Supporting Information for

Copper-catalyzed asymmetric allylic alkylation of racemic inert cyclic allylic ethers under batch and flow conditions

Jun Li [a], *Xiao Song* [a], *Yan Wang*[a], *Junrong Huang** [a,b], *Hengzhi You** [a,b], *Fen-Er Chen** [a,b,c]

[a] School of science, Harbin Institute of Technology (Shenzhen), Taoyuan Street, Nanshan District, Shenzhen, 518055, China.

[b] Green Pharmaceutical Engineering Research Center, Harbin Institute of Technology (Shenzhen), Taoyuan Street, Nanshan, District, Shenzhen, 518055, China.

[c] Engineering Center of Catalysis and Synthesis for Chiral Molecules, Department of Chemistry, Fudan University, Shanghai, 200433, China.

* Corresponding authors

E-mail: hjunrong@hit.edu.cn; youhengzhi@hit.edu.cn; rfchen@fudan.edu.cn

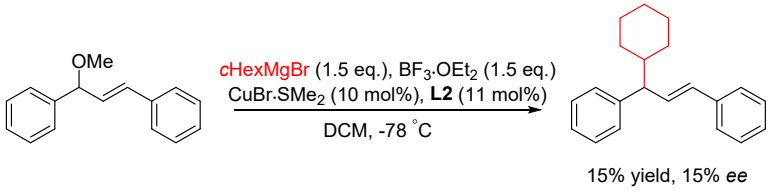
Table of Contents

1 General information

All reactions were carried out under argon atmosphere with flame-dried glassware. Solvents were redistilled under nitrogen before use to remove water and oxygen. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded on a Quantum-I 400M in $CDCl_3$, and chemical shift (δ) are given in ppm relative to residual $CHCl_3$. Coupling constants (*J*) are reported in Hertz (Hz). The residual solvent peak was used as an internal reference: ^{1}H NMR (chloroform δ 7.26) and ^{13}C NMR (chloroform δ 77.0). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Evolution of reaction was followed by GC-MS (EI mode) on an Agilent 7890B-5977B. Optical rotations were recorded on an IP-digi300/2 polarimeter at 25 °C in a 5 cm cell in the stated solvent. Enantiomeric ratio was determined by chiral GC measurement either on an Agilent 7890B with the stated column or UltiMate 3000 with the stated column using isopropanol and *n*-hexane as mobile phase. Temperature programs are described as follows: initial temperature (°C) - initial time (min) - temperature gradient (°C/min) - final temperature (°C); retention times (RT) are given in min. Column chromatography purifications were performed by flash chromatography on Santai Technologies Inc. SepaBean® machine T using Merck silica gel 60 Å or neutral alumina. All substrates and ligands were prepared according to the published procedures. Other reagents were received from commercial sources. Microreactor was received from E-zheng. The absolute configuration was assigned according to the literature report.[1-6]

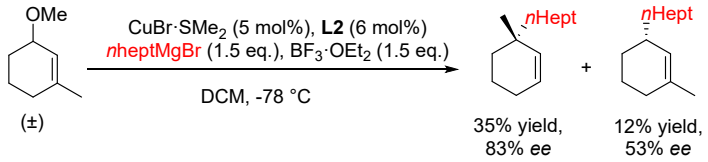
2 Substrate scope

2.1 (*E*)- allylic ether



Scheme S1 AAA reaction of (*E*)- allylic ether

2.2 3-methoxy-1-methylcyclohex-1-ene.



Scheme S2 AAA reaction of *rac*-3-methoxy-1-methylcyclohex-1-ene

3 Experimental parts

A) Procedure used in the synthesis of racemic products:

In a flame-dried Schlenk tube under argon atmosphere, CuTc (0.05 mmol, 10 mol%) and PPh_3 (0.055 mmol, 11 mol%) was dissolved in dry DCM (2 mL) and the solution was stirred for 15 min at room temperature. Then, the cyclic allylic bromide (0.5 mmol) was added and the solution was cooled to -78 °C. After 10 min at this temperature, the corresponding Grignard reagent (0.75 mmol, 1.5 equiv.) was added dropwise to the reaction mixture under nitrogen. Once the addition was complete, the mixture was stirred for another 1 h at -78 °C. The reaction was quenched with an aqueous solution of saturated aqueous NH_4Cl solution (2 mL) and extracted with DCM (15 mL). Organic layer was washed with the saturated aqueous NH_4Cl solution (15 mL) and brine (15 mL), dried over Na_2SO_4, filtered and concentrated on *vacuo*. Crude mixture was purified on silica gel chromatography column (pentane). Desired product was recovered as a colorless liquid.

B) General procedure for copper catalyzed asymmetric allylic alkylation

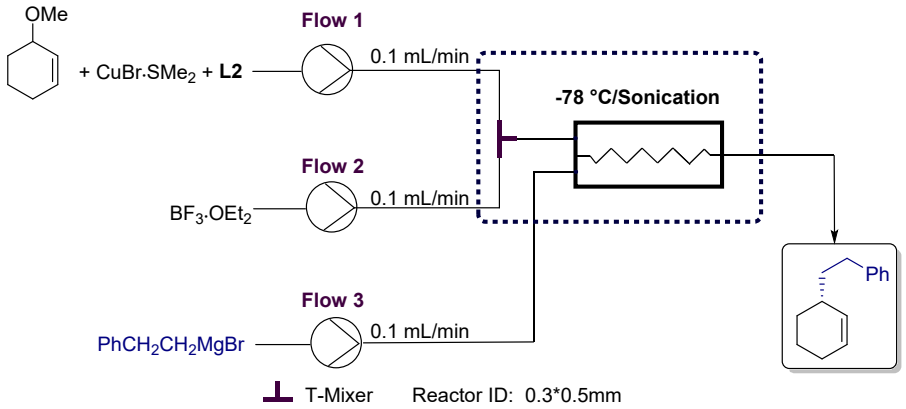
In a flame-dried Schlenk tube under argon atmosphere, $CuBr{\cdot}SMe_2$ (0.04 mmol, 10 mol%) and the appropriate ligand (0.044 mmol, 11 mol%) were dissolved in dry DCM (4 mL) and the solution was stirred for 15 min at room temperature. Then, the cyclic allylic ethers (0.4 mmol) and $BF_3{\cdot}OEt_2$ (0.6 mmol, 1.5 equiv.) was added at -78 °C. After 10 min at this temperature, the corresponding Grignard reagent (0.6 mmol, 0.5 or 1 M in Et_2O, 1.5 equiv.) was added dropwise to the reaction mixture. Once the addition was complete, the mixture was stirred for another 1 h at -78 °C. The reaction was quenched with an aqueous solution of saturated aqueous NH_4Cl solution (2 mL) and extracted with DCM (15 mL). Organic layer was washed with the saturated aqueous NH_4Cl solution (15 mL) and brine (15 mL), dried

over Na_2SO_4, filtered and concentrated on *vacuo*. Crude mixture was purified on silica gel chromatography column (pentane). Desired product was recovered as a colorless liquid.

C) Derivatization of products to epoxides for *ee* determination:

A sample of the isolated product was treated with 2.0 equiv. *m*CPBA and 3.0 equiv. Na_2HPO_4 in DCM. After 2 h, DCM (10 mL) was added and the reaction was quenched with an aqueous solution of saturated Na_2SO_3. The organic layer was washed two times with an aqueous solution of 1 M NaOH, dried over Na_2SO_4, filtered and concentrated on *vacuo*. The crude mixture of two diastereoisomeric epoxides was directly analyzed in chiral GC.

D) General Procedure of Flow AAA reaction



The AAA reaction was conducted in an 18 µL microreactor made of stainless steel (0.3*0.5mm inner diameter, 120 mm length). The CuBr·SMe_2 (0.7 mmol, 10 mol%) and **L2** (0.77 mmol, 11 mol%) were dissolved in 70 mL DCM and the mixture was stirred at room temperature for 30 min. Then, the cyclic allylic methyl ether (7 mmol) was directly added to the mixture. After that, the solution of CuBr·SMe_2, **L2** and cyclic allylic methyl ether was introduced at one inlet at a flow rate of 0.1 mL/min, BF_3·OEt_2 (10.5 mmol) in DCM (70 mL) was introduced from other inlet at the 0.1 mL/min flow rate. The two solutions were combined in a T-mixer and injected into the microreactor at -78 °C with sonication. Meanwhile, Grignard reagent (10.5 mmol, 0.15 M, 1.5 equiv.) was injected into the microreactor at the 0.1 mL/min flow rate. The microreactor were cooled to -78 °C with sonication. Total output was 0.3 mL/min (3.6 s of residence time). The reaction mixture was collected, quenched with EtOH or saturated NH_4Cl solution (0.5 mL) and extracted with DCM (15 mL). Organic layer was washed with the saturated NH_4Cl solution (15 mL) and brine (15 mL), dried over Na_2SO_4, filtered and concentrated in

vacuo. Crude mixture was purified on silica gel chromatography column (pentane). The desired product was recovered as a colorless liquid.

4 Experiments under flow

4.1 Selected optimization under continuous flow

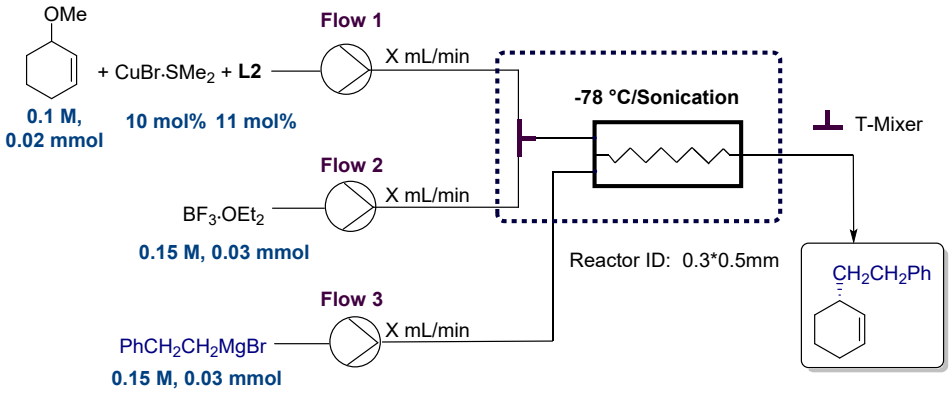
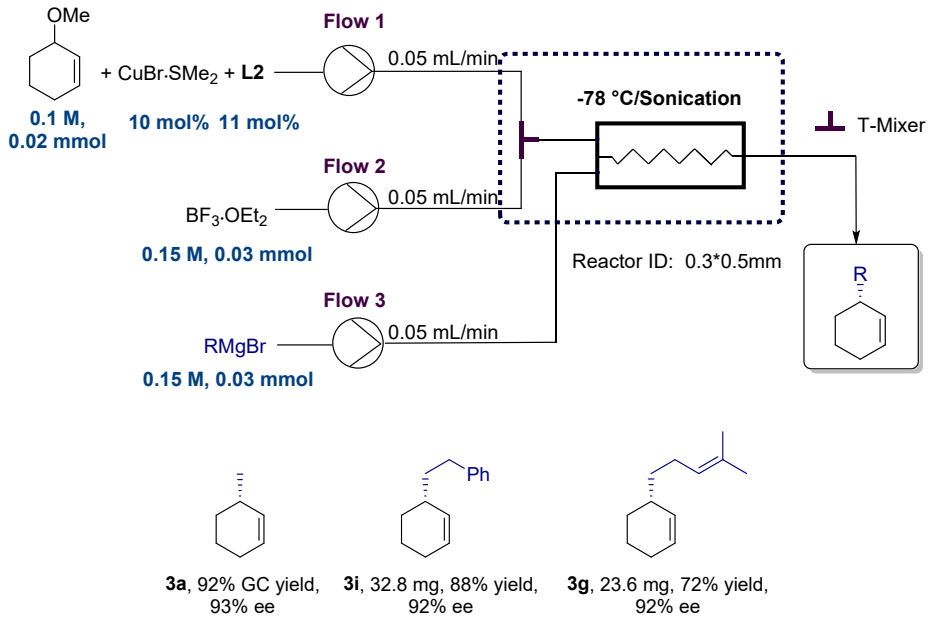


Table S1. Selected optimization under continuous flow[a]

Entry	X	*ee*	Yield
1	0.1	92%	95%
2	0.2	83%	86%
3	0.3	81%	85%
4	0.4	80%	68%
5	0.6	81%	65%
6	0.05	92%	95%
7[b]	0.05	87%	60%
8[b,c]	0.05	80%	92%

a: NMR yield. b: 5% catalyst loading. c: 3 eq. Grignard reagent and $BF_3{\cdot}OEt_2$.

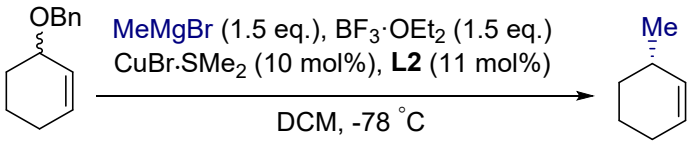
4.2 Substrate scope under continuous flow



Scheme S3 Substrate scope under continuous flow

5 Mechanistic analysis

5.1 GCMS traces of 3c in AAA reaction



In a flame-dried Schlenk tube under argon atmosphere, CuBr·SMe_2 (0.04 mmol, 10 mol%) and the appropriate ligand (0.044 mmol, 11mol%) were dissolved in dry DCM (4 mL) and the solution was stirred for 15 min at room temperature. Then, 3-benzyloxycyclohexene (0.4 mmol) and BF_3·OEt_2 (0.6 mmol, 1.5 equiv.) was added at -78 °C. After 10 min at this temperature, the MeMgBr (0.6 mmol, 0.5 M in Et_2O, 1.5 equiv.) was added dropwise to the reaction mixture. Once the addition was complete, the mixture was stirred for another 1 h at -78 °C and quenched with EtOH (0.2 mL).

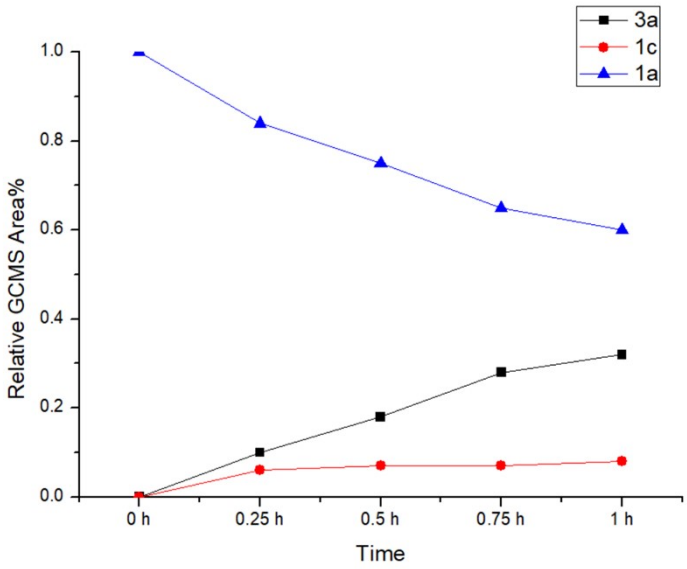


Fig. S1 GCMS traces of 3c in AAA reaction

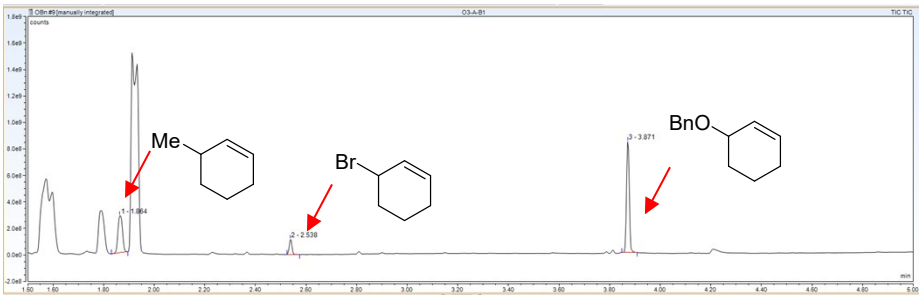
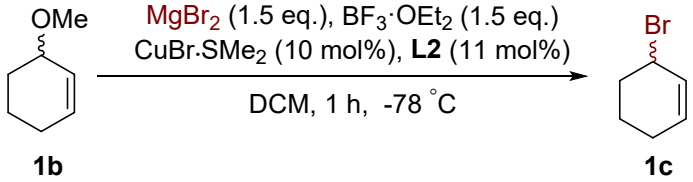


Fig. S2 GCMS traces of 3c in AAA reaction for 1 h

5.2 GCMS traces of 3c *in situ*



1b : **1c** = 55:45

In a flame-dried Schlenk tube under argon atmosphere, $CuBr{\cdot}SMe_2$ (0.04 mmol, 10 mol%) and the appropriate ligand (0.044 mmol, 11 mol%) were dissolved in dry DCM (4 mL) and the solution was stirred for 15 min at room temperature. Then, the cyclic allylic methyl ether (0.4 mmol) and $BF_3{\cdot}OEt_2$ (0.6 mmol, 1.5 equiv.) was added at -78 °C. After 10 min at this temperature, the $MgBr_2$ (0.6 mmol, 1.5 equiv.) was added to the reaction mixture. Once the addition was complete, the mixture was stirred for another 1 h at -78 °C.

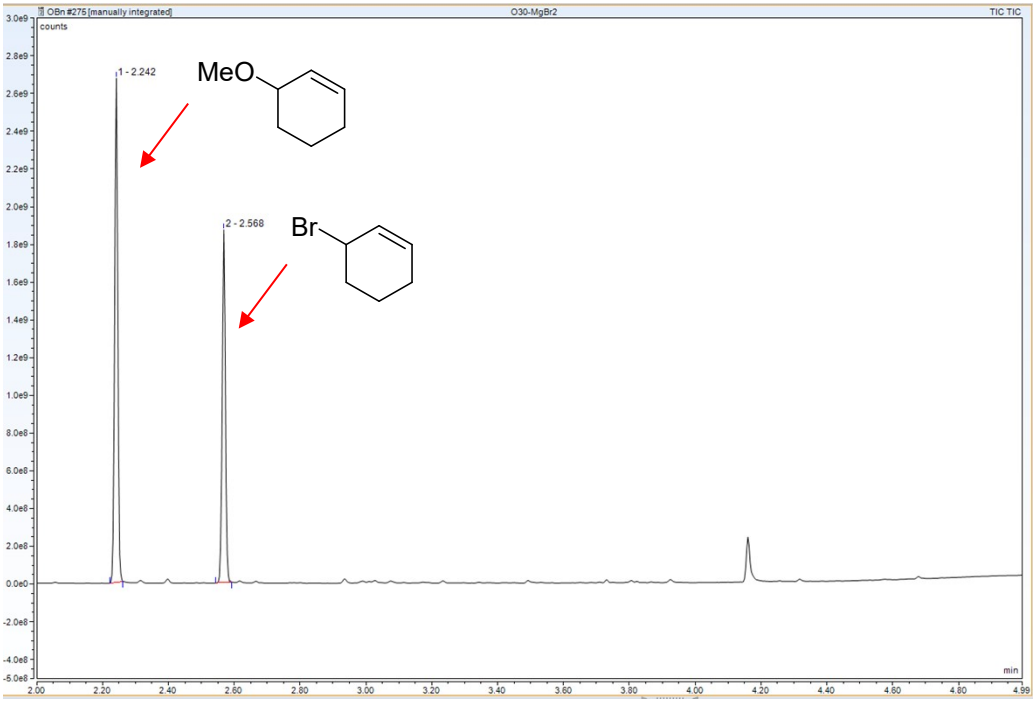


Fig. S3 GCMS traces of 3c *in situ*

6 Number of equivalents of catalyst loading

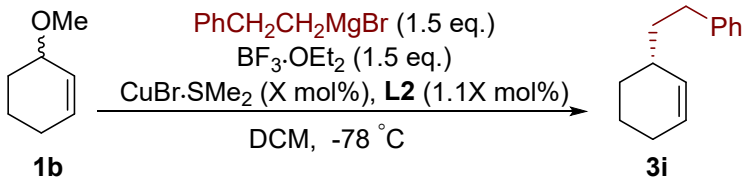


Table S2. Number of equivalents of catalyst loading

Entry	X	ee	Time	Conversion
1	10	95%	1 h	100%
2	5	95%	1 h	92%
3	1	94%	4 h	78%

7 References

1. Langlois, J. B.; Alexakis, A., Dynamic kinetic asymmetric transformation in copper catalyzed allylic alkylation. *Chem. Commun.* **2009,** (26), 3868-70.

2. Langlois, J.-B.; Alexakis, A., Copper-Catalyzed Asymmetric Allylic Alkylation of Racemic Cyclic Substrates: Application of Dynamic Kinetic Asymmetric Transformation (DYKAT). *Adv. Synth. Catal.* **2010,** *352* (2-3), 447-457.

3. Langlois, J.-B.; Emery, D.; Mareda, J.; Alexakis, A., Mechanistic identification and improvement of a direct enantioconvergent transformation in copper-catalyzed asymmetric allylic alkylation. *Chem. Sci.* **2012,** *3* (4), 1062-

1069.
4. You, H.; Rideau, E.; Sidera, M.; Fletcher, S. P., Non-stabilized nucleophiles in Cu-catalysed dynamic kinetic asymmetric allylic alkylation. *Nature* **2015,** *517* (7534), 351-5.
5. Rideau, E.; You, H.; Sidera, M.; Claridge, T. D. W.; Fletcher, S. P., Mechanistic Studies on a Cu-Catalyzed Asymmetric Allylic Alkylation with Cyclic Racemic Starting Materials. *J. Am. Chem. Soc.* **2017,** *139* (15), 5614-5624.
6. Li, J.; Song, X.; Wu, F.; You, H.; Chen, F.-E., Cu-Catalyzed Asymmetric Allylic Alkylation of Racemic Cyclic Allyl Bromides with Organolithium Compounds. *Eur. J. Org. Chem.* **2022,** *2022* (34), e202200860.

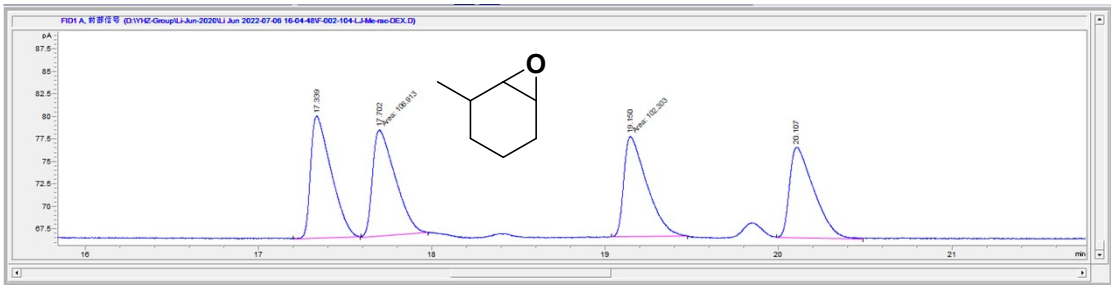
8 Spectroscopic and Chromatographic datas

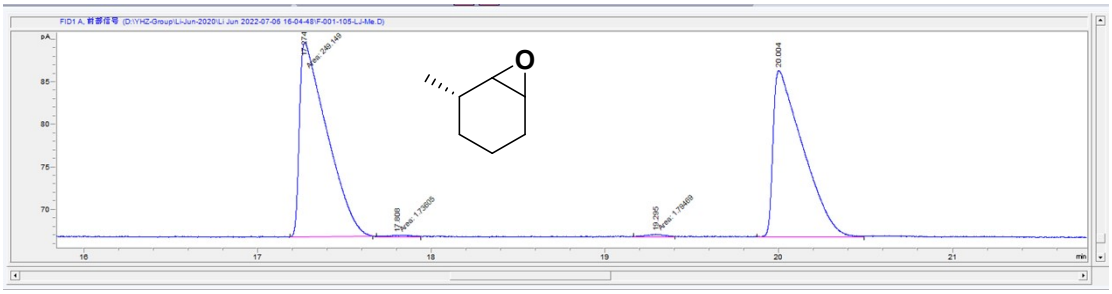
(*S*)-3-methylcyclohex-1-ene (3a)

Highly volatile colorless oil. 99% GC yield, 98% *ee*. The enantiomeric excess was determined by GC on chiral stationary phase (Supelco γ-Dex-225 column, Method: 25-35-10-200-5, RT: 29.04 (R), 29.27 (S) min). The enantiomeric excess was also determined by GC on a chiral stationary phase after derivatisation in corresponding epoxides. (CP-Chiralsil-Dex-CB column, Method: 60-0-1-170, RT: 17.27, 17.81, 19.30, 20.00 min) ^{1}H NMR (400 MHz, Chloroform-d) δ_H /ppm ^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.70 – 5.57 (m, 1H), 5.57 – 5.48 (m, 1H), 2.26 – 2.08 (m, 1H), 2.04 – 1.90 (m, 2H), 1.84 – 1.64 (m, 2H), 1.59 – 1.44 (m, 1H), 1.27 – 1.10 (m, 1H), 0.97 (d, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ_C /ppm 133.6, 126.3, 31.3, 30.1, 25.1, 21.7, 21.4.

HRMS (ESI) calcd for $C_7H_{13}^+$ [(M+H)$^+$] 97.1012, found 97.1010.

GC traces





Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	17.274	MM	0.1819	249.14888	22.82720	51.34979
2	17.808	MM	0.1440	1.73605	2.00960e-1	0.35780
3	19.295	MM	0.1045	1.79469	2.86319e-1	0.36989
4	20.004	BB	0.1571	232.51979	19.55562	47.92252

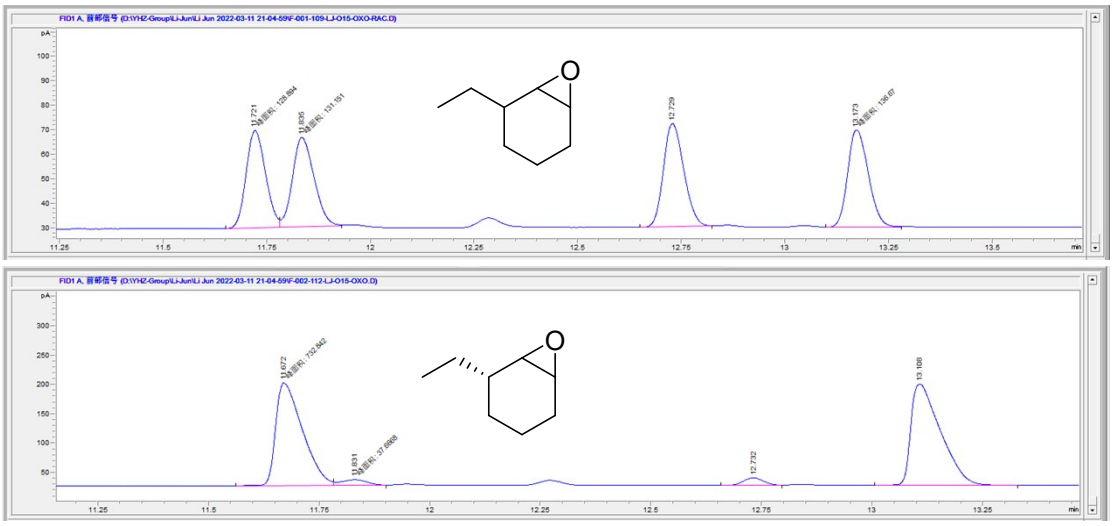
(*S*)-3-ethylcyclohex-1-ene (3b)

Volatile colorless oil. 31.2 mg, 71% isolated yield, 91% *ee*. The enantiomeric excess was determined by GC on a chiral stationary phase after derivatisation in corresponding epoxides (Hydrodex β-6 TBDM column, Method: 60-0-5-170-5, RT:11.67, 11.83, 12.73, 13.11 min). ^{1}H NMR (400 MHz, Chloroform-*d*) δ_H /ppm 5.73 – 5.63 (m, 1H), 5.62 – 5.53 (m, 1H), 2.03 – 1.87 (m, 3H), 1.82 – 1.67 (m, 2H), 1.54 – 1.45 (m, 1H), 1.38 – 1.18 (m, 3H), 0.91 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ_C /ppm 132.1, 126.7, 36.9, 29.0, 28.7, 25.4, 21.6, 11.4.

$[\alpha]^{25}_{589}$ = -82.4 (c = 0.1 in $CHCl_3$)

HRMS (ESI) calcd for $C_8H_{15}^+$ [$(M+H)^+$] 111.1168, found 111.1172.

GC traces



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	11.672	MF	0.0698	732.84210	174.98895	45.55416
2	11.831	FM	0.0674	37.66683	9.31460	2.34141
3	12.732	BB	0.0496	39.78463	12.61672	2.47305
4	13.108	BB	0.0645	798.43341	172.15292	49.63138

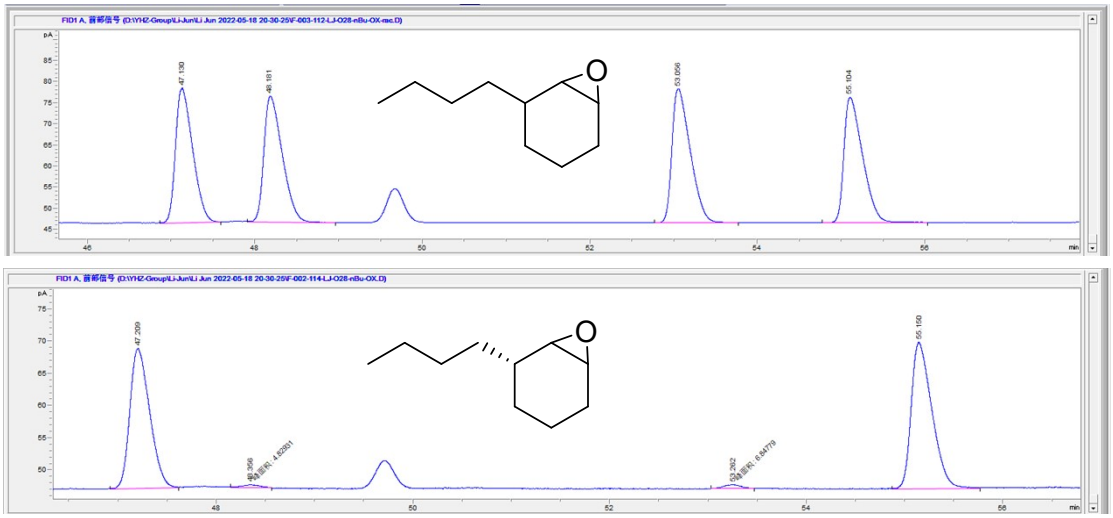
(*S*)-3-butylcyclohex-1-ene 3c

Volatile colorless oil. 45.9 mg, 83% isolated yield, 96% *ee*. The enantiomeric excess was determined by GC on a chiral stationary phase after derivatisation in corresponding epoxides (Hydrodex β-6 TBDM column, Method: 60-0-1-170-5, RT: 47.21, 48.36, 53.26, 55.15 min). ^{1}H NMR (400 MHz, Chloroform-*d*) δ_H /ppm 5.70 – 5.62 (m, 1H), 5.62 – 5.55 (m, 1H), 2.09 – 2.00 (m, 1H), 2.00 – 1.94 (m, 2H), 1.83 – 1.64 (m, 2H), 1.60 – 1.44 (m, 1H), 1.37 – 1.18 (m, 7H), 0.97 – 0.83 (m, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ_C /ppm 132.3, 126.5, 36.2, 35.2, 29.3, 29.2, 25.4, 23.0, 21.6, 14.1.

$[\alpha]^{25}_{589}$ = -62.3 (c = 0.21 in $CHCl_3$)

HRMS (ESI) calcd for $C_{10}H_{19}^{+}$ [$(M+H)^{+}$] 139.1481, found 139.1480.

GC traces



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	47.209	BB	0.1921	303.37531	21.67071	46.96106
2	48.356	MM	0.1874	4.82931	4.29422e-1	0.74755
3	53.262	MM	0.1906	6.84779	5.98719e-1	1.06000
4	55.150	BB	0.2189	330.96216	22.69435	51.23138

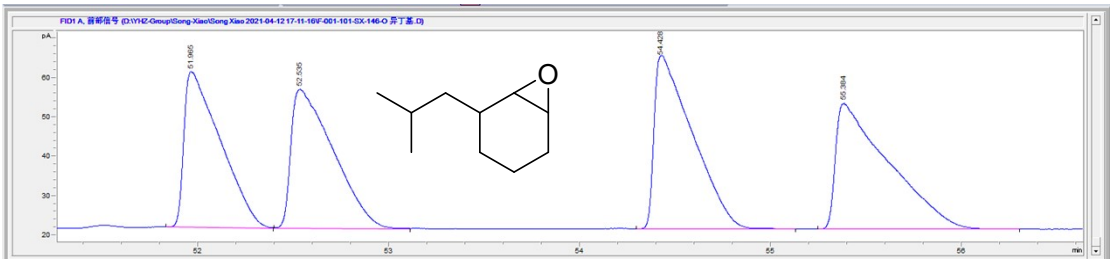
(*R*)-3-isobutylcyclohex-1-ene (3d)

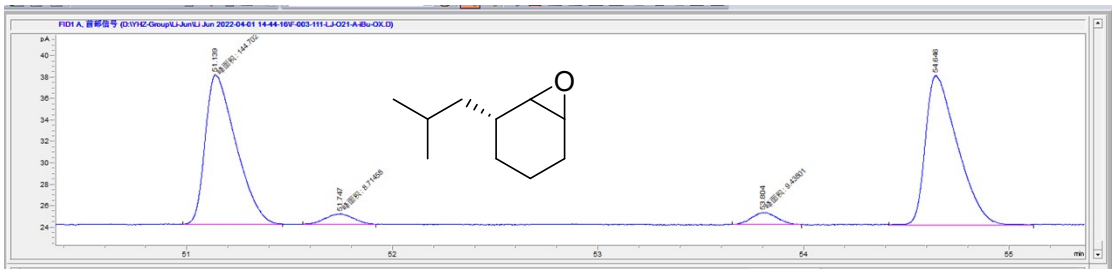
Volatile colorless oil. 43.8 mg, 79% isolated yield, 88% *ee*. The enantiomeric excess was determined by GC on a chiral stationary phase after derivatisation in corresponding epoxides (CP-Chiralsil-Dex-CB column, Method: 60-0-1-120-0-10-200-5, RT: 51.14, 51.75, 53.80, 54.65 min) ^{1}H NMR (400 MHz, Chloroform-*d*) δ_H /ppm 5.68 – 5.61 (m, 1H), 5.60 – 5.52 (m, 1H), 2.18 – 2.07 (m, 1H), 2.03 – 1.91 (m, 2H), 1.82 – 1.65 (m, 3H), 1.58 – 1.45 (m, 1H), 1.24 – 1.07 (m, 3H), 0.89 (t, J = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ_C /ppm 132.4, 126.5, 45.9, 32.7, 29.3, 25.5, 24.9, 23.1, 22.5, 21.4.

$[\alpha]^{25}_{589}$ = -40.6 (c = 0.14 in $CHCl_3$)

HRMS (ESI) calcd for $C_{10}H_{19}^{+}$ [$(M+H)^{+}$] 139.1481, found 139.1482.

GC traces





Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	51.139	MM	0.1727	144.70184	13.96224	46.08189
2	51.747	MM	0.1541	8.71458	9.42241e-1	2.77525
3	53.804	MM	0.1413	9.43801	1.11350	3.00564
4	54.646	BB	0.1584	151.15579	13.95419	48.13722

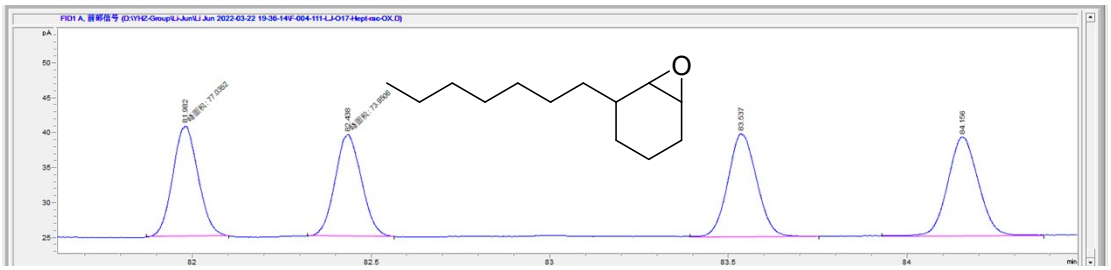
(S)-3-heptylcyclohex-1-ene (3e)

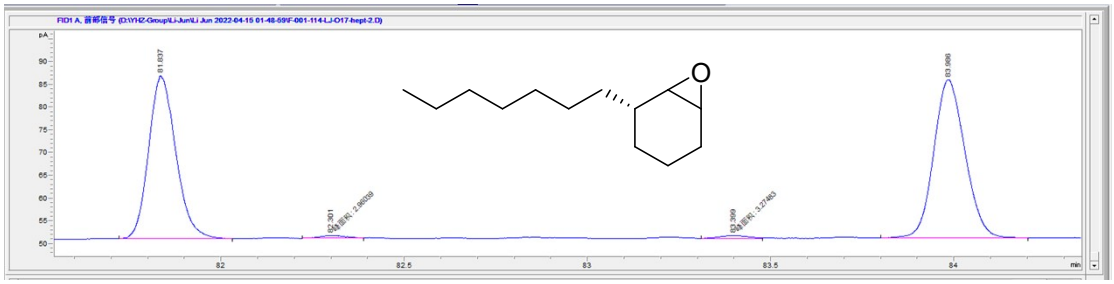
Colorless oil. 57.5 mg, 80% isolated yield, 97% *ee*. The enantiomeric excess was determined by GC on a chiral stationary phase after derivatisation in corresponding epoxides (Hydrodex β-6 TBDM column, Method: 60-0-1-140-0-20-170-5, RT: 81.84, 82,30, 83.40, 83.99 min).^{1}H NMR (400 MHz, Chloroform-*d*) δ_H /ppm 5.70 – 5.61 (m, 1H), 5.62 – 5.54 (m, 1H), 2.13 – 1.89 (m, 3H), 1.82 – 1.65 (m, 2H), 1.55 – 1.43 (m, 1H), 1.33 – 1.21 (m, 13H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ_C /ppm 132.4, 126.6, 36.4, 35.2, 31.9, 29.9, 29.4, 29.1, 27.0, 25.4, 22.7, 21.6, 14.1.

$[\alpha]^{25}_{589}$ = -5.4 (c = 0.18 in $CHCl_3$)

HRMS (ESI) calcd for $C_{13}H_{25}^{+}$ [$(M+H)^{+}$] 181.1951, found 181.1948.

GC traces





Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	81.837	BB	0.0753	184.42480	35.80082	46.45978
2	82.301	MM	0.0831	2.96039	5.93749e-1	0.74577
3	83.399	MM	0.0841	3.27483	6.49026e-1	0.82499
4	83.986	BB	0.0933	206.29578	34.74703	51.96946

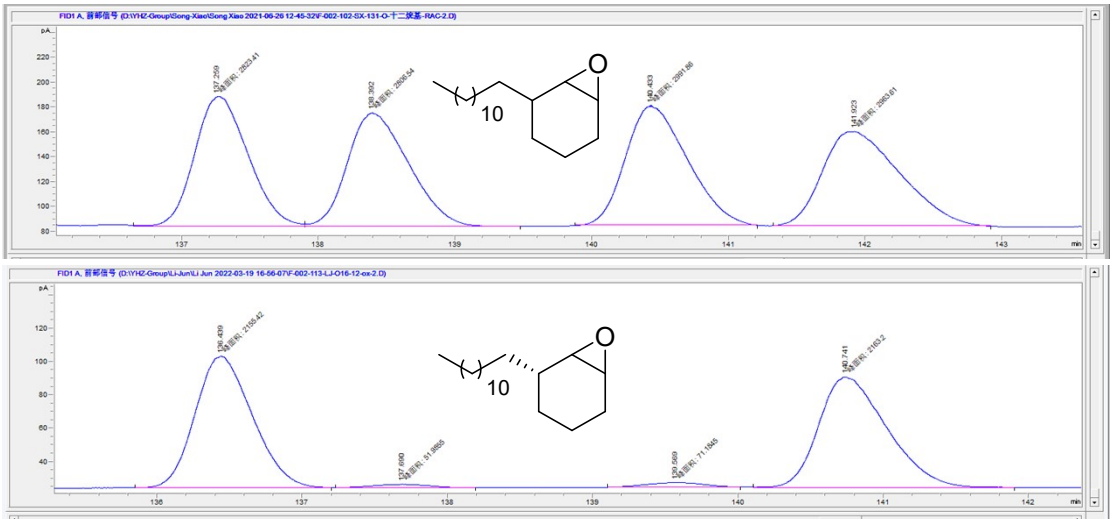
(S)-3-dodecylcyclohex-1-ene (3f)

Colorless oil. 95% NMR yield, 94% *ee*. The enantiomeric excess was determined by GC on a chiral stationary phase after derivatisation in corresponding epoxides (CP-Chiralsil-Dex-CB column, Method: 50-0-1-170-30-10-200-5, RT: 81.84, 82,30, 83.40, 83.99 min). ^{1}H NMR (400 MHz, Chloroform-*d*) δ_H /ppm 5.68 – 5.62 (m, 1H), 5.62 – 5.54 (m, 1H), 2.10 – 1.91 (m, 3H), 1.85 – 1.67 (m, 2H), 1.59 – 1.47 (m, 1H), 1.33 – 1.26 (m, 23H), 0.89 (t, J = 6.9 Hz, 3H).; ^{13}C NMR (100 MHz, Chloroform-*d*) δ_C /ppm 132.4, 126.6, 36.4, 35.2, 31.9, 29.9, 29.7 (m, 5C), 29.4, 29.1, 27.0, 25.4, 22.7, 21.6, 14.1.

$[\alpha]^{25}_{589}$ = -25.4 (c = 0.45 in $CHCl_3$)

HRMS (ESI) calcd for $C_{18}H_{35}^{+}$ [$(M+H)^{+}$] 251.2733, found 251.2728.

GC traces



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	136.439	MM	0.4558	2155.41577	78.81336	48.52590
2	137.690	MM	0.4272	51.98553	2.02816	1.17037
3	139.569	MM	0.4463	71.18447	2.65829	1.60261
4	140.741	MM	0.5426	2163.19849	66.44946	48.70112

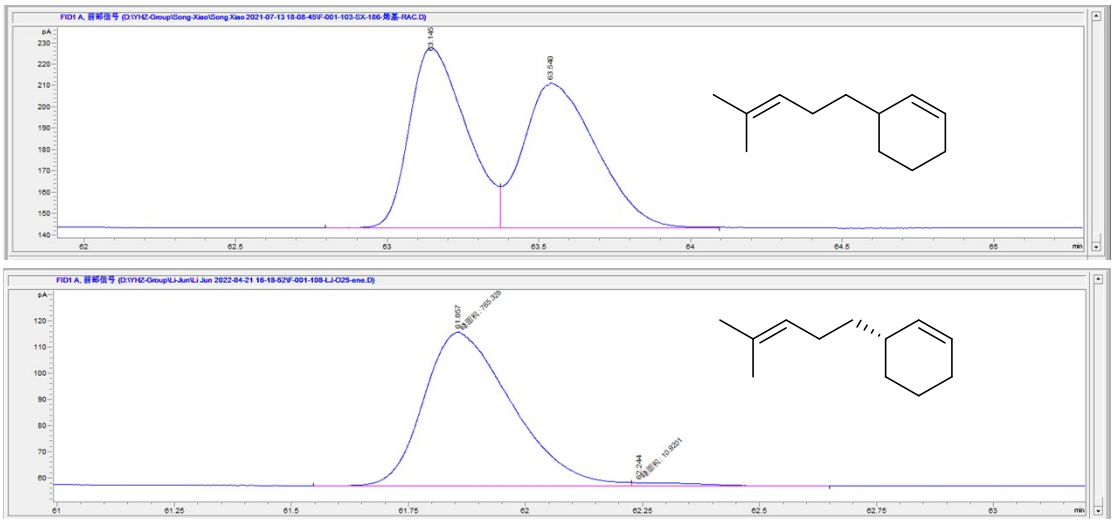
(R)-3-(4-methylpent-3-en-1-yl)cyclohex-1-ene (3g)

Colorless oil. 51.3 mg, 78% isolated yield, 97% *ee*. The enantiomeric excess was determined by GC on a chiral stationary phase (Hydrodex B3P column, Method: 40-0-1-110-0-5-170-5, RT: 61.86, 62.24 min). ^{1}H NMR (400 MHz, Chloroform-*d*) δ_H /ppm 5.73 – 5.63 (m, 1H), 5.62 – 5.52 (m, 1H), 5.14 – 5.08 (m, 1H), 2.08 – 2.01 (m, 2H), 2.00 – 1.92 (m, 3H), 1.82 – 1.74 (m, 1H), 1.69 (s, 3H), 1.61 (s, 3H), 1.54 – 1.45 (m, 1H), 1.43 – 1.13 (m, 4H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ_C /ppm 132.2, 131.3, 126.7, 124.7, 36.4, 34.7, 29.0, 25.7, 25.4, 21.5, 17.6.

$[\alpha]^{25}_{589}$ = -62.7 (c = 0.35 in $CHCl_3$)

HRMS (ESI) calcd for $C_{12}H_{21}^{+}$ [$(M+H)^{+}$] 165.1638, found 165.1637.

GC traces



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	61.857	MF	0.2167	765.32806	58.85297	98.59322
2	62.244	FM	0.1505	10.92007	1.20915	1.40678

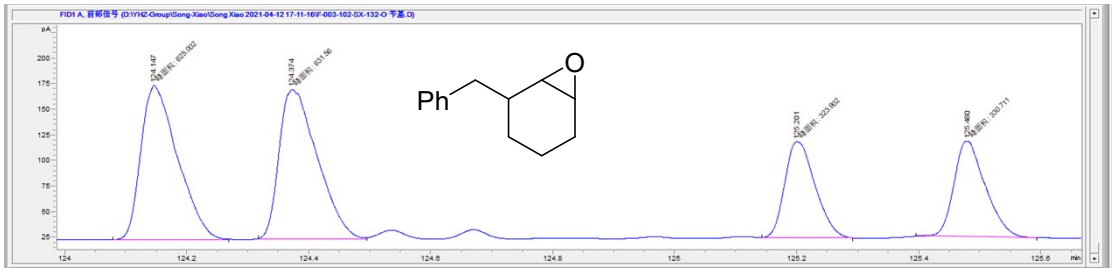
(R)-(cyclohex-2-en-1-ylmethyl)benzene (3h)

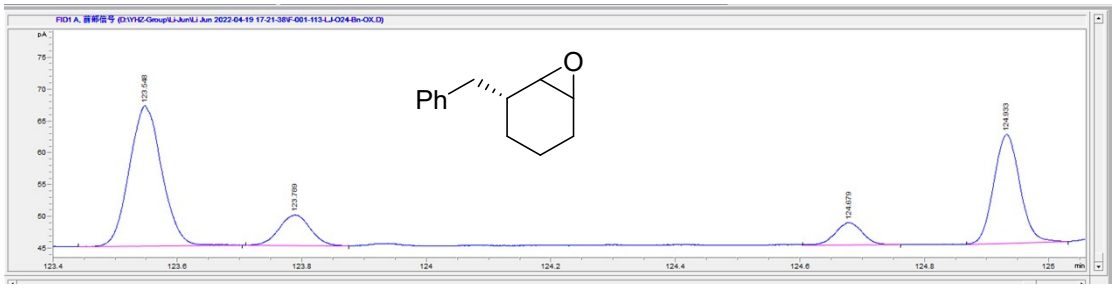
Colorless oil. 62 mg, 90% isolated yield, 65% *ee*. The enantiomeric excess was determined by GC on a chiral stationary phase after derivatisation in corresponding epoxides (CP-Chiralsil-Dex-CB column, Method: 30-0-1-150-0-10-200-5, RT: 123.55, 123.79, 124.68, 124.93 min). ^{1}H NMR (400 MHz, Chloroform-*d*) δ_H /ppm 7.31 – 7.23 (m, 2H), 7.22 – 7.12 (m, 3H), 5.75 – 5.64 (m, 1H), 5.62 – 5.51 (m, 1H), 2.70 – 2.58 (m, 1H), 2.56 – 2.48 (m, 1H), 2.42 – 2.30 (m, 1H), 2.05 – 1.92 (m, 2H), 1.77 – 1.62 (m, 2H), 1.56 – 1.41 (m, 1H), 1.33 – 1.18 (m, 1H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ_C /ppm 140.8, 131.3, 129.1, 128.1, 127.3, 125.7, 42.7, 37.2, 28.9, 25.4, 21.3.

$[\alpha]^{25}_{589}$ = -18.5 (c = 0.21 in $CHCl_3$)

HRMS (ESI) calcd for $C_{13}H_{17}^{+}$ [$(M+H)^{+}$] 173.1325, found 173.1322.

GC traces





Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	123.548	BB	0.0561	80.21606	22.04475	50.99786
2	123.789	BB	0.0544	16.81706	4.80495	10.69155
3	124.679	BB	0.0475	10.46578	3.51617	6.65369
4	124.933	BB	0.0460	49.79411	17.06130	31.65691

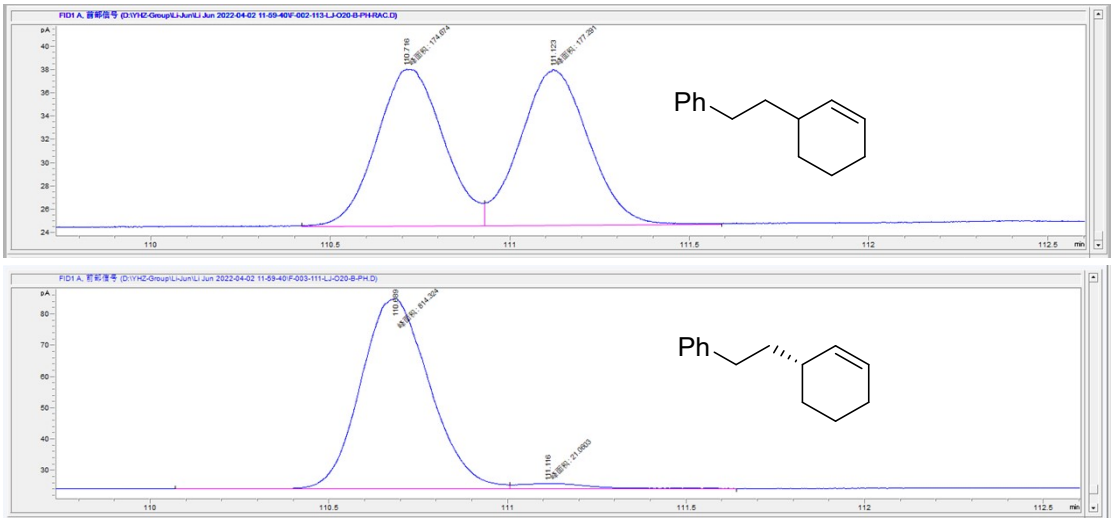
(R)-(2-(cyclohex-2-en-1-yl)ethyl)benzene (3i)

Colorless oil. 64.5 mg, 87% isolated yield, 95% *ee*. The enantiomeric excess was determined by GC on a chiral stationary phase (Hydrodex B3P column, Method: 60-30-1-150-0-20-170-5, RT: 110.69, 111.12 min). ^{1}H NMR (400 MHz, Chloroform-*d*) δ_H /ppm 7.31 – 7.26 (m, 2H), 7.23 – 7.13 (m, 3H), 5.74 – 5.66 (m, 1H), 5.66 – 5.59 (m, 1H), 2.71 – 2.61 (m, 2H), 2.14 – 2.05 (m, 1H), 2.03 – 1.94 (m, 2H), 1.88 – 1.80 (m, 1H), 1.79 – 1.70 (m, 1H), 1.69 – 1.56 (m, 2H), 1.54 – 1.46 (m, 1H), 1.32 – 1.27 (m, 1H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ_C /ppm 142.8, 131.7, 128.4, 128.3, 127.1, 125.6, 38.2, 34.7, 33.3, 29.0, 25.4, 21.5.

$[\alpha]^{25}_{589}$ = -25.8 (c = 0.36 in $CHCl_3$)

HRMS (ESI) calcd for $C_{14}H_{19}^{+}$ [$(M+H)^{+}$] 187.1481, found 187.1480.

GC traces

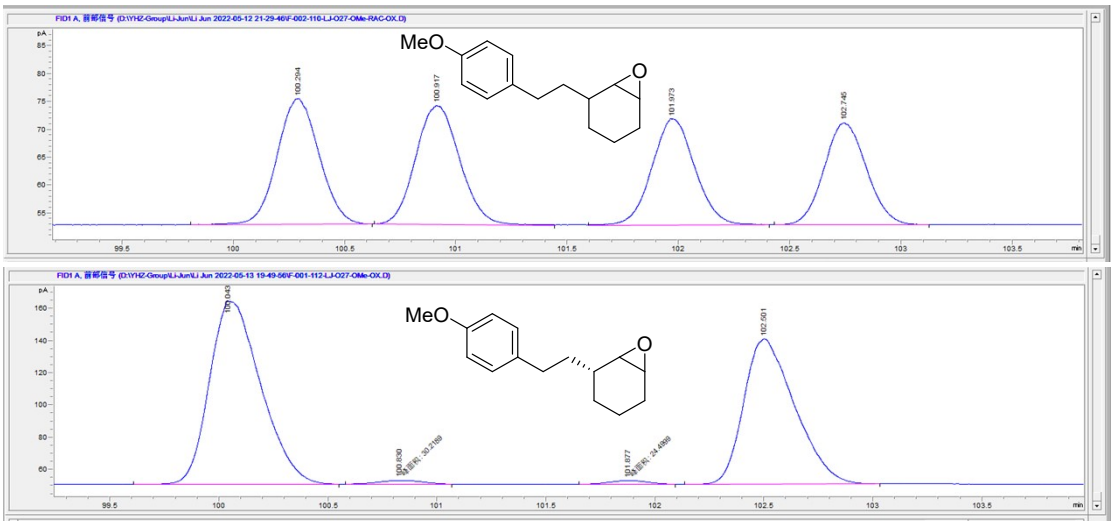


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	110.689	MF	0.2230	814.32385	60.84980	97.47897
2	111.116	FM	0.2179	21.06026	1.61104	2.52103

(R)-1-(2-(cyclohex-2-en-1-yl)ethyl)-4-methoxybenzene (3j)

Colorless oil, 96% *ee*. $[\alpha]^{25}_{589}$ = -49.3 (c = 0.1 in $CHCl_3$). HRMS (ESI) calcd for $C_{15}H_{21}O^+$ $[(M+H)^+]$ 217.1587, found 217.1585. Colorless oil isolated after derivatisation in corresponding epoxides. After treatment with *m*CPBA, **2-(4-methoxyphenethyl)-7-oxabicyclo[4.1.0]heptane (6j)** is isolated as a mixture of diastereoisomeric epoxides (1:1). 75.4 mg, 81% isolated yield (after two steps). The enantiomeric excess was determined by GC on a chiral stationary phase after derivatisation in corresponding epoxides (CP-Chiralsil-Dex-CB column, Method: 80-0-1-200-10, RT: 100.04, 100.83, 101.88, 102.50 min). ^{1}H NMR (400 MHz, Chloroform-*d*) δ_H /ppm δ 7.16 – 7.09 (m, 2H), 6.88 – 6.80 (m, 2H), 3.79 (s, 3H), 3.21 – 3.10 (m, 1.5H), 2.92 – 2.89 (m, 0.5H), 2.74 – 2.61 (m, 2H), 2.12 – 2.02 (m, 0.5H), 1.91 – 1.62 (m, 5H), 1.56 – 1.46 (m, 0.5H), 1.45 – 1.29 (m, 1.5H), 1.25 – 1.08 (m, 1H), 0.95 – 0.82 (m, 0.5H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ_C /ppm 157.7, 157.6, 134.5, 143.1, 129.2, 113.8, 113.7, 56.3, 55.5, 55.2, 52.9, 52.8, 36.1, 35.1, 34.1, 33.7, 32.4, 32.2, 27.2, 25.2, 24.8, 23.9, 19.8, 17.2. HRMS (ESI) calcd for $C_{15}H_{21}O_2^+$ $[(M+H)^+]$ 233.1536, found 233.1536.

GC traces



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	100.043	BB	0.1984	1863.43774	113.72225	55.11419
2	100.830	MM	0.2196	30.21889	2.29393	0.89377
3	101.877	MM	0.1848	24.49990	2.20961	0.72462
4	102.501	BB	0.2063	1462.89233	90.05285	43.26741

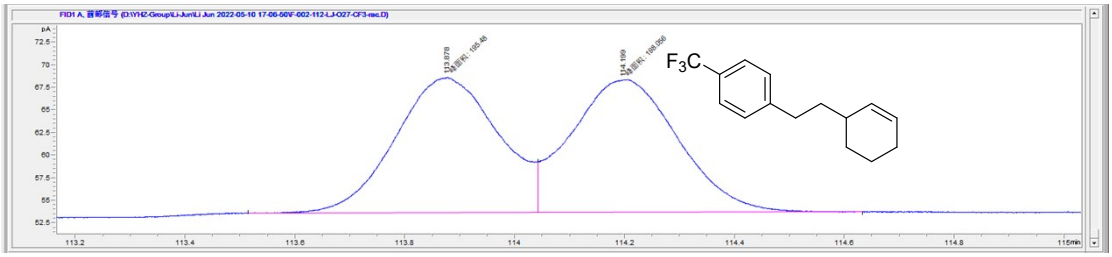
(R)-1-(2-(cyclohex-2-en-1-yl)ethyl)-4-(trifluoromethyl)benzene (3k)

Colorless oil. 65.7 mg, 65% isolated yield, 97% *ee*. The enantiomeric excess was determined by GC on a chiral stationary phase (Hydrodex B3P column, Method: 60-30-1-170-5, RT: 113.87, 114.18 min). ^{1}H NMR (400 MHz, Chloroform-*d*) δ_H /ppm δ 7.56 – 7.51 (m, 2H), 7.34 – 7.27 (m, 2H), 5.77 – 5.68 (m, 1H), 5.67 – 5.58 (m, 1H), 2.79 – 2.65 (m, 2H), 2.19 – 2.06 (m, 1H), 2.05 – 1.95 (m, 2H), 1.90 – 1.80 (m, 1H), 1.80 – 1.58 (m, 3H), 1.57 – 1.47 (m, 1H), 1.35 – 1.22 (m, 1H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ_C /ppm 147.0, 131.3,128.6 128.0 (q, J = 32.3 Hz), 127.5, 125.2 (q, J = 4.0 Hz), 124.4 (q, J = 272.7 Hz), 37.9, 34.7, 33.1, 29.0, 25.3, 21.4. ^{19}F NMR (380 MHz, Chloroform-*d*) δ -62.2.

$[\alpha]^{25}_{589}$ = -15.7 (c = 0.25 in $CHCl_3$)

HRMS (ESI) calcd for $C_{15}H_{18}F_3^+$ $[(M+H)^+]$ 255.1355, found 255.1355.

GC traces



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	113.867	MF	0.2256	377.86826	27.91684	98.67796
2	114.176	FM	0.1110	5.06249	7.60022e-1	1.32204

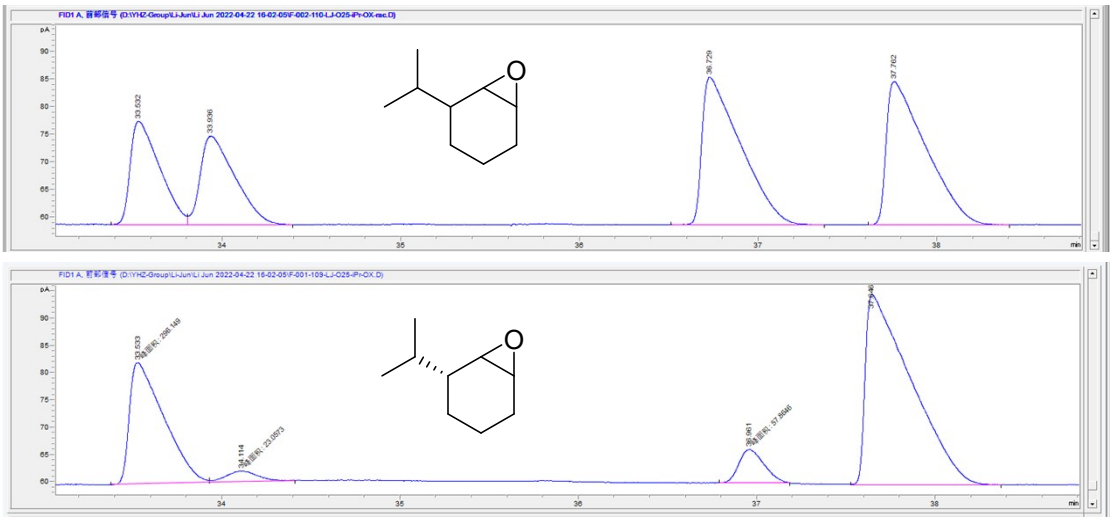
(R)-3-isopropylcyclohex-1-ene (3l)

Colorless oil. 41.1 mg, 83% isolated yield, 82% *ee*. The enantiomeric excess was determined by GC on a chiral stationary phase after derivatisation in corresponding epoxides (CP-Chiralsil-Dex-CB column, Method: 60-0-1-110-0-20-200-5, RT: 33.53, 34.11, 36.96, 37.65 min).^{1}H NMR (400 MHz, Chloroform-*d*) δ_H /ppm 5.76 – 5.65 (m, 1H), 5.63 – 5.53 (m, 1H), 2.05 – 1.87 (m, 3H), 1.85 – 1.63 (m, 2H), 1.61 – 1.43 (m, 2H), 1.35 – 1.21 (m, 1H), 0.89 (d, J = 6.8 Hz, 3H), 0.87 (d, J = 6.8 Hz, 3H).; ^{13}C NMR (100 MHz, Chloroform-*d*) δ_C /ppm 130.9, 127.4, 41.7, 32.2, 25.6, 25.4, 22.2, 19.7, 19.4.

$[\alpha]^{25}_{589}$ = -25.2(c = 0.1 in $CHCl_3$)

HRMS (ESI) calcd for $C_9H_{17}^+$ [$(M+H)^+$] 125.1325, found 125.1322.

GC traces



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	33.533	MF	0.2218	296.14883	22.24910	29.64119
2	34.114	FM	0.1976	23.05734	1.94451	2.30778
3	36.961	MM	0.1600	57.86464	6.02668	5.79160
4	37.646	BB	0.2263	622.04156	34.77803	62.25942

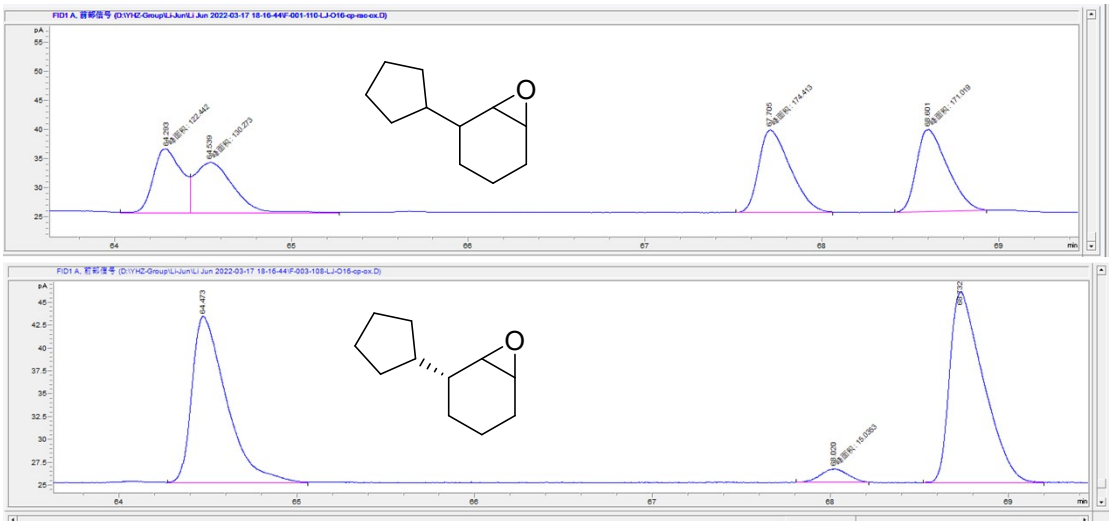
(R)-3-cyclopentylcyclohex-1-ene(3m)

Colorless oil. 56 mg, 93% isolated yield, 90% *ee*. The enantiomeric excess was determined by GC on a chiral stationary phase after derivatisation in corresponding epoxides (CP-Chiralsil-Dex-CB column, Method: 60-0-1-170-5, RT: 64.47, 68.02, 68.73 min). ^{1}H NMR (400 MHz, Chloroform-*d*) δ_H /ppm δ 5.74 – 5.56 (m, 2H), 2.00 – 1.94 (m, 2H), 1.93 – 1.85 (m, 1H), 1.82 – 1.69 (m, 4H), 1.68 – 1.44 (m, 6H), 1.32 – 1.10 (m, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ_C /ppm 131.3, 127.0, 45.7, 40.9, 30.7, 30.2, 28.5, 25.4, 25.4, 25.3, 21.8.

$[\alpha]^{25}_{589}$ = -97.2 (c = 0.34 in $CHCl_3$)

HRMS (ESI) calcd for $C_{11}H_{19}^{+}$ [$(M+H)^{+}$] 151.1481, found 151.1483.

GC traces



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	64.473	BB	0.1672	244.15001	18.16501	45.66834
2	68.020	MM	0.1744	15.03534	1.43679	2.81236
3	68.732	BB	0.1775	275.43008	20.93190	51.51929

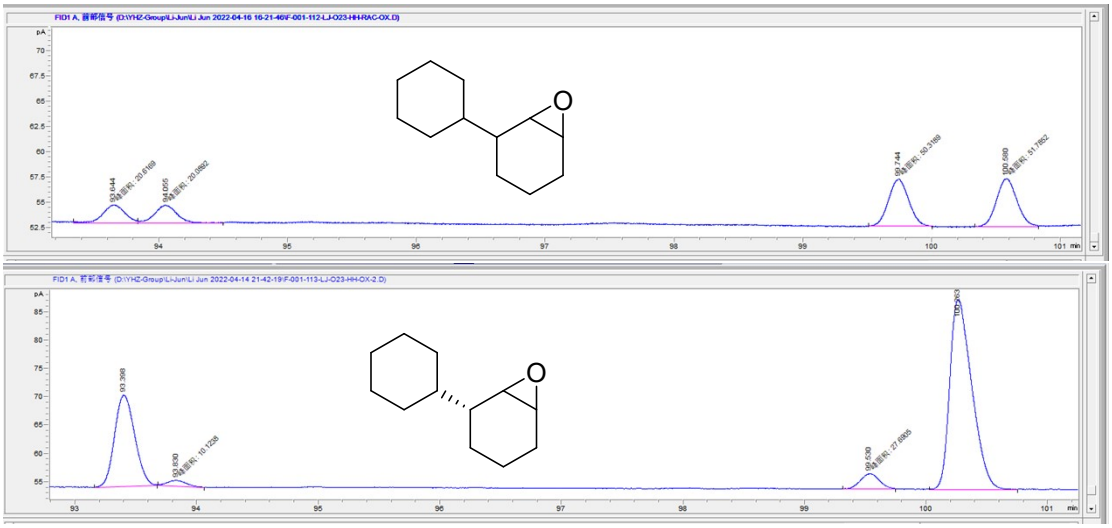
(R)-3-cyclohexylcyclohex-1-ene (3n)

Colorless oil. 92% NMR yield, 88% *ee*. The enantiomeric excess was determined by GC on a chiral stationary phase after derivatisation in corresponding epoxides (Hydrodex β-6 TBDM column, Method: 60-0-1-170-0-10-200-5, RT: 93.40, 93.83, 99.53, 100.26 min). ^{1}H NMR (400 MHz, Chloroform-*d*) δ_H /ppm 5.73 – 5.65 (m, 1H), 5.64 – 5.57 (m, 1H), 2.00 – 1.88 (m, 3H), 1.75 – 1.64 (m, 7H), 1.54 – 1.42 (m, 1H), 1.23 – 0.95 (m, 7H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ_C /ppm 131.1, 127.2, 42.7, 40.9, 30.3, 29.9, 26.8, 25.8, 25.5, 22.2.

$[\alpha]^{25}_{589}$ = -52.0 (c = 0.36 in $CHCl_3$)

HRMS (ESI) calcd for $C_{12}H_{21}^{+}$ [$(M+H)^{+}$] 165.1638, found 165.1638.

GC traces



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	93.398	BB	0.1423	185.14151	16.08185	28.70292
2	93.830	MM	0.1692	10.12377	9.97490e-1	1.56951
3	99.530	MM	0.1750	27.69049	2.63781	4.29292
4	100.263	BB	0.1639	422.07104	33.48516	65.43465

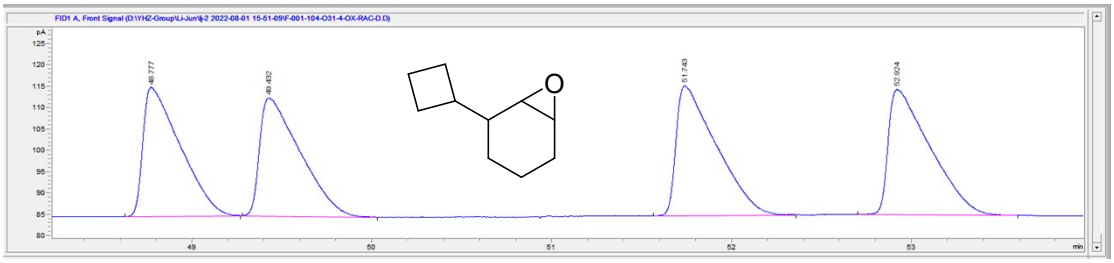
(R)-3-cyclobutylcyclohex-1-ene (3o)

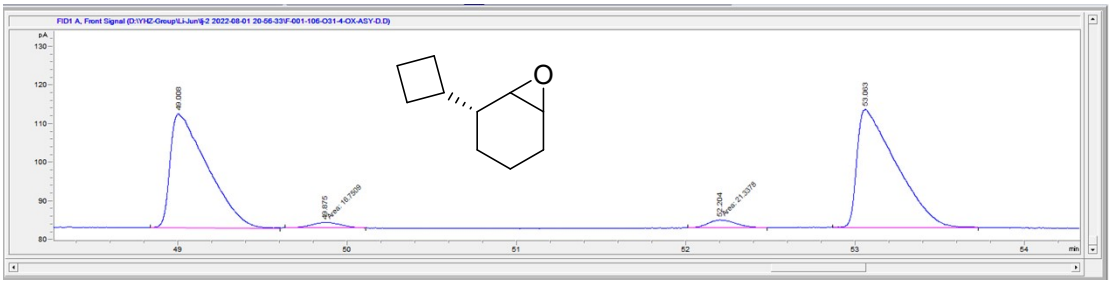
Colorless oil. 48.3 mg, 89% isolated yield, 92% *ee*. The enantiomeric excess was determined by GC on a chiral stationary phase after derivatisation in corresponding epoxides (CP-Chiralsil-Dex-CB column, Method: 60-0-1-170-5, RT: 49.01, 49.88, 52.20, 53.06 min). ^{1}H NMR (400 MHz, Chloroform-*d*) δ_H /ppm 5.73 – 5.64 (m, 1H), 5.63 – 5.54 (m, 1H), 2.14 – 1.93 (m, 6H), 1.88 – 1.66 (m, 6H), 1.54 – 1.42 (m, 1H), 1.16 – 1.01 (m, 1H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ_C /ppm 129.2, 127.0, 41.8, 41.18, 26.7, 26.5, 26.4, 25.4, 21.3, 18.1.

$[\alpha]^{25}_{589}$ = -43.4 (c = 0.03 in $CHCl_3$)

HRMS (ESI) calcd for $C_{10}H_{17}^{+}$ [$(M+H)^{+}$] 137.1325, found 137.1328.

GC traces



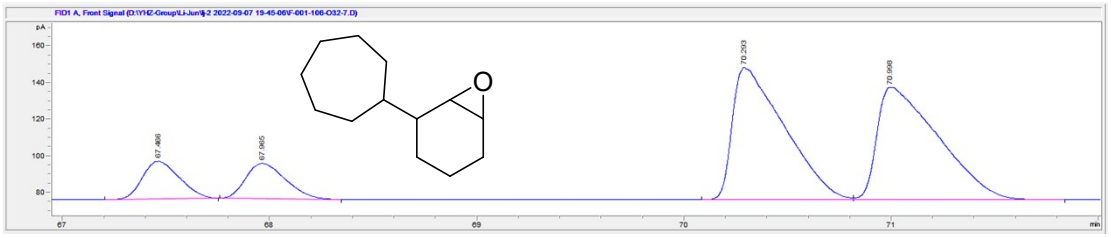


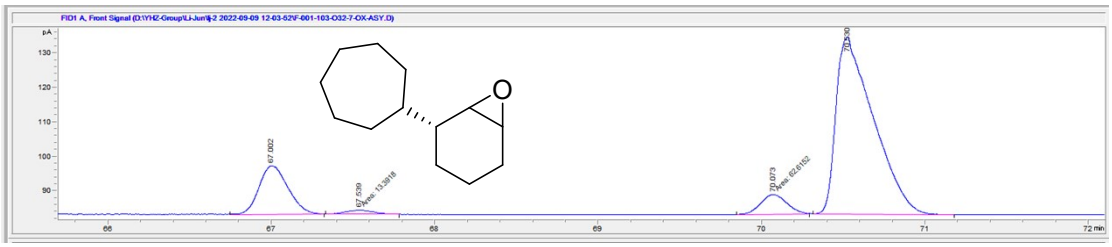
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	49.008	BB	0.1950	448.72110	29.50691	45.84940
2	49.875	MM	0.1984	16.75086	1.40741	1.71157
3	52.204	MM	0.1817	21.33775	1.95689	2.18025
4	53.063	BB	0.2043	491.87497	30.60146	50.25878

(R)-cyclohex-2-en-1-ylcycloheptane (3p)

Colorless oil, 86% *ee*. $[\alpha]^{25}_{589}$ = -20.0 (c = 0.11 in $CHCl_3$). HRMS (ESI) calcd for $C_{13}H_{23}^+$ $[(M+H)^+]$ 179.1794, found 179.1797. Colorless oil isolated after derivatisation in corresponding epoxides. After treatment with *m*CPBA, **2-cycloheptyl-7-oxabicyclo[4.1.0]heptane (6p)** is isolated as a mixture of diastereoisomericepoxides (82:18). 67.8 mg, 87% isolated yield (after two steps). The enantiomeric excess was determined by GC on a chiral stationary phase after derivatisation in corresponding epoxides (CP-Chiralsil-Dex-CB column, Method: 80-0-1-155-0-10-170-5, RT: 67.00, 67.54, 70.07, 70.53 min). ^{1}H NMR (400 MHz, Chloroform-d) δ_H /ppm ^{1}H NMR (400 MHz, Chloroform-*d*) δ 3.15 – 3.10 (m, 1H), 3.09 – 3.05 (m, 0.18H), 2.91 – 2.87 (m, 0.82H), 2.15 – 1.98 (m, 1H), 1.86 – 1.74 (m, 1H), 1.74 – 1.64 (m, 4H), 1.64 – 1.55 (m, 4H), 1.50 – 1.42 (m, 4H), 1.41 – 1.33 (m, 3H), 1.33 – 1.15 (m, 2H), 0.98 – 0.85 (m, 1H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ_C /ppm 55.9, 55.2, 53.0, 51.6, 43.0, 42.9, 42.0, 41.2, 31.9, 31.8, 31.7, 31.4, 28.4, 28.3, 28.1, 27.9, 27.6, 27.5, 26.9, 26.8, 25.2, 23.8, 23.7, 22.1, 21.1, 17.6. HRMS (ESI) calcd for $C_{13}H_{23}O^+$ $[(M+H)^+]$ 195.1743, found 195.1744.

GC traces





Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	67.002	BB	0.1515	173.11807	14.00114	16.21157
2	67.539	MM	0.1964	13.39177	1.13656	1.25407
3	70.073	MM	0.1835	62.61515	5.68822	5.86357
4	70.530	BB	0.1930	818.74231	51.41635	76.67079

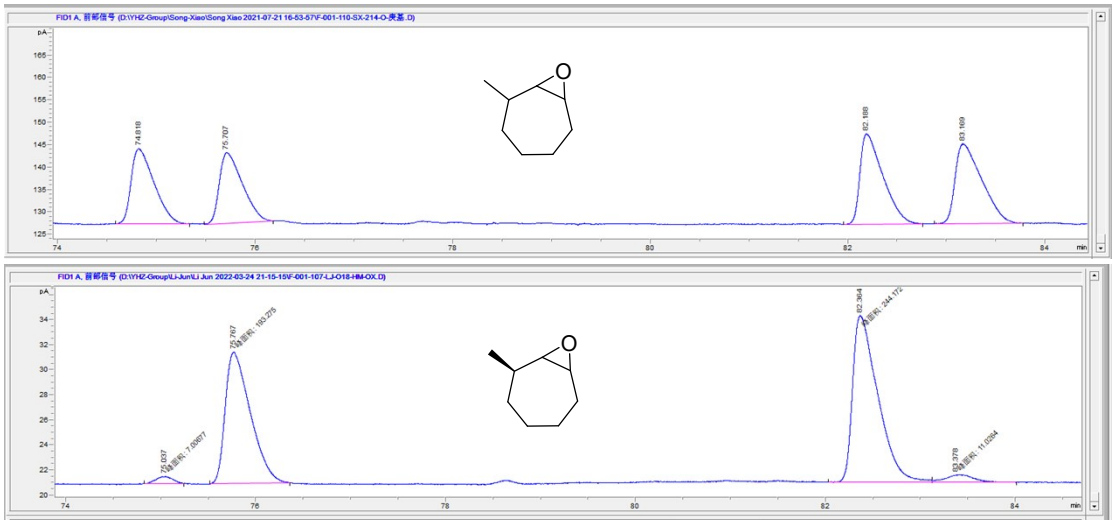
(*R*)-3-methylcyclohept-1-ene (4a)

Volatile colorless oil. 33.2 mg, 75% isolated yield, 91% *ee*. The enantiomeric excess was determined by GC on a chiral stationary phase after derivatisation in corresponding epoxides (Hydrodex β-6 TBDM column, Method: 50-30-1-120-5-10-180-9, RT: 75.04, 75.77, 82.36, 83.38 min). ^{1}H NMR (400 MHz, Chloroform-d) δ_H /ppm 5.77 – 5.65 (m, 1H), 5.54 – 2.39 (m, 1H), 2.42 – 2.27 (m, 1H), 2.21 – 2.02 (m, 2H), 1.98 – 1.85 (m, 1H), 1.73 – 1.63 (m, 1H), 1.60 – 1.49 (m, 2H), 1.35 – 1.27 (m, 1H), 1.25 – 1.16 (m, 1H), 1.03 (d, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ_C /ppm 139.4, 130.6, 35.9, 34.5, 30.6, 28.9, 27.0, 23.2.

$[\alpha]^{25}_{589}$ = +9.9 (c = 0.13 in $CHCl_3$)

HRMS (ESI) calcd for $C_8H_{15}^+$ [$(M+H)^+$] 111.1168, found 111.1169.

GC traces



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	75.037	MM	0.2047	7.00677	5.70579e-1	1.53833
2	75.767	MM	0.3069	193.27498	10.49551	42.43321
3	82.364	MF	0.3062	244.17232	13.29194	53.60764
4	83.378	FM	0.3157	11.02638	5.82189e-1	2.42082

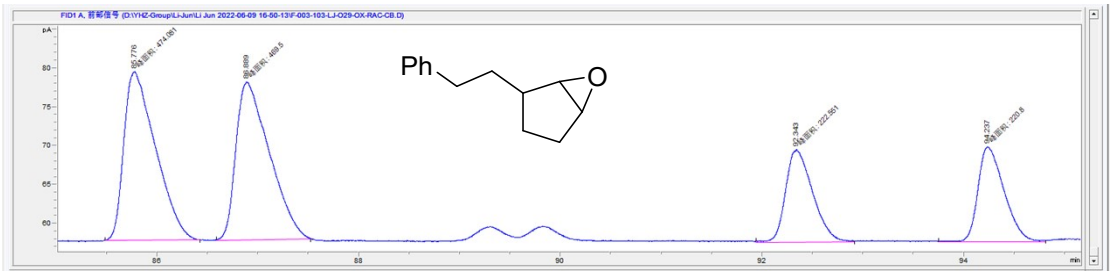
(R)-(2-(cyclopent-2-en-1-yl)ethyl)benzene(5a)

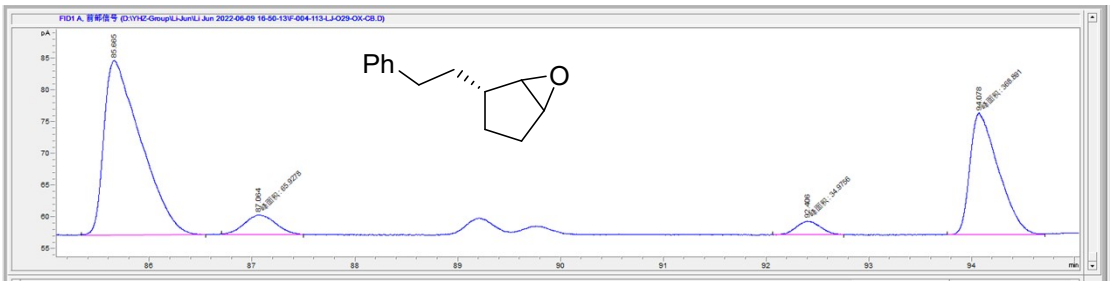
Colorless oil. 56.7 mg, 82% isolated yield, 83% *ee*. The enantiomeric excess was determined by GC on a chiral stationary phase after derivatisation in corresponding epoxides (CP-Chiralsil-Dex-CB column, Method: 80-0-1-120-30-1-150-0-20-200-5, RT: 85.67, 87.06, 92.41, 94.08 min). ^{1}H NMR (400 MHz, Chloroform-d) δ_H /ppm 7.30 – 7.25 (m, 2H), 7.22 – 7.13 (m, 3H), 5.77 – 5.67 (m, 2H), 2.72 – 2.58 (m, 3H), 2.42 – 2.22 (m, 2H), 2.15 – 2.01 (m, 1H), 1.80 – 1.69 (m, 1H), 1.66 – 1.57 (m, 1H), 1.51 – 1.40 (m, 1H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ_C /ppm 142.8, 134.9, 130.5, 128.4, 128.3, 125.6, 45.2, 37.9, 34.3, 32.0, 29.8.

$[\alpha]^{25}_{589}$ = -82.1 (c = 0.13 in $CHCl_3$)

HRMS (ESI) calcd for $C_{13}H_{17}^{+}$ [$(M+H)^{+}$] 173.1325, found 173.1321.

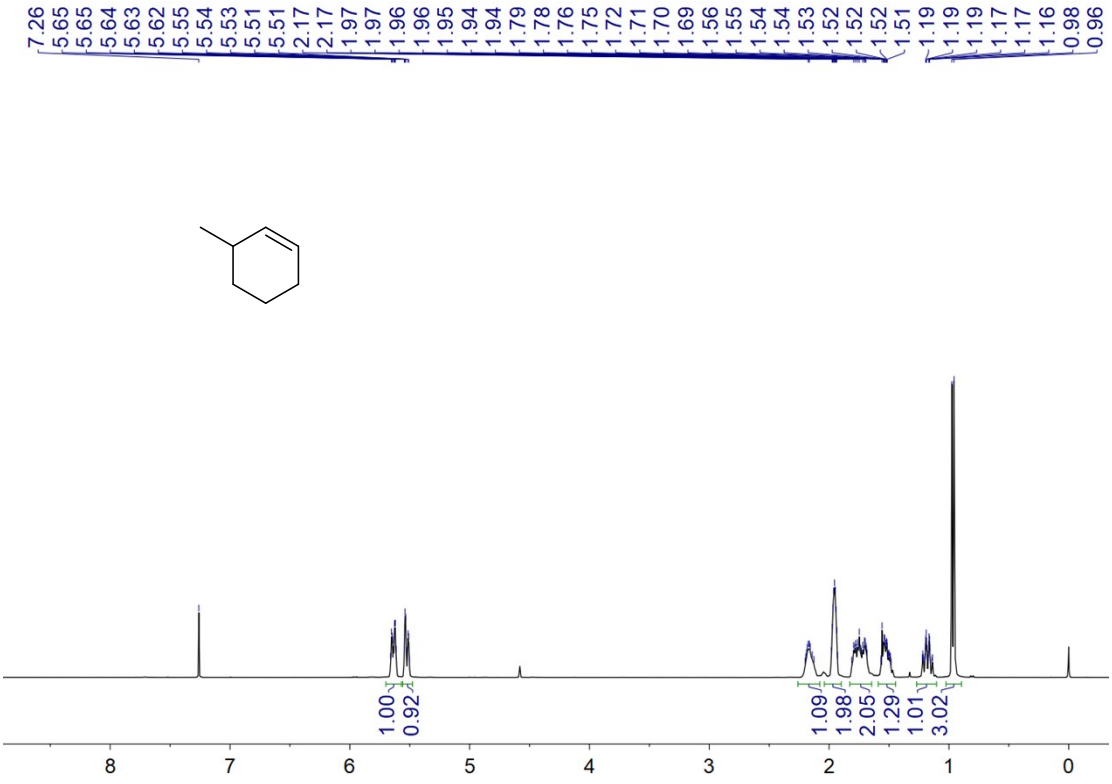
GC traces



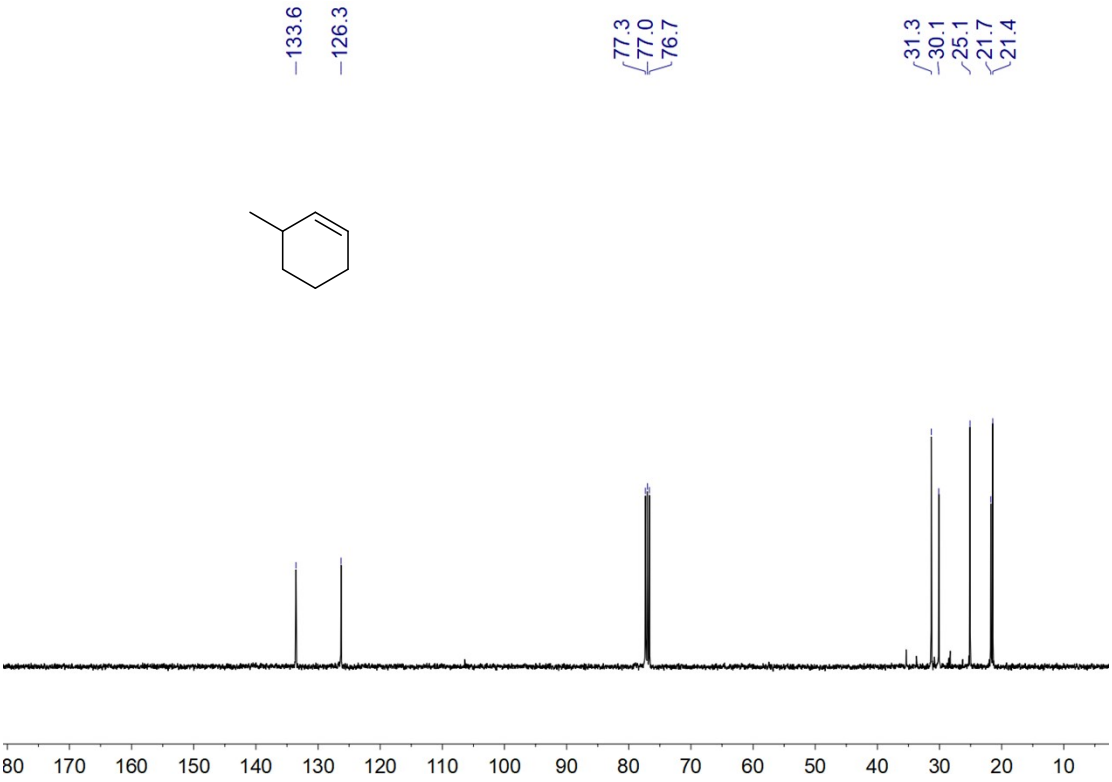


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	85.665	BB	0.2943	687.93622	27.49742	59.42108
2	87.064	MM	0.3536	65.92777	3.10786	5.69457
3	92.406	MM	0.2712	34.97562	2.14926	3.02105
4	94.078	MM	0.3213	368.89133	19.13802	31.86330

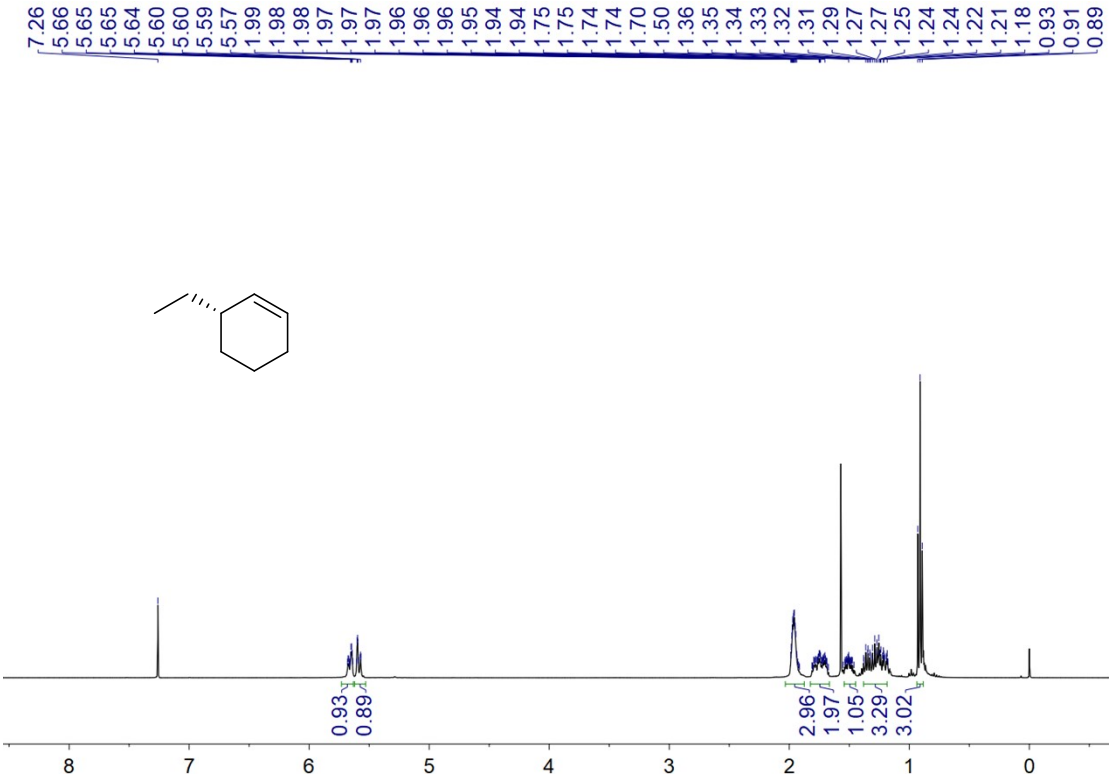
^{1}H NMR spectrum of **3a** in $CDCl_3$



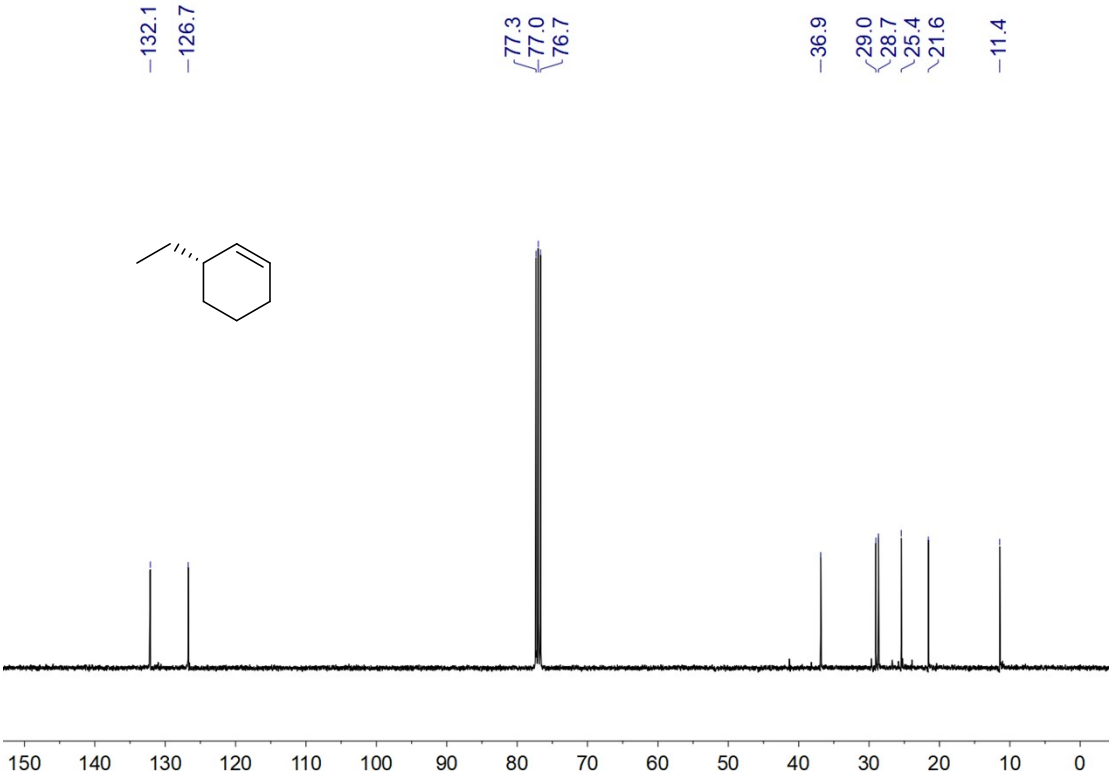
^{13}C NMR spectrum of **3b** in $CDCl_3$



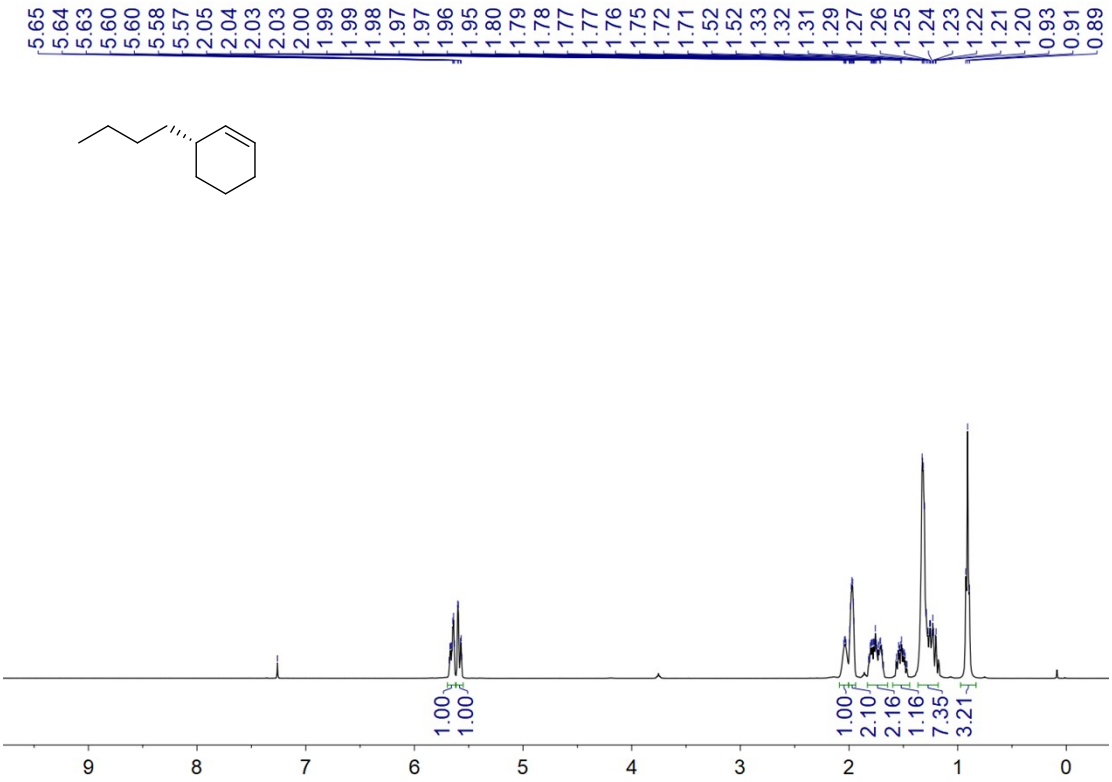
^{1}H NMR spectrum of **3b** in $CDCl_3$



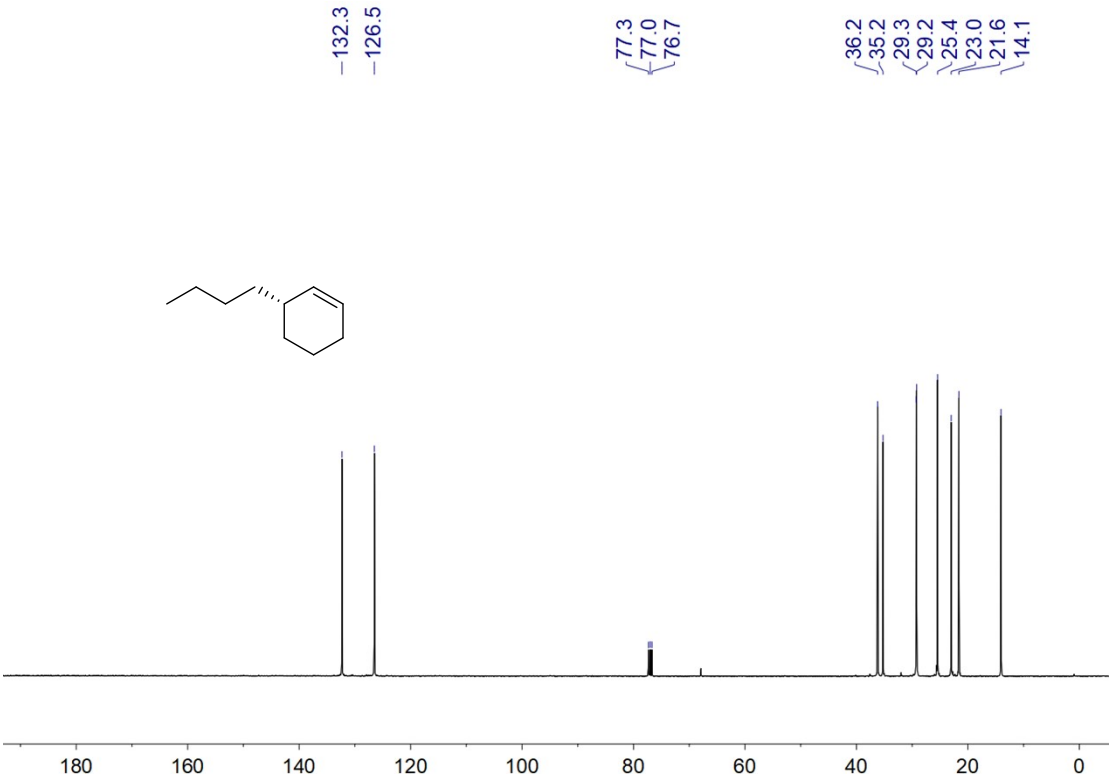
^{13}C NMR spectrum of **3b** in $CDCl_3$



^{1}H NMR spectrum of **3c** in $CDCl_3$

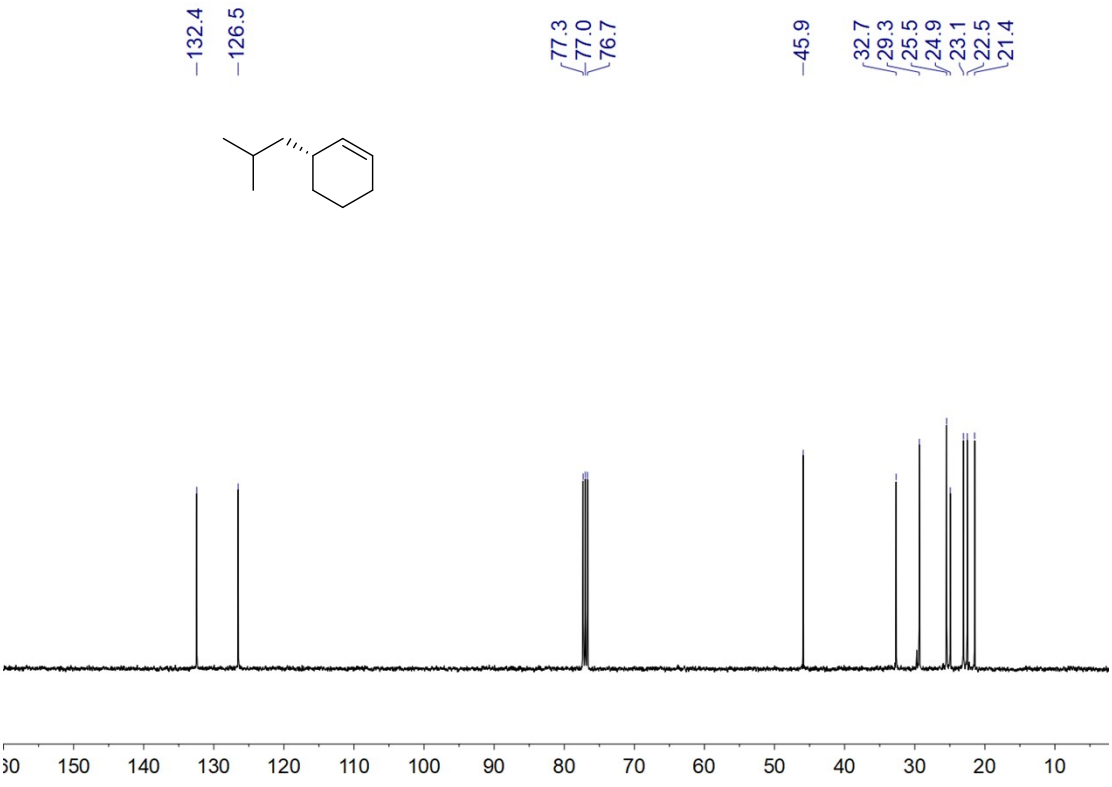


^{13}C NMR spectrum of **3c** in $CDCl_3$

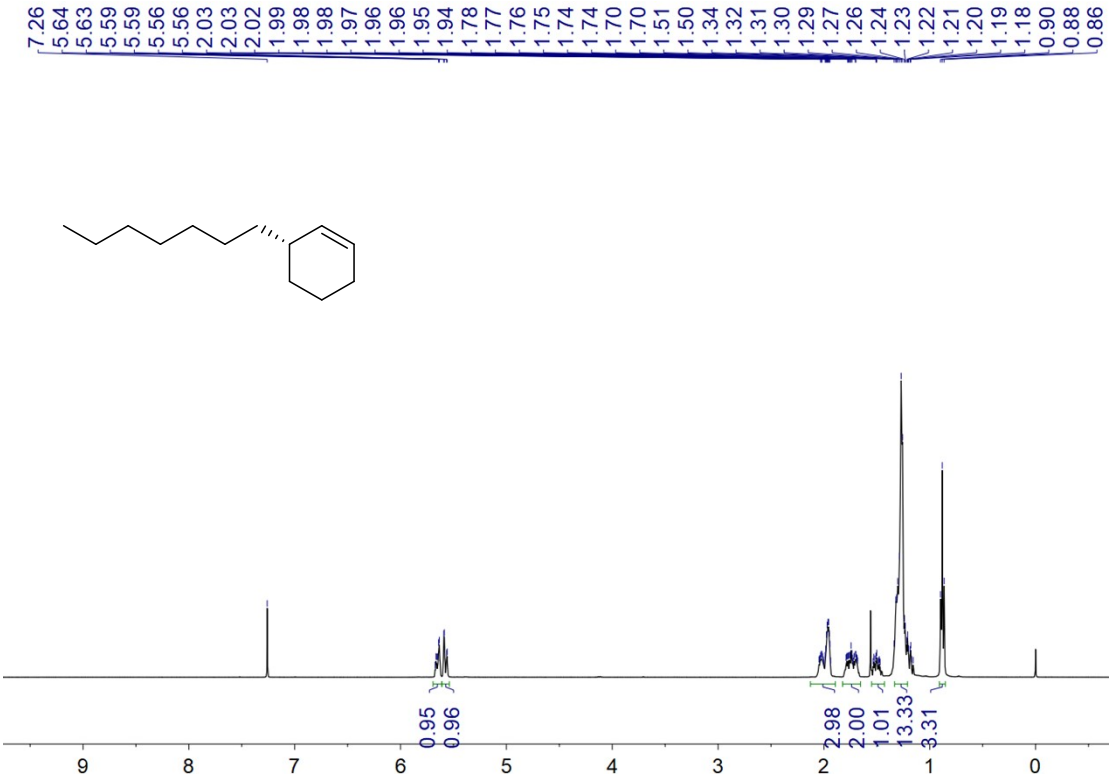


^{1}H NMR spectrum of **3d** in $CDCl_3$

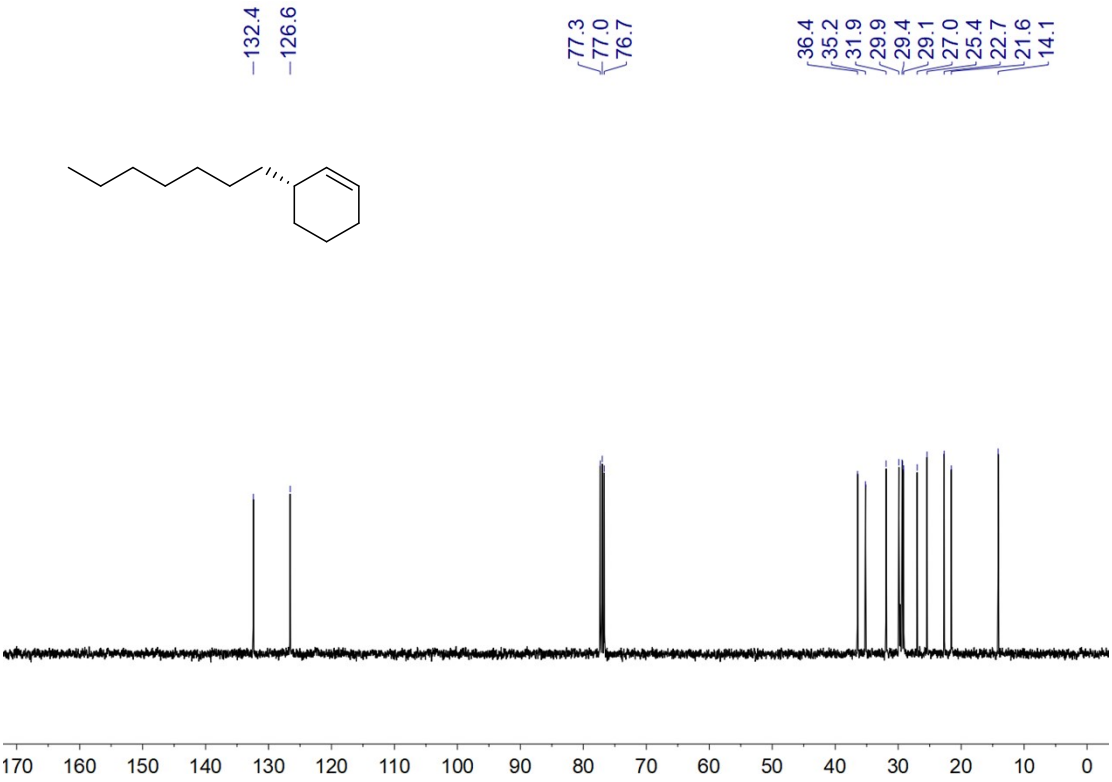
^{13}C NMR spectrum of **3d** in $CDCl_3$



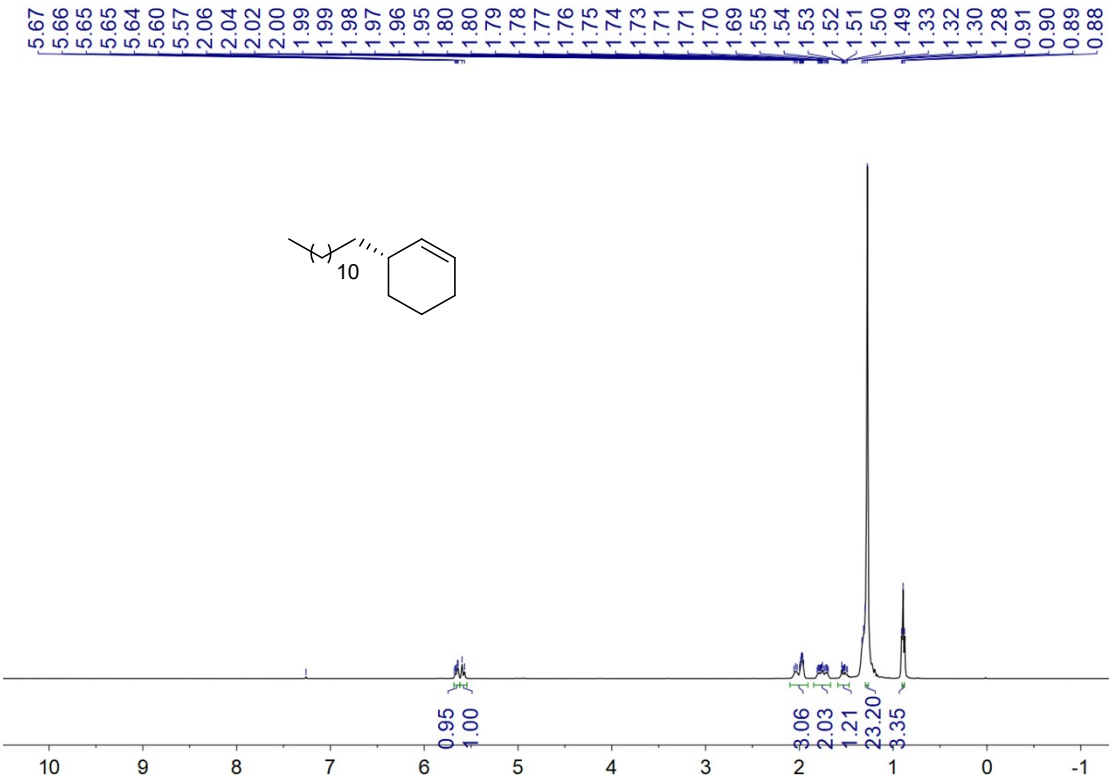
^{1}H NMR spectrum of **3e** in $CDCl_3$



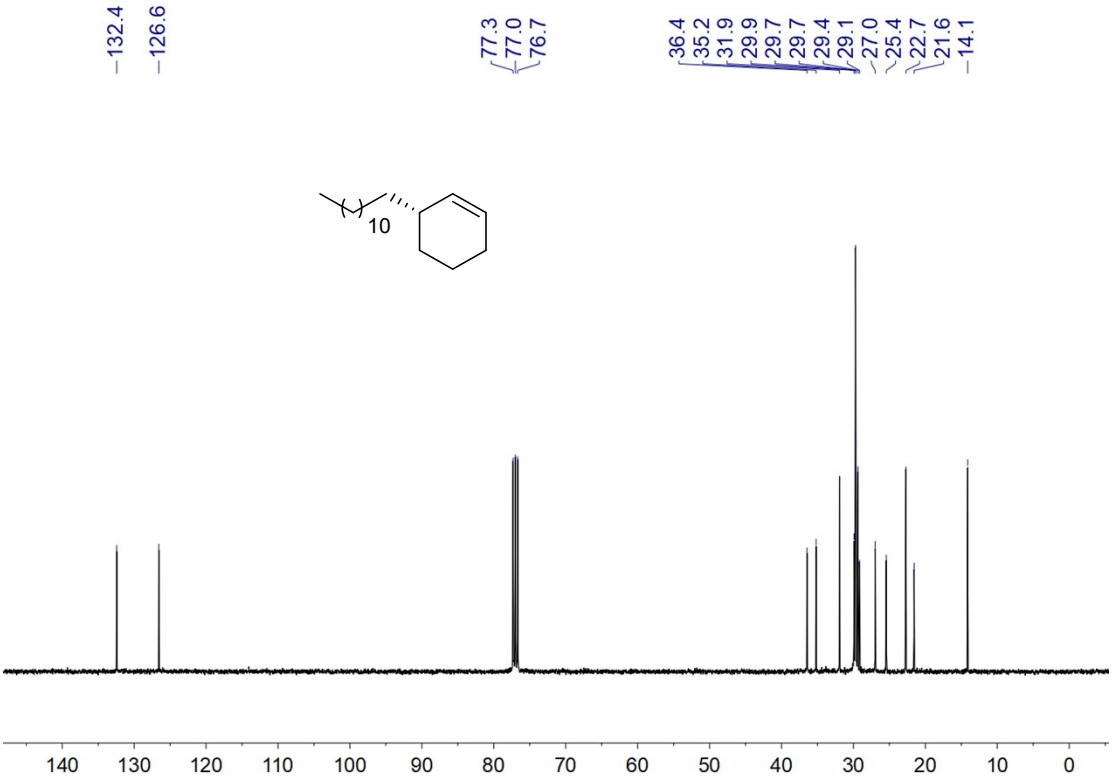
^{13}C NMR spectrum of **3e** in $CDCl_3$



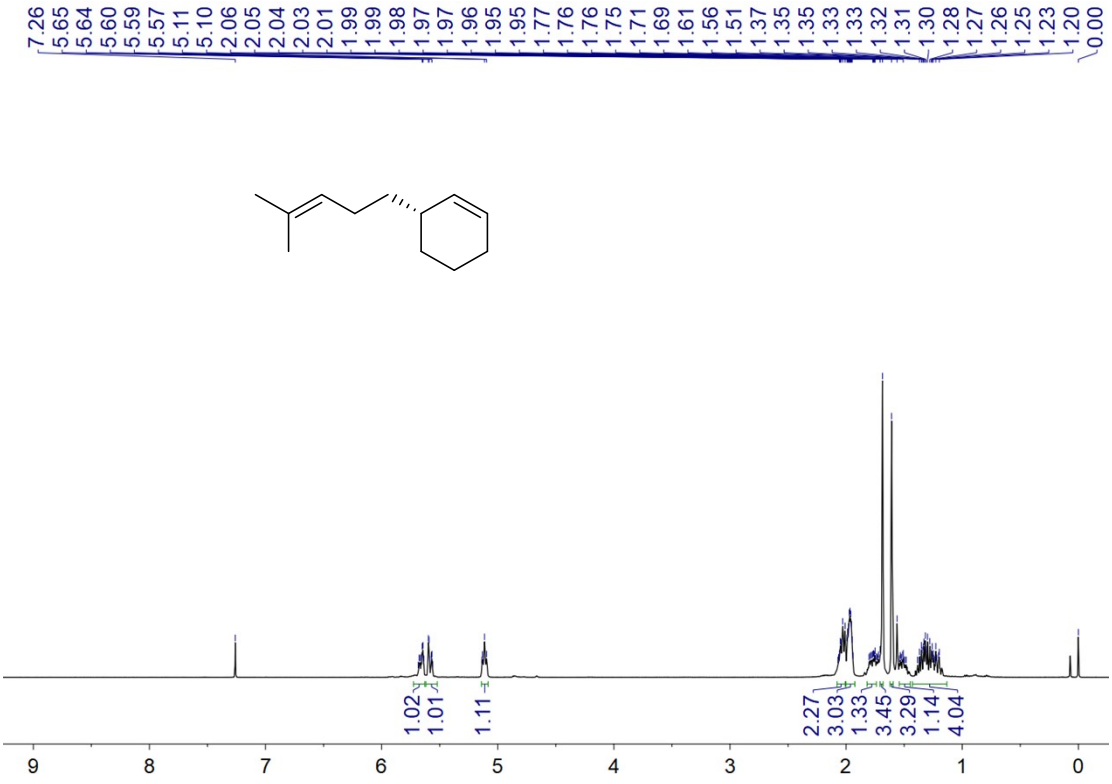
^{1}H NMR spectrum of **3f** in $CDCl_3$



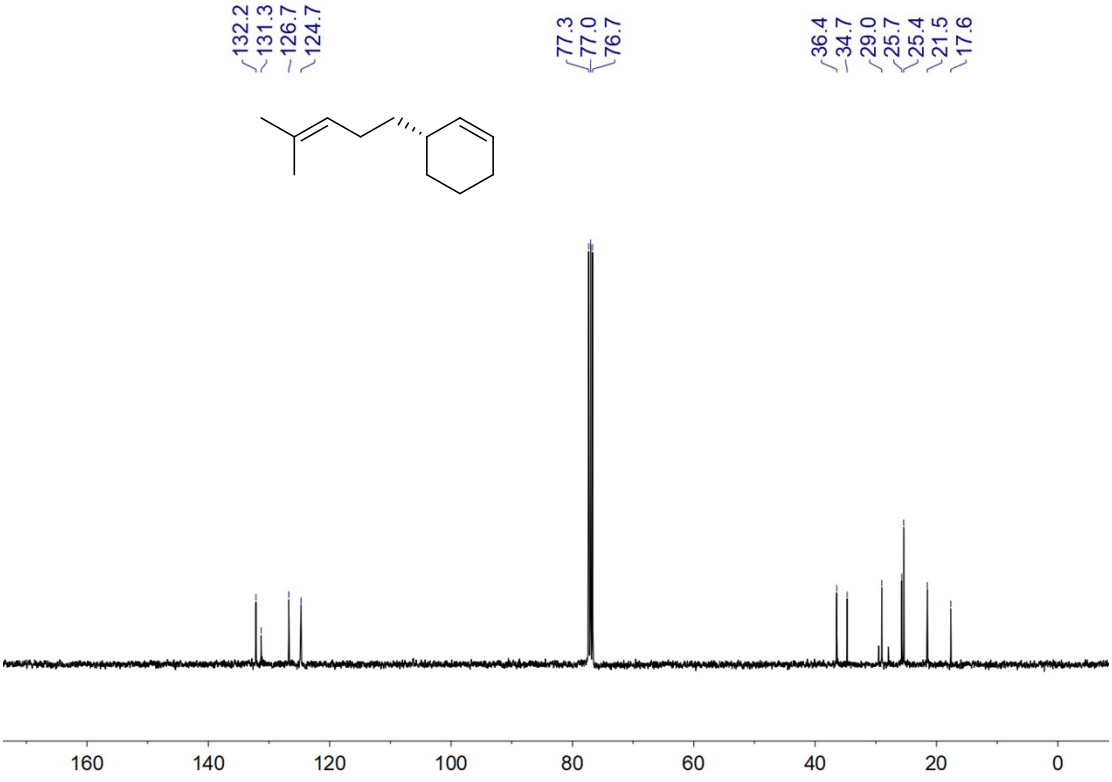
^{13}C NMR spectrum of **3f** in $CDCl_3$



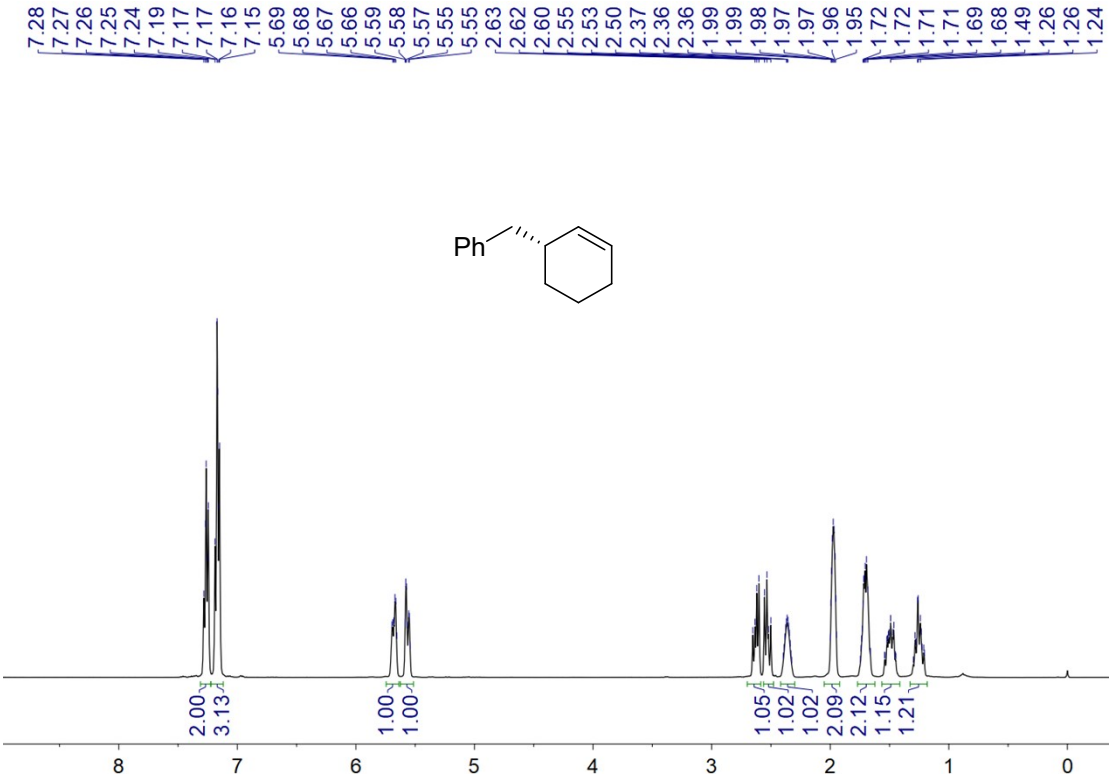
^{1}H NMR spectrum of **3g** in $CDCl_3$



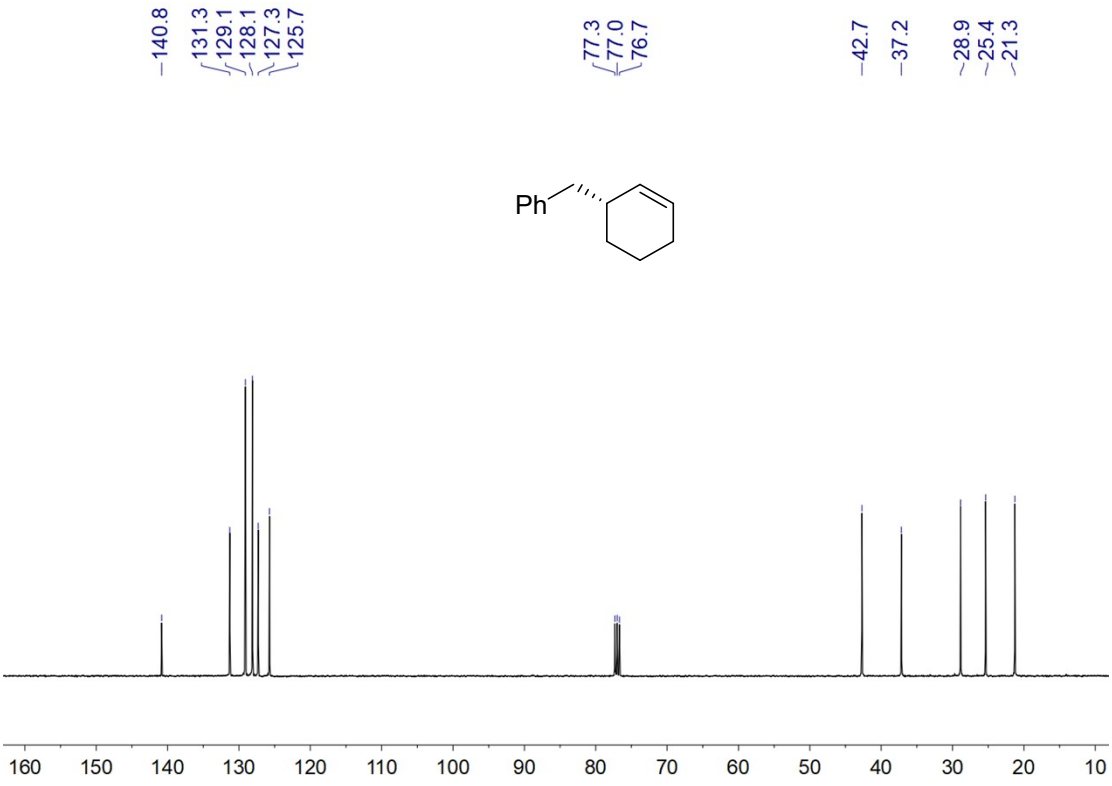
^{13}C NMR spectrum of **3g** in $CDCl_3$



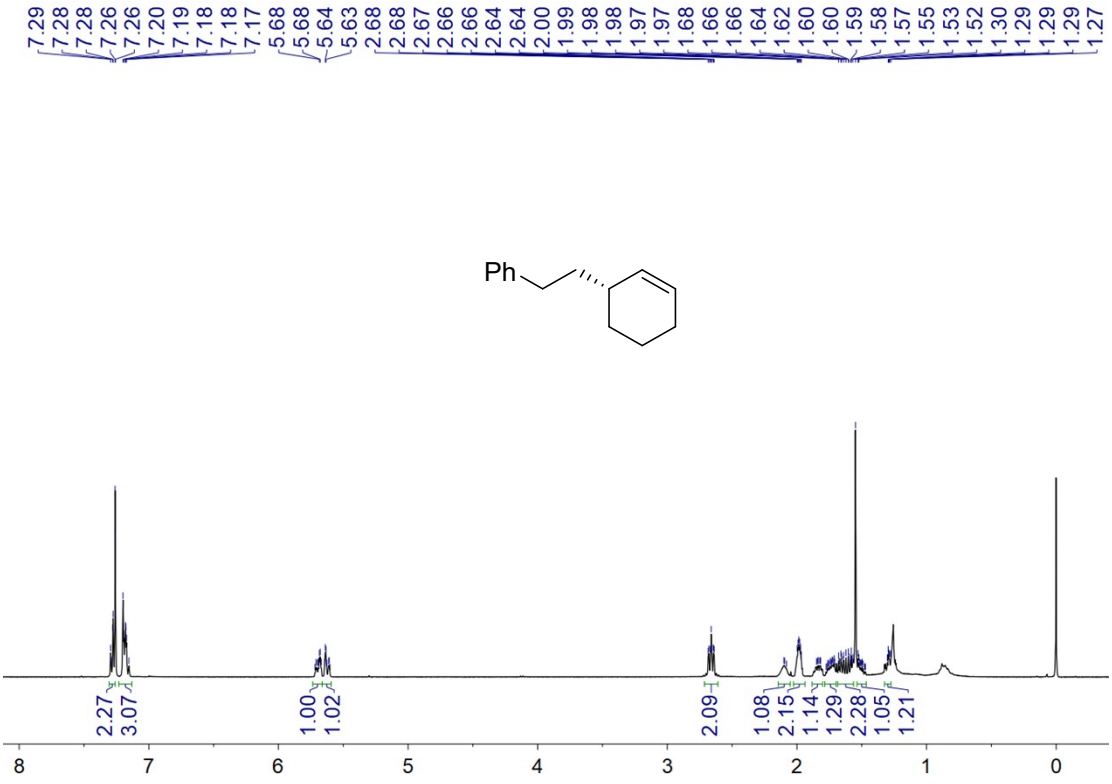
^{1}H NMR spectrum of **3h** in $CDCl_3$



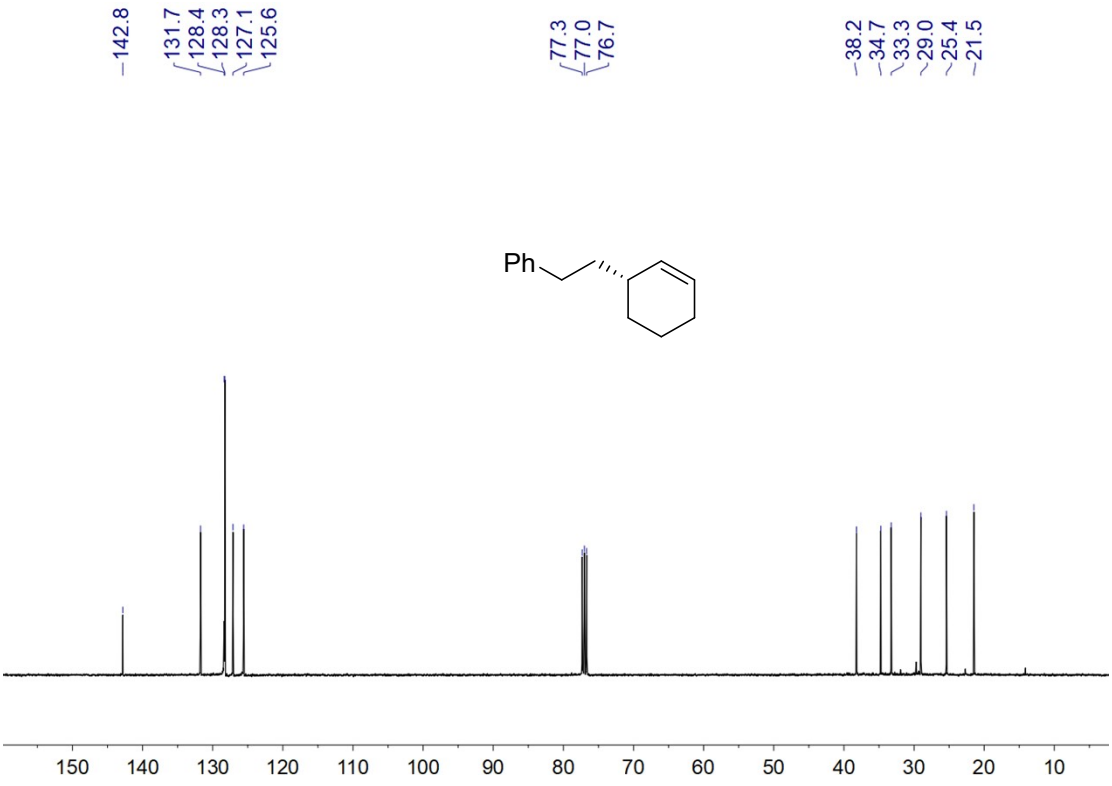
^{13}C NMR spectrum of **3h** in $CDCl_3$



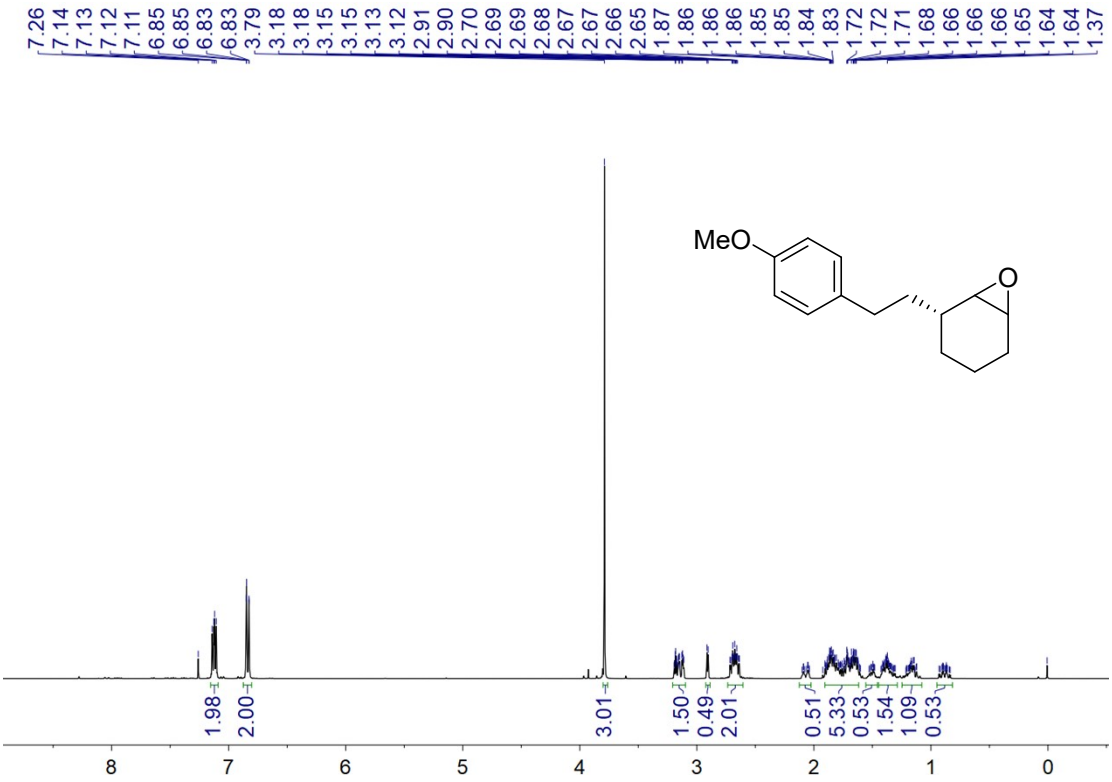
^{1}H NMR spectrum of **3i** in $CDCl_3$



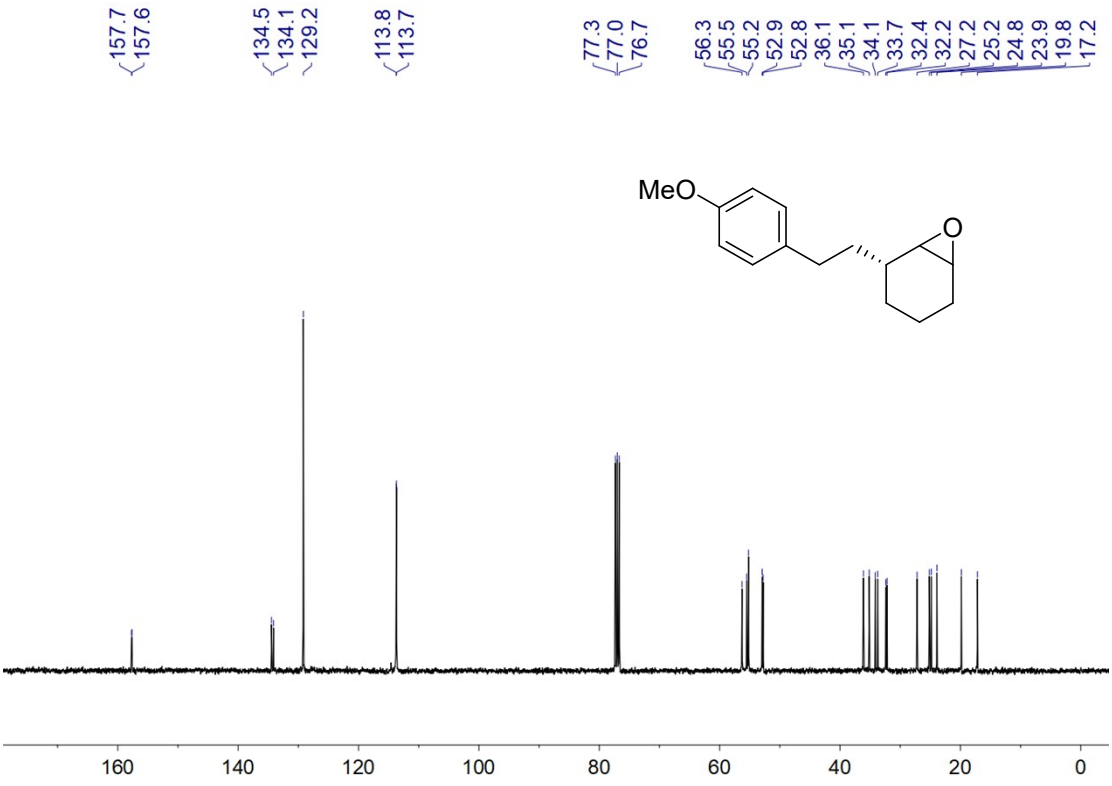
^{13}C NMR spectrum of **3i** in $CDCl_3$



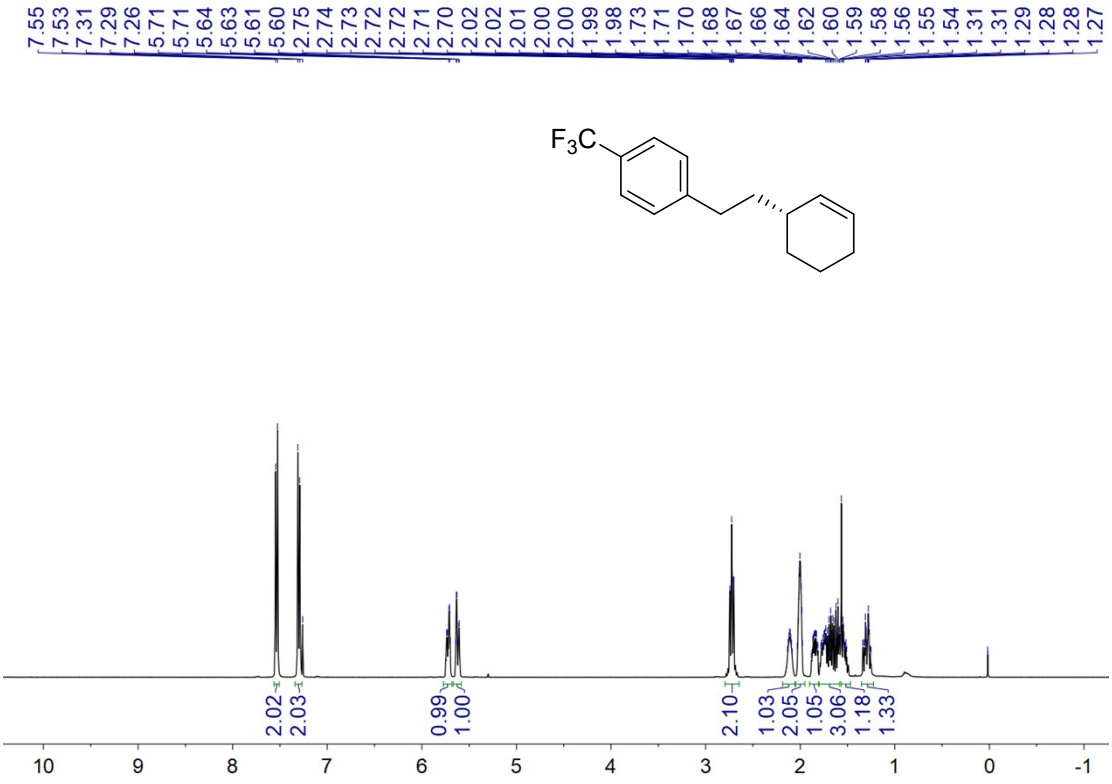
^{1}H NMR spectrum of **6j** in $CDCl_3$



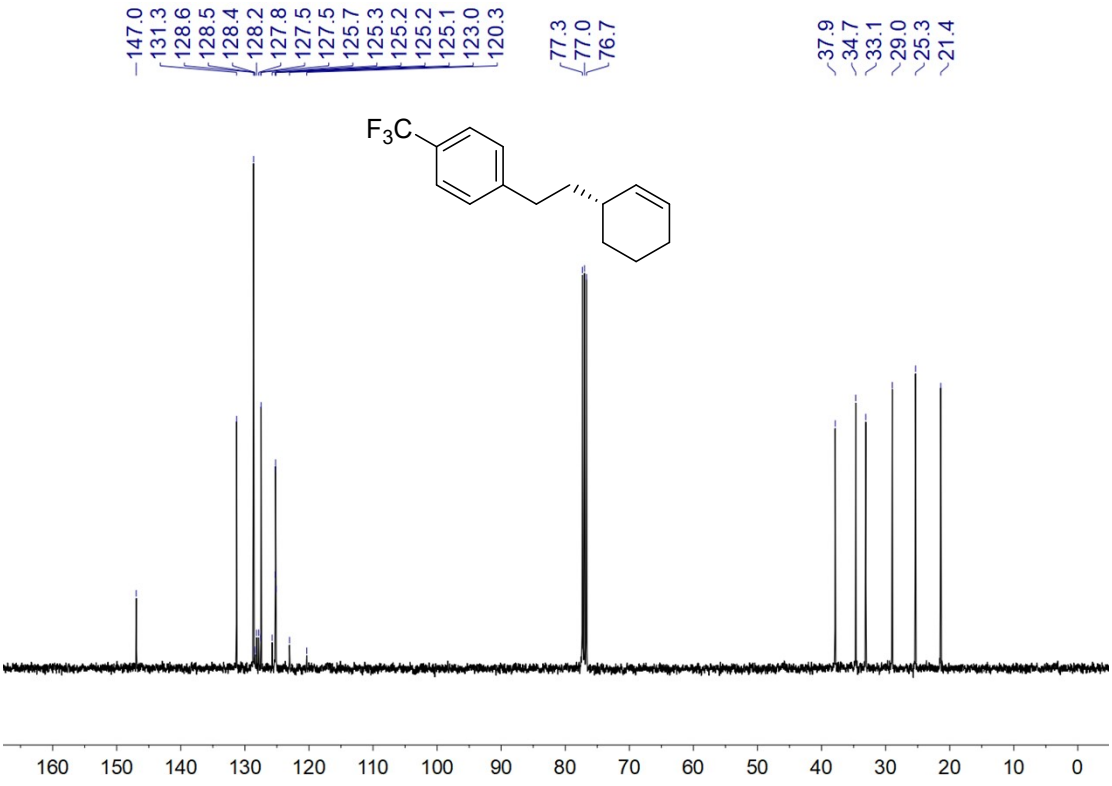
^{13}C NMR spectrum of **6j** in $CDCl_3$



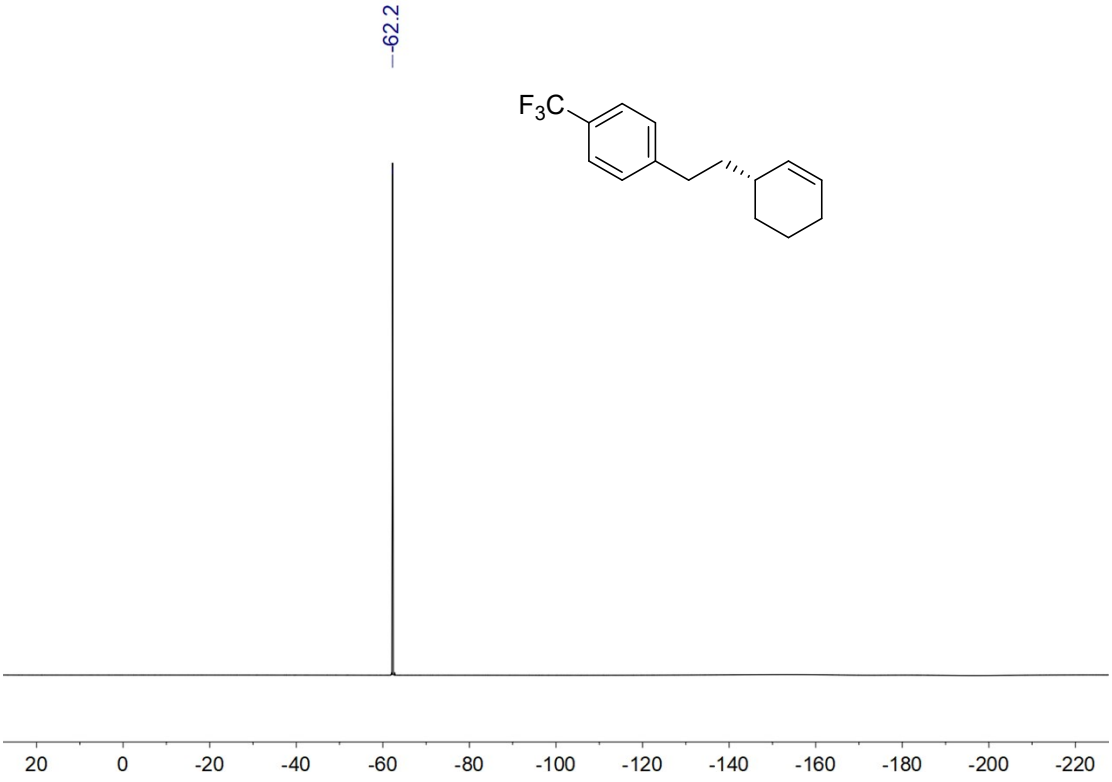
^{1}H NMR spectrum of **3k** in $CDCl_3$



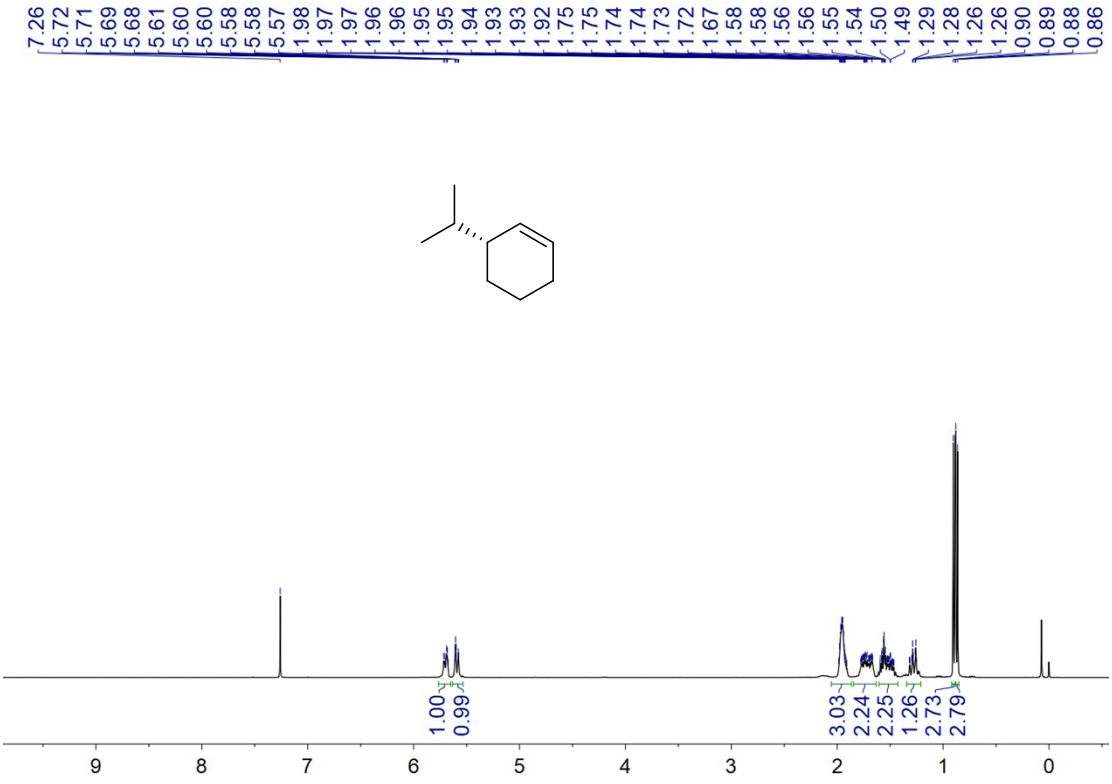
^{13}C NMR spectrum of **3k** in $CDCl_3$



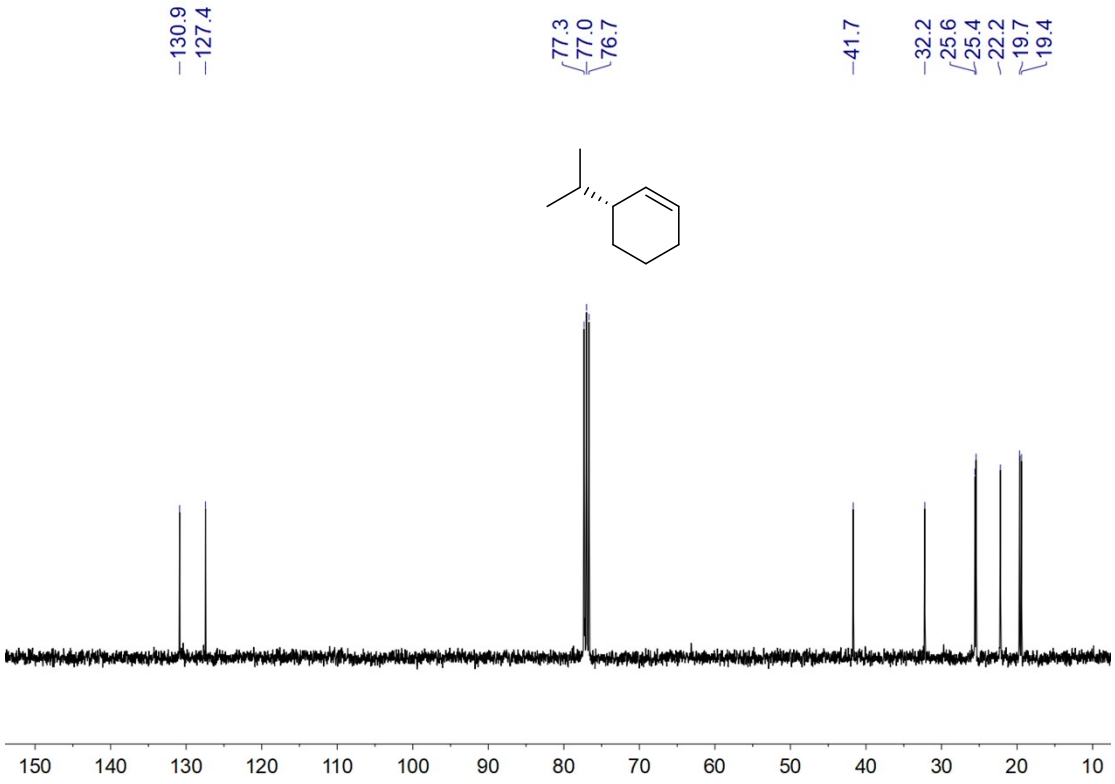
^{19}F NMR spectrum of **3k** in $CDCl_3$



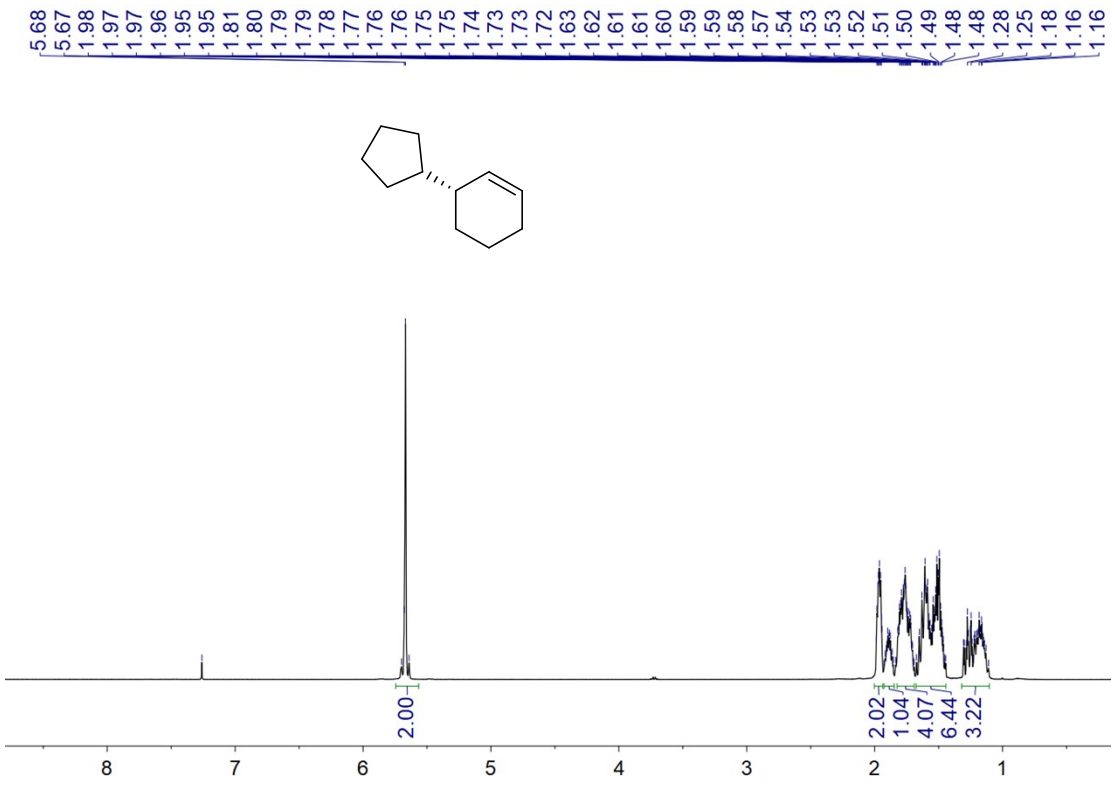
^{1}H NMR spectrum of **3l** in $CDCl_3$



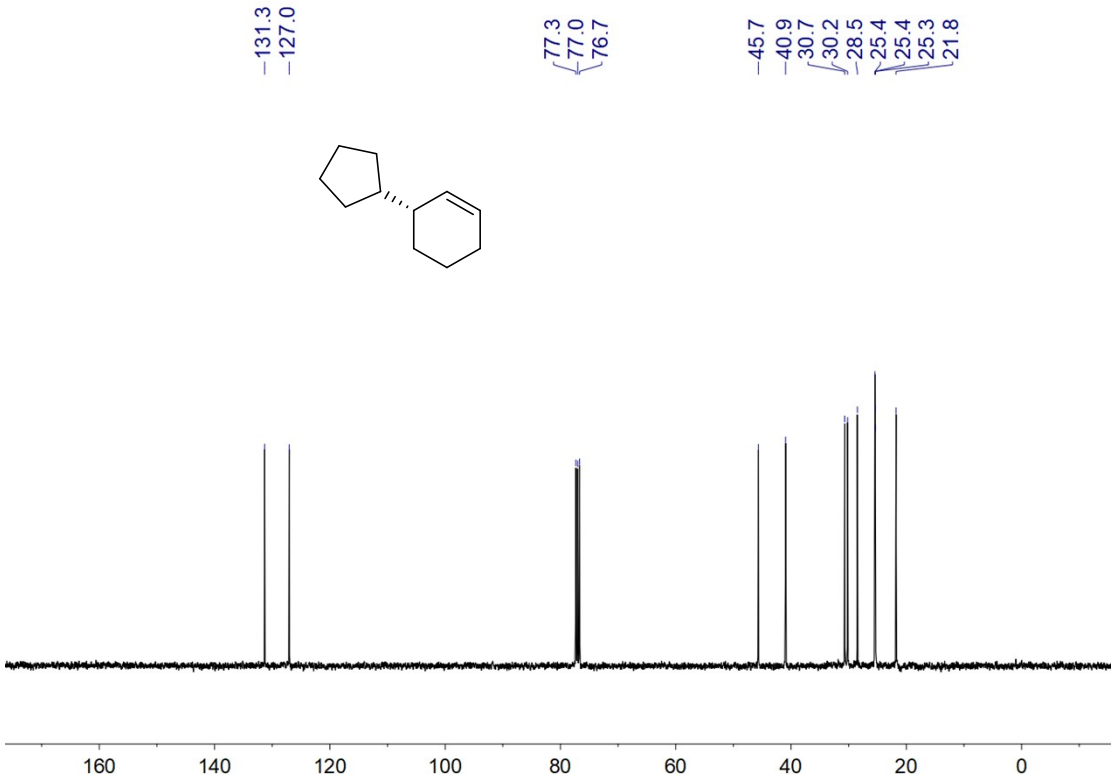
^{13}C NMR spectrum of **3l** in $CDCl_3$



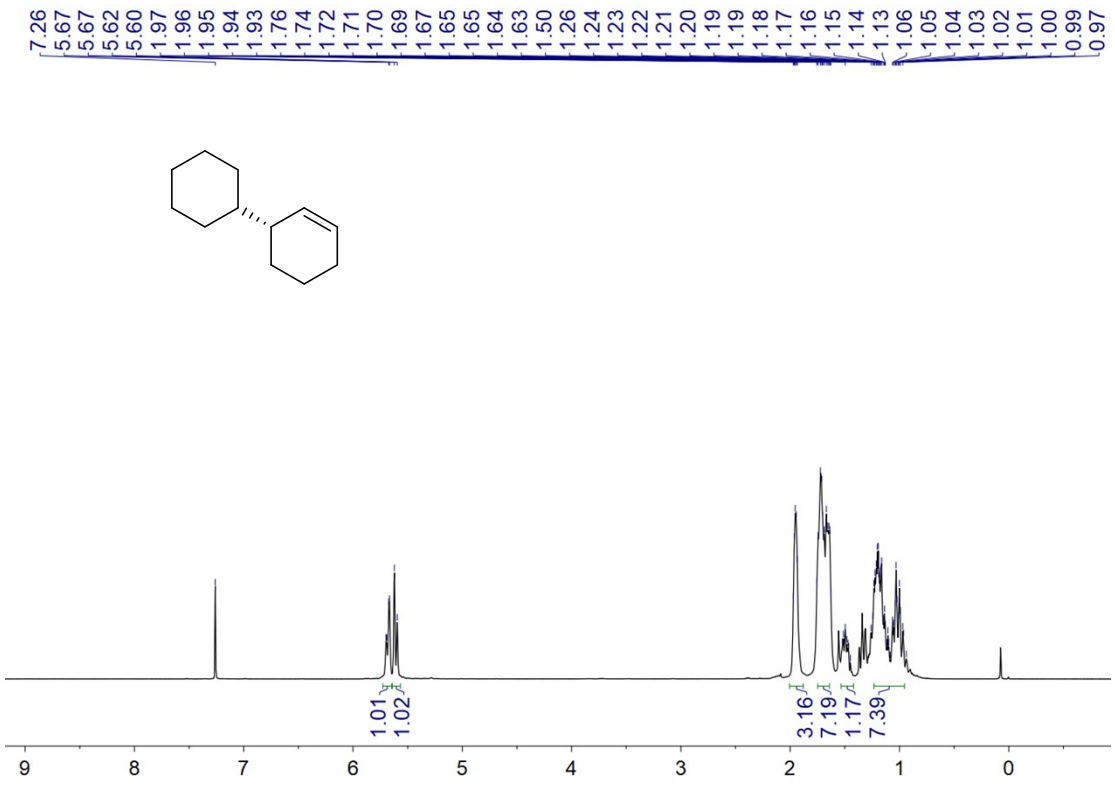
^{1}H NMR spectrum of **3m** in $CDCl_3$



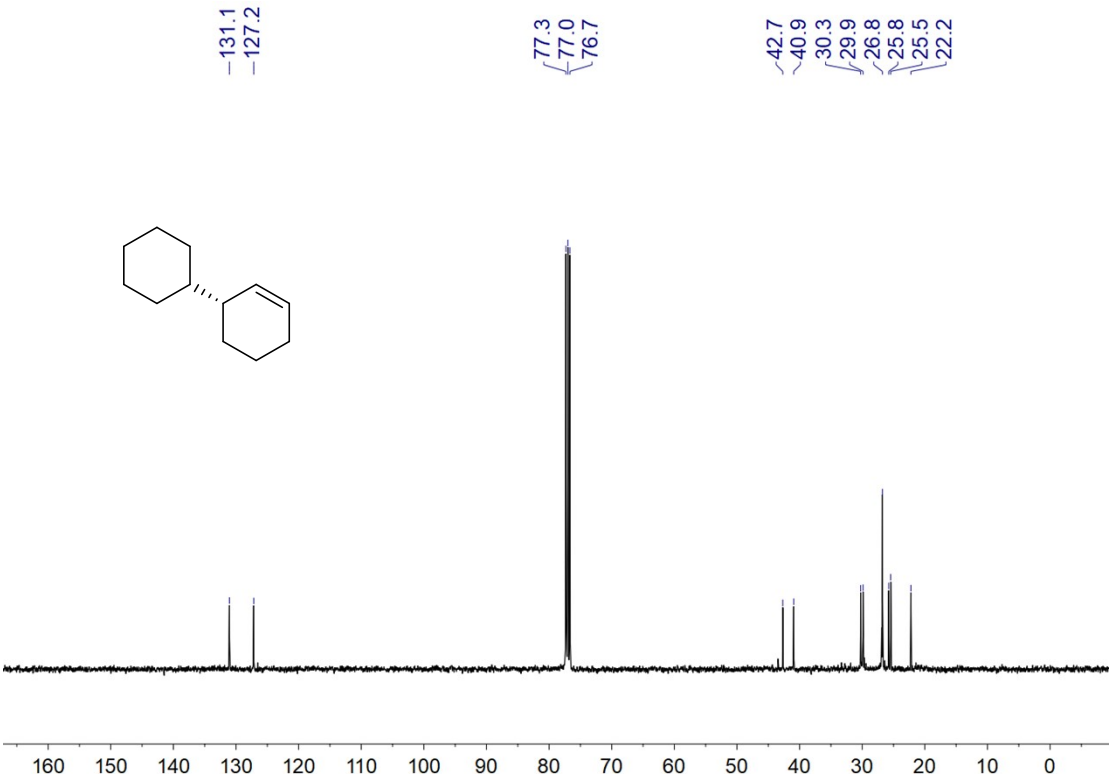
^{13}C NMR spectrum of **3m** in $CDCl_3$



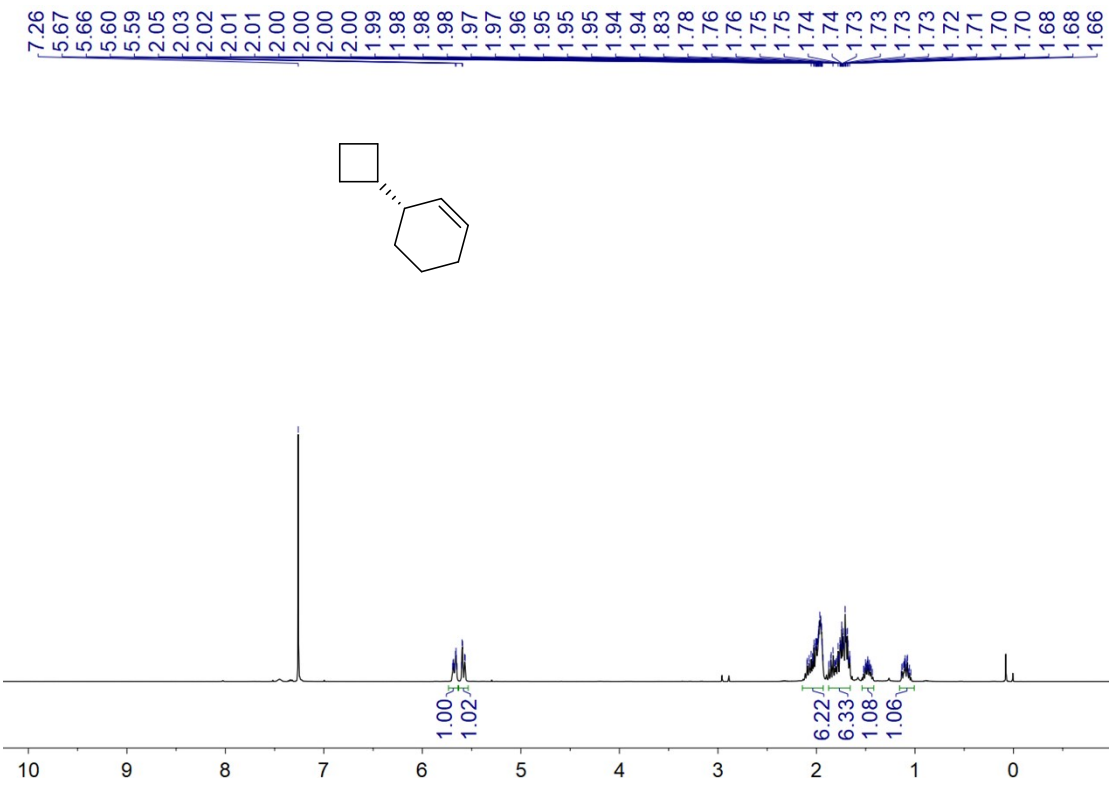
^{1}H NMR spectrum of **3n** in $CDCl_3$



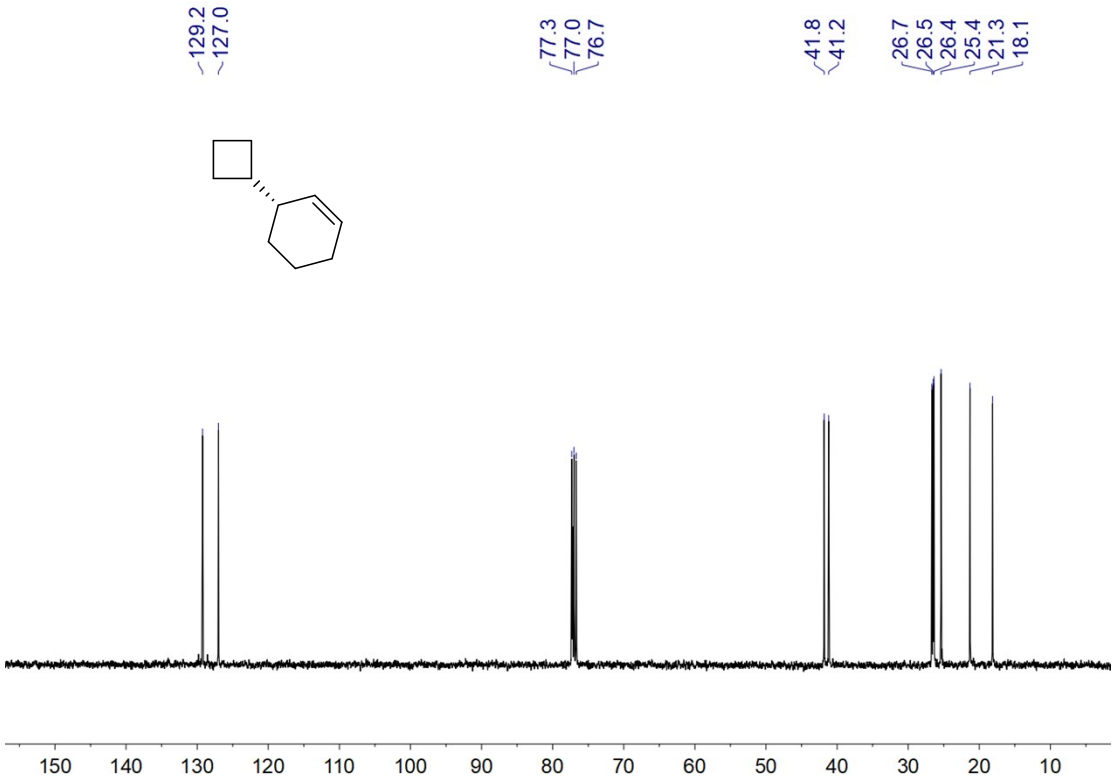
^{13}C NMR spectrum of **3n** in $CDCl_3$



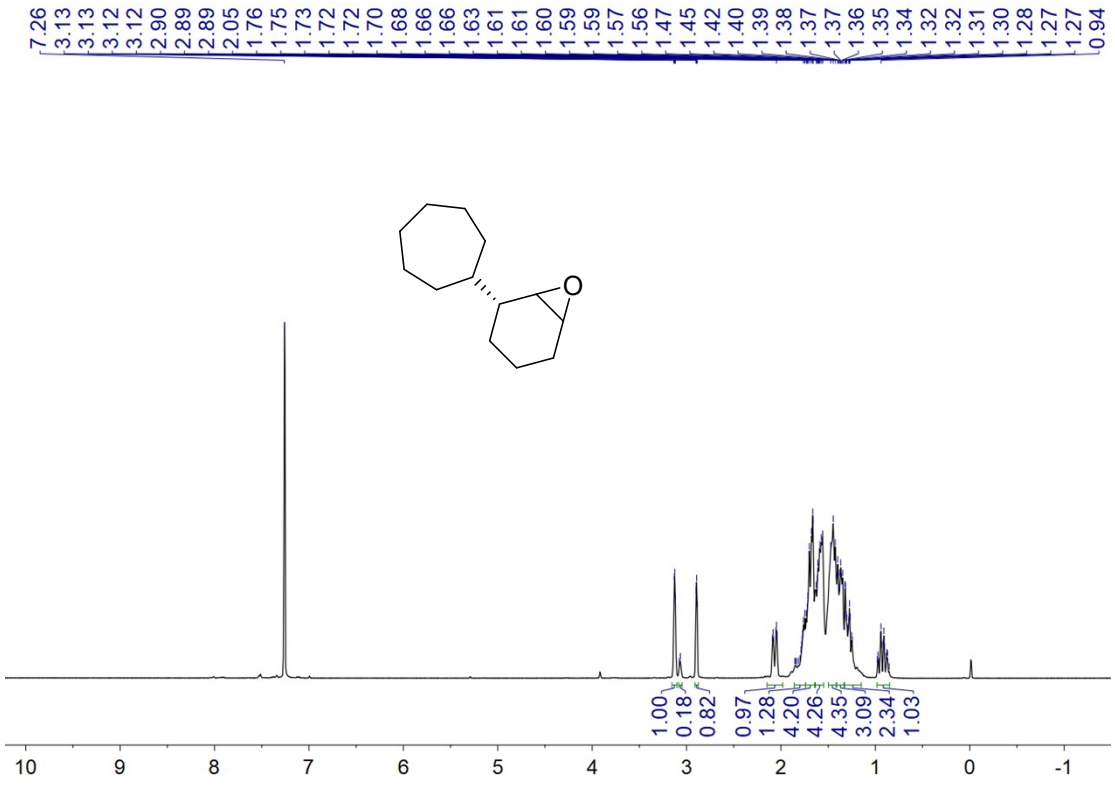
^{1}H NMR spectrum of **3o** in $CDCl_3$



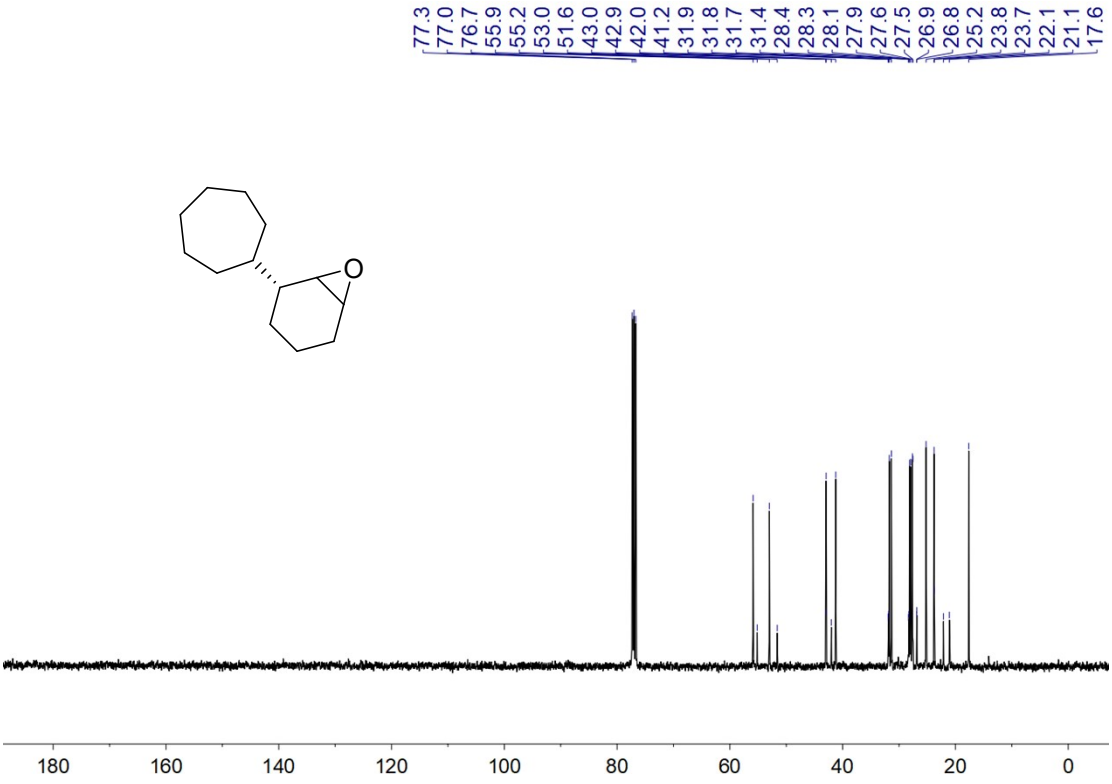
^{13}C NMR spectrum of **3o** in $CDCl_3$



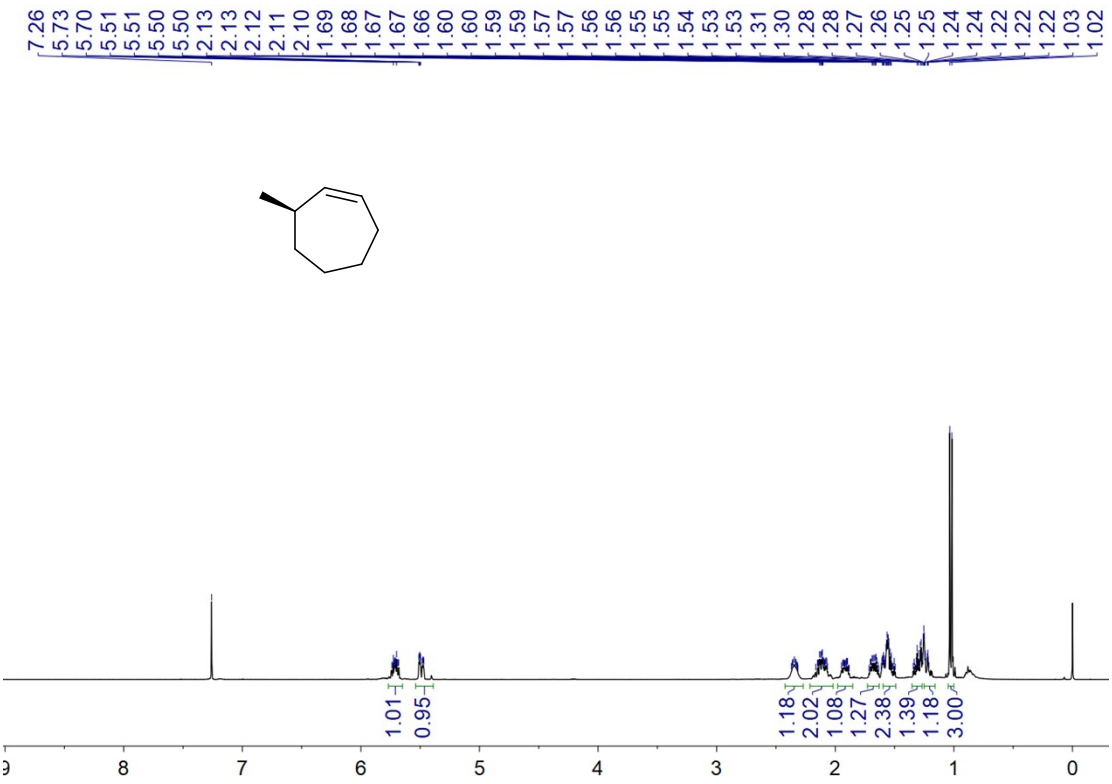
^{1}H NMR spectrum of **6p** in $CDCl_3$



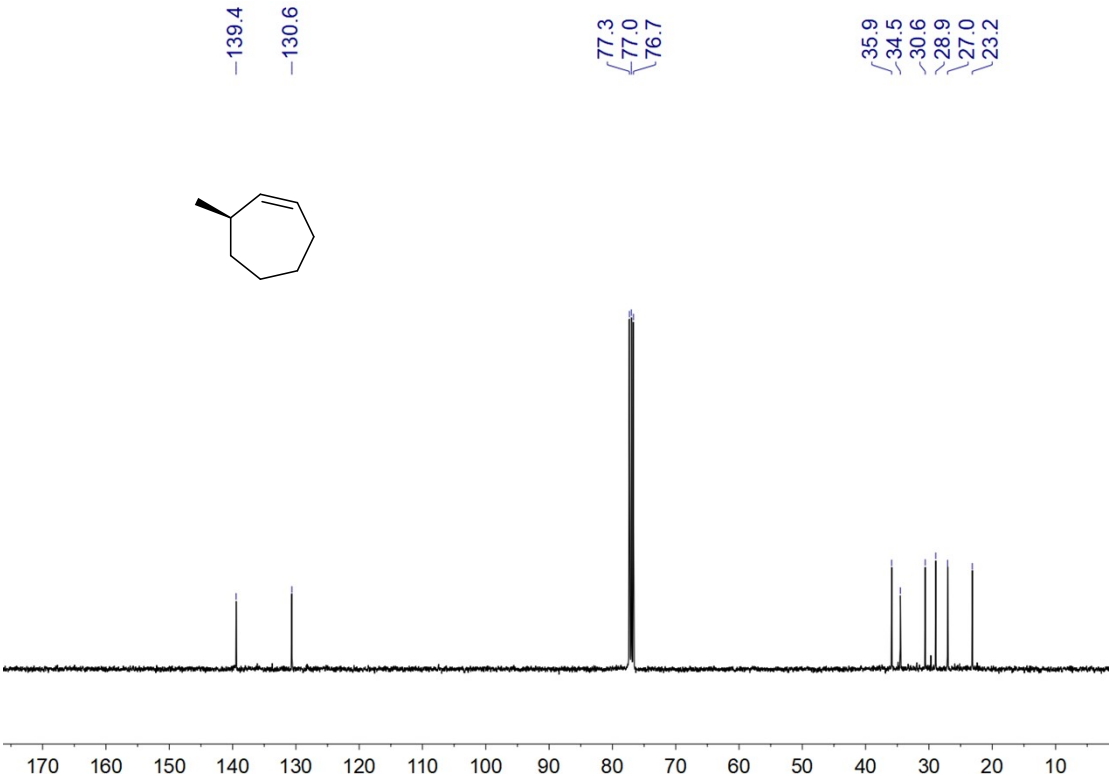
^{13}C NMR spectrum of **6p** in $CDCl_3$



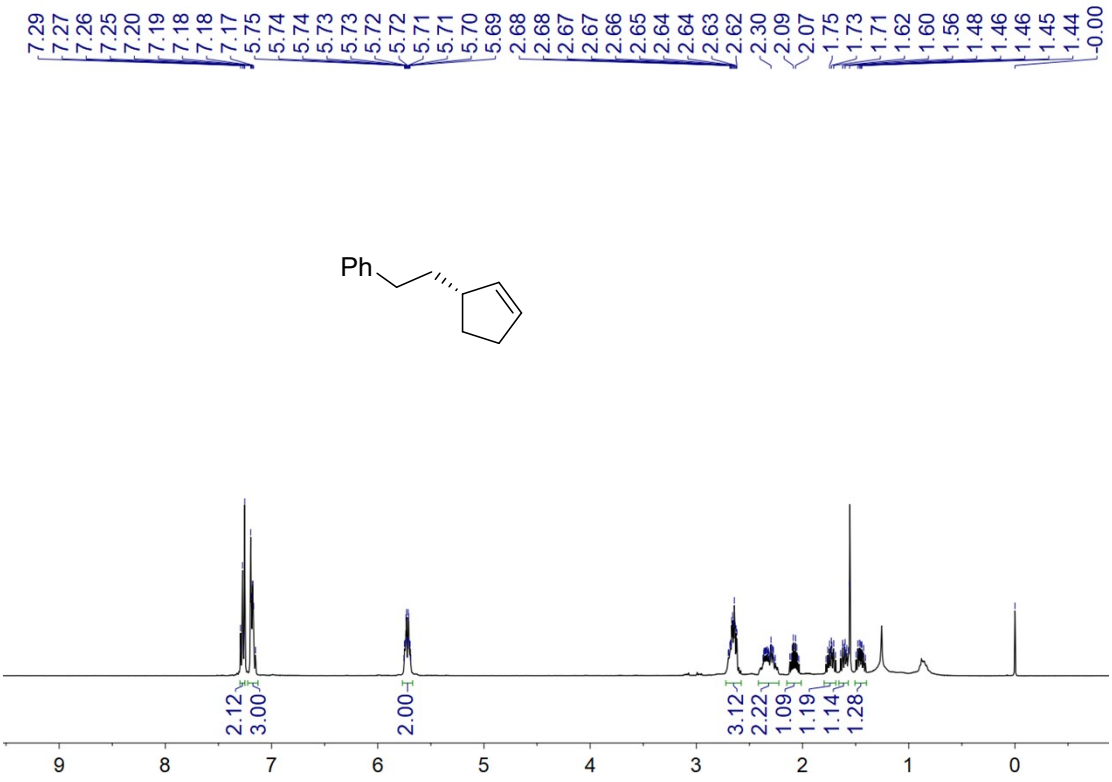
^{1}H NMR spectrum of **4a** in $CDCl_3$



^{13}C NMR spectrum of **4a** in $CDCl_3$



^{1}H NMR spectrum of **5a** in $CDCl_3$



^{13}C NMR spectrum of **5a** in $CDCl_3$