Supporting information

Photoinduced synthesis of functionalized spiro[2.3]hexane via additive-free

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General information

Unless otherwise noted, all commercially available compounds were used as provided without further purification. Solvents were dried and purified according to the procedure from "Purification of Laboratory Chemicals book". Column chromatography was performed using silica gel. Reactions were monitored by TLC and visualized by UV lamp (254 nm) and stained with ethanolic solution of concentrated potassium permanganate. Yields generally referred to chromatographically isolated yields, unless otherwise noted. ^{1}H NMR (400 MHz), ^{13}C NMR (101 MHz) and ^{19}F NMR (376 MHz) spectra are recorded on a Bruker AV-400 spectrometer in $CDCl_3$ with TMS as internal standard. For ^{1}H NMR (400 MHz), $CDCl_3$ (δ = 7.26 ppm) served as internal standard and data are reported as follows: chemical shift (in ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, brs = broad singlet), coupling constant (in Hz), and integration. GC-MS analysis was performed on 7890A-5975C/Agilent. HR-MS spectra were recorded on a Waters Xevo G2QTOF/UPLC mass spectrometer using TOF as the mass analyzer type. The photoreaction instrument (WPP-TEC-1020SL) was purchased from WATTCAS, China.

SPECTROPHOTOCOLORMETER ANALYSIS REPORT

Color Parameters:

CIE(1931:) x =0.1776 y =0.0296

CIE(1960:) u =0.2367 v =0.0592

CIE (1976:) u' =0.2367 v' =0.0888

Color Temperature： Tc=25000K Dominant Wave: WL.D=435.20nm Purity: PUR=93.54

Peak Wave: WL.P=392.5nm Delta Wave: WL.H=18.0nm

Color Tolerance: SDCM=186.7 Ra:Ra=15.0

CRI1=56.1 CRI2=16.3 CRI3=0.0 CRI4=0.0 CRI5=47.6

CRI6=0.0 CRI7=0.0 CRI8=0.0 CRI9=0.0 CRI10=0.0

CRI11=0.0 CRI12=0.0 CRI13=42.0 CRI14=6.3 CRI15=66.7

Photology Parameters:

Lum Flux: Φ(lm)=4.75lm Optical Power: Φe(mW)=2769.6mW η(lm/W)=0.4lm/W

Eletric Parameters:

Forward Voltage: VF = 22.68 V Forward Current: IF = 498.9 mA Power = 11.32 W

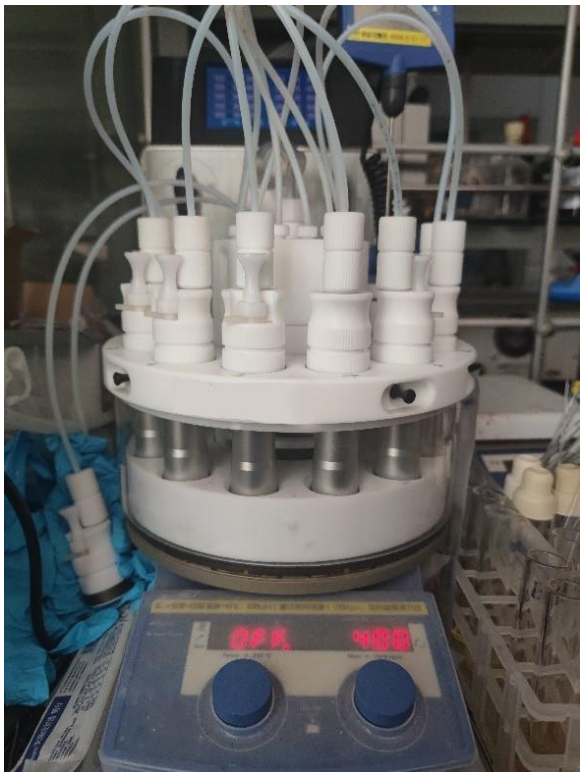


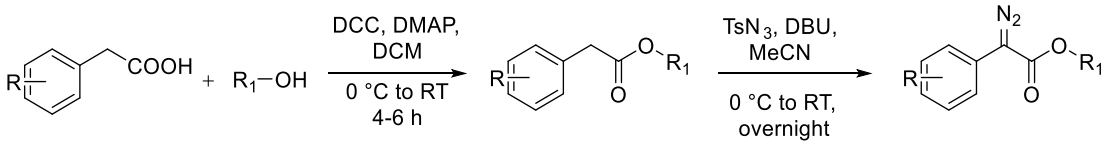
Figure S1. Photoreactor for photoreaction

Important Safety Note

Handling of diazo compounds should only be done in a well-ventilated fume cupboard using an additional blast shield. No incidents occurred handling of diazoalkanes during the preparation of this manuscript, yet the reader should be aware of carcinogenicity and explosiveness of the herein described diazo compounds. General safety precautions when working with diazomethane and its derivatives should be followed. Any reactions described in this manuscript should not be performed without strict risk assessment and proper safety precautions.

Synthesis of starting materials

Synthesis of diazoacetates 1a-1t[1]



Step-I: To a stirred, ice cooled solution of the phenylacetic acid derivatives (10 mmol, 1 equiv.), and alcohol (12 mmol, 1.2 equiv.) in 200 mL DCM was added a solution of DCC (13 mmol, 1.3 equiv.) and DMAP (1 mmol, 0.1 equiv.) in 100 mL DCM at once. The solution was stirred 4-6 h while

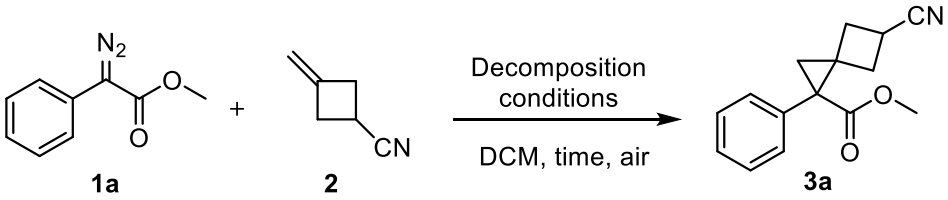
slowly warming up to room temperature. After finishing the reaction, the solid was filtered off and washed with Et_2O. The solvent was evaporated, and the residue was purified by silica gel column chromatography (pentane : ethyl acetate = 20:1) provided the desired ester.

Step-II: To a stirred, ice cooled solution of the ester (5 mmol, 1 equiv.) and p-Tosyl azide (5.5 mmol, 1.1 equiv.) in 100 mL MeCN were added DBU (7 mmol, 1.4 equiv.) dropwise. The solution was stirred over night while slowly warming up to room temperature. DCM was added, and the organic layer was washed two times with sat. aq. NH_4Cl solution. The organic layer was dried over $MgSO_4$ and the solvent was removed in vacuum. The crude product was purified by silica gel column chromatography using (pentane : ethyl acetate = 10:1) provided the desired diazo compound as a orange oil.

The starting material 3-methylenecyclobutanecarbonitrile 2a was purchased from Shanghai Aladdin Bio-Chem Technology Co., China.

Reaction Optimization

Table S1. Initial attempts on the photochemical cycloaddition reaction



Entry	Decomposition conditions	Time(h)	Yield (%)
1	dark	8	0
2[c]	50 °C	8	11
3	1W 465 nm blue LEDs	8	30
4	1W 465 nm blue LEDs	4	33
5	1W 465 nm blue LEDs	2	35
6	1W 465 nm blue LEDs	1	35

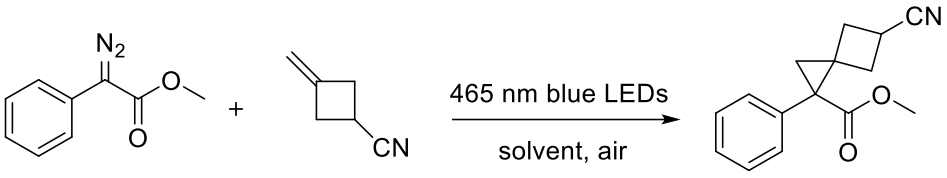
[a] Reaction conditions: **1a** (0.10 mmol, 1.0 equiv.), **2** (0.15 mmol, 1.5 equiv.), DCM (1.0 mL), under air.

Table S2. Initial evaluations on the photochemical cycloaddition reaction conditions[a]

Entry	Additive	Yield[b] (%)
1	KH_2PO_4	27
2	NH_4Cl	32
3	$Cu(OTf)_2$	15
4	K_2HPO_4	31
5	$NaHCO_3$	29

[a] Reaction conditions: **1a** (0.10 mmol, 1.0 equiv.), **2** (0.15 mmol, 1.5 equiv.), DCM (1.0 mL), additive (0.2 mmol, 0.2 equiv.) 1 W 465 nm blue LEDs, 1 h, under air. [b] Isolated yield after column chromatography.

Table S3. Optimization of reaction solvents[a]

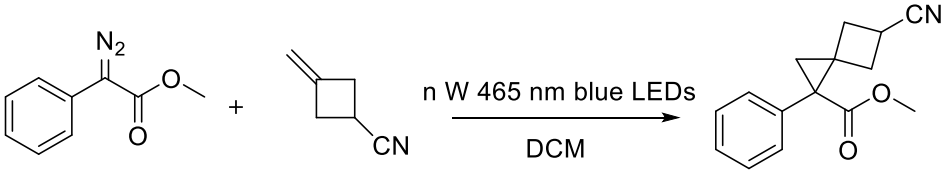


1a **2** **3a**

Entry	Solvent	Yield [b] (%)
1	DCM	35
2	DCE	29
3	EA	15
4	MeCN	13
5	ACE	<5
6	THF	N.D.
7	1,4-Dioxane	N.D.
8	DMSO	N.D.
9	DMF	N.D.

[a] Reaction conditions: **1a** (0.10 mmol, 1.0 equiv.), **2** (0.15 mmol, 1.5 equiv.), solvent (1.0 mL), 1 W 465 nm blue LEDs, 1 h, under air. [b] Isolated yield after column chromatography. N.D.: no detected.

Table S4. Screening of reaction light intensity and atmospheres [a]



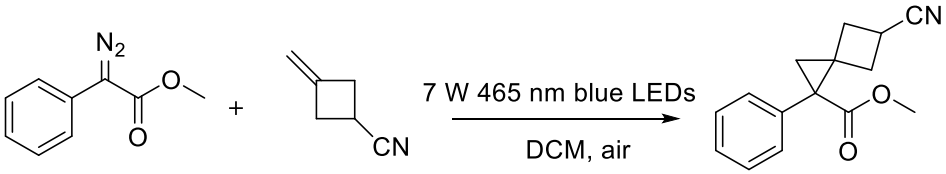
1a **2** **3a**

Entry	Light intensity	Atmosphere	Yield [b] (%)
1	1 W 465 nm blue LEDs	air	35
2	2 W 465 nm blue LEDs	air	40
3	3 W 465 nm blue LEDs	air	48
4	4 W 465 nm blue LEDs	air	54

5	5 W 465nm blue LEDs	air	65
6	6 W 465 nm blue LEDs	air	68
7	7 W 465 nm blue LEDs	air	76
8	8 W 465 nm blue LEDs	air	66
9	9 W 465 nm blue LEDs	air	62
10	10 W 465 nm blue LEDs	air	55
11	7 W 465 nm blue LEDs	N_2	76

[a] Reaction conditions: **1a** (0.10 mmol, 1.0 equiv.), **2** (0.15 mmol, 1.5 equiv.), DCM (1.0 mL), 1 h. [b] Isolated yield after column chromatography.

Table S5 Screening of reaction substrates radio [a]



1a **2** **3a**

Entry	**2**	Yield [b] (%)
1	1.0 equiv.	63
2	1.5 equiv.	77
3	3.0 equiv.	88
4	4.0 equiv.	93
5	5.0 equiv.	92

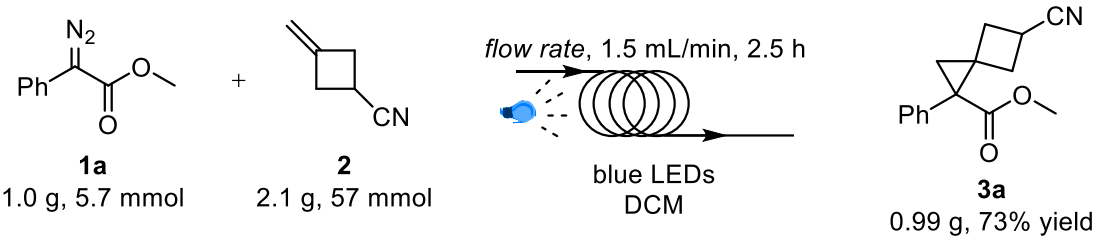
[a] Reaction conditions: **3-a1**(1.0 equiv.), **2**, DCM (1.0 mL), 7 W 465 nm blue LEDs, 1 h, under air. [b] Isolated yield after column chromatography.

General procedure for the multicomponent synthesis of spiro[2.3]hexane

1a **2** **3a**

An oven dried 50 mL reaction vial was charged with a stir bar. Substrate **1a** (0.1 mmol, 1 eq), **2a** (1 mmol, 4 eq) was added with 1 mL DCM. The reaction mixture was stirred and irradiated with 7 W blue LEDs lamp (WATTCAS： WPTEC-1020SL) for 1 hours until the reaction was completed(monitored by TLC). After reaction, the solvent was removed by rotary evaporation. Purified by flash column chromatography on silica gel(petroleum ether: ethyl acetate = 10:1) afforded spiro[2.3]hexane as a colorless oil. R_f = 0.2

General procedure for the gram-scale flow reaction



An oven dried 250 mL erlenmeyer flask was charged with a stir bar. Substrate **1a** (1.0 g, 5.7 mmol, 1 eq), **2a** (2.1 g, 57 mmol, 4 eq) was added with 100 mL DCM. The reaction mixture was stirred and irradiated with commercially available blue light bulbs and flow pump for 2.5 hours. After reaction, the solvent was removed by rotary evaporation. Purified by flash column chromatography on silica gel(petroleum ether: ethyl acetate = 10:1) afforded spiro[2.3]hexane(0.99g, 73% yield) as a colorless oil. R_f= 0.2

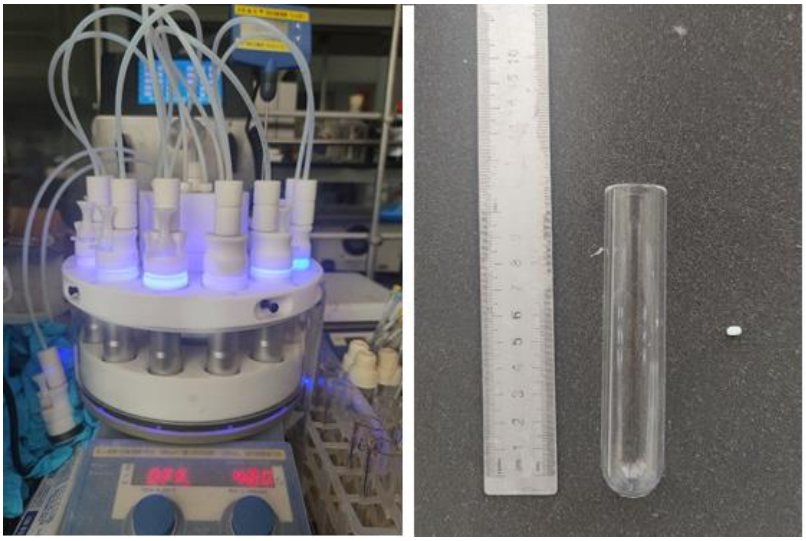


Figure S2. Reaction setup for general photoreactions

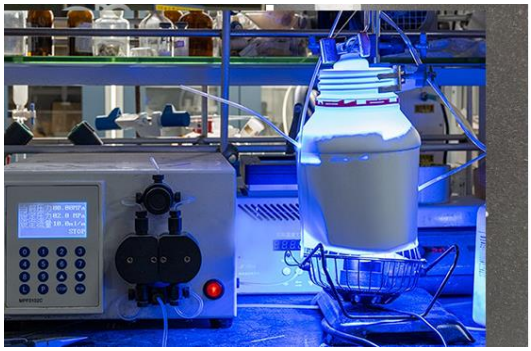


Figure S3. Flow reactor of photoreactions

UV-vis absorbance spectra of diazoacetates 1

Before the quenching experiments, the emission spectrum of methyl 2-diazo-2-phenylacetate (0.002 mM in DCM, 1 mL) was measured after added 2 mL DCM to serve as the background experiment, in which the emission maximum λ_{max} was determined at 432 nm (Figure S4).

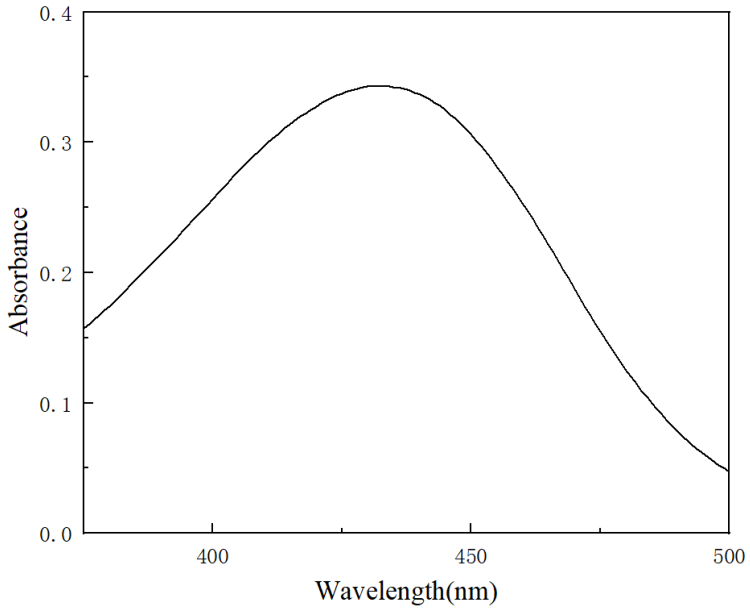


Figure S4. Emission spectrum of methyl 2-diazo-2-phenylacetate. Concentration = 6.67×10^{-4}mM (0.002/3 mM)

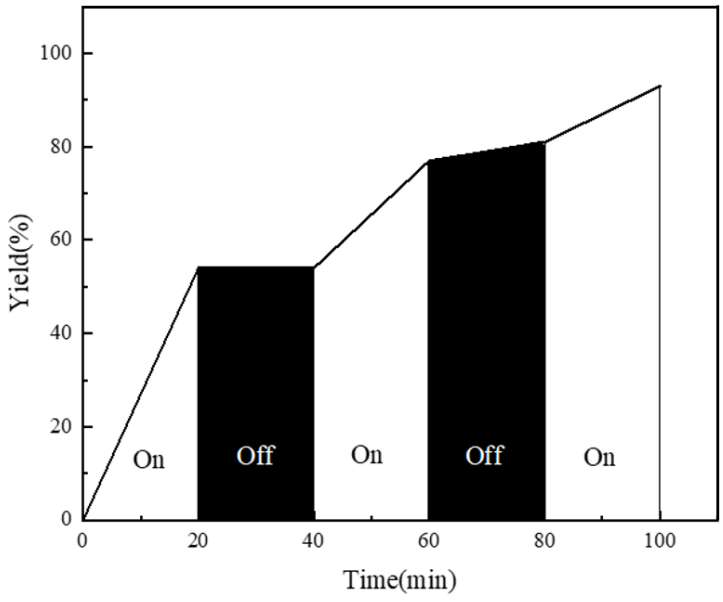
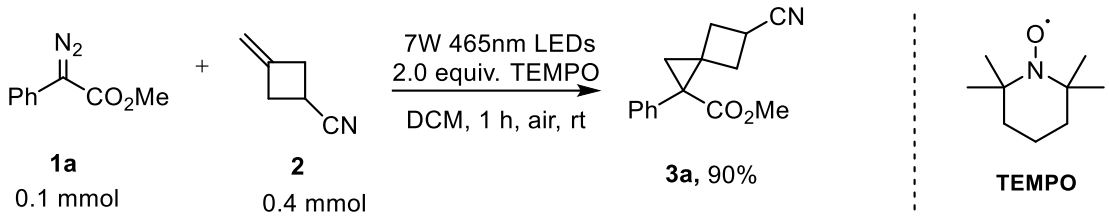
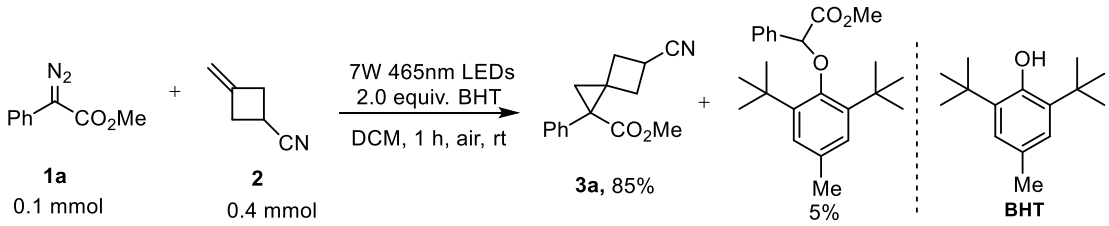


Figure S5. On/off light irradiation experiments

Control experiments



An oven dried 50 mL reaction vial was charged with a stir bar. Substrate **1a** (0.1 mmol, 1 eq), **2a** (1 mmol, 4 eq) , TEMPO (0.5 mmol, 2 eq) was added with 1 mL dcm. The reaction mixture was stirred and irradiated with 7 W blue LEDs lamp (WATTCAS: WPTEC-1020SL) for 1 hours until the reaction was completed(monitored by TLC). After reaction, the solvent was removed by rotary evaporation. Purified by flash column chromatography on silica gel (petroleum ether: ethyl acetate = 10:1) afforded vinyloxetane(90% yield) as a colorless oil.



An oven dried 50 mL reaction vial was charged with a stir bar. Substrate **1a** (0.1 mmol, 1 eq), **2a** (1 mmol, 4 eq) , BHT (0.5 mmol, 2 eq) was added with 1 mL DCM. The reaction mixture was stirred and irradiated with 7 W blue LEDs lamp (WATTCAS: WPTEC-1020SL) for 1 hours until the reaction was completed(monitored by TLC). After reaction, the solvent was removed by rotary evaporation. Purified by flash column chromatography on silica gel (petroleum ether: ethyl acetate = 10:1) afforded vinyloxetane (85% yield) as a colorless oil.

On/off light irradiation experiments

An oven dried 50 mL reaction vial was charged with a stir bar. Substrate **1a** (0.1 mmol, 1 eq), **2a** (1 mmol, 4 eq) was added with 1 mL DCM. The reaction mixture was stirred and irradiated with 7 W blue LEDs lamp (WATTCAS: WPTEC-1020SL) for 1 hours until the reaction was completed(monitored by TLC). After reaction, the solvent was removed by rotary evaporation. Purified by flash column chromatography on silica gel(petroleum ether: ethyl acetate = 10:1) afforded spiro[2.3]hexane as a colorless oil. R_f = 0.2

DFT Calculations

The calculations were performed using DFT implemented in the Dmol^3 package. The exchange correlation effects were accounted for by using the GGA-PBE function employed for the exchanged-correlation functional together with the double-numerical quality basis set with polarisation functions (DNP with 3.5 basis file) [1,2]. A global orbital cut off of 3.7 Å was adopted to improve the computational performance. Grimme's semi-empirical DFT-D scheme for dispersion

correction was adopted to describe the van der Waals interactions. The tolerances of the energy, gradient, and displacement convergence were 10^{-5} hartree (1 hartree = 27.2114 eV), 0.002 hartree per Å, and 0.005 Å, respectively. The SCF tolerance was set as 10^{-6}. To better simulate the reaction in real solvent solutions, a conductor-like screening model (COSMO) with a dielectric constant of 4.806 was adopted for all systems[3].

[1] B. Delley, J. Chem. Phys. 92, 508 (1990).
[2] B. Delley, J. Chem. Phys. 113, 7756 (2000).
[3] A. Klamt, G. Schuurmann, COSMO: a new approach to dielectric screening in solvents with explicit expressions for the screening energy and its gradient, J Chem Soc Pakistan 2 (1993) 799.

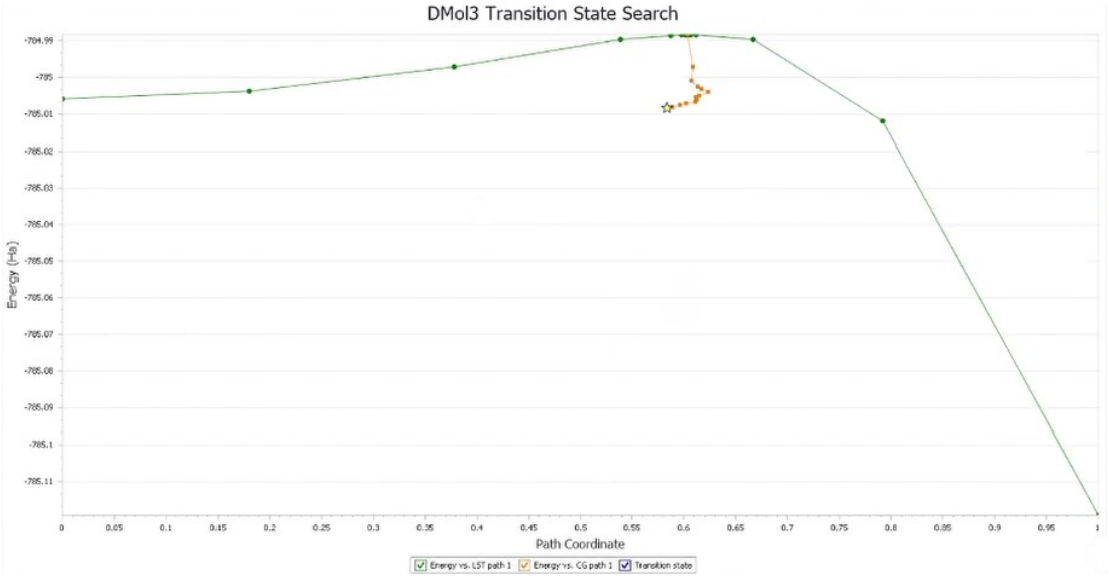


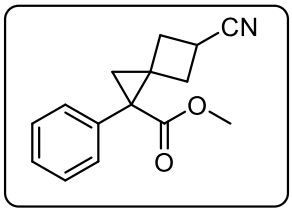
Figure S5. DMol^3 Transition State Search

The multiple attempts to search for the critical transition state in the Dmol^3 package revealed a tiny energy barrier during the process of forming the transition state. The transition state was stabilized at an energy lower than the starting substrate, providing evidence that the reaction occurred spontaneously.

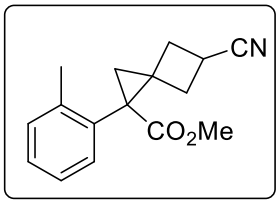
Entry	Energy kcal/mol	ΔG kal/mol
1	-180220.0487	
2a	-312269.5436	
TS1	-492,483.9516	5.64070651

3a	-492543.5349	-53.94262712
3b	-492544.0654	-54.47305564

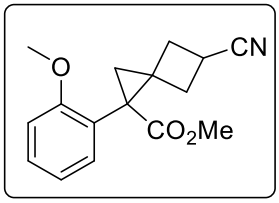
Characterization Data of Products



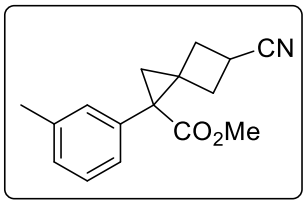
Compound 3a: colorless oil, d.r.=1.9:1, 22.5 mg. **major**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 - 7.37 (m, 4H), 7.34 - 7.31 (m, 4H), 7.29 - 7.26 (m, 2H), 3.68 (s, 5H), 3.30 - 3.13 (m, 3H), 2.89 - 2.73 (m, 4H), 2.49 (dd, J = 12.5, 7.8 Hz, 2H), 2.08 - 1.99 (m, 2H), 1.89 (d, J = 5.0 Hz, 2H), 1.53 (d, J = 5.0 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.20, 135.29, 130.73, 128.49, 127.64, 122.28, 52.49, 36.72, 34.19, 32.87, 32.26, 26.47, 16.85. **minor**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 - 7.37 (m, 2H), 7.34 - 7.31 (m, 3H), 3.67 (s, 3H), 3.30 - 3.13 (m, 1H), 2.89 - 2.73 (m, 2H), 2.36 (dd, J = 12.7, 9.5 Hz, 1H), 2.15 (dd, J = 12.7, 6.1 Hz, 1H), 1.95 (d, J = 5.3 Hz, 1H), 1.58 (d, J = 5.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.20, 135.37, 130.68, 128.49, 127.64, 122.61, 52.42, 36.89, 33.44, 32.80, 32.31, 26.10, 17.43. **HRMS (ESI) m/z:** $C_{15}H_{16}NO_2^+$ $[M+H]^+$ 242.1176, found 242.1179.



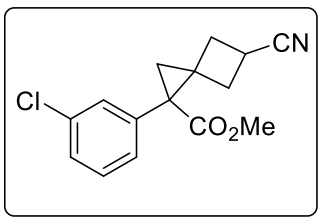
Compound 3b: colorless oil, d.r.=1.5:1, 18.9 mg. **major**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.23 (m, 3H), 7.20 (ddd, J = 8.7, 6.0, 2.0 Hz, 2H), 7.14 (dd, J = 7.7, 3.2 Hz, 2H), 3.66 (s, 5H), 3.28 (p, J = 8.7 Hz, 2H), 3.02 (ddd, J = 13.9, 9.0, 6.0 Hz, 2H), 2.85 (ddd, J = 12.8, 6.6, 2.4 Hz, 2H), 2.41 (s, 5H), 2.40 – 2.34 (m, 2H), 2.01 (td, J = 10.5, 10.0, 5.0 Hz, 2H), 1.85 (d, J = 4.8 Hz, 1H), 1.53 (d, J = 4.8 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.45, 139.01, 134.11, 130.55, 129.73, 127.83, 126.07, 122.17, 52.35, 35.50, 34.47, 33.13, 32.37, 28.20, 19.82, 16.60. **minor**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.23 (m, 2H), 7.20 (ddd, J = 8.7, 6.0, 2.0 Hz, 1H), 7.14 (dd, J = 7.7, 3.2 Hz, 1H), 3.65 (s, 3H), 3.23 – 3.14 (m, 1H), 3.02 (ddd, J = 13.9, 9.0, 6.0 Hz, 1H), 2.85 (ddd, J = 12.8, 6.6, 2.4 Hz, 1H), 2.32 (s, 3H), 2.26 (d, J = 10.8 Hz, 1H), 2.12 (dd, J = 12.9, 5.8 Hz, 1H), 1.92 (d, J = 5.1 Hz, 1H), 1.59 (d, J = 5.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.45, 138.78, 134.16, 130.38, 130.03, 127.83, 126.19, 122.78, 52.32, 35.55, 33.39, 32.48, 32.01, 28.23, 19.56, 17.50. **HRMS (ESI) m/z:** $C_{16}H_{18}NO_2^+$ $[M+H]^+$ 256.1332, found 256.1334.



Compound 3c: light yellow oil, d.r.=1.3:1, 21.5 mg. **major**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 - 7.31 (m, 1H), 7.09 (ddd, J = 7.4, 4.7, 1.8 Hz, 1H), 7.00 - 6.93 (m, 3H), 3.98 (s, 4H), 3.63 (s, 4H), 3.27 - 3.13 (m, 1H), 3.03 - 2.93 (m, 1H), 2.86 - 2.78 (m, 1H), 2.21 (m, 1H), 2.07 - 1.98 (m, 1H), 1.74 (d, J = 5.0 Hz, 1H), 1.44 (dd, J = 5.2, 3.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.6, 159.0, 130.1, 129.2, 124.6, 122.8, 120.5, 110.5, 55.7, 52.1, 33.6, 32.6, 32.3, 27.0, 16.4. **minor**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 - 7.31 (m, 1H), 7.09 (ddd, J = 7.4, 4.7, 1.8 Hz, 1H), 7.00 - 6.93 (m, 2H), 3.90 (s, 3H), 3.62 (s, 3H), 3.27 - 3.13 (m, 1H), 3.03 - 2.93 (m, 1H), 2.86 - 2.78 (m, 1H), 2.21 (m, 1H), 2.07 - 1.98 (m, 1H), 1.76 (d, J = 5.3 Hz, 1H), 1.44 (dd, J = 5.2, 3.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.6, 159.0, 130.5, 124.9, 123.0, 120.9, 110.6, 55.6, 52.1, 33.4, 32.8, 31.4, 26.2, 17.7. **HRMS (ESI) m/z:** $[M + H]^+$ Calcd for $C_{16}H_{18}O_3N$: 272.1281; Found: 272.1279.

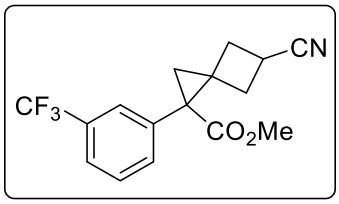


Compound 3d: colorless oil, d.r.=1.4:1, 19.5 mg. **major**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.25 (m, 3H), 7.14 (d, J = 7.1 Hz, 3H), 3.67 (s, 4H), 3.29 – 3.21 (m, 1H), 2.88 – 2.70 (m, 3H), 2.50 (dd, J = 12.5, 7.9 Hz, 1H), 2.40 (s, 4H), 2.07 – 1.98 (m, 2H), 1.86 (d, J = 4.9 Hz, 1H), 1.52 (d, J = 5.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.31, 138.09, 135.19, 131.33, 128.43, 127.81, 122.30, 52.45, 36.61, 34.27, 32.97, 32.33, 26.54, 21.51, 16.84. **minor**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14 (d, J = 7.1 Hz, 3H), 7.08 (dt, J = 4.1, 1.7 Hz, 2H), 3.66 (s, 3H), 3.21 – 3.14 (m, 1H), 2.88 – 2.70 (m, 2H), 2.39 (s, 3H), 2.36 (d, J = 9.6 Hz, 1H), 2.15 (dd, J = 12.8, 6.1 Hz, 1H), 1.92 (d, J = 5.2 Hz, 1H), 1.57 (d, J = 5.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.31, 138.09, 135.26, 131.27, 128.33, 128.31, 122.66, 52.38, 36.81, 33.48, 32.71, 32.25, 26.17, 21.51, 17.41. **HRMS (ESI) m/z:** $[M + H]^+$ Calcd for $C_{16}H_{18}O_2N$: 256.1332; Found: 256.1334.

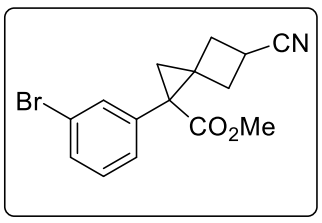


Compound 3e: yellow oil, d.r.=1:1, 22.6 mg. **major**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.25 (m, 4H), 3.68 (s, 3H), 3.30 – 3.22 (m, 1H), 2.87 – 2.72 (m, 2H), 2.46

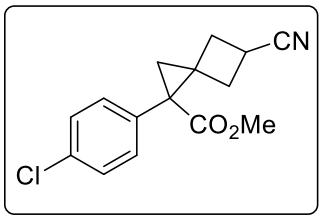
(dd, J = 12.5, 7.9 Hz, 1H), 2.04 (ddd, J = 12.0, 9.0, 2.5 Hz, 1H), 1.89 (d, J = 5.1 Hz, 1H), 1.51 (d, J = 5.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.55, 137.35, 134.23, 130.61, 129.72, 129.20, 122.45, 52.57, 36.34, 34.17, 32.94, 32.86, 26.42, 16.89. **minor**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.25 (m, 3H), 7.18 – 7.13 (m, 1H), 3.67 (s, 3H), 3.22 – 3.14 (m, 1H), 2.87 – 2.72 (m, 2H), 2.36 (dd, J = 12.8, 9.5 Hz, 1H), 2.15 (dd, J = 12.8, 6.0 Hz, 1H), 1.96 (d, J = 5.4 Hz, 1H), 1.57 (d, J = 5.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.55, 137.44, 134.23, 130.80, 128.92, 127.91, 122.07, 52.51, 36.52, 33.39, 32.48, 32.21, 26.15, 17.42. **HRMS (ESI) m/z:** $[M + H]^+$ Calcd for $C_{15}H_{15}O_2NCl$: 276.0786; Found: 276.0783.



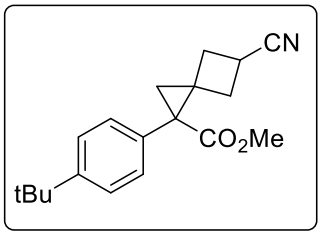
Compound 3f: yellow oil, d.r.=1.1:1, 24.8 mg. **major**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (dd, J = 7.7, 1.9 Hz, 2H), 7.53 (d, J = 6.7 Hz, 2H), 7.51 – 7.45 (m, 1H), 3.66 (s, 3H), 3.20 (ddd, J = 9.4, 6.0, 3.4 Hz, 1H), 2.80 – 2.73 (m, 2H), 2.13 (dd, J = 12.8, 5.9 Hz, 1H), 2.08 – 2.02 (m, 1H), 1.94 (d, J = 5.2 Hz, 1H), 1.55 (d, J = 5.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.41, 136.52, 134.22, 130.88 (q, J = 34.0, 33.1 Hz), 128.98, 127.36 (q, J = 3.5 Hz), 124.53 (q, J = 3.4 Hz), 122.39, 52.49, 36.57, 33.40, 32.95, 32.17, 26.11, 17.40. **minor**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (dd, J = 7.7, 1.9 Hz, 2H), 7.53 (d, J = 6.7 Hz, 2H), 7.51 – 7.45 (m, 1H), 3.67 (s, 3H), 3.30 – 3.22 (m, 1H), 2.85 (dd, J = 12.8, 8.2 Hz, 2H), 2.41 (dd, J = 12.5, 7.8 Hz, 1H), 2.32 (dd, J = 12.8, 9.5 Hz, 1H), 2.01 (d, J = 5.4 Hz, 1H), 1.61 (d, J = 5.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.41, 136.45, 134.58, 130.88 (q, J = 34.0, 33.1 Hz), 127.07 (q, J = 3.5 Hz), 124.53 (q, J = 3.4 Hz), 122.01, 52.56, 36.43, 34.15, 32.85, 32.52, 26.27, 16.92. **HRMS (ESI) m/z:** $[M + H]^+$ Calcd for $C_{16}H_{15}O_2F_3N$: 310.1049; Found: 310.1056.



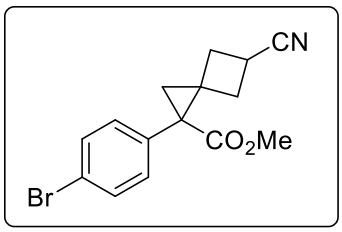
Compound 3g: light yellow oil, d.r.=1.1:1, 24 mg. **major**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (ddt, J = 10.1, 8.4, 1.8 Hz, 2H), 7.32 – 7.19 (m, 2H), 3.67 (s, 4H), 3.29 – 3.22 (m, 1H), 2.86 – 2.70 (m, 2H), 2.46 (dd, J = 12.4, 7.9 Hz, 1H), 2.08 – 2.00 (m, 1H), 1.89 (d, J = 5.1 Hz, 1H), 1.51 (d, J = 5.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.53, 137.64, 133.46, 130.01, 129.72, 122.39, 122.07, 52.58, 36.31, 34.17, 32.87, 32.50, 26.42, 16.90. **minor**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (ddt, J = 10.1, 8.4, 1.8 Hz, 2H), 7.32 – 7.19 (m, 2H), 3.66 (s, 3H), 3.21 – 3.14 (m, 1H), 2.86 – 2.70 (m, 2H), 2.36 (dd, J = 12.7, 9.5 Hz, 1H), 2.15 (ddd, J = 12.7, 6.0, 1.3 Hz, 1H), 1.95 (d, J = 5.4 Hz, 1H), 1.56 (d, J = 5.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.53, 137.72, 133.67, 130.82, 129.43, 122.45, 122.39, 52.52, 36.48, 33.39, 32.95, 32.21, 26.17, 17.42. **HRMS (ESI) m/z:** $[M + H]^+$ Calcd for $C_{15}H_{15}O_2NBr$: 320.0280; Found: 320.0284.



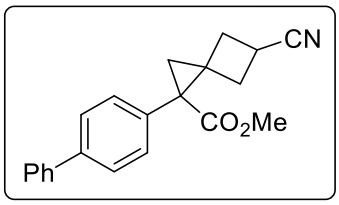
Compound 3h: yellow oil, d.r.=1.3:1, 24.8 mg. **major**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (ddd, J = 8.6, 5.1, 1.5 Hz, 3H), 7.29 – 7.25 (m, 3H), 7.23 – 7.19 (m, 3H), 3.67 (s, 4H), 3.29 – 3.21 (m, 1H), 2.86 – 2.74 (m, 3H), 2.43 (dd, J = 12.5, 7.7 Hz, 1H), 2.08 – 2.01 (m, 1H), 1.89 (d, J = 5.1 Hz, 1H), 1.48 (d, J = 5.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.70, 133.87, 133.55, 132.08, 128.72, 122.15, 52.53, 36.13, 34.08, 32.80, 32.43, 26.40, 16.90. **minor**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (ddd, J = 8.6, 5.1, 1.5 Hz, 2H), 7.23 – 7.19 (m, 2H), 3.66 (s, 3H), 3.20 – 3.13 (m, 1H), 2.86 – 2.74 (m, 2H), 2.34 (dd, J = 11.5, 9.6 Hz, 1H), 2.13 (dd, J = 12.8, 6.0 Hz, 1H), 1.95 (d, J = 5.4 Hz, 1H), 1.54 (d, J = 5.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.70, 133.95, 133.87, 132.02, 128.72, 122.46, 52.46, 36.24, 33.39, 32.89, 32.19, 26.17, 17.41. **HRMS (ESI) m/z:** $[M + H]^+$ Calcd for $C_{15}H_{15}O_2NCl$: 276.0786; Found: 276.0783.



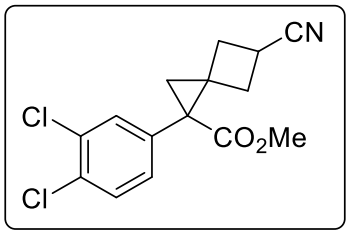
Compound 3i: colorless oil, d.r.=1.6:1, 23.3 mg. **major**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 - 7.36 (m, 3H), 7.27 - 7.23 (m, 3H), 3.67 (s, 5H), 3.21 (m, 2H), 2.86 - 2.71 (m, 3H), 2.49 (dd, J = 12.5, 7.8 Hz, 2H), 2.04 (tt, J = 9.3, 1.6 Hz, 2H), 1.86 (d, J = 4.9 Hz, 2H), 1.51 (d, J = 4.9 Hz, 2H), 1.35 (s, 15H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.4, 150.3, 132.1, 130.3, 125.4, 122.4, 52.4, 36.4, 34.2, 33.4, 32.3, 31.4, 26.3, 16.8. **minor**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 - 7.36 (m, 2H), 7.21 - 7.17 (m, 2H), 3.66 (s, 3H), 3.21 (m, 1H), 2.86 - 2.71 (m, 2H), 2.36 (dd, J = 12.7, 9.5 Hz, 1H), 2.16 (dd, J = 12.7, 6.3 Hz, 1H), 1.92 (d, J = 5.3 Hz, 1H), 1.55 (d, J = 5.3 Hz, 1H), 1.35 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.4, 150.4, 132.2, 130.2, 125.4, 122.7, 52.4, 36.5, 34.6, 32.9, 32.8, 31.4, 25.9, 17.4. **HRMS (ESI) m/z**: $[M + H]^+$ Calcd for $C_{19}H_{24}O_2N$: 298.1802; Found: 298.1806.



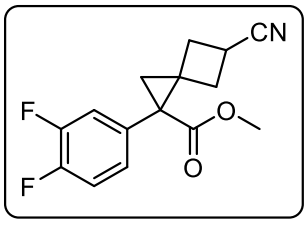
Compound 3j: yellow oil, d.r.=1.3:1, 26.9 mg. **major**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (ddd, J = 8.7, 5.1, 1.9 Hz, 2H), 7.21 (dd, J = 8.4, 1.9 Hz, 2H), 3.67 (s, 4H), 3.30 - 3.13 (m, 1H), 2.78 (qd, J = 12.7, 5.8 Hz, 3H), 2.43 (dd, J = 12.5, 7.7 Hz, 1H), 2.04 (dd, J = 12.2, 9.3 Hz, 1H), 1.89 (d, J = 3.5 Hz, 1H), 1.48 (d, J = 3.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 134.4, 132.4, 131.7, 122.1, 121.8, 52.6, 36.2, 34.1, 32.8, 32.4, 26.4, 16.9. **minor**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (ddd, J = 8.7, 5.1, 1.9 Hz, 2H), 7.15 (dd, J = 8.5, 1.9 Hz, 2H), 3.66 (s, 3H), 3.30 - 3.13 (m, 1H), 2.78 (qd, J = 12.7, 5.8 Hz, 2H), 2.34 (dd, J = 12.8, 9.6 Hz, 1H), 2.13 (dd, J = 12.7, 5.3 Hz, 1H), 1.95 (d, J = 3.7 Hz, 1H), 1.54 (d, J = 3.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 134.5, 132.4, 131.7, 122. 5, 121.7, 52.5, 36.3, 33.4, 32.9, 32.2, 26.1, 17.4. **HRMS (ESI) m/z**: $[M + H]^+$ Calcd for $C_{15}H_{15}O_2NBr$: 320.0281; Found: 320.0285.



Compound 3k: brown oil, d.r.=1.4:1, 28.9 mg. **major**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.60 (m, 6H), 7.49 (t, J = 7.6 Hz, 3H), 7.46 – 7.37 (m, 3H), 7.40 – 7.32 (m, 1H), 3.71 (s, 4H), 3.23 – 3.17 (m, 1H), 2.91 – 2.75 (m, 3H), 2.54 (dd, J = 12.5, 7.8 Hz, 1H), 2.11 – 2.05 (m, 1H), 1.93 (d, J = 5.0 Hz, 1H), 1.57 (d, J = 5.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.15, 140.59, 140.42, 134.34, 131.12, 128.87, 127.48, 127.20, 122.30, 52.52, 36.47, 34.22, 32.95, 32.93, 26.47, 16.90. **minor**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.60 (m, 4H), 7.49 (t, J = 7.6 Hz, 2H), 7.46 – 7.37 (m, 2H), 7.40 – 7.32 (m, 1H), 3.70 (s, 3H), 3.31 – 3.23 (m, 1H), 2.91 – 2.75 (m, 2H), 2.42 (dd, J = 12.6, 9.6 Hz, 1H), 2.19 (dd, J = 12.5, 5.8 Hz, 1H), 1.99 (d, J = 5.3 Hz, 1H), 1.63 (d, J = 5.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.15, 140.56, 140.46, 134.40, 131.07, 128.87, 127.52, 127.14, 122.62, 52.45, 36.62, 33.50, 32.47, 32.33, 26.13, 17.46. **HRMS (ESI) m/z**: $[M + H]^+$ Calcd for $C_{21}H_{20}O_2N$: 318.1489; Found: 318.1485.

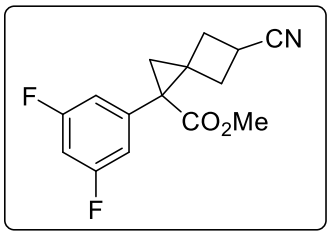


Compound 3l: yellow oil, d.r.=1.2:1, 24.2 mg. **major**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (t, J = 8.1 Hz, 1H), 7.39 (d, J = 2.1 Hz, 1H), 7.22 (dd, J = 8.3, 2.2 Hz, 1H), 3.68 (s, 4H), 3.31 - 3.14 (m, 1H), 2.85 - 2.72 (m, 3H), 2.44 (dd, J = 12.5, 7.8 Hz, 1H), 2.10 - 2.02 (m, 1H), 1.91 (d, J = 5.2 Hz, 1H), 1.49 (d, J = 5.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.2, 135.6, 132.5, 132.4, 130.5, 130.1, 122.0, 52.7, 35.9, 34.1, 32.8, 32.6, 26.4, 17.0. **minor**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (t, J = 8.1 Hz, 1H), 7.37 (d, J = 2.1 Hz, 1H), 7.12 (dd, J = 8.3, 2.1 Hz, 1H), 3.67 (s, 3H), 3.31 - 3.14 (m, 1H), 2.85 - 2.72 (m, 2H), 2.36 (dd, J = 12.8, 9.5 Hz, 1H), 2.16 (dd, J = 12.0, 6.5 Hz, 1H), 1.98 (d, J = 5.4 Hz, 1H), 1.55 (d, J = 5.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.2, 135.7, 132.6, 131.9, 130.4, 130.1, 122.3, 52.6, 36.0, 33.4, 33.1, 32.2, 26.3, 17.4. **HRMS (ESI) m/z**: $[M + H]^+$ Calcd for $C_{15}H_{14}O_2NCl_2$: 310.0396; Found: 310.0394.

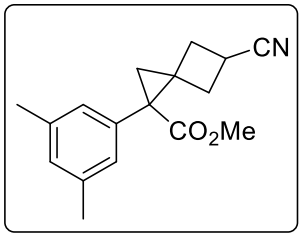


Compound 3m: yellow oil, d.r.=1.4:1, 19.7 mg. **major**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 - 7.09 (m, 3H), 7.09 - 7.04 (m, 1H), 3.67 (s, 4H), 3.30 - 3.21 (m, 1H), 2.84 - 2.69 (m, 3H), 2.44 (dd, J = 12.5, 7.8 Hz, 1H), 2.10 - 2.01 (m, 1H), 1.89 (d, J = 5.2 Hz, 1H), 1.47 (d, J = 5.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.40, 151.16 (dd, J = 23.8, 12.6 Hz), 132.40 (q, J = 6.5 Hz), 126.92 (dd, J = 6.3, 3.5 Hz), 122.04, 119.77, 119.60, 117.18, 52.56, 35.96, 34.05, 32.76, 32.60, 26.51, 16.90. **minor**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 - 7.09 (m, 2H), 6.99 (ddt, J = 8.2, 3.9, 1.8 Hz, 1H), 3.66 (s, 3H), 3.21 - 3.13 (m, 1H), 2.84 - 2.69 (m, 2H), 2.36 (dd, J = 12.8, 9.5 Hz,

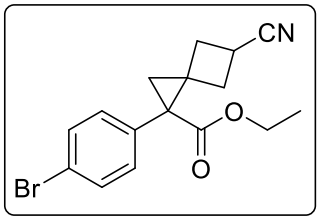
1H), 2.15 (dd, J = 12.9, 5.8 Hz, 1H), 1.96 (d, J = 5.5 Hz, 1H), 1.53 (d, J = 5.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.40, 148.69 (dd, J = 24.1, 12.7 Hz), 132.40 (q, J = 6.5 Hz), 126.71 (dd, J = 6.4, 3.5 Hz), 122.39, 119.85, 119.68, 117.35, 52.50, 36.09, 33.34, 33.03, 32.12, 26.31, 17.39. ^{19}F NMR (376 MHz, $CDCl_3$) δ -137.23 (dd, J = 21.2, 10.2 Hz), -138.85 (t, J = 28.9 Hz). **HRMS (ESI) m/z**: $[M + H]^+$ Calcd for $C_{15}H_{14}O_2NF_2$: 287.0987; Found: 278.0993.



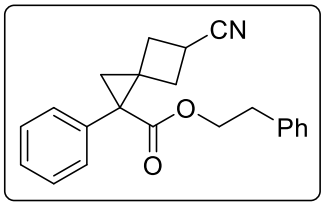
Compound 3n: yellow oil, d.r.=1.1:1, 17.5 mg. **major**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.90 – 6.85 (m, 1H), 6.85 – 6.74 (m, 2H), 3.69 (s, 3H), 3.31 – 3.22 (m, 1H), 2.86 – 2.78 (m, 1H), 2.78 – 2.71 (m, 1H), 2.46 (dd, J = 12.5, 7.9 Hz, 1H), 2.11 – 2.04 (m, 2H), 1.90 (d, J = 5.2 Hz, 1H), 1.50 (d, J = 5.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.02, 164.01, 161.67, 139.11 (q, J = 9.8 Hz), 121.90, 113.55 (dd, J = 6.9, 3.5 Hz), 103.41 (t, J = 25.2 Hz), 52.64, 36.29, 34.12, 32.76, 32.72, 26.44, 16.89. **minor**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.90 – 6.85 (m, 1H), 6.85 – 6.74 (m, 2H), 3.68 (s, 3H), 3.18 (tt, J = 9.4, 5.1 Hz, 1H), 2.86 – 2.78 (m, 1H), 2.78 – 2.71 (m, 1H), 2.37 (dd, J = 12.8, 9.5 Hz, 1H), 2.21 – 2.14 (m, 1H), 1.97 (d, J = 5.5 Hz, 1H), 1.55 (d, J = 5.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.02, 164.14, 161.54, 139.11 (q, J = 9.8 Hz), 122.32, 113.73 (dd, J = 6.8, 3.6 Hz), 103.41 (t, J = 25.2 Hz), 52.57, 36.45, 33.35, 33.21, 32.10, 26.21, 17.42. ^{19}F NMR (376 MHz, $CDCl_3$) δ -109.50 (q, J = 11.2, 9.8 Hz). **HRMS (ESI) m/z**: $[M + H]^+$ Calcd for $C_{15}H_{14}O_2NF_2$: 287.0987; Found: 278.0993.



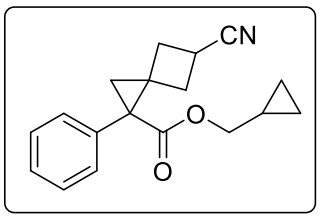
Compound 3o: colorless oil, d.r.=1.5:1, 19.7 mg. **major**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.96 (s, 2H), 6.93 (s, 3H), 3.67 (s, 4H), 3.29 – 3.21 (m, 2H), 2.88 – 2.71 (m, 3H), 2.52 (dd, J = 12.4, 8.0 Hz, 2H), 2.36 (s, 9H), 2.05 – 1.98 (m, 2H), 1.84 (d, J = 4.9 Hz, 2H), 1.50 (d, J = 4.9 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.46, 137.91, 135.09, 129.41, 128.43, 122.32, 52.45, 36.49, 34.35, 33.06, 32.18, 26.65, 21.39, 16.82.**minor**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.96 (s, 1H), 6.87 (s, 2H), 3.66 (s, 3H), 3.21 – 3.14 (m, 1H), 2.88 – 2.71 (m, 2H), 2.43 – 2.38 (m, 1H), 2.35 (s, 6H), 2.15 (dd, J = 12.7, 6.1 Hz, 1H), 1.89 (d, J = 5.2 Hz, 1H), 1.55 (d, J = 5.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.46, 137.91, 135.15, 129.41, 128.43, 122.71, 52.38, 36.75, 33.50, 32.62, 32.38, 26.25, 21.39, 17.41. **HRMS (ESI) m/z**: $[M + H]^+$ Calcd for $C_{17}H_{20}O_2N$: 270.1489; Found: 270.1492.



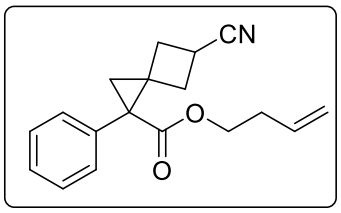
Compound 3p: yellow oil, d.r.=1.4:1, 21.7 mg. **major**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (ddd, J = 8.4, 5.0, 1.7 Hz, 3H), 7.23 - 7.19 (m, 3H), 4.18 - 4.07 (m, 3H), 3.29 - 3.10 (m, 1H), 2.86 - 2.68 (m, 3H), 2.41 (dd, J = 12.5, 7.8 Hz, 1H), 2.05 - 1.98 (m, 1H), 1.88 (d, J = 5.1 Hz, 1H), 1.46 (d, J = 5.1 Hz, 1H), 1.20 (tdd, J = 7.0, 3.2, 1.4 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 134.5, 132.4, 131.6, 122.1, 121.6, 61.4, 36.3, 34.2, 32.8, 32.3, 25.9, 25.8, 17.4, 16.9, 14.3. **minor**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (ddd, J = 8.4, 5.0, 1.7 Hz, 2H), 7.16 - 7.13 (m, 2H), 4.18 - 4.07 (m, 2H), 3.29 - 3.10 (m, 1H), 2.86 - 2.68 (m, 2H), 2.36 - 2.28 (m, 1H), 2.10 (ddd, J = 12.7, 5.8, 1.5 Hz, 1H), 1.95 (dd, J = 5.4, 1.3 Hz, 1H), 1.53 (d, J = 5.4 Hz, 1H), 1.20 (tdd, J = 7.0, 3.2, 1.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 134.6, 132.4, 131.6, 122.5, 121.6, 61.4, 36.4, 33.4, 32.7, 32.2, 25.8, 17.4, 14.3. **HRMS (ESI) m/z**: $[M + H]^+$ Calcd for $C_{16}H_{17}O_2NBr$: 334.0437; Found: 334.0440.



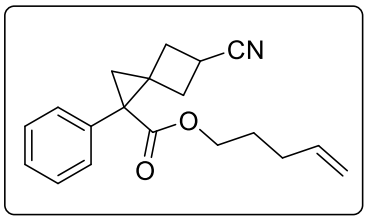
Compound 3q: light yellow oil, d.r.=1.3:1, 27.9 mg. **major**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 - 7.25 (m, 10H), 7.10 - 7.06 (m, 3H), 4.39 (dt, J = 11.0, 6.6 Hz, 1H), 4.26 - 4.17 (m, 1H), 3.26 - 3.16 (m, 1H), 2.88 (td, J = 6.7, 2.9 Hz, 3H), 2.75 - 2.60 (m, 2H), 2.48 (dd, J = 12.4, 7.9 Hz, 1H), 1.99 (ddd, J = 12.0, 8.9, 2.3 Hz, 1H), 1.82 (d, J = 4.9 Hz, 1H), 1.49 (d, J = 5.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 137.8, 135.3, 130.8, 129.1, 128.5, 128.4, 127.5, 126.6, 122.2, 65.7, 36.7, 35.1, 33.3, 32.9, 32.2, 26.4, 16.8. **minor**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 - 7.25 (m, 6H), 7.24 - 7.19 (m, 2H), 7.10 - 7.06 (m, 2H), 4.39 (dt, J = 11.0, 6.6 Hz, 1H), 4.26 - 4.17 (m, 1H), 3.08 (tt, J = 9.3, 6.5 Hz, 1H), 2.88 (td, J = 6.7, 2.9 Hz, 2H), 2.75 - 2.60 (m, 2H), 2.31 (dd, J = 12.7, 9.4 Hz, 1H), 2.13 (dd, J = 12.7, 6.3 Hz, 1H), 1.88 (d, J = 5.3 Hz, 1H), 1.52 (d, J = 5.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.5, 137.9, 135.4, 130.8, 129.1, 128.5, 128.4, 127.6, 126.6, 122.6, 65.6, 37.0, 34.0, 32.7, 32.3, 32.2, 25.8, 17.4. **HRMS (ESI) m/z**: $[M + H]^+$ Calcd for $C_{22}H_{22}O_2N$: 332.1645; Found: 332.1646.



Compound 3r: light yellow oil, d.r.=1.4:1, 25.9 mg. **major**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 - 7.26 (m, 7H), 4.01 - 3.86 (m, 3H), 2.86 (dd, J = 12.3, 8.0 Hz, 1H), 2.80 - 2.73 (m, 1H), 2.47 (dd, J = 12.4, 7.9 Hz, 1H), 2.04 - 1.99 (m, 1H), 1.90 (d, J = 5.0 Hz, 2H), 1.53 (d, J = 5.0 Hz, 1H), 1.09 (pq, J = 8.2, 4.6 Hz, 1H), 0.58 - 0.50 (m, 3H), 0.24 (dq, J = 6.0, 4.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.7, 135.5, 130.7, 128.4, 127.5, 122.3, 69.6, 36.9, 34.4, 32.9, 32.2, 25.9, 16.9, 10.0, 3.2. **minor**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 - 7.26 (m, 5H), 4.01 - 3.86 (m, 2H), 2.86 (dd, J = 12.3, 8.0 Hz, 1H), 2.80 - 2.73 (m, 1H), 2.36 (dd, J = 12.6, 9.5 Hz, 1H), 2.12 (ddd, J = 12.7, 6.0, 1.4 Hz, 1H), 1.97 (d, J = 5.4 Hz, 1H), 1.58 (d, J = 5.3 Hz, 1H), 1.09 (pq, J = 8.2, 4.6 Hz, 1H), 0.58 - 0.50 (m, 2H), 0.24 (dq, J = 6.0, 4.5 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.7, 135.5, 130.6, 128.4, 127.5, 122.7, 69.6, 37.1, 33.6, 32.6, 32.3, 25.6, 17.4, 9.9, 3.2. **HRMS (ESI) m/z**: $[M + H]^+$ Calcd for $C_{18}H_{20}O_2N$: 282.1489; Found: 282.1488.

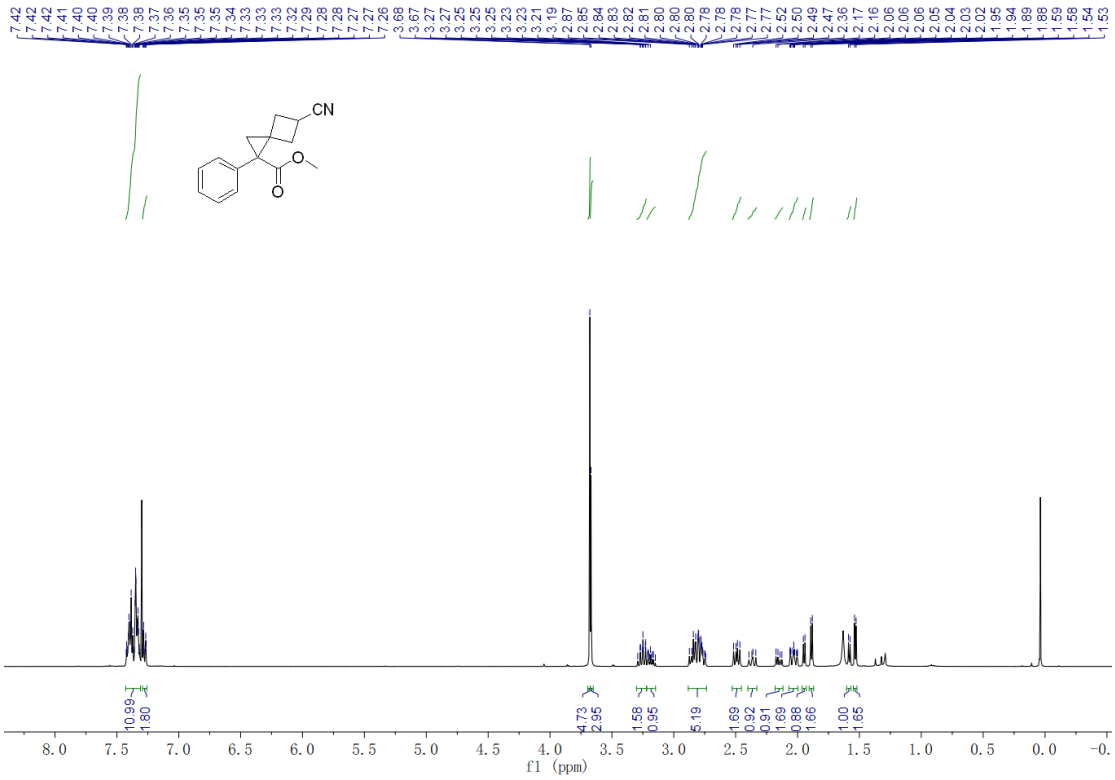


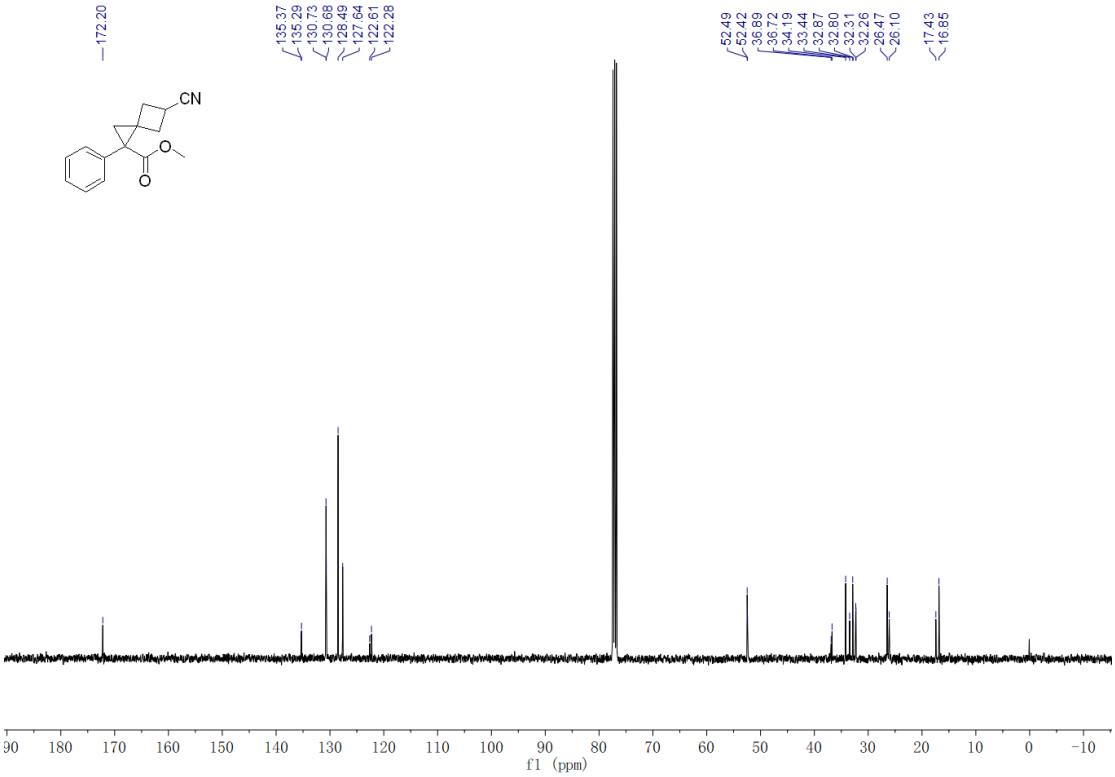
Compound 3s: yellow oil, d.r.=1.2:1, 21.4 mg. **major**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (dt, J = 7.7, 5.4 Hz, 2H), 7.31 - 7.27 (m, 2H), 7.25 - 7.21 (m, 1H), 5.74 - 5.62 (m, 1H), 5.08 - 5.01 (m, 2H), 4.17 (dq, J = 10.8, 6.8 Hz, 1H), 4.04 (dt, J = 10.6, 6.5 Hz, 1H), 3.26 - 3.09 (m, 1H), 2.85 - 2.69 (m, 2H), 2.45 (dd, J = 12.4, 7.9 Hz, 1H), 2.34 - 2.28 (m, 2H), 1.99 (tt, J = 9.2, 1.7 Hz, 1H), 1.84 (d, J = 5.0 Hz, 1H), 1.49 (d, J = 5.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 135.3, 133.9, 130.7, 128.4, 127.5, 122.6, 117.5, 64.2, 36.8, 34.3, 33.2, 32.9, 32.2, 26.1, 16.9. **minor**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (dt, J = 7.7, 5.4 Hz, 2H), 7.31 - 7.27 (m, 2H), 7.25 - 7.21 (m, 1H), 5.74 - 5.62 (m, 1H), 5.08 - 5.01 (m, 2H), 4.17 (dq, J = 10.8, 6.8 Hz, 1H), 4.04 (dt, J = 10.6, 6.5 Hz, 1H), 3.26 - 3.09 (m, 1H), 2.85 - 2.69 (m, 2H), 2.34 - 2.28 (m, 3H), 2.11 (dd, J = 12.7, 6.1 Hz, 1H), 1.91 (d, J = 5.3 Hz, 1H), 1.54 (d, J = 5.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 135.4, 134.0, 130.7, 128.4, 127.5, 122.2, 117.4, 64.2, 37.0, 33.6, 33.2, 32.7, 32.3, 25.7, 17.4. **HRMS (ESI) m/z**: $[M + H]^+$ Calcd for $C_{18}H_{20}O_2N$: 282.1489; Found: 282.1488.

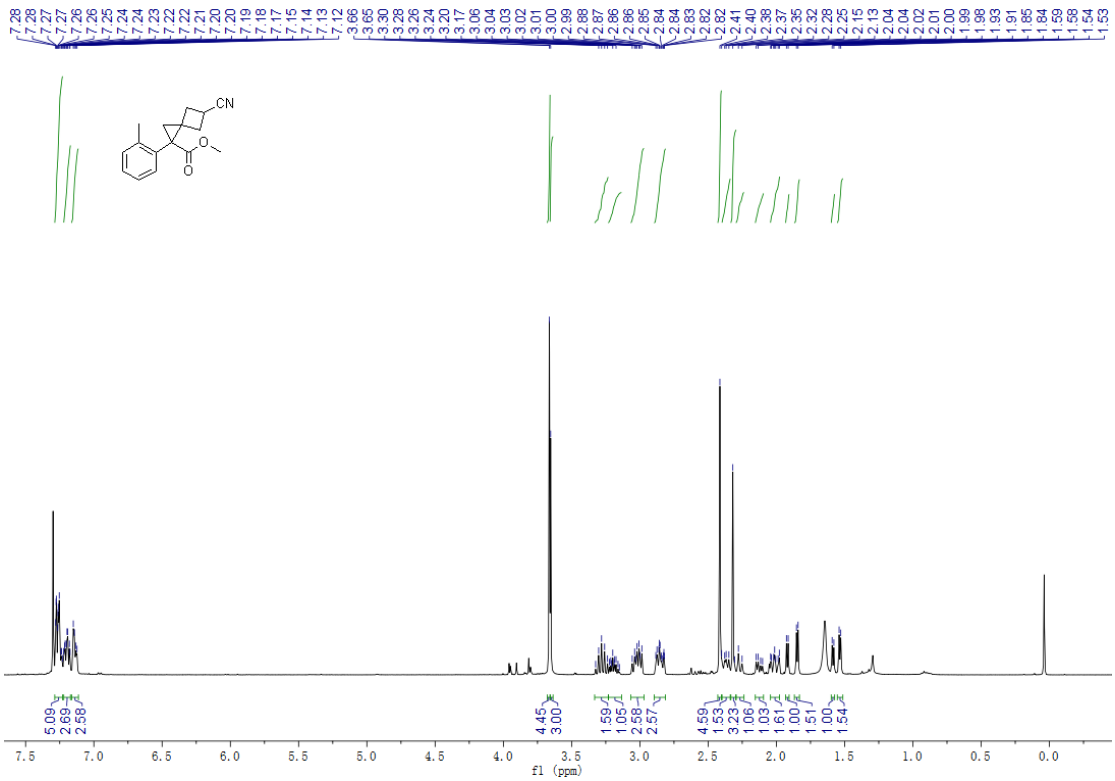


Compound 3t: yellow oil, d.r.=1.4:1, 18.4 mg. **major**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.30 (m, 7H), 5.83 – 5.77 (m, 1H), 5.04 – 4.94 (m, 3H), 4.12 (ddt, J = 10.8, 8.5, 6.6 Hz, 1H), 4.07 – 3.99 (m, 1H), 3.29 – 3.21 (m, 1H), 2.84 (ddd, J = 12.2, 8.5, 3.5 Hz, 1H), 2.80 – 2.72 (m, 1H), 2.49 (dd, J = 12.4, 7.9 Hz, 1H), 2.08 – 1.98 (m, 3H), 1.87 (d, J = 5.0 Hz, 1H), 1.62 – 1.54 (m, 3H), 1.52 (d, J = 5.0 Hz, 1H), 1.38 (qd, J = 8.0, 3.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.70, 138.33, 135.40, 130.68, 128.38, 127.50, 122.25, 114.87, 65.14, 36.86, 34.28, 33.13, 32.93, 32.32, 27.97, 26.11, 25.09, 16.90. **minor**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.30 (m, 3H), 7.29 – 7.25 (m, 2H), 5.77 – 5.72 (m, 1H), 5.04 – 4.94 (m, 2H), 4.12 (ddt, J = 10.8, 8.5, 6.6 Hz, 1H), 4.07 – 3.99 (m, 1H), 3.21 – 3.13 (m, 1H), 2.84 (ddd, J = 12.2, 8.5, 3.5 Hz, 1H), 2.80 – 2.72 (m, 1H), 2.40 – 2.34 (m, 1H), 2.14 (ddt, J = 12.7, 6.0, 1.4 Hz, 1H), 2.08 – 1.98 (m, 3H), 1.94 (d, J = 5.3 Hz, 1H), 1.62 – 1.54 (m, 3H), 1.38 (qd, J = 8.0, 3.2 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.70, 138.29, 135.47, 130.63, 128.38, 127.53, 122.62, 114.90, 65.08, 37.02, 33.53, 33.13, 32.59, 32.14, 27.97, 25.78, 25.10, 17.45. **HRMS (ESI) m/z**: $[M + H]^+$ Calcd for $C_{19}H_{22}O_2N$: 296.1645; Found: 296.1644.

^{1}H NMR and ^{13}C NMR Spectra for Products



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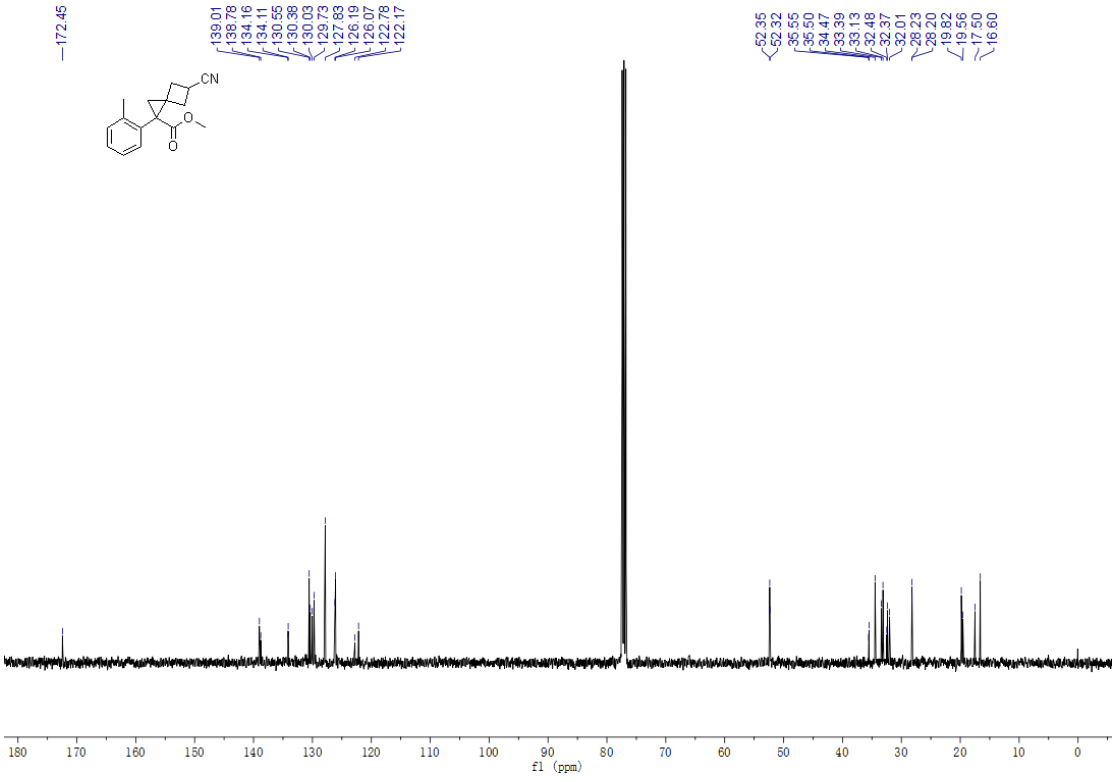
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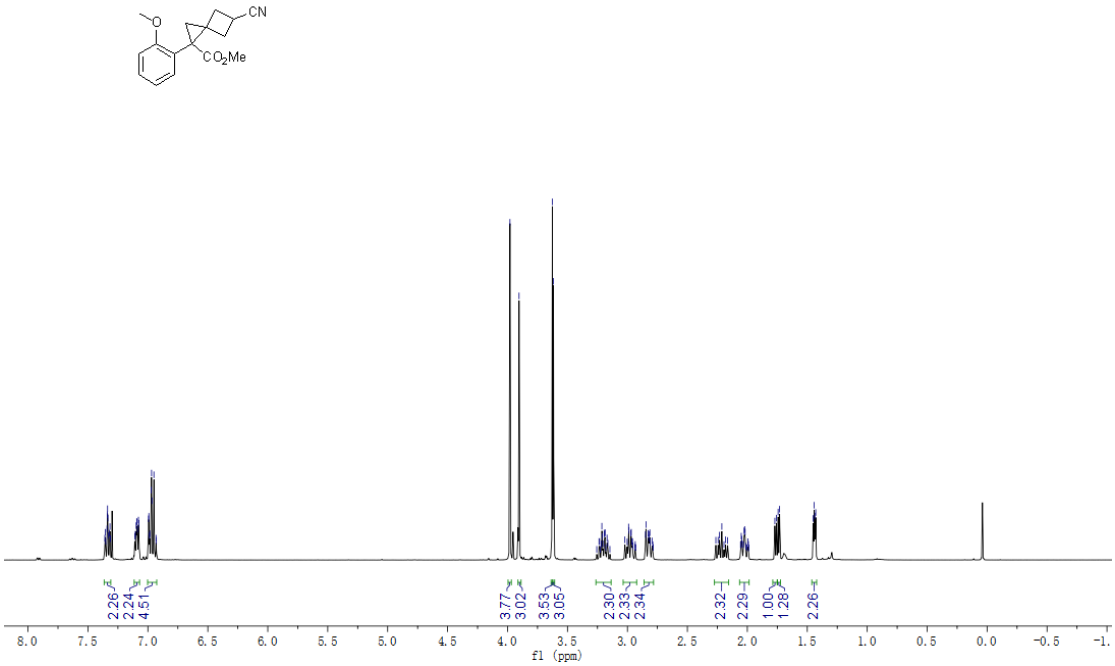
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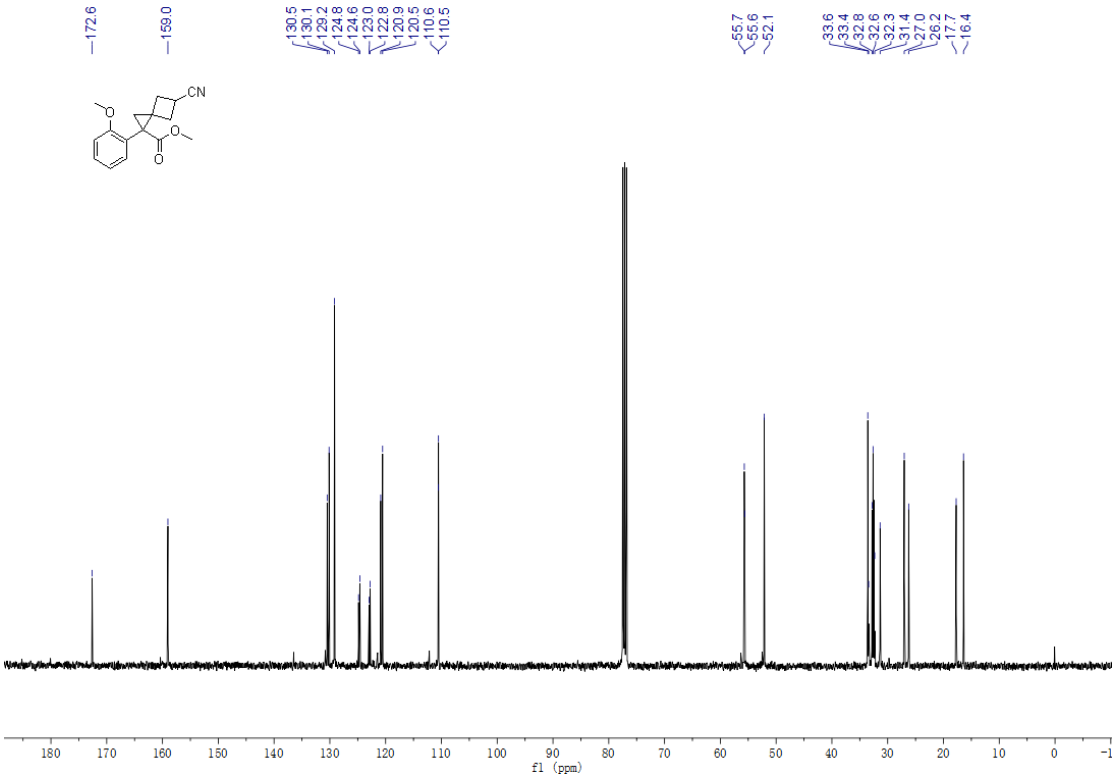
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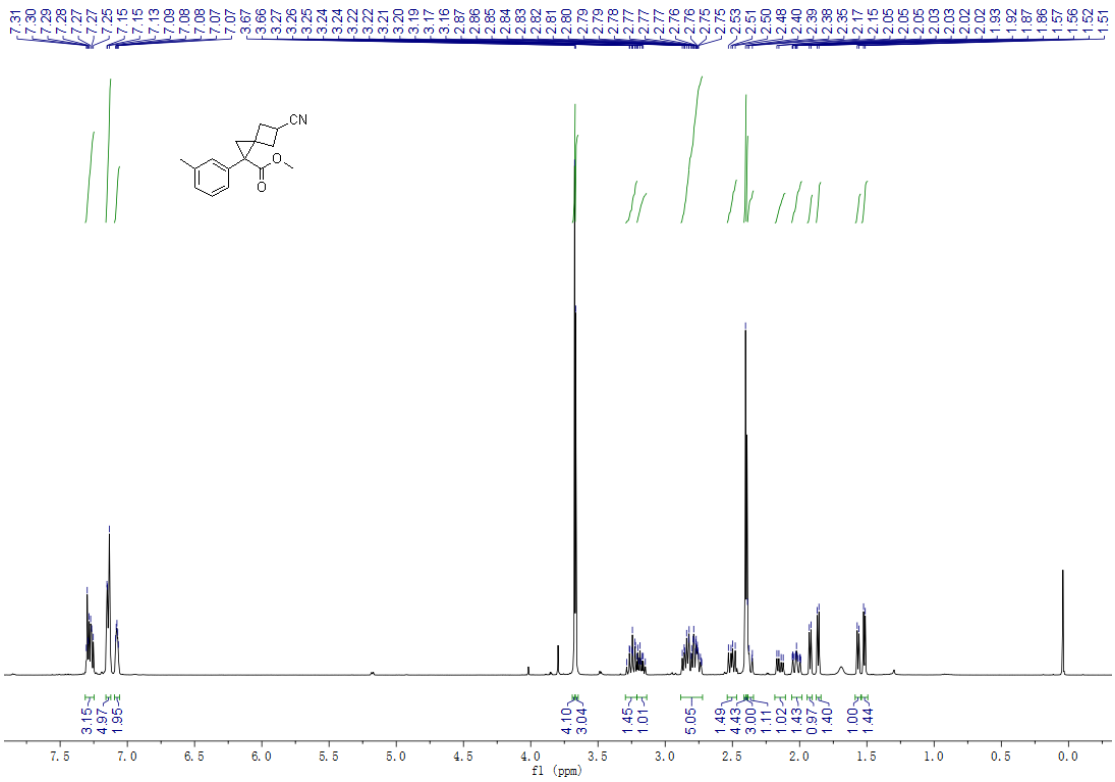
f1 (ppm)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O
O
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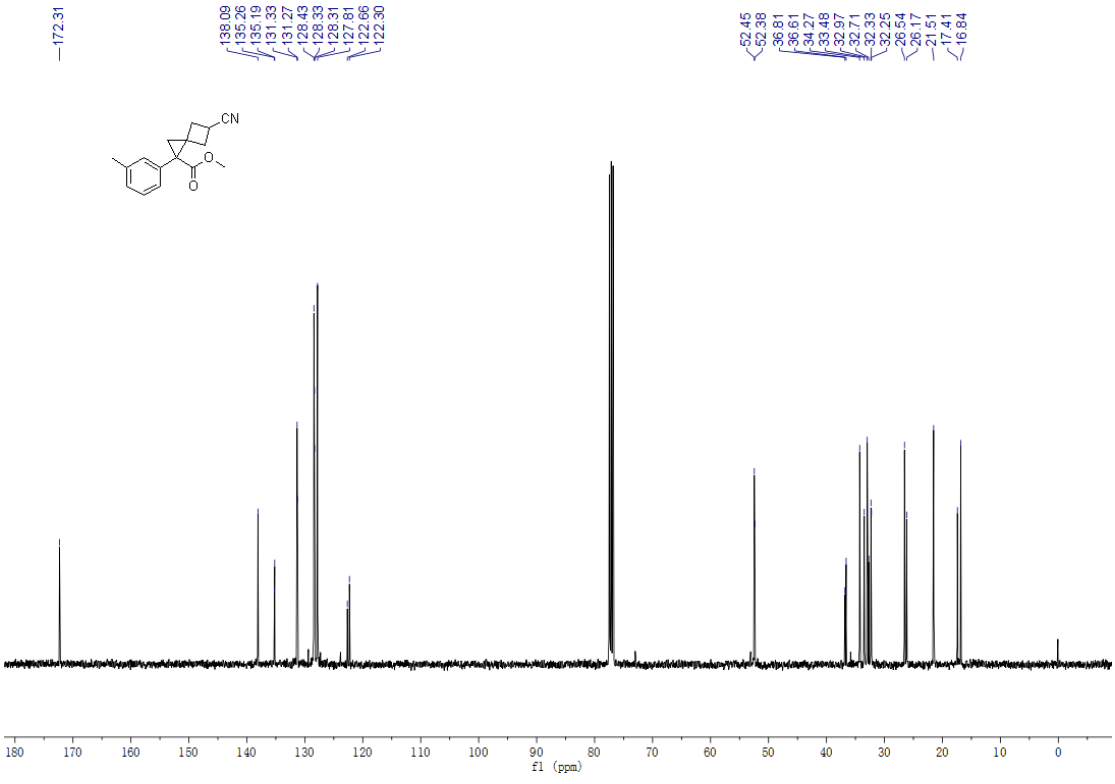
f1 (ppm)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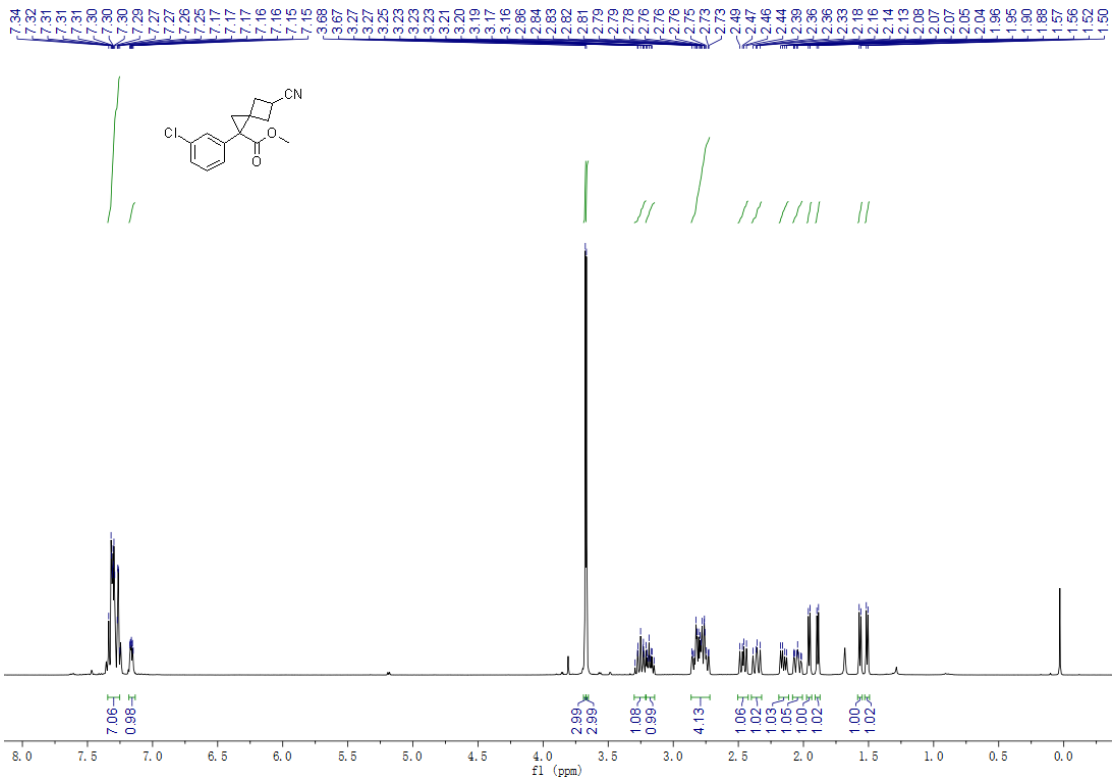
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2.49 2.47 2.46 2.44 2.39 2.36 2.36 2.33 2.18 2.16 2.14 2.13 2.08 2.07 2.07 2.05 2.04 1.96 1.95 1.90 1.88 1.57 1.56 1.52 1.50
CN
Cl
O
O
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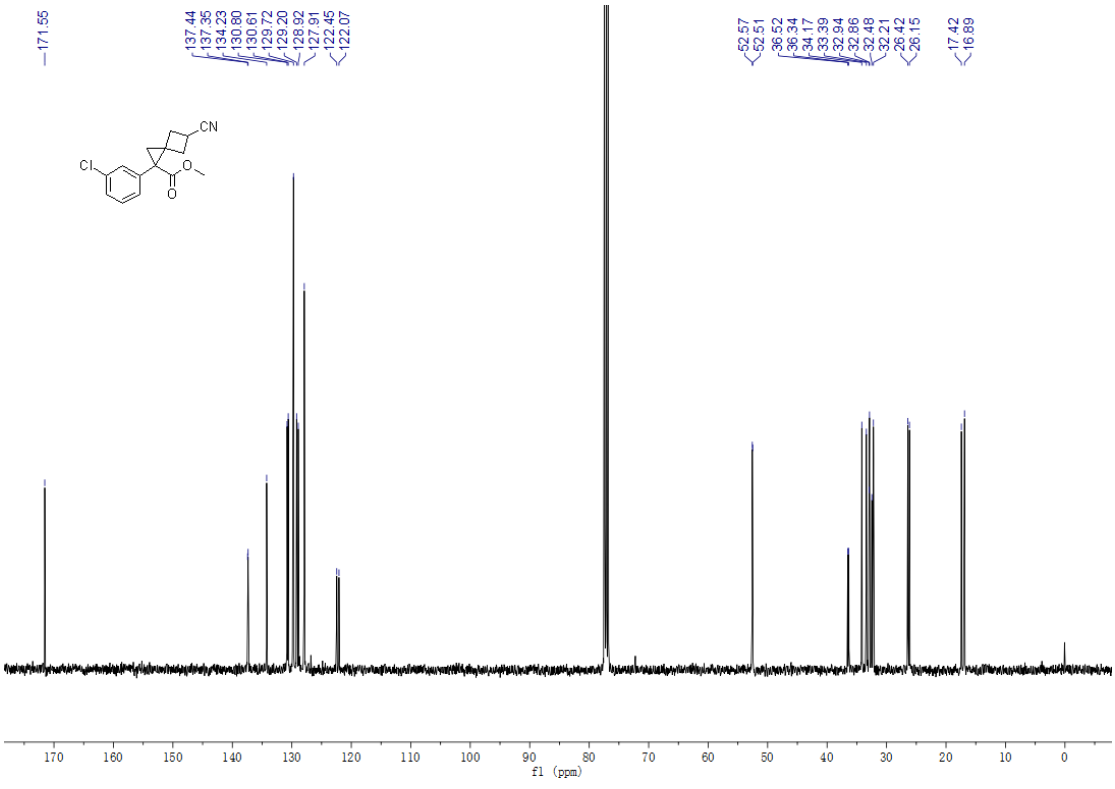
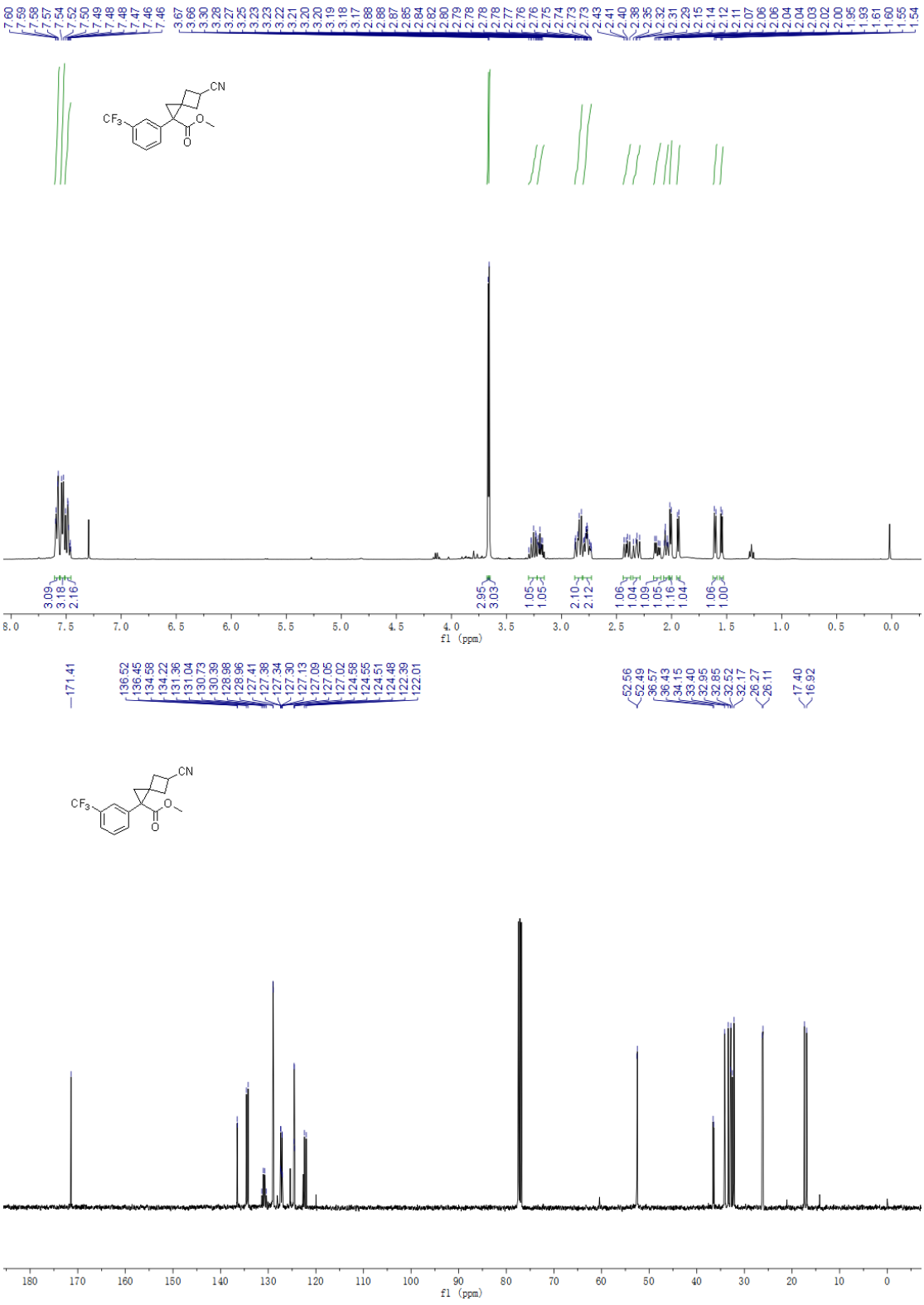
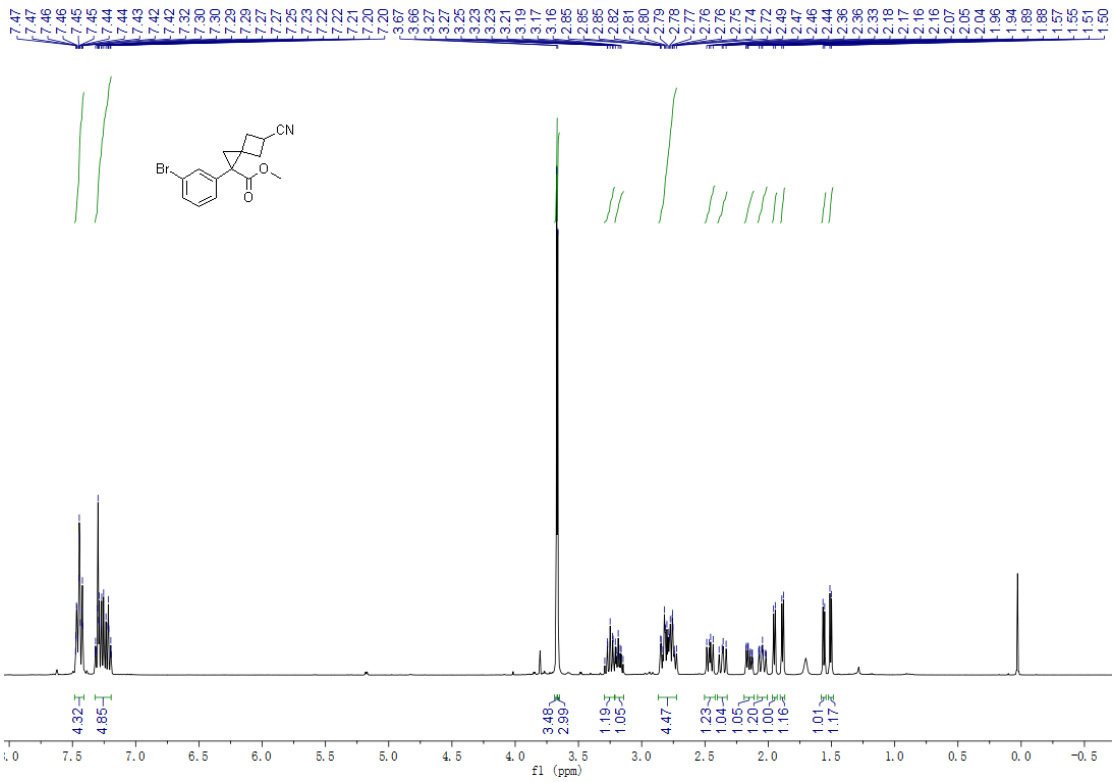
f1 (ppm)


171.55
137.44 137.35 134.23 130.80 130.61 129.72 129.20 128.92 127.91 122.45 122.07
52.57 52.51 36.52 36.34 34.17 33.39 32.94 32.86 32.48 32.21 26.42 26.15 17.42 16.89
CN
Cl
O
O
f1 (ppm)


CN
CF3
O
O
f1 (ppm)
f1 (ppm)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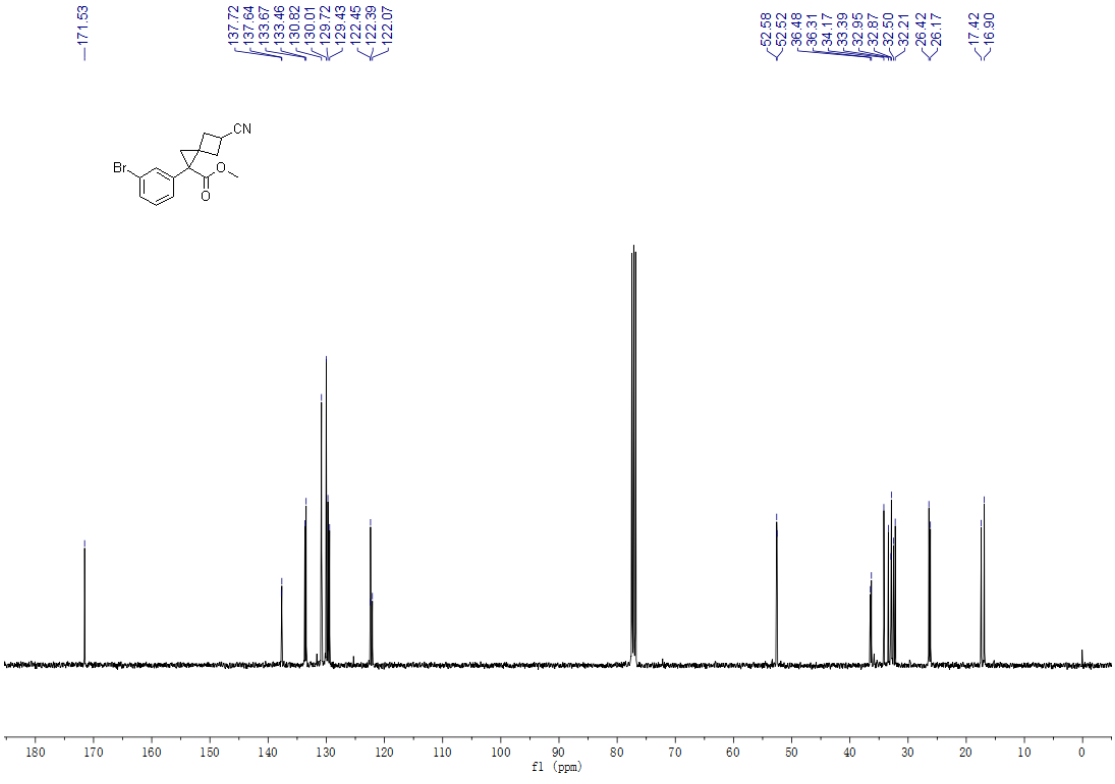
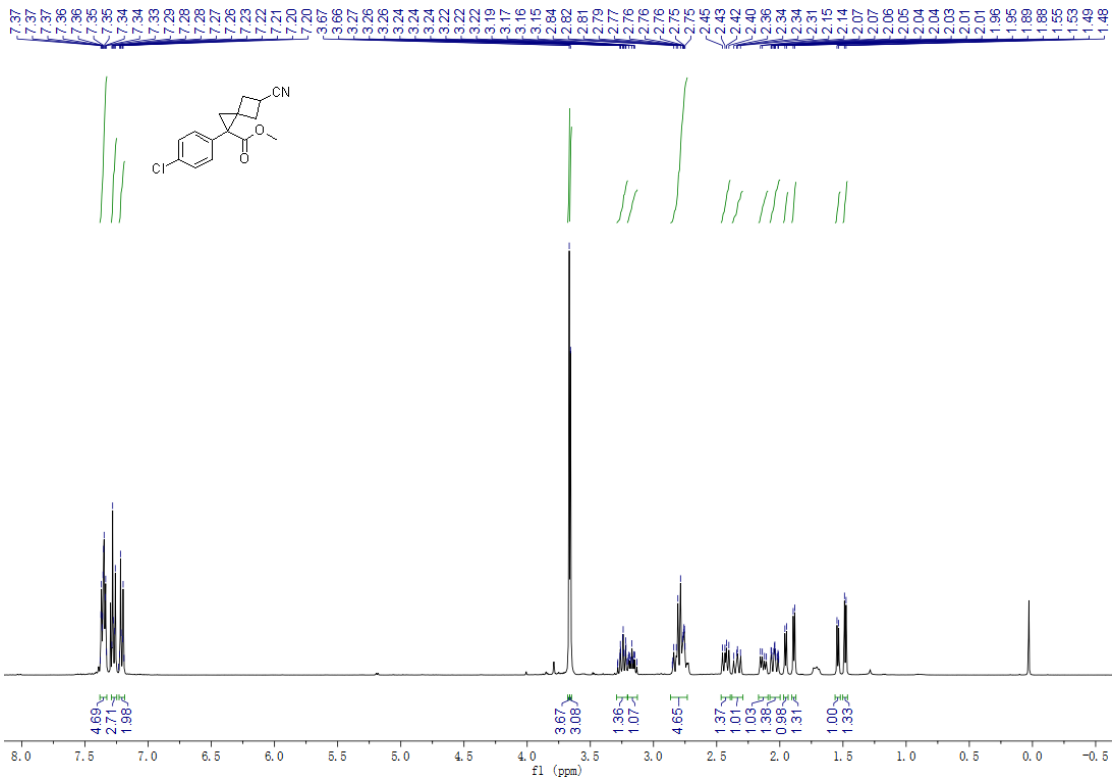
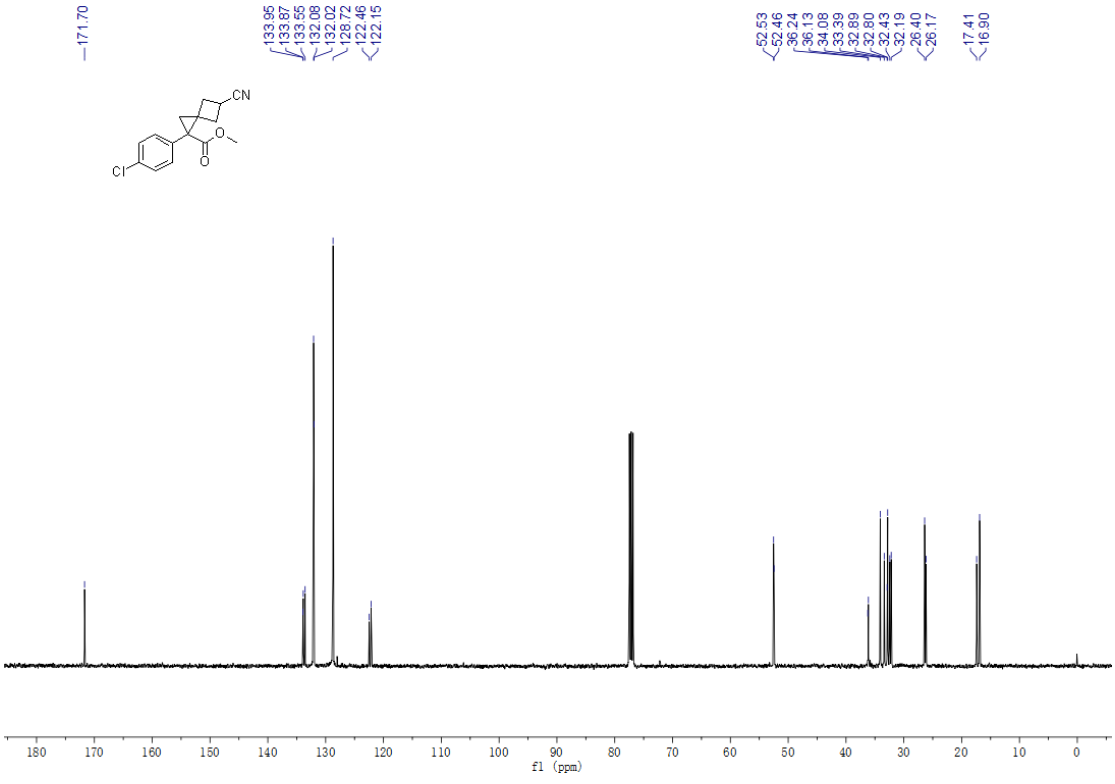
Br
O
O
f1 (ppm)


CN
Br
O
O
f1 (ppm)


7.37 7.37 7.36 7.36 7.35 7.35 7.34 7.34 7.33 7.29 7.28 7.27 7.26 7.23 7.22 7.21 7.20 7.20 3.67 3.66 3.27 3.26 3.26 3.24 3.24 3.24 3.22 3.22 3.19 3.17 3.16 3.15 2.84 2.82 2.81 2.79 2.77 2.76 2.76 2.76 2.75 2.75 2.45 2.43 2.42 2.40 2.36 2.34 2.34 2.31 2.15 2.14 2.07 2.07 2.06 2.05 2.04 2.04 2.03 2.01 2.01 1.96 1.95 1.89 1.88 1.55 1.53 1.49 1.48
CN
O
O
Cl
4.69
2.71
1.98
3.67
3.08
1.36
1.07
4.65
1.37
1.01
1.03
1.38
0.98
1.31
1.00
1.33
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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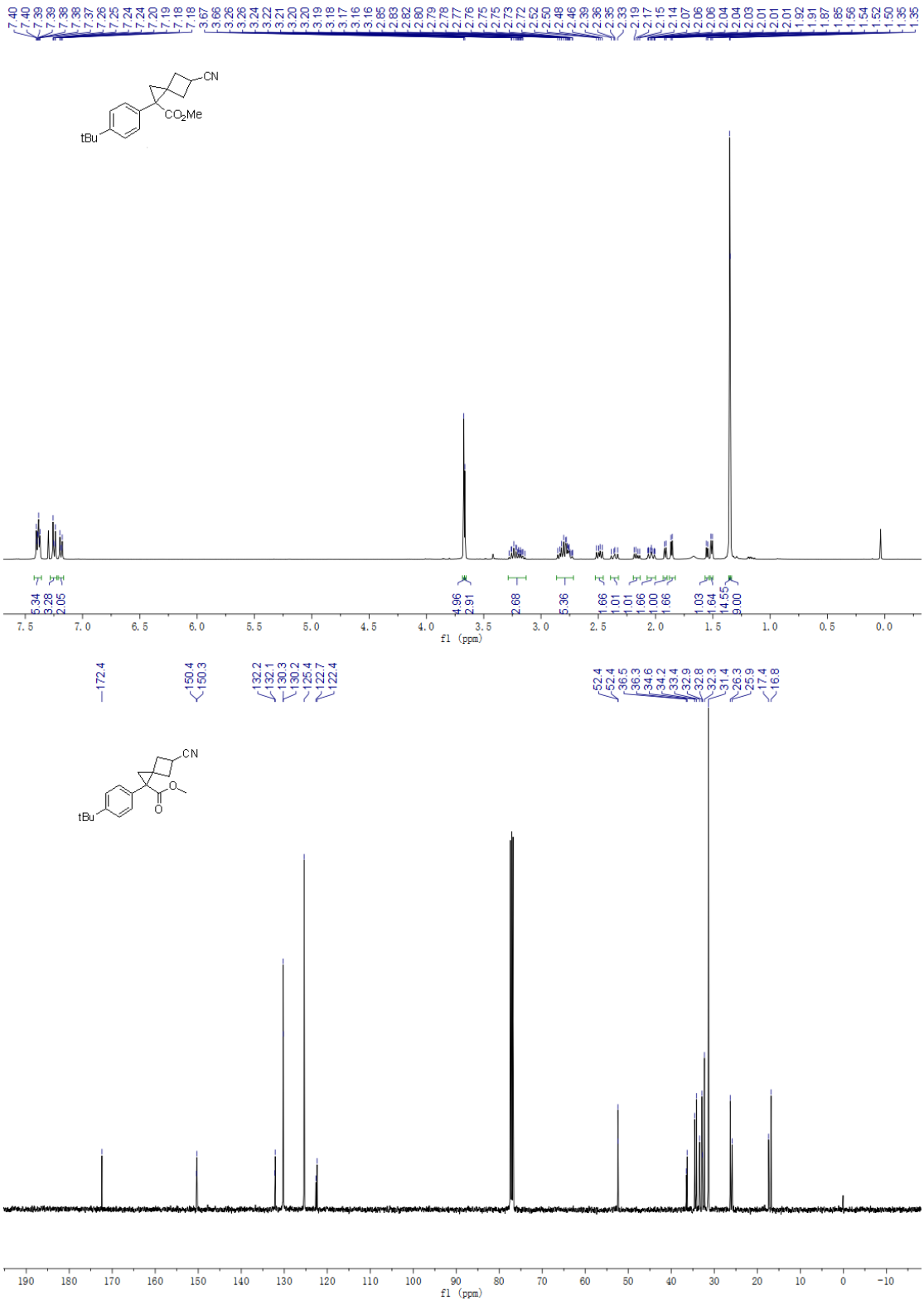
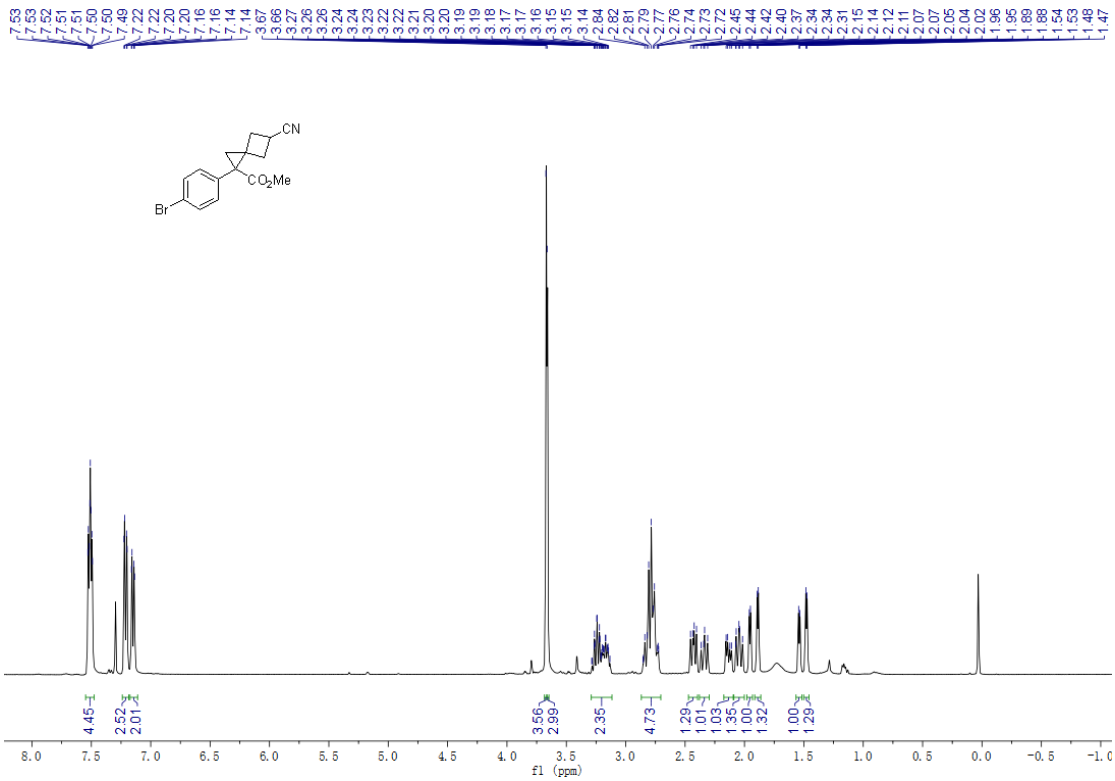
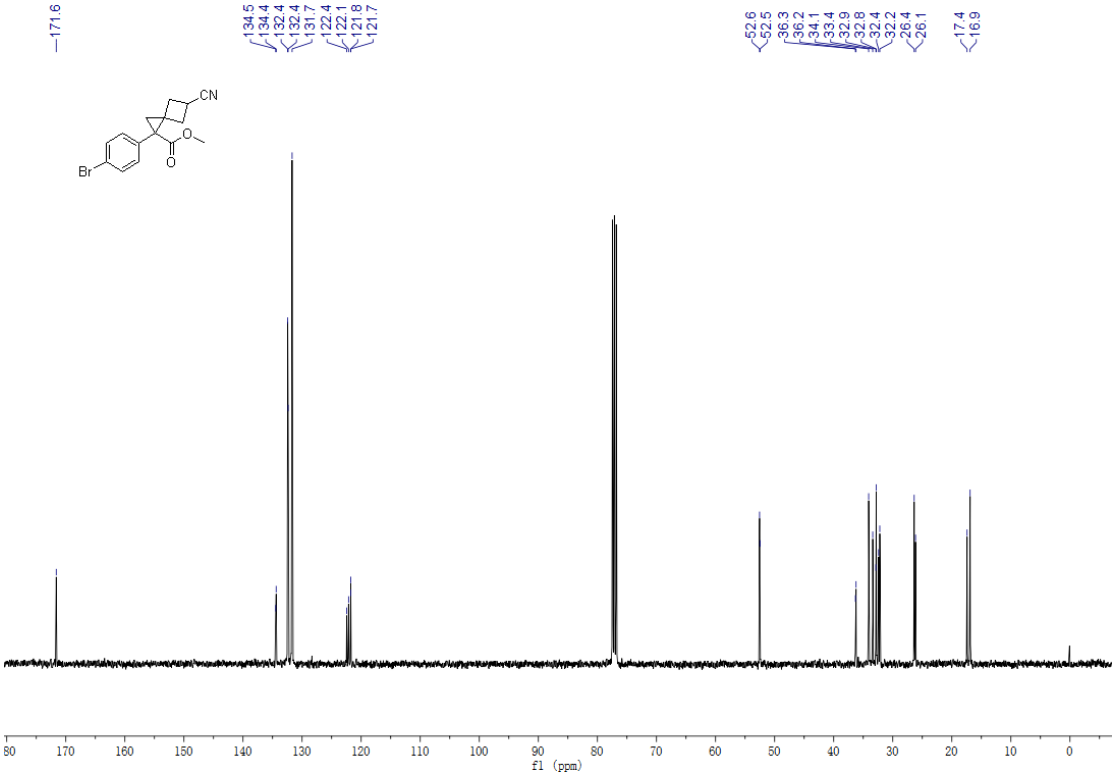
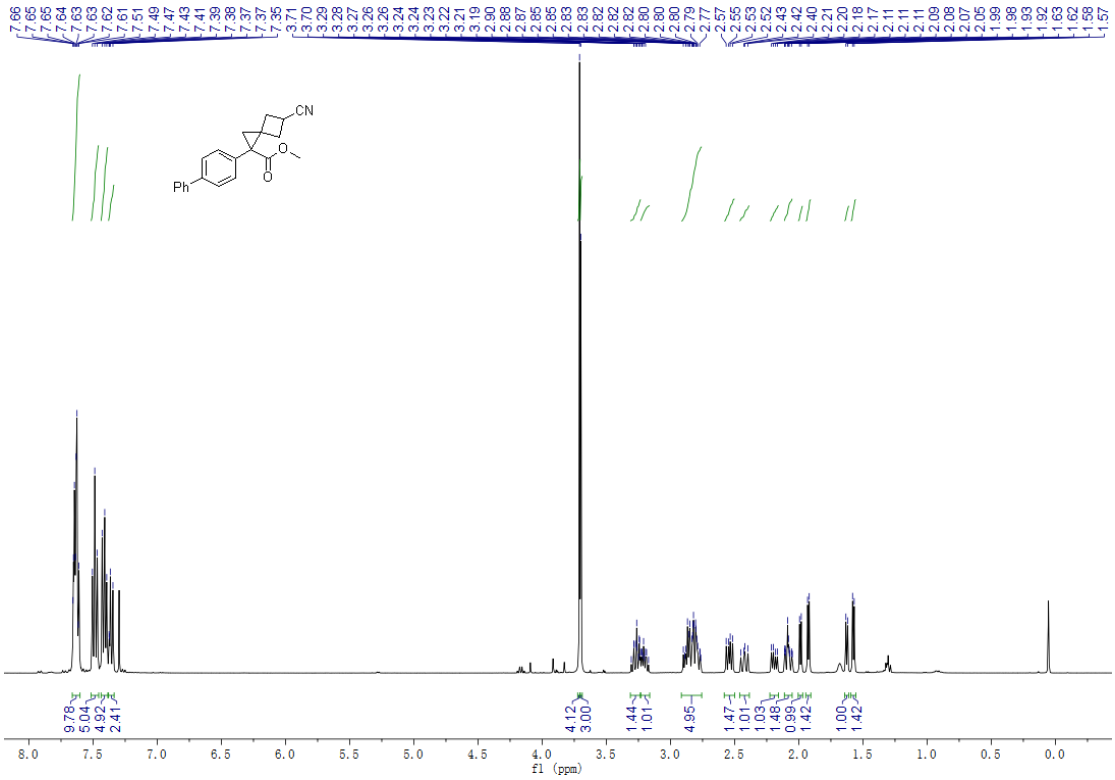
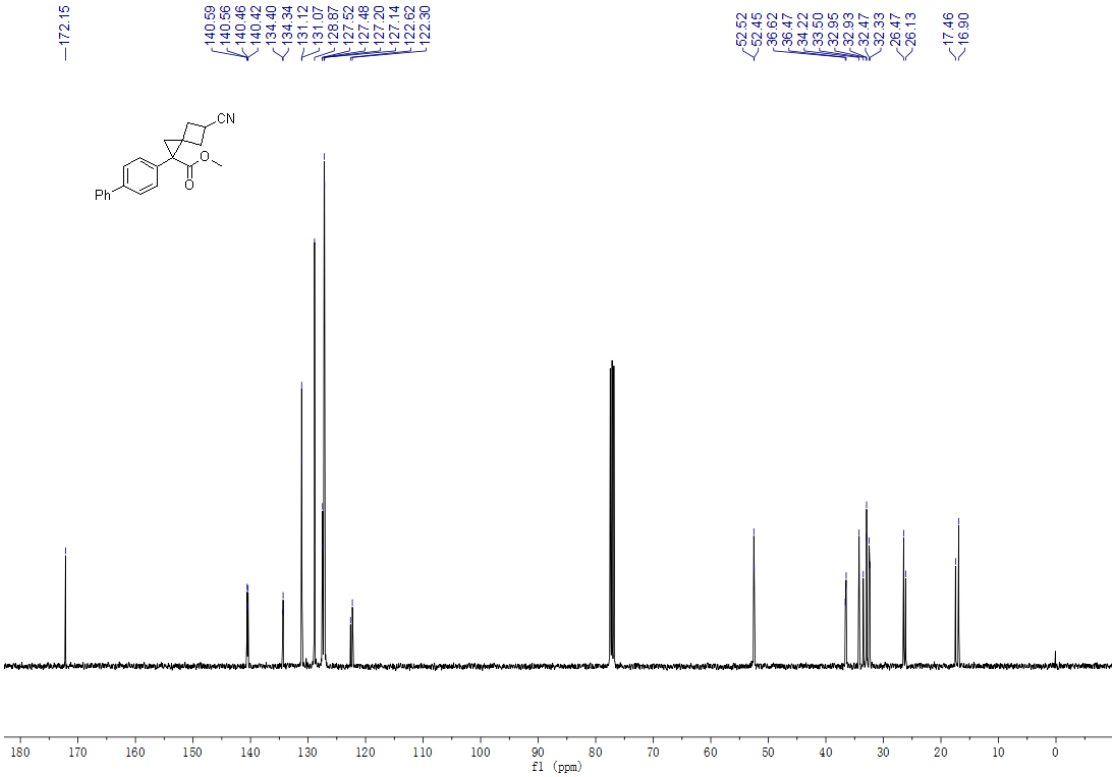
133.95
133.87
133.55
132.08
132.02
128.72
122.46
122.15
52.53
52.46
36.24
36.13
34.08
33.39
32.89
32.80
32.43
32.19
26.40
26.17
17.41
16.90
CN
O
O
Cl
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

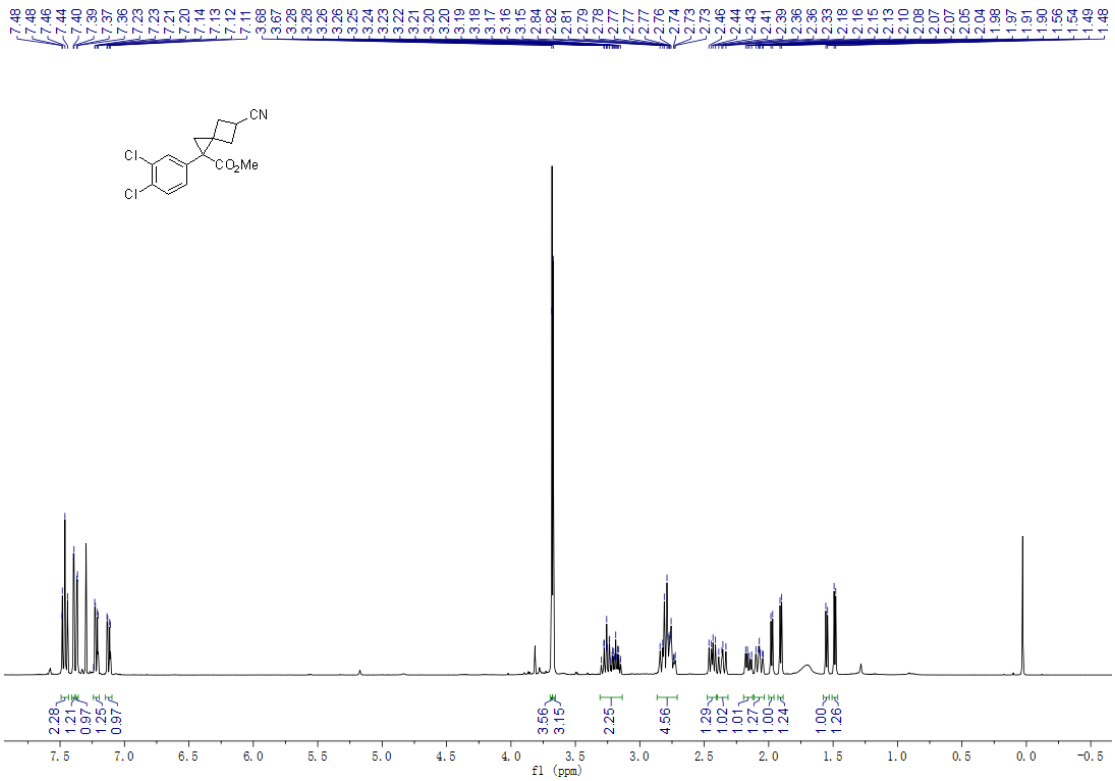

CN
CO2Me
tBu
7.40 7.40 7.39 7.39 7.38 7.38 7.37 7.26 7.25 7.24 7.24 7.20 7.19 7.18 7.18
3.67 3.66 3.26 3.26 3.24 3.22 3.21 3.20 3.20 3.19 3.18 3.17 3.16 3.16 2.85 2.83 2.82 2.80 2.79 2.78 2.77 2.76 2.75 2.75 2.73 2.72 2.52 2.50 2.48 2.46 2.39 2.36 2.35 2.33 2.19 2.17 2.15 2.14 2.07 2.06 2.04 2.04 2.03 2.01 2.01 2.01 1.92 1.91 1.87 1.85 1.56 1.54 1.52 1.50 1.35 1.35
5.34 3.28 2.05 4.96 2.91 2.68 5.36 1.66 1.01 1.01 1.00 1.00 1.66 1.03 1.64 14.55 9.00
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
f1 (ppm)
172.4
150.4 150.3
132.2 132.1 130.3 130.2 125.4 122.7 122.4
52.4 52.4 36.5 36.3 34.6 34.2 33.4 32.9 32.8 32.3 31.4 26.3 25.9 17.4 16.8
CN
O
O
tBu
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

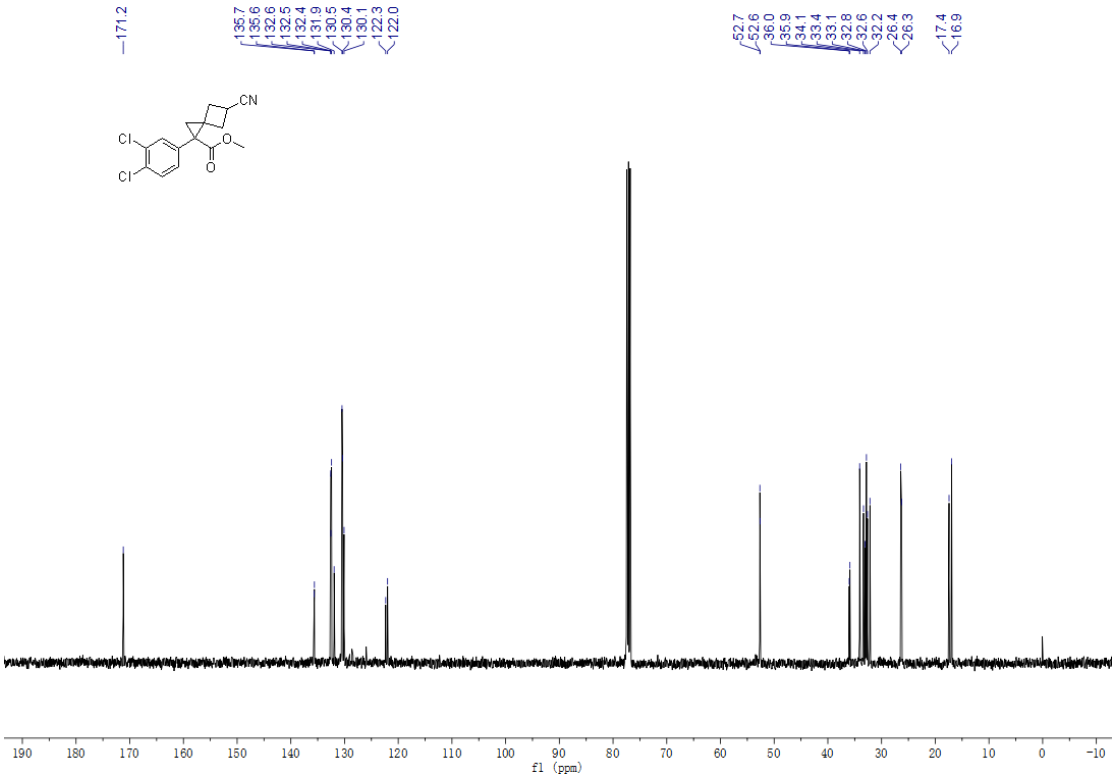

CN
CO2Me
Br
f1 (ppm)

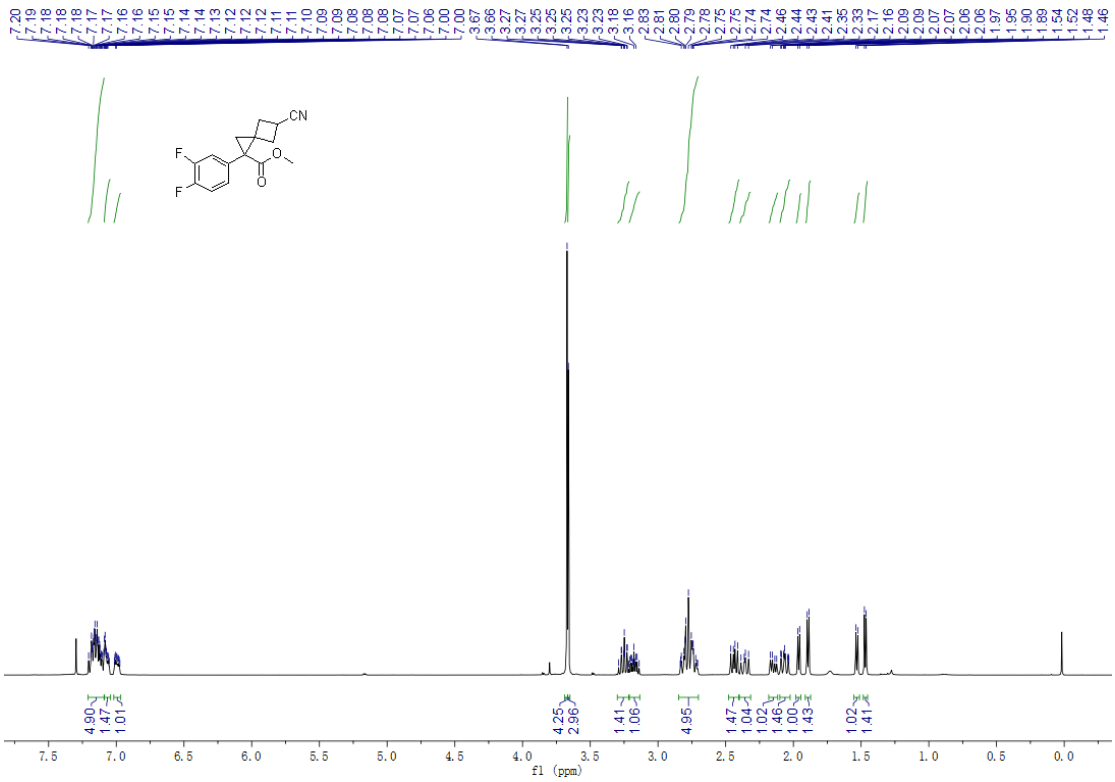

CN
O
O
Br
f1 (ppm)

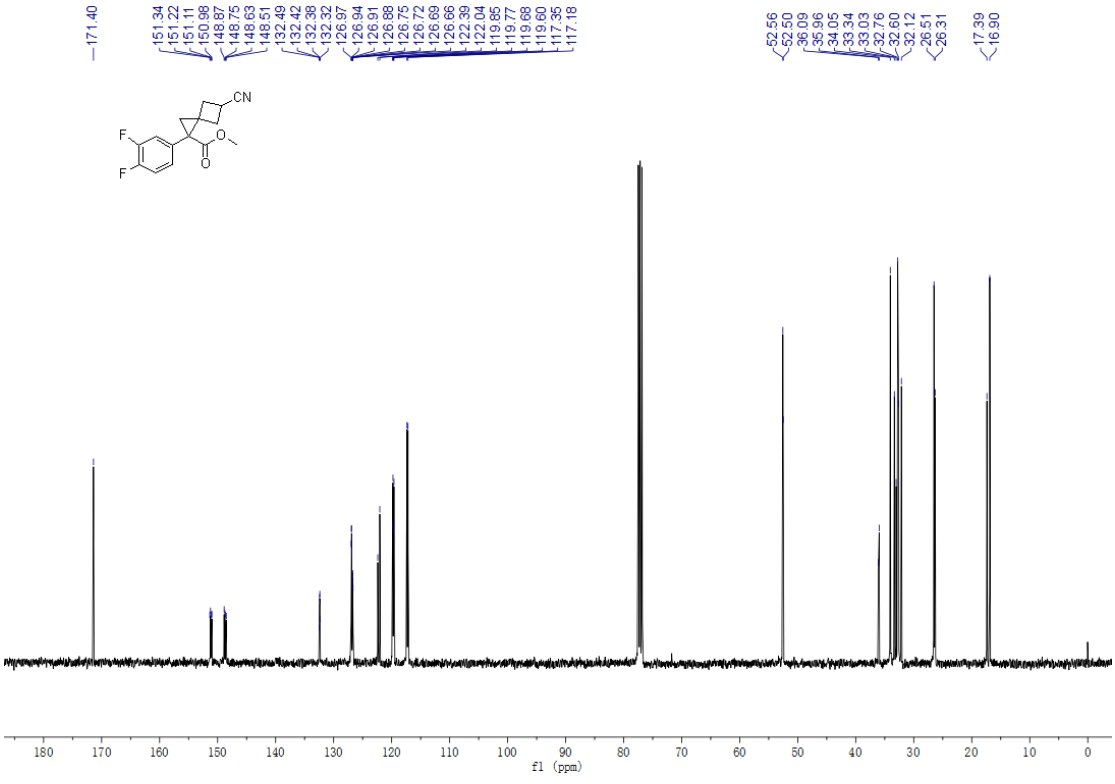

CN
Ph
O
O
f1 (ppm)

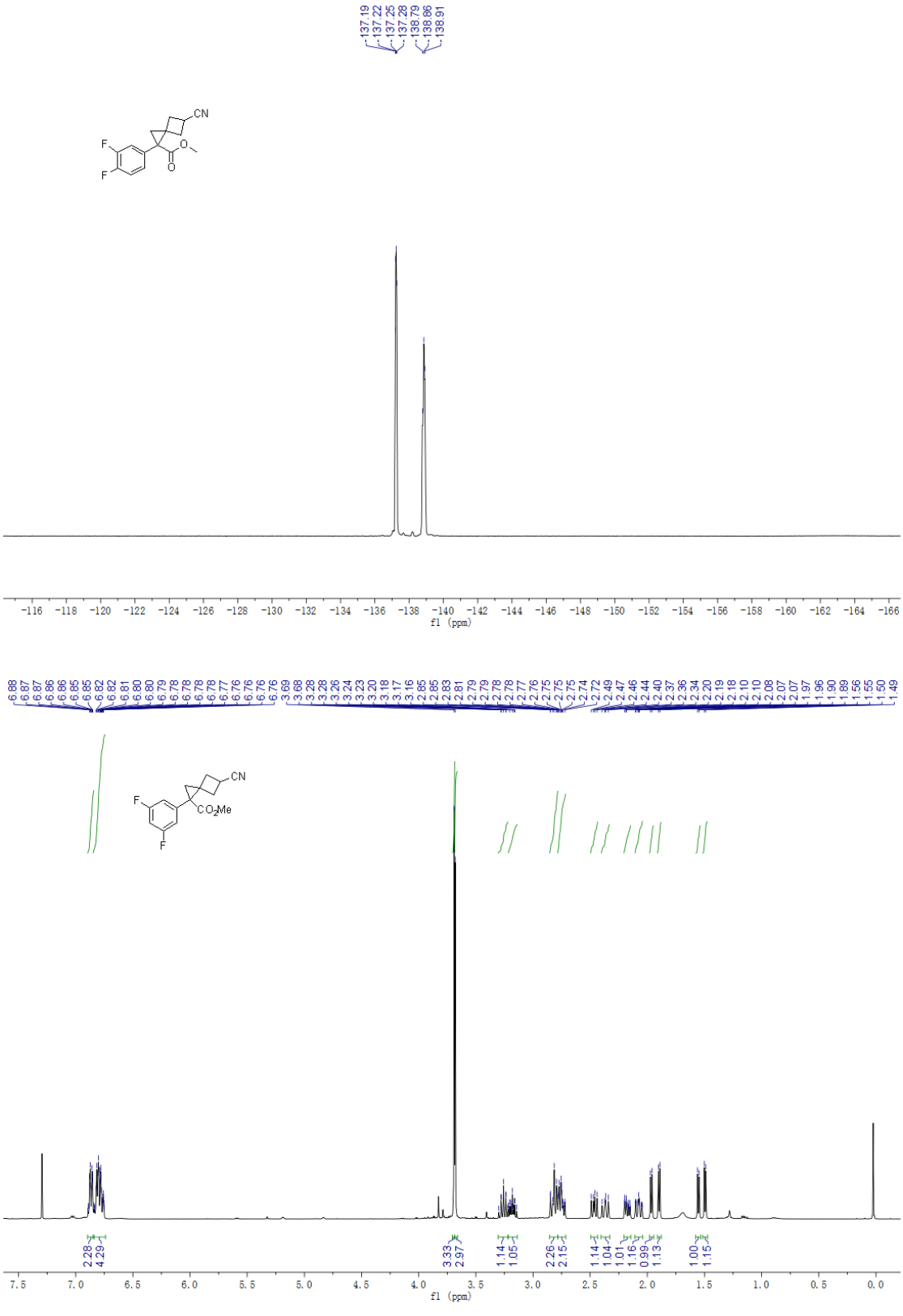

CN
Ph
O
O
f1 (ppm)

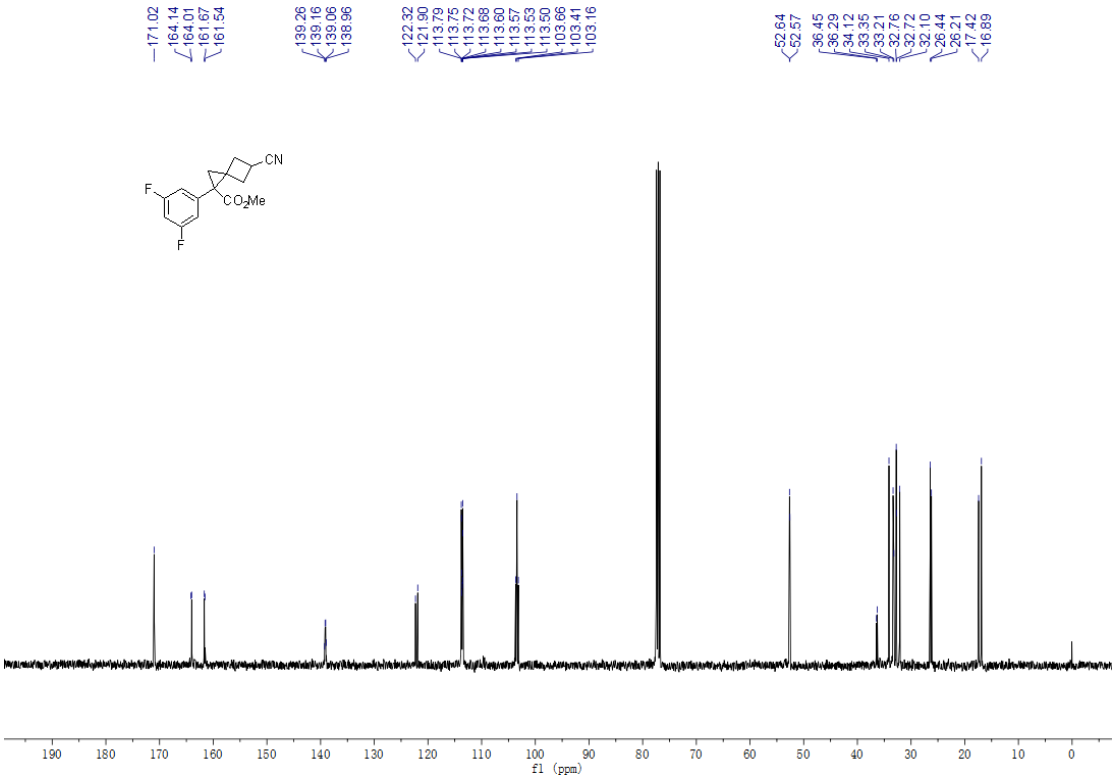

CN
Cl
Cl
CO2Me
f1 (ppm)


CN
Cl
Cl
O
O
f1 (ppm)


7.20 7.19 7.18 7.18 7.18 7.17 7.17 7.16 7.16 7.15 7.15 7.14 7.14 7.13 7.12 7.12 7.11 7.11 7.10 7.09 7.09 7.08 7.08 7.07 7.07 7.06 7.00 7.00
3.67 3.66 3.27 3.25 3.25 3.23 3.23 3.18 3.16 2.83 2.81 2.80 2.79 2.78 2.75 2.75 2.74 2.74 2.46 2.44 2.43 2.41 2.35 2.33 2.17 2.16 2.09 2.09 2.07 2.07 2.06 2.06 1.97 1.95 1.90 1.89 1.54 1.52 1.48 1.46
CN
F
F
O
O
4.90 1.47 1.01 4.25 2.96 1.41 1.06 4.95 1.47 1.04 1.02 1.46 1.00 1.43 1.02 1.41
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
f1 (ppm)


171.40
151.34 151.22 151.11 150.98 148.87 148.75 148.63 148.51 132.49 132.42 132.38 132.32 126.97 126.94 126.91 126.88 126.75 126.72 126.69 126.66 122.39 122.04 119.85 119.77 119.68 119.60 117.35 117.18
52.56 52.50 36.09 35.96 34.05 33.34 33.03 32.76 32.60 32.12 26.51 26.31 17.39 16.90
CN
F
F
O
O
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


137.19
137.22
137.25
137.28
138.79
138.86
138.91
CN
F
F
O
O
-116 -118 -120 -122 -124 -126 -128 -130 -132 -134 -136 -138 -140 -142 -144 -146 -148 -150 -152 -154 -156 -158 -160 -162 -164 -166
f1 (ppm)
CN
F
F
CO2Me
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
f1 (ppm)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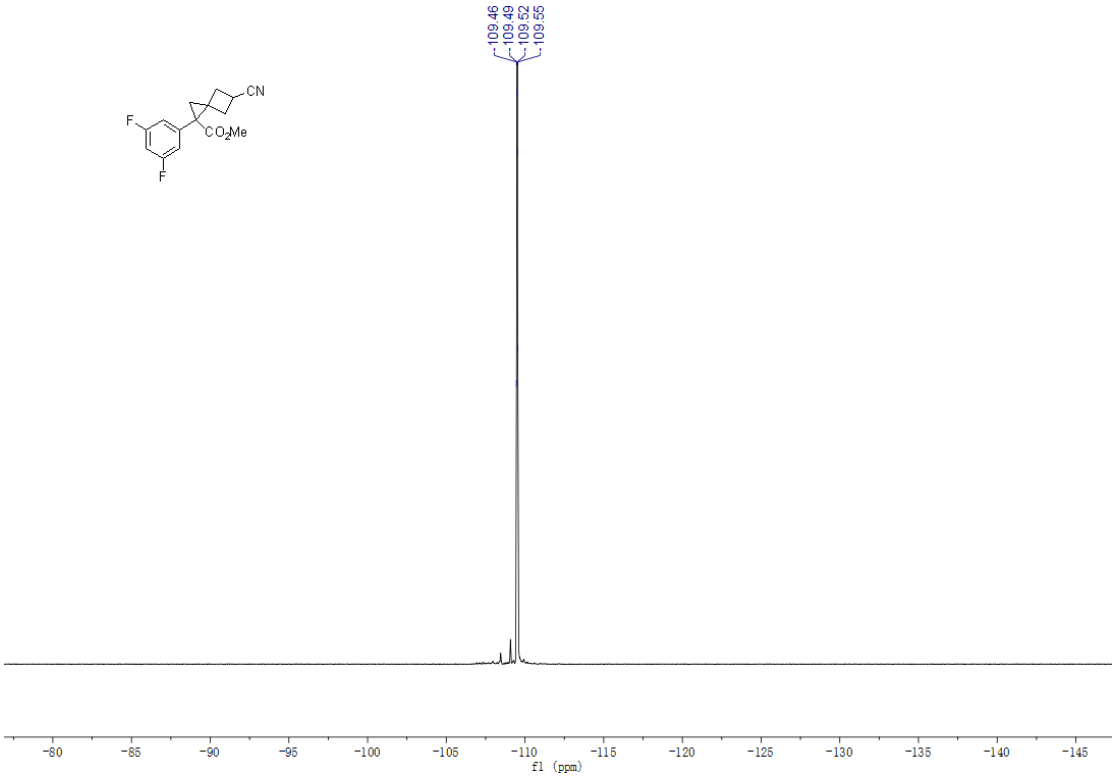
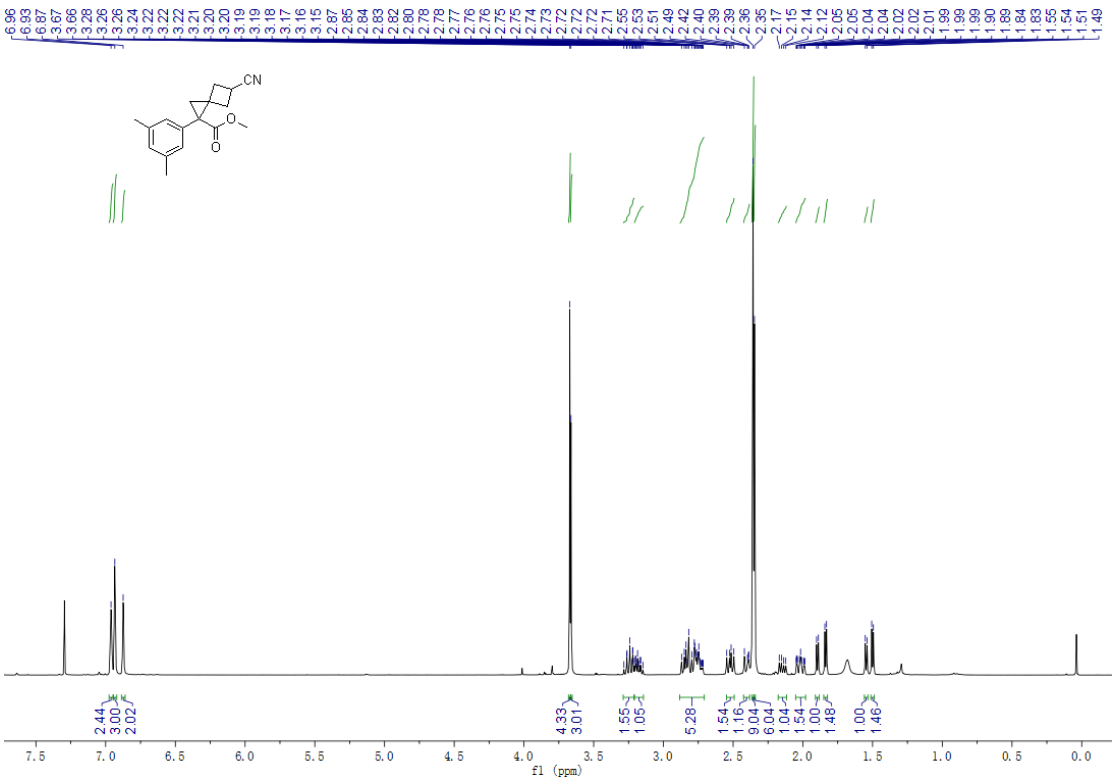
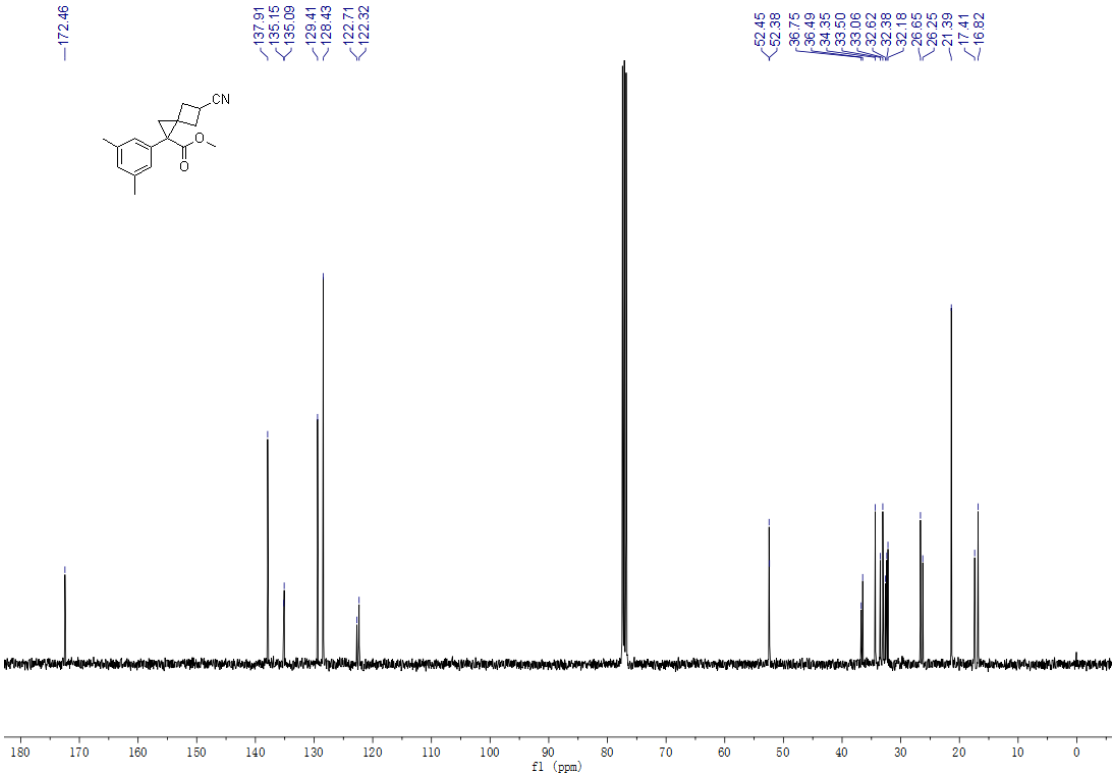
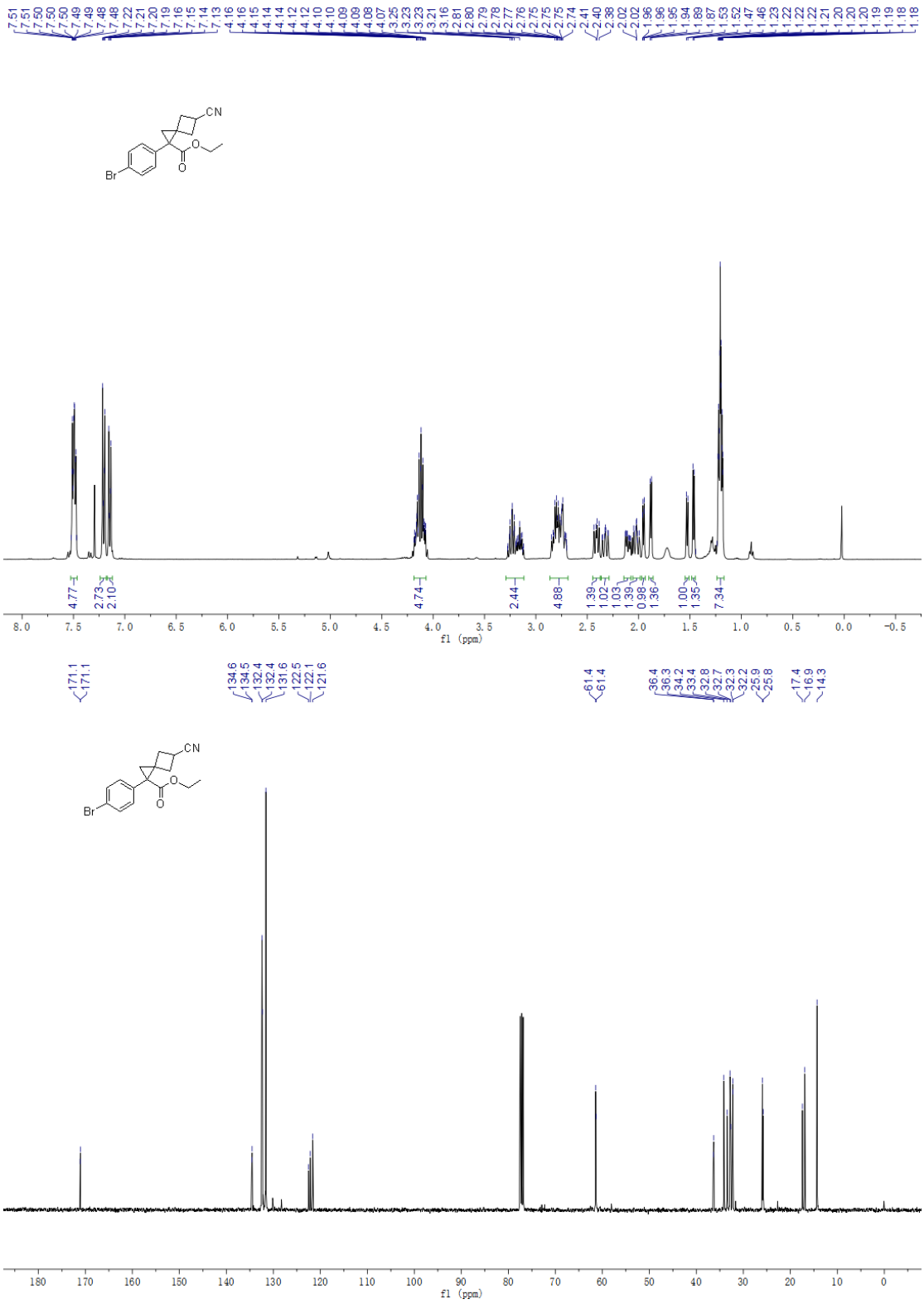
164.14
164.01
161.67
161.54
139.26
139.16
139.06
138.96
122.32
121.90
113.79
113.75
113.72
113.68
113.60
113.57
113.53
113.50
103.66
103.41
103.16
52.64
52.57
36.45
36.29
34.12
33.35
33.21
32.76
32.72
32.10
26.44
25.21
17.42
16.89
CN
F
CO2Me
F
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


109.46
109.49
109.52
109.55
CN
F
CO2Me
F
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
-140
-145
f1 (ppm)


CN
O
O
f1 (ppm)


CN
O
O
f1 (ppm)


CN
Br
O
O
4.77
2.73
2.10
4.74
2.44
4.88
1.39
1.02
1.03
0.98
1.36
1.00
1.35
7.34
f1 (ppm)
171.1
171.1
134.6
134.5
132.4
132.4
131.6
122.5
122.1
121.6
61.4
61.4
36.4
36.3
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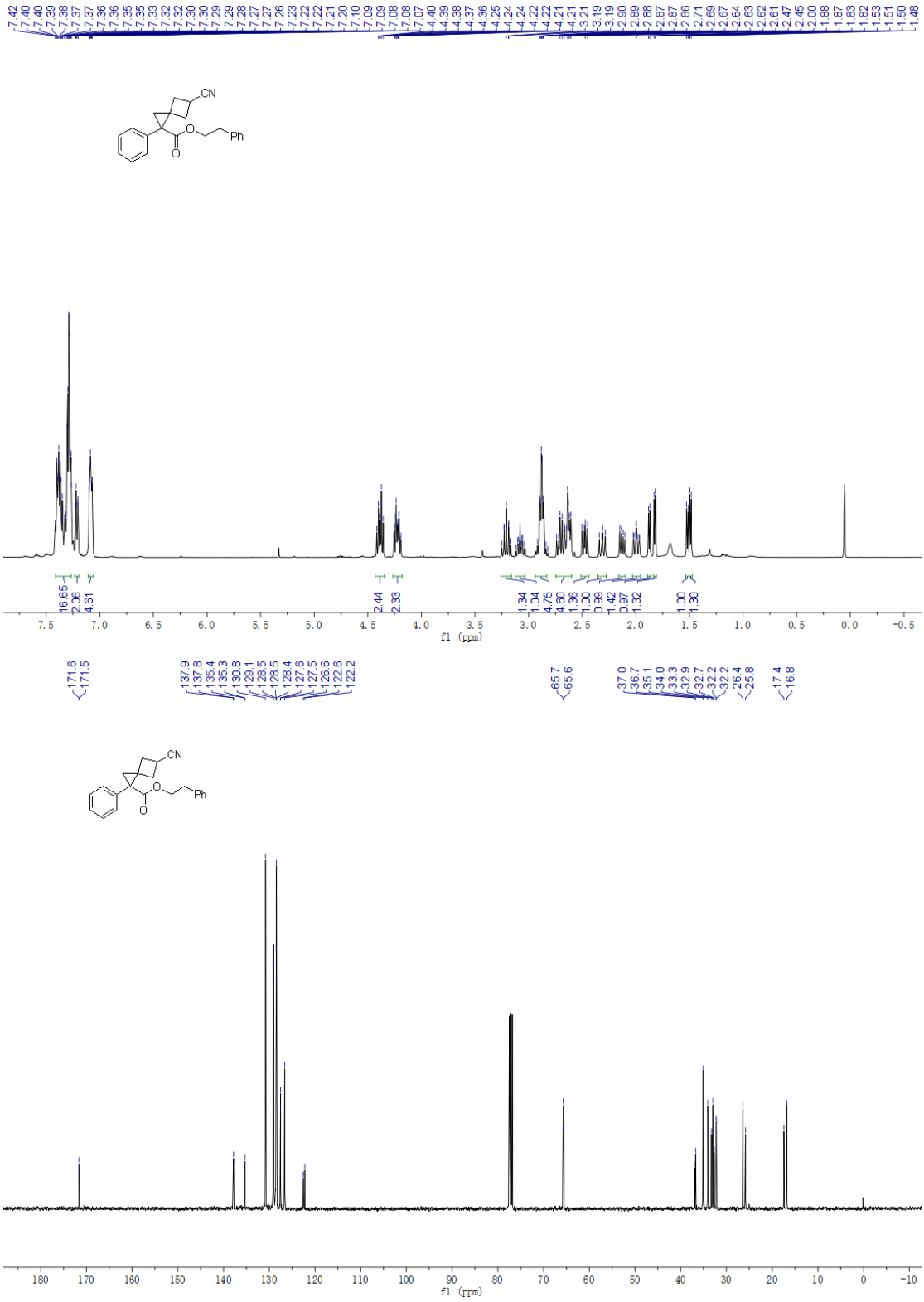
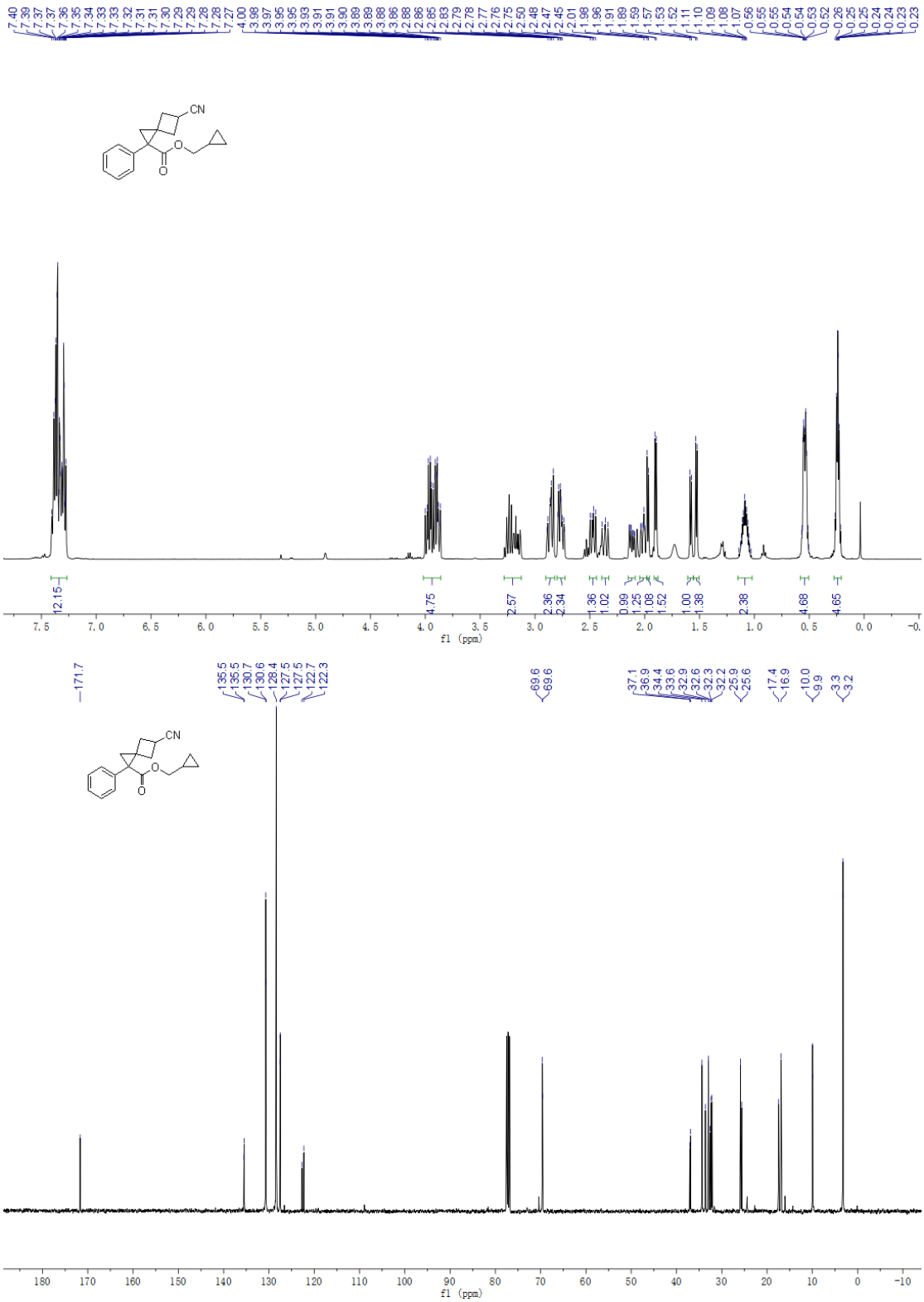
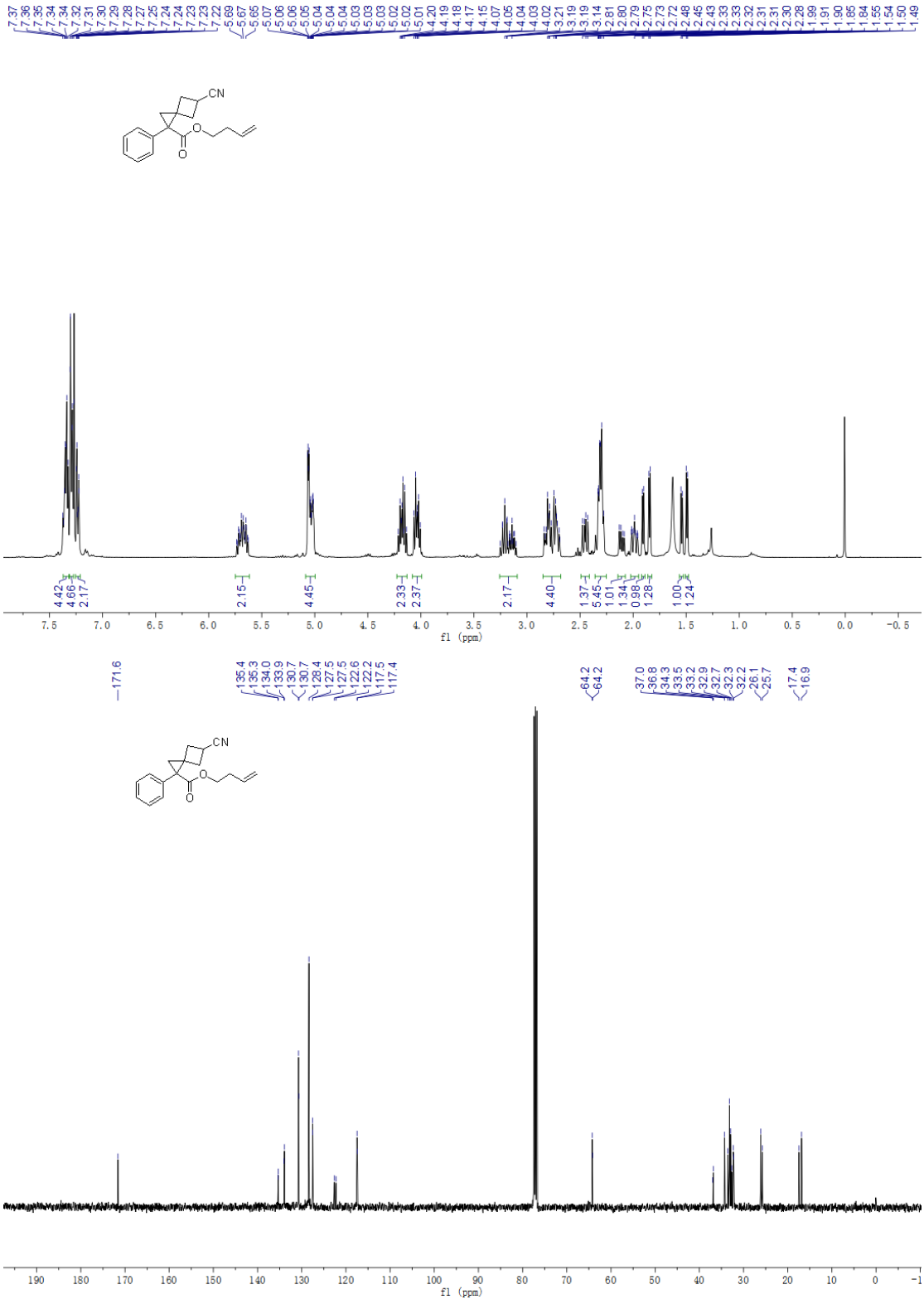
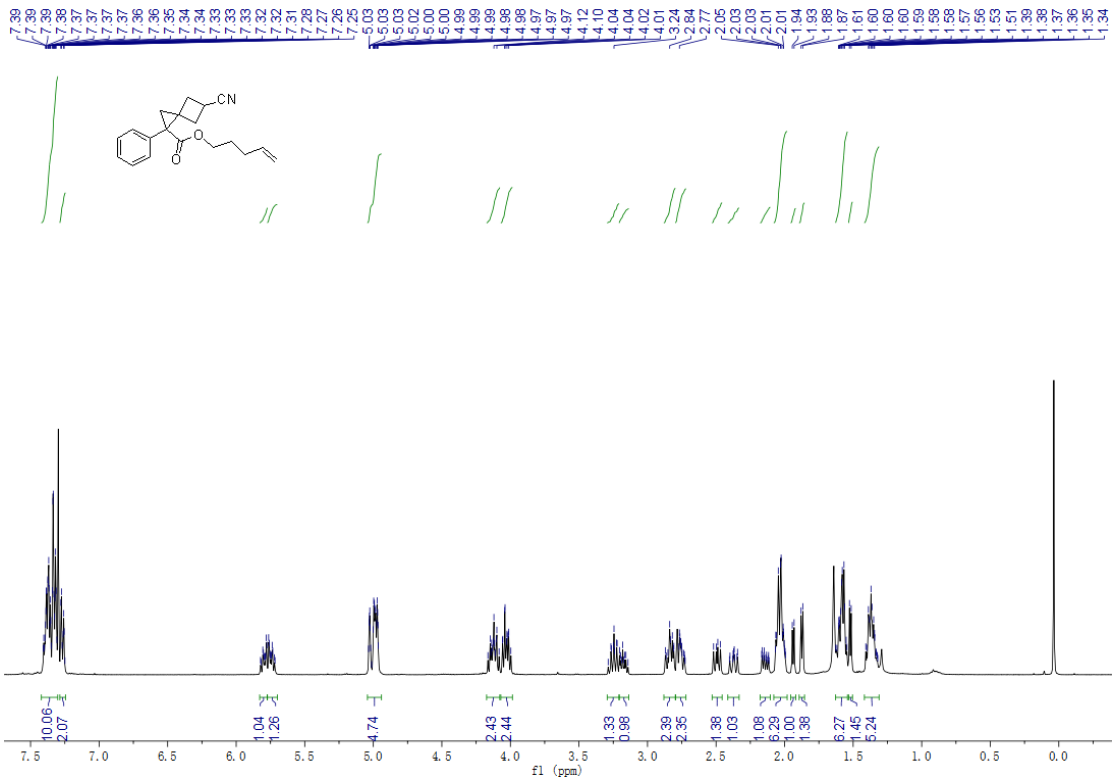
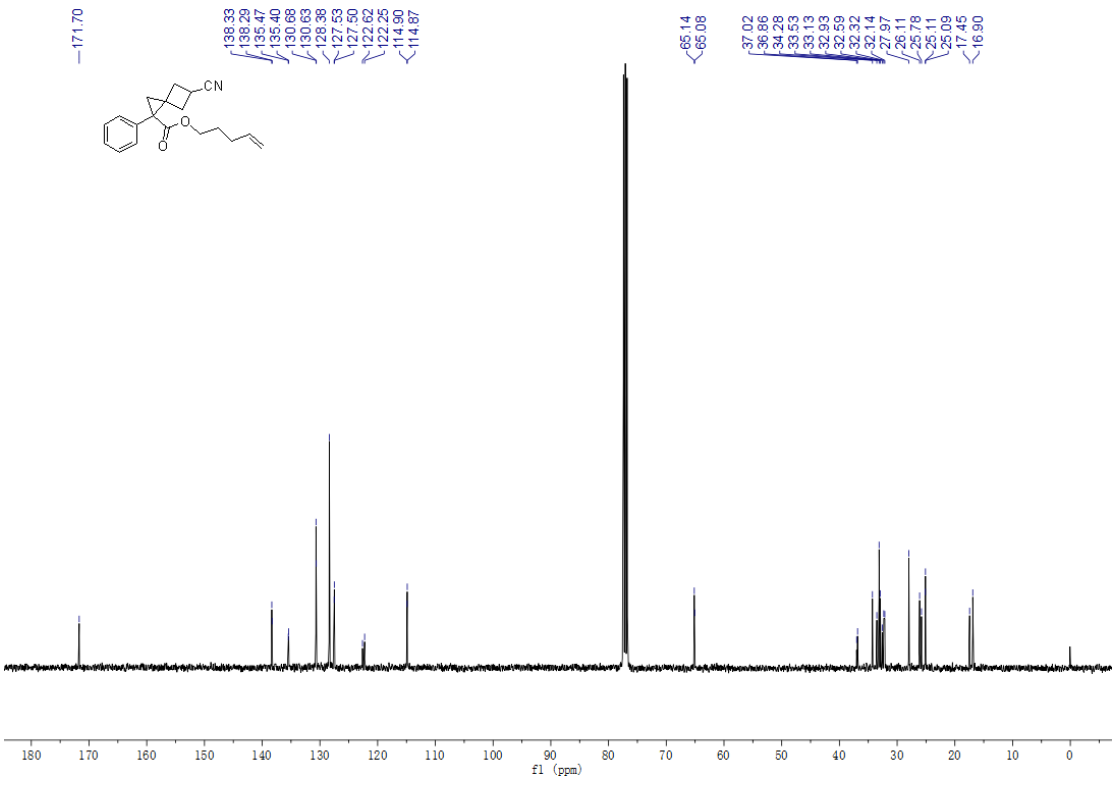
25.9
25.8
17.4
16.9
14.3
f1 (ppm)


CN
O
O
Ph
7.42 7.40 7.40 7.39 7.38 7.37 7.37 7.36 7.36 7.35 7.35 7.33 7.32 7.32 7.30 7.30 7.29 7.29 7.28 7.27 7.27 7.26 7.23 7.22 7.22 7.21 7.20 7.10 7.09 7.09 7.08 7.08 7.08 7.07 4.40 4.39 4.38 4.37 4.36 4.25 4.24 4.24 4.22 4.22 4.21 4.21 3.21 3.19 3.19 2.90 2.89 2.88 2.87 2.87 2.86 2.71 2.69 2.67 2.64 2.63 2.62 2.61 2.47 2.45 2.00 1.88 1.87 1.83 1.82 1.53 1.51 1.50 1.48
16.65 2.06 4.61 2.44 2.33 1.34 1.04 4.75 4.60 1.36 1.00 0.99 1.42 0.97 1.32 1.00 1.30
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)
171.6 171.5 137.9 137.8 135.4 135.3 130.8 129.1 128.5 128.5 128.4 127.6 127.5 126.6 122.6 122.2 65.7 65.6 37.0 36.7 35.1 34.0 33.3 32.9 32.7 32.2 32.2 26.4 25.8 17.4 16.8
CN
O
O
Ph
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


CN
O
O
f1 (ppm)
CN
O
O
f1 (ppm)


CN
O
O
f1 (ppm)
CN
O
O
f1 (ppm)


7.39 7.39 7.39 7.38 7.37 7.37 7.37 7.37 7.36 7.36 7.35 7.34 7.34 7.33 7.33 7.33 7.32 7.32 7.31 7.28 7.27 7.26 7.25
5.03 5.03 5.02 5.00 5.00 4.99 4.99 4.98 4.98 4.97 4.97 4.97 4.12 4.10 4.04 4.04 4.02 4.01 3.24 2.84 2.77 2.05 2.03 2.01 2.01 1.94 1.93 1.88 1.87 1.61 1.60 1.60 1.60 1.59 1.58 1.58 1.57 1.56 1.53 1.51 1.39 1.38 1.37 1.36 1.35 1.34
CN
O
O
10.06 2.07 1.04 1.26 4.74 2.43 2.44 1.33 0.98 2.39 2.35 1.38 1.03 1.08 6.29 1.00 1.38 6.27 1.45 5.24
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
f1 (ppm)


171.70
138.33 138.29 135.47 135.40 130.68 130.63 128.38 127.53 127.50 122.62 122.25 114.90 114.87
65.14 65.08
37.02 36.86 34.28 33.53 33.13 32.93 32.59 32.32 32.14 27.97 26.11 25.78 25.11 25.09 17.45 16.90
CN
O
O
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)