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Supporting Information

# Pd$^{II}$-Catalyzed Enantioselective C(sp$^3$)–H Activation/Cross-Coupling Reactions of Free Carboxylic Acids

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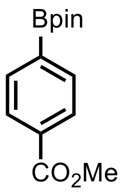
# 1. General Information

Carboxylic acids were obtained from the commercial sources or synthesized following literature procedures. Alkyl iodides were obtained from the commercial sources. Solvents were obtained from Sigma-Aldrich, Oakwood and Acros and used directly without further purification. Analytical thin layer chromatography was performed on 0.25 mm silica gel 60-F254. Visualization was carried out with UV light and Bromocresol Green Stain. $^{1}$H NMR was recorded on Bruker DRX-600 instrument (600 MHz). Chemical shifts were quoted in parts per million (ppm) referenced to the literature values of tetramethylsilane. The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, br = broad. Coupling constants, *J*, were reported in Hertz unit (Hz). $^{13}$C NMR spectra were recorded on Bruker DRX-600 instrument (150 MHz), and were fully decoupled by broad band proton decoupling. Chemical shifts were reported in ppm referenced to either the center line of a triplet at 77.0 ppm of chloroform-*d* or the center line of a multiplet at 29.84 ppm of acetone-$d^{6}$. High-resolution mass spectra (HRMS) were recorded on an Agilent Mass spectrometer using ESI-TOF (electrospray ionization-time of flight). Enantiomeric ratio (er) were determined on a Agilent SFC system or Waters SFC system using commercially available chiral columns.

## 2. Substrate Structures

Substrates **1a**, **1p**, **4a**, **4q**, **4u** were purchased from commercial sources. **1q-1u**, **4p**, **4r-4t** was synthesized from the reported procedure.[1,5,14]

**Arylboronic acid pinacol ester**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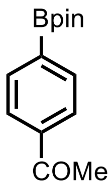
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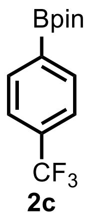
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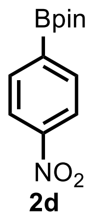
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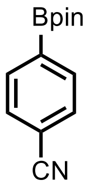
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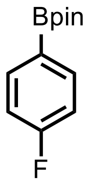
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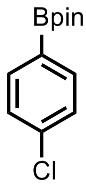
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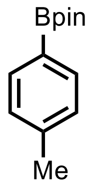
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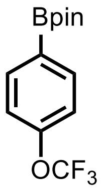
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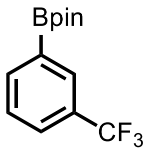
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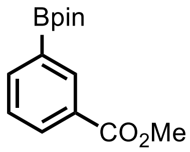
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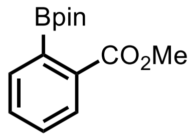
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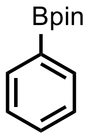
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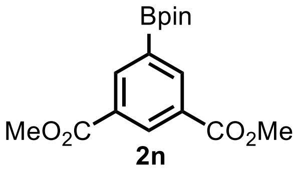
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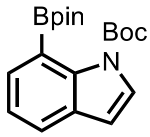
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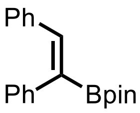
**Vinylboronic acid pinacol esters**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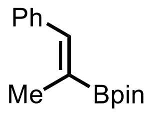
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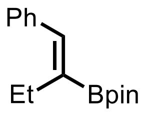
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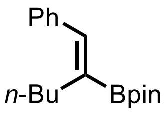
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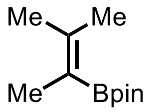
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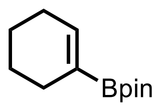
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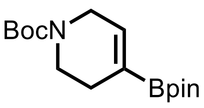
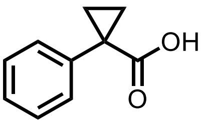

**7g**

## *α*-Substituted cyclopropanecarboxylic acids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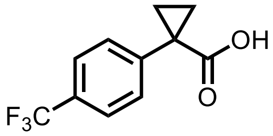
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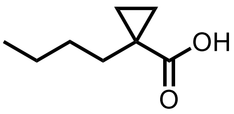
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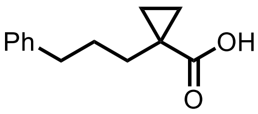
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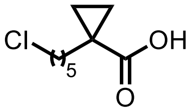
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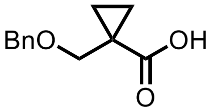
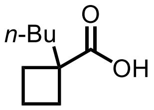

**1u**

## *α*-Substituted cyclobutanecarboxylic acids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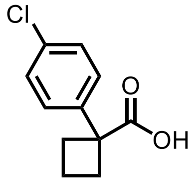
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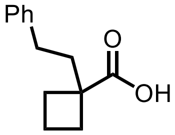
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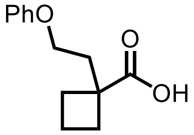
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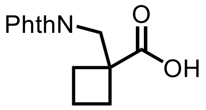
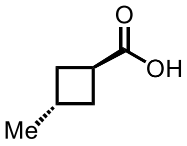
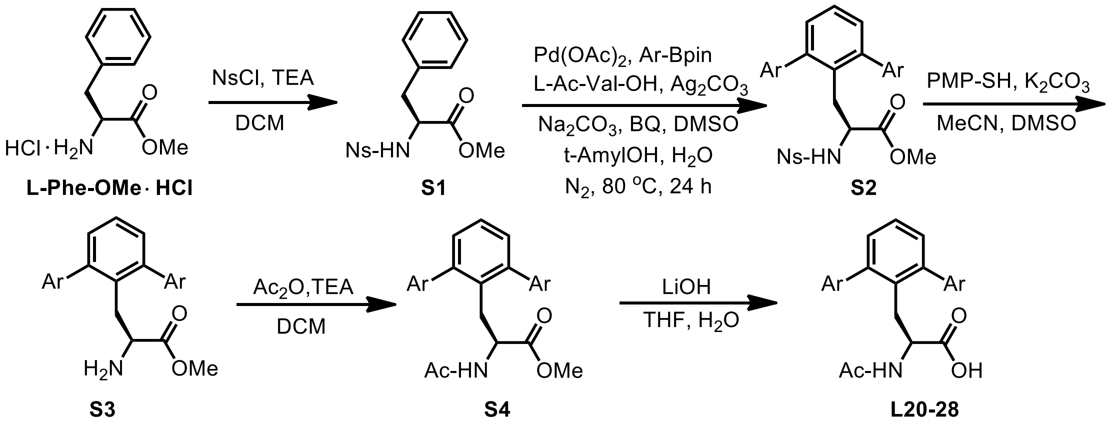

**4t**

## Unsuccessfull substrate


14% yield

# 3. Experimental Section

## 3.1.1 General Procedure for the Preparation of Ligands L20-28



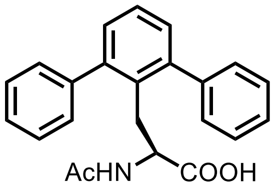
4-Nitrobenzenesulfonyl chloride (NsCl, 50 mmol, 1.0 equiv) was added to a cooled (0 °C) solution of L-phenylalanine methyl ester hydrochloride (L-Phe-OMe·HCl, 50 mmol, 1.0 equiv) and triethylamine (TEA, 150 mmol, 3.0 equiv) in DCM (150 mL). After being stirred at room temperature for 12 h, the reaction mixture was poured into $H_2O$. The organic layer was separated, dried over anhydrous $Na_2SO_4$, filtered and concentrated under vacuum. The residue was purified by trituration with a mixture of 50% DCM/hexane to give **S1**.

**S1** (8.0 mmol, 1.0 equiv), $Pd(OAc)_2$ (0.075 equiv), Ar-BPin (2.0 equiv), L-Ac-Val-OH (0.2 equiv), $Ag_2CO_3$ (2.0 equiv), $Na_2CO_3$ (2.0 equiv), BQ (0.5 equiv), $H_2O$ (5.0 equiv), and DMSO (0.4 equiv) were weighed in air and placed in a Schlenk tube with a magnetic stir bar. *t*-AmylOH (50 mL) was added, and the reaction vessel was evacuated and backfilled with nitrogen (×3). The reaction mixture was heated to 80 °C for 24 h under vigorous stirring. After being cooled to room temperature, the reaction mixture was diluted with EtOAc and filtered through a pad of Celite eluting with EtOAc. The filtrate was concentrated under vacuum and the resulting residue was purified by flash chromatography on silica gel (eluent: EtOAc/hexane = 1: 3) to give **S2**.

4-Methoxybenzenethiol (PMP-SH, 20.0 mmol, 4.0 equiv) and potassium carbonate (20.0 mmol, 4.0 equiv) were added to a solution of **S2** (5.0 mmol, 1.0 equiv) in MeCN (40 mL) and DMSO (1.5 mL). After being stirred at room temperature for 12 h, the reaction mixture was diluted with EtOAc, washed with $H_2O$ and brine, dried over anhydrous $Na_2SO_4$, filtered, and concentrated under vacuum. The residue was purified by column chromatography on silica gel (eluent: EtOAc/hexane = 1: 1) to give **S3**.

$Ac_2O$ (12.0 mmol, 3.0 equiv) was added to a solution of **S3** (4.0 mmol, 1.0 equiv) and triethylamine (12.0 mmol, 3.0 equiv) in DCM (20 mL). After being stirred at room temperature for 3 h, the reaction mixture was quenched with saturated $NH_4Cl$ solution and extracted with DCM. The combined organic layers were dried over anhydrous $Na_2SO_4$, filtered and concentrated to give **S4**, which could be used directly in the next step without further purification.

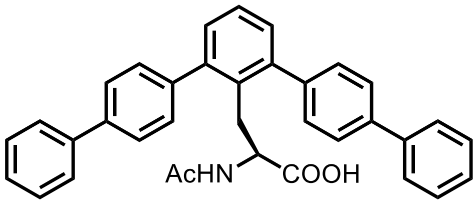
LiOH (8.0 mmol) was added to a suspension of **S4** in THF (8 mL), and $H_2O$ (4 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 8 h. The reaction mixture was quenched with 10% aqueous citric acid solution and extracted EtOAc (3 x 20 mL). The combined organic layers were washed with brine, dried over anhydrous $Na_2SO_4$, filtered and concentrated to give the desired ligand, further purification could be conducted by recrystallization or reversed phase flash column.



**(*S*)-3-([1,1':3',1''-terphenyl]-2'-yl)-2-acetamidopropanoic acid (L20)**

$^1$H NMR (600 MHz, DMSO-*d*$_6$) δ 11.92 (s, 1H), 7.47 – 7.40 (m, 4H), 7.39 – 7.33 (m, 7H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.11 (d, *J* = 7.6 Hz, 2H), 3.66 (q, *J* = 7.7 Hz, 1H), 3.13 (dd, *J* = 14.1, 7.5 Hz, 1H), 3.01 (dd, *J* = 14.1, 8.1 Hz, 1H), 1.55 (s, 3H); $^{13}$C NMR (150 MHz, DMSO-*d*$_6$) δ 172.52, 168.26, 143.23, 141.67, 132.30, 129.32, 129.21, 128.19, 126.91, 126.13, 51.59, 31.04, 22.12.

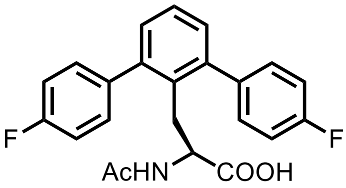
HRMS (ESI-TOF) *m/z* Calcd for $C_{23}H_{22}NO_3^+$ $[M+H]^+$ 360.1600, found 360.1601.



**(*S*)-3-([1,1':4',1'':3'',1''':4''',1''''-quinquephenyl]-2''-yl)-2-acetamidopropanoic acid (L21)**

$^1$H NMR (600 MHz, DMSO-*d*$_6$) δ 11.99 (s, 1H), 7.83 – 7.66 (m, 8H), 7.53 – 7.45 (m, 9H), 7.41 – 7.37 (m, 2H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.19 (d, *J* = 7.6 Hz, 2H), 3.80 (q, *J* = 7.7 Hz, 1H), 3.26 (dd, *J* = 14.1, 7.4 Hz, 1H), 3.11 (dd, *J* = 14.1, 8.2 Hz, 1H), 1.56 (s, 3H); $^{13}$C NMR (150 MHz, DMSO-*d*$_6$) δ 172.60, 168.32, 142.90, 140.87, 139.72, 138.49, 132.51, 129.89, 129.41, 128.99, 127.47, 126.57, 126.41, 126.29, 51.64, 31.33, 22.15.

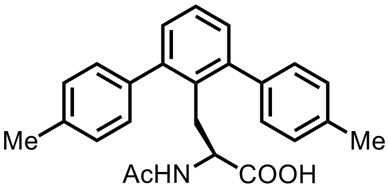
HRMS (ESI-TOF) *m/z* Calcd for $C_{35}H_{30}NO_3^+$ $[M+H]^+$ 512.2226, found 512.2228.



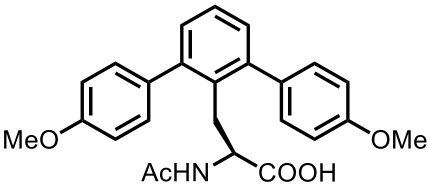
**(*S*)-2-acetamido-3-(4,4''-difluoro-[1,1':3',1''-terphenyl]-2'-yl)propanoic acid (L22)**

$^1$H NMR (600 MHz, DMSO-*d*$_6$) δ 12.02 (s, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.40 – 7.36 (m, 4H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.25 (d, *J* = 8.8 Hz, 4H), 7.12 (d, *J* = 7.6 Hz, 2H), 3.70 (q, *J* = 7.8 Hz, 1H), 3.11 (dd, *J* = 14.1, 7.3 Hz, 1H), 2.96 (dd, *J* = 14.2, 8.2 Hz, 1H), 1.57 (s, 3H); $^{13}$C NMR (150 MHz, DMSO-*d*$_6$) δ 172.51, 168.32, 161.34 (d, *J* = 241.5 Hz), 42.21, 137.87 (d, *J* = 3.0 Hz), 132.75, 131.20 (d, *J* = 9.0 Hz), 129.52, 126.22, 115.03 (d, *J* = 21.0 Hz), 51.36, 31.21, 22.15; $^{19}$F NMR (376 MHz, DMSO) δ -116.14.

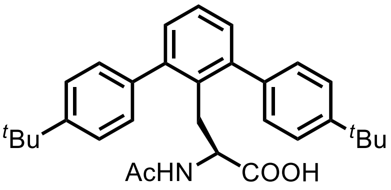
HRMS (ESI-TOF) *m/z* Calcd for $C_{23}H_{20}F_2NO_3^+$ $[M+H]^+$ 369.1411, found 369.1409.



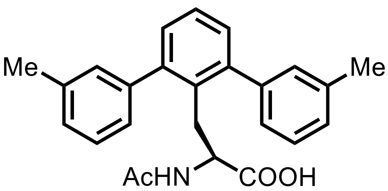
**(*S*)-2-acetamido-3-(4,4''-dimethyl-[1,1':3',1''-terphenyl]-2'-yl)propanoic acid (L23)**
$^1$H NMR (600 MHz, DMSO-$d_6$) δ 11.92 (s, 1H), 7.33 (d, *J* = 7.6 Hz, 1H), 7.23 (s, 9H), 7.06 (d, *J* = 7.6 Hz, 2H), 3.69 (q, *J* = 7.8 Hz, 1H), 3.14 (dd, *J* = 14.0, 7.5 Hz, 1H), 3.04 – 2.99 (m, 1H), 2.35 (s, 6H), 1.56 (s, 3H); $^{13}$C NMR (150 MHz, DMSO-$d_6$) δ 172.57, 168.34, 143.20, 138.87, 135.86, 132.34, 129.25, 129.11, 128.80, 126.06, 51.62, 31.06, 22.14, 20.80.
HRMS (ESI-TOF) *m/z* Calcd for $C_{25}H_{26}NO_3^+$ [M+H]$^+$ 388.1913, found 388.1914.



**(*S*)-2-acetamido-3-(4,4''-dimethoxy-[1,1':3',1''-terphenyl]-2'-yl)propanoic acid (L24)**
$^1$H NMR (600 MHz, DMSO-$d_6$) δ 11.93 (s, 1H), 7.32 (d, *J* = 7.6 Hz, 1H), 7.29 – 7.26 (m, 4H), 7.24 (d, *J* = 7.6 Hz, 1H), 7.06 (d, *J* = 7.5 Hz, 2H), 7.00 – 6.96 (m, 4H), 3.79 (s, 6H), 3.70 (q, *J* = 7.7 Hz, 1H), 3.15 (dd, *J* = 14.0, 7.3 Hz, 1H), 3.01 (dd, *J* = 14.0, 8.4 Hz, 1H), 1.57 (s, 3H); $^{13}$C NMR (150 MHz, DMSO-$d_6$) δ 172.63, 168.30, 158.12, 142.91, 134.05, 132.71, 130.32, 129.25, 126.01, 113.62, 55.06, 51.57, 31.12, 22.17.
HRMS (ESI-TOF) *m/z* Calcd for $C_{25}H_{26}NO_5^+$ [M+H]$^+$ 420.1811, found 420.1818.



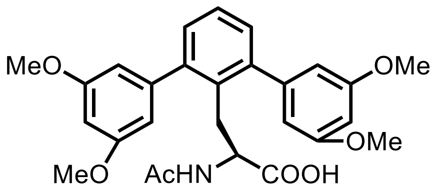
**(*S*)-2-acetamido-3-(4,4''-di-tert-butyl-[1,1':3',1''-terphenyl]-2'-yl)propanoic acid (L25)**
$^1$H NMR (600 MHz, DMSO-$d_6$) δ 11.89 (s, 1H), 7.46 – 7.41 (m, 4H), 7.35 (d, *J* = 7.4 Hz, 1H), 7.30 – 7.26 (m, 5H), 7.09 (d, *J* = 7.6 Hz, 2H), 3.65 (q, *J* = 7.6 Hz, 1H), 3.14 (dd, *J* = 14.1, 7.6 Hz, 1H), 3.00 (dd, *J* = 14.1, 7.7 Hz, 1H), 1.54 (s, 3H), 1.32 (s, 18H); $^{13}$C NMR (150 MHz, DMSO-$d_6$) δ 172.75, 168.09, 149.01, 143.09, 138.81, 132.59, 129.26, 128.88, 126.08, 124.92, 51.63, 40.07, 34.25, 31.19, 22.11.
HRMS (ESI-TOF) *m/z* Calcd for $C_{31}H_{38}NO_3^+$ [M+H]$^+$ 472.2852, found 472.2847.



**(*S*)-2-acetamido-3-(3,3''-dimethyl-[1,1':3',1''-terphenyl]-2'-yl)propanoic acid (L26)**
$^1$H NMR (600 MHz, DMSO-$d_6$) δ 11.93 (s, 1H), 7.36 – 7.26 (m, 4H), 7.18 – 7.12 (m, 6H), 7.08 (d, *J* = 7.6 Hz, 2H), 3.70 (q, *J* = 7.7 Hz, 1H), 3.13 (dd, *J* = 14.0, 7.3 Hz, 1H), 2.99 (dd, *J* = 14.1, 8.2 Hz, 1H), 2.35 (s, 6H), 1.56 (s, 3H); $^{13}$C NMR (150 MHz, DMSO-$d_6$) δ 172.59,

168.27, 143.28, 141.66, 137.19, 132.31, 129.86, 129.18, 128.06, 127.53, 126.29, 125.99, 51.72, 31.13, 22.14, 21.13.

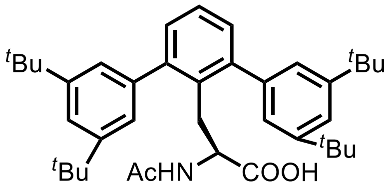
HRMS (ESI-TOF) *m/z* Calcd for $C_{25}H_{26}NO_3^+$ $[M+H]^+$ 388.1913, found 388.1914.



**(*S*)-2-acetamido-3-(3,3'',5,5''-tetramethoxy-[1,1':3',1''-terphenyl]-2'-yl)propanoic acid (L27)**

$^1$H NMR (600 MHz, DMSO-$d_6$) δ 11.99 (s, 1H), 7.40 (d, *J* = 7.7 Hz, 1H), 7.26 (dd, *J* = 7.9, 7.2 Hz, 1H), 7.11 (d, *J* = 7.6 Hz, 2H), 6.50 – 6.48 (m, 6H), 3.89 – 3.84 (m, 1H), 3.77 (s, 12H), 3.20 (dd, *J* = 14.1, 7.1 Hz, 1H), 3.04 (dd, *J* = 14.1, 8.6 Hz, 1H), 1.60 (s, 3H); $^{13}$C NMR (150 MHz, DMSO-$d_6$) δ 172.70, 168.39, 160.07, 143.63, 143.08, 132.32, 129.06, 125.91, 107.48, 99.05, 55.21, 51.62, 31.36, 22.15.

HRMS (ESI-TOF) *m/z* Calcd for $C_{27}H_{30}NO_7^+$ $[M+H]^+$ 480.2022, found 480.2026.

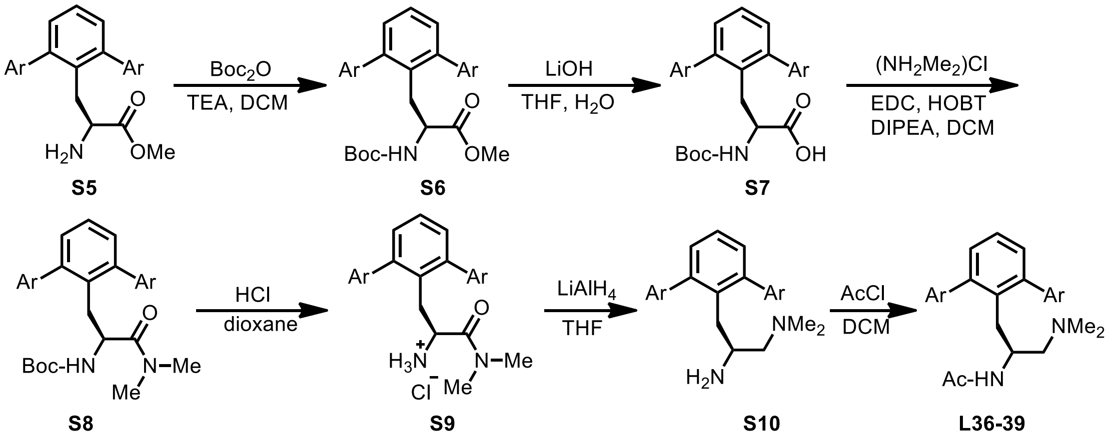


**(*S*)-2-acetamido-3-(3,3'',5,5''-tetra-tert-butyl-[1,1':3',1''-terphenyl]-2'-yl)propanoic acid (L28)**

$^1$H NMR (600 MHz, $CDCl_3$) δ 7.44 (t, *J* = 1.8 Hz, 2H), 7.35 (dd, *J* = 8.1, 7.0 Hz, 1H), 7.28 – 7.26 (m, 2H), 7.21 (d, *J* = 1.9 Hz, 4H), 5.12 (d, *J* = 7.2 Hz, 1H), 4.07 (ddd, *J* = 11.9, 7.1, 3.4 Hz, 1H), 3.28 (dd, *J* = 14.6, 3.5 Hz, 1H), 3.14 (dd, *J* = 14.6, 11.8 Hz, 1H), 1.75 (s, 3H), 1.36 (s, 36H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 172.81, 170.97, 150.76, 143.93, 140.08, 130.99, 129.35, 126.32, 120.92, 52.75, 34.54, 31.06, 29.33, 22.44.

HRMS (ESI-TOF) *m/z* Calcd for $C_{39}H_{54}NO_3^+$ $[M+H]^+$ 584.4104, found 584.4114.

### 3.1.2 General Procedure for the Preparation of Ligands L36-39



Boc$_2$O (8.0 mmol, 2.0 equiv) was added to a solution of **S5** (4.0 mmol, 1.0 equiv) and triethylamine (8.0 mmol, 2.0 equiv) in DCM (20 mL). After being stirred at room temperature for 3 h, the reaction mixture was quenched with saturated $NH_4Cl$ solution and extracted with

DCM. The combined organic layers were dried over anhydrous $Na_2SO_4$, filtered and concentrated to give **S6**, which could be used directly in the next step without further purification.

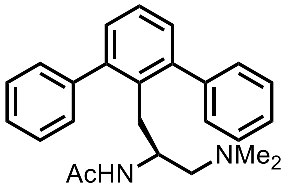
LiOH (8.0 mmol) was added to a suspension of **S6** in THF (8 mL), and $H_2O$ (4 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 8 h. The reaction mixture was quenched with 10% aqueous citric acid solution and extracted EtOAc (3 x 20 mL). The combined organic layers were washed with brine, dried over anhydrous $Na_2SO_4$, filtered and concentrated to give **S7**, further purification could be conducted by recrystallization or reversed phase flash column.

The corresponding Boc-protected amino acid (**S7**) (4 mmol), dimethylammonium chloride (8.8 mmol, 2.2 equiv) and benzotriazol-1-ol hydrate (HOBt) (4 mmol, 1.0 equiv) were added to a round bottom flask equipped with a magnetic stir bar. The solid mixture was dissolved in DCM (40 mL), and 1-ethyl-(3-(3-dimethylamino)propyl)-carbodiimide hydrochloride (EDC) (4.8 mmol, 1.2 equiv) was added at 0 °C. The resulting solution was stirred at 0 °C as N-ethyl-N,N-diisopropylamine (DIPEA) (9.6 mmol, 2.4 equiv) was added slowly. The reaction solution was allowed to warm to r.t. and stirred for about 3 h, after which the solution was poured into a separatory funnel, diluted to 150 mL with additional DCM, and washed with approximately 25 mL of 10% w/w aqueous citric acid. The organic layer was separated and subsequently washed with 25 mL each of saturated aqueous $NaHCO_3$ and brine. The organics were dried over anhydrous $Na_2SO_4$, filtered, and concentrated in vacuo to provide corresponding amide (**S8**) which could be directly used in the next step without further purification.

To the Boc-protected amino amide (**S8**) was added 4 N HCl/dioxane solution (4 ml). The resulting solution was stirred at room temperature for 2 h. Then, the volatile components were evaporated in vacuo, and the residue was subsequently used in the following reduction step.

To a solution of **S9** in THF (24 ml) was added a solution of $LiAlH_4$ in THF (6.0 mmol, 1.5 equiv) dropwise under $N_2$ at 0 °C. Then, the mixture was heated to reflux for 12 h, before being cooled down and diluted with ether. The mixture was cooled to 0 °C, and 0.28 ml of water was added slowly followed by 15% w/w NaOH aqueous solution (0.28 ml) and water (0.84 ml). The resulting suspension was then warmed to room temperature and stirred for 15 min before $MgSO_4$ was added. The mixture was stirred for additional 15 min before filtration. The filtrate was collected, and the solvent was removed in vacuo to provide diamine compound (**S10**) which could be used in next step without purification.

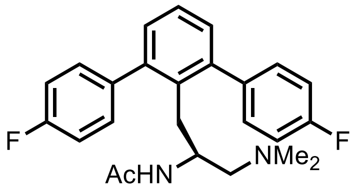
To a solution of the synthesized diamine compound (**S10**) in DCM (8 ml) was added acetyl chloride (8 mmol, 2.0 equiv) at 0 °C. Then the solution was stirred at room temperature for 2 h. The volatile components were evaporated in vacuo, and the residue was dissolved in 8 ml of water. The resulting solution was extracted with ether (10 ml x 3), then the aqueous phase was alkalized with 15% w/w NaOH aqueous solution until pH>13. The alkalized mixture was extracted with ether (10 ml x 3), and the organic layers were concentrated to provide the desired MPAAM Ligand. Further purification could be conducted by recrystallization or reversed phase flash column.



**(*S*)-N-(1-([1,1':3',1''-terphenyl]-2'-yl)-3-(dimethylamino)propan-2-yl)acetamide (L36)**

$^1$H NMR (600 MHz, $CDCl_3$) δ 7.46 – 7.40 (m, 8H), 7.38 – 7.35 (m, 2H), 7.29 – 7.27 (m, 1H), 7.20 – 7.17 (m, 2H), 4.60 (d, *J* = 8.7 Hz, 1H), 3.74 (dd, *J* = 10.0, 5.8 Hz, 1H), 3.12 (dd, *J* = 14.2, 4.2 Hz, 1H), 2.80 (dd, *J* = 14.2, 10.7 Hz, 1H), 1.85 (dd, *J* = 12.0, 7.0 Hz, 1H), 1.72 (s, 6H), 1.69 (s, 3H), 1.61 (dd, *J* = 12.0, 7.8 Hz, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 169.00, 143.33, 142.40, 133.44, 129.76, 129.59, 128.36, 127.02, 126.03, 63.99, 48.06, 45.20, 32.38, 23.41.

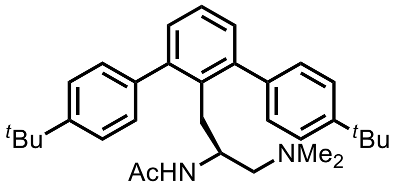
HRMS (ESI-TOF) *m/z* Calcd for $C_{25}H_{29}N_2O^+$ [M+H]$^+$ 373.2280, found 373.2282.



**(*S*)-N-(1-(4,4''-difluoro-[1,1':3',1''-terphenyl]-2'-yl)-3-(dimethylamino)propan-2-yl)acetamide (L37)**

$^1$H NMR (600 MHz, $CDCl_3$) δ 7.37 (dd, *J* = 8.5, 5.5 Hz, 4H), 7.29 – 7.27 (m, 1H), 7.17 – 7.12 (m, 5H), 4.74 (d, *J* = 8.8 Hz, 1H), 3.78 – 3.71 (m, 1H), 3.03 (dd, *J* = 14.2, 4.2 Hz, 1H), 2.77 (dd, *J* = 14.2, 10.4 Hz, 1H), 1.92 (dd, *J* = 12.1, 7.5 Hz, 1H), 1.80 (s, 6H), 1.70 (s, 3H), 1.67 – 1.62 (m, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 169.05, 162.04 (d, *J* = 246.0 Hz), 142.36, 138.22 (d, *J* = 3.0 Hz), 133.58, 131.27 (d, *J* = 7.5 Hz), 129.86, 126.19, 115.27 (d, *J* = 21.0 Hz), 63.66, 47.68, 45.05, 32.71, 23.34; $^{19}$F NMR (376 MHz, $CDCl_3$) δ -115.70.

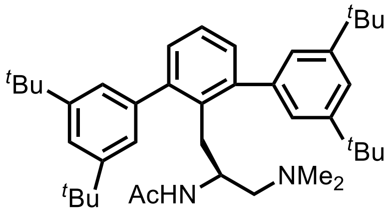
HRMS (ESI-TOF) *m/z* Calcd for $C_{25}H_{26}F_2N_2O^+$ [M+H]$^+$ 409.2091, found 409.2096.



**(*S*)-N-(1-(4,4''-di-tert-butyl-[1,1':3',1''-terphenyl]-2'-yl)-3-(dimethylamino)propan-2-yl)acetamide (L38)**

$^1$H NMR (600 MHz, $CDCl_3$) δ 7.48 – 7.44 (m, 4H), 7.36 – 7.32 (m, 4H), 7.25 – 7.23 (m, 1H), 7.18 – 7.15 (m, 2H), 4.59 (d, *J* = 9.0 Hz, 1H), 3.80 – 3.72 (m, 1H), 3.22 (dd, *J* = 14.2, 3.4 Hz, 1H), 2.70 (dd, *J* = 14.3, 11.2 Hz, 1H), 1.89 (dd, *J* = 11.9, 6.3 Hz, 1H), 1.69 (s, 6H), 1.68 (s, 3H), 1.65 – 1.60 (m, 1H), 1.37 (s, 18H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 168.50, 149.38, 142.77, 138.97, 133.30, 129.10, 129.00, 125.52, 124.83, 63.89, 47.81, 44.79, 34.12, 31.64, 30.96, 22.97.

HRMS (ESI-TOF) *m/z* Calcd for $C_{33}H_{45}N_2O^+$ [M+H]$^+$ 485.3532, found 485.3529.

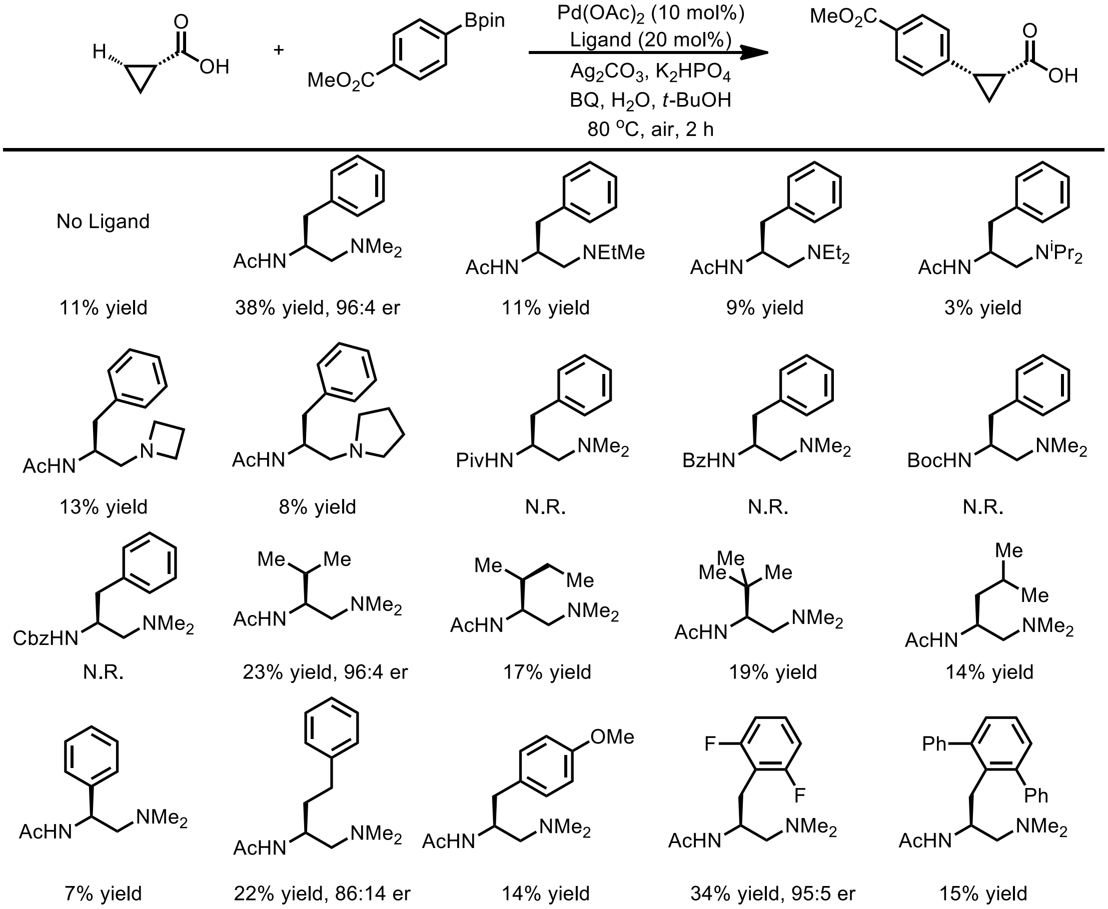


**(*S*)-N-(1-(dimethylamino)-3-(3,3'',5,5''-tetra-tert-butyl-[1,1':3',1''-terphenyl]-2'-yl)propan-2-yl)acetamide (L39)**

$^1$H NMR (600 MHz, CDCl$_3$) δ 7.42 (t, *J* = 1.8 Hz, 2H), 7.30 – 7.26 (m, 5H), 7.20 (d, *J* = 7.5 Hz, 2H), 4.72 (d, *J* = 9.2 Hz, 1H), 3.87 – 3.81 (m, 1H), 3.14 (dd, *J* = 14.2, 3.8 Hz, 1H), 2.80 (dd, *J* = 14.1, 11.1 Hz, 1H), 1.93 (d, *J* = 7.0 Hz, 1H), 1.72 (s, 6H), 1.69 (s, 3H), 1.66 – 1.62 (m, 1H), 1.38 (s, 36H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 168.91, 150.86, 150.71, 144.30, 141.51, 133.34, 129.63, 125.94, 120.89, 64.25, 47.49, 45.04, 34.97, 32.40, 31.58, 23.52. HRMS (ESI-TOF) *m/z* Calcd for $C_{41}H_{61}N_2O^+$ [M+H]$^+$ 597.4784, found 597.4791.

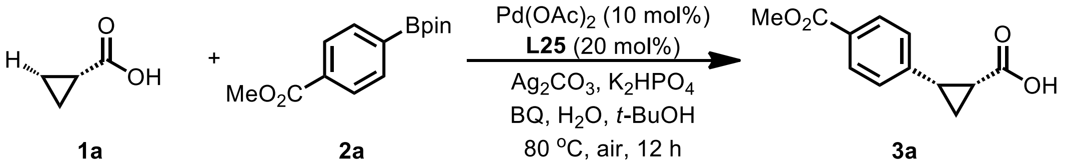
### 3.2 Optimization of Conditions of Arylation for Cyclopropanecarboxylic Acid

Screening of Ligands[a,b]



[a] Conditions: **1a** (0.1 mmol), **2a** (1.5 equiv), Pd(OAc)$_2$ (10 mol%), Ligand (20 mol%), Ag$_2$CO$_3$ (1.5 equiv), K$_2$HPO$_4$ (1.5 equiv), BQ (0.5 equiv), H$_2$O (10.0 equiv), *t*-BuOH (1.0 mL), 80 °C, air, 12 h. [b] $^1$H NMR yields, using CH$_2$Br$_2$ as an internal standard.

Screening of Ag Salts and Pd source[a,b]

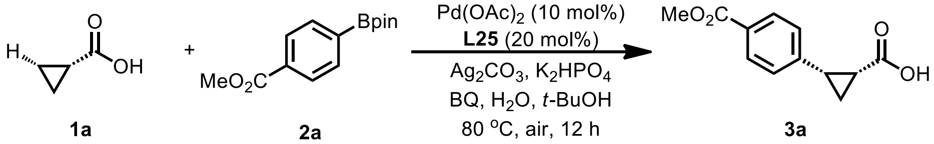


| Ag Salt | Yield | er |
|---|---|---|
| no change | 70% | 97:3 |
| AgOAc | 43% | 96:4 |
| AgOPiv | 10% | - |
| AgTFA | NR | - |
| AgF | 8% | - |
| $Ag_2O$ | 31% | 93:7 |

| Pd source | Yield | er |
|---|---|---|
| $PdCl_2$ | 16% | - |
| $Pd(TFA)_2$ | 37% | 96:4 |
| $Pd(MeCN)_4(BF_4)_2$ | 34% | 94:6 |
| $Pd(MeCN)_2Cl_2$ | 35% | 93:7 |
| $Pd(PhCN)_2Cl_2$ | 30% | 94:6 |
| $[Pd(allyl)Cl]_2$ | 23% | 92:8 |
| $Pd(pph_3)_2Cl_2$ | 20% | 91:9 |

[a] Conditions: **1a** (0.1 mmol), **2a** (1.5 equiv), Pd (10 mol%), **L25** (20 mol%), Ag (1.5 equiv), $K_2HPO_4$ (1.5 equiv), BQ (0.5 equiv), $H_2O$ (10.0 equiv), *t*-BuOH (1.0 mL), 80 °C, air, 12 h. [b] $^1H$ NMR yields, using $CH_2Br_2$ as an internal standard.

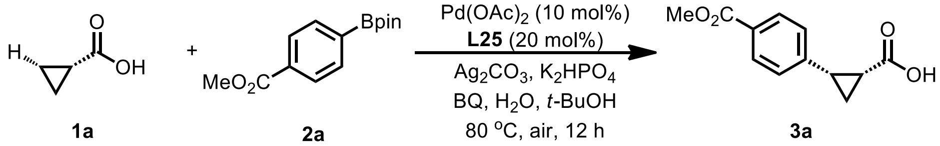
Screening of Solvent and Temperature[a,b]



| Entry | Solvent | Temperature | Yield | er |
|---|---|---|---|---|
| 1 | t-BuOH | 80 °C | 70% | 97:3 |
| 2 | t-AmylOH | 80 °C | 56% | 94:6 |
| 3 | THF | 80 °C | 16% | - |
| 4 | Dioxane | 80 °C | 19% | - |
| 5 | MeCN | 80 °C | N.R. | - |
| 6 | HFIP | 80 °C | 21% | 89:11 |
| 7 | DMF | 80 °C | N.R. | - |
| 8 | t-BuOH | 70 °C | 61% | 97:3 |
| 9 | t-BuOH | 90 °C | 71% | 90:10 |

[a] Conditions: **1a** (0.1 mmol), **2a** (1.5 equiv), $Pd(OAc)_2$ (10 mol%), **L25** (20 mol%), $Ag_2CO_3$ (1.5 equiv), $K_2HPO_4$ (1.5 equiv), BQ (0.5 equiv), $H_2O$ (10.0 equiv), *t*-BuOH (1.0 mL), 80 °C, air, 12 h. [b] $^1H$ NMR yields, using $CH_2Br_2$ as an internal standard.

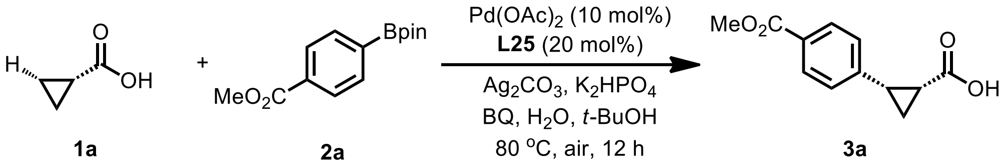
Screening of Bases[a,b]



| Base | Yield | er | Base | Yield | er |
|---|---|---|---|---|---|
| None | 3% | - | LiF | NR | - |
| NaOAc | 11% | - | KOAc | 32% | 94:6 |
| $NaHCO_3$ | 9% | - | $KHCO_3$ | 12% | - |
| $Na_2CO_3$ | 23% | 94:6 | $K_2CO_3$ | 29% | 94:6 |
| $NaH_2PO_4$ | NR | - | $KH_2PO_4$ | 18% | - |
| $Na_2HPO_4$ | 5% | - | $K_2HPO_4 \cdot 3H_2O$ | 45% | 93:7 |
| $Na_3PO_4$ | 18% | - | $K_3PO_4$ | 47% | 96:4 |
| $Li_2CO_3$ | NR | - | KF | 11% | - |
| LiOAc | NR | - | $Cs_2CO_3$ | 26% | 95:5 |
| $Li_3PO_4$ | NR | - | CsOAc | 11% | - |

[a] Conditions: **1a** (0.1 mmol), **2a** (1.5 equiv), Pd(OAc)$_2$ (10 mol%), **L25** (20 mol%), $Ag_2CO_3$ (1.5 equiv), $K_2HPO_4$ (1.5 equiv), BQ (0.5 equiv), $H_2O$ (10.0 equiv), *t*-BuOH (1.0 mL), 80 °C, air, 12 h. [b] $^1$H NMR yields, using $CH_2Br_2$ as an internal standard.

Screening of loading of reagents[a,b]

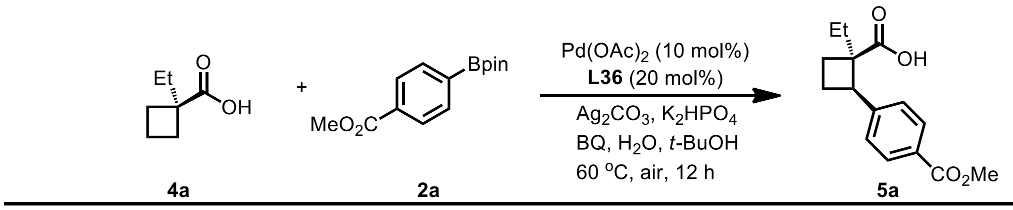


| Change | Yield | Base | Yield |
|---|---|---|---|
| No Change | 70% | $Ag_2CO_3$ (1.0 equiv) | 57% |
| $K_2HPO_4$ (1.0 equiv) | 61% | $Ag_2CO_3$ (2.0 equiv) | 68% |
| $K_2HPO_4$ (2.0 equiv) | 67% | ArBpin (1.0 equiv) | 57% |
| $K_2HPO_4$ (3.0 equiv) | 46% | ArBpin (2.0 equiv) | 70% |

[a] Conditions: **1a** (0.1 mmol), **2a** (1.5 equiv), Pd(OAc)$_2$ (10 mol%), **L25** (20 mol%), $Ag_2CO_3$ (1.5 equiv), $K_2HPO_4$ (1.5 equiv), BQ (0.5 equiv), $H_2O$ (10.0 equiv), *t*-BuOH (1.0 mL), 80 °C, air, 12 h. [b] $^1$H NMR yields, using $CH_2Br_2$ as an internal standard.

## 3.3 Optimization of Conditions of Arylation for Cyclobutanecarboxylic Acid

Screening of Solvent and Temperature[a,b]

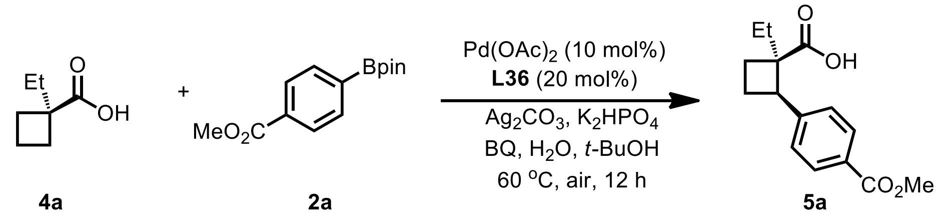


**4a** **2a** **5a**

| Entry | Solvent | Temperature | Yield | er |
|---|---|---|---|---|
| 1 | t-BuOH | 60 °C | 62% | 94:6 |
| 2 | t-AmylOH | 60 °C | 38% | 85:15 |
| 3 | THF | 60 °C | 23% | 86:14 |
| 4 | Dioxane | 60 °C | 12% | - |
| 5 | MeCN | 60 °C | N.R. | - |
| 6 | HFIP | 60 °C | 32% | 64:36 |
| 7 | DMF | 60 °C | N.R. | - |
| 8 | t-BuOH | 80 °C | 60% | 90:10 |
| 9 | t-BuOH | 50 °C | 46% | 94:6 |

[a] Conditions: **4a** (0.1 mmol), **2a** (1.5 equiv), $Pd(OAc)_2$ (10 mol%), **L36** (20 mol%), $Ag_2CO_3$ (2.0 equiv), $K_2HPO_4$ (1.5 equiv), BQ (0.5 equiv), $H_2O$ (5.0 equiv), *t*-BuOH (1.0 mL), 60 °C, air, 12 h. [b] $^1H$ NMR yields, using $CH_2Br_2$ as an internal standard.

Screening of loading of reagents[a,b]



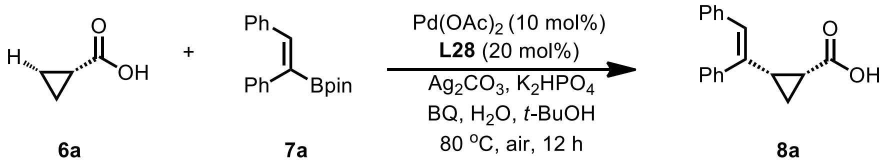
**4a** **2a** **5a**

| Change | Yield | Base | Yield |
|---|---|---|---|
| No Change | 62% | $Ag_2CO_3$ (1.0 equiv) | 53% |
| $K_2HPO_4$ (1.0 equiv) | 50% | $Ag_2CO_3$ (2.0 equiv) | 62% |
| $K_2HPO_4$ (2.0 equiv) | 52% | ArBpin (1.0 equiv) | 51% |
| $K_2HPO_4$ (3.0 equiv) | 43% | ArBpin (2.0 equiv) | 62% |

[a] Conditions: **4a** (0.1 mmol), **2a** (1.5 equiv), $Pd(OAc)_2$ (10 mol%), **L36** (20 mol%), $Ag_2CO_3$ (2.0 equiv), $K_2HPO_4$ (1.5 equiv), BQ (0.5 equiv), $H_2O$ (5.0 equiv), *t*-BuOH (1.0 mL), 60 °C, air, 12 h. [b] $^1H$ NMR yields, using $CH_2Br_2$ as an internal standard.

### 3.4 Optimization of Conditions of Vinylation for Cyclopropanetanecarboxylic Acid

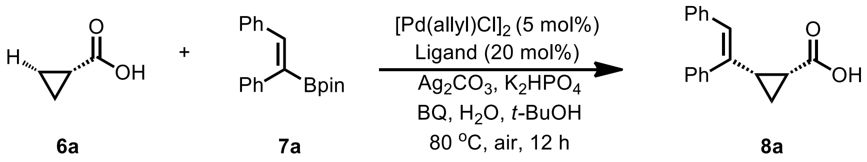
Screening of Ag Salts and Pd source[a,b]

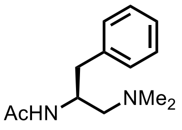


| Ag Salt | Yield | er | Pd source | Yield | er |
|---|---|---|---|---|---|
| no change | 48% | 96:4 | $PdCl_2$ | 18% | - |
| AgOAc | 19% | - | $Pd(TFA)_2$ | 52% | 95:5 |
| AgOPiv | 12% | - | $Pd(MeCN)_4(BF_4)_2$ | 63% | 98:2 |
| AgTFA | 7% | - | $Pd(MeCN)_2Cl_2$ | 53% | 97:4 |
|  |  |  | $Pd(PhCN)_2Cl_2$ | 52% | 96:4 |
| AgF | 17% | - | $[Pd(allyl)Cl]_2$ | 71% | 98:2 |
| $Ag_2O$ | 29% | 96:4 | $Pd(pph_3)_2Cl_2$ | 54% | 96:4 |

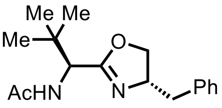
[a] Conditions: **6a** (0.1 mmol), **7a** (2.0 equiv), Pd (10 mol%), **L28** (20 mol%), Ag (1.5 equiv), $K_2HPO_4$ (1.5 equiv), BQ (0.5 equiv), $H_2O$ (2.0 equiv), *t*-BuOH (1.0 mL), 80 °C, air, 12 h. [b] $^1H$ NMR yields, using $CH_2Br_2$ as an internal standard.

### Screening of Ligand[a,b]

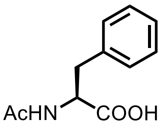




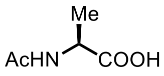
**L1**
34% yield, 92:8 er



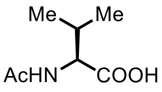
**L2**
17% yield



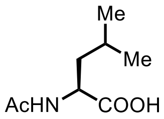
**L4**
48% yield, 95:5 er



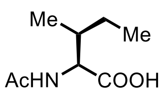
**L10**
36% yield, 95:5 er



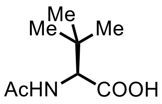
**L11**
32% yield, 96:4 er



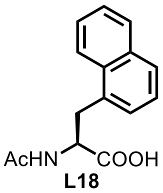
**L12**
35% yield, 96:4 er



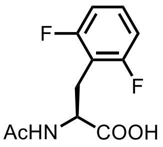
**L13**
41% yield, 95:5 er



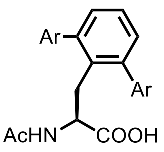
**L14**
37% yield, 97:3 er



**L18**
38% yield, 96:4 er



**L19**
41% yield, 95:5 er



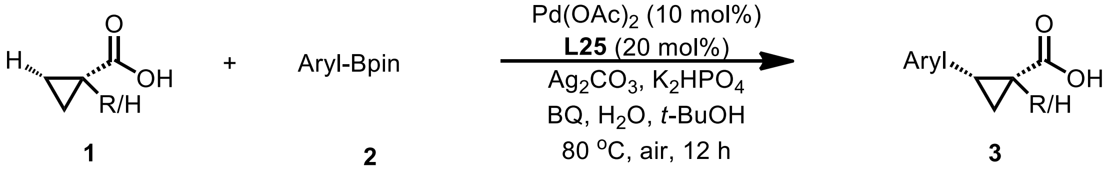
**L20**, Ar = $C_6H_5$
46% yield, 96:4 er
**L21**, Ar = 4-$PhC_6H_4$
46% yield, 95:5 er
**L22**, Ar = 4-$FC_6H_4$
44% yield, 93:7 er
**L23** Ar = 4-$MeC_6H_4$
52% yield, 93:7 er
**L24**, Ar = 4-$OMeC_6H_4$
48% yield, 95:5 er

**L25**, Ar = 4-*t*-Bu-$C_6H_4$
62% yield, 95:5 er
**L26**, Ar = 3-$MeC_6H_4$
51% yield, 96:4 er
**L27**, Ar = 3,5-$OMeC_6H_3$
44% yield, 97:3 er
**L28**, Ar = 3,5-*t*-Bu-$C_6H_3$
71% yield, 98:2 er

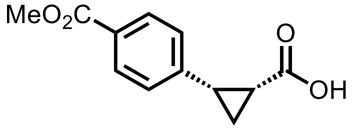
[a] Conditions: **6a** (0.1 mmol), **7a** (2.0 equiv), $[Pd(allyl)Cl]_2$ (5 mol%), Ligand (20 mol%), $Ag_2CO_3$ (1.5 equiv),

$K_2HPO_4$ (1.5 equiv), BQ (0.5 equiv), $H_2O$ (2.0 equiv), *t*-BuOH (1.0 mL), 80 °C, air, 12 h. $^b$ $^1$H NMR yields, using $CH_2Br_2$ as an internal standard.

### 3.5 Enantioselective Arylation of Cylcopropanecarboxylic acid



**General procedure for enantioselective arylation of cyclopropanecarboxylic acid**: A 2-dram vial equipped with a magnetic stir bar was charged with $Pd(OAc)_2$ (2.2 mg, 10 mol%) and **L25** (9.4 mg, 20 mol%) in *t*-BuOH (1.0 ml) and then stirred at the rate of 300 rpm at room temperature for 5 min. The appropriate cyclopropanecarboxylic acid substrate (0.10 mmol), $Ag_2CO_3$ (41.4 mg, 0.15 mmol), $K_2HPO_4$ (26.0 mg, 0.15 mmol), Aryl-Bpin (0.15 mmol), BQ (5.4 mg, 0.05 mmol), $H_2O$ (18.0 mg, 1.0 mmol)was then added. Subsequently the vial was capped and closed tightly. The reaction mixture was then stirred at the rate of 300 rpm at 80 °C for 12 h. After being allowed to cool to room temperature, the mixture was diluted with ethyl acetate and 0.1 ml of acetic acid was then added. The mixture was passed through a pad of Celite with ethyl acetate as the eluent to remove any insoluble precipitate. The resulting solution was concentrated, and the residual mixture was dissolved with a minimal amount of acetone and loaded onto a preparative TLC plate. The pure product was then isolated using preparative TLC with ethyl acetate and hexane (1/4 to 1/1) as the eluent and 1% v/v of acetic acid as additive.



**(1R,2S)-2-(4-(methoxycarbonyl)phenyl)cyclopropane-1-carboxylic acid (3a)**

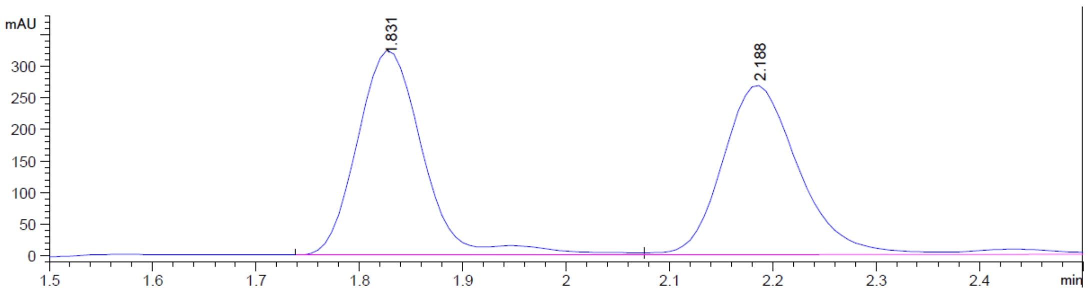
Substrate **1** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 2/1 with 1% v/v of acetic acid). The product was obtained as a white solid (70% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® AS-3 column, 30% $^i$PrOH / $CO_2$, flow rate 2 mL/min, retention time 1.825 min (major) and 2.171 min (minor), 97:3 er); $[\alpha]_D^{20} = -6.7$ (c = 1.0, $CHCl_3$).

$^1$H NMR (600 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.3 Hz, 2H), 7.29 (d, *J* = 7.8 Hz, 2H), 3.91 (s, 3H), 2.63 (q, *J* = 8.5 Hz, 1H), 2.08 (ddd, *J* = 9.2, 7.8, 5.6 Hz, 1H), 1.69 (dt, *J* = 7.6, 5.4 Hz, 1H), 1.42 (ddd, *J* = 8.5, 7.8, 5.1 Hz, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 176.11, 167.05, 141.35, 129.30, 129.23, 128.59, 52.02, 26.32, 21.65, 12.24.

HRMS (ESI-TOF) *m/z* Calcd for $C_{12}H_{13}O_4^+$ $[M+H]^+$ 221.0808, found 221.0814.

The absolute stereochemistry was assigned based on comparing the specific rotation of **3m** with literature.



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Peak RetTime Type  Width     Area       Height      Area
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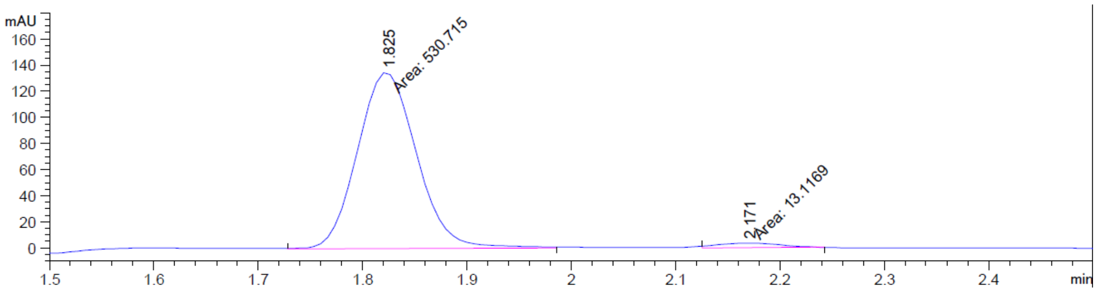
   1    1.831 BV R  0.0670 1432.96143  323.97009  50.1015
   2    2.188 VV R  0.0791 1427.15442  268.27094  49.8985
```



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Peak RetTime Type  Width     Area       Height      Area
  #    [min]        [min]    [mAU*s]     [mAU]        %
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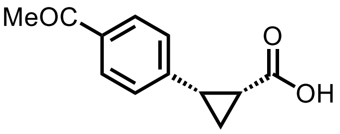
   1    1.825 MM    0.0653  530.71539  135.44972  97.5881
   2    2.171 MM    0.0651   13.11685    3.35660   2.4119
```



**(1R,2S)-2-(4-acetylphenyl)cyclopropane-1-carboxylic acid (3b)**

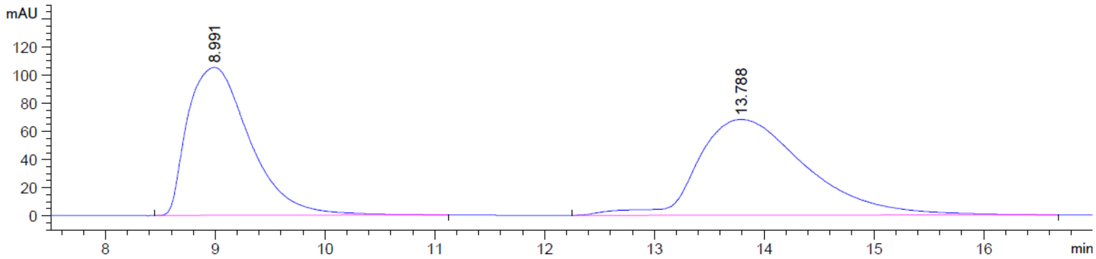
Substrate **1** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 2/1 with 1% v/v of acetic acid). The product was obtained as a white solid (62% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® AS-3 column, 5% $^{i}$PrOH / $CO_2$, flow rate 2 mL/min, retention time 9.023 min (major) and 14.154 min (minor), 98:2 er);

$^{1}$H NMR (600 MHz, $CDCl_3$) δ 7.84 (d, $J$ = 8.3 Hz, 2H), 7.32 (d, $J$ = 8.1 Hz, 2H), 2.64 (q, $J$ = 8.5 Hz, 1H), 2.58 (s, 3H), 2.10 (ddd, $J$ = 9.3, 7.8, 5.6 Hz, 1H), 1.71 (dt, $J$ = 7.8, 5.4 Hz, 1H), 1.44 (td, $J$ = 8.2, 5.2 Hz, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 197.95, 175.99, 141.63, 135.66, 129.47, 128.04, 26.58, 26.32, 21.70, 12.29.

HRMS (ESI-TOF) $m/z$ Calcd for $C_{12}H_{13}O_3^+$ $[M+H]^+$ 205.0859, found 205.0857.

The absolute stereochemistry was assigned based on comparing the specific rotation of **3m** with literature.



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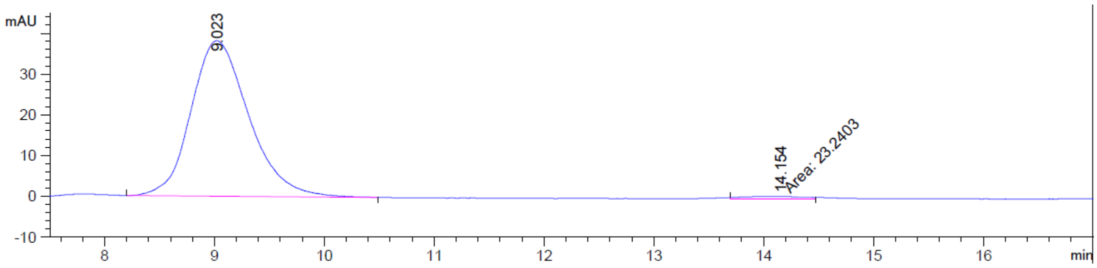
   2  13.788 BB    1.0413 4662.78320   68.06223  52.9447
```



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Peak RetTime Type  Width      Area       Height      Area
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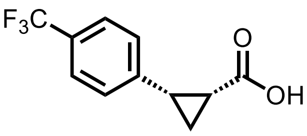
   1   9.023 BB    0.5499 1393.16235   38.16215  98.3592
   2  14.154 MM    0.6197   23.24029 6.25024e-1   1.6408
```



**(1R,2S)-2-(4-(trifluoromethyl)phenyl)cyclopropane-1-carboxylic acid (3c)**

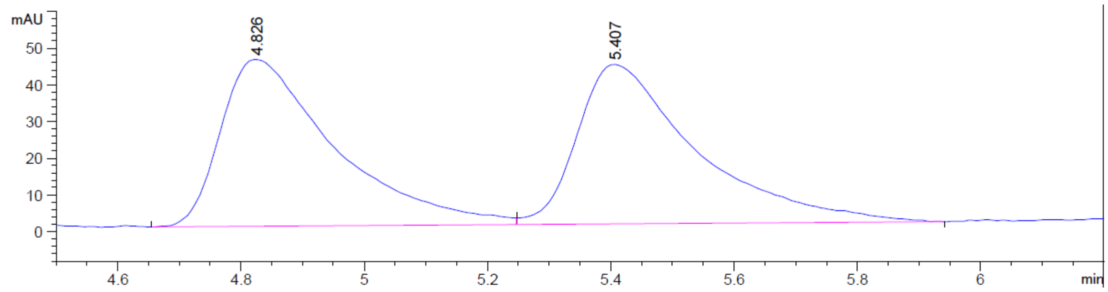
Substrate **1** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 5/1 with 1% v/v of acetic acid). The product was obtained as a pale-yellow solid (69% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® OJ-3 column, 5% $^i$PrOH / $CO_2$, flow rate 1 mL/min, retention time 4.897 min (major) and 5.495 min (minor), 97:3 er);

$^1$H NMR (600 MHz, $CDCl_3$) δ 7.49 (d, $J$ = 8.5 Hz, 2H), 7.33 (d, $J$ = 8.4 Hz, 2H), 2.64 (q, $J$ = 8.6 Hz, 1H), 2.09 (ddd, $J$ = 9.3, 7.7, 5.6 Hz, 1H), 1.69 (dt, $J$ = 7.7, 5.4 Hz, 1H), 1.43 (ddd, $J$ = 8.7, 7.8, 5.2 Hz, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 176.43, 140.02 (q, $J$ = 1.5 Hz), 129.59, 128.97 (q, $J$ = 31.5 Hz), 124.82 (q, $J$ = 3 Hz), 124.22 (q, $J$ = 270 Hz), 26.09, 21.58, 12.16. $^{19}$F NMR (376 MHz, $CDCl_3$) δ -62.69.

HRMS (ESI-TOF) *m/z* Calcd for $C_{11}H_{10}F_3O_2^+$ $[M+H]^+$ 231.0627, found 231.0631.

The absolute stereochemistry was assigned based on comparing the specific rotation of **3m** with literature.



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   1   4.826 BV    0.1818  583.19299  45.41054  50.0033
   2   5.407 VB    0.1866  583.11597  43.42923  49.9967
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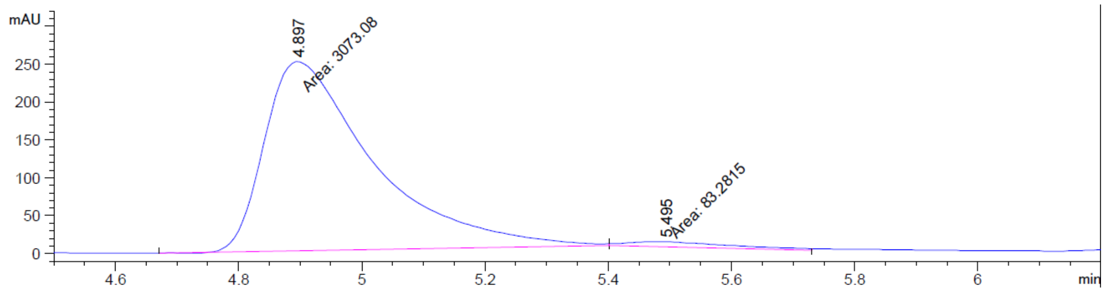

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   2   5.495 MM    0.2029   83.28146    6.84065   2.6385
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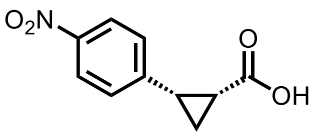


**(1R,2S)-2-(4-nitrophenyl)cyclopropane-1-carboxylic acid (3d)**

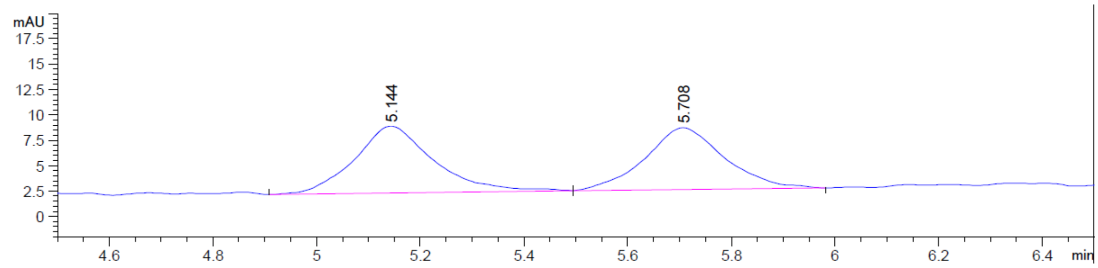
Substrate **1** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 2/1 with 1% v/v of acetic acid). The product was obtained as a pale-yellow solid (63% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® OJ-3 column, 5% $^i$PrOH / $CO_2$, flow rate 2 mL/min, retention time 5.160 min (major) and 5.715 min (minor), 97:3 er);

$^1$H NMR (600 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.8 Hz, 2H), 7.39 (d, *J* = 8.7 Hz, 2H), 2.67 (q, *J* = 8.5 Hz, 1H), 2.15 (ddd, *J* = 9.3, 7.8, 5.6 Hz, 1H), 1.72 (dt, *J* = 7.7, 5.5 Hz, 1H), 1.53 – 1.47 (m, 1H); $^{13}C$ NMR (150 MHz, $CDCl_3$) δ 175.87, 146.84, 143.71, 130.14, 123.13, 26.05, 21.90, 12.57.

HRMS (ESI-TOF) *m/z* Calcd for $C_{10}H_{10}NO_4^+$ $[M+H]^+$ 208.0604, found 208.0607.

The absolute stereochemistry was assigned based on comparing the specific rotation of **3m** with literature.



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Peak RetTime Type  Width      Area       Height      Area
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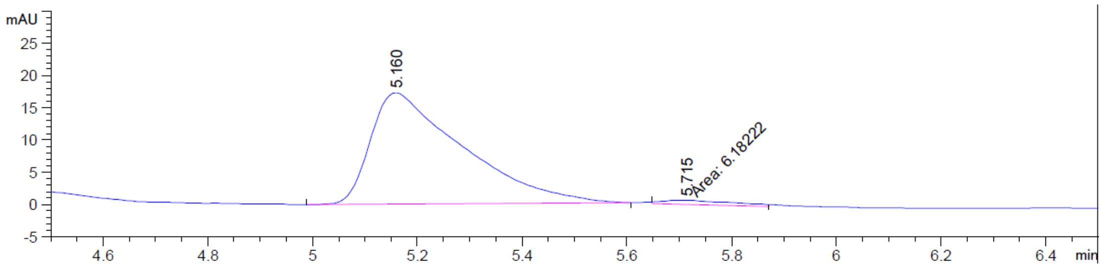
----|-------|----|-------|----------|----------|--------|
  1    5.144 BV    0.1571   55.05377    4.97626  49.4209
  2    5.706 VB    0.1719   56.34407    4.69940  50.5791
```



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Peak RetTime Type  Width      Area       Height      Area
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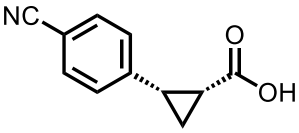
  2    5.715 MM    0.1533    6.18222 6.72103e-1   2.8397
```



**(1R,2S)-2-(4-cyanophenyl)cyclopropane-1-carboxylic acid (3e)**

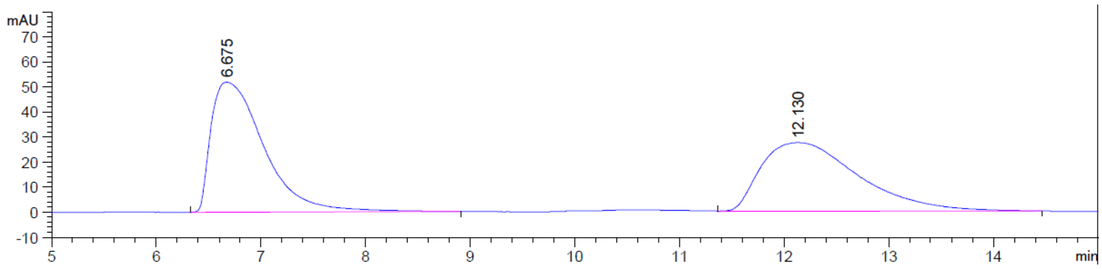
Substrate **1** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 2/1 with 1% v/v of acetic acid). The product was obtained as a pale-yellow solid (66% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® AS-3 column, 5% $^i$PrOH / $CO_2$, flow rate 2 mL/min, retention time 6.706 min (major) and 12.382 min (minor), 97:3 er);

$^1H$ NMR (600 MHz, $CDCl_3$) δ 7.54 (d, $J$ = 8.3 Hz, 2H), 7.33 (d, $J$ = 8.2 Hz, 2H), 2.64 (q, $J$ = 8.5 Hz, 1H), 2.12 (ddd, $J$ = 9.2, 7.8, 5.6 Hz, 1H), 1.69 (dt, $J$ = 7.8, 5.5 Hz, 1H), 1.51 – 1.40 (m, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 176.23, 141.55, 131.68, 130.06, 118.90, 110.52, 26.28, 21.82, 12.27.

HRMS (ESI-TOF) *m/z* Calcd for $C_{11}H_{10}NO_2^+$ $[M+H]^+$ 188.0706, found 188.0704.

The absolute stereochemistry was assigned based on comparing the specific rotation of **3m** with literature.



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Peak RetTime Type  Width     Area       Height      Area
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   1   6.675 BB    0.5512 1818.46094   51.84768  50.6245
   2  12.130 BB    0.8779 1773.59778   27.37505  49.3755
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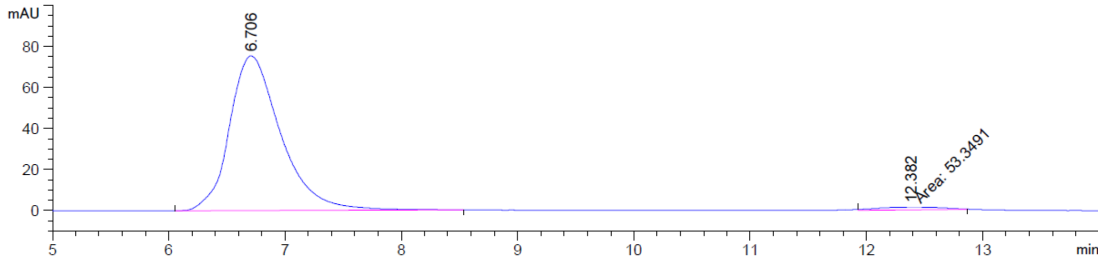

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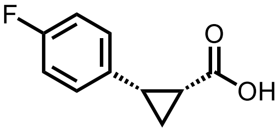
Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   6.706 BB    0.4634 2305.85181   75.26052  97.7387
   2  12.382 MM    0.6413   53.34911    1.38640   2.2613
```



**(1R,2S)-2-(4-fluorophenyl)cyclopropane-1-carboxylic acid (3f)**

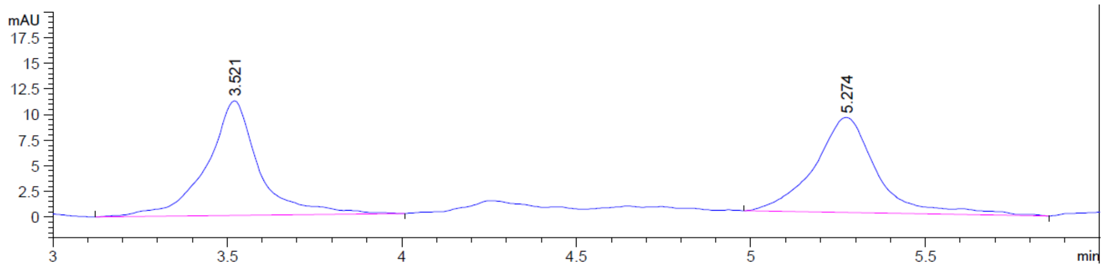
Substrate **1** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 5/1 with 1% v/v of acetic acid). The product was obtained as a pale-yellow solid (51% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® OJ-3 column, 5% $^i$PrOH / $CO_2$, flow rate 2 mL/min, retention time 3.394 min (major) and 5.098 min (minor), 97:3 er);

$^1$H NMR (600 MHz, $CDCl_3$) δ 7.20 (dd, *J* = 8.4, 5.5 Hz, 2H), 6.93 (t, *J* = 8.7 Hz, 2H), 2.59 (q, *J* = 8.5 Hz, 1H), 2.05 (ddd, *J* = 9.3, 7.9, 5.5 Hz, 1H), 1.63 (dt, *J* = 7.6, 5.4 Hz, 1H), 1.38 (ddd, *J* = 8.7, 7.7, 5.1 Hz, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 175.84, 161.74 (d, *J* = 243 Hz), 131.58 (d, *J* = 1.5 Hz), 130.75 (d, *J* = 7.5 Hz), 114.80 (d, *J* = 22.5 Hz), 25.70, 21.22, 12.21; $^{19}$F NMR (376 MHz, $CDCl_3$) δ -116.34.

HRMS (ESI-TOF) *m/z* Calcd for $C_{10}H_{10}FO_2^+$ $[M+H]^+$ 181.0659, found 181.0658.

The absolute stereochemistry was assigned based on comparing the specific rotation of **3m** with literature.



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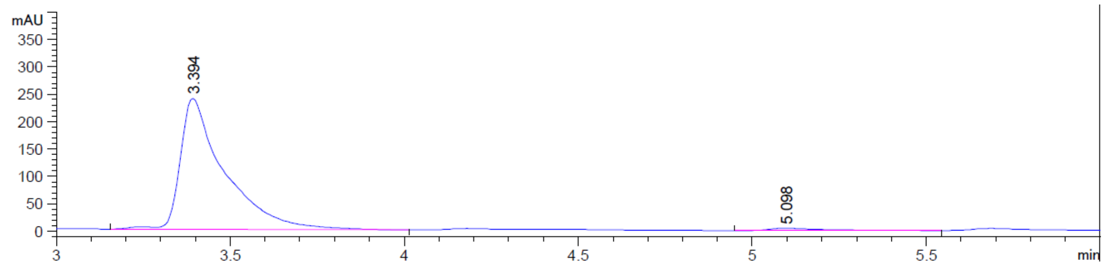
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   3.521 BB    0.1459  116.74403   11.17264  50.2261
   2   5.274 BB    0.1798  115.69290    9.25463  49.7739
```



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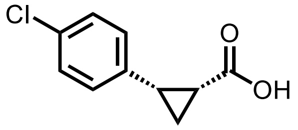
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   3.394 VB R  0.1222 2117.96899  239.30923  97.4252
   2   5.098 BV    0.1702   55.97525    4.46813   2.5748
```



**(1R,2S)-2-(4-chlorophenyl)cyclopropane-1-carboxylic acid (3g)**

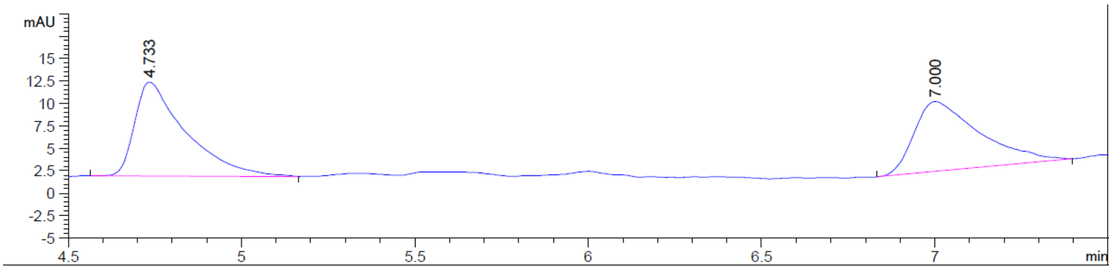
Substrate **1** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 5/1 with 1% v/v of acetic acid). The product was obtained as a pale-yellow solid (70% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® OJ-3 column, 5% $^{i}$PrOH / CO$_2$, flow rate 2 mL/min, retention time 4.726 min (major) and 6.986 min (minor), 97:3 er);

$^{1}$H NMR (600 MHz, CDCl$_3$) δ 7.22 (d, *J* = 8.5 Hz, 2H), 7.17 (d, *J* = 8.1 Hz, 2H), 2.58 (q, *J* = 8.5 Hz, 1H), 2.08 – 2.03 (m, 1H), 1.64 (dt, *J* = 7.7, 5.4 Hz, 1H), 1.39 (ddd, *J* = 8.7, 7.7, 5.1 Hz, 1H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 175.83, 134.40, 132.56, 130.59, 128.10, 25.82, 21.34, 12.15.

HRMS (ESI-TOF) *m/z* Calcd for $C_{10}H_{10}ClO_2^+$ [M+H]$^+$ 197.0364, found 197.0362.

The absolute stereochemistry was assigned based on comparing the specific rotation of **3m** with literature.



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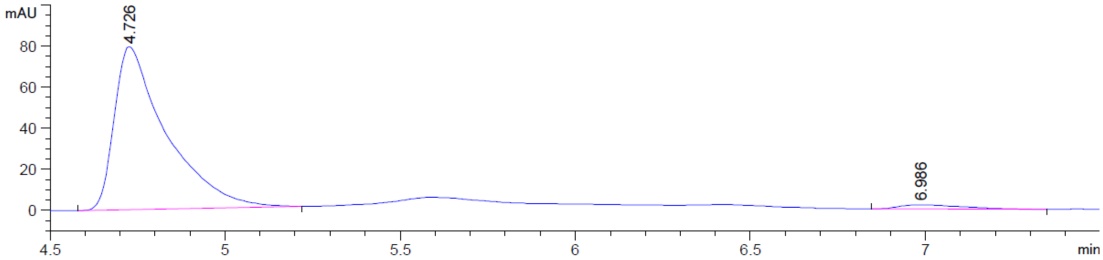
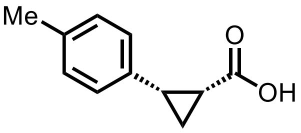
Peak RetTime Type  Width      Area       Height      Area
  #   [min]         [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1    4.733 BB    0.1428  107.01307   10.51189  51.2681
   2    7.000 BB    0.1884  101.71914    7.78732  48.7319
```



```
Peak RetTime Type  Width      Area       Height      Area
  #   [min]         [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1    4.726 BB    0.1442  818.38550   79.45596  97.1407
   2    6.986 BB    0.1774   24.08867    2.01673   2.8593
```



**(1R,2S)-2-(p-tolyl)cyclopropane-1-carboxylic acid (3h)**

Substrate **1** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 5/1 with 1% v/v of acetic acid). The product was obtained as a pale-yellow solid (62%

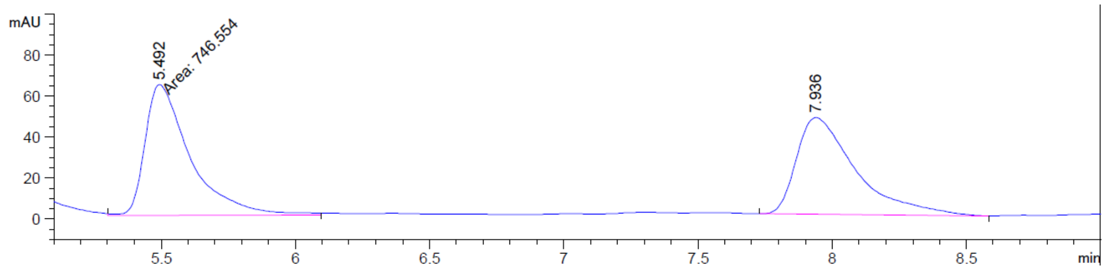
yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® OJ-3 column, 5% $^i$PrOH / $CO_2$, flow rate 2 mL/min, retention time 5.470min (major) and 7.932 min (minor), 99:1 er);

$^1$H NMR (600 MHz, $CDCl_3$) δ 7.13 (d, *J* = 7.7 Hz, 2H), 7.05 (d, *J* = 7.7 Hz, 2H), 2.59 (q, *J* = 8.6 Hz, 1H), 2.30 (s, 3H), 2.06 – 2.00 (m, 1H), 1.64 (dt, *J* = 7.8, 5.4 Hz, 1H), 1.35 (td, *J* = 8.2, 4.9 Hz, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 175.58, 136.28, 132.85, 129.09, 128.69, 26.17, 21.23, 21.09, 12.06.

HRMS (ESI-TOF) *m/z* Calcd for $C_{11}H_{13}O_2^+$ $[M+H]^+$ 177.0910, found 177.0905.

The absolute stereochemistry was assigned based on comparing the specific rotation of **3m** with literature.



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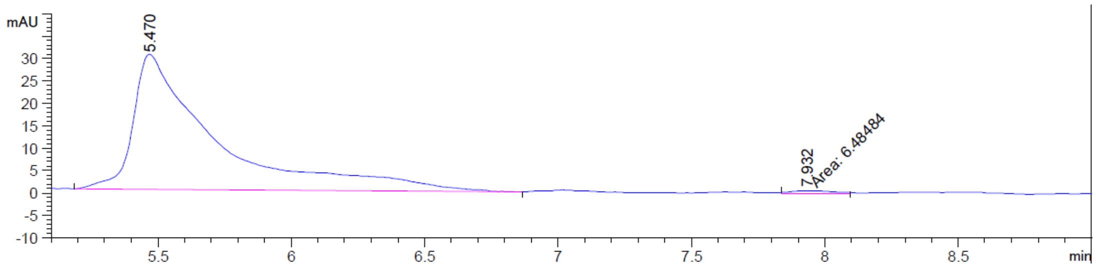
Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]      [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.492 MM    0.1950  746.55359   63.81255  50.8004
   2   7.936 BB    0.2329  723.02826   47.15403  49.1996
```



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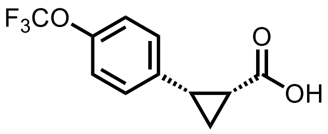
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.470 BB    0.2745  642.39697  30.15806  99.0006
   2   7.932 MM    0.1920    6.48484 5.62989e-1  0.9994
```



**(1R,2S)-2-(4-(trifluoromethoxy)phenyl)cyclopropane-1-carboxylic acid (3i)**

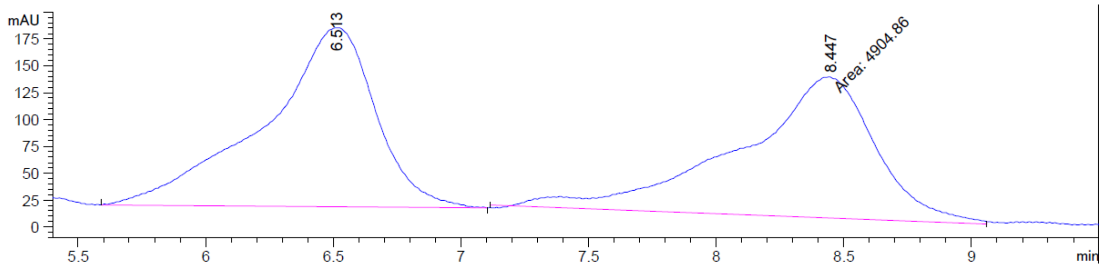
Substrate **1** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 3/1 with 1% v/v of acetic acid). The product was obtained as a pale-yellow solid (73% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® OJ-3 column, 3% $^i$PrOH / $CO_2$, flow rate 1 mL/min, retention time 6.532 min (major) and 8.508 min (minor), 97:3 er);

$^1$H NMR (600 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.7 Hz, 2H), 7.08 (d, *J* = 8.3 Hz, 2H), 2.58 (q, *J* = 8.5 Hz, 1H), 2.04 (ddd, *J* = 9.1, 7.7, 5.6 Hz, 1H), 1.62 (dt, *J* = 7.7, 5.4 Hz, 1H), 1.38 (td, *J* = 8.2, 5.1 Hz, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 176.88, 147.98 (q, *J* = 1.5 Hz), 134.70, 130.58, 120.47 (q, *J* = 255 Hz), 120.37, 25.69, 21.45, 12.12; $^{19}$F NMR (376 MHz, $CDCl_3$) δ -58.12.

HRMS (ESI-TOF) *m/z* Calcd for $C_{11}H_{10}F_3O_3^+$ $[M+H]^+$ 247.0577, found 247.0579.

The absolute stereochemistry was assigned based on comparing the specific rotation of **3m** with literature.



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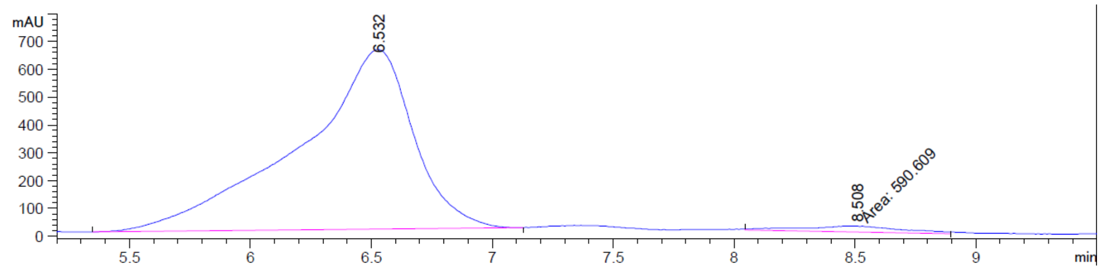
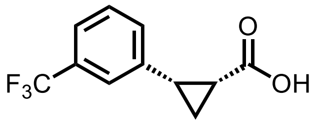
Peak RetTime Type  Width     Area       Height      Area
  #   [min]         [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   6.513 BV R  0.3599 5056.48486  166.71335  50.7611
   2   8.447 MM    0.6216 4904.86084  131.51088  49.2389
```



```
Peak RetTime Type  Width     Area       Height      Area
  #   [min]         [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   6.532 VV R  0.4272 2.12447e4   646.74084  97.2952
   2   8.508 MM    0.4780  590.60895   20.59183   2.7048
```



**(1R,2S)-2-(3-(trifluoromethyl)phenyl)cyclopropane-1-carboxylic acid (3j)**

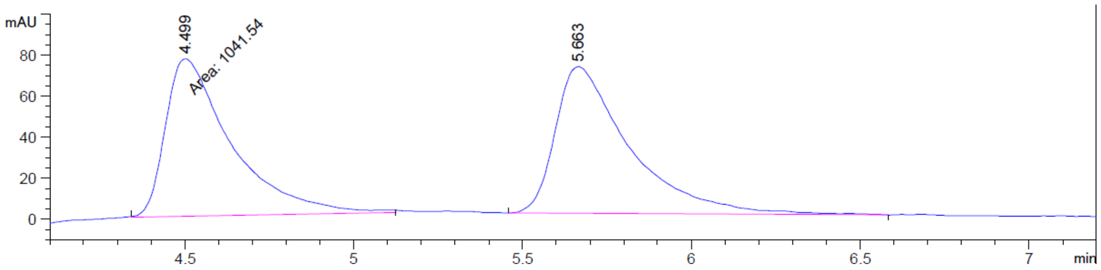
Substrate **1** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 5/1 with 1% v/v of acetic acid). The product was obtained as a pale-yellow oil (77% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® OJ-3 column, 5% $^i$PrOH / $CO_2$, flow rate 1 mL/min, retention time 4.529 min (major) and 5.711 min (minor), 92:8 er);

$^1$H NMR (600 MHz, $CDCl_3$) δ 7.48 (s, 1H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.39 (d, *J* = 7.8 Hz, 1H), 7.34 (t, *J* = 7.7 Hz, 1H), 2.64 (q, *J* = 8.6 Hz, 1H), 2.08 (ddd, *J* = 9.2, 7.8, 5.6 Hz, 1H), 1.68 (dt, *J* = 7.7, 5.4 Hz, 1H), 1.43 (ddd, *J* = 8.7, 7.8, 5.2 Hz, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 176.38, 136.92, 132.59, 130.28 (q, *J* = 31.5 Hz), 128.31, 126.11 (q, *J* = 4.5 Hz), 124.11 (q, *J* = 270 Hz), 123.62 (q, *J* = 4.5 Hz), 26.06, 21.40, 12.22; $^{19}$F NMR (376 MHz, $CDCl_3$) δ -62.90.

HRMS (ESI-TOF) *m/z* Calcd for $C_{11}H_{10}F_3O_2^+$ $[M+H]^+$ 231.0627, found 231.0628.

The absolute stereochemistry was assigned based on comparing the specific rotation of **3m** with literature.



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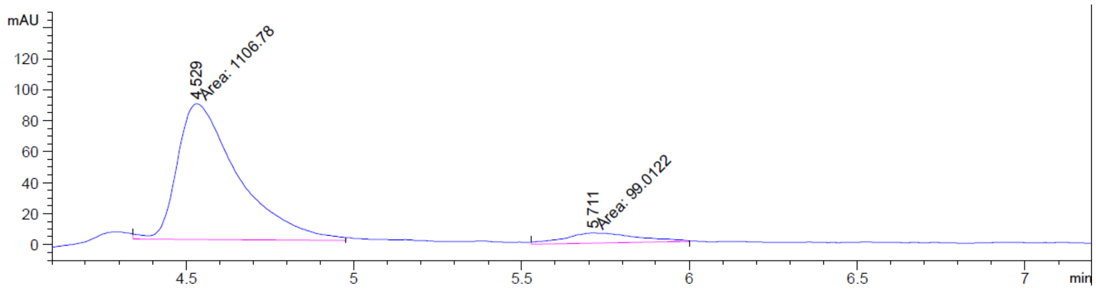
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   4.499 MM    0.2261 1041.54480   76.76731  48.7093
   2   5.663 BV R  0.2211 1096.74170   71.42764  51.2907
```



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Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   4.529 MM    0.2106 1106.78430   87.58733  91.7886
   2   5.711 MM    0.2513   99.01224    6.56730   8.2114
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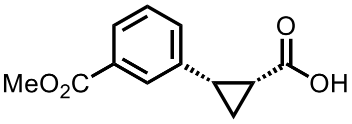


**(1R,2S)-2-(3-(methoxycarbonyl)phenyl)cyclopropane-1-carboxylic acid (3k)**

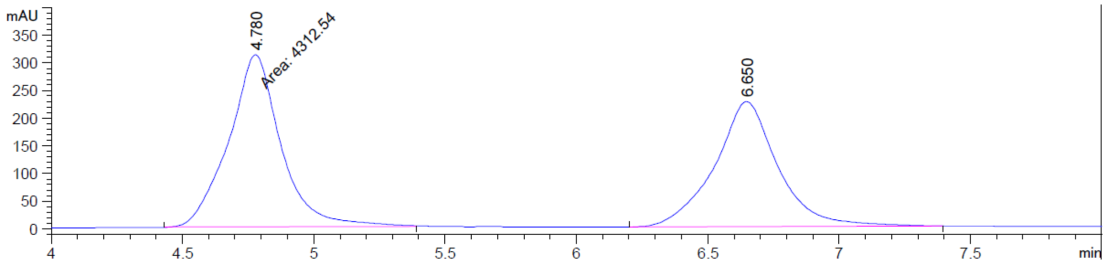
Substrate **1** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 2/1 with 1% v/v of acetic acid). The product was obtained as a white solid (67% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® OJ-3 column, 5% $^i$PrOH / $CO_2$, flow rate 2 mL/min, retention time 4.789 min (major) and 6.673 min (minor), 95:5 er);

$^1$H NMR (600 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.87 (d, *J* = 7.8 Hz, 1H), 7.40 (d, *J* = 7.6 Hz, 1H), 7.30 (t, *J* = 7.7 Hz, 1H), 3.91 (s, 3H), 2.64 (q, *J* = 8.5 Hz, 1H), 2.10 – 2.03 (m, 1H), 1.70 (dt, *J* = 7.7, 5.4 Hz, 1H), 1.41 (td, *J* = 8.2, 5.1 Hz, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 175.83, 167.06, 136.33, 133.70, 130.62, 129.87, 128.09, 127.97, 52.08, 26.11, 21.28, 12.15.

HRMS (ESI-TOF) *m/z* Calcd for $C_{12}H_{13}O_4^+$ $[M+H]^+$ 221.0808, found 221.0807.

The absolute stereochemistry was assigned based on comparing the specific rotation of **3m** with literature.



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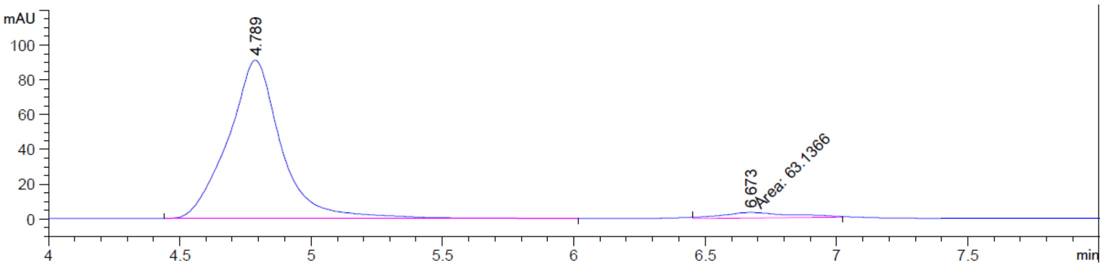
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   4.781 BB    0.1945  139.56223   10.01887  52.3888
   2   6.652 BB    0.2377  126.83482    7.48401  47.6112
```



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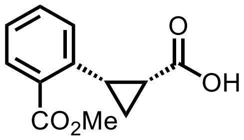
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   4.789 BB    0.1984 1284.97974   91.18695  95.3167
   2   6.673 MM    0.3232   63.13662    3.25587   4.6833
```



### (1R,2S)-2-(2-(methoxycarbonyl)phenyl)cyclopropane-1-carboxylic acid (3l)

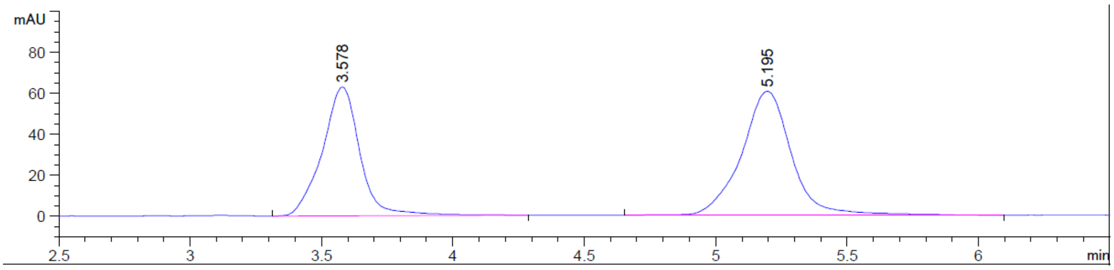
Substrate **1** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 2/1 with 1% v/v of acetic acid). The product was obtained as a white solid (54% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® OJ-3 column, 5% $^{i}$PrOH / $CO_2$, flow rate 2 mL/min, retention time 3.271 min (major) and 4.985 min (minor), 99:1 er);

$^{1}$H NMR (600 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.8 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 1H), 7.32 (d, *J* = 7.7 Hz, 1H), 7.30 – 7.25 (m, 1H), 3.82 (s, 3H), 2.98 (q, *J* = 8.6 Hz, 1H), 2.12 (ddd, *J* = 9.3, 7.7, 5.4 Hz, 1H), 1.60 (dt, *J* = 8.0, 5.2 Hz, 1H), 1.43 (td, *J* = 8.1, 5.0 Hz, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 177.08, 167.76, 137.61, 131.58, 131.08, 130.88, 130.08, 126.76, 51.95, 26.30, 21.71, 13.43.

HRMS (ESI-TOF) *m/z* Calcd for $C_{12}H_{13}O_4^+$ $[M+H]^+$ 221.0808, found 221.0807.

The absolute stereochemistry was assigned based on comparing the specific rotation of **3m** with literature.



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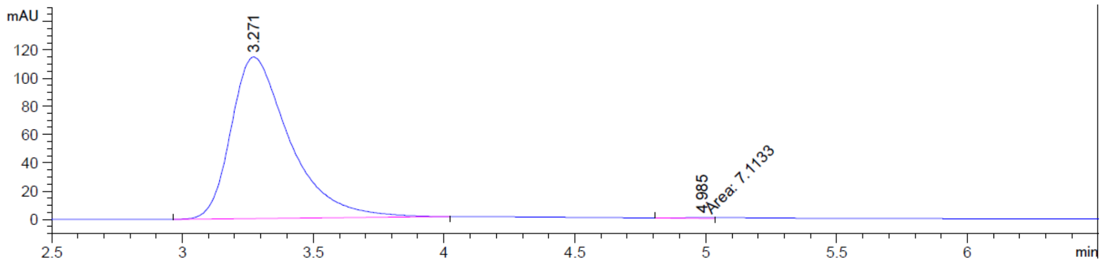
Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   3.578 MM    0.1670  629.59418   62.83921  47.7988
   2   5.195 MM    0.1983  687.58069   57.79146  52.2012
```



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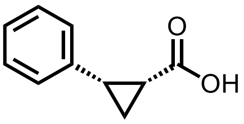
Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   3.271 BB     0.2318 1781.41797  114.32291  99.6023
   2   4.985 MM     0.1472    7.11330 8.05398e-1   0.3977
```



**(1R,2S)-2-phenylcyclopropane-1-carboxylic acid (3m)**

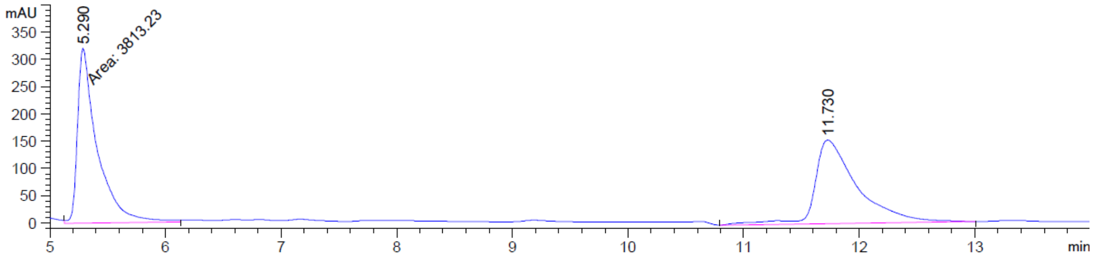
Substrate **1** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 5/1 with 1% v/v of acetic acid). The product was obtained as a pale-yellow solid (68% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® OJ-3 column, 5% $^i$PrOH / $CO_2$, flow rate 2 mL/min, retention time 5.287 min (major) and 11.697 min (minor), 98:2 er);

$^1$H NMR (600 MHz, $CDCl_3$) δ 7.26 – 7.22 (m, 4H), 7.20 (td, *J* = 5.9, 2.4 Hz, 1H), 2.62 (q, *J* = 8.6 Hz, 1H), 2.04 (ddd, *J* = 9.3, 7.7, 5.6 Hz, 1H), 1.66 (dt, *J* = 7.7, 5.3 Hz, 1H), 1.37 (ddd, *J* = 8.7, 7.7, 5.0 Hz, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 176.04, 135.91, 129.24, 127.94, 126.76, 26.48, 21.26, 12.00.

HRMS (ESI-TOF) *m/z* Calcd for $C_{10}H_{11}O_2^+$ $[M+H]^+$ 163.0754, found 163.0752.

The absolute stereochemistry was assigned based on comparing the specific rotation of **3m** with literature.



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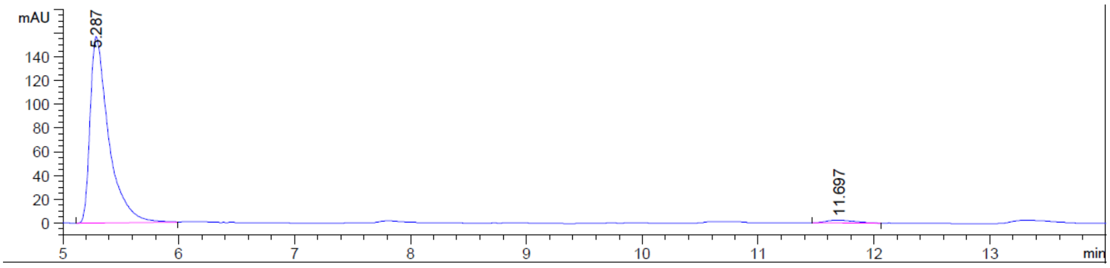
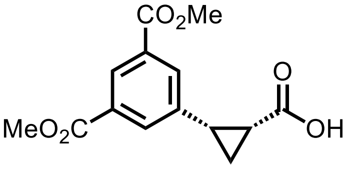
Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   5.290 MM     0.1982 3813.23438  320.63879  49.4393
   2  11.730 VB R   0.3614 3899.72827  153.09192  50.5607
```



```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.287 BB    0.1640 1745.86206  156.71941  97.9298
   2  11.697 BB    0.2069   36.90720    2.27959   2.0702
```



**(1R,2S)-2-(3,5-bis(methoxycarbonyl)phenyl)cyclopropanecarboxylic acid (3n)**

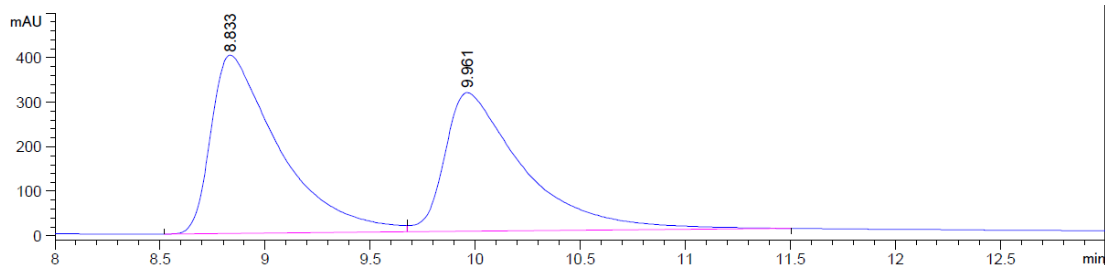
Substrate **1** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 2/1 with 1% v/v of acetic acid). The product was obtained as a white solid (66% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® OJ-3 column, 5% $^{i}$PrOH / $CO_2$, flow rate 1 mL/min, retention time 8.903 min (major) and 10.053 min (minor), 97:3 er);

$^{1}$H NMR (600 MHz, $CDCl_3$) δ 8.51 (s, 1H), 8.10 (s, 2H), 3.93 (s, 6H), 2.66 (s, 1H), 2.13 (d, *J* = 7.4 Hz, 1H), 1.75 (s, 1H), 1.46 (s, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 166.28, 161.00, 134.71, 130.27, 129.23, 116.15, 52.36, 24.68, 24.52, 12.32.

HRMS (ESI-TOF) *m/z* Calcd for $C_{14}H_{13}O_6^-$ $[M-H]^-$ 277.0712, found 277.0719.

The absolute stereochemistry was assigned based on comparing the specific rotation of **3m** with literature.



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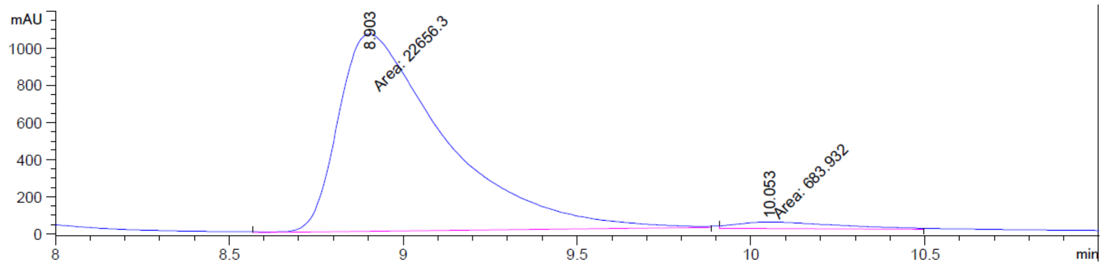
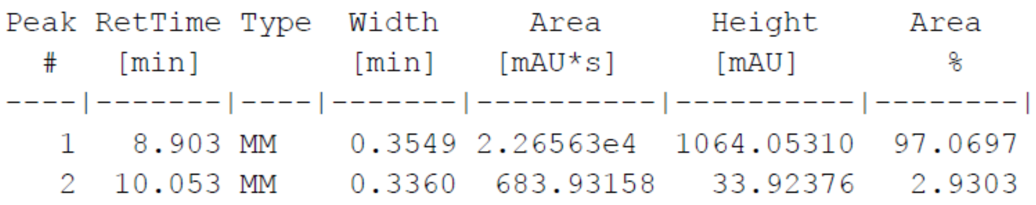
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   8.833 BV    0.3194 9046.69336  400.76804  52.8028
   2   9.961 VV R  0.3767 8086.30322  311.68176  47.1972
```





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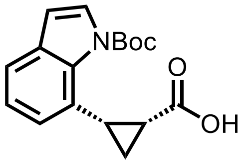
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   8.903 MM    0.3549 2.26563e4 1064.05310  97.0697
   2  10.053 MM    0.3360  683.93158   33.92376   2.9303
```



**(1R,2S)-2-(1-(tert-butoxycarbonyl)-1H-indol-7-yl)cyclopropanecarboxylic acid (3o)**

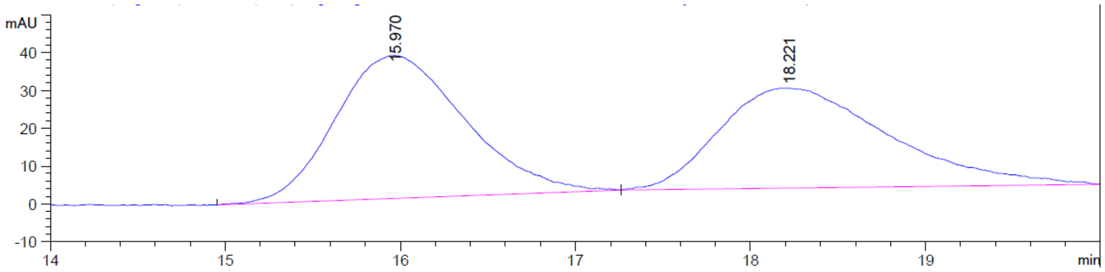
Substrate **1** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 2/1 with 1% v/v of acetic acid). The product was obtained as a white solid (47% yield).

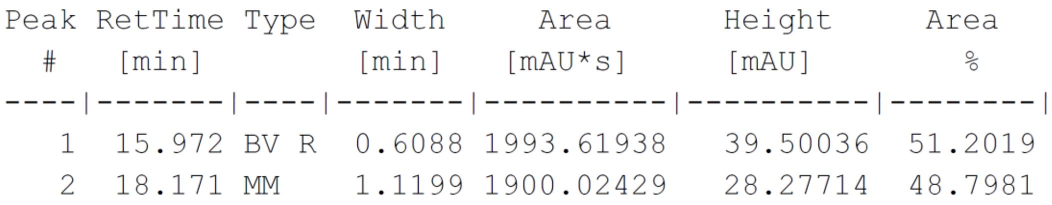
The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® AS-3 column, 5% $^i$PrOH / $CO_2$, flow rate 1 mL/min, retention time 16.895 min (major) and 19.070 min (minor), 99:1 er);

$^1$H NMR (600 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.55 (d, *J* = 3.4 Hz, 1H), 7.42 (dd, *J* = 1.8, 0.9 Hz, 1H), 7.21 (dd, *J* = 8.5, 1.8 Hz, 1H), 6.49 (dd, *J* = 3.6, 0.8 Hz, 1H), 2.72 (q, *J* = 8.6 Hz, 1H), 2.08 – 2.02 (m, 1H), 1.74 – 1.70 (m, 1H), 1.66 (s, 9H), 1.41 – 1.37 (m, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 180.47, 175.83, 149.77, 130.43, 130.20, 126.03, 125.72, 121.42, 114.60, 107.25, 28.19, 26.56, 21.32, 12.26, 9.05.

HRMS (ESI-TOF) *m/z* Calcd for $C_{17}H_{18}NO_4^-$ $[M-H]^-$ 300.1236, found 300.1228.

The absolute stereochemistry was assigned based on comparing the specific rotation of **3m** with literature.





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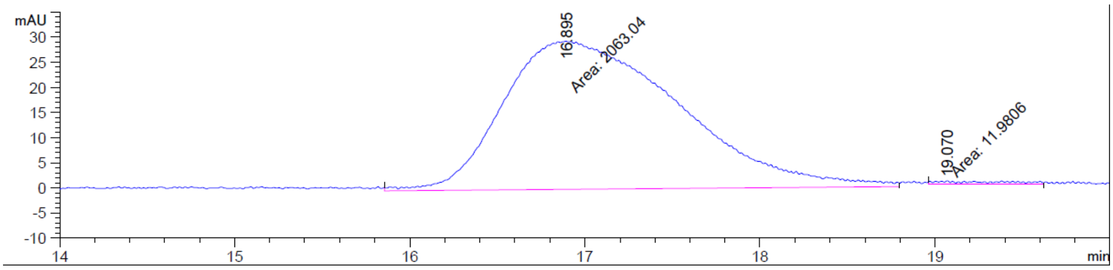
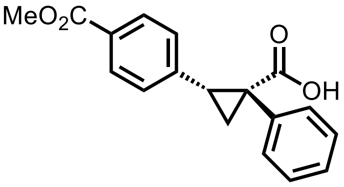
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  15.972 BV R  0.6088 1993.61938   39.50036  51.2019
   2  18.171 MM    1.1199 1900.02429   28.27714  48.7981
```



```
Peak RetTime Type  Width      Area       Height      Area
  #   [min]        [min]    [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
  1  16.895 MM    1.1670 2063.04224   29.46432  99.4226
  2  19.070 MM    0.3590   11.98057 5.56213e-1  0.5774
```



**(1R,2R)-2-(4-(methoxycarbonyl)phenyl)-1-phenylcyclopropane-1-carboxylic acid (3p)**

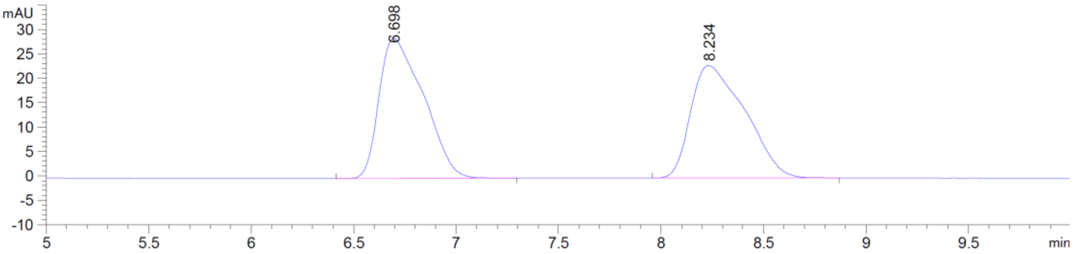
Substrate **1p** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 2/1 with 1% v/v of acetic acid). The product was obtained as a white solid (64% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® AD-3 column, 20% $^{i}$PrOH / $CO_2$, flow rate 2 mL/min, retention time 6.300 min (major) and 7.776 min (minor), 98:2 er);

$^{1}$H NMR (600 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.3 Hz, 2H), 7.48 – 7.41 (m, 2H), 7.35 (td, *J* = 7.9, 5.7 Hz, 4H), 7.31 – 7.27 (m, 1H), 3.93 (s, 3H), 2.89 (t, *J* = 8.4 Hz, 1H), 2.26 (dd, *J* = 7.8, 5.0 Hz, 1H), 1.70 (dd, *J* = 9.0, 5.0 Hz, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 175.85, 167.05, 141.33, 139.32, 130.19, 129.37, 129.20, 128.66, 128.38, 127.66, 52.06, 37.83, 34.38, 19.25.

HRMS (ESI-TOF) *m/z* Calcd for $C_{18}H_{16}O_4Na^+$ $[M+Na]^+$ 319.0941, found 319.0943.

The absolute stereochemistry was assigned based on comparing the specific rotation of **3m** with literature.



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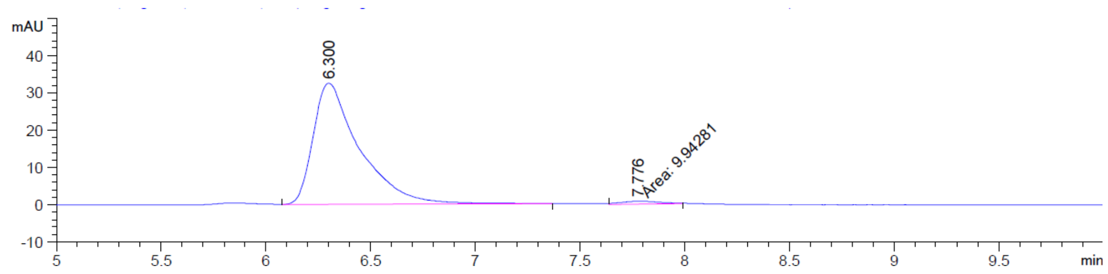
Peak RetTime Type  Width      Area       Height      Area
  #   [min]        [min]    [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
  1    6.698 BB    0.2132  431.89594   28.76545  50.3701
  2    8.234 BB    0.2627  425.54874   23.11917  49.6299
```



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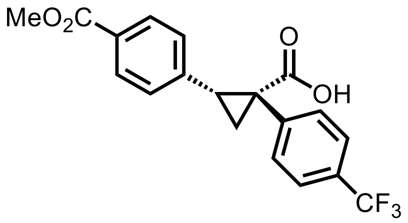
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   6.300 BB    0.2215  500.26663   32.50945  98.0512
   2   7.776 MM    0.2147    9.94281 7.71851e-1   1.9488
```



### (1R,2R)-2-(4-(methoxycarbonyl)phenyl)-1-(4-(trifluoromethyl)phenyl)cyclopropane-1-carboxylic acid (3q)

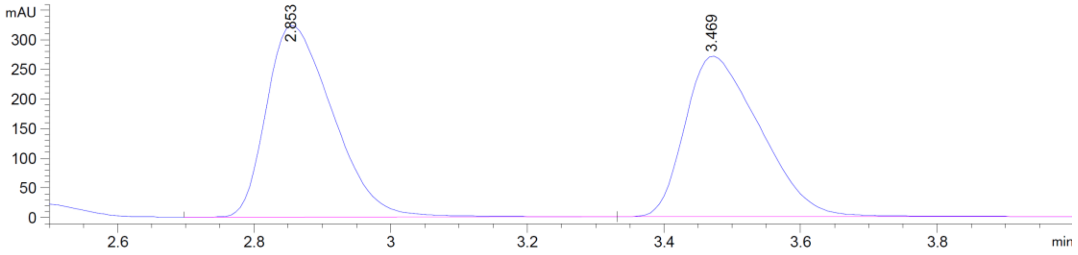
Substrate **1q** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 2/1 with 1% v/v of acetic acid). The product was obtained as a white solid (69% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® AD-3 column, 20% $^i$PrOH / $CO_2$, flow rate 2 mL/min, retention time 2.741 min (major) and 3.339 min (minor), 97:3 er);

$^1$H NMR (600 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.4 Hz, 2H), 7.60 (d, *J* = 8.1 Hz, 2H), 7.55 (d, *J* = 8.1 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 3.93 (s, 3H), 2.88 (t, *J* = 8.5 Hz, 1H), 2.31 (dd, *J* = 7.9, 5.2 Hz, 1H), 1.72 (dd, *J* = 9.0, 5.2 Hz, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 175.49, 167.02, 143.07, 140.67, 130.63, 129.87 (q, *J* = 33.0 Hz), 129.98, 129.76, 129.54, 129.43, 129.18, 128.87, 125.35 (q, *J* = 3.0 Hz), 123.97 (q, *J* = 270 Hz), 52.12, 37.41, 34.51, 19.20; $^{19}$F NMR (376 MHz, CDCl3) δ -62.82.

HRMS (ESI-TOF) *m/z* Calcd for $C_{19}H_{16}F_3O_4^+$ $[M+H]^+$ 365.0995, found 365.0994.

The absolute stereochemistry was assigned based on comparing the specific rotation of **3m** with literature.



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Peak RetTime Type  Width      Area       Height      Area
  #    [min]        [min]    [mAU*s]      [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   2.853 BB    0.1063 2174.49072  323.80118  51.2016
   2   3.469 BB    0.1233 2072.42944  270.79803  48.7984
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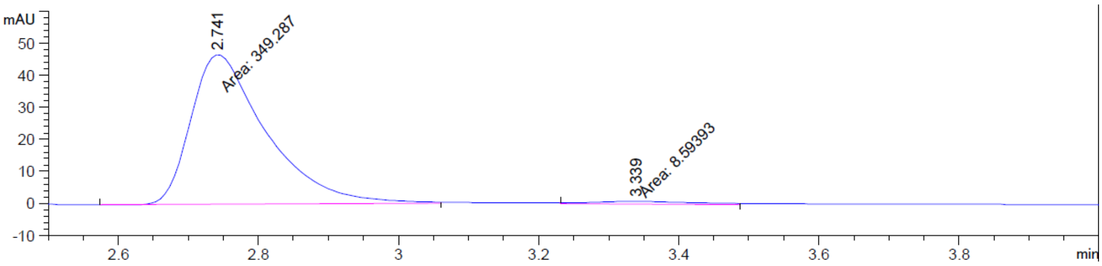

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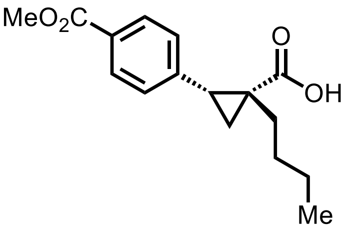
Peak RetTime Type  Width      Area       Height      Area
  #    [min]        [min]    [mAU*s]      [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   2.741 MM    0.1243  349.28665   46.85023  97.5987
   2   3.339 MM    0.1612    8.59393 8.88326e-1   2.4013
```



**(1R,2R)-1-butyl-2-(4-(methoxycarbonyl)phenyl)cyclopropane-1-carboxylic acid (3r)**

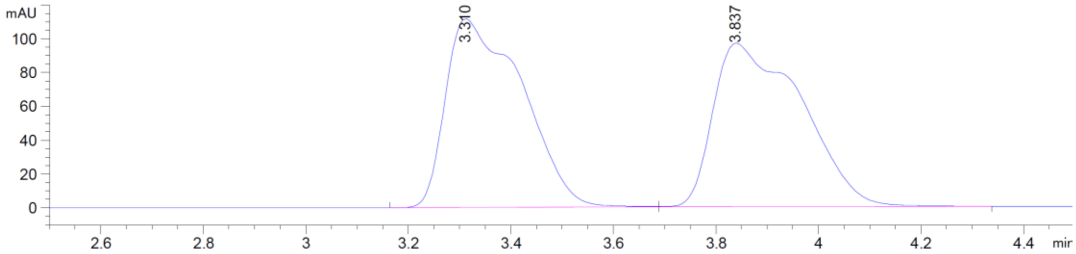
Substrate **1r** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 2/1 with 1% v/v of acetic acid). The product was obtained as a pale-yellow solid (63% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® AD-3 column, 20% $^i$PrOH / $CO_2$, flow rate 2 mL/min, retention time 3.240 min (major) and 3.738 min (minor), 95:5 er);

$^1$H NMR (600 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.2 Hz, 2H), 3.90 (s, 3H), 2.38 (t, *J* = 8.0 Hz, 1H), 2.06 – 1.98 (m, 1H), 1.88 (ddd, *J* = 7.5, 5.0, 1.0 Hz, 1H), 1.52 – 1.39 (m, 2H), 1.35 – 1.26 (m, 3H), 1.18 (dd, *J* = 8.7, 5.1 Hz, 1H), 0.91 (t, *J* = 7.3 Hz, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 177.71, 167.10, 142.12, 129.14, 129.02, 128.22, 35.27, 33.44, 33.23, 29.74, 22.72, 18.63, 13.93.

HRMS (ESI-TOF) *m/z* Calcd for $C_{16}H_{20}O_4^+$ $[M+H]^+$ 277.1434, found 277.1437.

The absolute stereochemistry was assigned based on comparing the specific rotation of **3m** with literature.



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Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   3.310 BV    0.1411 1157.89111  111.58231  49.9134
   2   3.837 VB    0.1621 1161.91125   96.72337  50.0866
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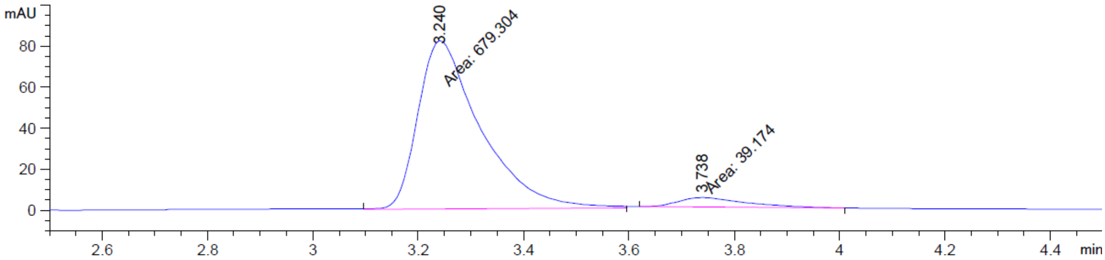

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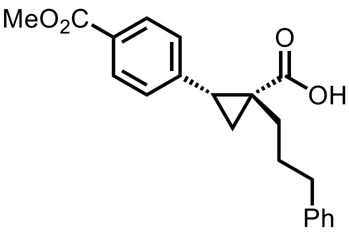
Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   3.240 MM    0.1378  679.30371   82.13483  94.5476
   2   3.738 MM    0.1443   39.17395    4.52614   5.4524
```



**(1R,2R)-2-(4-(methoxycarbonyl)phenyl)-1-(3-phenylpropyl)cyclopropane-1-carboxylic acid (3s)**

Substrate **1s** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 2/1 with 1% v/v of acetic acid). The product was obtained as a pale-yellow oil (44% yield).

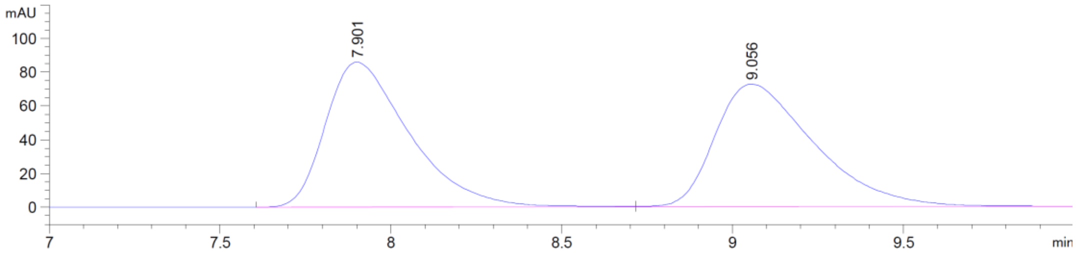
The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® AD-3 column, 20% $^i$PrOH / $CO_2$, flow rate 2 mL/min, retention time 7.675 min (major) and 8.768 min (minor), 96:4 er);

$^1$H NMR (600 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.3 Hz, 2H), 7.28 (t, *J* = 7.6 Hz, 2H), 7.22 – 7.15 (m, 5H), 3.88 (s, 3H), 2.63 (t, *J* = 7.7 Hz, 2H), 2.36 (t, *J* = 8.1 Hz, 1H), 2.05 (ddd, *J* = 13.7, 10.9, 5.1 Hz, 1H), 1.93 – 1.76 (m, 3H), 1.37 (ddd, *J* = 13.8, 11.0, 5.2 Hz, 1H), 1.16 (dd, *J* =

8.7, 5.0 Hz, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 177.54, 167.08, 141.97, 141.91, 129.15, 129.05, 128.31, 128.29, 125.77, 51.97, 35.78, 35.14, 33.55, 32.98, 29.17, 18.78.

HRMS (ESI-TOF) *m/z* Calcd for $C_{21}H_{23}O_4^+$ $[M+H]^+$ 339.1591, found 339.1595.

The absolute stereochemistry was assigned based on comparing the specific rotation of **3m** with literature.



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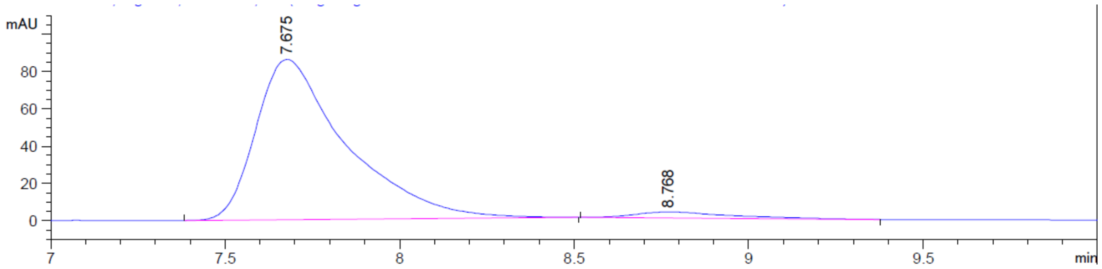
Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   7.901 BV    0.2568 1463.35474   85.87017  50.0170
   2   9.056 VBA   0.3032 1462.35803   72.52623  49.9830
```



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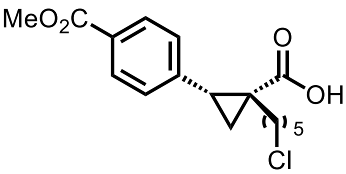
Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   7.675 BB    0.2599 1545.83704   85.93114  96.1478
   2   8.768 BB    0.2778   61.93466    3.19981   3.8522
```



**(1R,2R)-1-(5-chloropentyl)-2-(4-(methoxycarbonyl)phenyl)cyclopropane-1-carboxylic acid (3t)**

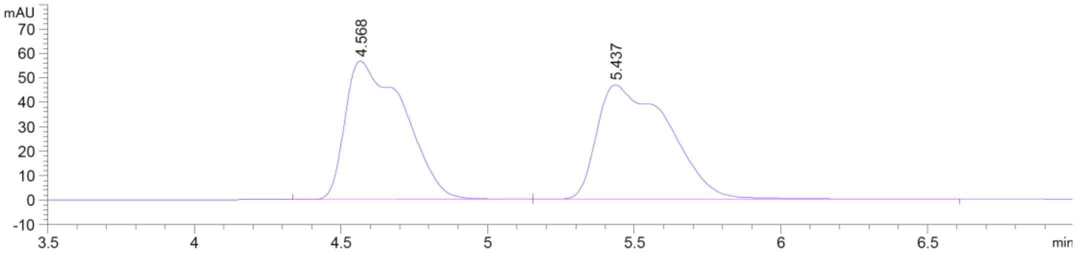
Substrate **1t** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 2/1 with 1% v/v of acetic acid). The product was obtained as a pale-yellow oil (62% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® AD-3 column, 20% $^i$PrOH / $CO_2$,flow rate 2 mL/min, retention time 4.489 min (major) and 5.300 min (minor), 96:4 er);

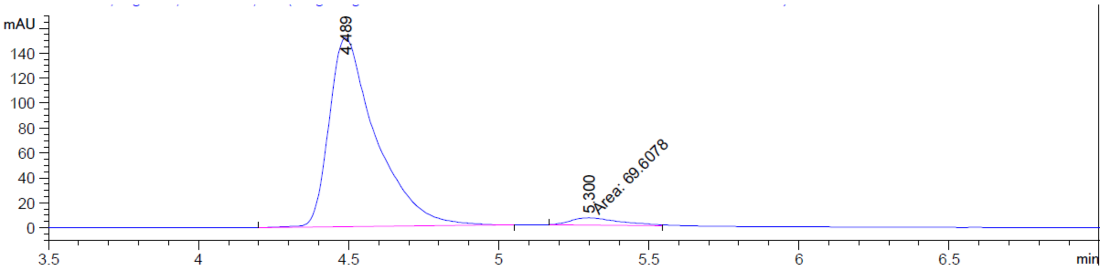
$^1$H NMR (600 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.4 Hz, 2H), 7.22 (d, *J* = 8.1 Hz, 2H), 3.90 (s, 3H), 3.53 (t, *J* = 6.7 Hz, 2H), 2.39 (t, *J* = 8.1 Hz, 1H), 2.04 (ddd, *J* = 14.5, 10.6, 4.2 Hz, 1H), 1.92 – 1.86 (m, 1H), 1.79 (p, *J* = 6.8 Hz, 2H), 1.57 – 1.42 (m, 4H), 1.33 (ddd, *J* = 13.8, 10.5, 5.4 Hz, 1H), 1.20 (dd, *J* = 8.7, 5.1 Hz, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 177.61, 167.06, 141.89, 129.14, 129.03, 128.28, 51.98, 44.95, 35.36, 33.53, 33.01, 32.34, 26.86, 26.82, 18.72.

HRMS (ESI-TOF) *m/z* Calcd for $C_{17}H_{22}ClO_4^+$ $[M+H]^+$ 325.1201, found 325.1205.

The absolute stereochemistry was assigned based on comparing the specific rotation of **3m** with literature.



```
Peak RetTime Type  Width      Area       Height      Area
  #   [min]        [min]    [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   4.568 BB    0.1887  791.70410   56.76482  49.7234
   2   5.437 BB    0.2299  800.51172   46.70959  50.2766
```



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Peak RetTime Type  Width      Area       Height      Area
  #   [min]        [min]    [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   4.489 BB    0.1568 1645.09912  151.36237  95.9405
   2   5.300 MM    0.1949   69.60776    5.95382   4.0595
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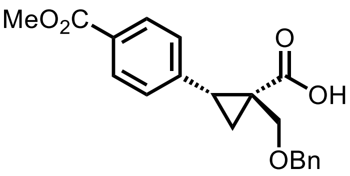


**(1R,2R)-1-((benzyloxy)methyl)-2-(4-(methoxycarbonyl)phenyl)cyclopropane-1-carboxylic acid (3u)**

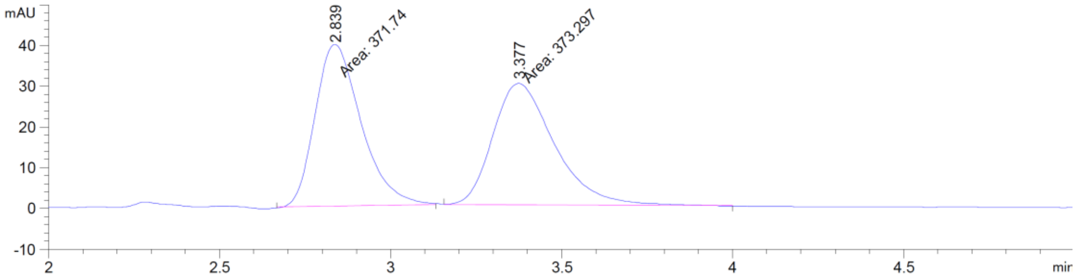
Substrate **1u** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 2/1 with 1% v/v of acetic acid). The product was obtained as a pale-yellow solid (57% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® AS-3 column, 20% $^{i}$PrOH / $CO_2$, flow rate 2 mL/min, retention time 2.835 min (major) and 3.830 min (minor), 98:2 er);

$^{1}$H NMR (600 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.0 Hz, 2H), 7.37 – 7.27 (m, 5H), 7.24 (d, *J* = 8.0 Hz, 2H), 4.58 (s, 2H), 3.87 (d, *J* = 12.2 Hz, 4H), 3.59 (d, *J* = 10.1 Hz, 1H), 2.58 (t, *J* = 8.3 Hz, 1H), 1.96 (dd, *J* = 7.7, 5.1 Hz, 1H), 1.41 (dd, *J* = 8.9, 5.1 Hz, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 175.29, 167.00, 141.19, 137.70, 129.23, 129.13, 128.53, 128.43, 127.78, 127.68, 73.15, 71.85, 51.98, 32.79, 31.00, 16.76.

HRMS (ESI-TOF) *m/z* Calcd for $C_{20}H_{21}O_5^+$ $[M+H]^+$ 341.1383, found 341.1383.

The absolute stereochemistry was assigned based on comparing the specific rotation of **3m** with literature.



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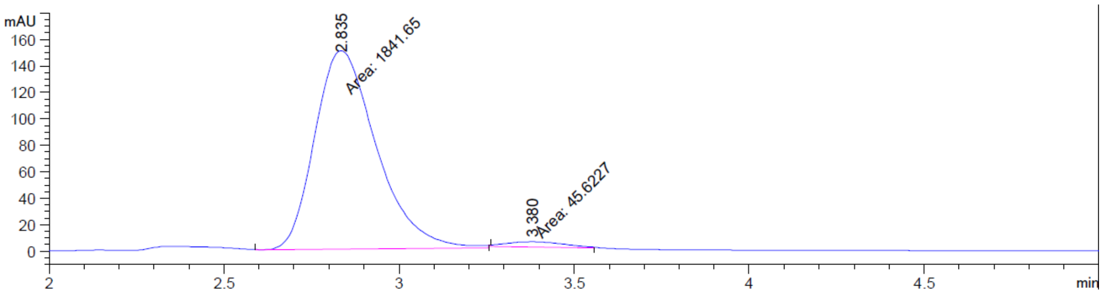
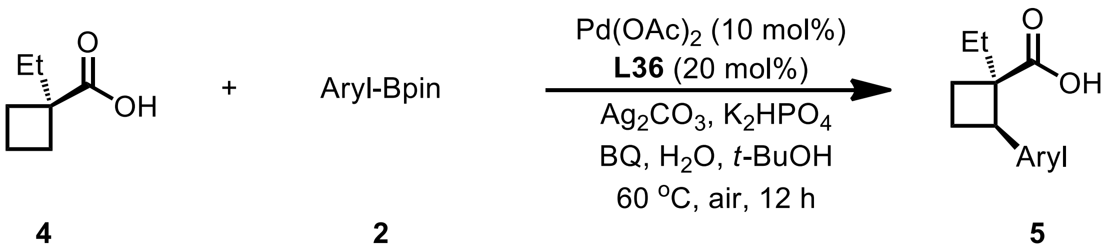
Peak RetTime Type  Width      Area       Height      Area
  #   [min]        [min]    [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   2.839 MM    0.1558  371.74030   39.76003  49.8956
   2   3.377 MM    0.2087  373.29666   29.81713  50.1044
```



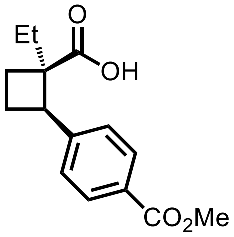
```
Peak RetTime Type  Width      Area       Height      Area
  #   [min]        [min]    [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   2.835 MM    0.2044 1841.64624  150.13182  97.5826
   2   3.380 MM    0.1923   45.62273    3.95362   2.4174
```

### 3.6 Enantioselective Arylation of Cylcobutanecarboxylic acid



**General procedure for enantioselective arylation of cyclobutanecarboxylic acid**:

A 2-dram vial equipped with a magnetic stir bar was charged with $Pd(OAc)_2$ (2.2 mg, 10 mol%) and **L36** (7.4 mg, 20 mol%) in *t*-BuOH (1.0 ml) and then stirred at the rate of 300 rpm at room temperature for 5 min. The appropriate cyclopropanecarboxylic acid substrate (0.10 mmol), $Ag_2CO_3$ (55.2 mg, 0.2 mmol), $K_2HPO_4$ (26.0 mg, 0.15 mmol), Aryl-Bpin (0.15 mmol), BQ (5.4 mg, 0.05 mmol), $H_2O$ (9.0 mg, 0.5 mmol) was then added. Subsequently the vial was capped and closed tightly. The reaction mixture was then stirred at the rate of 300 rpm at 60 °C for 12 h. After being allowed to cool to room temperature, the mixture was diluted with ethyl acetate and 0.1 ml of acetic acid was then added. The mixture was passed through a pad of Celite with ethyl acetate as the eluent to remove any insoluble precipitate. The resulting solution was concentrated, and the residual mixture was dissolved with a minimal amount of acetone and loaded onto a preparative TLC plate. The pure product was then isolated using preparative TLC with ethyl acetate and hexane (1/4 to 1/1) as the eluent and 1% v/v of acetic acid as additive.



**(1R,2R)-1-ethyl-2-(4-(methoxycarbonyl)phenyl)cyclobutanecarboxylic acid (5a)**

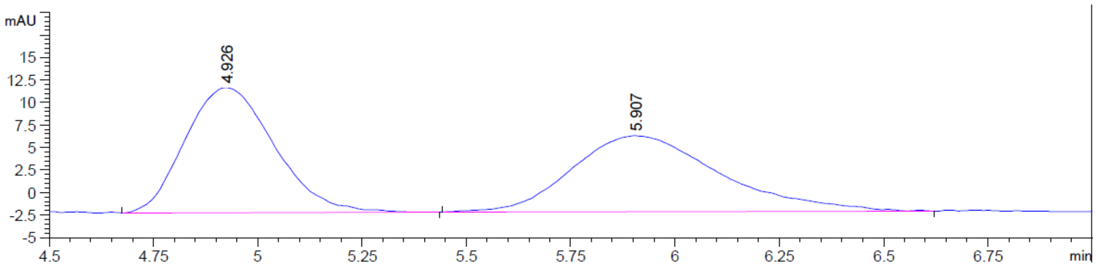
Substrate **4** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 2/1 with 1% v/v of acetic acid). The product was obtained as a pale-yellow solid (62% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® AS-3 column, 15% $^i$PrOH / $CO_2$, flow rate 1 mL/min, retention time 4.910 min (miner) and 5.923 min (major), 94:6 er); $[\alpha]_D{}^{20}$ = –11.8 (c = 1.0, $CHCl_3$).

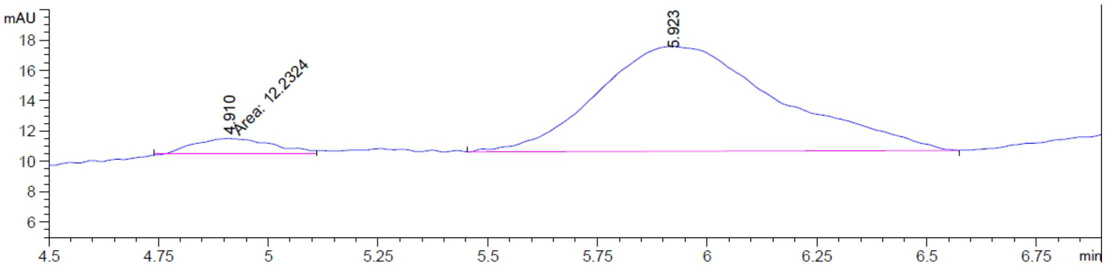
$^1$H NMR (600 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.4 Hz, 2H), 7.24 (d, *J* = 8.2 Hz, 2H), 3.89 (s, 3H), 3.57 (t, *J* = 8.9 Hz, 1H), 2.54 (td, *J* = 10.5, 3.9 Hz, 1H), 2.50 – 2.43 (m, 1H), 2.24 (dtd, *J* = 11.5, 8.9, 3.9 Hz, 1H), 2.17 (dt, *J* = 14.4, 7.2 Hz, 1H), 1.92 – 1.86 (m, 1H), 1.79 – 1.73 (m, 1H), 0.86 (t, *J* = 7.4 Hz, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 177.15, 167.05, 145.89, 129.45, 128.45, 127.33, 56.43, 51.98, 50.03, 32.25, 25.37, 21.18, 9.08.

HRMS (ESI-TOF) *m/z* Calcd for $C_{15}H_{17}O_4^-$ $[M-H]^-$ 261.1127, found 261.1132.

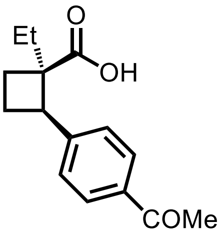
The absolute stereochemistry was assigned based on comparing the specific rotation of **5u** with literature.



```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   4.926 BB    0.2330  206.27145   13.90880  49.7158
   2   5.907 BB    0.3484  208.62941    8.43910  50.2842
```



```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   4.910 MM    0.2084   12.23242 9.78333e-1   5.8295
   2   5.923 BB    0.3590  197.60303    6.92348  94.1705
```



**(1R,2R)-2-(4-acetylphenyl)-1-ethylcyclobutanecarboxylic acid (5b)**

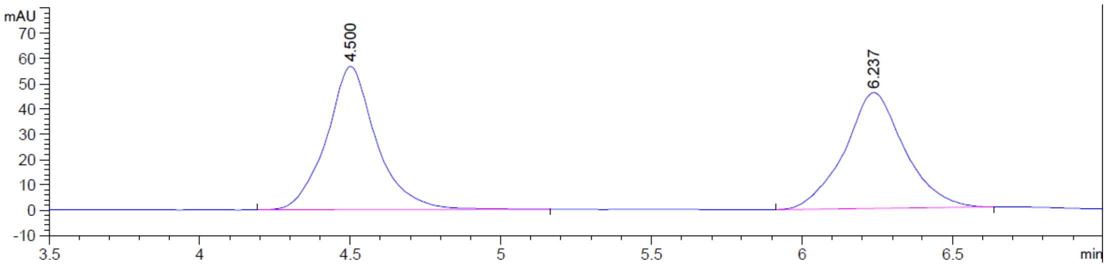
Substrate **4** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 2/1 with 1% v/v of acetic acid). The product was obtained as a colorless oil (65% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® OJ-3 column, 5% $^{i}$PrOH / $CO_2$, flow rate 2 mL/min, retention time 4.255 min (miner) and 5.859 min (major), 93:7 er);

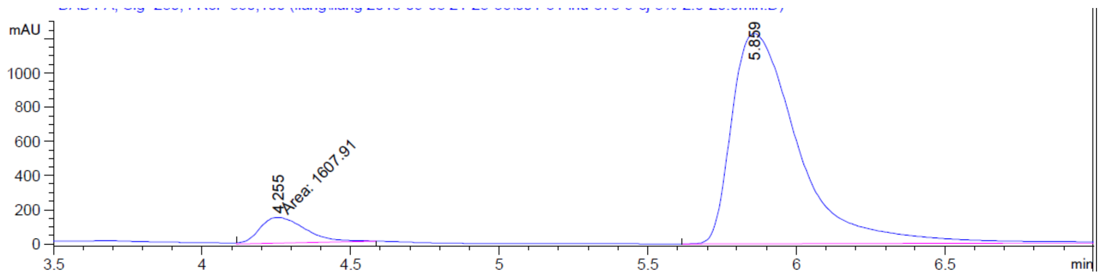
$^{1}$H NMR (600 MHz, $CDCl_3$) δ 7.86 (d, $J$ = 8.3 Hz, 2H), 7.26 (s, 2H), 3.57 (t, $J$ = 8.8 Hz, 1H), 2.57 (s, 3H), 2.54 (dd, $J$ = 10.9, 4.1 Hz, 1H), 2.47 (dd, $J$ = 11.2, 8.8 Hz, 1H), 2.27 – 2.23 (m, 1H), 2.17 (d, $J$ = 6.2 Hz, 1H), 1.92 – 1.87 (m, 1H), 1.77 (dd, $J$ = 13.6, 7.2 Hz, 1H), 0.86 (t, $J$ = 7.4 Hz, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 197.86, 177.29, 146.20, 135.55, 128.26, 127.52, 56.43, 50.01, 32.27, 26.54, 25.41, 21.22, 9.10.

HRMS (ESI-TOF) *m/z* Calcd for $C_{15}H_{17}O_3^-$ [M-H]$^-$ 261.1127, found 261.1132.

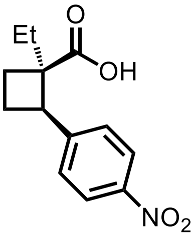
The absolute stereochemistry was assigned based on comparing the specific rotation of **5u** with literature.



```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   4.500 BB    0.1665  653.67517   56.71861  50.7258
   2   6.237 BB    0.1997  634.97046   45.81872  49.2742
```



```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   4.255 MM    0.1771 1607.90540  151.29349   7.5327
   2   5.859 BV R  0.2455 1.97379e4  1229.25208  92.4673
```



**(1R,2R)-1-ethyl-2-(4-nitrophenyl)cyclobutanecarboxylic acid (5c)**

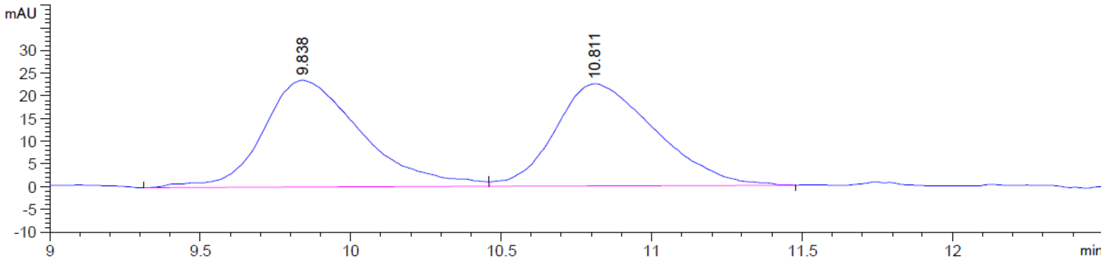
Substrate **4** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 2/1 with 1% v/v of acetic acid). The product was obtained as a pale-yellow solid (43% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® OJ-3 column, 5% $^i$PrOH / $CO_2$, flow rate 1 mL/min, retention time 9.557 min (miner) and 10.402 min (major), 94:6 er);

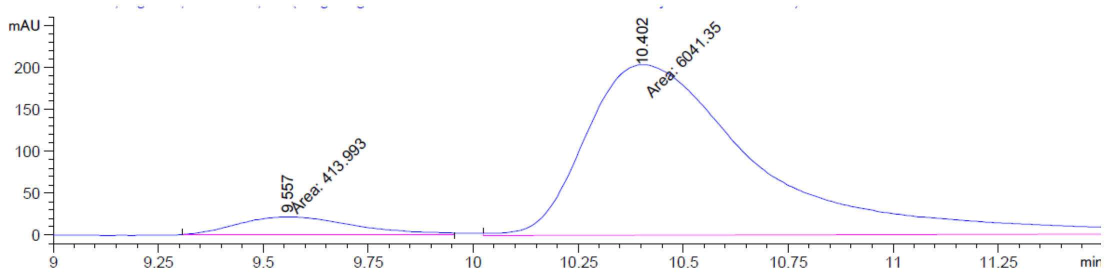
$^1$H NMR (600 MHz, CDCl$_3$) δ 8.13 (d, *J* = 8.7 Hz, 2H), 7.32 (d, *J* = 8.3 Hz, 2H), 3.61 (t, *J* = 8.8 Hz, 1H), 2.57 – 2.53 (m, 1H), 2.49 – 2.43 (m, 1H), 2.29 (ddd, *J* = 9.1, 7.1, 4.4 Hz, 1H), 2.19 – 2.15 (m, 1H), 1.95 – 1.91 (m, 1H), 1.80 – 1.75 (m, 1H), 0.86 (t, *J* = 7.4 Hz, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 177.10, 148.26, 146.72, 128.12, 123.35, 56.52, 49.63, 32.24, 25.39, 21.23, 9.03.

HRMS (ESI-TOF) *m/z* Calcd for $C_{13}H_{14}NO_4^-$ [M-H]$^-$ 248.0923, found 248.0923.

The absolute stereochemistry was assigned based on comparing the specific rotation of **5u** with literature.



```
Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
  1    9.838 BV    0.3208  539.44019   23.58702  50.7821
  2   10.811 VB    0.3290  522.82501   22.50610  49.2179
```



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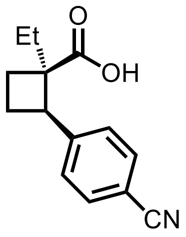
Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
  1    9.557 MM    0.3248  413.99335   21.24576   6.4132
  2   10.402 MM    0.4934 6041.35449  204.07893  93.5868
```



### (1R,2R)-2-(4-cyanophenyl)-1-ethylcyclobutanecarboxylic acid (5d)

Substrate **4** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 2/1 with 1% v/v of acetic acid). The product was obtained as a white solid (50%

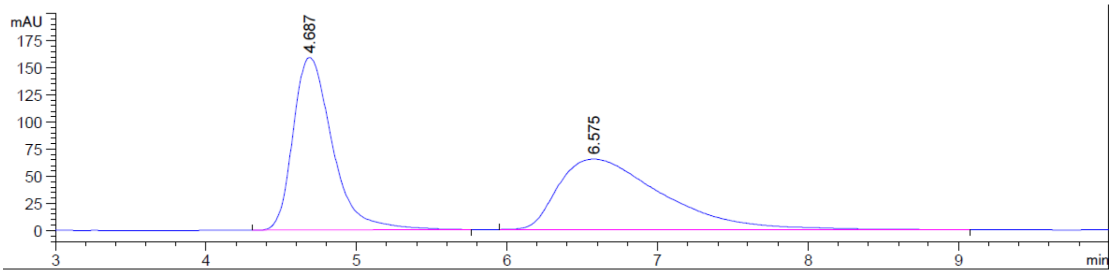
yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® AS-3 column, 5% $^{i}$PrOH / $CO_2$, flow rate 2 mL/min, retention time 4.597 min (miner) and 6.464 min (major), 95:5 er);

$^{1}$H NMR (600 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.3 Hz, 2H), 7.25 (d, *J* = 8.2 Hz, 2H), 3.55 (t, *J* = 8.8 Hz, 1H), 2.51 (ddd, *J* = 11.4, 9.6, 4.2 Hz, 1H), 2.42 (dq, *J* = 11.7, 9.0 Hz, 1H), 2.25 (dtd, *J* = 11.5, 8.9, 4.2 Hz, 1H), 2.17 – 2.11 (m, 1H), 1.90 (dt, *J* = 11.5, 8.8 Hz, 1H), 1.75 (dt, *J* = 13.3, 7.4 Hz, 1H), 0.86 (t, *J* = 7.4 Hz, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 178.94, 146.04, 131.86, 128.06, 118.93, 110.31, 56.48, 49.85, 32.17, 25.23, 20.96, 9.06.

HRMS (ESI-TOF) *m/z* Calcd for $C_{14}H_{14}NO_2^-$ $[M-H]^-$ 228.1025, found 228.1023.

The absolute stereochemistry was assigned based on comparing the specific rotation of **5u** with literature.



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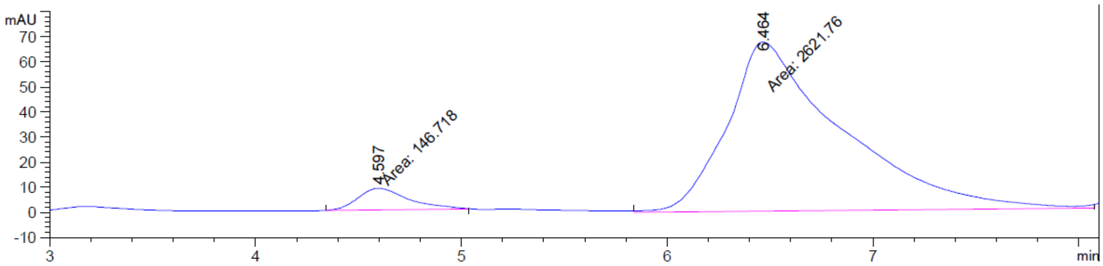
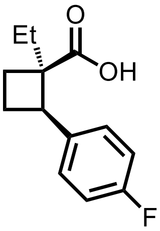
Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   4.687 BB    0.2816 2886.38135  159.12334  48.1444
   2   6.575 BB    0.7145 3108.88110   64.94115  51.8556
```



```
Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   4.597 MM    0.2843  146.71846    8.60063   5.2996
   2   6.464 MM    0.6480 2621.76270   67.42942  94.7004
```



**(1R,2R)-1-ethyl-2-(4-fluorophenyl)cyclobutanecarboxylic acid (5e)**

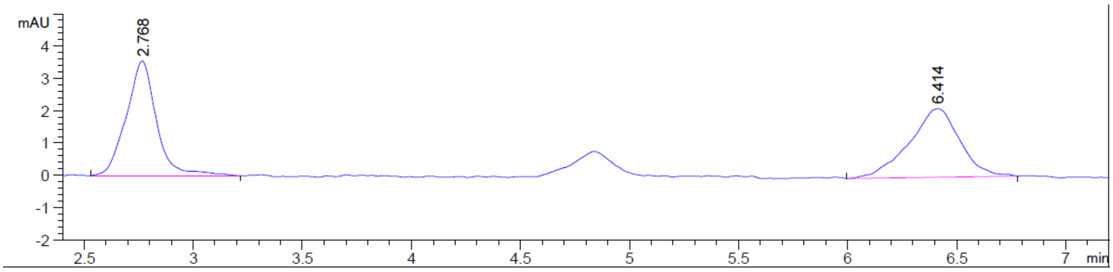
Substrate **4** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 5/1 with 1% v/v of acetic acid). The product was obtained as a pale-yellow oil (62% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® OJ-3 column, 5% $^i$PrOH / CO$_2$, flow rate 2 mL/min, retention time 2.639 min (miner) and 6.111 min (major), 95:5 er);

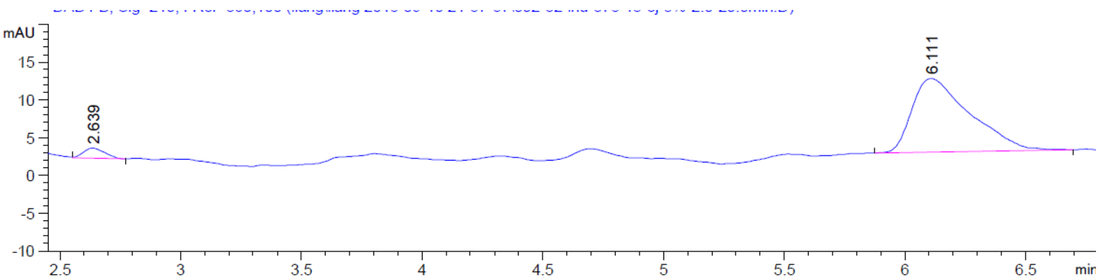
$^1$H NMR (600 MHz, CDCl$_3$) δ 7.11 (ddd, *J* = 6.0, 5.4, 2.7 Hz, 2H), 6.93 (t, *J* = 8.7 Hz, 2H), 3.48 (t, *J* = 9.0 Hz, 1H), 2.52 – 2.46 (m, 1H), 2.43 – 2.35 (m, 1H), 2.20 (dtd, *J* = 11.4, 9.0, 4.0 Hz, 1H), 2.16 – 2.10 (m, 1H), 1.86 – 1.80 (m, 1H), 1.70 (dt, *J* = 13.3, 7.4 Hz, 1H), 0.84 (t, *J* = 7.4 Hz, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 178.73, 161.67 (d, *J* = 243 Hz), 136.07 (d, *J* = 3.0 Hz), 128.74 (d, *J* = 7.5 Hz), 114.85 (d, *J* = 21 Hz), 56.42, 49.54, 32.14, 25.14, 21.52, 9.09; $^{19}$F NMR (376 MHz, CDCl$_3$) δ -116.70.

HRMS (ESI-TOF) *m/z* Calcd for $C_{13}H_{14}FO_2^-$ [M-H]$^-$ 221.0978, found 221.0979.

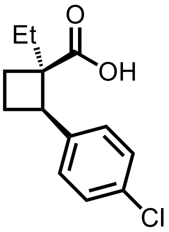
The absolute stereochemistry was assigned based on comparing the specific rotation of **5u** with literature.



```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   2.768 BB    0.1382   34.19260    3.55512  50.0155
   2   6.414 BB    0.2279   34.17139    2.12114  49.9845
```



```
Peak RetTime Type  Width      Area       Height      Area
  #    [min]        [min]    [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1    2.639 VB    0.0920    8.37479    1.35660    4.8913
   2    6.111 BB    0.2422  162.84474    9.78151   95.1087
```



**(1R,2R)-2-(4-chlorophenyl)-1-ethylcyclobutanecarboxylic acid (5f)**

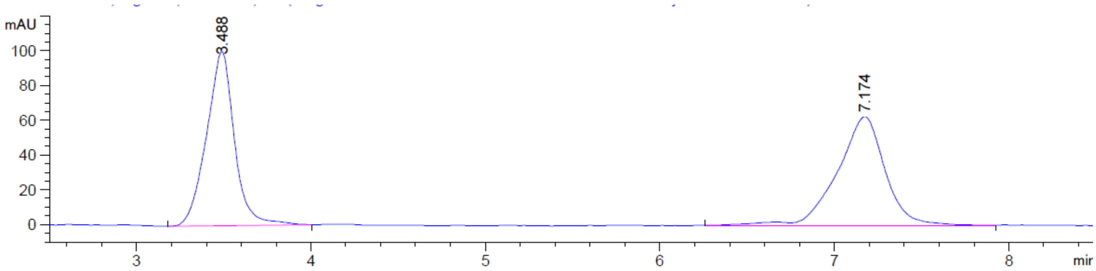
Substrate **4** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 5/1 with 1% v/v of acetic acid). The product was obtained as a white solid (63% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® OJ-3 column, 5% $^i$PrOH / $CO_2$, flow rate 2 mL/min, retention time 3.581 min (miner) and 7.103 min (major), 92:8 er);

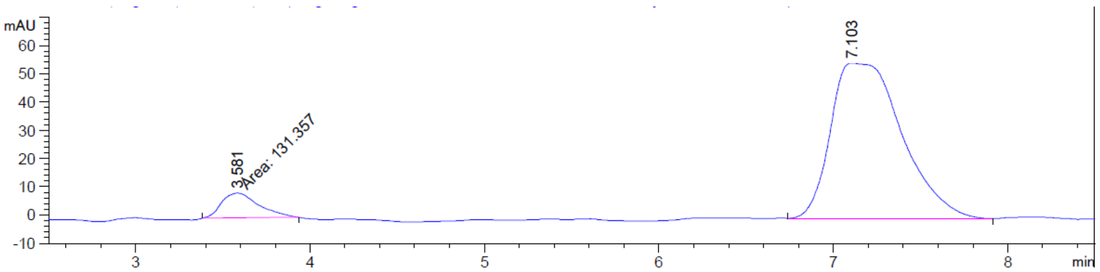
$^1$H NMR (600 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.5 Hz, 2H), 7.09 (d, *J* = 8.1 Hz, 2H), 3.48 (t, *J* = 9.0 Hz, 1H), 2.53 – 2.47 (m, 1H), 2.44 – 2.34 (m, 1H), 2.23 – 2.17 (m, 1H), 2.15 – 2.10 (m, 1H), 1.85 (dt, *J* = 11.4, 8.9 Hz, 1H), 1.75 – 1.67 (m, 1H), 0.85 (t, *J* = 7.4 Hz, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 178.68, 138.92, 132.33, 128.64, 128.20, 56.38, 49.58, 32.19, 25.22, 21.36, 9.10.

HRMS (ESI-TOF) *m/z* Calcd for $C_{13}H_{14}ClO_2^-$ [M-H]$^-$ 237.0682, found 237.0687.

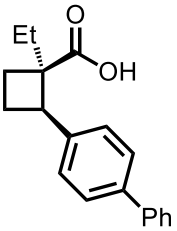
The absolute stereochemistry was assigned based on comparing the specific rotation of **5u** with literature.



```
Peak RetTime Type  Width      Area       Height      Area
  #    [min]        [min]    [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1    3.487 BB    0.1609   27.71568    2.47056   50.5590
   2    7.174 BB    0.2517   27.10285    1.53749   49.4410
```



```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   3.581 MM    0.2478  131.35725    8.83608   7.7650
   2   7.103 BB    0.3747 1560.30310   55.04886  92.2350
```



**(1R,2R)-2-([1,1'-biphenyl]-4-yl)-1-ethylcyclobutanecarboxylic acid (5g)**

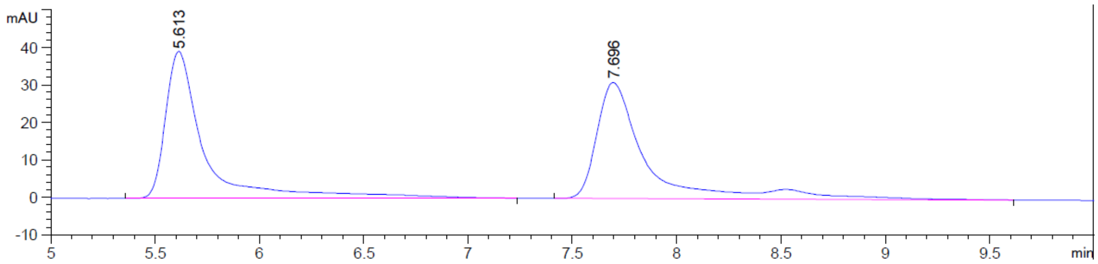
Substrate **4** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 5/1 with 1% v/v of acetic acid). The product was obtained as a white solid (62% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® OD-3 column, 10% $^i$PrOH / $CO_2$, flow rate 2 mL/min, retention time 5.720 min (major) and 7.662 min (minor), 95:5 er);

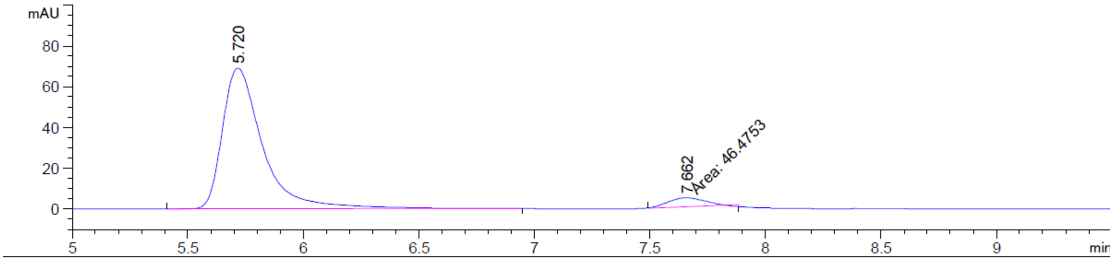
$^1$H NMR (600 MHz, $CDCl_3$) δ 7.56 – 7.54 (m, 2H), 7.48 (d, $J$ = 8.3 Hz, 2H), 7.42 – 7.39 (m, 2H), 7.33 – 7.30 (m, 1H), 7.25 (d, $J$ = 8.1 Hz, 2H), 3.55 (t, $J$ = 8.9 Hz, 1H), 2.56 – 2.45 (m, 2H), 2.24 – 2.16 (m, 2H), 1.88 – 1.83 (m, 1H), 1.76 – 1.72 (m, 1H), 0.84 (t, $J$ = 7.4 Hz, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 178.01, 140.91, 139.58, 139.38, 128.66, 127.75, 127.05, 126.96, 126.77, 56.46, 50.02, 32.27, 25.33, 21.44, 9.16.

HRMS (ESI-TOF) *m/z* Calcd for $C_{19}H_{19}O_2^-$ $[M-H]^-$ 279.1385, found 279.1388.

The absolute stereochemistry was assigned based on comparing the specific rotation of **5u** with literature.



```
Peak RetTime Type  Width     Area      Height     Area
  #    [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.613 BB    0.1876  509.75204   39.23637  49.4105
   2   7.696 BV R  0.2306  521.91632   30.98957  50.5895
```



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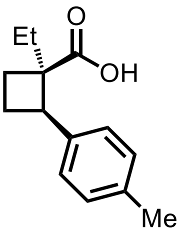
Peak RetTime Type  Width     Area      Height     Area
  #    [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.720 BB    0.1814  836.39392   69.02428  94.7359
   2   7.662 MM    0.1813   46.47529    4.27189   5.2641
```



**(1R,2R)-1-ethyl-2-(p-tolyl)cyclobutanecarboxylic acid (5h)**

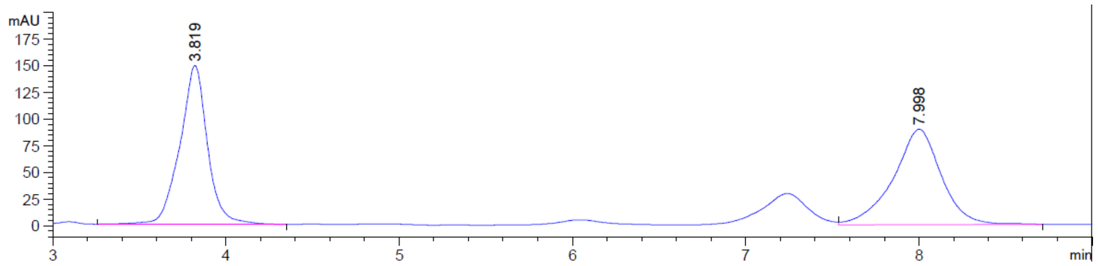
Substrate **1** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 5/1 with 1% v/v of acetic acid). The product was obtained as a white solid (54% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® OJ-3 column, 5% $^i$PrOH / $CO_2$, flow rate 2 mL/min, retention time 3.734 min (miner) and 7.674 min (major), 92:8 er);

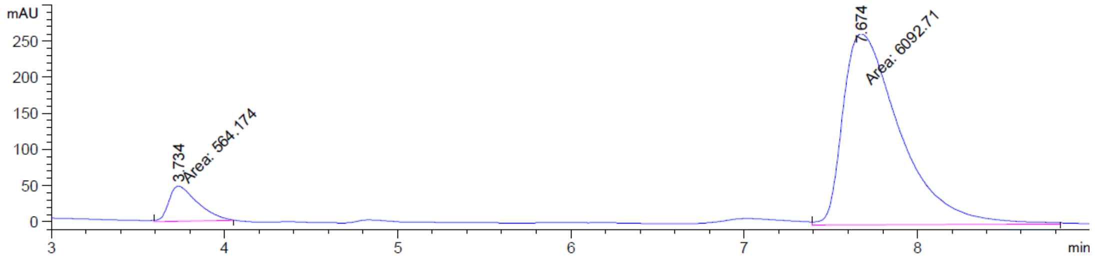
$^1$H NMR (600 MHz, $CDCl_3$) δ 7.06 (s, 4H), 3.47 (t, *J* = 9.0 Hz, 1H), 2.53 – 2.48 (m, 1H), 2.45 – 2.39 (m, 1H), 2.29 (s, 3H), 2.21 – 2.13 (m, 2H), 1.85 – 1.79 (m, 1H), 1.73 – 1.68 (m, 1H), 0.84 (t, *J* = 7.4 Hz, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 178.49, 137.38, 136.06, 128.80, 127.19, 56.47, 50.12, 32.22, 25.31, 21.55, 21.03, 9.13.

HRMS (ESI-TOF) *m/z* Calcd for $C_{14}H_{17}O_2^-$ [M-H]$^-$ 217.1229, found 217.1226.

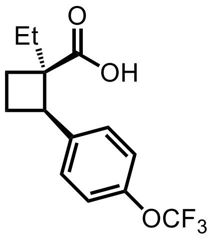
The absolute stereochemistry was assigned based on comparing the specific rotation of **5u** with literature.



```
Peak RetTime Type  Width      Area       Height      Area
  #    [min]        [min]    [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1    3.819 BB    0.1596 1652.83459  148.80081  49.0380
   2    7.998 VB    0.2784 1717.68567   89.28466  50.9620
```



```
Peak RetTime Type  Width      Area       Height      Area
  #    [min]        [min]    [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1    3.734 MM    0.1929  564.17365   48.75217   8.4750
   2    7.674 MM    0.3841 6092.70898  264.39890  91.5250
```



**(1R,2R)-1-ethyl-2-(4-(trifluoromethoxy)phenyl)cyclobutaneca (5i)**

Substrate **1** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 5/1 with 1% v/v of acetic acid). The product was obtained as a pale-yellow oil (56% yield).

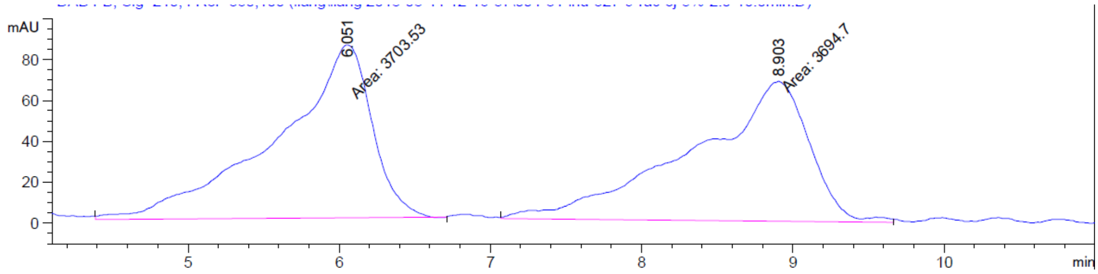
The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® OJ-3 column, 4% $^i$PrOH / $CO_2$, flow rate 1 mL/min, retention time 5.888 min (miner) and 8.670 min (major), 93:7 er);

$^1$H NMR (600 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.3 Hz, 2H), 7.09 (d, *J* = 7.8 Hz, 2H), 3.51 (t, *J* =

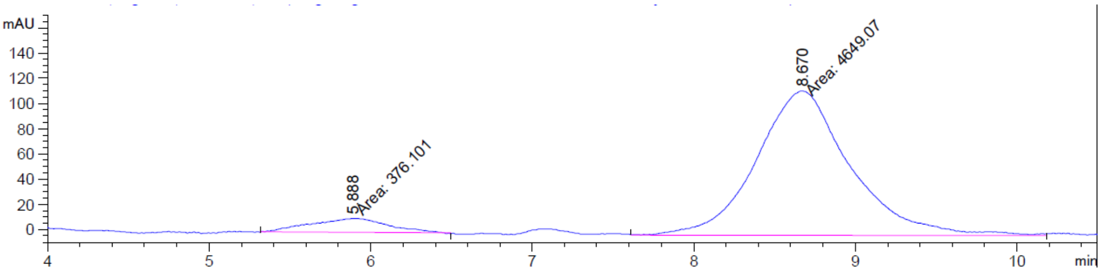
9.0 Hz, 1H), 2.52 – 2.46 (m, 1H), 2.40 (dtd, *J* = 11.5, 9.5, 8.5 Hz, 1H), 2.25 – 2.19 (m, 1H), 2.17 – 2.11 (m, 1H), 1.88 – 1.83 (m, 1H), 1.74 – 1.69 (m, 1H), 0.84 (t, *J* = 7.4 Hz, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 178.86, 147.89, 139.15, 128.58, 120.50, 120.47 (q, *J* = 255 Hz), 56.41, 49.48, 32.15, 25.19, 21.41, 9.01; $^{19}$F NMR (376 MHz, $CDCl_3$) δ -58.14.

HRMS (ESI-TOF) *m/z* Calcd for $C_{14}H_{14}F_3O_3^-$ [M-H]$^-$ 287.0895, found 287.0898.

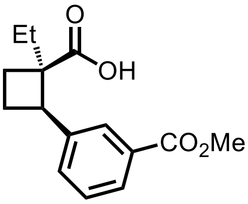
The absolute stereochemistry was assigned based on comparing the specific rotation of **5u** with literature.



```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.051 MM    0.7287 3703.52539   84.70240  50.0597
   2   8.903 MM    0.8979 3694.69897   68.58344  49.9403
```



```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.888 MM    0.5542  376.10083   11.30990   7.4843
   2   8.670 MM    0.6762 4649.07373  114.59574  92.5157
```



**(1R,2R)-1-ethyl-2-(3-(methoxycarbonyl)phenyl)cyclobutanecarbox (5j)**

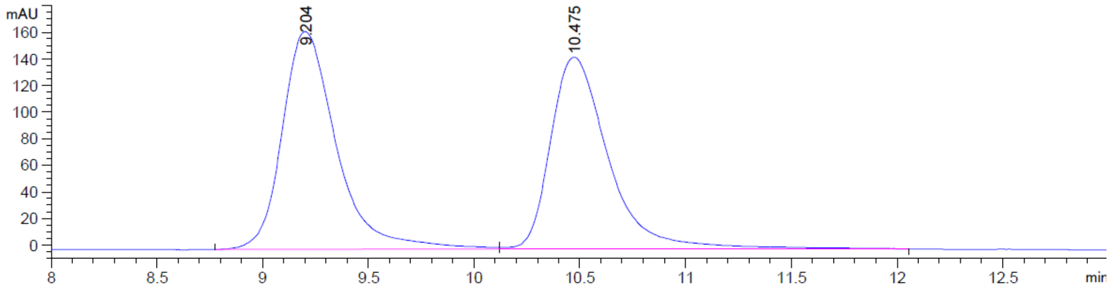
Substrate **1** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 2/1 with 1% v/v of acetic acid). The product was obtained as a white solid (64% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® AD-3 column, 10% ${}^{i}$PrOH / $CO_2$, flow rate 1 mL/min, retention time 9.159 min (major) and 10.557 min (minor), 89:11 er);

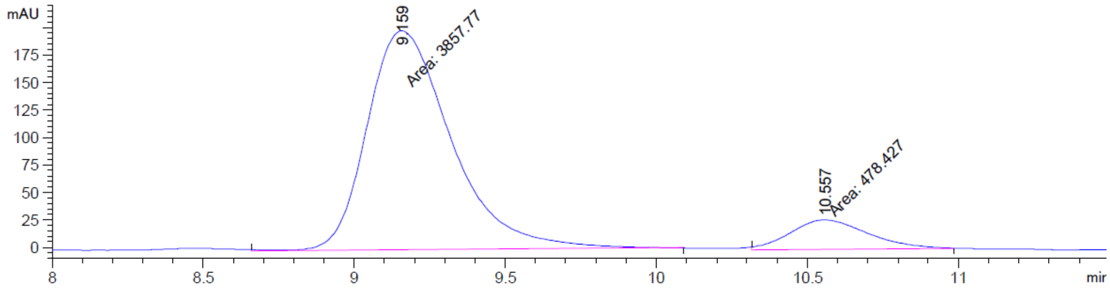
${}^{1}$H NMR (600 MHz, $CDCl_3$) δ 7.85 (d, $J$ = 7.7 Hz, 1H), 7.82 (s, 1H), 7.35 (d, $J$ = 7.7 Hz, 1H), 7.29 (t, $J$ = 7.7 Hz, 1H), 3.90 (s, 3H), 3.55 (t, $J$ = 8.8 Hz, 1H), 2.53 – 2.43 (m, 2H), 2.25 – 2.19 (m, 1H), 2.15 (dt, $J$ = 14.5, 7.2 Hz, 1H), 1.89 – 1.84 (m, 1H), 1.75 – 1.70 (m, 1H), 0.83 (t, $J$ = 7.4 Hz, 3H); ${}^{13}$C NMR (150 MHz, $CDCl_3$) δ 178.60, 167.17, 140.78, 131.73, 129.87, 128.59, 128.12, 127.92, 56.39, 52.05, 49.86, 32.20, 25.25, 21.23, 9.09.

HRMS (ESI-TOF) $m/z$ Calcd for $C_{15}H_{17}O_4^-$ $[M-H]^-$ 261.1127, found 261.1130.

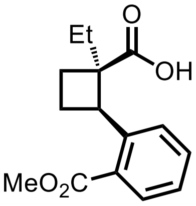
The absolute stereochemistry was assigned based on comparing the specific rotation of **5u** with literature.



```
Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
  1    9.204 BV    0.2686 2927.27808  163.69240  51.5808
  2   10.475 VB    0.2883 2747.85449  144.24396  48.4192
```



```
Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
  1    9.159 MM    0.3229 3857.77026  199.13843  88.9667
  2   10.557 MM    0.2999  478.42657   26.58735  11.0333
```



**(1R,2R)-1-ethyl-2-(2-(methoxycarbonyl)phenyl)cyclobutanecarboxylic acid (5k)**

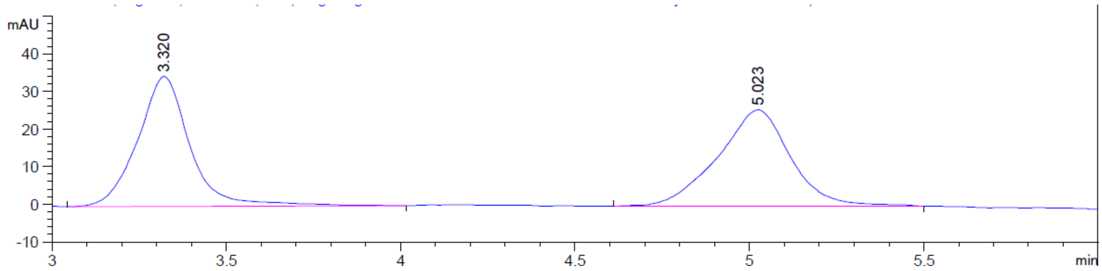
Substrate **1** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 2/1 with 1% v/v of acetic acid). The product was obtained as a colorless oil (60% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® OJ-3 column, 5% $^i$PrOH / $CO_2$, flow rate 2 mL/min, retention time 3.181 min (miner) and 4.768 min (major), 92:8 er);

$^1$H NMR (600 MHz, $CDCl_3$) δ 7.69 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.62 – 7.59 (m, 1H), 7.54 (td, *J* = 7.6, 1.4 Hz, 1H), 7.28 (td, *J* = 7.6, 1.2 Hz, 1H), 3.96 (s, 3H), 3.91 – 3.87 (m, 1H), 2.80 (d, *J* = 12.1 Hz, 1H), 2.42 – 2.38 (m, 1H), 2.25 – 2.20 (m, 2H), 1.97 – 1.92 (m, 2H), 0.92 (t, *J* = 7.4 Hz, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 174.90, 171.37, 141.55, 132.75, 130.48, 129.59, 127.18, 126.72, 55.95, 53.03, 45.81, 31.05, 25.13, 21.05, 9.07.

HRMS (ESI-TOF) *m/z* Calcd for $C_{15}H_{17}O_4^-$ $[M-H]^-$ 261.1127, found 261.1122.

The absolute stereochemistry was assigned based on comparing the specific rotation of **5u** with literature.



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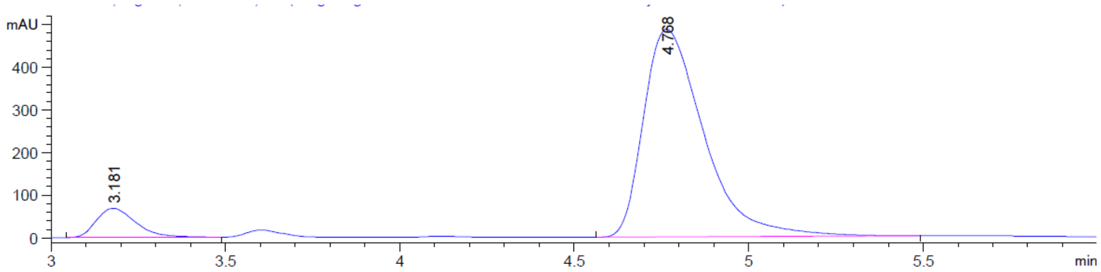
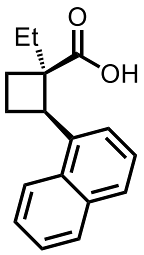
Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   3.320 BB    0.1505  363.30420   34.61173  49.2798
   2   5.023 BB    0.2119  373.92389   25.67123  50.7202
```



```
Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   3.181 BV    0.1234  549.15814   68.62186   8.5895
   2   4.768 BB    0.1839 5844.23730  487.40265  91.4105
```



**(1R,2R)-1-ethyl-2-(naphthalen-1-yl)cyclobutanecarboxylic acid (5l)**

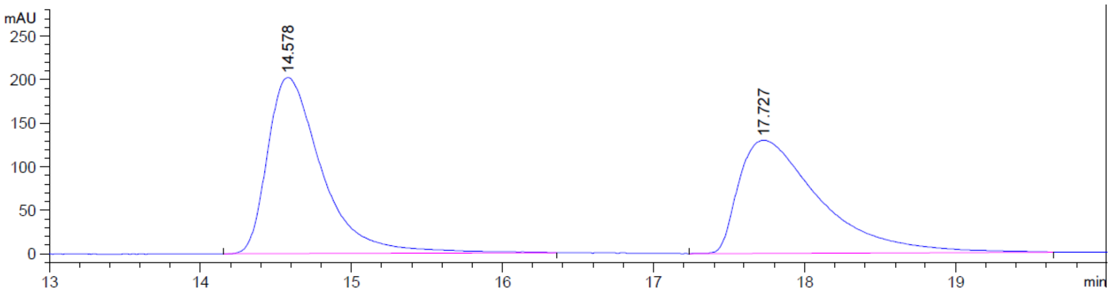
Substrate **1** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 5/1 with 1% v/v of acetic acid). The product was obtained as a colorless oil (56% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® AD-3 column, 10% $^i$PrOH / $CO_2$, flow rate 1 mL/min, retention time 14.396 min (major) and 17.263 min (minor), 92:8 er);

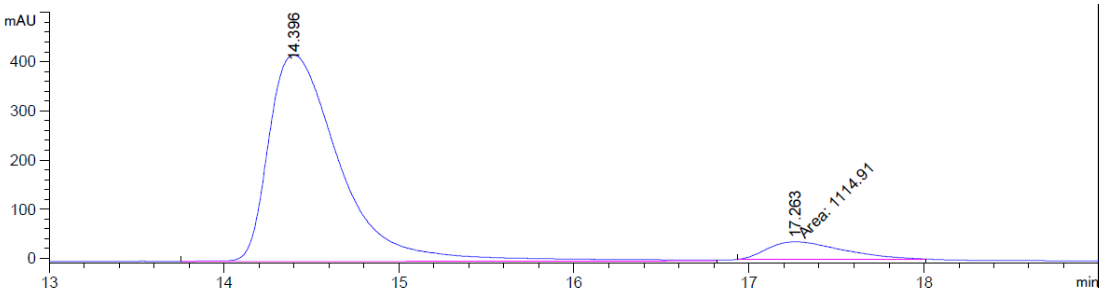
$^1$H NMR (600 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.4 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.68 (d, *J* = 8.1 Hz, 1H), 7.50 – 7.43 (m, 2H), 7.41 (d, *J* = 7.1 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 4.40 (t, *J* = 9.1 Hz, 1H), 2.76 – 2.67 (m, 1H), 2.57 – 2.51 (m, 1H), 2.37 – 2.32 (m, 1H), 2.20 (dtd, *J* = 11.5, 8.6, 3.1 Hz, 1H), 1.96 – 1.88 (m, 2H), 0.85 (t, *J* = 7.4 Hz, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 178.08, 136.09, 133.64, 132.39, 128.64, 127.25, 125.67, 125.36, 125.28, 123.82, 123.66, 57.96, 45.41, 32.49, 24.95, 20.91, 9.38.

HRMS (ESI-TOF) *m/z* Calcd for $C_{17}H_{17}O_2^-$ $[M-H]^-$ 253.1229, found 253.1225.

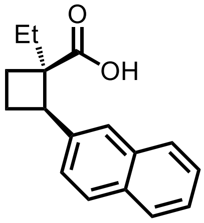
The absolute stereochemistry was assigned based on comparing the specific rotation of **5u** with literature.



```
Peak RetTime Type  Width     Area      Height      Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  14.578 BB    0.3782 5065.38818  202.24588  51.1350
   2  17.727 BB    0.5496 4840.53320  129.64720  48.8650
```



```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  14.396 BV    0.4351 1.18436e4  419.91861  91.3963
   2  17.263 MM    0.5120 1114.90845  36.29034   8.6037
```



**(1R,2R)-1-ethyl-2-(naphthalen-2-yl)cyclobutanecarboxylic acid (5m)**

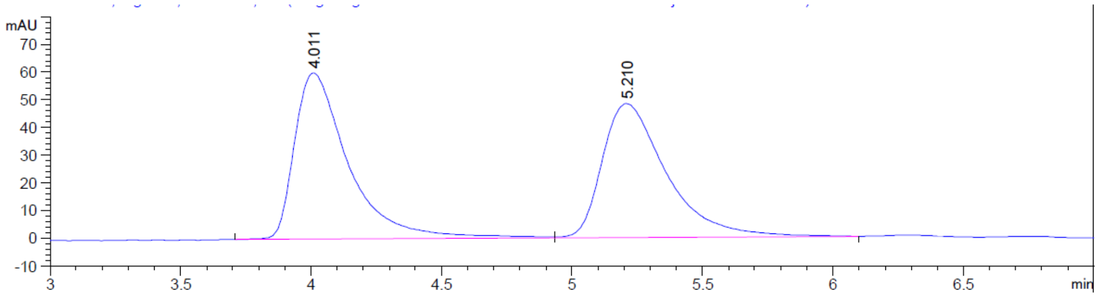
Substrate **1** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 5/1 with 1% v/v of acetic acid). The product was obtained as a colorless oil (58% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® IC-3 column, 10% $^i$PrOH / $CO_2$, flow rate 2 mL/min, retention time 3.941 min (major) and 5.166 min (minor), 92:8 er);

$^1$H NMR (600 MHz, $CDCl_3$) δ 7.78 – 7.74 (m, 2H), 7.66 (d, *J* = 8.5 Hz, 1H), 7.58 (s, 1H), 7.45 – 7.38 (m, 2H), 7.27 (dd, *J* = 8.5, 1.8 Hz, 1H), 3.65 (t, *J* = 8.8 Hz, 1H), 2.59 – 2.48 (m, 2H), 2.25 (ddd, *J* = 10.9, 2.9, 1.4 Hz, 1H), 2.20 – 2.15 (m, 1H), 1.89 – 1.83 (m, 1H), 1.75 (dt, *J* = 13.4, 7.4 Hz, 1H), 0.77 (t, *J* = 7.4 Hz, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 178.20, 138.03, 133.29, 132.39, 127.81, 127.54, 127.51, 126.14, 125.79, 125.52, 125.35, 56.50, 50.38, 32.33, 25.36, 21.35, 9.06.

HRMS (ESI-TOF) *m/z* Calcd for $C_{17}H_{17}O_2^-$ $[M-H]^-$ 253.1229, found 253.1227.

The absolute stereochemistry was assigned based on comparing the specific rotation of **5u** with literature.



```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   4.011 BV    0.2155  861.07312  59.99102  50.9482
   2   5.210 VB    0.2598  829.02124  48.40171  49.0518
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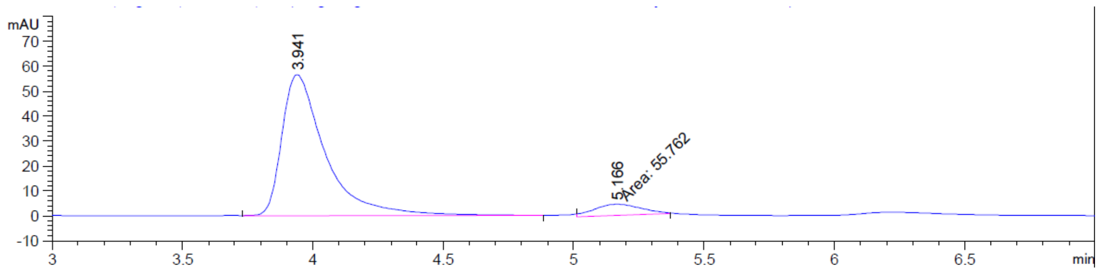
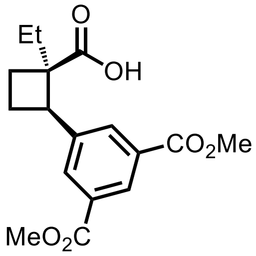


```
Peak RetTime Type  Width      Area        Height      Area
  #   [min]        [min]    [mAU*s]       [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   3.941 BB     0.1709  653.11957   56.48904  92.1338
   2   5.166 MM     0.2074   55.76199    4.48052   7.8662
```



**(1R,2R)-2-(3,5-bis(methoxycarbonyl)phenyl)-1-ethylcyclobutanecarboxylic acid (5n)**

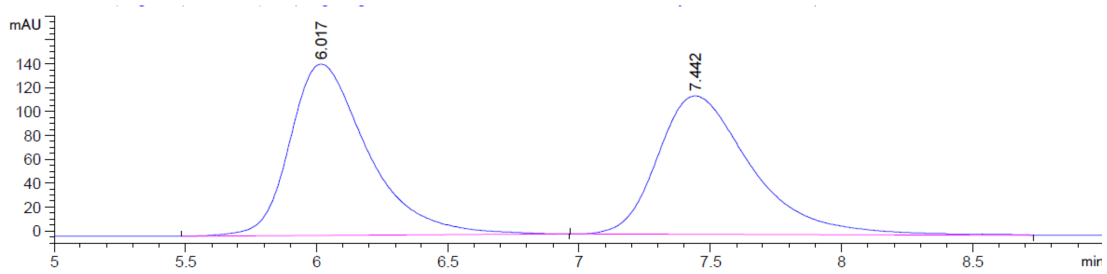
Substrate **1** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 2/1 with 1% v/v of acetic acid). The product was obtained as a white solid (60% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® IC-3 column, 10% $^i$PrOH / $CO_2$, flow rate 2 mL/min, retention time 5.983 min (major) and 7.467 min (minor), 92:8 er);

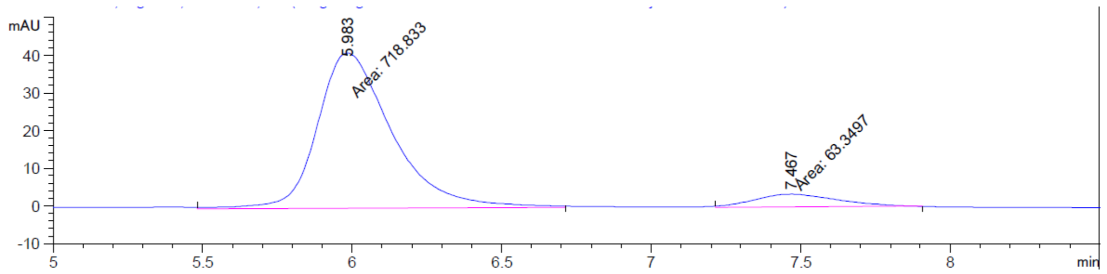
$^1$H NMR (600 MHz, $CDCl_3$) δ 8.49 (t, *J* = 1.6 Hz, 1H), 8.02 (dd, *J* = 1.6, 0.6 Hz, 2H), 3.92 (s, 6H), 3.60 (t, *J* = 8.5 Hz, 1H), 2.56 – 2.48 (m, 2H), 2.28 – 2.22 (m, 1H), 2.20 – 2.13 (m, 1H), 1.92 – 1.86 (m, 1H), 1.77 – 1.71 (m, 1H), 0.82 (t, *J* = 7.4 Hz, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 178.03, 166.28, 141.46, 132.71, 130.34, 129.09, 56.43, 52.30, 49.48, 32.17, 25.26, 21.18, 9.01.

HRMS (ESI-TOF) *m/z* Calcd for $C_{17}H_{19}O_6^-$ $[M-H]^-$ 319.1182, found 319.1180.

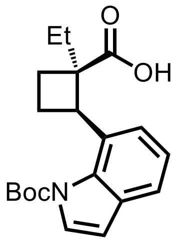
The absolute stereochemistry was assigned based on comparing the specific rotation of **5u** with literature.



```
Peak RetTime Type  Width      Area       Height      Area
  #   [min]        [min]    [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   6.017 BB    0.3138 2983.80957  143.97331  50.7996
   2   7.442 BB    0.3782 2889.87183  116.17687  49.2004
```



```
Peak RetTime Type  Width      Area       Height      Area
  #   [min]        [min]    [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   5.983 MM    0.2907  718.83331   41.21288  91.9009
   2   7.467 MM    0.3175   63.34967    3.32499   8.0991
```



**(1R,2R)-2-(1-(tert-butoxycarbonyl)-1H-indol-7-yl)-1-ethylcyclobutanecarboxylic acid (5o)**

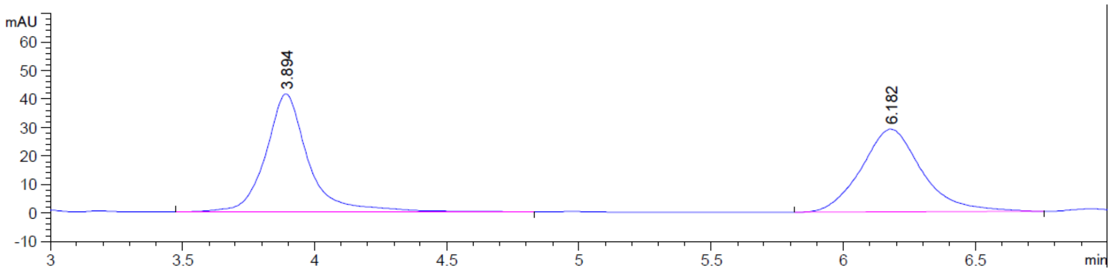
Substrate **1** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 2/1 with 1% v/v of acetic acid). The product was obtained as a pale-yellow solid (42% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® OJ-3 column, 5% $^i$PrOH / CO$_2$, flow rate 2 mL/min, retention time 3.688 min (miner) and 5.836 min (major), 91:9 er);

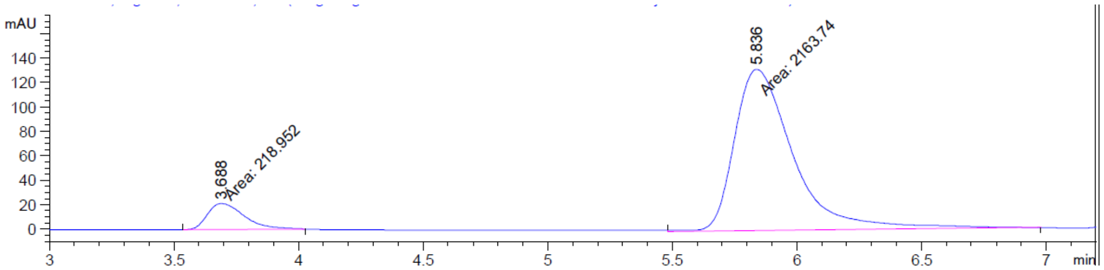
$^1$H NMR (600 MHz, CDCl$_3$) δ 7.99 (s, 1H), 7.53 (d, *J* = 3.5 Hz, 1H), 7.36 (dd, *J* = 1.7, 0.8 Hz, 1H), 7.13 (d, *J* = 8.6 Hz, 1H), 6.49 (dd, *J* = 3.7, 0.8 Hz, 1H), 3.61 (t, *J* = 8.6 Hz, 1H), 2.53 – 2.51 (m, 1H), 2.25 – 2.20 (m, 1H), 2.20 – 2.16 (m, 1H), 1.88 – 1.79 (m, 2H), 1.74 – 1.71 (m, 1H), 1.66 (s, 9H), 0.81 (t, *J* = 7.3 Hz, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 182.67, 178.39, 149.78, 134.81, 130.53, 125.89, 124.05, 119.25, 114.65, 107.37, 56.65, 50.40, 32.23, 29.41, 28.18, 25.26, 21.69, 9.11.

HRMS (ESI-TOF) *m/z* Calcd for $C_{20}H_{24}NO_4^-$ $[M-H]^-$ 342.1705, found 342.1700.

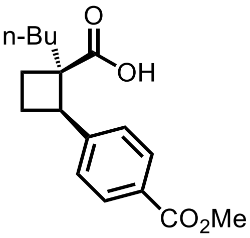
The absolute stereochemistry was assigned based on comparing the specific rotation of **5u** with literature.



```
Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
  1   3.894 BB    0.1610  466.13464   41.49893  50.1091
  2   6.182 BB    0.2362  464.10437   29.07586  49.8909
```



```
Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
  1   3.688 MM    0.1705  218.95163   21.39905   9.1893
  2   5.836 MM    0.2735 2163.74097  131.86678  90.8107
```



**(1R,2R)-1-butyl-2-(4-(methoxycarbonyl)phenyl)cyclobutanecarboxylic acid (5p)**

Substrate **4p** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 2/1 with 1% v/v of acetic acid). The product was obtained as a pale-yellow oil (60% yield).

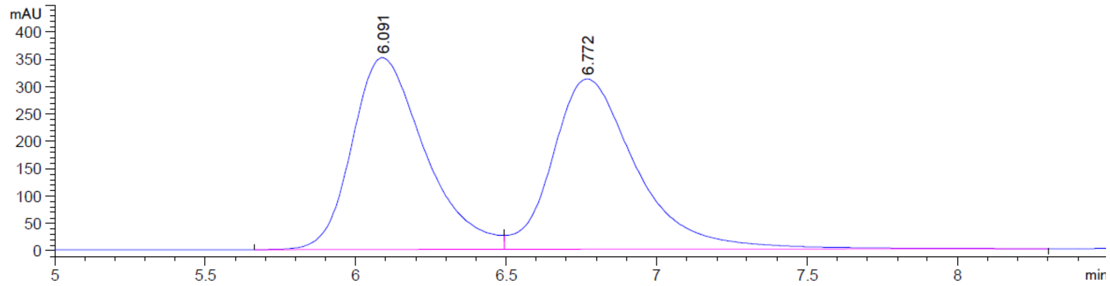
The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK®

IC-3 column, 10% $^{i}$PrOH / $CO_2$, flow rate 2 mL/min, retention time 5.918 min (major) and 6.620 min (minor), 86:14 er);

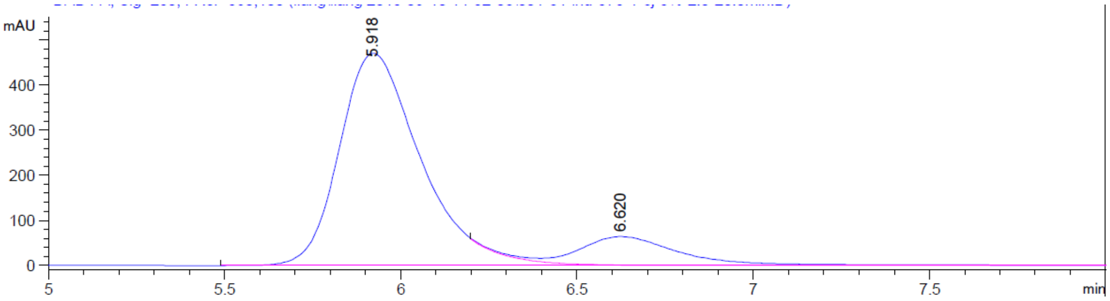
$^{1}$H NMR (600 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.4 Hz, 2H), 7.24 (s, 2H), 3.90 (s, 3H), 3.78 – 3.71 (m, 2H), 3.15 – 3.09 (m, 1H), 2.71 – 2.67 (m, 1H), 2.16 – 2.11 (m, 2H), 1.61 (p, *J* = 7.7 Hz, 2H), 1.47 (dt, *J* = 14.6, 7.3 Hz, 2H), 1.26 – 1.24 (m, 1H), 1.00 (t, *J* = 7.3 Hz, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 173.68, 167.01, 145.95, 129.40, 128.25, 126.91, 61.87, 52.02, 43.98, 38.44, 28.13, 27.02, 23.37, 14.04.

HRMS (ESI-TOF) *m/z* Calcd for $C_{17}H_{21}O_4^-$ $[M-H]^-$ 289.1440, found 289.1436.

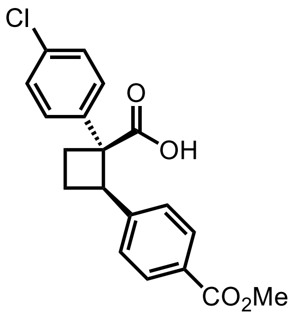
The absolute stereochemistry was assigned based on comparing the specific rotation of **5u** with literature.



```
Peak RetTime Type  Width     Area      Height      Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   6.091 BV    0.2566 5919.68555  351.25800  49.4354
   2   6.772 VB    0.2928 6054.89697  311.50253  50.5646
```



```
Peak RetTime Type  Width     Area      Height      Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   5.918 BV R  0.2421 7595.69092  471.12335  85.4971
   2   6.620 VB E  0.2998 1288.46021   63.22224  14.5029
```



### (1R,2R)-1-(4-chlorophenyl)-2-(4-(methoxycarbonyl)phenyl)cyclobutanecarboxylic acid (**5q**)

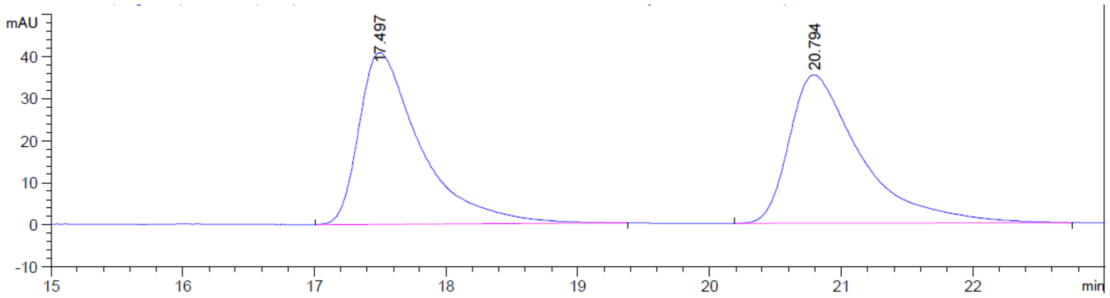
Substrate **4q** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 2/1 with 1% v/v of acetic acid). The product was obtained as a pale-yellow oil (53% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® OJ-3 column, 5% $^{i}$PrOH / CO$_2$, flow rate 2 mL/min, retention time 16.200 min (miner) and 19.175 min (major), 94:6 er);

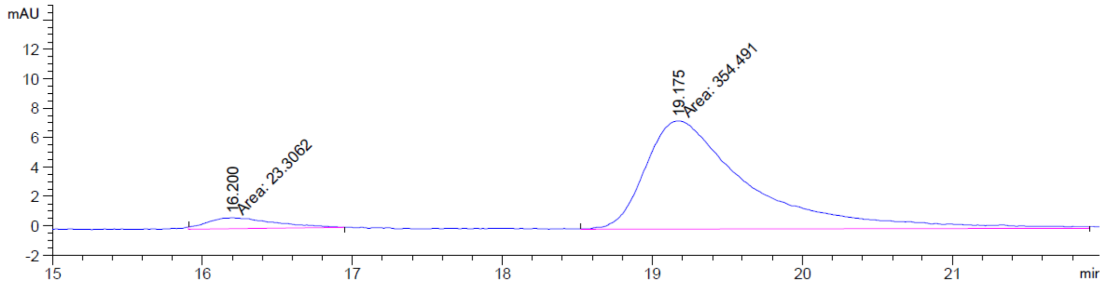
$^{1}$H NMR (600 MHz, CDCl$_3$) δ 8.00 (d, $J$ = 8.1 Hz, 2H), 7.41 (d, $J$ = 8.2 Hz, 2H), 7.33 (d, $J$ = 6.6 Hz, 2H), 7.25 (d, $J$ = 8.5 Hz, 2H), 4.17 (t, $J$ = 9.4 Hz, 1H), 3.92 (s, 3H), 2.99 – 2.93 (m, 1H), 2.69 – 2.63 (m, 1H), 2.38 – 2.30 (m, 2H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 175.96, 166.91, 145.48, 142.42, 132.91, 129.73, 129.07, 128.52, 127.91, 127.74, 58.68, 52.12, 50.13, 28.68, 23.15.

HRMS (ESI-TOF) *m/z* Calcd for C$_{19}$H$_{16}$ClO$_4^-$ [M-H]$^-$ 343.0737, found 343.0734.

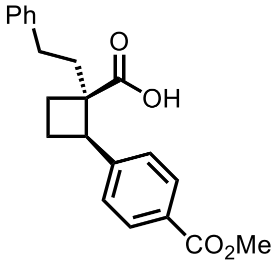
The absolute stereochemistry was assigned based on comparing the specific rotation of **5u** with literature.



```
Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]    [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  17.497 BB    0.4760 1321.17957   40.77972  49.8186
   2  20.794 BB    0.5283 1330.80139   35.26552  50.1814
```



```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  16.200 MM    0.5180   23.30623 7.49925e-1   6.1690
   2  19.175 MM    0.8021  354.49060    7.36629  93.8310
```



**(1S,2R)-2-(4-(methoxycarbonyl)phenyl)-1-phenethylcyclobutanecarboxylic acid (5r)**

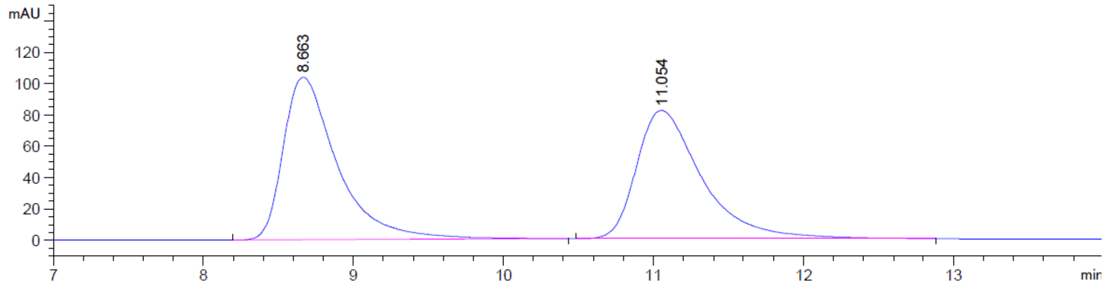
Substrate **4r** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 2/1 with 1% v/v of acetic acid). The product was obtained as a pale-yellow oil (65% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® IC-3 column, 10% $^i$PrOH / $CO_2$, flow rate 2 mL/min, retention time 9.028 min (major) and 11.620 min (minor), 93:7 er);

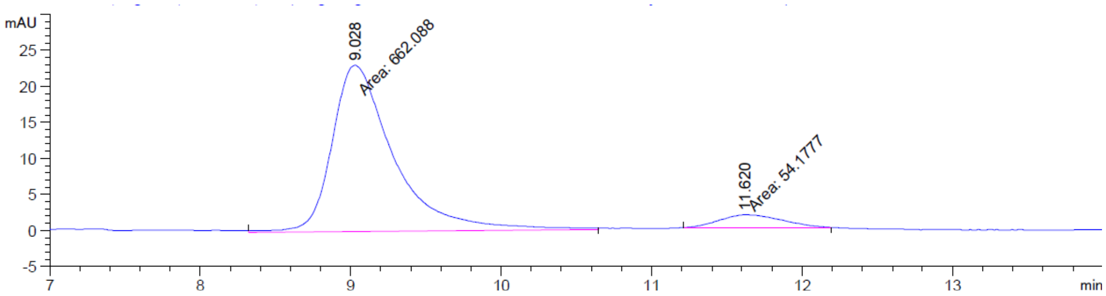
$^1$H NMR (600 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.4 Hz, 2H), 7.29 (t, *J* = 7.6 Hz, 2H), 7.24 – 7.15 (m, 5H), 3.79 (s, 3H), 3.60 (t, *J* = 8.6 Hz, 1H), 2.62 – 2.42 (m, 5H), 2.27 – 2.20 (m, 1H), 2.03 – 1.89 (m, 2H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 178.42, 166.98, 145.32, 141.68, 129.44, 128.56, 128.42, 128.37, 127.32, 125.95, 55.97, 51.92, 50.56, 41.80, 31.41, 26.01, 21.33.

HRMS (ESI-TOF) *m/z* Calcd for $C_{21}H_{21}O_4^-$ $[M-H]^-$ 337.1440, found 337.1438.

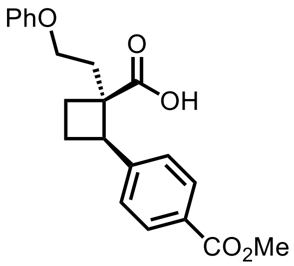
The absolute stereochemistry was assigned based on comparing the specific rotation of **5u** with literature.



```
Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]      [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   8.663 BB    0.3714 2609.29785  103.73867  51.2837
   2  11.054 BB    0.4535 2478.66602   81.79804  48.7163
```



```
Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]      [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   9.028 MM    0.4777  662.08783   23.09881  92.4361
   2  11.620 MM    0.4931   54.17773    1.83108   7.5639
```



**(1S,2R)-2-(4-(methoxycarbonyl)phenyl)-1-(2-phenoxyethyl)cyclobutanecarboxylic acid (5s)**

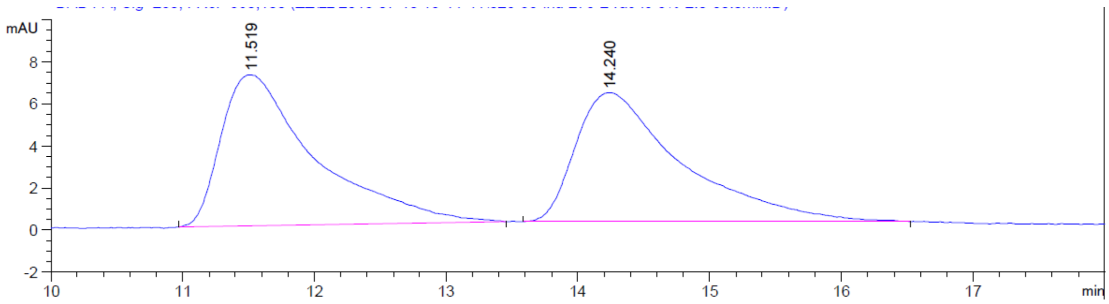
Substrate **4s** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 2/1 with 1% v/v of acetic acid). The product was obtained as a colorless oil (52% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® IC-3 column, 10% $^i$PrOH / $CO_2$, flow rate 2 mL/min, retention time 11.010 min (major) and 13.789 min (minor), 84:16 er);

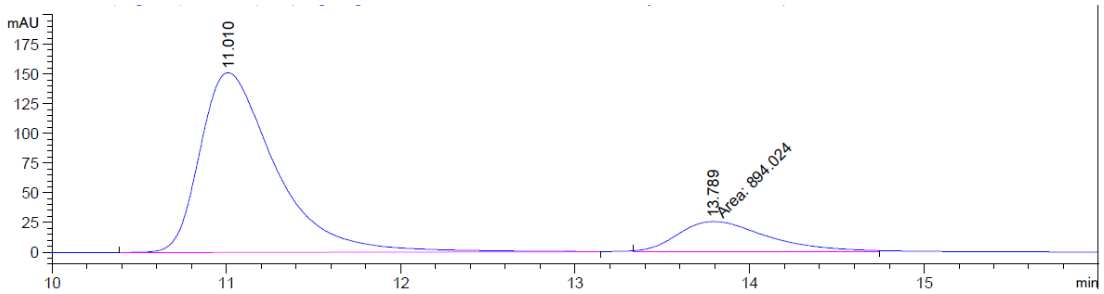
$^1$H NMR (600 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.1 Hz, 2H), 7.26 – 7.22 (m, 4H), 6.95 – 6.90 (m, 1H), 6.84 (d, *J* = 7.8 Hz, 2H), 4.03 – 3.94 (m, 2H), 3.87 (s, 3H), 3.73 (t, *J* = 9.0 Hz, 1H), 2.68 – 2.53 (m, 3H), 2.26 (td, *J* = 7.1, 3.2 Hz, 2H), 2.15 – 2.07 (m, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 177.97, 167.02, 158.53, 145.11, 129.48, 129.44, 128.65, 127.31, 120.76, 114.36, 64.31, 52.01, 50.36, 38.15, 26.23, 24.86, 21.76.

HRMS (ESI-TOF) *m/z* Calcd for $C_{21}H_{22}NaO_5^+$ [M+Na]$^+$ 377.1365, found 377.1369.

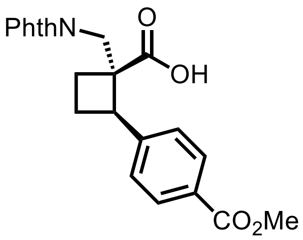
The absolute stereochemistry was assigned based on comparing the specific rotation of **5u** with literature.



```
Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  11.519 BB    0.5852  357.24802    7.19614  51.0097
   2  14.240 BB    0.6653  343.10483    6.14598  48.9903
```



```
Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  11.010 BB    0.4352 4528.30762  151.28094  83.5122
   2  13.789 MM    0.5916  894.02399   25.18769  16.4878
```



**(1R,2R)-1-((1,3-dioxoisoindolin-2-yl)methyl)-2-(4-(methoxycarbonyl)phenyl)cyclobutane carboxylic acid (5t)**

Substrate **4t** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 2/1 with 1% v/v of acetic acid). The product was obtained as a white solid (57% yield).

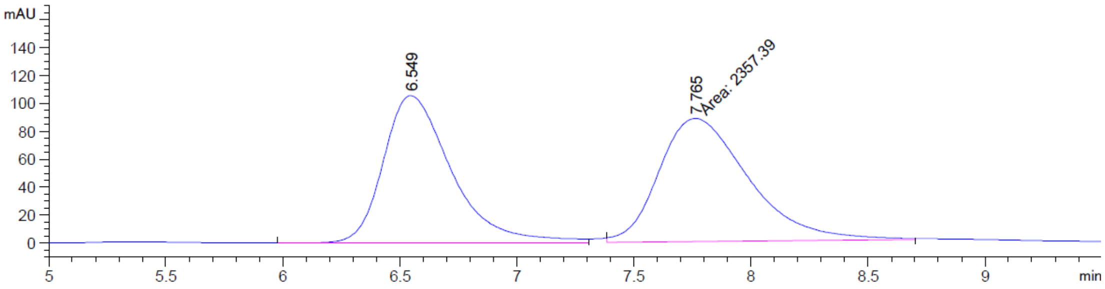
The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® AS-3 column, 10% $^{i}$PrOH / $CO_2$, flow rate 2 mL/min, retention time 6.848 min (miner) and 8.144 min (major), 93:7 er);

$^1$H NMR (600 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.1 Hz, 2H), 7.90 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.77 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.44 (d, *J* = 6.5 Hz, 2H), 4.20 (d, *J* = 15.3 Hz, 1H), 4.01 (d, *J* = 12.8

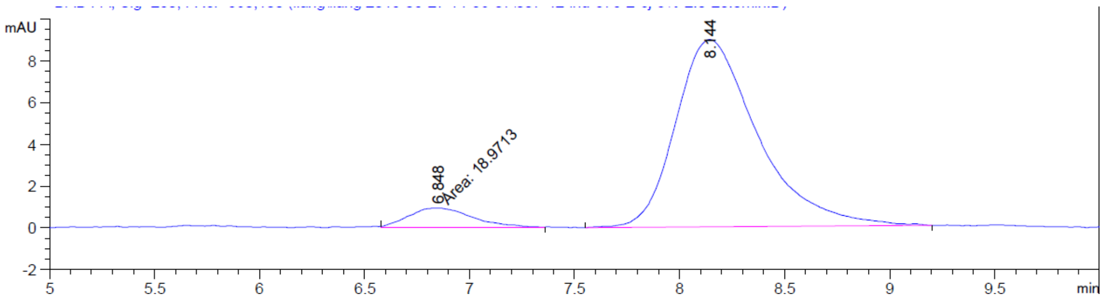
Hz, 1H), 3.89 (s, 3H), 3.81 – 3.76 (m, 1H), 2.61 – 2.55 (m, 1H), 2.41 (t, *J* = 10.2 Hz, 1H), 2.09 (dd, *J* = 18.4, 9.5 Hz, 2H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 185.59, 168.98, 167.10, 144.93, 134.31, 131.88, 129.52, 128.65, 127.47, 123.59, 123.45, 52.01, 45.70, 29.69, 29.21, 23.79, 21.18.

HRMS (ESI-TOF) *m/z* Calcd for $C_{22}H_{18}NO_6^-$ $[M-H]^-$ 392.1134, found 392.1127.

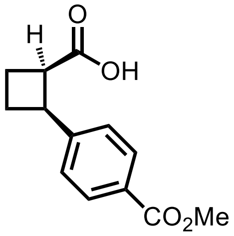
The absolute stereochemistry was assigned based on comparing the specific rotation of **5u** with literature.



```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   6.549 BV    0.3108 2141.92163  105.52997  47.6055
   2   7.765 MM    0.4455 2357.38965   88.19743  52.3945
```



```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   6.848 MM    0.3437   18.97134 9.19975e-1   7.1862
   2   8.144 BB    0.4041  245.02602    8.98688  92.8138
```



**(1R,2S)-2-(4-(methoxycarbonyl)phenyl)cyclobutanecarboxylic acid (5u)**

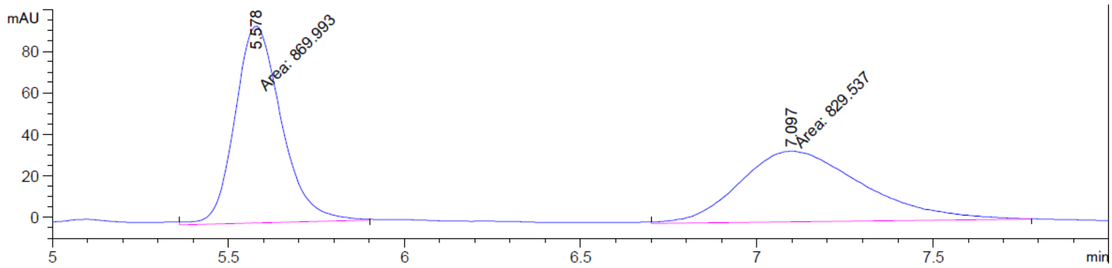
Substrate **4u** was arylated following the general arylation procedure (eluent: hexane/ethyl acetate = 2/1 with 1% v/v of acetic acid). The product was obtained as a white solid (61% yield).

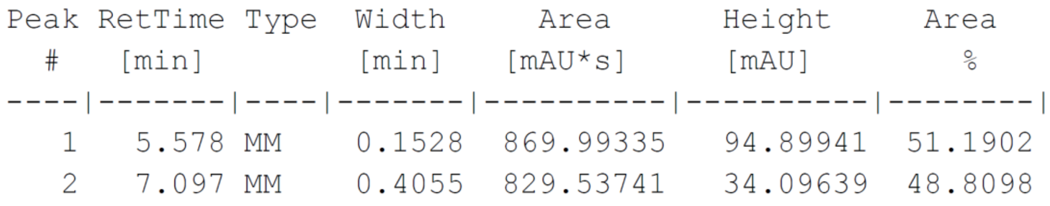
The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® AS-3 column, 15% $^{i}$PrOH / $CO_2$, flow rate 1 mL/min, retention time 5.554 min (major) and 7.770 min (minor), 92:8 er);

1H NMR (600 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.4 Hz, 2H), 7.25 (d, *J* = 8.2 Hz, 2H), 4.04 – 3.98 (m, 1H), 3.90 (s, 3H), 3.54 (q, *J* = 3.2, 2.4 Hz, 1H), 2.65 – 2.57 (m, 1H), 2.36 – 2.28 (m, 2H), 2.28 – 2.21 (m, 1H); $^{13}$C NMR (151 MHz, $CDCl_3$) δ 177.78, 167.09, 146.06, 129.50, 128.36, 127.13, 52.00, 44.56, 42.27, 24.44, 20.53.

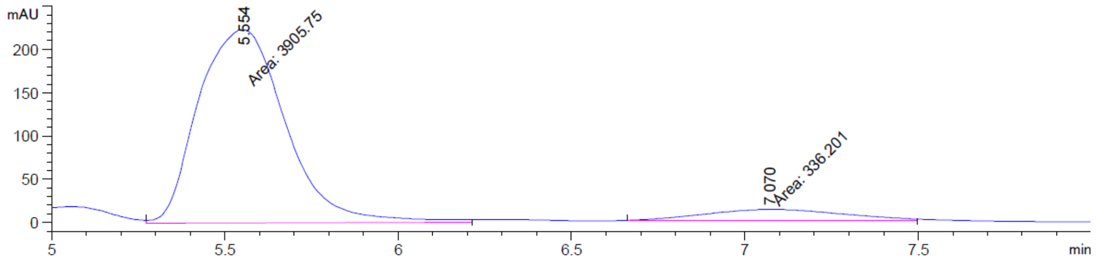
HRMS (ESI-TOF) *m/z* Calcd for $C_{13}H_{13}O_4^-$ $[M-H]^-$ 233.0814, found 233.0806.

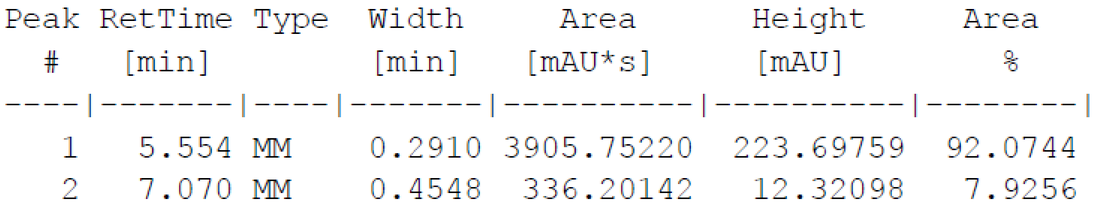
The absolute stereochemistry was assigned based on comparing the specific rotation of **5u** with literature.





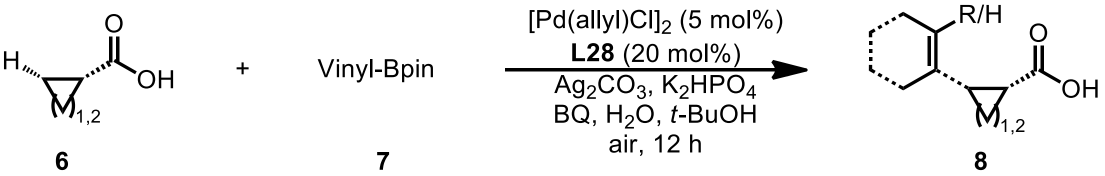
```
Peak RetTime Type  Width     Area        Height      Area
  #   [min]        [min]    [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
  1   5.578 MM    0.1528  869.99335   94.89941  51.1902
  2   7.097 MM    0.4055  829.53741   34.09639  48.8098
```



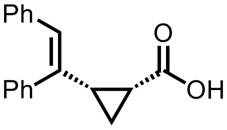


```
Peak RetTime Type  Width     Area        Height      Area
  #   [min]        [min]    [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
  1   5.554 MM    0.2910 3905.75220  223.69759  92.0744
  2   7.070 MM    0.4548  336.20142   12.32098   7.9256
```

### 3.7 Enantioselective Vinylation of Cylcopropanecarboxylic acid and Cylcobutanecarboxylic acid



**General procedure for enantioselective Vinylation of cyclopropanecarboxylic acid and cyclobutanecarboxylic acid**: A 2-dram vial equipped with a magnetic stir bar was charged with $[Pd(allyl)Cl]_2$ (1.9mg, 5 mol%) and **L28** (11.7 mg, 20 mol%) in *t*-BuOH (1.0 ml) and then stirred at the rate of 300 rpm at room temperature for 5 min. The appropriate acid substrate (0.10 mmol), $Ag_2CO_3$ (41.4 mg, 0.15 mmol), $K_2HPO_4$ (26.0 mg, 0.15 mmol), Vinyl-Bpin (0.2 mmol), BQ (5.4 mg, 0.05 mmol), $H_2O$ (3.6 mg, 0.2 mmol)was then added. Subsequently the vial was capped and closed tightly. The reaction mixture was then stirred at the rate of 300 rpm at 80 °C for 12 h. After being allowed to cool to room temperature, the mixture was diluted with ethyl acetate and 0.1 ml of acetic acid was then added. The mixture was passed through a pad of Celite with ethyl acetate as the eluent to remove any insoluble precipitate. The resulting solution was concentrated, and the residual mixture was dissolved with a minimal amount of acetone and loaded onto a preparative TLC plate. The pure product was then isolated using preparative TLC with ethyl acetate and hexane (1/4 to 1/1) as the eluent and 1% v/v of acetic acid as additive.



**(1R,2S)-2-((Z)-1,2-diphenylvinyl)cyclopropanecarboxylic acid (8a)**

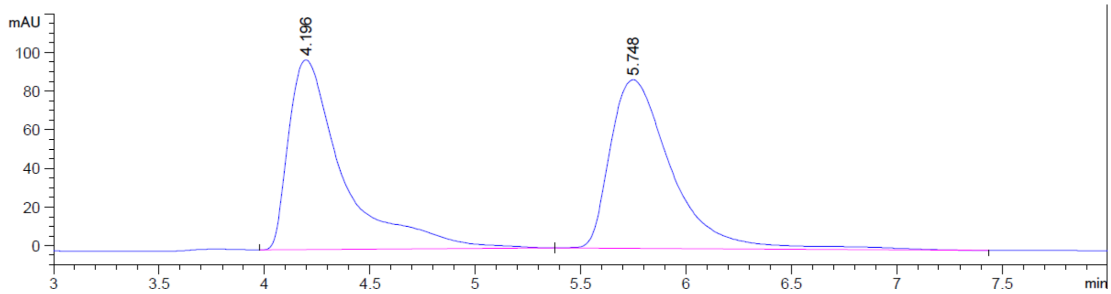
Substrate **6a** was vinylated following the general vinylation procedure (eluent: hexane/ethyl acetate = 5/1 with 1% v/v of acetic acid). The product was obtained as a colorless oil (71% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® IC-3 column, 10% $^i$PrOH / $CO_2$, flow rate 2 mL/min, retention time 4.352 min (minor) and 5.836 min (major), 98:2 er);

$^1$H NMR (600 MHz, $CDCl_3$) δ 7.18 – 7.11 (m, 5H), 7.07 (dt, *J* = 4.9, 1.8 Hz, 3H), 6.96 – 6.90 (m, 2H), 6.55 (s, 1H), 2.38 (q, *J* = 8.8, 8.1 Hz, 1H), 2.05 – 2.00 (m, 1H), 1.70 (dt, *J* = 7.9, 5.3 Hz, 1H), 1.31 (td, *J* = 8.0, 5.1 Hz, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 176.52, 140.97, 136.93, 135.51, 129.77, 129.28, 128.61, 128.41, 127.83, 127.05, 126.49, 30.91, 21.45, 12.34.

HRMS (ESI-TOF) *m/z* Calcd for $C_{18}H_{15}O_2^-$ $[M-H]^-$ 263.1072, found 263.1068.

The absolute stereochemistry was assigned based on comparing the specific rotation of **3m** with literature.



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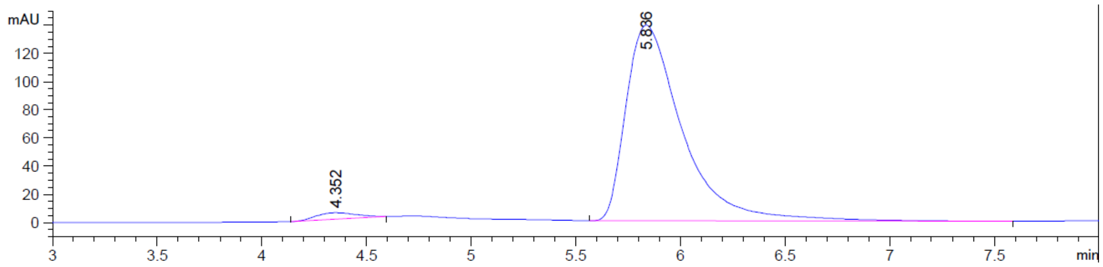
Peak RetTime Type  Width      Area       Height      Area
  #   [min]        [min]    [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   4.196 BB    0.2682 1770.29736   98.25798  49.8954
   2   5.748 BB    0.3115 1777.71936   87.32085  50.1046
```



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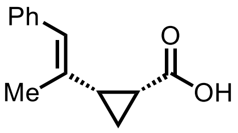
Peak RetTime Type  Width      Area       Height      Area
  #   [min]        [min]    [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   4.352 BB    0.2122   60.82872    4.54320   2.2811
   2   5.836 BB    0.2808 2605.83105  138.94025  97.7189
```



**(1R,2S)-2-((E)-1-phenylprop-1-en-2-yl)cyclopropanecarboxylic acid (8b)**

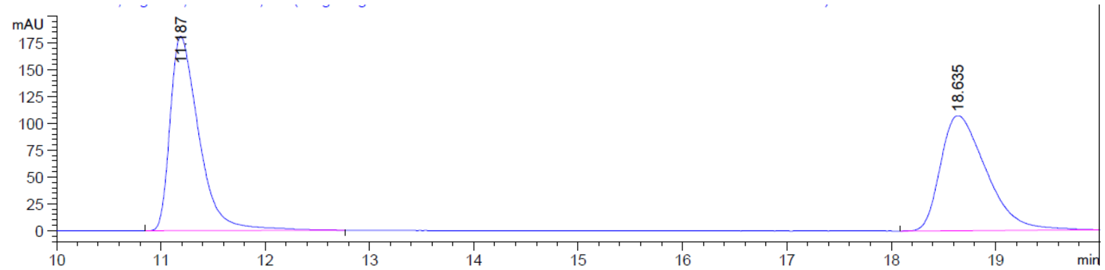
Substrate **6b** was vinylated following the general vinylation procedure (eluent: hexane/ethyl acetate = 5/1 with 1% v/v of acetic acid). The product was obtained as a white solid (70% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® OJ-3 column, 5% $^{i}$PrOH / $CO_2$, flow rate 2 mL/min, retention time 11.153 min (major) and 18.721 min (minor), 97:3 er);

$^{1}$H NMR (600 MHz, $CDCl_3$) δ 7.28 (dd, $J$ = 8.2, 7.1 Hz, 2H), 7.21 – 7.16 (m, 3H), 6.43 (s, 1H), 2.19 – 2.14 (m, 1H), 1.96 – 1.91 (m, 1H), 1.86 (s, 3H), 1.58 (dt, $J$ = 7.7, 5.2 Hz, 1H), 1.23 (td, $J$ = 8.0, 5.0 Hz, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 176.64, 137.87, 132.66, 128.85, 128.57, 128.00, 126.20, 30.85, 19.86, 18.65, 12.48.

HRMS (ESI-TOF) $m/z$ Calcd for $C_{13}H_{13}O_2^-$ $[M-H]^-$ 201.0916, found 201.0915.

The absolute stereochemistry was assigned based on comparing the specific rotation of **3m** with literature.



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Peak RetTime Type  Width      Area       Height      Area
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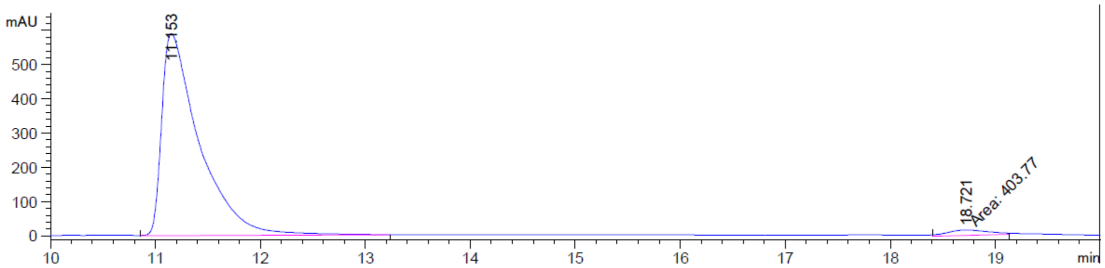
   1  11.187 BB    0.2919 3079.80225  164.88766  51.0895
   2  18.633 BB    0.4418 2948.44263   97.77589  48.9105
```



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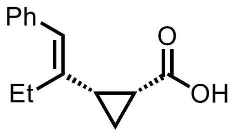
Peak RetTime Type  Width      Area       Height      Area
  #   [min]        [min]    [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  11.153 BB    0.3567 1.45963e4   589.75201  97.3082
   2  18.721 MM    0.4417  403.76981   15.23415   2.6918
```



**(1R,2S)-2-((E)-1-phenylbut-1-en-2-yl)cyclopropanecarboxylic acid (8c)**

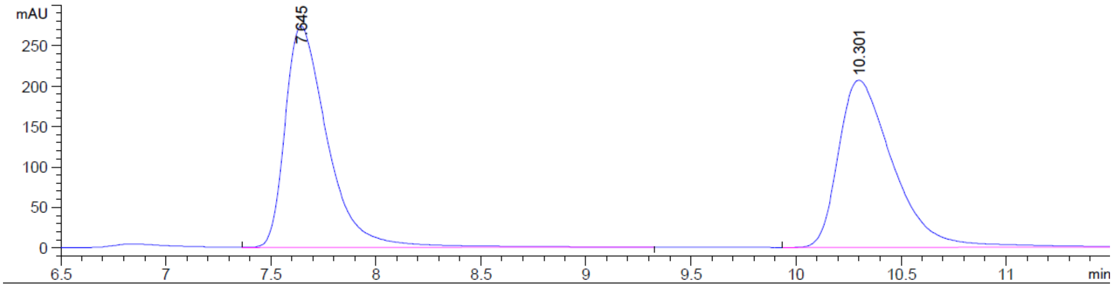
Substrate **6c** was vinylated following the general vinylation procedure (eluent: hexane/ethyl acetate = 5/1 with 1% v/v of acetic acid). The product was obtained as a colorless oil (63% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® OJ-3 column, 5% $^i$PrOH / $CO_2$, flow rate 2 mL/min, retention time 7.637 min (major) and 10.295 min (minor), 94:6 er);

$^1$H NMR (600 MHz, $CDCl_3$) δ 7.30 – 7.26 (m, 2H), 7.20 – 7.17 (m, 1H), 7.17 – 7.14 (m, 2H), 6.39 (s, 1H), 2.32 (dq, *J* = 15.0, 7.6 Hz, 1H), 2.21 – 2.15 (m, 2H), 1.97 (ddd, *J* = 9.3, 7.7, 5.4 Hz, 1H), 1.57 (dt, *J* = 7.8, 5.2 Hz, 1H), 1.26 – 1.21 (m, 1H), 1.08 (t, *J* = 7.6 Hz, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 177.08, 137.91, 137.59, 128.67, 128.13, 128.02, 126.21, 28.23, 25.18, 20.59, 12.79, 11.73.

HRMS (ESI-TOF) *m/z* Calcd for $C_{14}H_{15}O_2^-$ $[M-H]^-$ 215.1072, found 215.1070.

The absolute stereochemistry was assigned based on comparing the specific rotation of **3m** with literature.



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Peak RetTime Type  Width     Area      Height     Area
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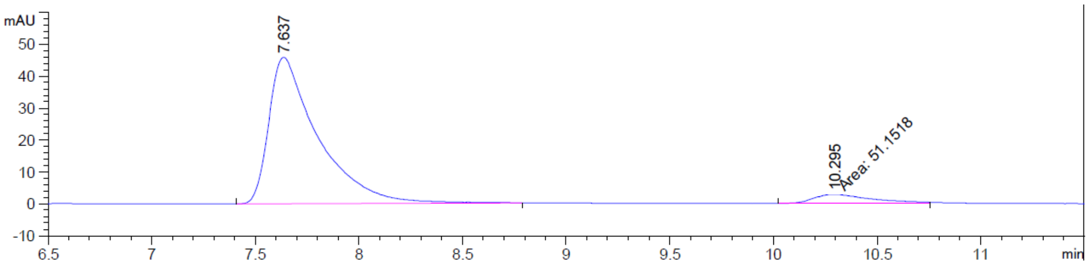
  1   7.645 VB    0.2135 3834.92285  273.60776  50.5871
  2  10.301 BB    0.2754 3745.91309  206.68524  49.4129
```



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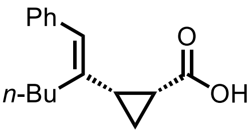
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
  1   7.637 BB    0.2301  756.30072   45.92109  93.6650
  2  10.295 MM    0.3111   51.15176    2.74055   6.3350
```



**(1R,2S)-2-((E)-1-phenylhex-1-en-2-yl)cyclopropanecarboxylic acid (8d)**

Substrate **6d** was vinylated following the general vinylation procedure (eluent: hexane/ethyl acetate = 5/1 with 1% v/v of acetic acid). The product was obtained as a colorless oil (61% yield).

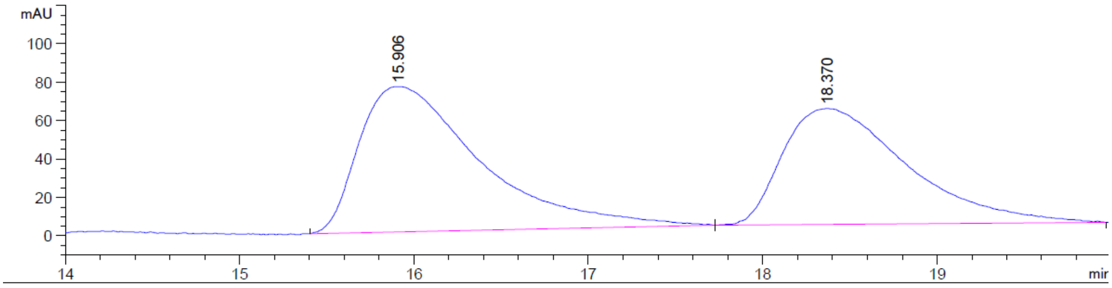
The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® OD-3 column, 5% $^i$PrOH / $CO_2$, flow rate 1 mL/min, retention time 15.860 min (minor) and 18.022 min (major), 92:8 er);

$^1$H NMR (600 MHz, $CDCl_3$) δ 7.29 – 7.26 (m, 2H), 7.21 – 7.12 (m, 3H), 6.41 (s, 1H), 2.32 (ddd, *J* = 13.9, 10.2, 6.4 Hz, 1H), 2.20 – 2.09 (m, 2H), 1.96 (ddd, *J* = 9.3, 7.7, 5.4 Hz, 1H), 1.60 – 1.54 (m, 1H), 1.51 – 1.47 (m, 1H), 1.33 – 1.20 (m, 4H), 0.85 (t, *J* = 7.4 Hz, 3H); $^{13}$C

NMR (150 MHz, $CDCl_3$) δ 176.78, 137.97, 136.60, 128.69, 128.56, 128.00, 126.17, 31.83, 30.28, 28.58, 22.78, 20.49, 13.88, 12.05.

HRMS (ESI-TOF) *m/z* Calcd for $C_{16}H_{19}O_2^-$ $[M-H]^-$ 243.1385, found 243.1384.

The absolute stereochemistry was assigned based on comparing the specific rotation of **3m** with literature.



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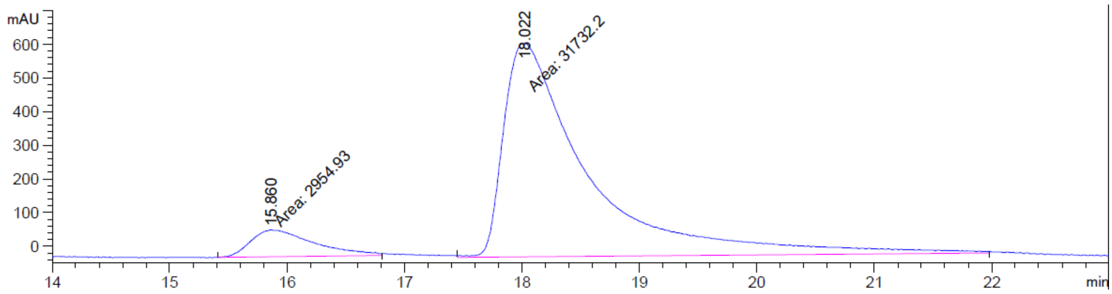
Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]      [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  15.875 VV R  0.5591 3928.37988   82.86909  53.1674
   2  18.365 MM    0.8272 3460.32300   69.71623  46.8326
```



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Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]      [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  15.860 MM    0.6183 2954.92944   79.65041   8.5188
   2  18.022 MM    0.8315 3.17322e4   636.05505  91.4812
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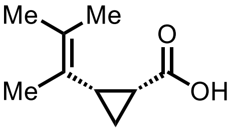


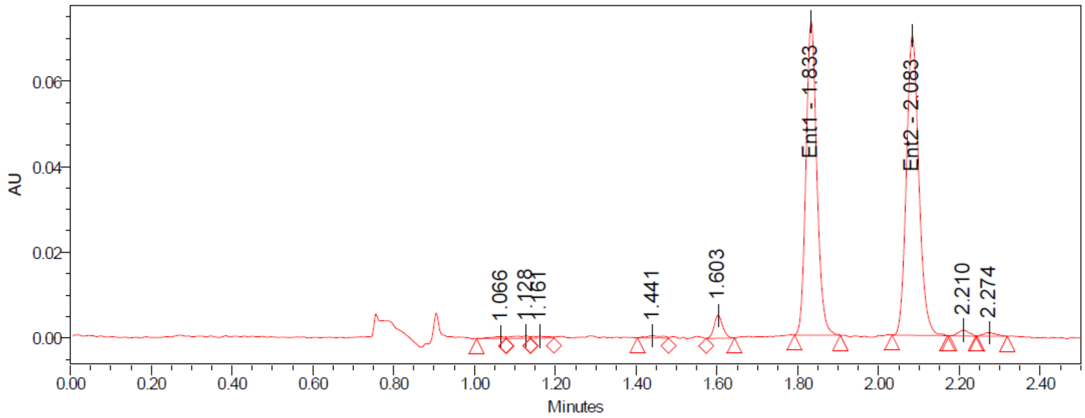
**(1R,2S)-2-(3-methylbut-2-en-2-yl)cyclopropanecarboxylic acid (8e)**

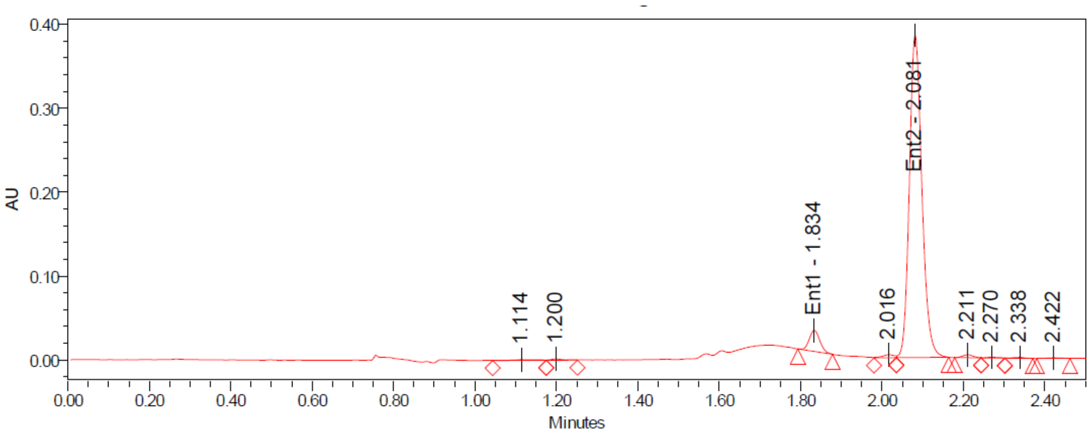
Substrate **6e** was vinylated following the general vinylation procedure (eluent: hexane/ethyl acetate = 5/1 with 1% v/v of acetic acid). The product was obtained as a colorless oil (50% yield).

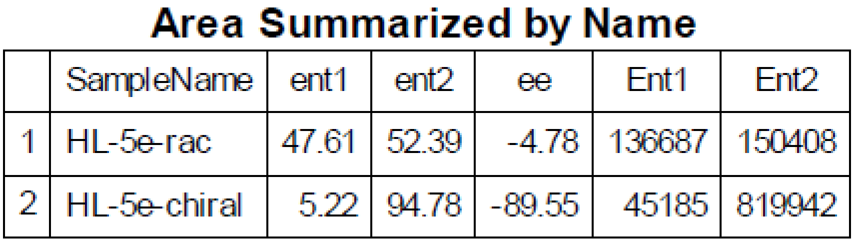
The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® IG-3 column, 5% MeOH/$CO_2$, flow rate 4 mL/min, retention time 1.834 min (miner) and 2.081 min (major), 95:5 er);

$^1H$ NMR (600 MHz, $CDCl_3$) δ 2.05 (t, *J* = 8.9 Hz, 1H), 1.92 (ddd, *J* = 8.9, 7.8, 5.3 Hz, 1H), 1.74 (s, 3H), 1.66 (s, 3H), 1.64 (s, 3H), 1.36 (dt, *J* = 8.0, 5.1 Hz, 1H), 1.22 – 1.18 (m, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 177.63, 130.57, 122.31, 27.08, 20.92, 20.86, 20.78, 18.25, 14.44. HRMS (ESI-TOF) *m/z* Calcd for $C_9H_{15}O_2^+$ $[M+H]^+$ 155.1072, found 155.1065.

The absolute stereochemistry was assigned based on comparing the specific rotation of **3m** with literature.

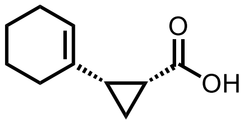






**Area Summarized by Name**

|  | SampleName | ent1 | ent2 | ee | Ent1 | Ent2 |
|---|---|---|---|---|---|---|
| 1 | HL-5e-rac | 47.61 | 52.39 | -4.78 | 136687 | 150408 |
| 2 | HL-5e-chiral | 5.22 | 94.78 | -89.55 | 45185 | 819942 |



**(1R,2S)-2-(cyclohex-1-en-1-yl)cyclopropanecarboxylic acid (8f)**

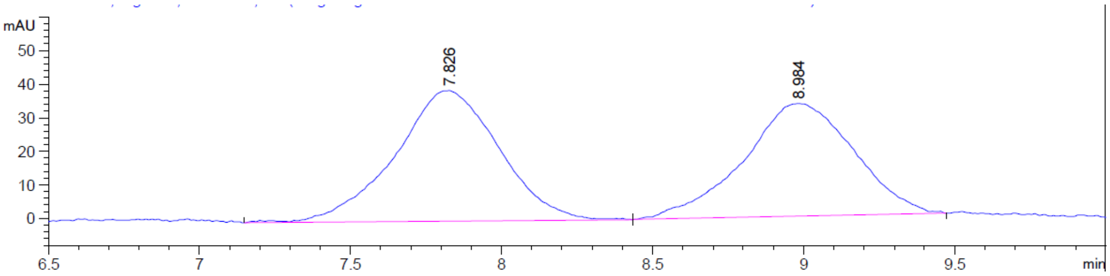
Substrate **6f** was vinylated following the general vinylation procedure (eluent: hexane/ethyl acetate = 5/1 with 1% v/v of acetic acid). The product was obtained as a colorless oil (47% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® AS-3 column, 10% $^{i}$PrOH / $CO_2$, flow rate 1 mL/min, retention time 7.816 min (major) and 9.113 min (minor), 98:2 er);

$^1$H NMR (600 MHz, $CDCl_3$) δ 5.60 (dq, *J* = 4.1, 1.9 Hz, 1H), 2.07 – 1.96 (m, 3H), 1.91 (t, *J* = 8.5 Hz, 1H), 1.82 (ddd, *J* = 9.2, 7.6, 5.5 Hz, 2H), 1.64 – 1.49 (m, 4H), 1.40 (dt, *J* = 7.7, 5.2 Hz, 1H), 1.10 (td, *J* = 8.0, 4.8 Hz, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 176.01, 131.41, 125.03, 28.74, 28.25, 24.74, 22.43, 21.94, 18.80, 10.91.

HRMS (ESI-TOF) *m/z* Calcd for $C_{10}H_{15}O_2^+$ $[M+H]^+$ 167.1072, found 167.1065.

The absolute stereochemistry was assigned based on comparing the specific rotation of **3m** with literature.



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Peak RetTime Type  Width     Area       Height      Area
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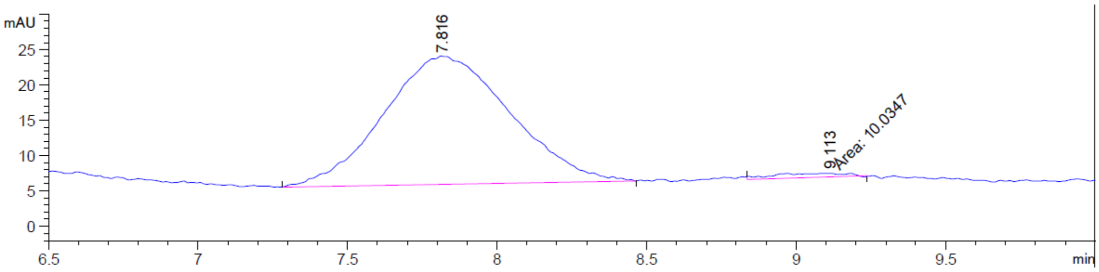
----|-------|----|-------|----------|----------|--------|
  1    7.826 VV R  0.3030  930.88171   38.93185  52.1549
  2    8.984 BV R  0.3058  853.95709   33.68350  47.8451
```



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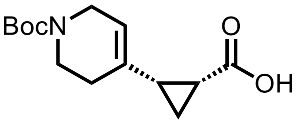
Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
  1    7.816 BV R  0.3457  532.12018   18.17036  98.1491
  2    9.113 MM    0.3155   10.03466 5.30117e-1   1.8509
```



**(1R,2S)-2-(1-(tert-butoxycarbonyl)-1,2,3,6-tetrahydropyridin-4-yl)cyclopropanecarboxylic acid (8g)**

Substrate **6g** was vinylated following the general vinylation procedure (eluent: hexane/ethyl acetate = 2/1 with 1% v/v of acetic acid). The product was obtained as a colorless oil (51% yield).

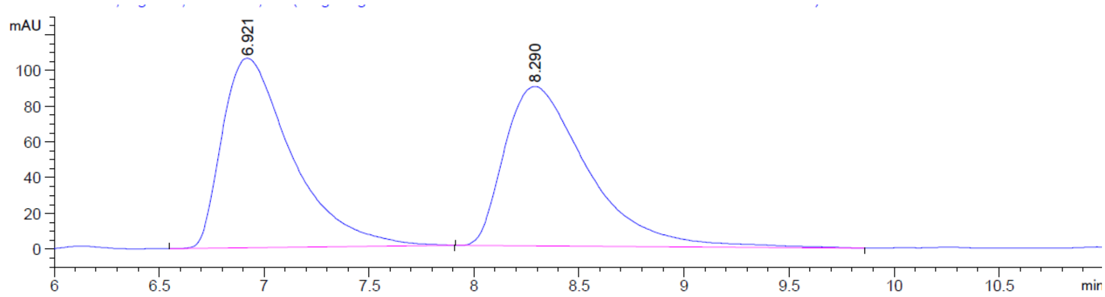
The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® IC-3 column, 10% $^i$PrOH / $CO_2$, flow rate 2 mL/min, retention time 6.855 min (major) and

8.383 min (minor), 97:3 er);

$^{1}$H NMR (600 MHz, CDCl$_3$) δ 5.53 (s, 1H), 3.99 – 3.81 (m, 2H), 3.55 (dt, *J* = 12.8, 5.4 Hz, 1H), 3.31 (s, 1H), 2.21 – 2.13 (m, 1H), 1.96 (q, *J* = 8.3 Hz, 2H), 1.86 (ddd, *J* = 9.1, 7.7, 5.5 Hz, 1H), 1.46 (s, 9H), 1.41 (dt, *J* = 7.9, 5.2 Hz, 1H), 1.16 (td, *J* = 8.1, 4.9 Hz, 1H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 176.84, 155.02, 131.07, 122.19, 79.55, 31.91, 29.68, 28.46, 27.63, 22.68, 14.11, 11.61.

HRMS (ESI-TOF) *m/z* Calcd for $C_{14}H_{20}NO_4^-$ [M-H]$^-$ 266.1392, found 266.1392.

The absolute stereochemistry was assigned based on comparing the specific rotation of **3m** with literature.



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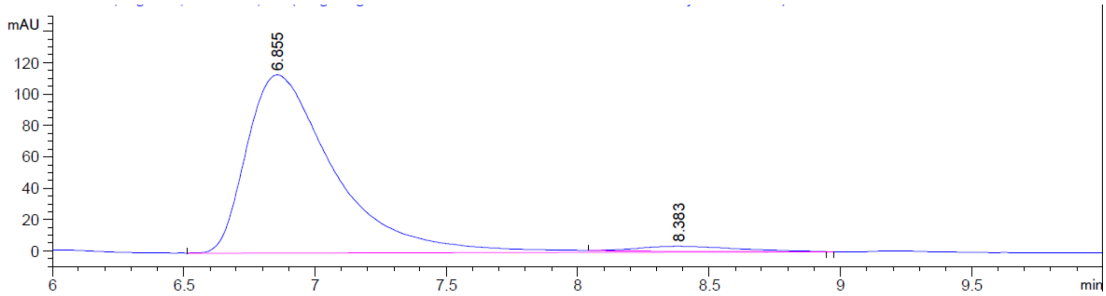
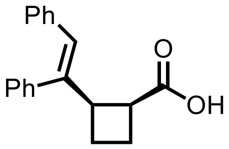
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.921 BB    0.3517 2451.06152  106.02688  49.9608
   2   8.290 BB    0.4135 2454.91040   89.08801  50.0392
```



```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.855 BV R  0.3346 2656.87109  113.72182  96.8827
   2   8.383 VB E  0.3269   85.48772    3.20762   3.1173
```



**(1S,2R)-2-((Z)-1,2-diphenylvinyl)cyclobutanecarboxylic acid (8h)**

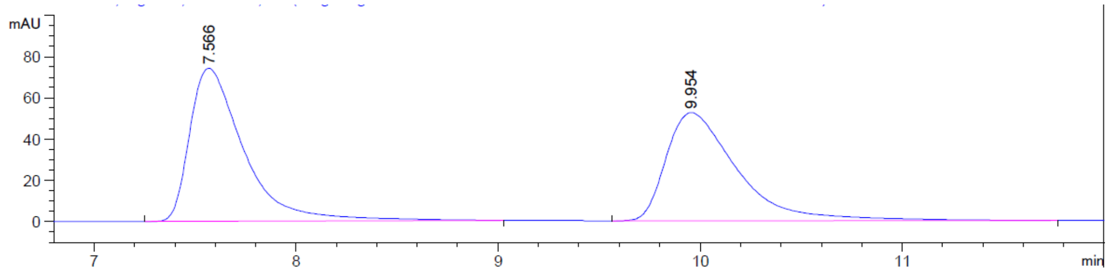
Substrate **6h** was vinylated following the general vinylation procedure (eluent: hexane/ethyl acetate = 2/1 with 1% v/v of acetic acid). The product was obtained as a colorless oil (61% yield).

The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® OJ-3 column, 5% $^{i}$PrOH / $CO_2$, flow rate 2 mL/min, retention time 7.478 min (major) and 9.876 min (minor), 88:12 er);

$^{1}$H NMR (600 MHz, $CDCl_3$) δ 7.19 (ddd, *J* = 4.3, 2.3, 1.2 Hz, 3H), 7.14 – 7.09 (m, 2H), 7.05 – 7.03 (m, 3H), 6.95 – 6.89 (m, 2H), 6.47 (s, 1H), 3.81 – 3.74 (m, 1H), 3.28 – 3.20 (m, 1H), 2.78 – 2.70 (m, 1H), 2.14 (dddd, *J* = 9.4, 7.9, 5.9, 3.4 Hz, 2H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 178.51, 141.42, 140.20, 137.07, 129.24, 128.75, 128.36, 127.78, 127.02, 126.91, 126.33, 45.18, 44.40, 24.50, 20.21.

HRMS (ESI-TOF) *m/z* Calcd for $C_{19}H_{17}O_2^-$ $[M-H]^-$ 277.1229, found 277.1226.

The absolute stereochemistry was assigned based on comparing the specific rotation of **5u** with literature.



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Peak RetTime Type  Width      Area       Height      Area
  #   [min]        [min]    [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   7.566 BB    0.2792 1382.54333   74.26161  51.8243
   2   9.954 BB    0.3741 1285.20544   52.41679  48.1757
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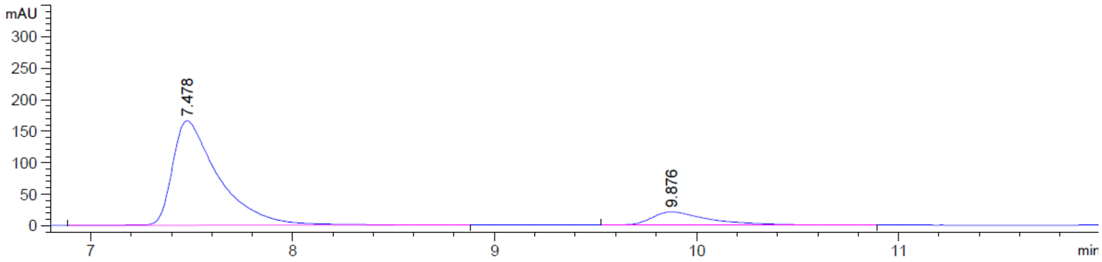

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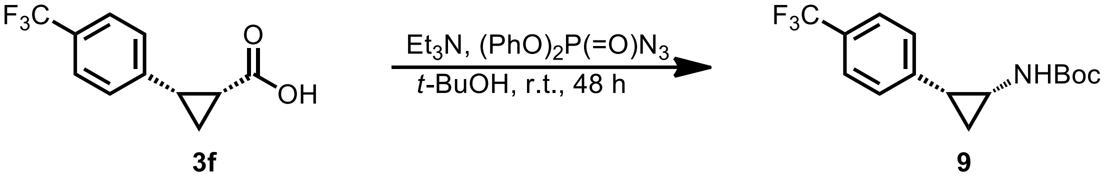
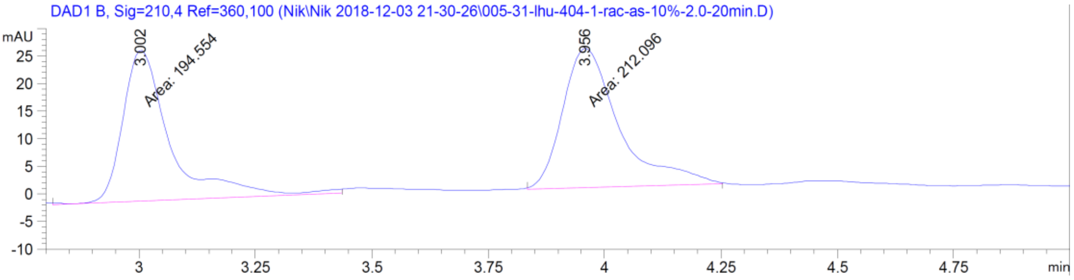
Peak RetTime Type  Width      Area       Height      Area
  #   [min]        [min]    [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   7.478 BB    0.2308 5079.21924  317.22769  88.1404
   2   9.876 MM    0.2967  683.42407   38.38791  11.8596
```

### 3.8 Synthesis of Cis-Chiral Amine from Carboxylic Acid



To a solution of tert-butyl ((1R,2R)-2-(4-(trifluoromethyl)phenyl)cyclopropyl)carbamate (46 mg, 0.2 mmol, 97:3 er.) and $Et_3N$ (31 uL, 0.22 mmol) in anhydrous *t*-BuOH (1 mL) was added diphenylphosphoryl azide (47 uL, 0.22 mmol) dropwise. The reaction was heated at 80 $^0$C and stirred for 48 h before cooling to r.t. and concentrating in vacuo. $Et_2O$ (20 mL) and water (40 mL) were added. The organic portion was isolated and the aqueous phase was extracted with $Et_2O$ (2 × 30 mL). The organics extracts were combined, washed with sat. aq. $NaHCO_3$ (20 mL) and brine (20 mL), dried over $Na_2SO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography (5 % EtOAc/hexane) to yield the title compound (43.3 mg, 72 %) as an white solid. $^1$H NMR (600 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.1 Hz, 2H), 7.32 (d, *J* = 7.9 Hz, 2H), 4.35 (s, 1H), 2.97 (s, 1H), 2.28 (d, *J* = 9.0 Hz, 1H), 1.37 (dt, *J* = 8.9, 6.8 Hz, 1H), 1.28 (s, 9H), 1.08 (s, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 156.17, 141.13, 129.01, 128.46 (q, *J* = 36.0 Hz), 124.83 (q, *J* = 4.5 Hz), 124.31(q, *J* = 270.0 Hz), 79.59, 29.65, 28.07, 22.43, 12.14; $^{19}$F NMR (375 MHz, $CDCl_3$) δ -62.62. $[\alpha]_D{}^{20}$ = 13.2 (c = 1.0, $CHCl_3$).
The enantiomeric purity of the substrate was determined by SFC analysis (CHIRALPAK® OD-3 column, 10% $^i$PrOH / $CO_2$, flow rate 2 mL/min, retention time 3.020 min (miner) and 3.986 min (major), 97:3 er);



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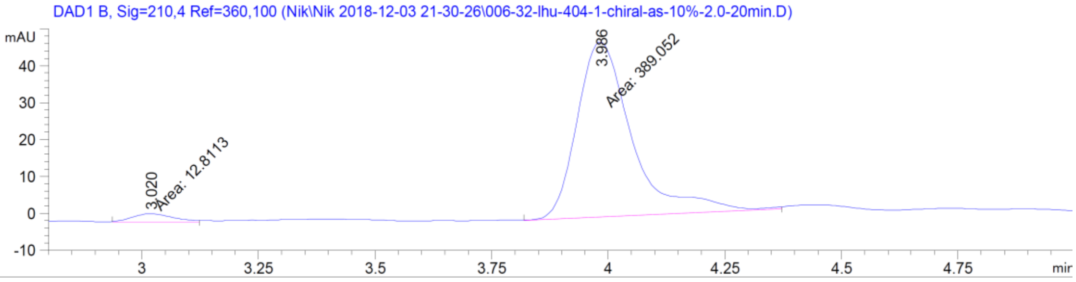
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
  1   3.002 MM    0.1183  194.55423   27.40913  47.8432
  2   3.956 MM    0.1399  212.09579   25.26016  52.1568
```



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Peak RetTime Type  Width     Area      Height     Area
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  2   3.986 MM    0.1363  389.05157   47.55794  96.8120
```

# 4. Reference

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## 5. X-Ray Crystallographic Data of Compounds

**Figure S1** X-Ray Structure **5p**

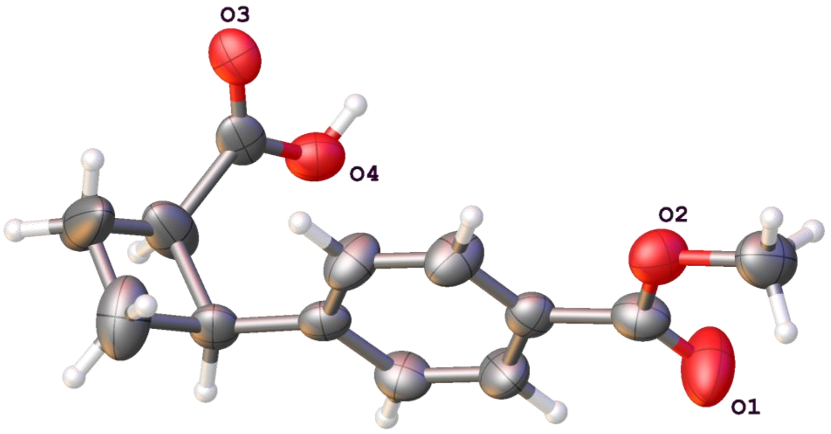
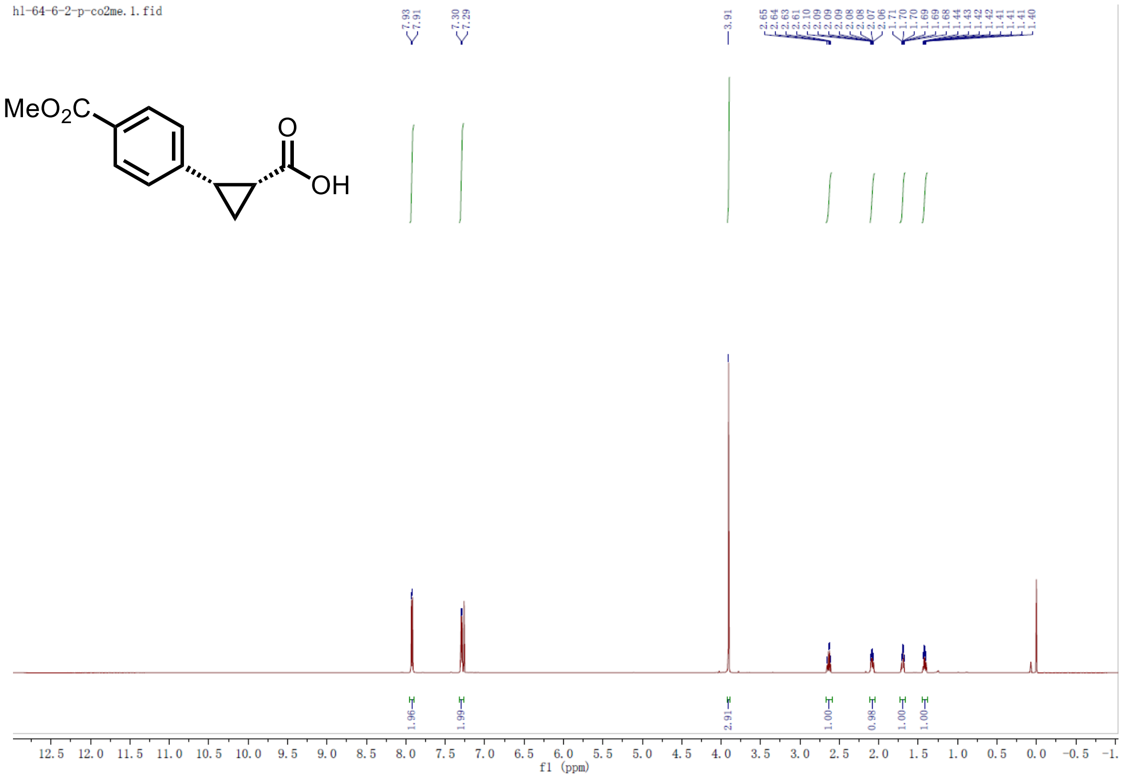


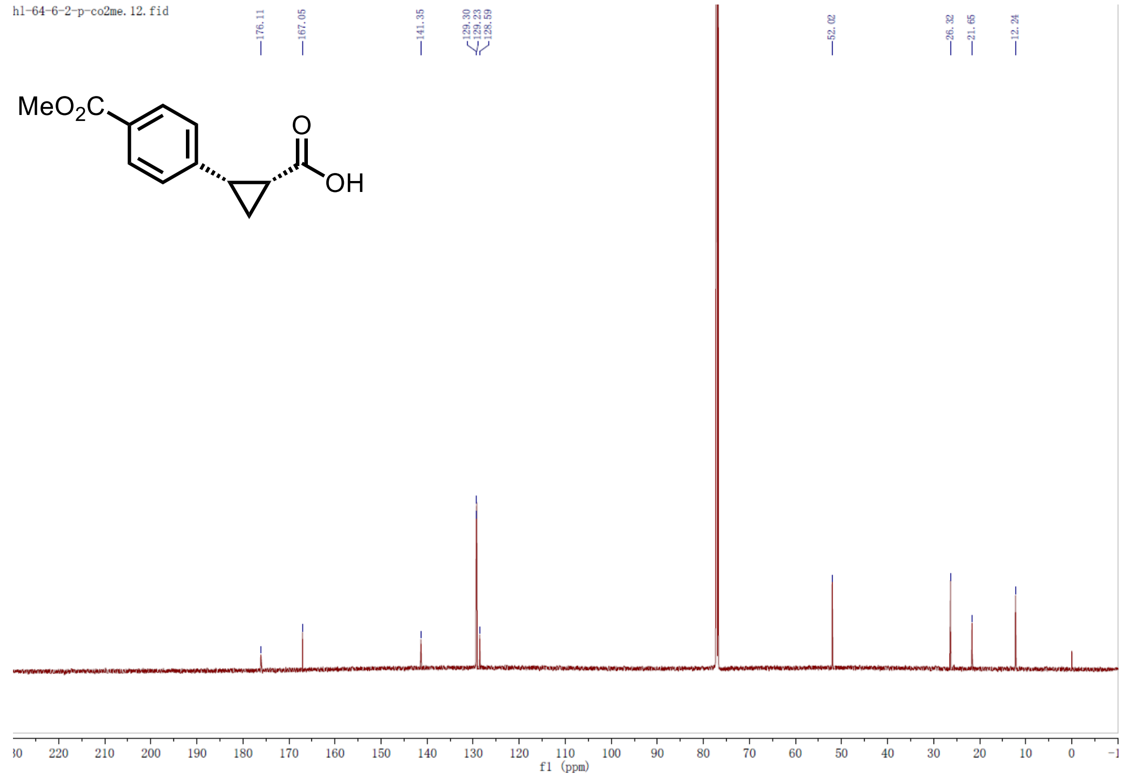
**Table 1**. Crystal data and structure refinement for **5p**

| | | |
|---|---|---|
| CCDC number | 1870087 | |
| Empirical formula | $C_{13} H_{14} O_4$ | |
| Formula weight | 234.24 | |
| Temperature | 100.0 K | |
| Wavelength | 1.54178 Å | |
| Crystal system | Trigonal | |
| Space group | $P3_1$ | |
| Unit cell dimensions | a = 15.8015(7) Å | = 90°. |
| | b = 15.8015(7) Å | = 90°. |
| | c = 16.3042(10) Å | = 120°. |
| Volume | 3525.5(4) $Å^3$ | |
| Z, Z’ | 12, 4 | |
| Density (calculated) | 1.324 $Mg/m^3$ | |
| Absorption coefficient | 0.815 $mm^{-1}$ | |
| F(000) | 1488 | |
| Crystal size | 0.20 x 0.17 x 0.11 $mm^3$ | |
| Theta range for data collection | 3.229 to 68.408°. | |
| Index ranges | -18<=h<=19, -19<=k<=19, -19<=l<=19 | |
| Reflections collected | 52265 | |
| Independent reflections | 8620 [R(int) = 0.0417] | |
| Completeness to theta = 67.679° | 100.0 % | |
| Absorption correction | Semi-empirical from equivalents | |
| Max. and min. transmission | 0.7531 and 0.6705 | |
| Refinement method | Full-matrix least-squares on $F^2$ | |

| | |
|---|---|
| Data / restraints / parameters | 8620 / 4 / 634 |
| Goodness-of-fit on $F^2$ | 1.039 |
| Final R indices [I>2sigma(I)] | R1 = 0.0398, wR2 = 0.1082 |
| R indices (all data) | R1 = 0.0413, wR2 = 0.1097 |
| Absolute structure parameter | 0.08(5) |
| Extinction coefficient | n/a |
| Largest diff. peak and hole | 0.328 and -0.171 e.$\text{Å}^{-3}$ |

# 6. NMR Spectra



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OH
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7.31
2.66
2.65
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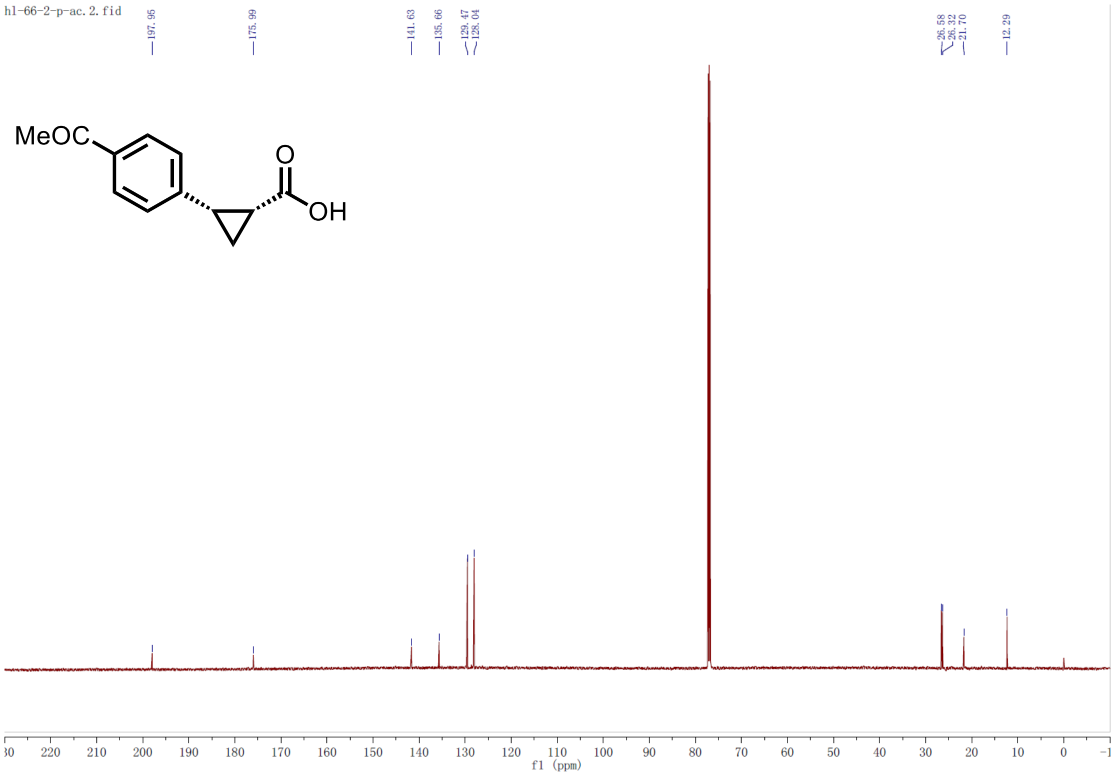
2.62
2.58
2.12
2.11
2.11
2.10
2.10
2.09
2.08
1.72
1.71
1.71
1.70
1.69
1.45
1.44
1.43
1.43
1.42
2.00
2.01
1.08
3.12
0.98
0.96
1.00
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)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128.04
26.58
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12.29
MeOC
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OH
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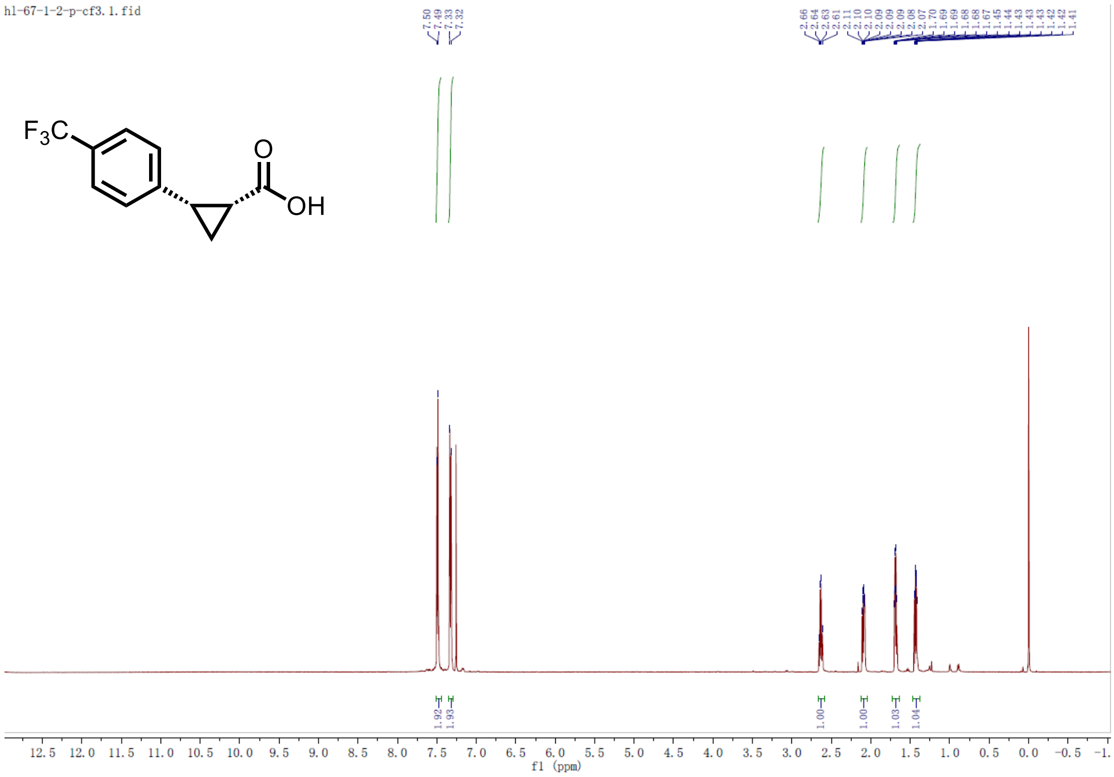
f1 (ppm)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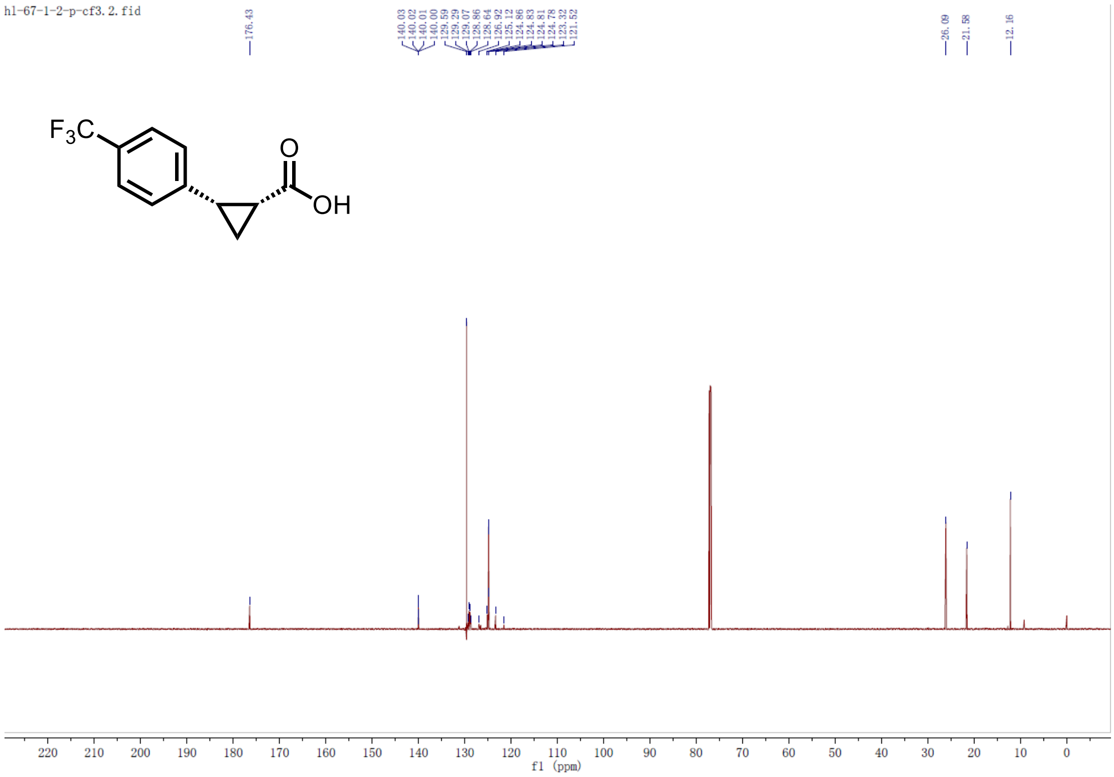
2.08
2.07
1.70
1.69
1.69
1.68
1.67
1.45
1.44
1.43
1.43
1.43
1.42
1.41
F3C
O
OH
1.92
1.93
1.00
1.00
1.03
1.04
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)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128.86
128.64
126.92
125.12
124.86
124.83
124.81
124.78
123.32
121.52
26.09
21.58
12.16
F3C
O
OH
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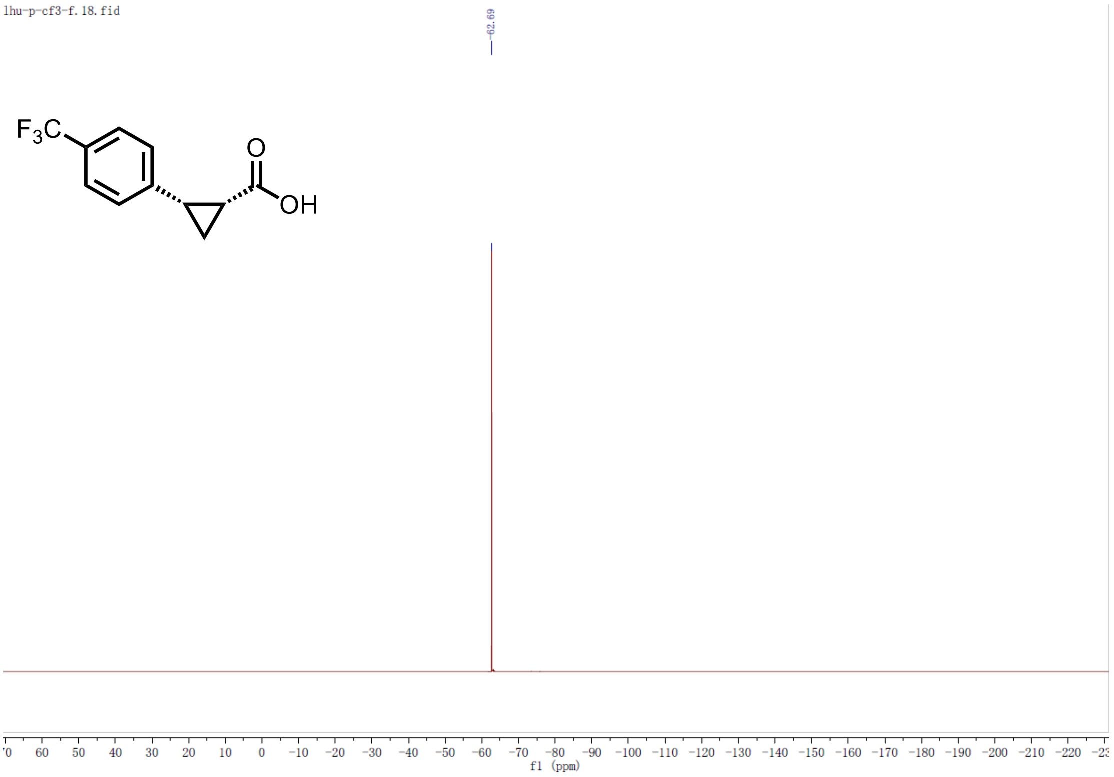
f1 (ppm)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O
OH
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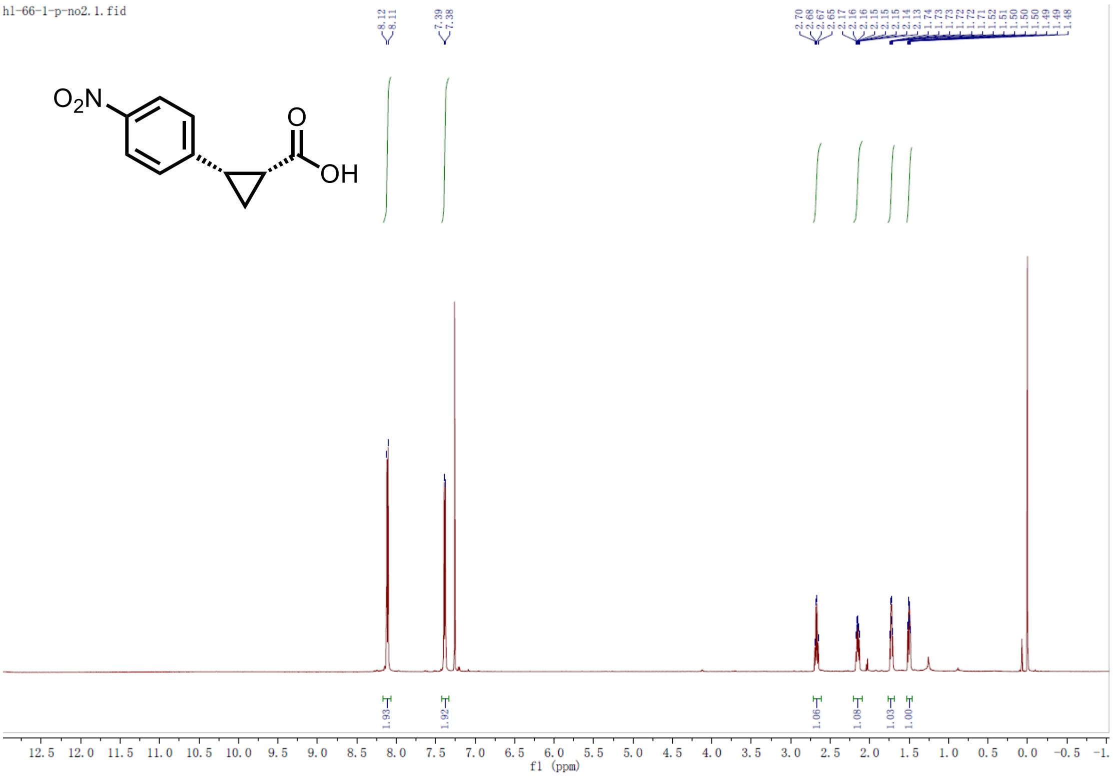
f1 (ppm)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1.49
1.49
1.48
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O
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1.92
1.06
1.08
1.03
1.00
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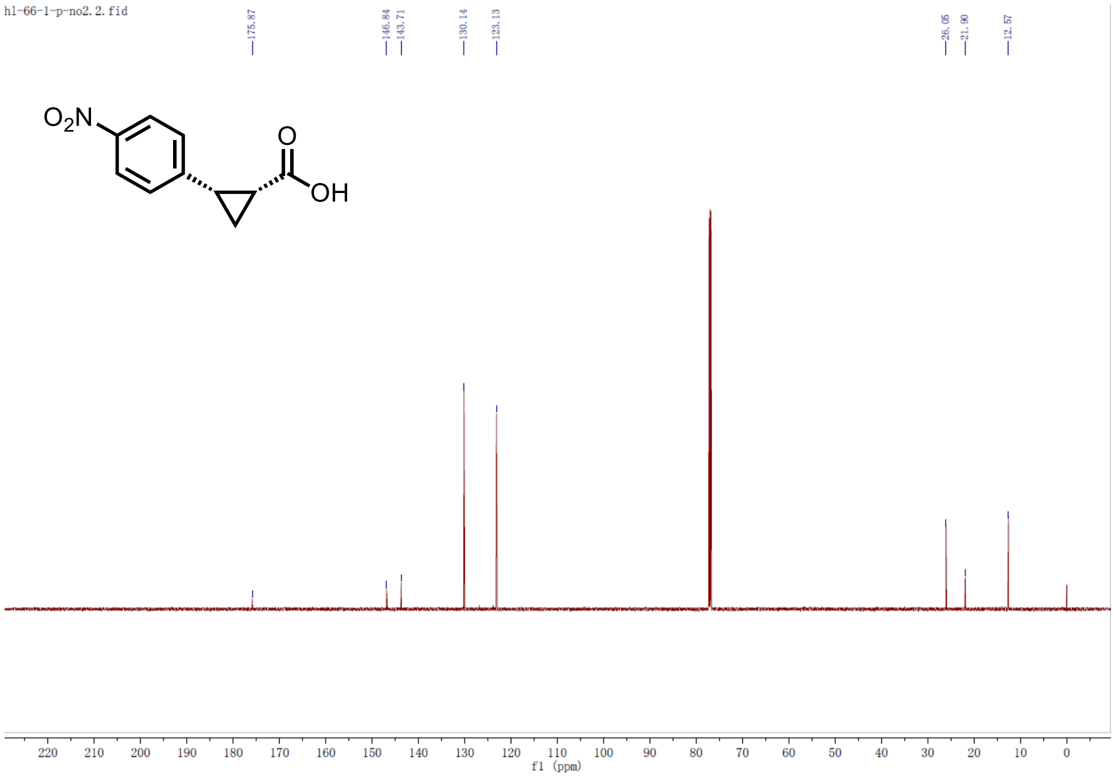
f1 (ppm)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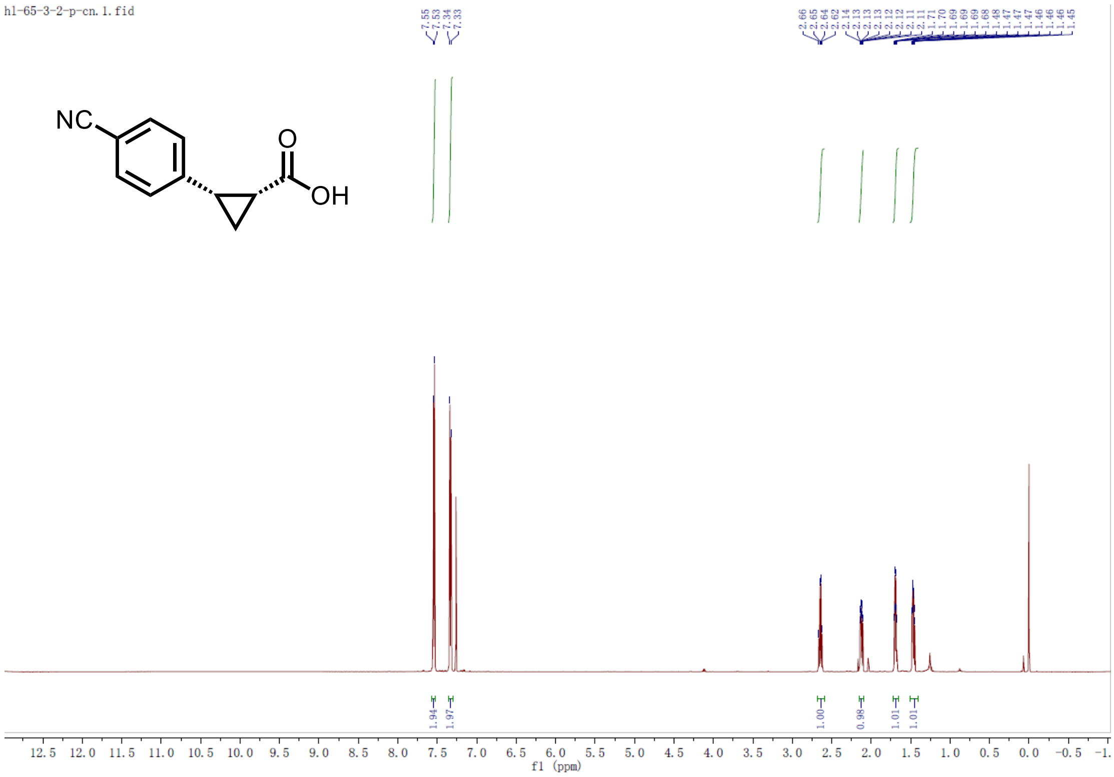
f1 (ppm)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1.47
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1.01
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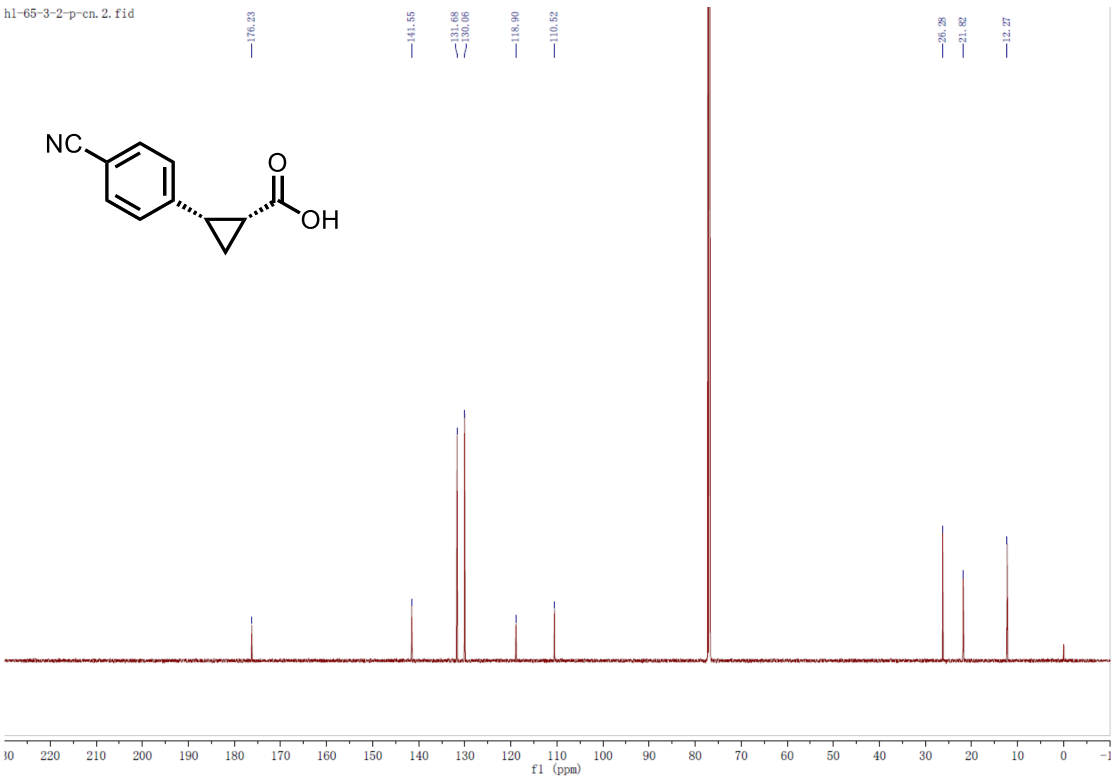
f1 (ppm)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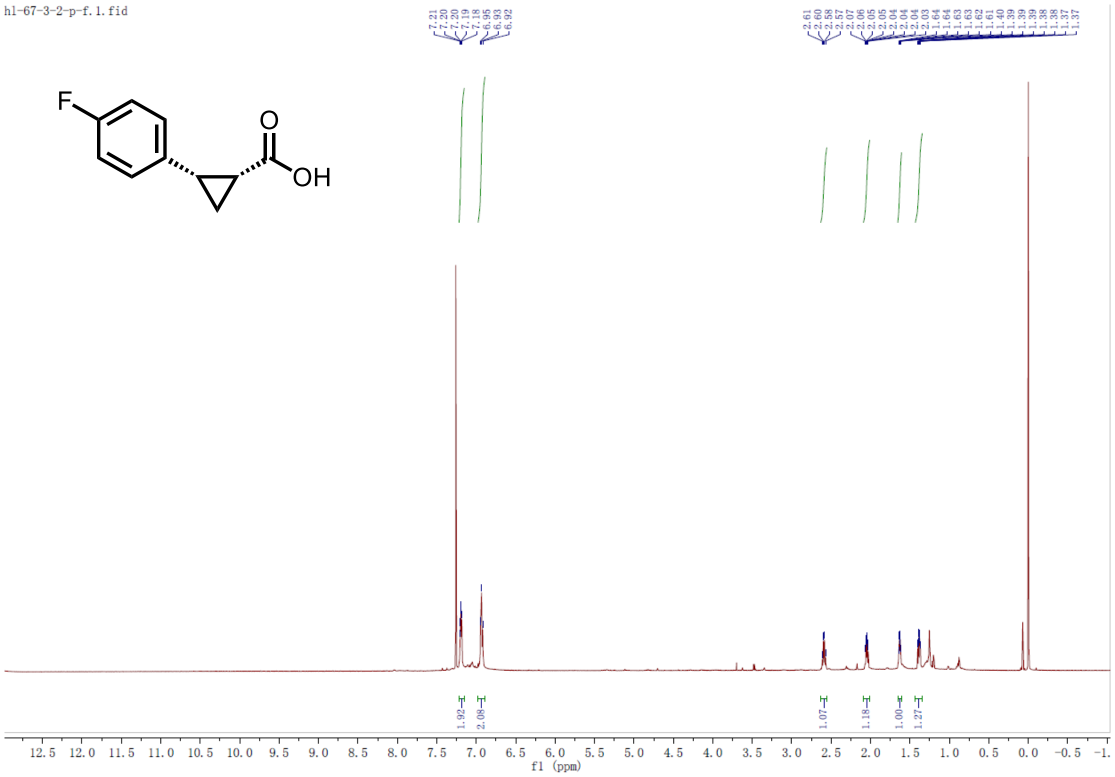
f1 (ppm)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2.05
2.05
2.04
2.04
2.04
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1.63
1.63
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1.38
1.38
1.37
1.37
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O
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2.08
1.07
1.18
1.00
1.27
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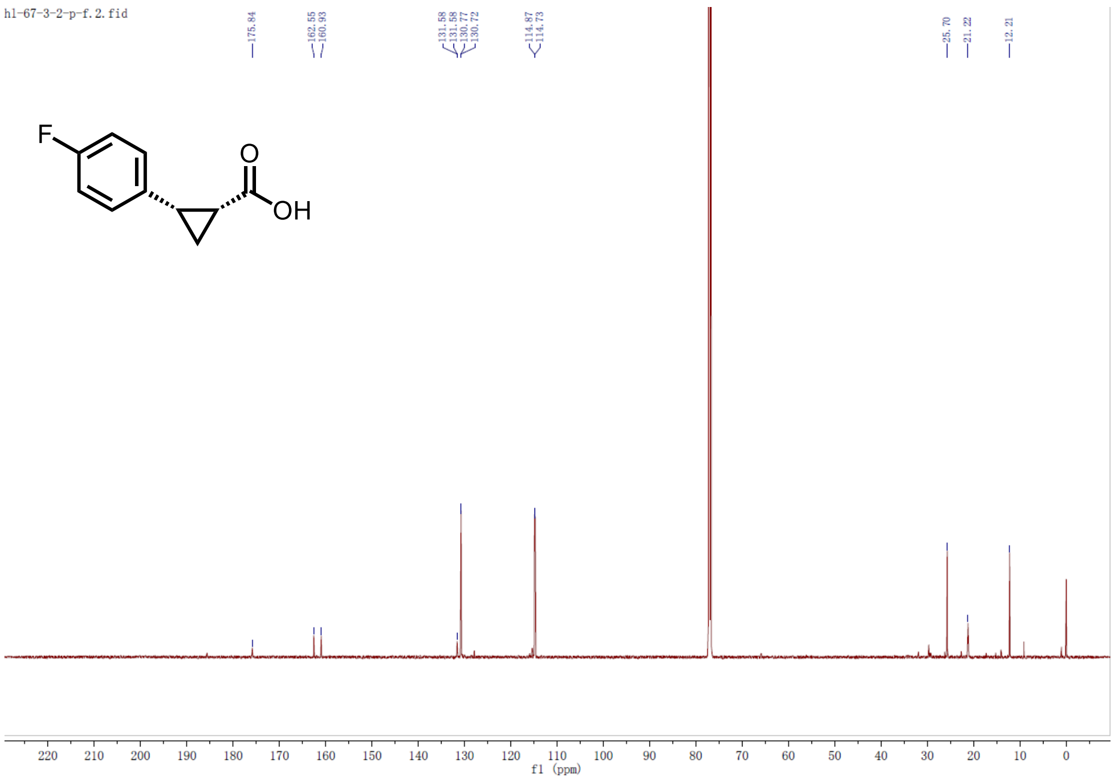
f1 (ppm)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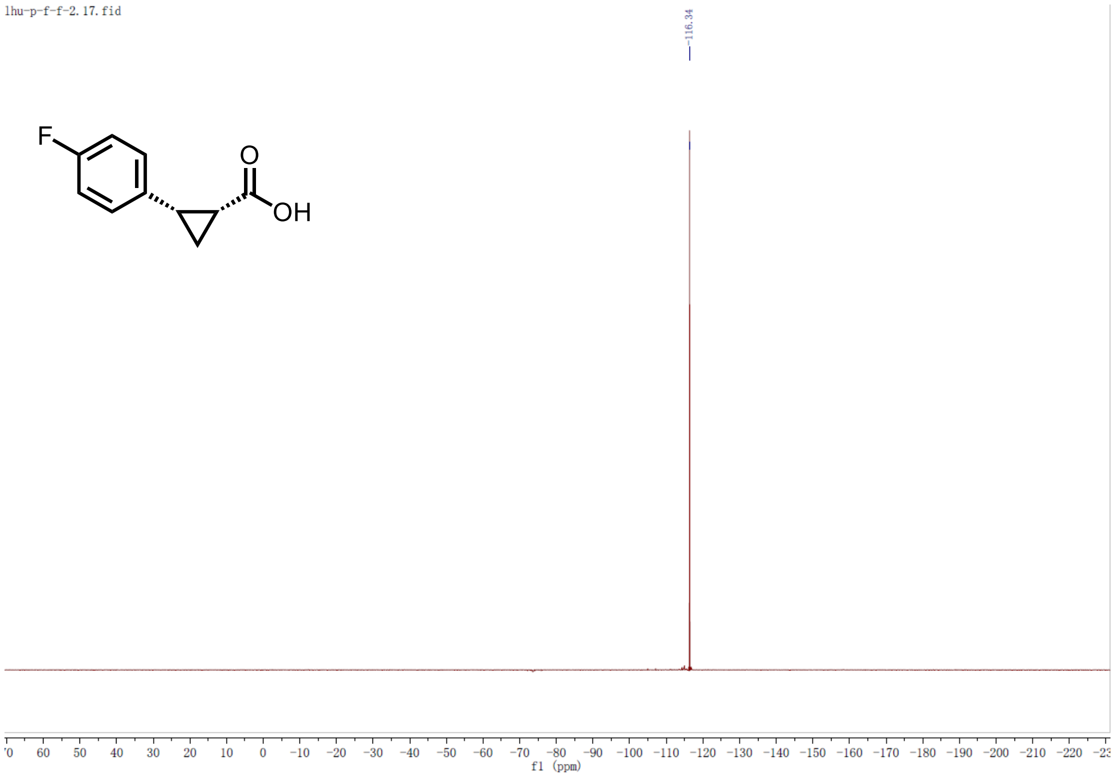
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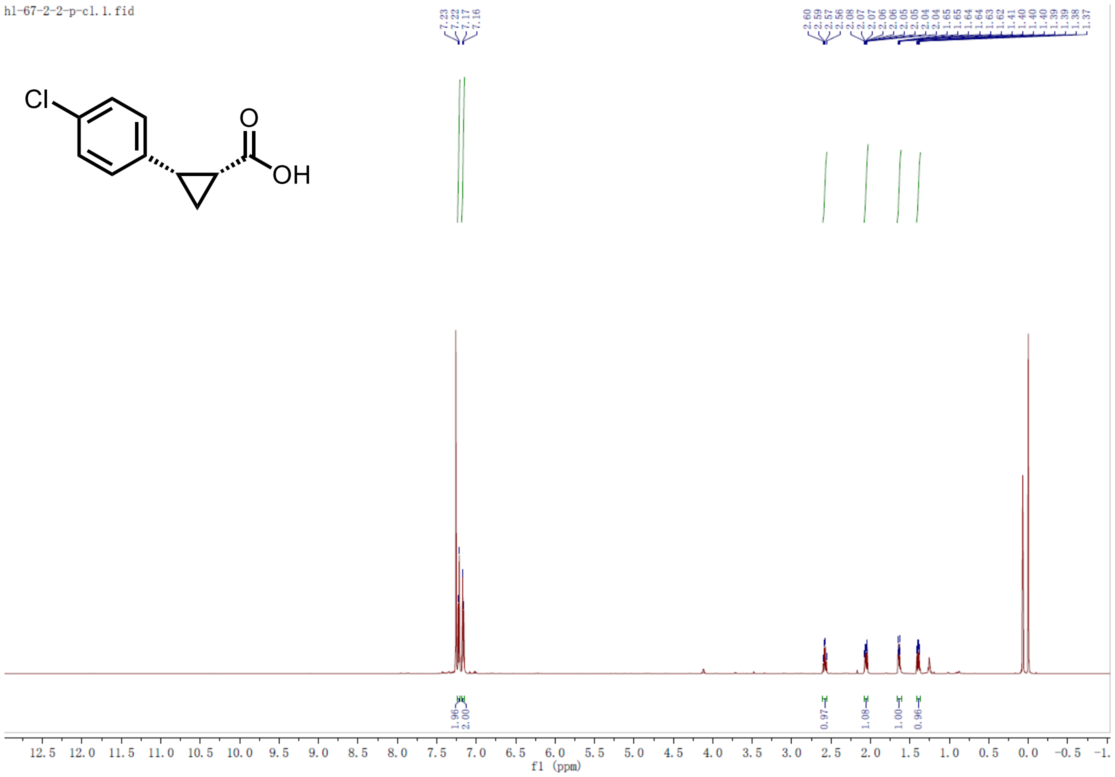
f1 (ppm)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1.38
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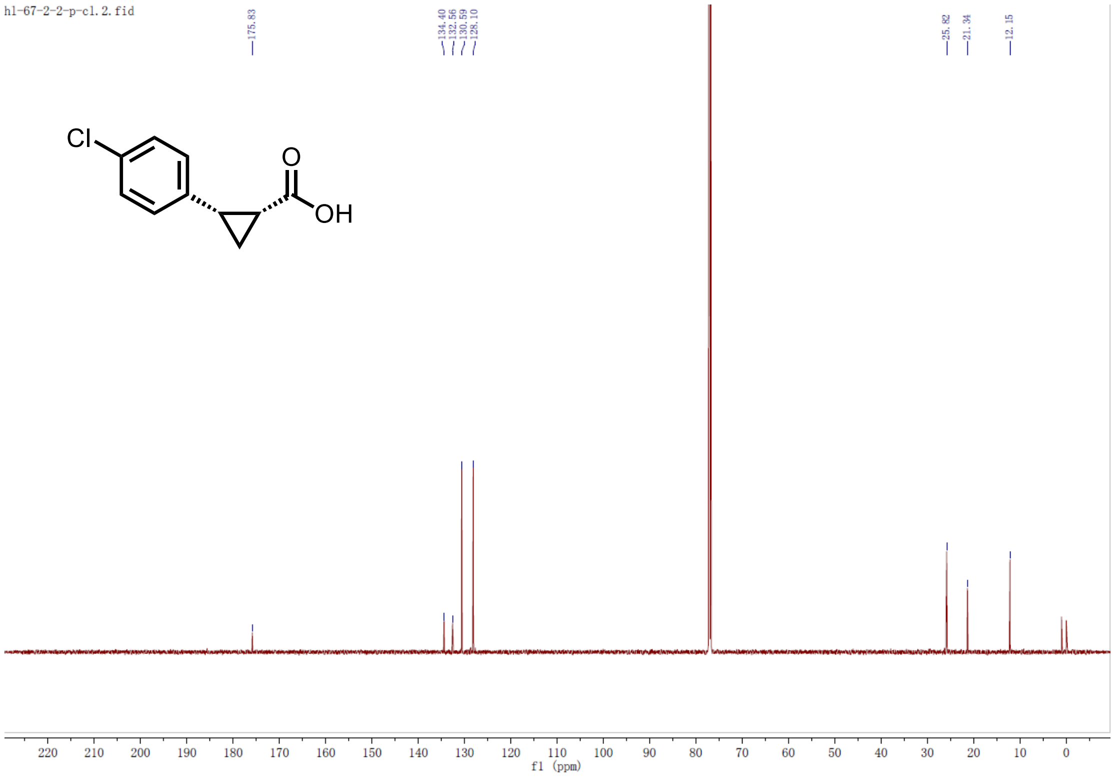
1.08
1.00
0.96
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)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12.15
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OH
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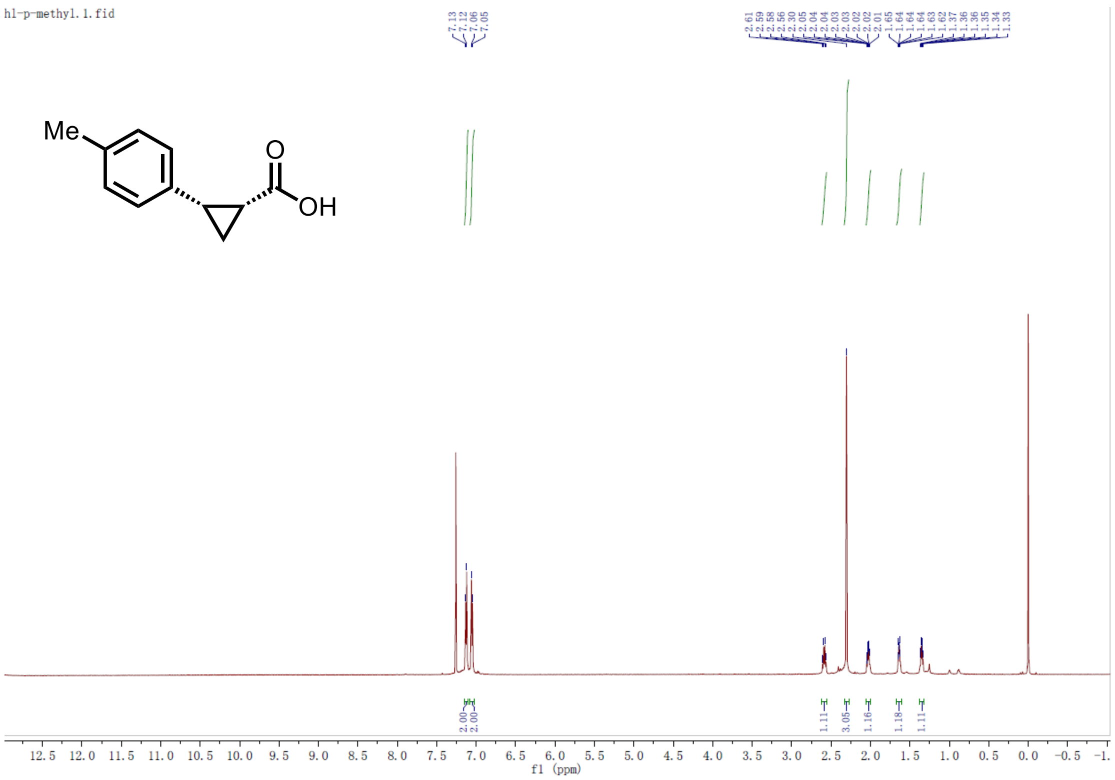
f1 (ppm)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1.33
Me
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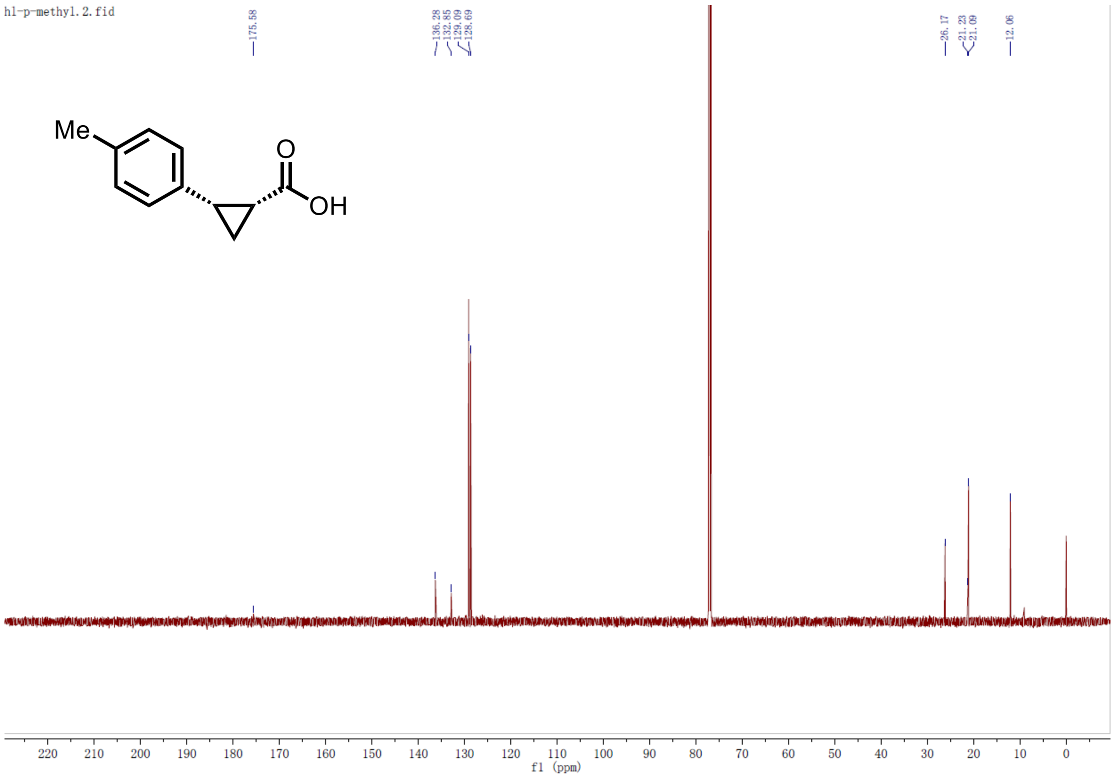
1.18
1.11
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)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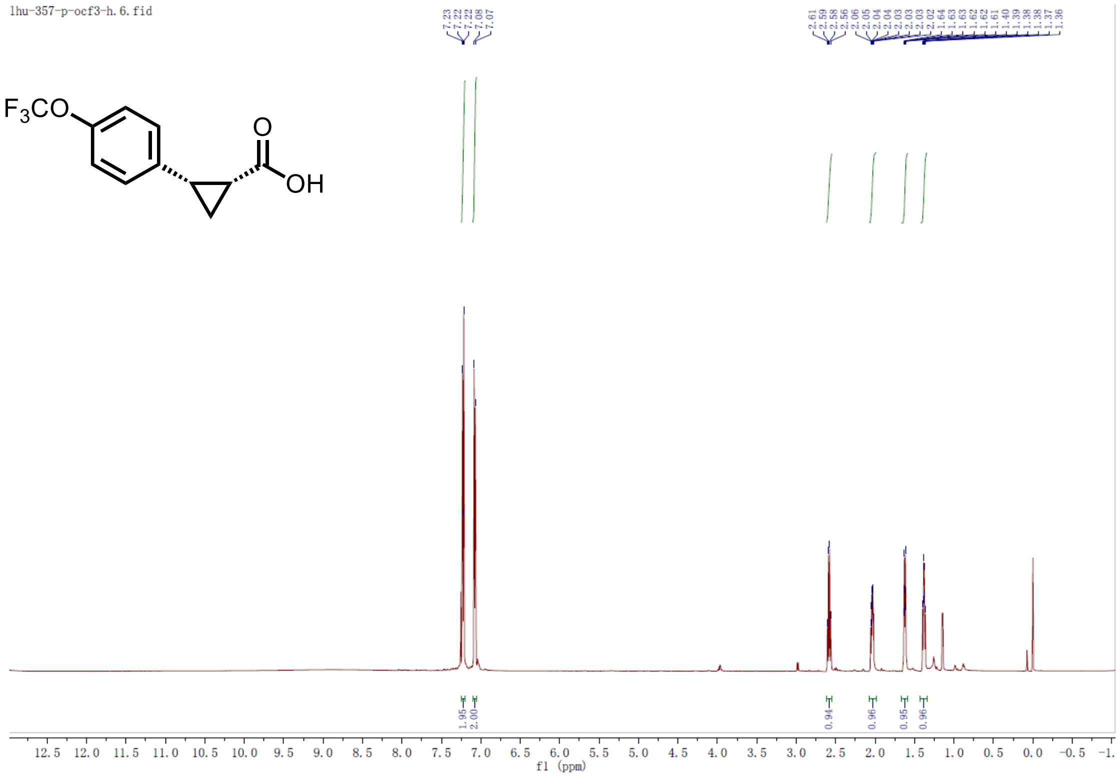
f1 (ppm)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1.62
1.61
1.40
1.39
1.38
1.38
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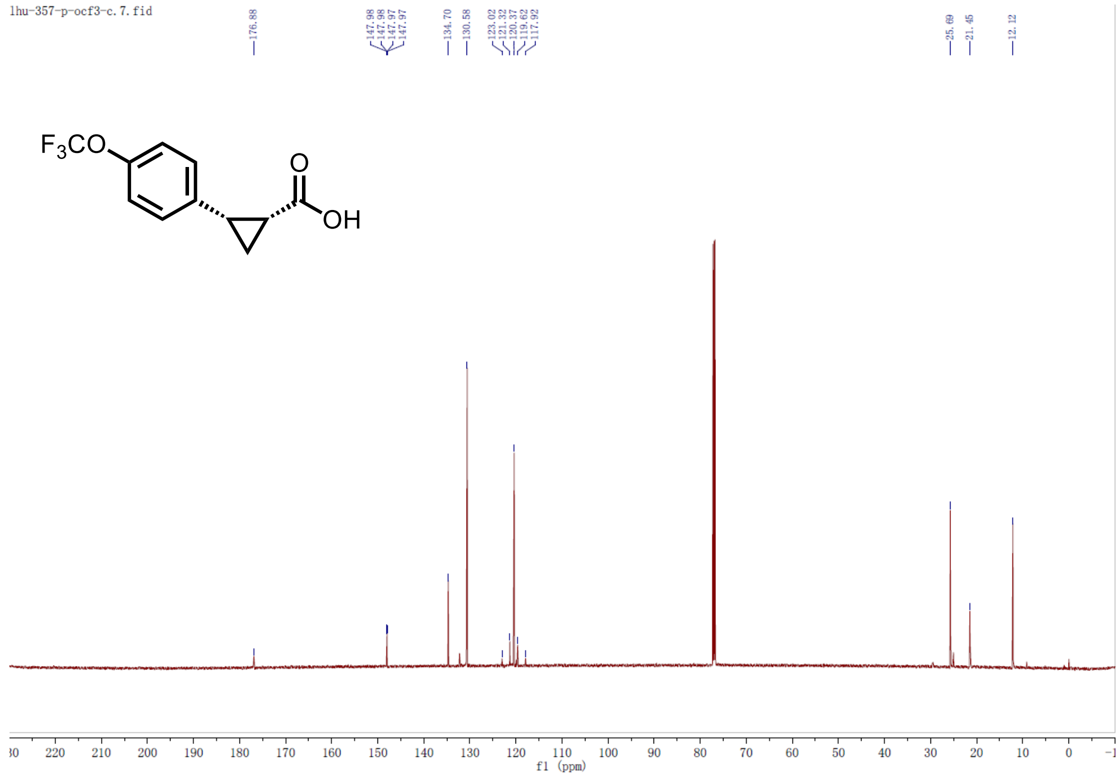
0.96
0.95
0.96
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)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147.97
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123.02
121.32
120.37
119.62
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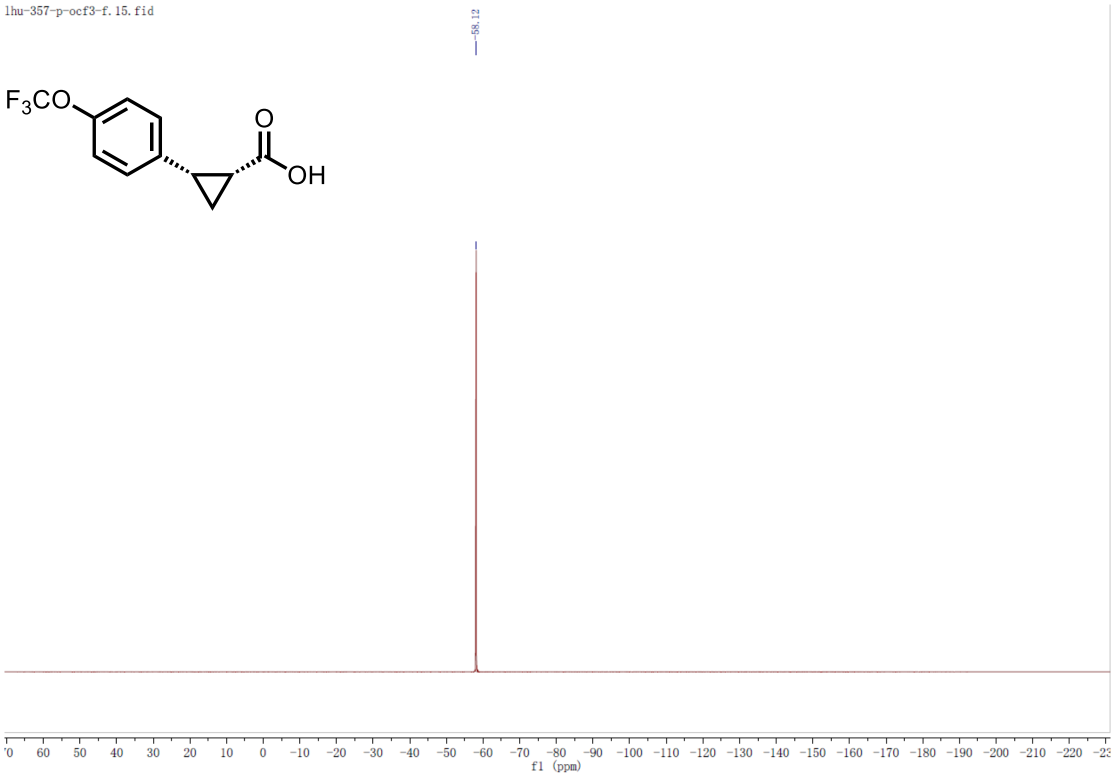
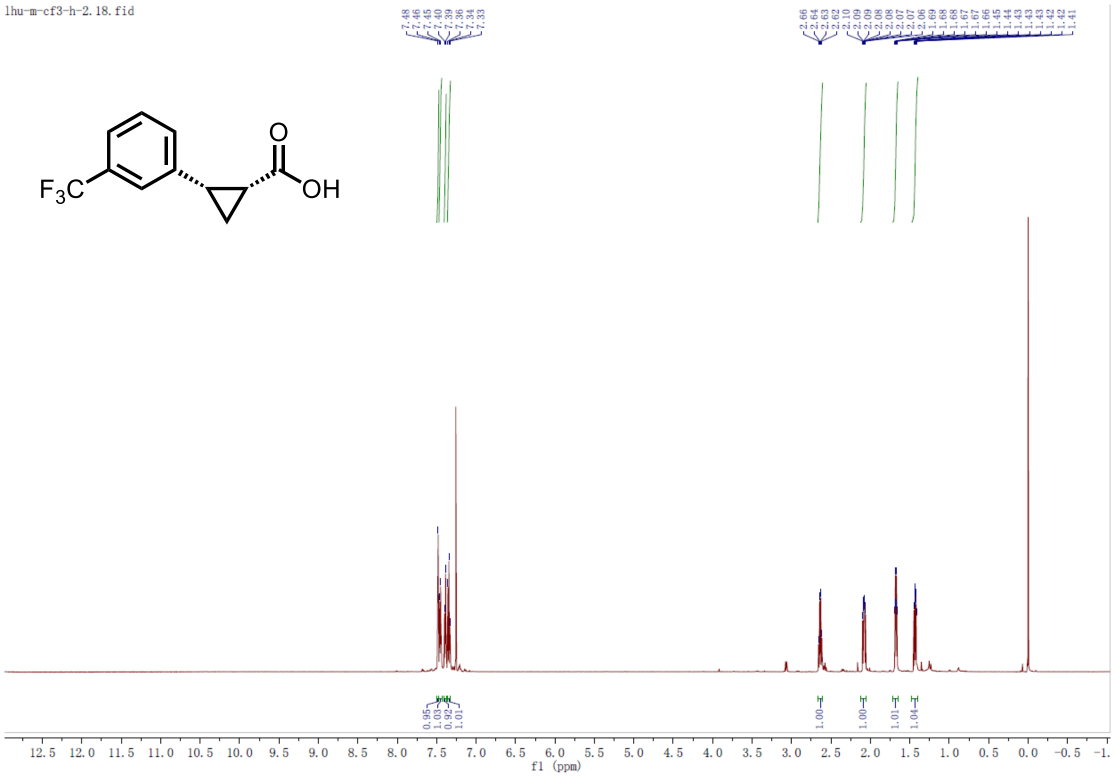
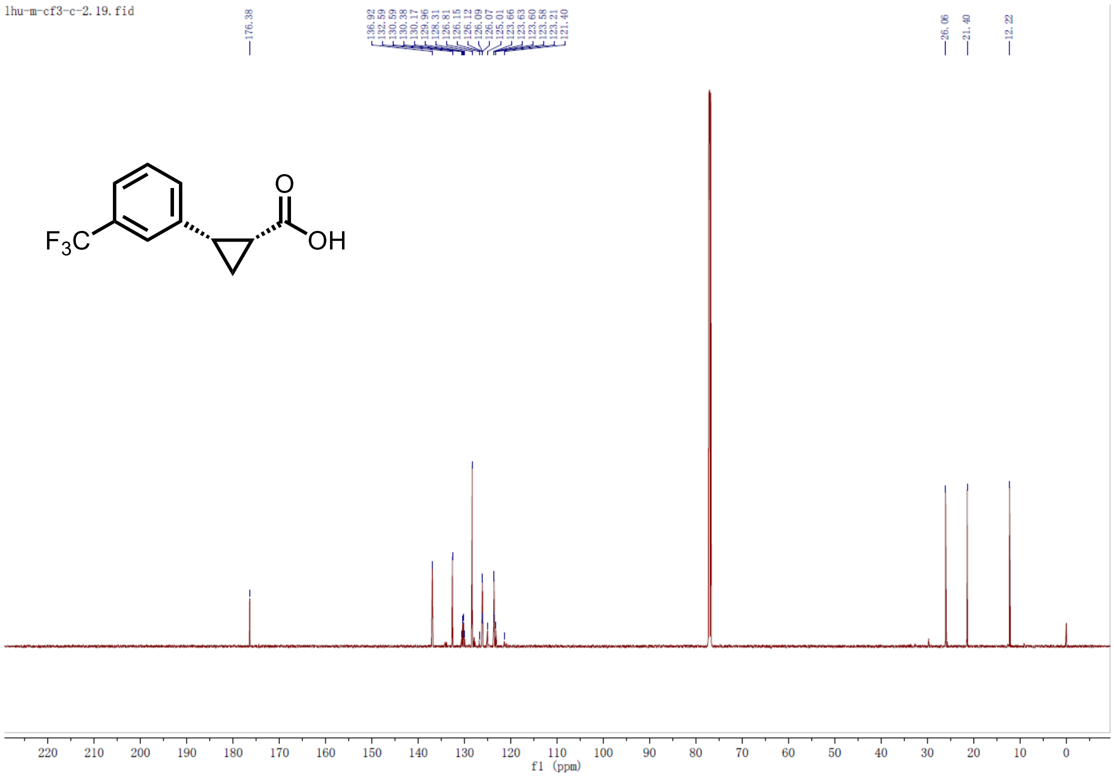
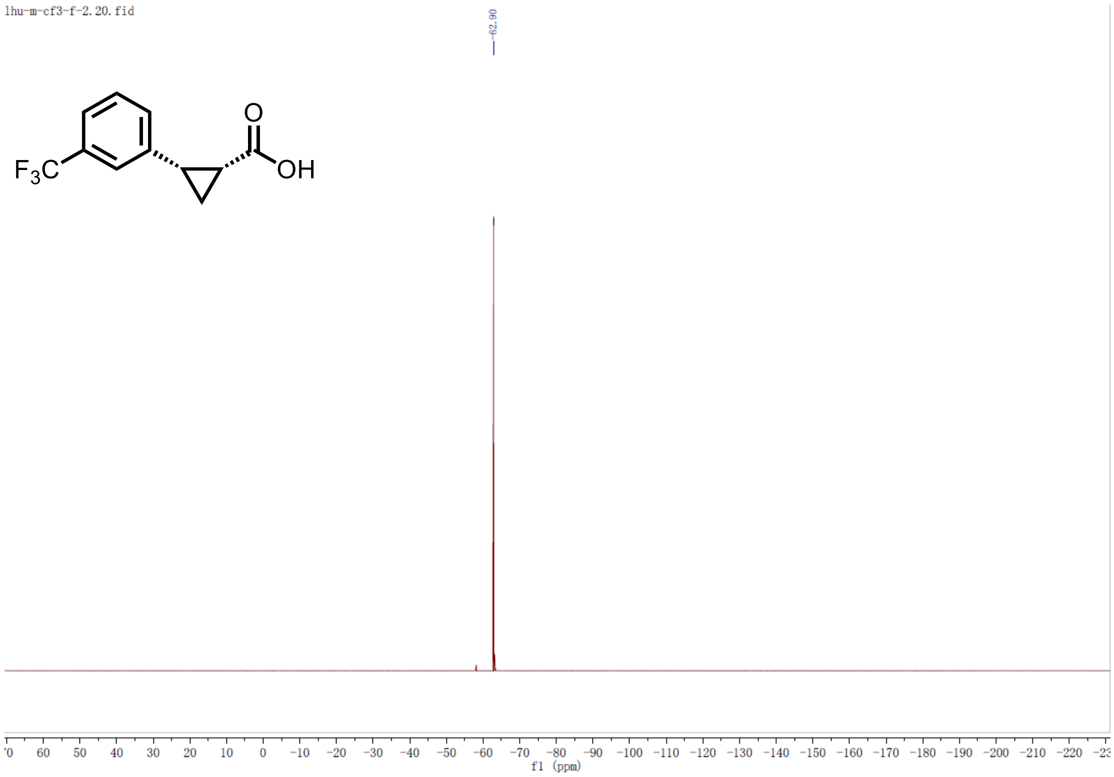
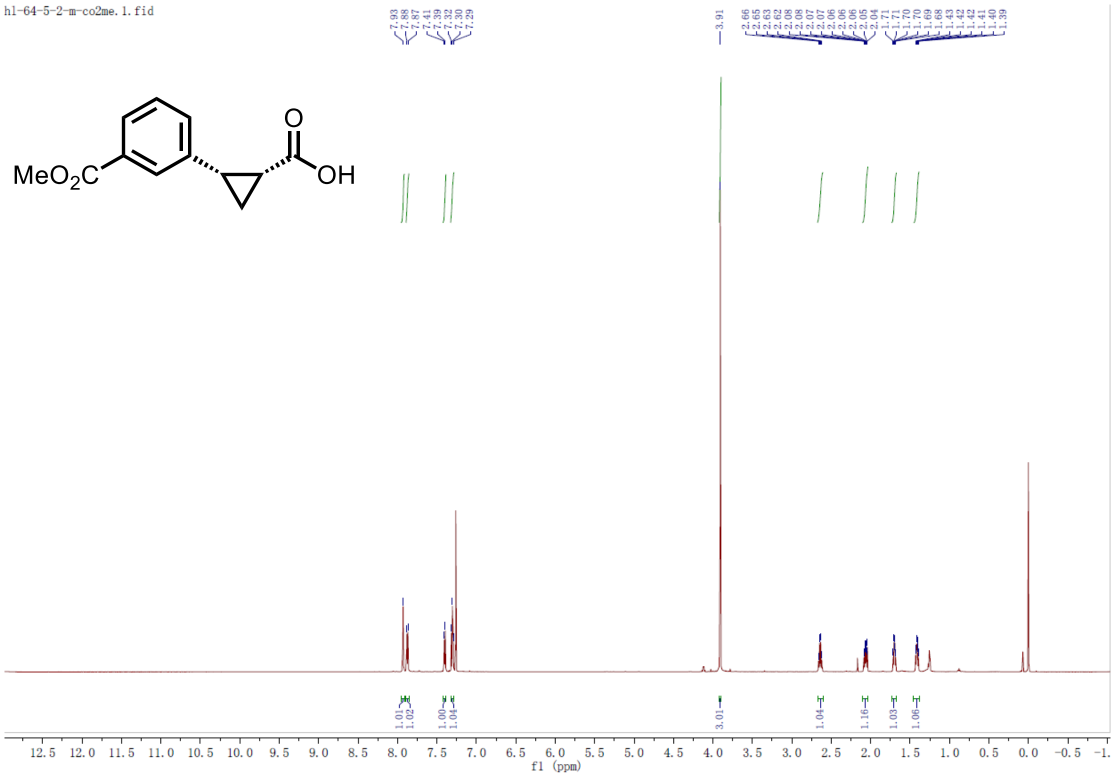
21.45
12.12
30 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

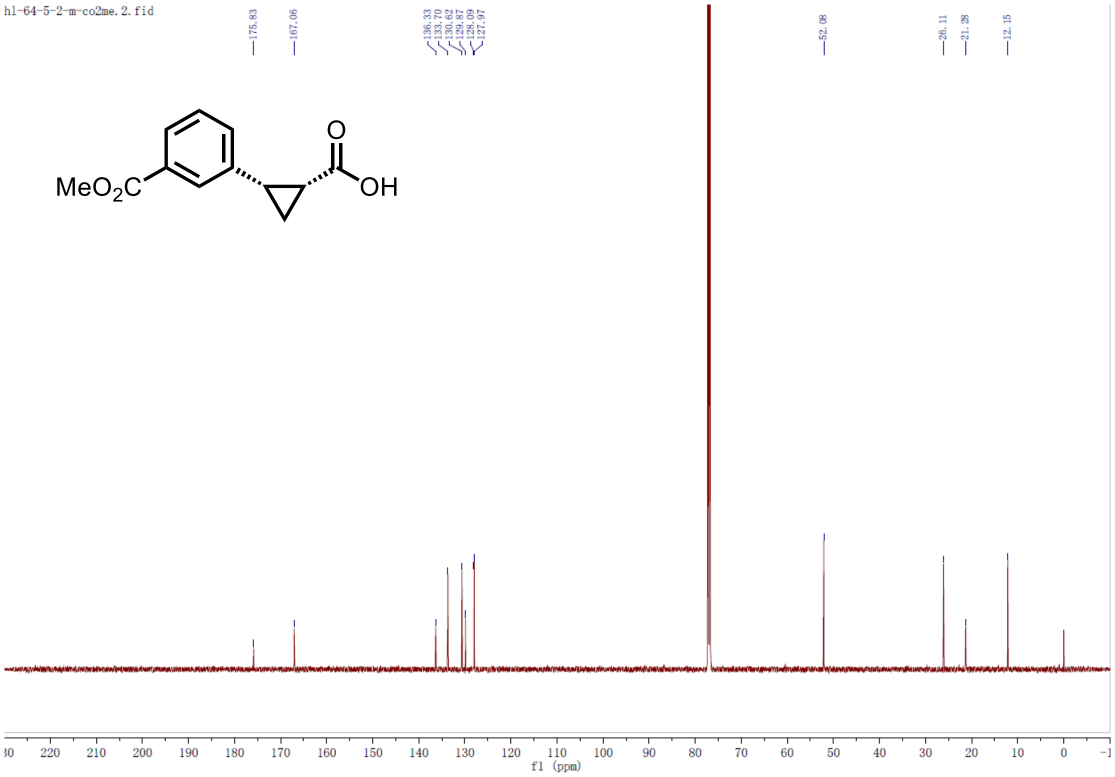

lhu-357-p-ocf3-f.15.fid
-58.12
F3CO
O
OH
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -23
f1 (ppm)

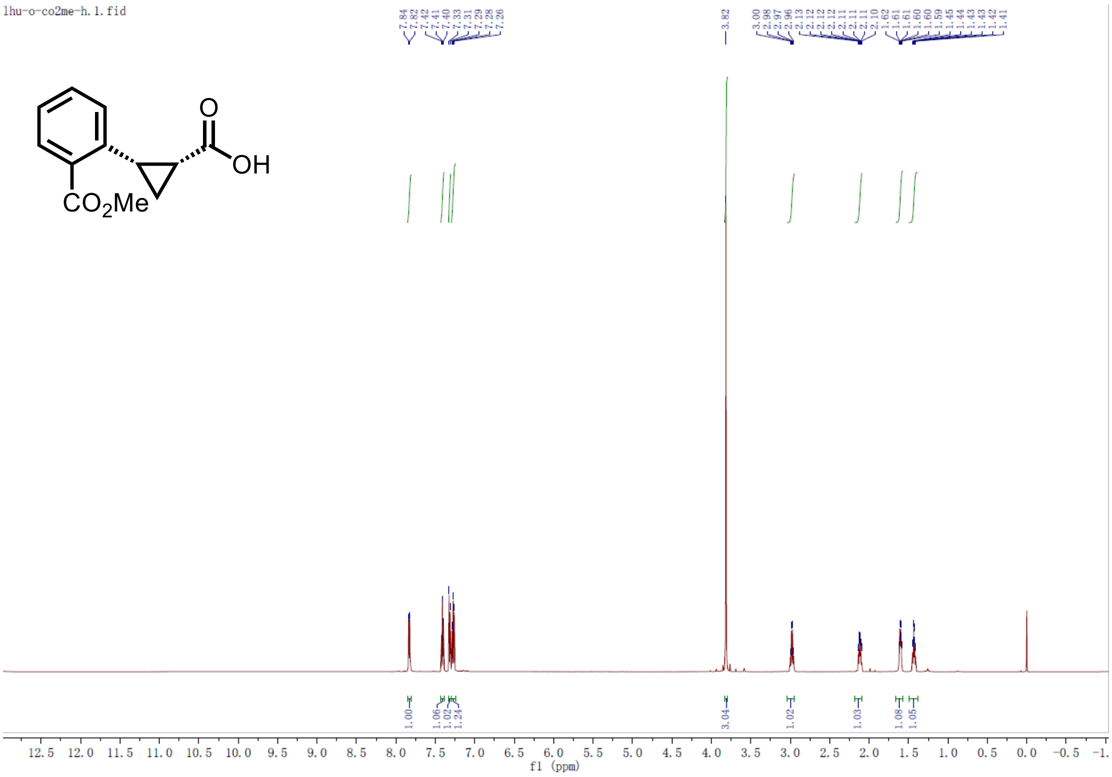

lhu-m-cf3-h-2.18.fid
7.48
7.46
7.45
7.40
7.39
7.36
7.34
7.33
2.66
2.64
2.63
2.62
2.10
2.09
2.09
2.08
2.08
2.07
2.07
2.06
1.69
1.68
1.68
1.67
1.67
1.66
1.45
1.44
1.43
1.43
1.43
1.42
1.42
1.41
F3C
O
OH
0.95
1.03
0.92
1.01
1.00
1.00
1.01
1.04
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

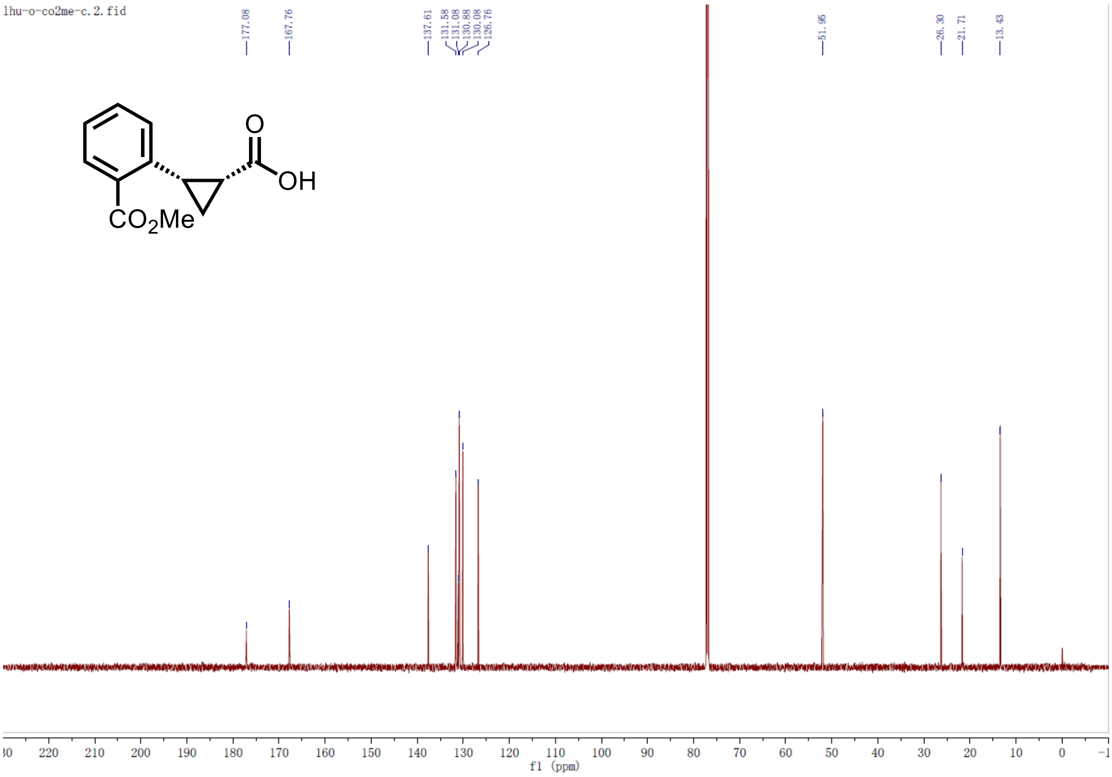

lhu-m-cf3-c-2.19.fid
176.38
136.92
132.59
130.59
130.38
130.17
129.96
128.31
126.81
126.15
126.12
126.09
126.07
125.01
123.66
123.63
123.60
123.58
123.21
121.40
26.06
21.40
12.22
F3C
O
OH
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

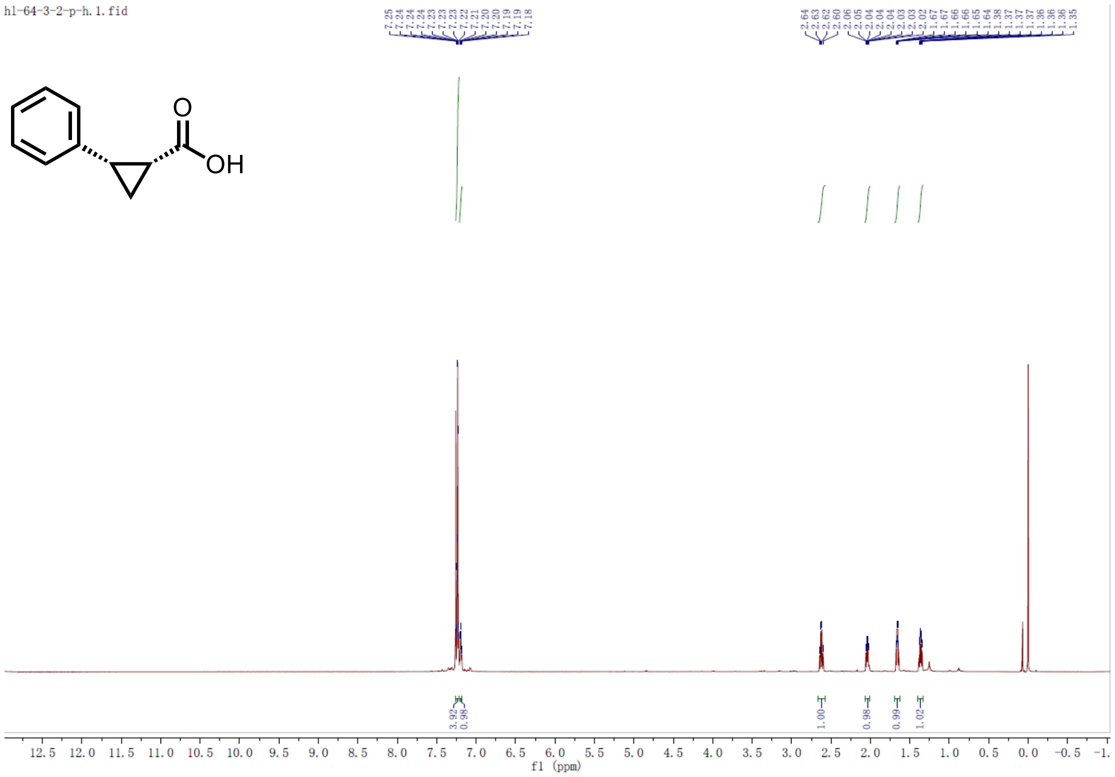

lhu-m-cf3-f-2.20.fid
-62.90
F3C
O
OH
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-23
f1 (ppm)

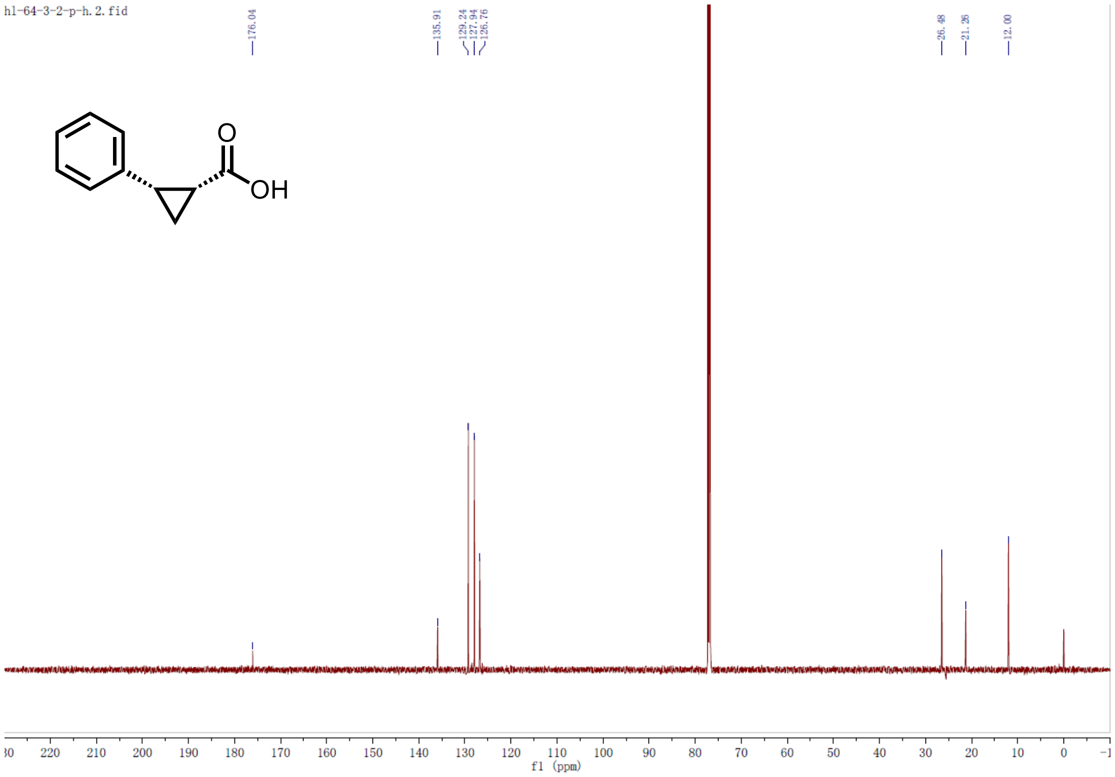

hl-64-5-2-m-co2me.1.fid
MeO$_2$C
O
OH
7.93
7.88
7.87
7.41
7.39
7.32
7.30
7.29
3.91
2.66
2.65
2.63
2.62
2.08
2.08
2.07
2.07
2.06
2.06
2.06
2.05
2.04
1.71
1.71
1.70
1.70
1.69
1.68
1.43
1.42
1.42
1.41
1.40
1.39
1.01
1.02
1.00
1.04
3.01
1.04
1.16
1.03
1.06
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.
f1 (ppm)

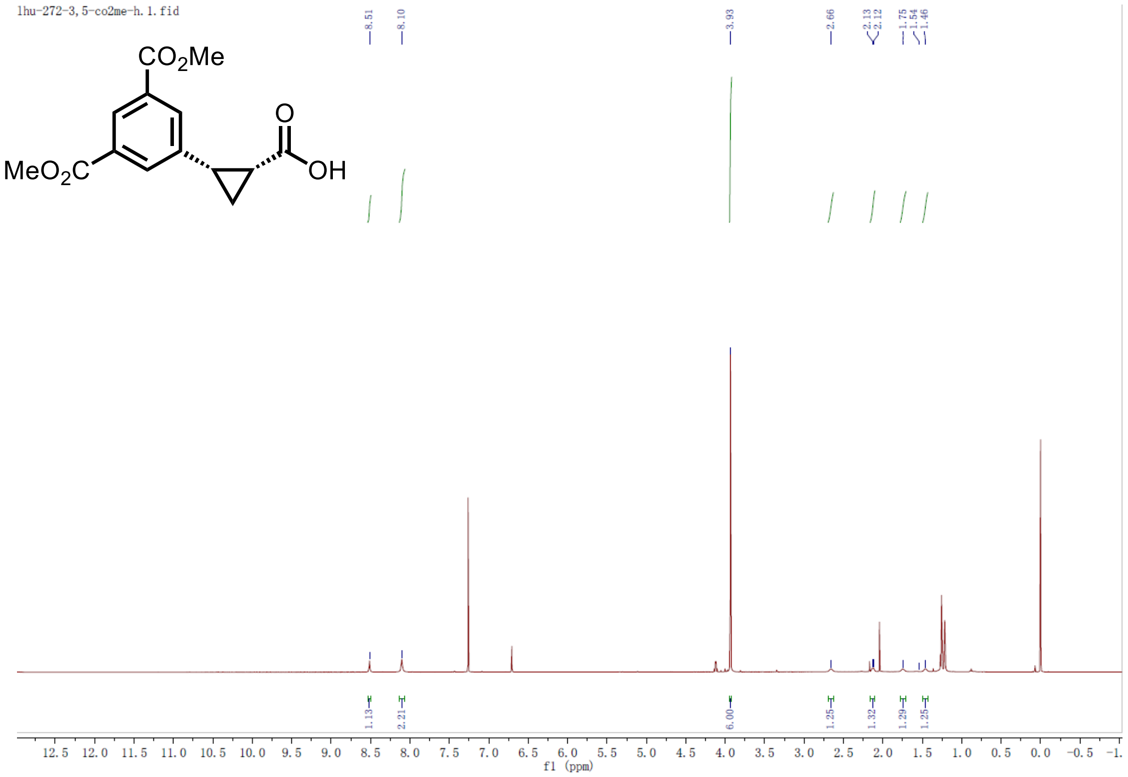

hl-64-5-2-m-co2me.2.fid
MeO$_2$C
O
OH
175.83
167.06
136.33
133.70
130.62
129.87
128.09
127.97
52.08
26.11
21.28
12.15
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

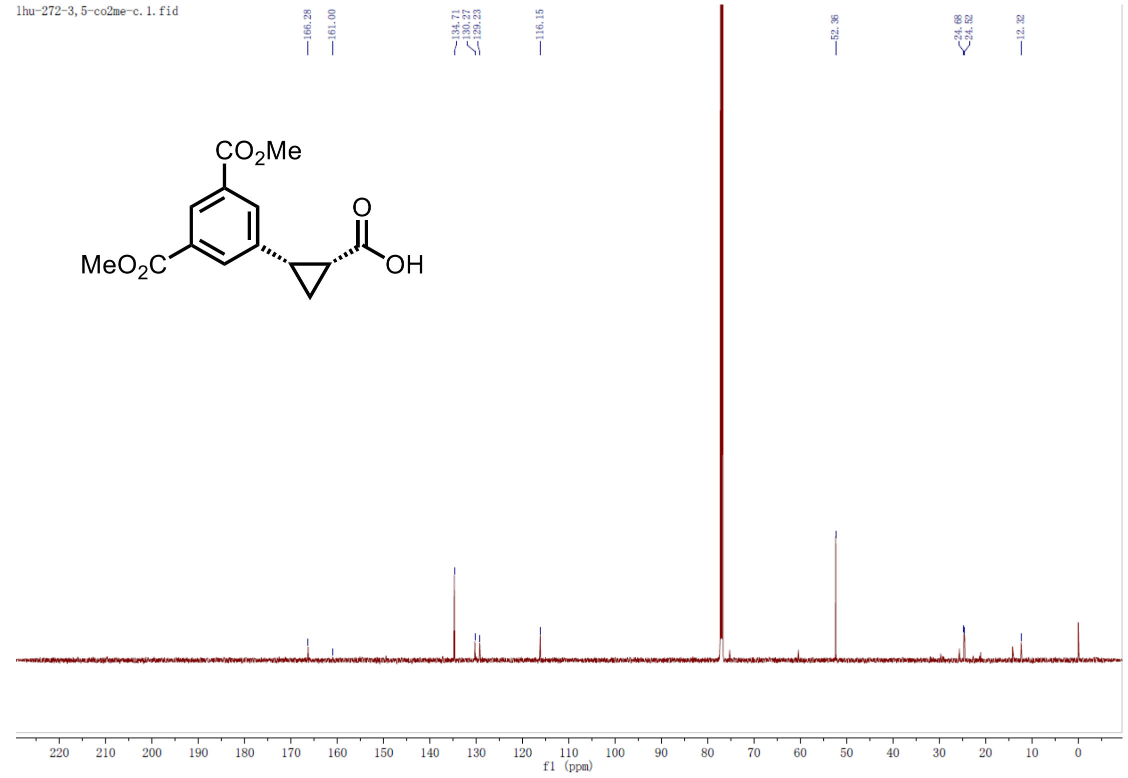

lhu-o-co2me-h.1.fid
CO2Me
O
OH
7.84
7.82
7.42
7.41
7.40
7.33
7.31
7.29
7.26
3.82
3.00
2.98
2.97
2.96
2.13
2.12
2.12
2.12
2.11
2.11
2.10
1.62
1.61
1.61
1.60
1.60
1.59
1.45
1.44
1.43
1.43
1.42
1.41
1.00
1.06
1.02
1.24
3.04
1.02
1.03
1.08
1.05
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

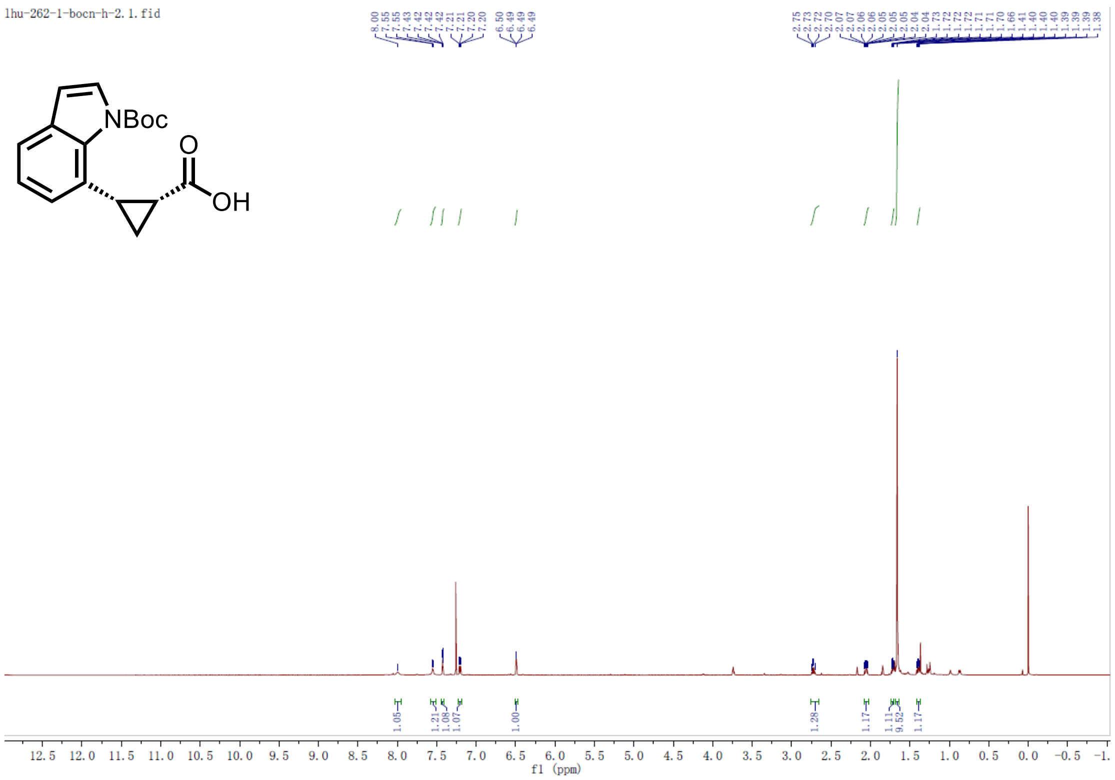

lhu-o-co2me-c.2.fid
CO2Me
O
OH
177.08
167.76
137.61
131.58
131.08
130.88
130.08
126.76
51.95
26.30
21.71
13.43
30 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

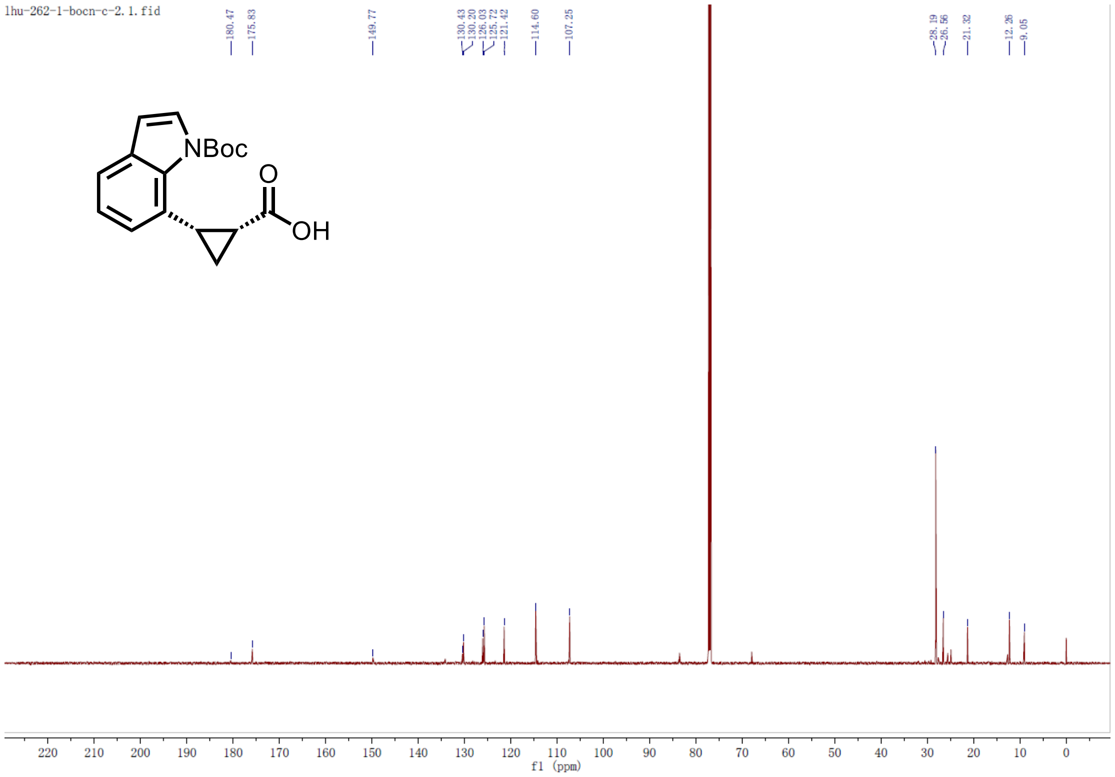

hl-64-3-2-p-h.1.fid
7.25
7.24
7.24
7.24
7.23
7.23
7.23
7.22
7.21
7.20
7.20
7.19
7.19
7.18
2.64
2.63
2.62
2.60
2.06
2.05
2.04
2.04
2.04
2.03
2.03
2.02
1.67
1.67
1.66
1.66
1.65
1.64
1.38
1.37
1.37
1.37
1.36
1.36
1.36
1.35
O
OH
3.92
0.98
1.00
0.98
0.99
1.02
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.
f1 (ppm)

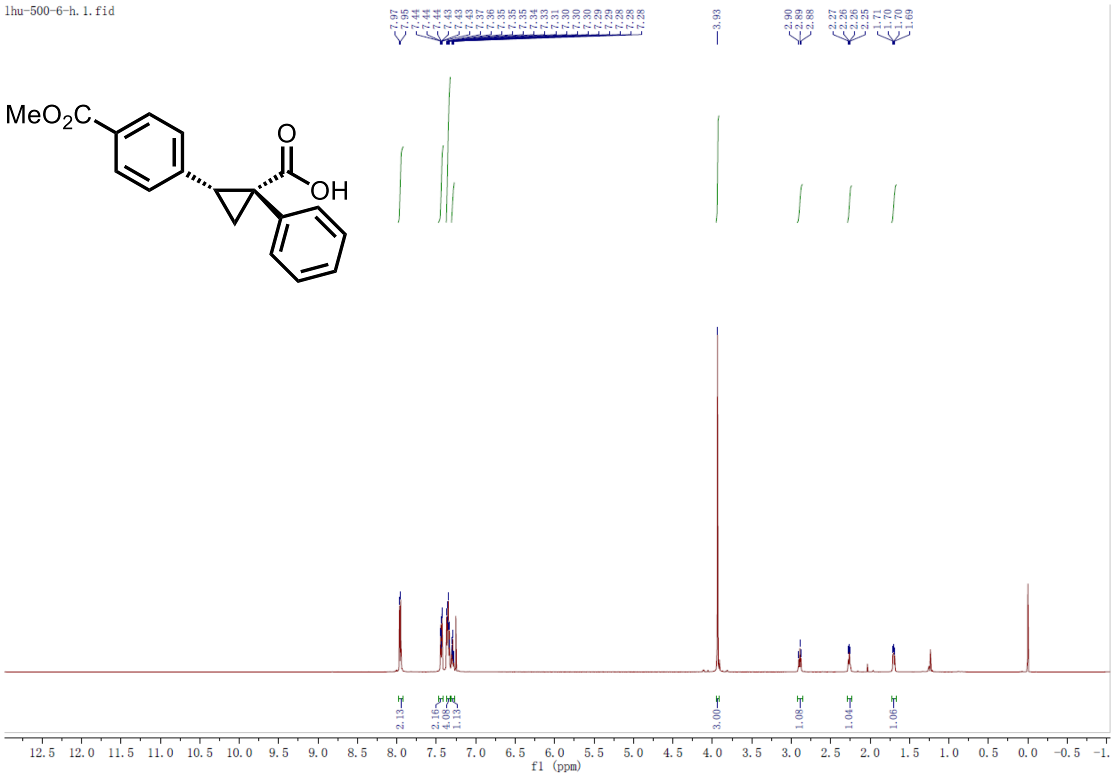

hl-64-3-2-p-h.2.fid
176.04
135.91
129.24
127.94
126.76
26.48
21.26
12.00
O
OH
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

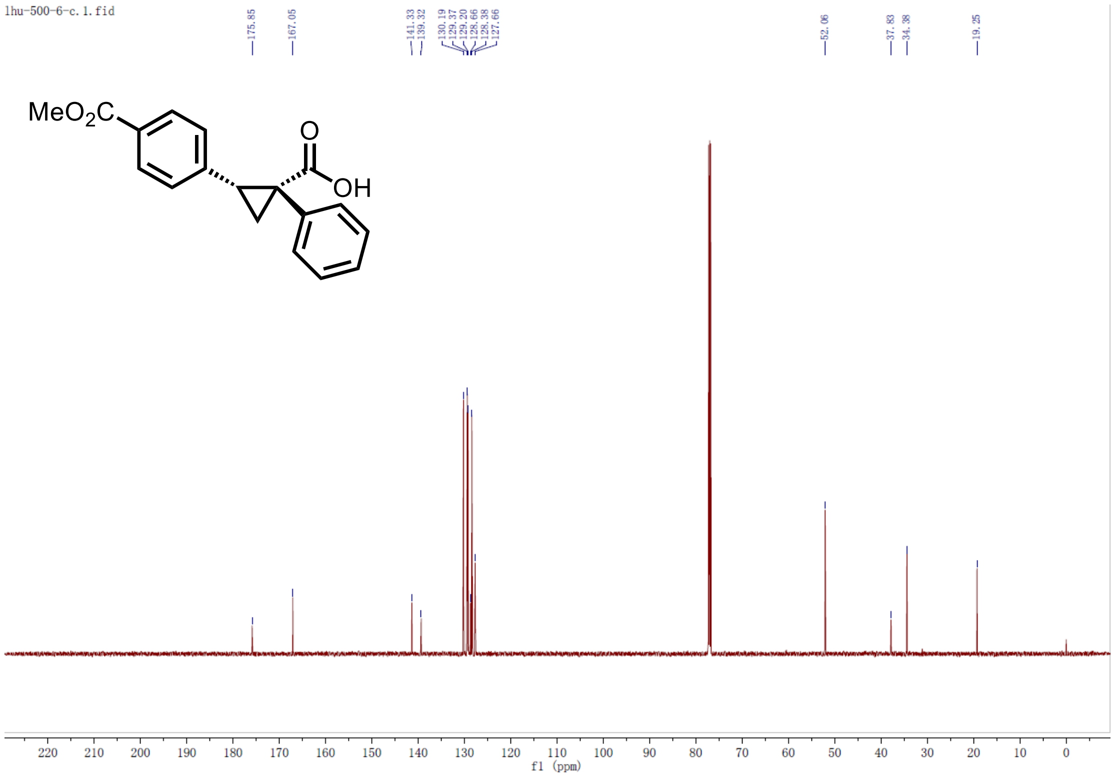

lhu-272-3,5-co2me-h.1.fid
CO2Me
MeO2C
O
OH
8.51
8.10
3.93
2.66
2.13
2.12
1.75
1.54
1.46
1.13
2.21
6.00
1.25
1.32
1.29
1.25
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

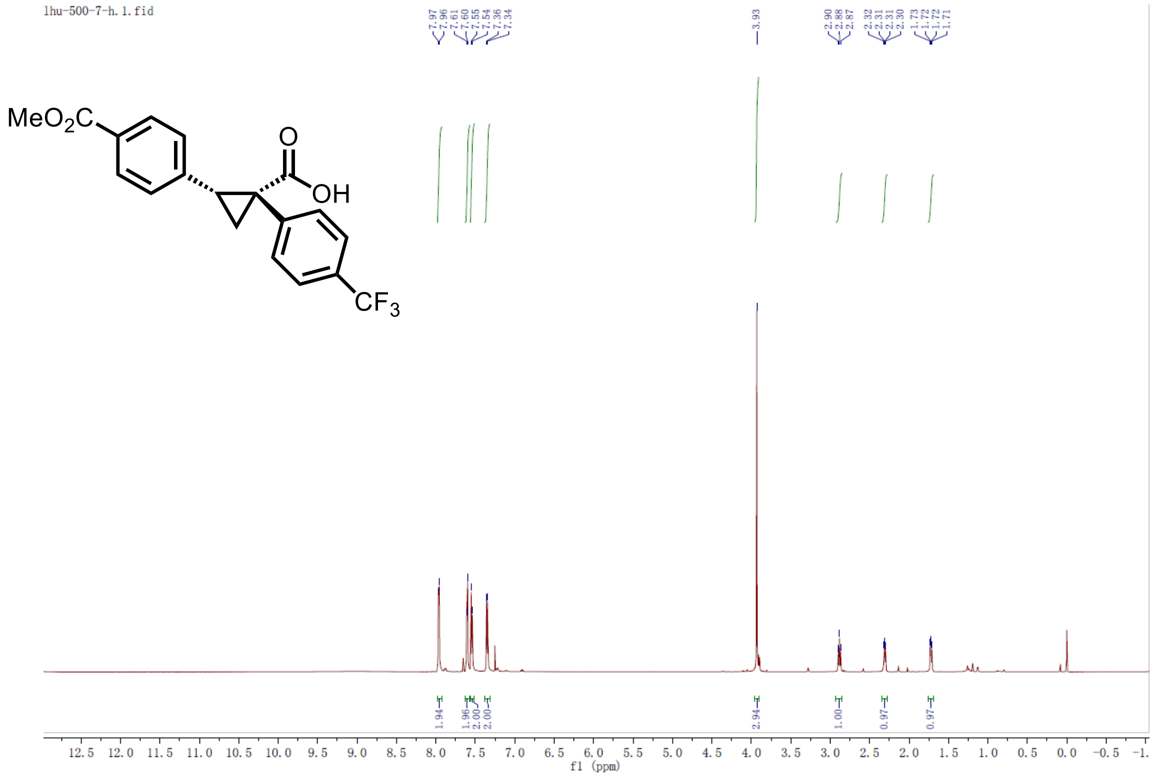

lhu-272-3,5-co2me-c.1.fid
166.28
161.00
134.71
130.27
129.23
116.15
52.36
24.68
24.52
12.32
CO2Me
MeO2C
O
OH
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

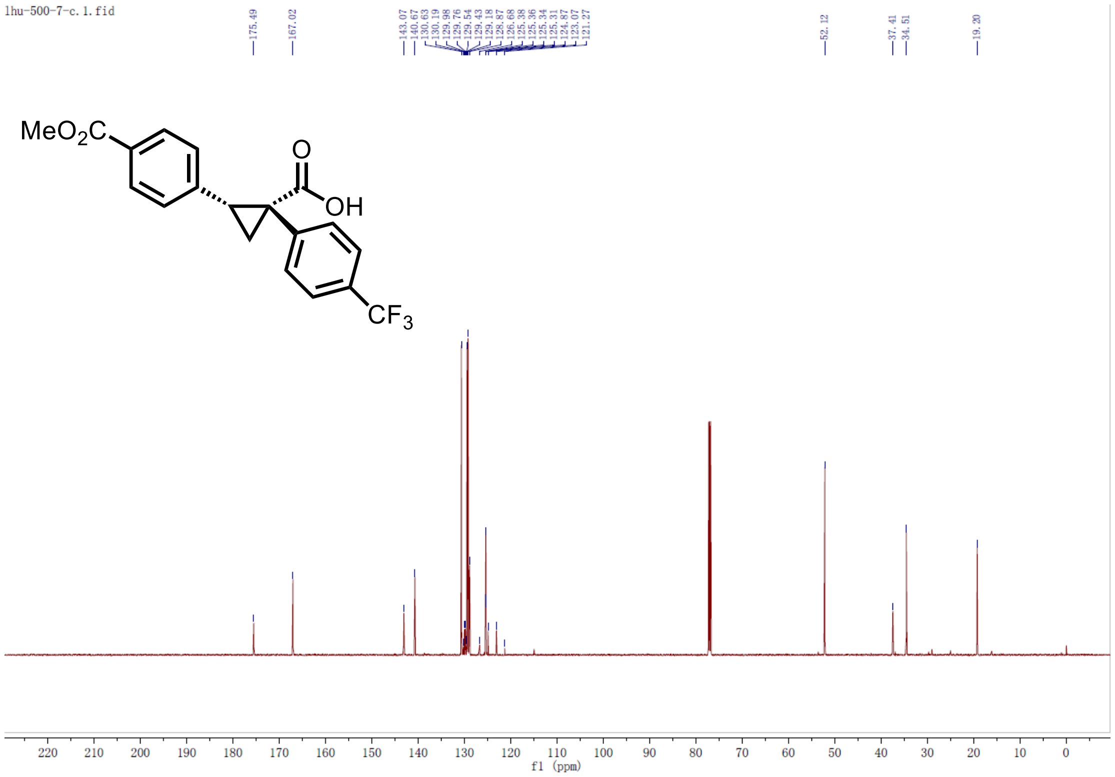

lhu-262-1-bocn-h-2.1.fid
NBoc
O
OH
8.00
7.55
7.55
7.43
7.42
7.42
7.42
7.21
7.21
7.20
7.20
6.50
6.49
6.49
6.49
2.75
2.73
2.72
2.70
2.07
2.07
2.06
2.06
2.05
2.05
2.05
2.04
2.04
1.73
1.72
1.72
1.72
1.71
1.71
1.70
1.66
1.41
1.40
1.40
1.40
1.39
1.39
1.39
1.38
1.05
1.21
1.08
1.07
1.00
1.28
1.17
1.11
9.52
1.17
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

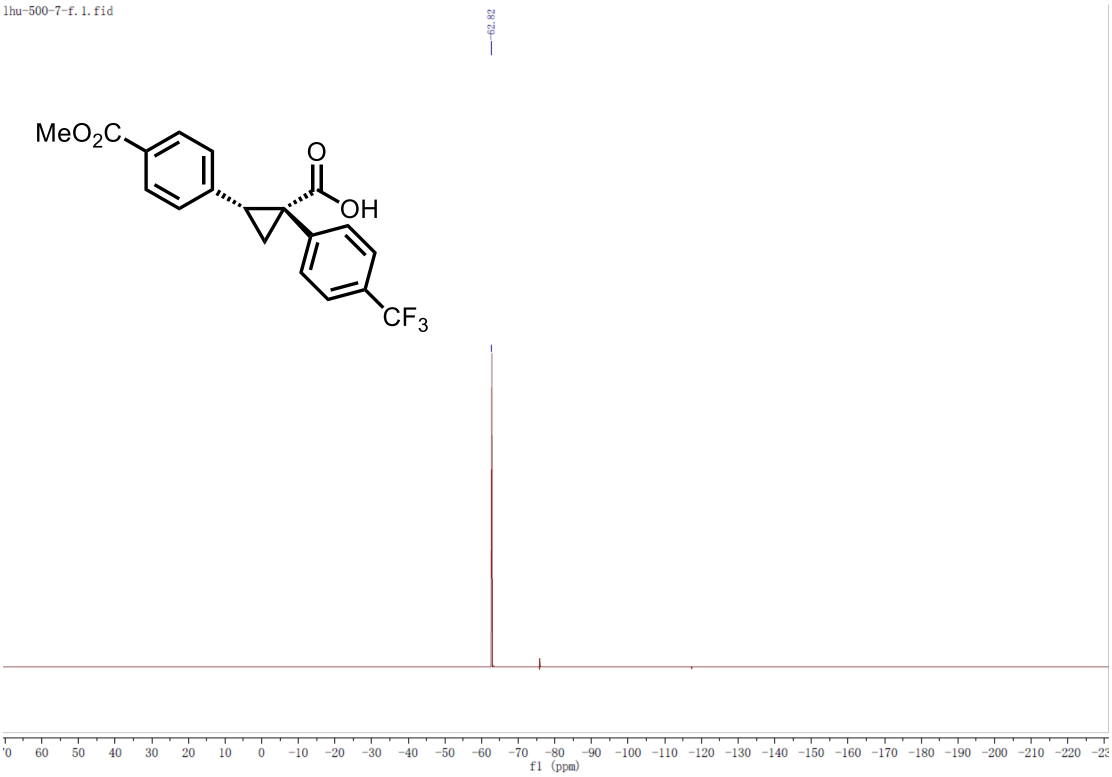

lhu-262-1-bocn-c-2.1.fid
NBoc
O
OH
180.47
175.83
149.77
130.43
130.20
126.03
125.72
121.42
114.60
107.25
28.19
26.56
21.32
12.26
9.05
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

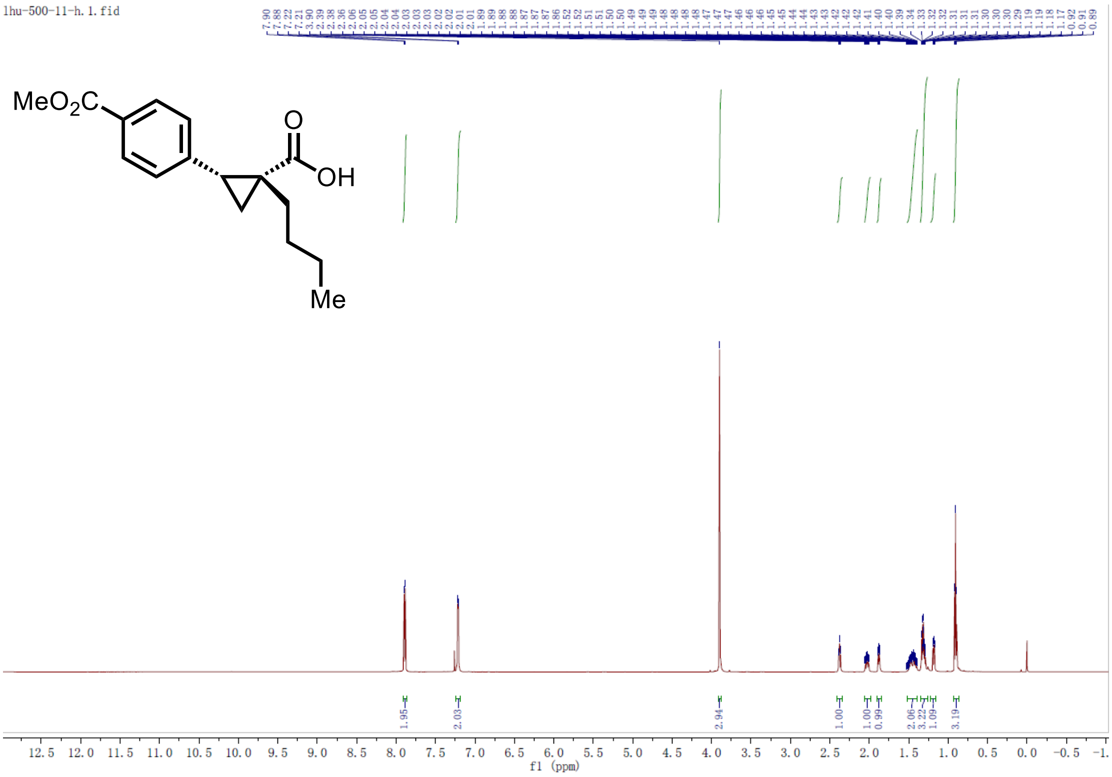

lhu-500-6-h.1.fid
7.97
7.95
7.44
7.44
7.44
7.43
7.43
7.43
7.37
7.36
7.35
7.35
7.35
7.34
7.33
7.31
7.30
7.30
7.30
7.29
7.29
7.28
7.28
7.28
3.93
2.90
2.89
2.88
2.27
2.26
2.26
2.25
1.71
1.70
1.70
1.69
MeO2C
O
OH
2.13
2.16
4.08
1.13
3.00
1.08
1.04
1.06
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

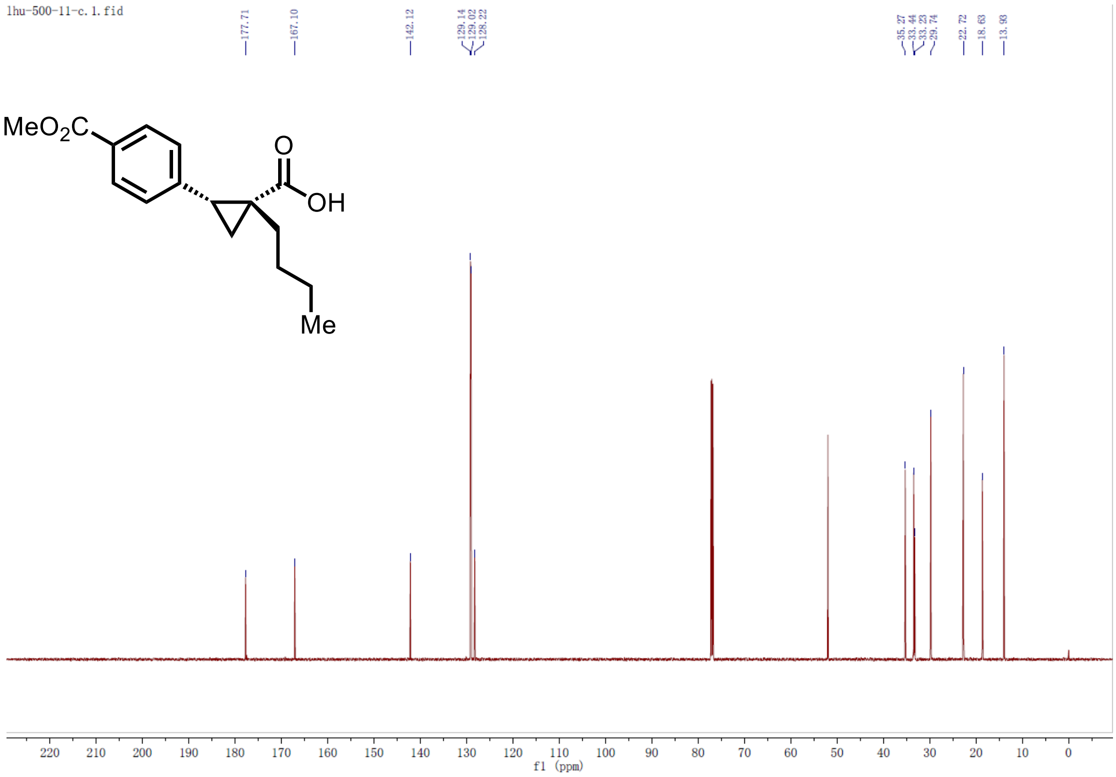

lhu-500-6-c.1.fid
175.85
167.05
141.33
139.32
130.19
129.37
129.20
128.66
128.38
127.66
52.06
37.83
34.38
19.25
MeO2C
O
OH
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

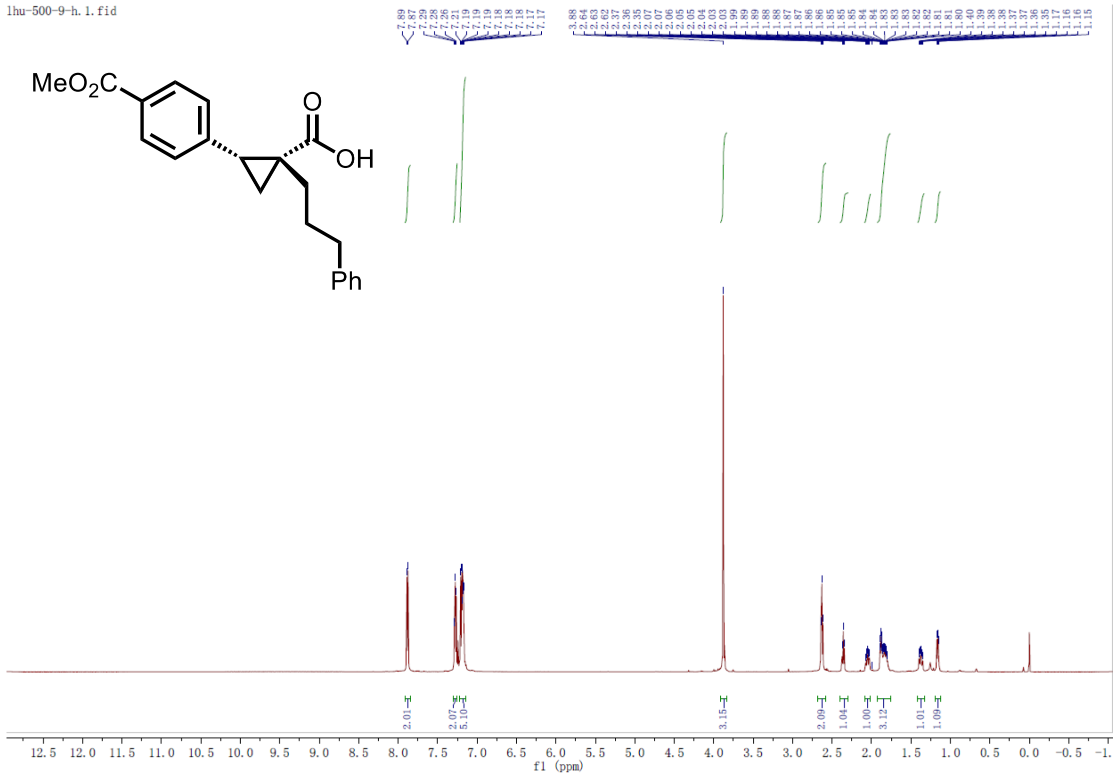

lhu-500-7-h.1.fid
7.97
7.96
7.61
7.60
7.55
7.54
7.36
7.34
3.93
2.90
2.88
2.87
2.32
2.31
2.31
2.30
1.73
1.72
1.72
1.71
MeO2C
O
OH
CF3
1.94
1.96
2.00
2.00
2.94
1.00
0.97
0.97
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

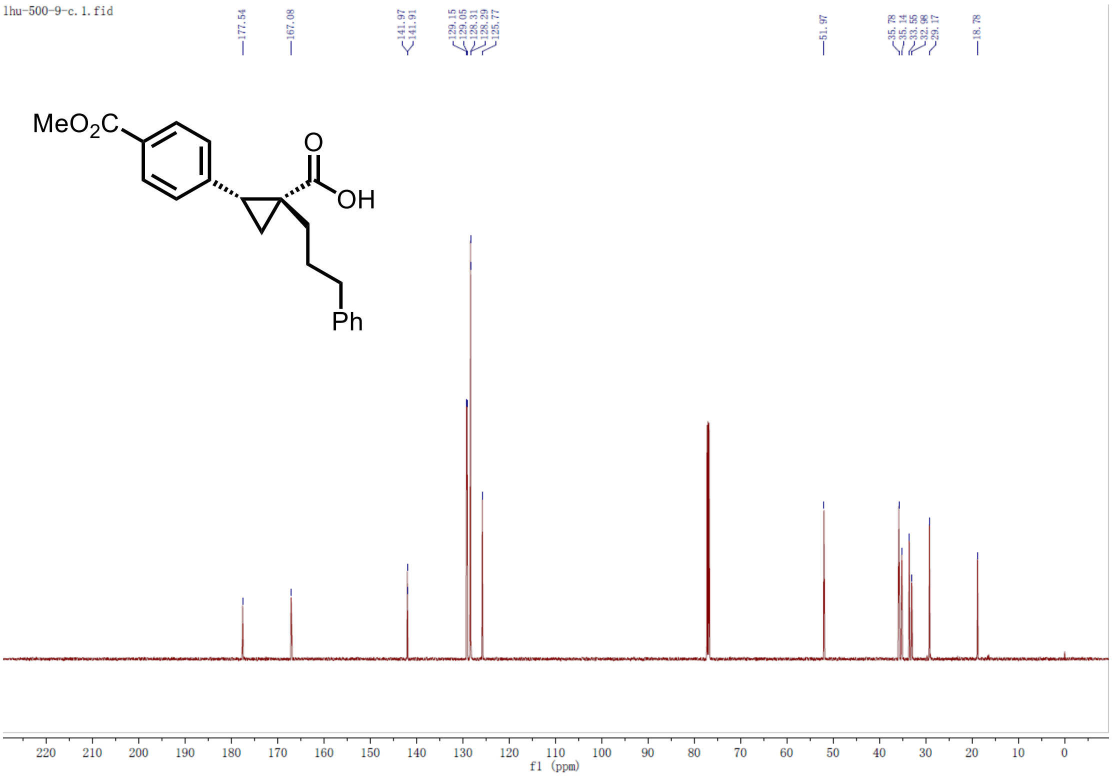

lhu-500-7-c.1.fid
175.49
167.02
143.07
140.67
130.63
130.19
129.98
129.76
129.54
129.43
129.18
128.87
126.68
125.38
125.36
125.34
125.31
124.87
123.07
121.27
52.12
37.41
34.51
19.20
MeO2C
O
OH
CF3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

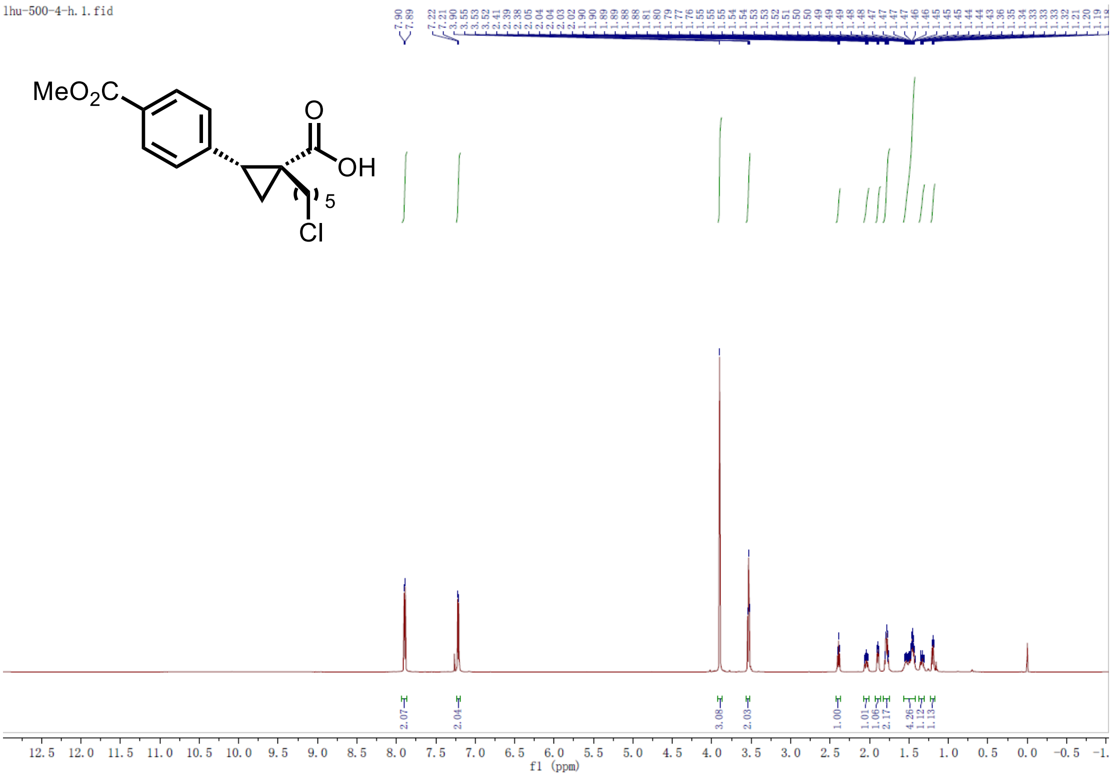

lhu-500-7-f.1.fid
-62.82
MeO$_2$C
O
OH
CF$_3$
'0 60 50 40 30 20 10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210 −220 −23
f1 (ppm)

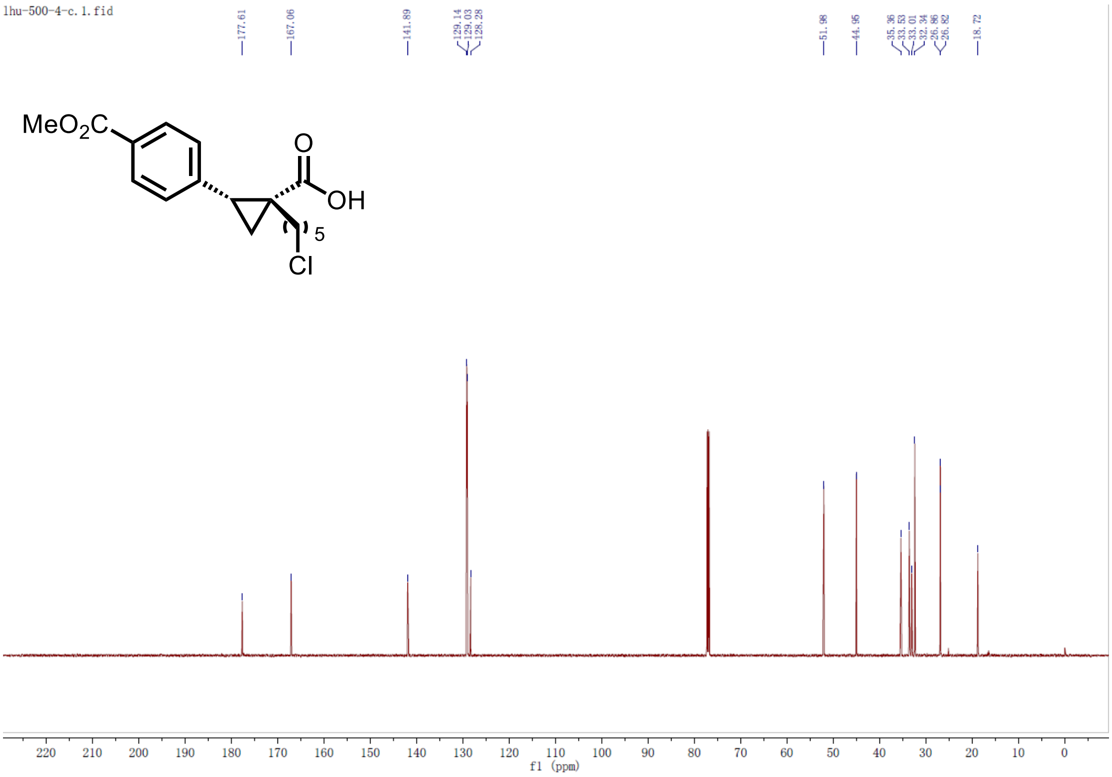

lhu-500-11-h.1.fid
7.90 7.88 7.22 7.21 3.90 2.39 2.38 2.36 2.06 2.05 2.05 2.04 2.04 2.03 2.03 2.03 2.02 2.02 2.01 2.01 1.89 1.89 1.88 1.88 1.87 1.87 1.87 1.86 1.52 1.52 1.51 1.51 1.50 1.50 1.49 1.49 1.49 1.48 1.48 1.48 1.48 1.47 1.47 1.47 1.46 1.46 1.46 1.45 1.45 1.44 1.44 1.43 1.43 1.42 1.42 1.42 1.41 1.40 1.40 1.39 1.34 1.33 1.32 1.32 1.31 1.31 1.31 1.30 1.30 1.30 1.29 1.19 1.19 1.18 1.17 0.92 0.91 0.89
MeO$_2$C
O
OH
Me
1.95
2.03
2.94
1.00
1.00
0.99
2.06
3.22
1.09
3.19
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.
f1 (ppm)


lhu-500-11-c.1.fid
177.71
167.10
142.12
129.14
129.02
128.22
35.27
33.44
33.23
29.74
22.72
18.63
13.93
MeO2C
O
OH
Me
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


lhu-500-9-h.1.fid
7.89 7.87 7.29 7.28 7.26 7.21 7.19 7.19 7.19 7.18 7.18 7.18 7.17 7.17
3.88 2.64 2.63 2.62 2.37 2.36 2.35 2.07 2.07 2.06 2.05 2.05 2.04 2.03 2.03 1.99 1.89 1.89 1.88 1.88 1.87 1.87 1.86 1.86 1.85 1.85 1.85 1.84 1.84 1.83 1.83 1.83 1.82 1.82 1.81 1.81 1.80 1.40 1.39 1.38 1.38 1.37 1.37 1.36 1.35 1.17 1.16 1.16 1.15
MeO2C
O
OH
Ph
2.01
2.07
5.10
3.15
2.09
1.04
1.00
3.12
1.01
1.09
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)


lhu-500-9-c.1.fid
177.54
167.08
141.97
141.91
129.15
129.05
128.31
128.29
125.77
51.97
35.78
35.14
33.55
32.98
29.17
18.78
MeO2C
O
OH
Ph
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


lhu-500-4-h.1.fid
7.90
7.89
7.22
7.21
3.90
3.55
3.53
3.52
2.41
2.39
2.38
2.05
2.04
2.03
2.02
1.90
1.90
1.89
1.89
1.88
1.88
1.81
1.80
1.79
1.77
1.76
1.55
1.55
1.55
1.54
1.54
1.53
1.53
1.52
1.51
1.50
1.50
1.49
1.49
1.49
1.48
1.48
1.47
1.47
1.47
1.47
1.46
1.46
1.45
1.45
1.45
1.44
1.44
1.43
1.36
1.35
1.34
1.33
1.33
1.33
1.32
1.21
1.20
1.19
1.1
MeO2C
O
OH
5
Cl
2.07
2.04
3.08
2.03
1.00
1.01
1.06
2.17
4.26
1.12
1.13
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)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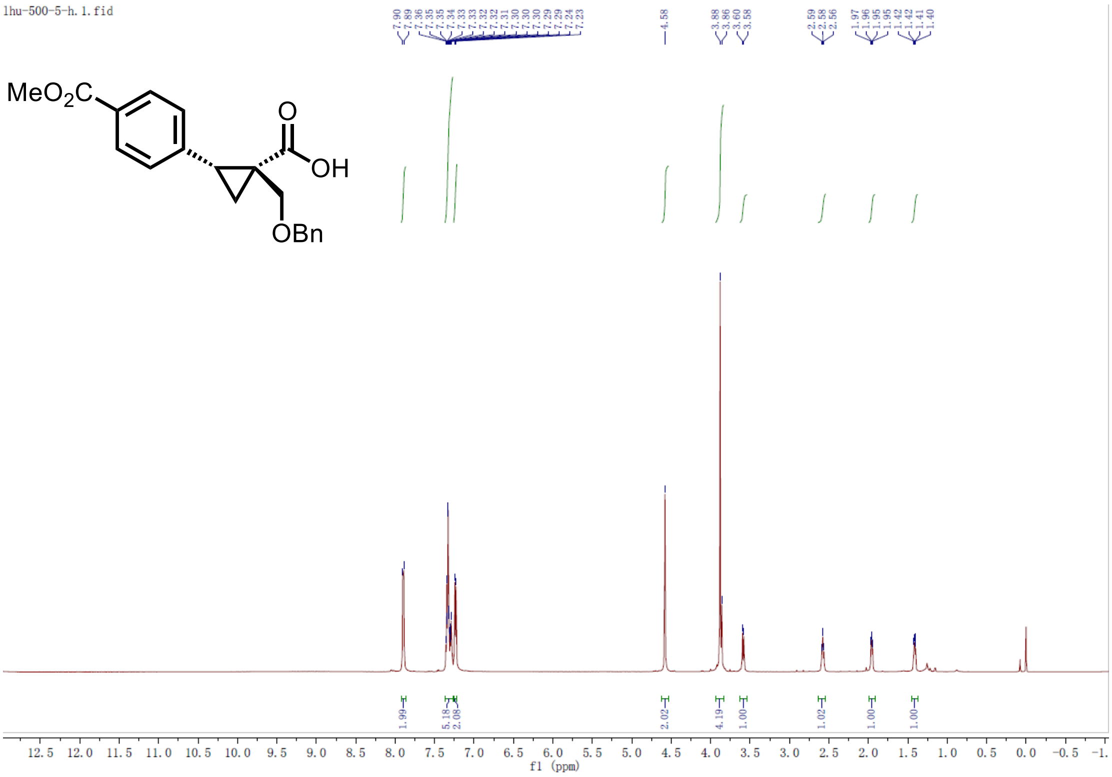
167.06
141.89
129.14
129.03
128.28
51.98
44.95
35.36
33.53
33.01
32.94
26.86
26.82
18.72
MeO2C
O
OH
5
Cl
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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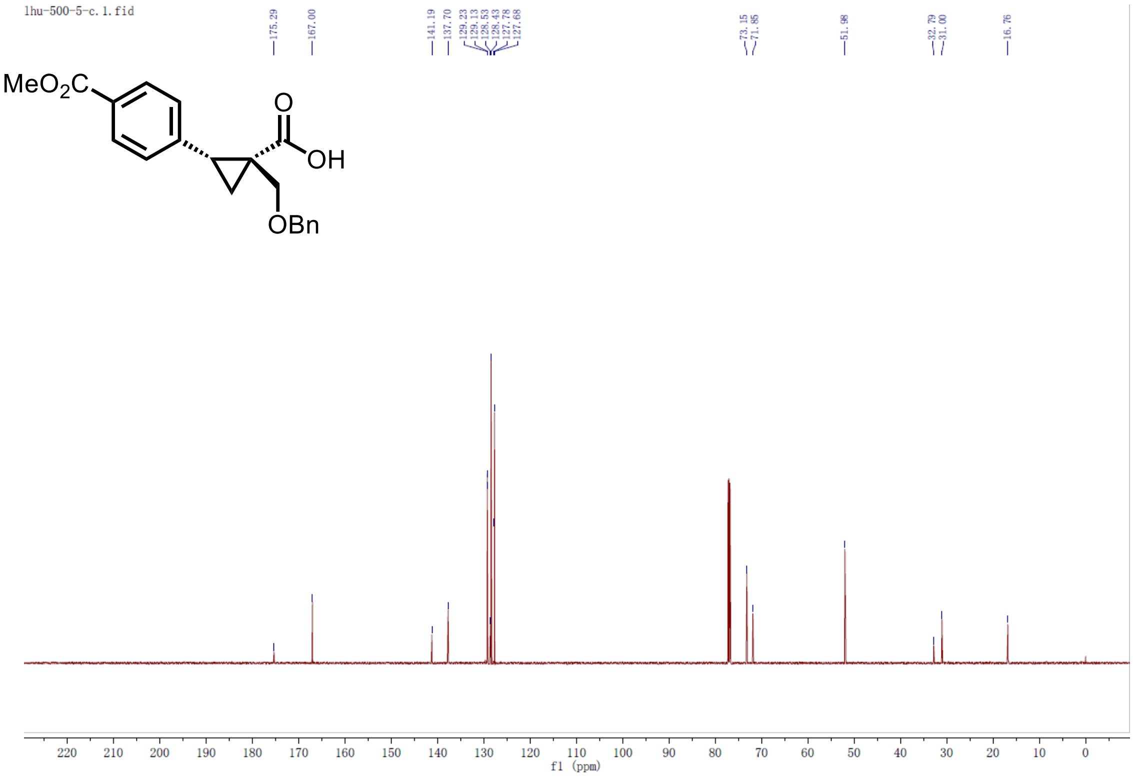
7.89
7.36
7.35
7.35
7.34
7.33
7.33
7.32
7.32
7.31
7.30
7.30
7.30
7.29
7.29
7.24
7.23
4.58
3.88
3.86
3.60
3.58
2.59
2.58
2.56
1.97
1.96
1.95
1.95
1.42
1.42
1.41
1.40
MeO2C
O
OH
OBn
1.99
5.18
2.08
2.02
4.19
1.00
1.02
1.00
1.00
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)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141.19
137.70
129.23
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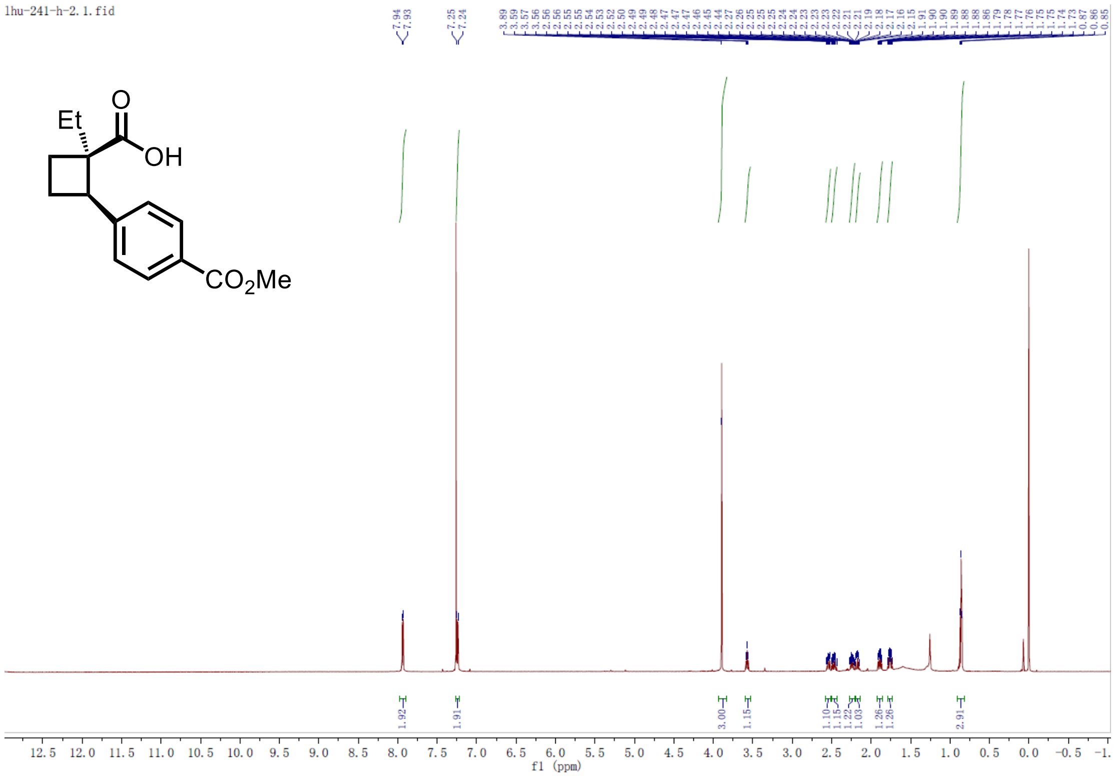
128.53
128.43
127.78
127.68
73.15
71.85
51.98
32.79
31.00
16.76
MeO2C
O
OH
OBn
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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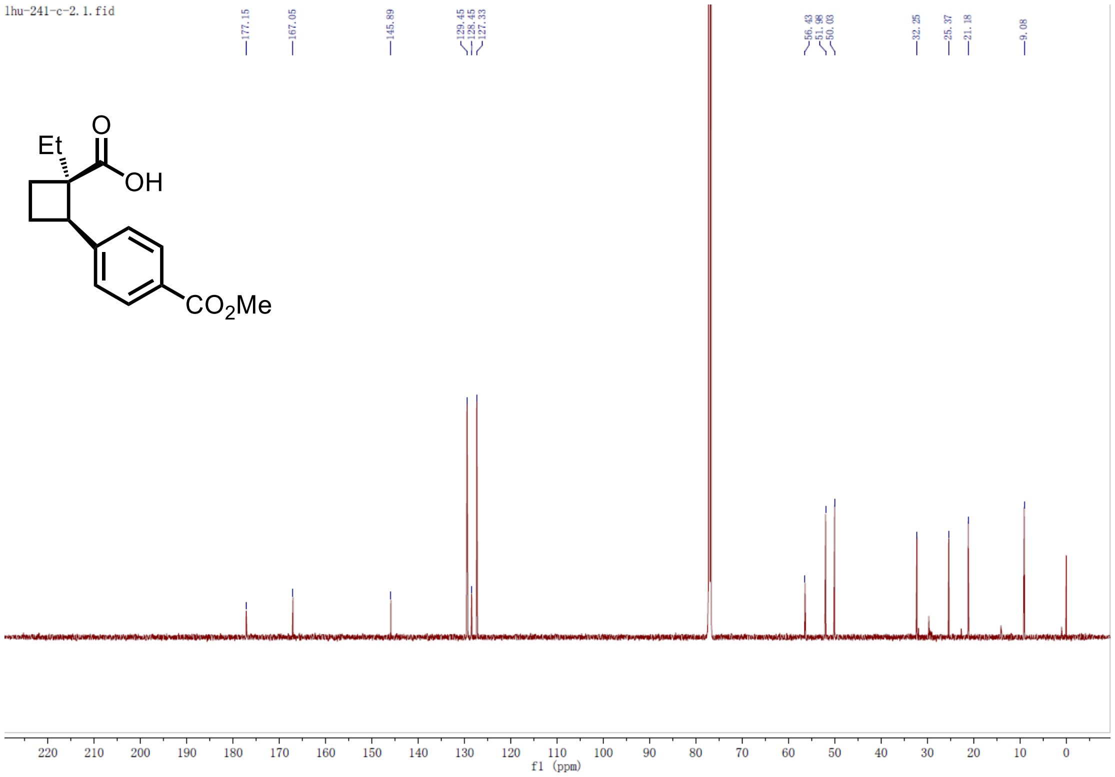
7.93
7.25
7.24
3.89 3.59 3.57 3.56 2.56 2.56 2.55 2.55 2.54 2.53 2.52 2.50 2.49 2.49 2.48 2.47 2.47 2.47 2.46 2.45 2.44 2.27 2.26 2.25 2.25 2.25 2.24 2.24 2.23 2.23 2.23 2.22 2.21 2.21 2.19 2.18 2.17 2.16 2.15 1.91 1.90 1.90 1.89 1.88 1.88 1.86 1.79 1.78 1.77 1.76 1.75 1.75 1.74 1.73 0.87 0.86 0.85
Et
O
OH
CO2Me
1.92
1.91
3.00
1.15
1.10
1.15
1.22
1.03
1.26
1.26
2.91
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)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145.89
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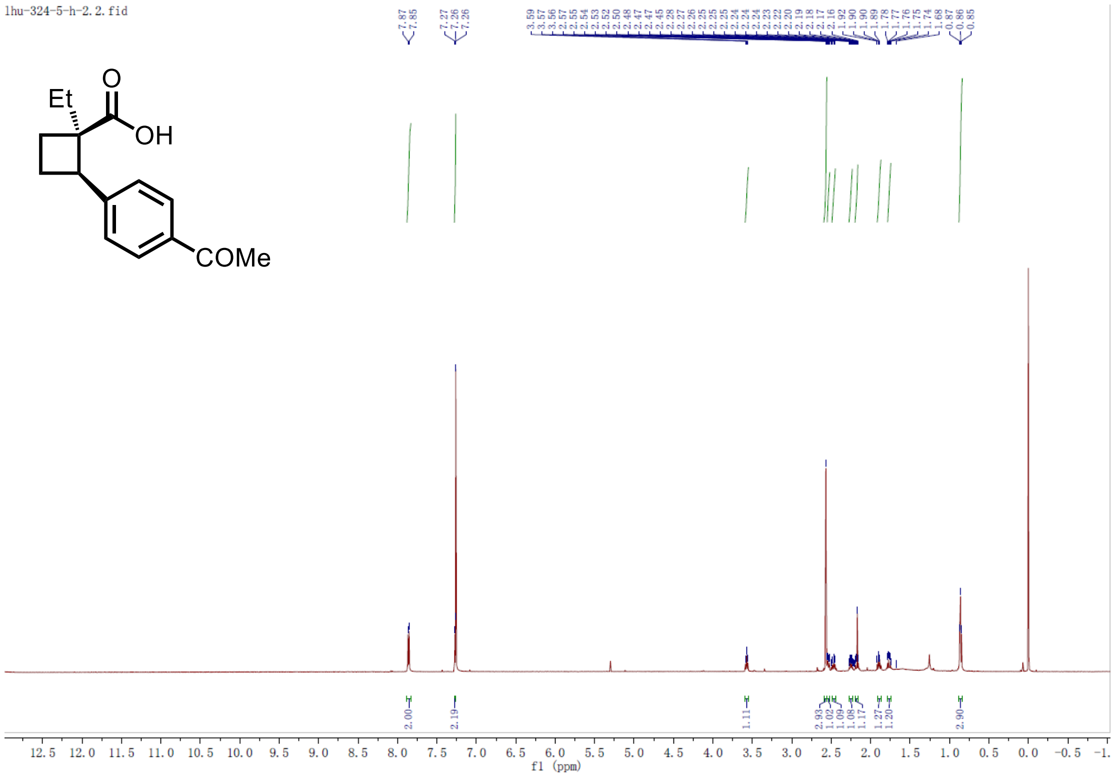
128.45
127.33
56.43
51.98
50.03
32.25
25.37
21.18
9.08
Et
O
OH
CO2Me
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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7.85
7.27
7.26
7.26
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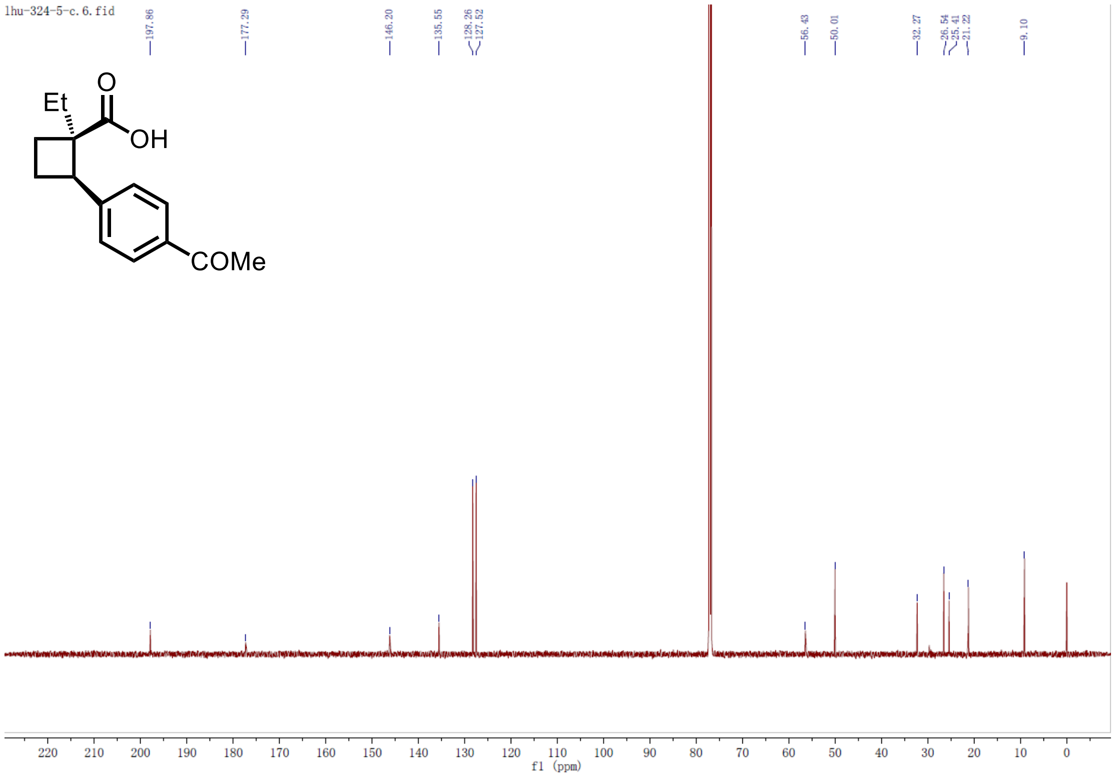
3.57
3.56
2.57
2.55
2.54
2.53
2.52
2.50
2.48
2.47
2.47
2.45
2.28
2.27
2.26
2.25
2.25
2.25
2.24
2.24
2.24
2.23
2.22
2.20
2.19
2.18
2.17
2.16
1.92
1.90
1.90
1.89
1.78
1.77
1.76
1.75
1.74
1.68
0.87
0.86
0.85
Et
O
OH
COMe
2.00
2.19
1.11
2.93
1.02
1.09
1.08
1.17
1.27
1.20
2.90
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)


lhu-324-5-c.6.fid
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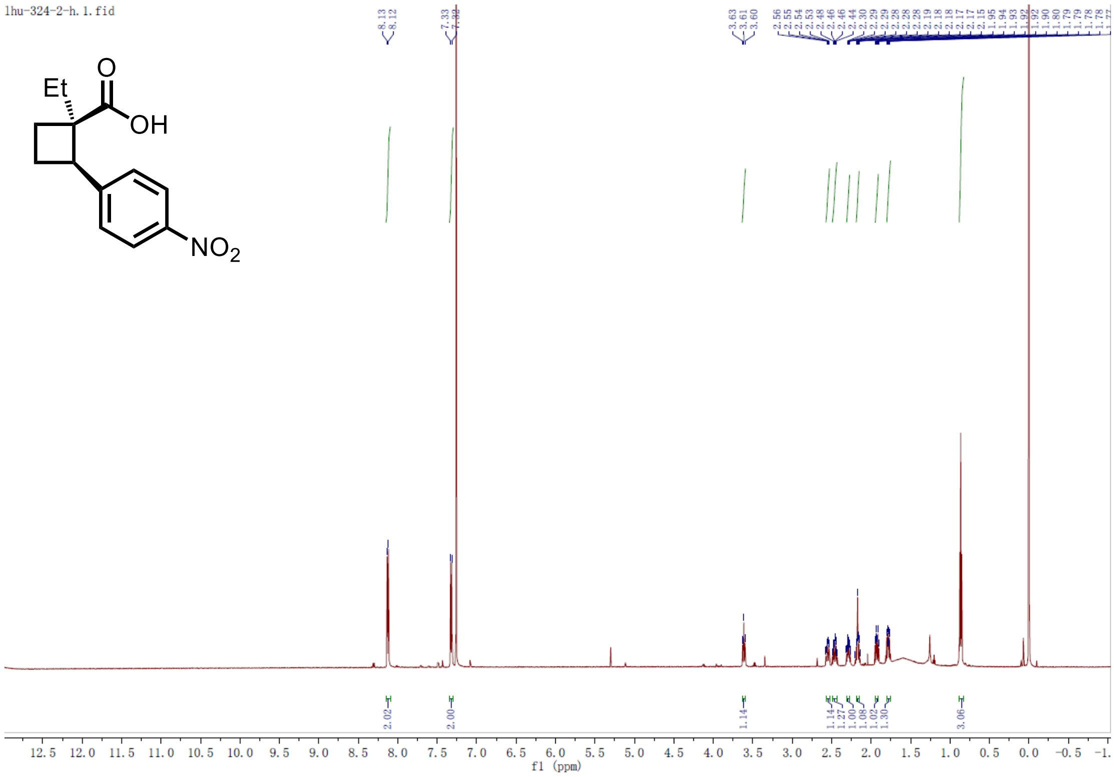
177.29
146.20
135.55
128.26
127.52
56.43
50.01
32.27
26.54
25.41
21.22
9.10
Et
O
OH
COMe
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


lhu-324-2-h.1.fid
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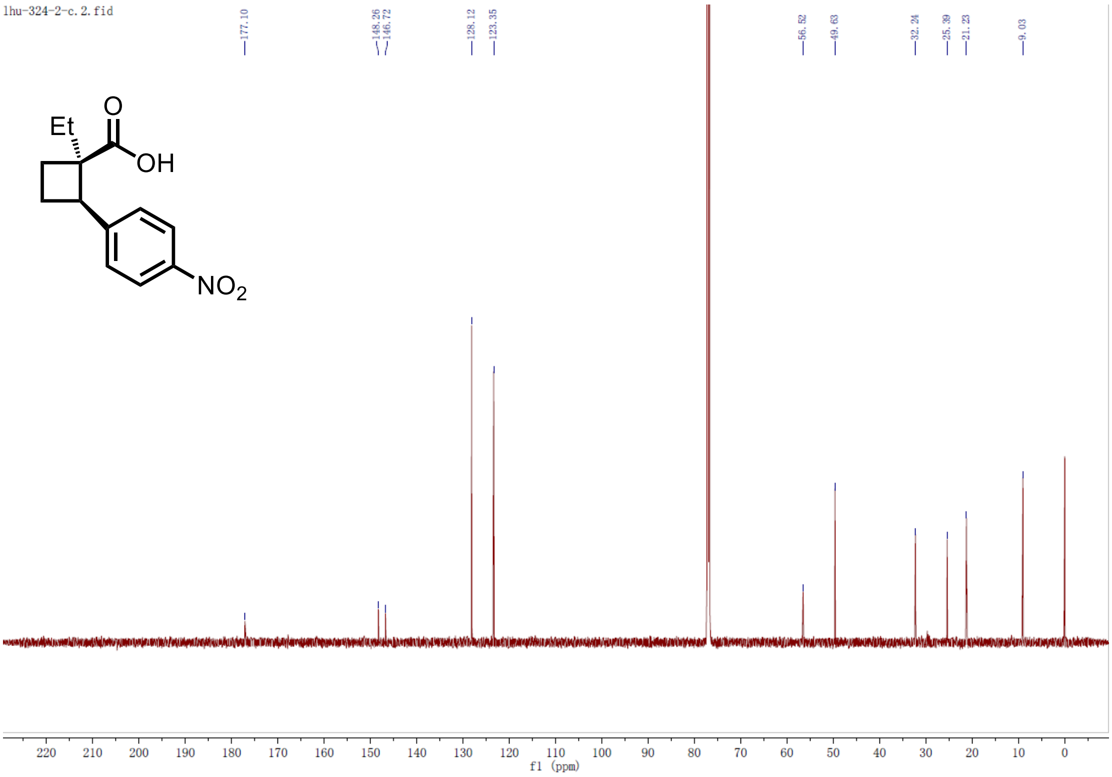
8.12
7.33
7.32
3.63
3.61
3.60
2.56
2.55
2.54
2.53
2.48
2.46
2.46
2.44
2.30
2.29
2.29
2.28
2.28
2.28
2.19
2.18
2.18
2.17
2.17
2.15
1.95
1.94
1.93
1.92
1.92
1.90
1.80
1.79
1.79
1.78
1.78
1.77
Et
O
OH
$NO_2$
2.02
2.00
1.14
1.14
1.27
1.00
1.08
1.02
1.30
3.06
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.
f1 (ppm)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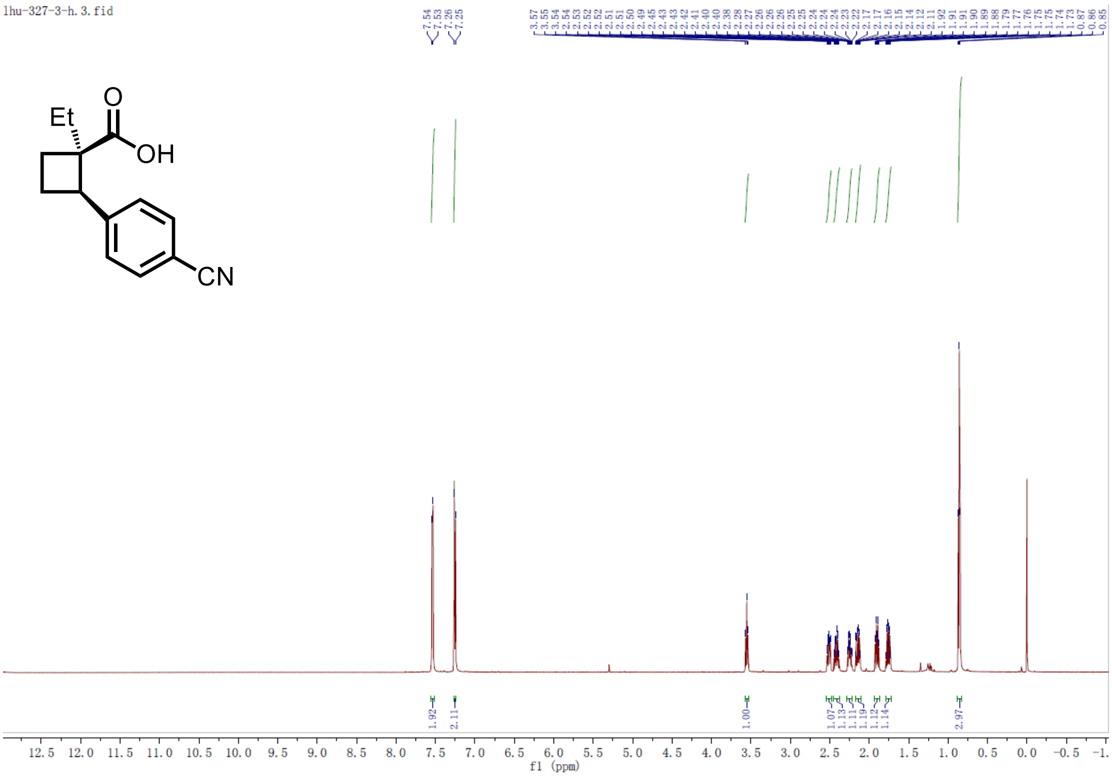
146.72
128.12
123.35
56.52
49.63
32.24
25.39
21.23
9.03
Et
O
OH
NO2
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.25
3.57
3.55
3.54
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2.53
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2.51
2.51
2.50
2.49
2.45
2.43
2.43
2.42
2.41
2.40
2.40
2.38
2.28
2.27
2.26
2.26
2.26
2.25
2.25
2.24
2.24
2.24
2.23
2.22
2.17
2.17
2.16
2.15
2.14
2.12
2.11
1.92
1.91
1.91
1.90
1.89
1.88
1.79
1.77
1.76
1.75
1.75
1.74
1.73
0.87
0.86
0.85
Et
O
OH
CN
1.92
2.11
1.00
1.07
1.13
1.11
1.19
1.12
1.14
2.97
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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2.0
1.5
1.0
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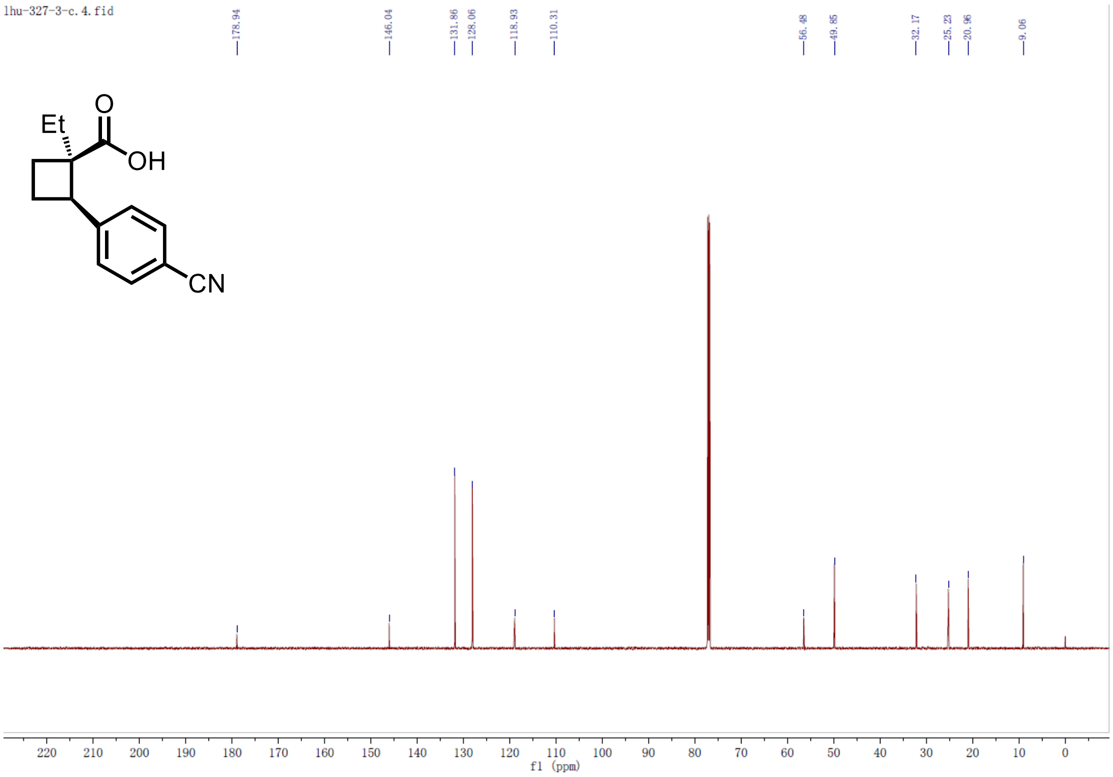
0.0
-0.5
-1.
f1 (ppm)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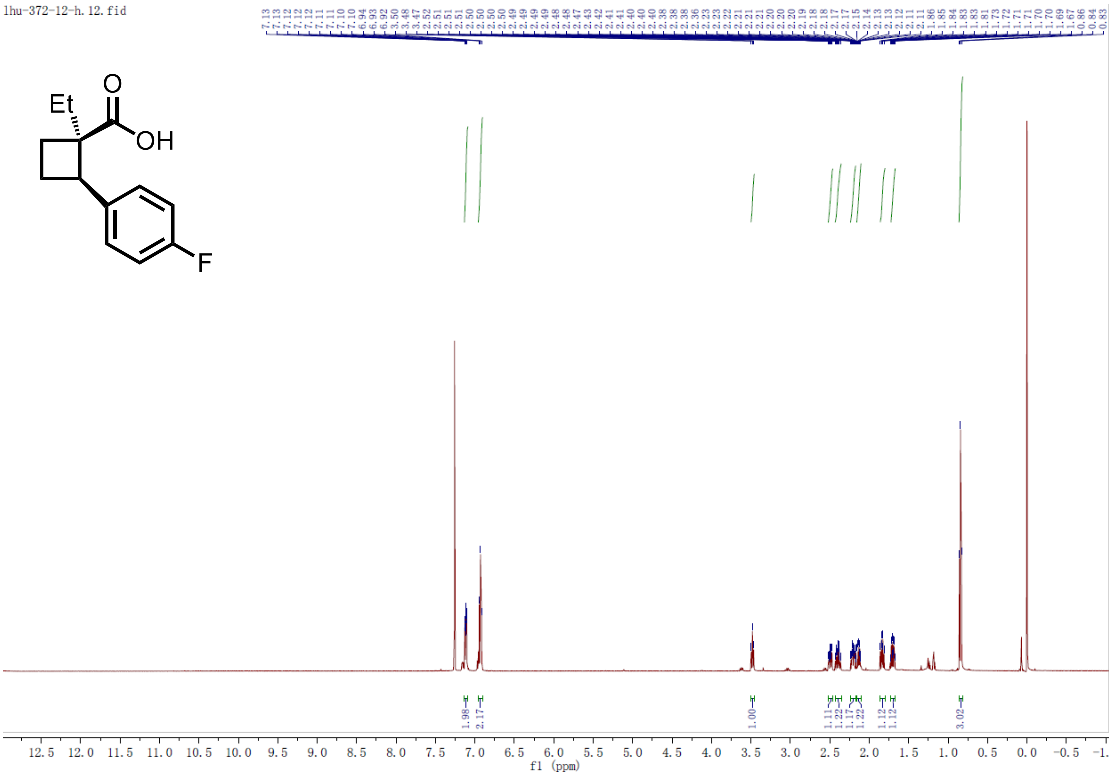
128.06
118.93
110.31
56.48
49.85
32.17
25.23
20.96
9.06
Et
O
OH
CN
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


lhu-372-12-h.12.fid
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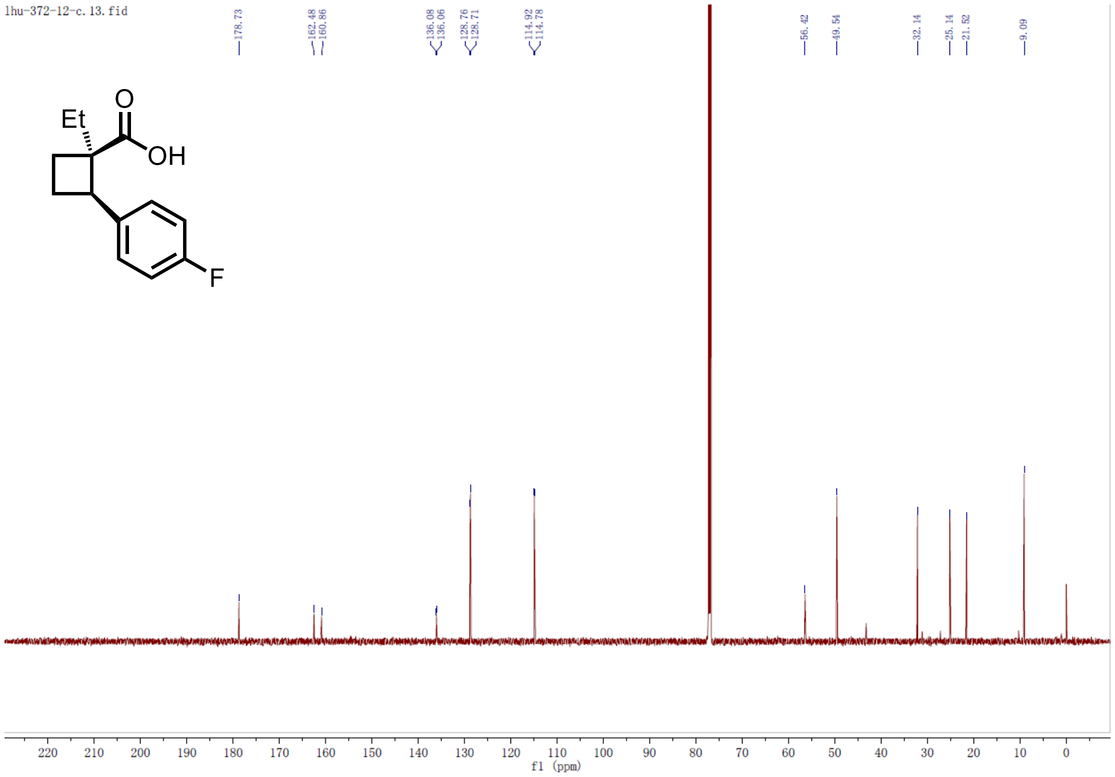
Et
O
OH
F
1.98
2.17
1.00
1.11
1.22
1.17
1.22
1.12
1.12
3.02
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)


lhu-372-12-c.13.fid
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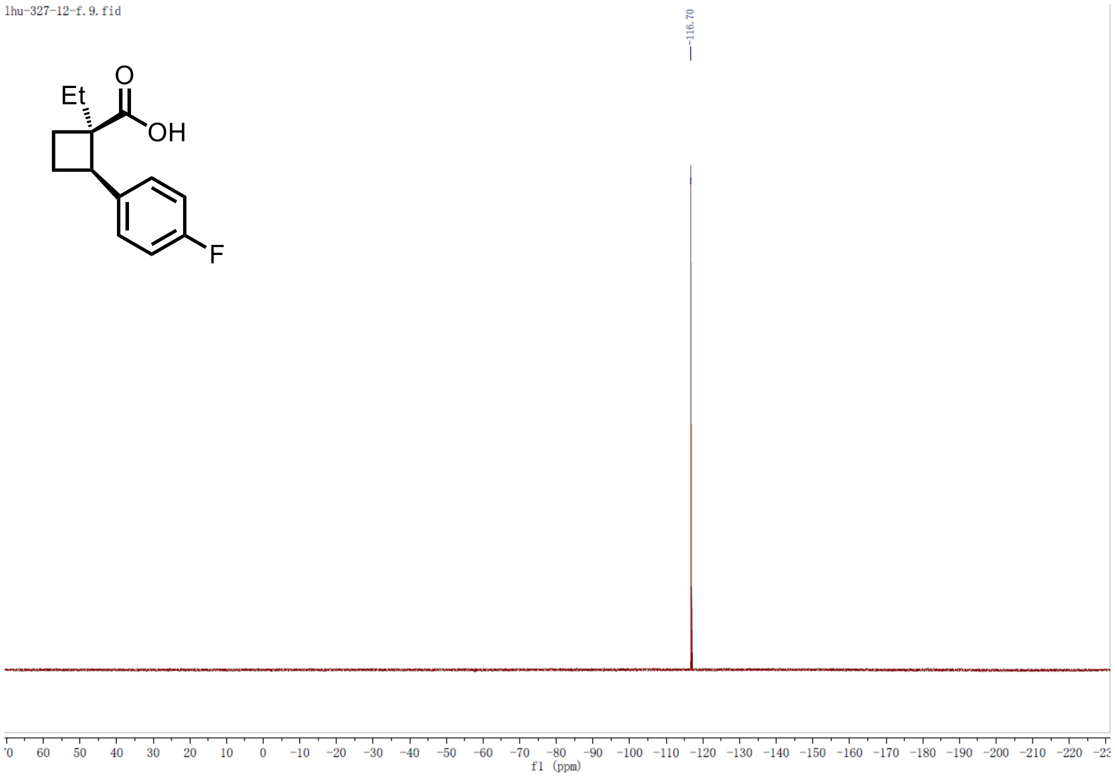
160.86
136.08
136.06
128.76
128.71
114.92
114.78
56.42
49.54
32.14
25.14
21.52
9.09
Et
O
OH
F
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


lhu-327-12-f.9.fid
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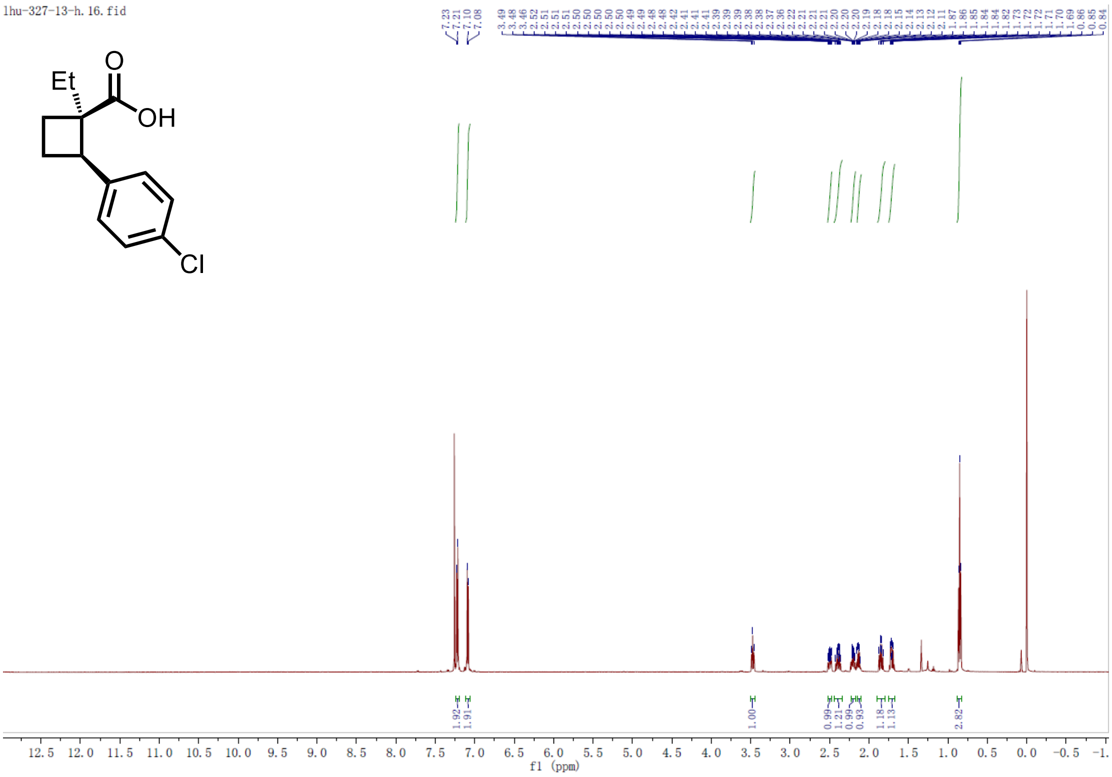
Et
O
OH
F
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -23
f1 (ppm)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O
OH
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2.51
2.50
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2.38
2.37
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2.22
2.21
2.21
2.21
2.20
2.20
2.20
2.19
2.18
2.18
2.15
2.14
2.13
2.12
2.11
1.87
1.86
1.85
1.84
1.84
1.82
1.73
1.72
1.72
1.71
1.70
1.69
0.86
0.85
0.84
1.92
1.91
1.00
0.99
1.21
0.99
0.93
1.18
1.13
2.82
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11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
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6.5
6.0
5.5
5.0
4.5
4.0
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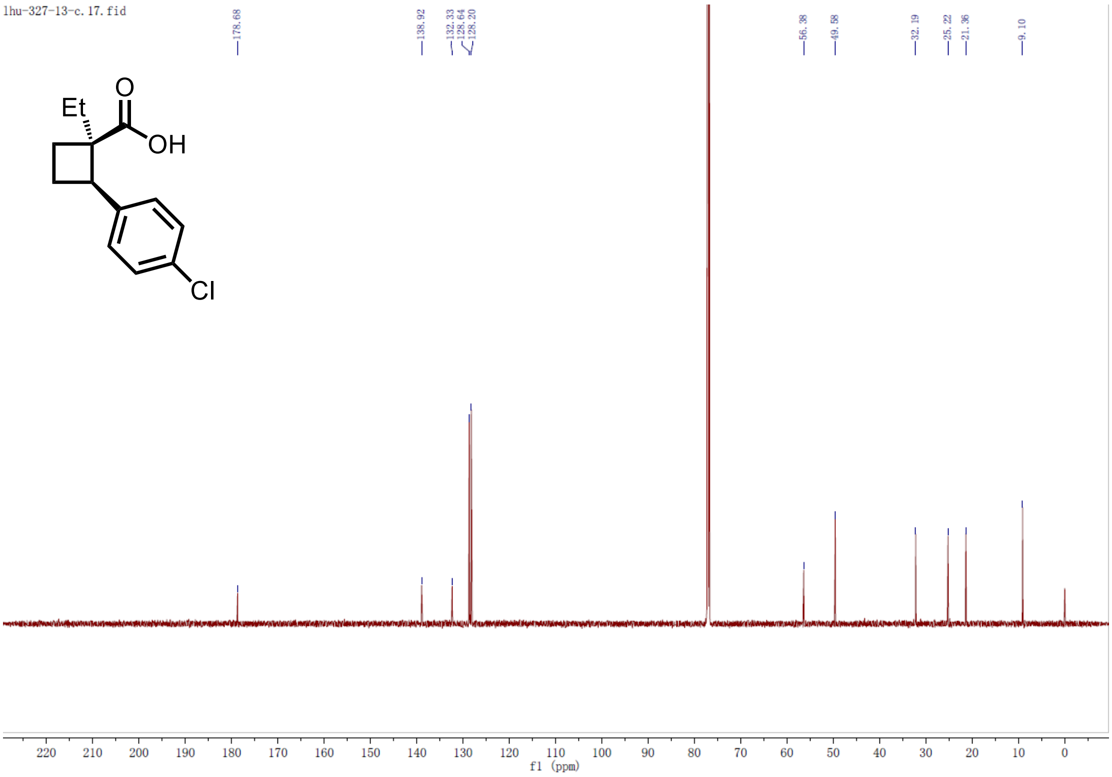
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.
f1 (ppm)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OH
Cl
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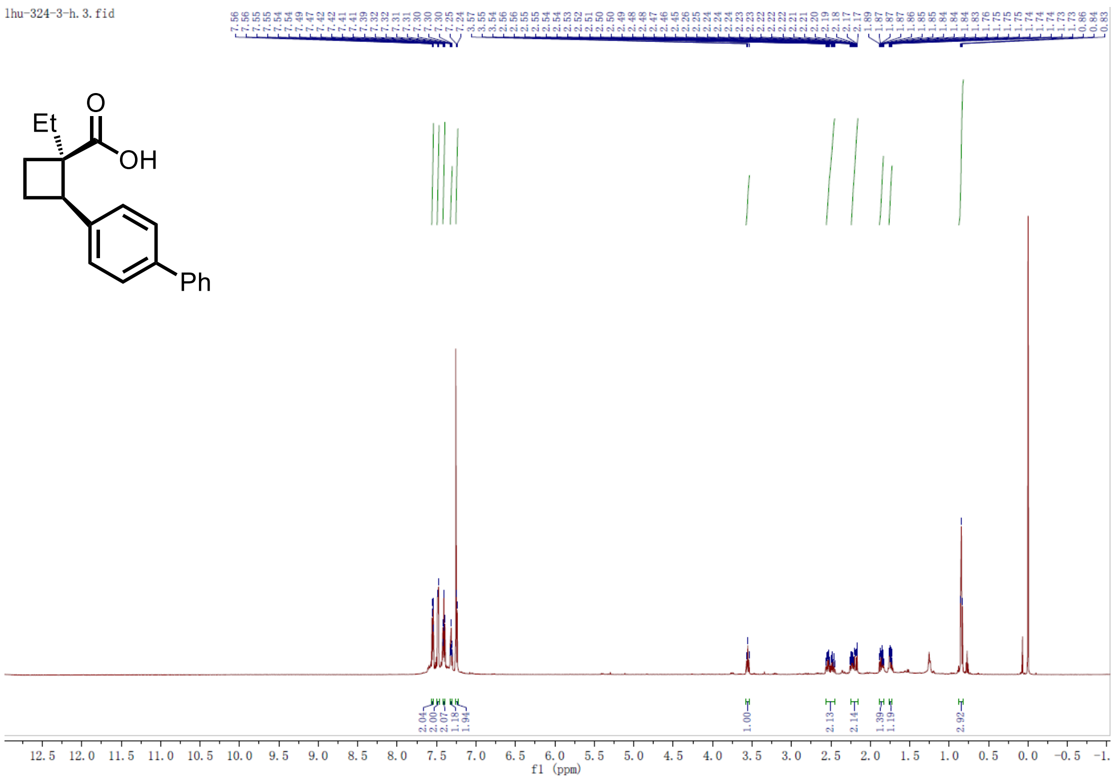
32.19
25.22
21.36
9.10
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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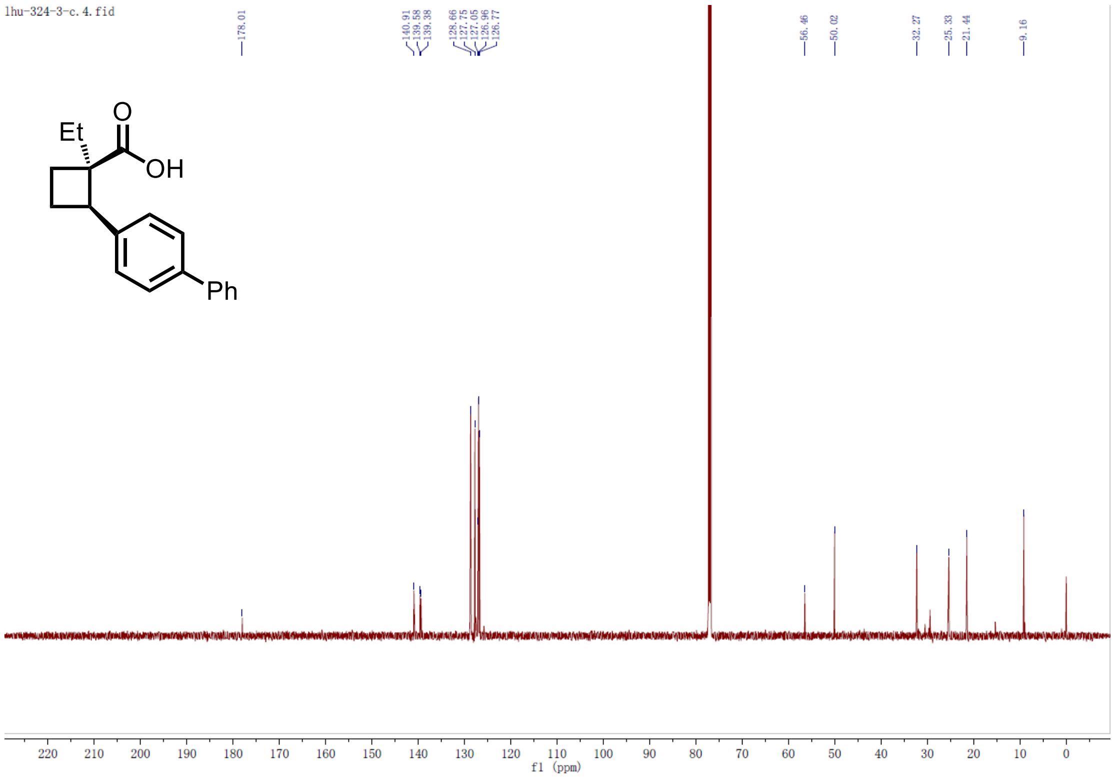
Et
O
OH
Ph
2.04
2.00
2.07
1.18
1.94
1.00
2.13
2.14
1.39
1.19
2.92
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)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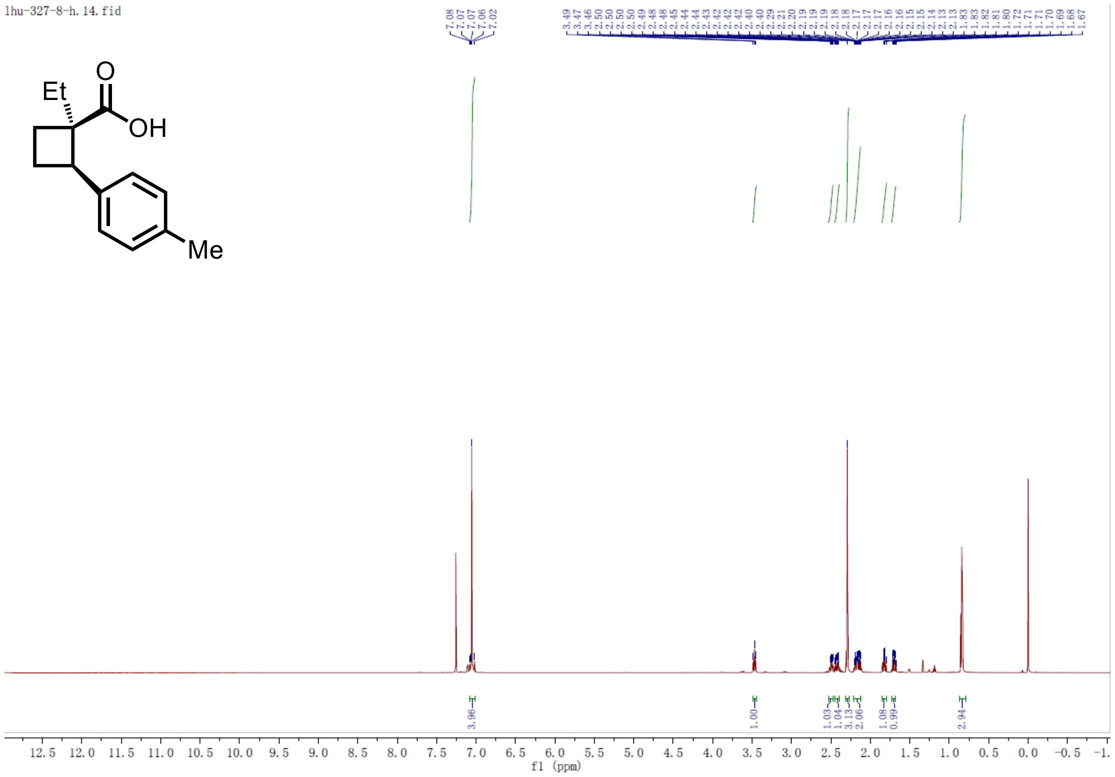
127.05
126.96
126.77
56.46
50.02
32.27
25.33
21.44
9.16
Et
O
OH
Ph
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


lhu-327-8-h.14.fid
Et
O
OH
Me
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7.07
7.06
7.02
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3.47
3.46
2.50
2.50
2.50
2.50
2.49
2.48
2.48
2.45
2.44
2.44
2.43
2.42
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2.40
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2.29
2.21
2.20
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2.19
2.18
2.18
2.17
2.17
2.17
2.16
2.16
2.15
2.15
2.14
2.13
2.13
1.83
1.83
1.82
1.81
1.80
1.72
1.71
1.71
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1.69
1.68
1.67
3.96
1.00
1.03
1.04
3.13
2.06
1.08
0.99
2.94
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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2.5
2.0
1.5
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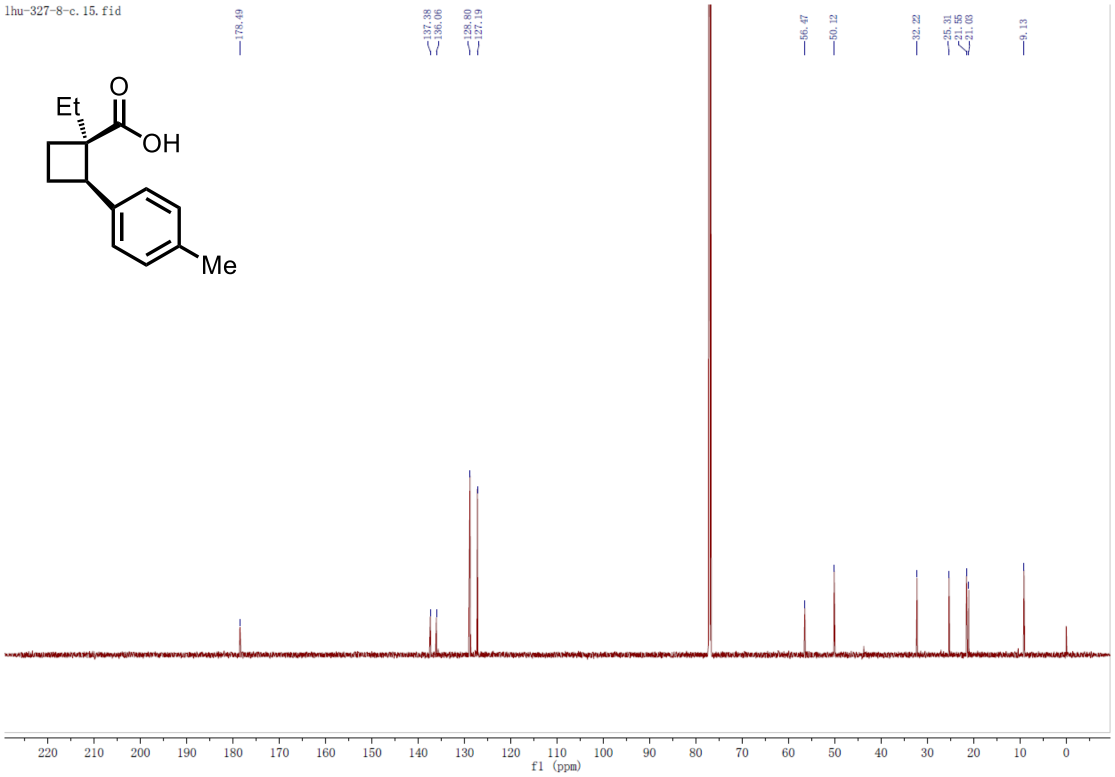
0.5
0.0
-0.5
-1.
f1 (ppm)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O
OH
Me
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127.19
56.47
50.12
32.22
25.31
21.55
21.03
9.13
220
210
200
190
180
170
160
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130
120
110
100
90
80
70
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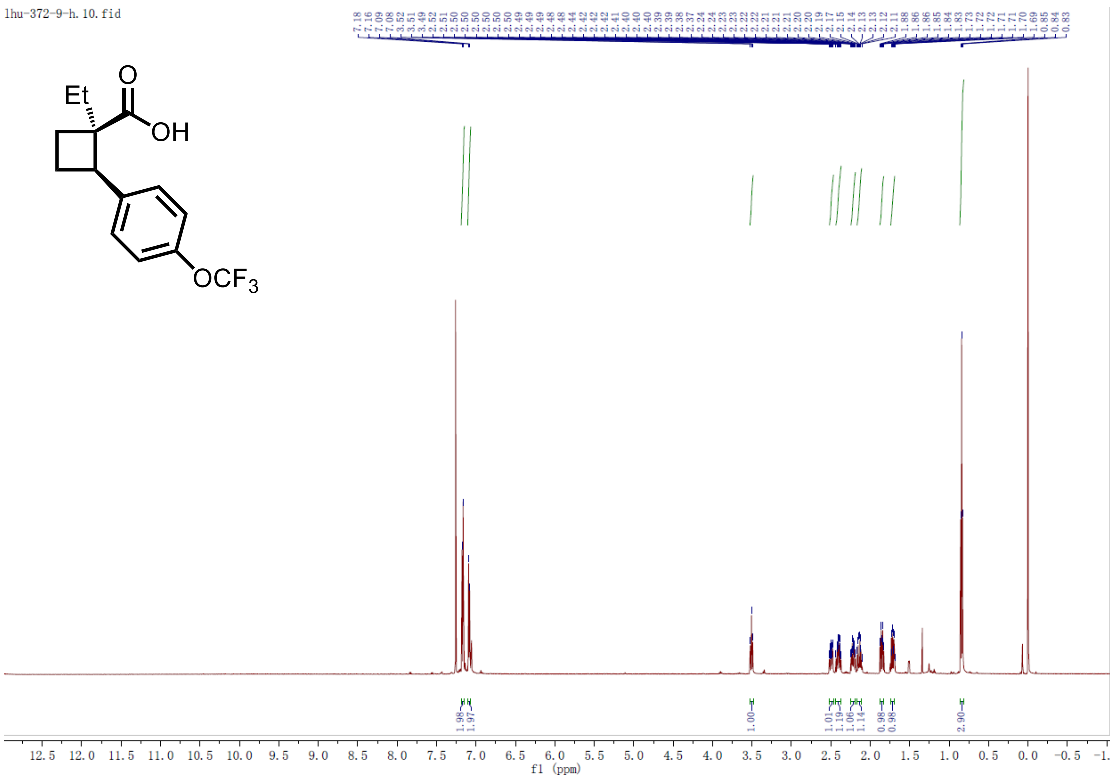
50
40
30
20
10
0
f1 (ppm)


lhu-372-9-h.10.fid
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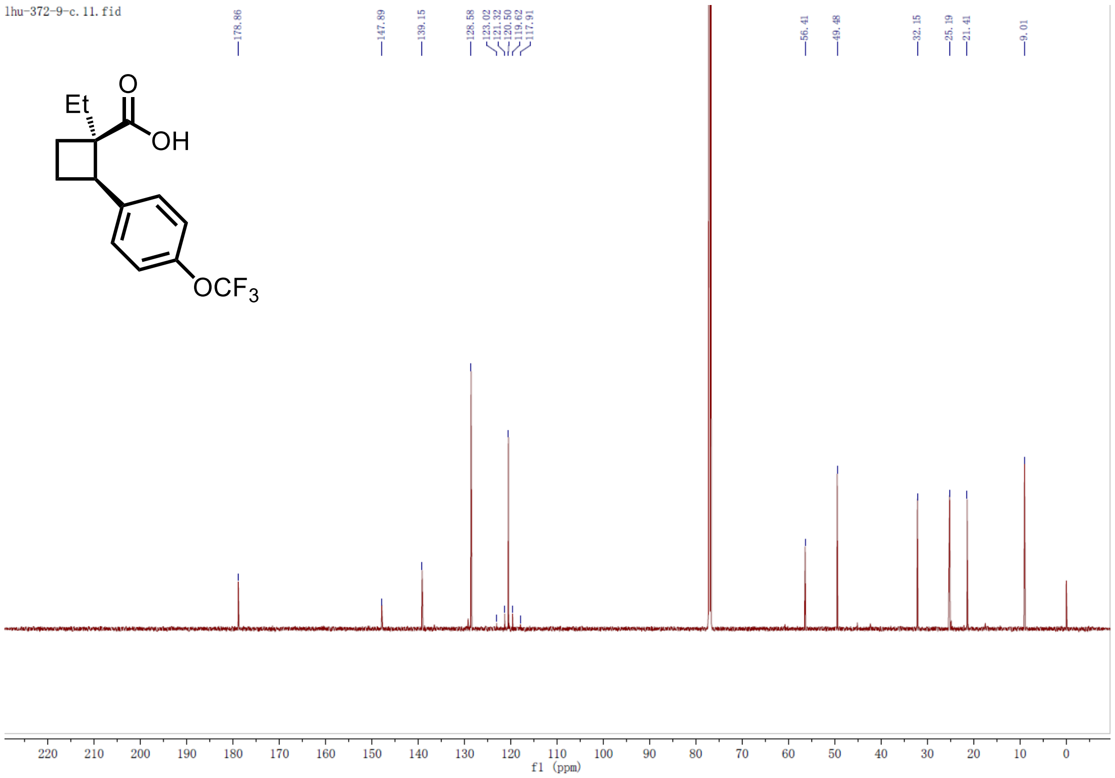
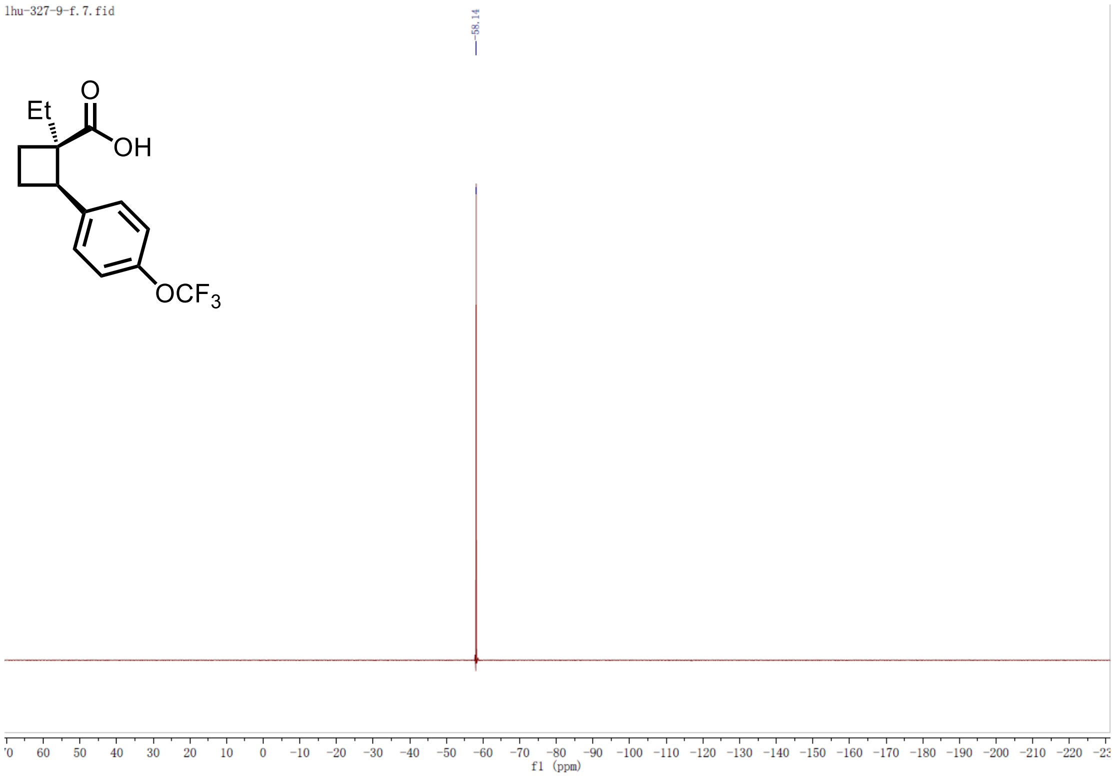
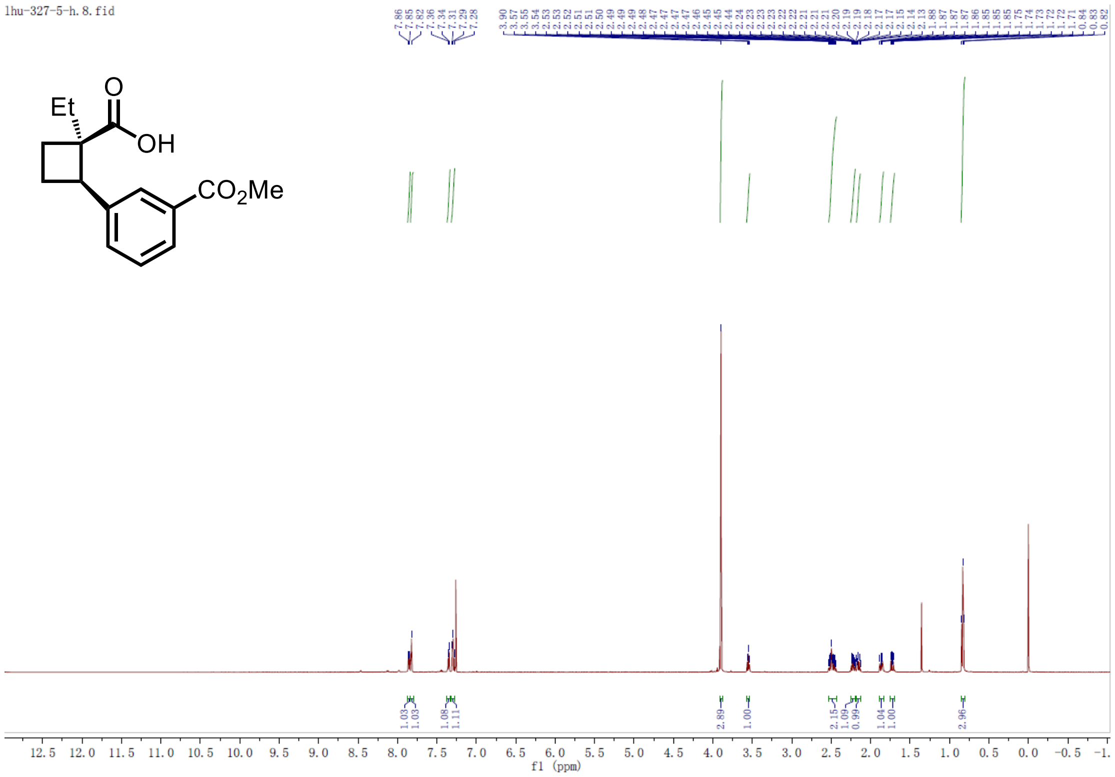
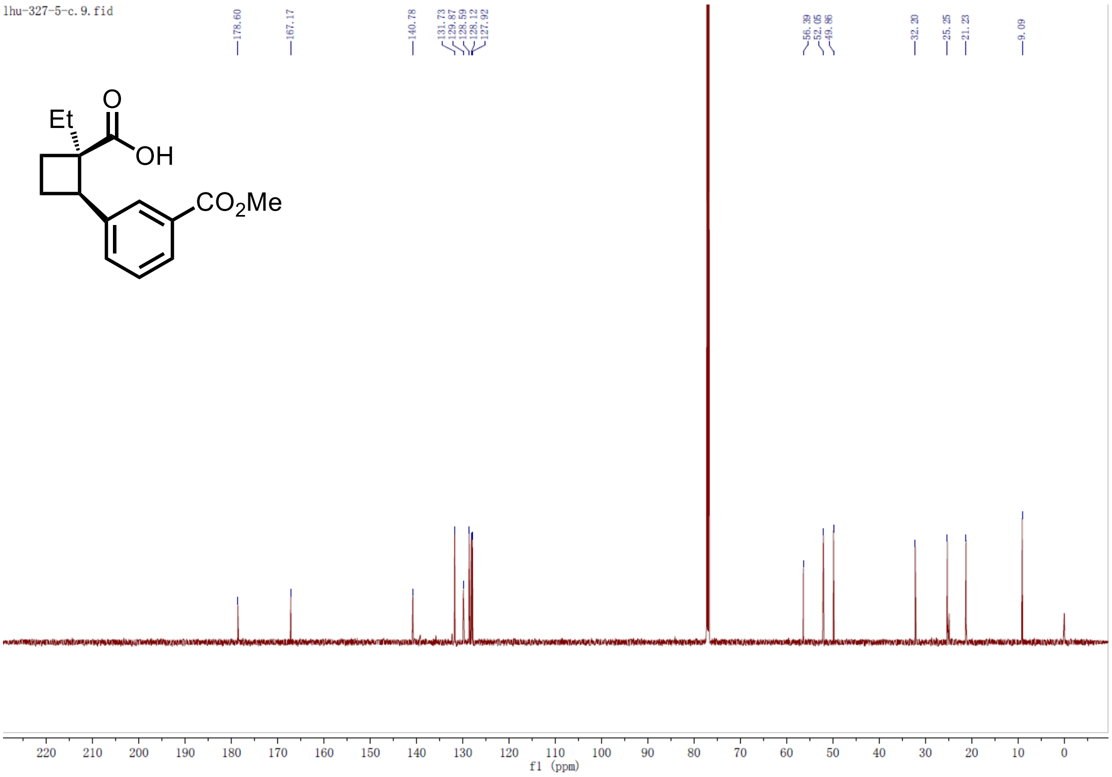
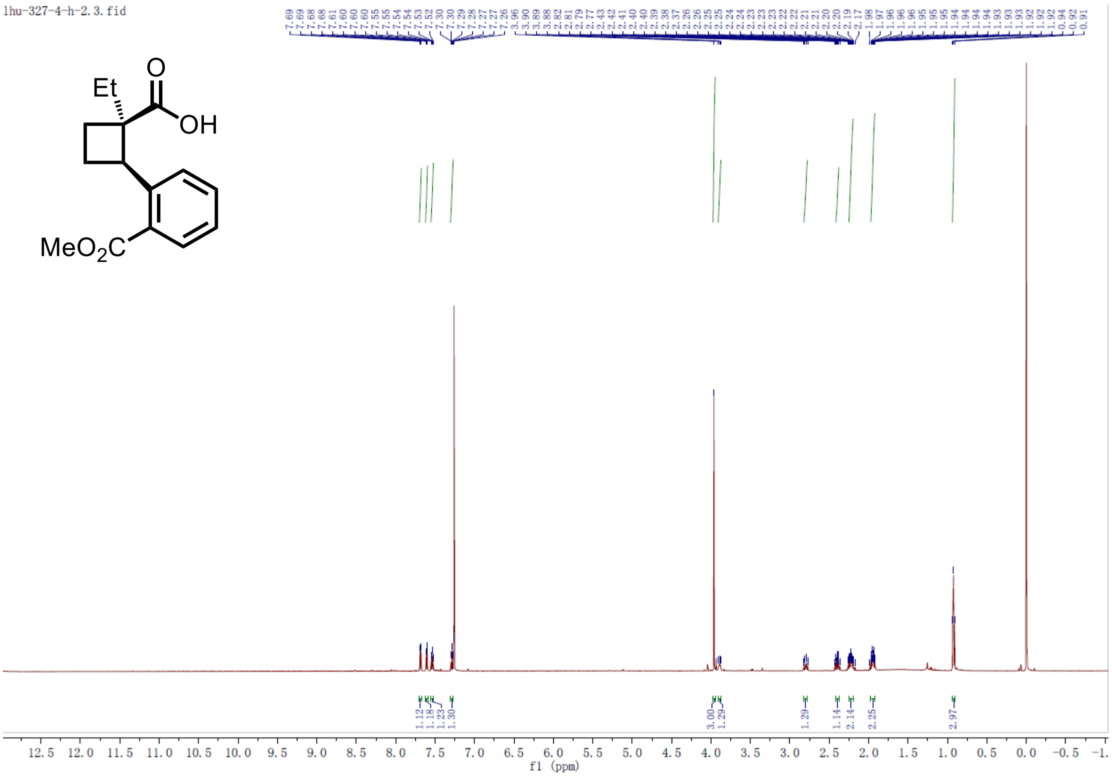
O
OH
OCF3
7.18 7.16 7.09 7.08 3.52 3.51 3.49 2.52 2.51 2.50 2.50 2.50 2.50 2.50 2.49 2.49 2.48 2.48 2.44 2.42 2.42 2.42 2.41 2.40 2.40 2.40 2.39 2.39 2.38 2.37 2.24 2.24 2.23 2.23 2.22 2.22 2.21 2.21 2.21 2.20 2.20 2.19 2.17 2.15 2.14 2.13 2.13 2.12 2.11 1.88 1.86 1.86 1.85 1.84 1.83 1.73 1.72 1.72 1.71 1.71 1.70 1.69 0.85 0.84 0.83
1.98 1.97 1.00 1.01 1.19 1.06 1.14 0.98 0.98 2.90
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)


lhu-372-9-c.11.fid
Et
O
OH
OCF3
178.86
147.89
139.15
128.58 123.02 121.32 120.50 119.62 117.91
56.41
49.48
32.15
25.19
21.41
9.01
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


lhu-327-9-f.7.fid
-58.14
Et
O
OH
OCF$_3$
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -23
f1 (ppm)


lhu-327-5-h.8.fid
7.86 7.85 7.82 7.36 7.34 7.31 7.29 7.28 3.90 3.57 3.55 3.54 2.53 2.53 2.52 2.51 2.51 2.50 2.49 2.49 2.49 2.48 2.47 2.47 2.47 2.47 2.46 2.45 2.45 2.44 2.24 2.23 2.23 2.23 2.22 2.22 2.21 2.21 2.21 2.20 2.19 2.19 2.18 2.17 2.17 2.15 2.14 2.13 1.88 1.87 1.87 1.87 1.86 1.85 1.85 1.85 1.75 1.74 1.73 1.72 1.72 1.71 0.84 0.83 0.82
Et
O
OH
CO$_2$Me
1.03 1.03 1.08 1.11 2.89 1.00 2.15 1.09 0.99 1.04 1.00 2.96
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)


lhu-327-5-c.9.fid
178.60
167.17
140.78
131.73
129.87
128.59
128.12
127.92
56.39
52.05
49.86
32.20
25.25
21.23
9.09
Et
O
OH
CO2Me
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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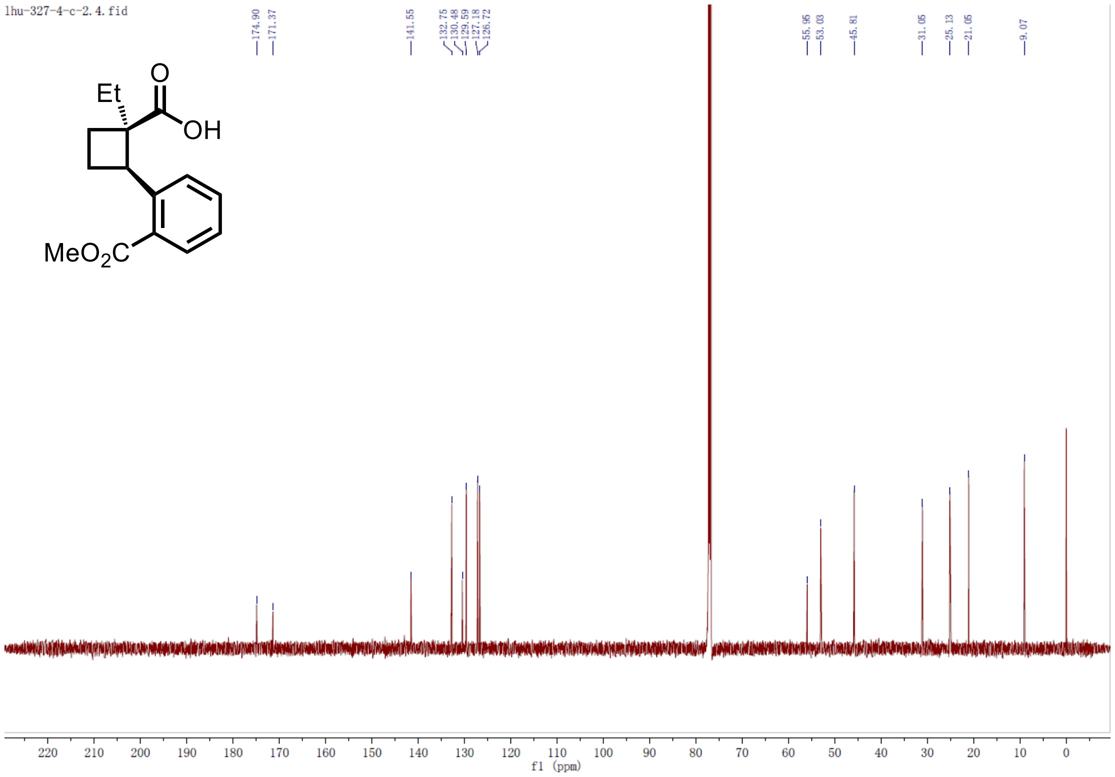
Et
O
OH
MeO2C
1.12
1.18
1.23
1.30
3.00
1.29
1.29
1.14
2.14
2.25
2.97
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)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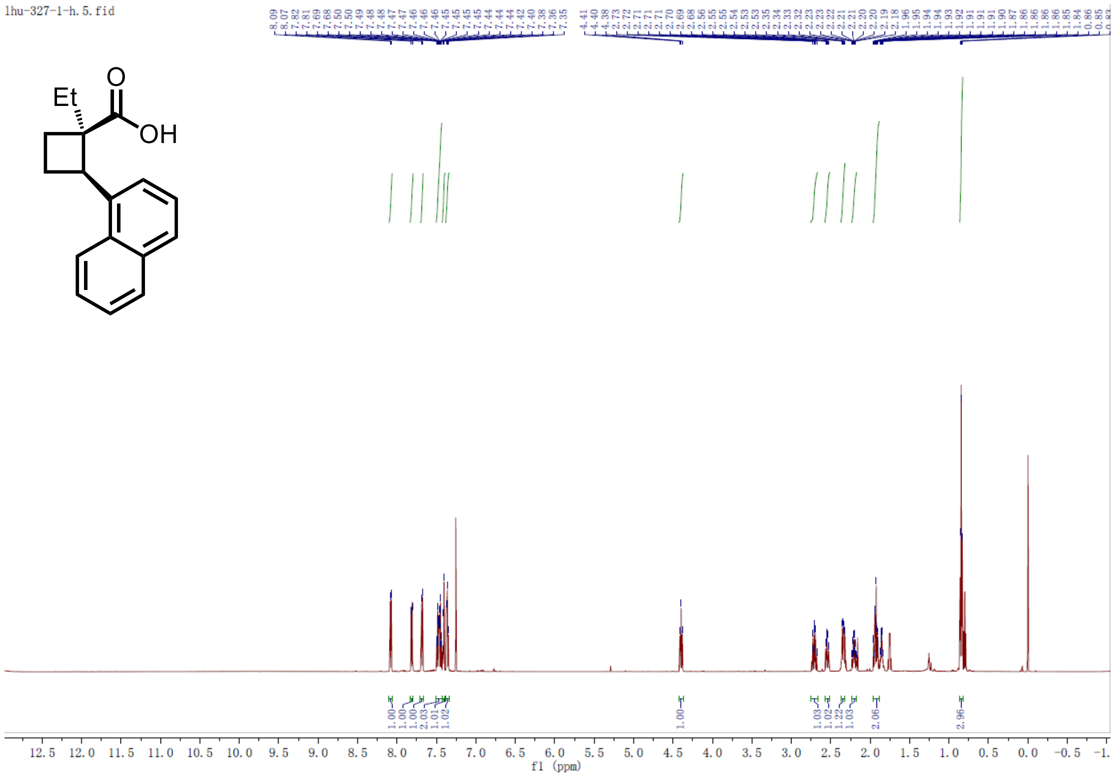
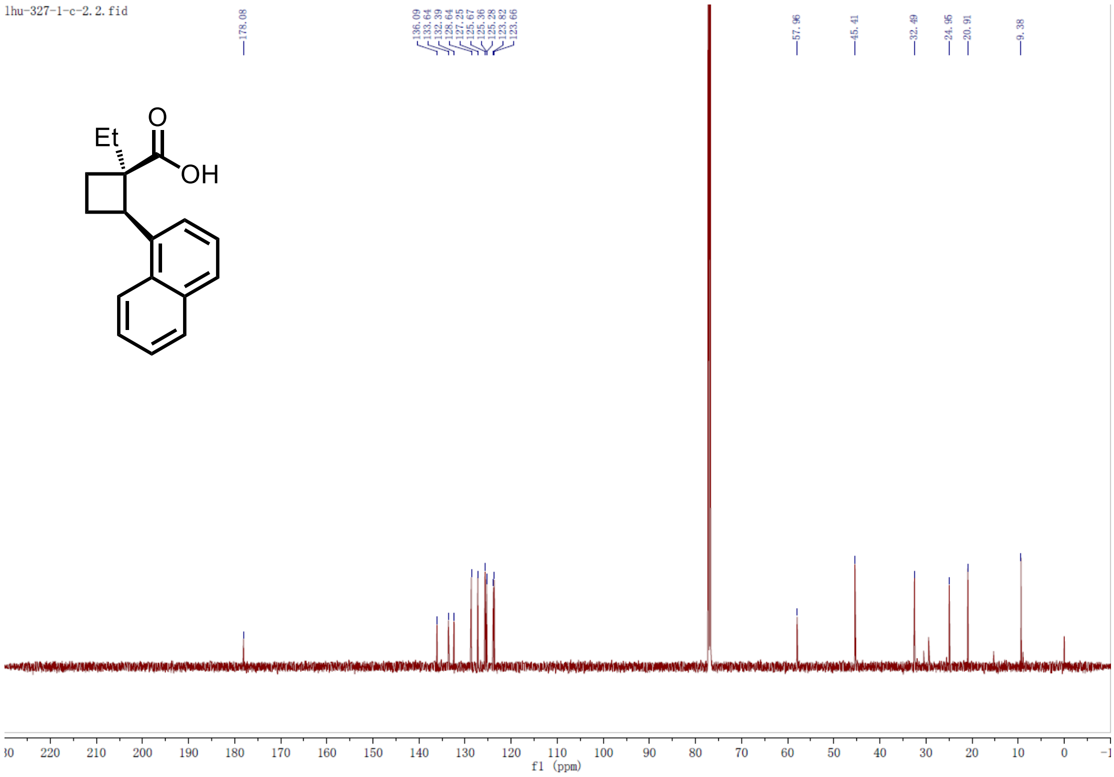
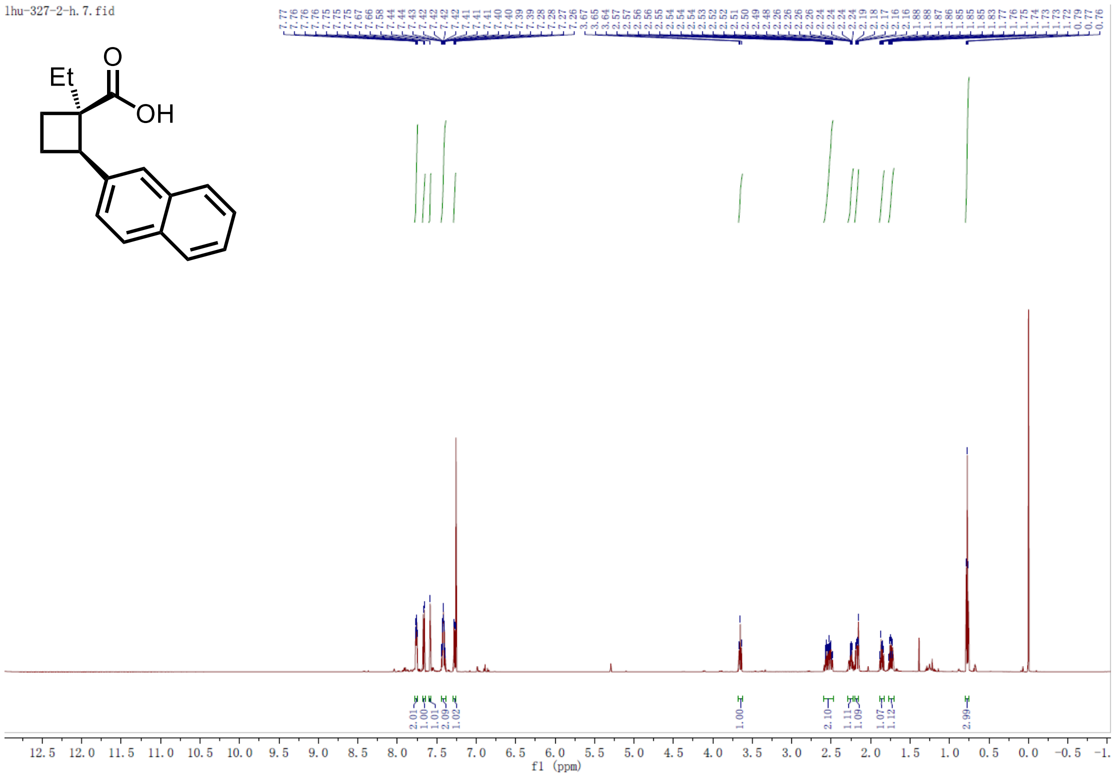
O
OH
MeO2C
174.90
171.37
141.55
132.75
130.48
129.59
127.18
126.72
55.95
53.03
45.81
31.05
25.13
21.05
9.07
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


lhu-327-1-h.5.fid
Et
O
OH
8.09 8.07 7.82 7.81 7.69 7.68 7.50 7.50 7.49 7.48 7.48 7.47 7.47 7.46 7.46 7.46 7.45 7.45 7.45 7.45 7.44 7.44 7.44 7.42 7.40 7.38 7.36 7.35
4.41 4.40 4.38 2.73 2.72 2.71 2.71 2.70 2.69 2.68 2.56 2.55 2.54 2.53 2.53 2.35 2.34 2.33 2.32 2.23 2.23 2.22 2.21 2.21 2.20 2.20 2.19 2.18 1.96 1.95 1.94 1.93 1.92 1.91 1.91 1.91 1.90 1.87 1.86 1.86 1.86 1.85 1.84 0.86 0.85
1.00
1.00
1.00
2.03
1.01
1.02
1.00
1.03
1.02
1.22
1.03
2.06
2.96
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)


lhu-327-1-c-2.2.fid
178.08
136.09
133.64
132.39
128.64
127.25
125.67
125.36
125.28
123.82
123.66
57.96
45.41
32.49
24.95
20.91
9.38
Et
O
OH
30 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −1
f1 (ppm)


lhu-327-2-h.7.fid
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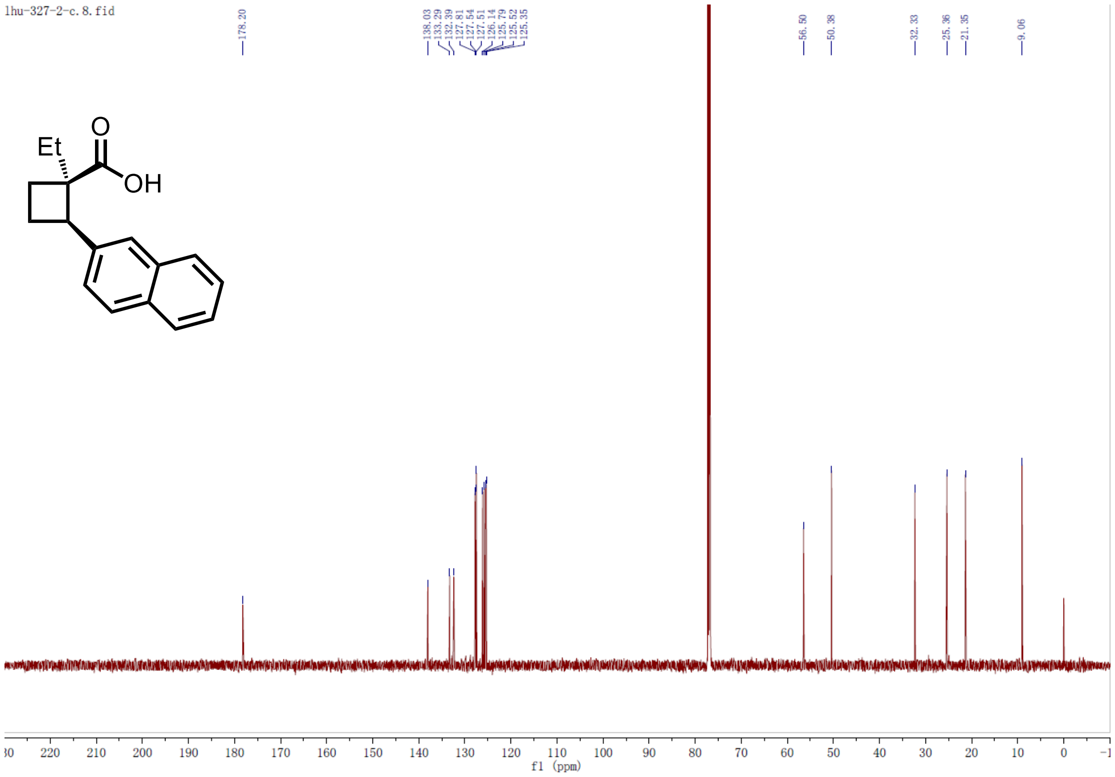
7.76
7.76
7.76
7.75
7.75
7.75
7.67
7.66
7.58
7.44
7.44
7.43
7.42
7.42
7.42
7.42
7.41
7.41
7.41
7.40
7.40
7.39
7.39
7.28
7.28
7.27
7.26
3.67
3.65
3.64
2.57
2.57
2.56
2.56
2.55
2.54
2.54
2.54
2.53
2.52
2.52
2.51
2.50
2.49
2.48
2.26
2.26
2.26
2.26
2.24
2.24
2.24
2.24
2.19
2.18
2.17
2.16
2.16
1.88
1.88
1.87
1.86
1.85
1.85
1.85
1.83
1.77
1.76
1.75
1.74
1.73
1.73
1.72
0.79
0.77
0.76
Et
O
OH
2.01
1.00
1.01
2.09
1.02
1.00
2.10
1.11
1.09
1.07
1.12
2.99
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.
f1 (ppm)


lhu-327-2-c.8.fid
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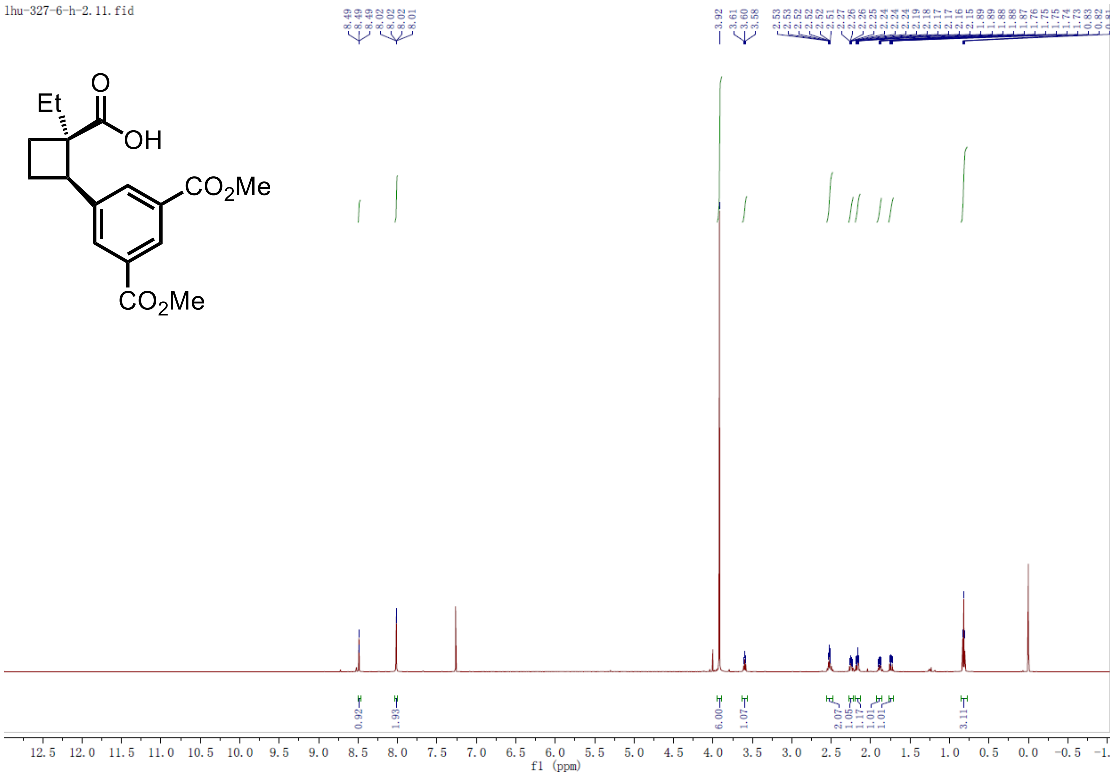
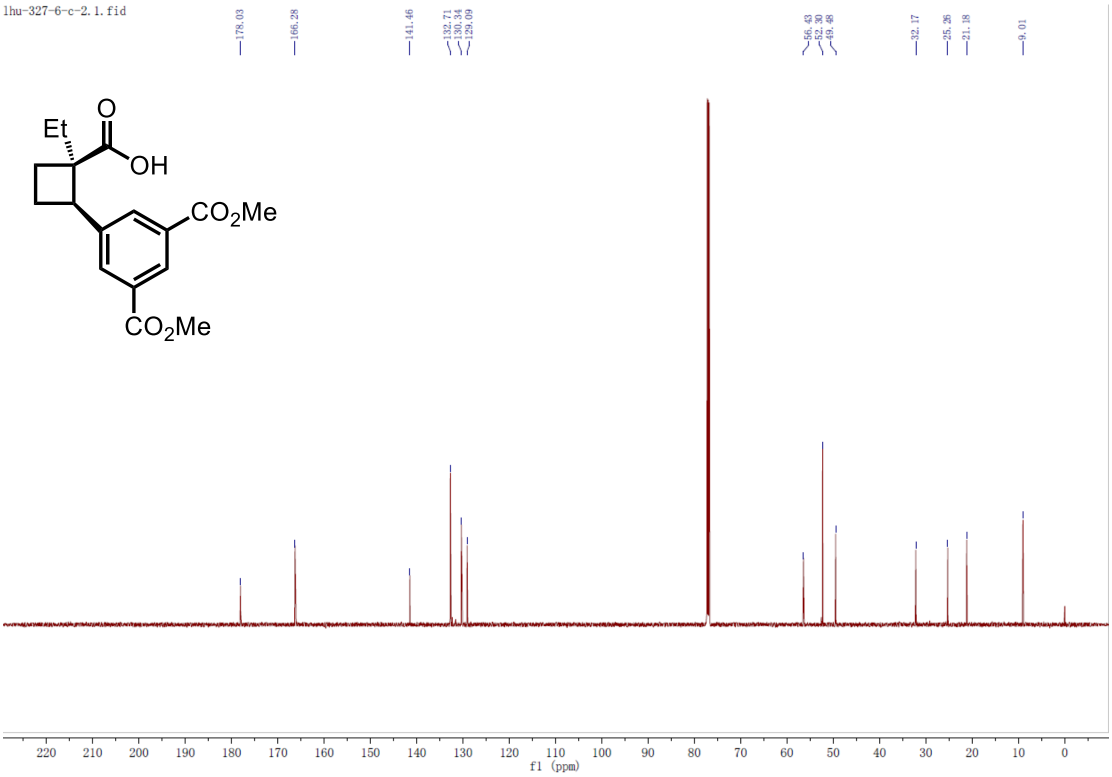
138.03
133.29
132.39
127.81
127.54
127.51
126.14
125.79
125.52
125.35
56.50
50.38
32.33
25.36
21.35
9.06
Et
O
OH
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−1
f1 (ppm)


lhu-327-6-h-2.11.fid
8.49
8.49
8.49
8.02
8.02
8.02
8.01
3.92
3.61
3.60
3.58
2.53
2.53
2.52
2.52
2.52
2.51
2.27
2.26
2.26
2.25
2.24
2.24
2.24
2.19
2.18
2.17
2.17
2.16
2.15
1.89
1.89
1.88
1.88
1.87
1.76
1.75
1.75
1.74
1.73
0.83
0.82
Et
O
OH
CO2Me
CO2Me
0.92
1.93
6.00
1.07
2.07
1.05
1.17
1.01
1.01
3.11
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
−1.
f1 (ppm)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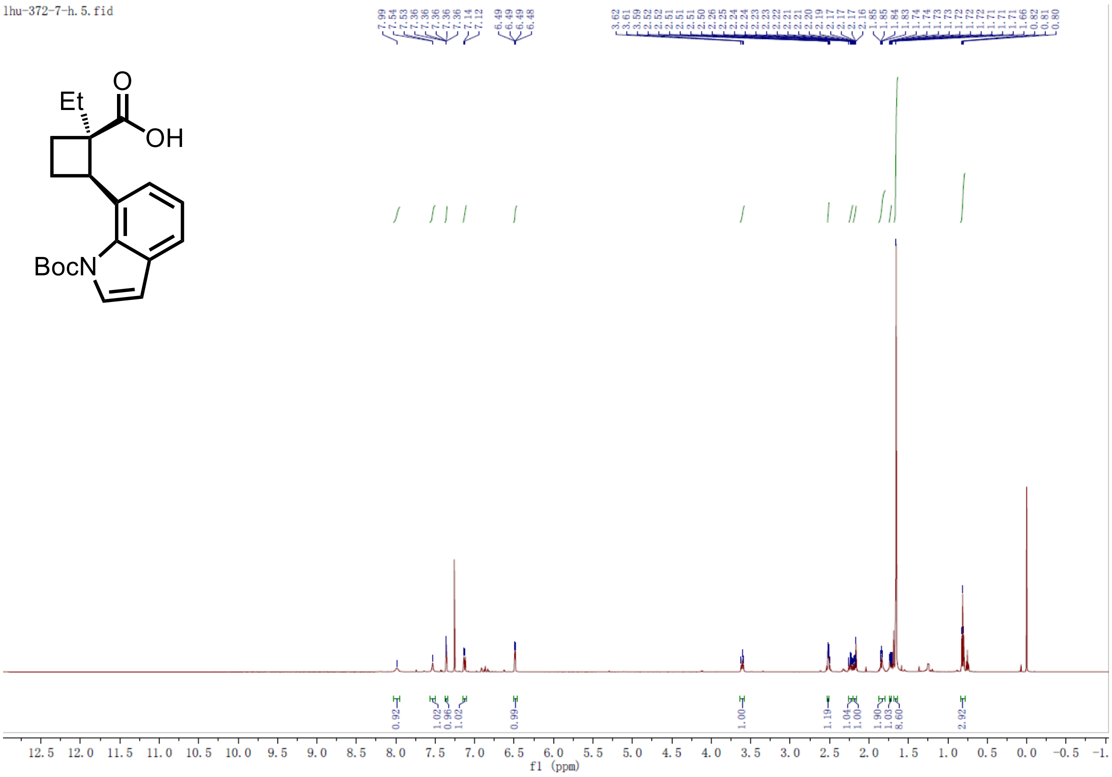
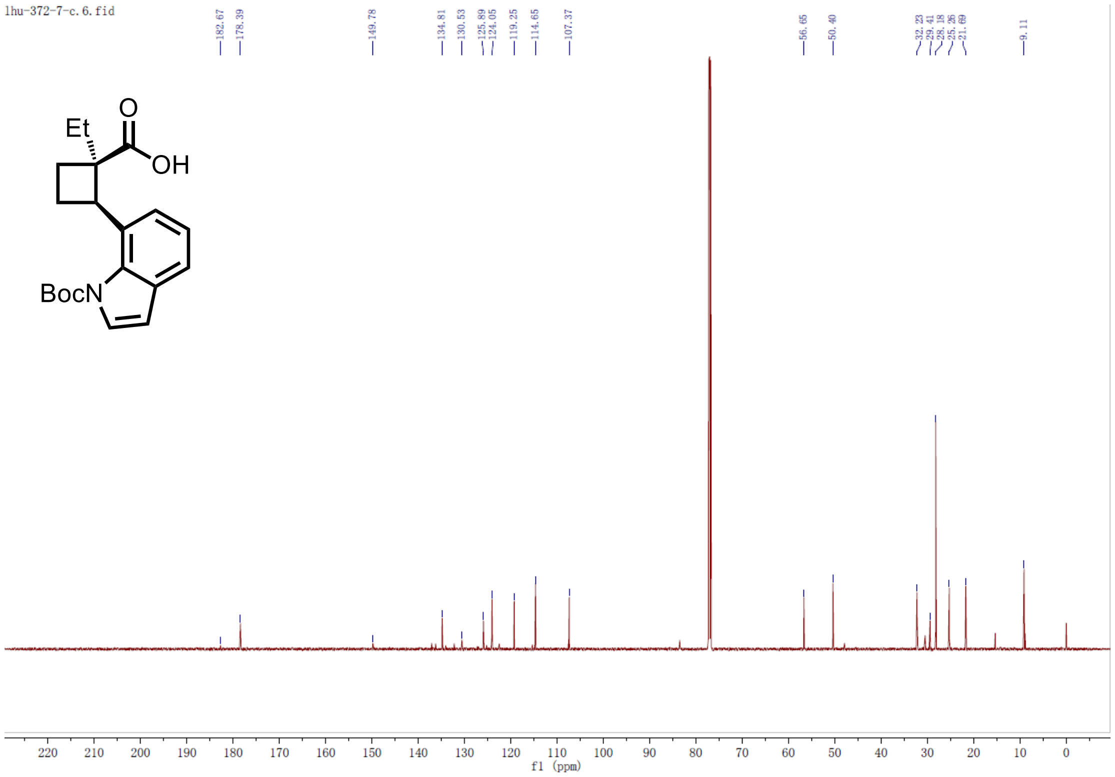
166.28
141.46
132.71
130.34
129.09
56.43
52.30
49.48
32.17
25.36
21.18
9.01
Et
O
OH
CO2Me
CO2Me
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


lhu-372-7-h.5.fid
7.99
7.54
7.53
7.36
7.36
7.36
7.36
7.36
7.14
7.12
6.49
6.49
6.49
6.48
3.62
3.61
3.59
2.52
2.52
2.51
2.51
2.51
2.50
2.26
2.25
2.24
2.24
2.23
2.23
2.22
2.21
2.21
2.20
2.19
2.17
2.17
2.17
2.16
1.85
1.85
1.84
1.83
1.74
1.74
1.73
1.73
1.72
1.72
1.72
1.71
1.71
1.71
1.66
0.82
0.81
0.80
Et
O
OH
BocN
0.92
1.02
0.96
1.02
0.99
1.00
1.19
1.04
1.00
1.90
1.03
8.60
2.92
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)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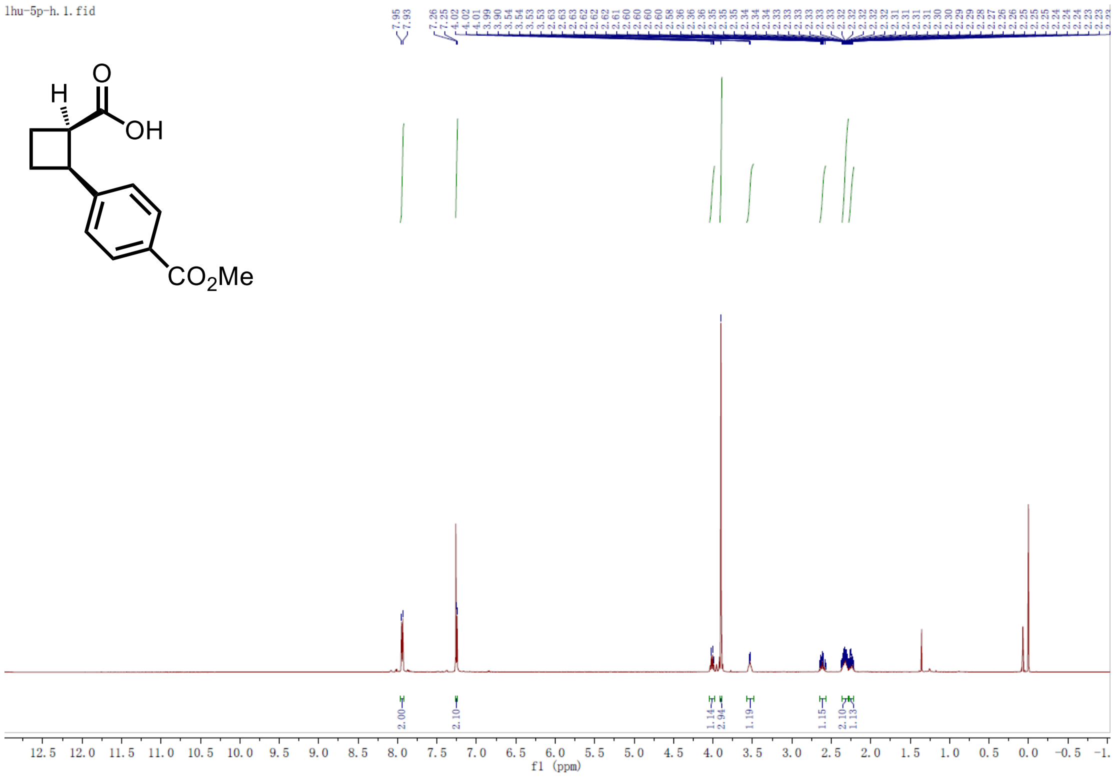
149.78
134.81
130.53
125.89
124.05
119.25
114.65
107.37
56.65
50.40
32.23
29.41
28.18
25.26
21.69
9.11
Et
O
OH
BocN
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


lhu-5p-h.1.fid
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7.93
7.26
7.25
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4.02
4.01
3.99
3.90
3.54
3.54
3.53
3.53
2.63
2.63
2.63
2.62
2.62
2.62
2.61
2.60
2.60
2.60
2.58
2.36
2.36
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2.35
2.34
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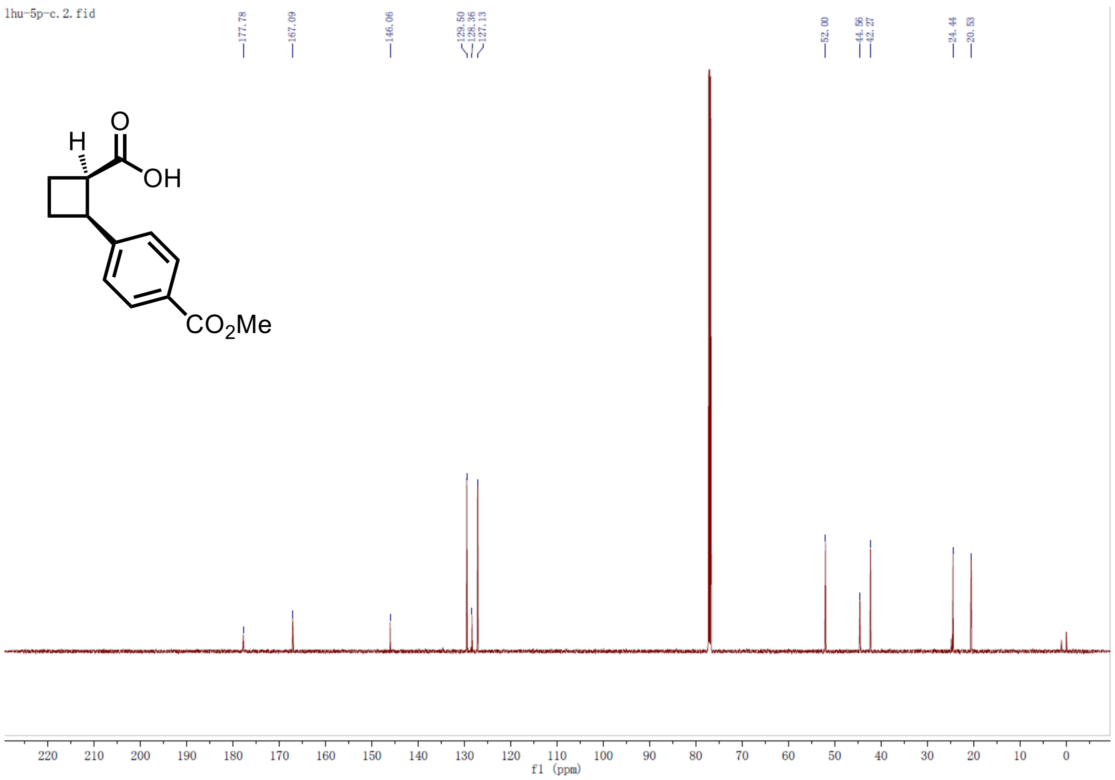
2.27
2.26
2.26
2.25
2.25
2.25
2.24
2.24
2.24
2.23
2.23
H
O
OH
CO2Me
2.00
2.10
1.14
2.94
1.19
1.15
2.10
1.13
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.
f1 (ppm)


lhu-5p-c.2.fid
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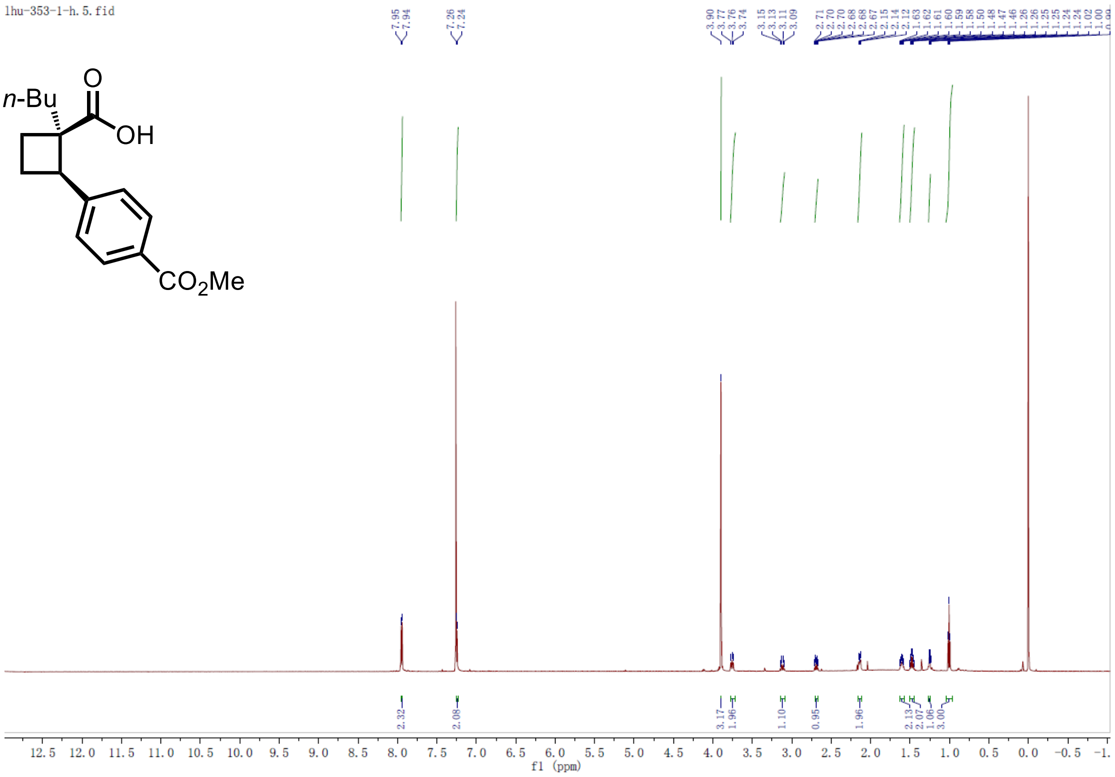
167.09
146.06
129.50
128.36
127.13
52.00
44.56
42.27
24.44
20.53
O
H
OH
CO2Me
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


lhu-353-1-h.5.fid
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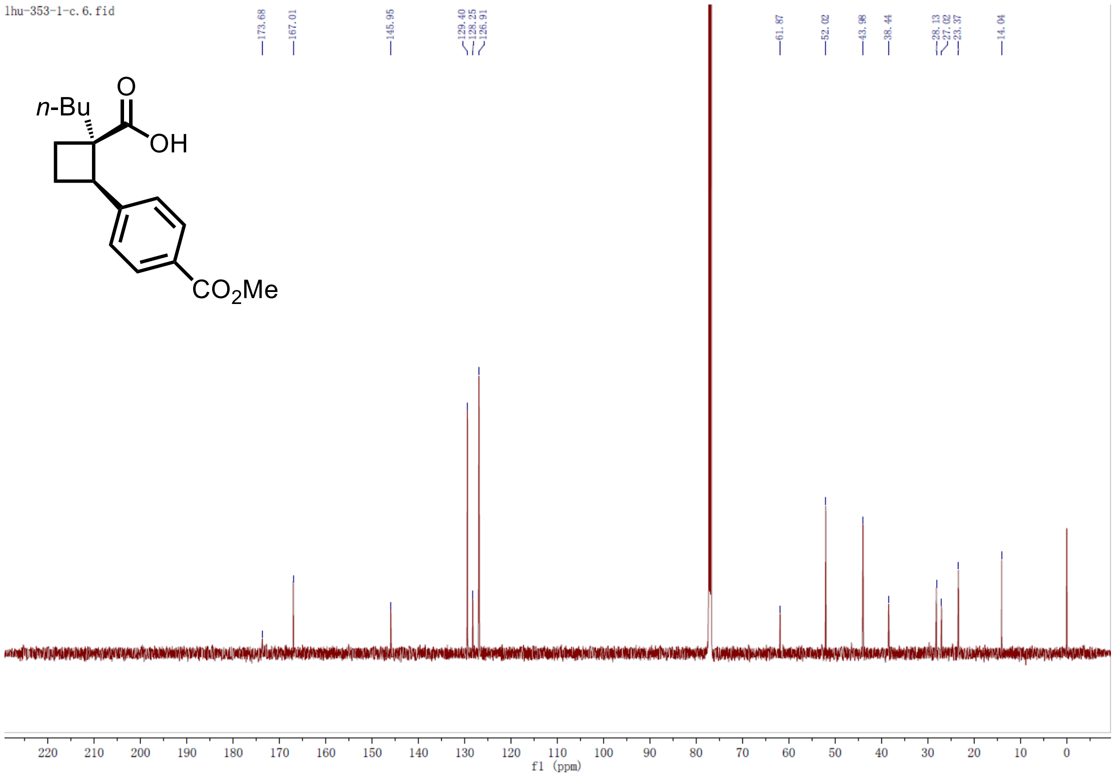
7.94
7.26
7.24
3.90
3.77
3.76
3.74
3.15
3.13
3.11
3.09
2.71
2.70
2.70
2.68
2.68
2.67
2.15
2.14
2.12
1.63
1.62
1.61
1.60
1.59
1.58
1.50
1.48
1.47
1.46
1.26
1.26
1.25
1.25
1.24
1.24
1.02
1.00
n-Bu
O
OH
CO2Me
2.32
2.08
3.17
1.96
1.10
0.95
1.96
2.13
2.07
1.06
3.00
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)


lhu-353-1-c.6.fid
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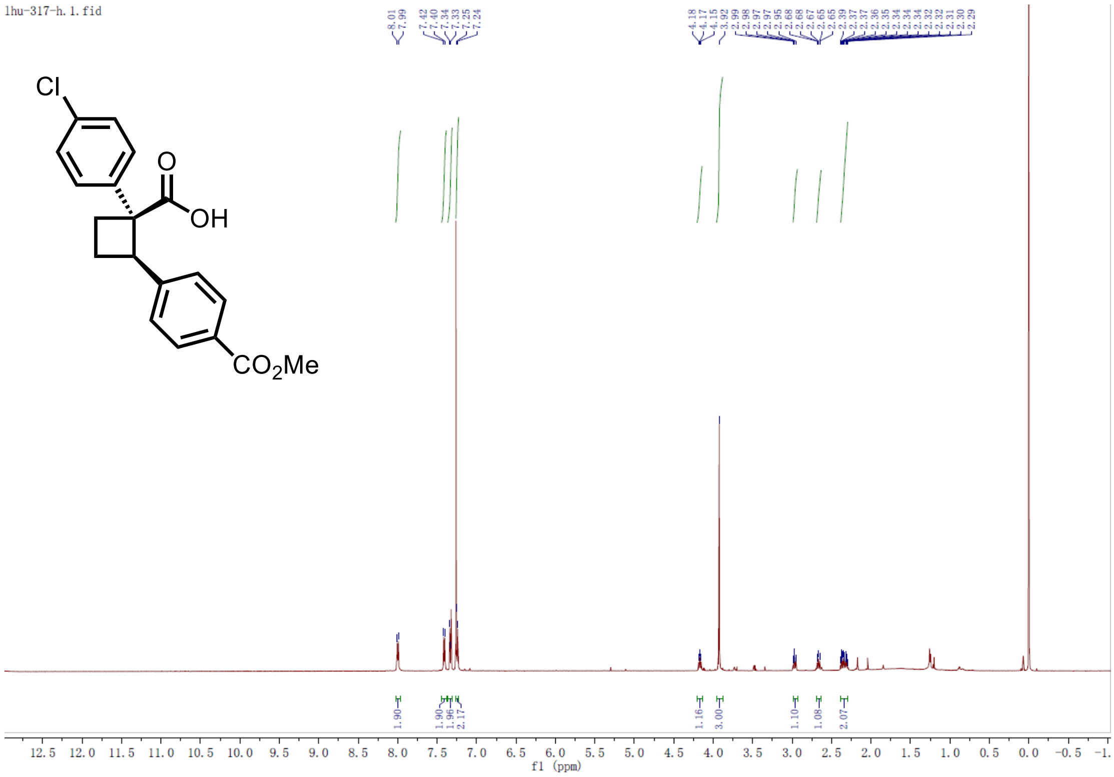
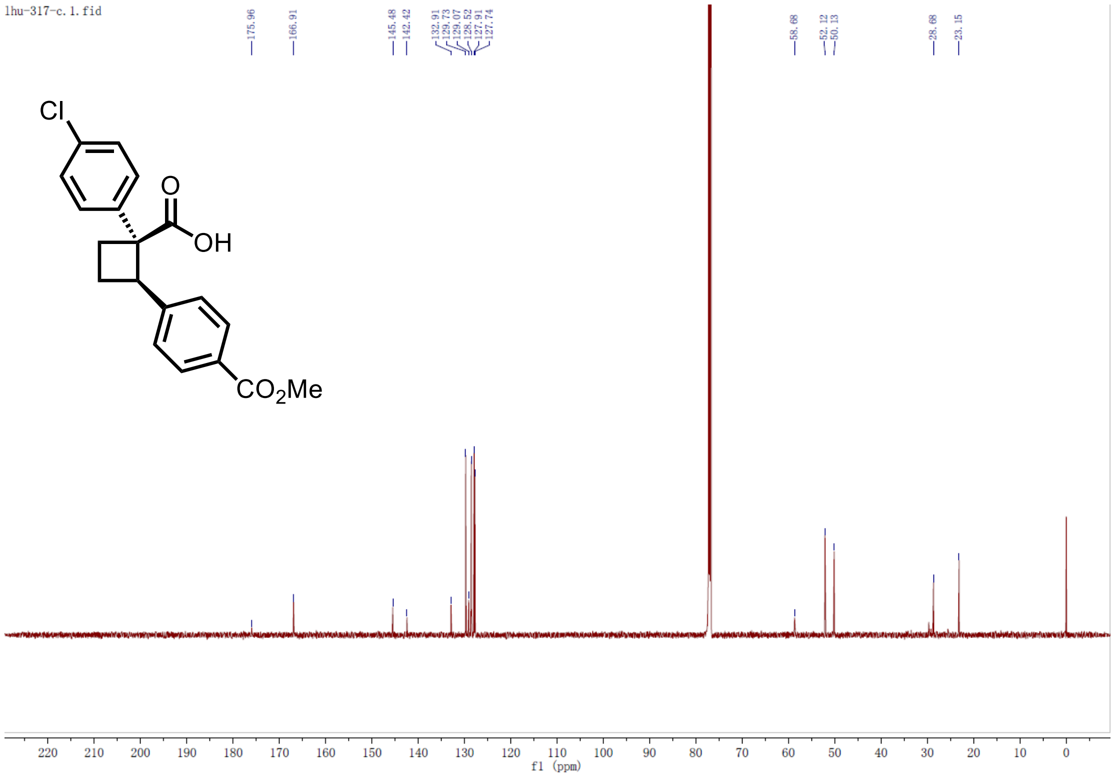
145.95
129.40
128.25
126.91
61.87
52.02
43.98
38.44
28.13
27.02
23.37
14.04
n-Bu
O
OH
CO2Me
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


lhu-317-h.1.fid
8.01
7.99
7.42
7.40
7.34
7.33
7.25
7.24
4.18
4.17
4.15
3.92
2.99
2.98
2.97
2.97
2.95
2.68
2.68
2.67
2.65
2.65
2.39
2.37
2.37
2.36
2.35
2.34
2.34
2.34
2.32
2.32
2.31
2.30
2.29
Cl
O
OH
CO2Me
1.90
1.90
1.96
2.17
1.16
3.00
1.10
1.08
2.07
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.
f1 (ppm)


lhu-317-c.1.fid
175.96
166.91
145.48
142.42
132.91
129.73
129.07
128.52
127.91
127.74
58.68
52.12
50.13
28.68
23.15
Cl
O
OH
CO2Me
220
210
200
190
180
170
160
150
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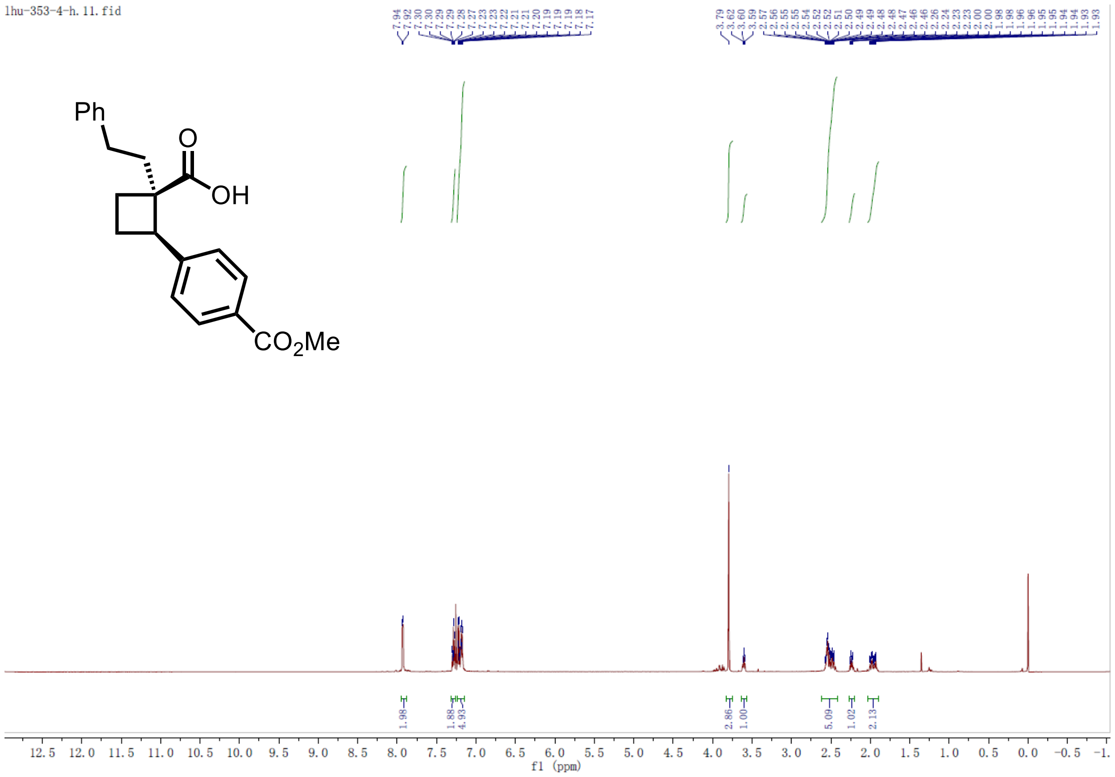
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


lhu-353-4-h.11.fid
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7.92
7.30
7.30
7.29
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7.21
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7.18
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2.51
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2.49
2.48
2.48
2.47
2.46
2.46
2.26
2.24
2.23
2.23
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2.00
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1.98
1.96
1.96
1.95
1.95
1.94
1.94
1.93
1.93
Ph
O
OH
CO2Me
1.98
1.88
4.93
2.86
1.00
5.09
1.02
2.13
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11.5
11.0
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10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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2.0
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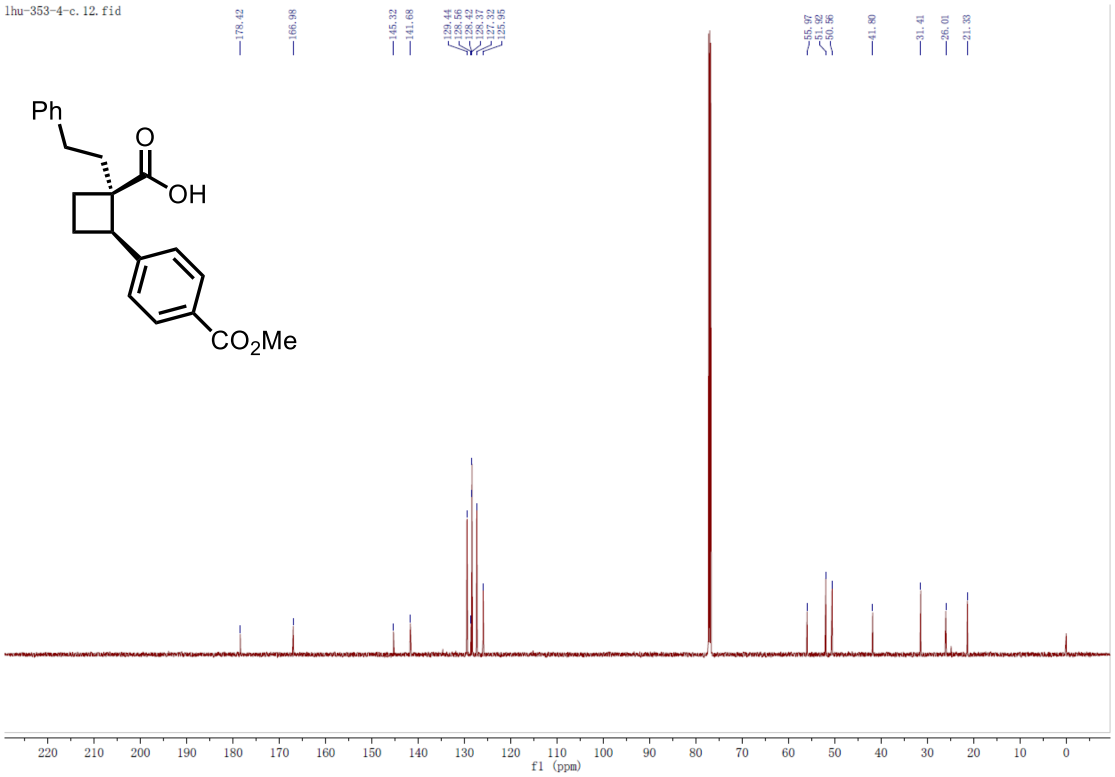
-1.
f1 (ppm)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128.37
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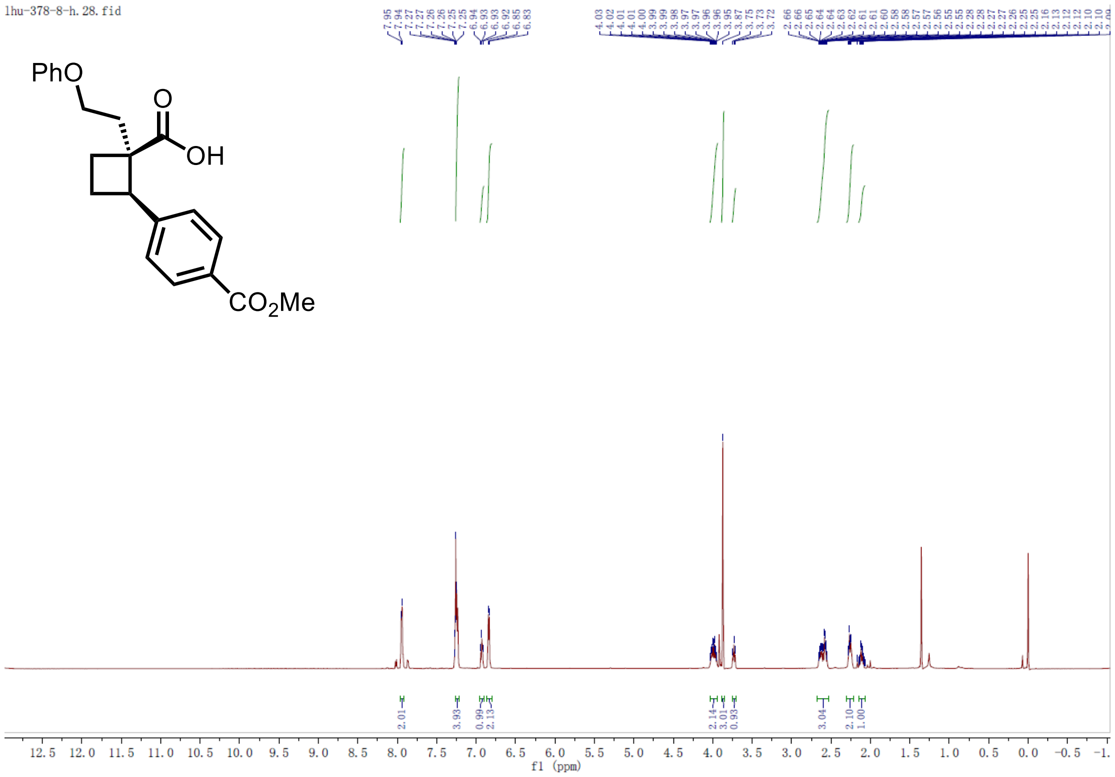
125.95
55.97
51.92
50.56
41.80
31.41
26.01
21.33
Ph
O
OH
CO2Me
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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6.83
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4.02
4.01
4.01
4.00
3.99
3.99
3.98
3.97
3.97
3.96
3.96
3.95
3.87
3.75
3.73
3.72
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2.66
2.65
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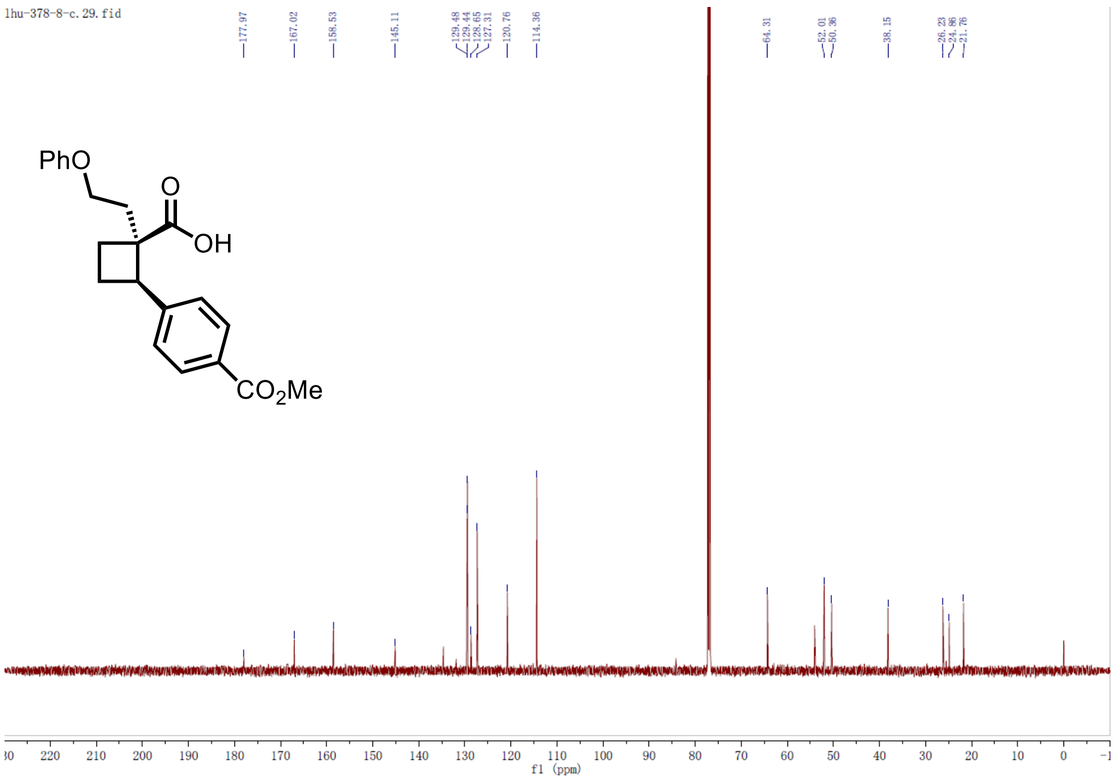
2.64
2.63
2.62
2.61
2.61
2.60
2.58
2.58
2.57
2.57
2.56
2.55
2.55
2.28
2.28
2.27
2.27
2.26
2.25
2.25
2.16
2.13
2.12
2.12
2.10
2.10
PhO
O
OH
CO2Me
2.01
3.93
0.99
2.13
2.14
3.01
0.93
3.04
2.10
1.00
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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127.31
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64.31
52.01
50.36
38.15
26.23
24.86
21.76
PhO
O
OH
CO2Me
220
210
200
190
180
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130
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90
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50
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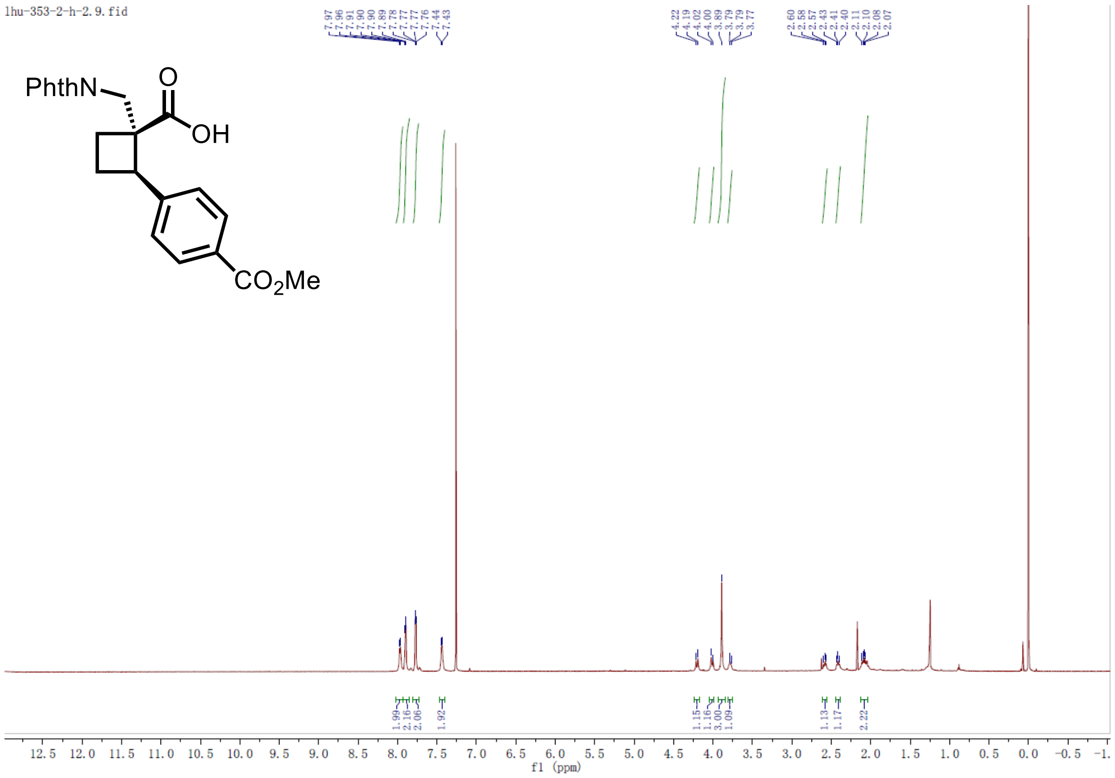
f1 (ppm)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7.90
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7.77
7.77
7.76
7.44
7.43
4.22
4.19
4.02
4.00
3.89
3.79
3.79
3.77
2.60
2.58
2.57
2.43
2.41
2.40
2.11
2.10
2.08
2.07
PhthN
O
OH
CO2Me
1.99
2.16
2.06
1.92
1.15
1.16
3.00
1.09
1.13
1.17
2.22
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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3.0
2.5
2.0
1.5
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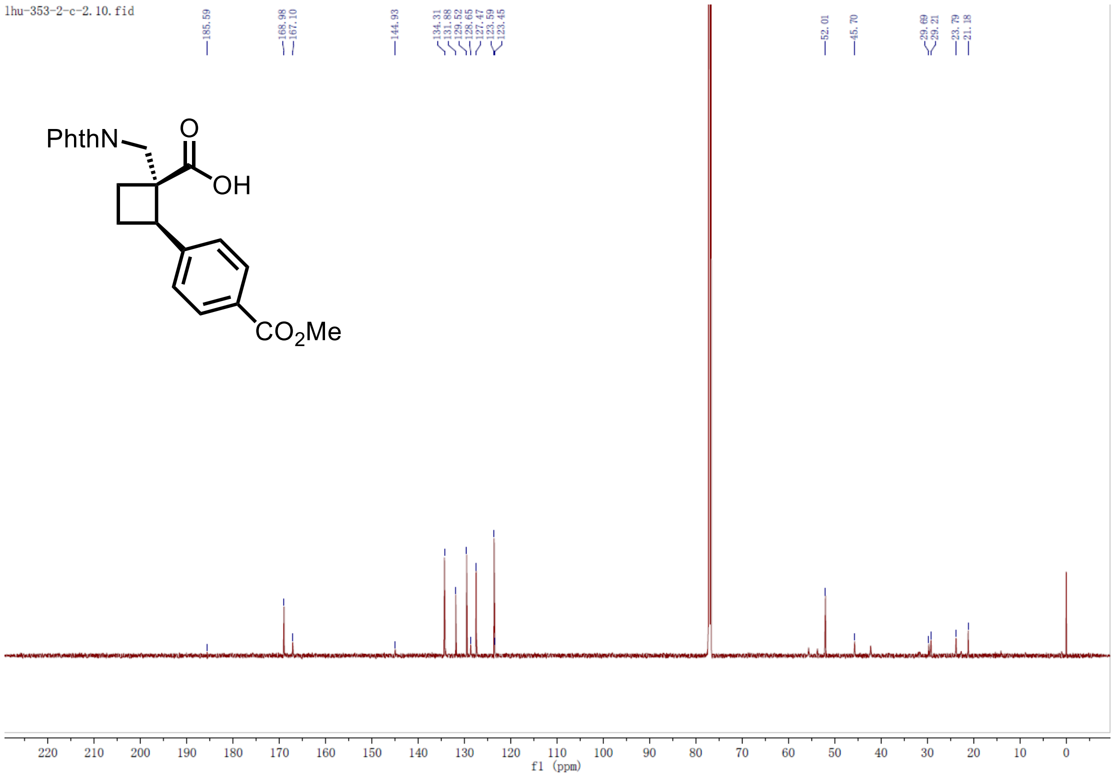
0.5
0.0
-0.5
f1 (ppm)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128.65
127.47
123.59
123.45
52.01
45.70
29.69
29.21
23.79
21.18
PhthN
O
OH
CO2Me
220
210
200
190
180
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130
120
110
100
90
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50
40
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10
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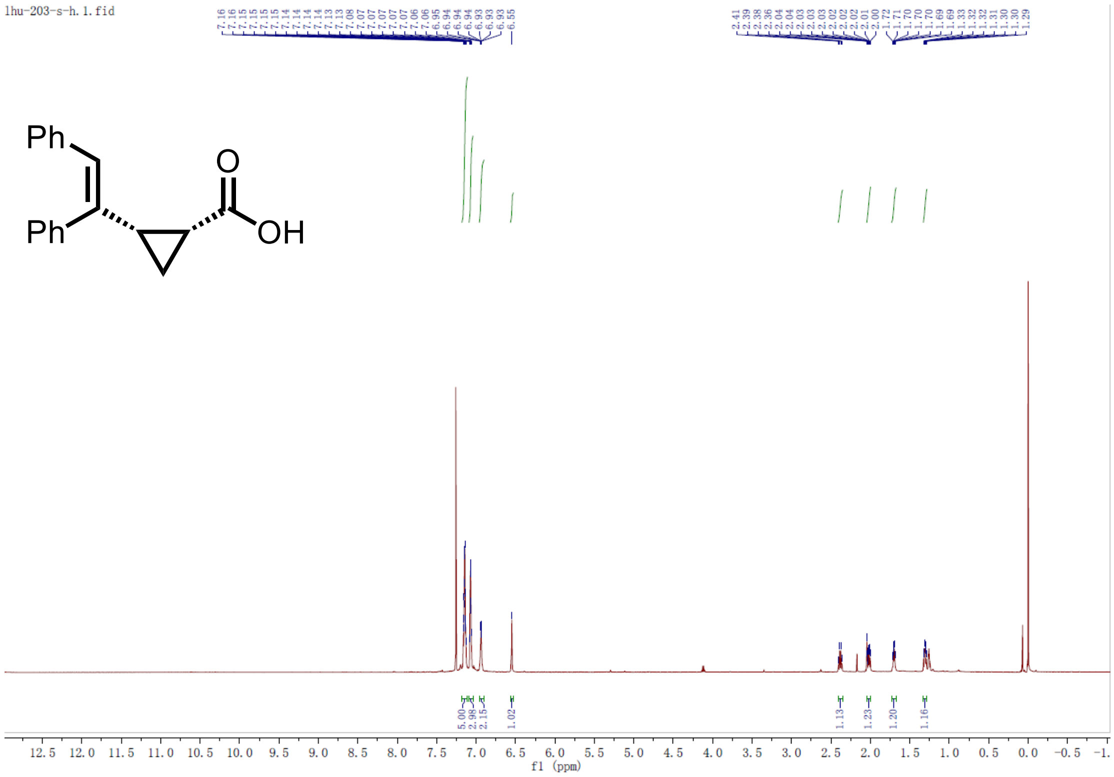
f1 (ppm)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7.14
7.14
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7.13
7.13
7.08
7.07
7.07
7.07
7.07
7.07
7.06
7.06
6.95
6.94
6.94
6.94
6.93
6.93
6.93
6.55
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2.39
2.38
2.36
2.04
2.04
2.03
2.03
2.03
2.02
2.02
2.02
2.01
2.00
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1.71
1.70
1.70
1.70
1.69
1.69
1.33
1.32
1.32
1.31
1.30
1.30
1.29
Ph
Ph
O
OH
5.00
2.98
2.15
1.02
1.13
1.23
1.20
1.16
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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2.5
2.0
1.5
1.0
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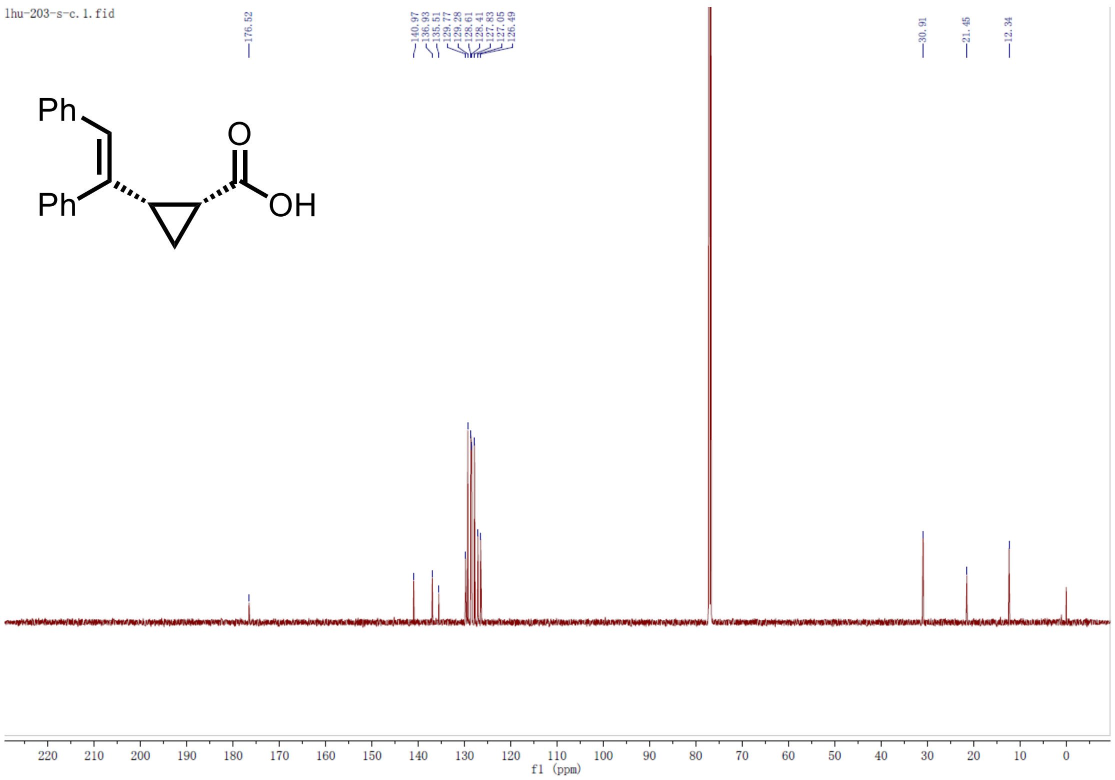
0.0
-0.5
-1.
f1 (ppm)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135.51
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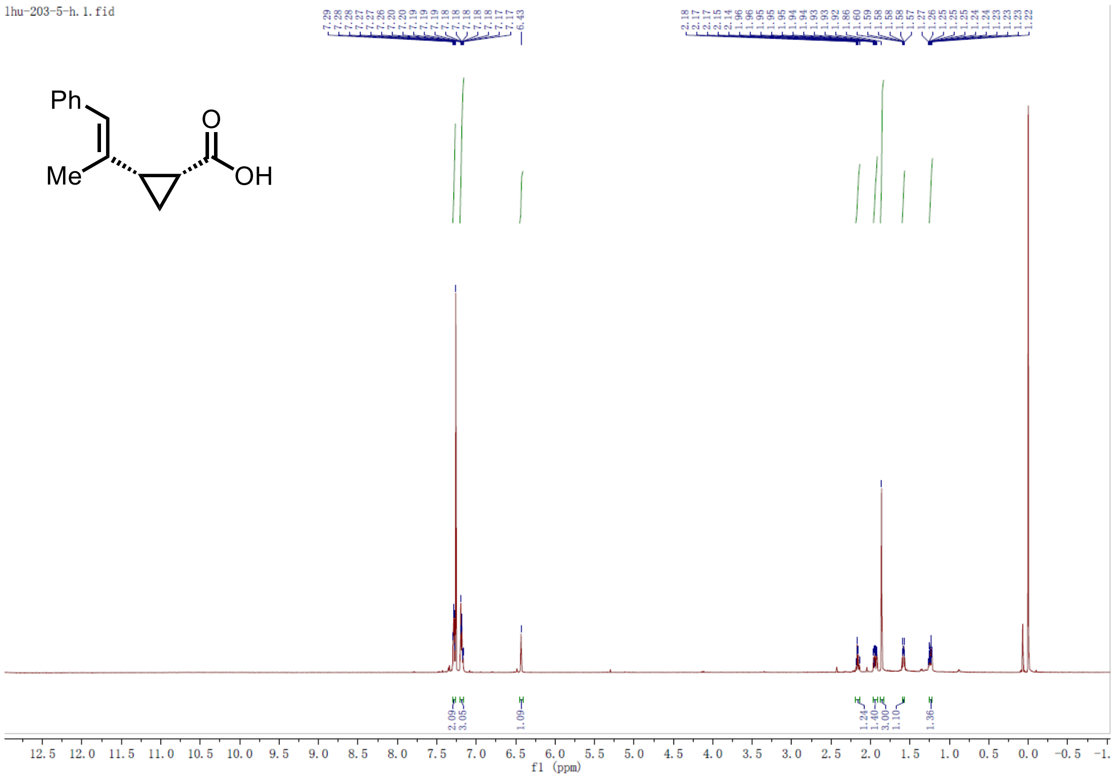
129.28
128.61
128.41
127.83
127.05
126.49
30.91
21.45
12.34
Ph
Ph
O
OH
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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7.28
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7.27
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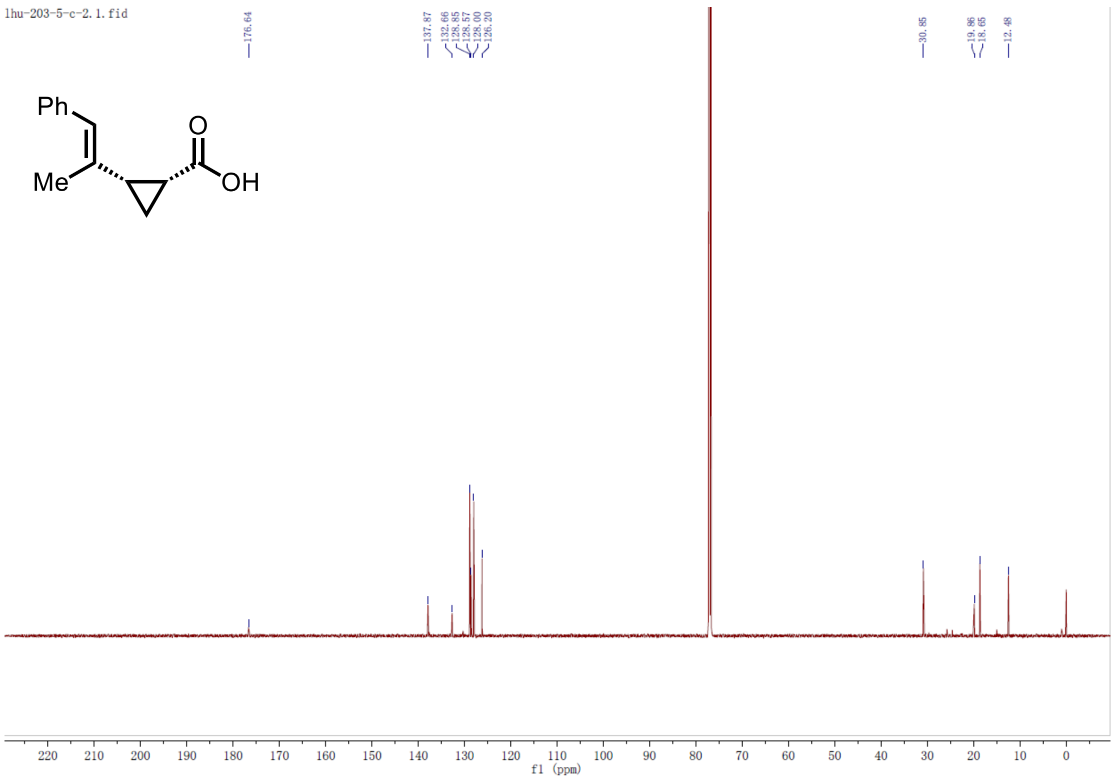
7.20
7.20
7.19
7.19
7.19
7.18
7.18
7.18
7.18
7.18
7.17
7.17
6.43
2.18
2.17
2.17
2.15
2.14
1.96
1.96
1.95
1.95
1.95
1.94
1.94
1.93
1.93
1.92
1.86
1.60
1.59
1.58
1.58
1.58
1.57
1.27
1.26
1.25
1.25
1.25
1.24
1.24
1.23
1.23
1.23
1.22
Ph
Me
O
OH
2.09
3.05
1.09
1.24
1.40
3.00
1.10
1.36
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)


lhu-203-5-c-2.1.fid
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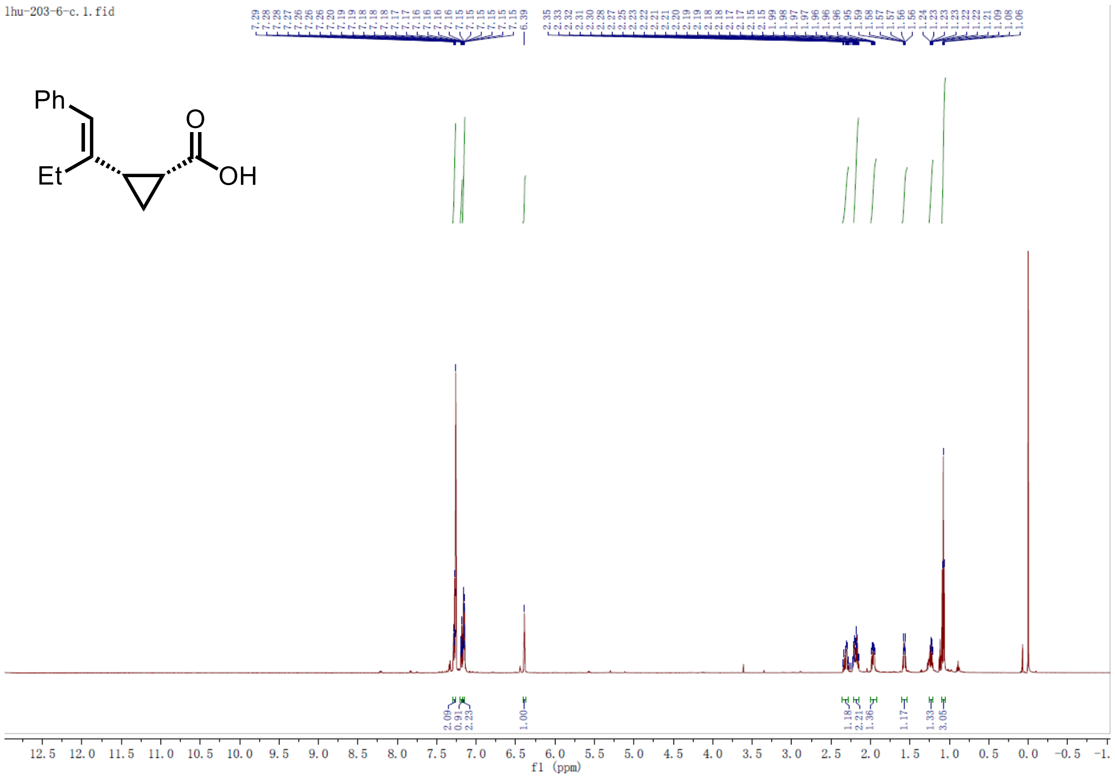
137.87
132.66
128.85
128.57
128.00
126.20
30.85
19.86
18.65
12.48
Ph
Me
O
OH
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


lhu-203-6-c.1.fid
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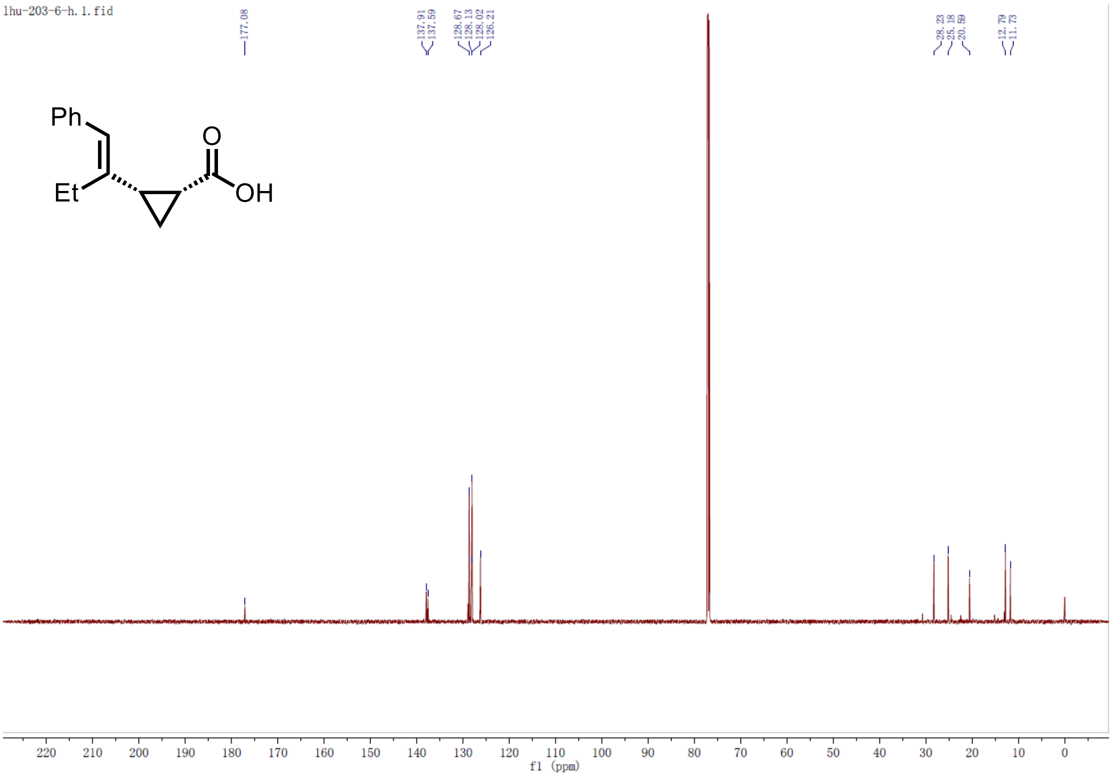
6.39
2.35 2.33 2.32 2.31 2.30 2.28 2.27 2.25 2.23 2.22 2.21 2.21 2.20 2.19 2.19 2.18 2.18 2.17 2.17 2.15 2.15 1.99 1.98 1.97 1.97 1.96 1.96 1.96 1.95 1.59 1.58 1.57 1.57 1.56 1.56 1.24 1.23 1.23 1.23 1.22 1.22 1.21 1.09 1.08 1.06
Ph
Et
O
OH
2.09
0.91
2.23
1.00
1.18
2.21
1.36
1.17
1.33
3.05
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)


lhu-203-6-h.1.fid
Ph
Et
O
OH
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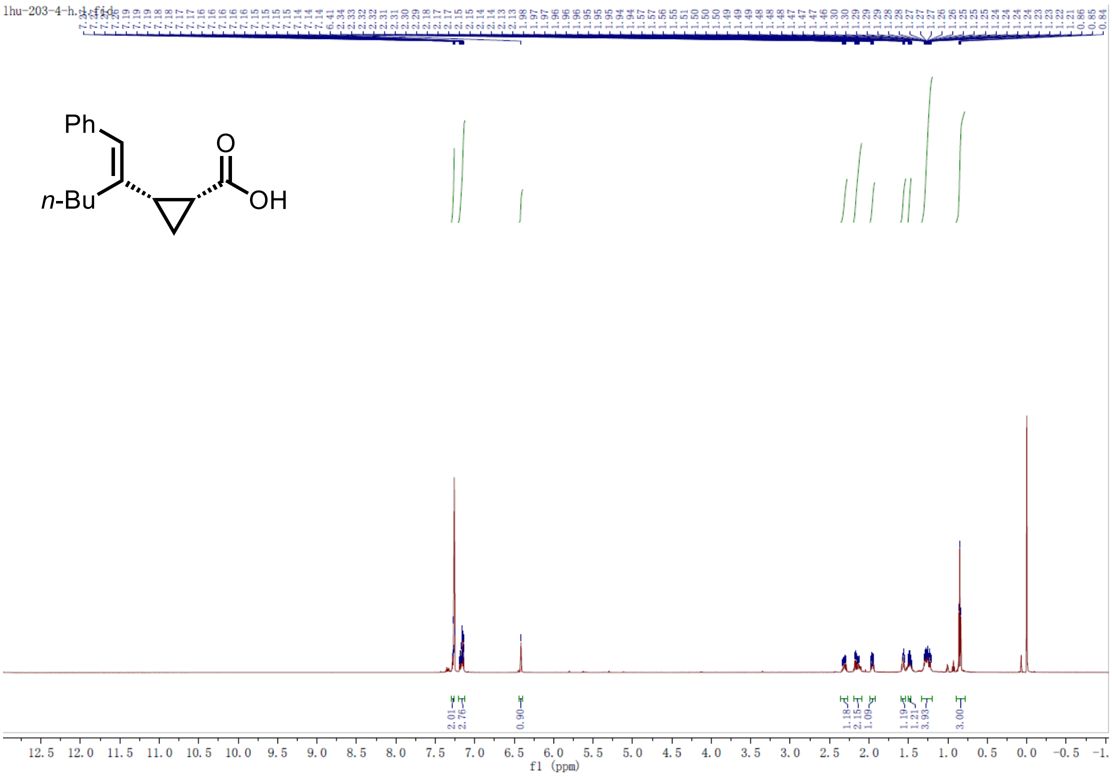
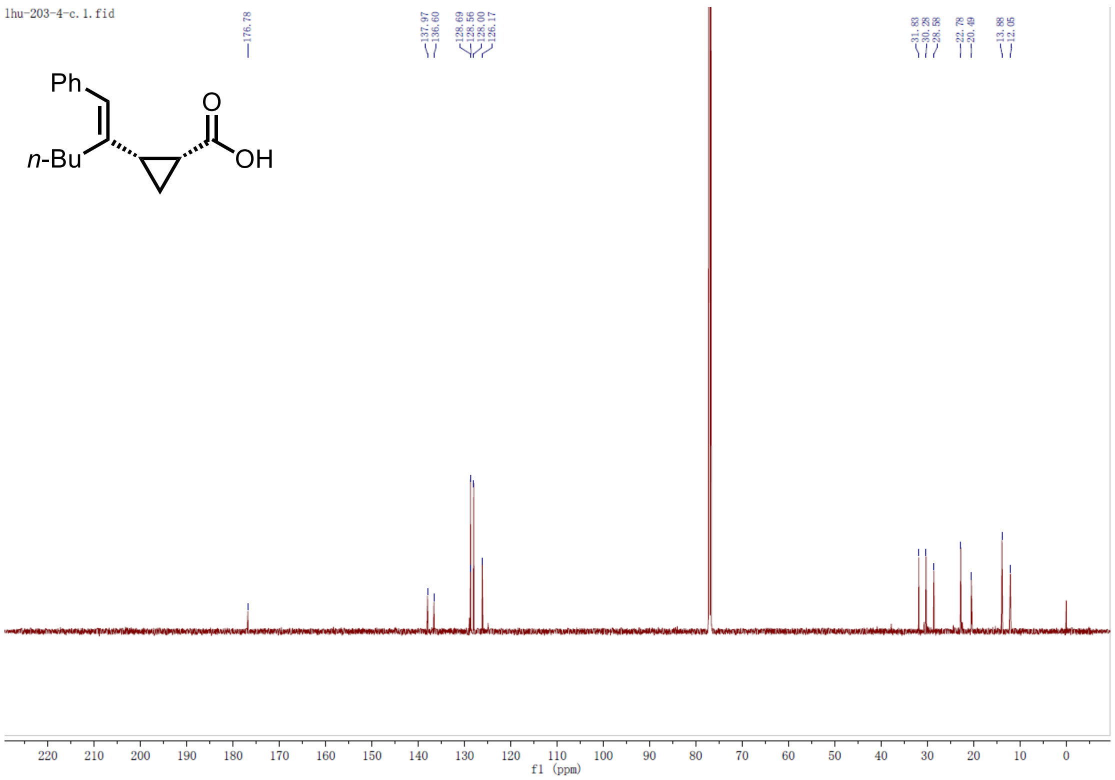
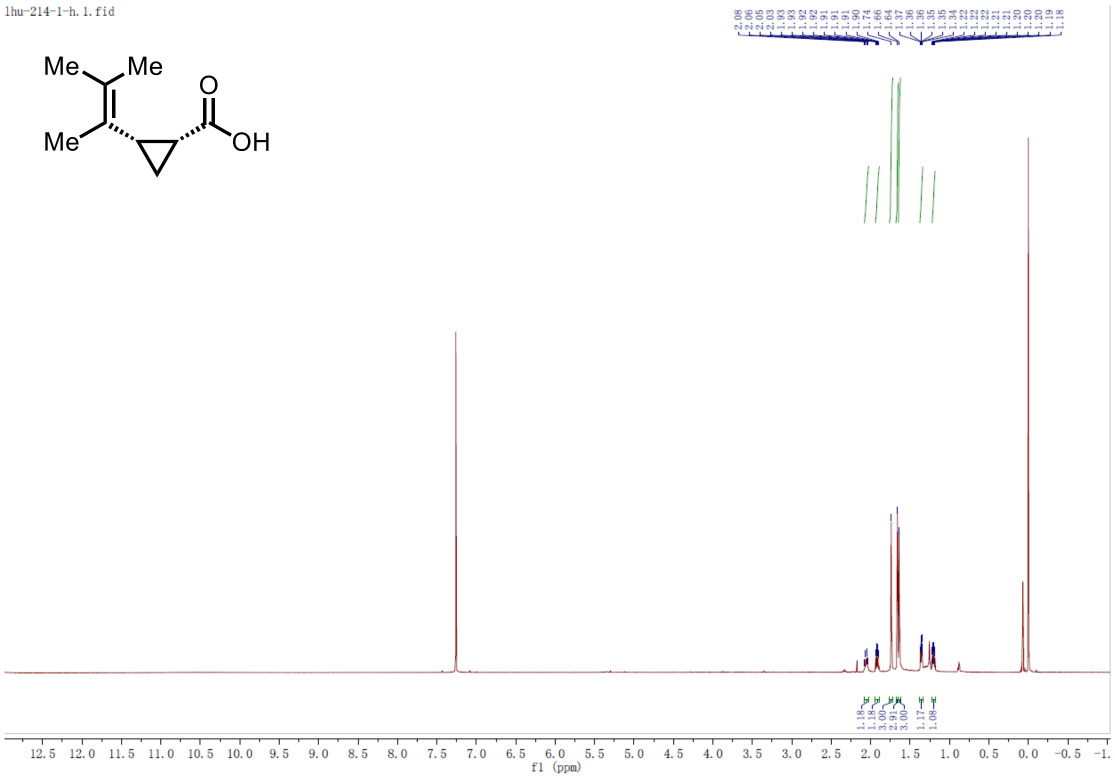
137.91
137.59
128.67
128.13
128.02
126.21
28.23
25.18
20.59
12.79
11.73
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


lhu-203-4-h.1.fid
Ph
n-Bu
O
OH
7.27 7.27 7.26 7.26 7.19 7.19 7.19 7.18 7.18 7.17 7.17 7.16 7.16 7.16 7.16 7.16 7.15 7.15 7.15 7.15 7.14 7.14 7.14 6.41 2.34 2.33 2.32 2.32 2.31 2.31 2.30 2.29 2.18 2.17 2.17 2.15 2.15 2.14 2.14 2.13 2.13 1.98 1.97 1.97 1.96 1.96 1.96 1.95 1.95 1.95 1.94 1.94 1.57 1.57 1.56 1.55 1.51 1.50 1.50 1.50 1.49 1.49 1.49 1.48 1.48 1.48 1.47 1.47 1.47 1.46 1.30 1.30 1.29 1.29 1.29 1.28 1.28 1.27 1.27 1.27 1.26 1.26 1.25 1.25 1.25 1.24 1.24 1.24 1.24 1.23 1.23 1.22 1.21 0.86 0.85 0.84
2.01
2.76
0.90
1.18
2.15
1.09
1.19
1.21
3.93
3.00
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)


lhu-203-4-c.1.fid
Ph
O
n-Bu
OH
176.78
137.97
136.60
128.69
128.56
128.00
126.17
31.83
30.28
28.58
22.78
20.49
13.88
12.05
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


lhu-214-1-h.1.fid
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Me
O
Me
OH
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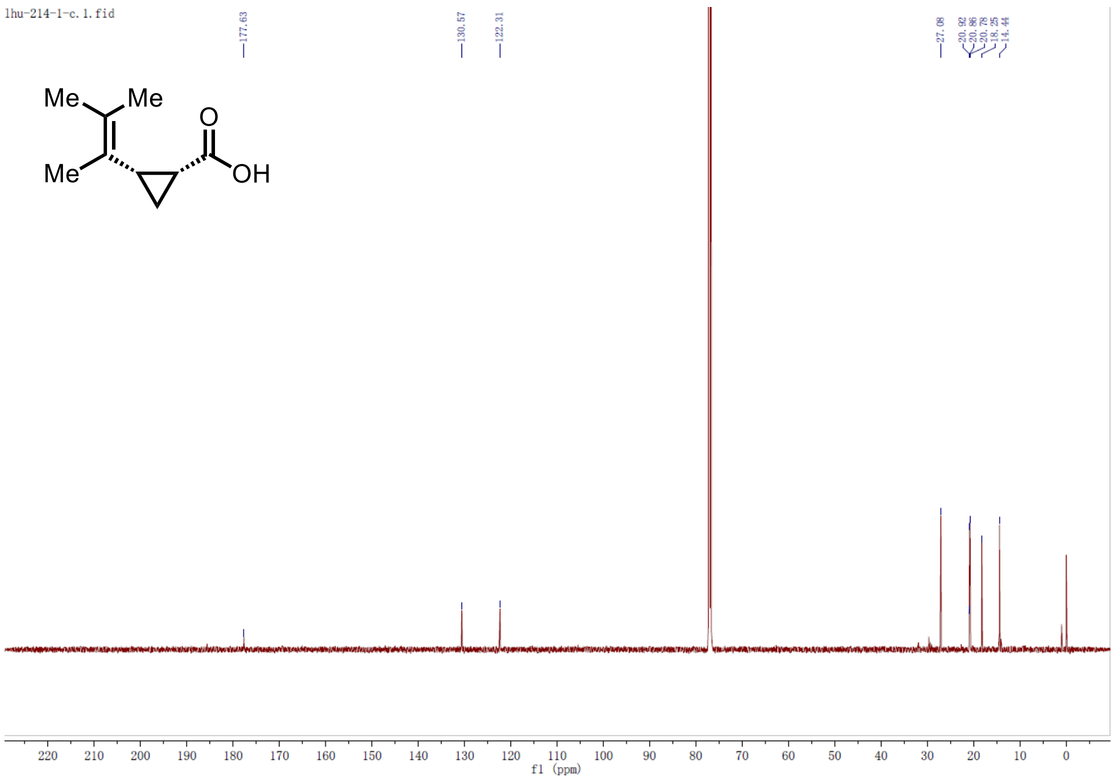
2.06
2.05
2.03
1.93
1.93
1.92
1.92
1.91
1.91
1.91
1.90
1.74
1.66
1.64
1.37
1.36
1.36
1.35
1.35
1.34
1.22
1.22
1.22
1.21
1.21
1.20
1.20
1.20
1.19
1.18
1.18
1.18
3.00
2.91
3.00
1.17
1.08
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)


lhu-214-1-c.1.fid
Me
Me
Me
O
OH
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122.31
27.08
20.92
20.86
20.78
18.25
14.44
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
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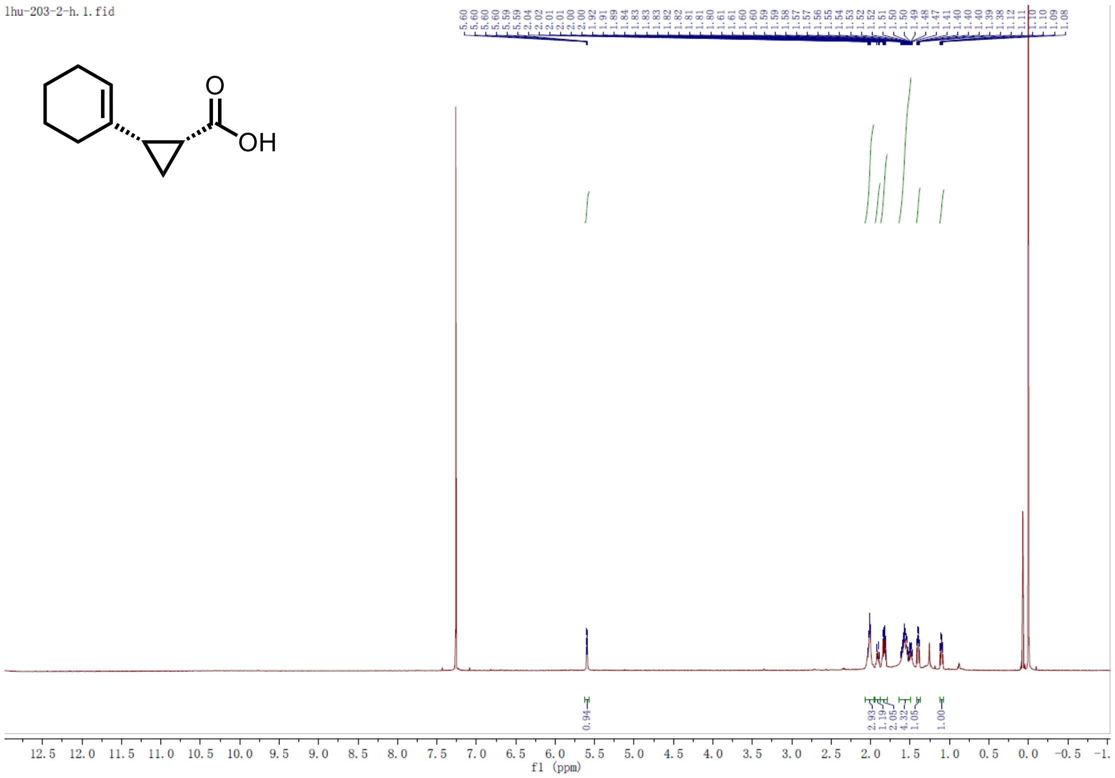
50
40
30
20
10
0
f1 (ppm)


lhu-203-2-h.1.fid
O
OH
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5.60
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5.59
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2.00
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1.60
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1.57
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1.56
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1.54
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1.52
1.51
1.50
1.50
1.49
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1.47
1.41
1.40
1.40
1.40
1.39
1.38
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1.11
1.10
1.10
1.09
1.08
0.94
2.93
1.19
2.05
4.32
1.05
1.00
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12.0
11.5
11.0
10.5
10.0
9.5
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6.5
6.0
5.5
5.0
4.5
4.0
3.5
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2.5
2.0
1.5
1.0
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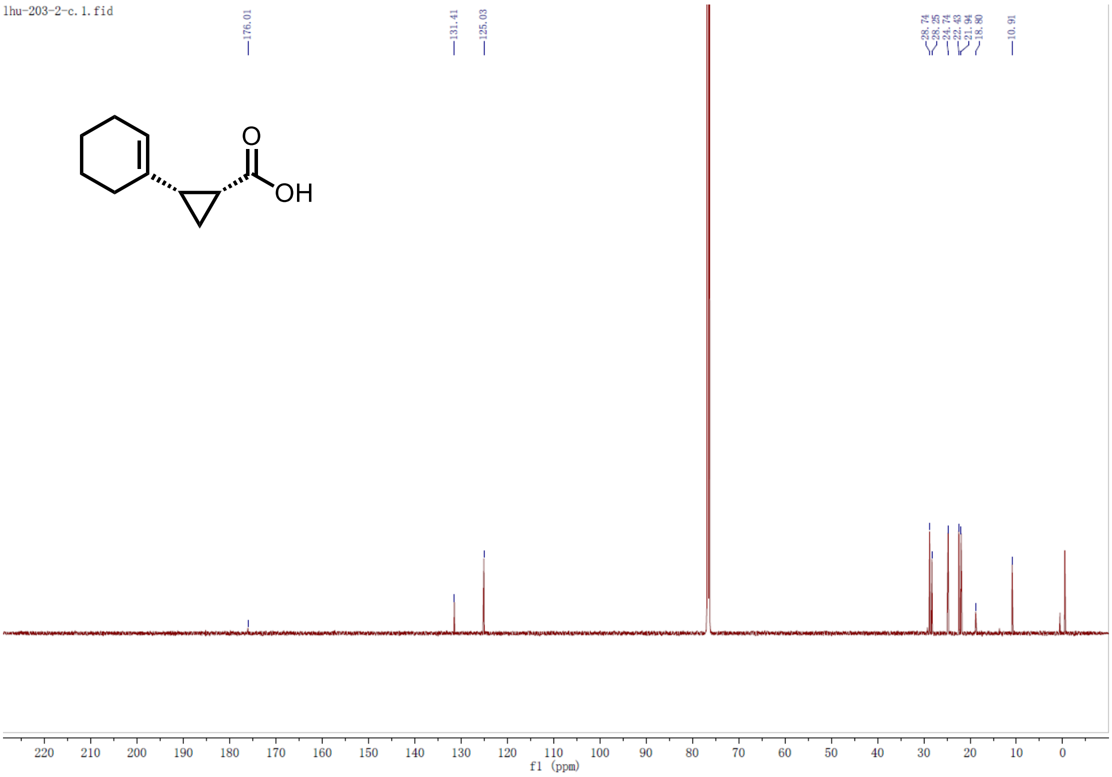
0.0
-0.5
-1.
f1 (ppm)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24.74
22.43
21.94
18.80
10.91
O
OH
220
210
200
190
180
170
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150
140
130
120
110
100
90
80
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50
40
30
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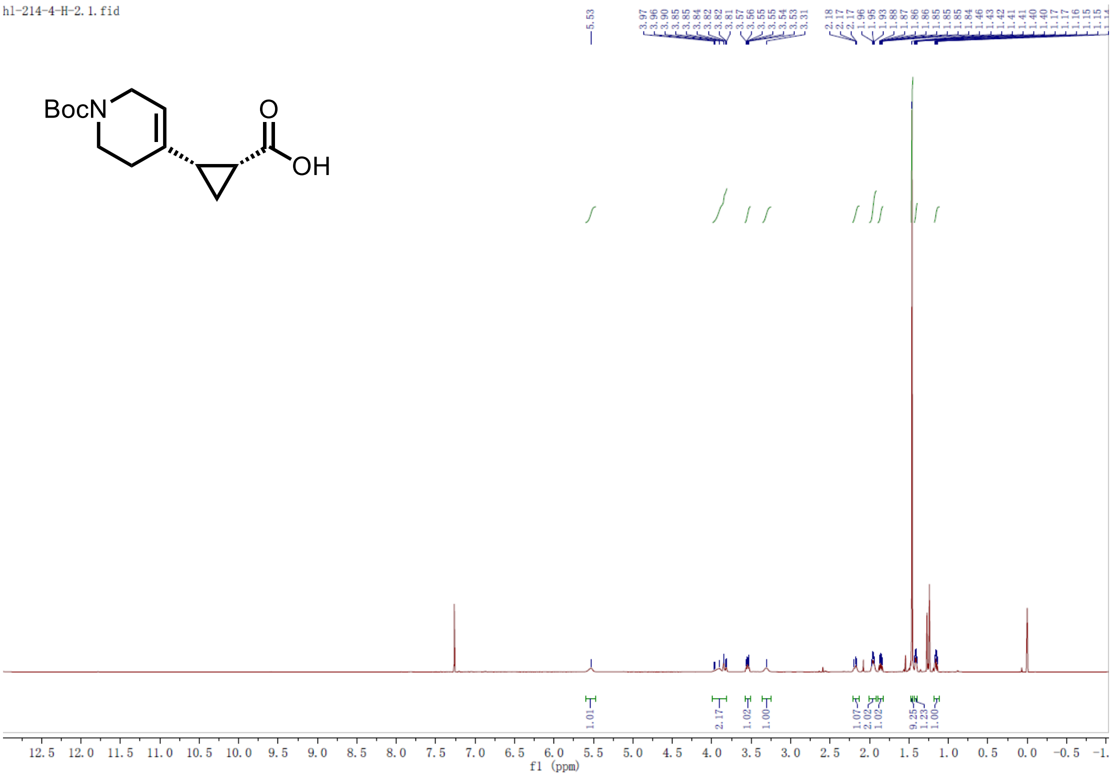
10
0
f1 (ppm)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3.81
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3.55
3.54
3.53
3.31
2.18
2.17
2.17
1.96
1.95
1.93
1.88
1.87
1.86
1.86
1.85
1.85
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1.84
1.46
1.43
1.42
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1.41
1.40
1.40
1.17
1.17
1.16
1.15
1.15
BocN
O
OH
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2.17
1.02
1.00
1.07
2.02
1.02
9.25
1.23
1.00
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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3.0
2.5
2.0
1.5
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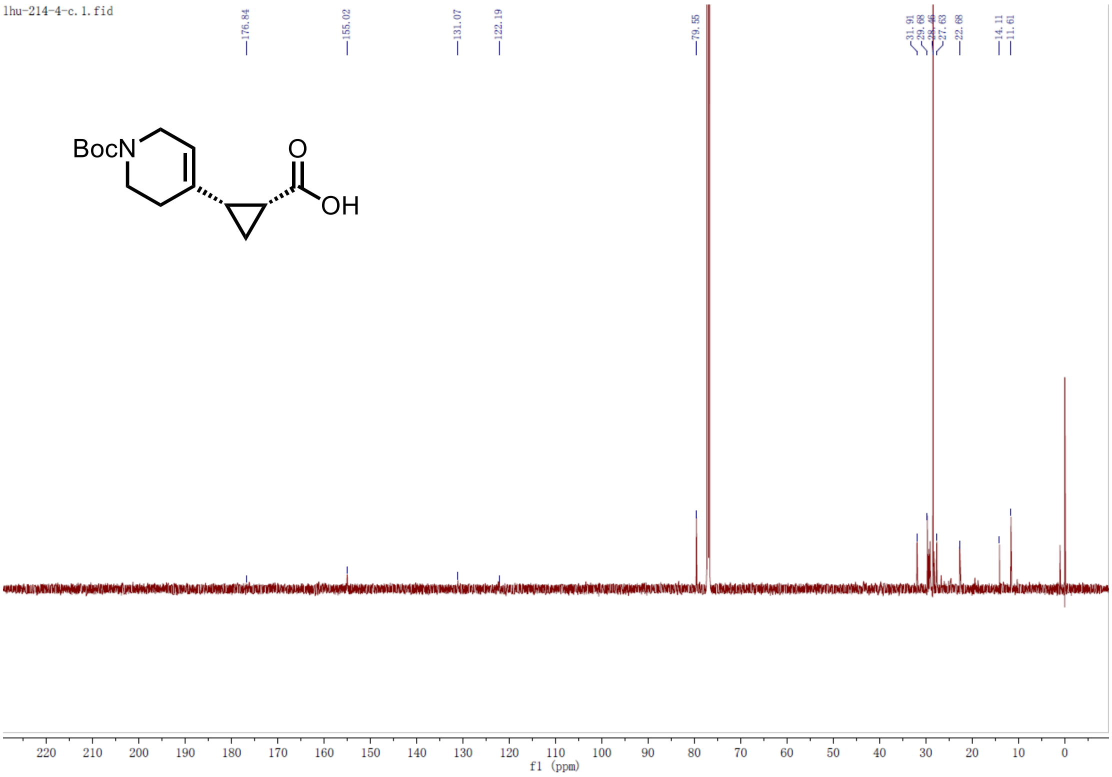
0.5
0.0
-0.5
f1 (ppm)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79.55
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29.68
28.46
27.63
22.68
14.11
11.61
BocN
O
OH
220
210
200
190
180
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110
100
90
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50
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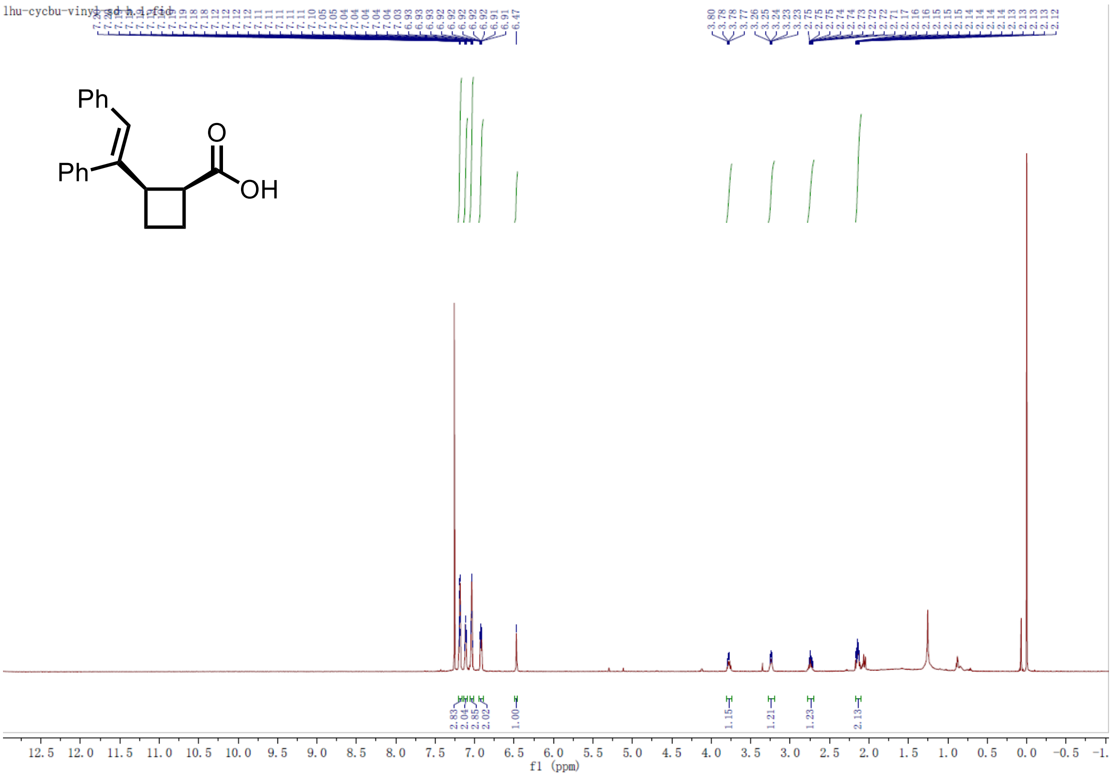
10
0
f1 (ppm)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6.47
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3.78
3.77
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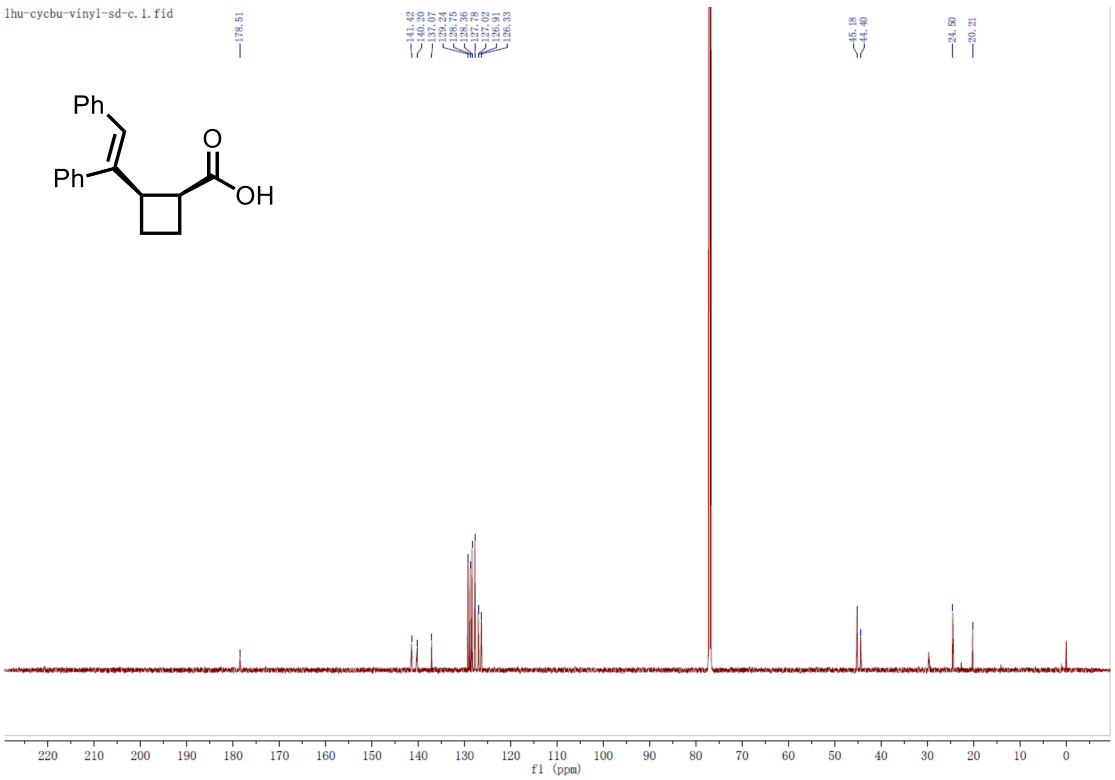
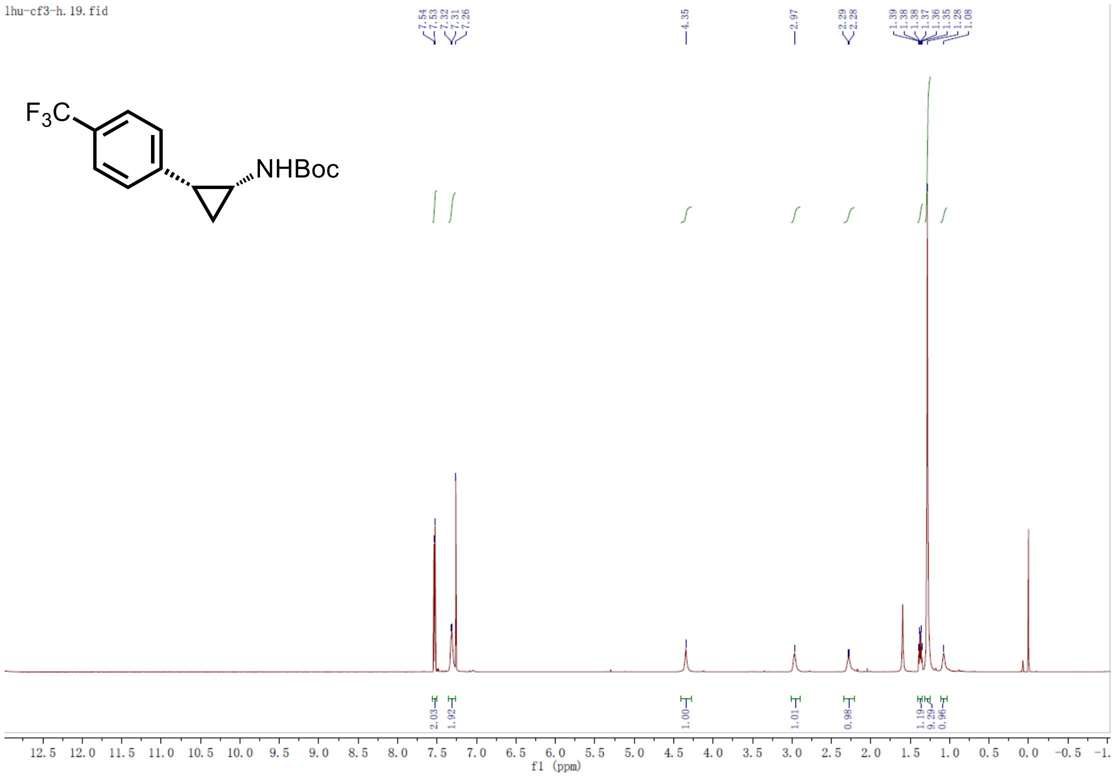
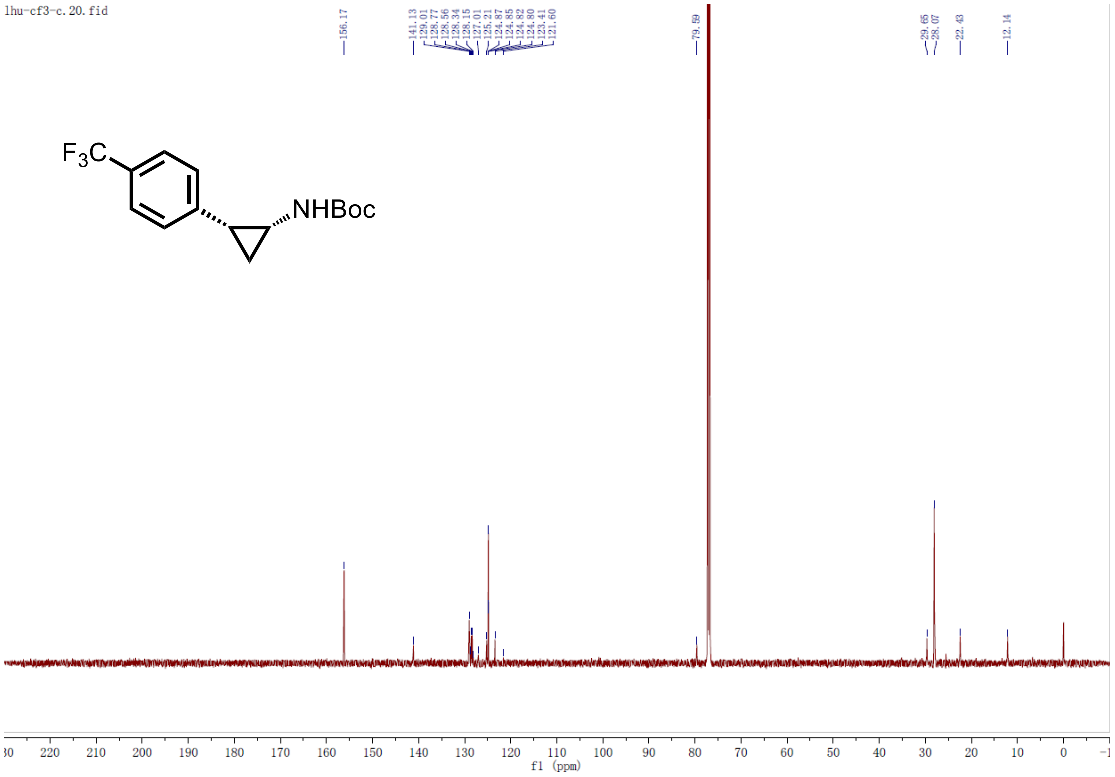
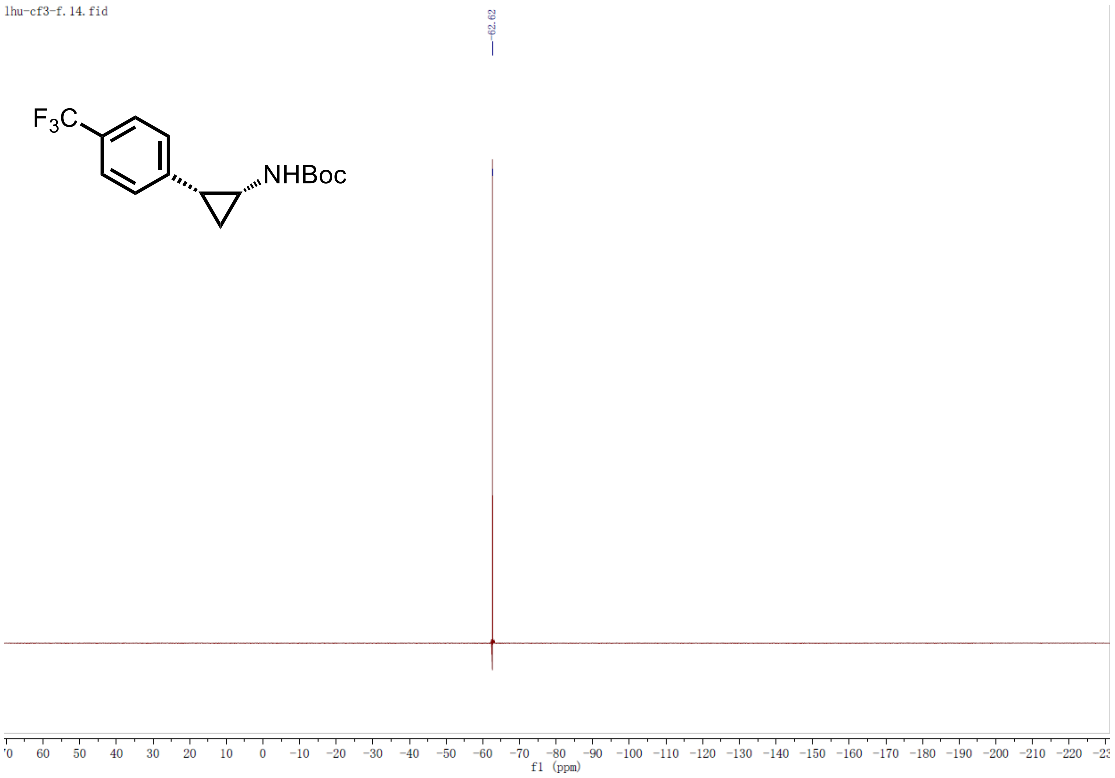
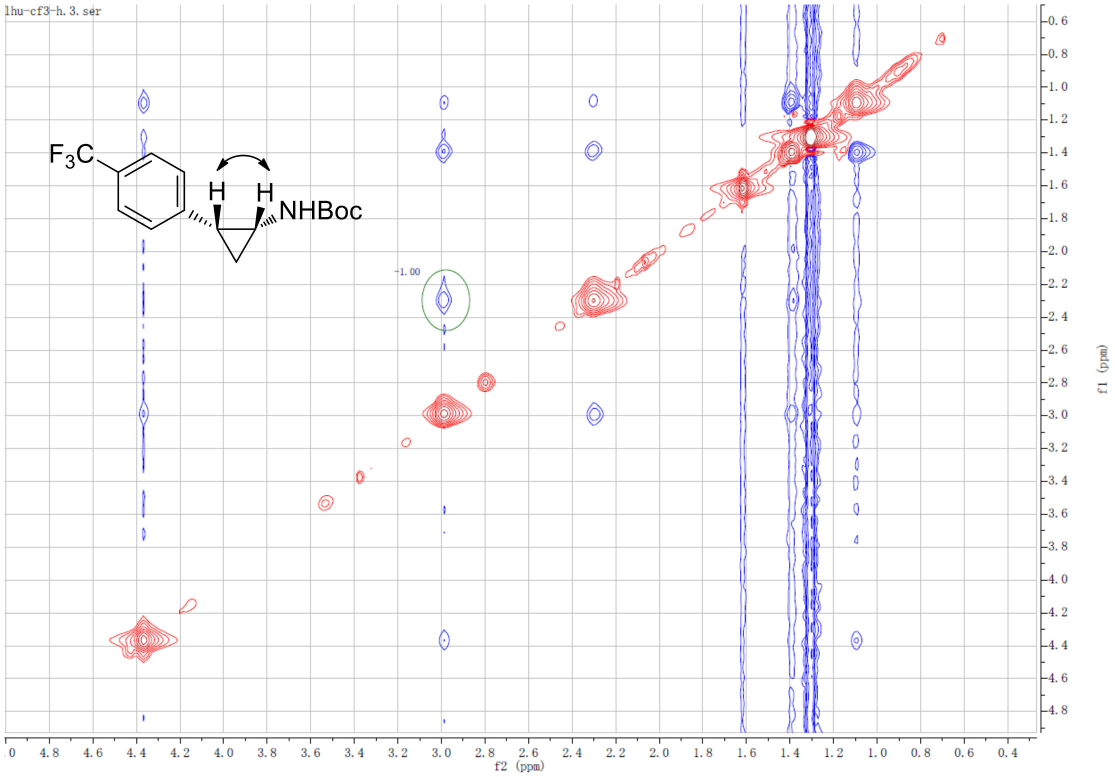
3.25
3.24
3.23
3.23
2.75
2.75
2.75
2.74
2.74
2.73
2.72
2.72
2.71
2.17
2.16
2.16
2.15
2.15
2.15
2.14
2.14
2.14
2.14
2.13
2.13
2.13
2.13
2.12
Ph
Ph
O
OH
2.83
2.04
2.85
2.02
1.00
1.15
1.21
1.23
2.13
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.
f1 (ppm)


lhu-cycbu-vinyl-sd-c.1.fid
178.51
141.42
140.20
137.07
129.24
128.75
128.36
127.78
127.02
126.91
126.33
45.18
44.40
24.50
20.21
Ph
Ph
O
OH
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


lhu-cf3-h.19.fid
7.54
7.53
7.32
7.31
7.26
4.35
2.97
2.29
2.28
1.39
1.38
1.38
1.37
1.36
1.35
1.28
1.08
F3C
NHBoc
2.03
1.92
1.00
1.01
0.98
1.19
9.29
0.96
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)


lhu-cf3-c.20.fid
156.17
141.13
129.01
128.77
128.56
128.34
128.15
127.01
125.21
124.87
124.85
124.82
124.80
123.41
121.60
79.59
29.65
28.07
22.43
12.14
F3C
NHBoc
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


lhu-cf3-f.14.fid
-62.62
F3C
NHBoc
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
f1 (ppm)


lhu-cf3-h.3.ser
$F_3C$
H
H
NHBoc
-1.00
.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
f2 (ppm)
0.6
0.8
1.0
1.2
1.4
1.6
1.8
2.0
2.2
2.4
2.6
2.8
3.0
3.2
3.4
3.6
3.8
4.0
4.2
4.4
4.6
4.8
f1 (ppm)