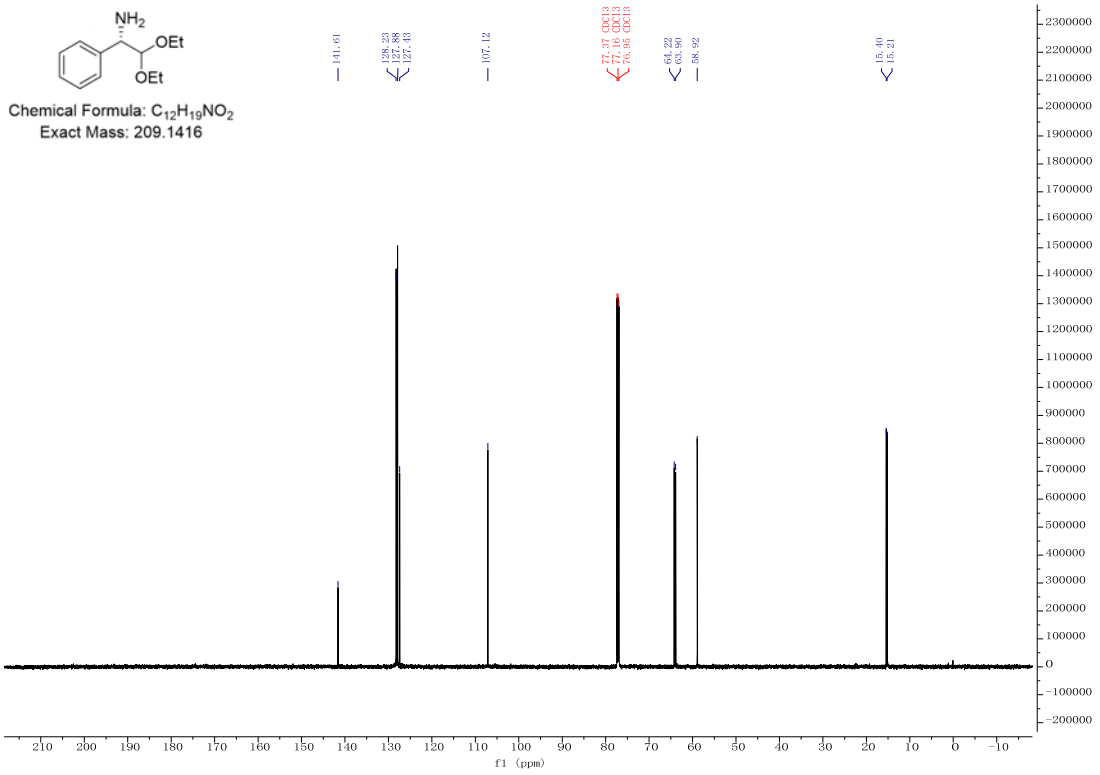
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **1t**



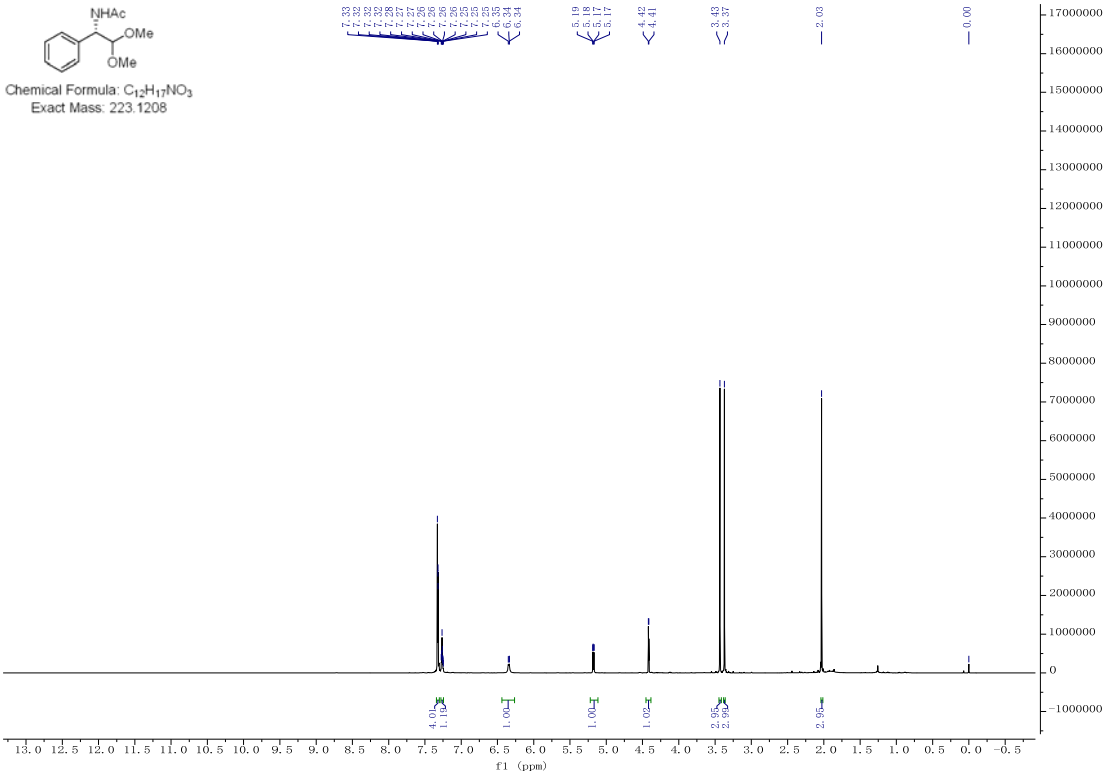
^{1}H NMR (600 MHz, Chloroform-d) of compound **2aa**



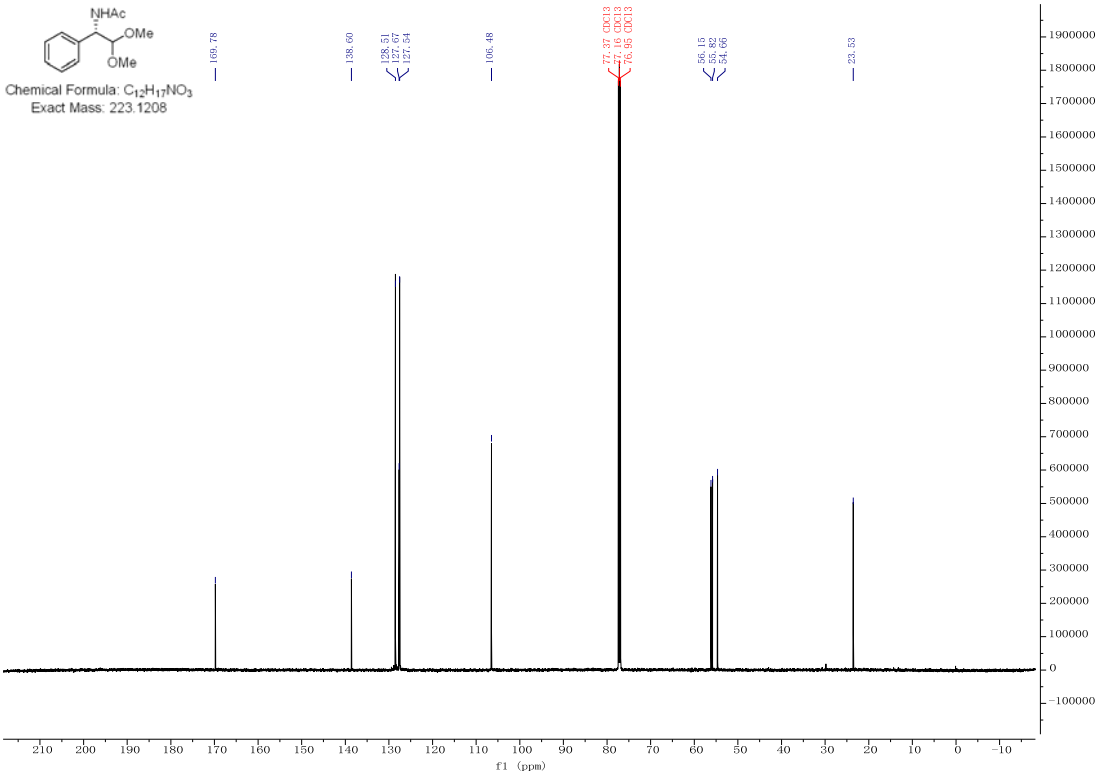
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **2aa**



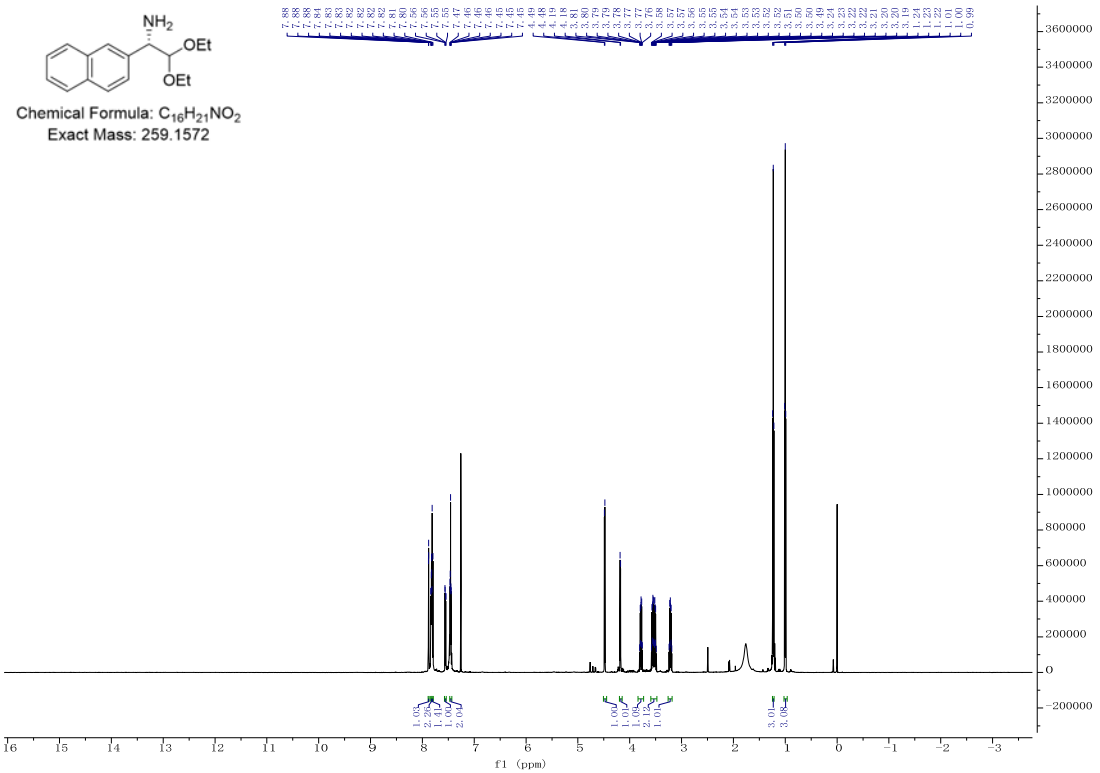
^{1}H NMR (600 MHz, Chloroform-d) of compound **2ab-Ac**



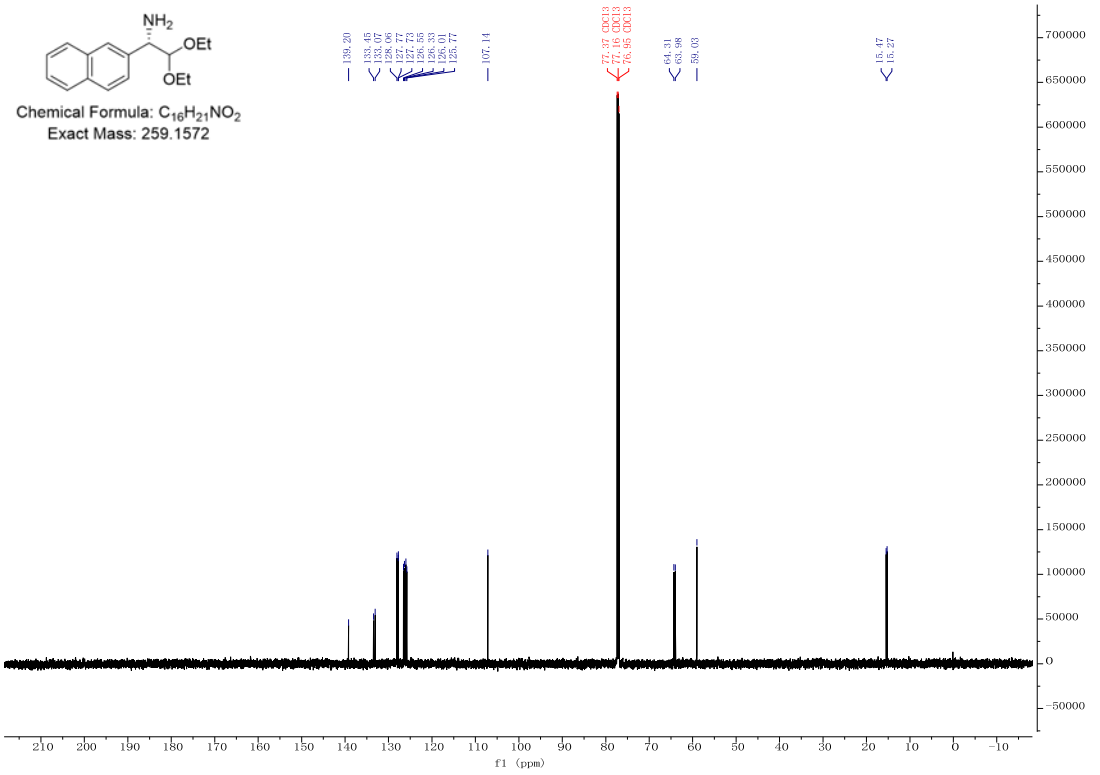
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **2ab-Ac**



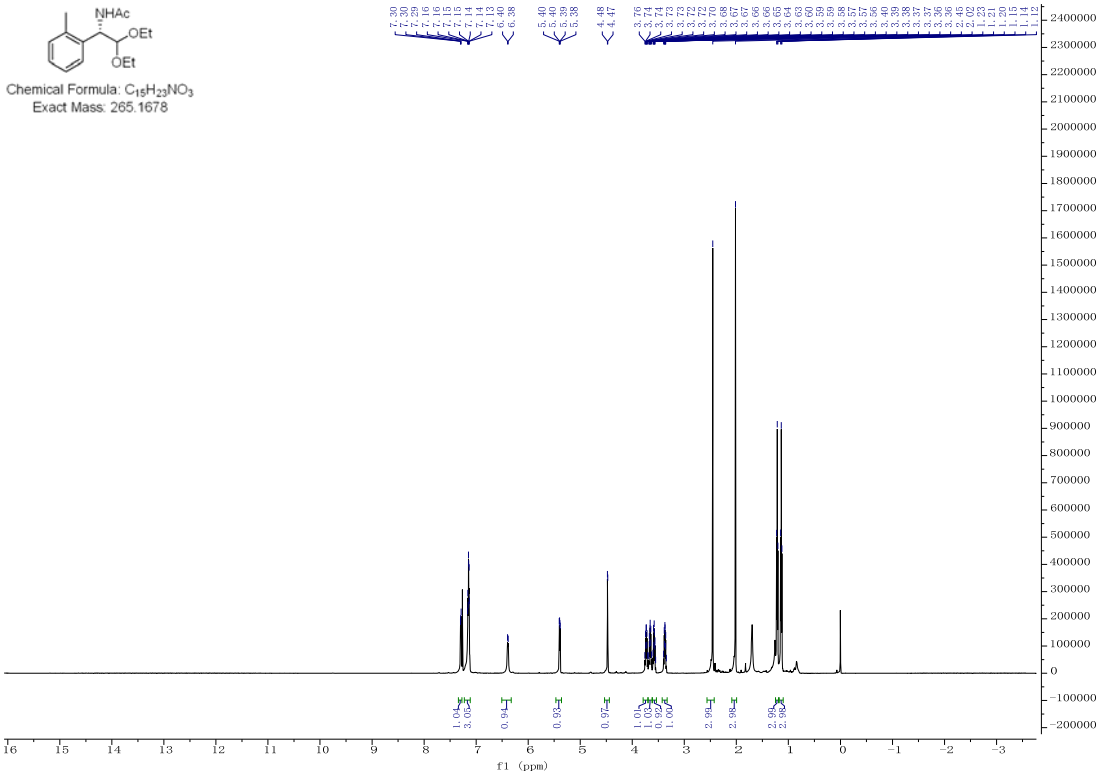
^{1}H NMR (600 MHz, Chloroform-d) of compound **2b**



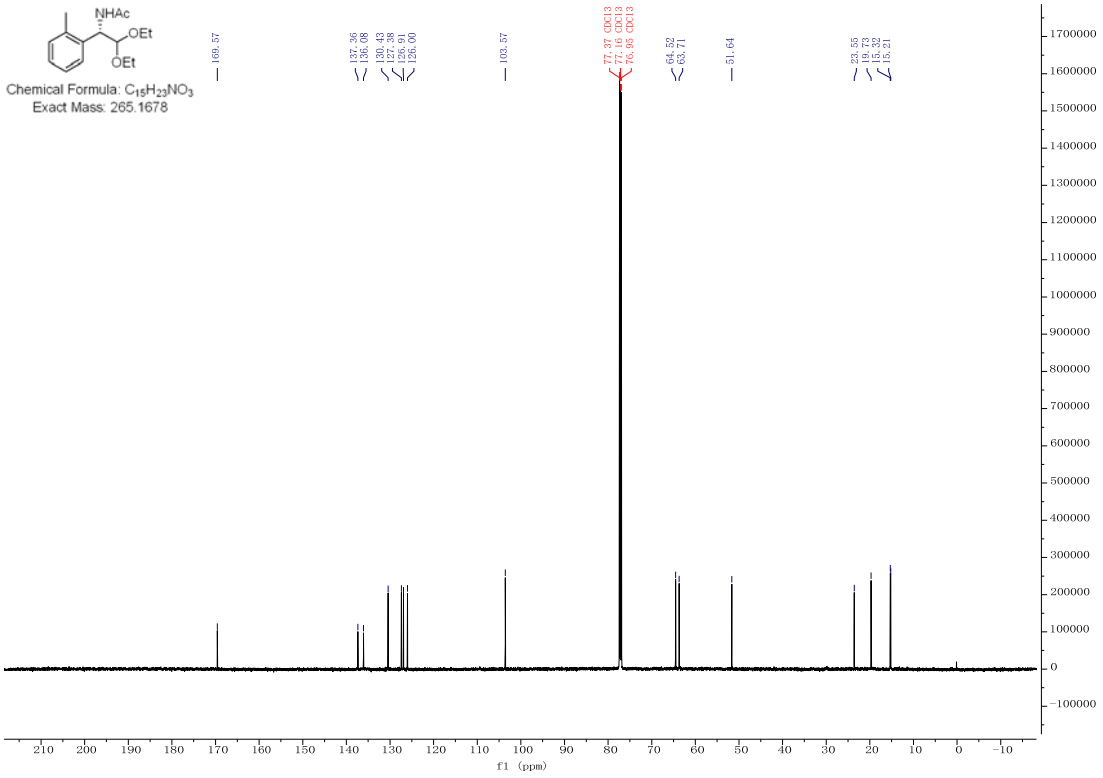
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **2b**



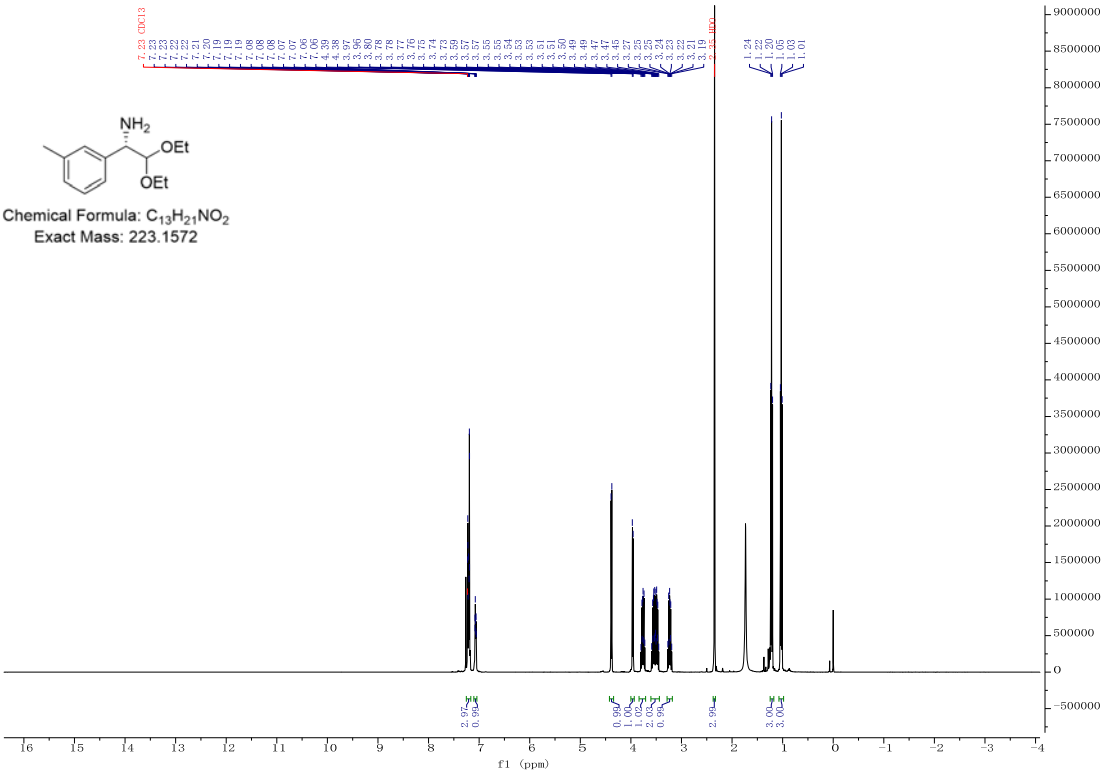
^{1}H NMR (600 MHz, Chloroform-d) of compound **2c-Ac**



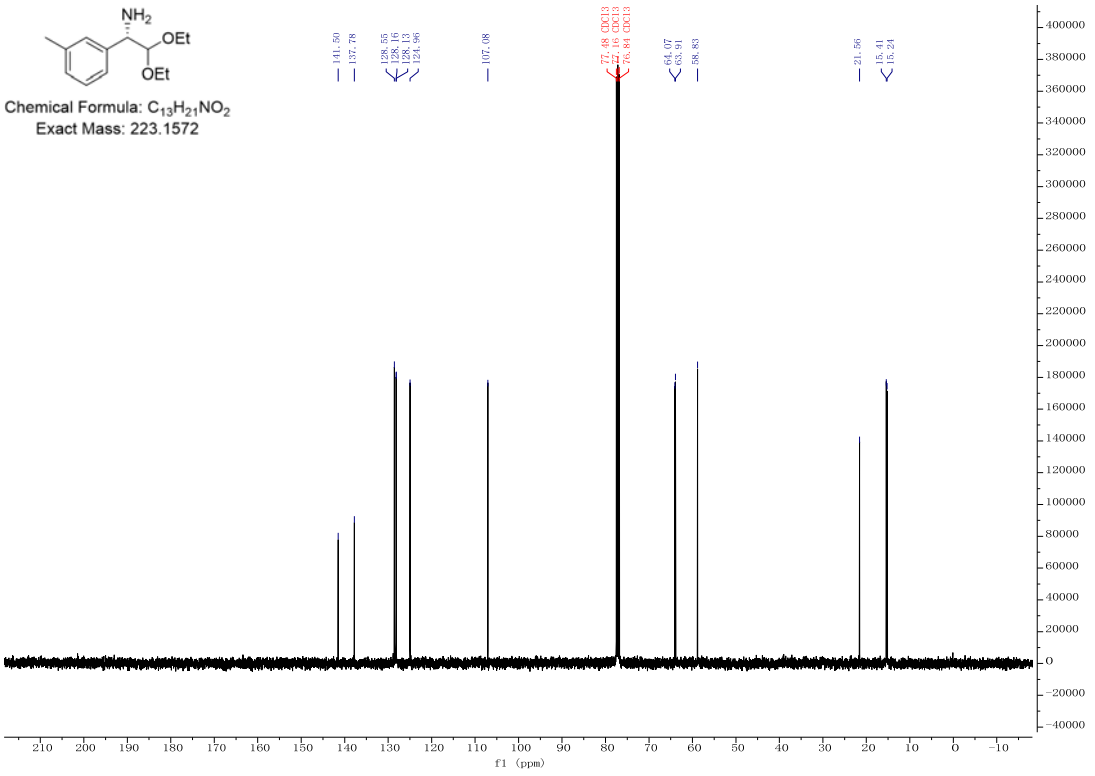
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **2c-Ac**



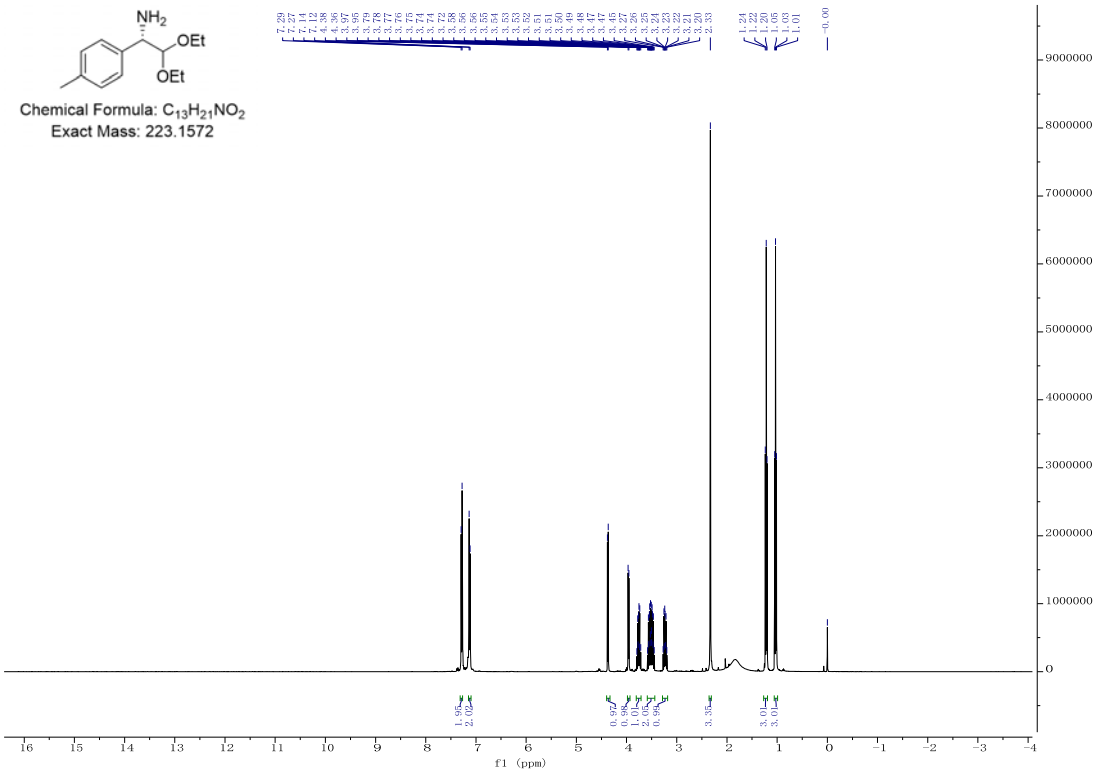
^{1}H NMR (400 MHz, Chloroform-d) of compound **2d**



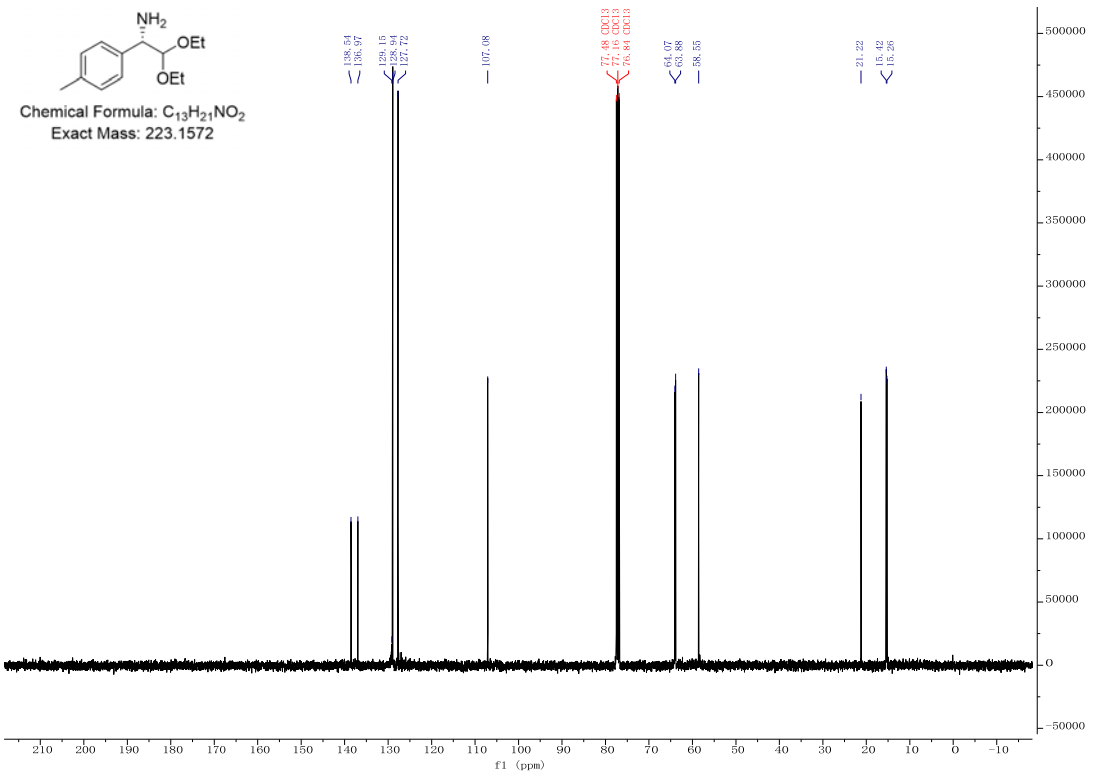
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **2d**



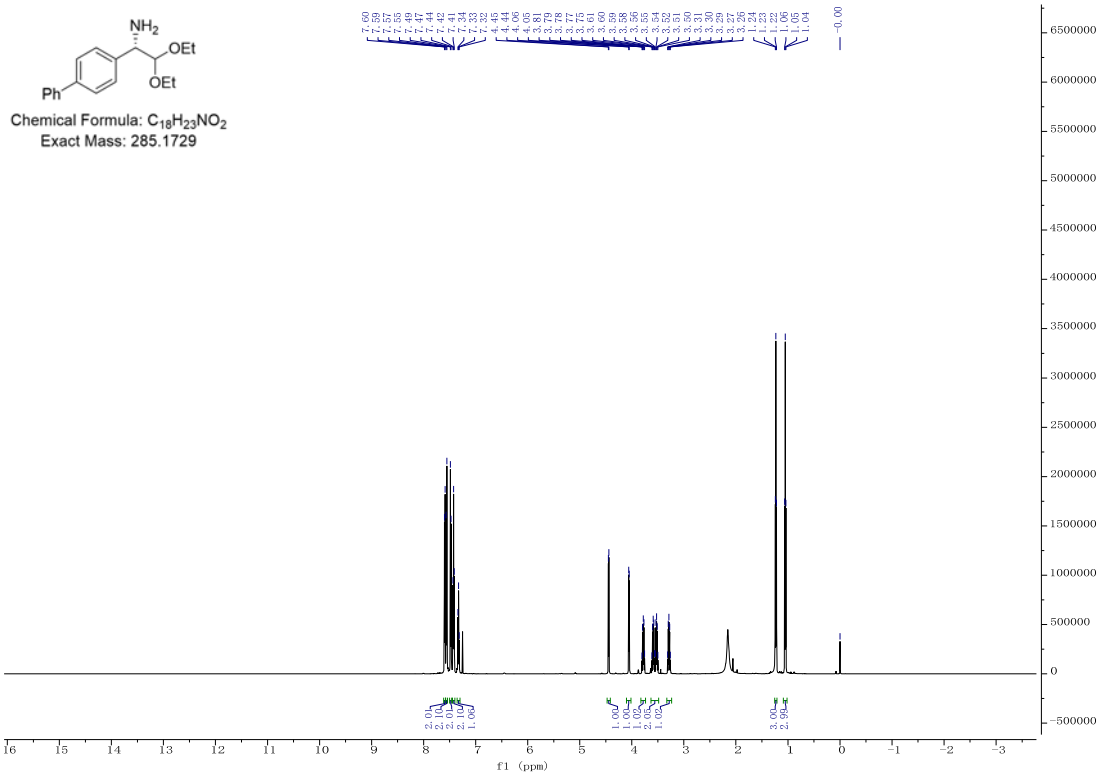
^{1}H NMR (400 MHz, Chloroform-d) of compound **2e**



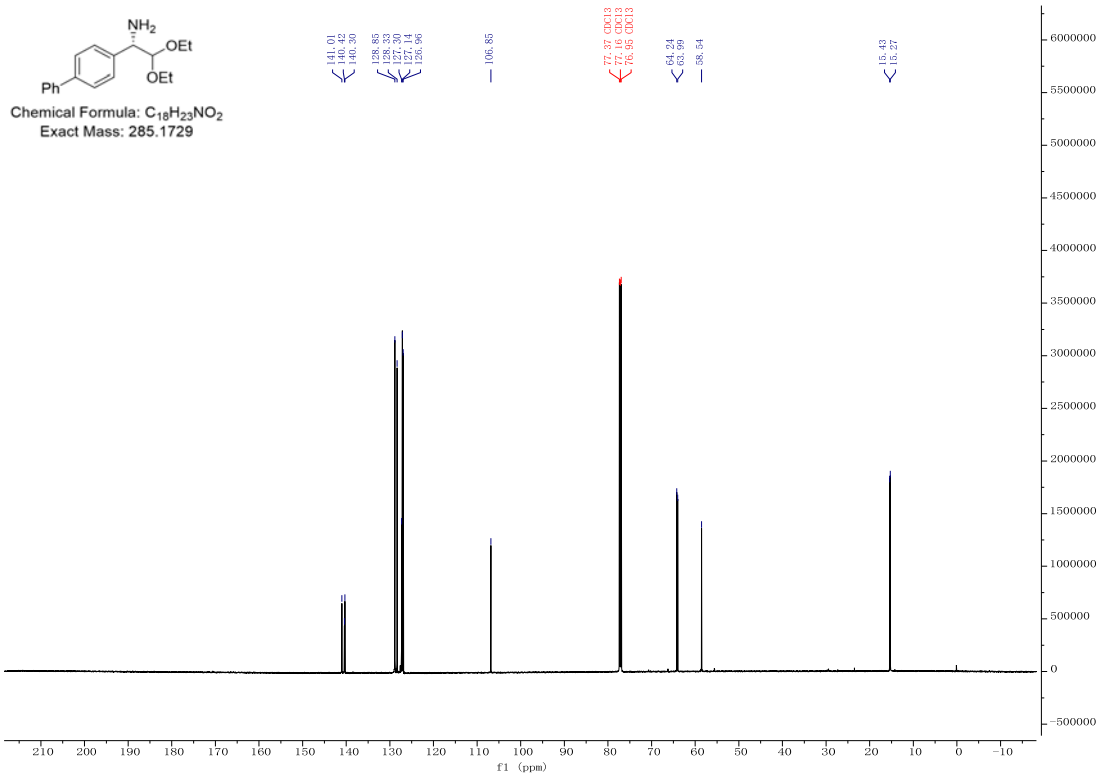
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **2a**



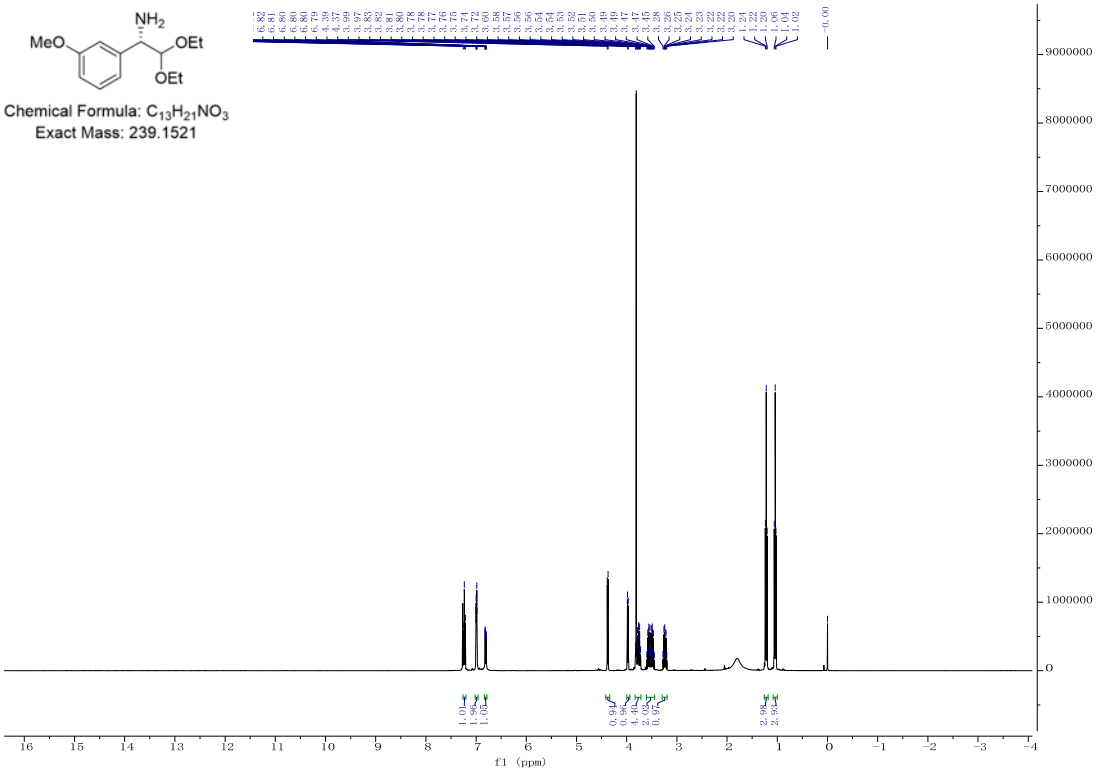
^{1}H NMR (600 MHz, Chloroform-d) of compound **2f**



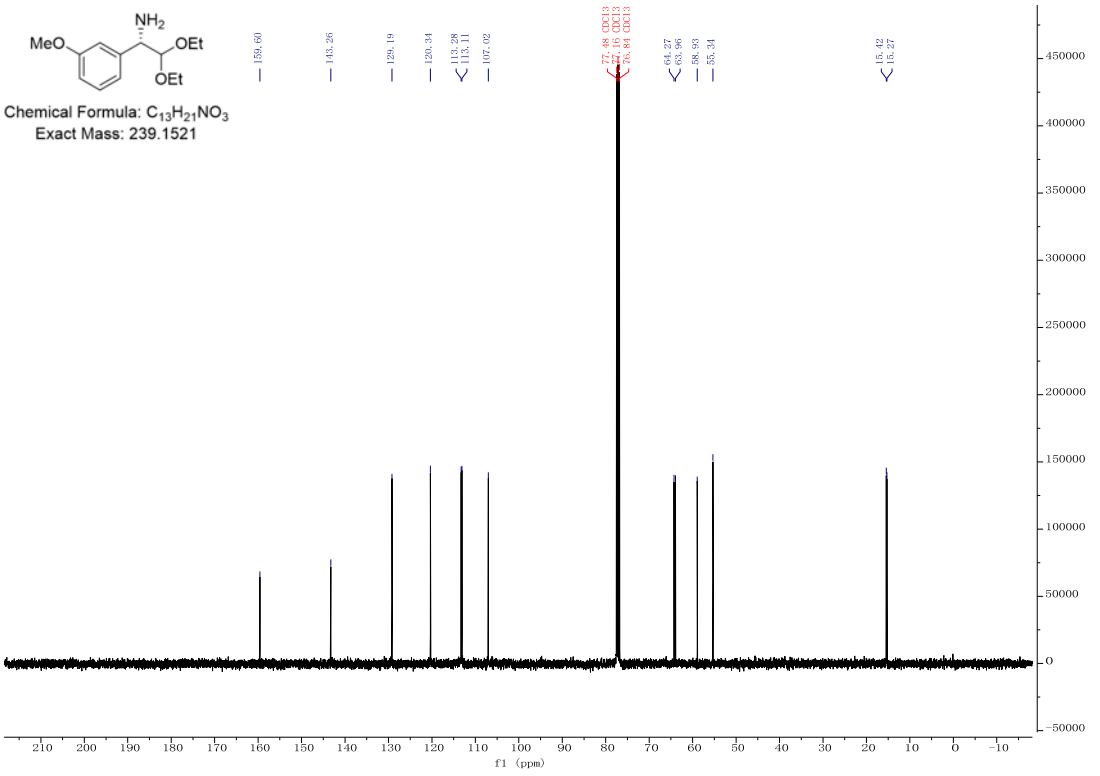
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **2f**



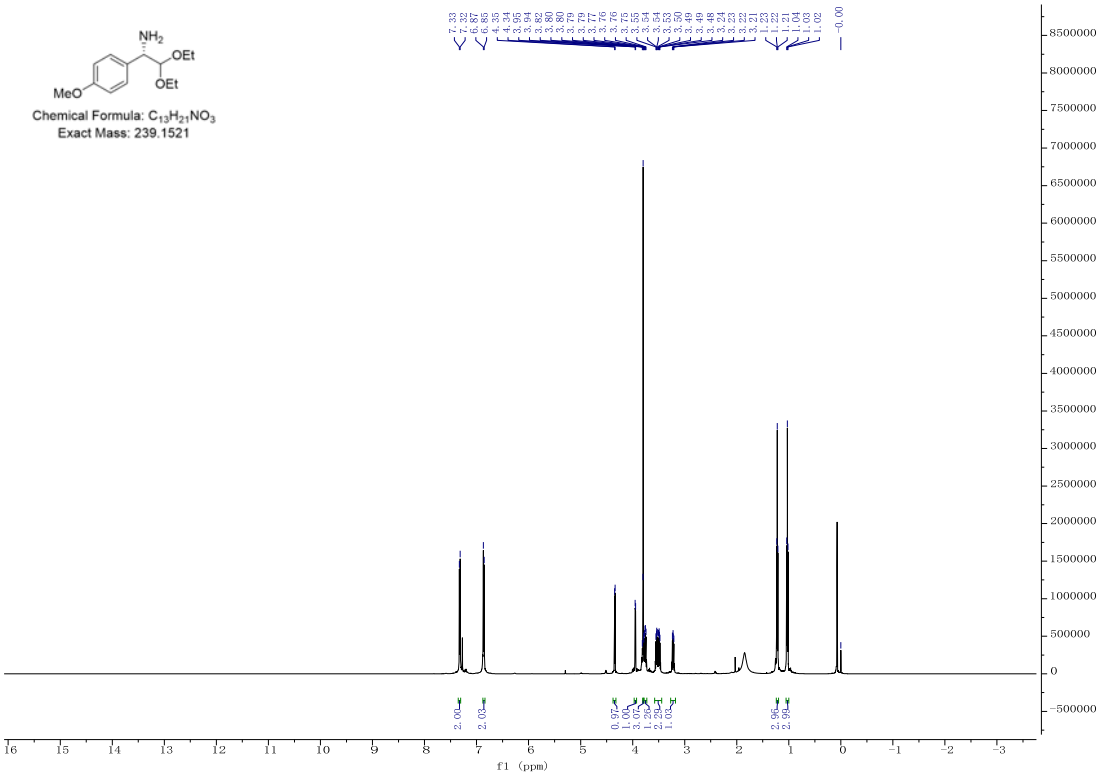
^{1}H NMR (400 MHz, Chloroform-d) of compound **2g**



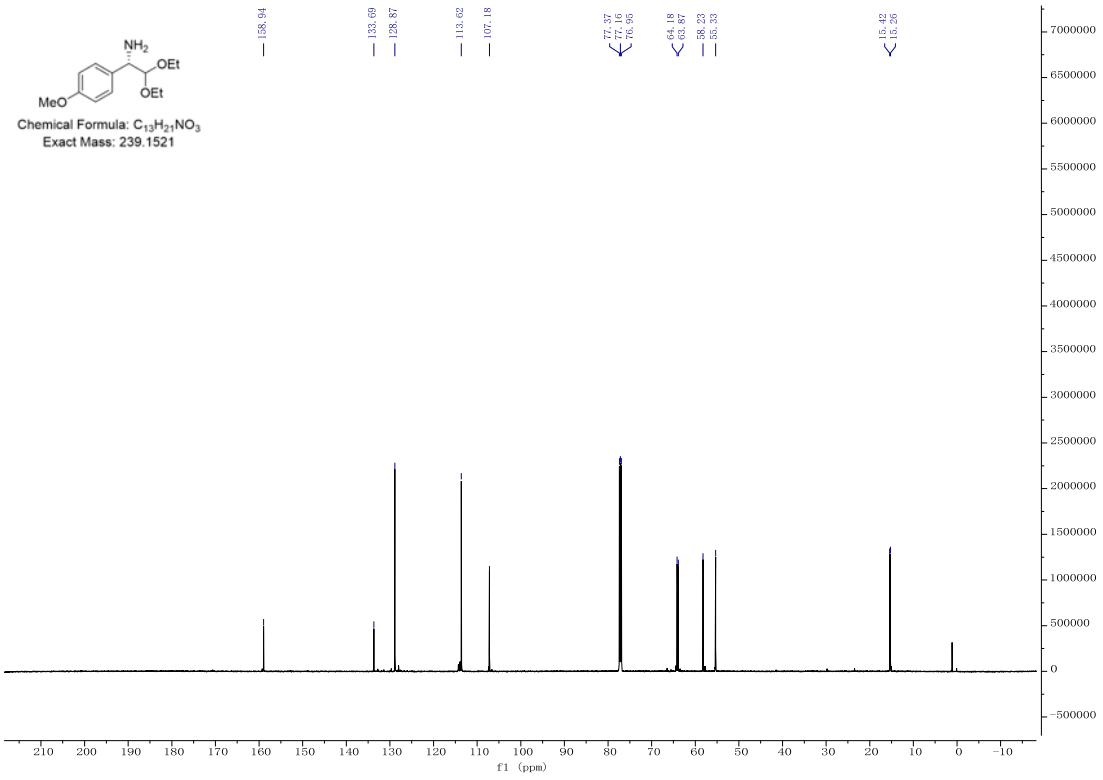
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **2g**



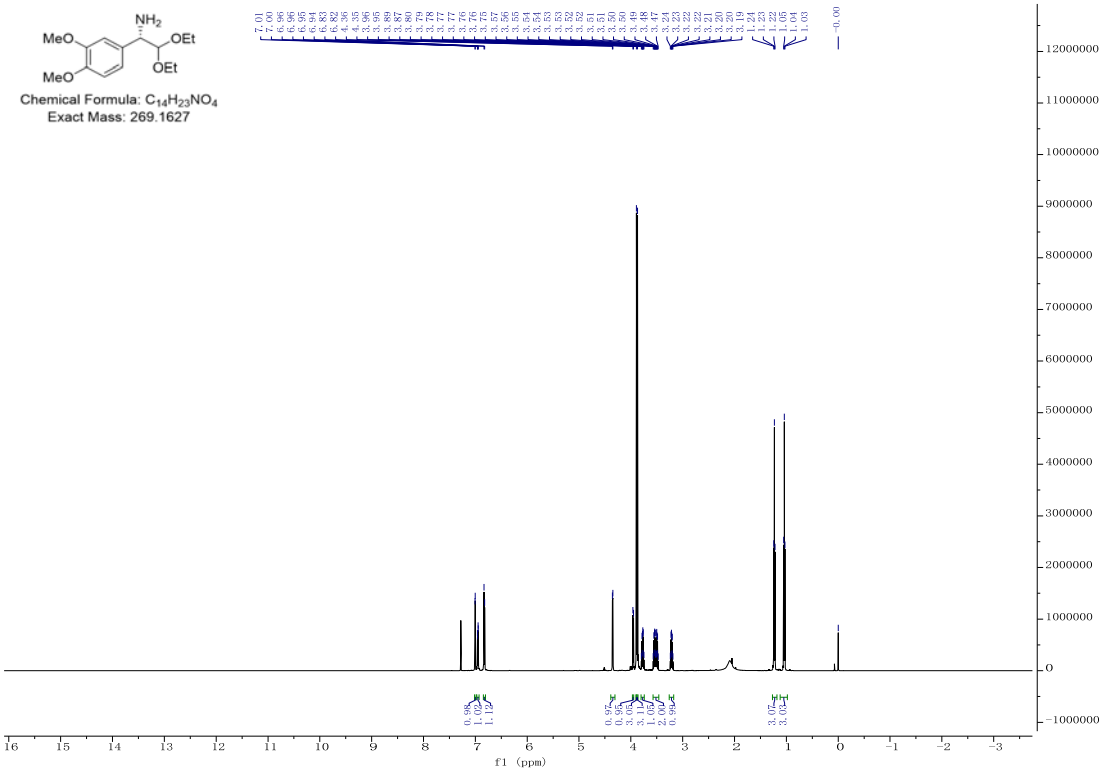
^{1}H NMR (600 MHz, Chloroform-d) of compound **2h**



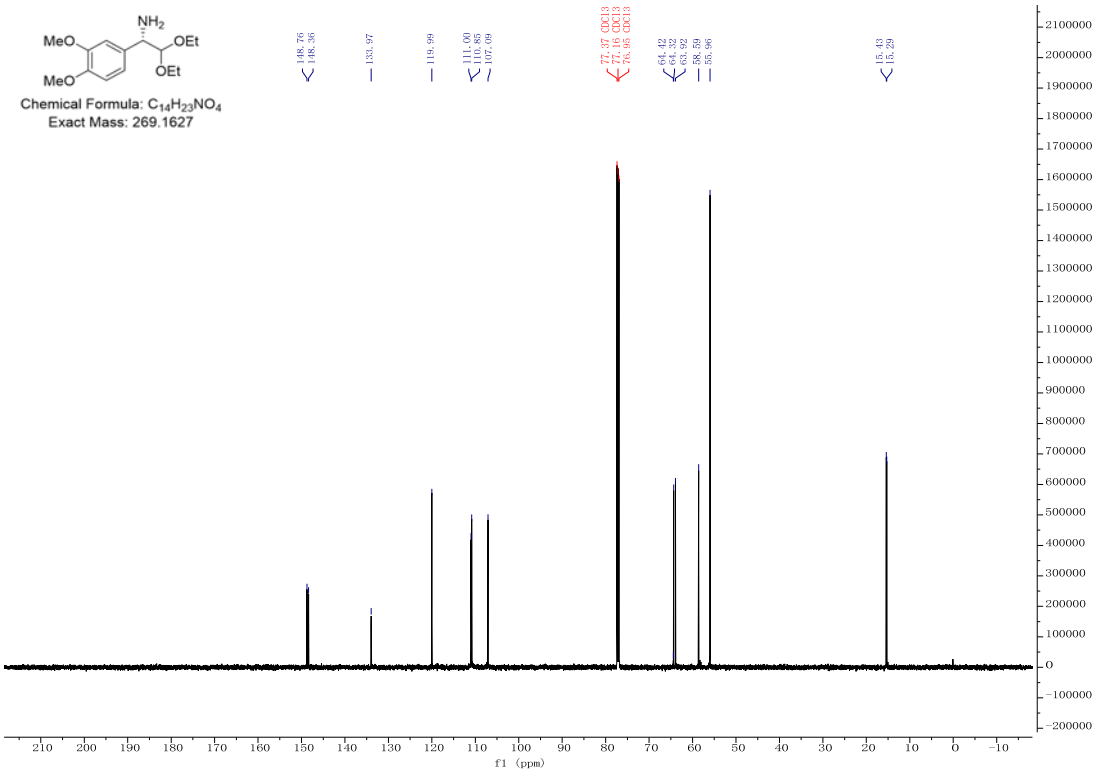
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **2h**



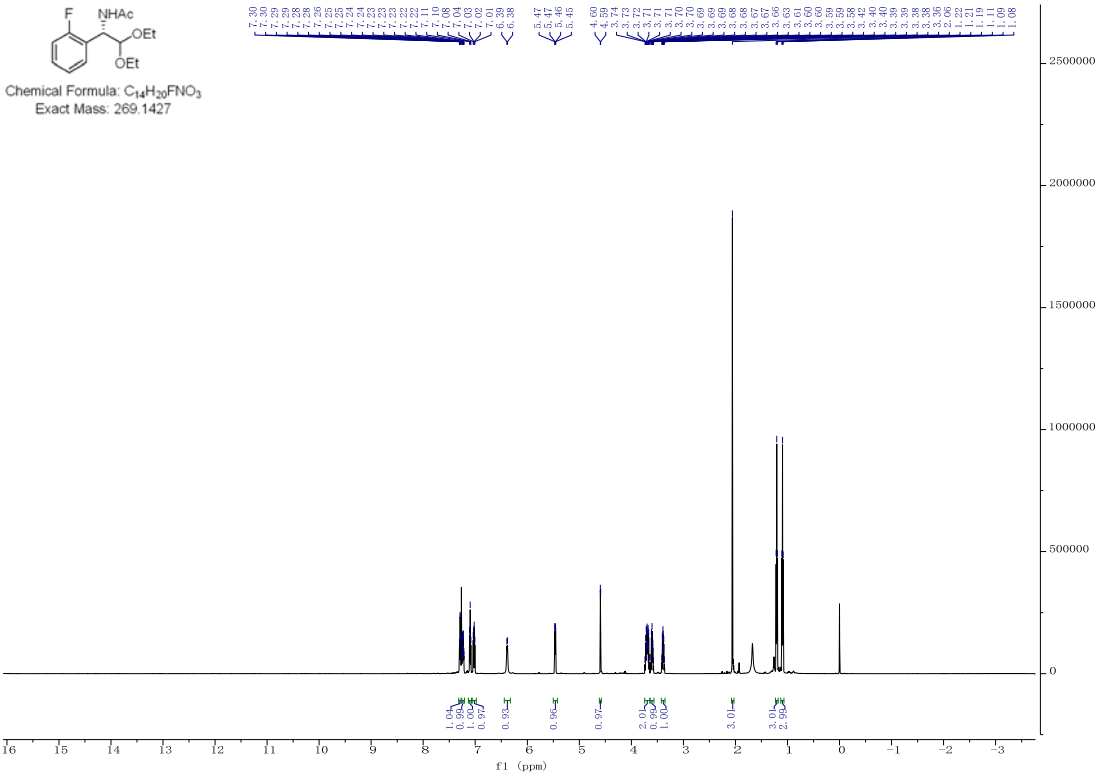
^{1}H NMR (600 MHz, Chloroform-d) of compound **2i**



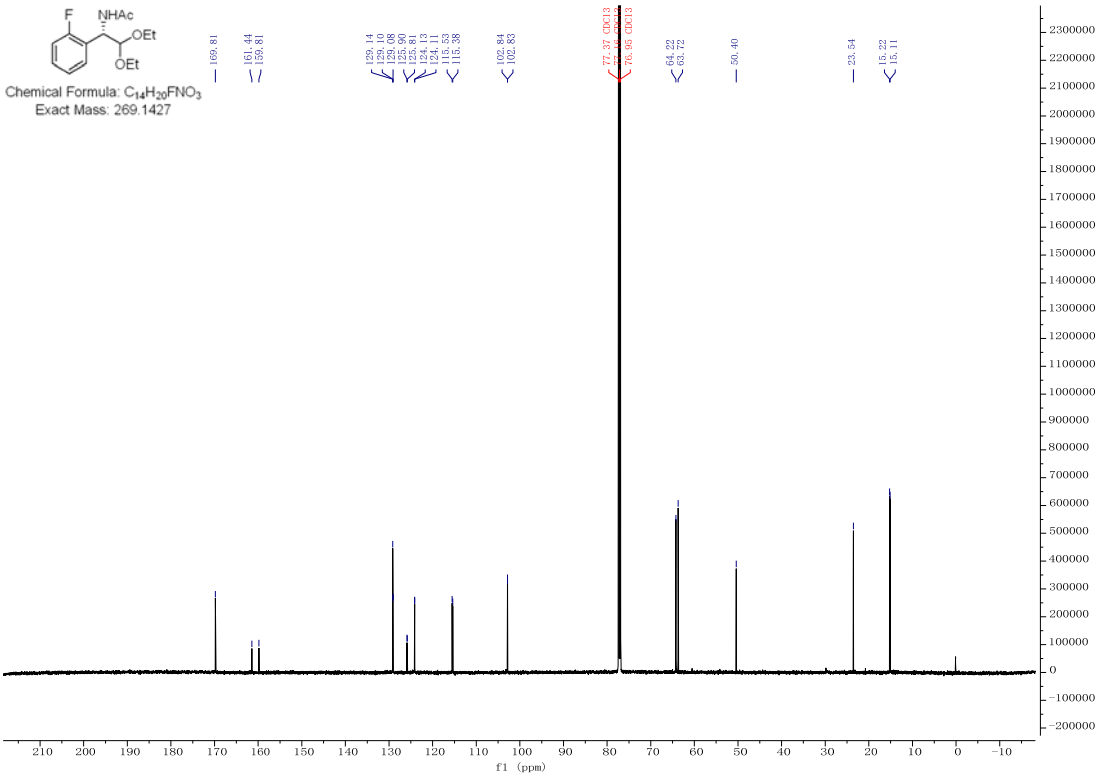
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **2i**



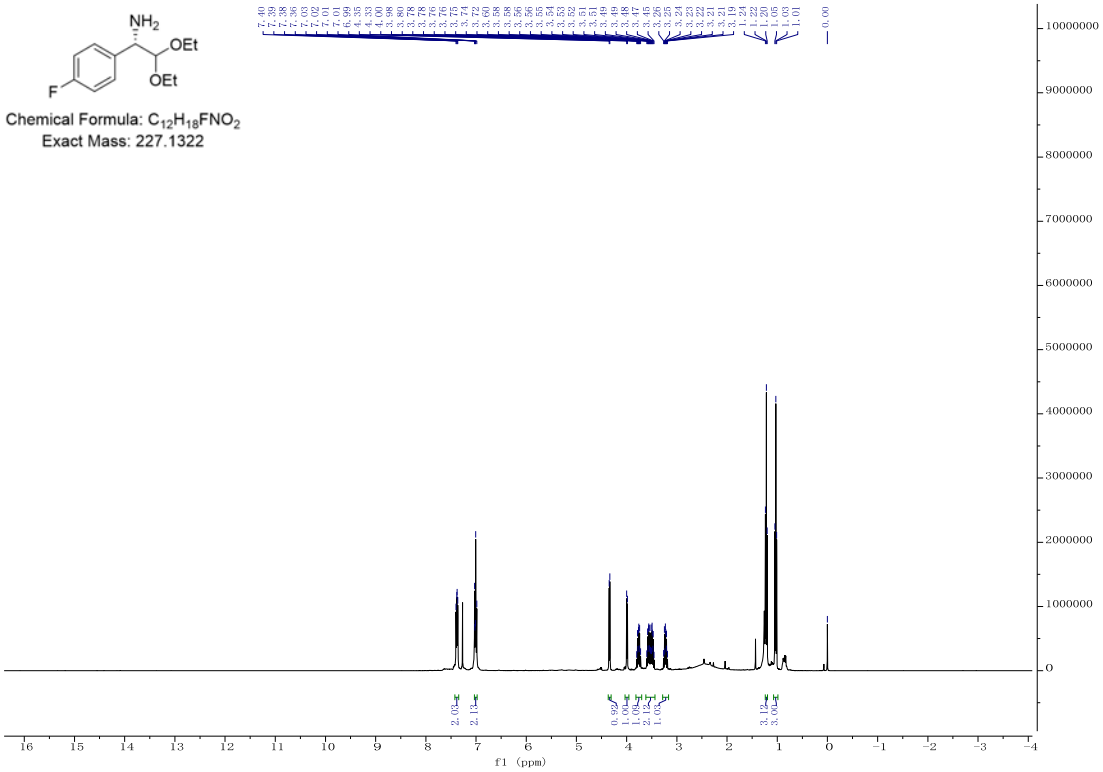
^{1}H NMR (400 MHz, Chloroform-d) of compound **2j-Ac**



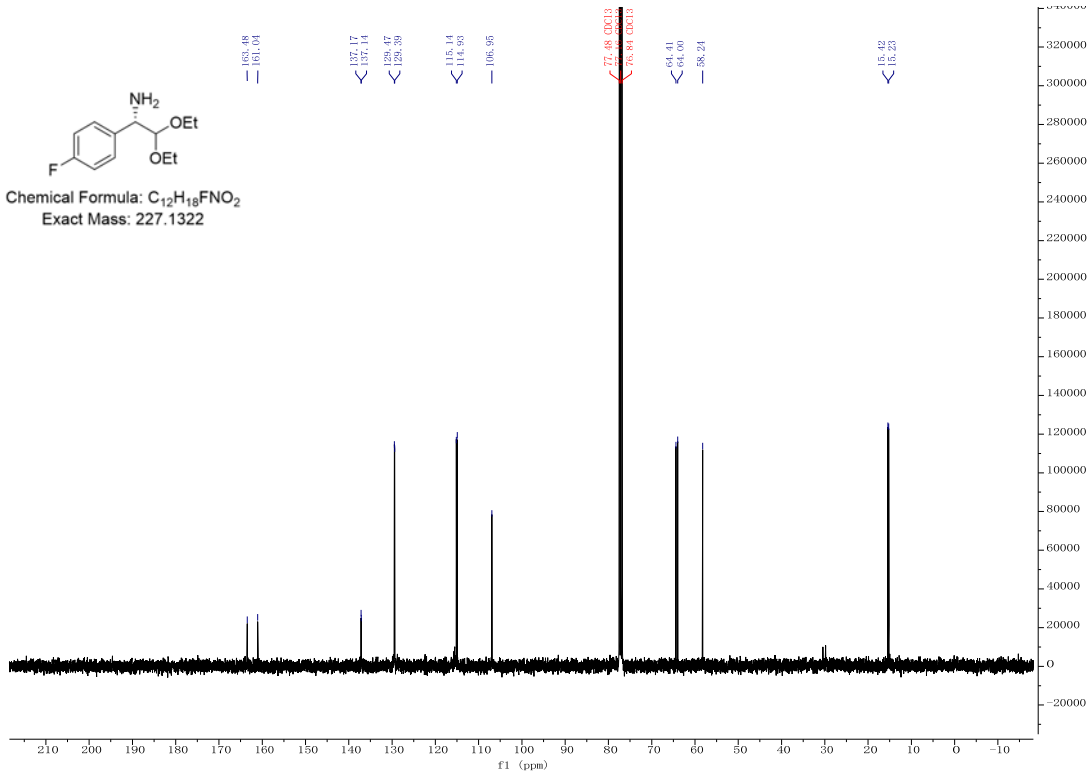
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **2j-Ac**



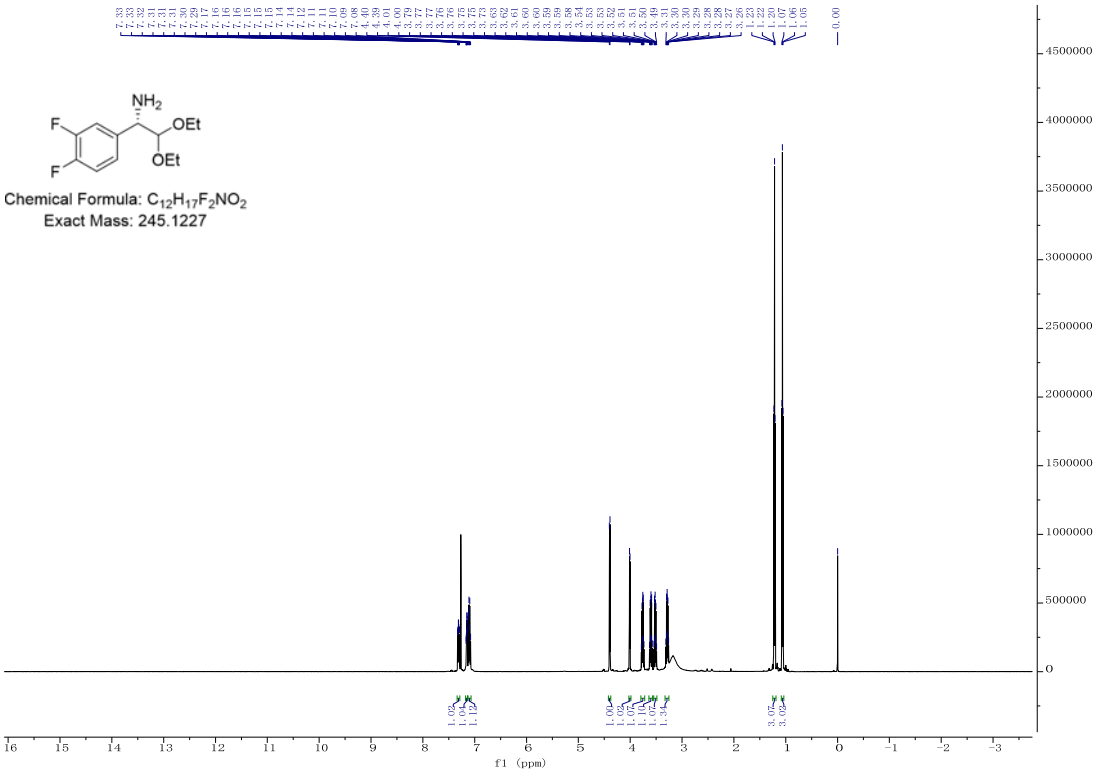
^{1}H NMR (400 MHz, Chloroform-d) of compound **2k**



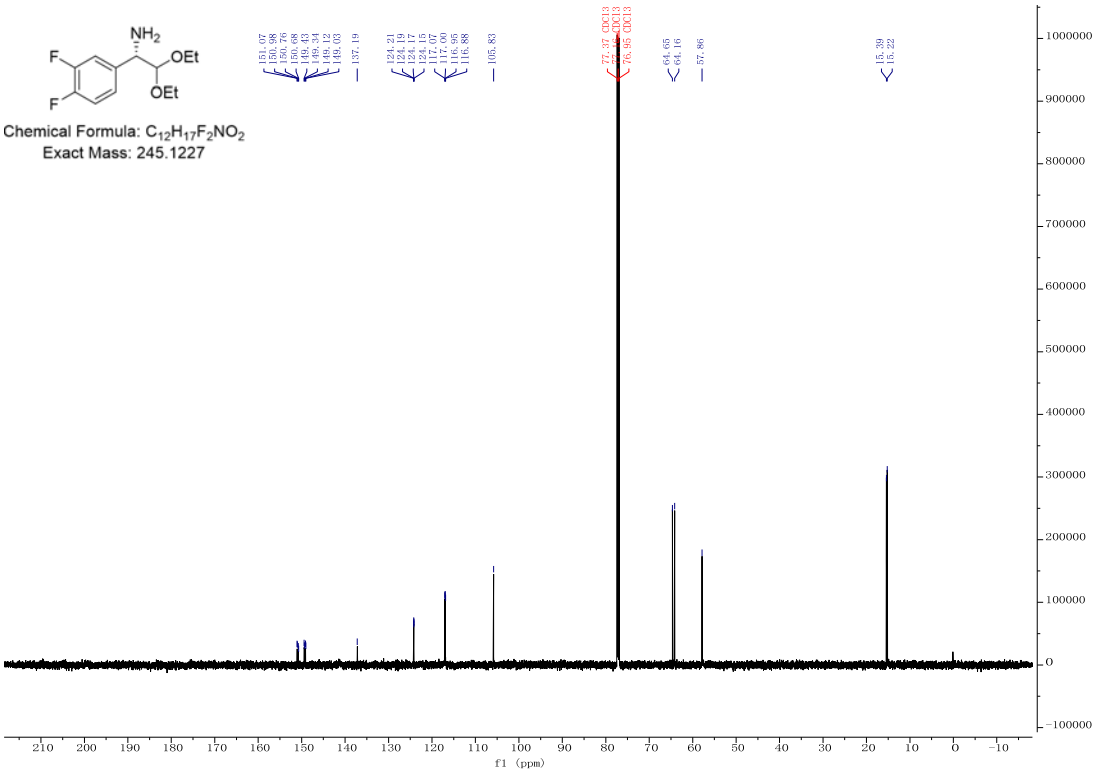
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **2k**



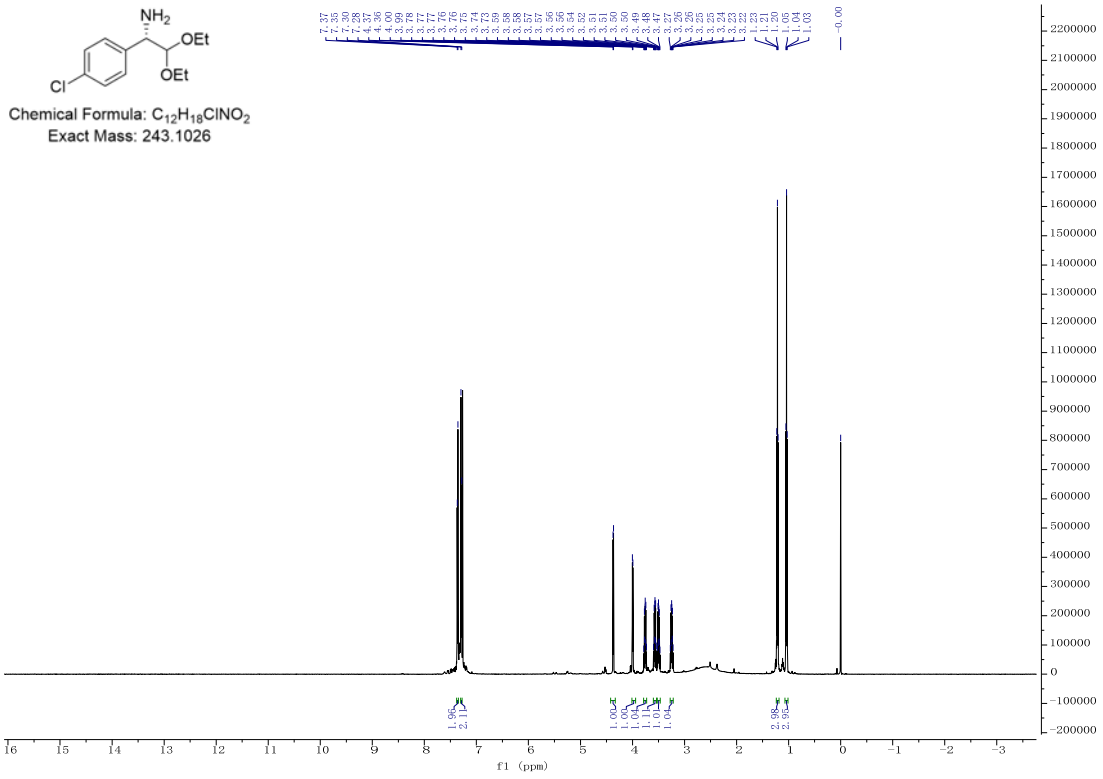
^{1}H NMR (600 MHz, Chloroform-d) of compound **2l**



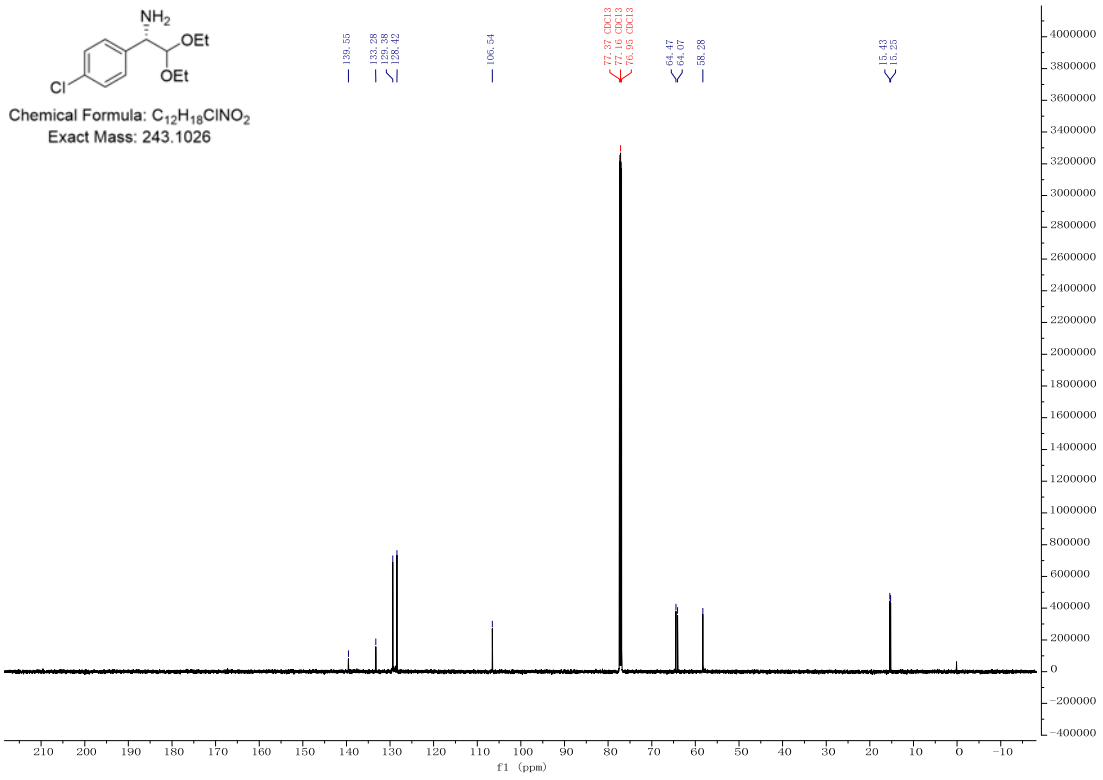
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **2l**



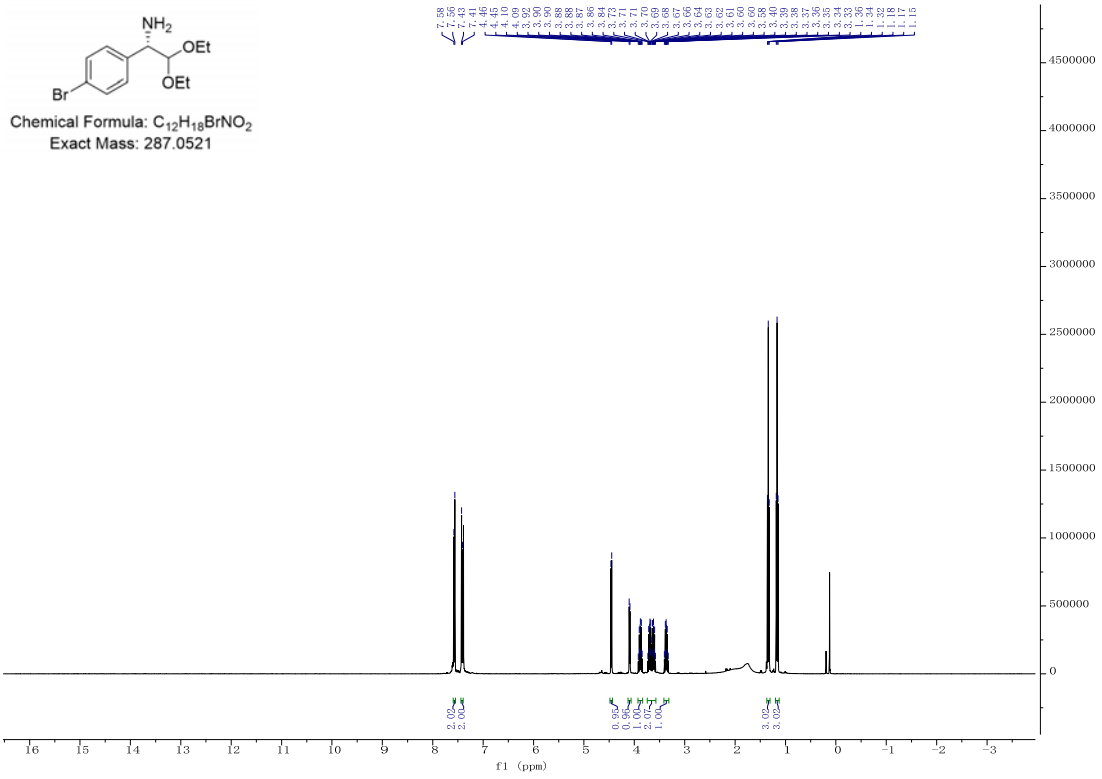
^{1}H NMR (600 MHz, Chloroform-d) of compound **2m**



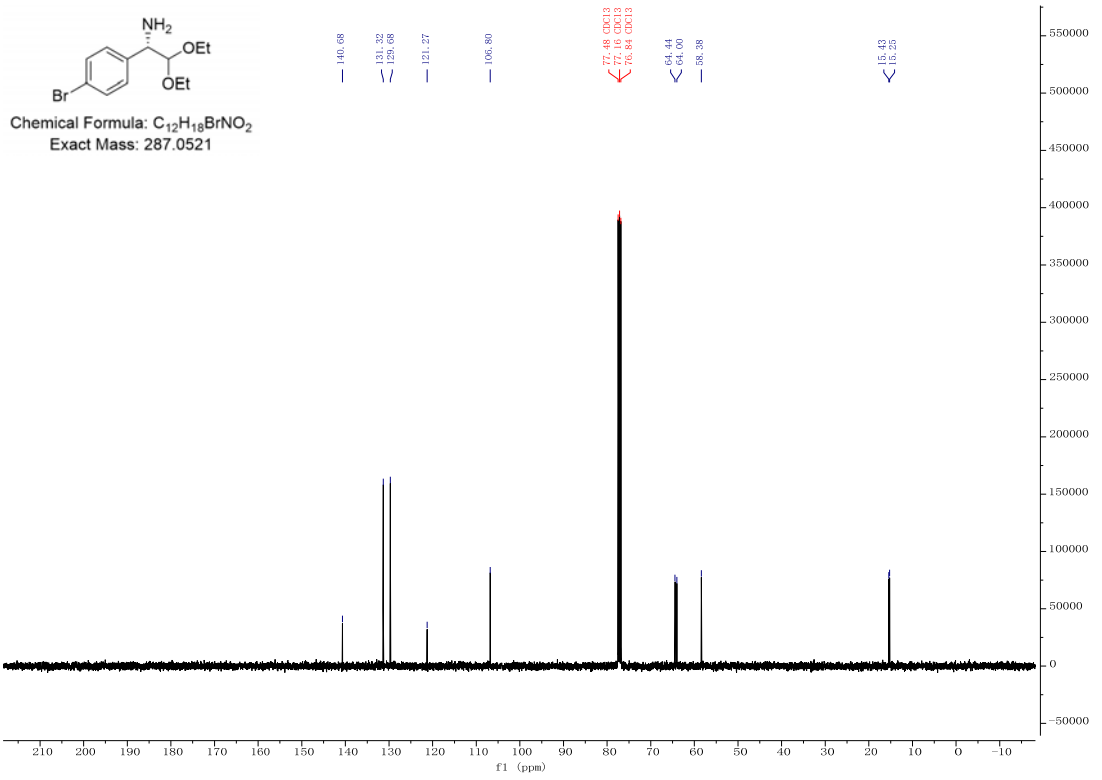
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **2m**



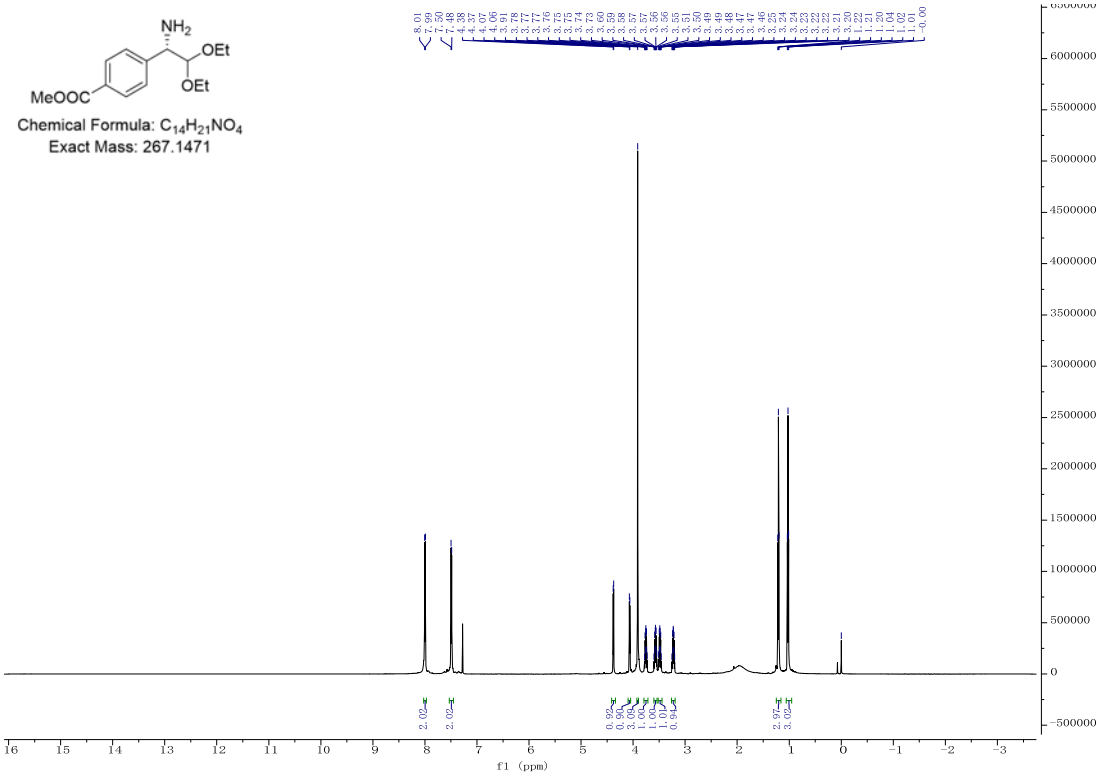
^{1}H NMR (400 MHz, Chloroform-d) of compound **2n**



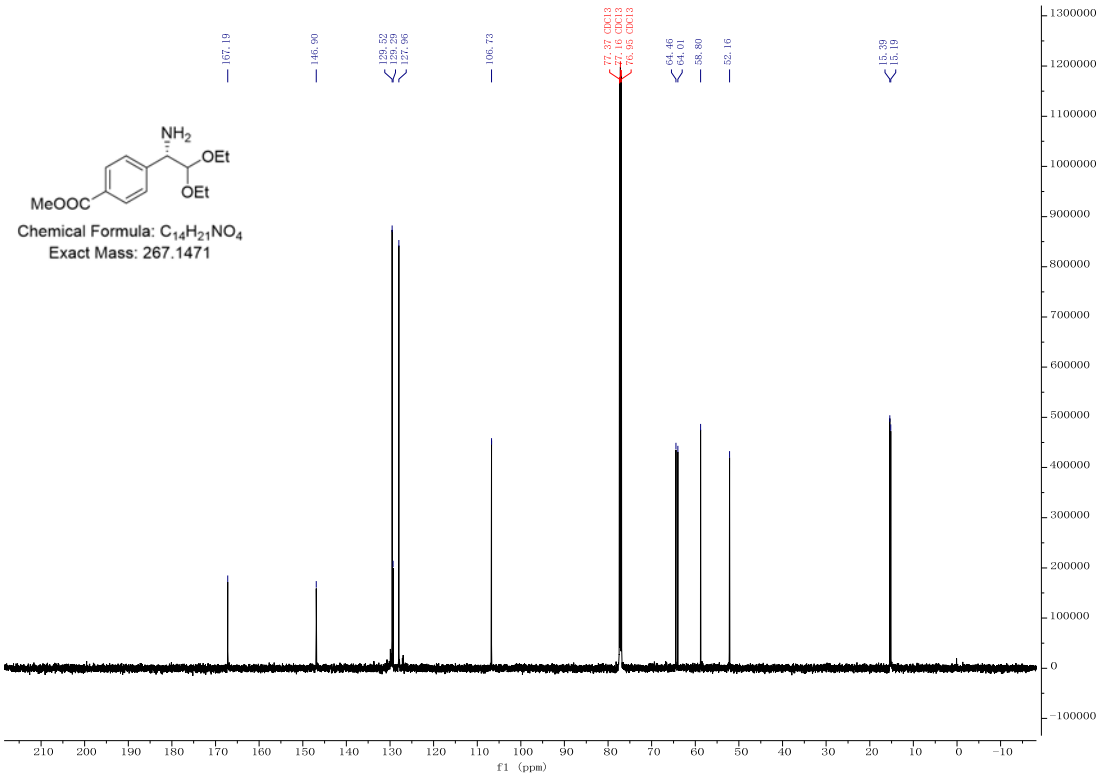
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **2n**



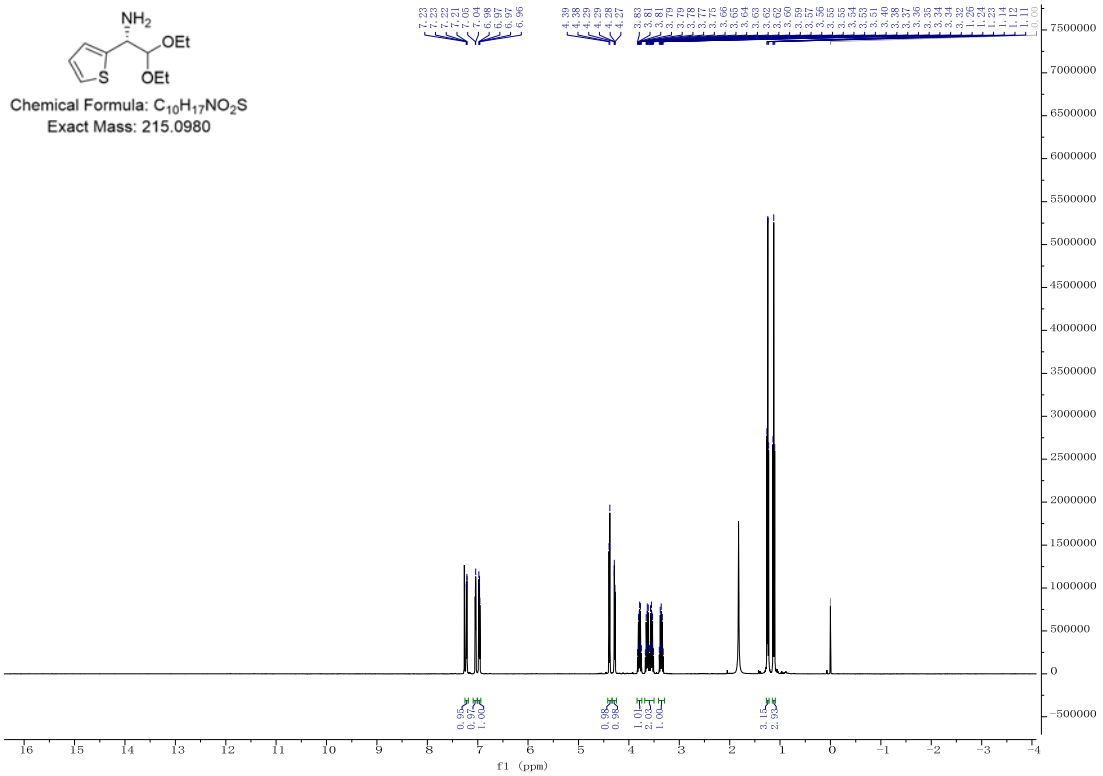
^{1}H NMR (600 MHz, Chloroform-d) of compound **2o**



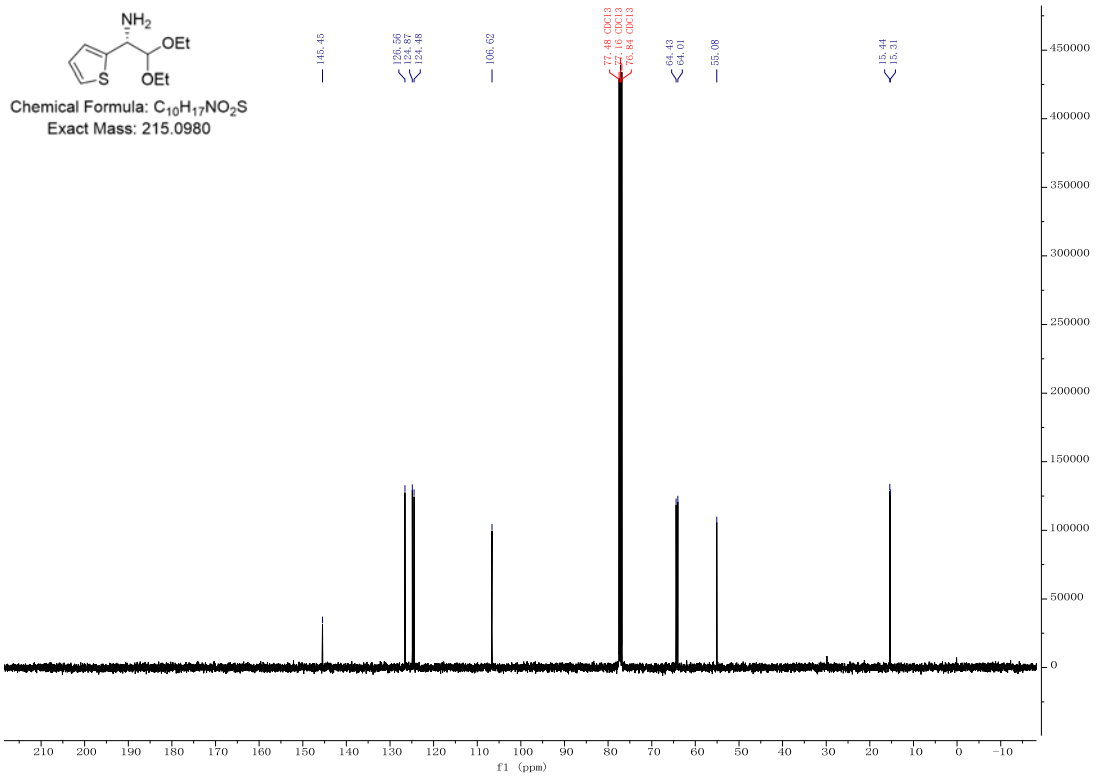
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **2o**



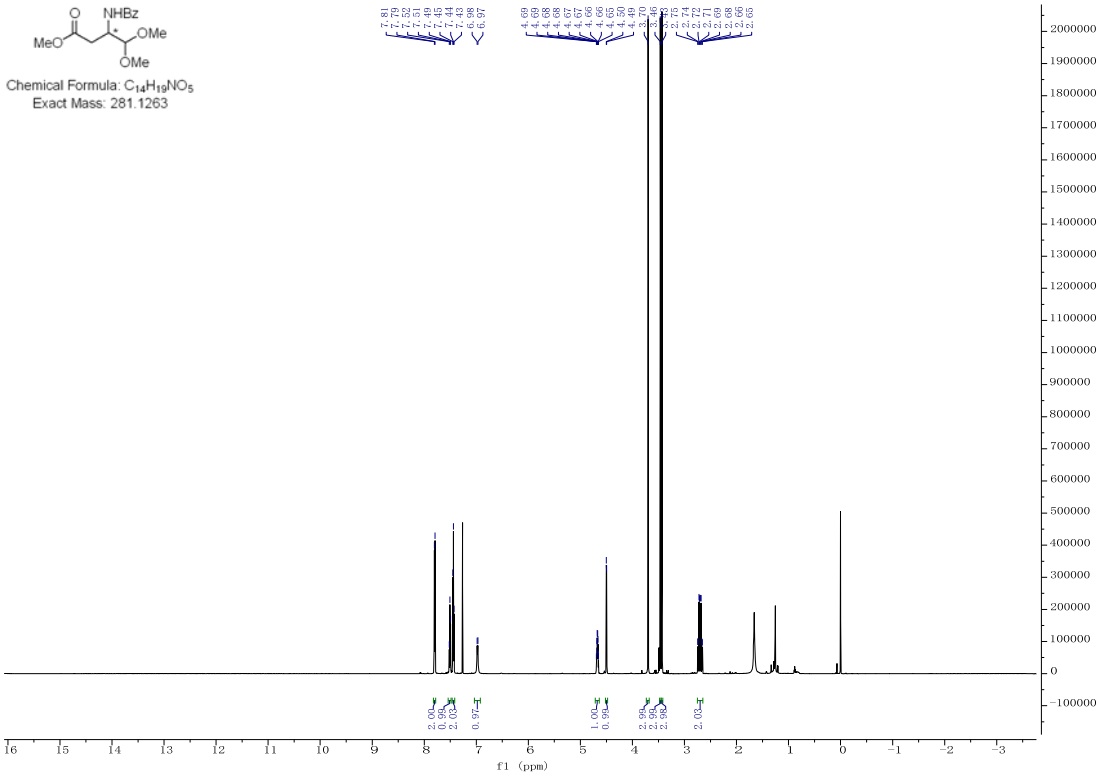
^{1}H NMR (400 MHz, Chloroform-d) of compound **2p**



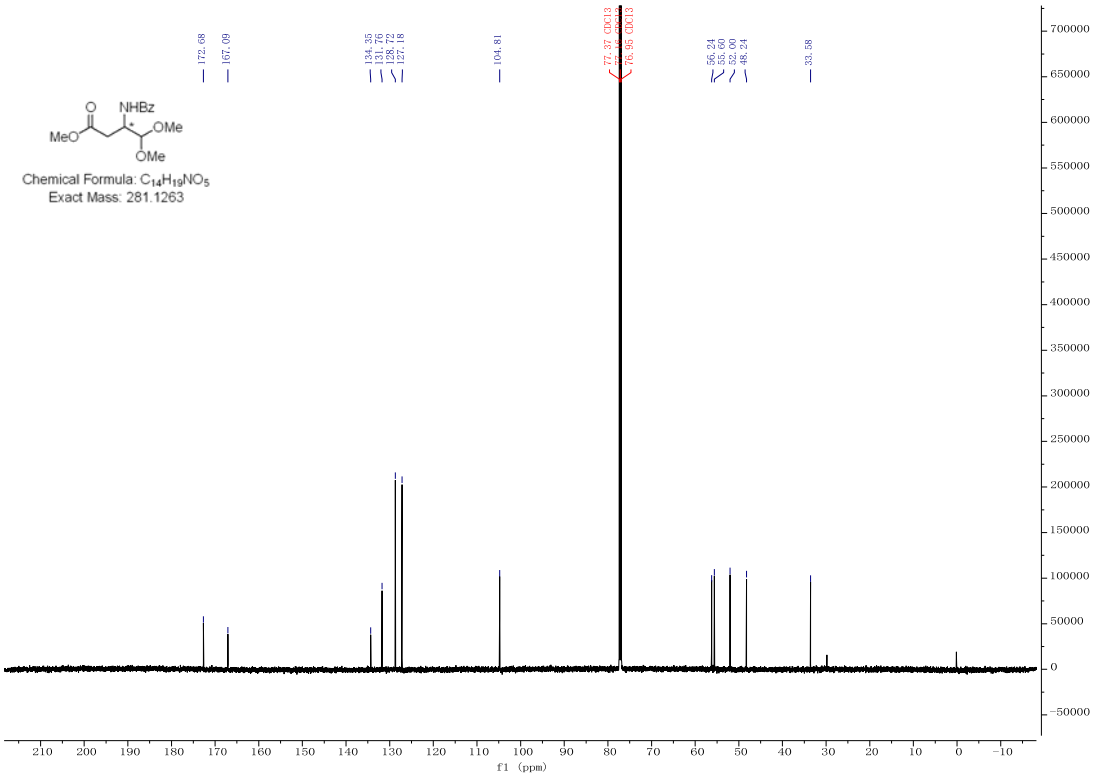
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **2p**



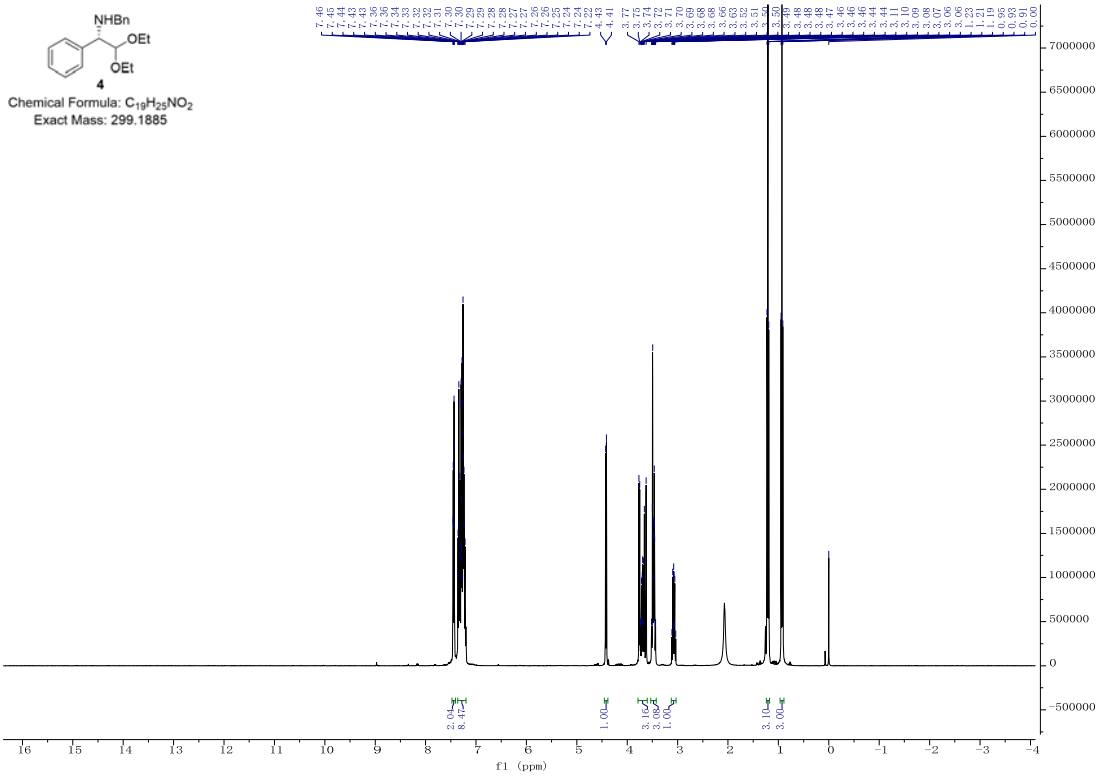
^{1}H NMR (600 MHz, Chloroform-d) of compound **2q-Bz**



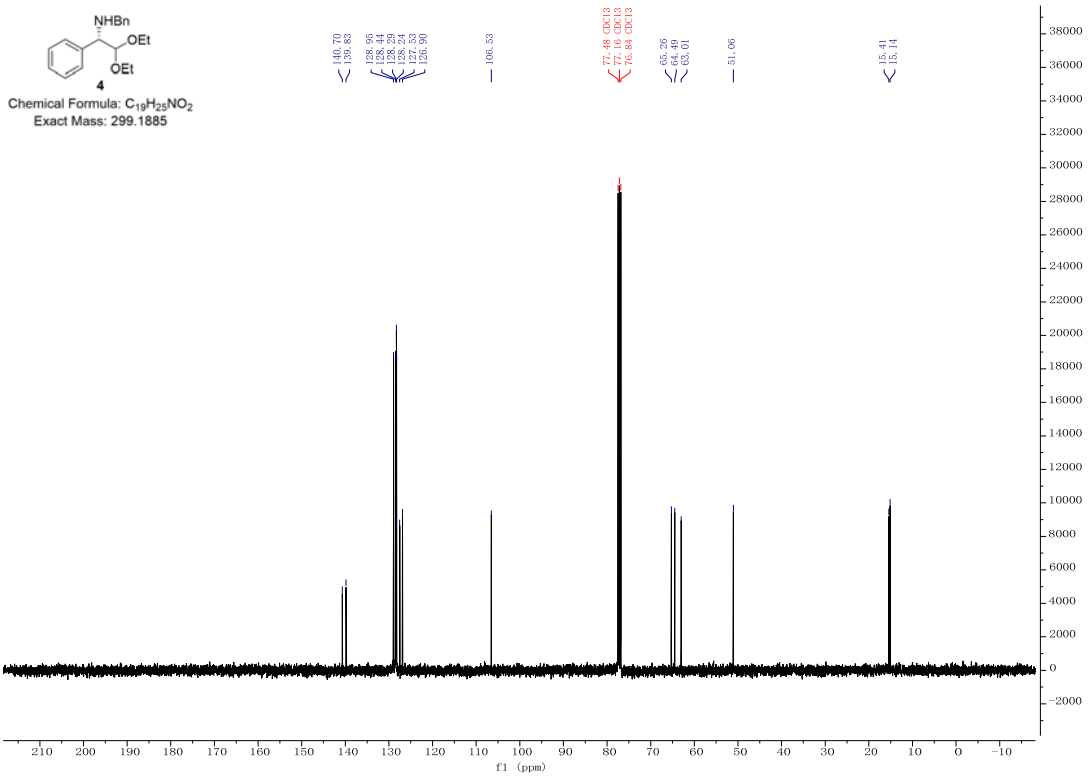
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **2q-Bz**



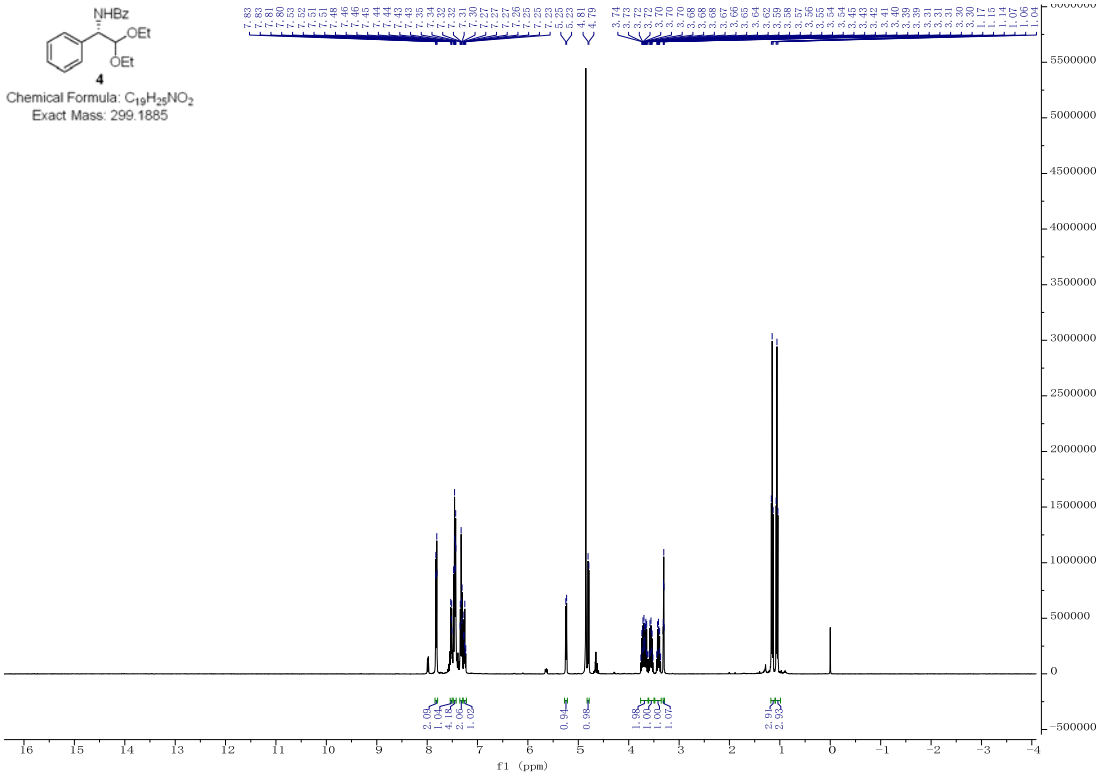
^{1}H NMR (400 MHz, Chloroform-d) of compound **3**



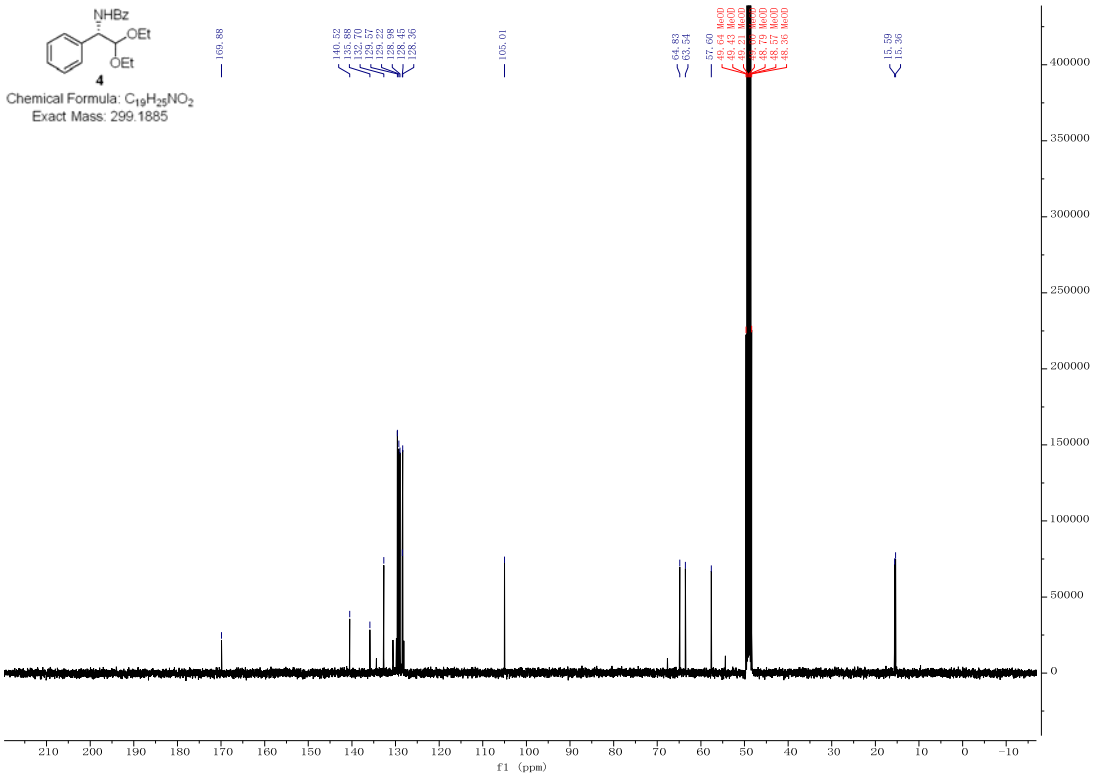
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **3**



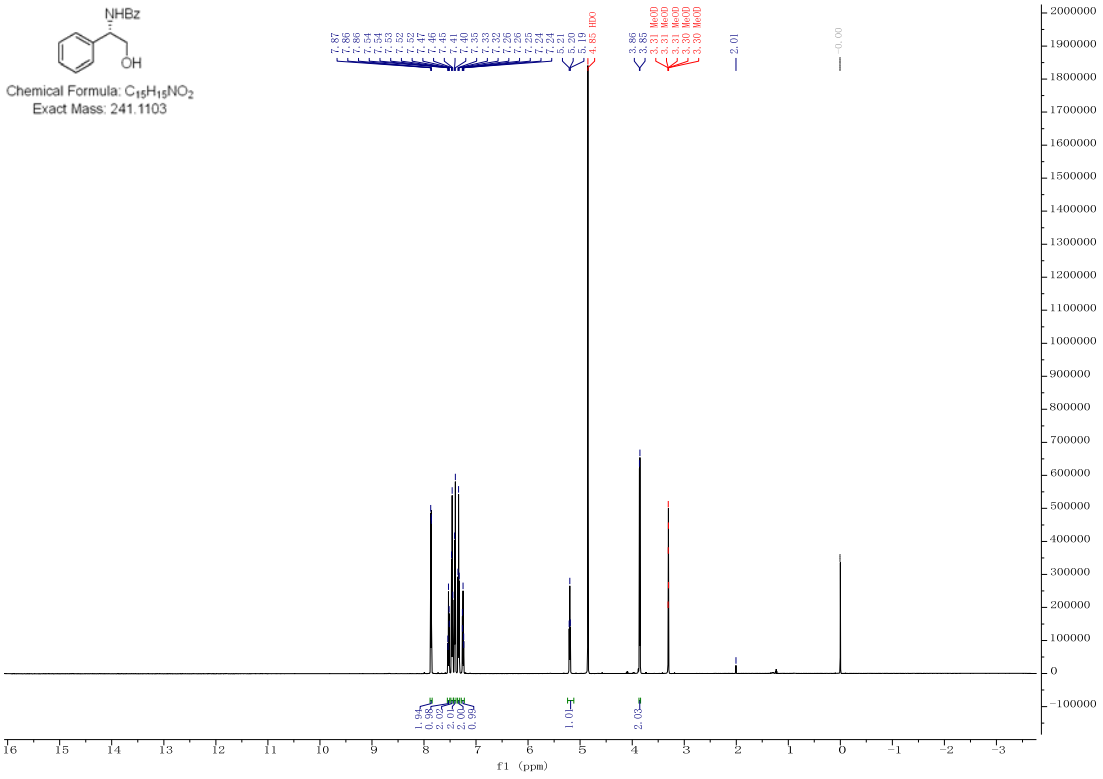
^{1}H NMR (400 MHz, Chloroform-d) of compound **4**



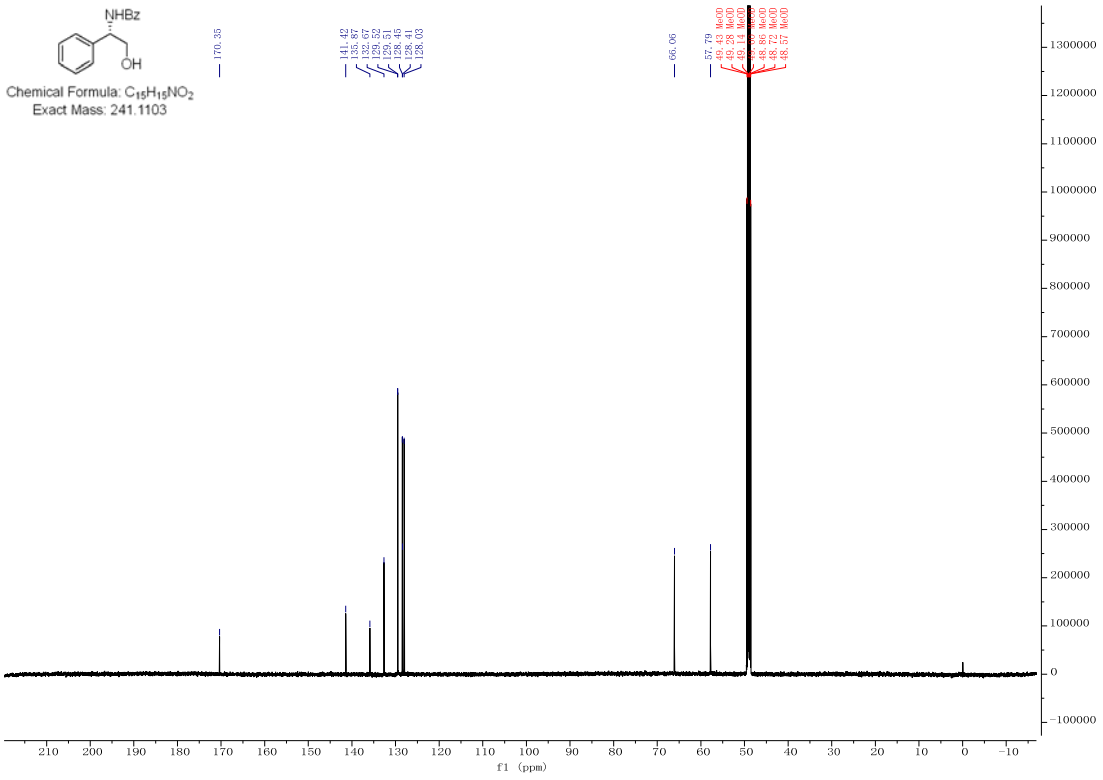
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **4**



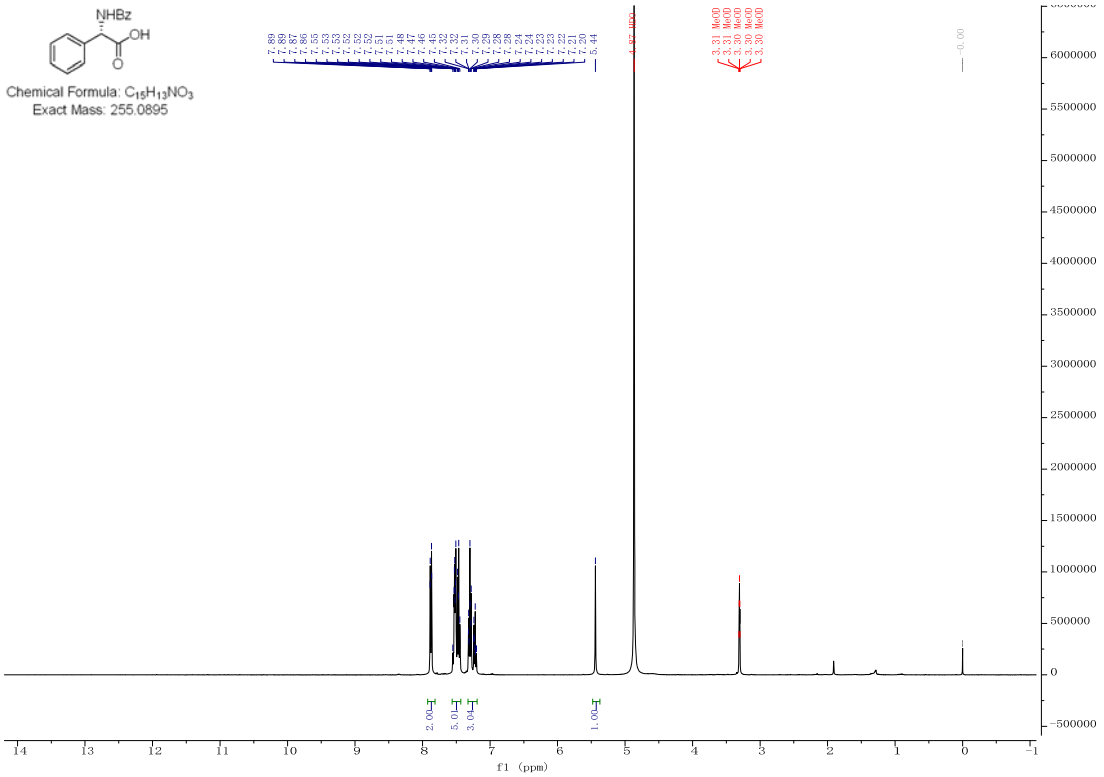
^{1}H NMR (600 MHz, Chloroform-d) of compound **5**



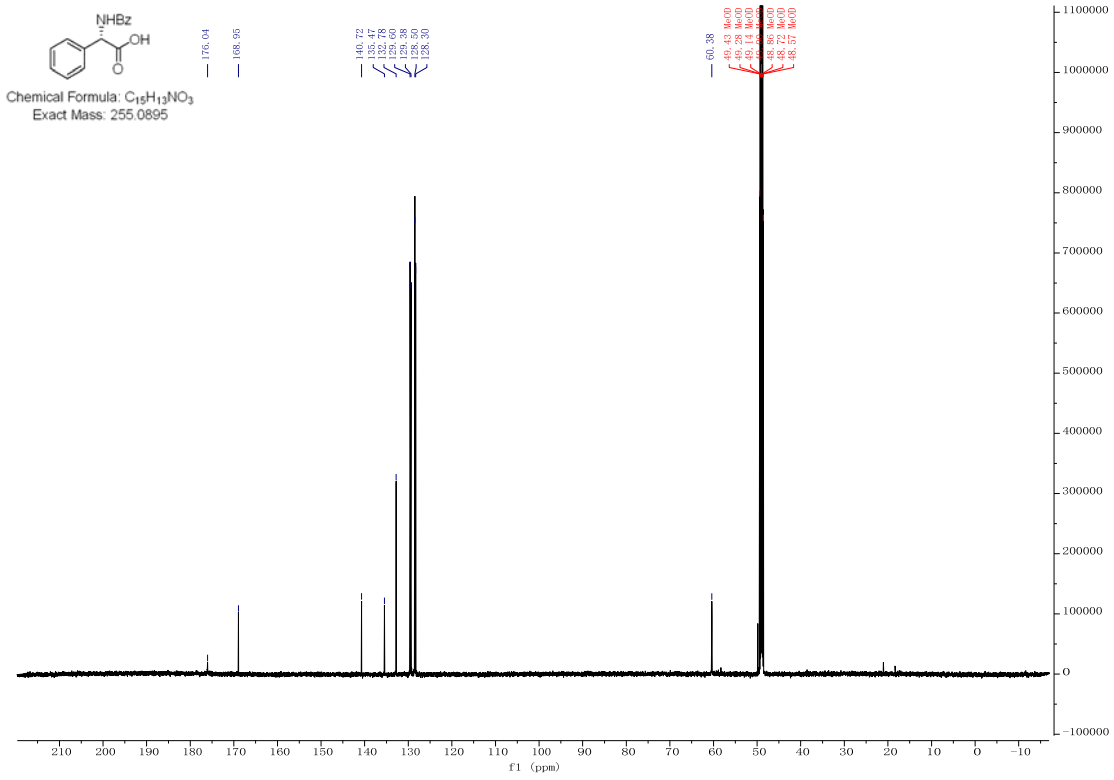
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **5**



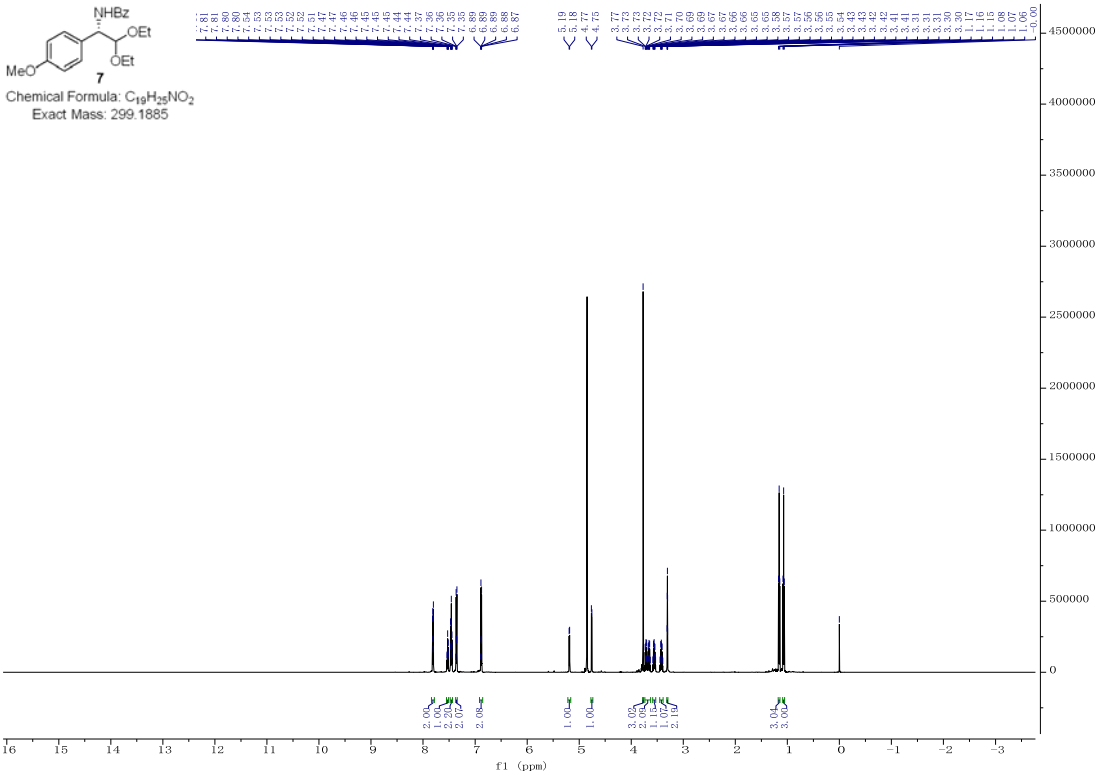
^{1}H NMR (400 MHz, Chloroform-d) of compound **6**



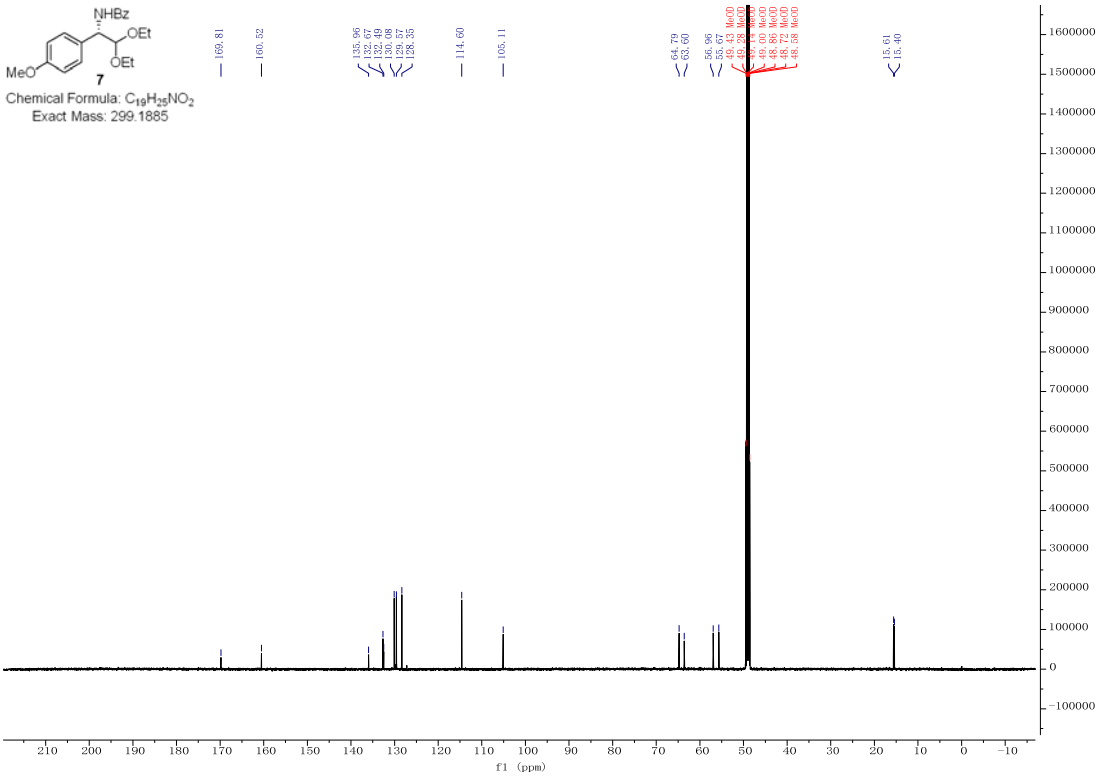
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **6**



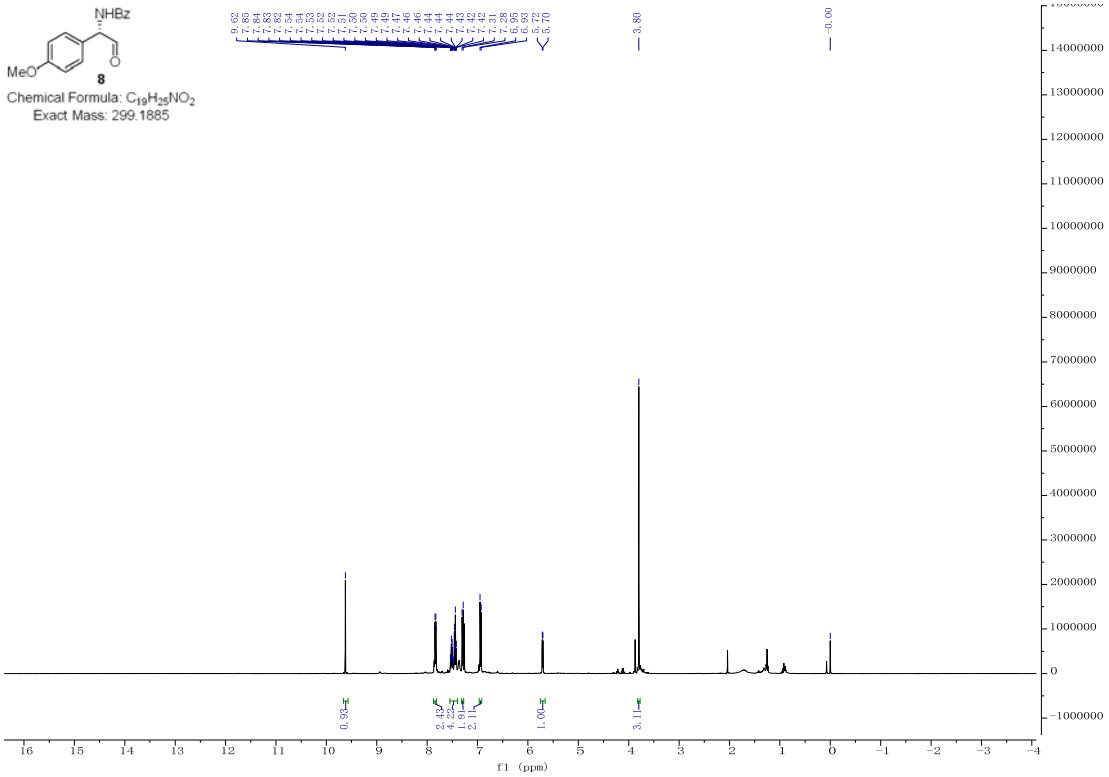
^{1}H NMR (600 MHz, Chloroform-d) of compound **7**



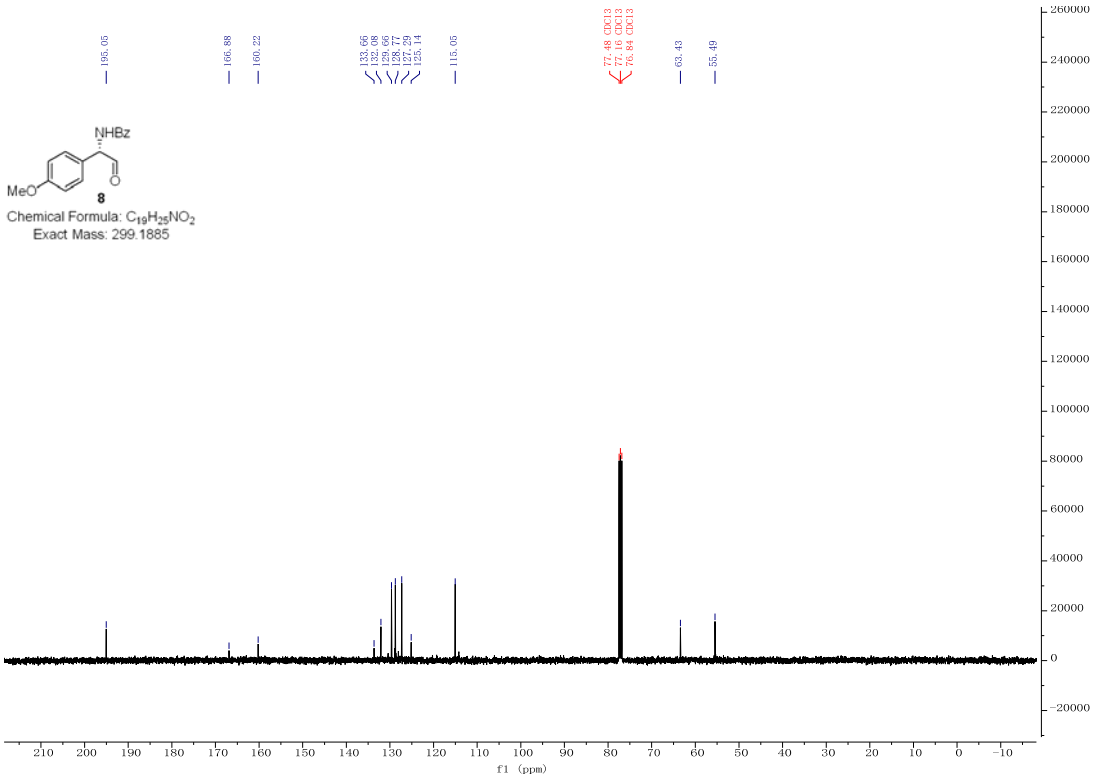
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **7**



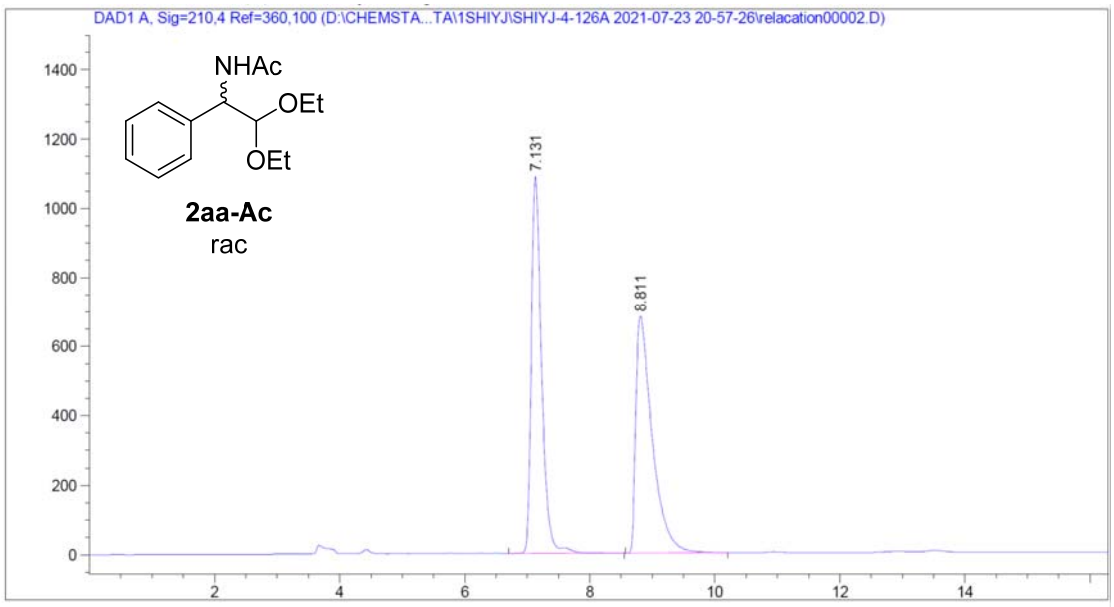
^{1}H NMR (400 MHz, Chloroform-d) of compound **8**



^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **8**

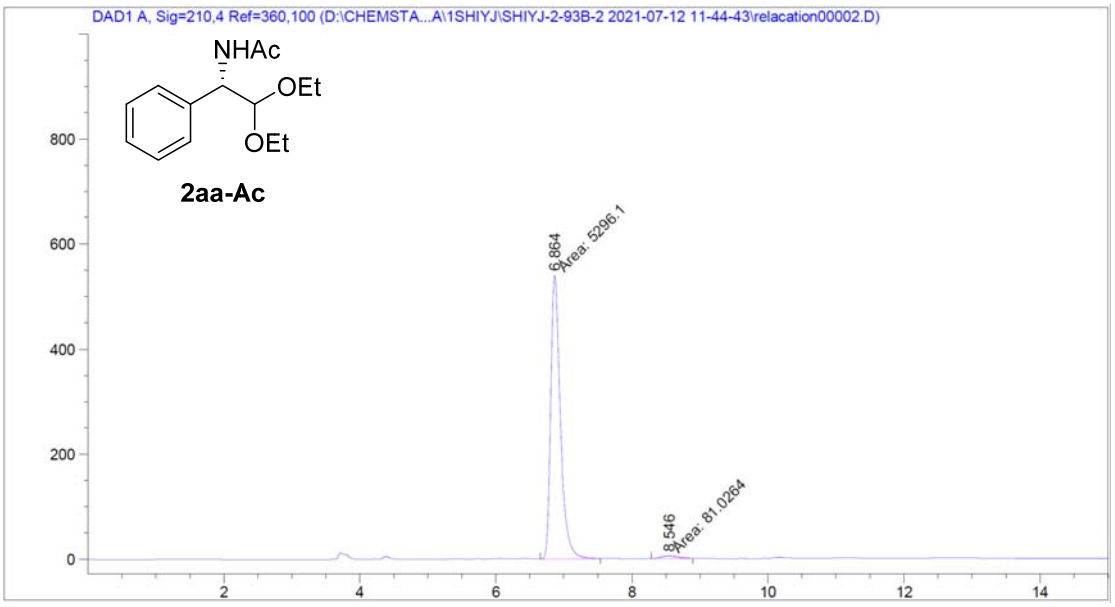


VII. HPLC spectra



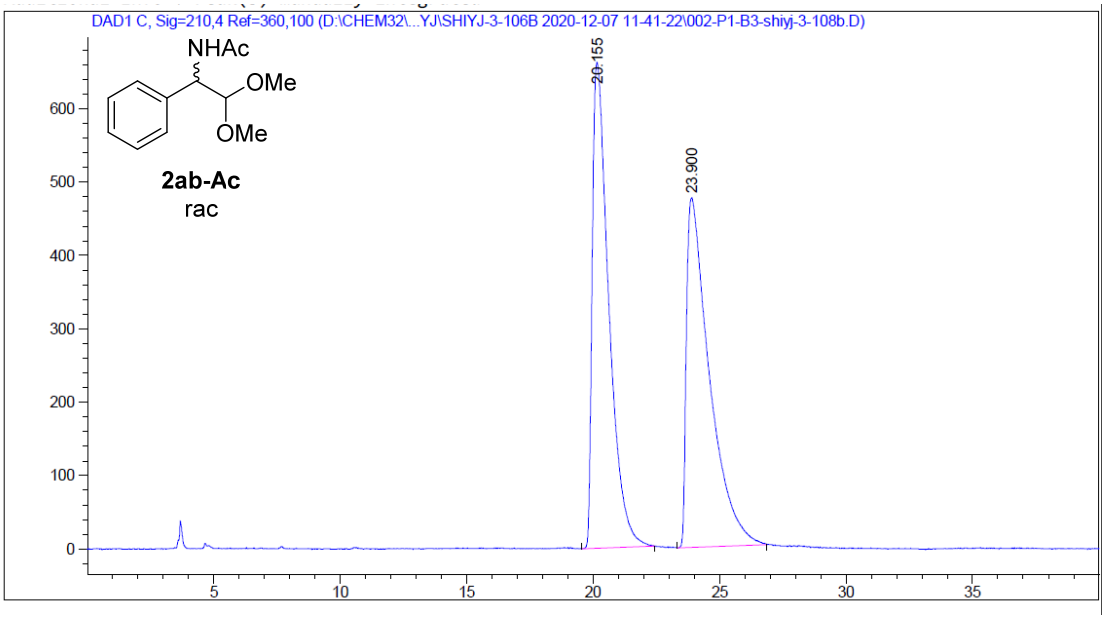
Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.131	BV R	0.1702	1.23824e4	1090.31726	49.9410
2	8.811	BB	0.2681	1.24117e4	682.86652	50.0590



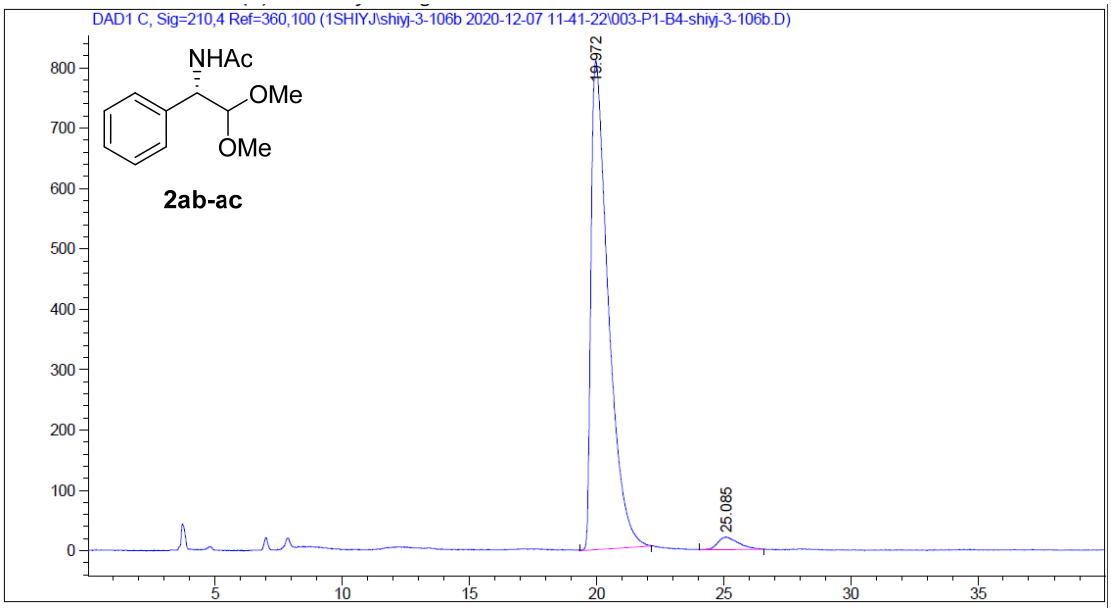
Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.864	MM	0.1634	5296.10010	540.15015	98.4931
2	8.546	MM	0.2960	81.02644	4.56172	1.5069



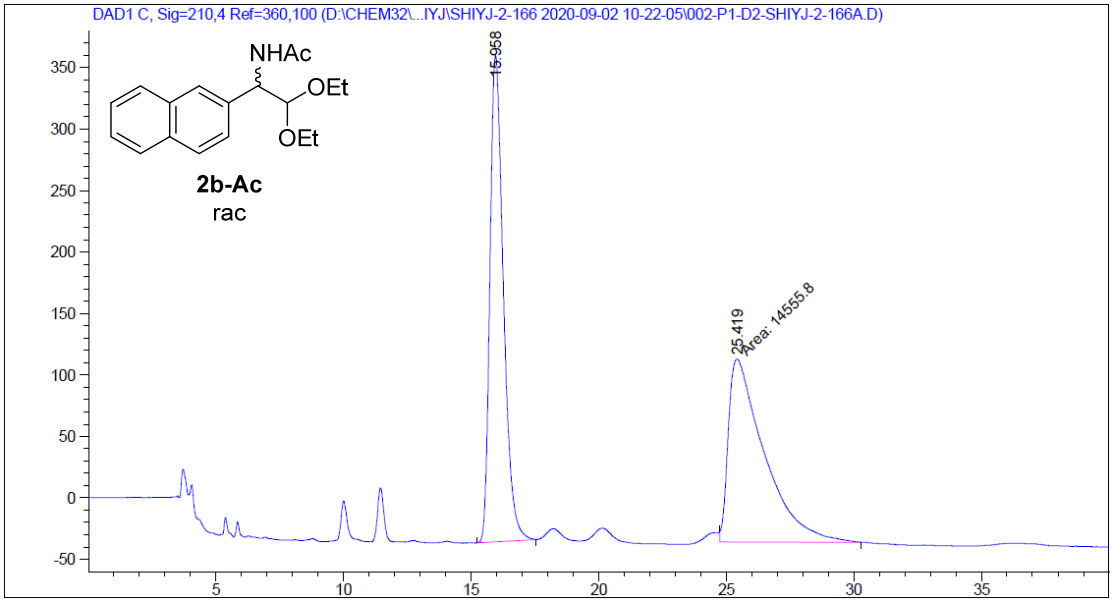
Signal 1: DAD1 C, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.155	BV R	0.6042	3.00069e4	662.72308	50.0026
2	23.900	BV R	0.8222	3.00038e4	476.48727	49.9974



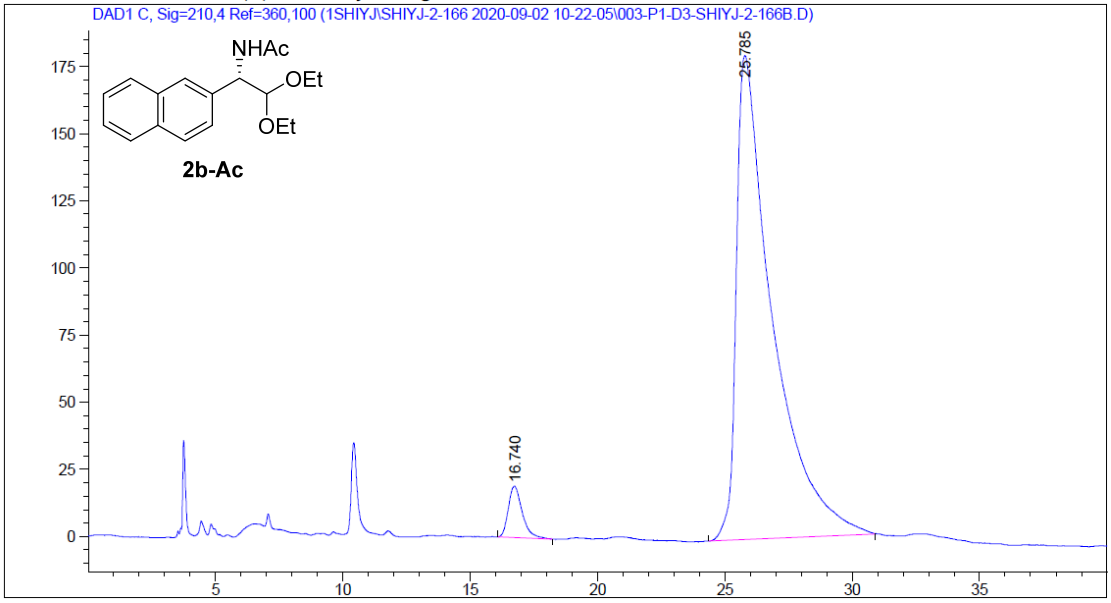
Signal 1: DAD1 C, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.972	VV R	0.6261	3.82208e4	810.60114	97.1150
2	25.085	VV R	0.6456	1135.42065	20.62930	2.8850



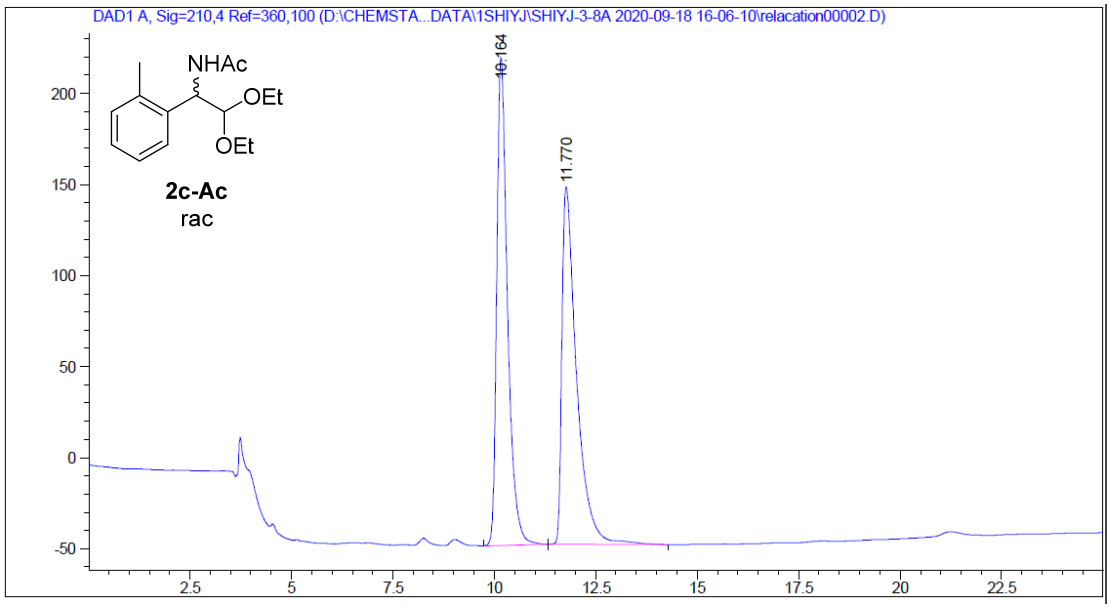
Signal 1: DAD1 C, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.958	BB	0.5593	1.44974e4	395.78857	49.8994
2	25.419	MM	1.6305	1.45558e4	148.78726	50.1006



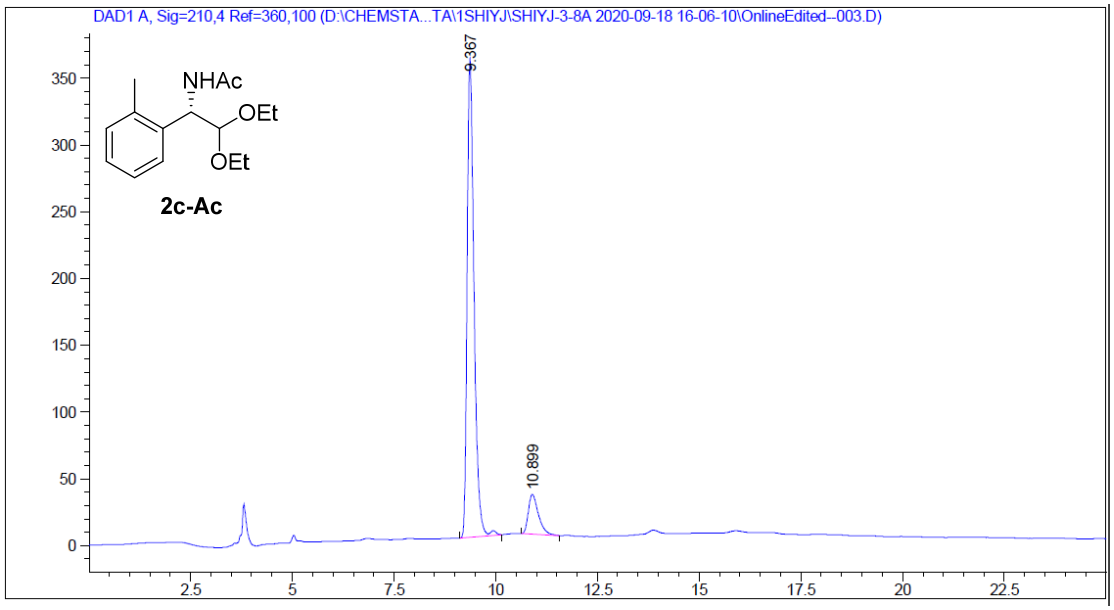
Signal 1: DAD1 C, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.740	BB	0.5339	730.16742	19.18851	3.9459
2	25.785	BB	1.3129	1.77742e4	180.17317	96.0541



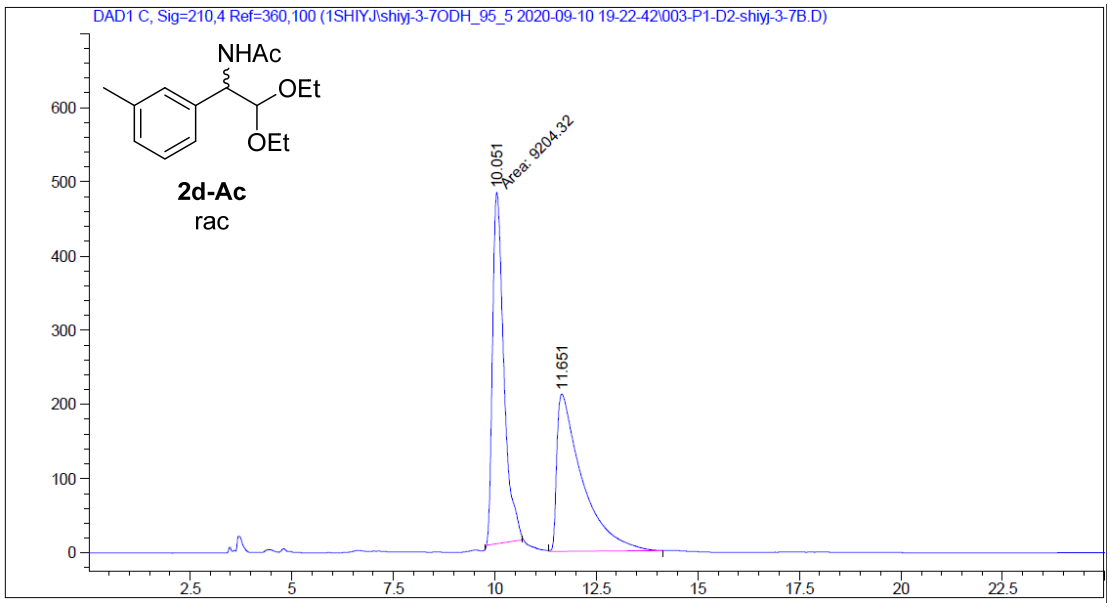
Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.164	BB	0.2792	4940.73193	267.86829	50.0590
2	11.770	BB	0.3690	4929.08740	196.27818	49.9410



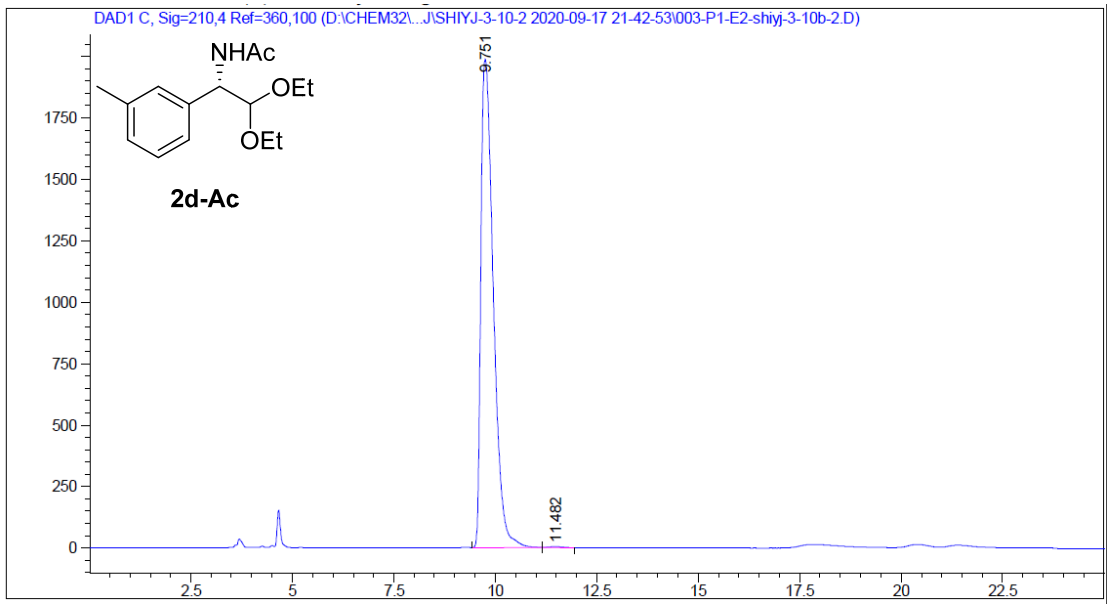
Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.367	BV R	0.1786	4235.14160	358.87387	89.1567
2	10.899	BB	0.2590	515.08105	29.90011	10.8433



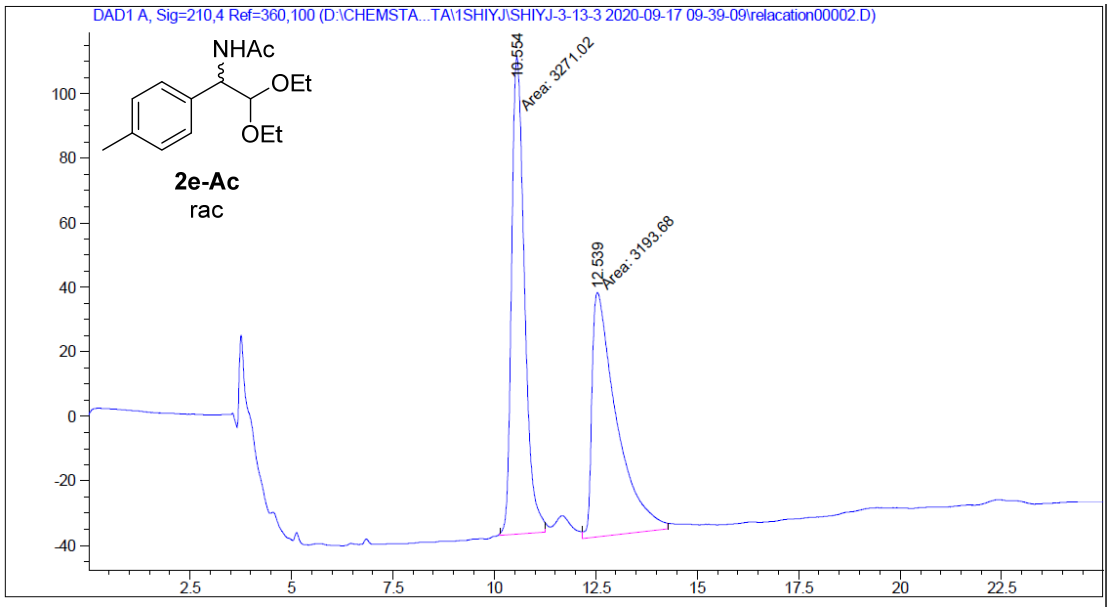
Signal 1: DAD1 C, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.051	MM	0.3238	9204.31738	473.81577	49.9131
2	11.651	VB	0.5960	9236.36035	212.12172	50.0869



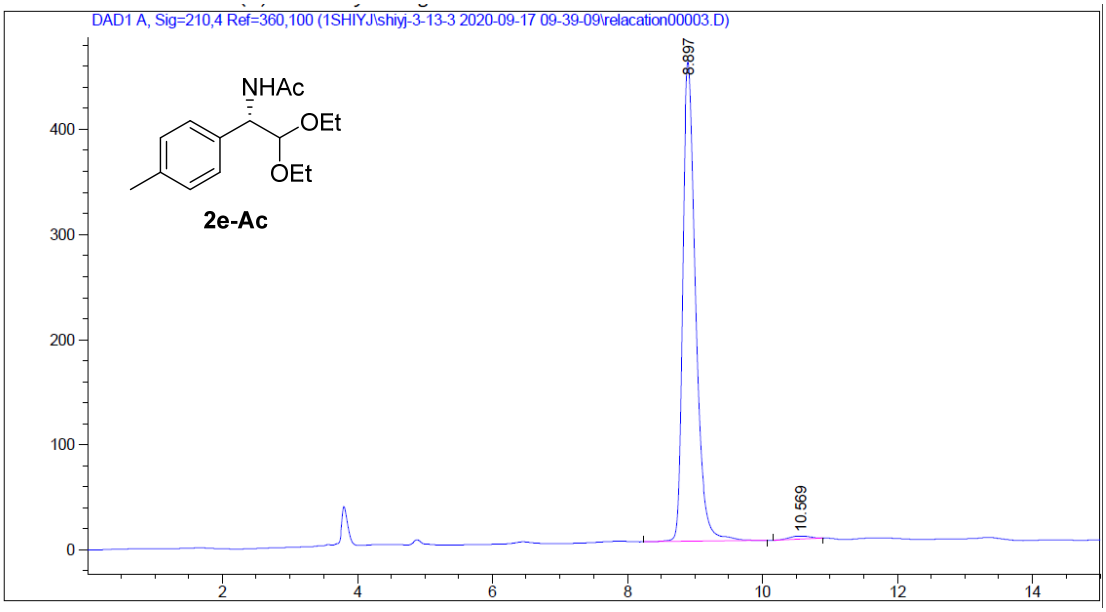
Signal 1: DAD1 C, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.751	BB	0.3307	4.23787e4	1987.67102	99.7895
2	11.482	BB	0.3087	89.38857	4.33246	0.2105



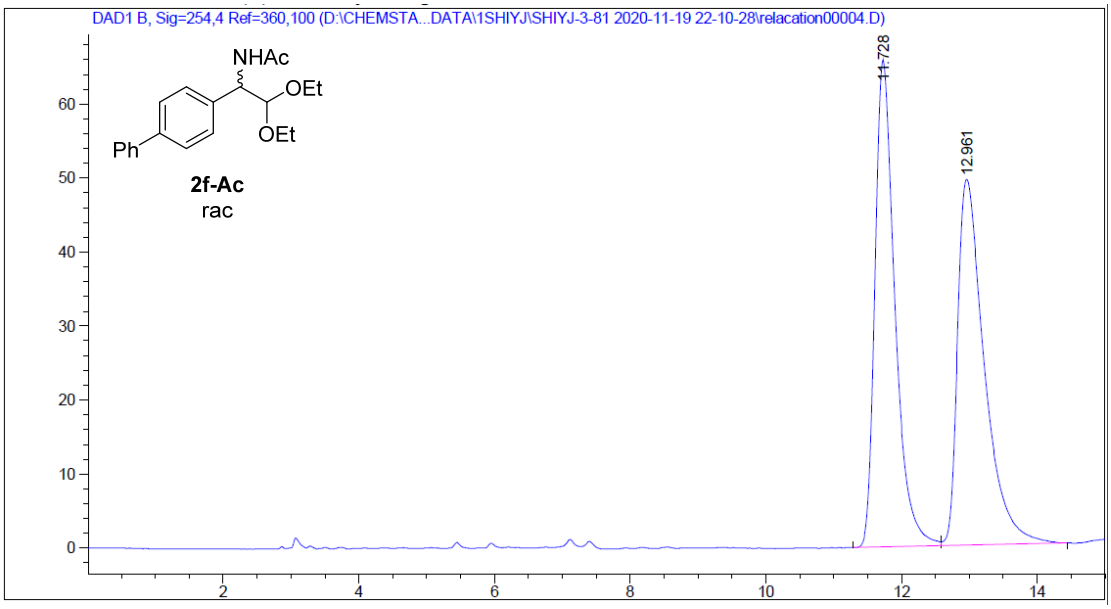
Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.554	MM	0.3686	3271.01880	147.91644	50.5982
2	12.539	MM	0.7031	3193.67505	75.70998	49.4018



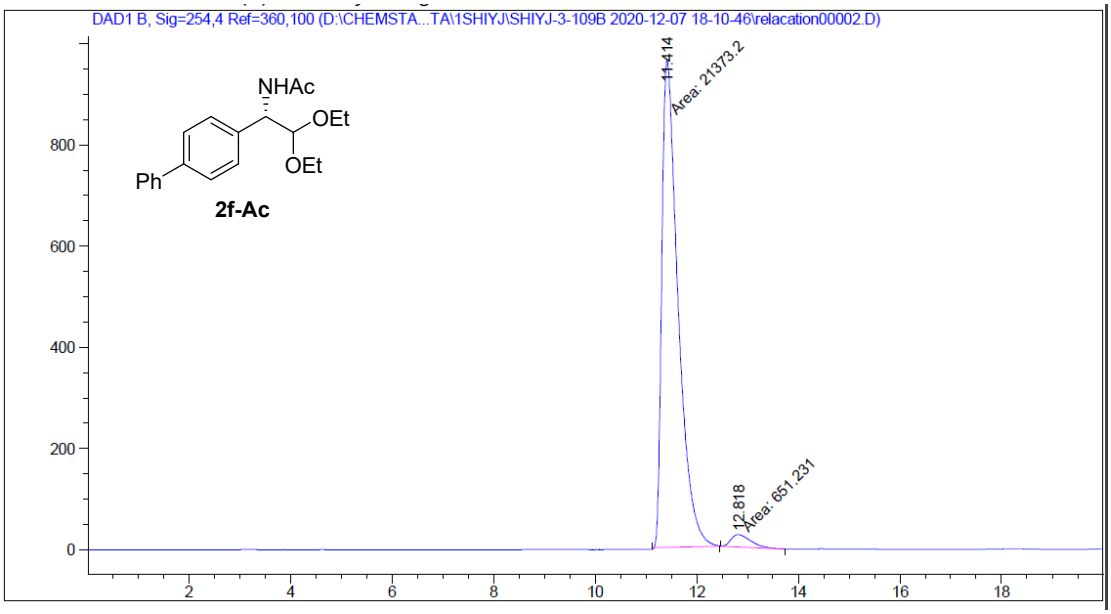
Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.897	BB	0.2021	6028.88477	456.33356	98.9748
2	10.569	BB	0.2920	62.44792	3.01062	1.0252



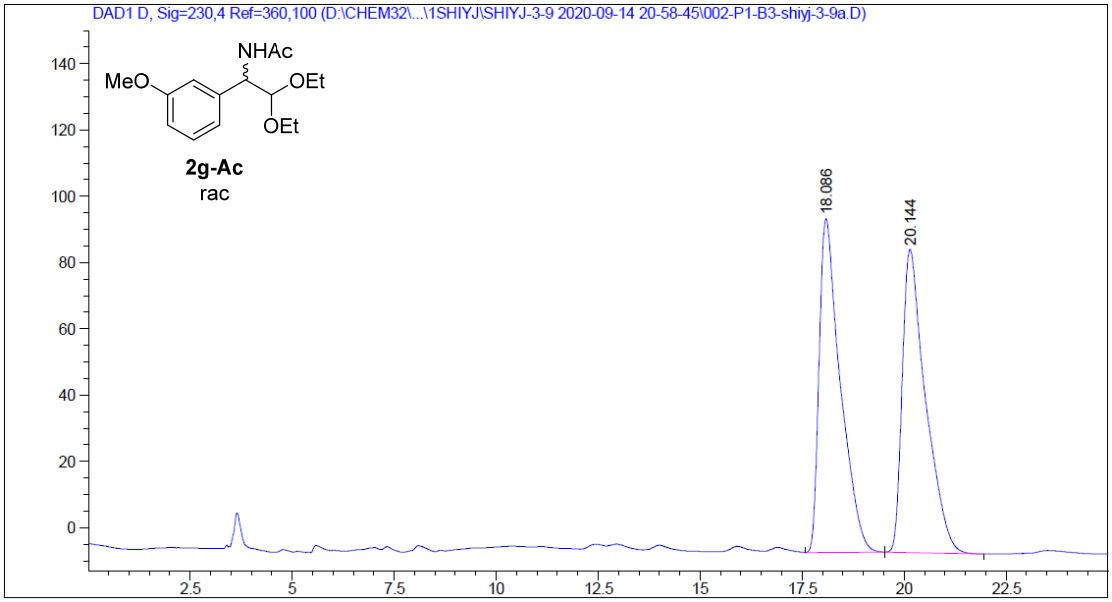
Signal 1: DAD1 B, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.728	BV	0.3084	1346.69177	65.91394	49.8920
2	12.961	VB	0.4049	1352.51953	49.48120	50.1080



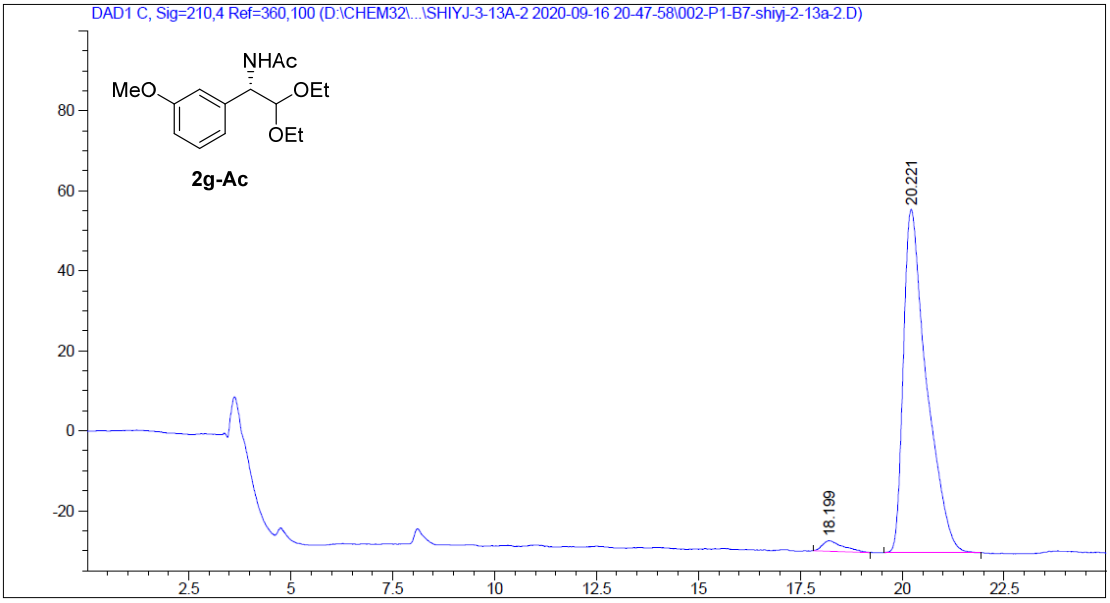
Signal 1: DAD1 B, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.414	MM	0.3703	2.13732e4	961.90515	97.0431
2	12.818	MM	0.4472	651.23108	24.26995	2.9569



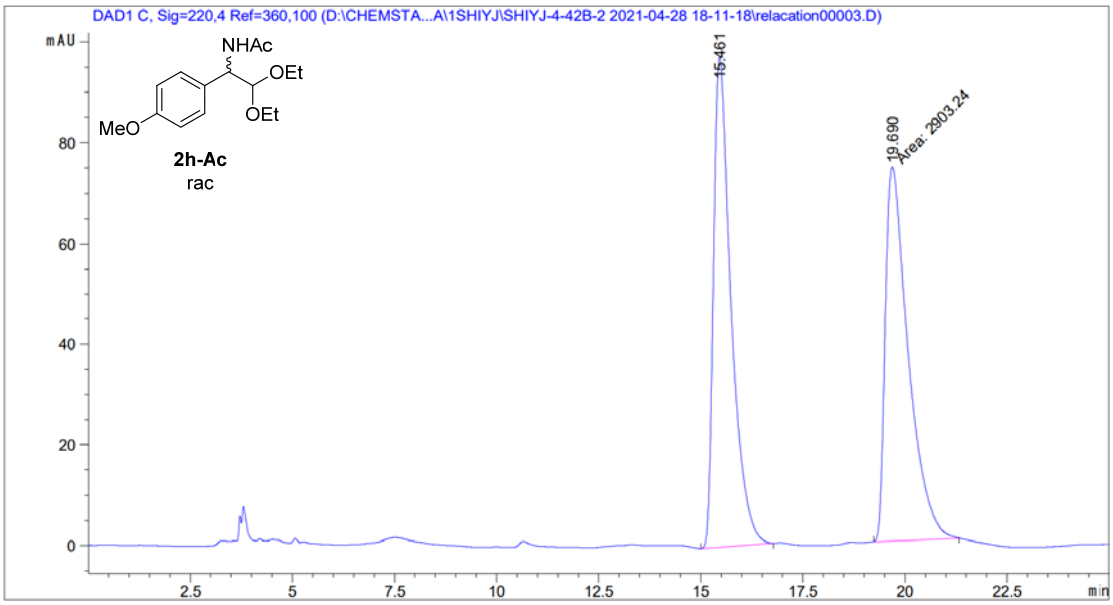
Signal 1: DAD1 D, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.086	BB	0.5206	3627.91333	100.64352	49.9370
2	20.144	BB	0.5737	3637.06958	91.51700	50.0630



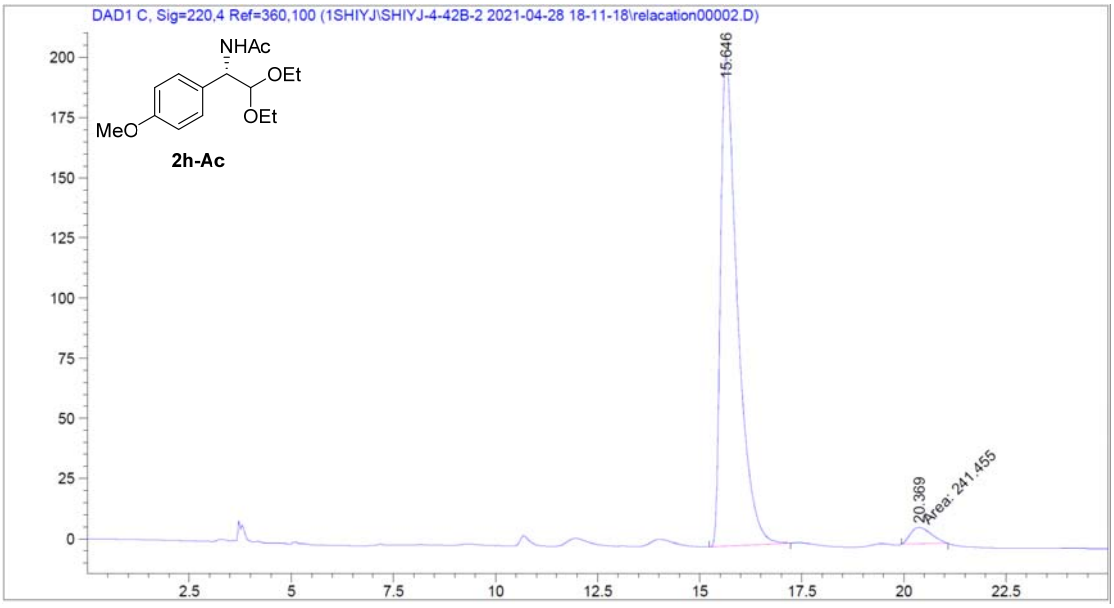
Signal 1: DAD1 C, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.199	BB	0.4280	93.63518	2.63865	2.6872
2	20.221	BB	0.5777	3390.84961	85.68890	97.3128



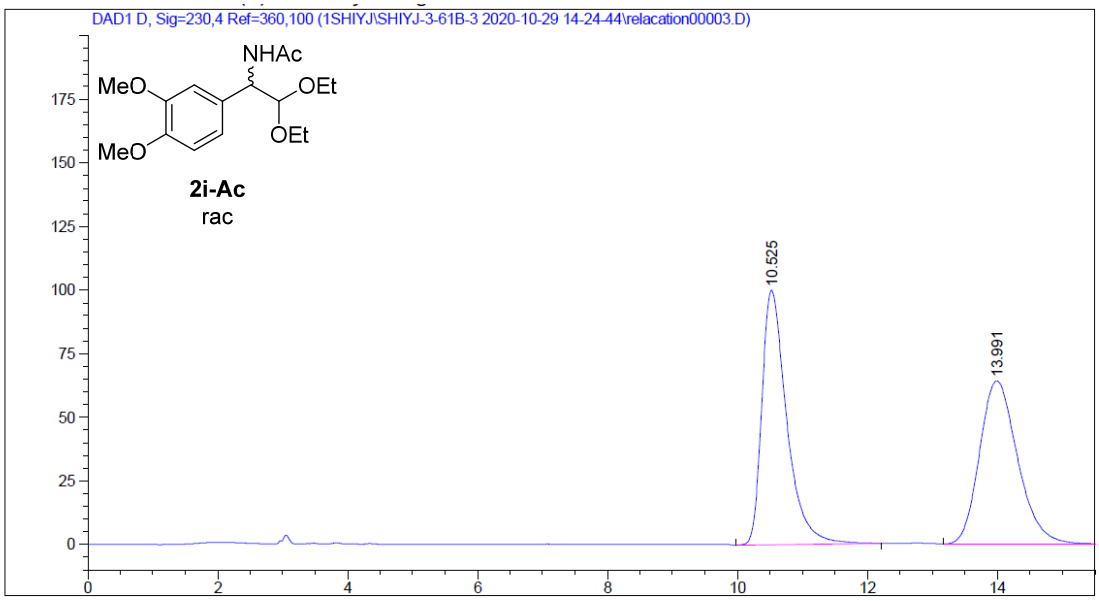
Signal 1: DAD1 C, Sig=220,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.646	BB	0.4287	5863.24609	203.16783	96.0448
2	20.369	MM	0.5906	241.45497	6.81371	3.9552



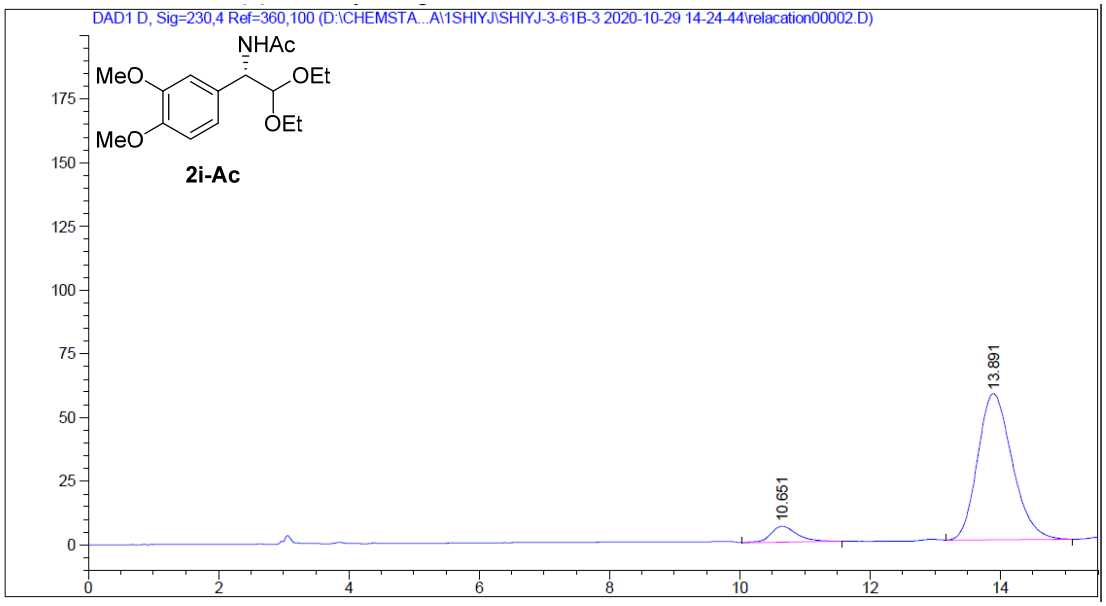
Signal 1: DAD1 C, Sig=220,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.646	BB	0.4287	5863.24609	203.16783	96.0448
2	20.369	MM	0.5906	241.45497	6.81371	3.9552



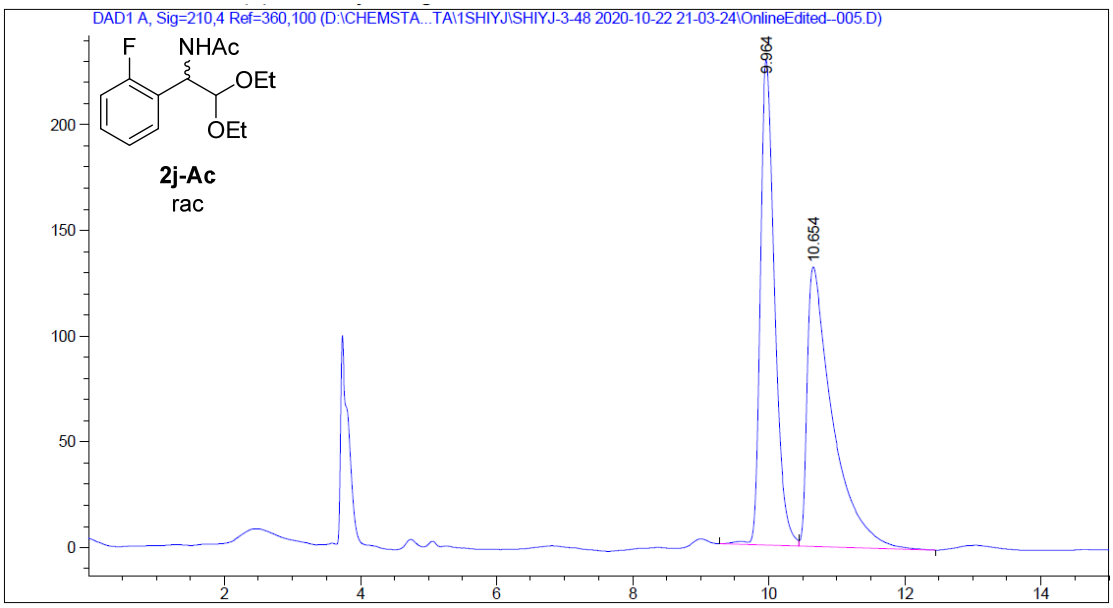
Signal 1: DAD1 D, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.525	BB	0.4019	2658.90991	100.11333	50.5419
2	13.991	BB	0.6195	2601.89478	64.10281	49.4581



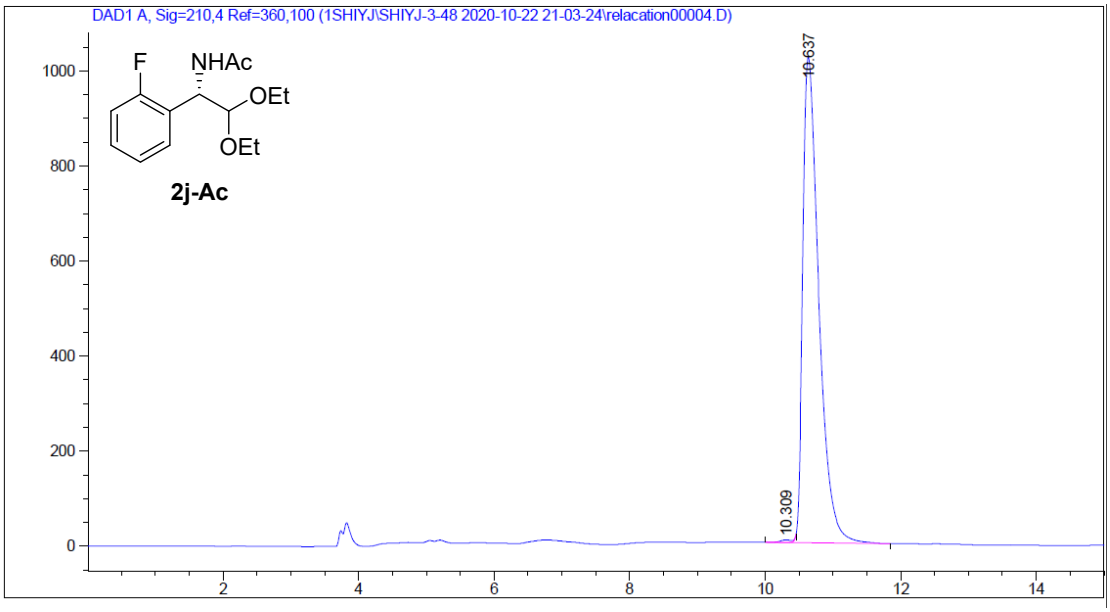
Signal 1: DAD1 D, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.651	BB	0.3955	173.95155	6.27411	7.6078
2	13.891	BB	0.5680	2112.53955	57.31940	92.3922



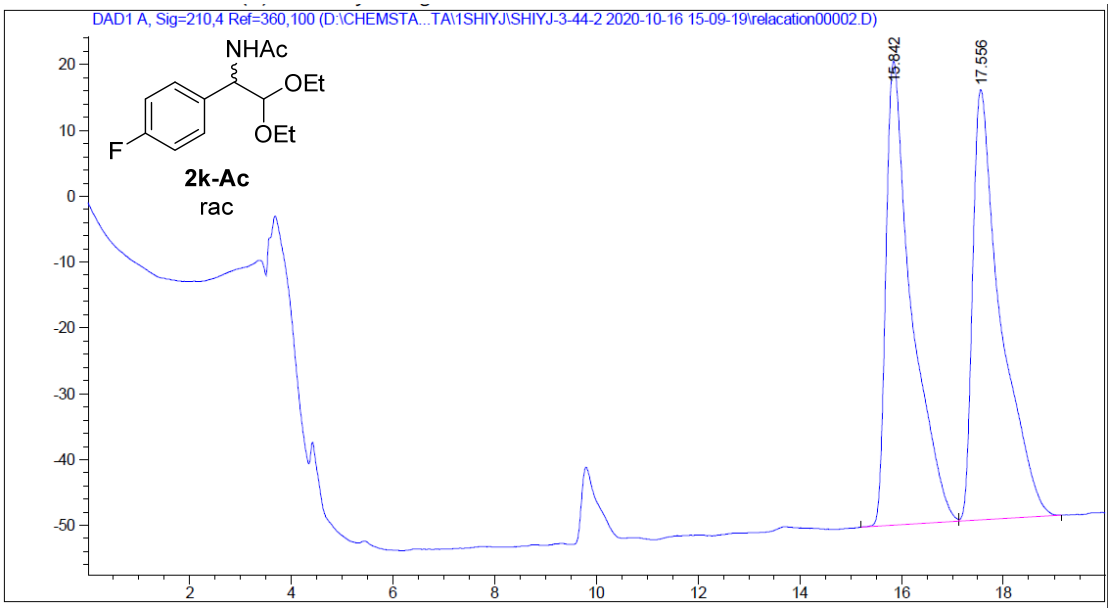
Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.964	VV R	0.2236	3360.18701	229.67091	49.6016
2	10.654	VB	0.3632	3414.16138	132.22545	50.3984



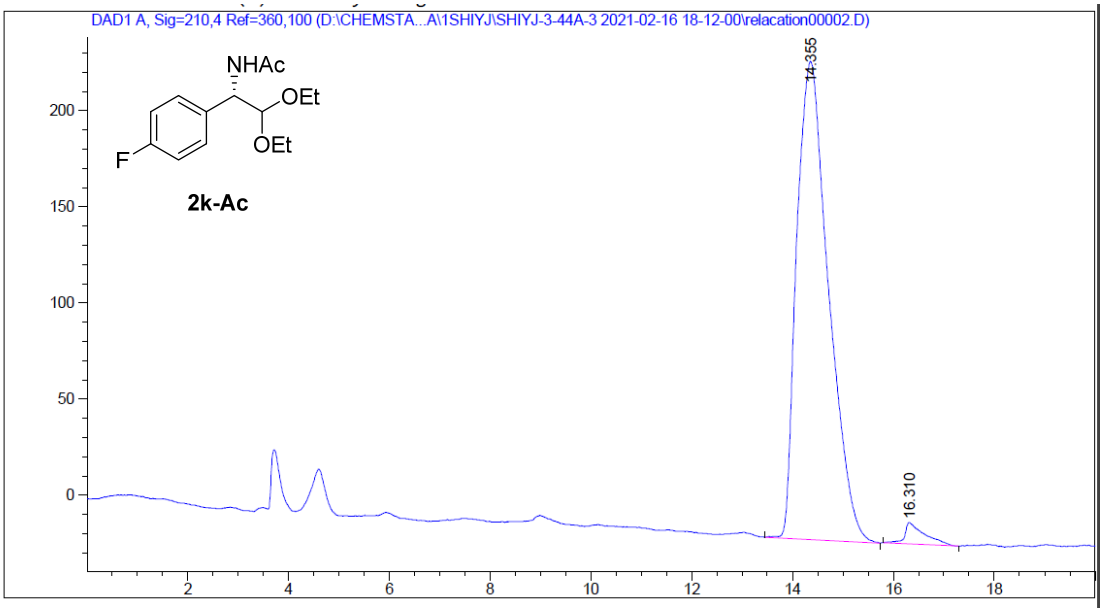
Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.309	BV E	0.1767	67.27077	5.65959	0.3994
2	10.637	VB R	0.2495	1.67752e4	1022.09692	99.6006



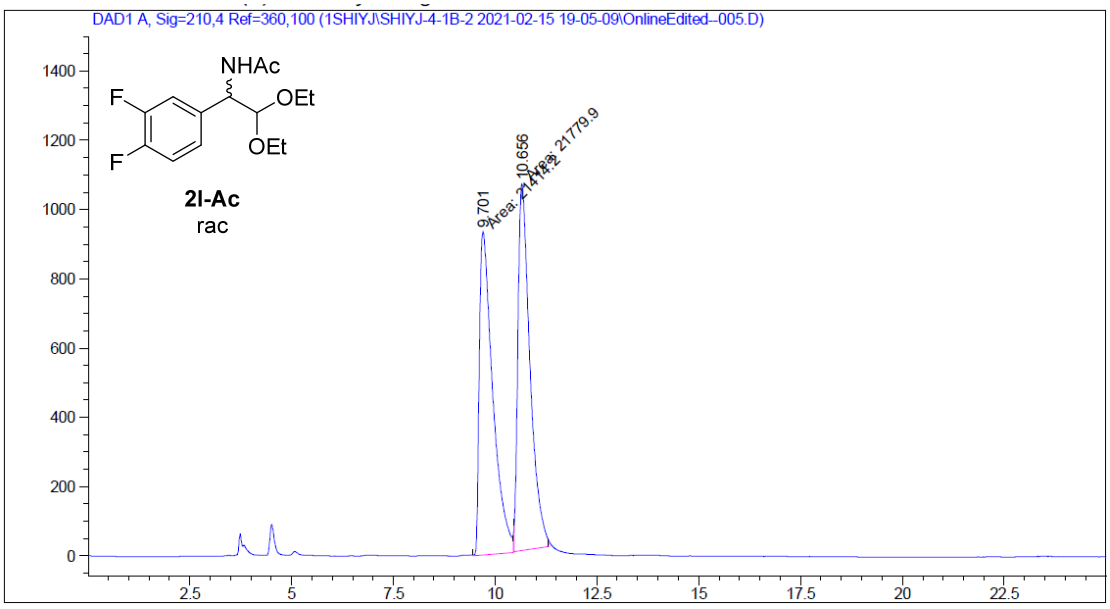
Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.842	BV	0.4933	2474.17627	70.53150	49.6480
2	17.556	VB	0.5397	2509.25879	65.38808	50.3520



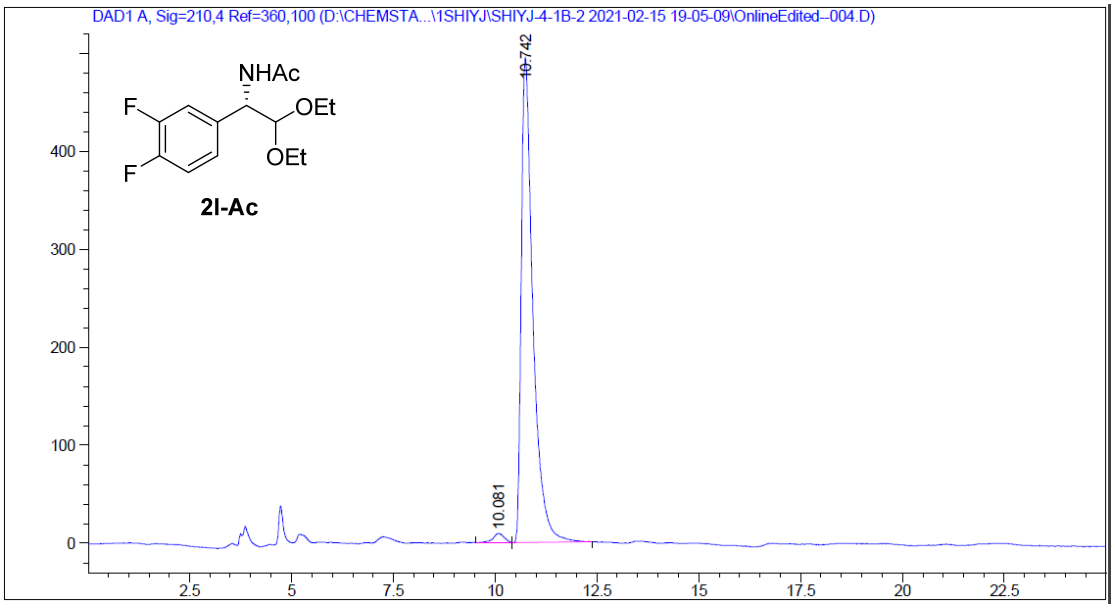
Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.355	VB R	0.6668	1.08888e4	248.71510	97.2413
2	16.310	VB R	0.3487	308.90768	11.23804	2.7587



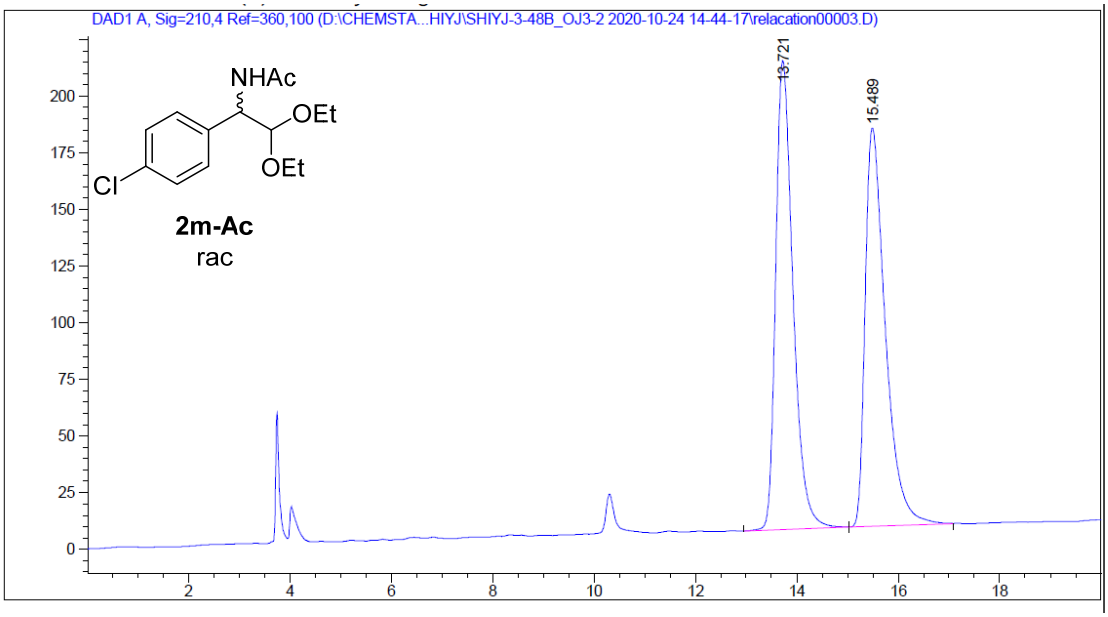
Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.701	MM	0.3821	2.14142e4	933.94714	49.5767
2	10.656	MM	0.3430	2.17799e4	1058.38904	50.4233



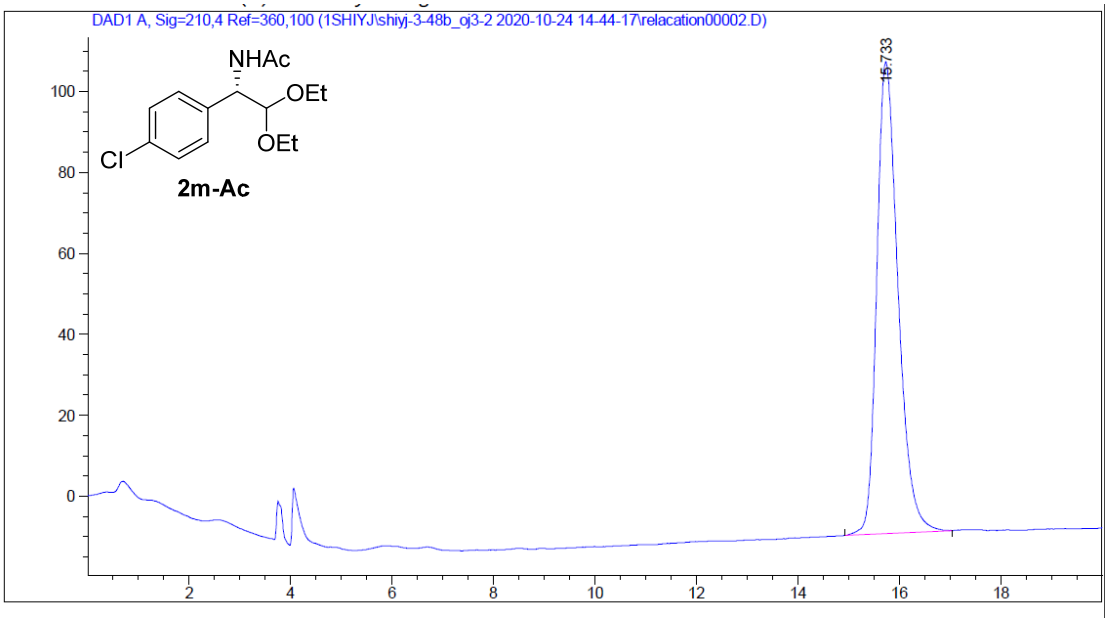
Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.081	VB R	0.2542	184.60168	9.52206	1.8352
2	10.742	BV R	0.2969	9874.18848	494.60416	98.1648



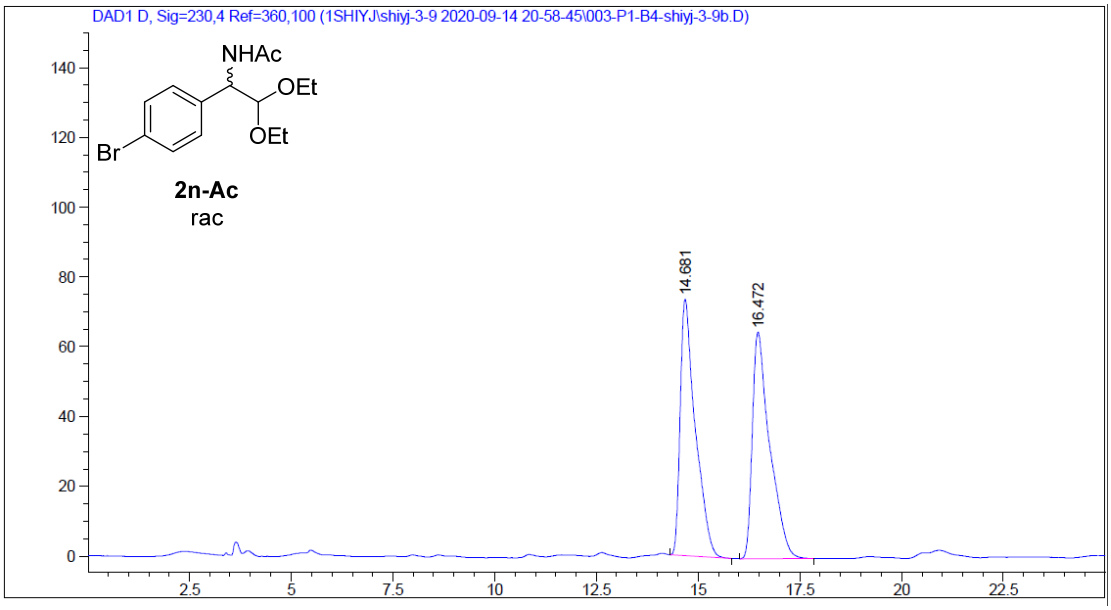
Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.721	BB	0.3626	4904.28613	206.86893	50.2624
2	15.489	BB	0.4161	4853.07178	175.77356	49.7376



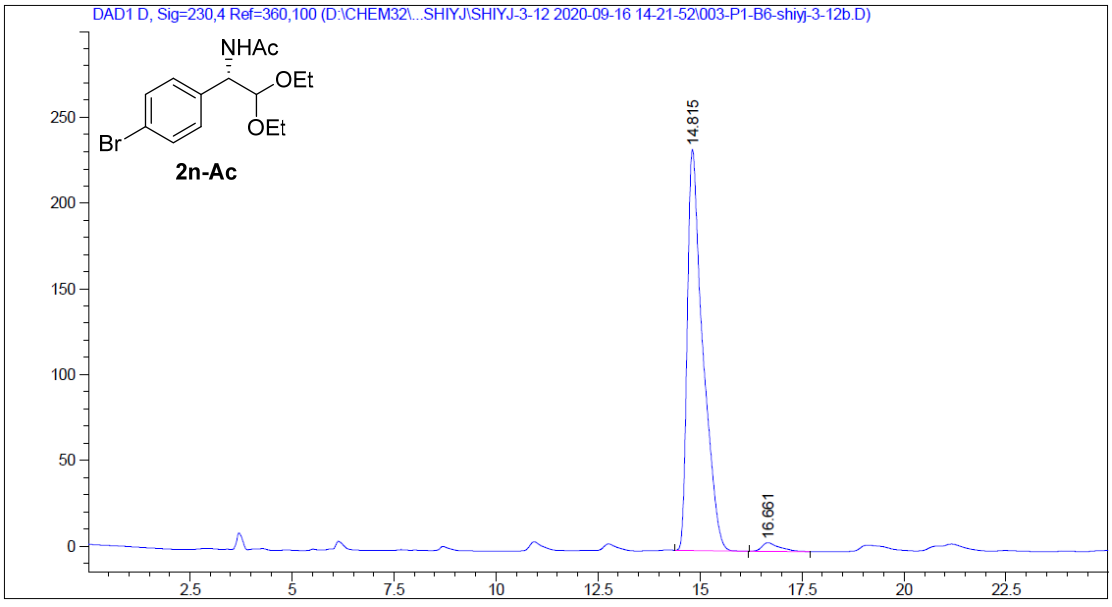
Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.733	BB	0.4418	3395.52173	116.59029	100.0000



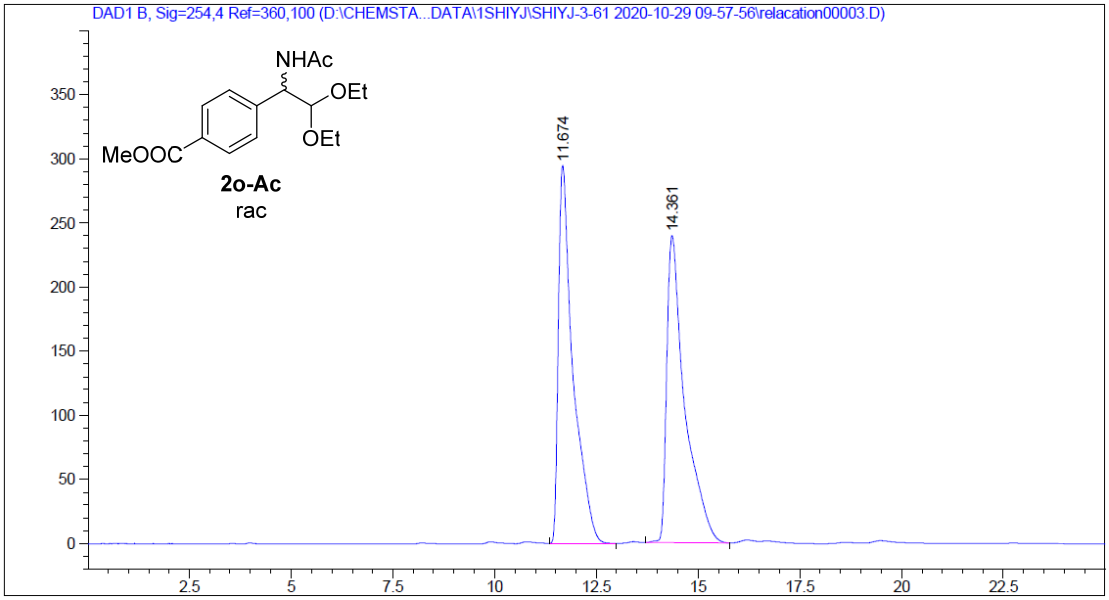
Signal 1: DAD1 D, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.681	BB	0.3712	1897.05835	73.48484	49.5575
2	16.472	BB	0.4228	1930.93872	64.95163	50.4425



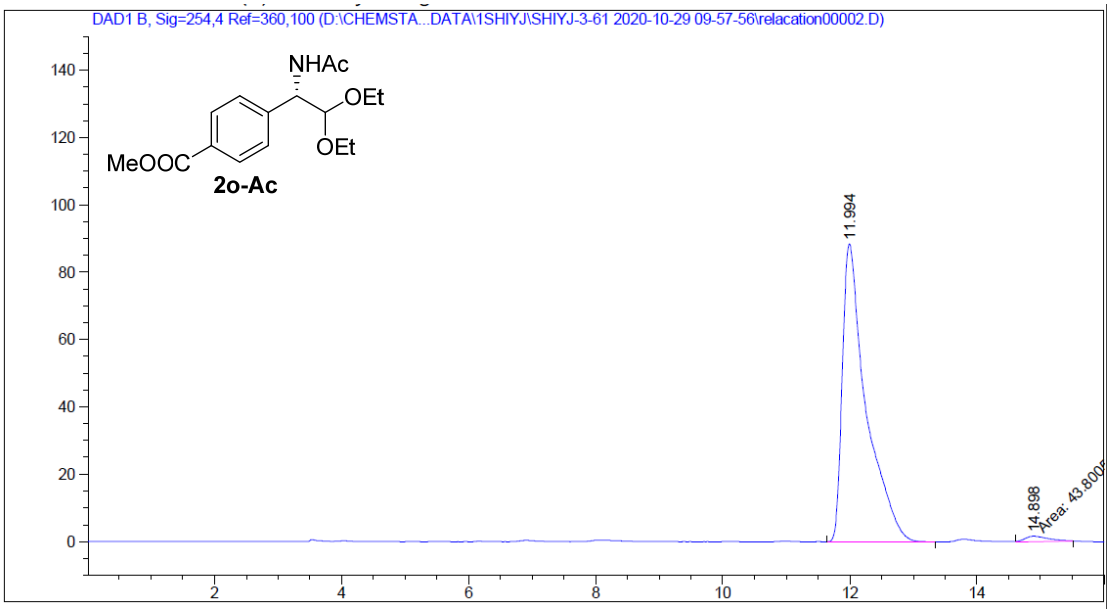
Signal 1: DAD1 D, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.815	BB	0.3814	6202.06348	233.89536	97.6576
2	16.661	BB	0.4122	148.76442	5.01272	2.3424



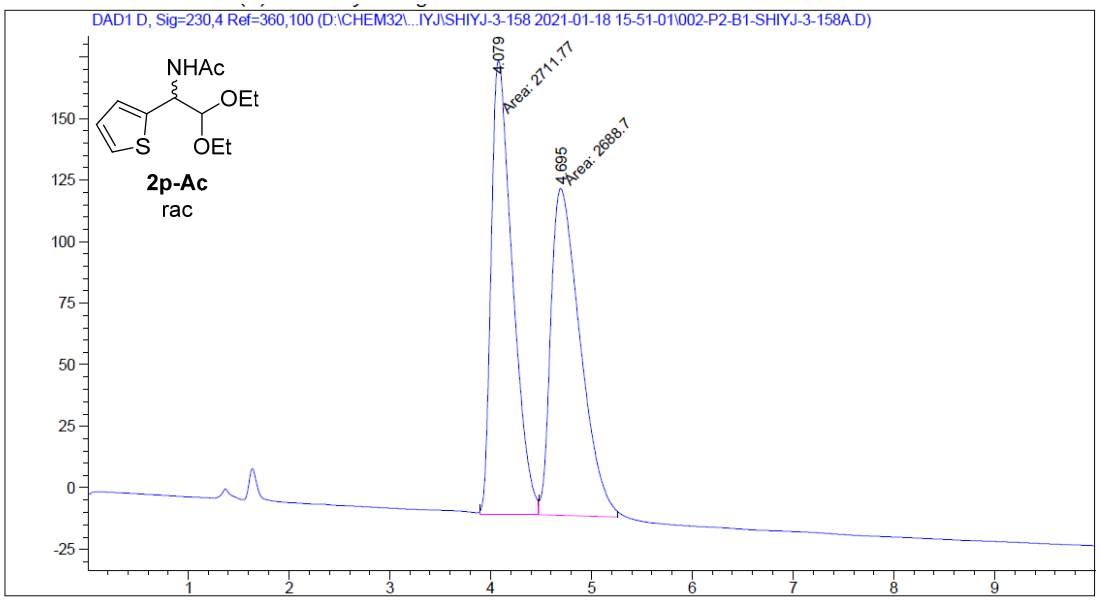
Signal 1: DAD1 B, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.674	BB	0.3550	7348.78662	294.62073	49.9317
2	14.361	BB	0.4389	7368.89453	239.52878	50.0683



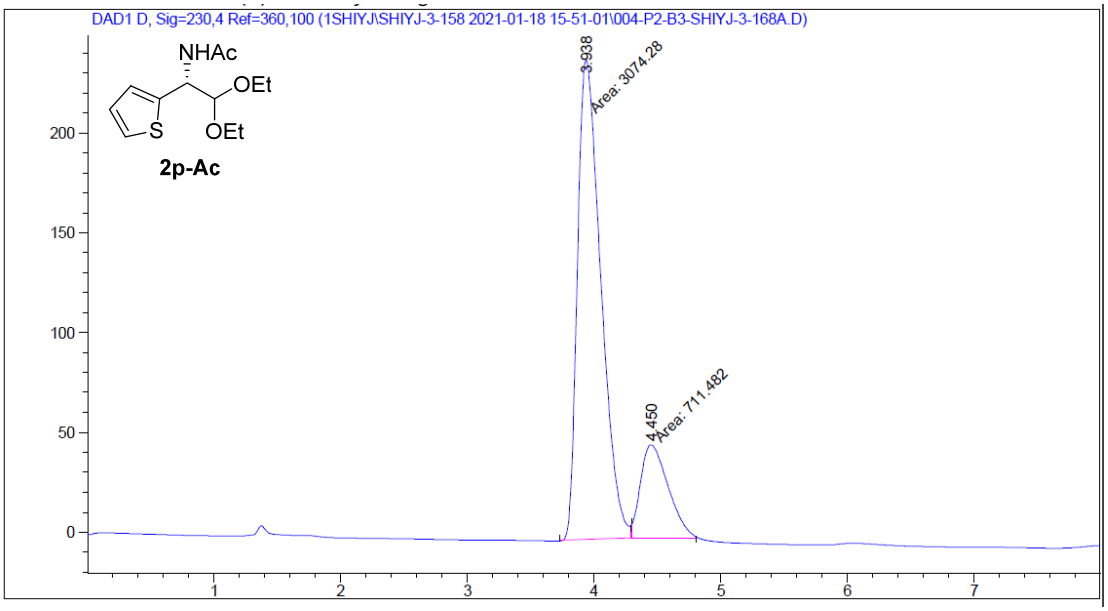
Signal 1: DAD1 B, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.994	BB	0.3666	2295.15405	88.48380	98.1273
2	14.898	MM	0.4385	43.80046	1.66472	1.8727



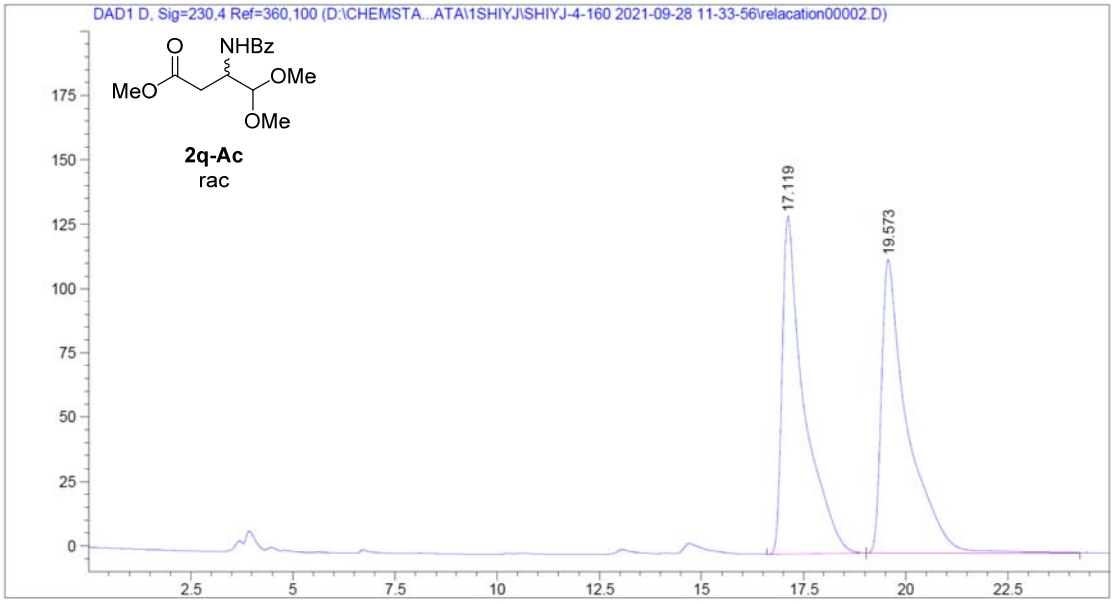
Signal 1: DAD1 D, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.079	MM	0.2449	2711.77124	184.55461	50.2136
2	4.695	MM	0.3374	2688.70483	132.80968	49.7864



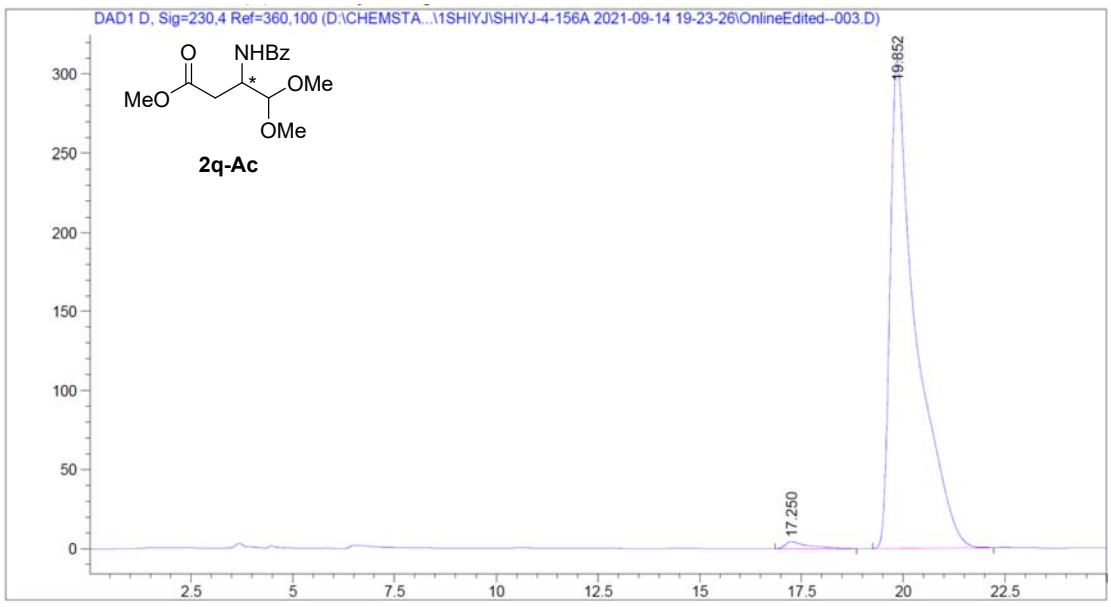
Signal 1: DAD1 D, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.938	MM	0.2134	3074.28076	240.12175	81.2064
2	4.450	MM	0.2530	711.48199	46.86198	18.7936



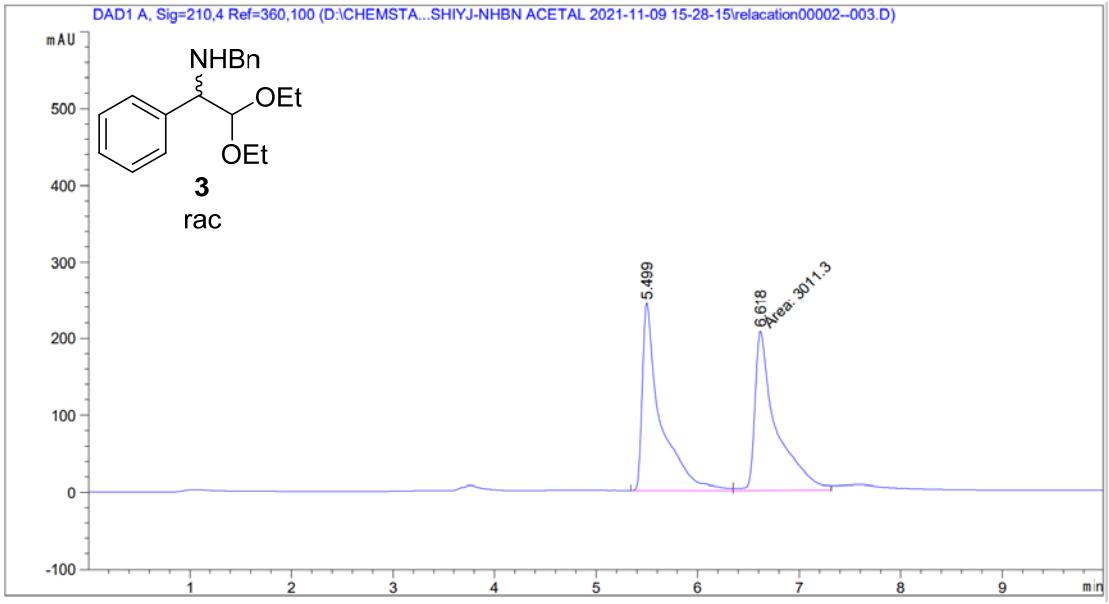
Signal 1: DAD1 D, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.119	BB	0.5108	4893.10986	131.28204	49.3576
2	19.573	BB	0.6012	5020.47412	114.13428	50.6424



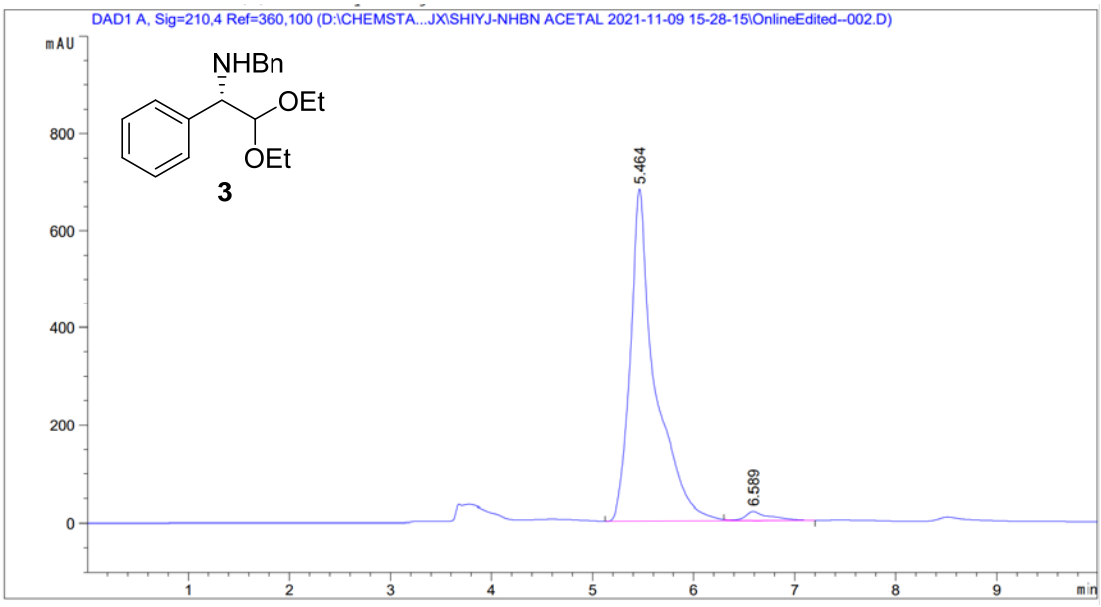
Signal 1: DAD1 D, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.250	BB	0.5141	165.28810	4.38208	1.2028
2	19.852	BB	0.6011	1.35771e4	308.71213	98.7972



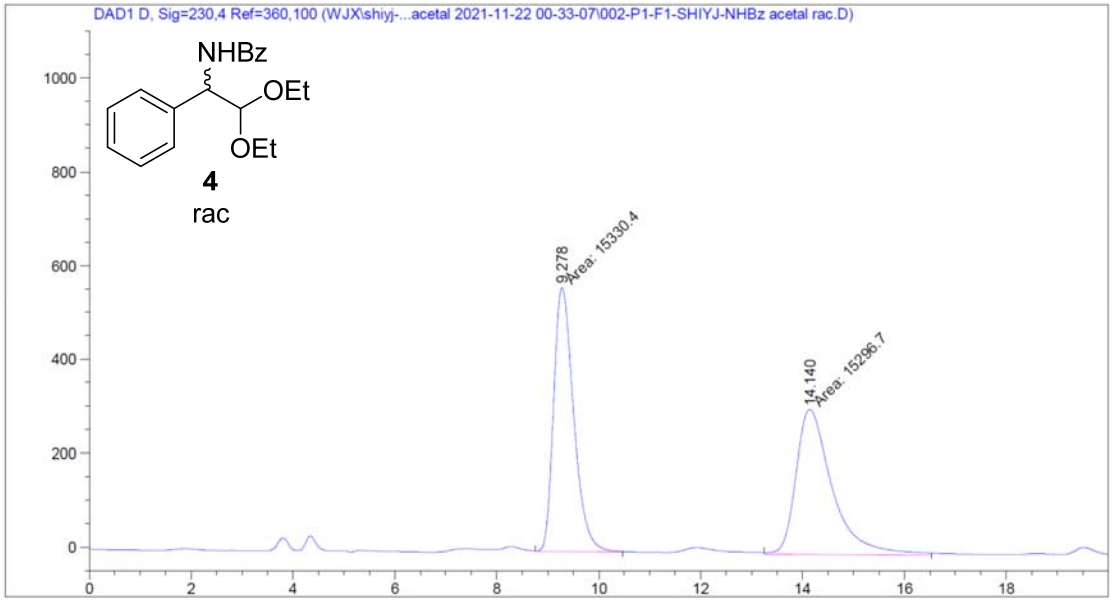
Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.499	BV	0.1687	3024.60596	243.94107	50.1102
2	6.618	MF	0.2427	3011.30396	206.77905	49.8898



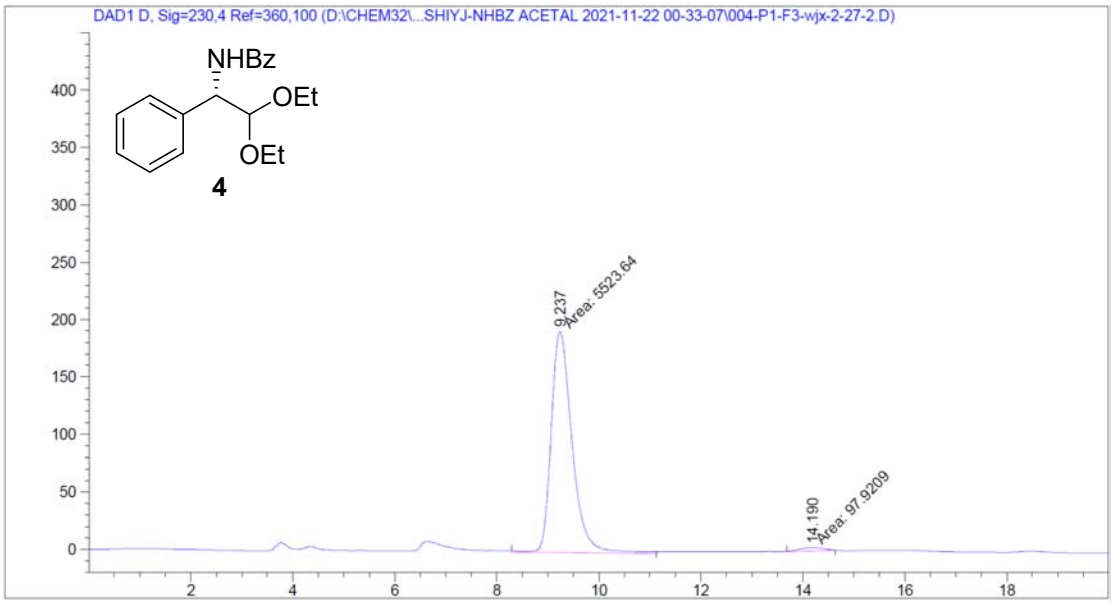
Signal 1: DAD1 A, Sig=210,4 Ref=360,100

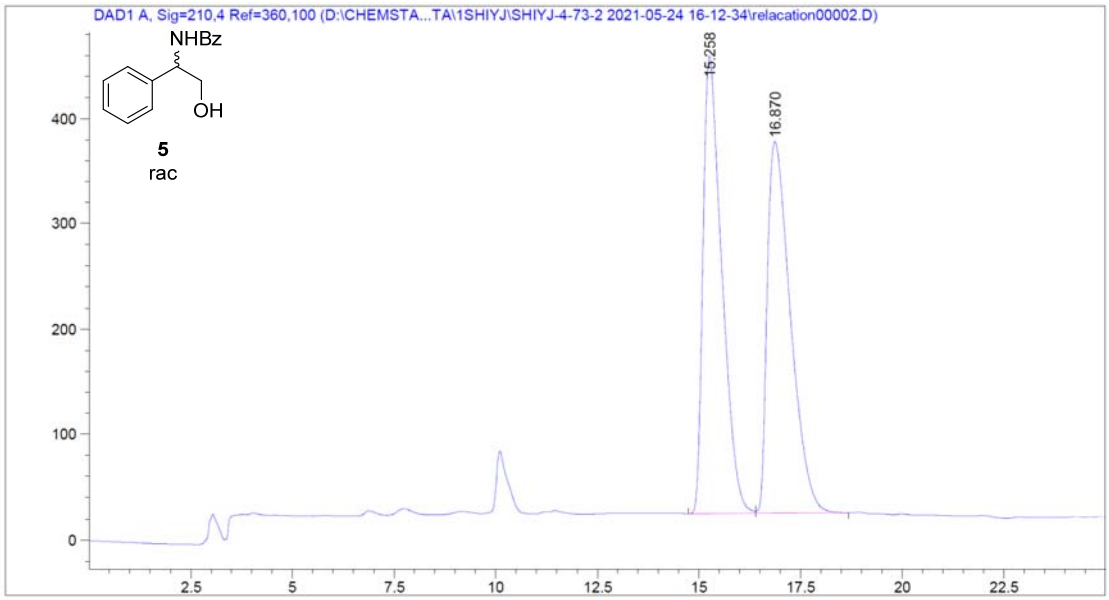
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.464	BV R	0.2291	1.16548e4	683.00140	97.2997
2	6.589	VB E	0.2249	323.44791	19.55738	2.7003



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

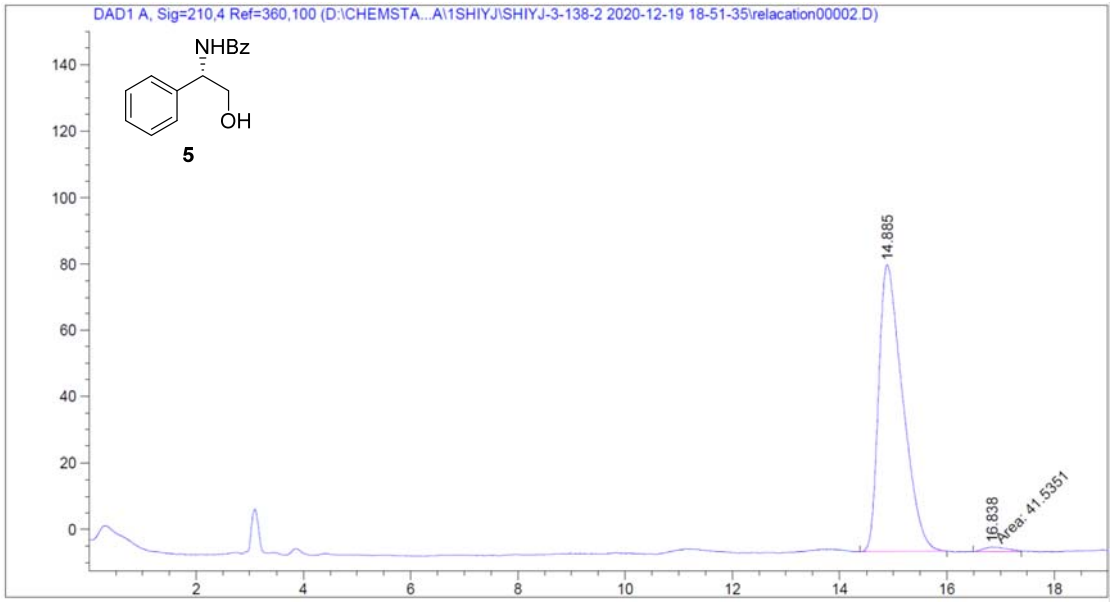
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.278	MM	0.4540	1.53304e4	562.76740	50.0550
2	14.140	MM	0.8282	1.52967e4	307.82202	49.9450





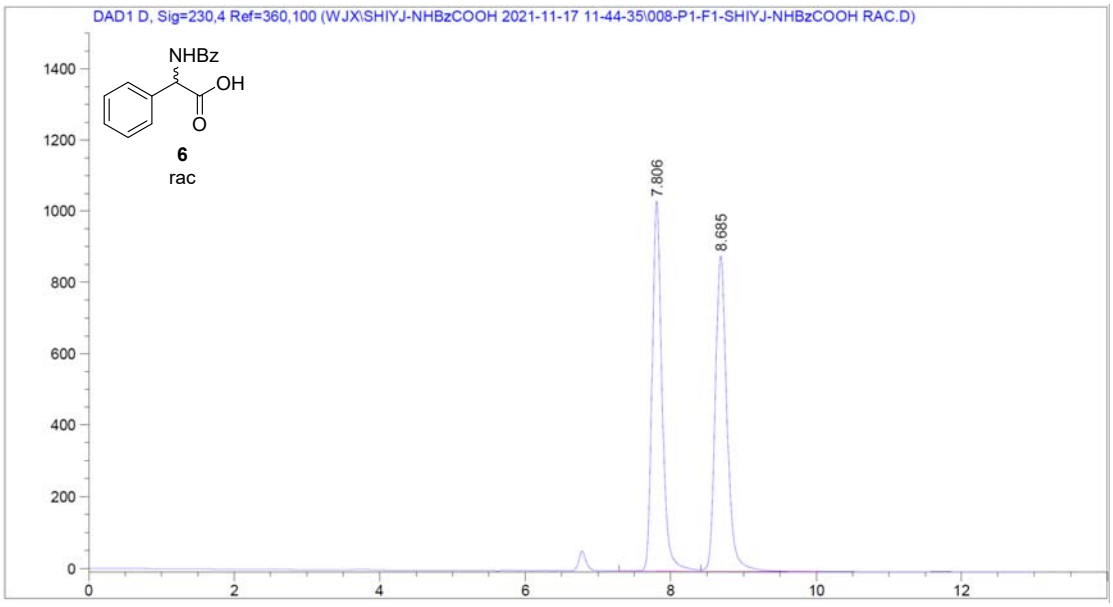
Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.258	BV	0.4743	1.39240e4	434.01779	49.9065
2	16.870	VB	0.6122	1.39761e4	352.75870	50.0935



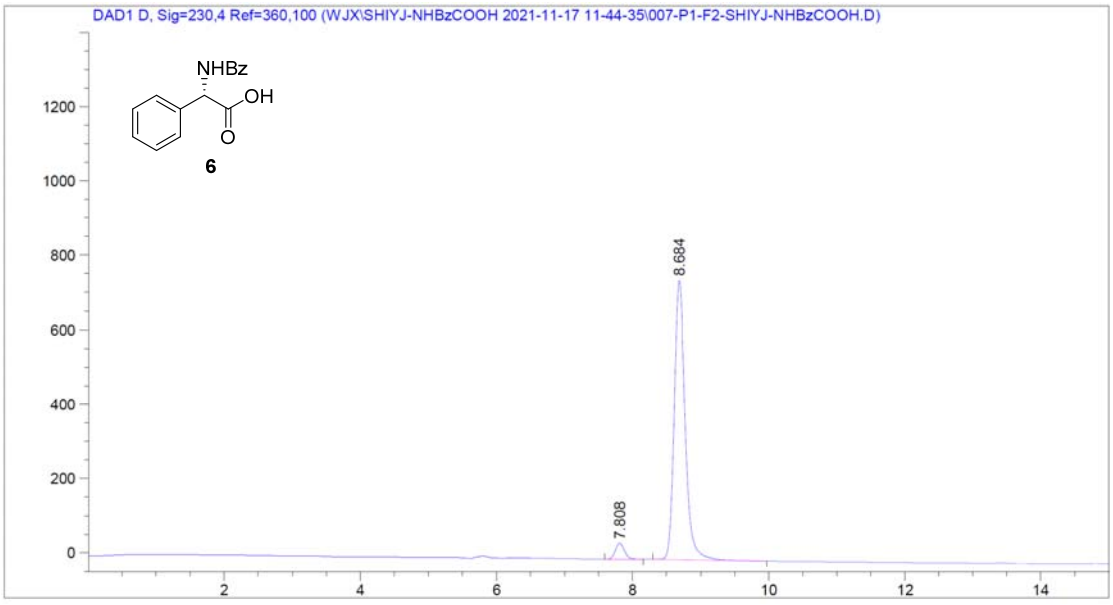
Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.885	BB	0.4504	2686.73535	86.48200	98.4776
2	16.838	MM	0.5199	41.53515	1.33141	1.5224



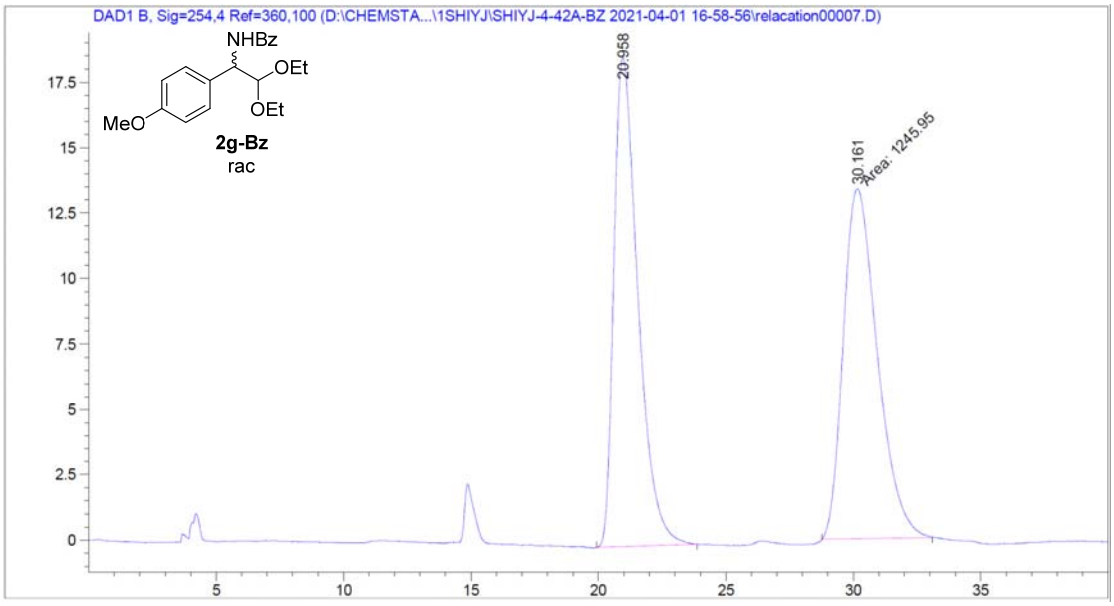
Signal 1: DAD1 D, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.806	BV	0.1447	9834.31445	1036.78589	49.8065
2	8.685	VB	0.1709	9910.74609	883.11548	50.1935



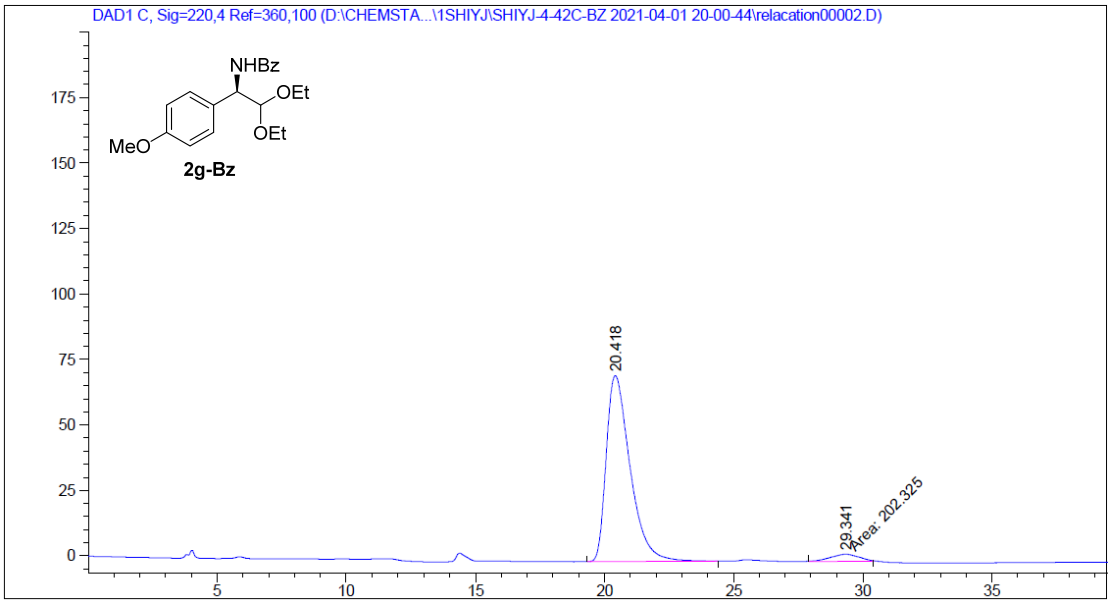
Signal 1: DAD1 D, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.808	BB	0.1412	403.29742	43.87557	4.5845
2	8.684	BB	0.1704	8393.61816	751.02795	95.4155



Signal 1: DAD1 B, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.958	BB	0.9554	1229.65405	18.69534	49.6709
2	30.161	MM	1.5518	1245.95081	13.38186	50.3291

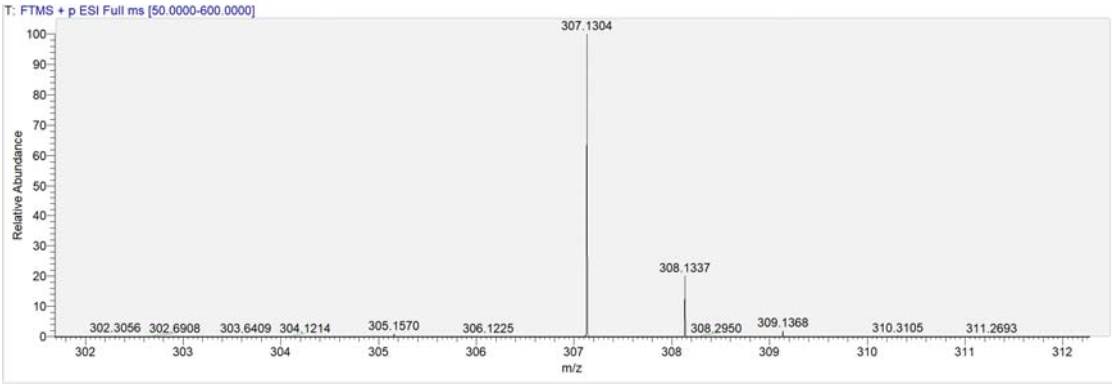


Signal 1: DAD1 C, Sig=220,4 Ref=360,100

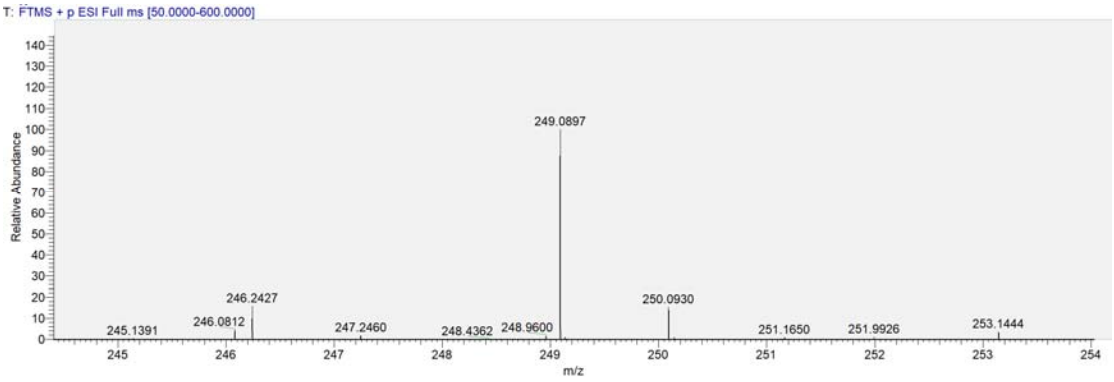
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.418	BB	0.9681	4584.30859	71.11302	95.7731
2	29.341	MM	1.2548	202.32512	2.68733	4.2269

VIII. HRMS spectra

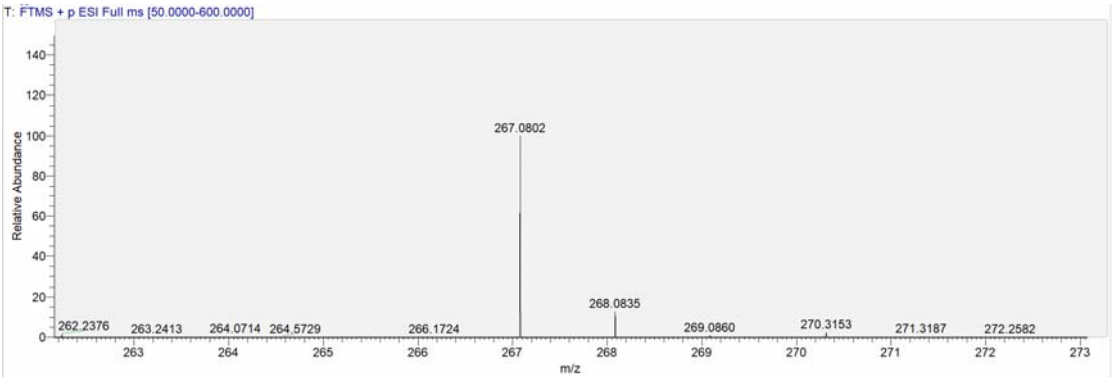
1-([1,1'-biphenyl]-4-yl)-2,2-diethoxyethan-1-one (1f)



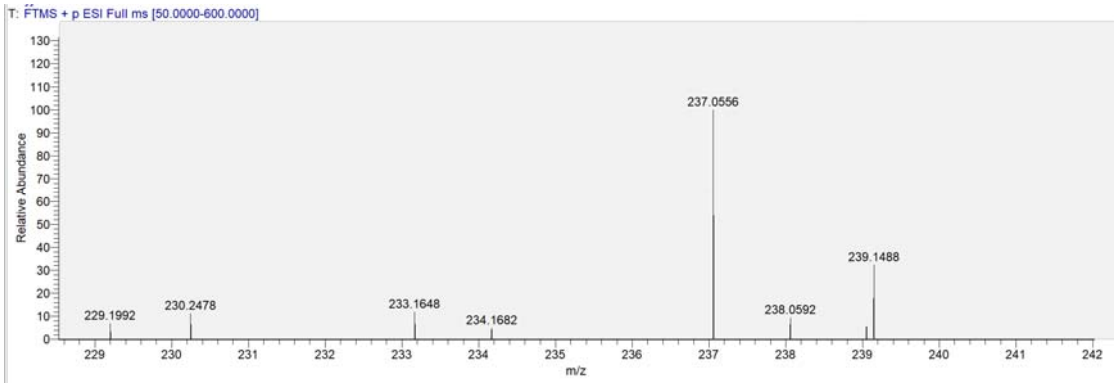
2,2-diethoxy-1-(2-fluorophenyl)ethan-1-one (1j)



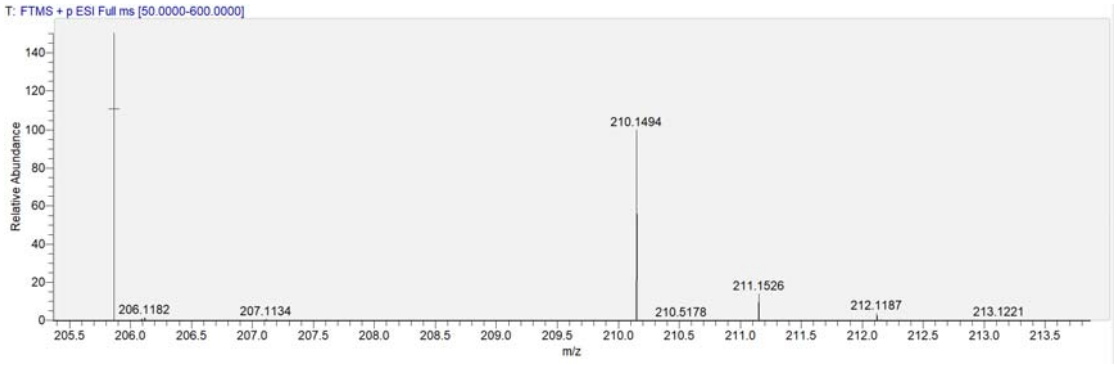
1-(3,4-difluorophenyl)-2,2-diethoxyethan-1-one (1l)



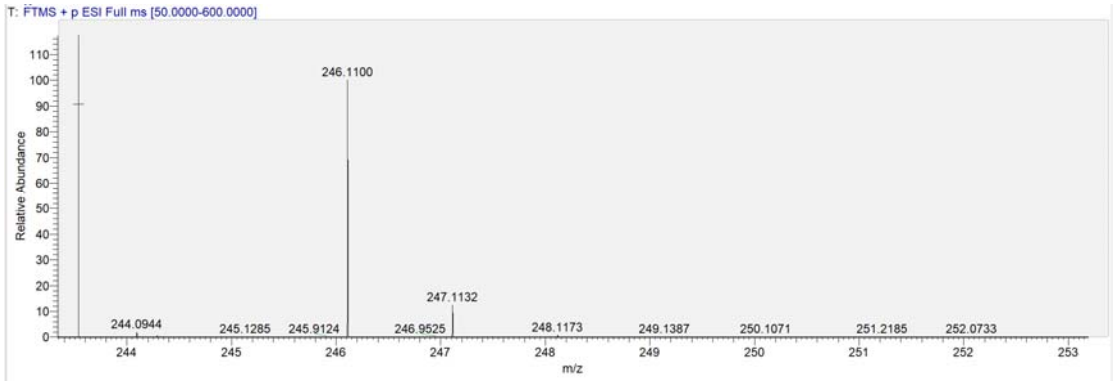
2,2-diethoxy-1-(thiophen-2-yl)ethan-1-one (1p)



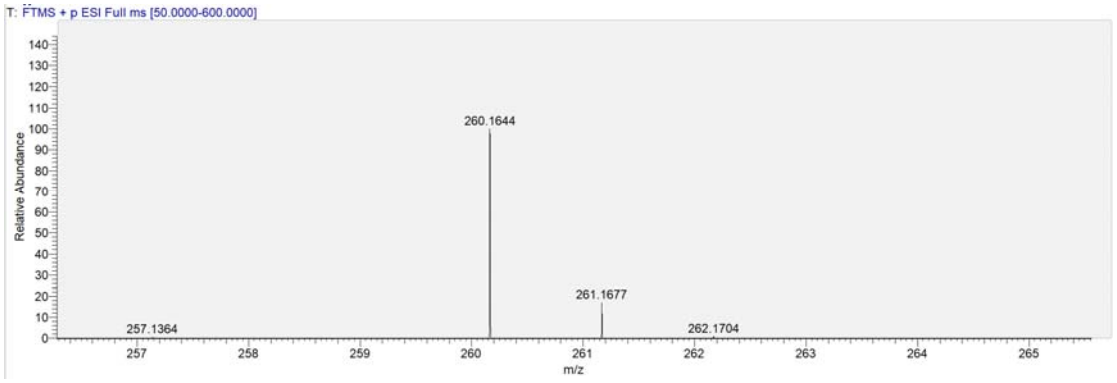
2-bromo-5,6-dihydro-[1,1'-biphenyl]-3(4H)-ol (2aa)



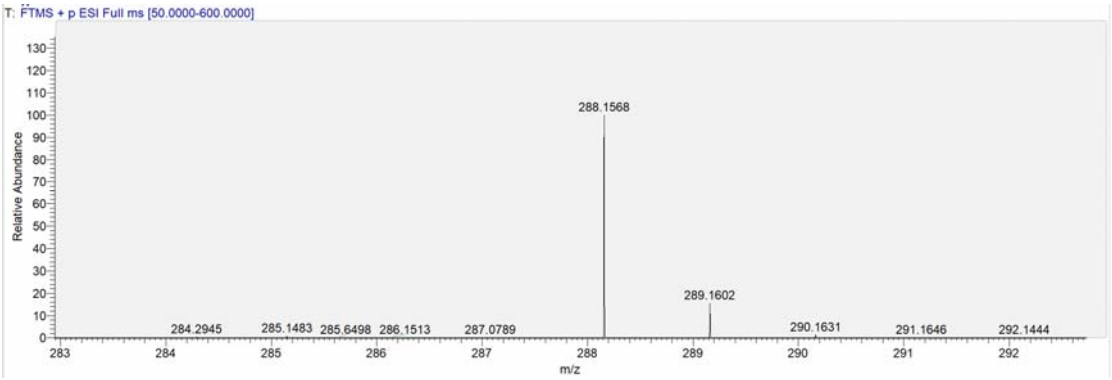
(*S*)-N-(2,2-dimethoxy-1-phenylethyl)acetamide (2ab-Ac)



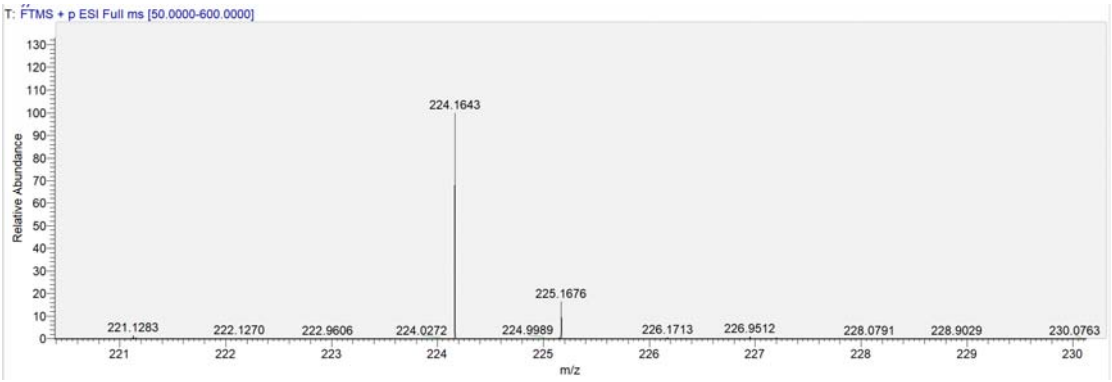
(*S*)-2,2-diethoxy-1-(naphthalen-2-yl)ethan-1-amine (2b)



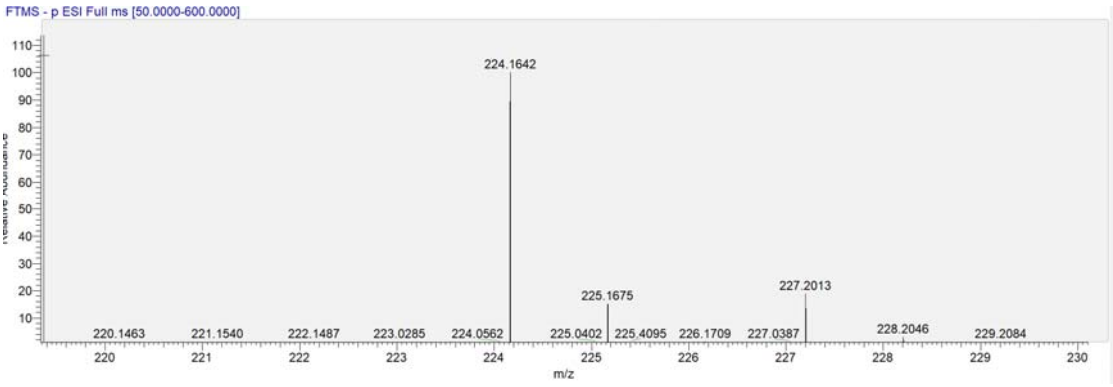
(*S*)-N-(2,2-diethoxy-1-(o-tolyl)ethyl)acetamide (2c-Ac)



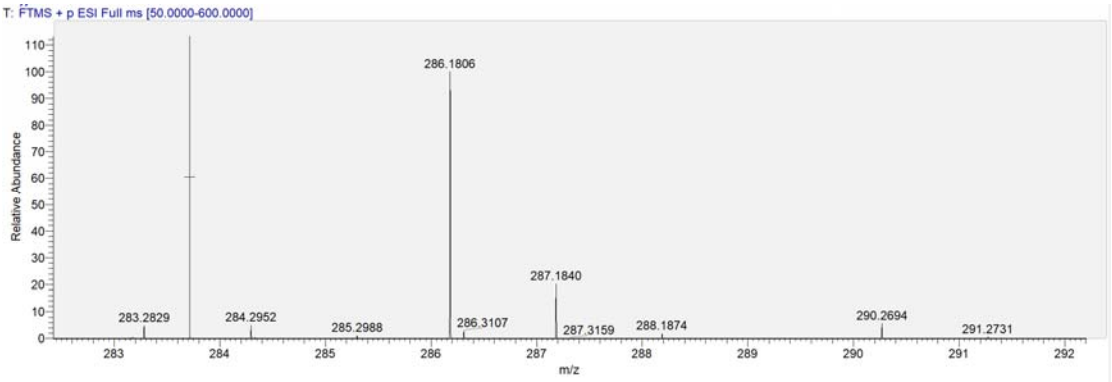
(*S*)-2,2-diethoxy-1-(m-tolyl)ethan-1-amine (2d)



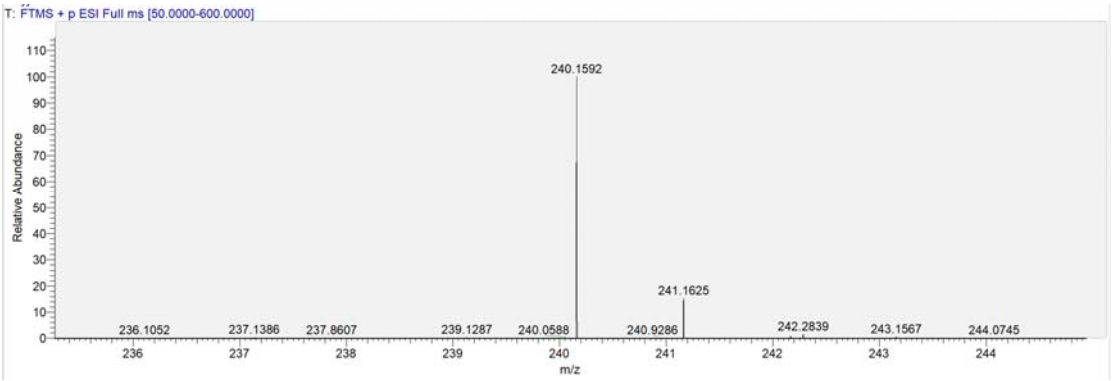
(*S*)-2,2-diethoxy-1-(p-tolyl)ethan-1-amine (2e)



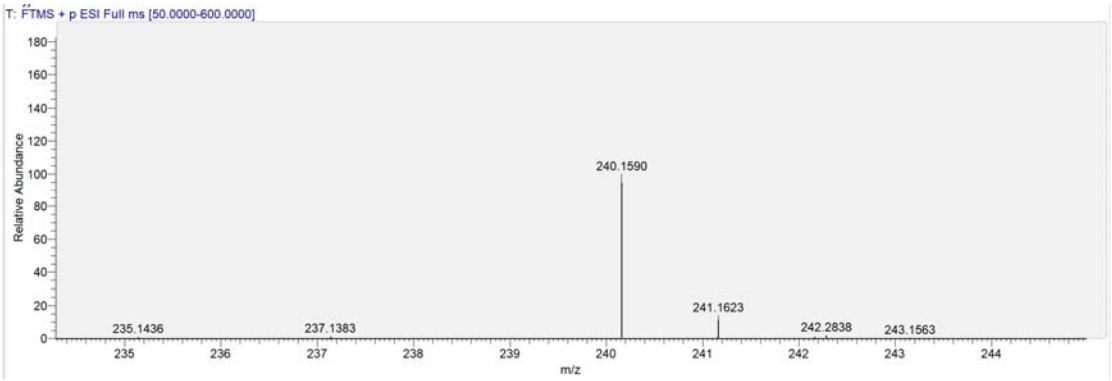
(*S*)-1-([1,1'-biphenyl]-4-yl)-2,2-diethoxyethan-1-amine (2f)



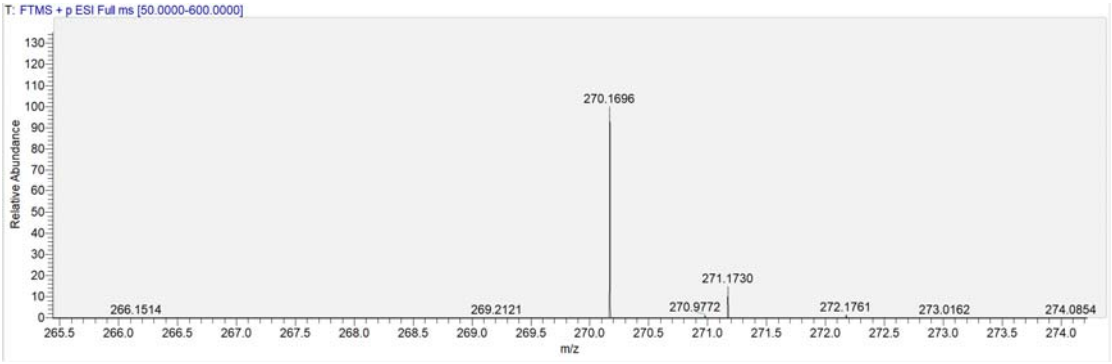
(*S*)-2,2-diethoxy-1-(3-methoxyphenyl)ethan-1-amine (2g)



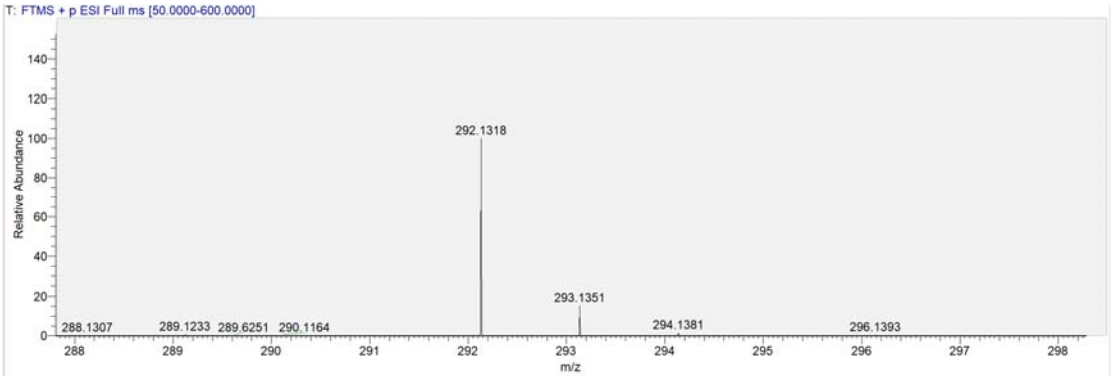
(*S*)-2,2-diethoxy-1-(4-methoxyphenyl)ethan-1-amine (2h)



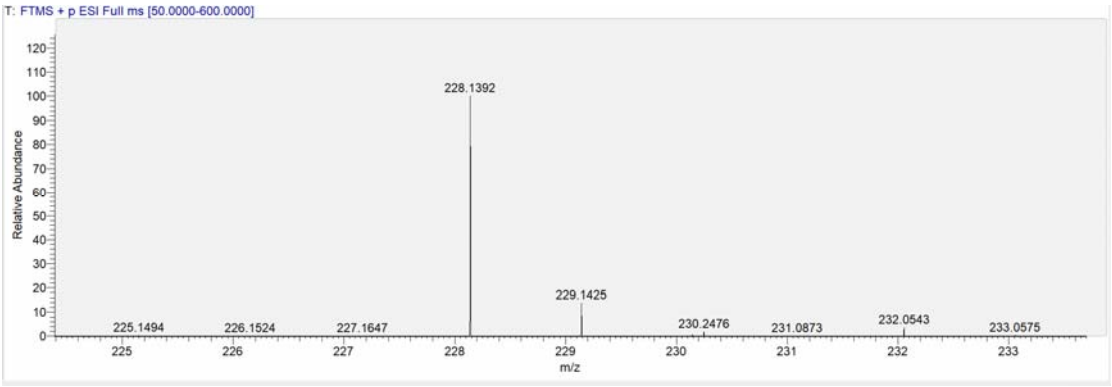
(*S*)-1-(3,4-dimethoxyphenyl)-2,2-diethoxyethan-1-amine (2i)



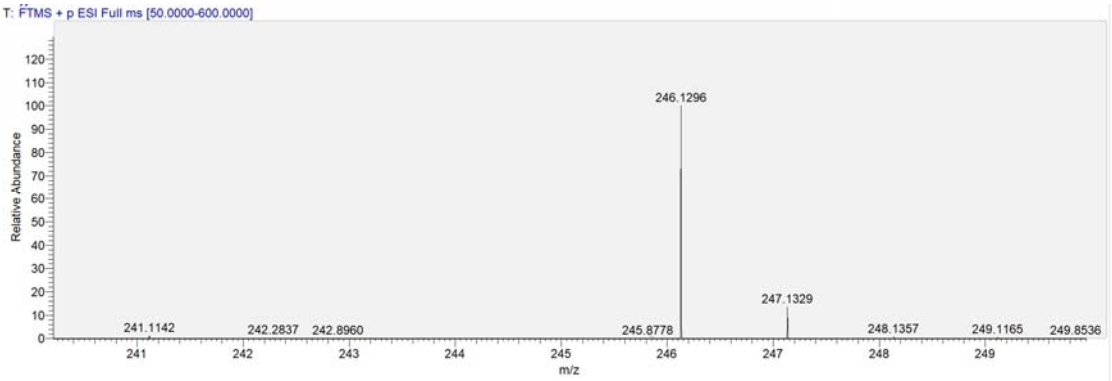
(*S*)-N-(2,2-diethoxy-1-(2-fluorophenyl)ethyl)acetamide (2j-Ac)



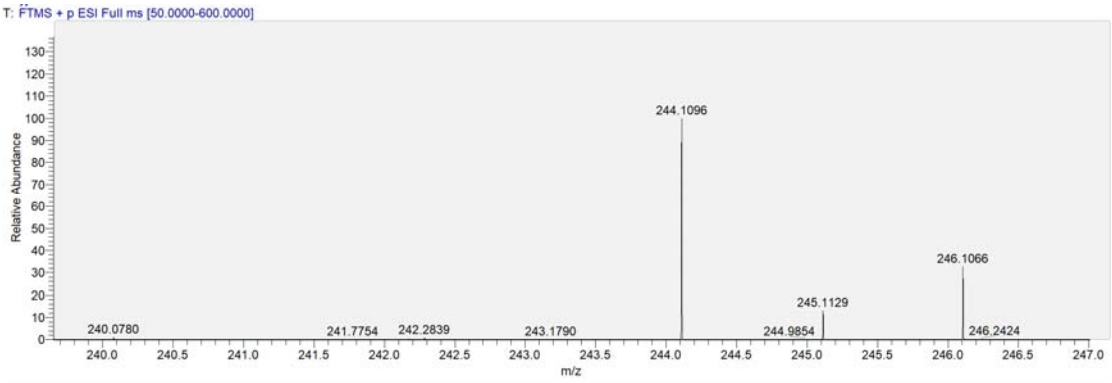
(*S*)-2,2-diethoxy-1-(4-fluorophenyl)ethan-1-amine (2k)



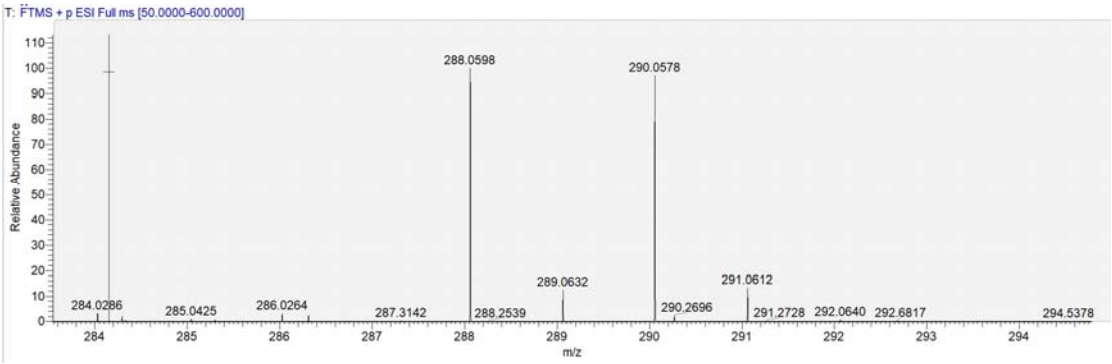
(*S*)-1-(3,4-difluorophenyl)-2,2-diethoxyethan-1-amine (2l)



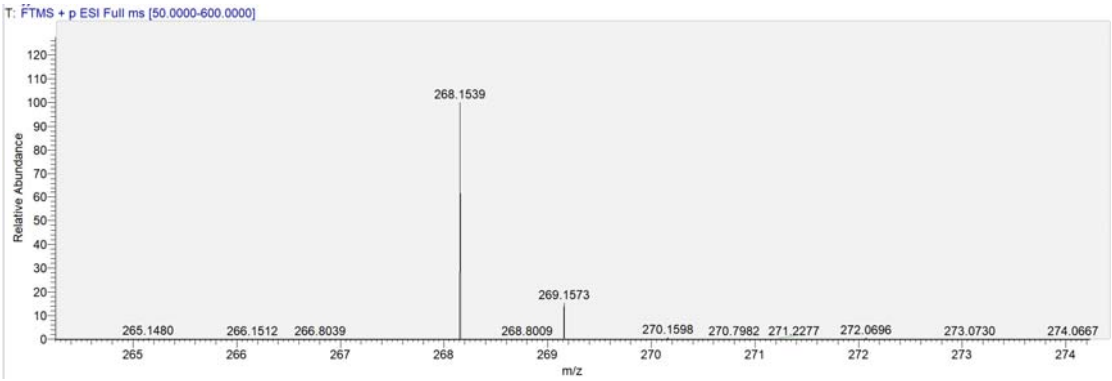
(*S*)-1-(4-chlorophenyl)-2,2-diethoxyethan-1-amine (2m)



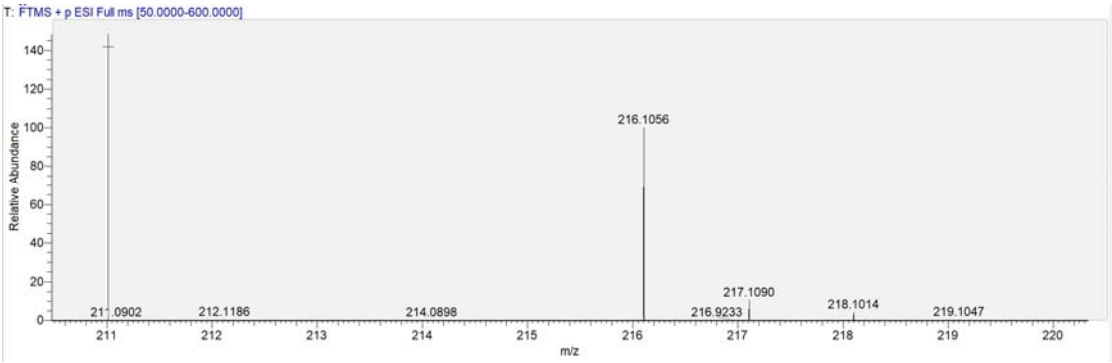
(*S*)-1-(4-bromophenyl)-2,2-diethoxyethan-1-amine (2n)



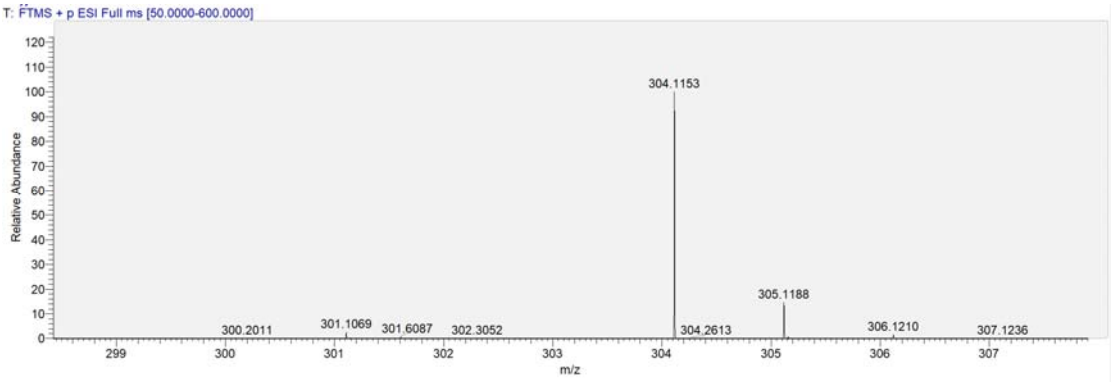
(*S*)-methyl (S)-4-(1-amino-2,2-diethoxyethyl)benzoate (2o)



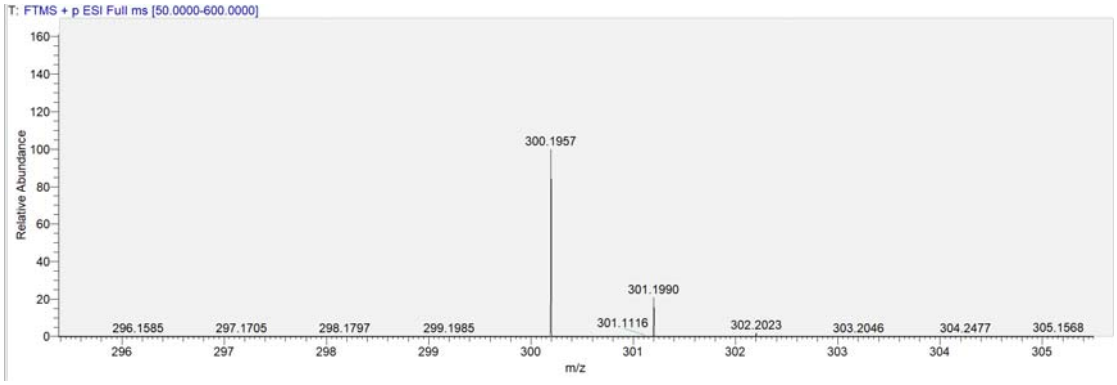
(*R*)-2,2-diethoxy-1-(thiophen-2-yl)ethan-1-amine (2p)



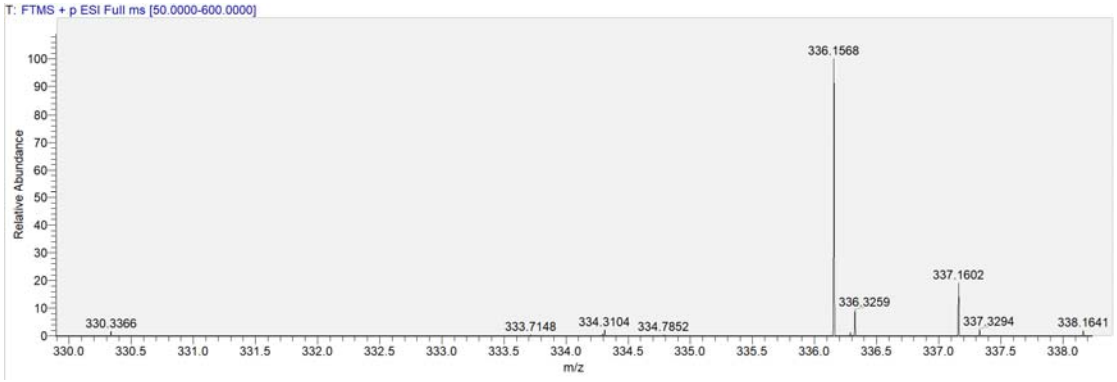
methyl 3-benzamido-4,4-dimethoxybutanoate (2q-Bz)



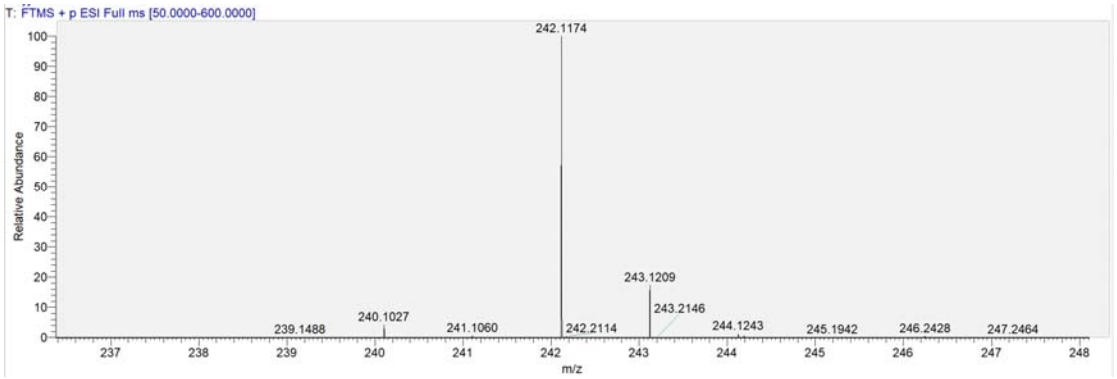
(*S*)-N-benzyl-2,2-diethoxy-1-phenylethan-1-amine (3)



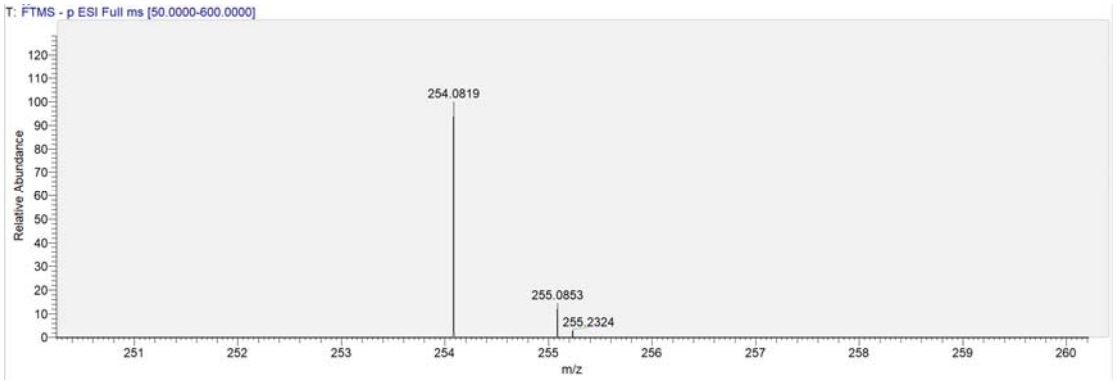
(*S*)-N-(2,2-diethoxy-1-phenylethyl)benzamide (4)



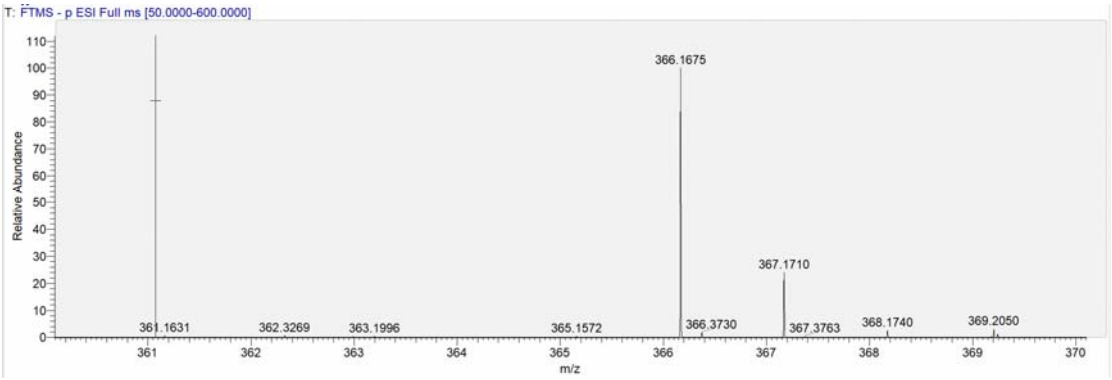
(*S*)-N-(2-hydroxy-1-phenylethyl)benzamide (5)



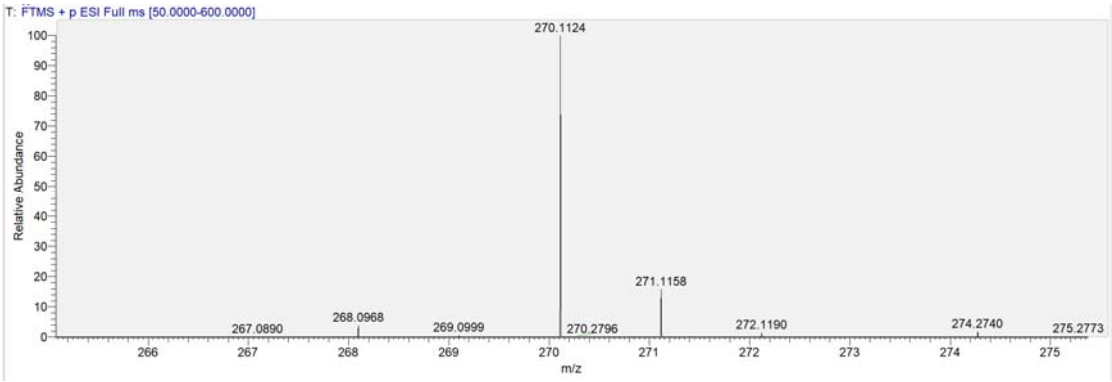
(*S*)-2-benzamido-2-phenylacetic acid (6)



(*S*)-N-(2,2-diethoxy-1-(4-methoxyphenyl)ethyl)benzamide (7)



(*S*)-N-(1-(4-methoxyphenyl)-2-oxoethyl)benzamide (8)



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