Supporting Information for:

Palladium-Catalyzed Synthesis of 4-Cyclohexylmorpholines from Reductive Coupling of Aryl Ethers and Lignin Model Compounds with Morpholines

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Experimental Section

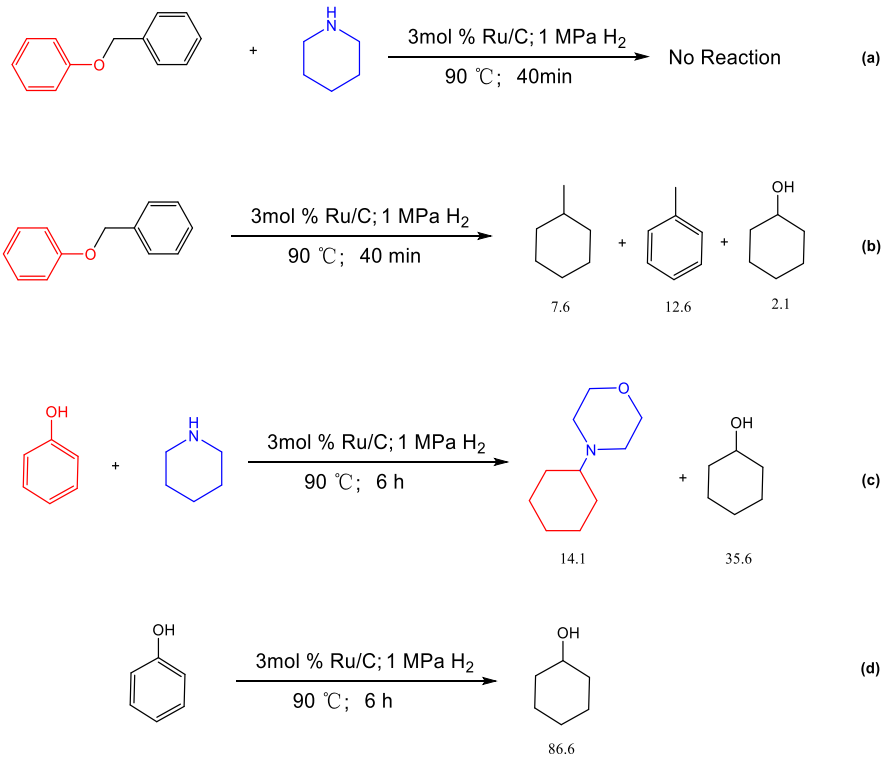
Materials. Benzyl phenyl ether (>98%), morpholine (99%), cyclohexanol (>98.5%), ruthenium on carbon (Ru/C, 5 wt% Ru, reduced, nominally 50% water wet), phenethoxybenzene (98%), and *m*-xylene (>99%) were purchased from Aladdin. Phenol (99.5%), *n*-dodecane (99.5%), and cyclohexanone (99%) were achieved from TCI. Methylmorpholine (97%), 2,2-dimethylmorpholine (97%), *(R)*-3-methylmorpholine (97%), and *(S)*-3-methylmorpholine (97%) were purchased from ARK. *cis*-2,6-Dimethylmorpholine (97%) was achieved from Alfa. Palladium on carbon (Pd/C, 10 wt% Pd, reduced, anhydrous), platinum on carbon (Pt/C, 10 wt% Pt, reduced, anhydrous), and palladium(II) 2,4-pentanedionate (34.7% Pd) were purchased from Innochem. Ethanol (99.9%) was obtained from Sinopharm. 2-Ethylmorpholine (97%) was purchased from Leyan. The compounds of 1b-1l were synthesized according to the literatures.[1,2]

Instruments. Conversion and yields were determined by a gas chromatography (Agilent 7890B) with the FID detector and a HP-5 column (30 m x 320 μm x 0.25μm). NMR data were recorded on a Bruker ARX 100 and Bruker ARX 400 spectrometers. High resolution transmission electron microscopy (HRTEM) was conducted on a Tecnai G2 F30 FETEM (FEI Corp.).

General procedures to conduct the reaction. The general procedure for the reaction of benzyl phenyl ether (1) with morpholine can be described as follows. In a 15 mL stainless steel reactor with a Teflon coating, the catalyst Pd/C (3 mol% Pd metal based on 1), aryl ether (1 mmol), morpholine (1.5 mmol), and *m*-xylene (3.5 mL) were combined and a magnetic stirring bar was added. The autoclave (15 mL) was purged three times with H_2 (1 MPa) and was then pressurized to the desired pressure with H_2. The autoclave was placed into an a constant-temperature air bath and heated to the desired temperature, and the reactions were stirred at 800 rpm for the desired reaction time. After the reaction, the products were analyzed quantitatively using *n*-dodecane as the internal standard by gas chromatography (GC) and gas chromatography coupled with mass spectroscopy (GC-MS).

General procedure for recycling experiment. To test the recyclability of Pd/C, the catalyst was separated from the reaction system by filtration, washed with ethanol for 4 times, and then dried under oven at 60 °C for 10 h. The sample was collected and

transferred into a ceramic boat, then moved to a tubular furnace for reduction under H_2/Ar atmosphere (containing 90% Ar) with a flow rate of 100 mL/min. The sample was heated with a heating rate of 10 °C min^{-1} from room temperature to 250 °C and held at this temperature for 5 h. Afterwards, the tubular furnace was cooled down to room temperature. Finally, the catalyst was used in the next catalytic cycle.



Scheme S1. Activity of Ru/C for several control experiments.

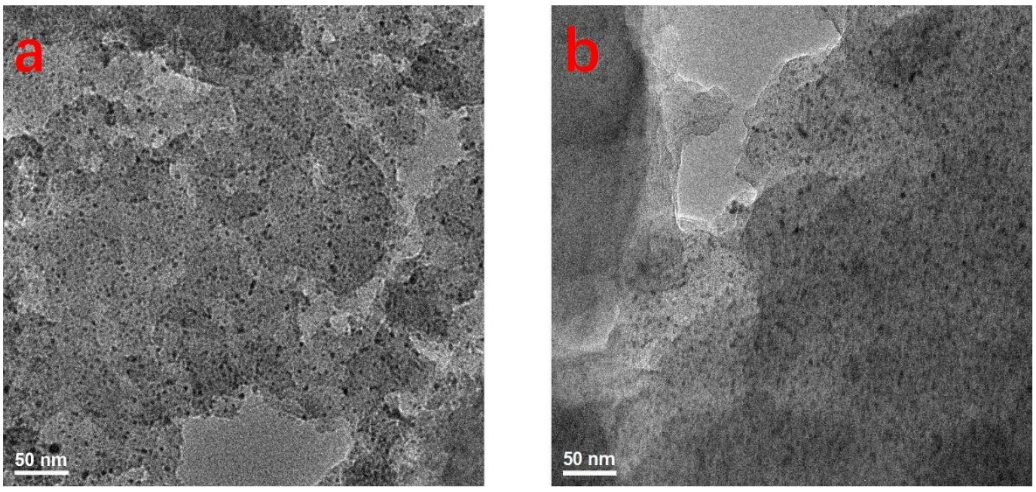
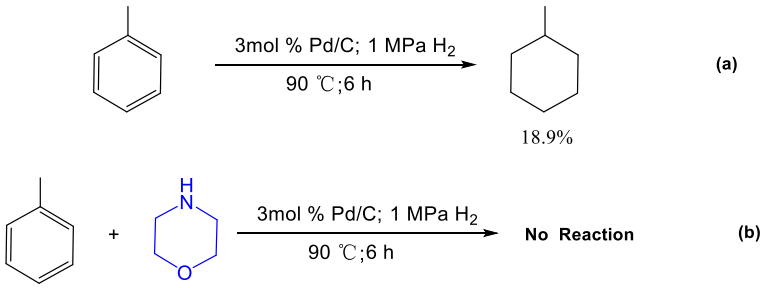
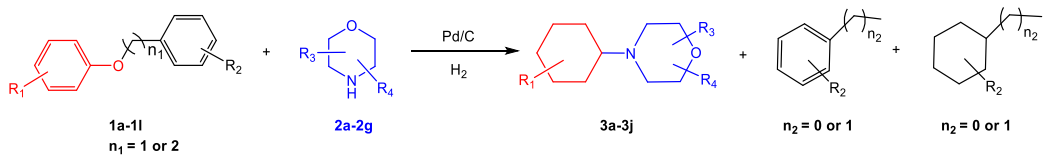


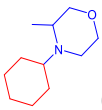
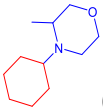
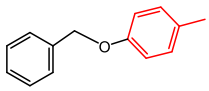
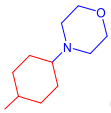
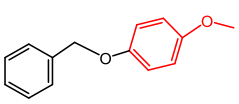
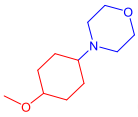
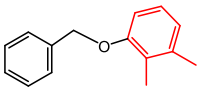
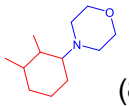
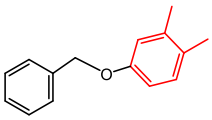
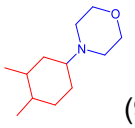
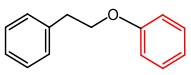
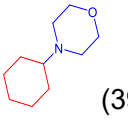
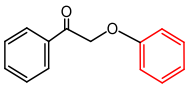
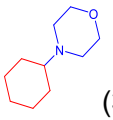
Figure S1. (a) The original Pd/C, and (b) the recycled Pd/C after three cycles (6 h).



Scheme S2. Hydrogenation of toluene.

Table S1. Pd-catalyzed reductive coupling of morpholine with benzyl aryl ethers.[a]

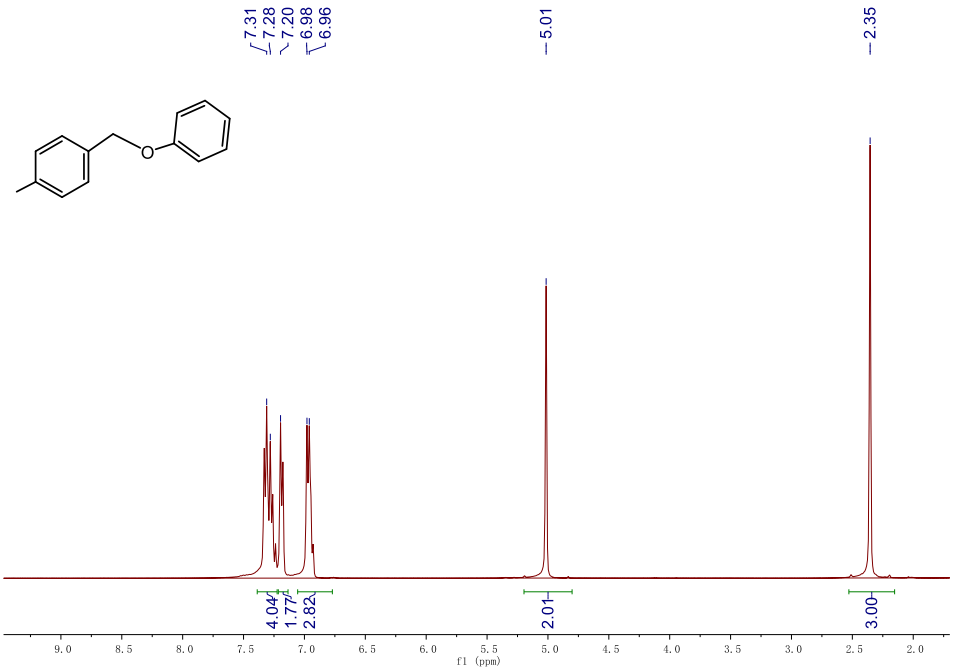


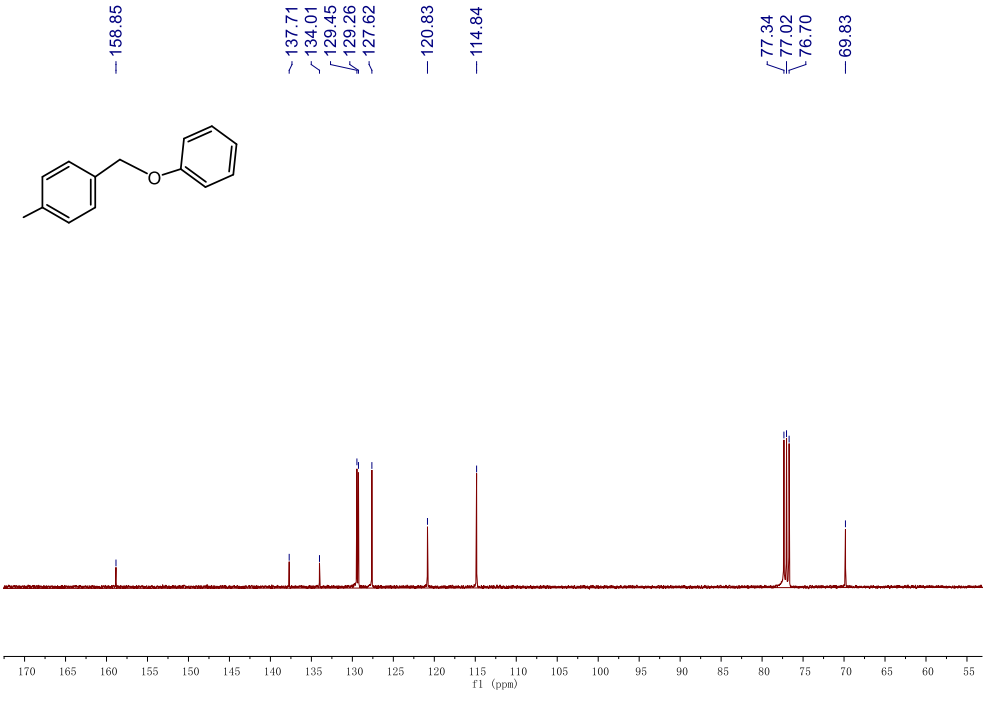
Entry	Substrates	Yield of major Products[b]		
1[c]	 2f	 (86.1)	 (87.6)	 (13.4)
2[c]	 2g	 (85.9)	 (86.0)	 (14.0)
3[d]	 1h	 (>99.0)	 (90.0)	 (9.2)
4[d]	 1i	 (99.0)	 (77.0)	 (22.0)
5[d]	 1j	 (84.7)	 (67.0)	 (17.6)
6[d]	 1k	 (96.5)	 (73.5)	 (23.5)
7[e]	 1l	 (39.4)	 (26.5)	 (8.7)
8[e]	 1m	 (35.0)	 (21.4)	 (3.4)

[a]Reaction conditions: 1, 1.0 mmol; 2, 1.5 mmol; catalyst, 3 mol% metal based on 1; *m*-xylene, 3.5 mL; H_2 pressure, 1 MPa. The aromatic ether of entry 1 and 2 was benzyl phenyl ether. The amine used in entries 3-8 was morpholine. [b]The yield were determined by GC using dodecane as a standard. [c]Reaction temperature, 120 °C; reaction time,12 h. [d]Catalyst, 6 mol% metal based on 1, reaction temperature,150 °C; H_2 pressure, 3 MPa; reaction time 12 h. [e]Catalyst, 9 mol% metal based on 1, reaction temperature, 170 °C; H_2 pressure, 3 MPa; reaction time, 24 h.

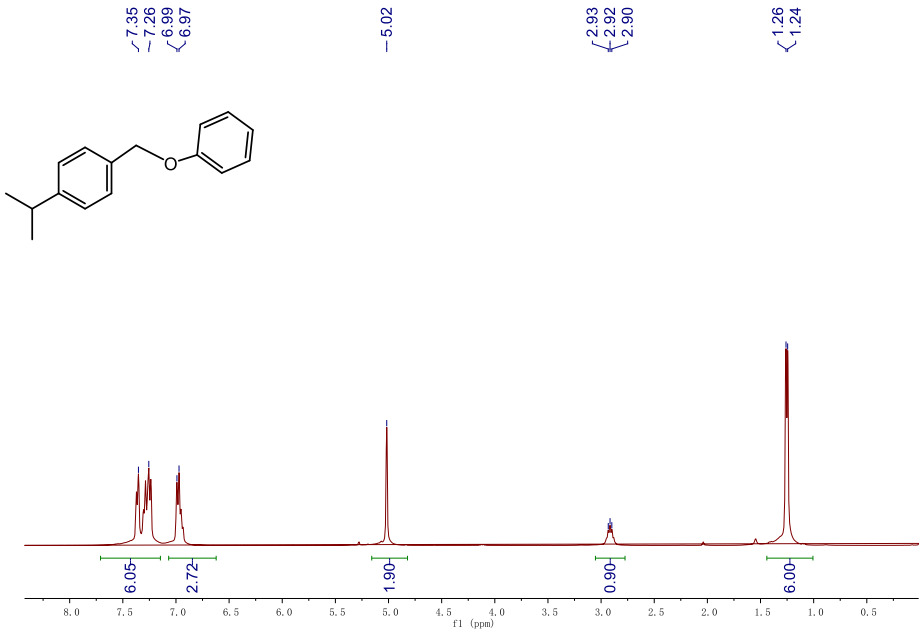
Copies of ^{1}H NMR and ^{13}C NMR

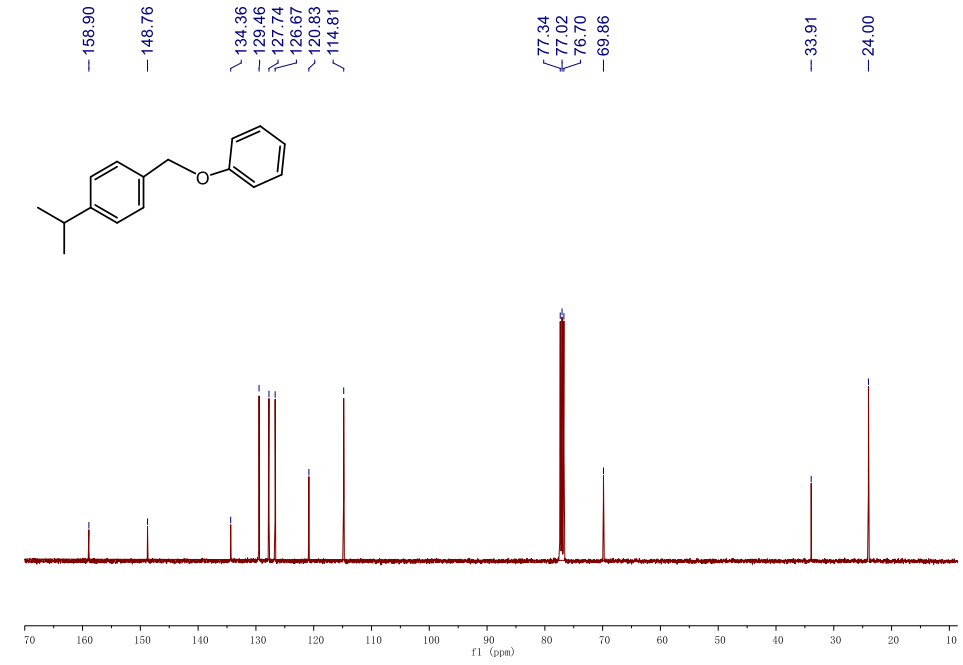
^{1}H and ^{13}C NMR spectra of compound 1b



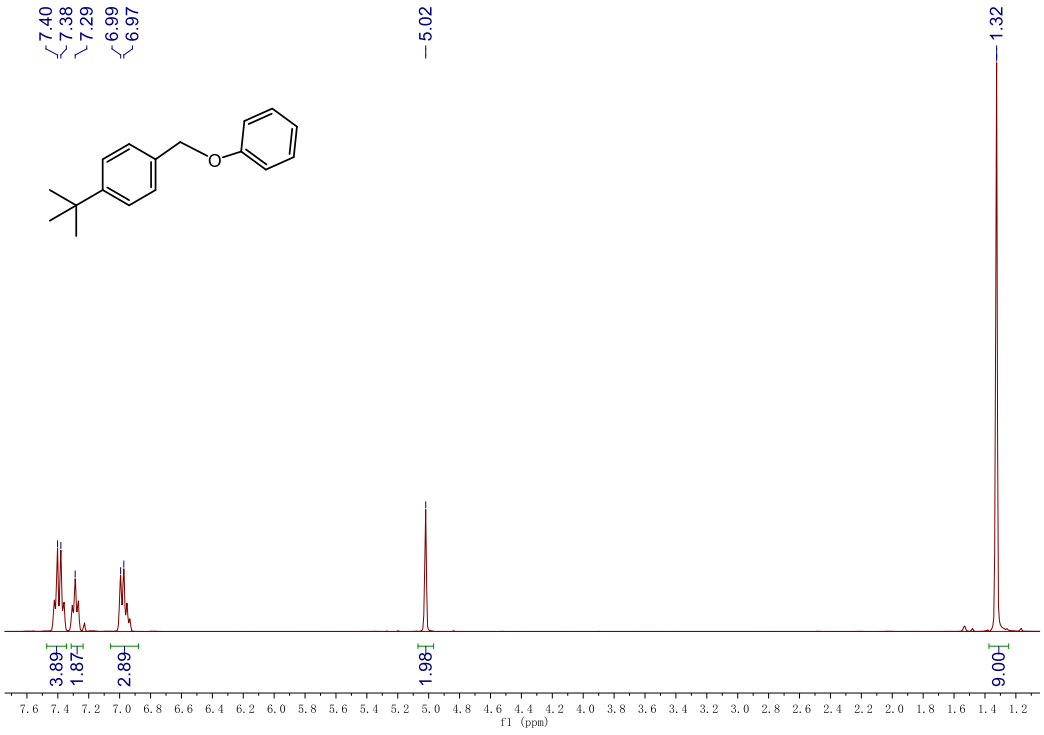


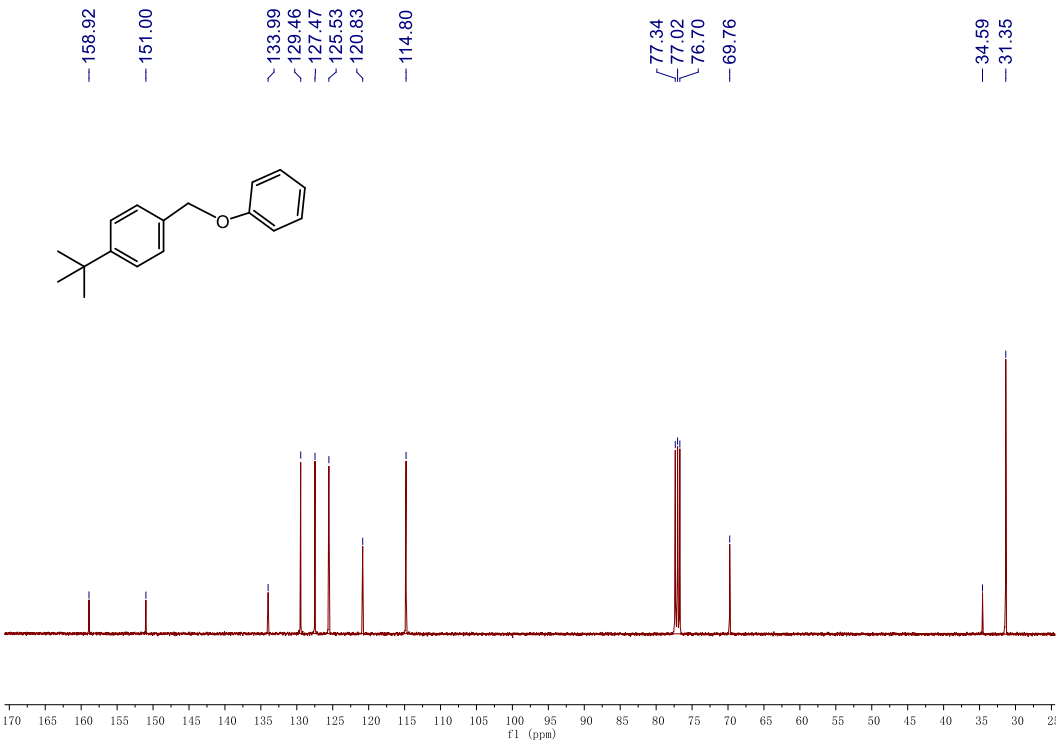
^{1}H and ^{13}C NMR spectra of compound 1c



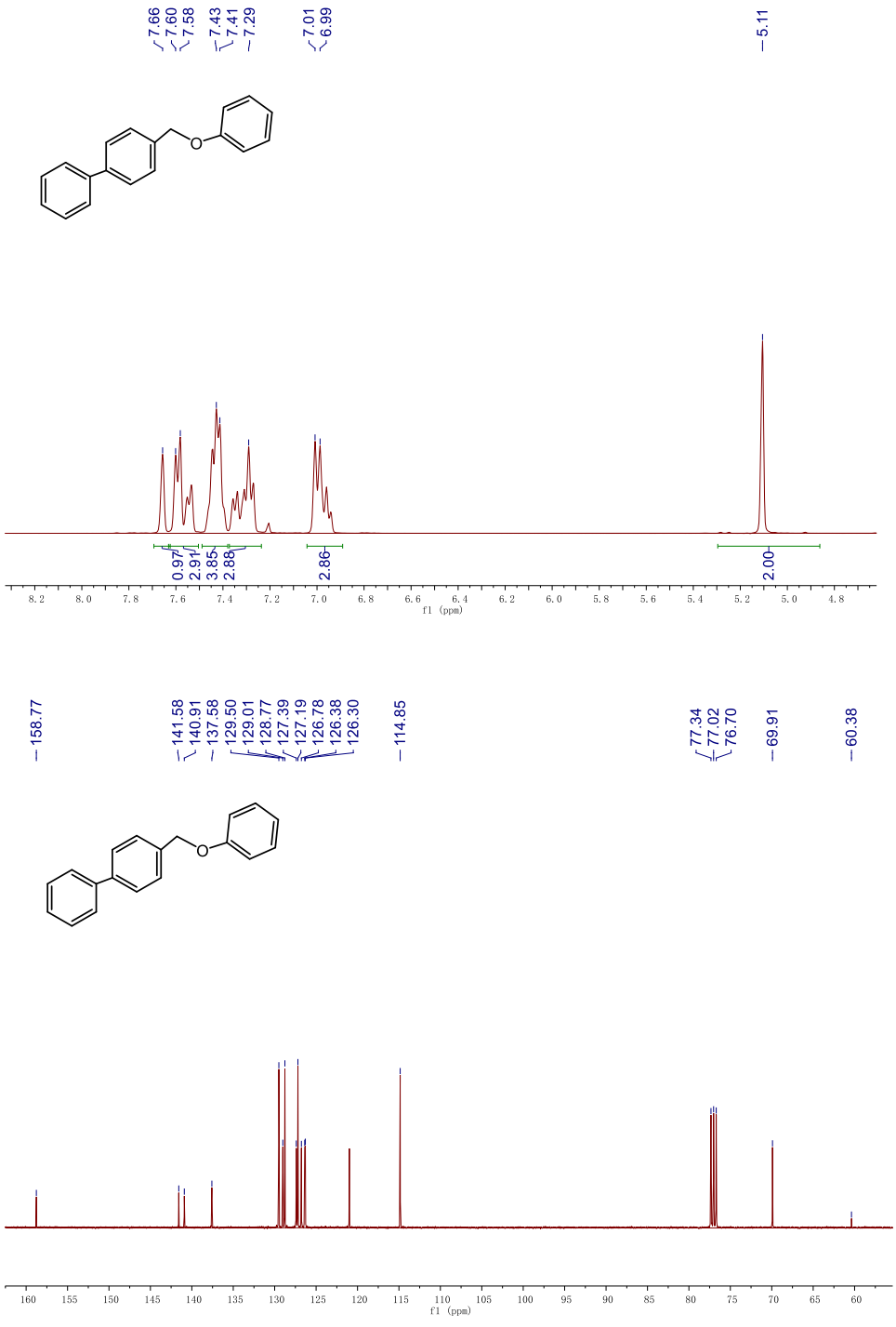


^{1}H and ^{13}C NMR spectra of compound 1d

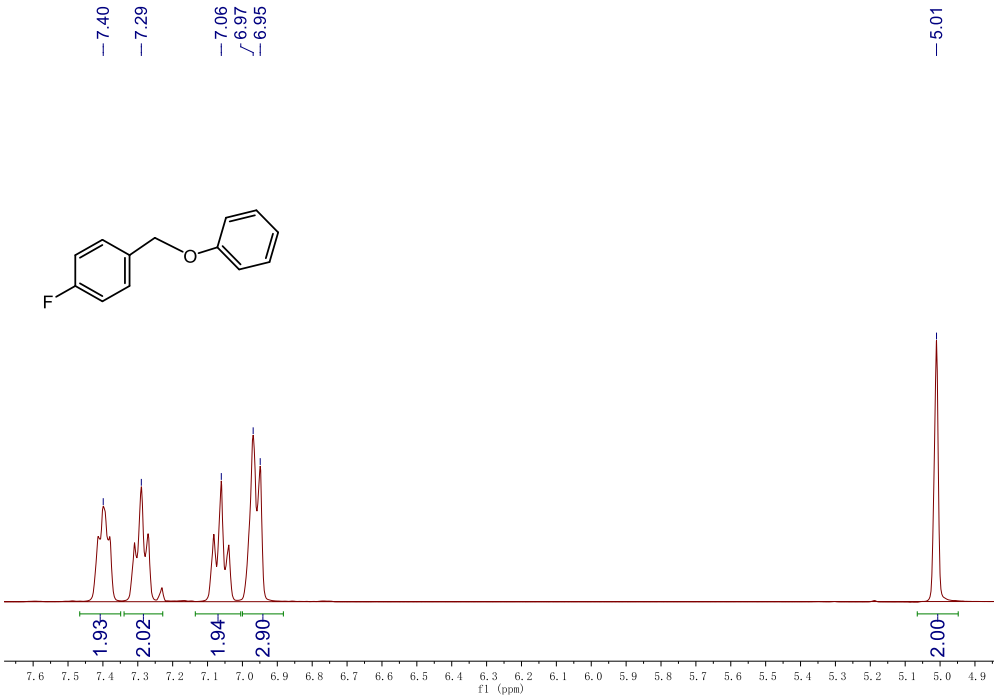


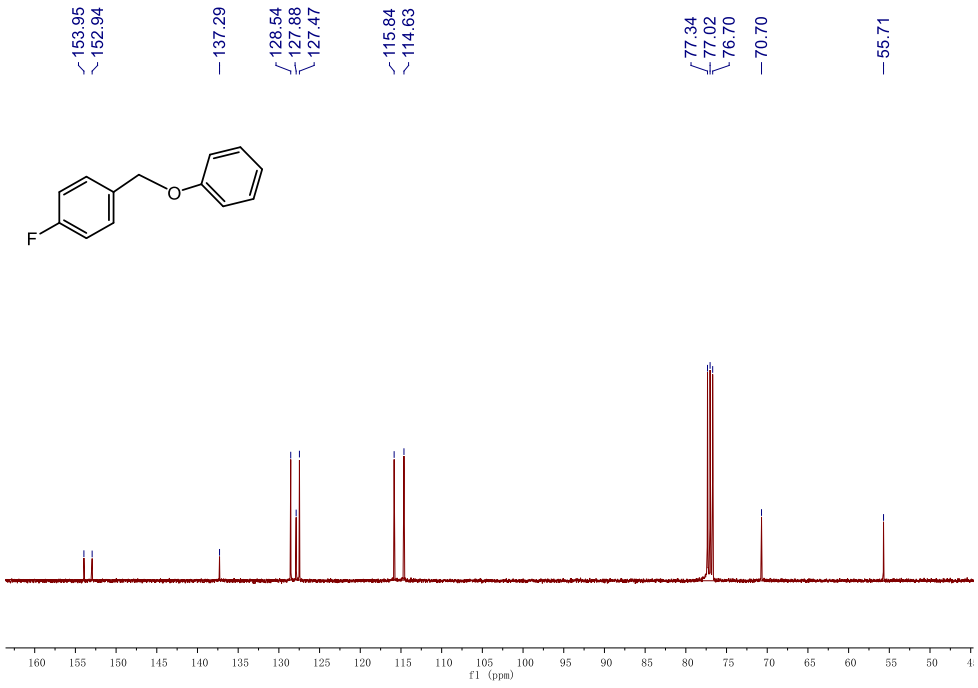


^{1}H and ^{13}C NMR spectra of compound 1e

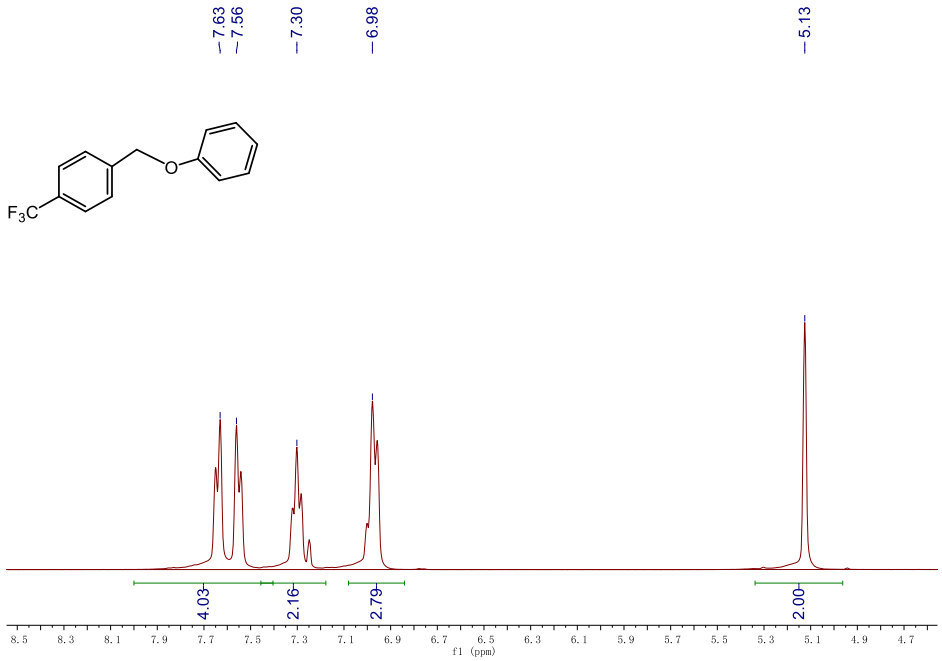


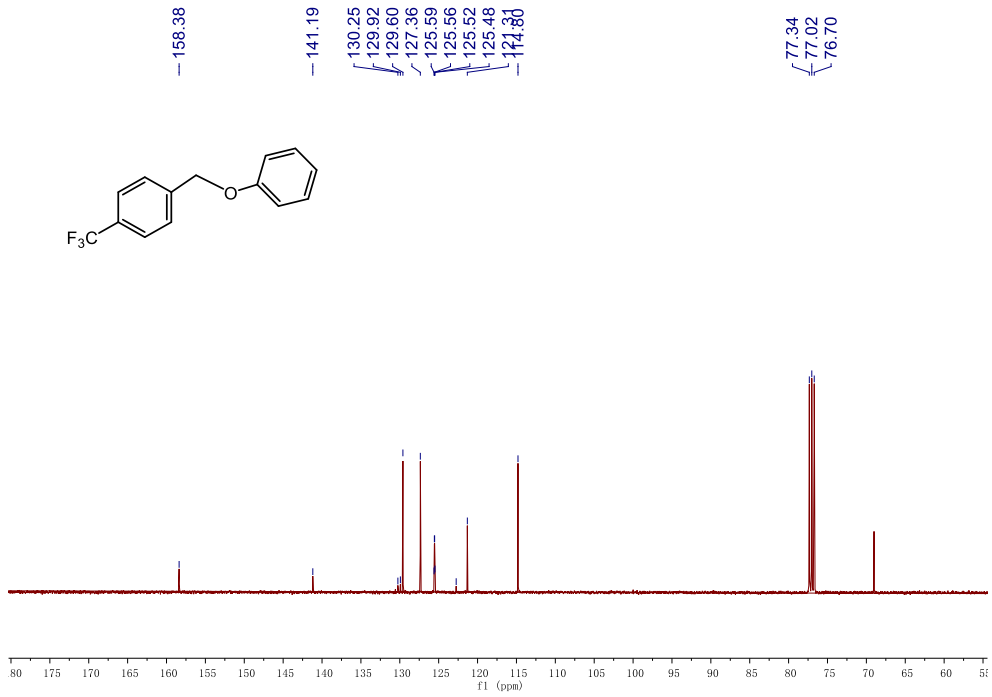
^{1}H and ^{13}C NMR spectra of compound 1f



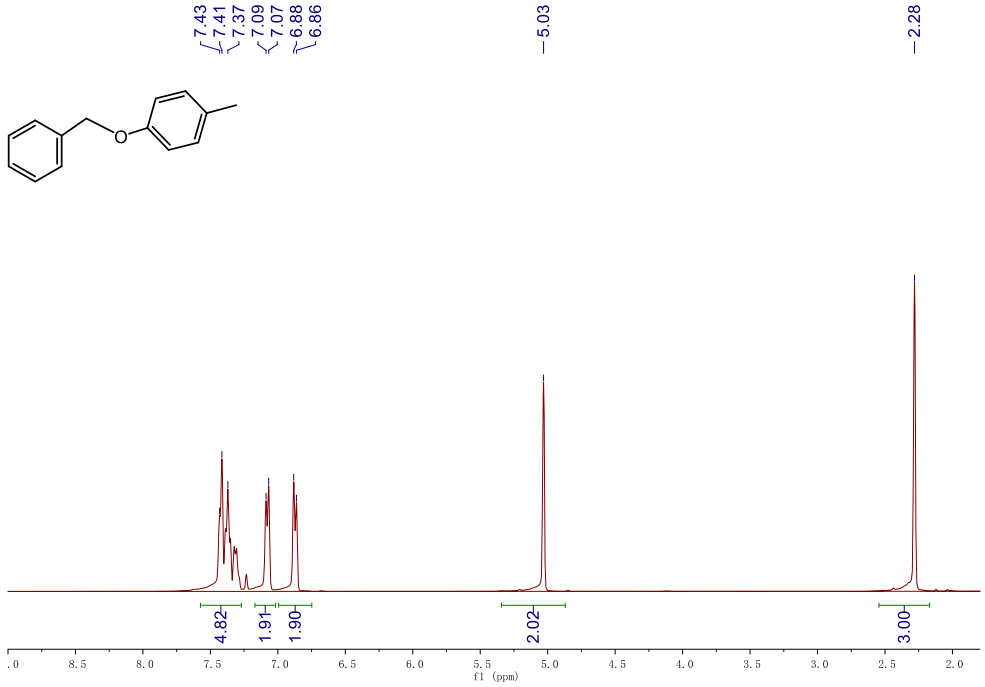


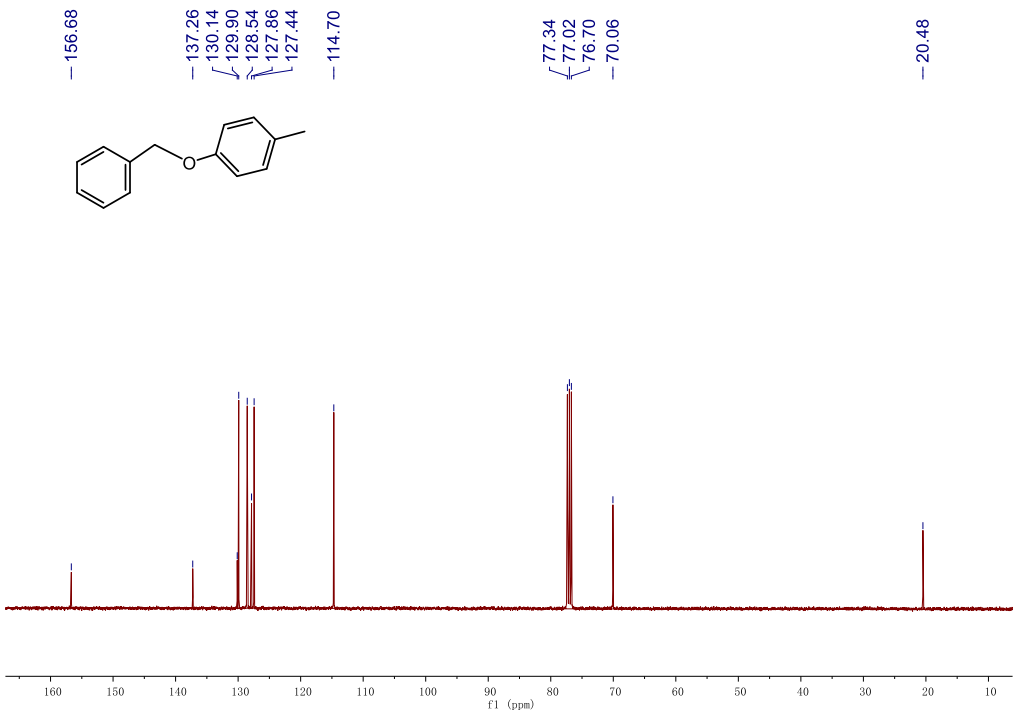
^{1}H and ^{13}C NMR spectra of compound 1g



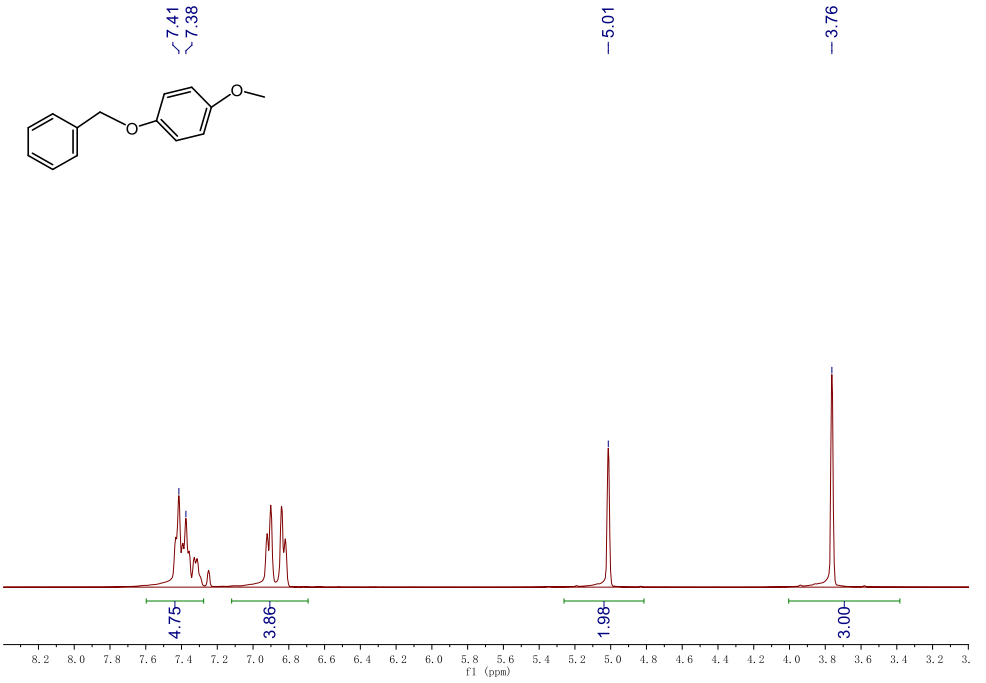


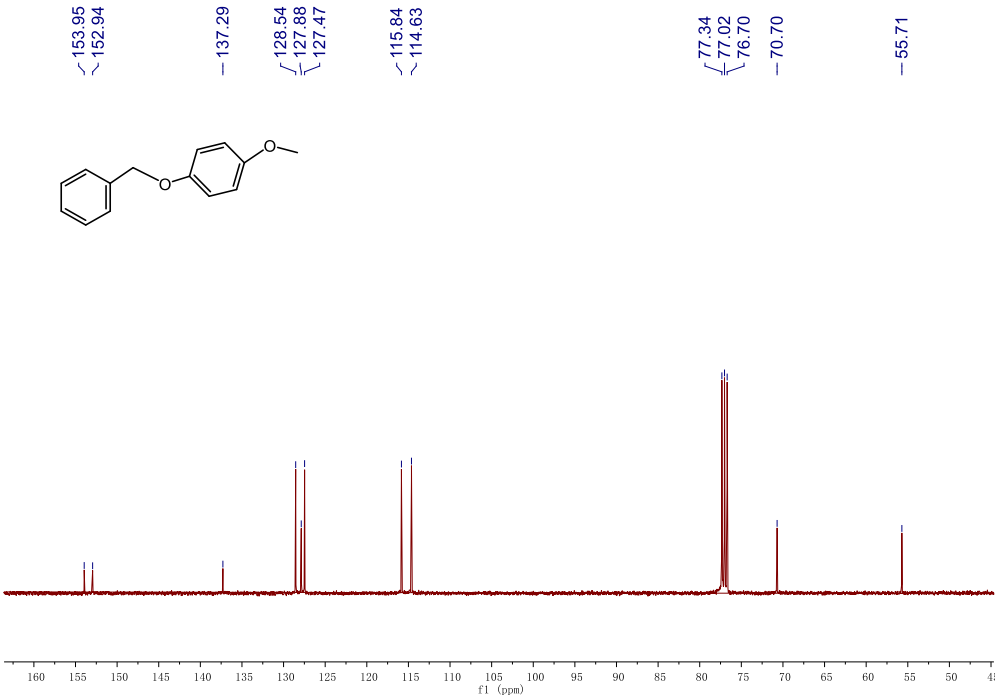
^{1}H and ^{13}C NMR spectra of compound 1h



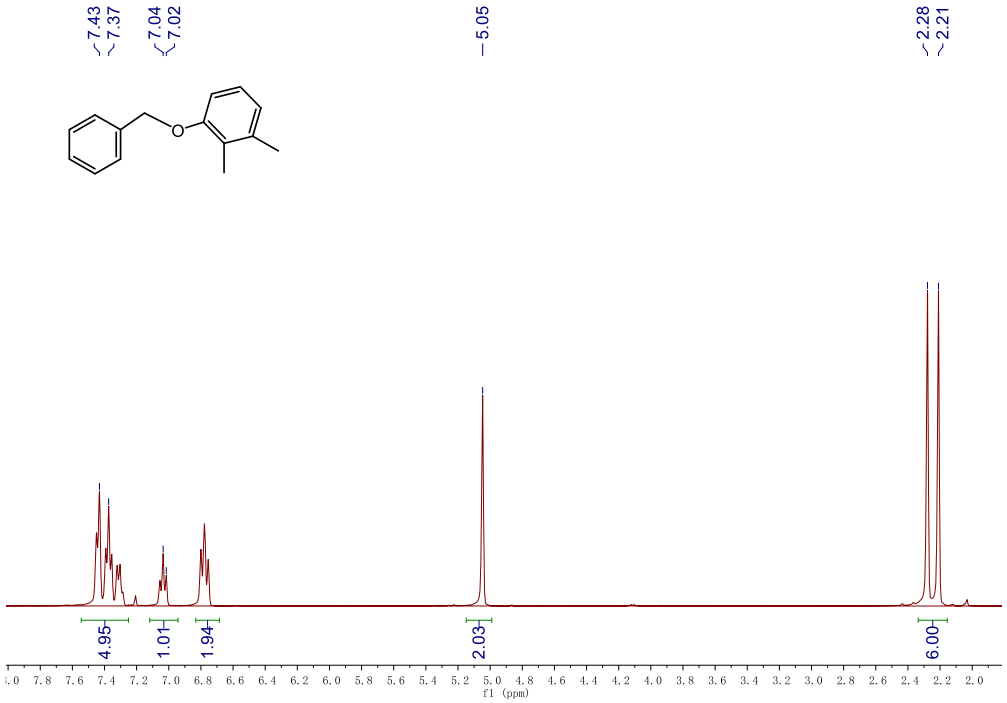


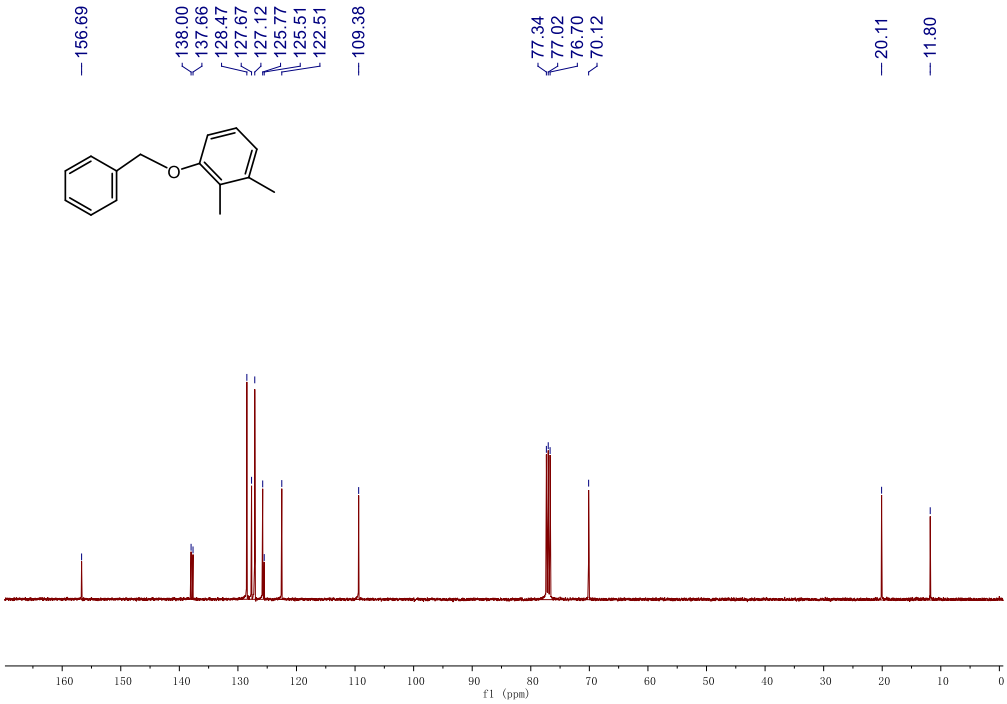
^{1}H and ^{13}C NMR spectra of compound 1i



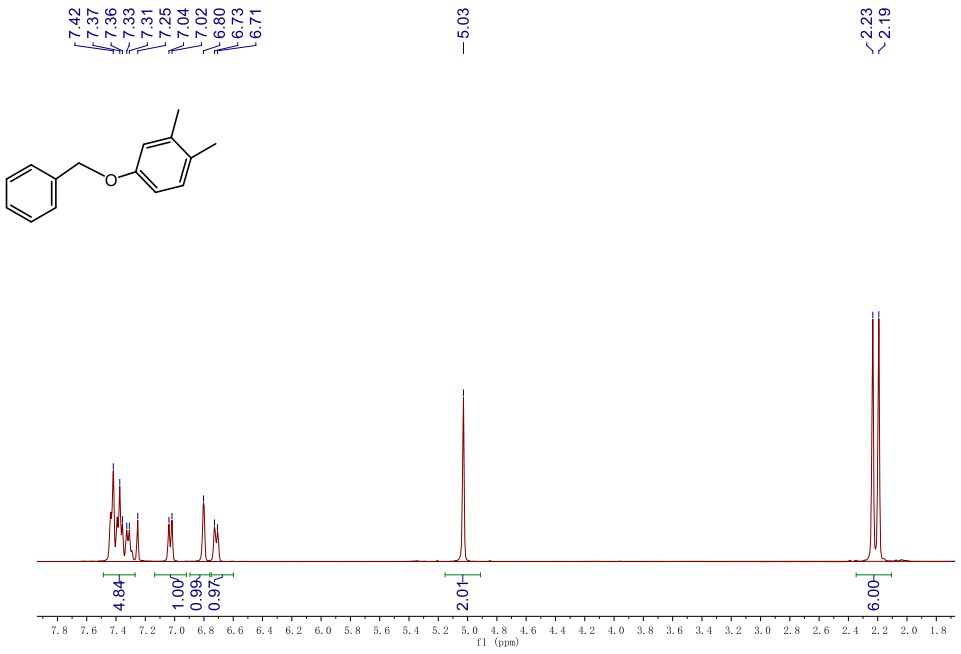


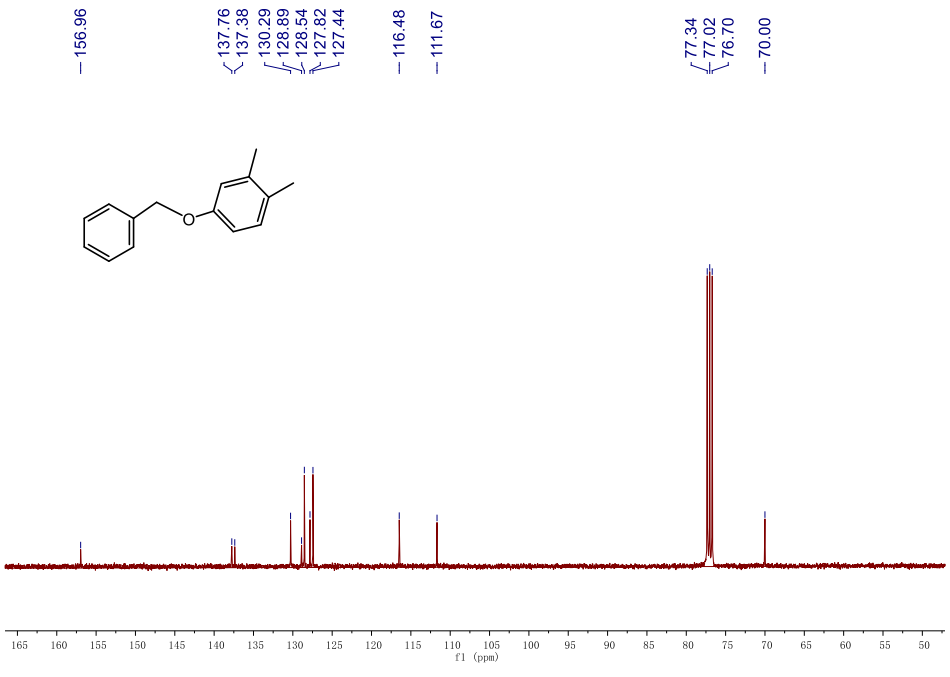
^{1}H and ^{13}C NMR spectra of compound 1j



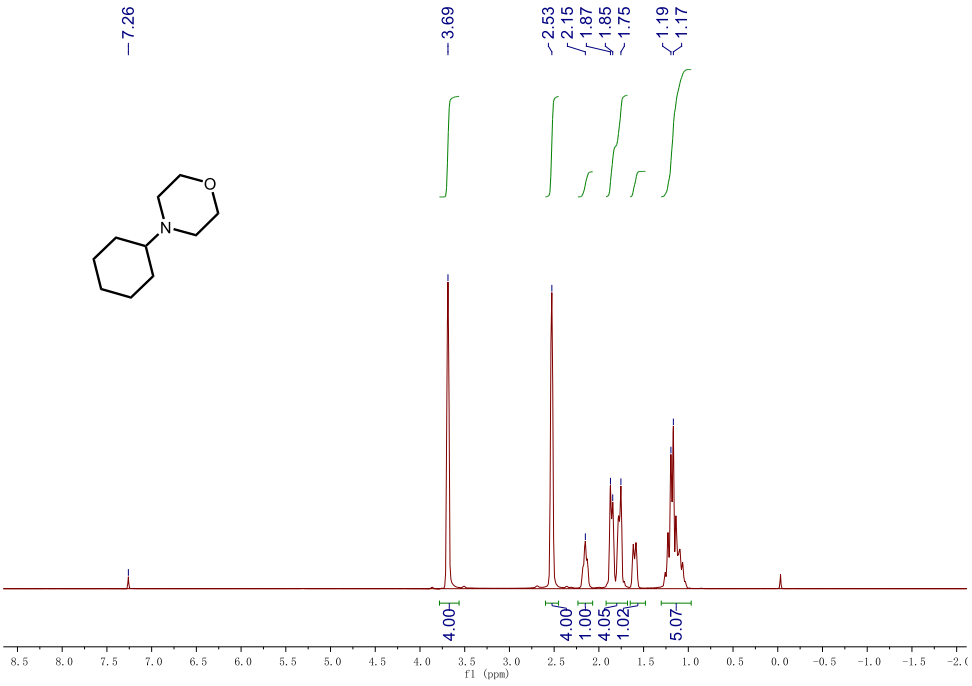


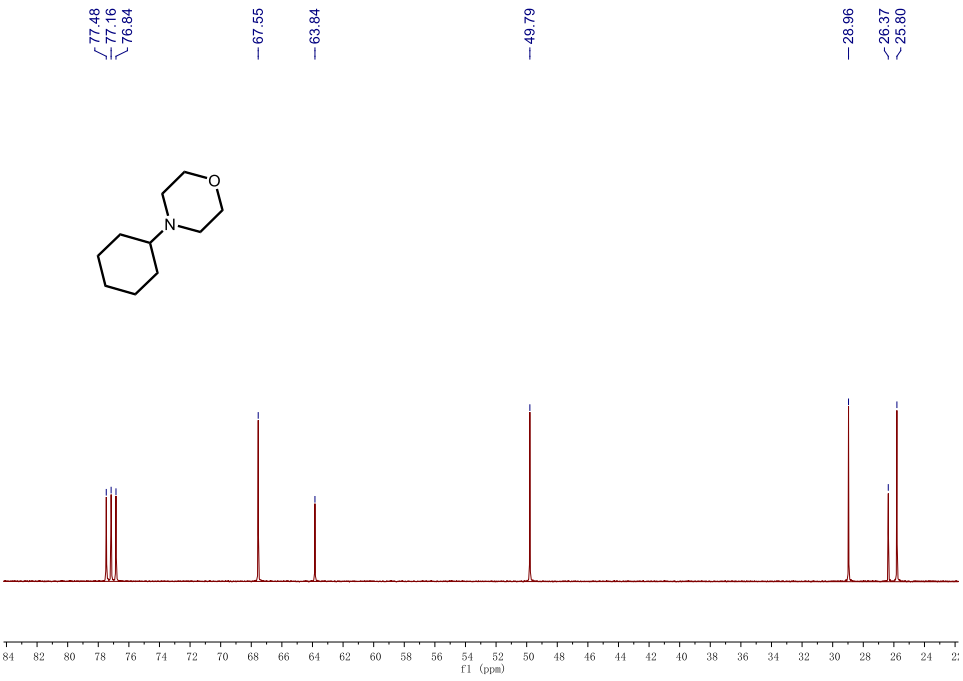
^{1}H and ^{13}C NMR spectra of compound 1k



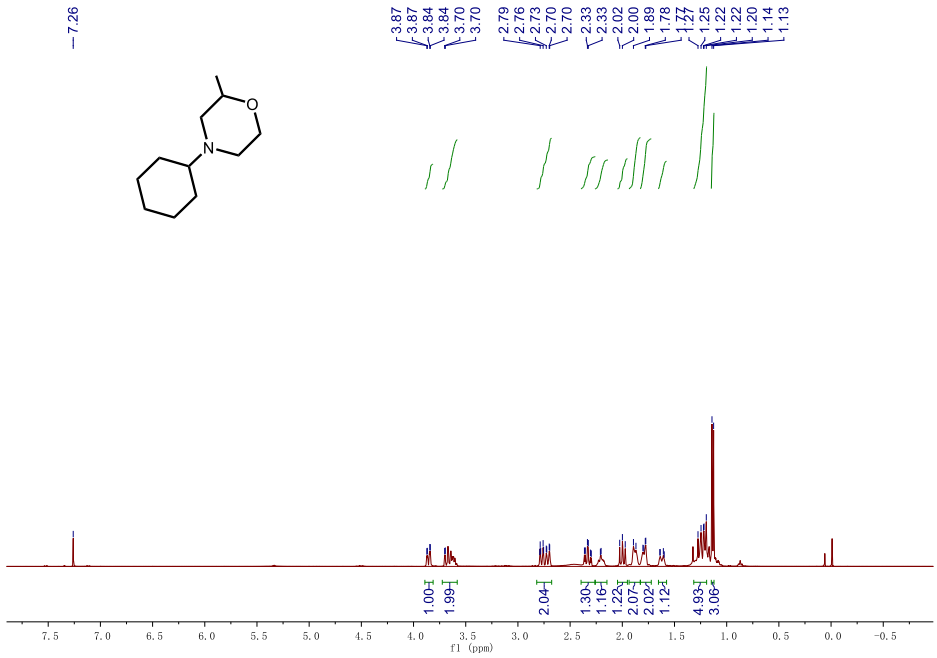


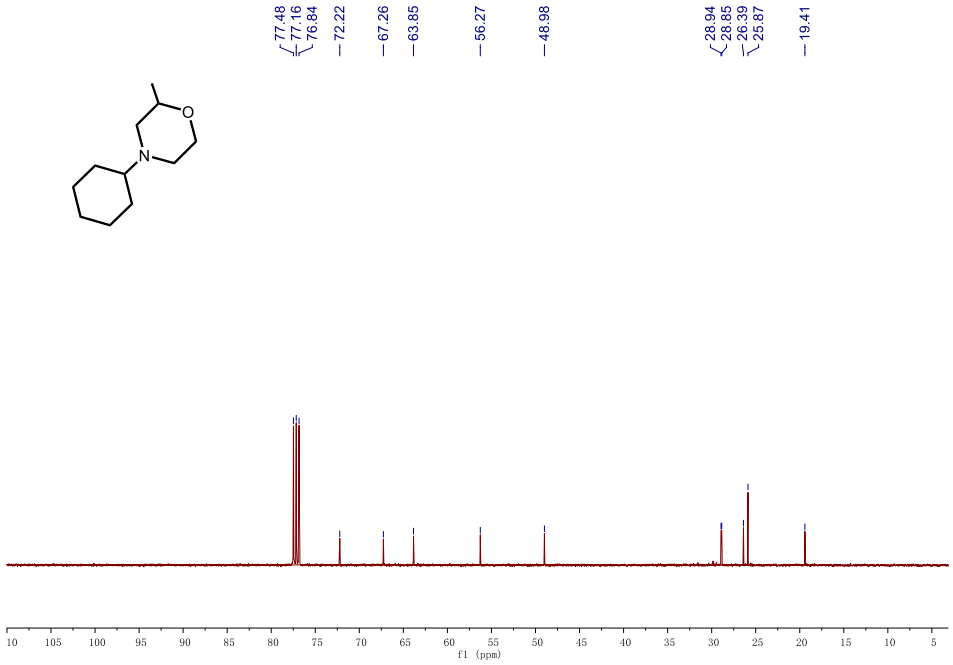
^{1}H and ^{13}C NMR spectra of compound 3a



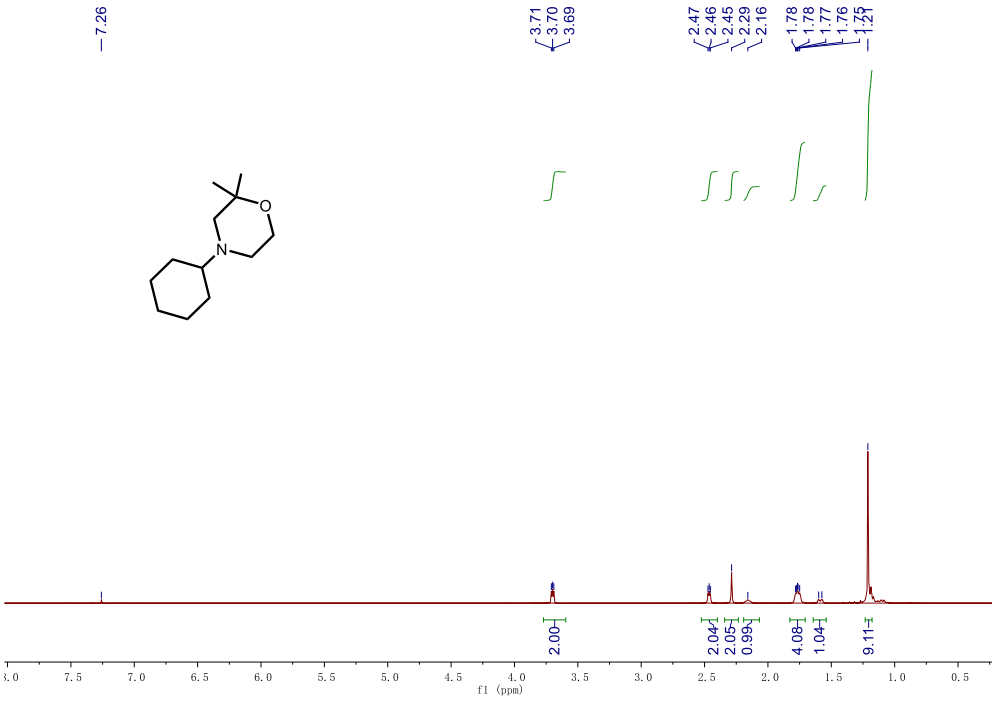


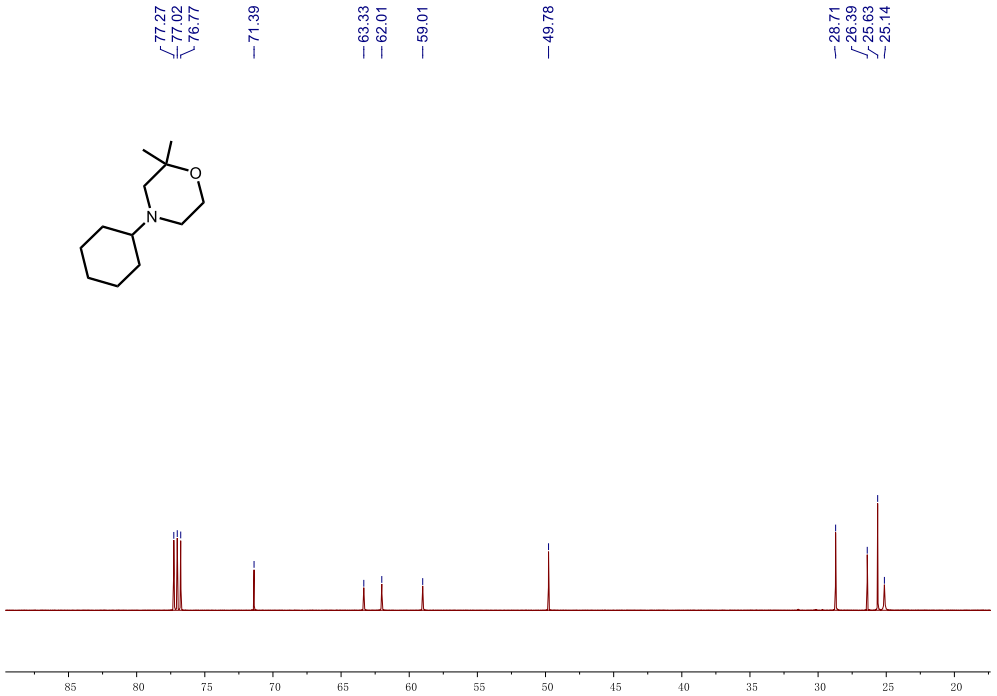
^{1}H and ^{13}C NMR spectra of compound 3b



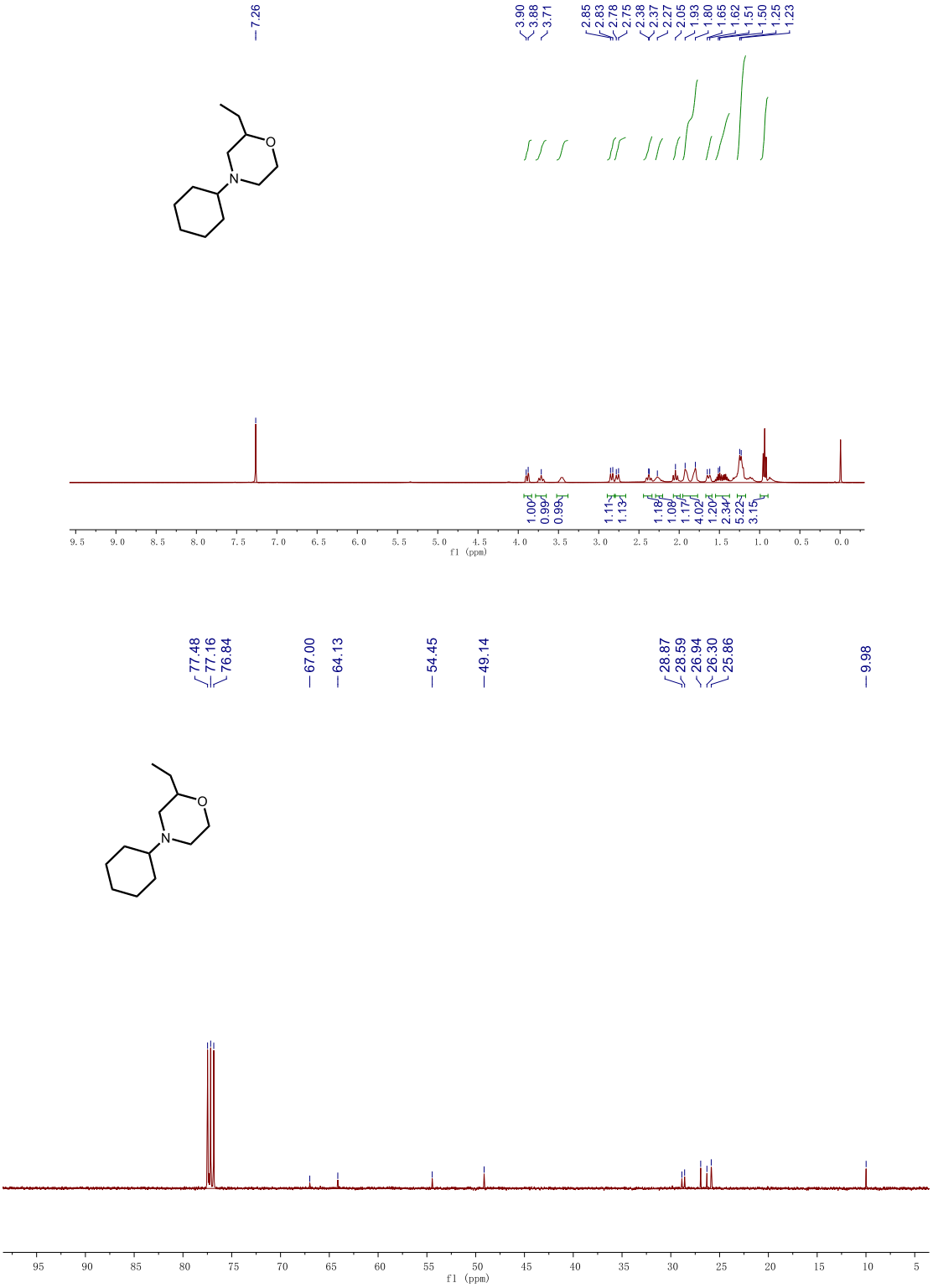


^{1}H and ^{13}C NMR spectra of compound 3c

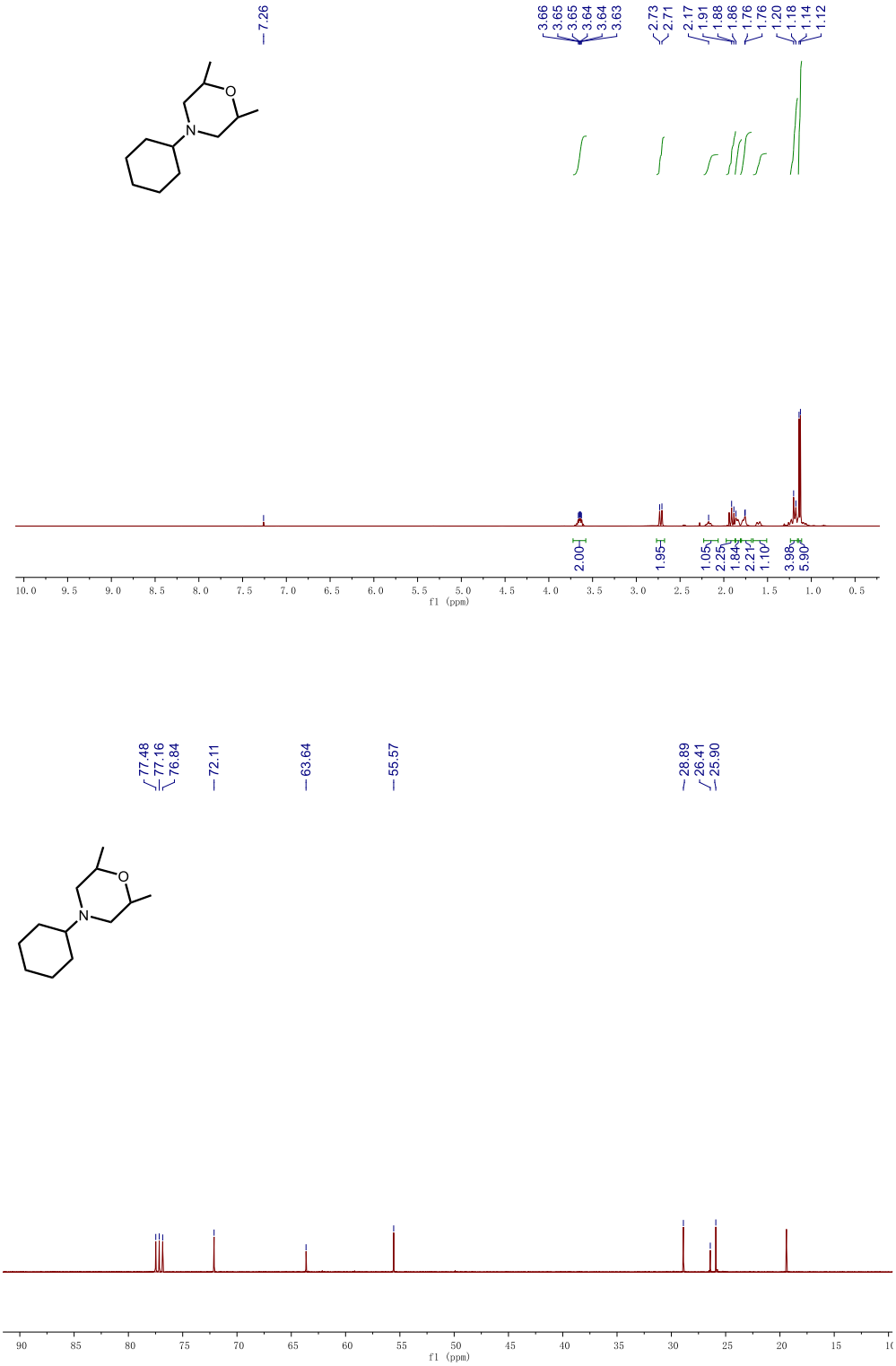




^{1}H and ^{13}C NMR spectra of compound 3d

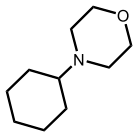


^{1}H and ^{13}C NMR spectra of compound 3e



HR-MS data

HR-MS for compound 3a

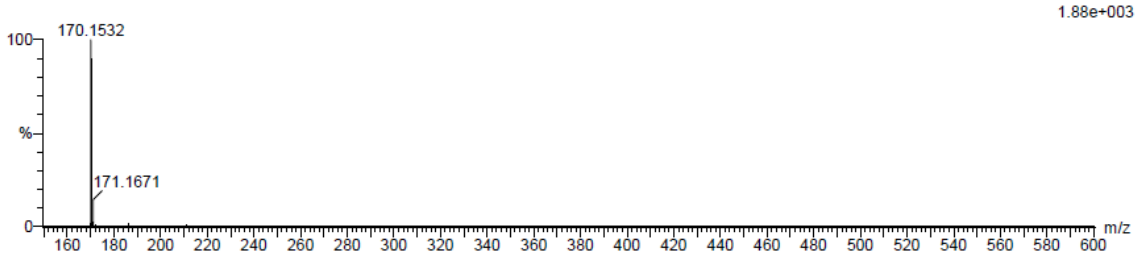


HRMS (ESI): Calcd for $C_{10}H_{20}NO$ $[M+H]^+$: 170.1545; Found: 170.1532.

Elemental Composition Report

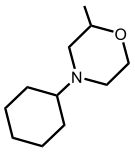
Single Mass Analysis
Tolerance = 500.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Even Electron Ions
1 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 10-10 H: 11-25 N: 1-1 O: 1-1 Na: 0-1
ZBX-1 89 (1.766)
1: TOF MS ES+



Minimum:				-1.5	
Maximum:		500.0	10.0	50.0	
Mass	Calc. Mass	mDa	PPM	DBE	Formula
170.1532	170.1545	-1.3	-7.6	1.5	C10 H20 N O

HR-MS for compound 3b

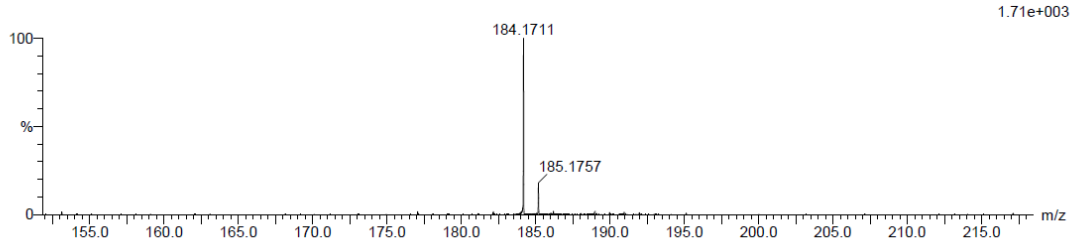


HRMS (ESI): Calcd for $C_{11}H_{22}NO$ $[M+H]^+$: 184.1701; Found: 184.1711.

Elemental Composition Report

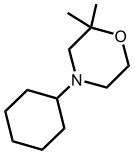
Single Mass Analysis
Tolerance = 500.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Even Electron Ions
4 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 11-11 H: 12-25 N: 1-1 O: 1-3 Na: 0-1
ZBX-1-0803 120 (2.352)
1: TOF MS ES+



Minimum:				-1.5	
Maximum:		500.0	10.0	50.0	
Mass	Calc. Mass	mDa	PPM	DBE	Formula
184.1711	184.1701	1.0	5.4	1.5	C11 H22 N O

HR-MS for compound 3c

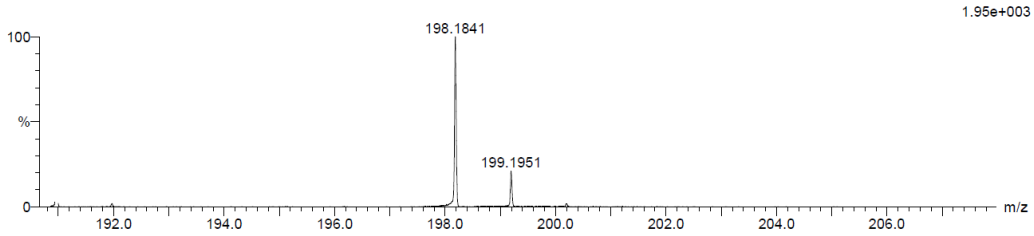


HRMS (ESI): Calcd for $C_{12}H_{24}NO$ $[M+H]^+$: 198.1858; Found: 198.1841.

Elemental Composition Report

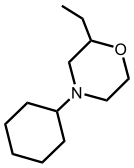
Single Mass Analysis
Tolerance = 500.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Even Electron Ions
4 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 12-12 H: 12-25 N: 1-1 O: 1-3 Na: 0-1
ZBX-2-0803 105 (2.077)
1: TOF MS ES+



Minimum:				-1.5	
Maximum:		500.0	10.0	50.0	
Mass	Calc. Mass	mDa	PPM	DBE	Formula
198.1841	198.1858	-1.7	-8.6	1.5	C12 H24 N O

HR-MS for compound 3d

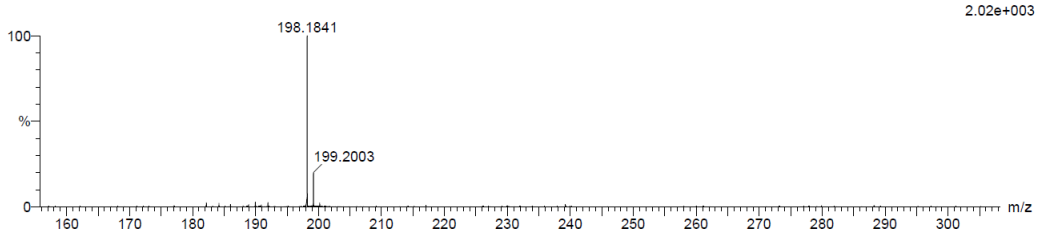


HRMS (ESI): Calcd for $C_{12}H_{24}NO$ $[M+H]^+$: 198.1858; Found: 198.1841.

Elemental Composition Report

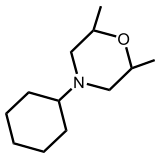
Single Mass Analysis
Tolerance = 500.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Even Electron Ions
4 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 12-12 H: 12-25 N: 1-1 O: 1-3 Na: 0-1
ZBX-3-0803 102 (2.006)
1: TOF MS ES+



Minimum:				-1.5	
Maximum:		500.0	10.0	50.0	
Mass	Calc. Mass	mDa	PPM	DBE	Formula
198.1841	198.1858	-1.7	-8.6	1.5	C12 H24 N O

HR-MS for compound 3e

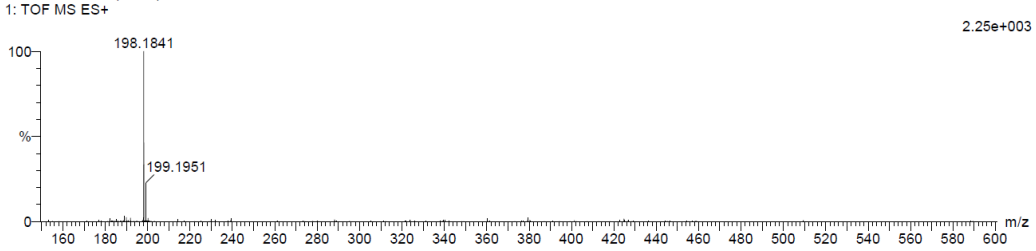


HRMS (ESI): Calcd for $C_{12}H_{24}NO$ $[M+H]^+$: 198.1858; Found: 198.1841.

Elemental Composition Report

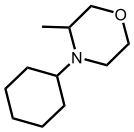
Single Mass Analysis
Tolerance = 500.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Even Electron Ions
4 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 12-12 H: 12-25 N: 1-1 O: 1-3 Na: 0-1
ZBX-4-0803 111 (2.179)
1: TOF MS ES+



Minimum:				-1.5	
Maximum:		500.0	10.0	50.0	
Mass	Calc. Mass	mDa	PPM	DBE	Formula
198.1841	198.1858	-1.7	-8.6	1.5	C12 H24 N O

HR-MS for compound 3f$_1$



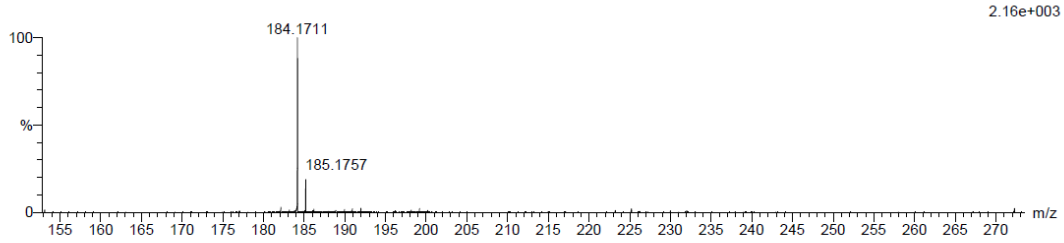
(cis/trans = 1 : 17: 0.25)

HRMS (ESI): Calcd for $C_{11}H_{22}NO$ $[M+H]^+$: 184.1701; Found: 184.1711.

Elemental Composition Report

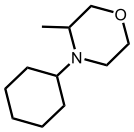
Single Mass Analysis
Tolerance = 500.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Even Electron Ions
4 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 11-11 H: 12-25 N: 1-1 O: 1-3 Na: 0-1
ZBX-5-0803 92 (1.817)
1: TOF MS ES+



Minimum:				-1.5	
Maximum:		500.0	10.0	50.0	
Mass	Calc. Mass	mDa	PPM	DBE	Formula
184.1711	184.1701	1.0	5.4	1.5	C11 H22 N O

HR-MS for compound 3f$_2$



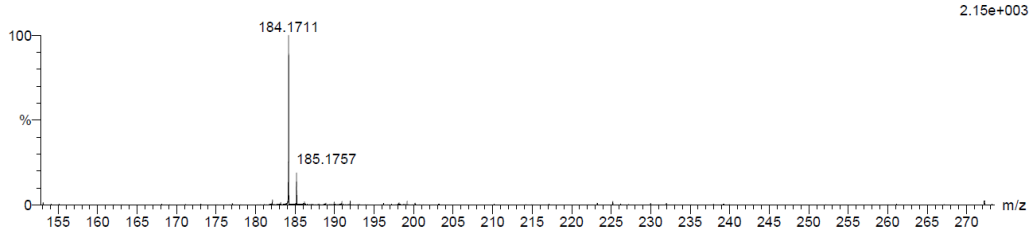
(cis/trans = 1:12.2)

HRMS (ESI): Calcd for $C_{11}H_{22}NO$ $[M+H]^+$: 184.1701; Found: 184.1711.

Elemental Composition Report

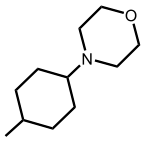
Single Mass Analysis
Tolerance = 500.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Even Electron Ions
4 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 11-11 H: 12-25 N: 1-1 O: 1-3 Na: 0-1
ZBX-6-0803 92 (1.817)
1: TOF MS ES+



Minimum:				-1.5	
Maximum:		500.0	10.0	50.0	
Mass	Calc. Mass	mDa	PPM	DBE	Formula
184.1711	184.1701	1.0	5.4	1.5	C11 H22 N O

HR-MS for compound 3g



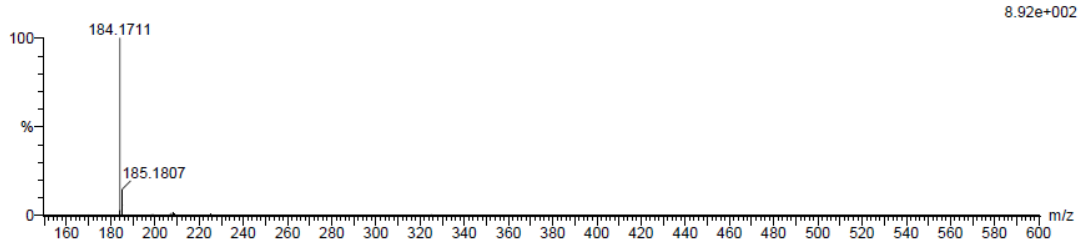
(cis/trans = 2.7 : 1)

HRMS (ESI): Calcd for $C_{11}H_{22}NO$ $[M+H]^+$: 184.1701; Found: 184.1711.

Elemental Composition Report

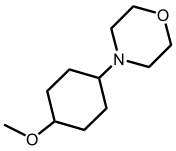
Single Mass Analysis
Tolerance = 500.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Even Electron Ions
1 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 11-11 H: 11-25 N: 1-1 O: 1-1 Na: 0-1
ZBX-2 17 (0.365)
1: TOF MS ES+



Minimum:				-1.5	
Maximum:		500.0	10.0	50.0	
Mass	Calc. Mass	mDa	PPM	DBE	Formula
184.1711	184.1701	1.0	5.4	1.5	C11 H22 N O

HR-MS for compound 3h



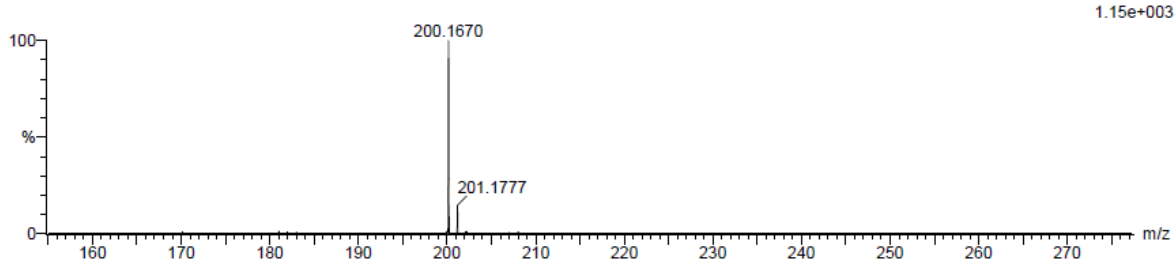
(cis/trans = 1.1 : 1)

HRMS (ESI): Calcd for $C_{11}H_{22}NO_2$ $[M+H]^+$: 200.1651; Found: 200.1670

Elemental Composition Report

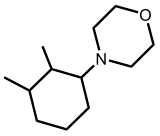
Single Mass Analysis
Tolerance = 500.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Even Electron Ions
9 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 11-11 H: 11-25 N: 1-2 O: 2-4 Na: 0-1
ZBX-3 18 (0.382)
1: TOF MS ES+



Minimum:				-1.5	
Maximum:		500.0	10.0	50.0	
Mass	Calc. Mass	mDa	PPM	DBE	Formula
200.1670	200.1651	1.9	9.5	1.5	C11 H22 N O2

HR-MS for compound 3i



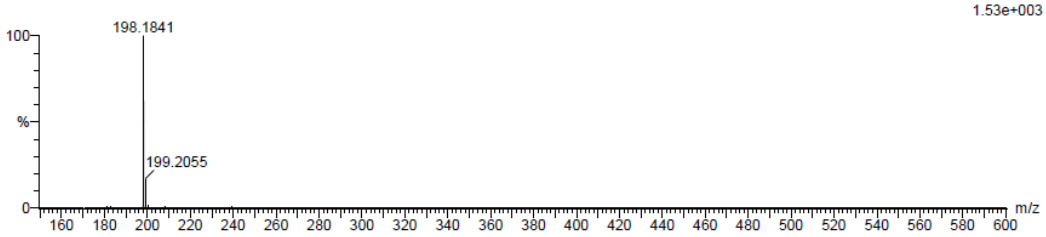
(cis/trans = 3.5 : 0.2 : 1 : 0.6)

HRMS (ESI): Calcd for $C_{12}H_{24}NO$ $[M+H]^+$: 198.1858; Found: 198.1841.

Elemental Composition Report

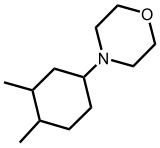
Single Mass Analysis
Tolerance = 500.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Even Electron Ions
1 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 12-12 H: 11-25 N: 1-1 O: 1-1 Na: 0-1
ZBX-4 19 (0.399)
1: TOF MS ES+



Minimum:				-1.5	
Maximum:		500.0	10.0	50.0	
Mass	Calc. Mass	mDa	PPM	DBE	Formula
198.1841	198.1858	-1.7	-8.6	1.5	C12 H24 N O

HR-MS for compound 3j



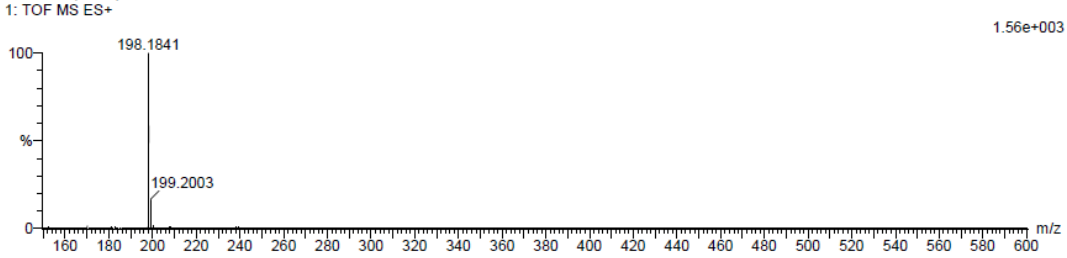
(cis/trans = 1 : 0.7 : 2.1 : 0.5)

HRMS (ESI): Calcd for $C_{12}H_{24}NO$ $[M+H]^+$: 198.1858; Found: 198.1841.

Elemental Composition Report

Single Mass Analysis
Tolerance = 500.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Even Electron Ions
1 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 12-12 H: 11-25 N: 1-1 O: 1-1 Na: 0-1
ZBX-5 19 (0.399)
1: TOF MS ES+



Minimum:				-1.5	
Maximum:		500.0	10.0	50.0	
Mass	Calc. Mass	mDa	PPM	DBE	Formula
198.1841	198.1858	-1.7	-8.6	1.5	C12 H24 N O

Reference:

(1) W. B. Wu and J. M. Huang, *J. Org. Chem.*, 2014, **79**, 10189-10195.

(2) A. S. Singh, S. S. Shendage and J. M. Nagarkar, *Tetrahedron Lett.*, 2014, **55**, 7243-7246.