10.1071/CH14187_AC

Australian Journal of Chemistry 2014, 67(7), 1119-1123

Chiral Bicylic Guanidine-Catalyzed Conjugate Addition of α-Fluoro-β-Ketoesters to Cyclic Enones

Zhenzhong Jing,[†] Jin Liu,[†] Kek Foo Chin,[‡] Wenchao Chen,[†] Choon-Hong Tan[‡] and Zhiyong Jiang[†,]*

[†] *Key Laboratory of Natural Medicine and Immuno-Engineering of Henan Province, Henan University, Kaifeng, Henan, P. R. China, 475004*

[‡] *Division of Chemistry and Biological Chemistry, Nanyang Technological University, 21 Nanyang Link, 637371, Singapore*

E-mail: chmjzy@henu.edu.cn

Supplementary Material

Table of Contents

1. General Informationc

General Procedures and Methods

Experiments involving moisture and/or air sensitive components were performed under a positive pressure of nitrogen in oven-dried glassware equipped with a rubber septum inlet. Dried solvents and liquid reagents were transferred by oven-dried syringes or hypodermic syringe cooled to ambient temperature in a desiccator. Reactions mixtures were stirred in 4 mL sample vial with Teflon-coated magnetic stirring bars unless otherwise stated. Moisture in non-volatile reagents/compounds was removed under high vacuum by means of an oil pump and subsequent purging with nitrogen. Solvents were removed in vacuo under ~30 mmHg and heated with a water bath at 30–35 °C using Changcheng rotary evaporator with Changcheng aspirator. The condenser was cooled with running water at 0 °C.

All experiments were monitored by analytical thin layer chromatography (TLC). TLC was performed on pre-coated plates, Qingdao Shenghai Chemicals (P. R. China) 60 F_{254}. After elution, plate was visualized under UV illumination at 254 nm for UV active material. Further visualization was achieved by staining $KMnO_4$, ceric molybdate, or anisaldehyde solution. For those using the aqueous stains, the TLC plates were heated on a hot plate.

Columns for flash chromatography (FC) contained silica gel 200-300 mesh (Qingdao Haiyang). Columns were packed as slurry of silica gel in petroleum ether and equilibrated solution using the appropriate solvent system. The elution was assisted by applying pressure of about 2 atm with an air pump.

Instrumentations

Proton nuclear magnetic resonance (^{1}H NMR), carbon NMR (^{13}C NMR), and fluorine (^{19}F NMR) spectra were recorded in $CDCl_3$ unless otherwise stated. ^{1}H (400 MHz), ^{13}C (100 MHz) and ^{19}F NMR (376 MHz) were performed on a Bruker AVANCE-III (400MHz) spectrometer. Chemical shifts are reported in parts per million (ppm), using the residual solvent signal as an internal standard: $CDCl_3$ (^{1}H NMR: δ 7.26, singlet; ^{13}C NMR: δ 77.0, triplet). Multiplicities were given as: *s* (singlet), *d* (doublet), *t* (triplet), *q* (quartet), *quintet*, *m* (multiplets), *dd* (doublet of doublets), *dt* (doublet of triplets), and *br* (broad). Coupling constants (*J*) were recorded in Hertz (Hz). The number of proton atoms (*n*) for a given resonance was indicated by *n*H. The number of carbon atoms (*n*) for a given resonance was indicated by *n*C. HRMS

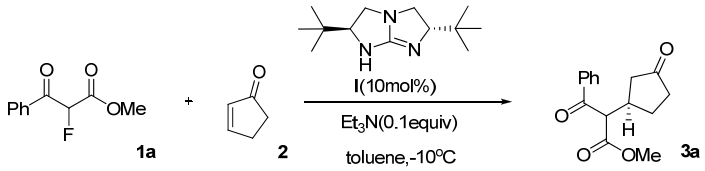
was reported in units of mass to charge ratio (m/z). Mass samples were dissolved in CH_3CN (HPLC Grade) unless otherwise stated.

Enantiomeric excesses were determined by chiral High Performance Liquid Chromatography (HPLC) analysis. UV detection was monitored at 254 nm and 210 nm at the same time. HPLC samples were dissolved in HPLC grade isopropanol (IPA) unless otherwise stated.

Materials

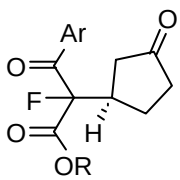
All commercial reagents were purchased from Sigma-Aldrich, J&K, Alfa-Aesar, TCI and Aladdin and were of the highest purity grade. They were used without further purification unless specified. All solvents used, mainly petroleum ether (PE) and ethyl acetate (EtOAc), were distilled. Anhydrous DCM and MeCN were freshly distilled from CaH_2 and stored under N_2 atmosphere. THF, Et_2O and toluene were freshly distilled from sodium/benzophenone before use. All compounds synthesized were stored in a −20 °C freezer and light-sensitive compounds were protected with aluminium foil.

2. Typical experimental procedure for Michael reaction catalyzed by chiral bicyclic guanidine



1a (14.7 mg, 0.075 mmol, 1.5 equiv.), Et_3N (0.5 mg, 0.005 mmol, 0.1 equiv.) and **I** (1.1 mg, 0.005 mmol, 0.1 equiv.) were added into toluene (0.1 mL) and stirred at −10 ^{o}C for 5 minutes. Then **2** (0.05 mmol, 1.0 equiv.) was added. The reaction mixture was stirred at −10 ^{o}C and monitored by TLC. Upon complete consumption of **2**, the reaction mixture was directly loaded onto a short silica gel column, followed by gradient elution with PE/EtOAc mixture (20/1 – 5/1 ratio). After removing the solvent, product **3a** (12.1 mg) was obtained as colorless oil in 93% yield.

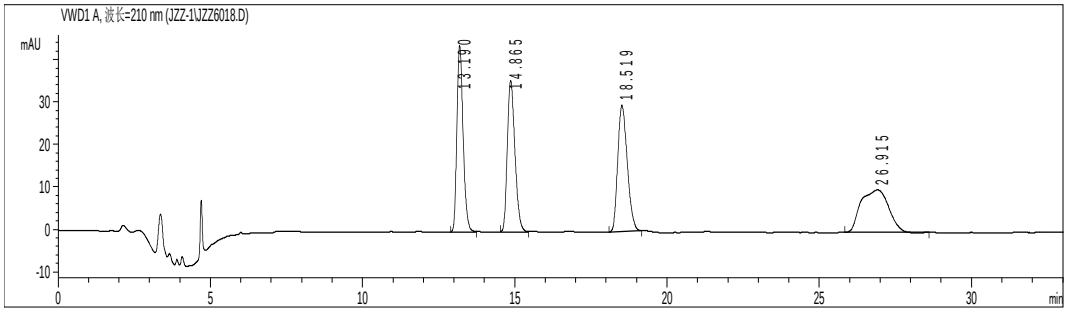
3. Characterization of Michael adducts



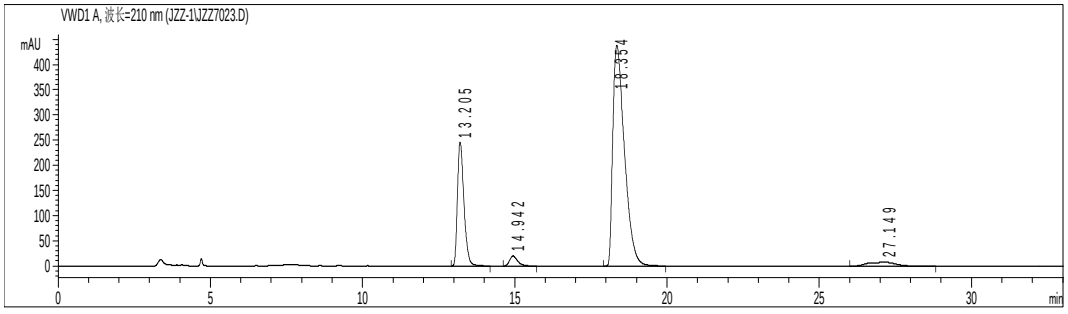
3a: Ar =Ph
R = Me

Colorless oil, 93% yield; 92% *ee*; *dr* = 3.0:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06–8.02 (m, 2H), 7.63–7.60 (m, 1H), 7.50–7.46 (m, 2H), 3.84–3.81 (m, 3H), 3.55–3.38 (m, 1H), 2.54–2.11 (m, 5H), 2.04–1.97 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 216.4, 216.0, 190.9, 167.4, 167.1, 134.5, 133.7, 130.0, 129.9, 128.9, 101.2 (d, $J_{C\text{-}F}$ = 201 Hz), 53.7, 41.1, 40.9, 40.7, 38.8 (two peaks), 38.3, 38.1, 23.0 (two peaks), 14.2;^{19}F NMR (376 MHz, $CDCl_3$) δ –172.98, –173.05. HRMS (ESI) m/z Found 279.1034 $[M+H]^+$, calc. for $C_{15}H_{16}FO_4$ 279.1033.

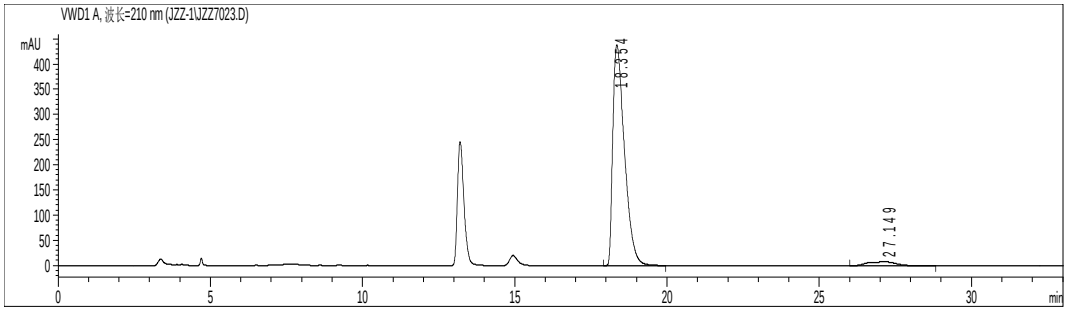
The *ee* was determined by HPLC analysis. CHIRALPAK ID (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 ^{o}C; 210 nm; retention time: 18.4 min (major), 27.1 min (minor).



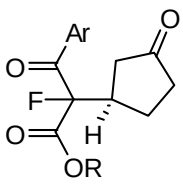
Peak #	Ret.Time	Area	Height	Area %
1	13.19	624.4	43.9	24.756
2	14.865	619.5	35.7	24.563
3	18.519	647.7	29.8	25.680
4	26.915	630.6	10	25.001
Total		2522.2	119.4	100.000



Peak #	Ret.Time	Area	Height	Area %
1	13.205	3663.4	246.5	22.579
2	14.942	373.8	20.1	2.304
3	18.354	11694.4	438.4	72.077
4	27.149	493.2	7.7	3.040
Total		16224.8	712.7	100.000



Peak #	Ret.Time	Area	Height	Area %
1	18.354	11694.4	438.4	95.953
2	27.149	493.2	7.7	4.047
Total		12187.6	446.1	100.000

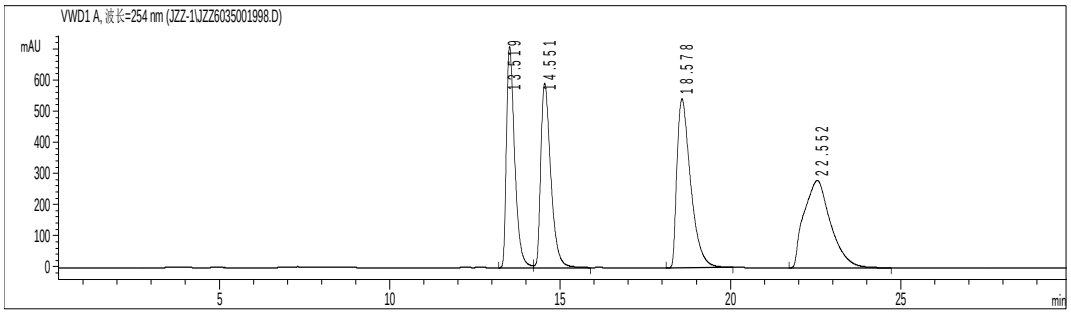


3b: Ar =Ph
R = Et

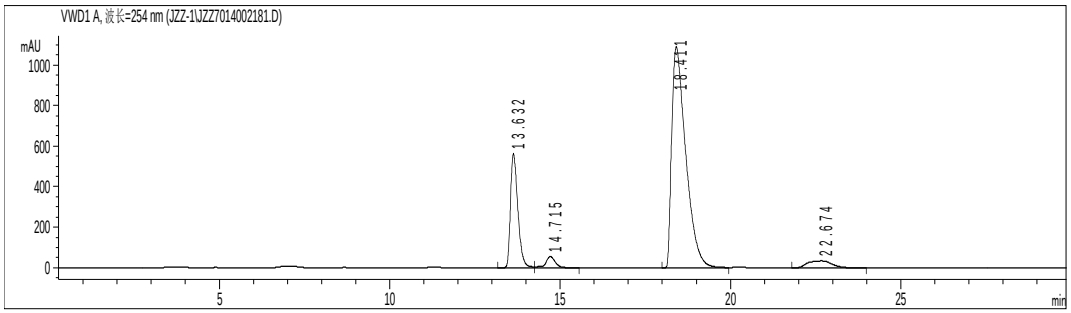
Colorless oil, 92% yield; 90% *ee*; *dr* = 3.0:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06-8.03 (m, 2H), 7.62–7.59 (m, 1H), 7.50–7.45 m, 2H), 4.37–4.21 (m, 2H), 3.54–3.38 (m, 1H), 2.55–2.11 (m, 5H), 2.04–2.0 (m, 1H), 1.26–1.21 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 216.4, 216.1, 191.1, 190.8, 166.8, 166.5, 134.3, 134.2, 133.6 (two peaks), 129.8 (two peaks), 128.8, 100.0 (d, $J_{C\text{-}F}$ = 201 Hz), 63.1, 63.0, 62.7, 62.6, 40.9, 40.7, 40.6, 40.4, 38.8, 38.7, 38.3 (two peaks), 38.2, 38.0, 23.1, 23.0, 22.8, 22.7, 16.3, 16.2, 14.0 (two peaks); ^{19}F NMR (376 MHz, $CDCl_3$) δ –172.96, –173.02.

HRMS (ESI) m/z Found 293.1190 $[M+H]^+$, calc. for $C_{16}H_{18}FO_4$ 293.1189.

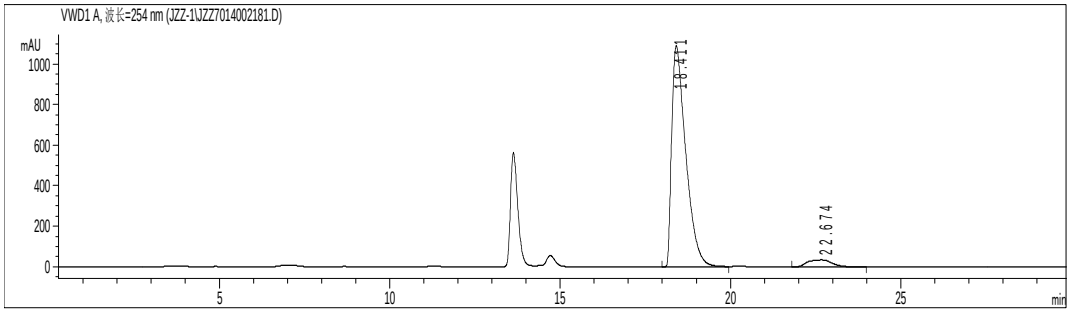
The *ee* was determined by HPLC analysis. CHIRALPAK ID (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 ^{o}C; 254 nm; retention time: 18.4 min (major), 22.7 min (minor).



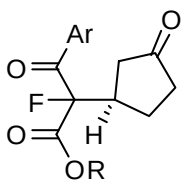
Peak #	Ret.Time	Area	Height	Area %
1	13.519	11913.3	711.2	21.864
2	14.551	12136.8	593.6	22.274
3	18.578	15172.2	543.2	27.845
4	22.552	15265.3	281.3	28.016
Total		54487.6	2129.3	100.000



Peak #	Ret.Time	Area	Height	Area %
1	13.632	8496.4	562.3	19.967
2	14.715	1073.6	55.6	2.523
3	18.411	31301.8	1091.4	73.560
4	22.674	1680.9	34.1	3.950
Total		42552.7	1743.4	100.000



Peak #	Ret.Time	Area	Height	Area %
1	18.411	31301.8	1091.4	94.904
2	22.674	1680.9	34.1	5.096
Total		32982.7	1125.5	100.000

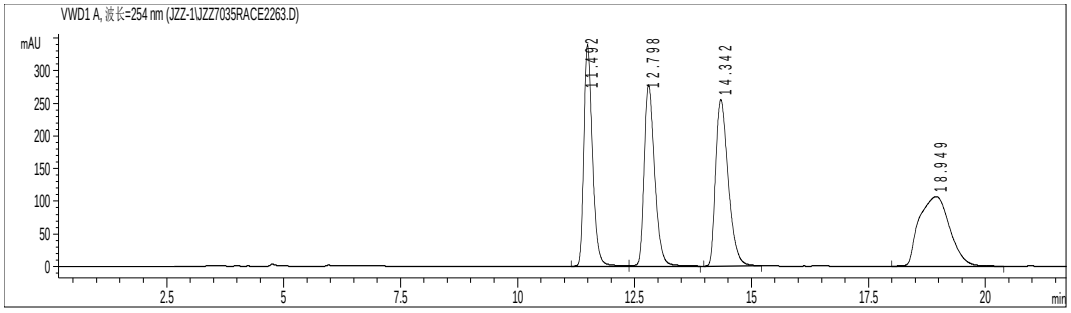


3c: Ar =4-FPh
R = Me

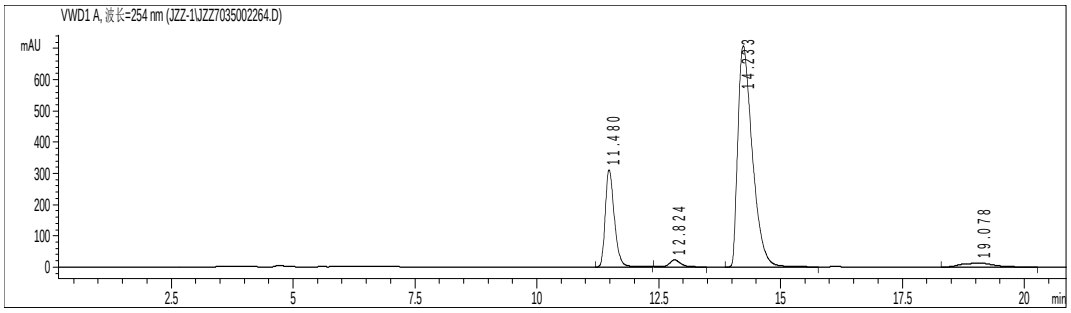
Colorless oil, 90% yield; 93% *ee*; *dr* = 3.6:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11–8.08 (m, 2H), 7.18–7.12 (m, 2H), 3.83–3.80 (m, 3H), 3.52–3.38 (m, 1H), 2.53–2.09 (m, 5H), 2.02–1.96 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 219.0, 216.0, 215.7, 189.4, 189.1, 167.6, 167.1, 166.9, 165.1, 132.9, 132.8, 132.8, 132.7, 129.9, 116.2, 115.9, 100.2 (d, $J_{C\text{-}F}$ = 201 Hz), 53.6, 40.7, 40.6, 40.4, 38.6 (two peaks), 38.2, 38.1, 37.9, 23.0, 23.0, 22.8, 22.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ –102.0, –102.1, –172.7, –172.8.

HRMS (ESI) m/z Found 297.0937 $[M+H]^+$, calc. for $C_{15}H_{16}FO_5$ 297.0938.

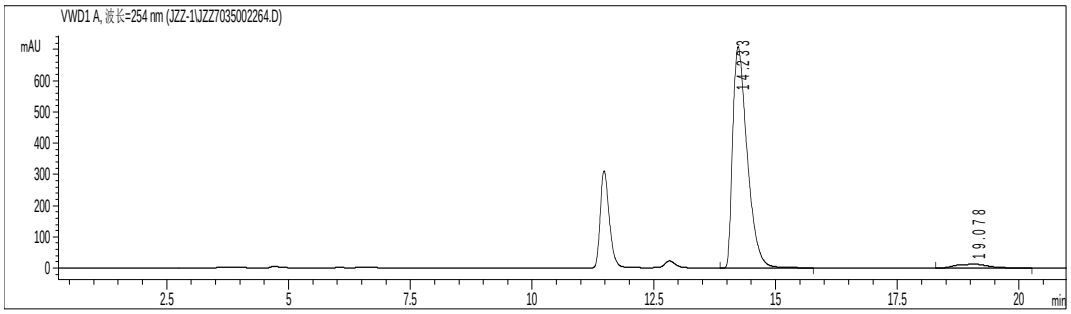
The *ee* was determined by HPLC analysis. CHIRALPAK ID (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 ^{o}C; 254 nm; retention time: 14.2 min (major), 19.1 min (minor).



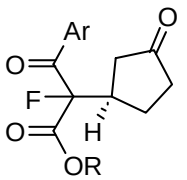
Peak #	Ret.Time	Area	Height	Area %
1	11.492	4310.3	339.4	23.615
2	12.798	4330.2	278	23.724
3	14.342	4786.1	254.9	26.222
4	18.949	4825.8	106.9	26.439
Total		18252.4	979.2	100.000



Peak #	Ret.Time	Area	Height	Area %
1	11.48	4027.3	310.5	20.557
2	12.824	363.7	22.3	1.856
3	14.233	14647.9	708	74.770
4	19.078	551.7	12.3	2.816
Total		19590.6	1053.1	100.000



Peak #	Ret.Time	Area	Height	Area %
1	14.233	14647.9	708	96.371
2	19.078	551.7	12.3	3.629
Total		15199.6	720.3	100.000

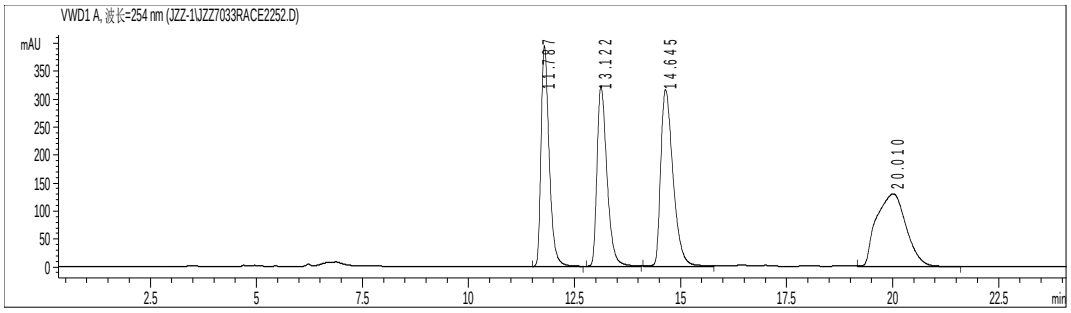


3d: Ar =4-ClPh
R = Me

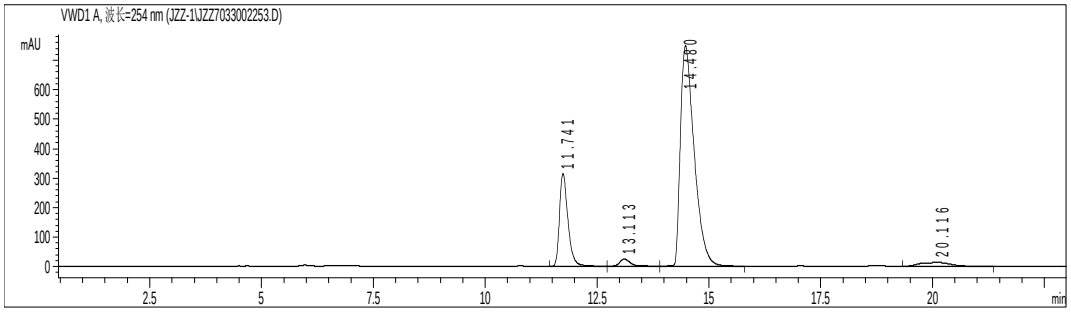
Colorless oil, 90% yield; 93% *ee*; *dr* = 3.5:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01–7.98 (m, 2H), 7.47–7.44 (m, 2H), 3.84–3.81 (m, 3H), 3.53 (m, 1H), 2.54–2.08 (m, 5H), 2.03–1.95 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 216.0, 215.6, 189.8, 189.6, 167.0, 166.8, 141.0, 131.8, 131.3, 131.2, 129.2, 128.8, 100.1 (d, $J_{C\text{-}F}$ = 201 Hz), 99.9, 53.7, 53.6, 40.9, 40.7, 40.6, 40.4, 38.6 (two peaks), 38.2 (two peaks), 38.1, 37.9, 22.9, 22.8 (two peaks); ^{19}F NMR (376 MHz, $CDCl_3$) δ –172.9, –173.0.

HRMS (ESI) m/z Found 313.0644 $[M+H]^+$, calc. for $C_{15}H_{14}FO_4$ 313.0643.

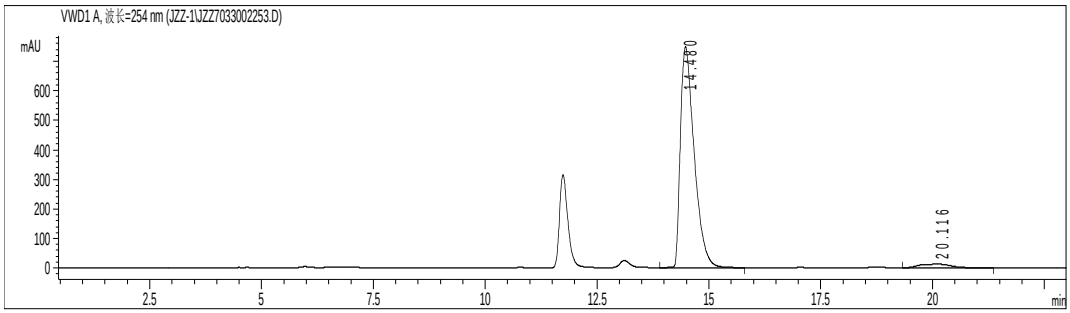
The *ee* was determined by HPLC analysis. CHIRALPAK ID (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 ^{o}C; 254 nm; retention time: 14.5 min (major), 20.1 min (minor).



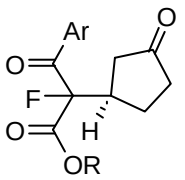
Peak #	Ret.Time	Area	Height	Area %
1	11.787	5233.3	394.4	22.605
2	13.122	5260.4	322.4	22.722
3	14.645	6394.0	316.2	27.619
4	20.010	6263.3	129.5	27.054
Total		23151	1162.5	100.000



Peak #	Ret.Time	Area	Height	Area %
1	11.741	4122.6	314.6	19.454
2	13.113	415	24.4	1.959
3	14.48	16070.5	748.7	75.834
4	20.116	583.4	12.4	2.753
Total		21191.5	1100.1	100.000



Peak #	Ret.Time	Area	Height	Area %
1	14.48	16070.5	748.7	96.497
2	20.116	583.4	12.4	3.503
Total		16653.9	761.1	100.000

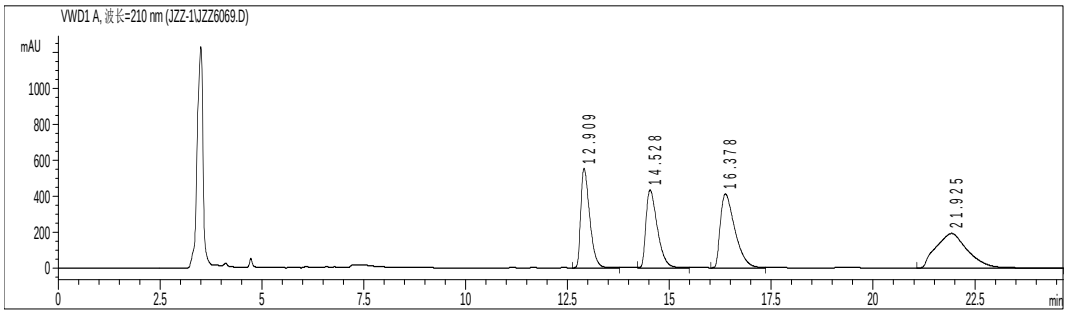


3e: Ar =4-BrPh
R = Me

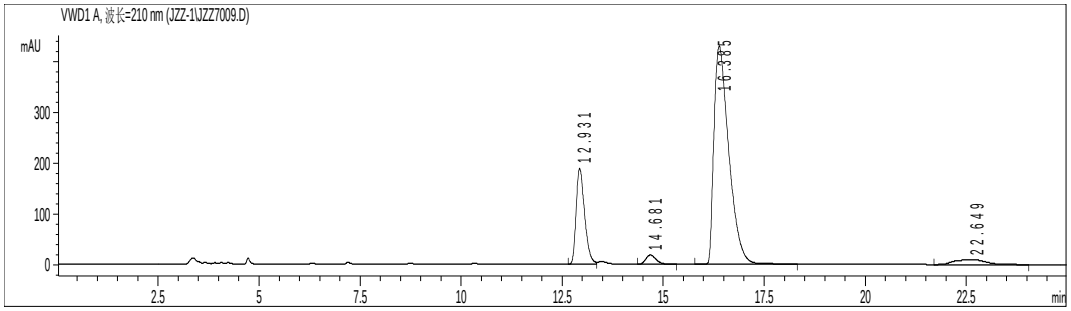
Colorless oil, 77% yield; 91% *ee*; *dr* = 3.8:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94–7.89 (m, 2H), 7.64–7.60 (m, 2H), 3.83–3.80 (m, 3H), 3.52–3.36 (m, 1H), 2.54–2.06 (m, 4H), 2.02–1.95 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 216.1, 190.2, 190.0, 167.2, 166.9, 132.3 (two peaks), 131.5, 131.4, 130.1, 100.3 (d, $J_{C\text{-}F}$ = 201 Hz), 53.8, 41.1, 40.8, 40.55, 38.8, 38.7, 38.4, 38.3 (two peaks), 38.04, 23.1, 22.9 (two peaks); ^{19}F NMR (376 MHz, $CDCl_3$) δ –173.0, –173.1.

HRMS (ESI) m/z Found 357.0137 $[M+H]^+$, calc. for $C_{15}H_{15}BrFO_4$ 357.0138.

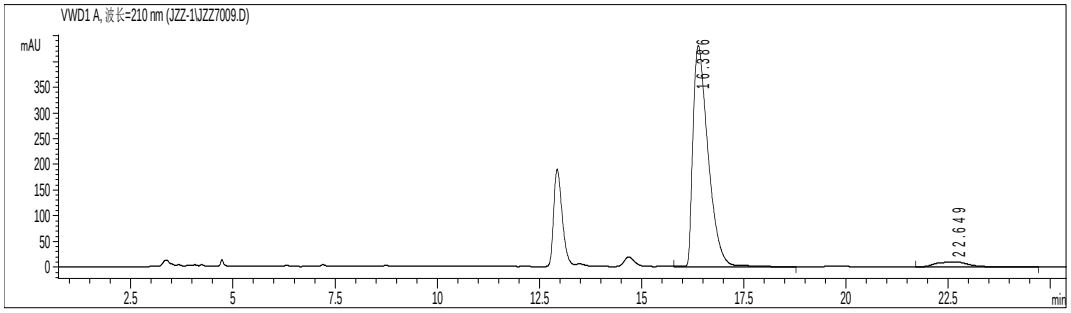
The *ee* was determined by HPLC analysis. CHIRALPAK ID (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 16.4 min (major), 22.6 min (minor).



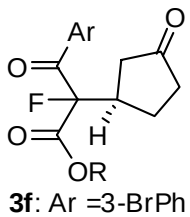
Peak #	Ret.Time	Area	Height	Area %
1	12.909	8506.7	552.3	22.422
2	14.528	8532.9	434	22.491
3	16.378	10364.4	412.9	27.319
4	21.925	10534.8	193.1	27.768
Total		37938.8	1592.3	100.000



Peak #	Ret.Time	Area	Height	Area %
1	12.932	2779.8	189.8	18.854
2	14.681	353.5	18.9	2.398
3	16.386	11087	430.3	75.198
4	22.649	523.4	9.8	3.550
Total		14743.7	648.8	100.000



Peak #	Ret.Time	Area	Height	Area %
1	16.386	11087	430.3	95.492
2	22.649	523.4	9.8	4.508
Total		11610.4	440.1	100.000

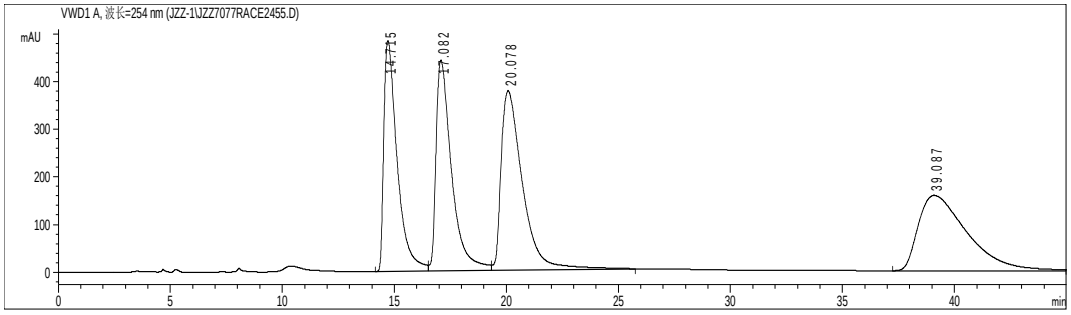


3f: Ar =3-BrPh
R = Me

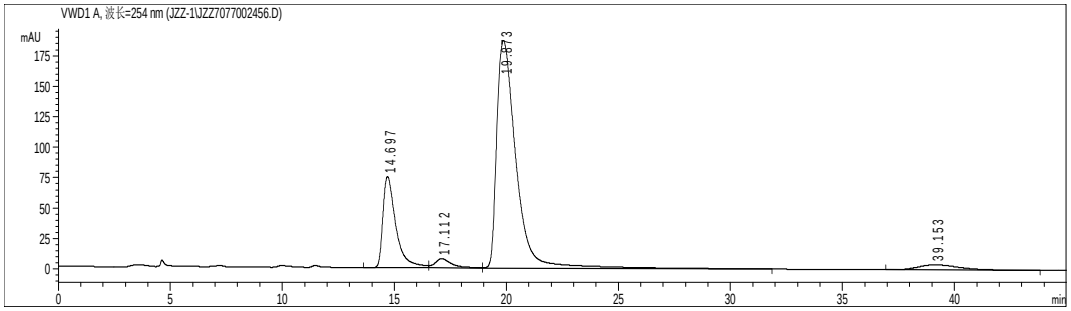
Colorless oil, 79% yield; 91% *ee*; *dr* = 2.9:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19–8.14 (m, 1H), 8.00–7.97 (m, 1H), 7.74 (d, *J* = 7.9 Hz, 1H), 7.39–7.34 (m, 1H), 3.85–3.82 (m, 3H), 3.52–3.36 (m, 1H), 2.52–2.36 (m, 2H), 2.32–2.19 (m, 2H), 2.16–2.09 (m, 1H),2.03–1.96 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 215.8, 190.3, 189.9, 189.6, 166.8, 166.6, 137.2, 137.1, 135.2, 135.1, 132.6 (two peaks), 132.6, 130.3, 128.4, 128.3, 123.0, 100.1 (d, $J_{C\text{-}F}$ = 201 Hz), 53.7 (two peaks), 41.0, 40.8, 40.7, 40.5, 38.6, 38.5, 38.2 two peaks), 38.1, 37.9, 23.0, 22.9, 22.8 (two peaks); ^{19}F NMR (376 MHz, $CDCl_3$) δ –173.19, –173.24.

HRMS (ESI) m/z Found 357.0138 $[M+H]^+$, calc. for $C_{15}H_{15}BrFO_4$ 357.0138.

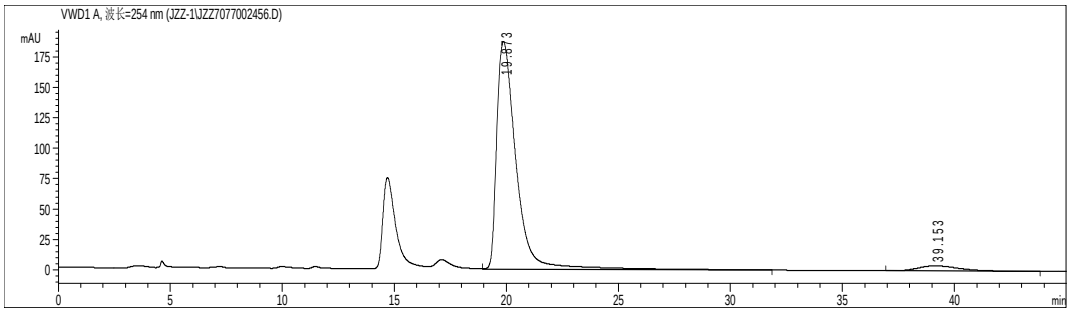
The *ee* was determined by HPLC analysis. LUX Amylose-2 (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 ^oC; 254 nm; retention time: 19.1 min (major), 39.2 min (minor).



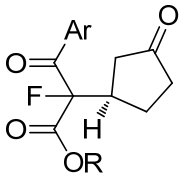
Peak #	Ret.Time	Area	Height	Area %
1	13.042	28330.1	1812.9	23.674
2	14.665	28348.2	1451	23.689
3	18.121	31364.7	1155.4	26.210
4	25.372	31625.3	460.8	26.427
Total		119668.3	4880.1	100.000



Peak #	Ret.Time	Area	Height	Area %
1	13.273	5652.8	362.5	54.938
2	15.034	376.9	20.3	3.663
3	18.657	3312	126.2	32.188
4	24.243	947.7	32.8	9.211
Total		10289.4	541.8	100.000



Peak #	Ret.Time	Area	Height	Area %
1	19.872	10634.5	186.3	95.400
2	39.164	512.7	4.2	4.600
Total		11147.2	190.5	100.000

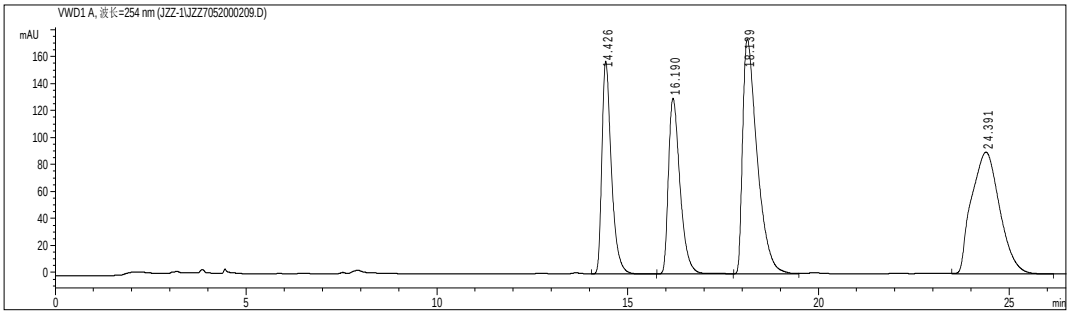


3g: Ar =2-FPh
R = Me

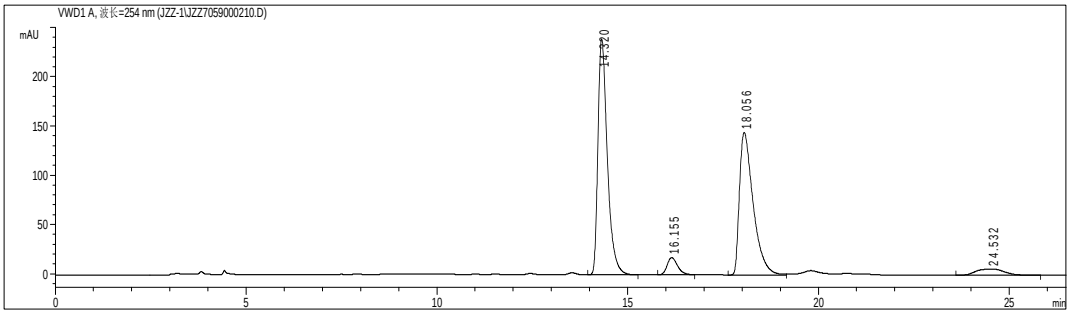
Colorless oil, 84% yield; 85% *ee*; *dr* = 1.5:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68–7.54 (m, 2H), 7.28–7.23(m, 1H), 7.17–7.11 (m, 1H), 3.90–3.87 (m, 3H), 3.49–3.33 (m, 1H), 2.44–1.98 (m, 5H), 1.88–1.78 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 215.7, 215.6, 192.7, 192.4, 166.0, 165.8, 165.6, 161.0, 159.4, 135.2, 135.1, 135.0, 130.6, 130.5, 124.6 (two peaks), 124.6, 124.5, 116.5 (two peaks), 116.3 (two peaks), 99.8 (d, $J_{C\text{-}F}$ = 202 Hz), 99.5 (d, $J_{C\text{-}F}$ = 202 Hz), 53.5, 53.4, 41.6, 41.4 (two peaks), 41.2, 38.4 (two peaks), 38.0 (two peaks), 29.7, 23.1, 23.0, 22.9 (two peaks); ^{19}F NMR (376 MHz, $CDCl_3$) δ –102.0,–102.1, –172.7, –172.8;

HRMS (ESI) m/z Found 297.0939 $[M+H]^+$, calc. for $C_{15}H_{15}F_2O_4$ 297.0938.

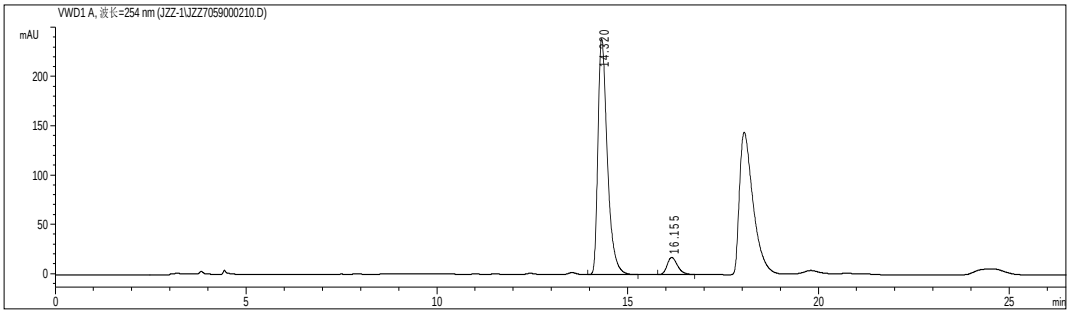
The *ee* was determined by HPLC analysis. CHIRALPAK ID (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 14.3 min (major), 16.2 min (minor).



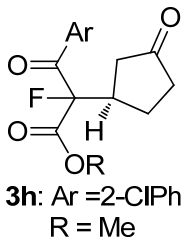
Peak #	Ret.Time	Area	Height	Area %
1	14.426	2721.5	157.6	18.521
2	16.19	2746.5	130.1	18.691
3	18.139	4595.7	174.1	31.276
4	24.391	4630.3	90.5	31.511
Total		14694	552.3	100.000



Peak #	Ret.Time	Area	Height	Area %
1	14.32	4107.7	239.2	49.065
2	16.155	336.5	17.5	4.019
3	18.056	3617.3	144.6	43.207
4	24.532	310.4	6.3	3.708
Total		8371.9	407.6	100.000



Peak #	Ret.Time	Area	Height	Area %
1	14.32	4107.7	239.2	92.429
2	16.155	336.5	17.5	7.571
Total		4444.2	256.7	100.000

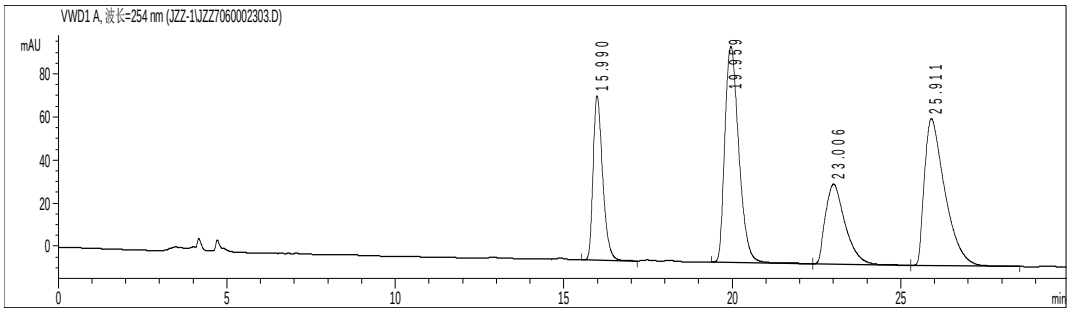


3h: Ar =2-ClPh
R = Me

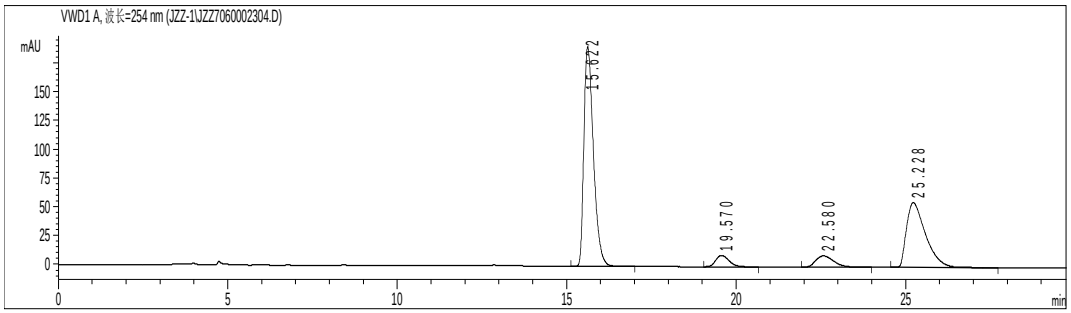
Colorless oil, 91% yield; 82% *ee*; *dr* = 1.6:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47–7.39 (m, 3H), 7.37–7.30 (m, 1H), 3.92–3.88 (m, 3H), 3.58–3.40 (m, 1H), 2.49–2.14 (m, 5H),1.99–1.83 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 215.5, 215.3, 195.3, 195.20, 195.0, 194.9, 166.0, 165.9, 165.8, 165.6, 135.2 (two peaks), 135.1 (two peaks), 132.5 (two peaks), 131.6 (two peaks), 130.7 (two peaks), 128.9 (two peaks), 128.8, 128.7, 126.5, 100.3 (d, $J_{C\text{-}F}$ = 202 Hz), 100.1 (d, $J_{C\text{-}F}$ = 202 Hz), 62.6(two peaks), 53.7(two peaks), 42.1, 41.9, 41.7, 38.2, 38.1, 37.8, 23.0, 22.9 (two peaks), 22.8, 16.2 (two peaks); ^{19}F NMR (376 MHz, $CDCl_3$) δ –176.1, –176.4.

HRMS (ESI) m/z Found 313.0642 $[M+H]^+$, calc. for $C_{15}H_{15}ClFO_4$ 313.0643

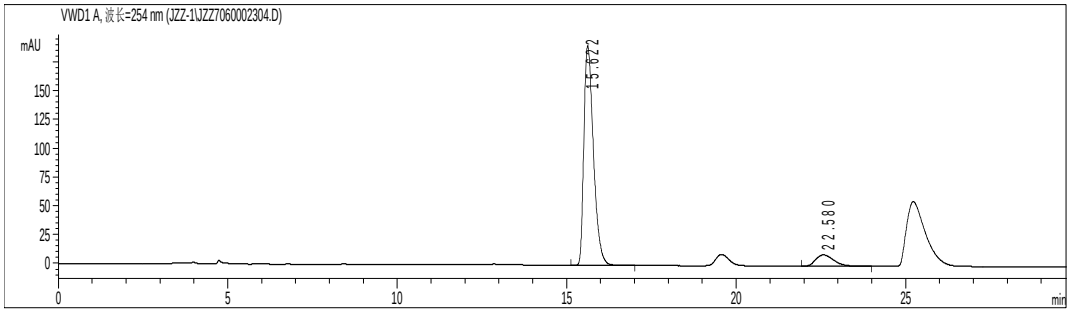
The *ee* was determined by HPLC analysis. CHIRALPAK ID (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 ^{o}C; 254 nm; retention time: 15.6 min (major), 22.6 min (minor).



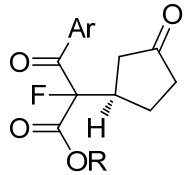
Peak #	Ret.Time	Area	Height	Area %
1	15.99	1501.7	76.4	17.149
2	19.959	2883	100.5	32.924
3	23.006	1500	37.2	17.131
4	25.911	2871.8	68.1	32.796
Total		8756.5	282.2	100.000



Peak #	Ret.Time	Area	Height	Area %
1	15.622	3718.7	191	56.723
2	19.57	270.9	10	4.132
3	22.58	360.7	9.8	5.502
4	25.228	2205.6	56.4	33.643
Total		6555.9	267.2	100.000



Peak #	Ret.Time	Area	Height	Area %
1	15.622	3718.7	191	91.158
2	22.58	360.7	9.8	8.842
Total		4079.4	200.8	100.000

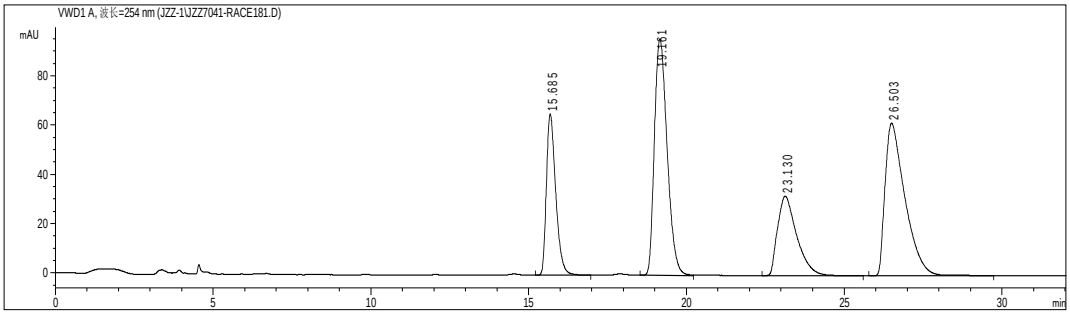


3i: Ar =2-BrPh
R = Me

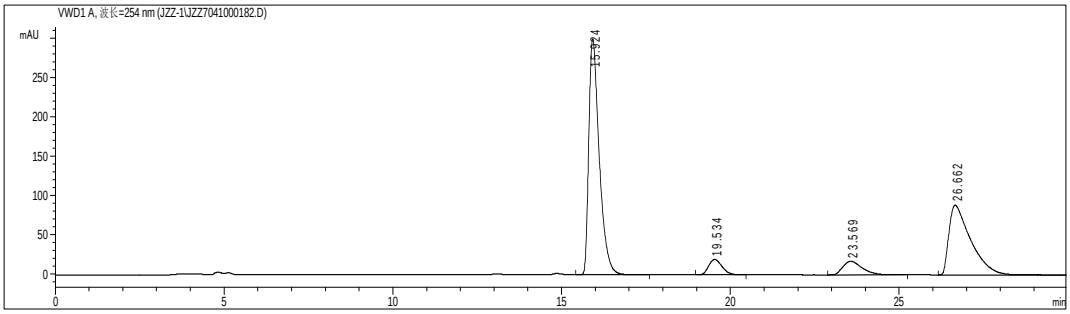
Colorless oil, 74% yield; 81% *ee*; *dr* = 1.5:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67–7.63 (m, 1H), 7.46–7.32 (m, 3H), 3.92–3.88 (m, 3H), 3.60–3.42 (m, 1H), 2.54–2.16 (m, 5H), 1.99–1.84 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 215.6, 215.4, 195.6, 195.4, 195.3, 195.1, 166.1, 166.0, 165.9, 165.7, 136.8 (three peaks), 134.1, 134.1, 132.6 (two peaks), 129.0 (two peaks), 128.8 (two peaks), 127.0, 100.0 (d, $J_{C\text{-}F}$ = 203 Hz), 53.8 (two peaks), 42.1, 41.9 (two peaks), 41.6, 38.4, 38.3, 38.2 (two peaks), 37.9, 23.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ –175.6, –175.9.

HRMS (ESI) m/z Found 357.0137 $[M+H]^+$, calc. for $C_{15}H_{15}BrFO_4$ 357.0138

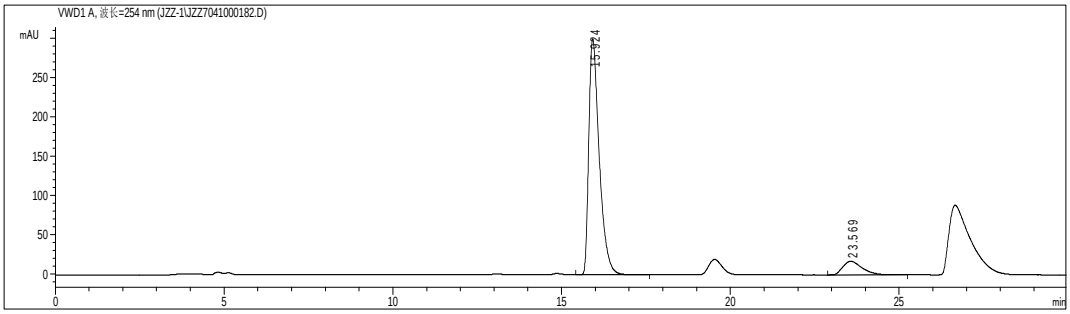
The *ee* was determined by HPLC analysis. CHIRALPAK ID (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 ^{o}C; 254 nm; retention time: 15.9 min (major), 23.6 min (minor).



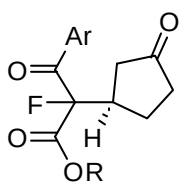
Peak #	Ret.Time	Area	Height	Area %
1	15.685	1344.9	65.3	16.612
2	19.161	2693.4	95.9	33.268
3	23.13	1357.5	32.3	16.768
4	26.503	2700.3	61.9	33.353
Total		8096.1	255.4	100.000



Peak #	Ret.Time	Area	Height	Area %
1	15.924	6461.9	299.7	55.448
2	19.534	542.1	19.5	4.651
3	23.569	686	17.3	5.887
4	26.662	3964	88.5	34.014
Total		11654.0	425	100.000



Peak #	Ret.Time	Area	Height	Area %
1	15.924	6461.9	299.7	90.403
2	23.569	686	17.3	9.597
Total		7147.9	317	100.000

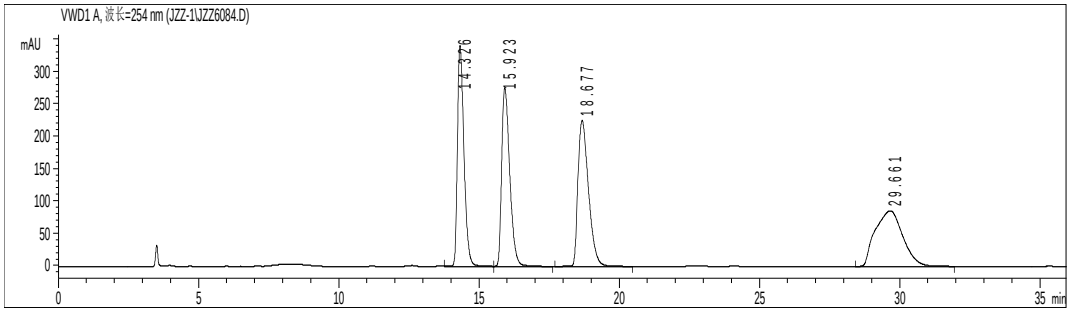


3j: Ar =4-MePh
R = Me

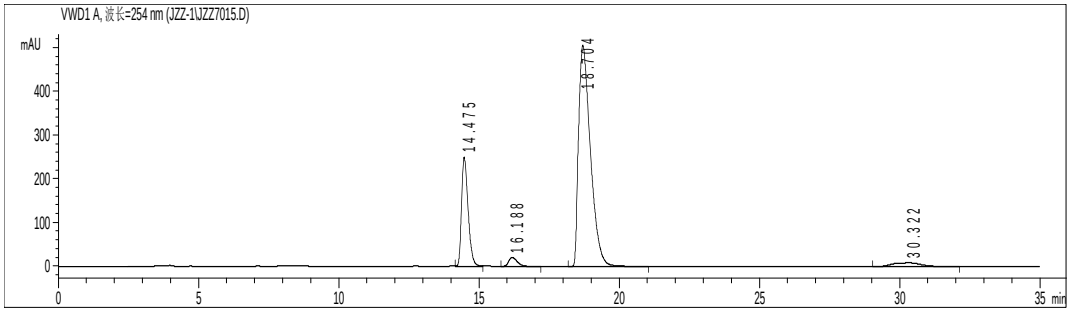
Colorless oil, 87% yield; 93% *ee*; *dr* = 3.6:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98–7.93 (m, 2H), 7.29–7.28 (m, 1H), 3.82–3.80 (m, 3H), 3.54–3.37 (m, 1H), 2.55–2.09 (m, 8H), 2.03–1.95 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 216.4, 216.0, 190.5, 190.2, 167.4, 167.2, 145.6, 131.1, 131.0 (three peaks), 129.5, 100.1 (d, $J_{C\text{-}F}$ = 201 Hz), 62.7, 62.6, 53.5, 41.01, 40.8, 40.7, 40.5, 38.8, 38.7, 38.4, 38.2, 38.0, 23.0, 22.9, 22.8, 21.8, 16.3, 16.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -172.8, -172.9.

HRMS (ESI) m/z Found 293.1190 $[M+H]^+$, calc. for $C_{16}H_{18}FO_4$ 293.1189

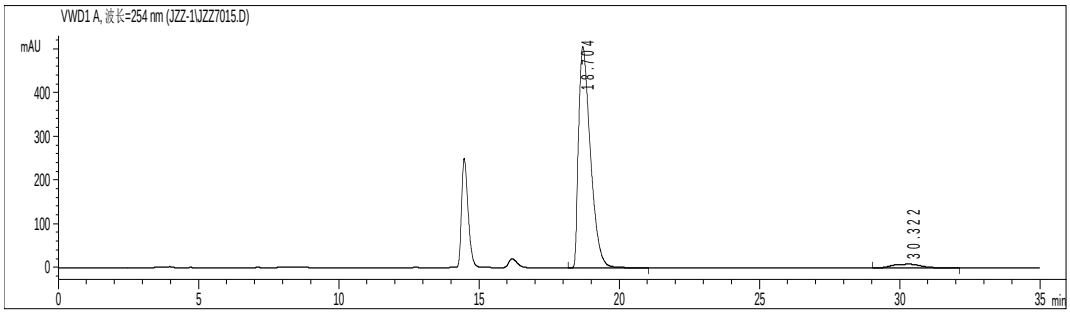
The *ee* was determined by HPLC analysis. CHIRALPAK ID (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 ^{o}C; 254 nm; retention time: 18.7 min (major), 30.3 min (minor).



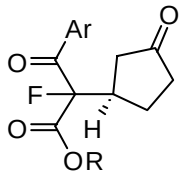
Peak #	Ret.Time	Area	Height	Area %
1	14.326	5534	341.5	24.226
2	15.923	5531.9	275.9	24.217
3	18.677	5907.4	225.8	25.861
4	29.661	5869.8	85.8	25.696
Total		22843.1	929.0	100.000



Peak #	Ret.Time	Area	Height	Area %
1	14.475	4064.7	249.4	20.406
2	16.188	441.8	20.7	2.218
3	18.704	14845.8	506.2	74.528
4	30.322	567.4	8.4	2.848
Total		19919.7	784.7	100.000



Peak #	Ret.Time	Area	Height	Area %
1	18.704	14845.8	506.2	96.319
2	30.322	567.4	8.4	3.681
Total		15413.2	514.6	100.000

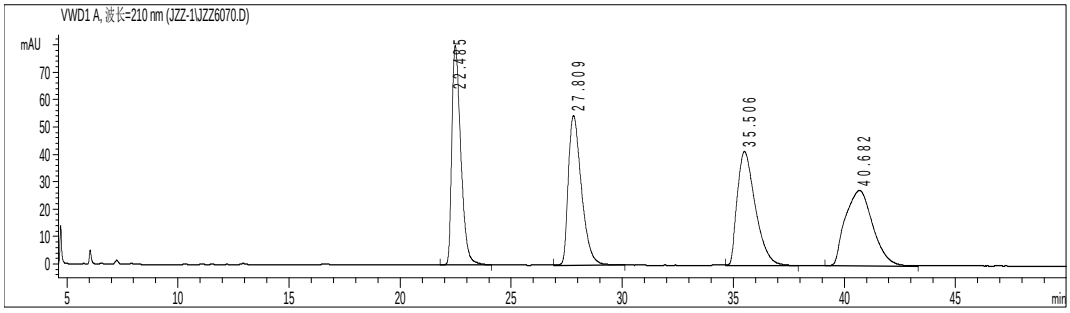


3k: Ar =4-MeOPh
R = Me

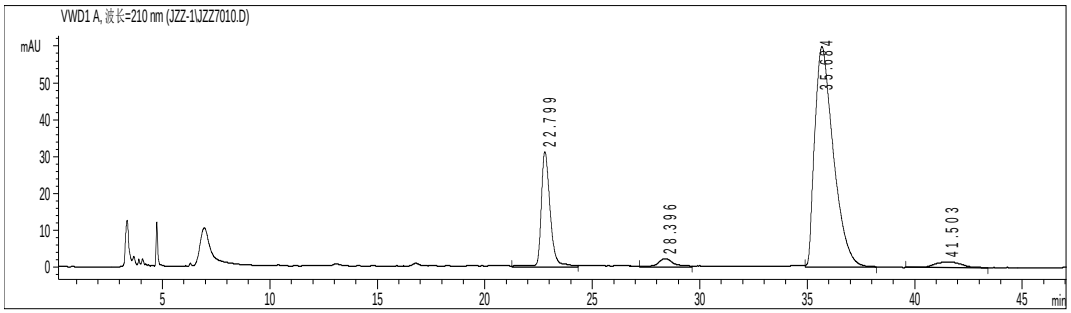
Colorless oil, 91% yield; 93% *ee*; *dr* = 3.6:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09–8.04 (m, 2H), 6.95–6.92 (m, 2H), 3.88–3.87 (m, 3H), 3.82–3.79 (m, 3H), 3.54–3.38 (m, 1H), 2.56–2.33 (m, 2H), 2.33–2.08 (m, 3H), 2.01–1.94 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 216.2, 190.6, 190.4, 167.2, 167.0, 159.8, 134.6, 129.8, 122.4 (two peaks), 121.2 (two peaks), 113.7, 113.6, 100.0 (d, $J_{C\text{-}F}$ = 202 Hz), 99.9, 55.4, 53.5, 40.7, 40.5, 38.7, 38.6, 38.1, 37.9, 22.8 (two peaks); ^{19}F NMR (376 MHz, $CDCl_3$) δ –172.36, –172.41.

HRMS (ESI) m/z Found 309.1137 $[M+H]^+$, calc. for $C_{16}H_{18}FO_5$ 309.1138

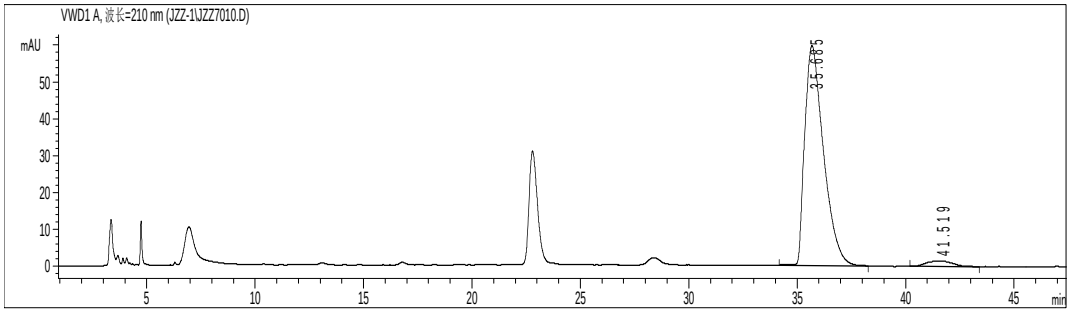
The *ee* was determined by HPLC analysis. CHIRALPAK ID (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 ^{o}C; 254 nm; retention time: 35.7 min (major), 41.5 min (minor).



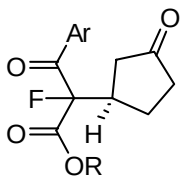
Peak #	Ret.Time	Area	Height	Area %
1	22.485	2245.4	80	24.317
2	27.809	2249.1	54.6	24.357
3	35.506	2366.8	41.7	25.632
4	40.682	2372.5	27.5	25.694
Total		9233.8	203.8	100.000



Peak #	Ret.Time	Area	Height	Area %
1	22.799	914.9	31.3	19.168
2	28.396	121.3	2.3	2.540
3	35.684	3600.7	59.8	75.438
4	41.503	136.2	1.5	2.854
Total		4773.1	94.9	100.000



Peak #	Ret.Time	Area	Height	Area %
1	35.685	3604.6	59.8	96.467
2	41.519	132	1.5	3.533
Total		3736.6	61.3	100.000

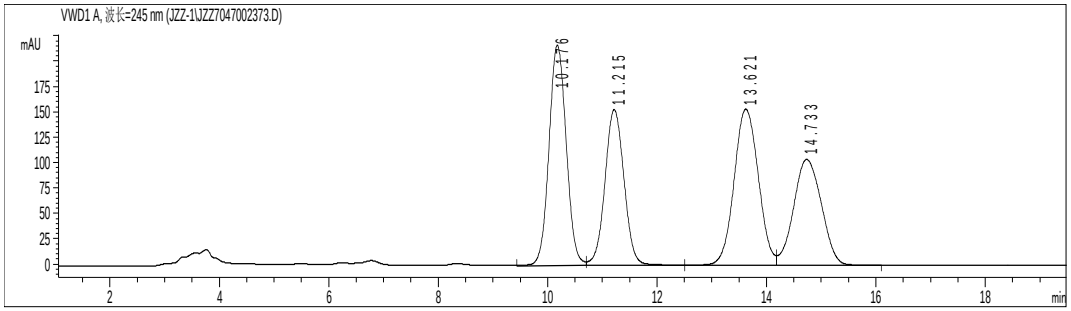


3l: Ar = 4-(4-BrPh)Ph
R = Me

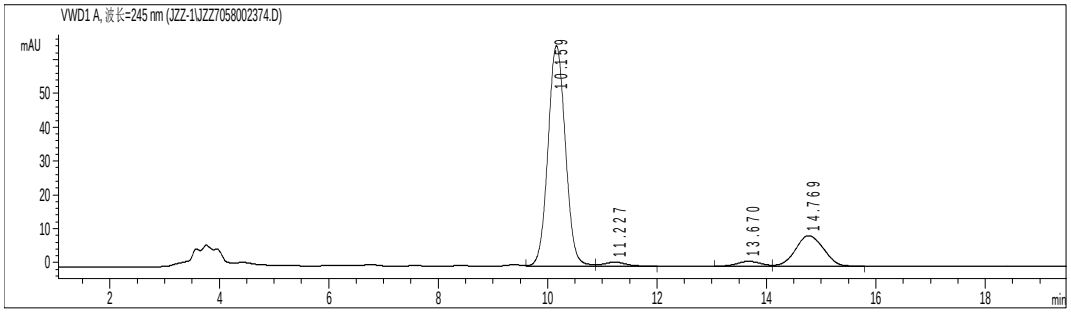
Colorless oil, 64% yield; 94% *ee*; *dr* = 4.3:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15–8.11 (m, 2H), 7.67–7.59 (m, 4H), 7.50–7.47 (m, 2H), 3.85–3.82 (m, 3H), 3.56–3.40 (m, 1H), 2.55–2.12 (m, 4H), 2.05–1.98 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 216.1, 215.8, 190.4, 190.1, 167.2, 167.0, 145.7, 138.4, 132.5, 132.5, 132.2, 130.6, 130.5, 128.8, 127.1, 123.1, 100.2 (d, $J_{C\text{-}F}$ = 201 Hz), 53.6, 41.0, 40.8, 40.7, 40.5, 38.68, 38.7, 38.3, 38.1, 37.9, 29.7, 23.0, 22.8 (two peaks); ^{19}F NMR (376 MHz, $CDCl_3$) δ –172.9, –173.0.

HRMS (ESI) m/z Found 455.0272 $[M+Na]^+$, calc. for $C_{21}H_{18}BrFMNaO_5$ 455.0270

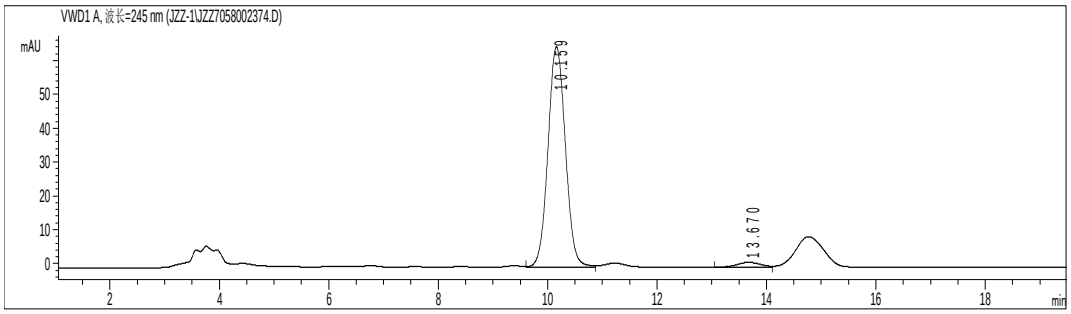
The *ee* was determined by HPLC analysis. CHIRALPAK ID (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 75/25; flow rate 1.0 mL/min; 25 ^{o}C; 254 nm; retention time: 10.2 min (major), 13.7 min (minor).



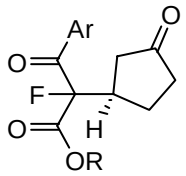
Peak #	Ret.Time	Area	Height	Area %
1	10.176	4761.8	217	28.053
2	11.215	3750	153.5	22.092
3	13.621	4765.6	154	28.074
4	14.733	3697.4	104.3	21.782
Total		16974.8	628.8	100.000



Peak #	Ret.Time	Area	Height	Area %
1	10.159	1442.5	65.1	78.268
2	11.227	35.3	1.2	1.914
3	13.67	43.3	1.4	2.347
4	14.769	322	9	17.471
Total		1843.1	76.7	100.000



Peak #	Ret.Time	Area	Height	Area %
1	10.159	1442.5	65.1	97.089
2	13.67	43.3	1.4	2.911
Total		1485.8	66.5	100.000

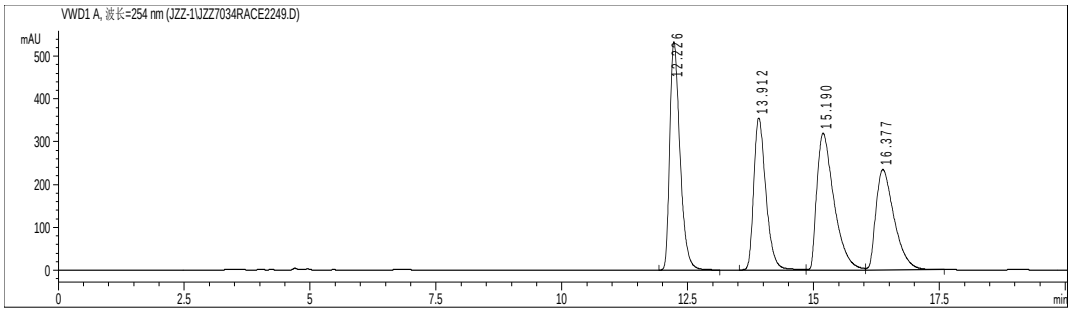


3m: Ar = 2-MePh
R = Me

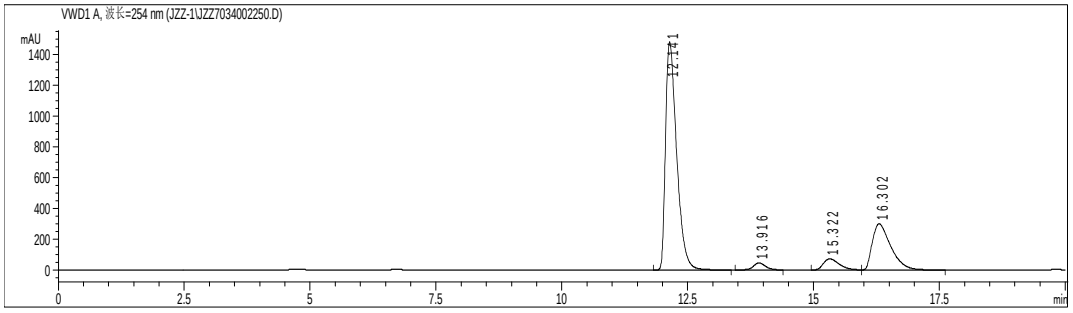
Colorless oil, 93% yield; 87% *ee*; *dr* = 3.0:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70–7.65 (m, 1H), 7.44–7.40 (m, 1H), 7.30–7.24 (m, 2H), 3.89–3.86 (m, 3H), 3.62–3.44 (m, 1H), 2.462.42 (m, 3H), 2.37–2.09 (m, 5H), 1.98–1.80 (m, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 216.0, 215.7, 195.6 195.4 167.0, 166.7, 139.2, 134.0, 132.3, 132.0, 129.2 (two peaks), 125.5, 100.0 (d, $J_{C\text{-}F}$ = 204 Hz), 53.6, 41.8, 41.7, 41.5, 41.3, 38.4, 38.3, 38.2 (two peaks), 37.9, 22.9, 20.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ –173.6 –173.7

HRMS (ESI) m/z Found 293.1190 $[M+H]^+$, calc. for $C_{16}H_{18}FO_4$ 293.1189

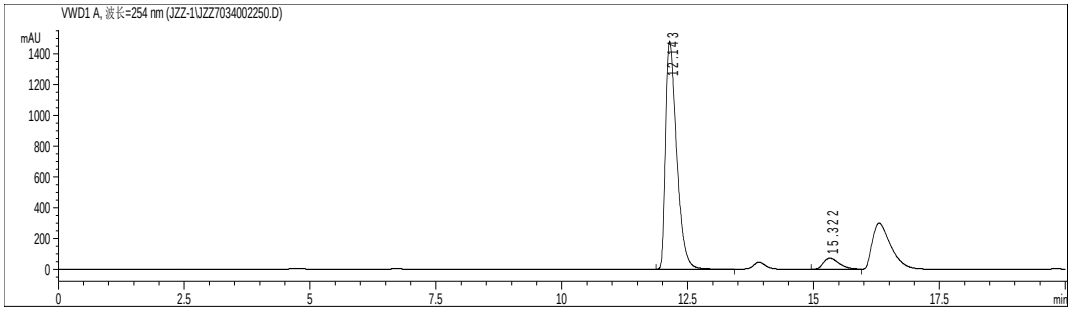
The *ee* was determined by HPLC analysis. CHIRALPAK ID (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 ^{o}C; 254 nm; retention time: 12.7 (major), 15.3 (minor).



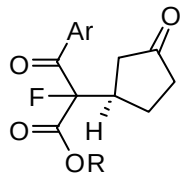
Peak #	Ret.Time	Area	Height	Area %
1	12.802	9977.9	678.3	27.679
2	14.632	8050	465.8	22.331
3	15.991	9979.8	399.9	27.684
4	17.315	8040.7	292.7	22.305
Total		36048.4	1836.7	100.000



Peak #	Ret.Time	Area	Height	Area %
1	12.17	6956.7	495.6	68.319
2	13.885	252.6	14.6	2.481
3	15.348	597.6	23.5	5.869
4	16.376	2375.8	98.7	23.331
Total		10102.7	632.4	100.000



Peak #	Ret.Time	Area	Height	Area %
1	12.143	22704.6	1480.1	93.453
2	15.322	1590.7	72.4	6.547
Total		24295.3	1552.5	100.000

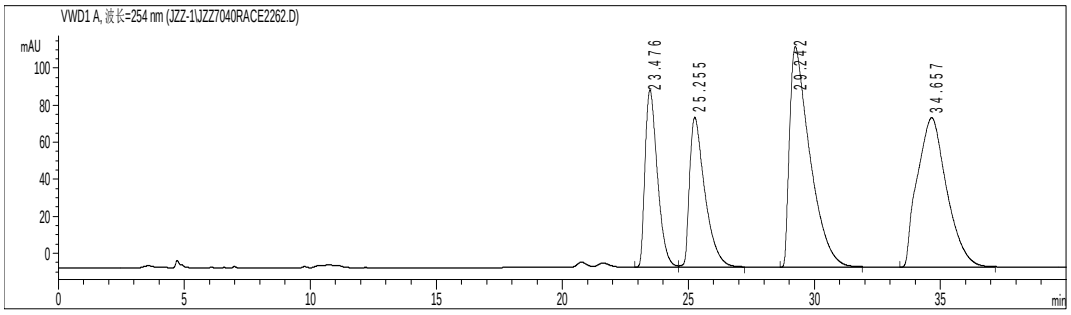


3n: Ar = 2-MeOPh
R = Me

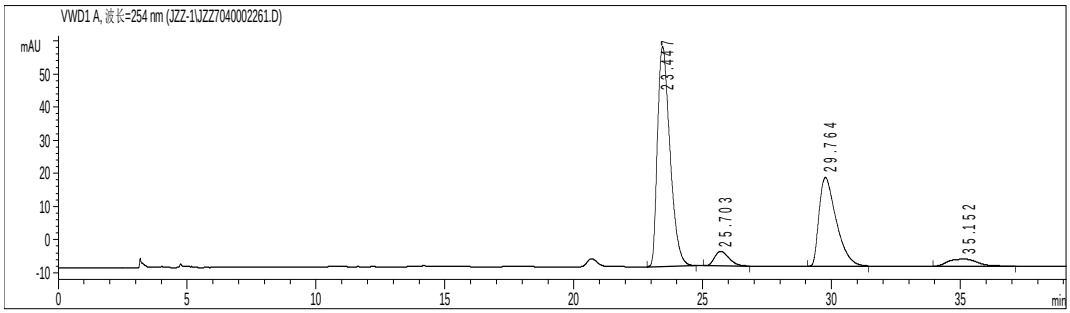
Colorless oil, 92% yield; 84% *ee*; *dr* = 1.8:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53–7.41 (m, 2H), 7.06–7.01 (m, 1H), 6.97–6.94 (m, 1H), 3.87–3.83 (m, 3H), 3.81–3.79 (m, 3H), 2.40–1.97 (m, 5H), 1.84–1.74 (m, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 216.2, 216.1, 196.0, 195.7, 166.4, 166.1, 165.9, 158.1, 134.2, 130.1, 130.0 (two peaks), 126.2 (two peaks), 126.0, 121.1 (two peaks), 111.4 (two peaks), 99.7 (d, $J_{C\text{-}F}$ = 201 Hz), 99.3 (d, $J_{C\text{-}F}$ = 201 Hz), 55.3, 55.2, 53.0, 52.9, 41.7, 41.6, 41.5, 41.4, 38.6 (two peaks), 38.5 (two peaks), 38.1, 38.0, 23.1, 23.0 (two peaks); ^{19}F NMR (376 MHz, $CDCl_3$) δ –173.5, –173.7.

HRMS (ESI) m/z Found 309.1137 $[M+H]^+$, calc. for $C_{16}H_{18}FO_5$ 309.1138

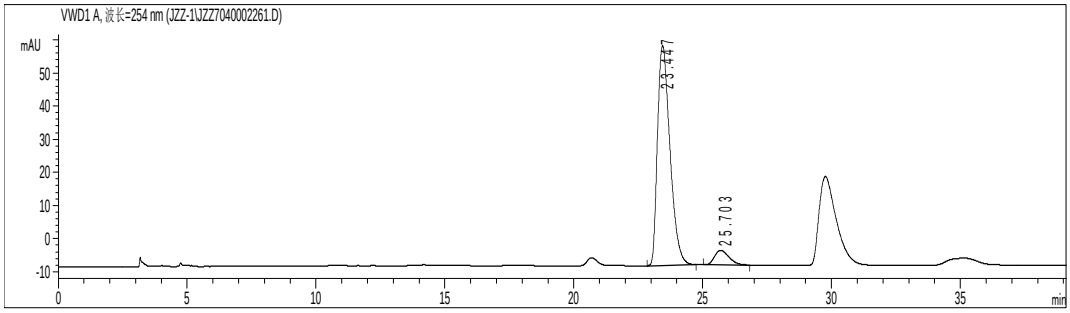
The *ee* was determined by HPLC analysis. CHIRALPAK ID (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 ^{o}C; 254 nm; retention time: 23.4 min (major), 25.7 min (minor).



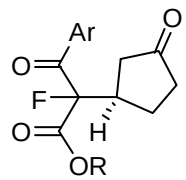
Peak #	Ret.Time	Area	Height	Area %
1	23.476	3263.2	95.9	16.399
2	25.255	3426	81.1	17.218
3	29.242	6684.9	119.2	33.596
4	34.657	6524	80.8	32.787
Total		19898.1	377.0	100.000



Peak #	Ret.Time	Area	Height	Area %
1	23.447	2236.8	66.4	58.459
2	25.703	176	4.5	4.600
3	29.764	1248.9	26.9	32.641
4	35.152	164.5	2.1	4.300
Total		3826.2	99.9	100.000



Peak #	Ret.Time	Area	Height	Area %
1	23.447	2236.8	66.4	92.705
2	25.703	176	4.5	7.295
Total		2412.8	70.9	100.000

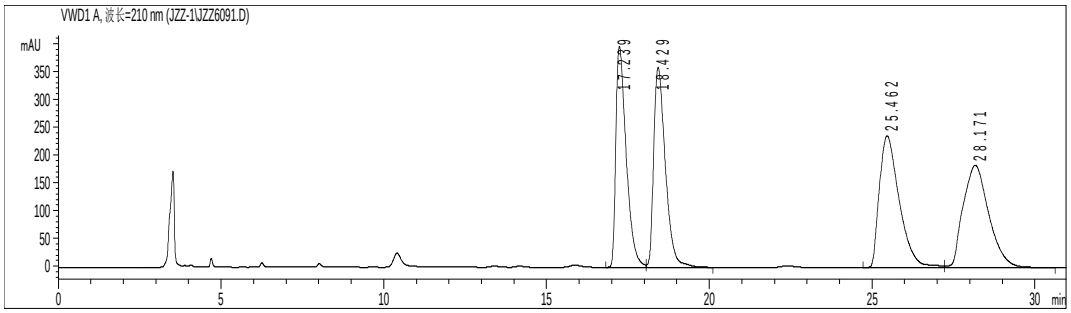


3o: Ar = 3-MeOPh
R = Me

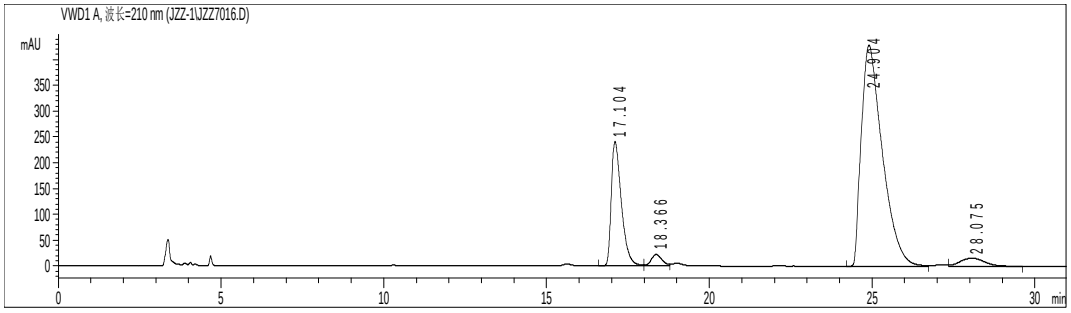
Colorless oil, 95% yield; 92% *ee*; *dr* = 3.7:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68–7.63 (m, 1H), 7.56–7.54 (m, 1H), 7.40–7.35 (m, 1H), 7.17–7.14 (m, 1H), 3.86–3.85 (m, 3H), 3.83–3.80 (m, 3H), 3.53–3.37 (m, 1H), 2.56–2.09 (m, 5H), 2.05–1.95 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 216.4, 216.0, 190.5, 190.2, 167.4, 167.2, 145.6, 131.1 (two peaks), 130.0 (two peaks), 129.5, 100.1 (d, $J_{C\text{-}F}$ = 201 Hz), 62.7, 62.6, 53.5, 41.0, 40.8, 40.7, 40.5, 38.8, 38.7, 38.34, 38.2, 38.0, 23.0, 22.9, 22.8, 21.8, 16.3, 16.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ –172.6, –172.7.

HRMS (ESI) m/z Found 309.1139 $[M+H]^+$, calc. for $C_{16}H_{18}FO_5$ 309.1138

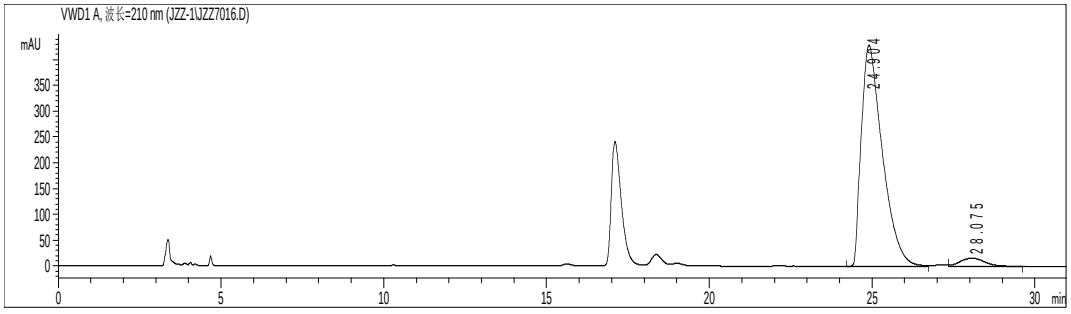
The *ee* was determined by HPLC analysis. CHIRALPAK ID (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 ^oC; 254 nm; retention time: 24.9 (major), 28.2 (minor).



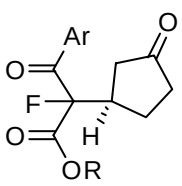
Peak #	Ret.Time	Area	Height	Area %
1	17.239	8779.6	397.5	23.159
2	18.429	8981.7	359.6	23.692
3	25.462	10072.6	236.9	26.569
4	28.171	10076.5	184.3	26.580
Total		37910.4	1178.3	100.000



Peak #	Ret.Time	Area	Height	Area %
1	17.104	5218.4	241.6	20.217
2	18.366	520.7	22.4	2.017
3	24.904	19233.1	428.9	74.512
4	28.075	839.9	15.7	3.254
Total		25812.1	708.6	100.000



Peak #	Ret.Time	Area	Height	Area %
1	24.904	19233.1	428.9	95.816
2	28.075	839.9	15.7	4.184
Total		20073	444.6	100.000

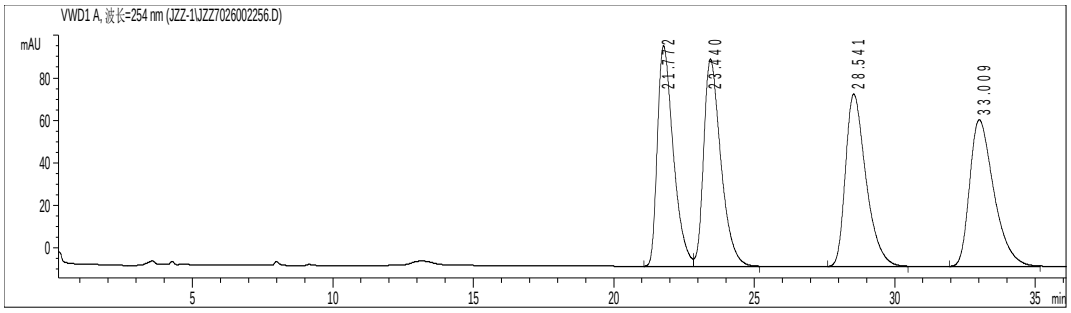


3p: Ar =2-furyl
R = Me

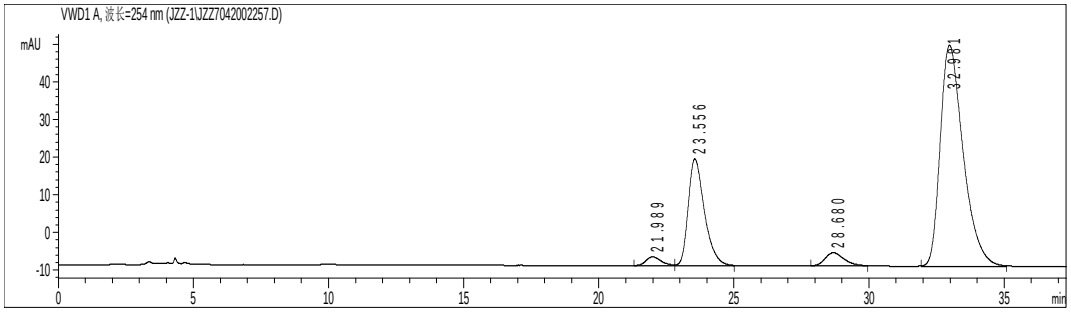
Colorless oil, 92% yield; 90% *ee*; *dr* = 2.8:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73–7.72(m, 1H), 7.57–7.52 (m, 1H), 6.61–6.57 (m, 1H), 3.83–3.80 (m, 3H), 3.53–3.36 (m, 1H), 2.52–2.10 (m, 6H), 2.10–1.80 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 215.9, 215.6, 195.7, 195.4, 167.0, 166.7, 139.4, 139.2, 134.1, 132.3 (two peaks), 132.0 (two peaks), 129.2, 129.1, 125.5, 100.0 (d, $J_{C\text{-}F}$ = 204 Hz), 53.6, 41.8, 41.5, 38.3 (two peaks), 38.1, 37.9, 22.9 (two peaks), 20.8 (two peaks); ^{19}F NMR (376 MHz, $CDCl_3$) δ –176.4, –176.8.

HRMS (ESI) m/z Found 309.1139 $[M+H]^+$, calc. for $C_{16}H_{18}FO_5$ 309.1138

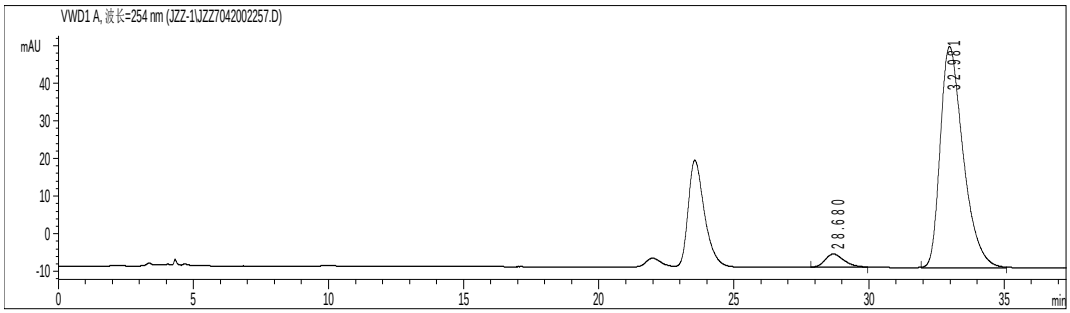
The *ee* was determined by HPLC analysis. CHIRALPAK ID (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 ^{o}C; 254 nm; retention time: 28.7 (minor), 33.0 min (major).



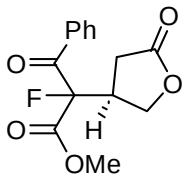
Peak #	Ret.Time	Area	Height	Area %
1	21.772	4089.1	103.8	24.816
2	23.44	4141.2	97.5	25.132
3	28.541	4120.7	81.1	25.007
4	33.009	4126.9	69.1	25.04
Total		16477.9	351.5	100.000



Peak #	Ret.Time	Area	Height	Area %
1	21.989	90.1	2.3	1.835
2	23.556	1182.2	28.4	24.077
3	28.68	175	3.5	3.563
4	32.981	3462.7	58.8	70.524
Total		4910	93.0	100.000



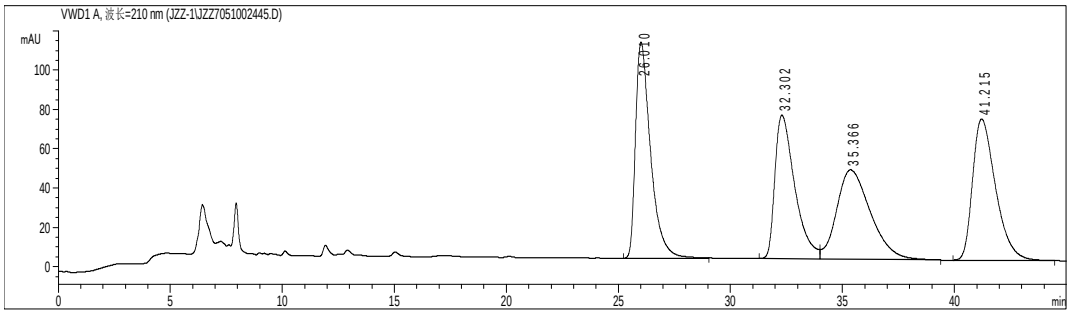
Peak #	Ret.Time	Area	Height	Area %
1	28.68	175	3.5	4.810
2	32.981	3462.7	58.8	95.190
Total		3637.7	62.3	100.000



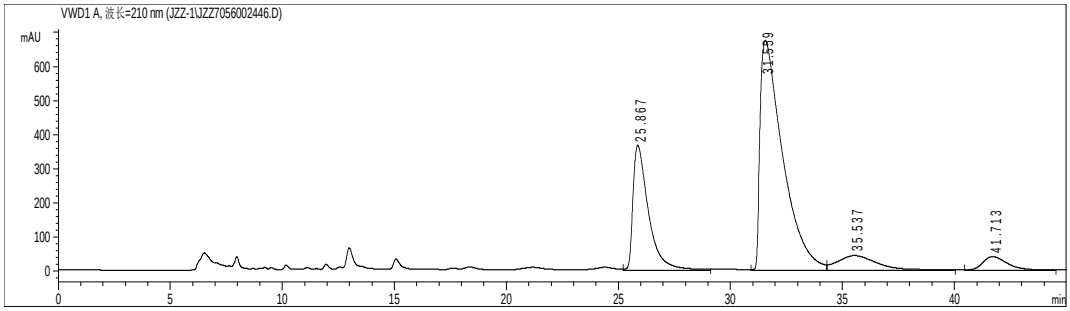
5 Colorless oil, 43% yield; 82% *ee*; *dr* = 2.3:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05–8.02 (m, 2H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.50 (t, *J* = 7.8 Hz, 2H), 4.68 and 4.46 (t, *J* = 9.0 Hz, 1H), 4.37 and 4.20 (dd, *J* = 9.5, 7.5 Hz, 1H), 3.86–3.80 (m, 3H), 3.78–3.68 (m, 1H), 2.83−2.71 (m, 1H), 2.65-2.54 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.3, 190.0, 175.0, 174.8, 166.4, 166.1, 134.9, 134.7, 133.0 (two peaks), 132.8 (two peaks), 129.8 (four peaks), 129.0, 128.9, 98.0 (d, $J_{C\text{-}F}$ = 203 Hz), 67.9 (two peaks), 67.0, 66.9, 53.9, 39.6, 39.5, 39.4, 39.2, 28.8 (two peaks), 28.0, 27.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ –167.0, –171.5.

HRMS (ESI) m/z Found 281.0825 $[M+H]^+$, calc. for $C_{14}H_{14}FO_5$ 281.0825

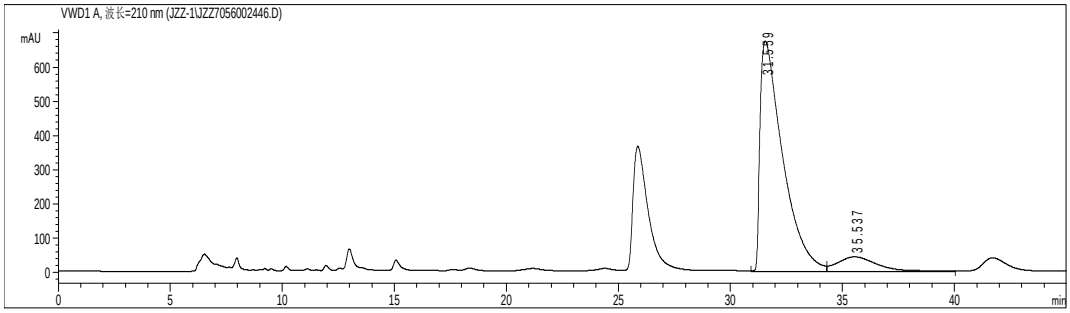
The *ee* was determined by HPLC analysis. LUX Cellulose−2 and LUX Amylose−2 (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 60/40; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 31.6 (major), 35.5 min (minor).



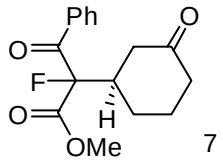
Peak #	Ret.Time	Area	Height	Area %
1	26.01	5106.1	109.9	26.237
2	32.302	4490.7	73	23.075
3	35.366	4738.4	45.4	24.347
4	41.215	5126.4	71.9	26.341
Total		19461.6	300.2	100.000



Peak #	Ret.Time	Area	Height	Area %
1	25.867	17064.5	363.8	23.820
2	31.559	47046.6	671.9	65.671
3	35.537	4716.6	41.1	6.584
4	41.713	2812.1	38.7	3.925
Total		71639.8	1115.5	100.000



Peak #	Ret.Time	Area	Height	Area %
1	31.559	47046.6	671.9	90.888
2	35.537	4716.6	41.1	9.112
Total		51763.2	713	100.000

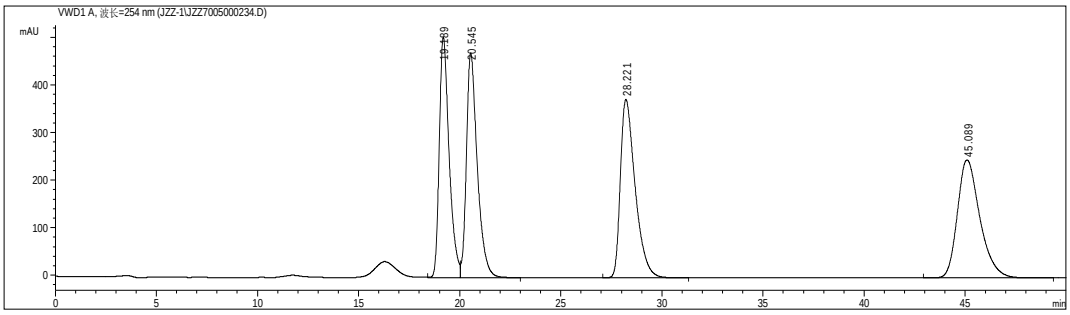


7

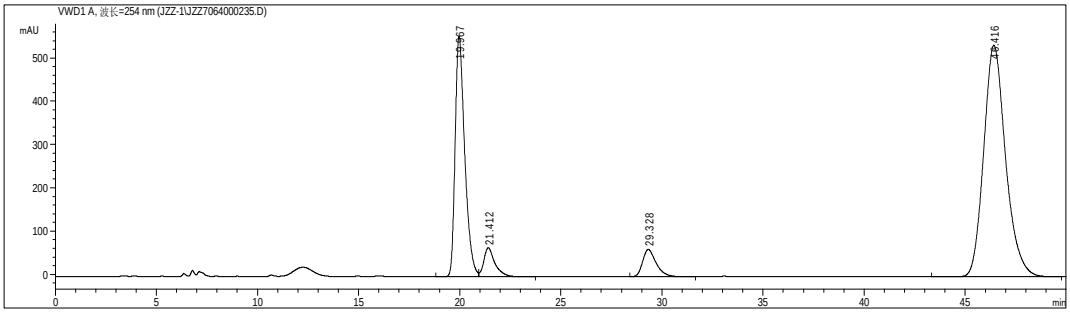
Colorless oil, 88% yield; 86% *ee*; *dr* = 2.4:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04–7.99 (m, 2H), 7.60 (dd, *J* = 13.4, 7.3 Hz, 1H), 7.47 (dd, *J* = 14.7, 6.9 Hz, 2H), 3.83–3.81 (m, 3H), 3.23–3.05 (m, 1H), 2.48–2.40 (m, 4H), 2.15–2.06 (m, 1H), 1.77–1.57 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.2, 209.0, 191.4, 191.2, 166.9, 166.7, 134.1, 129.8 (three peaks), 129.7, 128.6, 101.9 (d, $J_{C\text{-}F}$ = 203 Hz), 53.6, 53.5, 42.7, 42.5, 42.3, 42.1, 41.4, 41.1 (two peaks), 40.9, 40.8, 24.8 (two peaks), 24.2, 24.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ –172.0, –173.1.

HRMS (ESI) m/z Found 293.1190 $[M+H]^+$, calc. for $C_{16}H_{18}FO_4$ 293.1189

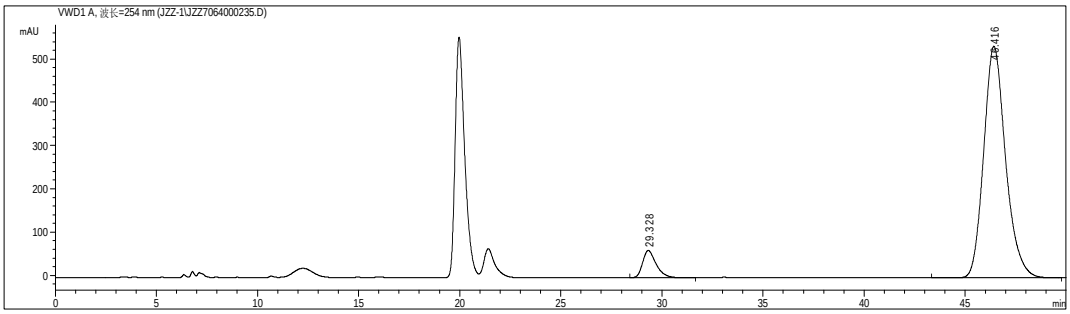
The *ee* was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 90/10; flow rate 1.0 mL/min; 25 ^{o}C; 254 nm; retention time: 29.3 (minor), 46.4 min (major).



Peak #	Ret.Time	Area	Height	Area %
1	19.189	17065.8	505.1	23.492
2	20.545	17578.5	471.9	24.198
3	28.221	18950.7	374.6	26.087
4	45.089	19049.7	247.7	26.223
Total		72644.7	1599.3	100.000



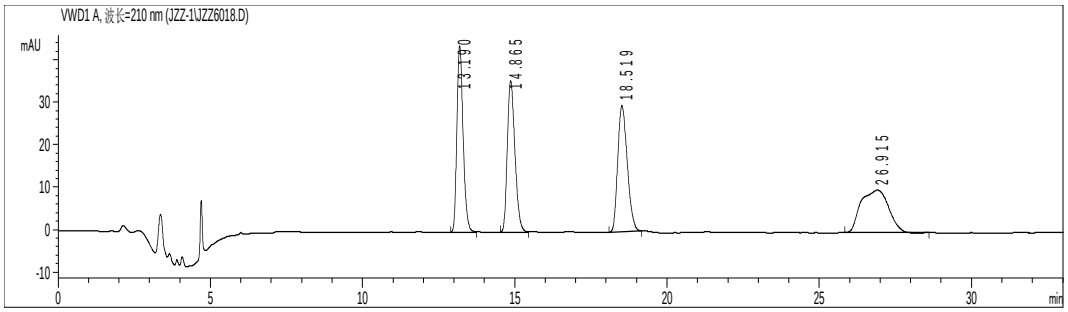
Peak #	Ret.Time	Area	Height	Area %
1	19.967	18269.8	556.5	28.563
2	21.412	2562	67.3	4.005
3	29.328	2899.9	62.8	4.534
4	46.416	40231.2	535	62.898
Total		63962.9	1221.6	100.000

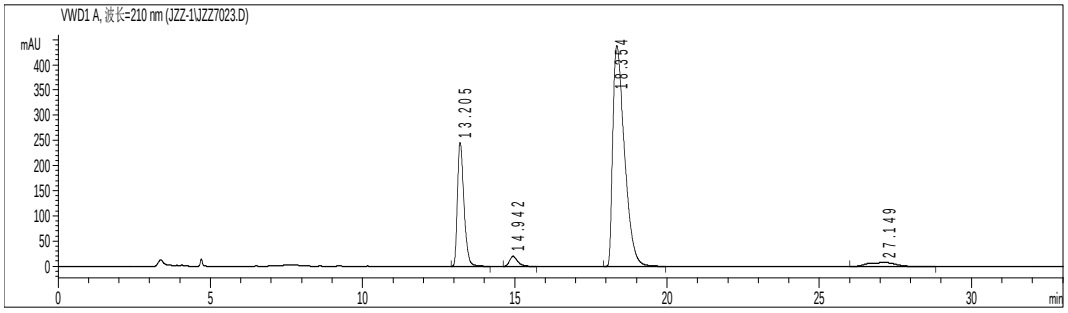


Peak #	Ret.Time	Area	Height	Area %
1	29.328	2899.9	62.8	6.723
2	46.416	40231.2	535	93.277
Total		43131.1	597.8	100.000

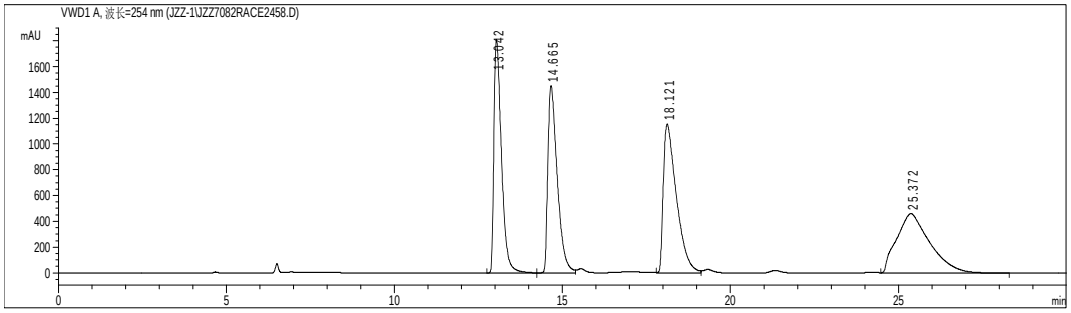
4. The comparison of HPLC spectra of 3a and 10

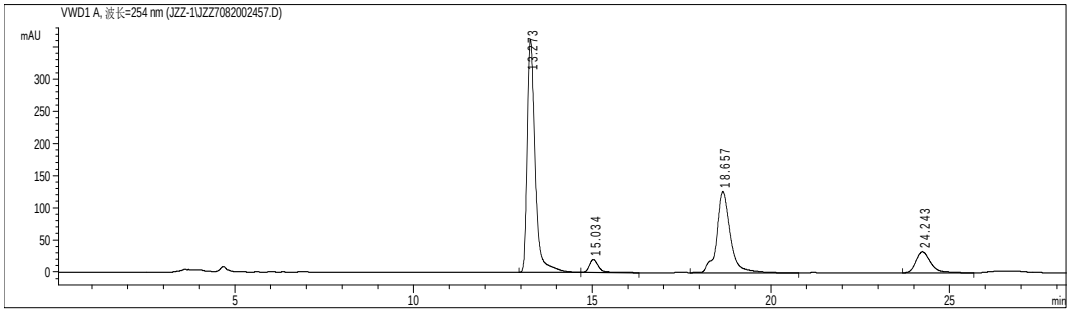
3a: dr:1:3





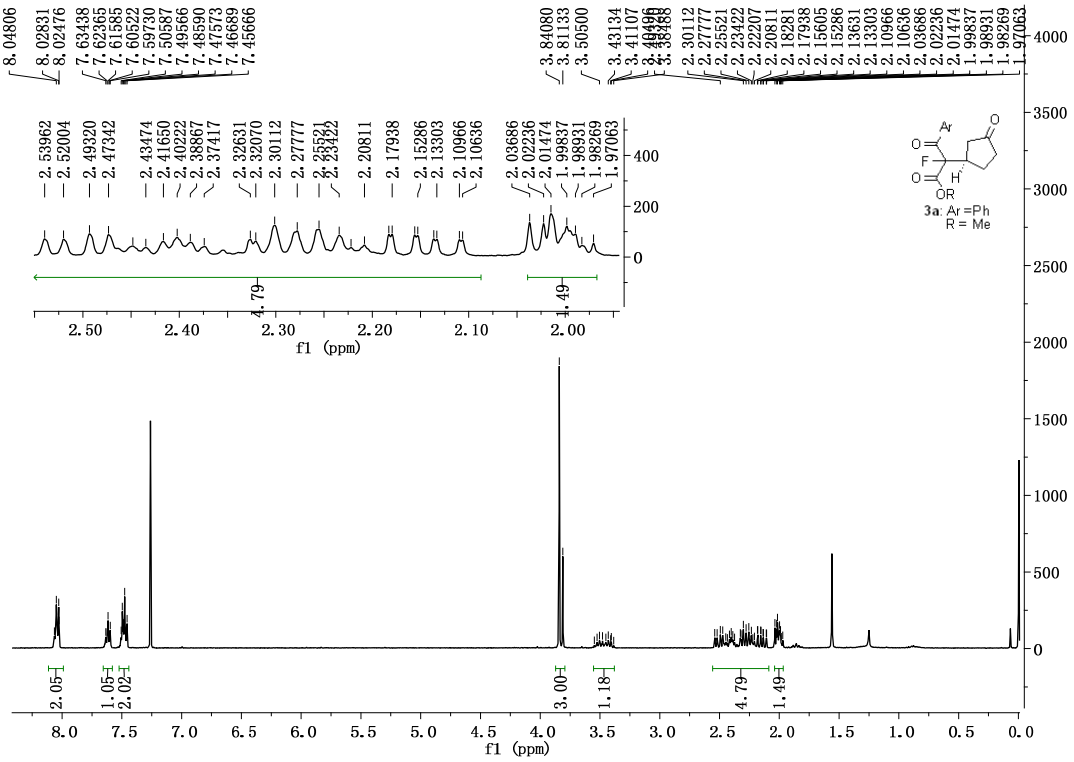
10: dr: 3:2

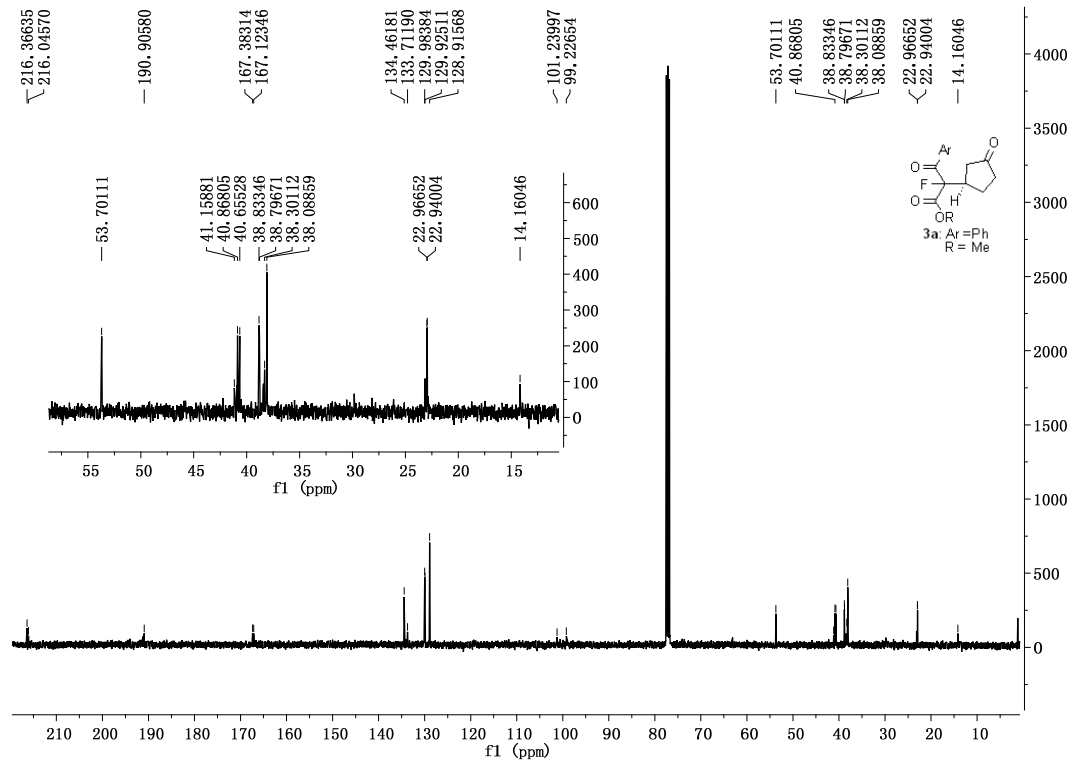


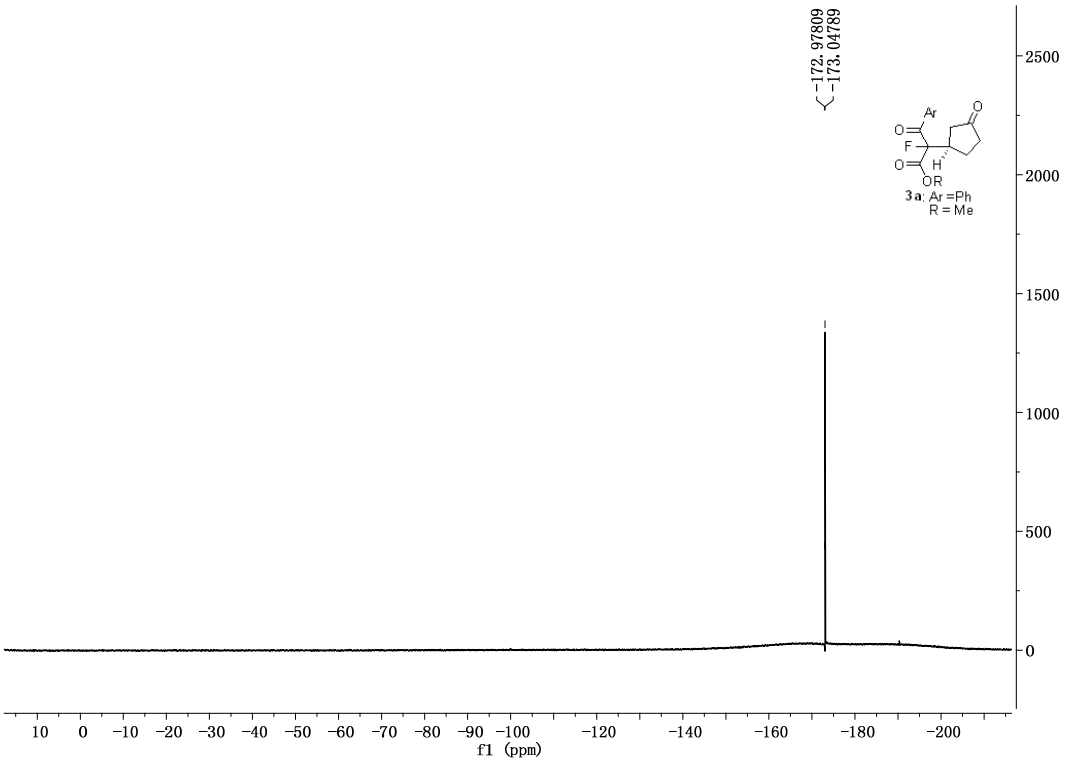


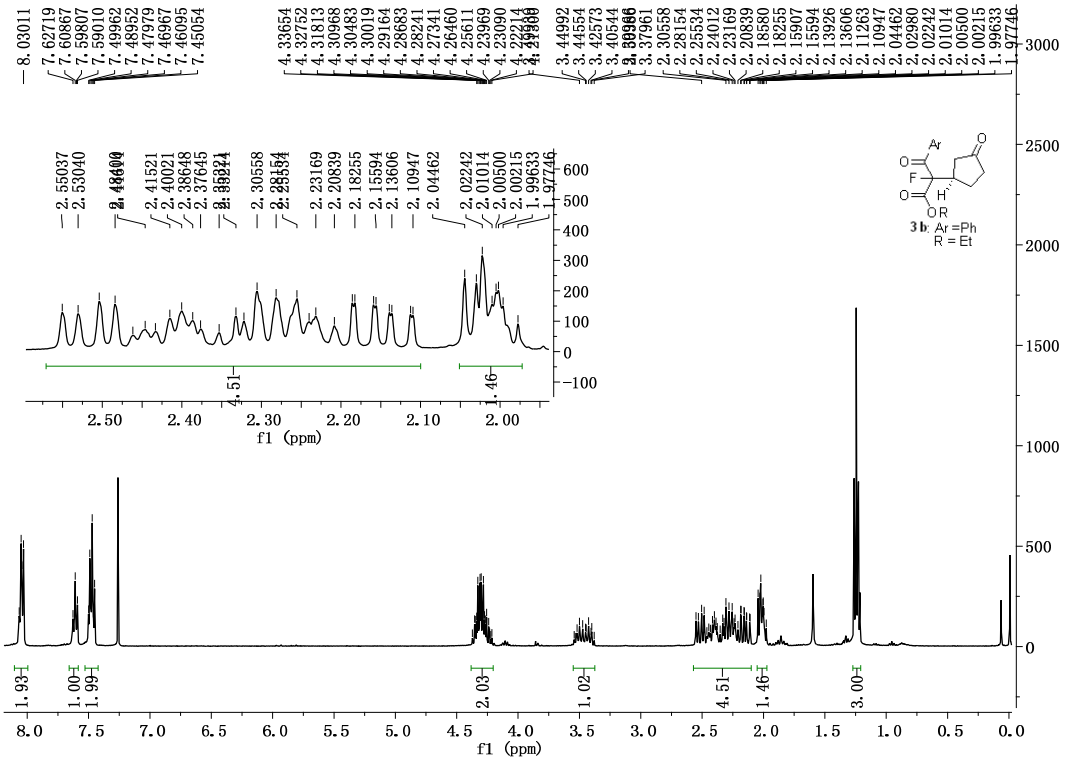
Same enantioselectivity but opposite diastereoselective results.

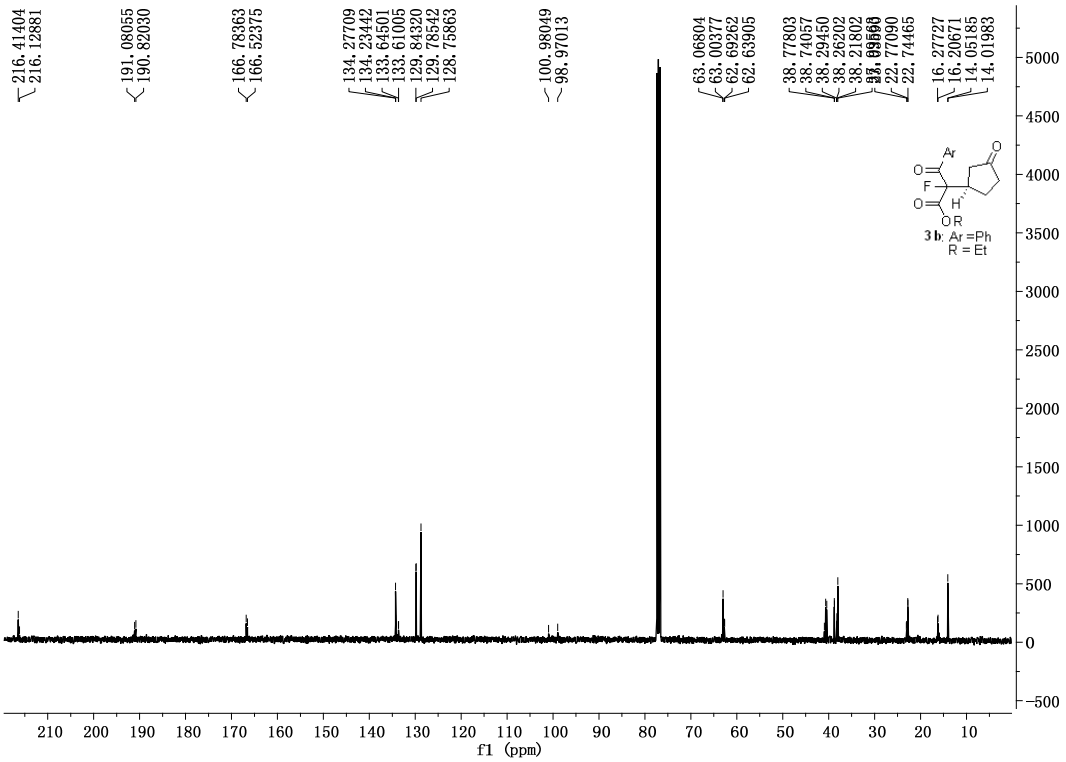
5. NMR spectra

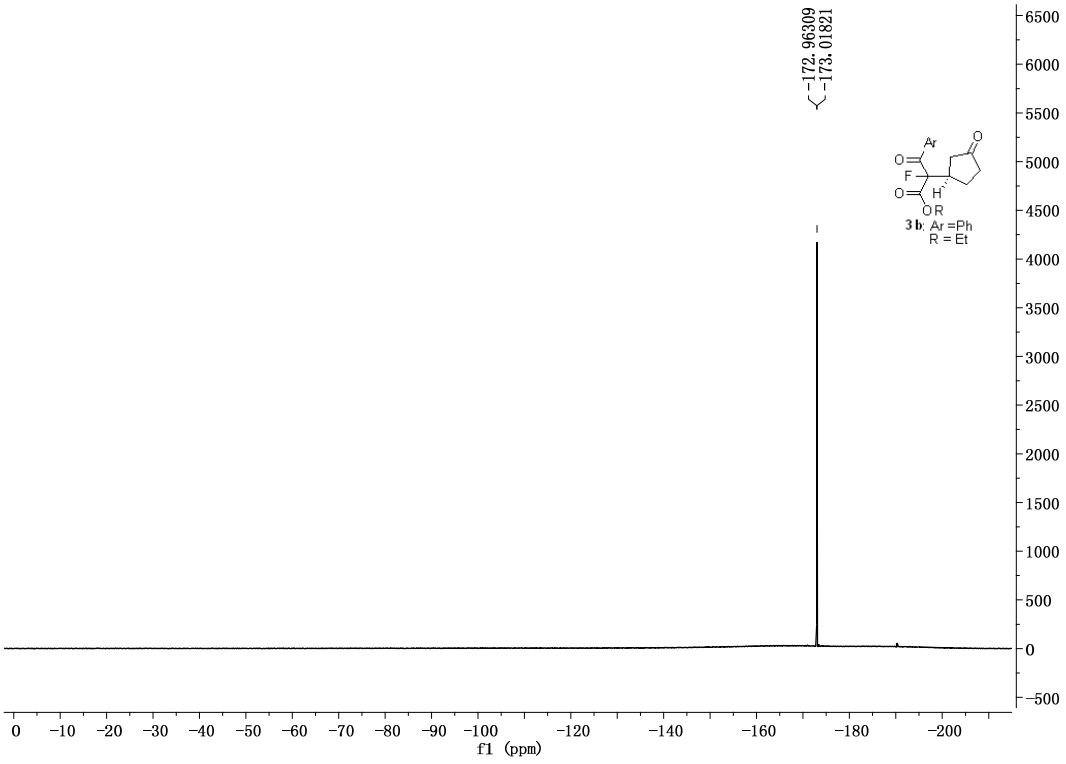


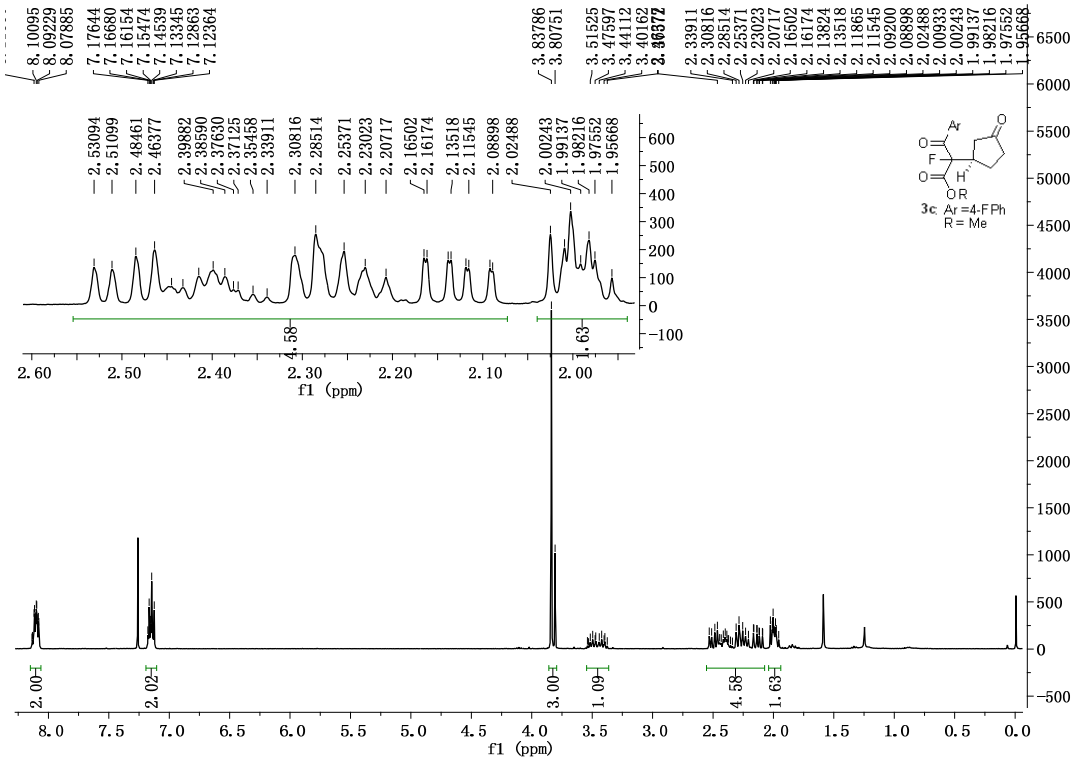


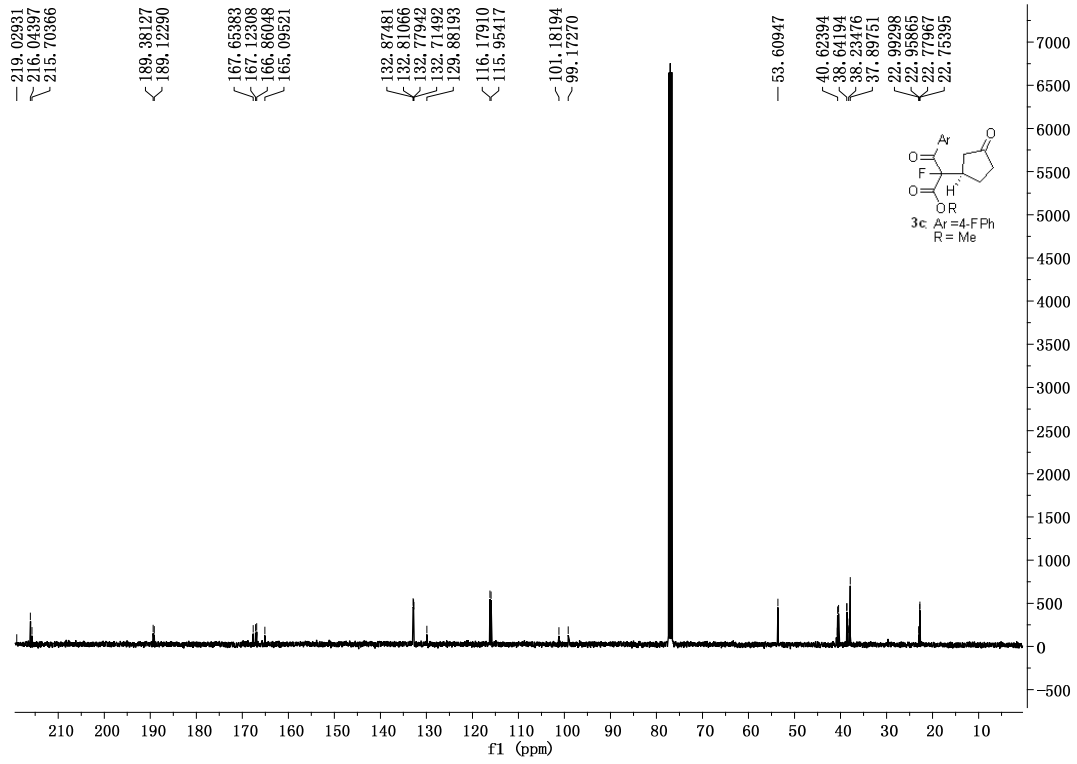

-172.97809
-173.04789
3a: Ar =Ph
R = Me
f1 (ppm)

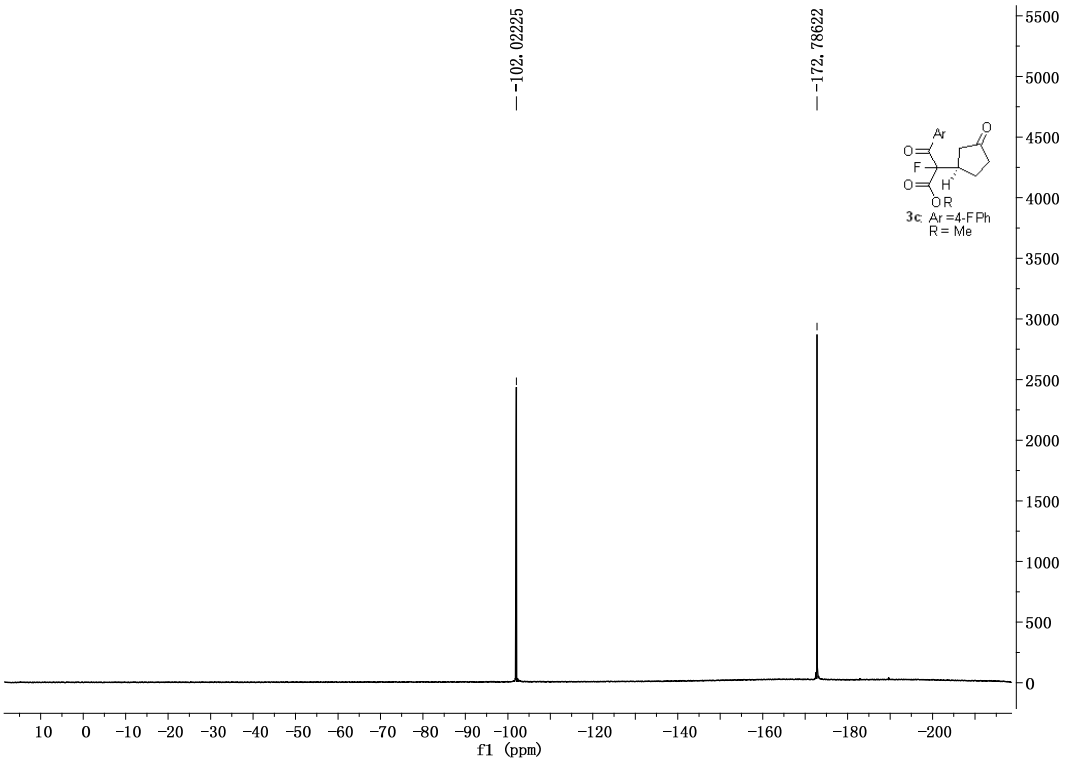

3b: Ar =Ph
R = Et
4.51
1.46
f1 (ppm)
1.93
1.00
1.99
2.03
1.02
4.51
1.46
3.00

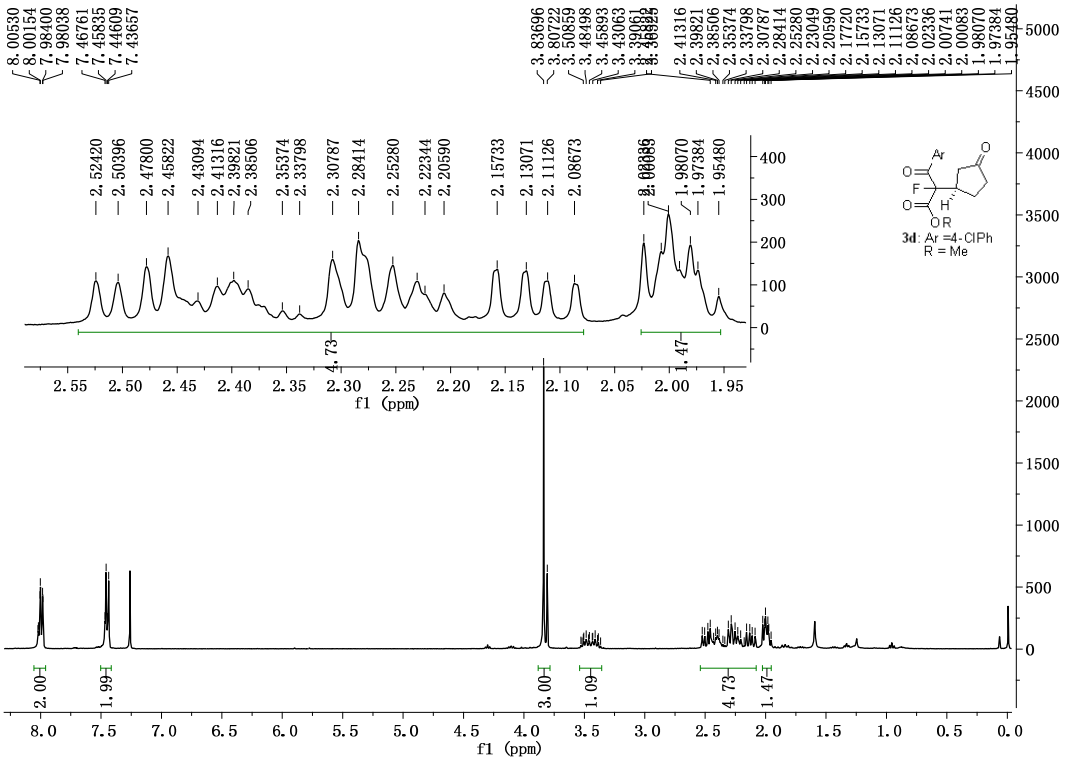

216.41404
216.12881
191.08055
190.82030
166.78363
166.52375
134.27709
134.23442
133.64501
133.61005
129.84320
129.78542
128.75863
100.98049
98.97013
63.06804
63.00377
62.69262
62.63905
38.77803
38.74057
38.29450
38.26202
38.21802
22.77090
22.74465
16.27727
16.20671
14.05185
14.01983
Ar
O
F
H
OR
3b: Ar =Ph
R = Et
f1 (ppm)

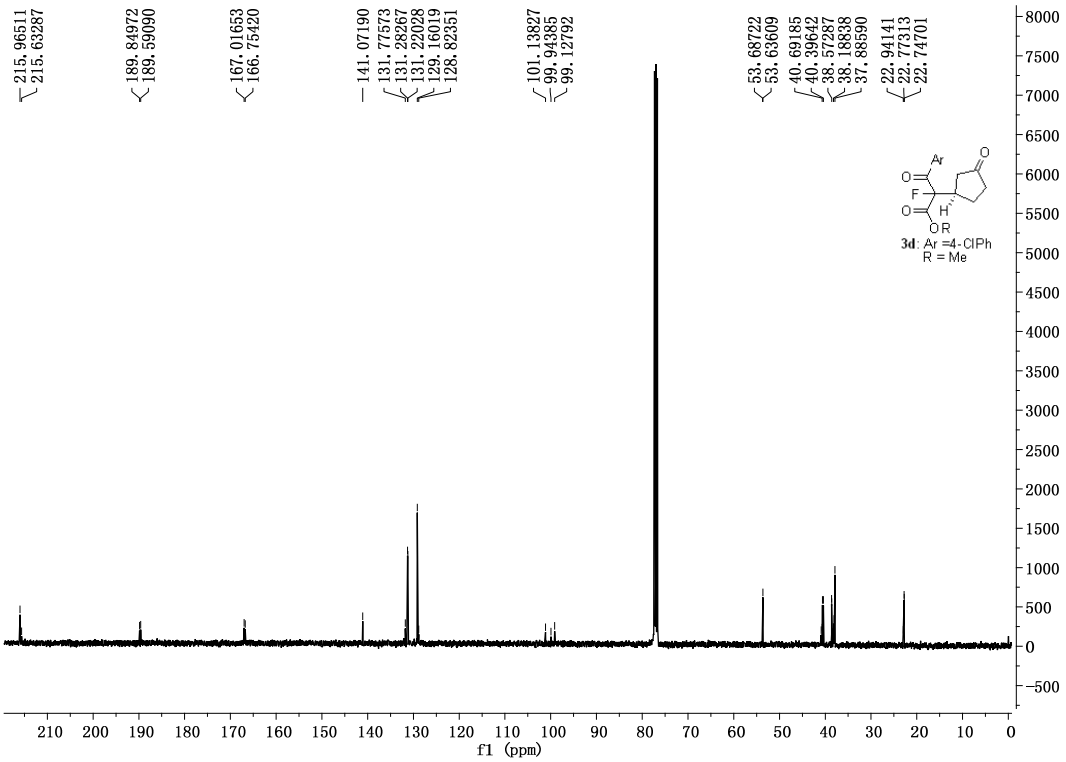

-172.96309
-173.01821
Ar
O
F
H
OR
3b: Ar =Ph
R = Et
f1 (ppm)

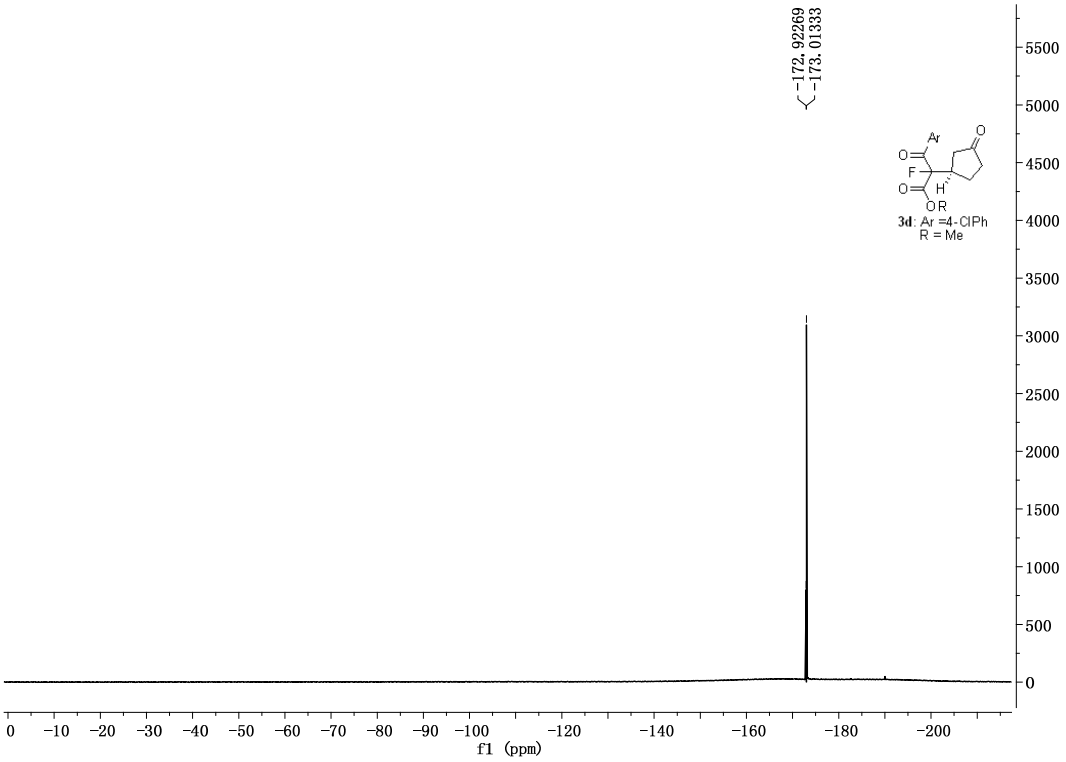

3c: Ar =4-FPh
R = Me
f1 (ppm)

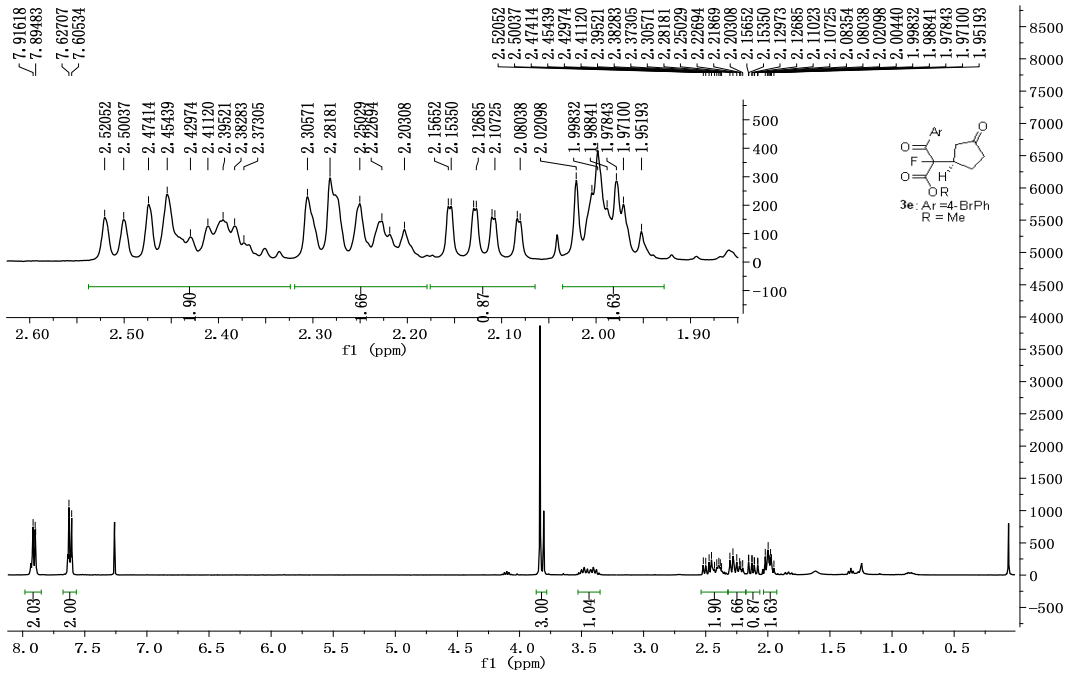

3c: Ar =4-FPh
R = Me
f1 (ppm)

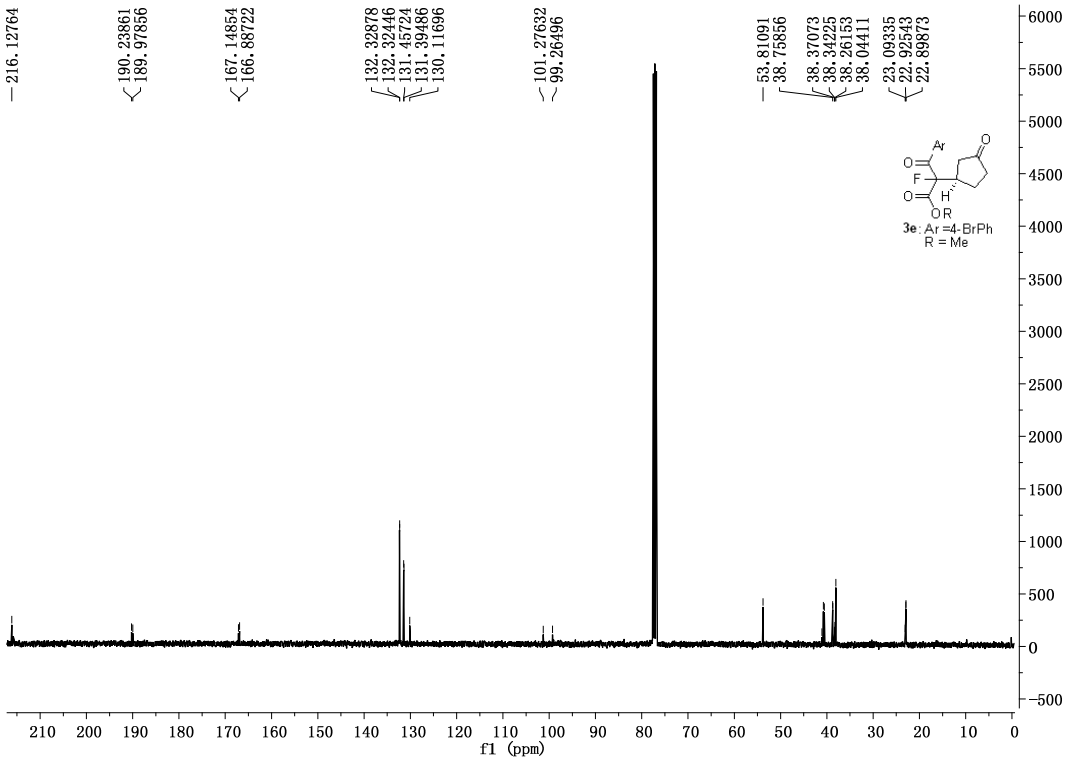

-102.02225
-172.78622
3c: Ar =4-FPh
R = Me
f1 (ppm)

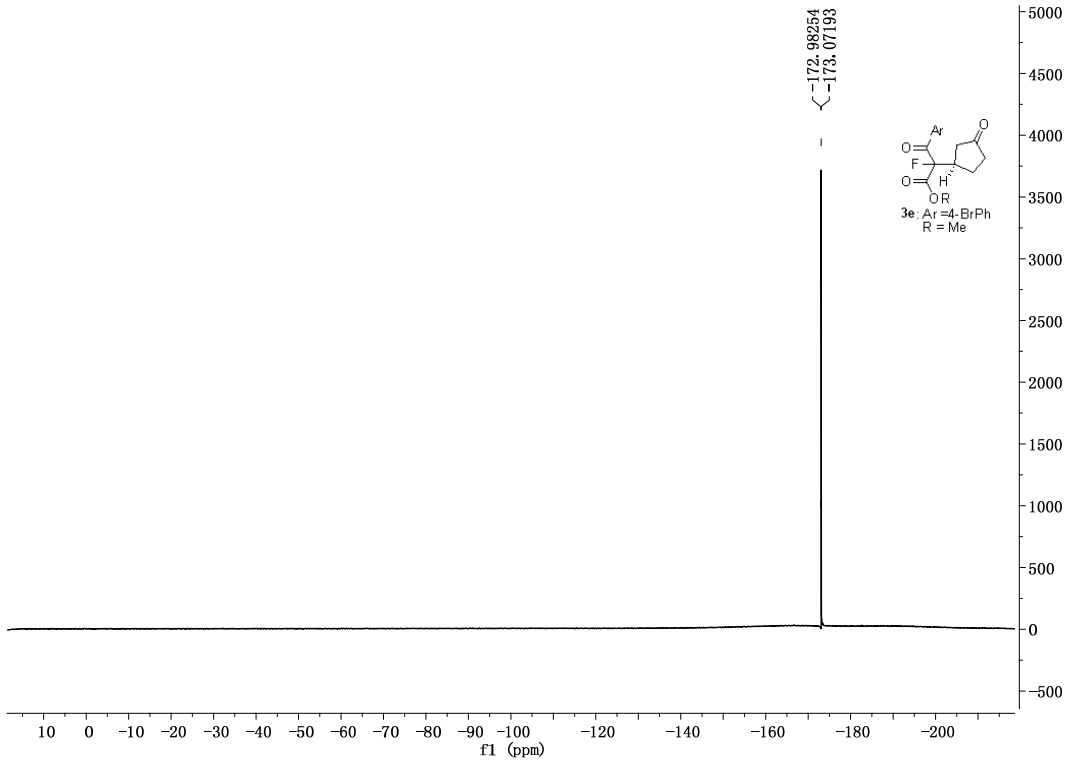

3d: Ar =4-ClPh
R = Me
f1 (ppm)

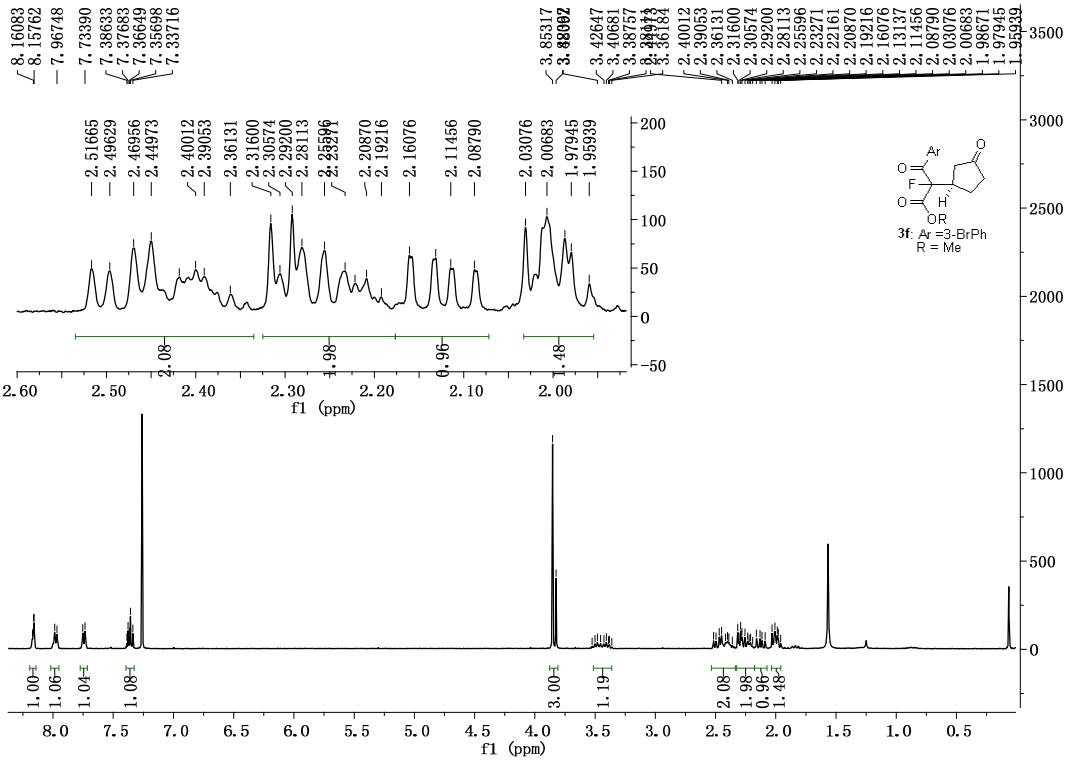

215.96511
215.63287
189.84972
189.59090
167.01653
166.75420
141.07190
131.77573
131.28267
131.22028
129.16019
128.82351
101.13827
99.94385
99.12792
53.68722
53.63609
40.69185
40.39642
38.57287
38.18838
37.88590
22.94141
22.77313
22.74701
Ar
O
F
H
OR
3d: Ar =4-ClPh
R = Me
f1 (ppm)

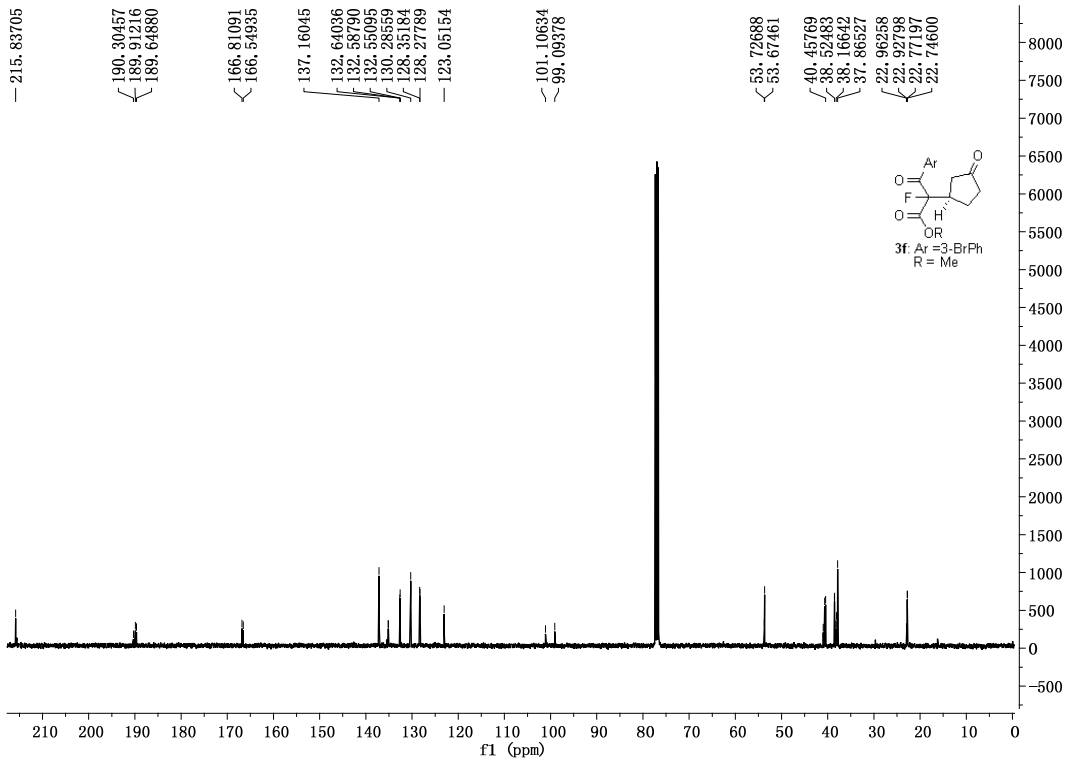

-172.92269
-173.01333
Ar
O
F
H
OR
3d: Ar =4-ClPh
R = Me
f1 (ppm)

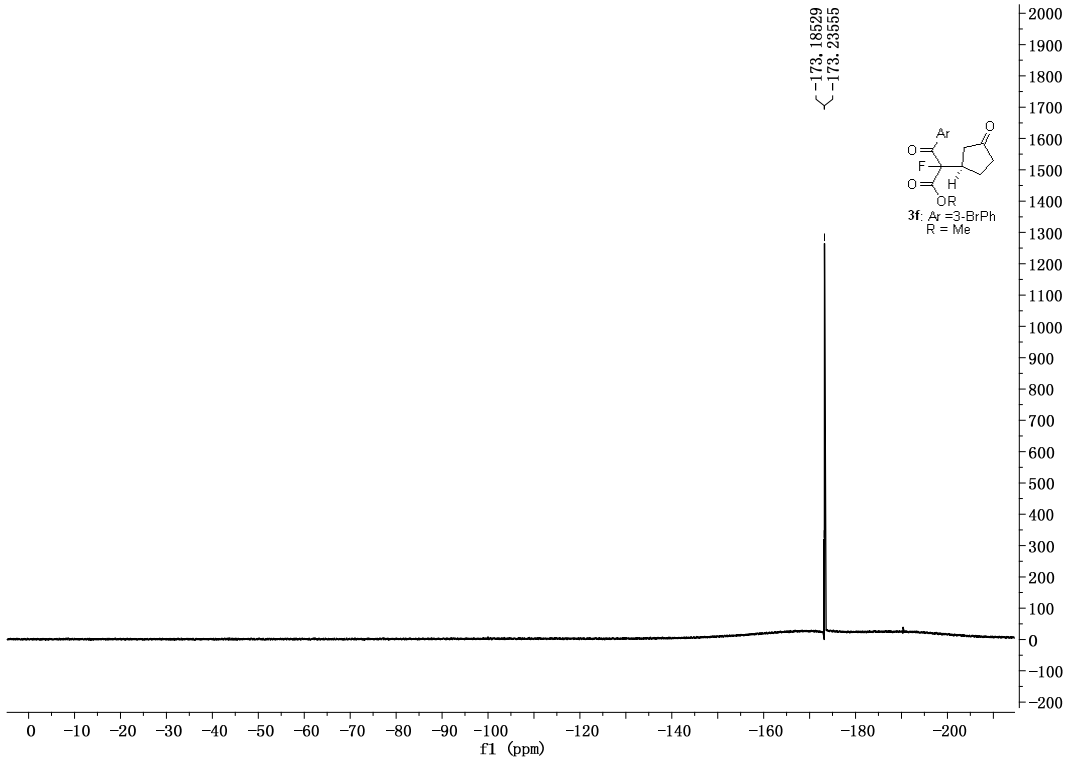

7.91618
7.89483
7.62707
7.60534
2.52052
2.50037
2.47414
2.45439
2.42974
2.41120
2.39521
2.38283
2.37305
2.30571
2.28181
2.25029
2.22694
2.21869
2.20308
2.15652
2.15350
2.12973
2.12685
2.11023
2.10725
2.08354
2.08038
2.02098
2.00440
1.99832
1.98841
1.97843
1.97100
1.95193
Ar
O
F
H
OR
3e: Ar =4-BrPh
R = Me
1.90
1.66
0.87
1.63
f1 (ppm)
2.03
2.00
3.00
1.04
1.90
1.66
0.87
1.63
f1 (ppm)

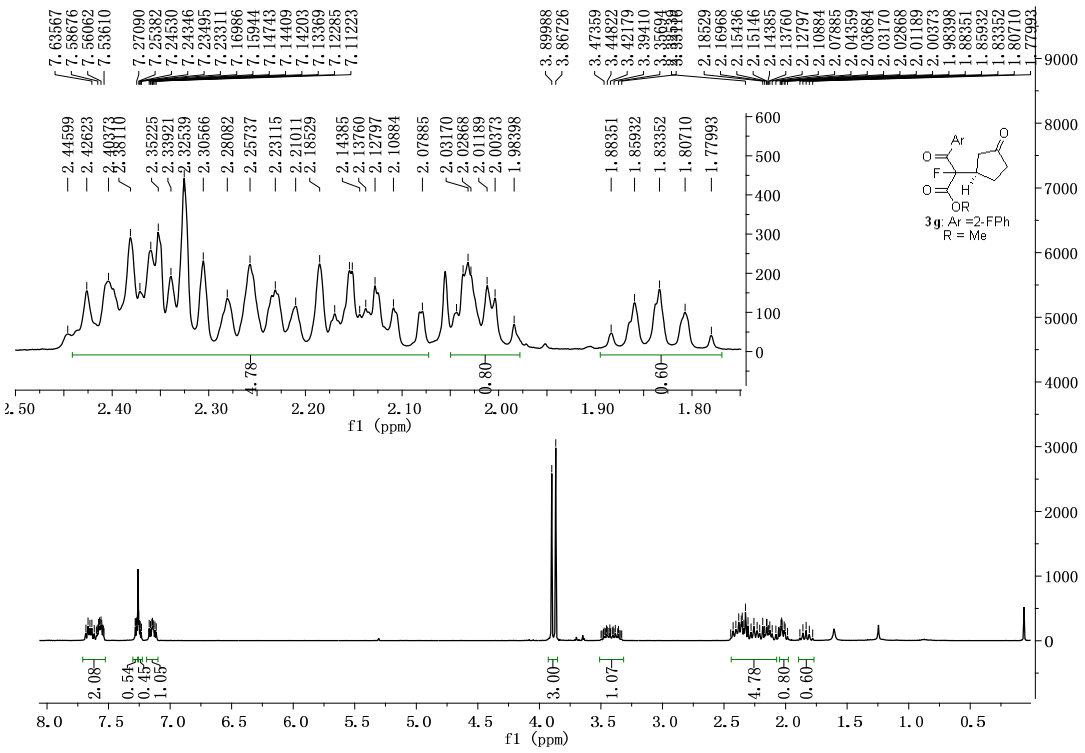

216.12764
190.23861
189.97856
167.14854
166.88722
132.32878
132.32446
131.45724
131.39486
130.11696
101.27632
99.26496
53.81091
38.75856
38.37073
38.34225
38.26153
38.04411
23.09335
22.92543
22.89873
Ar
O
F
H
OR
3e: Ar =4-BrPh
R = Me
f1 (ppm)

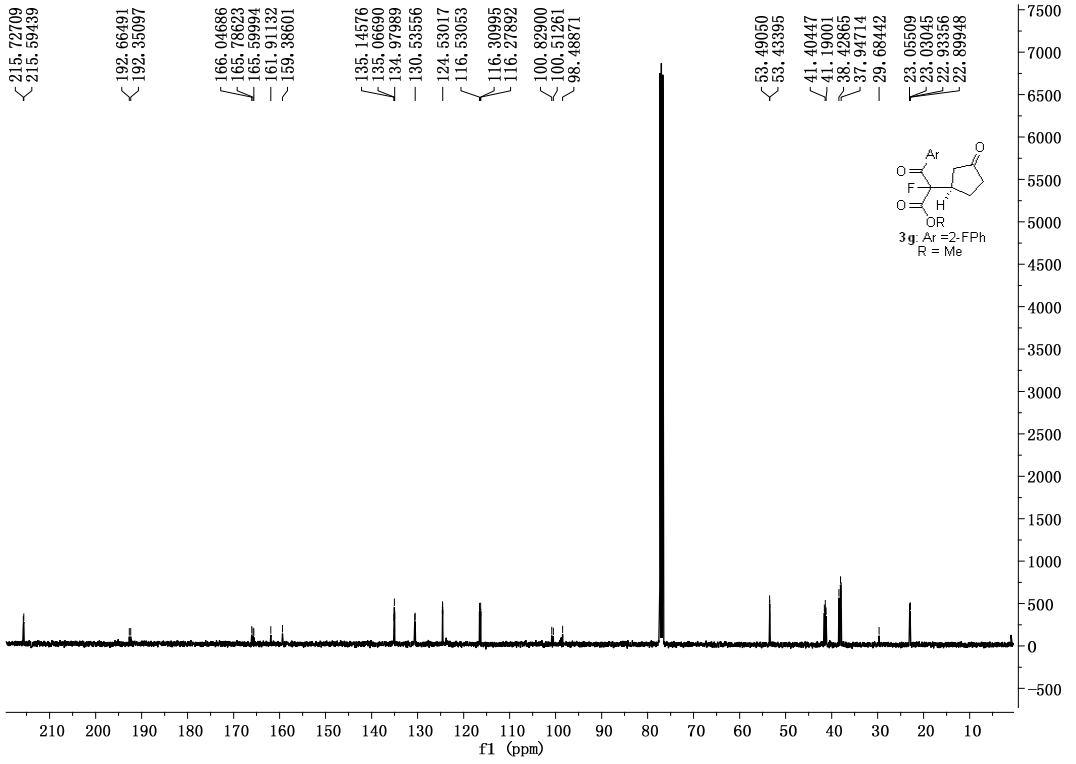

172.98254
173.07193
3e: Ar =4-BrPh
R = Me
f1 (ppm)

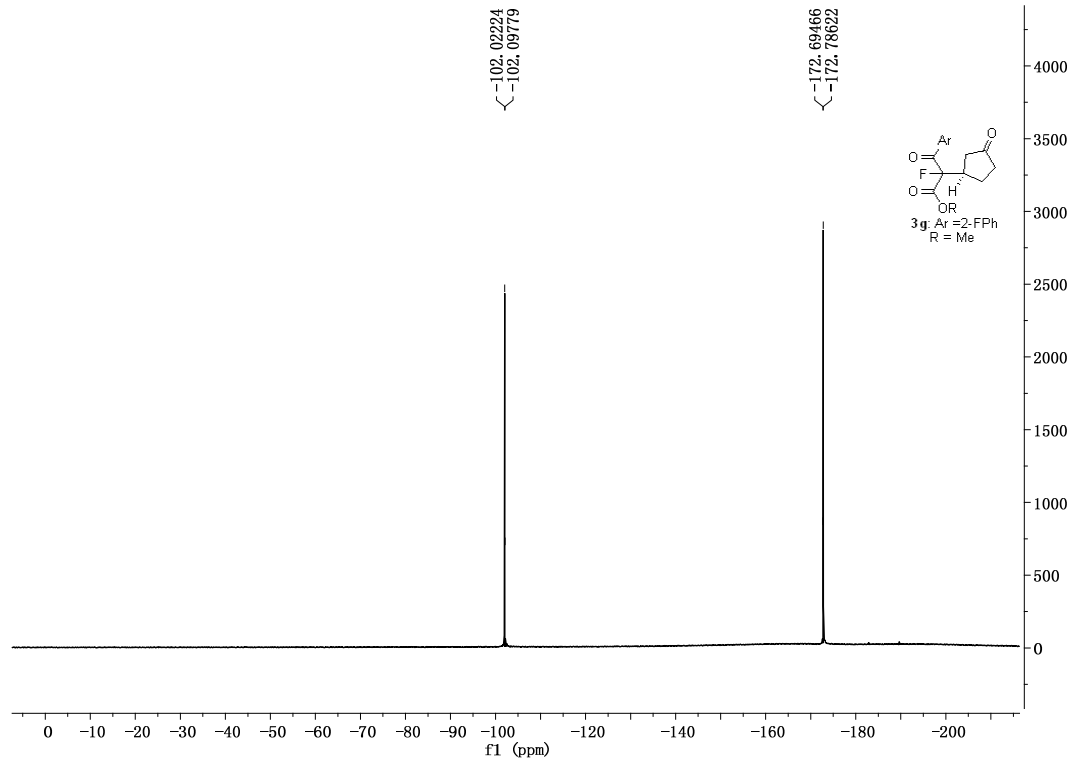

3f: Ar =3-BrPh
R = Me
f1 (ppm)

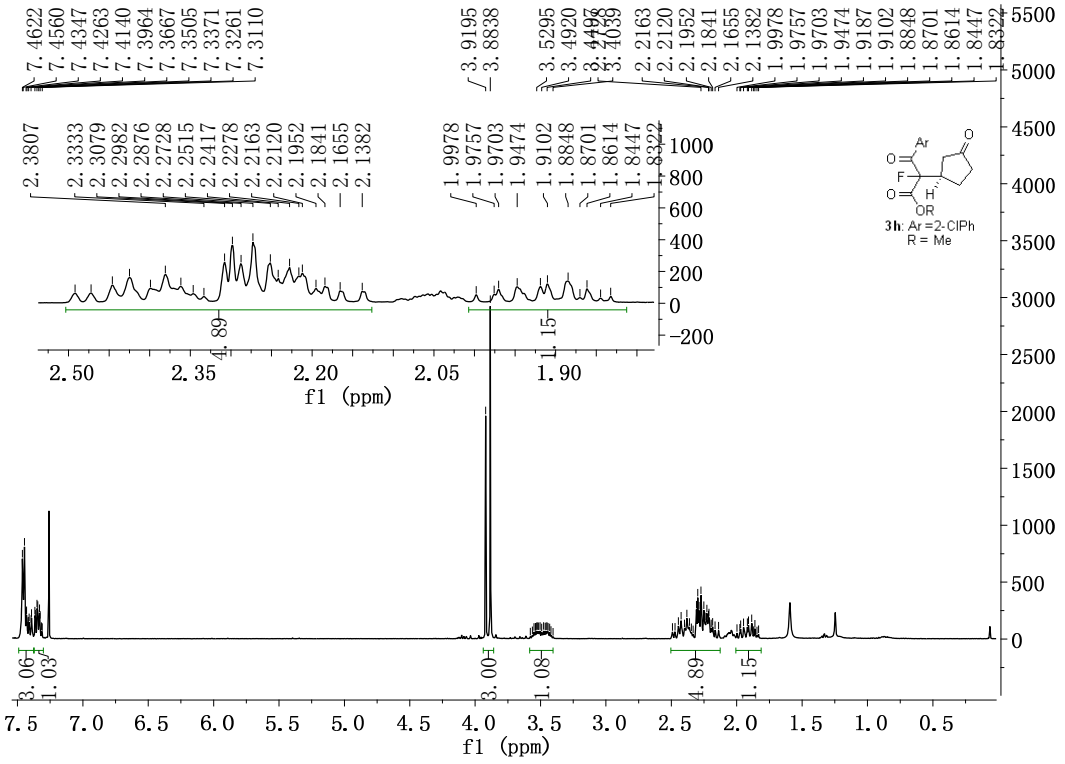

215.83705
190.30457
189.91216
189.64880
166.81091
166.54935
137.16045
132.64036
132.58790
132.55095
130.28559
128.35184
128.27789
123.05154
101.10634
99.09378
53.72688
53.67461
40.45769
38.52483
38.16642
37.86527
22.96258
22.92798
22.77197
22.74600
Ar
O
F
H
OR
3f: Ar =3-BrPh
R = Me
f1 (ppm)

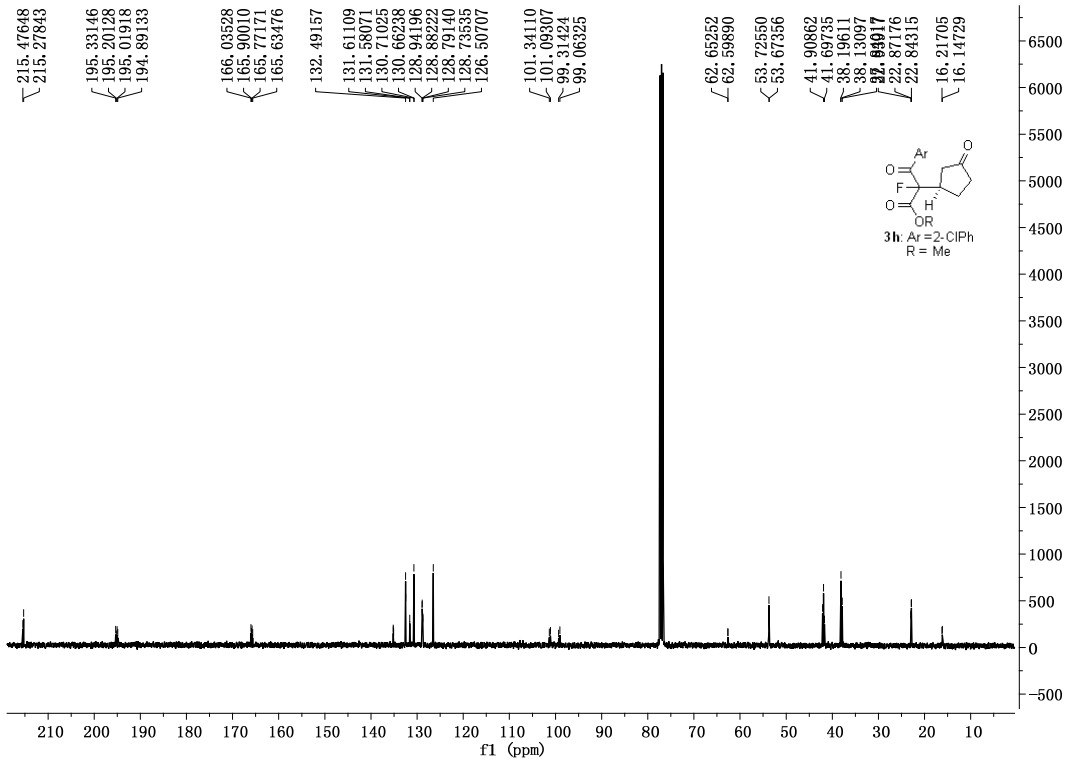

-173.18529
-173.23555
Ar
O
F
H
OR
3f: Ar =3-BrPh
R = Me
f1 (ppm)

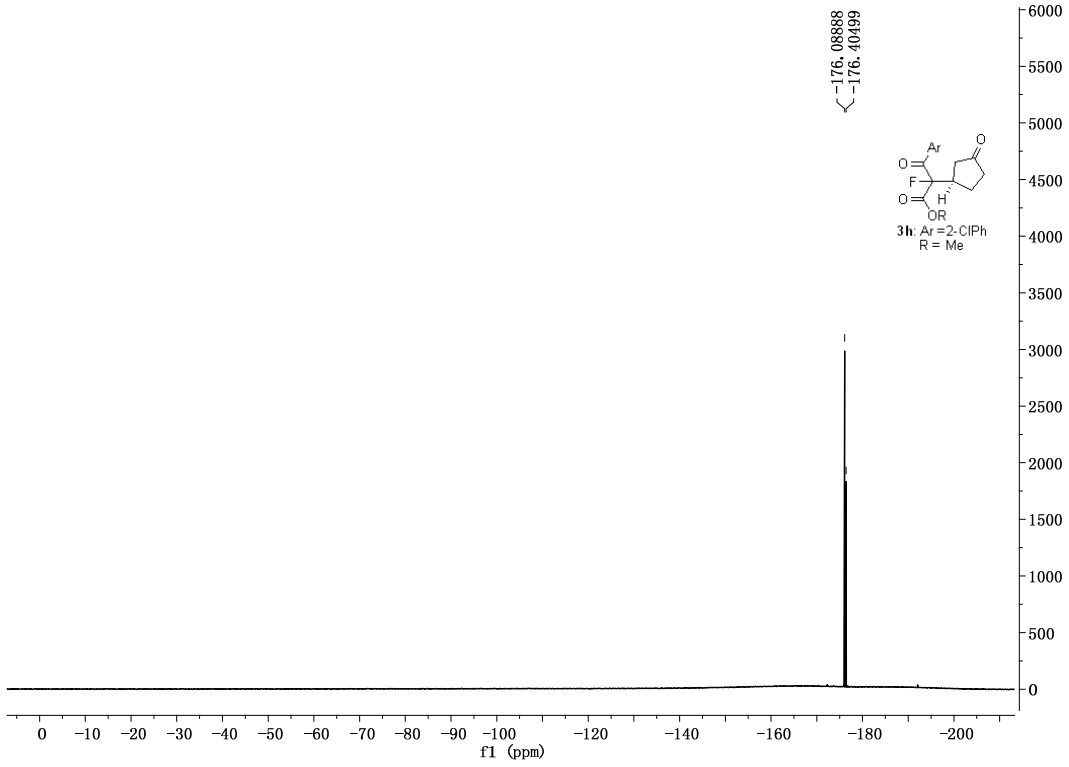

3g: Ar =2-FPh
R = Me
f1 (ppm)

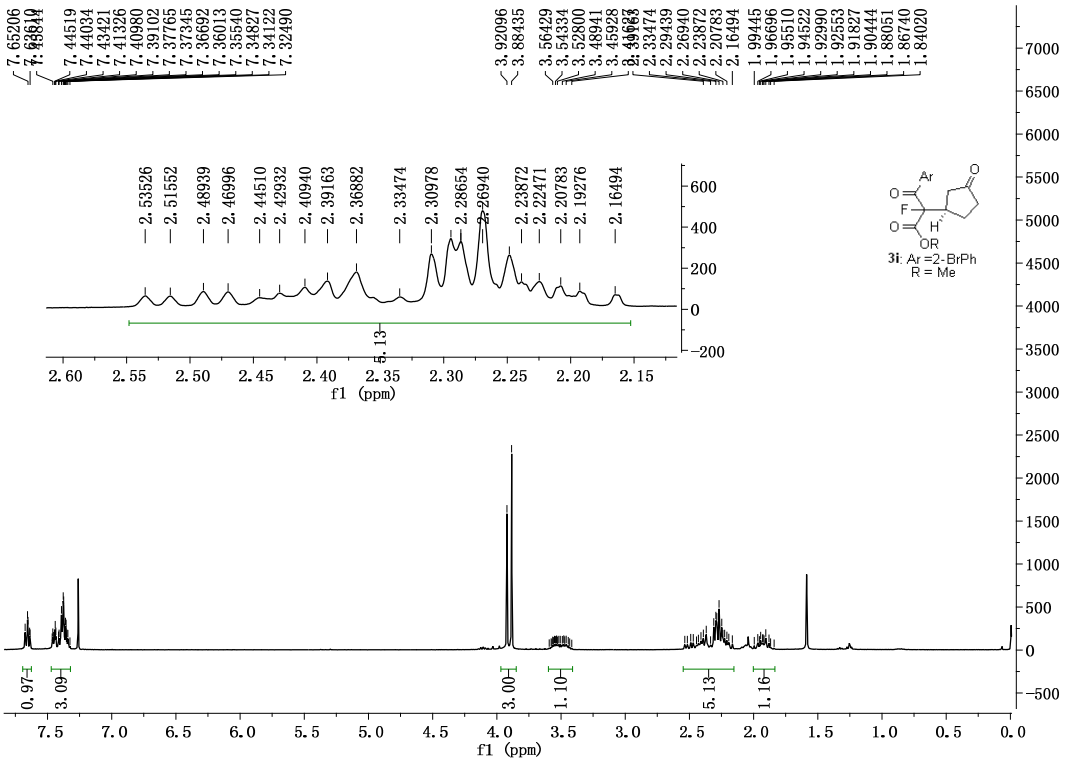

3g: Ar =2-FPh
R = Me
f1 (ppm)

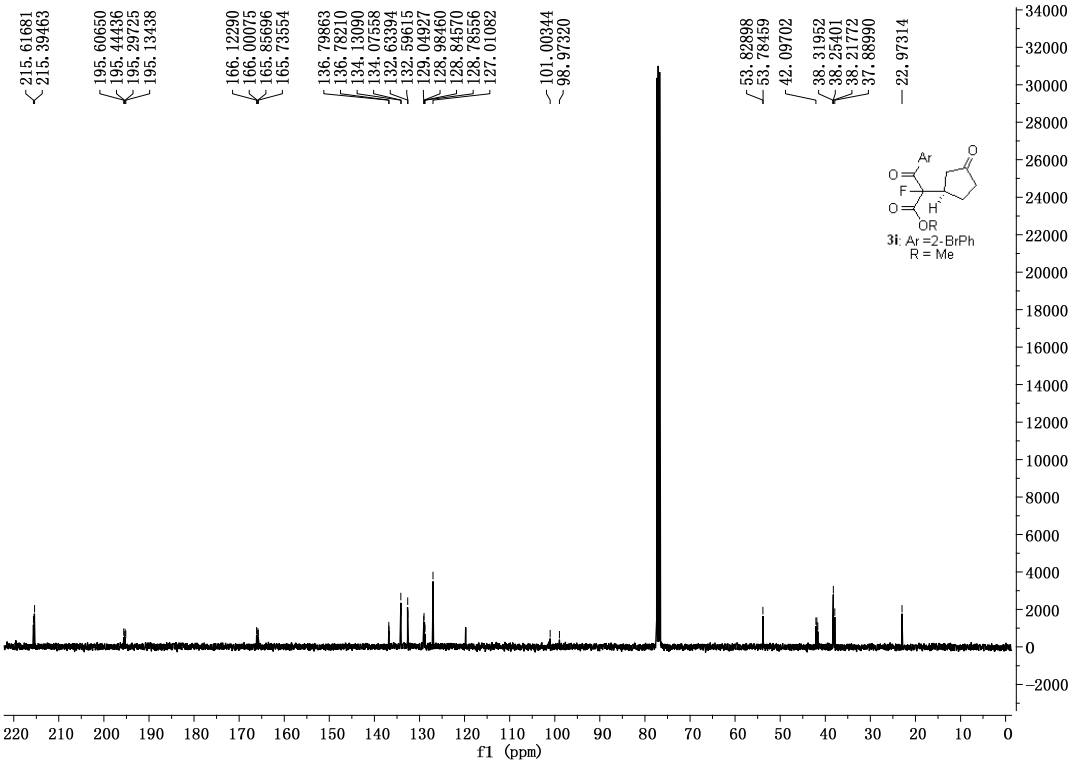

-102.02224
-102.09779
-172.69466
-172.78622
3g: Ar =2-FPh
R = Me
f1 (ppm)

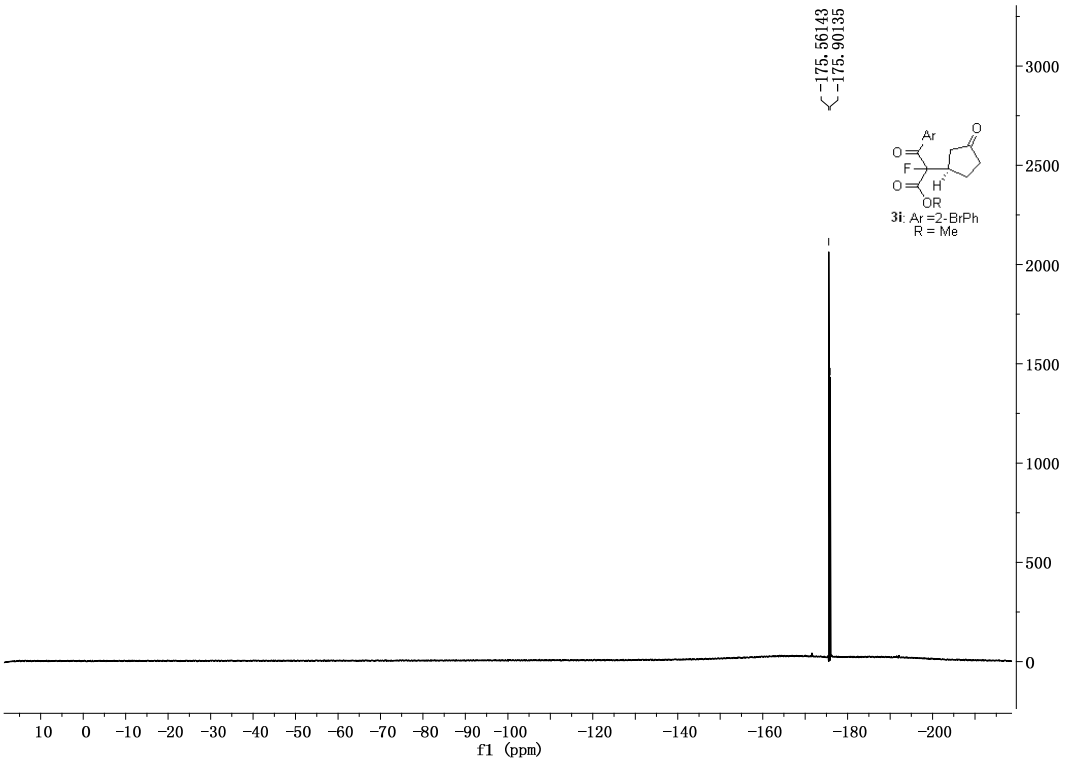

3h: Ar =2-ClPh
R = Me
f1 (ppm)

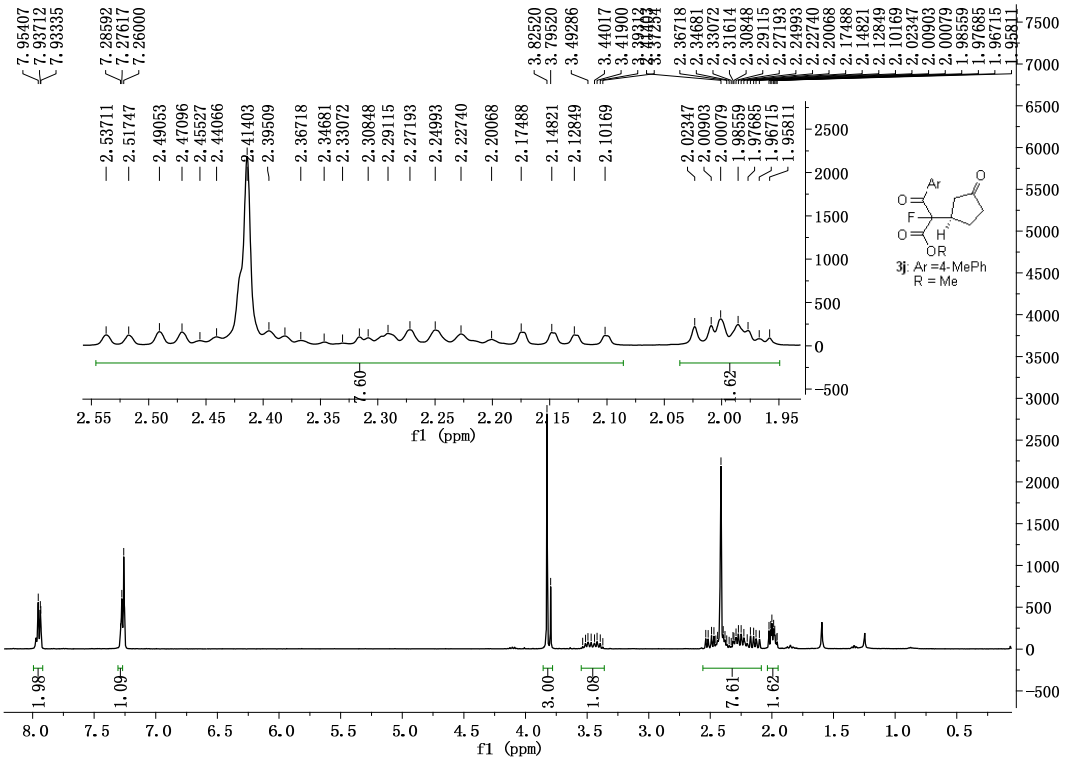

215.47648
215.27843
195.33146
195.20128
195.01918
194.89133
166.03528
165.90010
165.77171
165.63476
132.49157
131.61109
131.58071
130.71025
130.66238
128.94196
128.88222
128.79140
128.73535
126.50707
101.34110
101.09307
99.31424
99.06325
62.65252
62.59890
53.72550
53.67356
41.90862
41.69735
38.19611
38.13097
22.87176
22.84315
16.21705
16.14729
Ar
O
F
H
OR
3h: Ar =2-ClPh
R = Me
f1 (ppm)

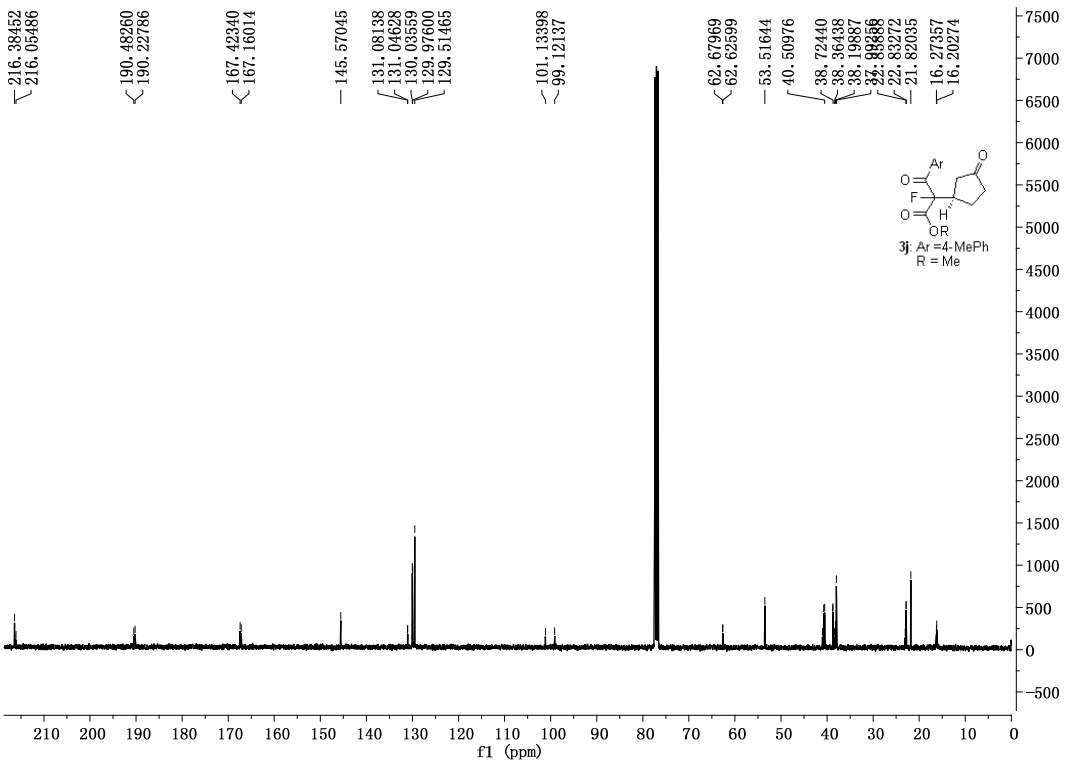

-176.08888
-176.40499
Ar
O
F
H
OR
3h: Ar =2-ClPh
R = Me
f1 (ppm)

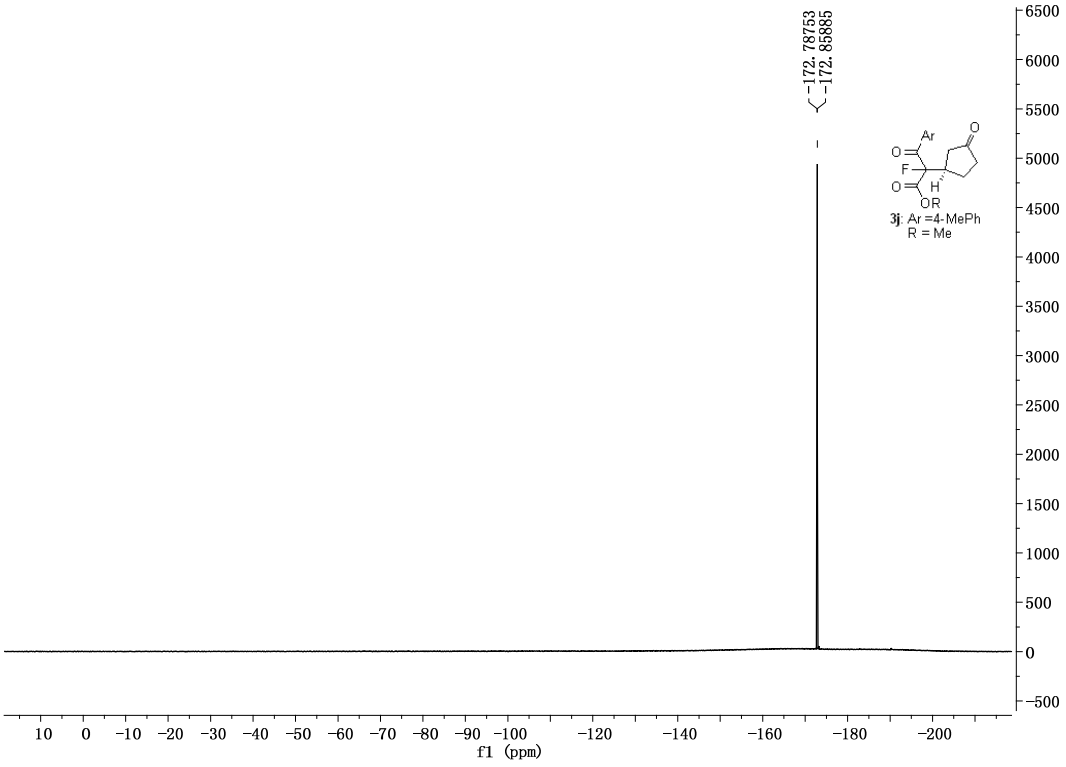

7.65206
7.44519
7.44034
7.43421
7.41326
7.40980
7.39102
7.37765
7.37345
7.36692
7.36013
7.35540
7.34827
7.34122
7.32490
3.92096
3.88435
3.56429
3.54334
3.52800
3.48941
3.45928
2.33474
2.29439
2.26940
2.23872
2.20783
2.16494
1.99445
1.96696
1.95510
1.94522
1.92990
1.92553
1.91827
1.90444
1.88051
1.86740
1.84020
2.53526
2.51552
2.48939
2.46996
2.44510
2.42932
2.40940
2.39163
2.36882
2.33474
2.30978
2.28654
2.26940
2.23872
2.22471
2.20783
2.19276
2.16494
5.13
f1 (ppm)
Ar
O
F
H
OR
3i: Ar =2-BrPh
R = Me
0.97
3.09
3.00
1.10
5.13
1.16
f1 (ppm)

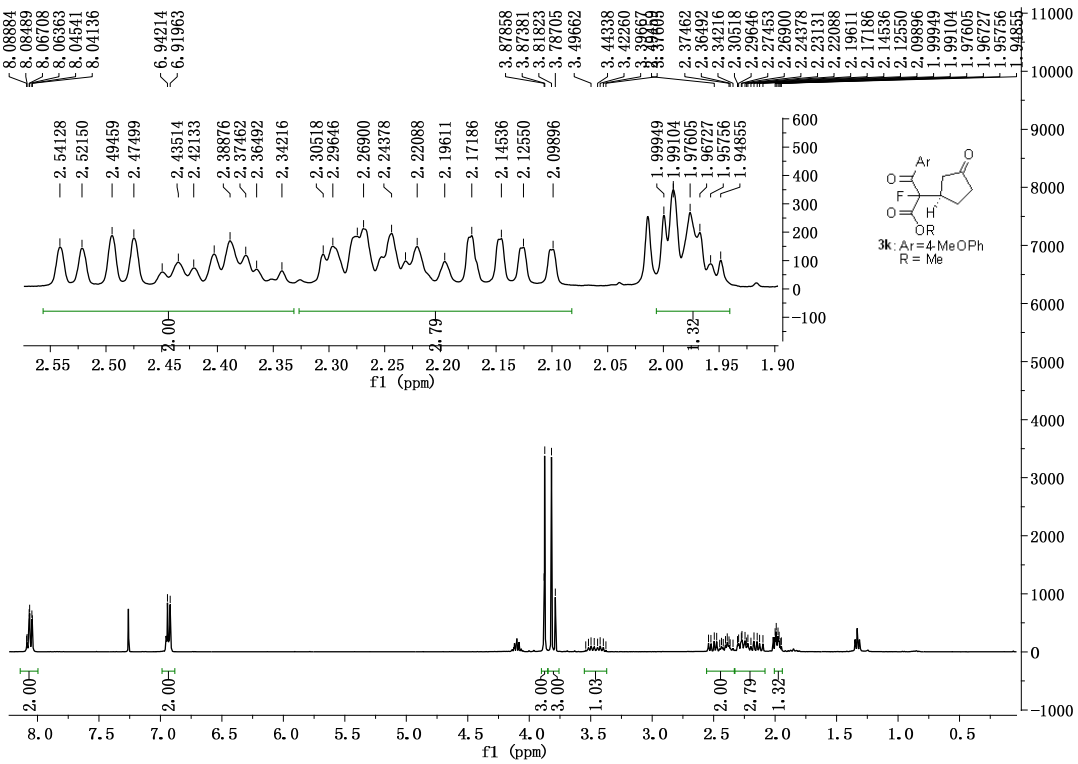

215.61681
215.39463
195.60650
195.44436
195.29725
195.13438
166.12290
166.00075
165.85696
165.73554
136.79863
136.78210
134.13090
134.07558
132.63394
132.59615
129.04927
128.98460
128.84570
128.78556
127.01082
101.00344
98.97320
53.82898
53.78459
42.09702
38.31952
38.25401
38.21772
37.88990
22.97314
Ar
O
F
H
OR
3i: Ar =2-BrPh
R = Me
f1 (ppm)

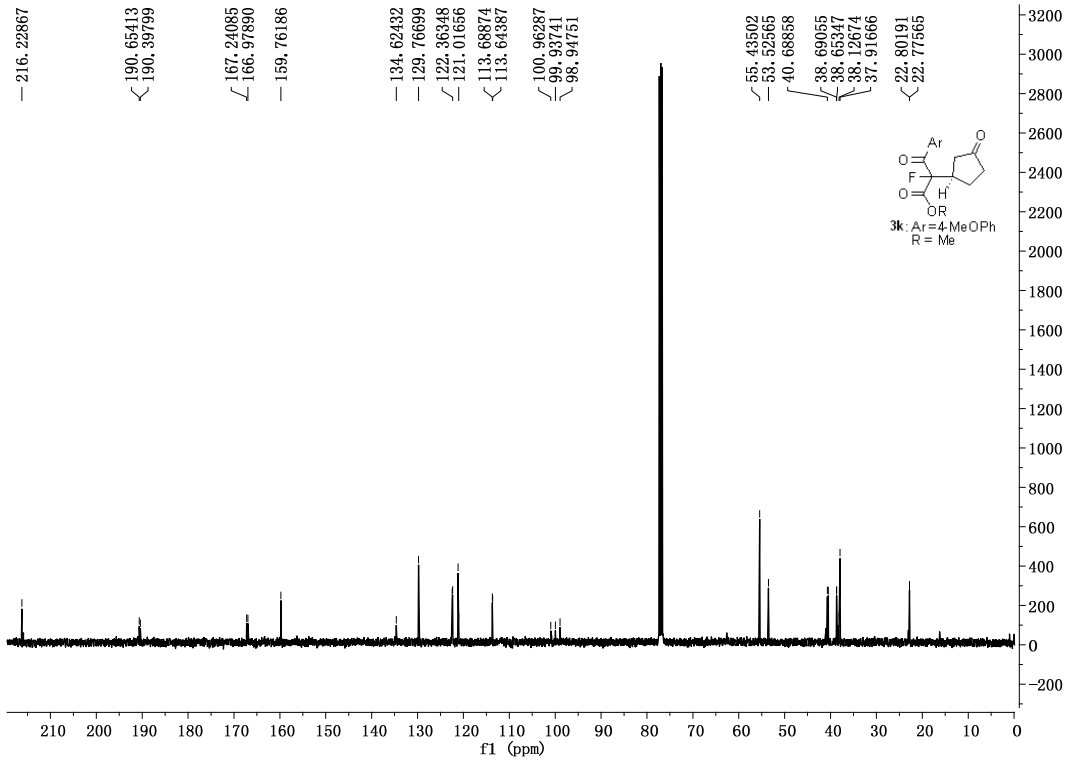

-175.56143
-175.90135
Ar
O
F
H
OR
3i: Ar =2-BrPh
R = Me
f1 (ppm)

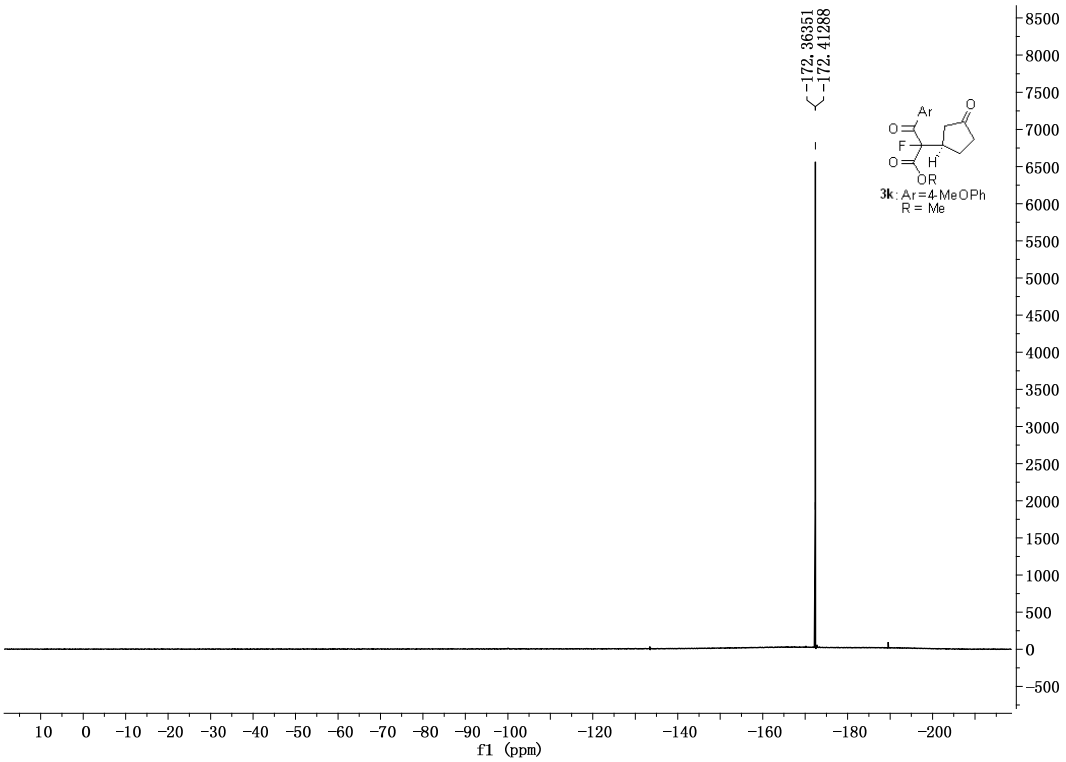

7.95407
7.93712
7.93335
7.28592
7.27617
7.26000
3.82520
3.79520
3.49286
2.53711
2.51747
2.49053
2.47096
2.45527
2.44066
2.41403
2.39509
2.36718
2.34681
2.33072
2.30848
2.29115
2.27193
2.24993
2.22740
2.20068
2.17488
2.14821
2.12849
2.10169
2.02347
2.00903
2.00079
1.98559
1.97685
1.96715
1.95811
7.60
1.62
1.98
1.09
3.00
1.08
7.61
1.62
3j: Ar =4-MePh
R = Me
f1 (ppm)

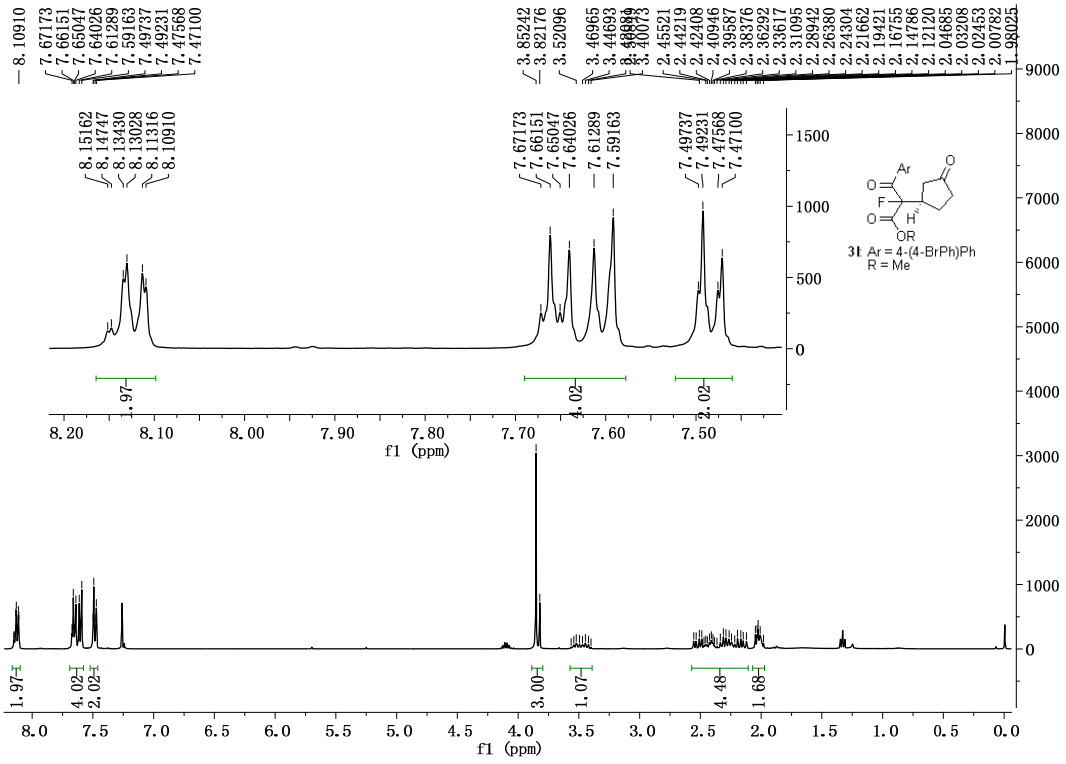

216.38452
216.05486
190.48260
190.22786
167.42340
167.16014
145.57045
131.08138
131.04628
130.03559
129.97600
129.51465
101.13398
99.12137
62.67969
62.62599
53.51644
40.50976
38.72440
38.36438
38.19887
22.83272
21.82035
16.27357
16.20274
Ar
O
F
H
OR
3j: Ar =4-MePh
R = Me
f1 (ppm)

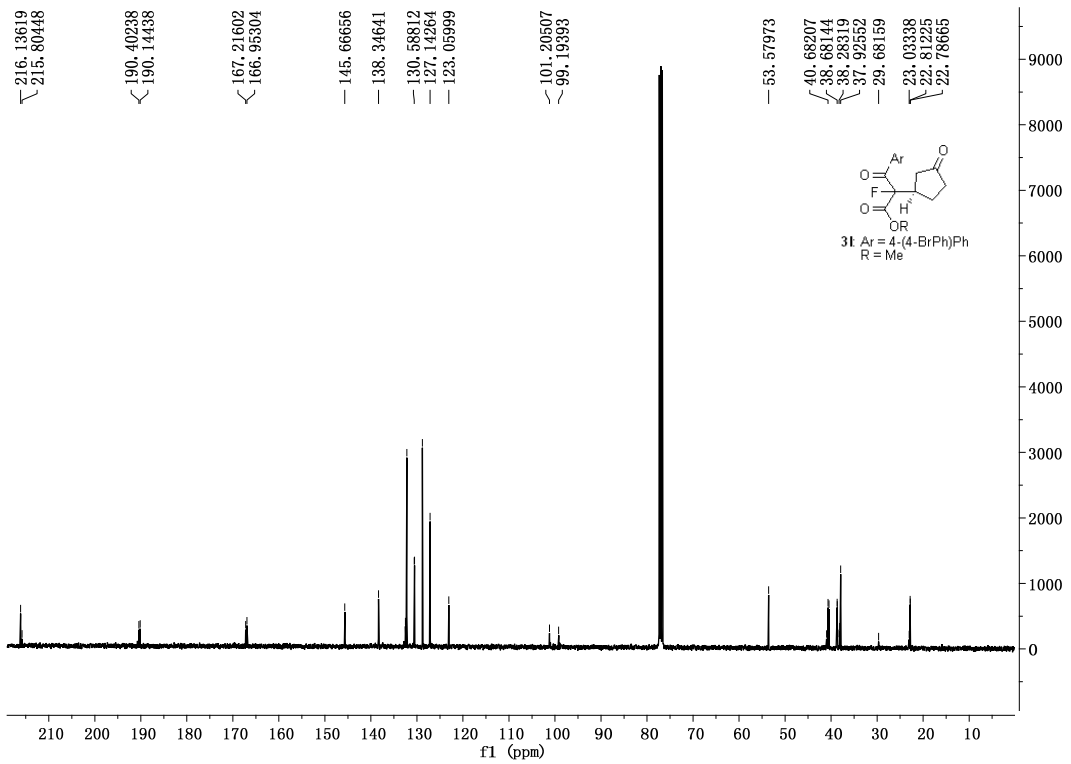

-172.78753
-172.85885
Ar
O
F
H
OR
3j: Ar =4-MePh
R = Me
f1 (ppm)

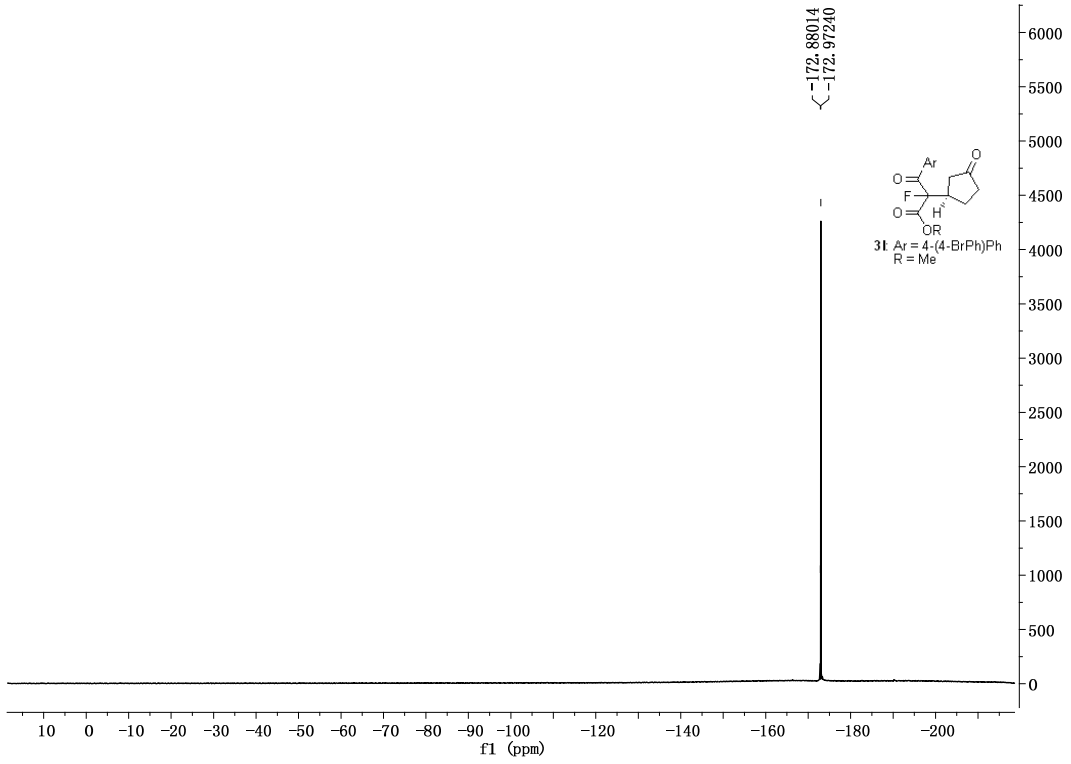

3k: Ar=4-MeOPh
R = Me
f1 (ppm)

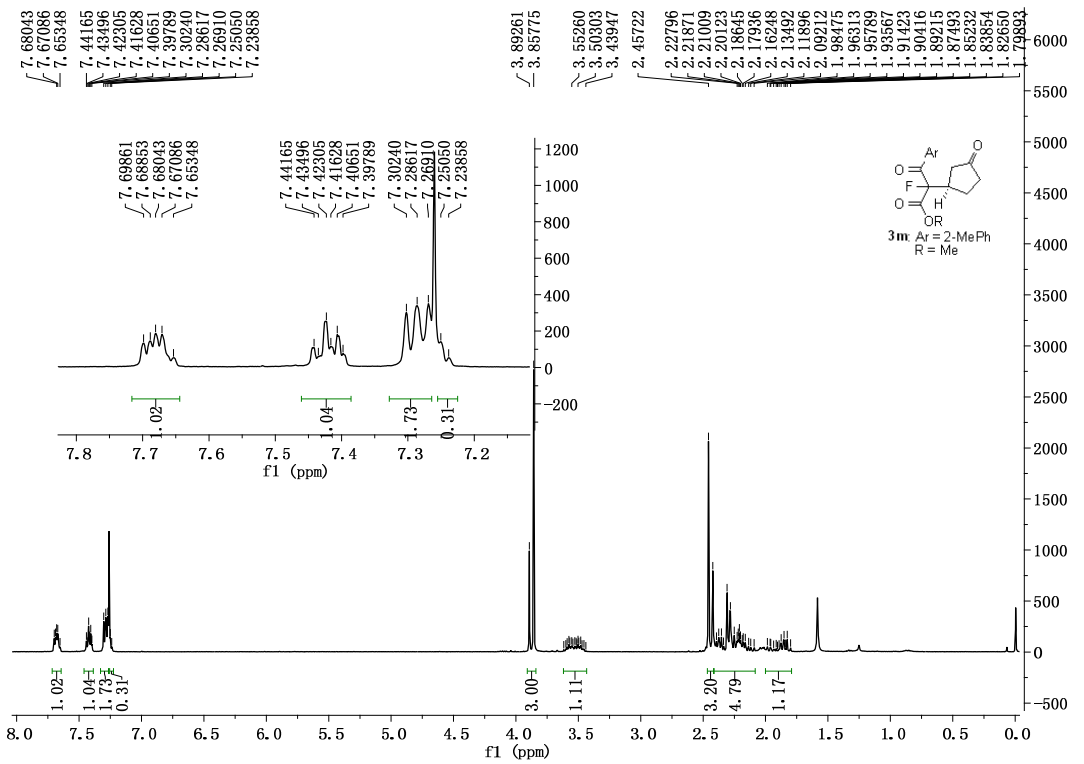

3k: Ar=4-MeOPh
R = Me
f1 (ppm)

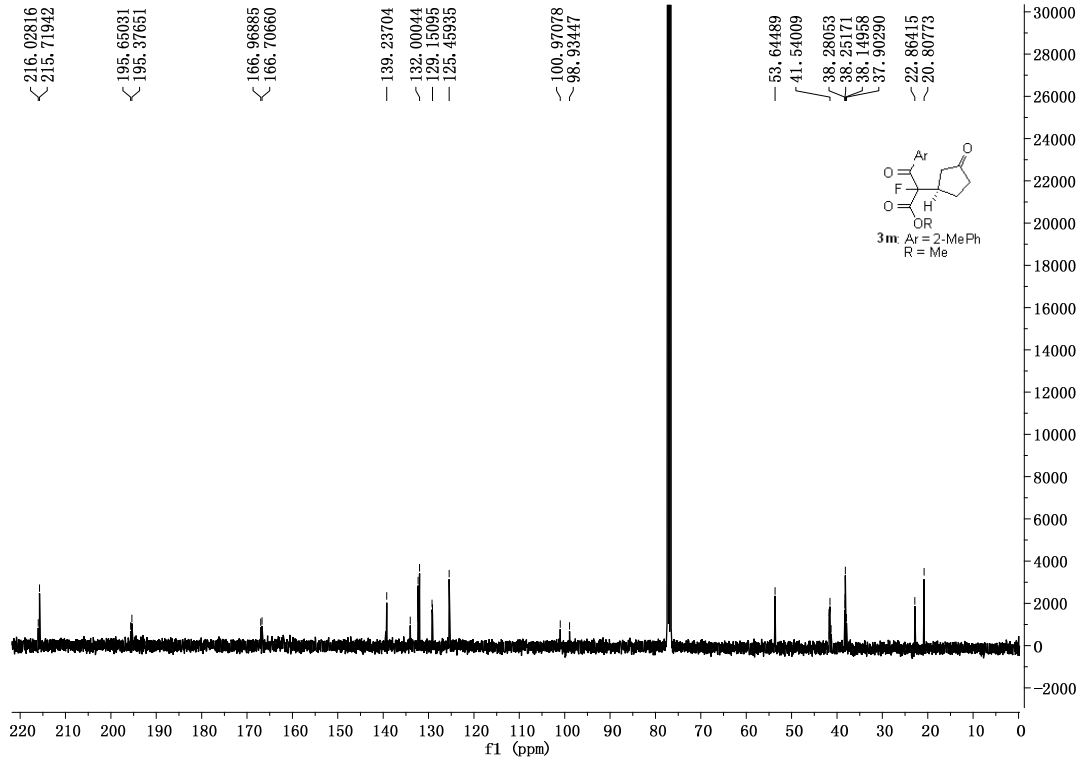

-172.36351
-172.41288
Ar
O
F
H
OR
3k: Ar=4-MeOPh
R = Me
f1 (ppm)

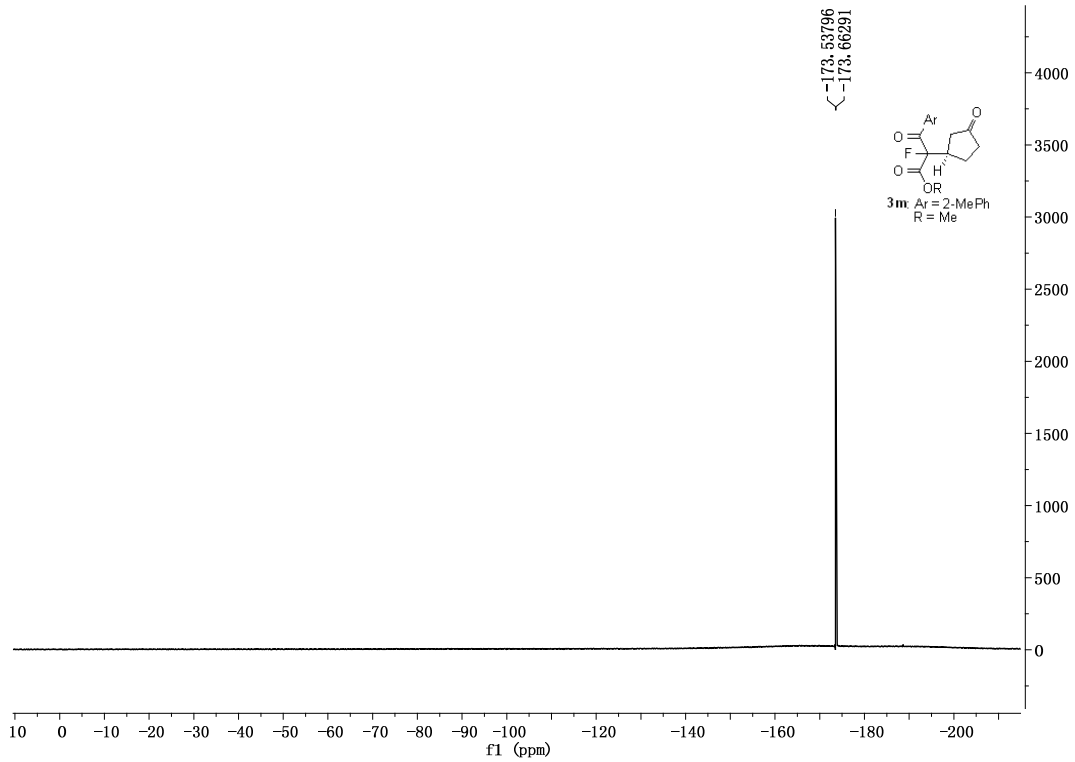

8.10910
7.67173
7.66151
7.65047
7.64026
7.61289
7.59163
7.49737
7.49231
7.47568
7.47100
3.85242
3.82176
3.52096
3.46965
3.44693
3.40073
2.45521
2.44219
2.42408
2.40946
2.39587
2.38376
2.36292
2.33617
2.31095
2.28942
2.26380
2.24304
2.21662
2.19421
2.16755
2.14786
2.12120
2.04685
2.03208
2.02453
2.00782
1.98025
8.15162
8.14747
8.13430
8.13028
8.11316
8.10910
7.67173
7.66151
7.65047
7.64026
7.61289
7.59163
7.49737
7.49231
7.47568
7.47100
1.97
4.02
2.02
3.00
1.07
4.48
1.68
31: Ar = 4-(4-BrPh)Ph
R = Me
f1 (ppm)

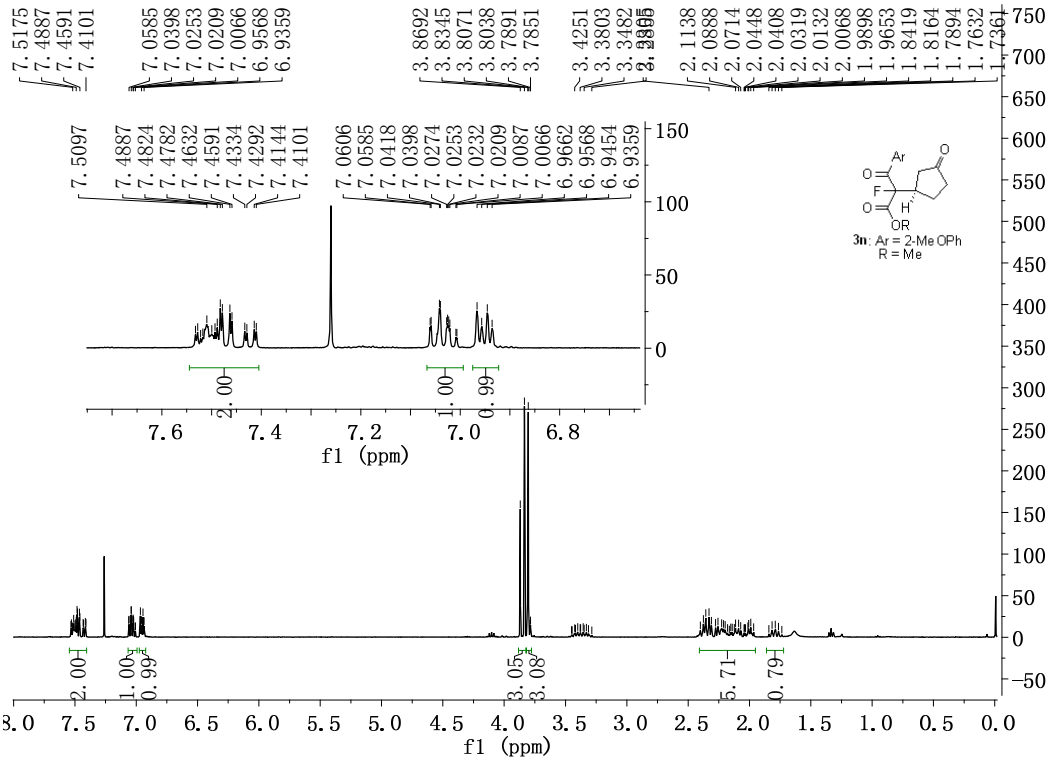

216.13619
215.80448
190.40238
190.14438
167.21602
166.95304
145.66656
138.34641
130.58812
127.14264
123.05999
101.20507
99.19393
53.57973
40.68207
38.68144
38.28319
37.92552
29.68159
23.03338
22.81225
22.78665
Ar
O
F
H
OR
3l Ar = 4-(4-BrPh)Ph
R = Me
f1 (ppm)

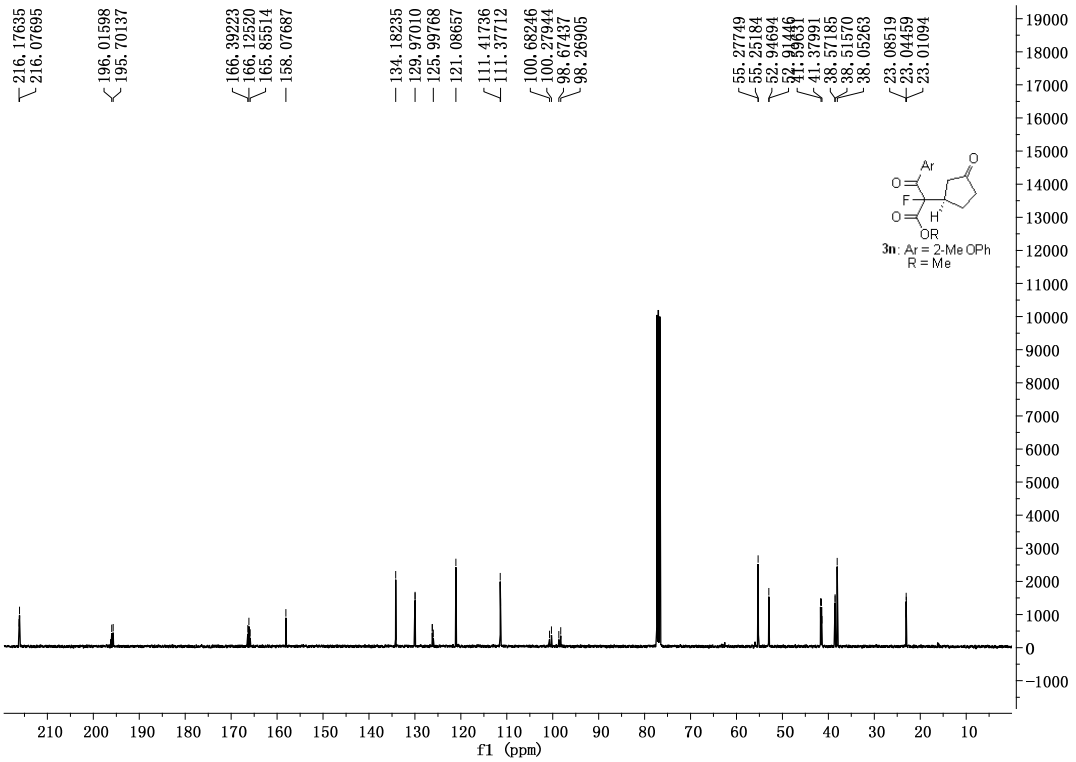

-172.88014
-172.97240
Ar
O
F
H
OR
3l Ar = 4-(4-BrPh)Ph
R = Me
f1 (ppm)

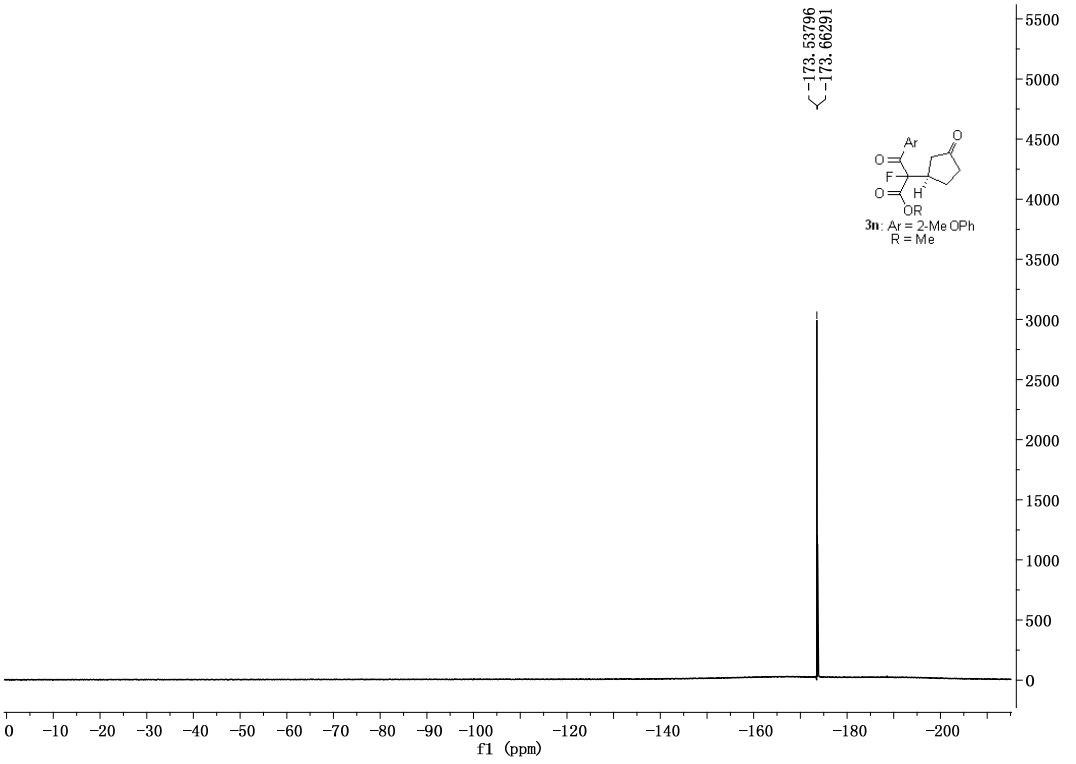

7.68043
7.67086
7.65348
7.44165
7.43496
7.42305
7.41628
7.40651
7.39789
7.30240
7.28617
7.26910
7.25050
7.23858
3.89261
3.85775
3.55260
3.50303
3.43947
2.45722
2.22796
2.21871
2.21009
2.20123
2.18645
2.17936
2.16248
2.13492
2.11896
2.09212
1.98475
1.96313
1.95789
1.93567
1.91423
1.90416
1.89215
1.87493
1.85232
1.83854
1.82650
1.79893
Ar
O
F
H
OR
3m: Ar = 2-MePh
R = Me
f1 (ppm)

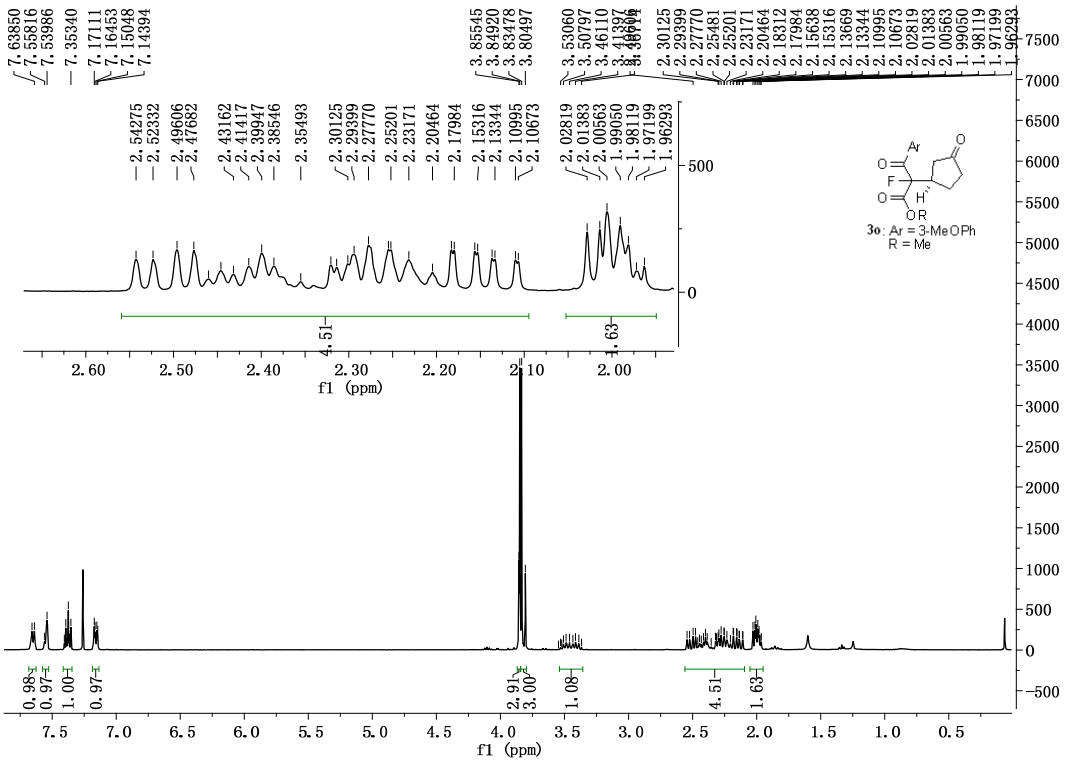

216.02816
215.71942
195.65031
195.37651
166.96885
166.70660
139.23704
132.00044
129.15095
125.45935
100.97078
98.93447
53.64489
41.54009
38.28053
38.25171
38.14958
37.90290
22.86415
20.80773
Ar
O
F
H
OR
3m: Ar = 2-MePh
R = Me
f1 (ppm)

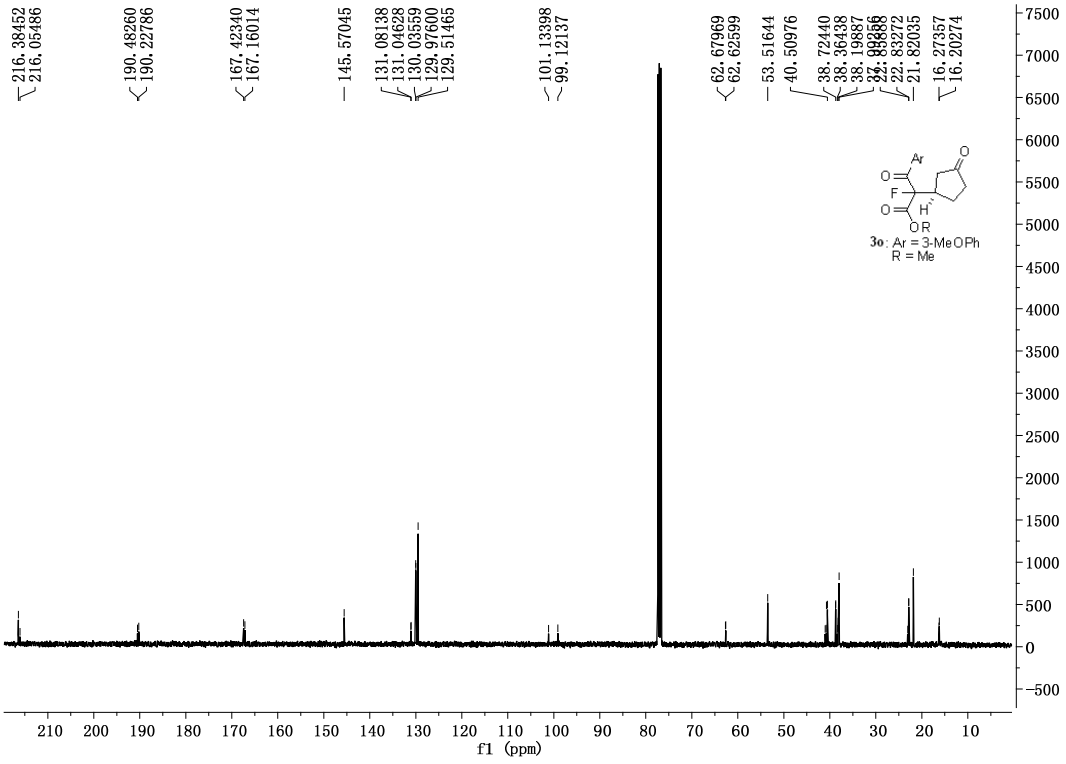

-173.53796
-173.66291
3m: Ar = 2-MePh
R = Me
f1 (ppm)

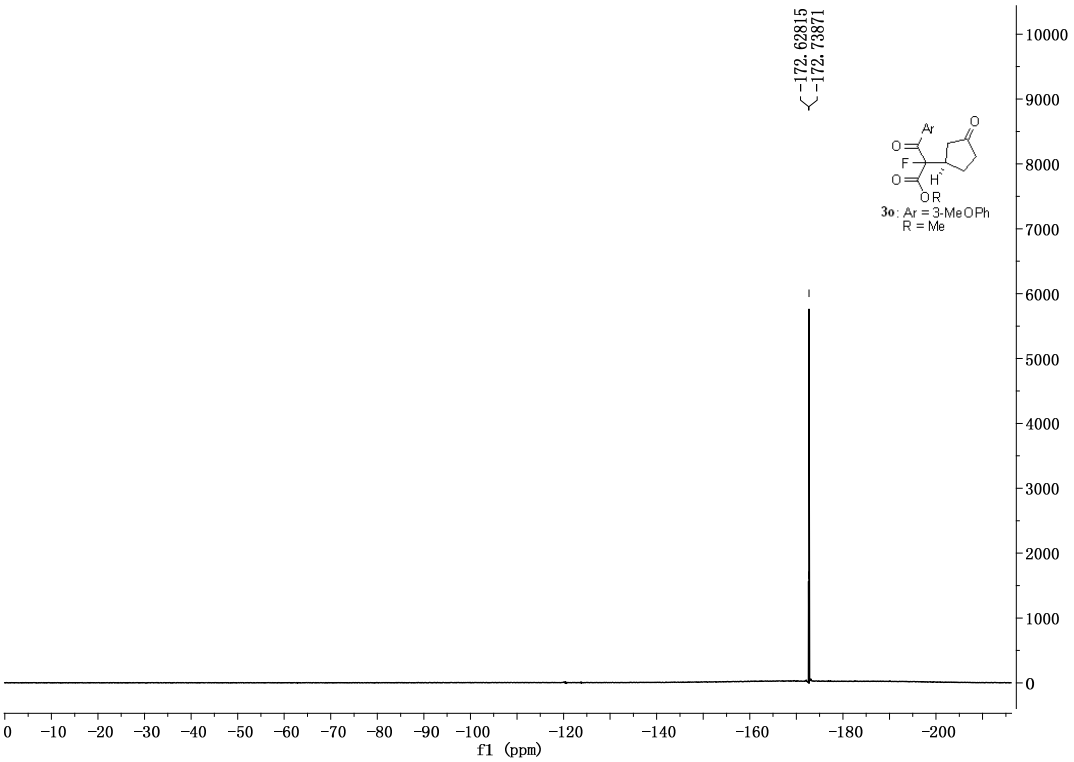

3m: Ar = 2-Me OPh
R = Me
f1 (ppm)

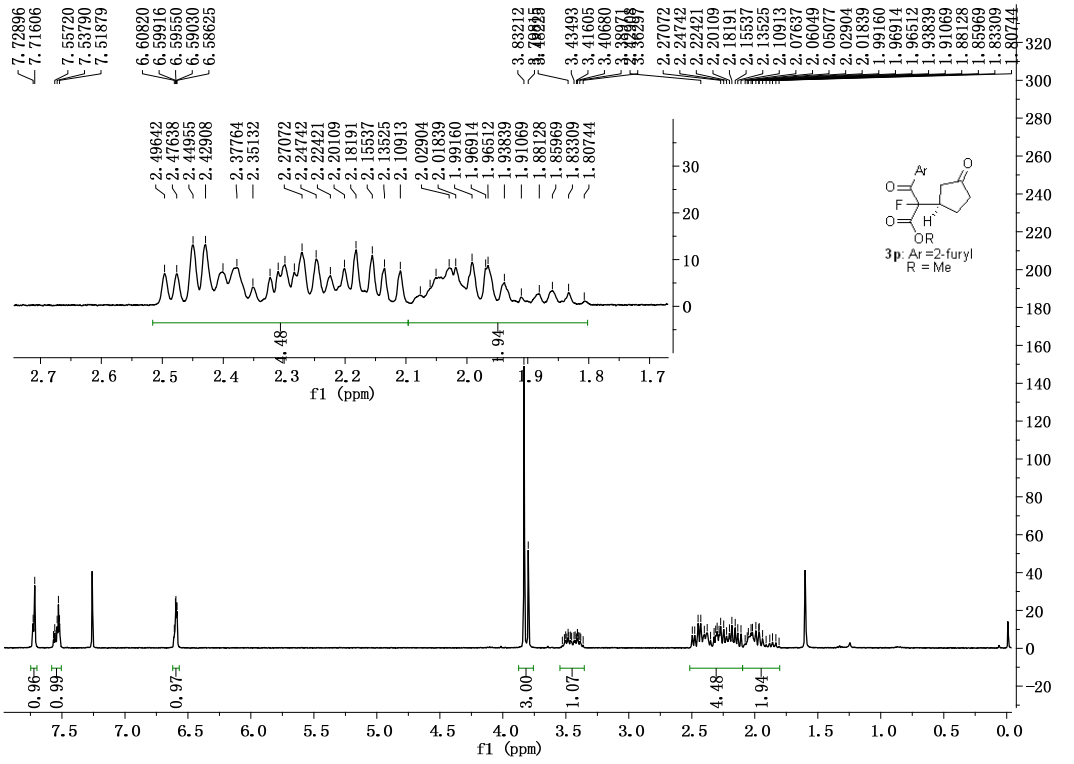

216.17635
216.07695
196.01598
195.70137
166.39223
166.12520
165.85514
158.07687
134.18235
129.97010
125.99768
121.08657
111.41736
111.37712
100.68246
100.27944
98.67437
98.26905
55.27749
55.25184
52.94694
41.37991
38.57185
38.51570
38.05263
23.08519
23.04459
23.01094
Ar
O
F
H
OR
3n: Ar = 2-MeOPh
R = Me
f1 (ppm)

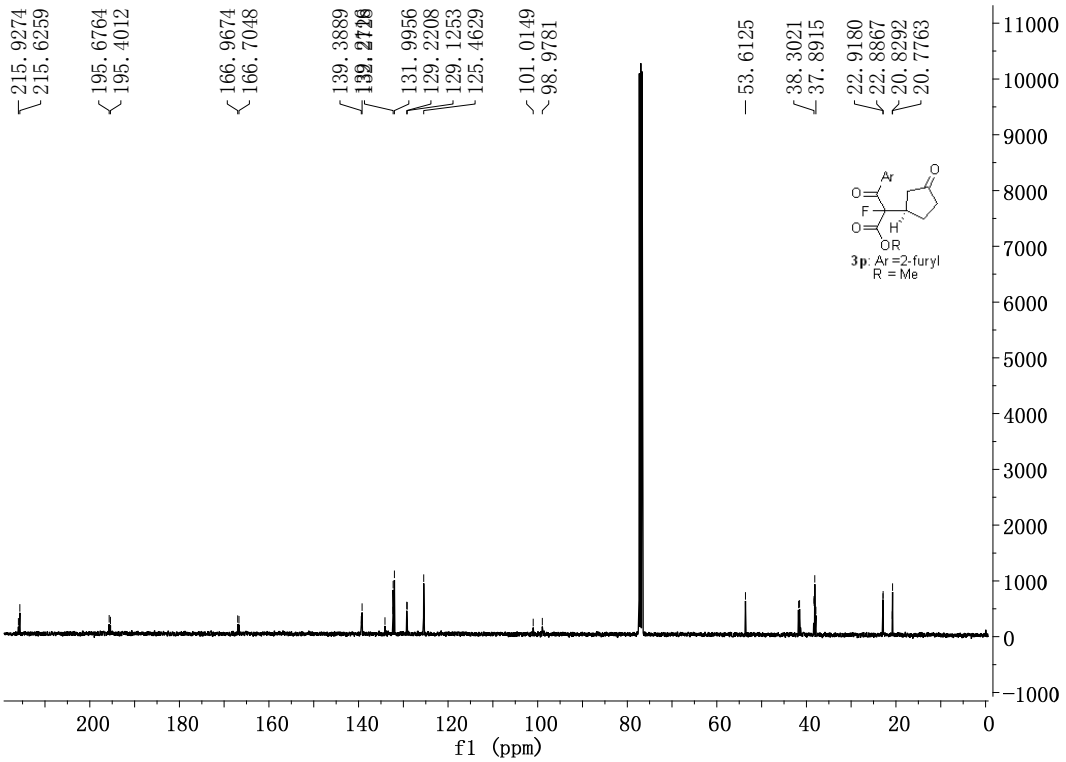

-173.53796
-173.66291
Ar
O
F
H
OR
3n: Ar = 2-MeOPh
R = Me
f1 (ppm)

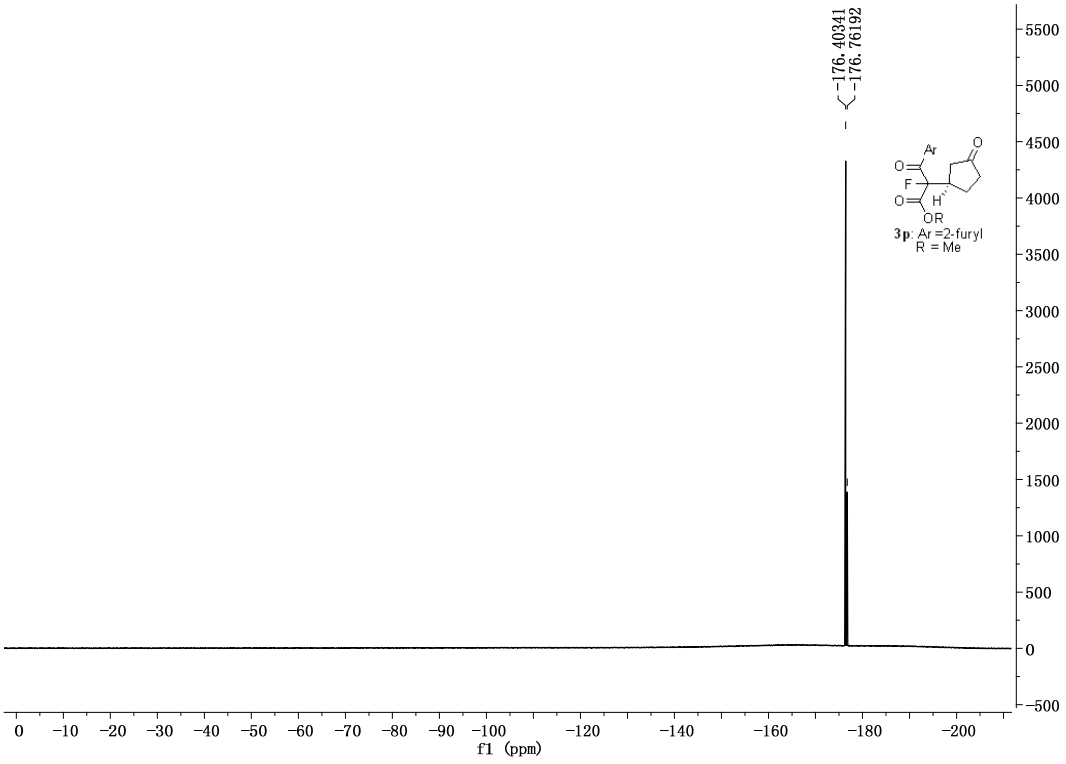

3o: Ar = 3-MeOPh
R = Me
f1 (ppm)

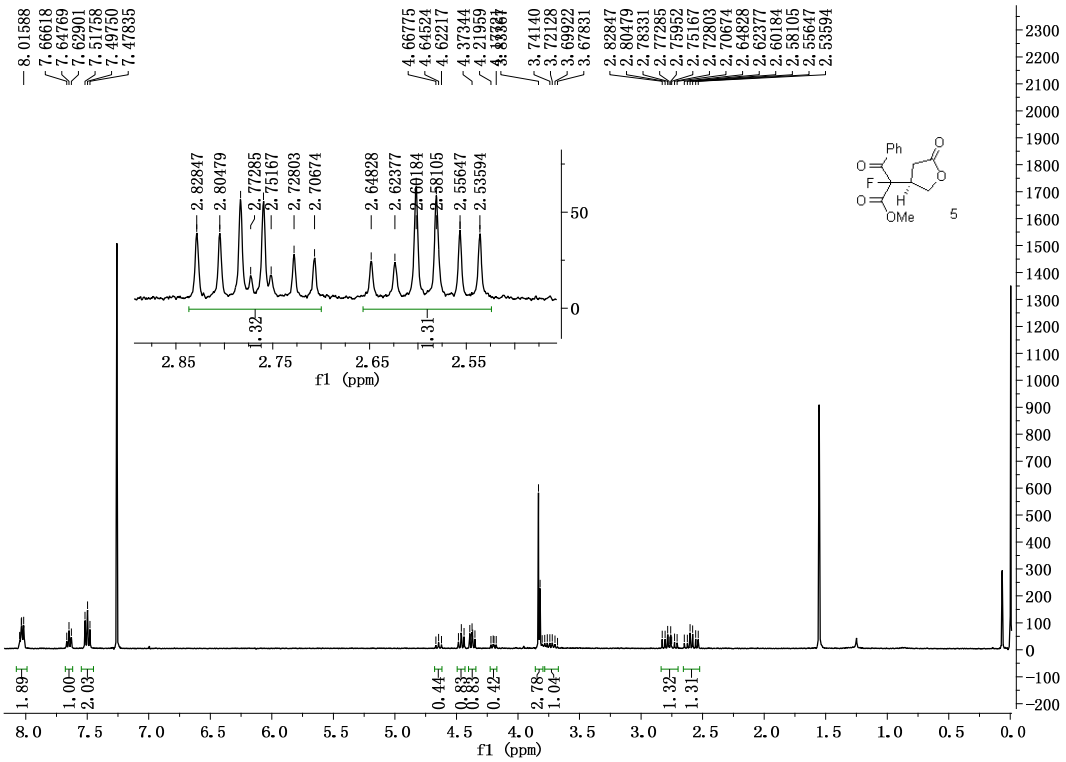

3o: Ar = 3-MeOPh
R = Me
f1 (ppm)

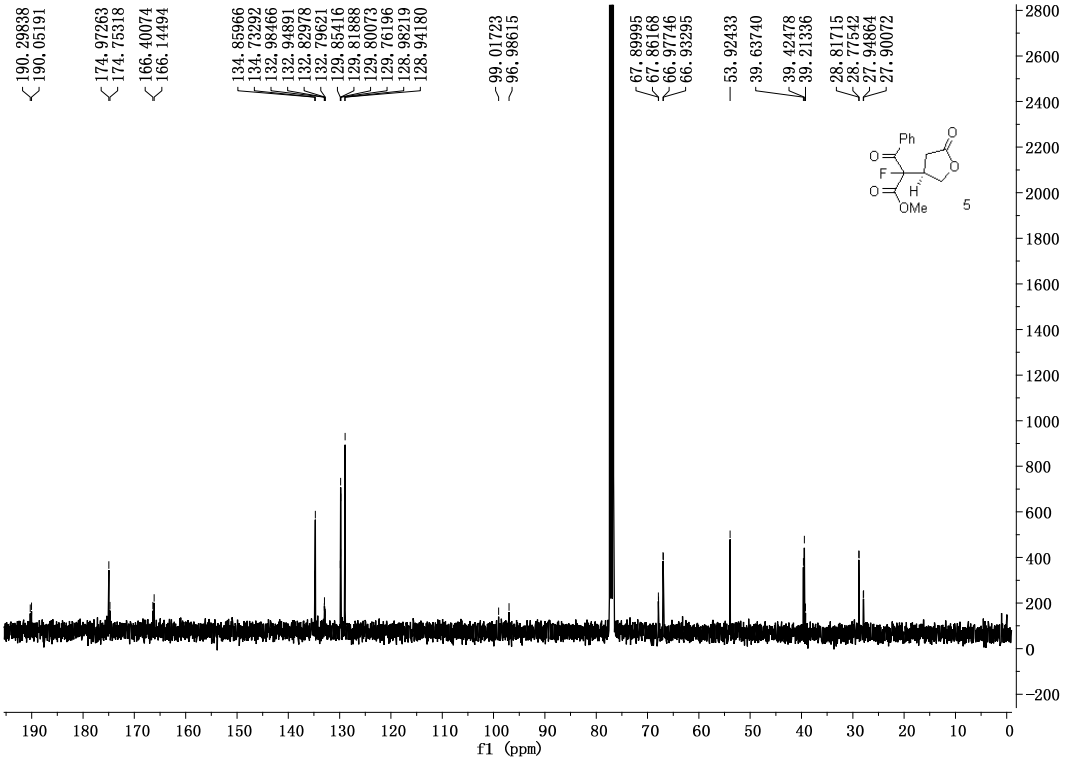

-172.62815
-172.73871
3o: Ar = 3-MeOPh
R = Me
f1 (ppm)

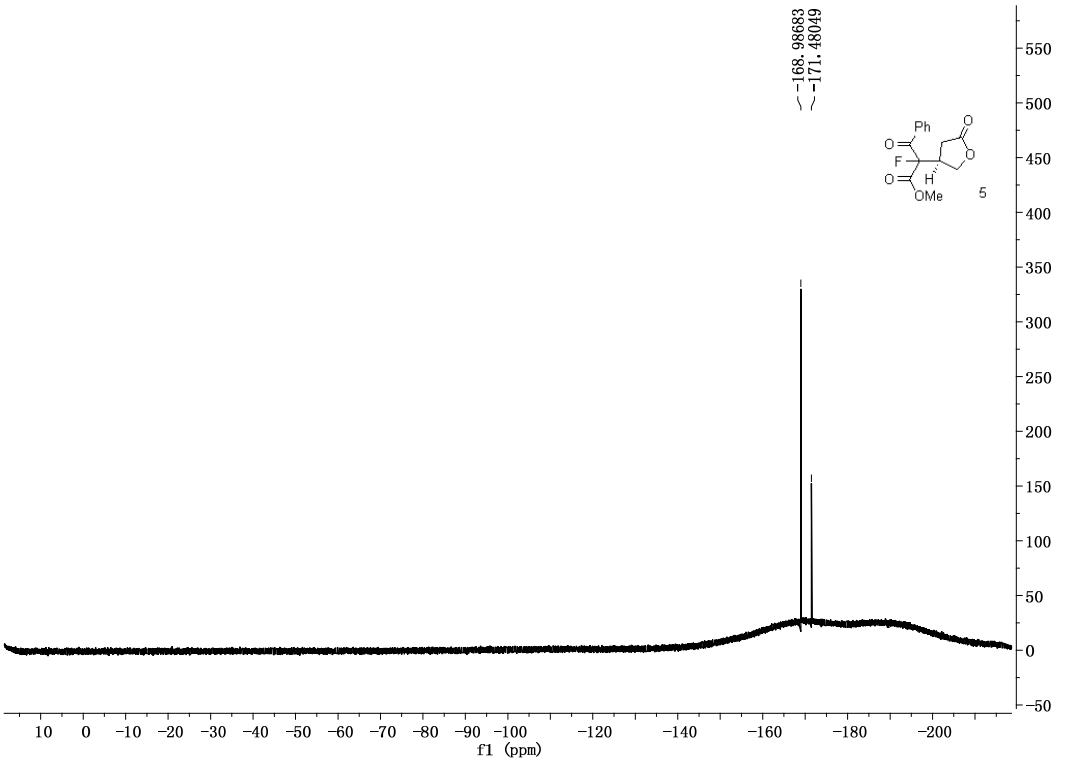

3p: Ar =2-furyl
R = Me
4.48
1.94
f1 (ppm)

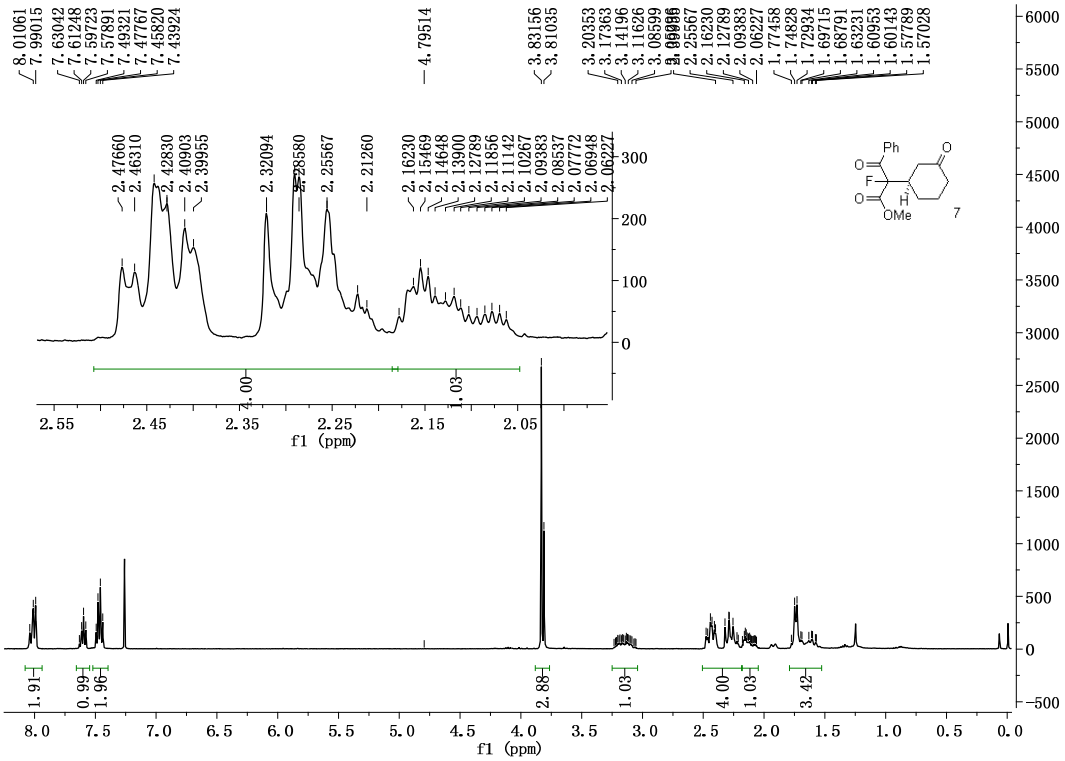

215.9274
215.6259
195.6764
195.4012
166.9674
166.7048
139.3889
131.9956
129.2208
129.1253
125.4629
101.0149
98.9781
53.6125
38.3021
37.8915
22.9180
22.8867
20.8292
20.7763
Ar
O
F
H
OR
3p: Ar =2-furyl
R = Me
f1 (ppm)

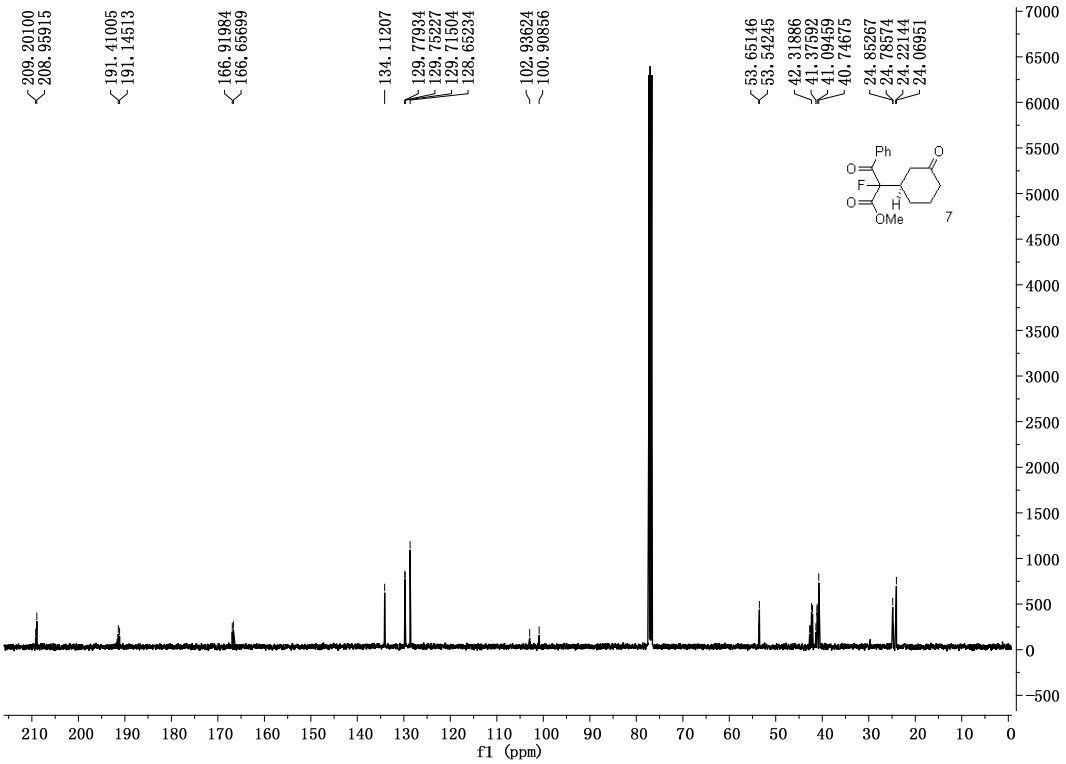

176.40341
176.76192
Ar
O
F
H
OR
3p: Ar =2-furyl
R = Me
f1 (ppm)

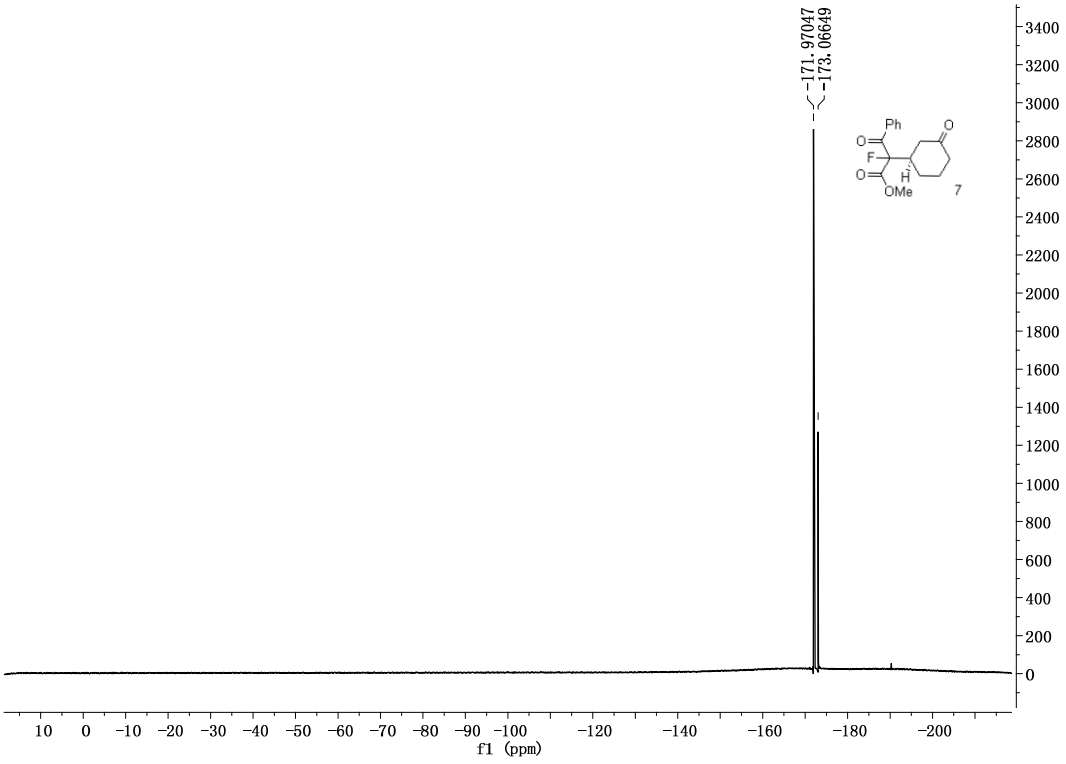

8.01588
7.66618
7.64769
7.62901
7.51758
7.49750
7.47835
4.66775
4.64524
4.62217
4.37344
4.21959
3.74140
3.72128
3.69922
3.67831
2.82847
2.80479
2.78331
2.77285
2.75952
2.75167
2.72803
2.70674
2.64828
2.62377
2.60184
2.58105
2.55647
2.53594
Ph
O
F
H
OMe
5
f1 (ppm)


190.29838
190.05191
174.97263
174.75318
166.40074
166.14494
134.85966
134.73292
132.98466
132.94891
132.82978
132.79621
129.85416
129.81888
129.80073
129.76196
128.98219
128.94180
99.01723
96.98615
67.89995
67.86168
66.97746
66.93295
53.92433
39.63740
39.42478
39.21336
28.81715
28.77542
27.94864
27.90072
Ph
O
F
H
OMe
5
f1 (ppm)


-168.98683
-171.48049
Ph
O
F
H
OMe
5
f1 (ppm)


8.01061
7.99015
7.63042
7.61248
7.59723
7.57891
7.49321
7.47767
7.45820
7.43924
4.79514
3.83156
3.81035
2.47660
2.46310
2.42830
2.40903
2.39955
2.32094
2.28580
2.25567
2.21260
2.16230
2.15469
2.14648
2.13900
2.12789
2.11856
2.11142
2.10267
2.09383
2.08537
2.07772
2.06948
2.06227
1.91
0.99
1.96
2.88
1.03
4.00
1.03
3.42
Ph
F
H
OMe
7
f1 (ppm)


209.20100
208.95915
191.41005
191.14513
166.91984
166.65699
134.11207
129.77934
129.75227
129.71504
128.65234
102.93624
100.90856
53.65146
53.54245
42.31886
41.37592
41.09459
40.74675
24.85267
24.78574
24.22144
24.06951
Ph
O
F
H
OMe
7
f1 (ppm)


-171.97047
-173.06649
Ph
O
F
H
OMe
7
f1 (ppm)