Synthesis of Allyl Selenides by Palladium-Catalyzed Decarboxylative Coupling

Shelli R. Waetzig and Jon A. Tunge*
Department of Chemistry, The University of Kansas, Lawrence, KS 66045

Supporting Information

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Experimental:

General Information:

All reactions were run in flame-dried glassware under Ar atmosphere using standard Schlenk techniques, unless otherwise stated. CH_2Cl_2 and toluene were dried over activated alumina. THF was dried over sodium in the presence of benzophenone indicator. Commericially available reagents were used without additional purification unless otherwise stated. *N*-chlorosuccinimide (NCS) was recrystallized from glacial acetic acid. Compound purification was effected by flash chromatography using 230-400 mesh, 60 Å porosity silica obtained from Sorbent Technologies. For the synthesis of the allyl selenocarbonates, *the purification required the premium Rf silica gel* also obtained from Sorbent Technologies. ^{1}H NMR and ^{13}C NMR spectra were obtained on a Bruker Avance 400 or a Bruker Avance 500 DRX spectrometer and referenced to residual protio solvent signals (most spectra were taken using a QNP cryoprobe). Structural assignments are based on ^{1}H, ^{13}C, DEPT-135, COSY, HSQC and IR spectroscopies. Mass spectra were obtained using FAB+, ESI+ and EI+ techniques. Chiral-phase gas chromatography was performed on a Shimadzu GC-17A instrument with an AOC-20i autoinjector using Chiraldex B-DM column. Chiral-phase high pressure liquid chromatography was performed on a Shimadzu SCL-10AVP instrument using Daicel Chiralpak AD and OD-H columns using hexane and isopropanol as the elution solvents. All enantioenriched samples were compared to the retention times of a racemic sample of the same substrate.

General procedure for the synthesis of allyl selenocarbonates

The selenocarbonates were synthesized using a modified procedure from Tian and coworkers.[1] To a solution of the appropriate allylic alcohol (1.5 mmol) in 1,2-dichloroethane (10 mL) was added 1,1'-carbonyl diimidazole (2.3 mmol) and the resulting solution was heated to reflux for 4 hours. The solution was allowed to cool to room temperature and then diluted with Et_2O (20 mL) and washed with brine (2 × 3 mL). The organic layer was dried over $MgSO_4$ and concentrated.

[1] F. Tian, J-L. Montchamp and J. W. Frost. *J. Org. Chem.*, 1996, **61**, 7373.

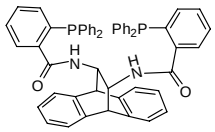
The crude imidazolyl carbamate was then subjected to flash column chromatography using 90:10 hexane:ethyl acetate.
The resulting carbamate (1.2 mmol) was dissolved in 1,2-dichloroethane (5 mL). To this mixture was added 4Å mol sieves (4 beads, ~ 0.15 g) and benzeneselenol (2.4 mmol) and the reaction was heated to reflux for 4 hours. The solution was then cooled to room temperature and concentrated. Purification of the crude residue was achieved via flash column chromatography using 99:1 hexane:ethyl acetate as the eluent.

*Note: After completing a significant portion of this project, a new batch of silica gel was opened, and the higher activity of the fresh silica gel caused significant or total decarboxylation of the allyl selenocarbonates. Switching to the premium Rf silica gel purchased from Sorbent Technologies drastically reduced or completely suppressed the decarboxylation during flash column chromatography.

General procedure for the Pd-catalyzed decarboxylative selenylation
To a dried Schlenk flask was added the selenocarbonate (0.41 mmol) and CH_2Cl_2 (5 mL). $Pd(PPh_3)_4$ (24 mg, 0.02 mmol) was then added, and the resulting solution was stirred at room temperature. Upon reaction completion, as determined by TLC (2-24 h), the solution was concentrated and directly subjected to flash column chromatography affording the pure allyl selenides.

Procedure for the synthesis of allyl selenides using SmI_2
To a flame dried Schlenk flask was added $PdCl_2$ (0.0056 mmol), PPh_3 (0.022 mmol), and 0.1 M SmI_2 in THF (0.28 mmol) and was dissolved in THF. The dark blue solution was allowed to stir for 10 minutes at room temperature. PhSeSePh (0.112 mmol) and cyclohexenyl acetate (0.112 mmol) were added to the solution and the reaction turned a dark orange. The solution was stirred for 16 hours and checked by ^{1}H NMR spectroscopy. No product or degradation of the starting material was observed.

General procedure for the optimization of enantioselective selenylation
To a dried NMR tube was added Pd_2dba_3 (0.8 mg, 0.0008 mmol) and a chiral ligand (0.0017 mmol) and dissolved in the designated solvent (600 μL) (as listed in Table 2). Selenocarbonate **2** (0.035 mmol) was then added to the NMR tube and the solution was allowed to stand at room temperature for up to 24 hours, while monitoring the conversion by ^{1}H NMR spectroscopy. Once the reaction had stopped, even if complete conversion had not been reached, the solution was concentrated. The residue was purified on a silica plug with 100% hexane and subjected to chiral-phase high pressure liquid chromatography to determine the enantiomeric excess.

The structure of the bicyclic-Trost ligand from Table 2 is: 

Procedure for the kinetic resolution of selenocarbonates
To a flame-dried Schlenk flask was added the allyl selenocarbonate (0.61 mmol) and (*S*,*S*)-Naphthyl-Trost ligand (0.031 mmol) dissolved in toluene (4 mL). To the solution was added, via cannula, $Pd_2(dba)_3$ (0.015 mmol) dissolved in toluene (3 mL) and the solution was allowed to stir at room temperature for 2 hours. The solution was then concentrated and ^{1}H NMR spectroscopy of the residue confirmed the % completion of the reaction. The residue was then purified using flash column chromatography and both the allyl selenide and allyl selenocarbonate were obtained. The enantiomeric excess of each compound was determined using chiral-phase high pressure liquid chromatography.

Procedure for the synthesis of allyl amine 6g

The allylic amination was achieved using a previously reported procedure by Hopkins and coworkers.[2] To a dried Schlenk flask was added enantioenriched allyl selenide **5g** (0.067 mmol), Et_3N (0.338 mmol) and dry MeOH (337 μL). The reaction was cooled to –25 °C and NCS (0.067 mmol) was added to the solution. After 5 minutes, *p*-*t*butyl aniline was added at –20 °C. The solution was allowed to warm to room temperature over 1.5 hours. The solution was then concentrated and directly purified *via* flash column chromatography (95:5 hexane:ethyl acetate), where amine **6g** was isolated. The enantiomeric excess was determined by chiral-phase high pressure liquid chromatography.

Procedure for the synthesis of allylic chloride 7g

The allylic chlorination was achieved using a procedure by Sharpless.[3] To a dried NMR tube was added the enantioenriched allyl selenide **5g** (0.05 mmol) and *t*BuOMe (0.05 mmol, used as an internal standard) and was dissolved in CD_2Cl_2 (600 μL). An initial ^1H NMR spectrum was taken to calibrate the starting allyl selenide and the internal standard. Then NCS (0.045 mmol) was added to the mixture and the reaction was monitored for conversion by ^1H NMR spectroscopy, and the clean formation of allyl chloride **7** was observed, which occurred after one hour. The enantiomeric excess of the resulting allyl chloride was determined by chiral-phase gas chromatography. Spectral characterization in $CDCl_3$ was achieved following a vacuum distillation of the reaction mixture.

Determination of Stereochemistry of Allyl Selenides

Hydrolysis of Selenocarbonate (*S*)-2

An open air flask charged with selenocarbonate (*S*)-**2** (0.124 mmol) and $LiOH{\cdot}H_2O$ (0.248 mmol) and dissolved in THF (3 mL) and H_2O (0.4 mL). The resulting solution was stirred at room temperature for 48 hours and was added Et_2O (10 mL). The organic solution was then extracted with aqueous NH_4Cl solution (2x5 mL) and brine (2x5 mL). The organic layer was then dried over $MgSO_4$ and concentrated. The purified alcohol was confirmed by optical rotation to be the (-)-enantiomer, which corresponds to the literature reported (*S*)-configuration.[4]

Procedure for the oxidation of allyl selenide 3 to allylic alcohol (*S*)-1[5]

This procedure was also used to determine the stereochemistry of the allyl selenides. An open air flask was charged with a stir bar and enantioenriched allyl selenide (*R*)-**3** (0.042 mmol), N,N'-dimethylaminopyridine (0.21 mmol) and THF (0.21 mL). The solution was then cooled to -78 °C followed by the dropwise addition of 30% H_2O_2 solution (47.6 μL). After stirring for 20 minutes, the solution was allowed to warm to room temperature and continued stirring for 12 hours. The reaction was then diluted with 3 mL Et_2O and 1 mL hexane, dried over $MgSO_4$, filtered and concentrated. The crude residue was purified using flash column chromatography with 7:1 pentane:Et_2O as the eluent. Using chiral-phase gas chromatography, the product was determined to be of the same configuration as when the hydrolysis of the selenocarbonate was achieved. This result is expected since the oxidation proceeds through a rearrangement which inverts the initial (*R*)-stereochemistry.

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[2] Shea, R. G.; Fitzner, J. N; Fankhauser, J. E.; Spaltenstein, A.; Carpino, P. A.; Peevey, R. M.; Pratt, D. V.; Tenge, B. J.; Hopkins, P. B. *J. Org. Chem.* **1986**, *51*, 5243.

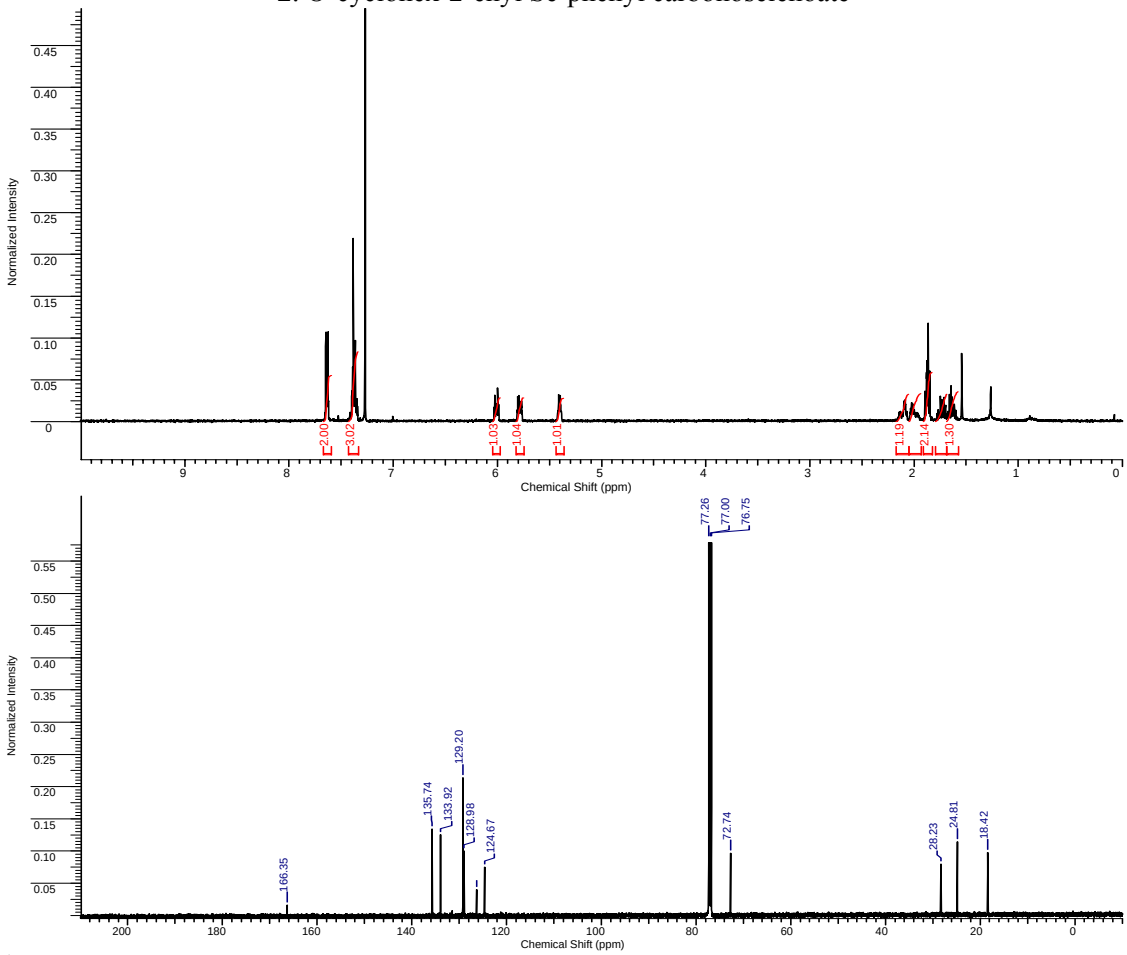
[3] T. Hori and K. B. Sharpless, *J. Org. Chem.* 1979, **44**, 4208.

[4] . H.-J. Gais, T. Jagusch, N. Spalthoff, F. Gerhards, M. Frank and G. Raabe, *Chem. Eur. J.*, 2003, **9**, 4202

[5] B. J. Albert, A. Sivaramakrishnan, T. Naka, N. L. Czaicki and K. Koide, *J. Am. Chem. Soc.* 2007, **129**, 2648.

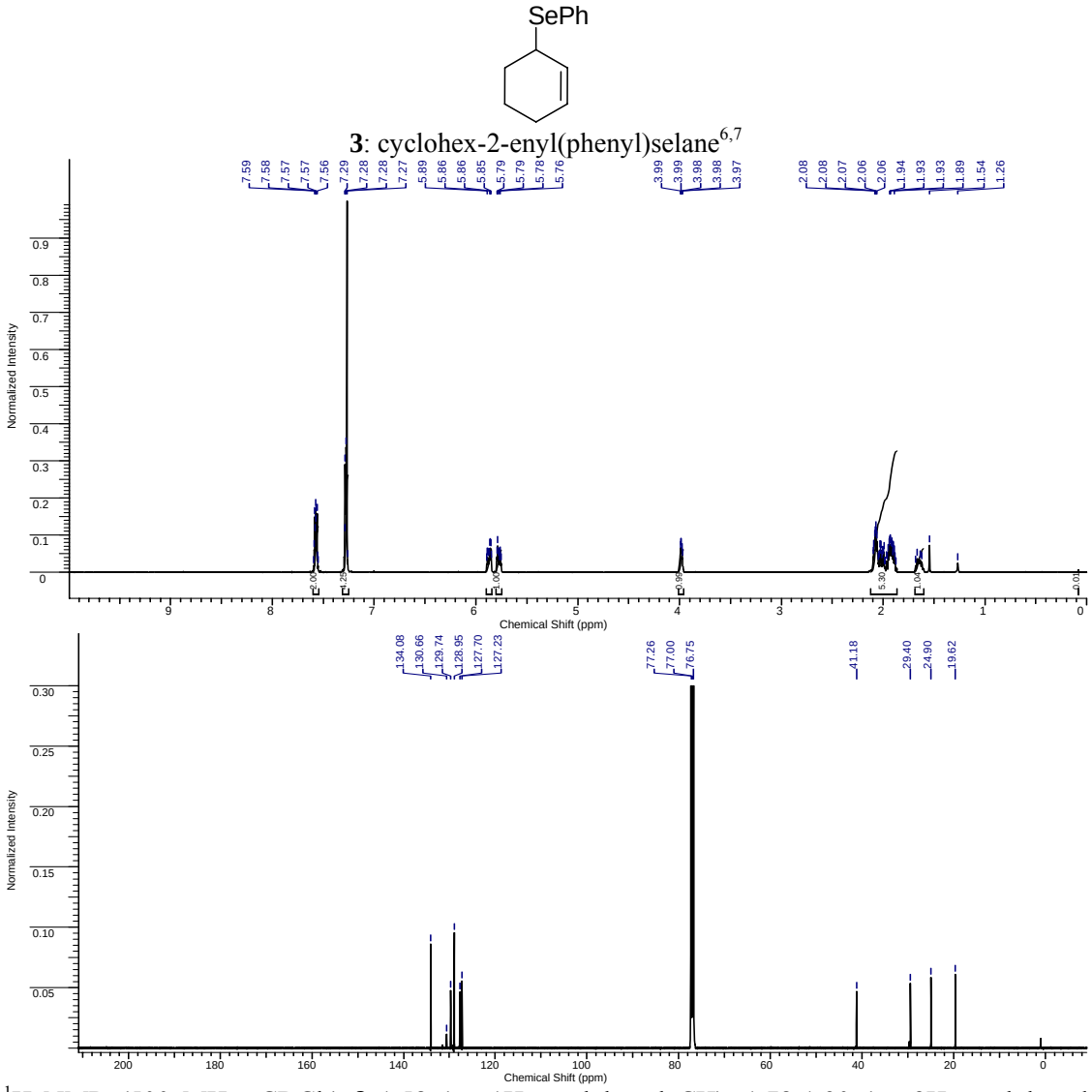
Spectral Characterization of Compounds:

2: O-cyclohex-2-enyl Se-phenyl carbonoselenoate



^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 1.64 (m, 1H: CH=CHCH$_2$C*H*H), 1.72 (m, 1H: CH=CHCH$_2$CH*H*), 1.86 (dt, 2H: *J* = 5.1, 7.6 Hz, OCHC*H*$_2$), 2.00 (m, 1H: CH=CHC*H*H), 2.10 (m, 1H: CH=CHCH*H*), 5.40 (m, 1H: C*H*OCOSePh), 5.79 (dddd, 1H: *J* = 2.0, 2.0, 4.0. 9.9 Hz, OCHC*H*=CH), 6.01 (dt, 1H: *J* = 3.8, 10.2 Hz, OCHCH=C*H*), 7.38 (m, 3H: Ar CH's), 7.64 (m, 2H: Ar CH's); ^{13}C NMR (126 MHz,$CDCl_3$) δ ppm 18.4 (*C*H$_2$CH$_2$CH=CH), 24.8 (CH=CH*C*H$_2$), 28.2 (OCH*C*H$_2$), 72.7 (*C*HO), 124.7 (OCH*C*H=CH), 126.3 (quat. Ar C), 129.0 (Ar CH), 129.2 (Ar CH's), 133.9 (OCHCH=*C*H), 135.7 (Ar CH's), 166.4 (C=O); FTIR (CH_2Cl_2) υ_{max}: 3055, 2947, 1720, 1650, 1579, 1477, 1438, 1257, 1126; HRMS: (ESI+) calcd for [M+Na] 305.0056, found 305.0069.

Chiral HPLC Column: Chiralpak OD-H **Eluent:** 99.1:0.9 hexane:isopropanol **Flow rate**: 1.0 mL/min **Wavelength**: 210 nm **Retention times:** 23.6 (major) and 26.2 minutes.

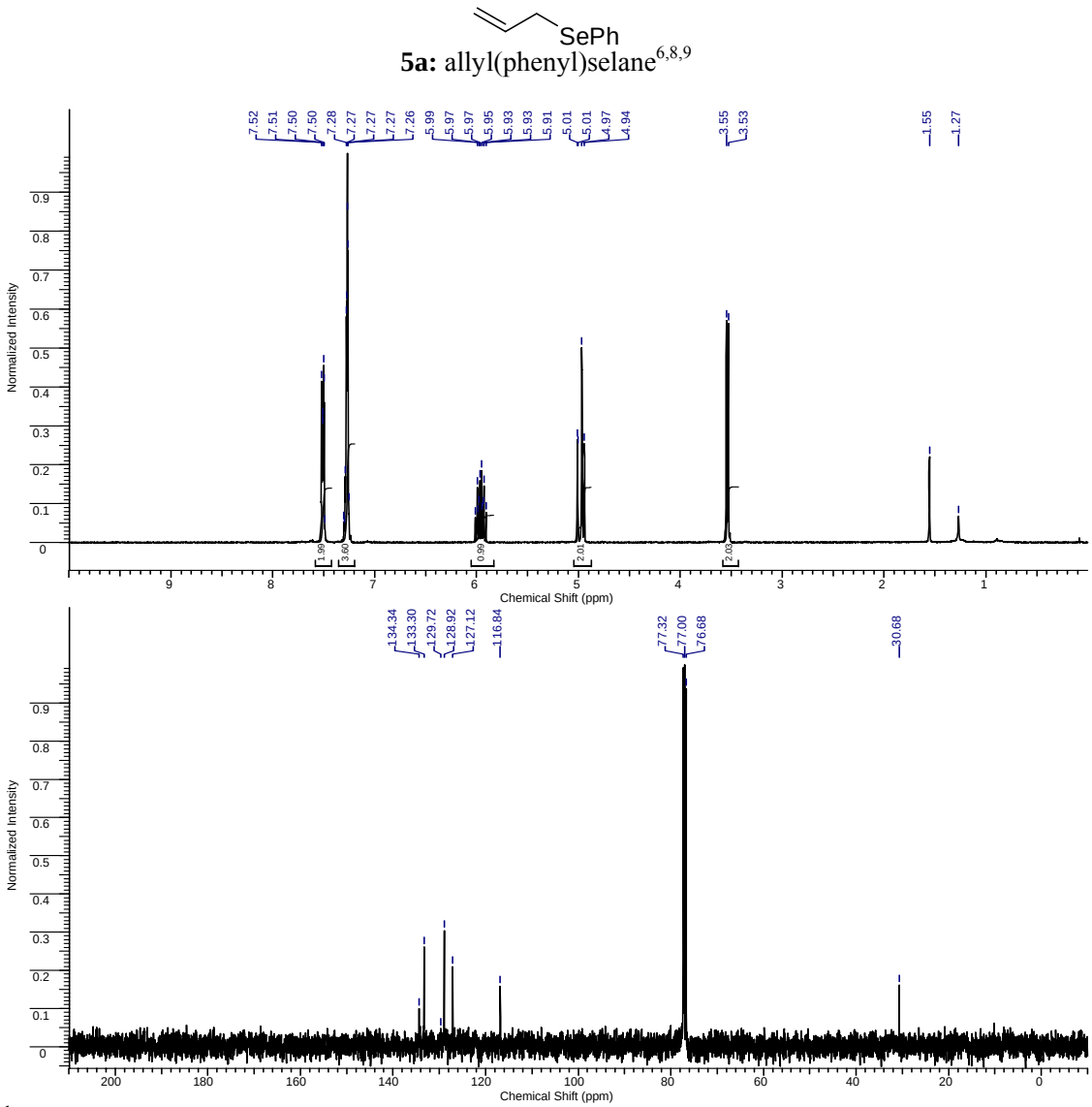


3: cyclohex-2-enyl(phenyl)selane[6,7]

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.58 (m, 1H: cyclohexyl CH), 1.78-1.90 (m, 2H: cyclohexyl CH's), 1.90-1.96 (m, 1H: cyclohexyl CH), 1.97-2.02 (m, 2H: cyclohexyl CH's), 3.91 (br. s, 1H: C*H*SePh), 5.67-5.72 (dt, 1H: *J* = 3.8, 6.0 Hz, PhSeCHC*H*=CH), 5.79 (dddd, 1H: *J* = 1.9, 1.9, 4.1, 9.8 Hz, PhSeCHCH=C*H*), 7.20 (m, 3H: Ar CH's), 7.50 (m, 2H: Ar CH's); ^{13}C NMR (126 MHz, $CDCl_3$) δ 18.6 (cyclohexyl CH_2), 23.9 (cyclohexyl CH_2), 28.4 (cyclohexyl CH_2), 40.2 (*C*HSePh), 127.2 (PhSeCHCH=*C*H), 127.7 (Ar CH's), 128.9 (PhSeCH*C*H=CH), 129.7 (quat. Ar C), 130.7 (Ar CH), 134.1 (Ar CH's); FTIR (CH_2Cl_2) υ_{max}: 3075, 2995, 2870, 1575, 1475, 1020; HRMS: (EI+) calcd for [M+] 238.0261, found 238.0251

Chiral HPLC Column: Chiralpak AD **Eluent:** 99.8:0.2 hexane:isopropanol **Flow rate**: 0.5 mL/min **Wavelength**: 210 nm **Retention times:** 9.6 (major) and 10.0 minutes.

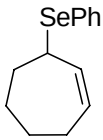
[6] O. A. Wallner and K. J. Szabo, *J. Org. Chem.*, 2005, **70**, 9215.
[7] B. C. Ranu, T. Mandal and S. Samanta, *Org. Lett.*, 2003, **5**, 1439.



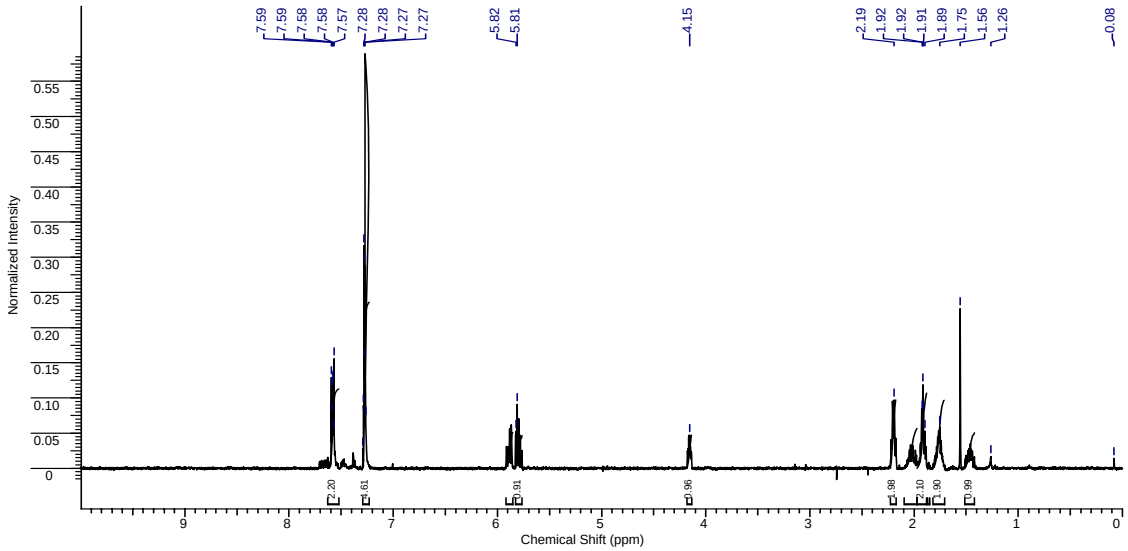
5a: allyl(phenyl)selane[6,8,9]

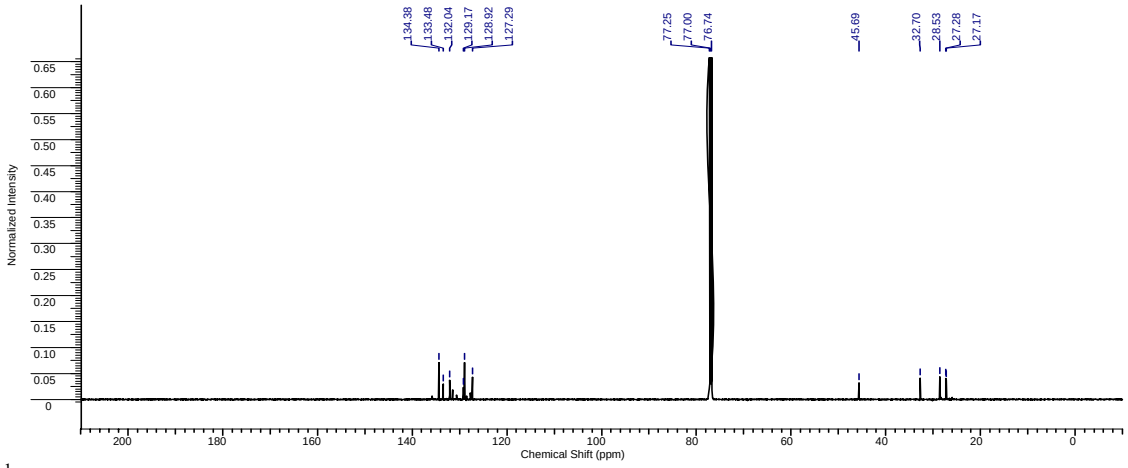
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.57 (d, 1H: J = 7.2 Hz, CH_2SePh), 4.97 (dt, 1H: J = 9.9, 0.9 Hz, H_B), 5.02 (dq, 1H: J = 1.4, 16.7 Hz, H_A), 5.93-6.06 (m, 1H: CH=CH_2), 7.27-7.33 (m, 2H: Ar CH's), 7.50-7.55 (m, 2H: Ar CH's); ^{13}C NMR (101 MHz, $CDCl_3$) δ 30.7 (CH_2SePh), 116.8 (CH=CH_2), 127.1 (Ar CH), 128.9 (Ar CH), 129.9 (quat. Ar C), 133.3 (Ar CH), 134.4 (CH=CH_2); HRMS: (EI+) calcd for [M+] 197.9948, found 197.9951.

[8] R. J. Cohen, D. L. Fox and R. N. Salvatore, *J. Org. Chem.* 2004, **69**, 4265.
[9] E. G. Kafaev, L. M. Kataeva and G. A. Chmutova, *Zh. Org. Khim.* 1966, **2**, 2244.

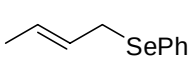


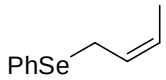
5b: (Z)-cyclohept-2-enyl(phenyl)selane



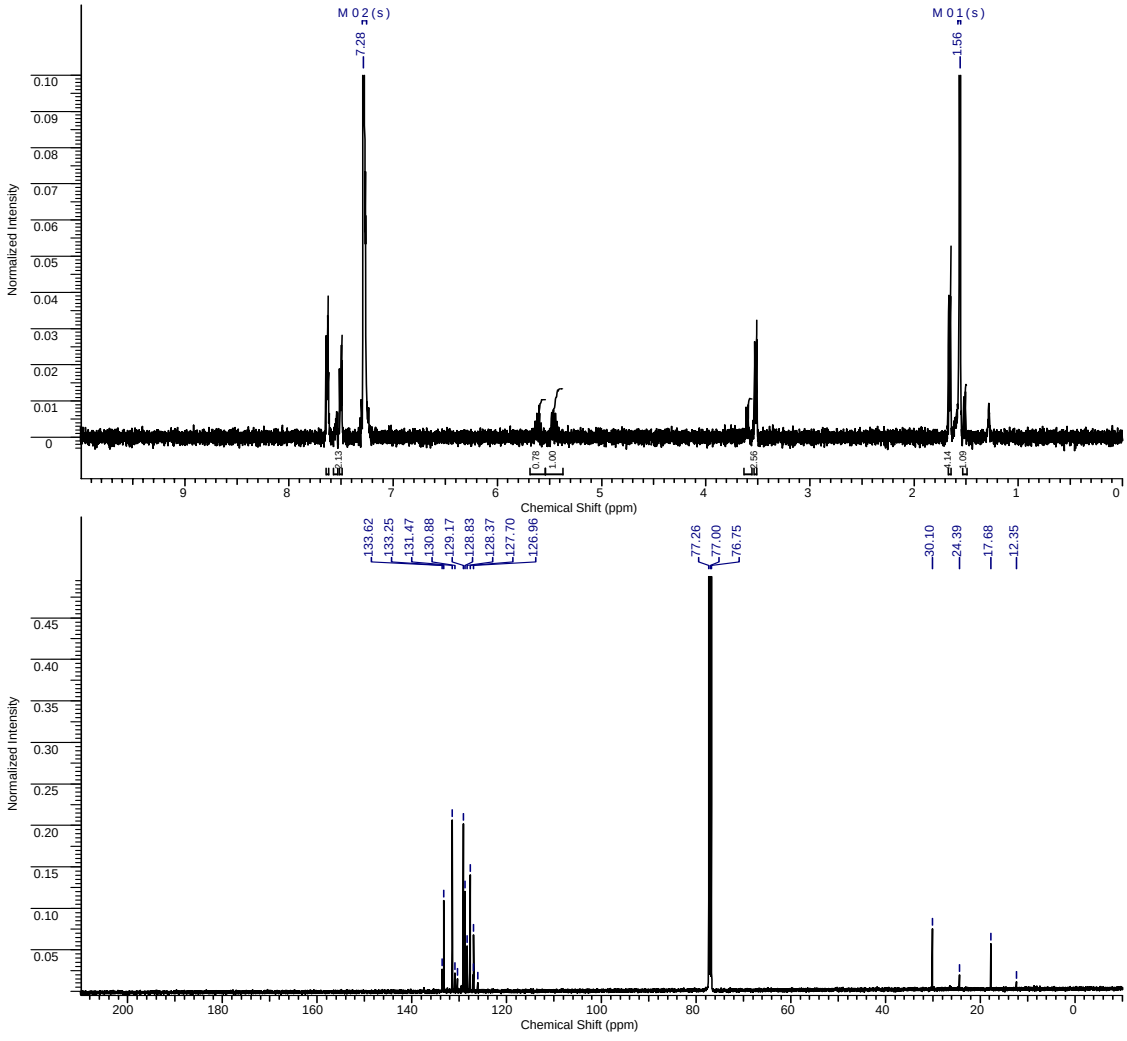


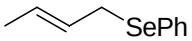
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.43-1.52 (m, 1H: cycloheptyl CH), 1.73-1.81 (m, 2H: cycloheptyl CH's), 1.92 (m, 2H: cycloheptyl CH's), 2.03 (m, 1H: cycloheptyl CH), 2.20 (app. q, 2H: J = 5.8 Hz, cycloheptyl CH), 4.15 (ddd, 1H: J = 3.4, 4.1, 5.8 Hz, C*H*SePh), 5.80 (dd, 1H: J = 5.8, 11.3 Hz, PhSeCHC*H*=CH), 5.87 (ddt, 1H: J = 1.0, 6.5, 11.3 Hz, PhSeCHCH=C*H*), 7.25-7.30 (m, 3H: Ar CH's), 7.55-7.60 (m, 2H: Ar CH's); ^{13}C NMR (126 MHz, $CDCl_3$) δ 27.2 (cycloheptyl CH_2), 27.3 (cycloheptyl CH_2), 28.5 (cycloheptyl CH_2), 32.7 (cycloheptyl CH_2), 45.7 (*C*HSePh), 127.3 (Ar CH's), 128.9 (Ar CH's), 129.2 (quat. Ar C), 132.0 (PhSeCH*C*H=CH), 133.5 (PhSeCHCH=*C*H), 134.4 (Ar CH); FTIR (CH_2Cl_2) υ_{max}: 3076, 2995, 1575, 1475, 1020.





5c: (*E*)-but-2-enyl(phenyl)selane and (Z)-but-2-enyl(phenyl)selane[8,10] isolated as 3.9:1 mixture of *E:Z* isomers

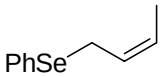




5c: (*E*)-but-2-enyl(phenyl)selane

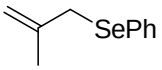
^{1}H NMR (500 MHz, $CDCl_3$) *E*-isomer δ 1.64 (ddt, 3H: *J* = 1.0, 1.6, 6.6 Hz, C*H*$_3$), 3.51 (dp, 2H: *J* = 1.3, 7.3 Hz, C*H*$_2$SePh), 5.44 (m, 1H: CH=C*H*CH$_3$), 5.59 (ddq, 1H: *J* = 1.6, 7.6, 15.1 Hz, C*H*=CHCH$_3$), 7.26 (m, 3H: Ar CH's), 7.48 (m, 2H: Ar CH's); ^{13}C NMR (126 MHz, $CDCl_3$) *E*-isomer δ 16.7 (*C*H$_3$), 29.1 (*C*H$_2$SePh), 125.9 (*C*H=CHCH$_3$), 125.98 (CH=*C*HCH$_3$), 127.8 (Ar CH's), 127.9 (Ar CH), 129.4. (quat. Ar C), 132.3 (Ar CH's); FTIR (CH_2Cl_2) υ_{max}: 3074, 2997, 1575, 1475, 1436, 1020, 999; HRMS: (EI+) calcd for [M+] 212.0104, found 212.0098.

[10] B. C. Ranu and T. Mandal, *J. Org. Chem.* 2004, **69**, 5793.

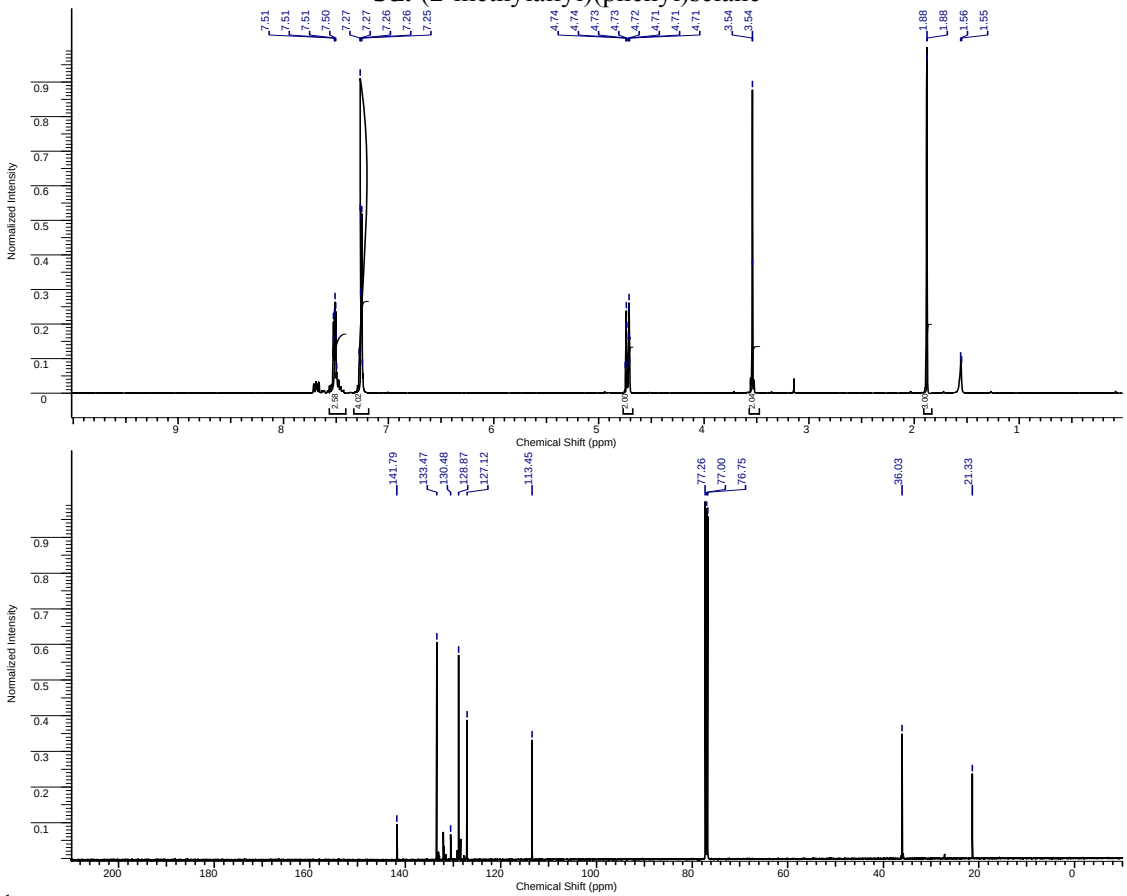


5c:(Z)-but-2-enyl(phenyl)selane
isolated as 3.9:1 mixture of *E/Z* isomers

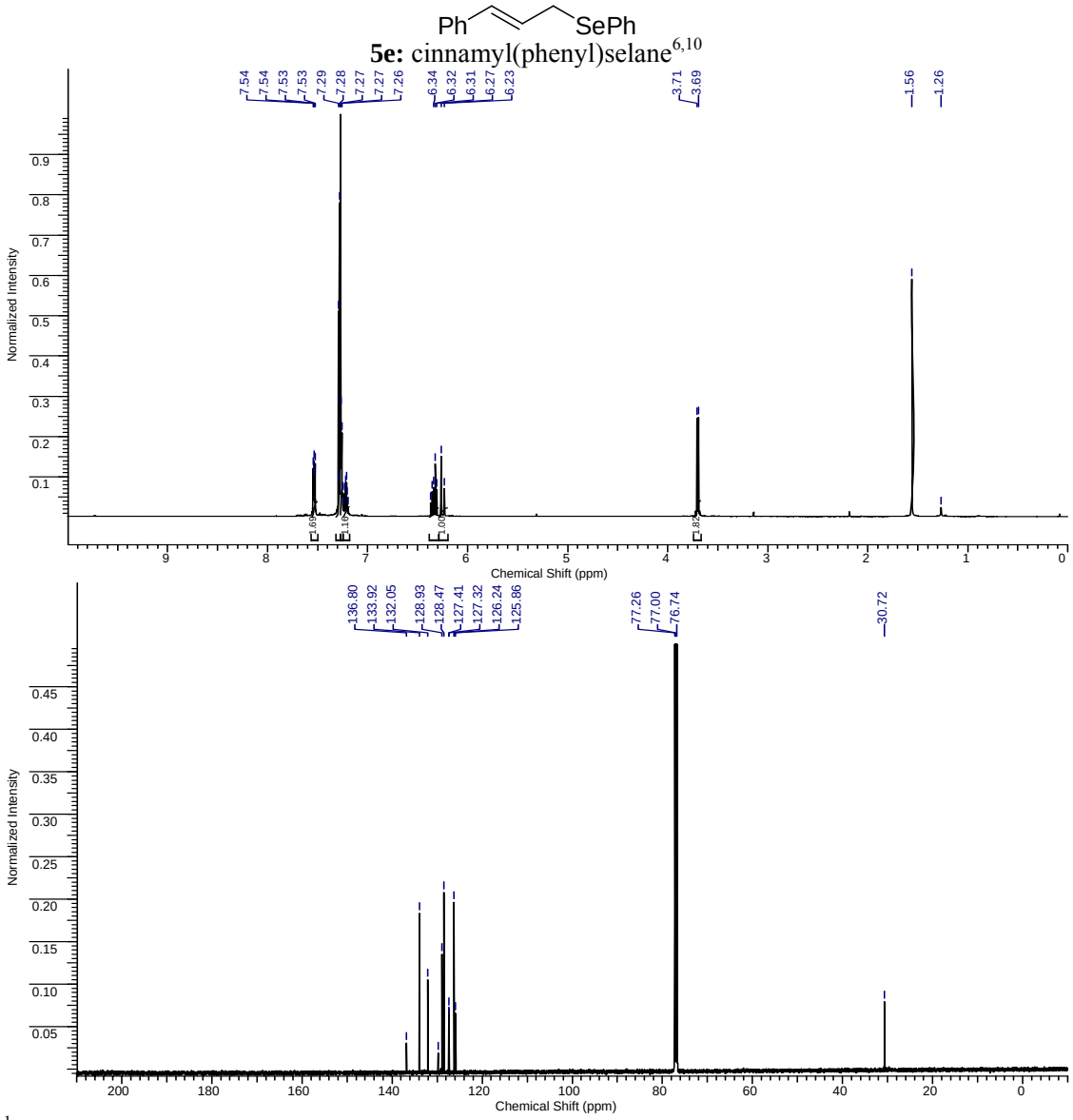
^{1}H NMR (500 MHz, $CDCl_3$) *Z*-isomer δ 1.50 (app. dd, 3H: *J* = 1.6, 6.9 Hz, C*H*$_3$), 3.59 (app. d, 2H: *J* = 8.2 Hz, C*H*$_2$SePh), 5.52 (m, 1H: CH=C*H*CH$_3$), 5.63 (m, 1H: C*H*=CHCH$_3$), 7.26 (m, 3H: Ar CH's), 7.54 (m, 2H: Ar CH's); ^{13}C NMR (126 MHz, $CDCl_3$) *Z*-isomer δ 11.4 (*C*H$_3$), 23.40 (PhSe*C*H$_2$), 126.03 (*C*H=CHCH$_3$), 126.10 (CH=*C*HCH$_3$), 127.4 (Ar CH's), 128.2 (Ar CH), 132.63 (Ar CH's), quat. Ar C not observed.



5d: (2-methylallyl)(phenyl)selane

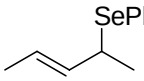


^{1}H NMR (400 MHz, $CDCl_3$) δ 1.88 (m, 3H: C*H*$_3$), 3.54 (app. d, 2H: C*H*$_2$SePh), 4.73 (app. d, 2H: R$_2$C=C*H*$_2$), 7.26 (m, 3H: Ar CH's), 7.51 (m, 2H: Ar CH's); ^{13}C NMR (500 MHz, $CDCl_3$) δ 21.3 (*C*H$_3$), 36.0 (*C*H$_2$CR=CH$_2$), 113.5 (*C*H$_2$=CR$_2$), 127.1 (Ar CH), 128.9 (Ar CH's), 130.5 (quat. Ar C), 133.5 (Ar CH's), 141.8 (CH$_2$=*C*R$_2$); FTIR (CH_2Cl_2) υ_{max}: 3076, 2975, 2939, 1643, 1577, 1477, 1436, 1188, 1120, 1020, 999; HRMS: (EI+) calcd for [M+] 212.0104, found 212.0095.

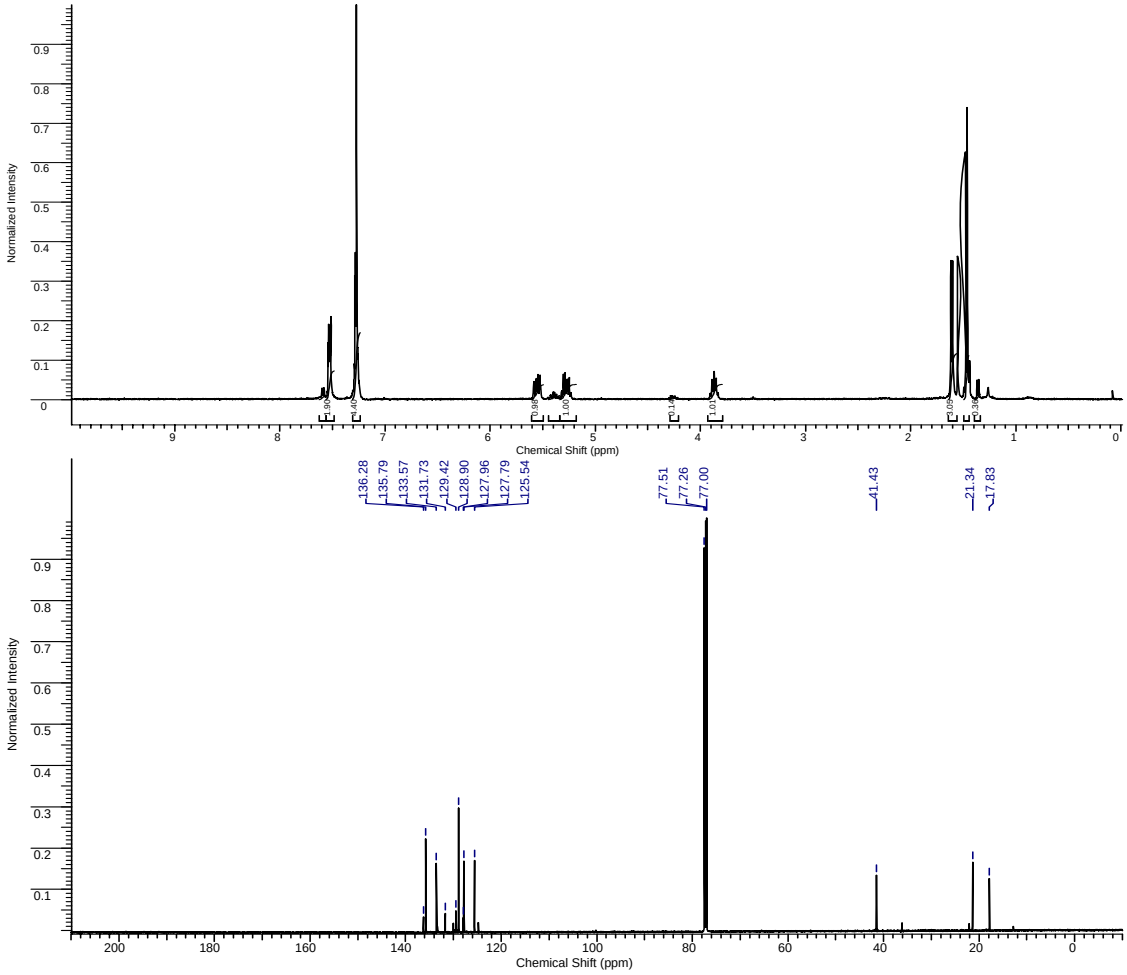


5e: cinnamyl(phenyl)selane[6,10]

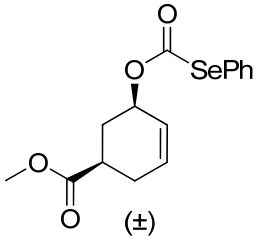
^{1}H NMR (500 MHz, $CDCl_3$) δ 3.70 (d, 2H: *J* = 7.5 Hz, C*H*$_2$SePh), 6.27 (app. t, 1H: *J* = 15.7 Hz, PhC*H*=CH), 6.35 (dd, 1H: *J* = 7.5, 15.7 Hz, PhCH=C*H*), 7.22 (m, 1H: Ar CH), 7.25 (m, 3H; Ar CH's), 7.28 (m, 4H; Ar CH's), 7.54 (m, 2H: Ar CH's); ^{13}C NMR (500 MHz, $CDCl_3$) δ 30.7 (*C*H_2SePh), 125.9 (PhCH=*C*HR), 126.2 (Ar CH's), 127.32 (Ar CH), 127.4 (Ar CH), 128.5 (Ar CH's), 128.9 (Ar CH's), 129.8 (quat. Ar C), 132.05 (Ph*C*H=CHR), 133.9 (Ar CH's), 136.8 (quat. Ar C); FTIR (CH_2Cl_2) υ_{max}: 3029, 2933, 1577, 1477, 1437, 1178, 1072, 1022, 962; HRMS (FAB+) calcd for [M+] 274.0261, found 274.0267.



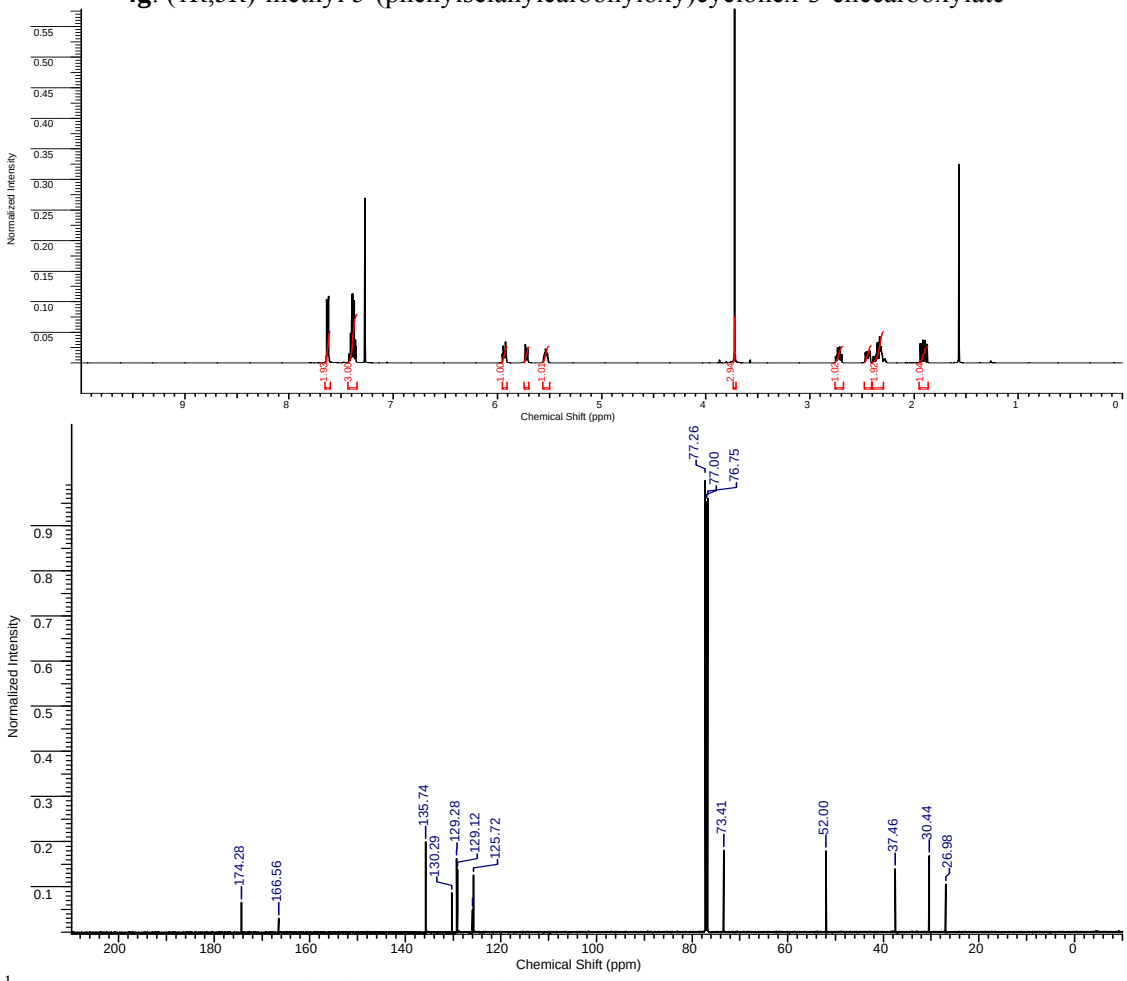
5f: (E)-pent-3-en-2-yl(phenyl)selane (major isomer)
isolated as a 10:1 mixture of *E*/*Z* isomers



^{1}H NMR (400 MHz, $CDCl_3$) *E*-isomer δ 1.48 (d, 2H: *J* = 6.7 Hz, PhSeCHC*H*$_3$), 1.63 (dd, 3H: *J* = 1.7, 6.5 Hz, CH=CHC*H*$_3$), 3.88 (p, 1 H: *J* = 7.2 Hz, C*H*SePh), 5.29 (ddd, 1 H: *J* = 1.7, 6.5, 15.3 Hz, CH=C*H*SePh), 5.55 (ddq, 1H: *J* =1.7, 8.6, 15.3 Hz, CH_3C*H*=CH), 7.30 (m, 3H: Ar CH's), 7.53 (m, 2H: Ar CH's); ^{13}C NMR (500 MHz, $CDCl_3$) *E*-isomer δ 17.8 (*C*H_3CH=CH), 21.3 (*C*H_3CHSePh), 41.4 (*C*HSePh), 125.5 (CH_3*C*H=CHR), 127.8 (Ar CH), 128.9 (Ar CH's), 131.7 (quat. Ar C), 133.6 (CH=*C*HCHSePh), 135.8 (Ar CH's); FTIR (CH_2Cl_2) υ_{max}: 3074, 2975, 1575, 1475, 1437, 1020

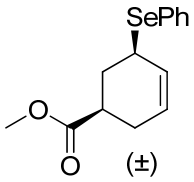


4g: (1*R*,5*R*)-methyl 5-(phenylselanylcarbonyloxy)cyclohex-3-enecarboxylate

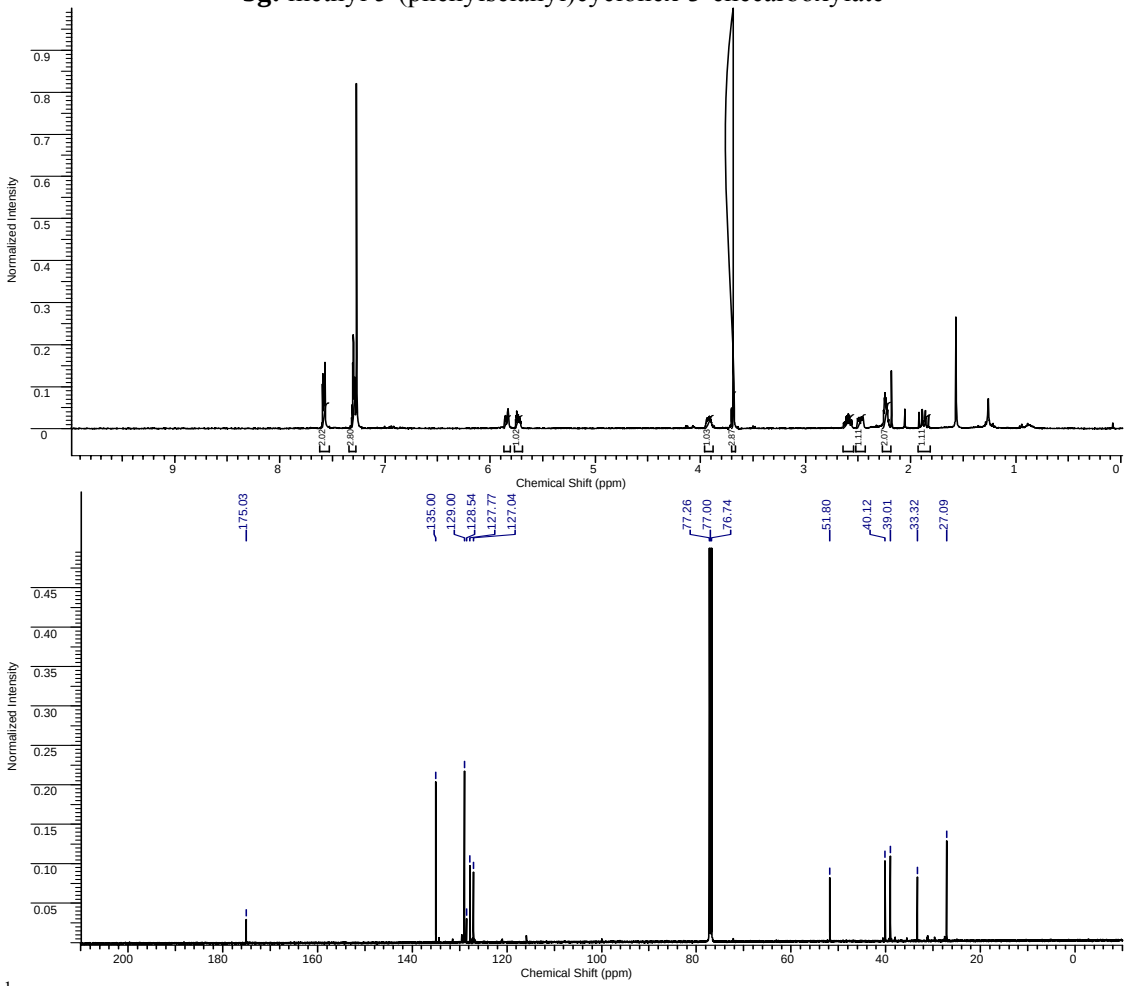


^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 1.93 (dd, 1H: *J* = 9.3, 12.5 Hz, OCHC*H*HCH$_2$), 2.33 (m, 2H: CH=CHC*H*$_2$), 2.45 (m, 1H: OCHCH*H*CH$_2$), 2.69 (ddd, 1H: *J* = 3.0, 6.1, 9.3 Hz, C*H*CO$_2$CH$_3$), 3.72 (s, 2H: OC*H*$_3$), 5.50 (br. s., 2H: C*H*OCOSePh), 5.72 (d, 1H: *J* = 10.9 Hz, OCHC*H*=CH), 5.92 (m, 1H: OCHCH=C*H*), 7.39 (m, 3H: Ar CH's), 7.63 (dd, 2H: *J* = 1.8, 7.8, Ar CH's); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 27.0 (CH=CH*C*H$_2$), 30.4 (OCH*C*H$_2$), 37.5 (*C*HCO$_2$CH$_3$), 52.0 (OCH$_3$), 73.4 (O*C*HCH=CH), 125.7 (OCH*C*H=CH), 126.0 (quat. Ar C), 129.1 (Ar CH), 129.3 (Ar CH), 130.3 (OCHCH=*C*H), 135.7 (Ar CH's), 166.6 (O*C*OSePh), 174.3 (*C*OCH$_3$); FTIR (CH_2Cl_2) υ_{max}: 3001, 2952, 1728, 1654, 1577, 1477, 1439, 1122; HRMS (ESI+) calcd for [M+Na] 363.0111, found 363.0096.

Chiral HPLC Column: Chiralpak OD-H **Eluent:** 99.5:0.5 hexane:isopropanol **Flow rate**: 1.0 mL/min **Wavelength**: 210 nm **Retention times:** 26.8 (major) and 30.0 minutes.

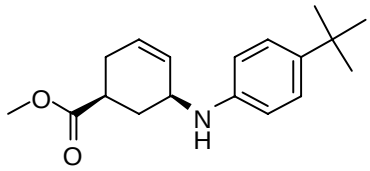


5g: methyl 5-(phenylselanyl)cyclohex-3-enecarboxylate

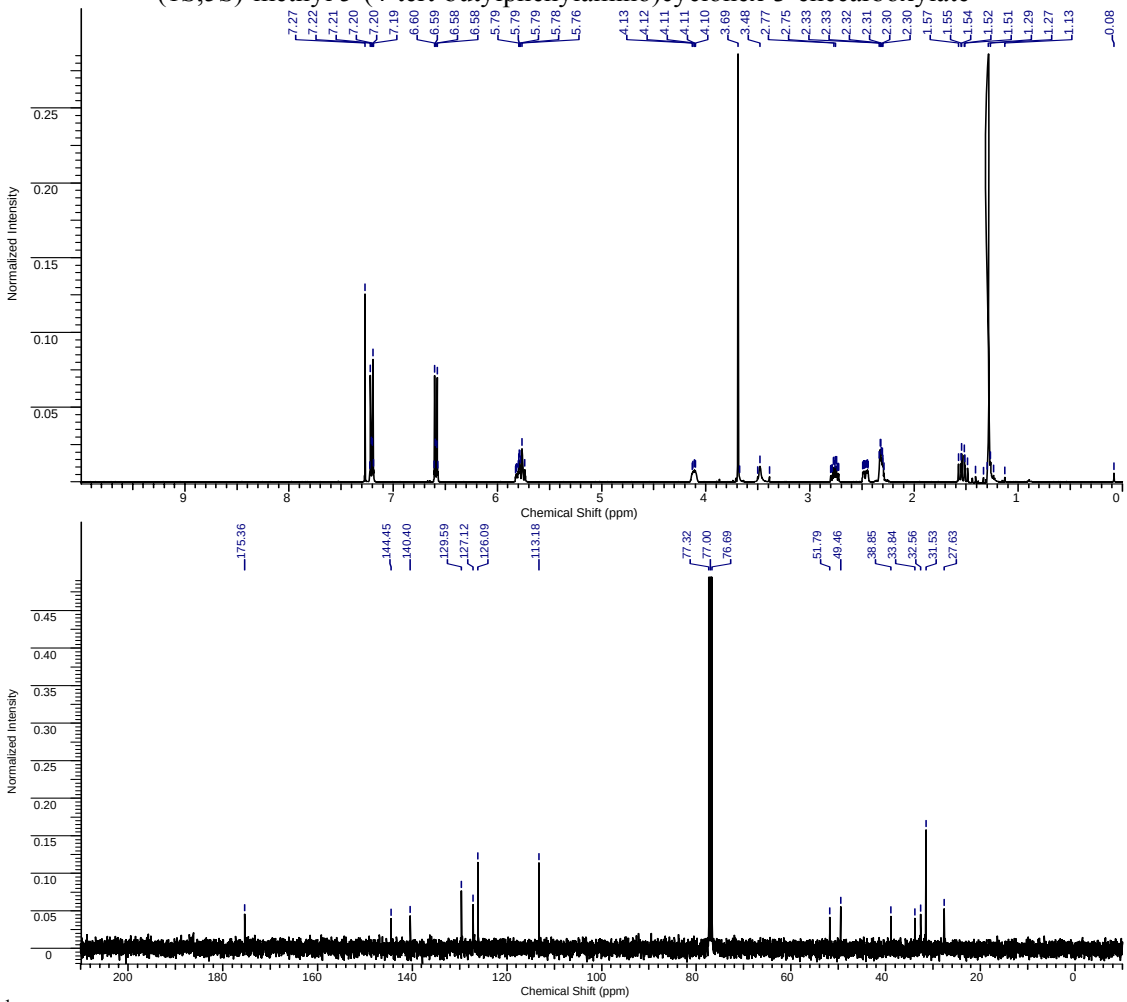


^{1}H NMR (400 MHz, $CDCl_3$) δ 1.89 (ddd, 1H: *J* = 10.6, 12.1, 13.2 Hz, PhSeCHC*H*H), 2.25 (m, 2H: CH=CHCH_2), 2.49 (ddd, 1H: *J* = 2.7, 6.0, 13.2 Hz, PhSeCHCH*H*), 2.61 (dddd, 1H: *J* = 2.7, 6.4, 9.2, 12.2, Hz, C*H*CO_2CH_3), 3.70 (s, 3H: OCH_3), 3.93 (m, 1H: C*H*SePh), 5.75 (m, 1H: PhSeCHCH=C*H*), 5.85 (app. d, 1H: *J* = 10.2 Hz, PhSeCHC*H*=CH), 7.31 (m, 3H: Ar CH's), 7.60 (m, 2H: Ar CH's); ^{13}C NMR (400 MHz, $CDCl_3$) δ 27.1 (*C*H_2CH=CH), 33.3 (*C*H_2CHSePh), 39.0 (*C*HSePh), 40.1 (*C*HCO_2R), 51.8 (O*C*H_3), 127.0 (*C*H=CHCHSePh), 127.8 (Ar CH), 128.5 (quat. Ar C), 128.98 (CH=*C*HCHSePh), 129.00 (Ar CH's), 135.0 (Ar CH's), 175.0 (*C*O_2CH_3); FTIR (CH_2Cl_2) υ_{max}: 3064, 2952, 1730, 1477, 1437, 1313, 1300, 1209, 1193, 1175, 1163, 1101; HRMS (FAB+) calcd for [M+] 296.0315, found 296.0303.

Chiral HPLC Column: Chiralpak AD **Eluent:** 99.5:0.5 hexane:isopropanol **Flow rate**: 0.5 mL/min **Wavelength**: 210 nm **Retention times:** 21.7 (major) and 22.3 minutes.

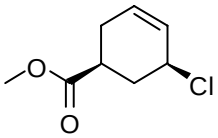


(1S,5S)-methyl 5-(4-tert-butylphenylamino)cyclohex-3-enecarboxylate

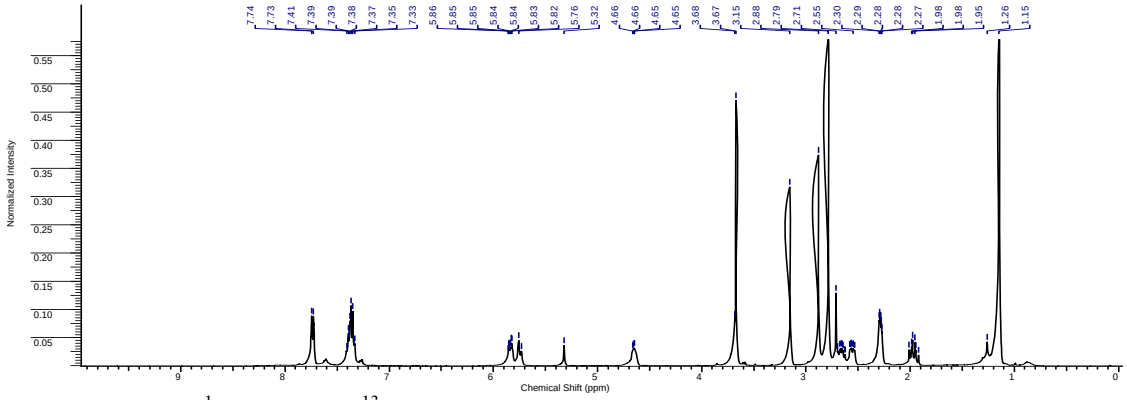


^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 1.28 (s, 9H: $C(CH_3)_3$), 1.54 (dd, 1H: *J* = 9.9, 12.5 Hz, NHCHCH*H*), 2.32 (ddd, 2H: *J* = 3.0, 3.3, 5.7 Hz, CH=CHCH_2), 2.46 (m, 1H: NHCHC*H*H), 2.76 (dddd, 1H: *J* =3.0, 3.2, 6.3, 12.1 Hz, C*H*CO_2CH_3), 3.44 - 3.55 (br s, 1H: NH), 3.69 (s, 3H: OCH_3), 4.11 (td, 1H: *J* = 2.4, 5.0 Hz, NHC*H*), 5.75 (m, 1H: NHCHCH=C*H*), 5.80 (m, 1H: NHCHC*H*=CH), 6.59 (d, 2H: *J* = 8.8 Hz, Ar CH's), 7.21 (d, 2H: *J* = 8.8 Hz, Ar CH's); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 27.6 (CH=CHCH_2), 31.5 ($C(CH_3)_3$), 32.6 (NHCHCH_2), 33.8 ($C(CH_3)_3$), 38.9 (NHCHCH_2), 49.5 (NH*C*H), 51.8 (OCH_3), 113.2 (Ar CH's), 126.1 (Ar CH's), 127.1 (NCH*C*H=CH), 129.6 (NCHCH=*C*H), 140.4 (quat. Ar. C), 144.5 (quat. Ar C), 175.4 (C=O); FTIR (CH_2Cl_2) υ_{max}: 3419, 3022, 2927, 1730, 1612, 1518, 1475, 1365, 1193, 1172, 908, 649; HRMS (ESI+) calcd for [M+H] 288.1963, found 288.1960.

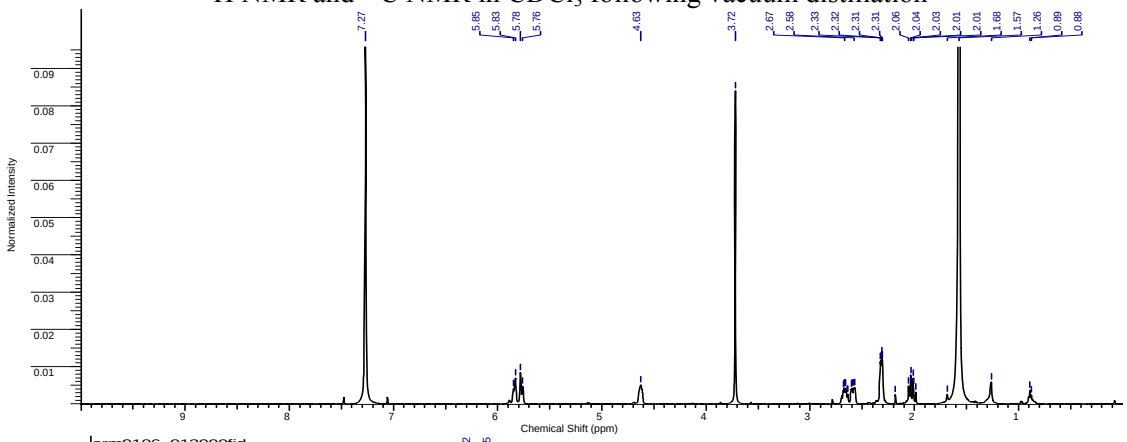
Chiral HPLC Column: Chiralpak AD **Eluent:** 95:5 hexane:isopropanol **Flow rate**: 0.5 mL/min **Wavelength**: 210 nm **Retention times:** 15.4 and 17.6 (major) minutes.

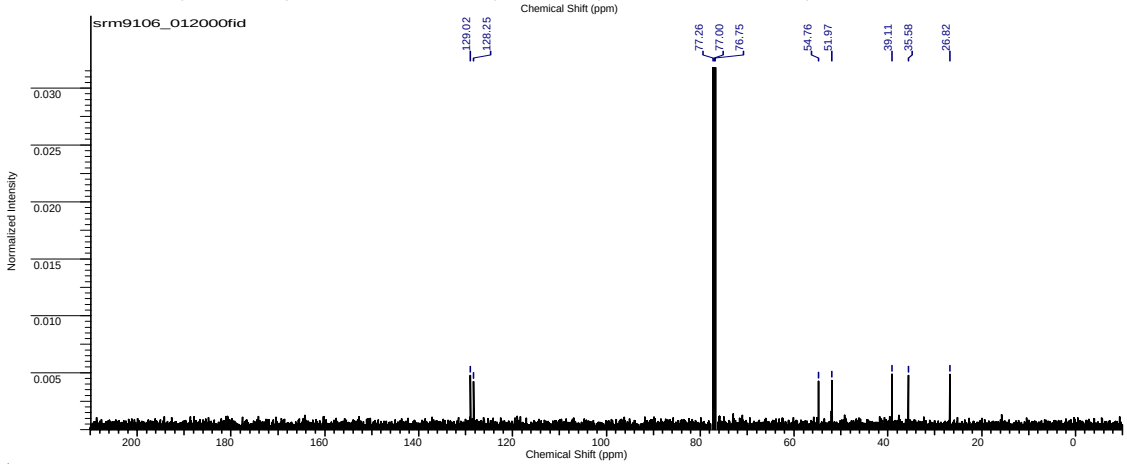


(1S,5S)-methyl 5-chlorocyclohex-3-enecarboxylate
NMR Reaction with tBuOMe as internal standard



^{1}H NMR and ^{13}C NMR in $CDCl_3$ following vacuum distillation





^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 1.89 (td, 1H: *J* = 9.9, 12.5 Hz, C*H*HCHCl), 2.21 (m, 2H: CH_2CH=CH), 2.47 (dd, 1H: *J* = 3.2, 6.0 Hz, CH*H*CHCl), 2.58 (ddd, 1H: *J* = 3.3, 8.7, 15.8 Hz, C*H*CO_2Me), 3.59 (s, 3H: CO_2CH_3), 4.57 (m, 1 H: C*H*Cl), 5.67 (app. d, 1H: *J* = 10.1 Hz, ClCHC*H*=CH), 5.76 (m, 1 H: ClCHCH=C*H*); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 26.8

(CH$_2$CH=CH), 35.6 (CH$_2$CHCl), 39.1 (CHCO$_2$Me), 52.0 (OCH$_3$), 54.8 (CHCl), 128.2 (ClCHCH=CH), 129.0 (ClCHCH=CH), 174.2 (CO$_2$CH$_3$);); FTIR (CH_2Cl_2) υ_{max}: 3001, 2974, 2952, 1733, 1647, 1604, 1454, 1436, 1205, 1172; HRMS (EI+) calcd for [M-HCl] 138.0681, found 138.0682.

Chiral GC Column: Chiraldex B-DM **Program:** Initial Hold Temp. 50 °C for 5 minutes, ramp 10 °C/minute to 120 °C, hold at 120 °C Inj. 200°C, Det. 250°C **Retention times:** 27.9 (major) and 29.3 minutes.