# Supporting Information

## Diastereoselective Synthesis of *C*-Aliphatic Homoallylic Amines and Biologically Important Cyclohexenylmine Analogues

Chi-Lik Ken Lee, Hui Yvonne Ling, Teck-Peng Loh*.

*Department of Chemistry, 3 Science Drive 3, National University of Singapore, Singapore 117543*

## General Information

Experiments involving moisture and/or sensitive compounds were performed under a positive pressure of nitrogen in flame-dried glassware equipped with a rubber septum inlet. Solvents and liquid reagents were transferred by oven-dried syringes cooled in a dessicator or via double-tipped cannular needles.

Reactions mixtures were stirred with Teflon-coated magnetic stirring bars unless otherwise stated. Moisture in non-volatile reagents/compounds was removed by the addition of the stated amount of anhydrous THF, followed by the removal of the solvent and traces of moisture *in vacuo* by means of an oil pump (~30 mmHg, 23-50 $^{o}$C) and subsequent purging with nitrogen.

All experiments were monitored by analytical thin layer chromatography (refer to section under "Chromatography").

Solvents were removed *in vacuo* under ~30 mmHg and heated with a water bath at 23 $^{o}$C using Büchi rotary evaporator cooled with running water at 0 $^{o}$C.

## Materials

Commercial solvents and reagents were used without further purification with the following exceptions:

Solvents:

Hexane, ethyl acetate, dichloromethane and water were freshly distilled prior to use. Anhydrous THF was obtained by distillation under nitrogen atmosphere from a deep purple solution resulting from sodium and benzophenone. Anhydrous dichloromethane was distilled over calcium hydride under nitrogen atmosphere.

Reagents:

(*S*)-Phenylglycine acid methyl ester was obtained by extracting (*S*)-phenylglycine acid methyl ester hydrogen chloride salt in saturated $Na_2CO_3$ with diethyl ether. It is then dried using anhydrous THF. Cyclohexanecarbaldehyde and 3-phenylpropanal were distilled over 4Å molecular sieve under nitrogen atmosphere. Activated Zn powder was obtained by "washing" commercial Zn powder using glacial acetic acid and subsequently filtered and

washed with diethyl ether. Saturated solutions of sodium chloride, sodium bicarbonate, and sodium carbonate were prepared from their respective solids.

## Chromatography

Analytical thin layer chromatography was performed using Merck 60 $F_{254}$ pre-coated silica gel plates (0.25 mm thickness). Subsequent to elution, ultraviolet illumination of the chromatogram at 254 nm allowed for visualization of UV active material. Further visualization was achieved by staining with $KMnO_4$ or ceric molybdate solution followed by heating on a hot plate.

Flash column chromatography was performed using Merck Silica Gel 60 (0.010-0.063 nm) and freshly distilled solvents. Columns were packed as slurry of silica gel in hexane and equilibrated with the appropriate solvent/solvent mixture prior to use. The analyte was loaded neat or as a concentrated solution using the appropriate solvent system. The elution was assisted by applying pressure of about 2 atm with an air pump.

## Instruments & Equipments

### Infrared Spectroscopy

Infrared spectra were recorded on a Bio-RAD FTS 165 FT-IR Spectrometer. Solid samples were analyzed as a KBr pressed-disk while liquid samples were either examined neat between KBr salt plates or as a solution in dichloromethane using NaCl liquid cells.

### Optical Rotation

Optical rotation was measured using a JASCO DIP-1000 Digital Polarimeter equipped with a sodium vapour lamp at 589 nm. Concentration is denoted as *c* and was calculated as grams per milliliters (g/100 mL) whereas the solvent was indicated in parentheses (*c*, solvent).

### Mass Spectroscopy

Mass spectrometries were performed by the staff from the Chemical and Molecular Analysis Center of the National University of Singapore. MS (EI) spectra were recorded on a Hewlett-Packard 5890A gas chromatogram, and HRMS (EI) spectra were recorded on a V>G> Micromass 7035. MS and HRMS (ESI) spectra were recorded on a Finnigan/MAT LCQ quadrupole ion trap mass spectrometer, coupled with the TSP4000 HPLC system and the Crystal 310 CE system. HRMS (FAB) spectra were recorded on a Finnigan MAT 95XL-

T. MS and HRMS were reported in units of mass of charge ratio (*m/z*). For full instrumentation details, please visit http://www.chemistry.nus.edu.sg/cmac/ms/MS_Instrument.html.

Nuclear Magnetic Resonance Spectroscopy

Proton nuclear magnetic resonance ($^1$H NMR) and carbon nuclear magnetic resonance ($^{13}$C NMR) spectroscopy were performed on a 300 MHz Bruker ACF 300, 300 MHz Bruker DPX 300 and 500 MHz Bruker AMX 500 NMR spectrometer.

Chemical shifts were reported as δ in units of parts per million (ppm) downfield from tetramethysilane (δ 0.00), using the residual solvent signal as an internal standard: deuterio chloroform-*d*, $CDCl_3$ ($^1$H NMR, δ 7.26, singlet; $^{13}$C NMR, δ 77.04, triplet).

Multiplicities were given as: s (singlet), d (doublet), t (triplet), q (quartet), qn (quintet), m (multiplets), br (broad), dd (doublet of doublets), dt (doublet of triplets), ddd (doublet of doublet of doublets) and ddt (doublet of doublet of triplets). Coupling constants (*J*) were recorded in Hertz (Hz). The number of protons (n) for a given resonance was indicated by nH.

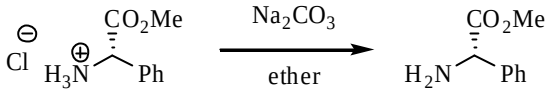
In cases where several diastereomers were obtained, only the major isomer will be assigned. The ratio of the isomers was determined by the integration of the respective signals in the $^1$H NMR spectra or by comparing the relative intensities of the signals in the $^{13}$C NMR spectra.

Nomenclature

Systematic nomenclature for the compounds would follow the numbering system as defined by IUPA. Compounds were named using the CS Chemdraw Ultra 8.0 program.

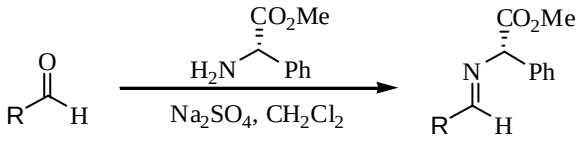
## Procedures and Data

### Preparation of (*S*)-Phenylglycine methyl ester for imine formation.

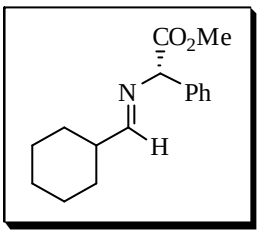



(*S*)-Phenylglycine acid methyl ester (10 g, 60 mmol) was dissolved in saturated $Na_2CO_3$ (150 mL) and was extracted with diethyl ether (5 x 100 mL). The combined organic phases were washed with brine, before drying over $MgSO_4$. The crude mixture was then filtered and concentrated in vacuo. The crude product was obtained as light yellow oil and was used for subsequent reaction without any purification.

### General procedure for the preparation of imines 1.




To a stirred solution of aldehyde (1 equiv) and $Na_2SO_4$ in dichloromethane (0.33M) under nitrogen at 0 $^{o}$ C was added (*S*)-Phenylglycine methyl ester (1.5 to 2.0 equiv). The reaction mixture was allowed to stir for 5 hrs. The resulting reaction mixture was then filtered concentrated in vacuo. The crude product obtained was used without purification for subsequent steps.

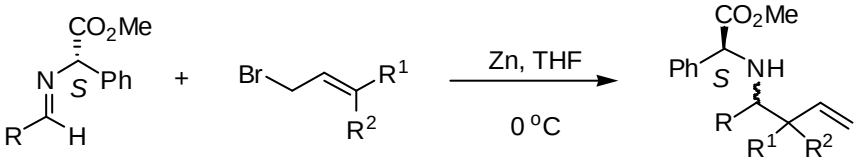



**1a: (*S*,*E*)-Methyl 2-(cyclohexylmethyleneamino)-2-phenylacetate**

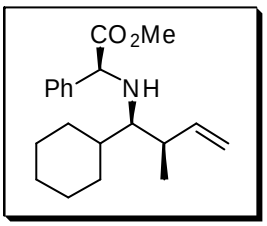
To a stirred solution of the cyclohexcarbaldehyde (0.19 mL, 1.5 mmol) and $Na_2SO_4$ (0.5 g) in dichloromethane (5 mL, 0.3M) under nitrogen at 0 $^{o}$ C was added (*S*)-Phenylglycine methyl ester (0.45 g, 1.8 mmol). The reaction mixture was allowed to stir for 5 hrs. The resulting reaction mixture was then filtered concentrated in vacuo. The crude product obtained was used without purification for subsequent steps.

**Zn Mediated Allylation of Imines**

**General reaction procedure for the preparation of chiral homoallylic amines 3 – 6.**




To a stirred suspension of the chiral imine (1 equiv.) in THF (0.2 M) and "activated" Zn powder (3.2 equiv.), was added the allylic bromide (3.0 equiv.) at 0 $^{o}$C and stirred for up to 7 hours. The reaction mixture was then quenched with saturated $NaHCO_3$ (10 mL) before being extracted with $CH_2Cl_2$ (3 x 10 mL). The mixture was then washed with water (2 x 10mL), before being dried with $Na_2SO_4$ and concentrated in vacuo. The crude product was purified by flash column chromatography.




**3a: (S)-Methyl 2-((1R,2R)-1-cyclohexyl-2-methylbut-3-enylamino)-2-phenylacetate**

To a stirred suspension of **1a** (0.26 g, 1 mmol) in THF (5 mL) and "activated" Zn powder (0.21 g, 3.2 mmol), was added the allylic bromide **2a** (0.26 mL, 3.0 mmol) at 0 $^{o}$C and stirred for up to 7 hours. The reaction mixture was then quenched with saturated $NaHCO_3$ (10 mL) before being extracted with $CH_2Cl_2$ (3 x 10 mL). The mixture was then washed with water (2 x 10mL), before being dried with $Na_2SO_4$ and concentrated in vacuo. The crude product was purified by flash column chromatography.

(60 % *de*; *syn* : *anti* = 75 : 25)

Light yellow oil (296 mg, 94 %);

$R_f$ = 0.58 (8:1 hexane/ethyl acetate);

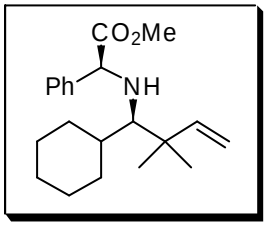
$[\alpha]^{25}$ = + 26.4 $^{o}$ (0.41, $CH_2Cl_2$);

$^{1}$H NMR (300 MHz, $CDCl_3$): d 7.38 – 7.27 (m, 5H), 5.93 – 5.80 (m, 1H), 5.07 – 4.98 (m, 2H), 4.48 (s, 1H), 3.66 (s, 3H), 2.45 – 2.39 (m, 1H), 2.19 – 2.11 (m, 1H), 1.64 – 1.46 (m, 5H), 1.44 – 1.33 (m, 1H), 1.21 – 1.04 (m, 8H);

$^{13}$C NMR (75.4 MHz, $CDCl_3$) d 173.9, 173.8, 143.3, 142.2, 128.3, 128.3, 127.9, 127.7, 114.4, 113.4, 65.2, 64.8, 64.1, 51.9, 51.8, 41.0, 40.7, 40.5, 39.7, 31.3, 31.1, 28.8, 28.6, 26.8, 26.7, 26.6, 26.6, 26.5, 17.8, 15.0;

FTIR (neat): 3839, 3064, 2925, 2851, 1738, 1491, 1451, 1169, 1001, 912, 730, 699 cm$^{-1}$;

HRMS (EI) Calcd for $C_{20}H_{29}NO_2$ [$M^+$]: 315.2198, found 316.2273 (M + 1).




**3b: (S)-Methyl 2-((R)-1-cyclohexyl-2,2-dimethylbut-3-enylamino)-2-phenylacetate**

(78 %*de*)

Light yellow oil (303 mg, 92 %);

$R_f$ = 0.69 (8:1 hexane/ethyl acetate);

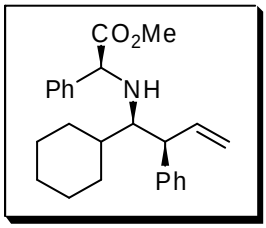
$[\alpha]^{25}$ = + 17.5 $^{o}$ (0.41, $CH_2Cl_2$);

$^{1}$H NMR (300 MHz, $CDCl_3$): d 7.42 – 7.28 (m, 5H), 5.90 (dd, *J* = 17.1, 11.2 Hz, 1H), 5.02 – 4.96 (m, 2H), 4.50 (s, 1H), 3.68 (s, 3H), 2.06 (d, *J* = 1.7 Hz, 1H), 1.74 – 1.62 (m, 5H), 1.32 – 1.24 (m, 1H), 1.09 – 0.99 (m, 11H);

$^{13}$C NMR (75.4 MHz, $CDCl_3$) d 173.9, 147.1, 139.5, 128.4, 127.8, 127.6, 111.6, 68.6, 66.2, 51.8, 43.0, 39.2, 35.6, 29.1, 27.4, 26.8, 26.5, 24.6, 23.6;

FTIR (neat): 3038, 3061, 2851, 2525, 1939, 1491, 1450, 1167, 1005, 912, 698, 575 $cm^{-1}$;

HRMS (EI) Calcd for $C_{21}H_{31}NO_2$ [$M^+$]: 329.2355, found 328.2271 (M - 1).




**3c: (S)-Methyl 2-((1R,2S)-1-cyclohexyl-2-phenylbut-3-enylamino)-2-phenylacetate**

(76 %*de*; *syn* : *anti* = 82 : 18)

Yellow oil (245 mg, 65 %);

$R_f$ = 0.59 (8:1 hexane/ethyl acetate);

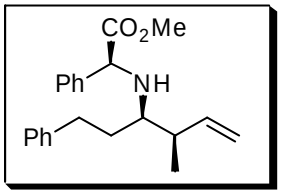
$[\alpha]^{25}$ = + 36.7 $^{o}$ (0.52, $CH_2Cl_2$);

$^{1}$H NMR (300 MHz, $CDCl_3$): d 7.35 – 7.24 (m, 8H), 7.20 – 7.17 (m, 2H), 6.06 (dt, *J* = 17.7, 9.4 Hz, 1H), 5.08 – 5.02 (m, 1H), 3.80 (s, 1H), 3.48 (s, 3H), 2.61 (dd, *J* = 8.7, 2.8 Hz, 1H), 1.82 (brs, 2H), 1.73 (brs, 4H), 1.50 – 1.44 (m, 1H), 1.21 – 1.11 (m, 5H);

$^{13}$C NMR (75.4 MHz, $CDCl_3$) d 173.4, 140.1, 139.2, 128.6, 128.4, 128.2, 128.1, 127.7, 126.5, 115.4, 64.2, 63.9, 55.0, 52.0, 40.4, 31.4, 31.5, 26.8, 26.6, 26.5;

FTIR (neat): 3700, 3356, 3062, 3029, 2926, 2851, 2665, 1948, 1871, 1805, 1737, 1635, 1599, 1491, 1305, 1247, 1173, 996, 915, 847, 760, 734, 517 $cm^{-1}$;

HRMS (EI) Calcd for $C_{25}H_{31}NO_2$ [$M^+$]: 377.2355, found 376.2274 (M - 1).




**4a: (S)-Methyl 2-((3R,4R)-4-methyl-1-phenylhex-5-en-3-ylamino)-2-phenylacetate**

(56 %*de*; *syn* : *anti* = 79 : 21)

Yellow oil (132 mg, 39 %);

$R_f$ = 0.58 (8:1 hexane/ethyl acetate);

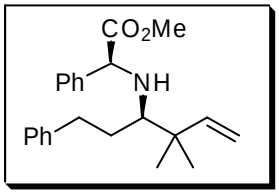
$[\alpha]^{25}$ = + 22.7 $^o$ (0.40, $CH_2Cl_2$);

$^1$H NMR (300 MHz, $CDCl_3$): d 7.29 – 7.05 (m, 10H), 5.75 – 5.58 (m, 1H), 5.10 – 5.04 (m, 1H), 4.16 (s, 1H), 3.61 (s, 3H), 2.74 – 2.68 (m, 3H), 2.58 – 2.51 (m, 2H), 2.17 – 2.05 (m, 1H), 0.8 (d, *J* = 6.9 Hz, 3H);

$^{13}$C NMR (75.4 MHz, $CDCl_3$) d 174.4, 142.0, 141.9, 141.8, 141.7, 140.2, 138.6, 137.1, 131.0, 128.7, 128.6, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 127.6, 127.5, 127.2, 127.0, 125.8, 125.7, 125.6, 116.0, 114.2, 68.4, 65.0, 62.2, 51.7, 42.2, 36.1, 34.9, 33.3, 30.6, 18.2, 13.6;

FTIR (neat): 3062, 3027, 2952, 1737, 1599, 1453, 1300, 1204, 1170, 997, 917, 733, 699, 551 $cm^{-1}$;

HRMS (ESI) Calcd for $C_{22}H_{27}NO_2$ [$M^+$]: 337.2042, found 338.2113 (M + 1).




**4b: (S)-Methyl 2-((R)-4,4-dimethyl-1-phenylhex-5-en-3-ylamino)-2-phenylacetate**

(78 %*de*)

Yellow oil (253 mg, 72 %);

$R_f$ = 0.70 (8:1 hexane/ethyl acetate);

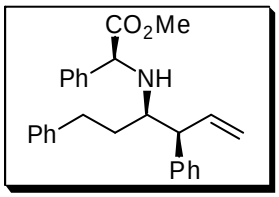
$[\alpha]^{25}$ = + 32.8 $^{o}$ (0.61, $CH_2Cl_2$);

$^1$H NMR (300 MHz, $CDCl_3$): d 7.42 – 7.09 (m, 10H), 5.88 (dd, *J* = 17.1, 11.5 Hz, 2H), 5.04 – 4.98 (m, 2H), 4.47 (s, 1H), 3.67 (s, 3H), 2.53 (dt, *J* = 5.6, 5.3 Hz, 1H), 2.28 – 2.17 (m, 2H), 1.86 – 1.74 (m, 1H), 1.49 – 1.37 (m, 1H), 1.04 (s, 3H), 1.02 (s, 3H);

$^{13}$C NMR (75.4 MHz, $CDCl_3$) d 173.9, 146.9, 142.7, 139.7, 128.9, 128.6, 128.5, 128.4, 128.2, 128.0, 127.9, 127.1, 125.6, 112.1, 65.2, 63.9, 52.1, 42.4, 34.3, 34.1, 24.1, 23.2;

FTIR (neat): 3027, 2954, 2868, 1737, 1600, 1454, 1361, 1307, 1253, 1201, 1169, 1004, 914, 738, 699 $cm^{-1}$;

HRMS (ESI) Calcd for $C_{23}H_{29}NO_2$ [$M^+$]: 351.2198, found 352.2281 (M + 1).




**4c: (S)-Methyl 2-((3R,4S)-1,4-diphenylhex-5-en-3-ylamino)-2-phenylacetate**

(76 %*de*; *syn* : *anti* = 90 : 10)

Dark Yellow oil (231 mg, 58 %);

$R_f$ = 0.48 (8:1 hexane/ethyl acetate);

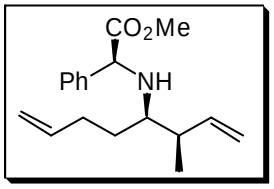
$[\alpha]^{25}$ = + 29.7 $^{o}$ (0.81, $CH_2Cl_2$);

$^1$H NMR (300 MHz, $CDCl_3$): d 7.34 – 6.95 (m, 15H), 6.08 (dt, *J* = 10.5, 9.4 Hz, 1H), 5.21 – 5.15 (m, 2H), 4.40 (s, 1H), 3.61 (3H), 3.57 – 3.48 (m, 1H), 2.86 (dt, *J* = 10.5, 3.8 Hz, 1H), 2.71 (ddd, *J* = 10.5, 5.6, 5.2 Hz, 1H), 2.44 (ddd, *J* = 10.5, 6.3, 5.6 Hz, 1H), 1.80 – 1.63 (m, 3H);

$^{13}$C NMR (75.4 MHz, $CDCl_3$) d 173.4, 142.6, 141.8, 138.9, 138.0, 128.6, 128.5, 128.4, 128.2, 128.1, 128.0, 127.8, 126.6, 125.6, 117.2, 63.0, 58.6, 53.4, 52.2, 32.8, 31.0;

FTIR (neat): 3027, 2949, 1737, 1601, 1491, 1452, 1305, 1171, 996, 920, 737, 700 $cm^{-1}$;

HRMS (ESI) Calcd for $C_{27}H_{29}NO_2$ [$M^+$]: 399.2198, found 400.2270 (M + 1).




**5a: (S)-methyl 2-((3R,4R)-3-methylocta-1,7-dien-4-ylamino)-2-phenylacetate**

(50 %*de*; *syn* : *anti* = 86 : 14)

Yellow oil (169 mg, 59 %);

$R_f$ = 0.66 (8:1 hexane/ethyl acetate);

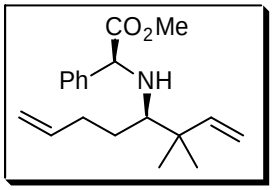
$[\alpha]^{25}$ = + 31.2 $^o$ (0.19, $CH_2Cl_2$);

$^1$H NMR (300 MHz, $CDCl_3$): d 7.40 – 7.29 (m, 5H), 5.88 – 5.63 (m, 2H), 5.10 – 5.02 (m, 2H), 4.91 – 4.85 (m, 2H), 4.51 (s, 1H), 3.67 (s, 3H), 2.47 – 2.41 (m, 1H), 2.39 – 2.32 (m, 1H), 2.19 – 2.09 (m, 1H), 1.99 – 1.86 (m, 1H), 1.49 – 1.41 (m, 1H), 1.38 – 1.29 (m, 1H), 0.98 (d, *J* = 6.9 Hz, 3H);

$^{13}$C NMR (75.4 MHz, $CDCl_3$) d 173.6, 141.7, 140.7, 138.9, 138.8, 138.7, 128.4, 127.8, 127.7, 127.5, 114.9, 114.4, 63.0, 62.8, 58.4, 52.1, 39.9, 39.3, 30.3, 30.1, 29.5, 15.4, 14.8;

FTIR (neat): 3072, 3029, 2958, 1739, 1600, 1639, 1452, 1373, 1315, 1252, 1203, 1171, 1132, 998, 912, 785, 733, 699 $cm^{-1}$;

HRMS (ESI) Calcd for $C_{18}H_{25}NO_2$ [$M^+$]: 287.1885, found 288.1961 (M + 1).




**5b: (S)-Methyl 2-((R)-3,3-dimethylocta-1,7-dien-4-ylamino)-2-phenylacetate**

(78 %*de*)

Yellow oil (197 mg, 72 %);

$R_f$ = 0.64 (8:1 hexane/ethyl acetate);

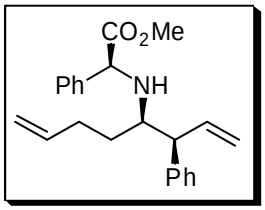
$[\alpha]^{25}$ = + 40.6 $^{o}$ (0.49, $CH_2Cl_2$);

$^1$H NMR (300 MHz, $CDCl_3$): d 7.38 – 7.28 (m, 5H), 5.88 (dd, *J* = 17.1, 11.5 Hz, 1H), 5.62 (ddt, *J* = 13.9, 10.5, 6.6 Hz, 1H), 5.05 – 4.99 (m, 2H), 4.86 – 4.76 (m, 2H), 4.47 (s, 1H), 3.68 (s, 3H), 2.21 (dd, *J* = 2.4, 7.3 Hz, 1H), 2.02 – 1.92 (m, 1H), 1.78 – 1.54 (m, 4H), 1.04 (s, 3H), 1.02 (s, 3H);

$^{13}$C NMR (75.4 MHz, $CDCl_3$) d 173.8, 138.6, 135.1, 128.6, 127.9, 127.5, 117.6, 114.5, 62.7, 53.8, 52.2, 38.3, 33.3, 29.7;

FTIR (neat): 3072, 2926, 2855, 1819, 1740, 1640, 1452, 1364, 1311, 1208, 1122, 1028, 995, 914, 736, 699 $cm^{-1}$;

HRMS (ESI) Calcd for $C_{17}H_{23}NO_2$ [$M^+$]: 273.1729, found 274.1796 (M + 1).




**5c: (S)-Methyl 2-((3S,4R)-3-phenylocta-1,7-dien-4-ylamino)-2-phenylacetate**

(80 %*de*; *syn* : *anti* = 95 : 5)

Dark Yellow oil (216 mg, 62 %);

$R_f$ = 0.55 (8:1 hexane /ethyl acetate);

$[\alpha]^{25}$ = + 33.8 $^{o}$ (0.62, $CH_2Cl_2$);

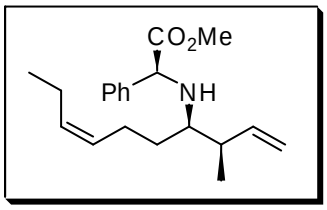
$^1$H NMR (300 MHz, $CDCl_3$): d 7.30 – 7.17 (m, 10H), 6.08 (dt, *J* = 16.7, 9.8 Hz, 1H), 5.64 (ddt, *J* = 13.9, 9.8, 6.6 Hz, 1H), 5.19 – 5.12 (m, 2H), 4.86 – 4.82 (m, 2H), 4.39 (s, 1H), 3.62

(s, 3H), 3.53 – 3.48 (m, 1H), 2.80 (q, *J* = 3.8 Hz, 1H), 2.21 – 2.11 (m, 1H), 2.09 – 1.93 (m, 1H), 1.49 – 1.43 (m, 1H);

$^{13}$C NMR (75.4 MHz, $CDCl_3$) d 173.2, 141.8, 138.6, 137.9, 128.4, 128.4, 128.1, 127.8, 127.6, 126.4, 117.0, 114.3, 62.7, 58.3, 23.3, 21.9, 29.9, 29.1;

FTIR (neat): 3063, 3028, 2947, 2405, 1738, 1639, 1600, 1492, 1450, 1309, 1207, 1172, 996, 915, 732, 700 $cm^{-1}$;

HRMS (ESI) Calcd for $C_{23}H_{27}NO_2$ [$M^+$]: 349.2042, found 350.2119 (M + 1).




**6a: (S)-Methyl 2-((Z,3R,4R)-3-methyldeca-1,7-dien-4-ylamino)-2-phenylacetate**

(60 %*de*; *syn* : *anti* = 81 : 19)

Yellow oil (167 mg, 53 %);

$R_f$ = 0.60 (8:1 hexane/ethyl acetate);

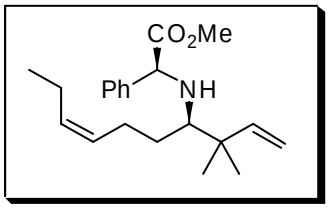
$[\alpha]^{25}$ = + 43.7 $^o$ (0.55, $CH_2Cl_2$);

$^1$H NMR (300 MHz, $CDCl_3$): d 7.41 – 7.28 (m, 5H), 5.83 (ddd, *J* = 13.6, 10.5, 6.9 Hz, 1H), 5.36 – 5.17 (m, 2H), 5.09 – 5.02 (m, 2H), 4.51 (s, 1H), 3.68 (s, 3H), 2.46 – 2.29 (m, 2H), 2.17 – 1.84 (m, 4H), 1.49 – 1.23 (m, 2H), 1.99 (d, *J* = 6.9 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H);

$^{13}$C NMR (75.4 MHz, $CDCl_3$) d 173.8, 141.0, 138.9, 131.8, 128.8, 128.6, 128.5, 127.9, 127.7, 127.5, 114.9, 62.9, 58.9, 52.2, 39.5, 31.1, 23.8, 20.5, 15.4, 14.3;

FTIR (neat): 3003, 2962, 1873, 1740, 1638, 1454, 1374, 1204, 1170, 999, 914, 731, 698 $cm^{-1}$;

HRMS (ESI) Calcd for $C_{20}H_{29}NO_2$ [$M^+$]: 315.2198, found 316.2277 (M + 1).




**6b: (S)-Methyl 2-((R,Z)-3,3-dimethyldeca-1,7-dien-4-ylamino)-2-phenylacetate**

(80 %*de*)

Yellow oil (303 mg, 92 %);

$R_f$ = 0.71 (8:1 hexane/ethyl acetate);

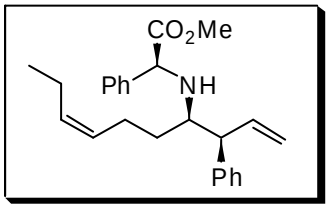
$[\alpha]^{25}$ = + 43.7 $^{o}$ (0.43, $CH_2Cl_2$);

$^1$H NMR (300 MHz, $CDCl_3$): d 7.41 – 7.28 (m, 5H), 5.92 (dd, *J* = 11.9, 10.4 Hz, 1H), 5.39 – 5.15 (m, 2H), 5.07 – 5.07 (m, 2H), 4.50 (s, 1H), 3.68 (s, 3H), 2.23 (dd, *J* = 6.9, 3.5 Hz, 1H), 2.06 (brs, 1H), 1.98 – 1.88 (m, 2H), 1.78 – 1.67 (m, 1H), 1.63 – 1.51 (m, 1H), 1.27 – 1.17 (m, 1H), 1.06 (s, 3H), 0.96 (s, 3H), 0.93 (t, *J* = 6.9 Hz, 3H);

$^{13}$C NMR (75.4 MHz, $CDCl_3$) d 173.8, 146.9, 139.4, 131.6, 128.8, 128.4, 127.8, 127.6, 111.8, 64.9, 63.8, 51.9, 42.1, 32.0, 25.8, 24.0, 22.9, 20.4, 14.3;

FTIR (neat): 3004, 2963, 2872, 1740, 1690, 1637, 1434, 1454, 1363, 1257, 1199, 1166, 1130, 1071, 913, 865, 728, 699 $cm^{-1}$;

HRMS (ESI) Calcd for $C_{21}H_{31}NO_2$ [$M^+$]: 329.2355, found 330.2441 (M + 1).




**6c: (S)-Methyl 2-((Z,3S,4R)-3-phenyldeca-1,7-dien-4-ylamino)-2-phenylacetate**

(80 %*de*; *syn* : *anti* = 88 : 12)

Dark Yellow oil (253 mg, 67 %);

$R_f$ = 0.55 (8:1 hexane/ethyl acetate);

$[\alpha]^{25}$ = + 39.2 $^{o}$ (0.33, $CH_2Cl_2$);

$^1$H NMR (300 MHz, $CDCl_3$): d 7.36 – 7.22 (m, 10H), 6.12 (ddd, *J* = 16.4, 15.3, 9.4 Hz, 1H), 5.37 – 5.15 (m, 4H), 4.42 (s, 1H), 3.63 (s, 3H), 3.52 (dd, *J* = 9.4, 7.3 Hz, 1H), 2.89 – 2.83 (m, 1H), 2.20 – 2.10 (m, 2H), 2.09 – 1.93 (m, 2H), 1.59 – 1.39 (m, 2H), 0.93 (t, *J* = 7.7 Hz, 3H);

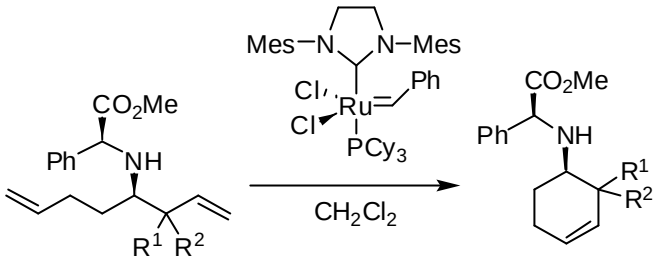
$^{13}$C NMR (75.4 MHz, $CDCl_3$) d 173.3, 141.8, 138.6, 138.2, 131.7, 128.8, 128.6, 128.4, 128.1, 127.9, 127.8, 127.5, 126.5, 116.8, 62.8, 58.6, 53.6, 51.9, 30.8, 22.5, 20.4, 14.3;

FTIR (neat): 3063, 3028, 3004, 2960, 2932, 2872, 1738, 1600, 1492, 1453, 1306, 1204, 1170, 995, 919, 731, 700 $cm^{-1}$;

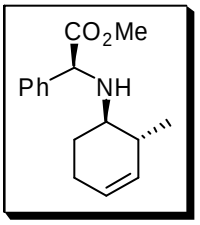
HRMS (ESI) Calcd for $C_{25}H_{31}NO_2$ [$M^+$]: 377.2355, found 378.2436 (M + 1).

**Ring closing metathesis of homoallylic amines.**

**General reaction procedure for the preparation of cyclohexenylamines 7.**




To a stirred suspension of the chiral homoallylic amine (1 equiv.) in $CH_2Cl_2$ (0.01 M) was added the Grubbs' 2nd generation catalyst (0.1 equiv.) at two portions (interval of 30 minutes) at 25 °C and stirred for up to 12 hours. Reactions were heated to the TLC showed starting material after 12 hours of stirring at room temperature The reaction mixture was then filtered through a pad of celite before being concentrated in vacuo. The crude product was purified by flash column chromatography.




**7a: (S)-Methyl 2-((1R,2R)-2-methylcyclohex-3-enylamino)-2-phenylacetate**

To a stirred suspension of the chiral homoallylic amine **6a** (0.29 g, 1 mmol) in $CH_2Cl_2$ (100 mL) was added the Grubbs' 2nd generation catalyst (0.085 g, 0.1 mmol) at two portions (interval of 30 minutes) at 25 °C and stirred for up to 12 hours. Reactions were reflux at 40 °C if the TLC showed starting material after 12 hours of stirring at room temperature The reaction mixture was then filtered through a pad of celite before being concentrated in vacuo. The crude product was purified by flash column chromatography.

Dark brown oil (218 mg, 84 %);

$R_f$ = 0.51 (8:1 hexane/ethyl acetate);

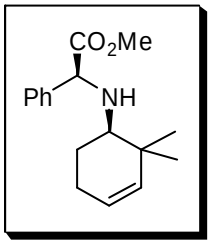
$[\alpha]^{25}$ = + 1.8 $^{o}$ (0.42, $CH_2Cl_2$);

$^{1}$H NMR (300 MHz, $CDCl_3$): d 7.41 – 7.27 (m, 5H), 5.63 – 5.59 (m, 1H), 5.45 (ddd, *J* = 10.2, 2.3, 1.8 Hz, 1H), 4.55 (s, 1H), 3.69 (s, 3H), 2.35 (dt, *J* = 9.7, 2.8 Hz, 1H), 2.14 – 1.93 (m, 3H), 1.87 – 1.82 (m, 1H), 1.45 – 1.38 (m, 1H), 1.09 (d, *J* = 6.9 Hz, 3H);

$^{13}$C NMR (75.4 MHz, $CDCl_3$) d 174.0, 138.9, 131.6, 128.6, 128.5, 127.9, 127.5, 127.3, 125.8, 125.6, 62.9, 58.2, 52.1, 36.4, 26.8, 23.8, 19.4;

FTIR (neat): 3018, 2953, 2926, 2870, 1737, 1453, 1250, 1205, 1168, 1137, 1016, 729, 698 $cm^{-1}$;

HRMS (EI) Calcd for $C_{16}H_{21}NO_2$ [$M^+$]: 259.1572, found 259.1574.




**7b: (S)-Methyl 2-((R)-2,2-dimethylcyclohex-3-enylamino)-2-phenylacetate**

Dark brown oil (251 mg, 92 %);

$R_f$ = 0.61 (8:1 hexane/ethyl acetate);

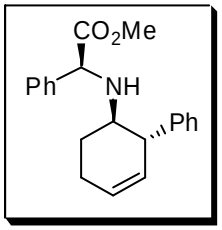
$[\alpha]^{25}$ = + 25.1 $^{o}$ (0.52, $CH_2Cl_2$);

$^{1}$H NMR (300 MHz, $CDCl_3$): d 7.45 – 7.28 (m, 5H), 5.50 (ddd, *J* = 10.2, 2.8, 1.8 Hz, 1H), 5.36 (dt, *J* = 10.2, 1.9 Hz, 1H), 5.54 (s, 1H), 3.69 (s, 3H), 2.43 (dd, *J* = 11.1, 2.8 Hz, 1H), 2.06 – 1.93 (m, 3H), 1.75 – 1.71 (m, 1H), 1.49 – 1.42 (m, 1H), 1.13 (s, 3H), 1.00 (s, 3H);

$^{13}$C NMR (75.4 MHz, $CDCl_3$) d 174.0, 139.1, 137.6, 128.5, 127.9, 127.3, 123.7, 63.7, 61.0, 51.9, 36.2, 28.4, 24.7, 24.4, 22.9;

FTIR (neat): 3013, 2954, 1738, 1454, 1363, 1298, 1204, 1168, 916, 737, 698 $cm^{-1}$;

HRMS (EI) Calcd for $C_{17}H_{23}NO_2$ [$M^+$]: 273.1729, found 273.1731.




**7c: (S)-Methyl 2-((1R,2S)-2-phenylcyclohex-3-enylamino)-2-phenylacetate**

Dark brown oil (276 mg, 86 %);

$R_f$ = 0.40 (8:1 hexane/ethyl acetate);

$[\alpha]^{25}$ = + 44.1 $^{o}$ (0.41, $CH_2Cl_2$);

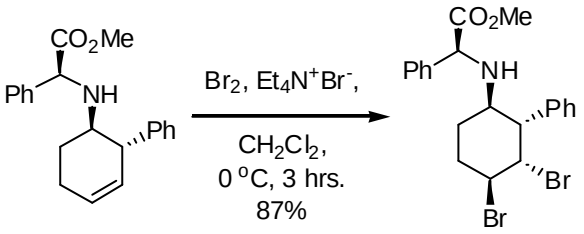
$^{1}$H NMR (300 MHz, $CDCl_3$): d 7.38 – 7.25 (m, 10H), 5.86 – 5.82 (m, 1H), 5.59 (ddd, *J* = 10.2, 2.3, 1.9 Hz, 1H), 4.40 (s, 1H), 3.50 (s, 3H), 3.36 – 3.33 (m, 1H), 2.72 (dt, *J* = 10.6, 2.8 Hz, 1H), 2.33 – 2.16 (m, 4H), 1.97 – 1.92 (m, 1H), 1.60 – 1.53 (m, 1H);

$^{13}$C NMR (75.4 MHz, $CDCl_3$) d 173.3, 143.4, 138.5, 129.0, 128.5, 128.4, 127.8, 127.3, 127.2, 126.7, 62.8, 58.1, 51.9, 49.2, 27.0, 24.0;

FTIR (neat): 3025, 2947, 2925, 2860, 1737, 1491, 1453, 1290, 1248, 1207, 1169, 1135, 1029, 787, 760, 733,701 $cm^{-1}$;

HRMS (EI) Calcd for $C_{21}H_{23}NO_2$ [$M^+$]: 321.1729, found 321.1730.

**Bromination of cyclohexenylamine 8.**




**7c** **8**

**8: (S)-Methyl 2-((1R,2S,3S,4S)-3,4-dibromo-2-phenylcyclohexylamino)-2-phenylacetate**

Tetraethylammonium bromide (1.09 g, 5.20 mmol) was added into a stirred solution of **7c** (0.17 g, 0.52 mmol) in $CH_2Cl_2$ (1.80 mL) at 0 $^{o}$C. After the reaction mixture had stirred for 15 minutes, bromine (0.08 mL, 1.56 mmol) was introduced slowly into the former at the same temperature. The resultant solution was allowed to stir for a further 3 hours. When TLC has shown the full depletion of the starting material **7c**, the reaction mixture was washed with

saturated $NaHSO_3$ (2 x 20 mL) and water (2 x 20 mL). After drying in $Na_2SO_4$, the reaction mixture was filtered and concentrated in vacuo. The crude product was purified *via* flash column chromatography (20:1 hexane/ethyl acetate), yielding 0.22 g (87% yield, 0.45 mmol) of the desired product **8** as a white solid.

$R_f$ = 0.50 (8:1 hexane/ethyl acetate);

$[\alpha]^{25}$ = + 24.6 $^{o}$ (0.11, $CH_2Cl_2$);

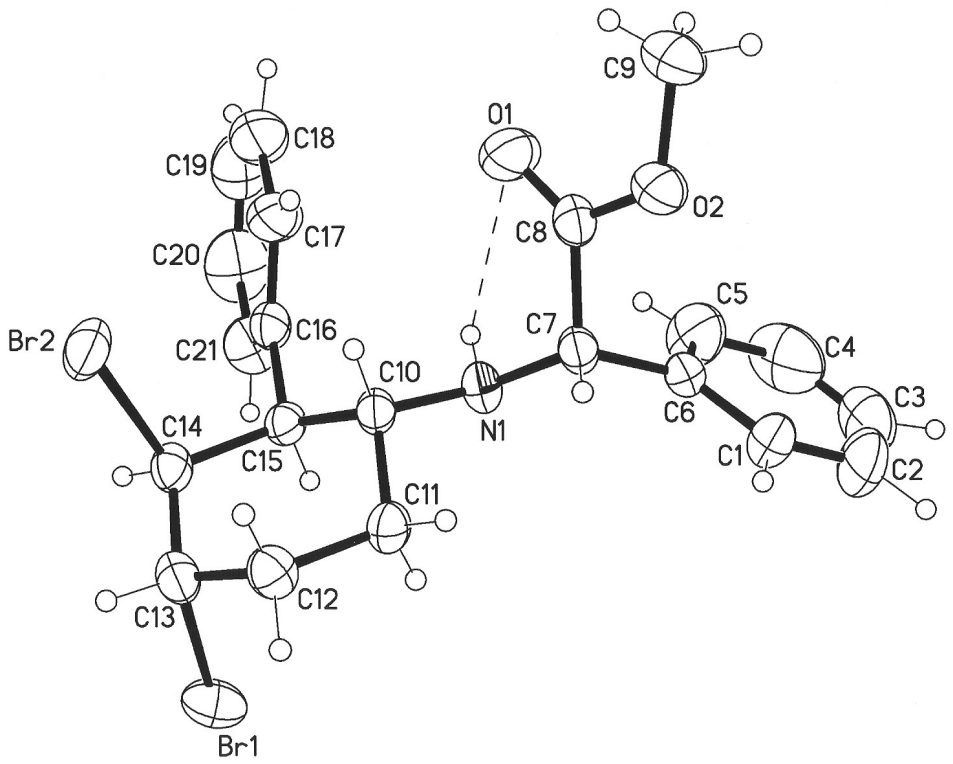
$^1$H NMR (300 MHz, $CDCl_3$): d 7.41 – 7.22 (m, 10H), 4.83 (d, *J* = 2.5 Hz, 1H), 4.55 (s, 1H), 4.52 (d, *J* = 1.9 Hz, 1H), 3.72 (s, 3H), 3.65 (dd, *J* = 10.8, 2.5 Hz, 1H), 3.53 (dt, *J* = 10.8, 3.8 Hz, 1H), 2.69 – 2.62 (m, 1H), 2.09 – 2.04 (m, 2H), 1.94 – 1.85 (m, 1H);

$^{13}$C NMR (75.4 MHz, $CDCl_3$) d 173.4, 138.3, 138.1, 129.5, 128.6, 128.3, 127.9, 127.6, 127.1, 61.9, 61.5, 53.8, 52.1, 51.5, 47.6, 27.4, 26.6;

FTIR (KBr): 3062, 3030, 2951, 1735, 1600, 1452, 1434, 1265, 1209, 1171, 1057, 855, 737, 700, 599 $cm^{-1}$;

HRMS (EI) Calcd for $C_{21}H_{23}Br_2NO_2$ [$M^+$]: 479.0096, found 481.0075.

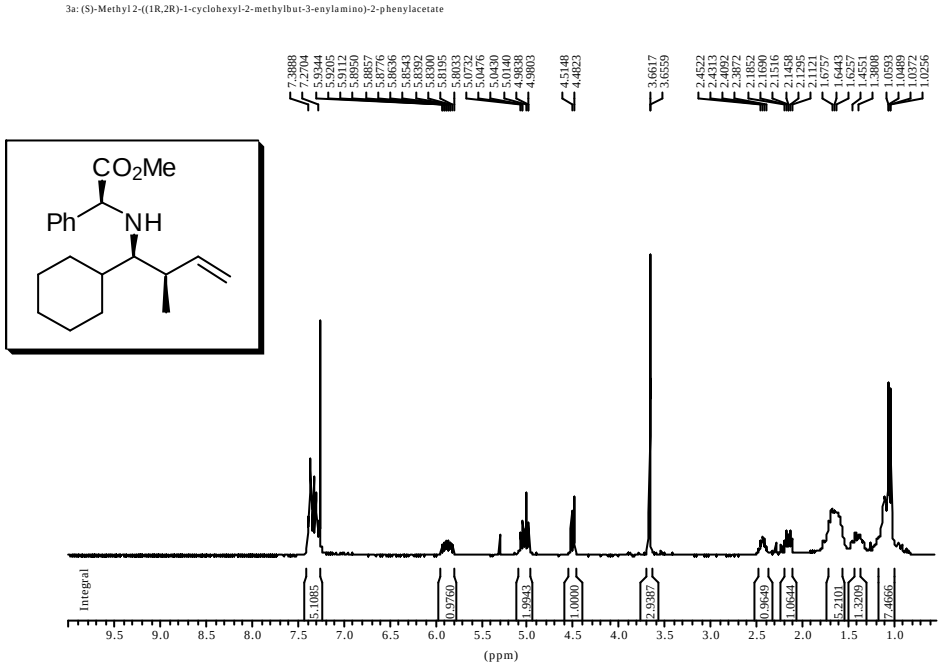
Crystal structure:

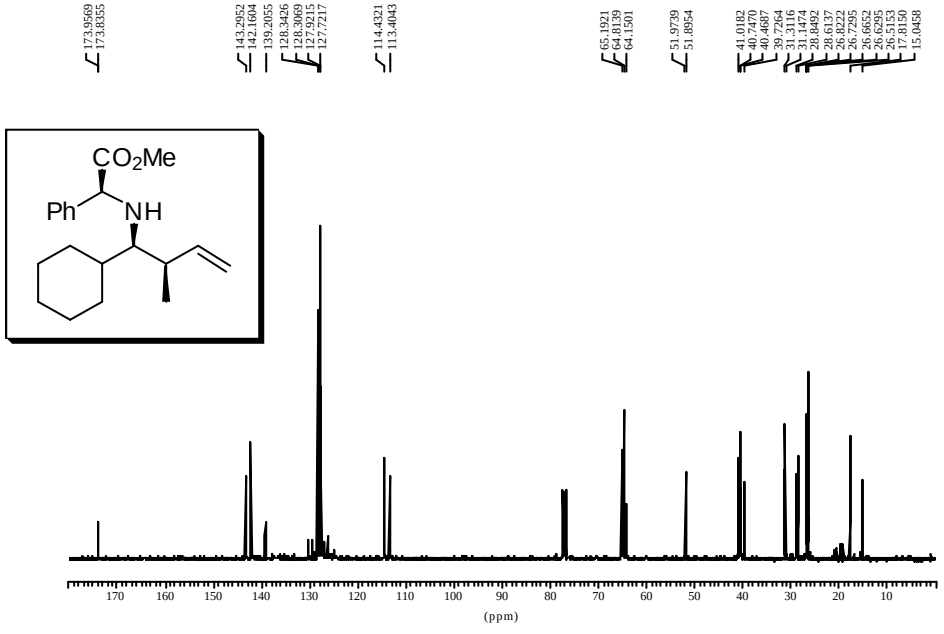


**Crystal Data and Structure Refinement for 8:**

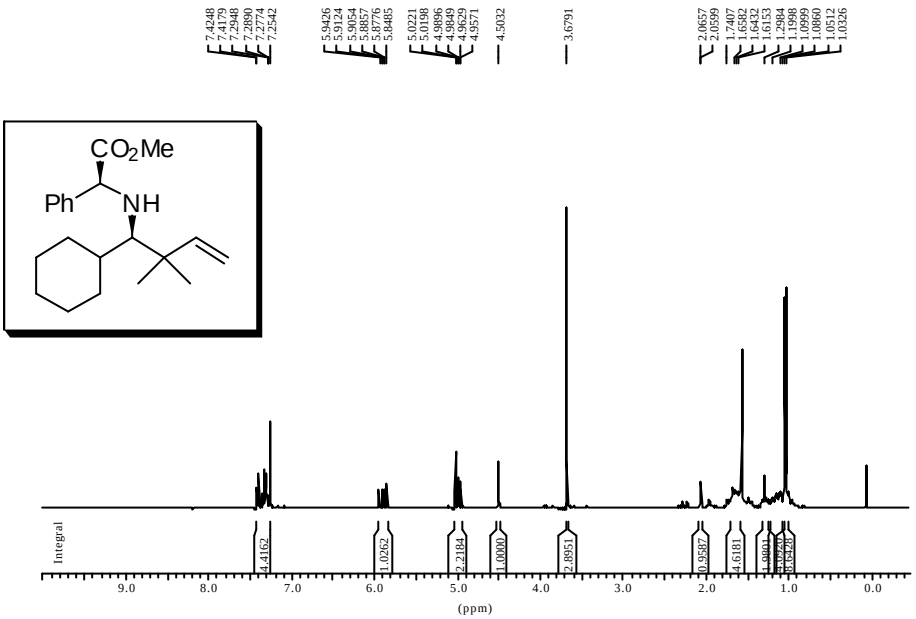
| | | |
|---|---|---|
| Crystal growing solvent | Dichloromethane and hexane | |
| Empirical formula | C21 H23 Br2 N O2 | |
| Formula weight | 481.22 | |
| Temperature | 293(2) K | |
| Wavelength | 0.71073 Å | |
| Crystal system | Triclinic | |
| Space group | P-1 | |
| Unite cell dimensions | a = 9.669(5) Å | $\alpha$ = 94.398(10)°. |
| | b = 10.054(5) Å | $\beta$ = 97.815(10)°. |
| | c = 11.307(6) Å | $\gamma$ = 110.743(9)°. |
| Volume | 1009.0(9) $Å^3$ | |
| Z | 2 | |
| Density (calculated) | 1.584 $Mg/m^3$ | |
| Absorption coefficient | 4.032 $mm^{-1}$ | |
| F(000) | 484 | |
| Crystal size | 0.30 x 0.48 x 0.56 $mm^3$ | |
| Theta range for data collection | 1.83 to 27.50°. | |
| Index ranges | -12<=h<=12, -13<=k<=13, -14<=l<=14 | |
| Reflections collected | 13167 | |
| Independent reflections | 4628 [R(int) = 0.0193] | |
| Completeness to theta = 27.50° | 99.9 % | |
| Absorption correction | Sadabs, (Sheldrick 2001) | |
| Refinement method | Full-matrix least-squares on $F^2$ | |
| Data / restraints / parameters | 4628 / 0 / 327 | |
| Goodness-of-fit on $F^2$ | 1.060 | |
| Final R indices [I>2sigma(I)] | R1 = 0.0256, wR2 = 0.0631 | |
| R indices (all data) | R1 = 0.0343, wR2 = 0.0661 | |
| Largest diff. peak and hole | 0.324 and -0.477 $e.Å^{-3}$ | |

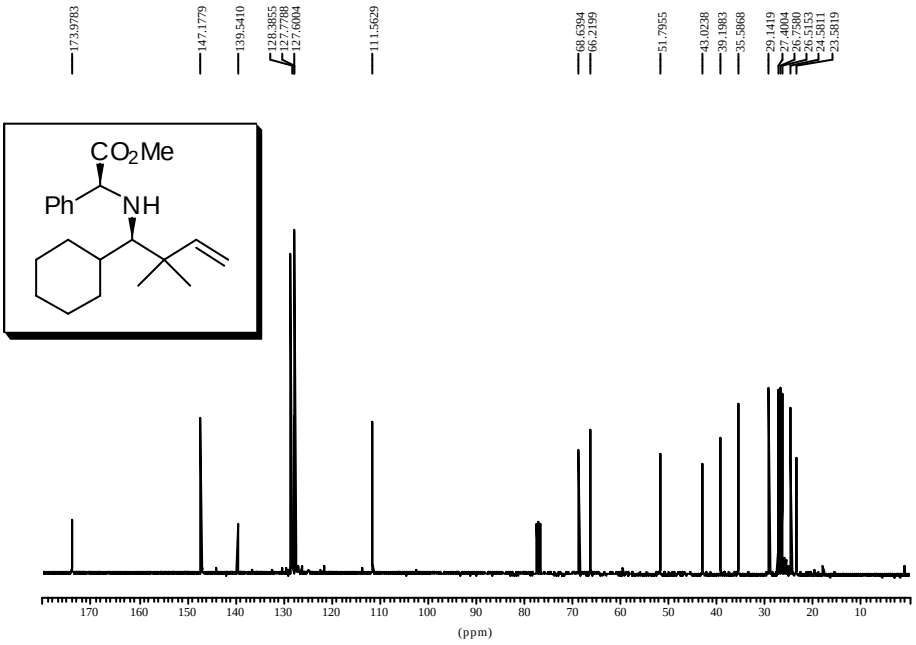
NMR and $^{13}$C NMR Spectra for Compounds **3 – 8**.



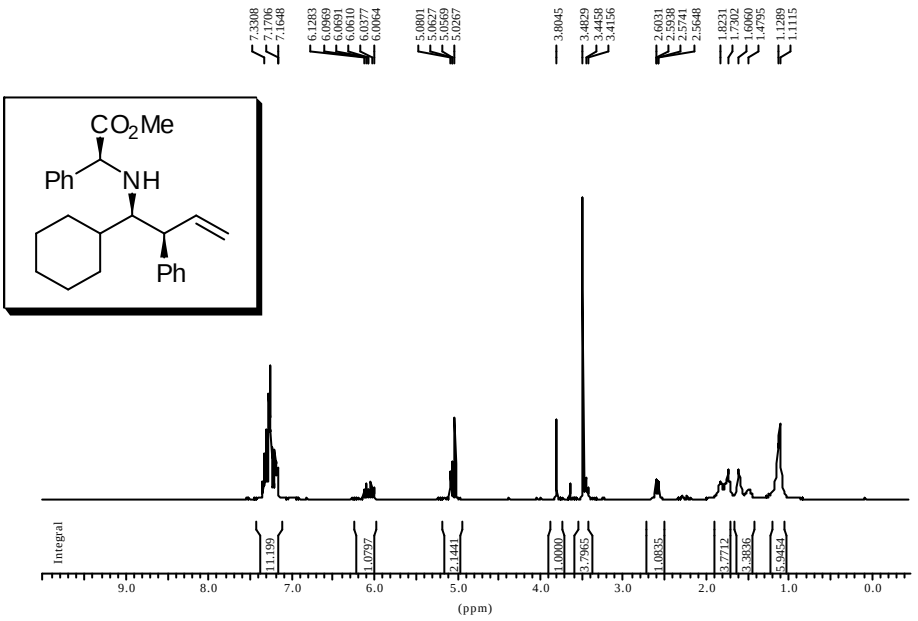



3b: (S)-Methyl 2-((R)-1-cyclohexyl-2,2-dimethylbut-3-enylamino)-2-phenylacetate

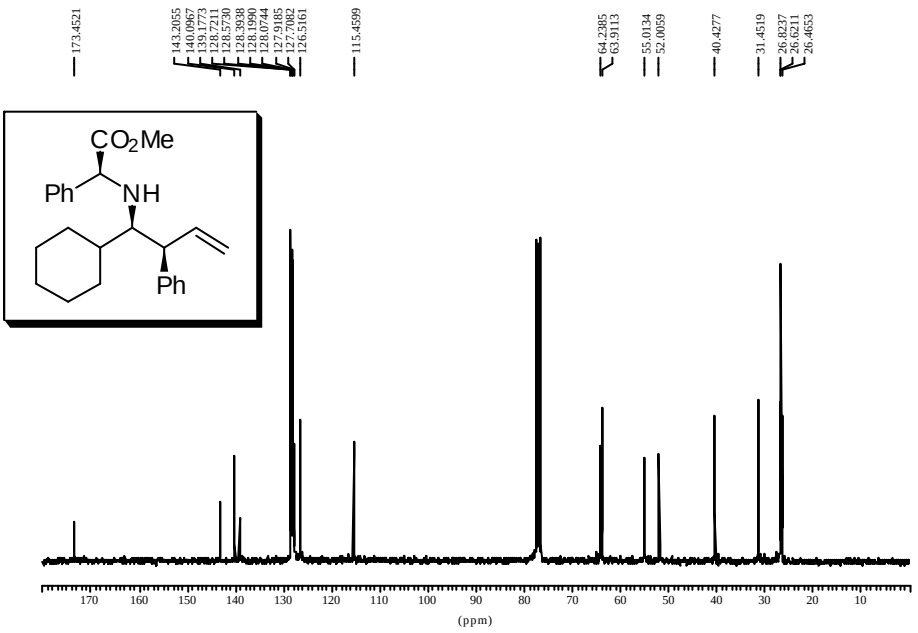


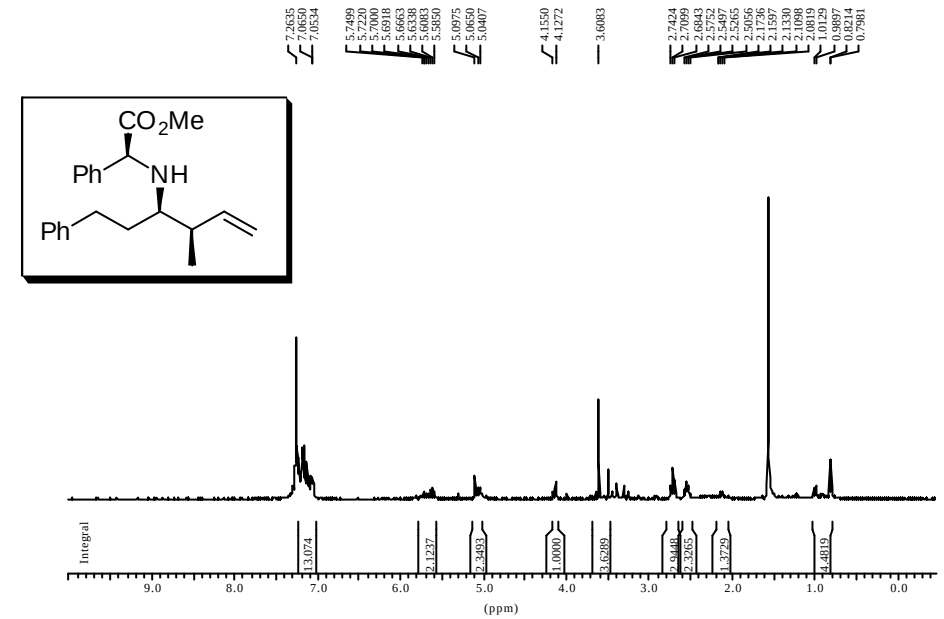
3c: (S)-Methyl 2-((1R,2S)-1-cyclohexyl-2-phenylbut-3-enylamino)-2-phenylacetate

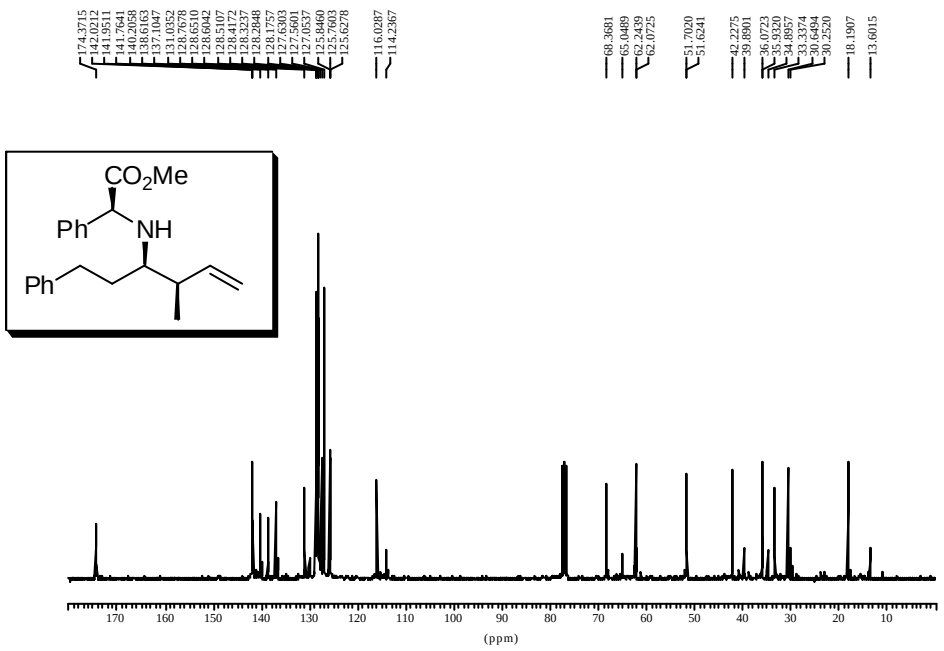



7112A 13C ag117112.43 5-1

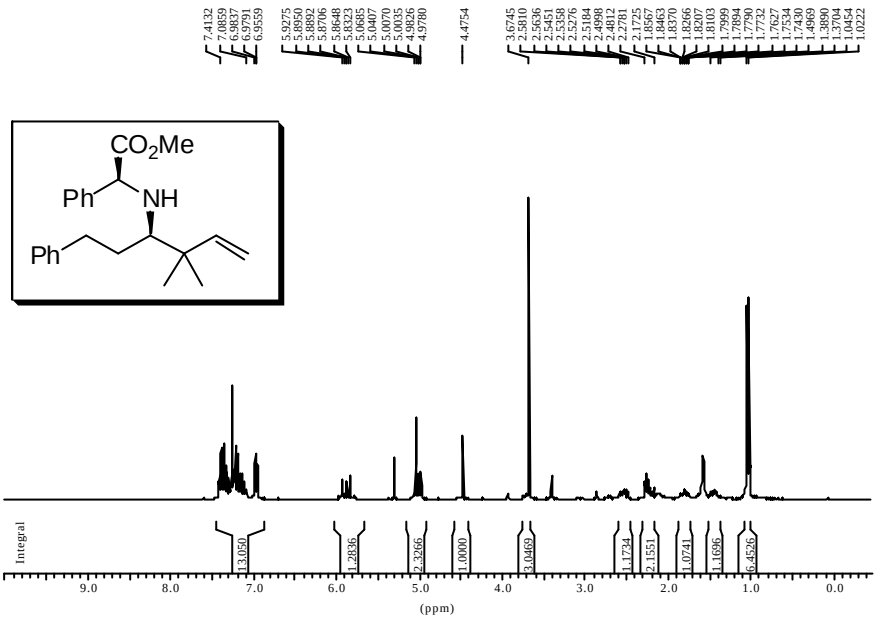


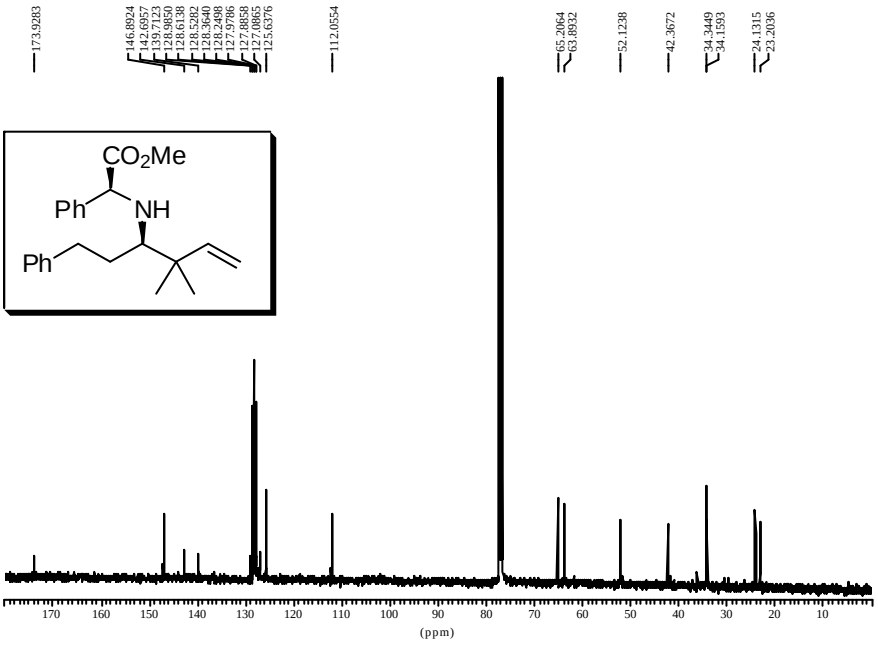
4a: (S)-Methyl 2-((3R,4R)-4-methyl-1-phenylhex-5-en-3-ylamino)-2-phenylacetate



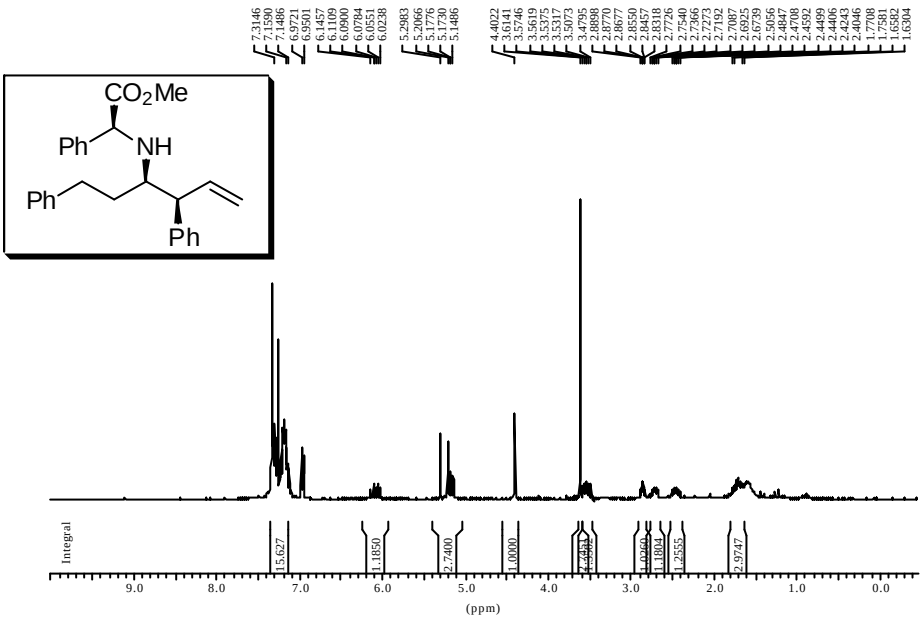



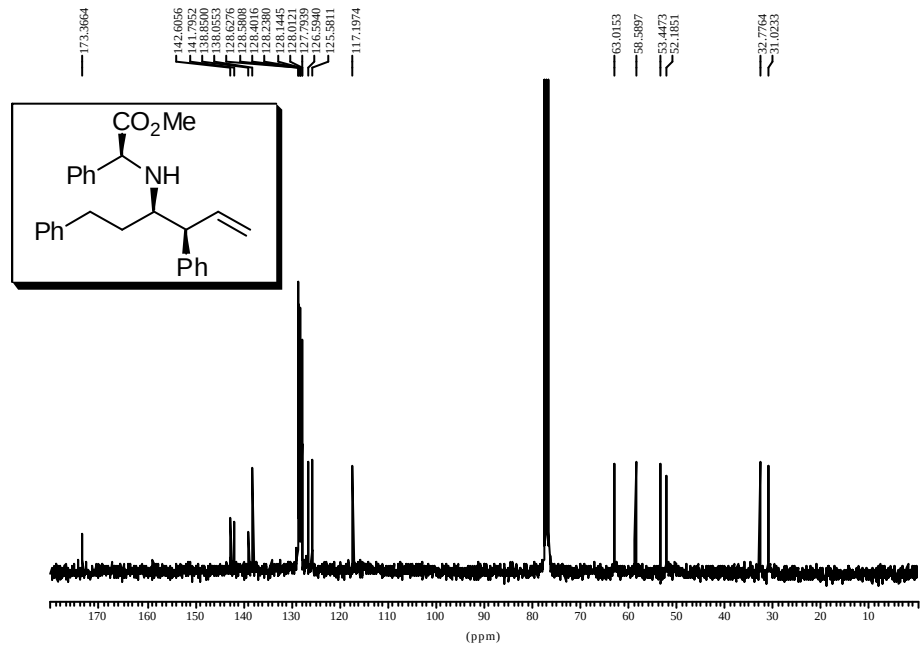
4b: (S)-Methyl 2-((R)-4,4-dimethyl-1-phenylhex-5-en-3-ylamino)-2-phenylacetate



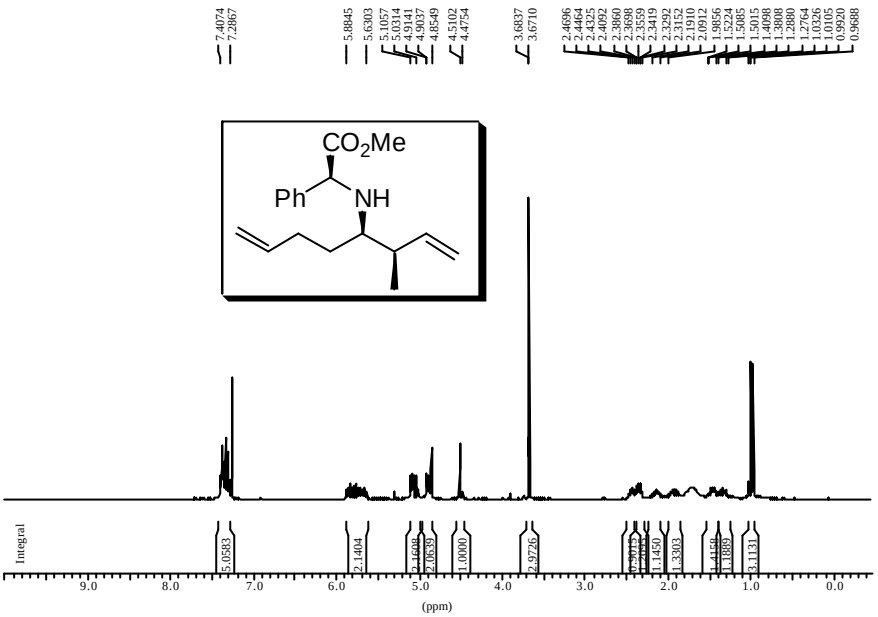



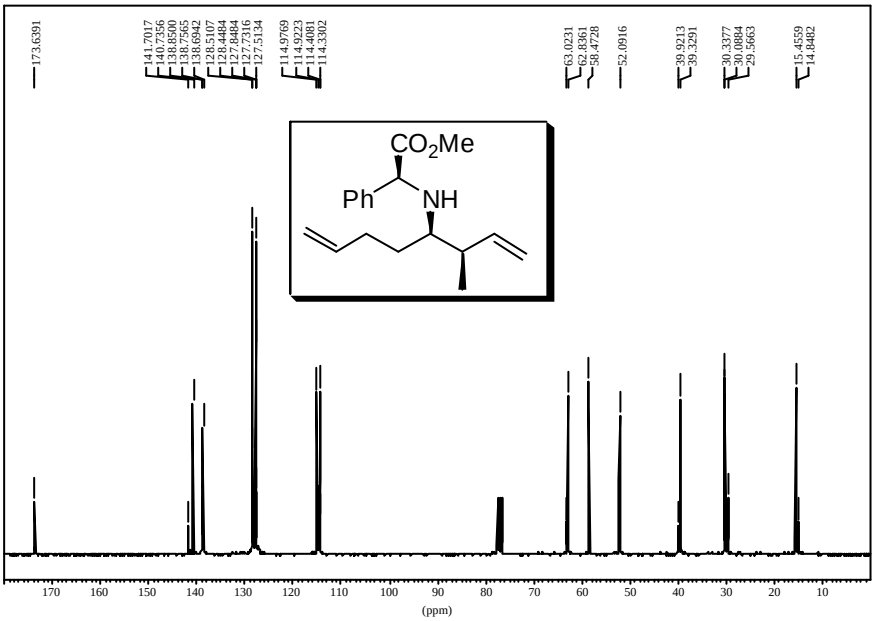
4c: (S)-Methyl 2-((3R,4S)-1,4-diphenylhex-5-en-3-ylamino)-2-phenylacetate



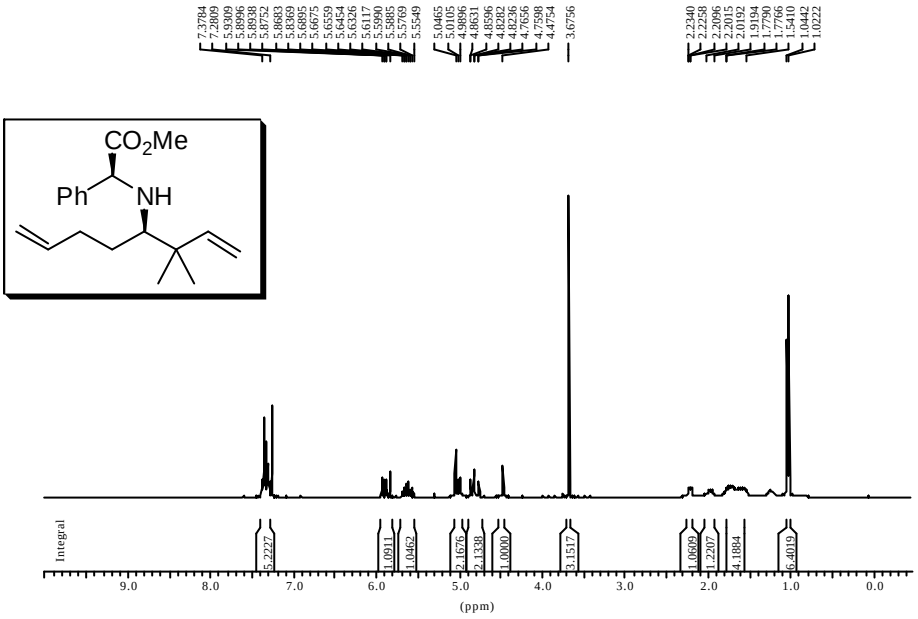



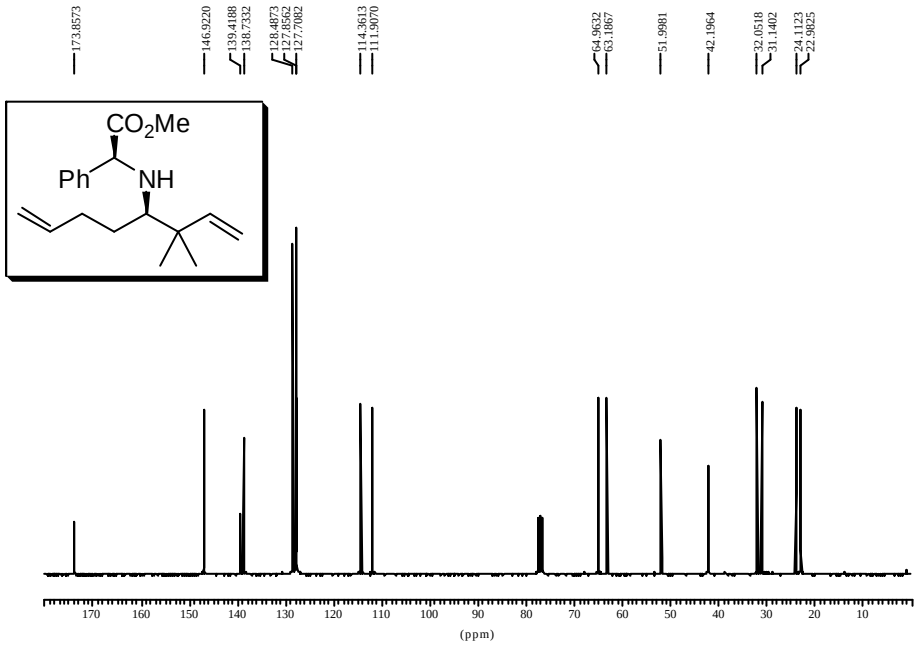
5a: (S)-methyl 2-((3R,4R)-3-methylocta-1,7-dien-4-ylamino)-2-phenylacetate



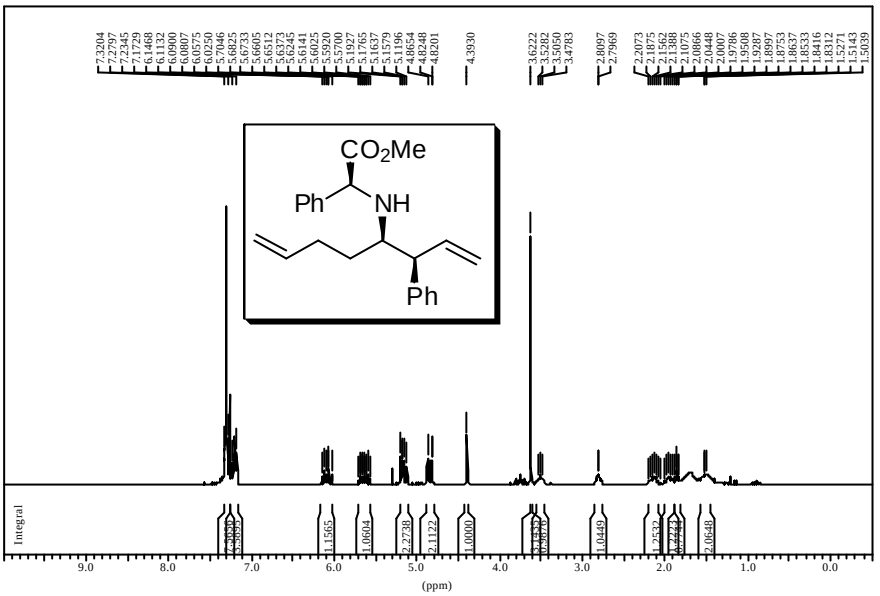



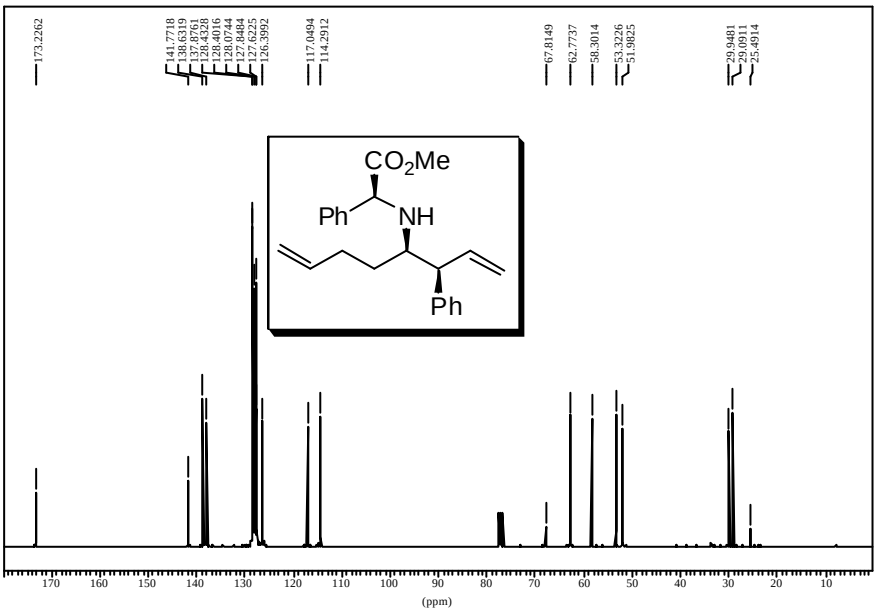
5b: (S)-Methyl 2-((R)-3,3-dimethylocta-1,7-dien-4-ylamino)-2-phenylacetate



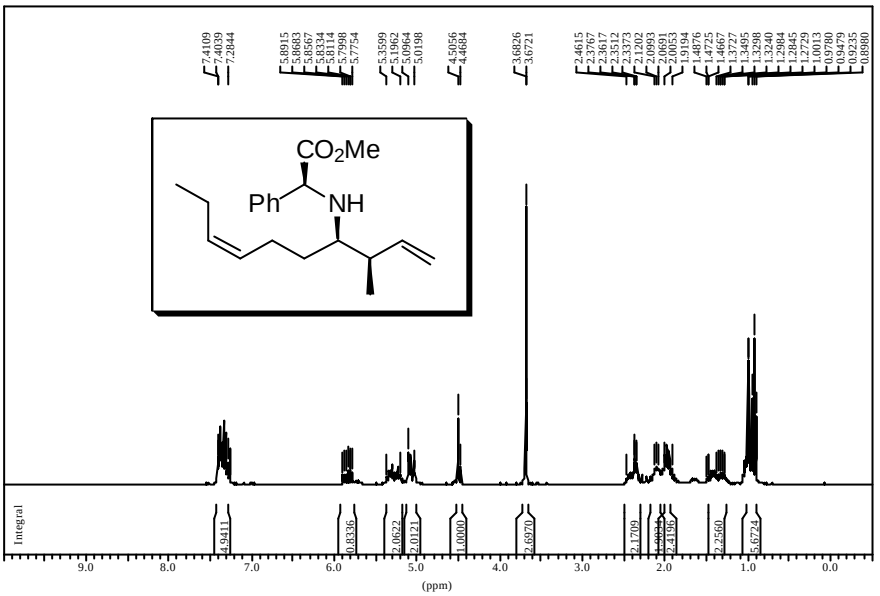



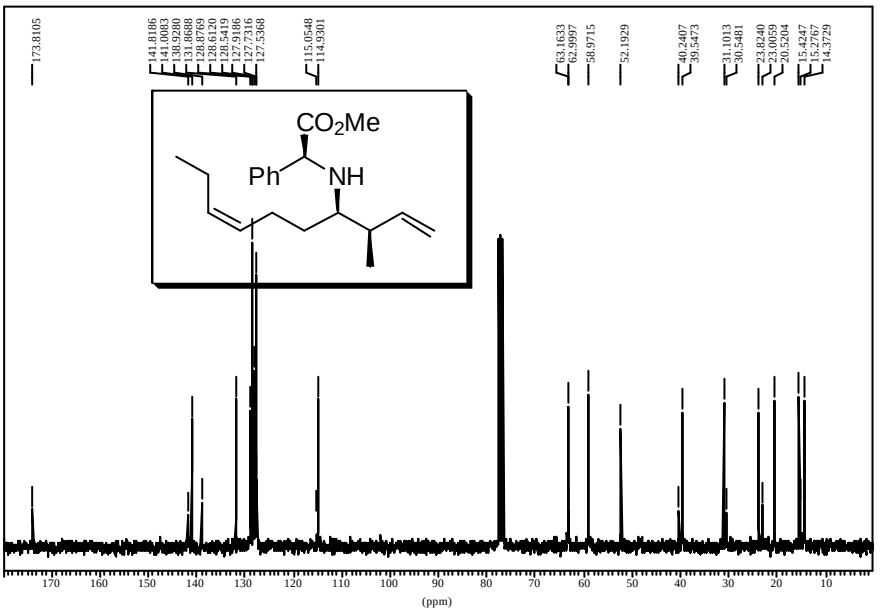
5c: (S)-Methyl 2-((3S,4R)-3-phenylocta-1,7-dien-4-ylamino)-2-phenylacetate



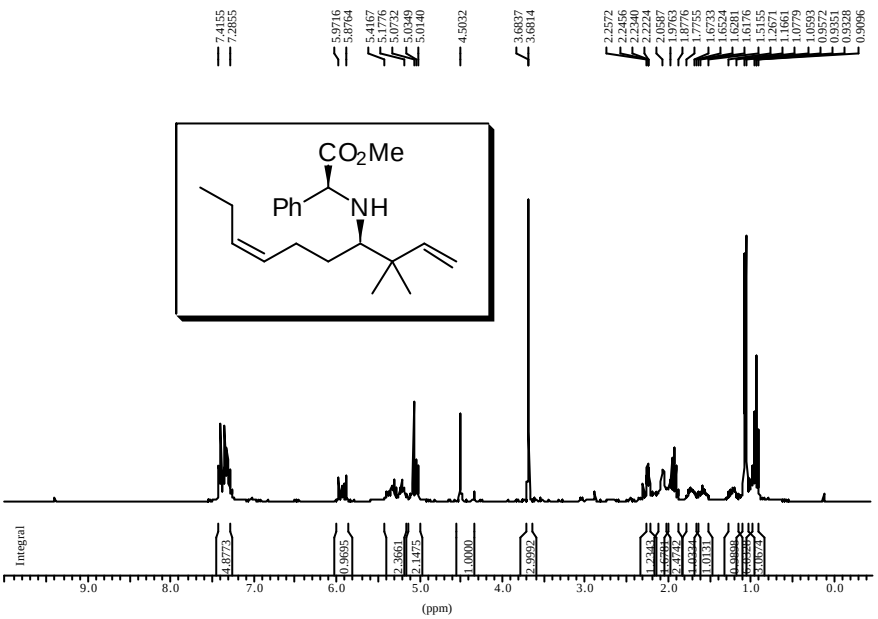



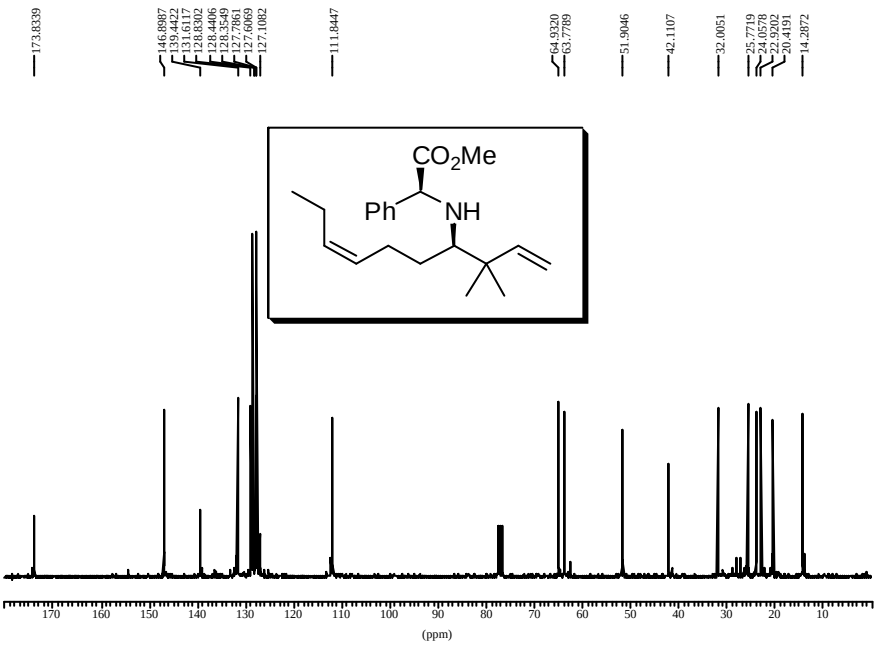
6a: (S)-Methyl 2-((Z,3R,4R)-3-methyldeca-1,7-dien-4-ylamino)-2-phenylacetate



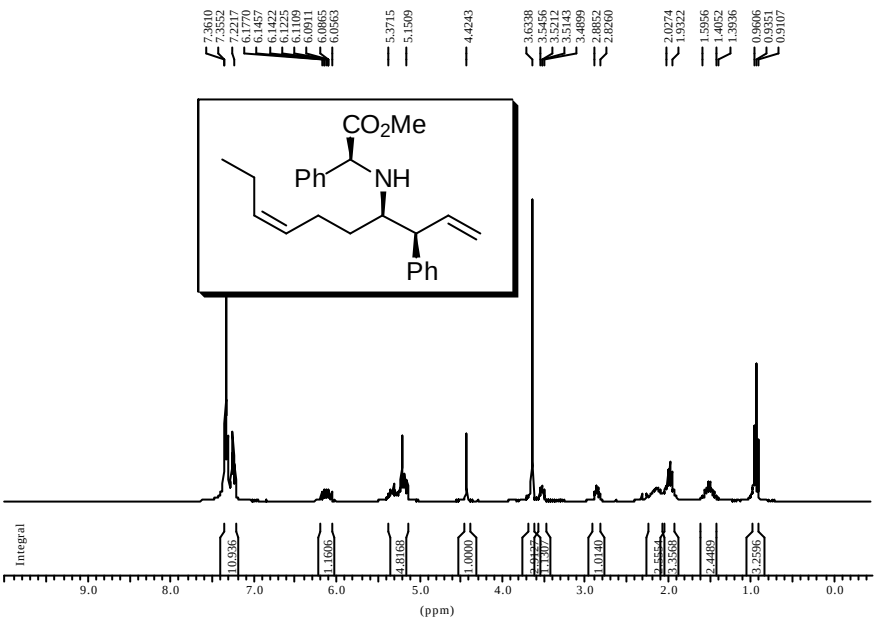



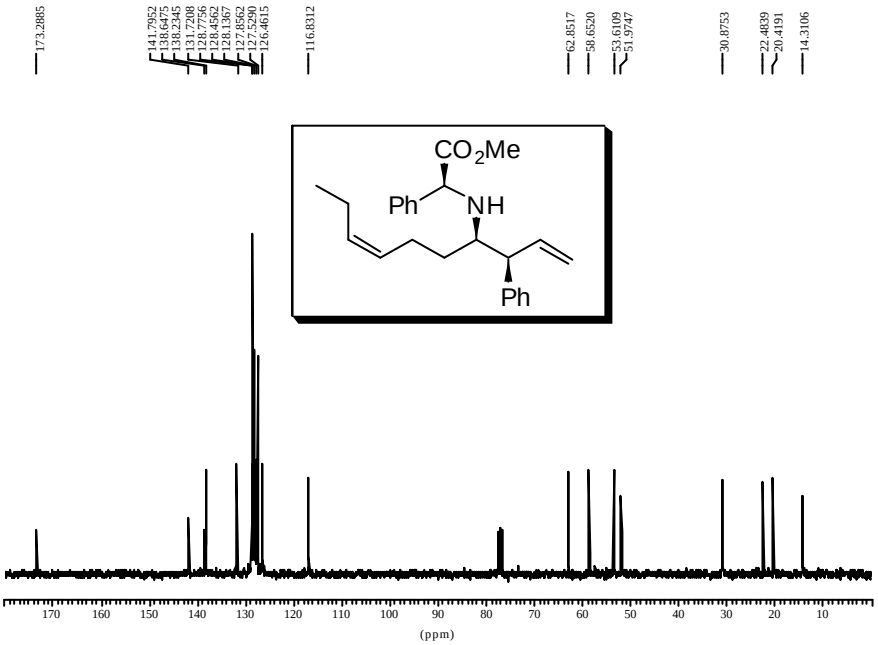
6b: (S)-Methyl 2-((R,Z)-3,3-dimethyldeca-1,7-dien-4-ylamino)-2-phenylacetate



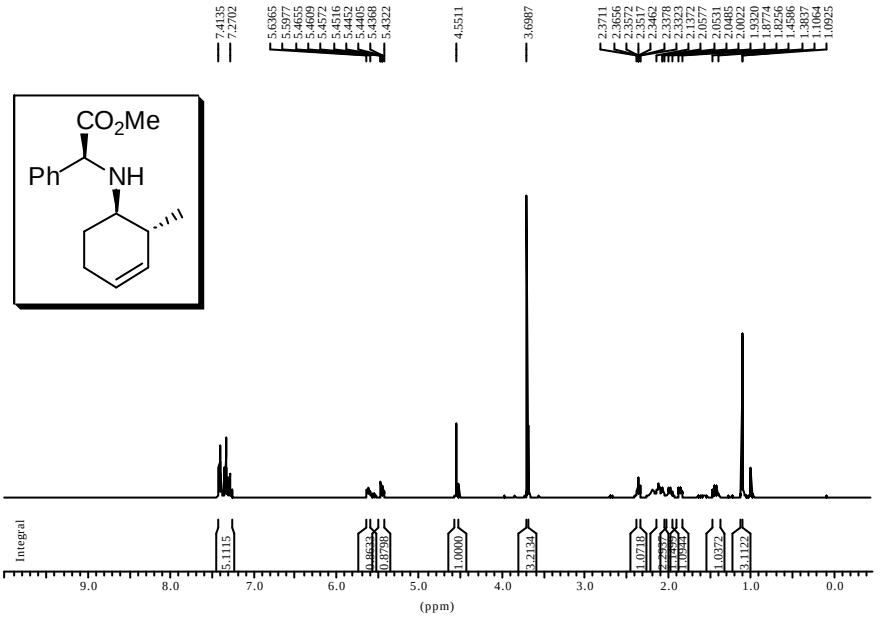



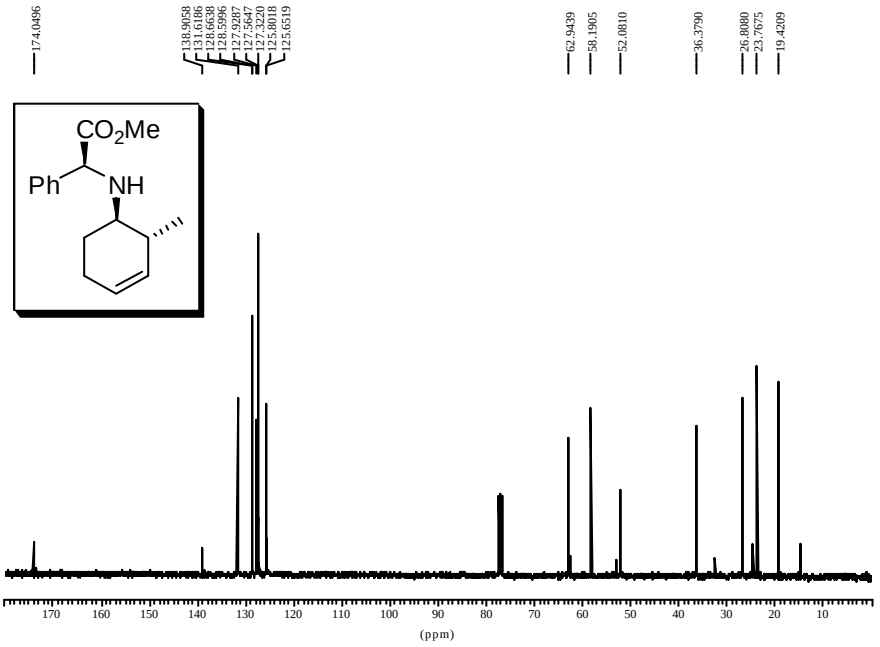
6c: (S)-Methyl 2-((Z,3S,4R)-3-phenyldeca-1,7-dien-4-ylamino)-2-phenylacetate



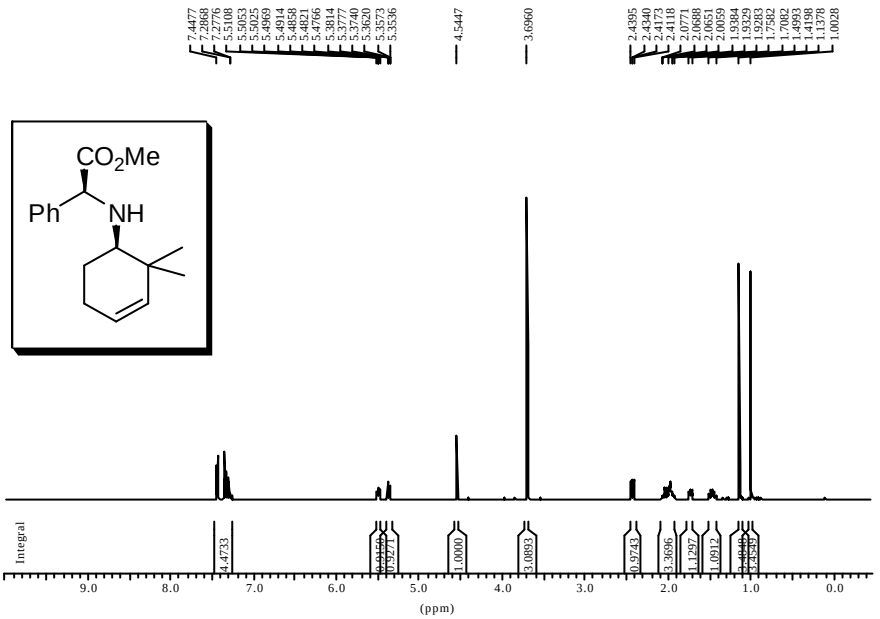



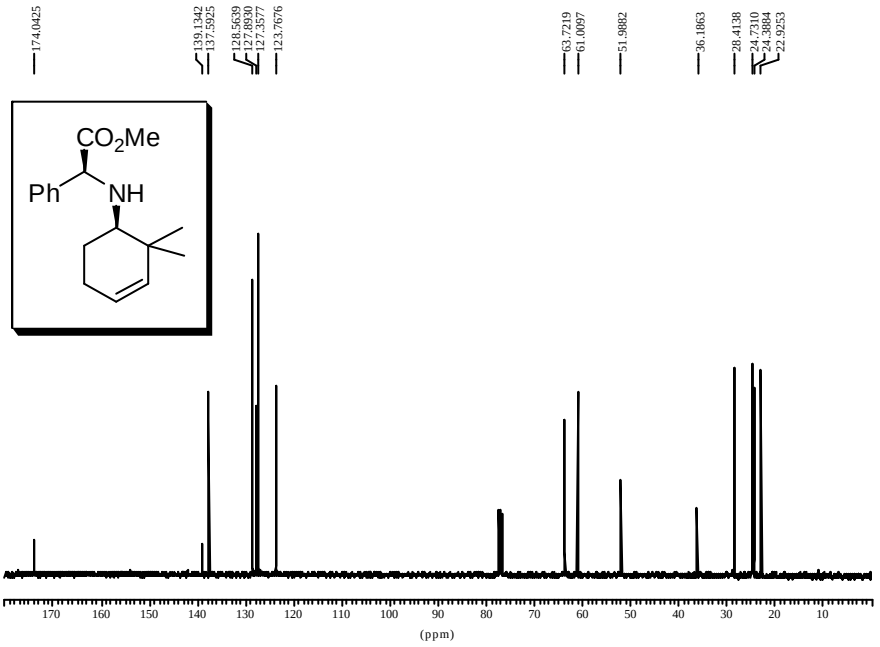
7a: (S)-Methyl 2-((1R,2R)-2-methylcyclohex-3-enylamino)-2-phenylacetate



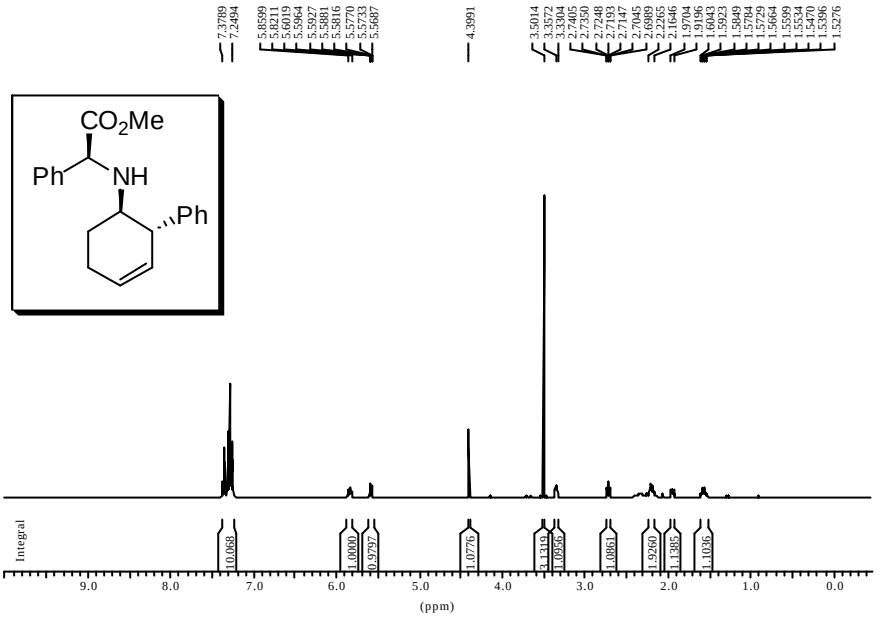



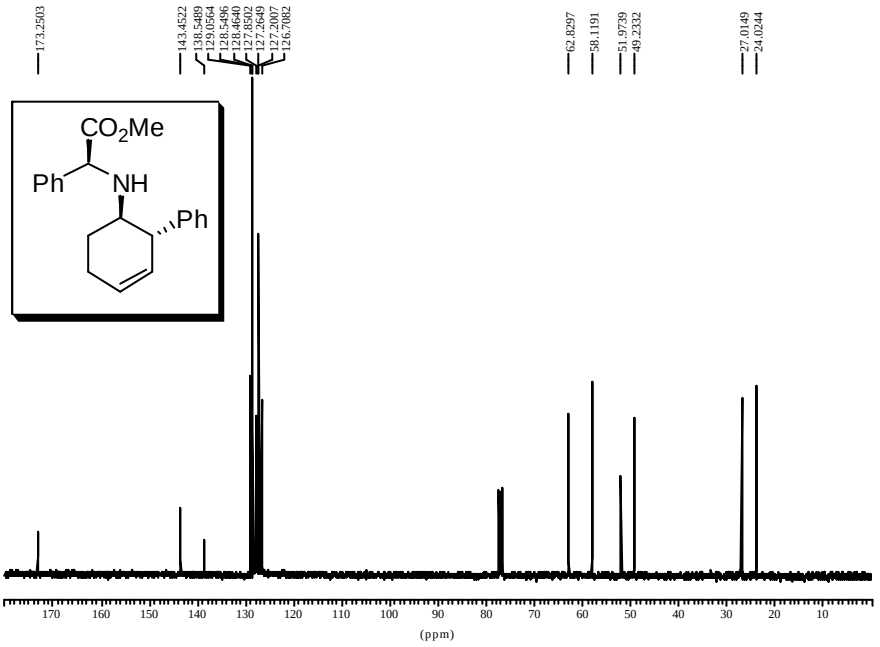
7b: (S)-Methyl 2-((R)-2,2-dimethylcyclohex-3-enylamino)-2-phenylacetate



7c: (S)-Methyl 2-((1R,2S)-2-phenylcyclohex-3-enylamino)-2-phenylacetate



8: (S)-Methyl 2-((1R,2S,3S,4S)-3,4-dibromo-2-phenylcyclohexylamino)-2-phenylacetate