Supporting Information

Highly Functionalized *tertiary*-Carbinols and Carbinamines from the Asymmetric γ-Alkoxyallylboration of Ketones and Ketimines with the Borabicyclodecanes

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General Methods

All experiments were carried out in pre-dried glassware (1 h, 150 °C) under a nitrogen atmosphere. Standard handling techniques for air-sensitive compounds were employed for all the operations. Nuclear magnetic resonance (NMR) spectra were obtained using Bruker Advance DPX-500 (^{1}H (500 MHz), ^{13}C (125 MHz)) or DPX-300 (^{1}H (300 MHz), ^{13}C (75 MHz), ^{31}P (121.5 MHz)) spectrometers. NMR were recorded in $CDCl_3$ or C_6D_6, unless otherwise noted, and the chemical shift are expressed in ppm relative to $CDCl_3$ (δ 7.26 and 77.0 for ^{1}H and ^{13}C NMR, respectively) and of C_6D_6 (δ 7.15 and 128.0 for ^{1}H and ^{13}C NMR, respectively) as the internal standard. Infrared spectra were recorded on a

Bruker Tensor 27 FTIR spectrophotometer with HELIOS ATR attachment. Mass spectral data were obtained with a Hewlett-Packard 5995A GC/MS spectrometer (70 eV), Fisons VG Autospect or a Hewlett-Packard 5971A Mass Selective Ion Detector. High-resolution mass spectral data were obtained from Emory University. Optical rotations were measured employing a Perkin-Elmer 243B polarimeter. Literature citations are provided for all known compounds together with selected repeated data to consolidate this information herein.

Organoboranes

The organoboranes used to prepare **1**, **11**, and **22** reported below, were prepared according to the literature procedures.[1,2] They are included herein to consolidate the information.

***B*-Methoxy-10-trimethylsilyl-9-borabicyclo[3.3.2]decane**

(A). To a solution of *B*-MeO-9-BBN (18.0 g, 118 mmol) in hexanes (110 mL), $TMSCHN_2$ in hexanes (130 mmol, 2 M) was added at 25 ^{o}C. The mixture was refluxed for 10 h and the solvent was removed under vacuum. The residue was distilled to give 27.2 g of **A** (97%, bp 80 °C, 0.10 mmHg): ^{1}H NMR (300 MHz, C_6D_6) δ 0.21 (s, 9H), 1.45-1.68 (m, 15H), 3.34 (s, 3H); ^{13}C NMR (75 MHz, C_6D_6) δ 1.1, 22.3, 22.5, 24.9, 25.8, 28.0, 29.2, 32.0, 33.2, 33.6, 52.5; ^{11}B NMR (96 MHz, C_6D_6) δ 54.9. IR (neat) 2950, 1466, 1324, 1092, 688 cm^{-1}; HRMS (EI) *m/z* calcd for $C_{13}H_{27}BOSi$ 238.1924, found 238.1929.

9-(1*S*,2*S*-Pseudoephedrinyl)-(10*R*)-(trimethylsilyl)-9-borabicyclo[3.3.2]-decane ((+)-B): To a mixture of (1*S*,2*S*)-pseudoephedrine (8.28 g, 50 mmol) in acetonitrile (110 mL) was added (±)-*B*–MeO-10-TMS-9-BBD (23.85 g, 100 mmol) dropwise. The reaction mixture was refluxed for 6 h and slowly cooled to 25 ^{o}C resulting in large crystals. The supernatant was decanted via cannula and the crystals were washed with hexanes (3 X 10 mL) to remove residual MeCN and organoborane impurities and dried *in vacuo* to give 14.1 g of (+)-**B** (38% yield, mp 106-109 °C): [α] $^{20}_{D}$ + 54.2 (*c* 4.5, $CDCl_3$) ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.12 (s, 9 H), 0.95 (d, *J* = 6.4 Hz, 3 H), 1.25 (m, 2 H), 1.40-1.67 (m, 13H), 1.8 (br s, 1 H), 2.45 (s, 3H), 2.62 (m, 1 H), 4.18 (d, *J* = 8.2 Hz, 1 H), 7.29 (m, 5 H); ^{13}C NMR (75 MHz, C_6D_6) δ 1.7, 15.1, 22.6, 23.1, 26.4, 27.6, 29.3, 31.0, 33.1, 35.4, 38.4, 65.0, 80.8, 127.0, 127.4, 128.1, 141.7; ^{11}B NMR (96 MHz, C_6D_6) δ 55.2, 17.4; HRMS *m/z* calcd for $C_{22}H_{38}BNOSi$ 371.2816, found 371.2825.

9-(1*R*,2*R*-Pseudoephedrinyl)-(10*S*)-(trimethylsilyl)-9-borabicyclo[3.3.2]-decane ((-)-B). The above supernatant together with the hexane washings were concentrated. The resulting residue was dissolved in acetonitrile (100 mL was mixed with 1*R*,2*R*-pseudoephedrine (8.28 g, 50 mmol). The reaction mixture was refluxed for 6 h, whereupon it was slowly cooled to 25 C forming large crystals The supernatant was removed and the crystals were washed as above and dried *in vacuo* to give 10.4 g of **(-)-B** (28% yield): [α] $^{28}_{D}$ -54.4 (*c* 4.3, $CDCl_3$).

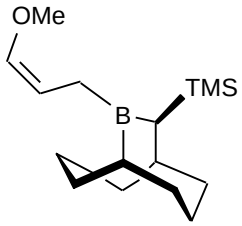
***B*-Allyl-10*R*-trimethylsilyl-9-borabicyclo[3.3.2]decane (RC).** A solution of 9-(1*S*,2*S*-pseudoephedrinyl)-(10*R*)-(trimethylsilyl)-9-borabicyclo[3.3.2]decane (1.48 g, 4.0 mmol) in ether (40 mL) was cooled to -78 °C and a solution of allylmagnesium bromide (4 mL of 1.0 M) in ether was added dropwise. The solution was allowed to reach 25 ^{o}C and was stirred for 1 h. Using standard techniques to prevent the exposure of the borane to the open atmosphere, the mixture was concentrated under vacuum, the residue was washed with pentane (6 x10 mL) and these washings were filtered through a celite pad. Concentration gives 0.97 g (98%) of *B*-Allyl-10*R*-TMS-9-BBD ^{1}H NMR (300 MHz, C_6D_6) δ 0.85 (m, 1H), 0.9 (s, 9H), 1.24 (m, 1H), 1.52 (m, 10H), 1.80 (m, 1H), 2.10 (m, 2H), 2.30 (m, 1H), 4.95 (m, 2H), 5.97 (m, 1H); ^{13}C NMR (75 MHz, C_6D_6) δ 1.8, 22.0, 25.3, 25.4, 29.5, 30.9, 31.2, 34.2, 35.2, 37.1, 39.9, 113.8, 136.4; ^{11}B NMR (96 MHz, $CDCl_3$) δ 84.6; $[\alpha]_D^{27}$ -23.7 (*c* 3.91, C_6D_6). *B*-Allyl-10*S*-trimethylsilyl-9-borabicyclo[3.3.2]decane is prepared by the same procedure starting with 9-(1*R*,2*R*-pseudoephedrinyl)-(10*S*)-(TMS)-9-borabicyclo[3.3.2]decane. (**SC**) $[\alpha]_D^{27}$ +23.3 (*c* 3.91, C_6D_6). Other data are essentially identical to *B*-Allyl-10*R*-TMS-9-BBD.

***B*-Methoxy-10*R*-trimethylsilyl-9-borabicyclo[3.3.2]decane (-) and (+)-A)**

A solution of *B*-allyl-10*R*-TMS-9-BBD

(5.48 g, 14.8 mmol) in ether (100 mL) was chilled to -78 °C. Allylmagnesium bromide (17.7 mmol, 1.0 M in ether) was added *via* cannula. The solution was allowed to warm to 25 ^{0}C and stirred for 1 h at 25 ^{o}C. Subsequently, the ether solvent was removed *in vacuo*. The resulting slurry was filtered through an oven-

dried celite pad with pentane. Concentration of the filtrate gave 3.4 g (98%) of *B*-MeO-10*R*-TMS-9-BBD. MeOH (~30 mL) was added and the solution was refluxed for 2 h. Removal of the MeOH *in vacuo* and subsequent distillation provided 2.02 g of *B*-MeO-10*R*-TMS-9-BBD (87%, bp 81 °C at 0.05 mm Hg, >98% purity by ^{13}C NMR): $[\alpha]_D^{29}$ -28.4 (*c* 2.62, C_6D_6). The spectroscopic data was identical to the racemic compound *B*-MeO-10-TMS-9-BBD. The *B*-MeO-10*S*-TMS-9-BBD ($[\alpha]_D^{22}$ +28.0 (*c* 2.54, C_6D_6)) was prepared by the same procedure as for *B*-MeO-10*R*-TMS-9-BBD, except from the corresponding complex 9-(1*R*,2*R*-pseudoephedrinyl)-(10*S*)-(trimethylsilyl)-9-borabicyclo[3.3.2]-decane.



(10*R*)-*B*-[(*Z*)-γ-Methoxyallyl]-10-trimethylsilyl-9-borabicyclo[3.3.2]decane ((-)-11*R*): To a stirred solution of allyl methyl ether (0.324 g, 4.5 mmol) in THF (4 mL) was added *sec*-butyllithium in cyclohexane (2.7 mL, 1.48 M, 4 mmol) at -78 ^{o}C, dropwise. The mixture was stirred at -78 ^{o}C for 30 min and to it was added *via* cannula *B*-MeO-10*R*-TMS-9-BBD in 3 mL of THF (0.714 g, 3 mmol). After the reaction mixture was stirred at -78 ^{o}C for 2 h, TMSCl (0.57 mL, 4.5 mmol) in 4.5

mL of THF was added via cannula at -78 ^{o}C. After 10 min, all the volatiles were removed at 25 ^{o}C under reduced pressure (0.1 mmHg). The residue was dissolved in 20 mL of dry pentane, filtered through a filter packed with celite and washed with pentane (2 X 20 mL). All volatiles were removed at 25 ^{o}C under reduced pressure (0.1 mmHg) to give 0.71 g (85%) of **11*R***. $[\alpha]_D^{22}$ -17.7 (*c* 1.6, C_6D_6) ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.25 (s, 10H), 1.19-2.45 (m, 16H), 3.26 (s, 3H), 4.64 (td, *J* = 8.1, 6.0 Hz, 1H), 5.88 (dt, *J* = 6.0, 1.5 Hz, 1H) ; ^{13}C NMR (75 MHz, C_6D_6) δ 1.8, 22.2, 25.2, 25.9, 26.5 (br), 29.5, 30.9 (br), 31.5, 34.3, 35.1, 33.6 (br), 58.8, 103.7, 145.7; ^{11}B NMR (96 MHz, C_6D_6) δ 85.1 (Figure 1). The **11*S*** is prepared by the same procedure starting with *B*-MeO-10*S*-TMS-9-BBD, $[\alpha]_D^{20}$ +17.9 (*c* 1.6, C_6D_6). Other data are essentially identical to **11*R***.

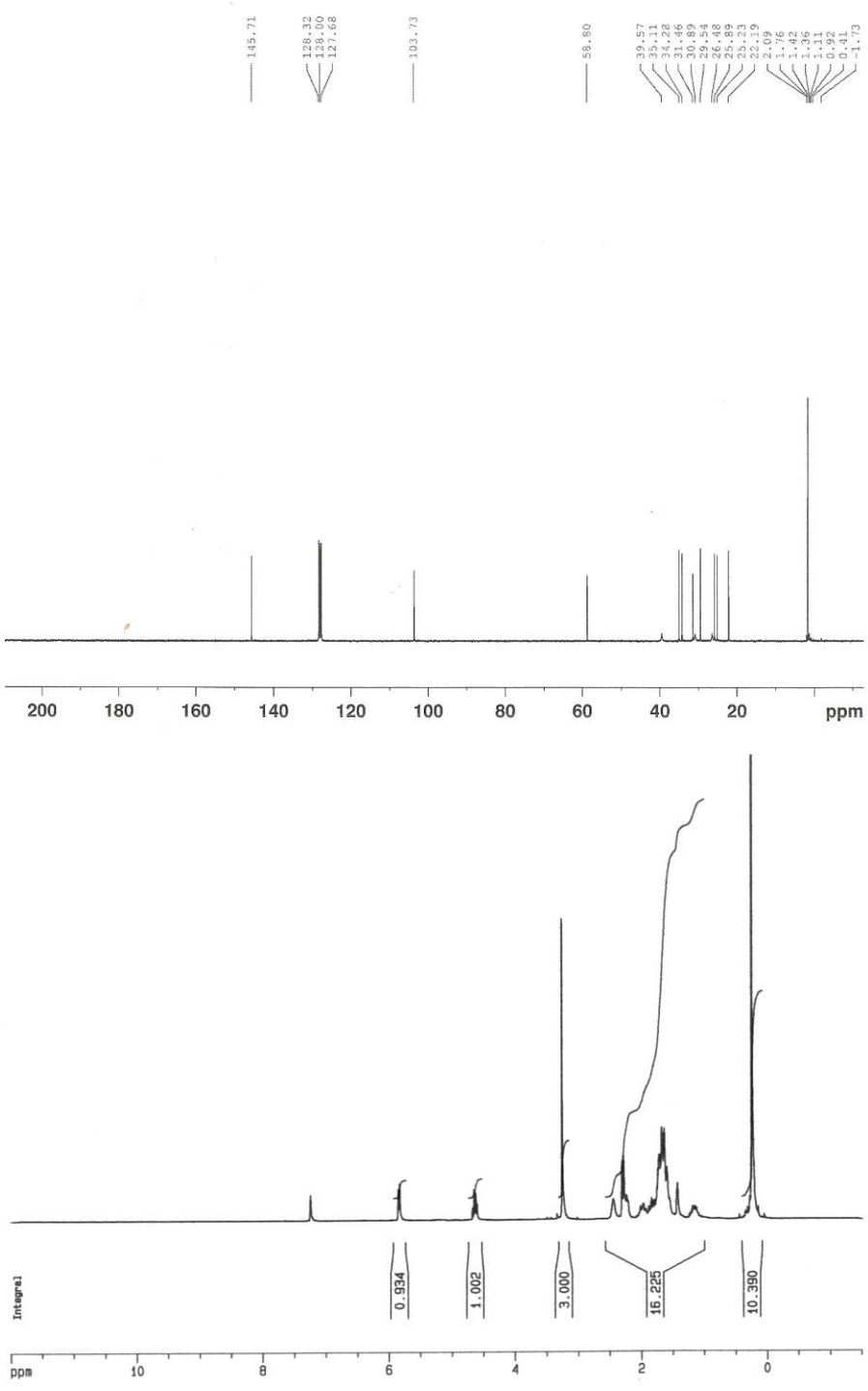
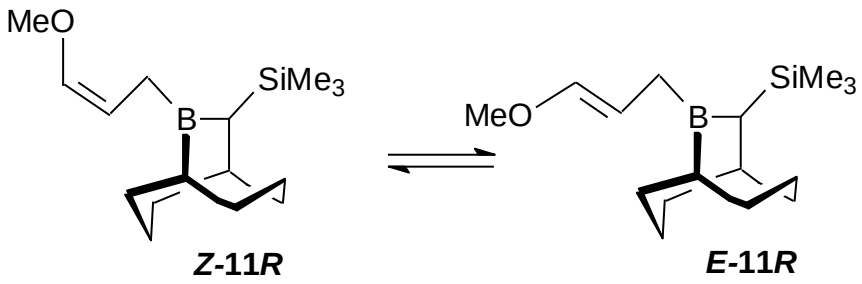


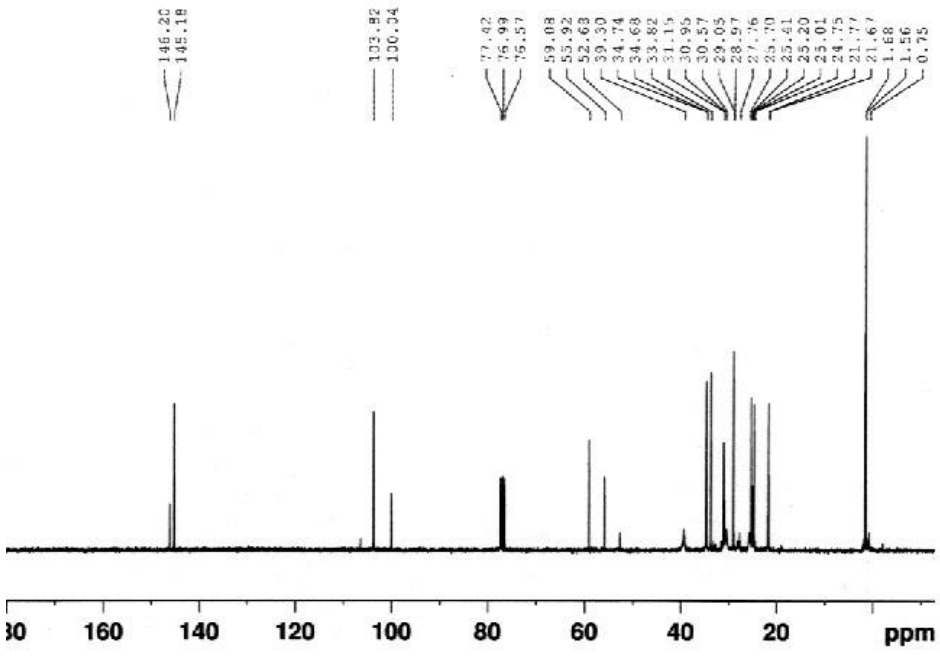
Figure 1. ^{13}C and ^{1}H NMR of **11**.



Z*-11*R ***E*-11*R***

(±)-*B*-[(*Z*/*E*)-γ-Methoxyallyl]-10-trimethylsilyl-9-borabicyclo[3.3.2]decane ((±)-(*Z*/*E*)-11*R*): To a stirred solution of allyl methyl ether (0.324 g, 4.5 mmol) in THF (4 mL) was added *sec*-butyllithium in cyclohexane (2.7 mL, 1.48 M, 4 mmol) at -78 ^{o}C, dropwise. The mixture was stirred at -78 ^{o}C for 30 min and to it was added via cannula *B*-MeO-10-TMS-9-BBD in 3 mL of THF (0.714 g, 3 mmol). After the reaction mixture was stirred at -78 ^{o}C for 2 h, trimethylsilyl chloride (0.57 mL, 4.5 mmol) in 4.5 mL of THF was added via cannula at -78 ^{o}C. After 10 min, the mixture was allowed to reach 25 ^{o}C and all of the volatiles were removed under reduced pressure (0.1 mmHg). The residue was dissolved in 20 mL of dry pentane, filtered through a filter packed with celite and washed with pentane (2 X 20 mL). All volatiles were again removed at 25 ^{o}C under reduced pressure (0.1 mmHg). After 10 mL of pentane were added, the round-bottomed flask was equipped with a reflux condensor and the mixture was heated at reflux for 4 d, cooled under N_2 atmosphere to obtain a ~70:30 *cis*/*trans* mixture (see Figure 2). This was used to obtain the diastereomers of the alcohols and determine the de by ^{31}P NMR analysis. Due to the complexity of the *cis*/*trans* mixture only some features of the ^{1}H NMR (300 MHz, $CDCl_3$) data are highlighted in Figure 3. ^{13}C NMR (75 MHz, $CDCl_3$) δ 1.6 (*cis*), 1.7 (*trans*), 21.7 (*trans*), 21.8 (*cis*), 24.8 (*cis*),

25.0 (*trans*), 25.2 (*trans*), 25.4 (*cis*), 25.7 (br), 29.0 (*trans*), 29.1 (*cis*), 30.6 (br), 30.1 (*trans*), 31.1 (*cis*), 33.8 (*cis*), 34.7 (*cis*), 34.7 (*trans*), 39.3 (br), 55.9 (*trans*), 59.1 (*cis*), 100.0 (*trans*), 103.8 (*cis*), 145.2 (*cis*), 146.2 (*trans*); ^{11}B NMR (96 MHz, C_6D_6) δ 85.1. A similar result was obtained when **11** in C_6D_6 (*ca.,* 1 M) was heated at reflux for 14 h. Some minor additional signals due to decomposition were observed in the NMR spectra of this *cis*/*trans* mixture which continued to decompose over the 36 h period for which it was monitored. The pentane isomerization at 36 ^{o}C is cleaner (*vide infra*). The attempted distillation of this material led to decomposition both in the distillate (bp 170-190 ^{o}C at ~0.1 mmHg) and in the residue as evidenced from the appearance of many additional signals in the NMR spectra of these mixtures.



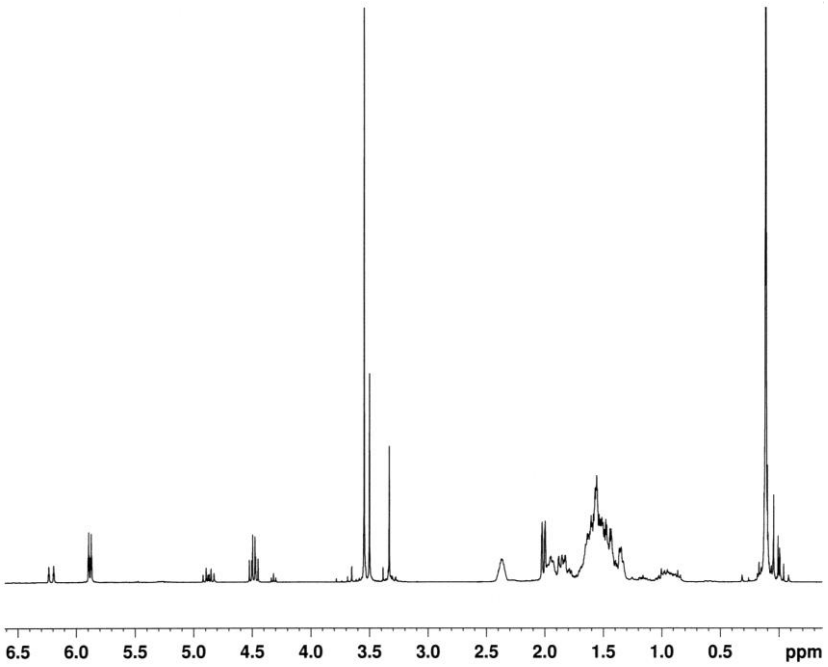


Figure 2. ^{13}C and ^{1}H NMR of **(±)-*(Z/E)*-11**.

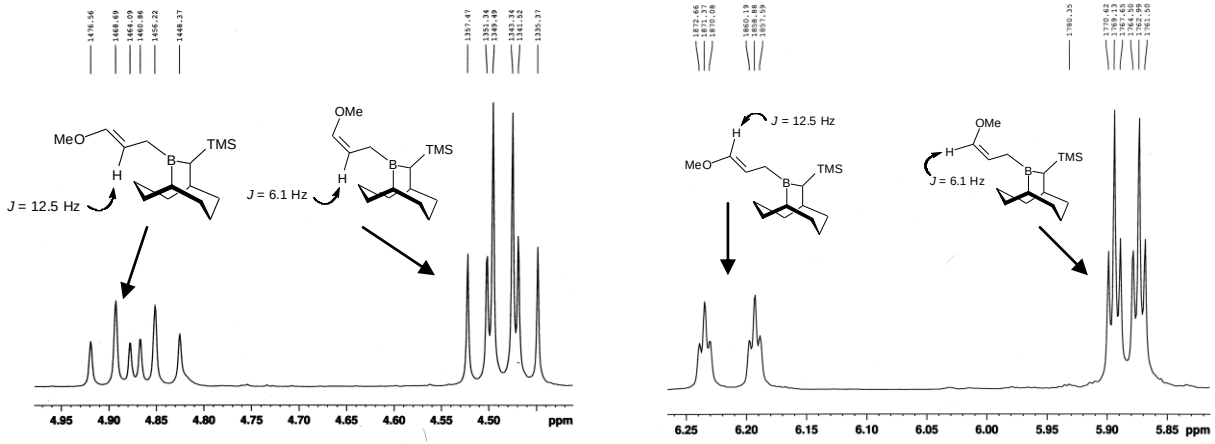


Figure 3. ^{1}H NMR expansions of *cis/trans* mixture of **11**.

(±)-*B*-Methoxy-10-phenyl-9-borabicyclo[3.3.2]decane ((±)-4). To a solution of *B*-MeO-9-BBN (18.0 g, 118 mmol) in hexanes (110 mL), $PhCHN_2$ in hexanes, (130 mmol, 2 M) was added dropwise at 0 °C. The mixture was stirred for 10 h

and the solvents were removed under vacuum. The residue was distilled to give 25.7 g of **(±)-4** (90%, bp 120 °C, 0.10 mmHg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.30-2.0 (m, 14H), 2.40 (m, 1H), 3.51 (s, 3H), 7.1-7.4 (m, 5H) ^{13}C NMR (75 MHz, C_6D_6) δ 21.5, 24.3, 26.5, 28.0, 29.1, 31.6, 38.8, 43.1, 53.7, 125.0, 128.1, 129.0, 130.4, 145.0; IR (cm $^{-1}$) 3020. 2908, 2851, 1467, 1323, 1288, 1254, 749, 717, 697; ^{11}B NMR (96 MHz, C_6D_6) δ 55.5. HRMS calcd. 242.18 found 242.15.

(+)-*B*-((1*S*,2*S*)-*N*-Methylpseudoephedrinyl))-(10*S*)-phenyl-9-borabicyclo-[3.3.2]decane (NMPE-10*S*-Ph-9-BBD). To a solution of (1*S*,2*S*)-*N*-methylpseudoephedrine (5.0 g, 27.9 mmol) in hexane (60 mL) was added **(±)-4** (13.5 g, 55.8 mmol) dropwise. The reaction mixture was refluxed for 6 h and slowly cooled to 25 ^{o}C resulting in small square, clear crystals. The supernatant was decanted *via* cannula and the crystals were washed with hexane (3 x 20 mL) and dried *in vacuo* to give 4.2 g (10.8 mmol) of NMPE-10*S*-Ph-9-BBD (38% yield). The supernatant is concentrated and fresh hexane (60 mL) is added the mixture is then refluxed for an additional 6 h. Upon cooling a second batch of crystals are obtained following the before-mentioned work-up. The second collection gives 4.4 g (11.2 mmol) of NMPE-10*S*-Ph-9-BBD. The overall yield of NMPE-10*S*-Ph-9-BBD is 79% (39.5% based upon **(±)-4**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.72 (s, 3H), 1.32 (m, 2H), 1.75-2.0 (m, 11H) 2.45 (m, 7H), 2.85 (m, 1H), 4.28 (m, 1H), 6.95-7.66 (m, 10H); ^{11}B NMR (96 MHz, CDCl3) δ 55.5, 10.0; mp = 130- 140 °C Anal. calcd for C 80.20, H 9.32, found C 79.99, H 9.44. $[\alpha]^{D}_{22}$ +66.3 (*c* 4.5, CH_2Cl_2).

(-)-*B*-((1*R*,2*R*)-*N*-Methylpseudoephedrinyl))-(10*R*)-phenyl-9-borabicyclo-[3.3.2]decane (NMPE-10*R*-Ph-9-BBD). The above supernatant was concentrated. The resulting residue was dissolved in hexane (60 mL) and mixed with (1*R*,2*R*)-*N*-methylpseudoephedrine (5.0 g, 27.9 mmol). The reaction mixture was refluxed for 6 h, whereupon it was slowly cooled to 25 ^{o}C forming small, square and clear crystals. The supernatant was decanted *via* cannula and the crystals were washed (3 x 20 mL) with hexane and dried *in vacuo* to give 4.1 g (10.5 mmol) of **NMPE-10*R*-Ph-9-BBD**. The supernatant is concentrated and fresh hexane (60 mL) is added the mixture is then refluxed for an additional 6 h. Upon cooling a second batch of crystals (2.0 g) are obtained following the above work-up. The overall yield of **NMPE-10*R*-Ph-9-BBD** is 56% (28% based upon **(±)-4**). mp = 135-140 °C $[\alpha]^{D}_{25}$ -66.6 (*c* 4.5, CH_2Cl_2). Pseudoephedrine can also be used to precipitate the residual isomer.

(+)-*B*-((1*S*,2*S*)-Pseudoephedrinyl))-(10*R*)-phenyl-9-borabicyclo[3.3.2]-decane. As above, with (1*S*,2*S*)-pseudoephedrine, 29%, $[\alpha]^{D}_{28}$ +25.45 (*c* 1.1, CH_2Cl_2).

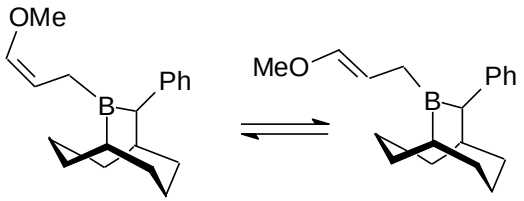
(+)-*B*-Allyl-10*S*-phenyl-9-borabicyclo[3.3.2]decane (*B*-Allyl-10*S*-Ph-9-BBD). A solution of (+)-*B*-((1*S*,2*S*)-pseudoephedrinyl))-(10*R*)-phenyl-9-borabi-cyclo[3.3.2]-decane (1.17 g, 3.0 mmol) in ether (10 mL) was cooled to -78 °C and a solution of allylmagnesium bromide (3.2 mL of 1.0 M) in ether was added dropwise. The solution was allowed to reach 25 ^{o}C and was stirred for 2 h and

the reaction mixture was quenched with 0.5 mmols of TMSCl. Using standard techniques to prevent the exposure of the borane to the open atmosphere, the mixture was concentrated under vacuum, the residue was washed with pentane (3 x 10 mL) and these washings were filtered through a celite pad. Concentration gives 0.74 g (98%) of *B*-Allyl-10*S*-Ph-9-BBD. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.99 (m, 15H), 4.77 (m, 2H), 5.85 (m, 1H), 7.23 (m, 5H); ^{13}C NMR (75 MHz, C_6D_6) δ 23.5, 23.6, 26.7, 27.7, 29.2, 30.7, 34.1, 36.2, 40.5, 52.4, 131.9, 124.8, 128.1, 130.0, 135.5, 146.5; ^{11}B NMR (96 MHz, $CDCl_3$) δ 84.6; $[\alpha]_D^{20}$ +42.8 (*c* 3.14, $CDCl_3$).

(-)-*B*-Allyl-10*R*-phenyl-9-borabicyclo[3.3.2]decane (*B*-Allyl-10*R*-Ph-9-BBD) is prepared by the same procedure starting with (+)-*B*-((1*S*,2*S*)-pseudoephedrinyl))-(10*R*)-phenyl-9-borabicyclo[3.3.2]-decane. $[\alpha]_D^{22}$ -42.3 (*c* 3.41, $CDCl_3$). Other data are essentially identical to *B*-Allyl-10*S*-Ph-9-BBD.

(10*S*)-*B*-[(*Z*)-γ-Methoxyallyl]-10-phenyl-9-borabicyclo[3.3.2]decane (1*S*). To a stirred solution of allyl methyl ether (0.324 g, 4.5 mmol) in THF (2 mL) was added *sec*-butyllithium in cyclohexane (2.7 mL, 1.48 M, 4 mmol) at -78 ^{o}C, dropwise. The mixture was stirred at -78 ^{o}C for 30 min and to it was added via cannula **4*S*** in 1 mL of THF (0.727 g, 3 mmol). After the reaction mixture was stirred at -78 ^{o}C for 2 h, TMSCl (0.57 mL, 4.5 mmol) in 0.5 mL of THF was added via cannula at -78 ^{o}C. After 30 min at -78 ^{o}C, the resultant solution was immediately used without purification. 87% Yield (calculated by ^{11}B NMR *via* comparison of

integration of δ 81.0 ppm (**1*S***) vs the 55.5 ppm (**4*S***) peaks). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.21 – 2.08 (m, 14 H), 2.25 (s, 2 H), 2.59 (s, 1H), 3.44 (s, 3 H), 4.34 (td, *J* = 7.8, 6.1 Hz, 1 H), 5.63 (d, *J* = 6.1, 1 H), 6.88 – 7.29 (m, 5 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 23.3, 23.5, 25.6 (br), 26.6, 28.1, 29.3, 30.6 (br), 34.1, 40.4, 52.0 (br), 59.1, 103.2, 124.5, 127.9, 129.9, 145.4, 147.0. The ***1R*** is prepared by the same procedure starting with **4*R***, NMR data is essentially identical to **4*S***.



1 **7**

(±)-*B*-[(*Z*/*E*)-γ-Methoxyallyl]-10-phenyl-9-borabicyclo[3.3.2]decane (1/7). To a stirring solution of allyl methyl ether (0.324 g, 4.5 mmol) in THF (2 mL) was added *sec*-butyllithium in cyclohexane (2.7 mL, 1.48 M, 4 mmol) at -78 ^{o}C, dropwise. The mixture was stirred at -78 ^{o}C for 30 min and to it was added via cannula **(±)-1** in 1 mL of THF (0.727 g, 3 mmol). After the reaction mixture was stirred at -78 ^{o}C for 2 h, trimethylsilyl chloride (0.57 mL, 4.5 mmol) in 0.5 mL of THF was added via cannula at -78 ^{o}C. After 10 min, the mixture was allowed to reach 25 ^{o}C and all of the volatiles were removed under reduced pressure (0.1 mmHg). The residue was dissolved in 20 mL of dry pentane, filtered through a filter packed with celite and washed with pentane (2 X 20 mL). All volatiles were again removed at 25 ^{o}C under reduced pressure (0.1 mmHg). After 1 h at 25 ^{o}C a ~84:16 *cis*/*trans* mixture, after 2.5 h at 25 ^{o}C a ~74:26 *cis*/*trans* mixture and after 24 h at 25 ^{o}C a ~54:46 *cis*/*trans* mixture was obtained (see Figures 4, 5).

This was used to verify the stability of the (±)-*B*-[(*Z/E*)-γ-methoxyallyl]-10-phenyl-9-borabicyclo[3.3.2]decane **(±)-(1/7)** vs the (±)-*B*-[(*Z/E*)-γ-Methoxyallyl]-10-trimethylsilyl-9-borabicyclo[3.3.2]decane [2] which retained its *cis* configuration upon warming to 25 ^{o}C and after heated at reflux for 4 d, cooled under N_2 atmosphere, a ~70:30 *cis*/*trans* mixture was obtained. Due to the complexity of the *cis*/*trans* mixture only some features of the ^{1}H NMR (300 MHz, $CDCl_3$) data are highlighted from Figure 5. ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.3 (*cis/trans*), 23.5 (*cis*), 23.7 (*trans*), 25.6 (br), 26.6 (*cis/trans*), 27.9 (*trans*), 28.1 (*cis*), 29.2 (trans), 29.3 (cis), 30.6 (br), 33.9 (trans), 34.1 (cis), 40.4 (cis/trans), 52.0 (br), 55.7 (trans), 59.1 (cis), 98.7 (trans), 103.2 (cis), 124.5 (cis), 124.7 (trans), 127.9 (cis), 128.1 (trans), 129.9 (cis), 130.0 (trans), 145.4 (cis), 146.5 (trans), 146.6 (trans), 147.01 (cis).

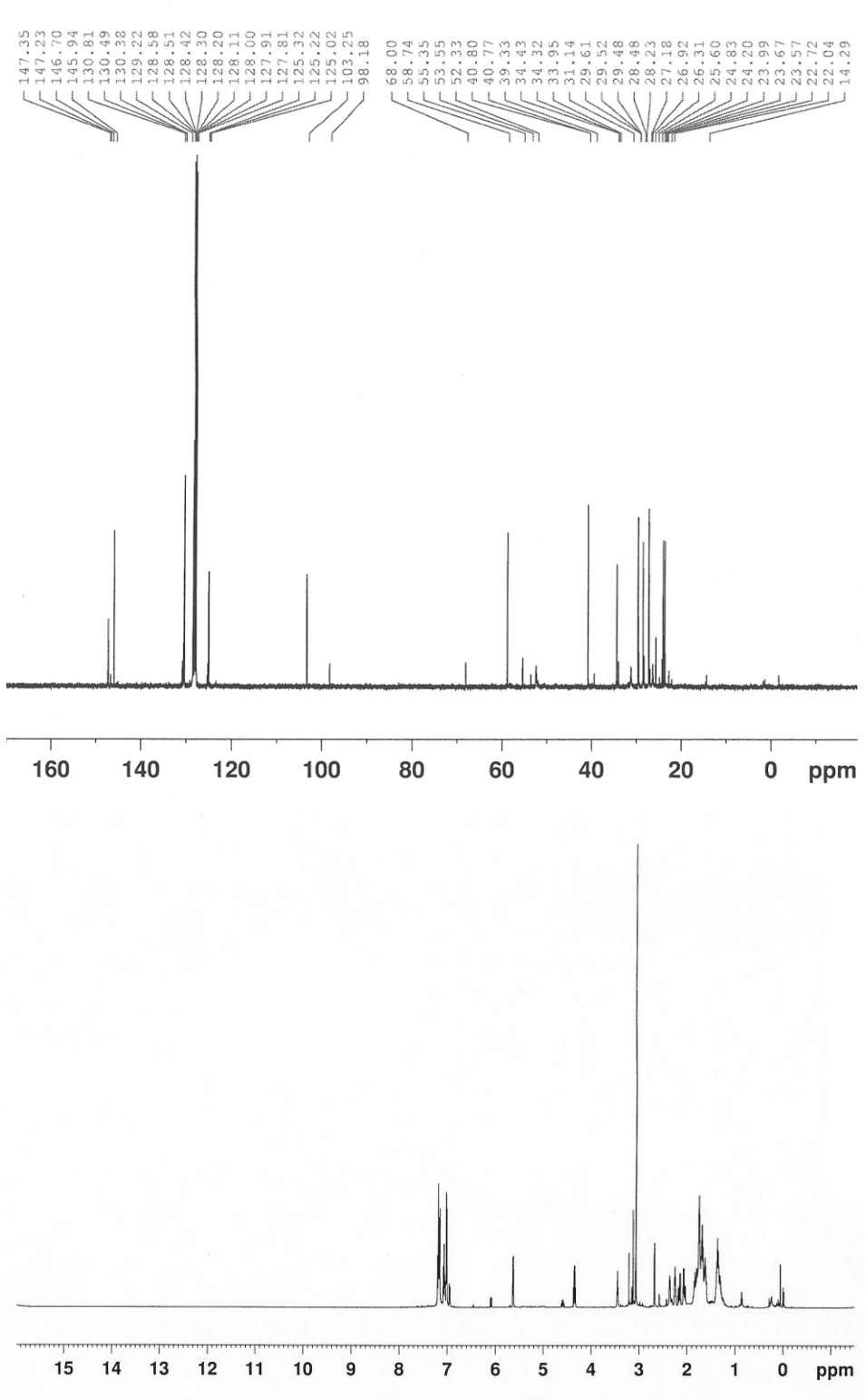


Figure 4. ^{13}C and ^{1}H NMR data of **(±)-(1/7)** after 1 h at 25 ^{o}C.

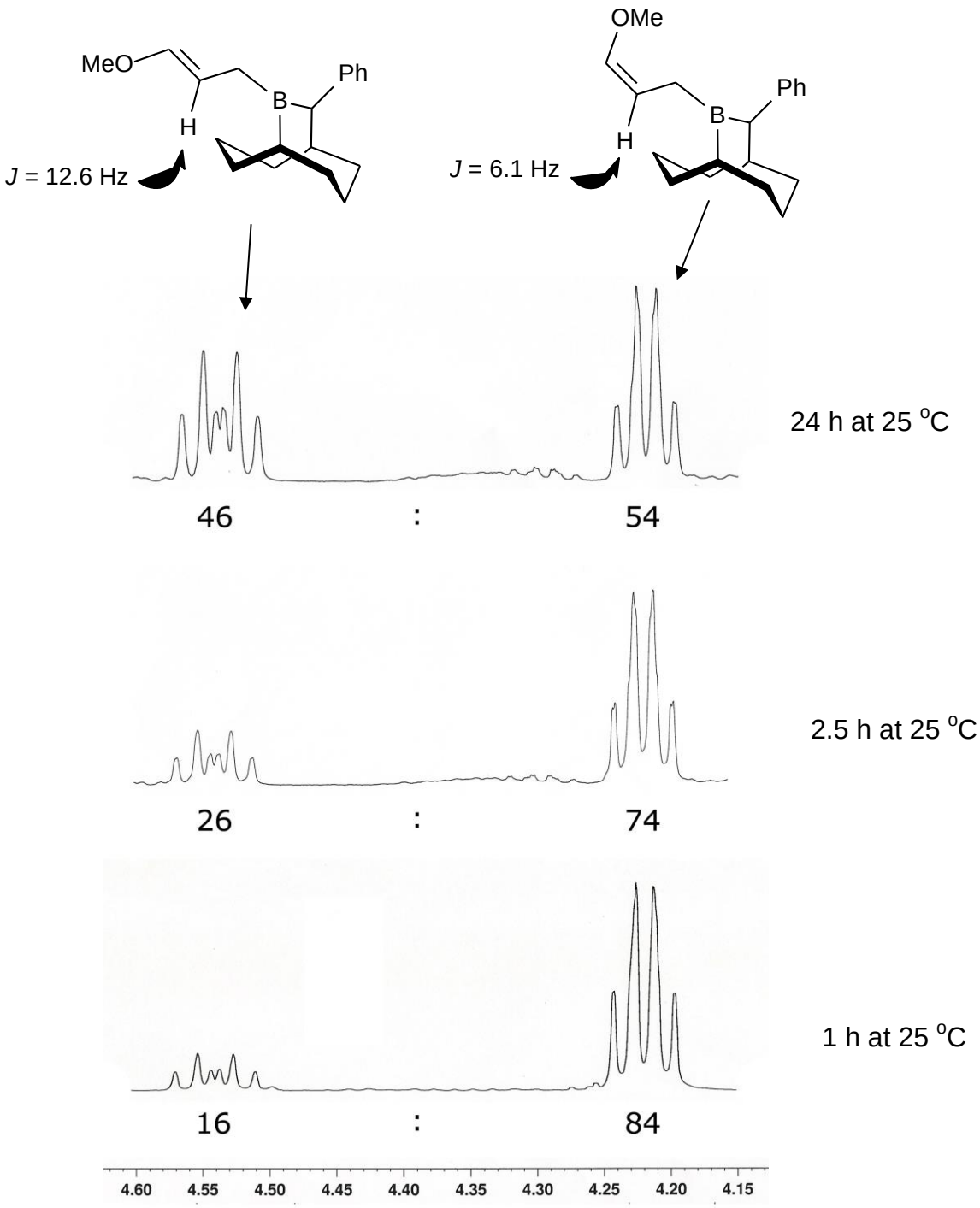
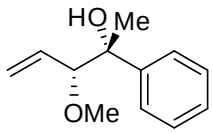


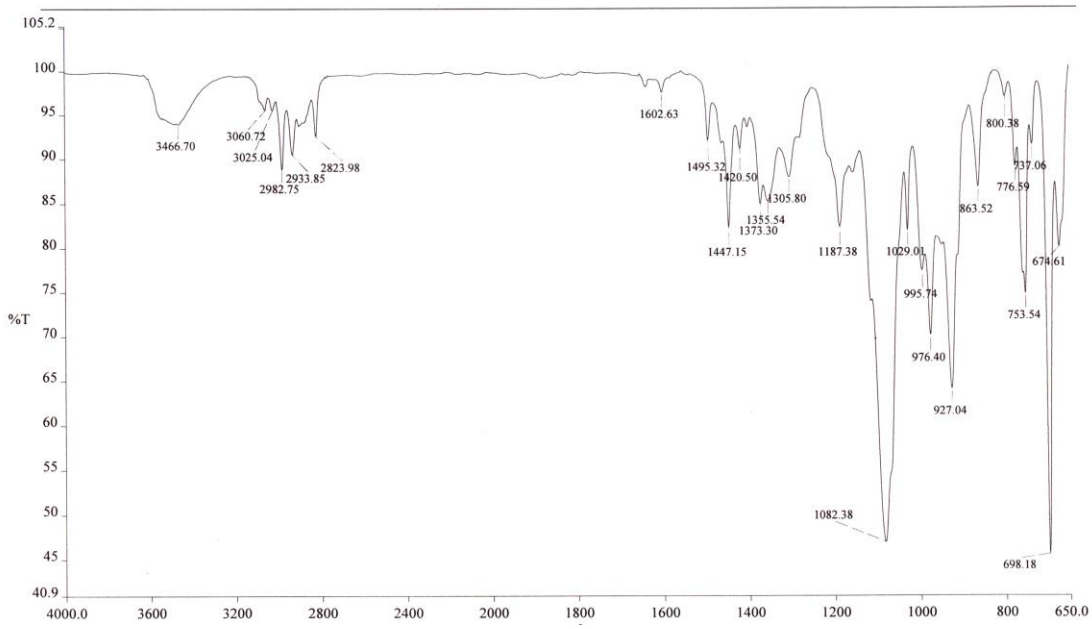
Figure 5. Selected ^{1}H NMR region of **(±)-(1/7)**.

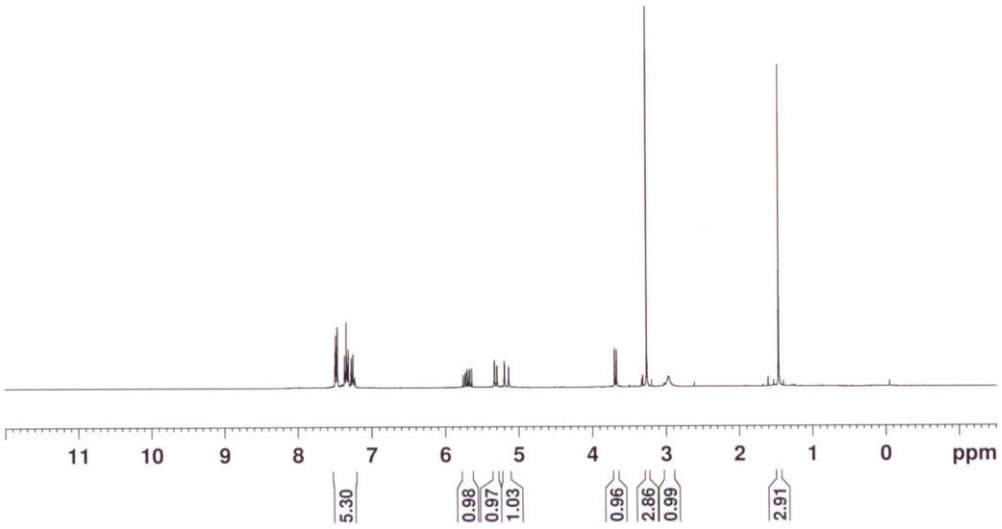
Addition to Ketones



(2*R*,3*R*)-3-Methoxy-2-phenylpent-4-en-2-ol (10a*RR*). Typical procedure for addition to ketones. Acetophenone (**8a**) (0.35 mL, 3 mmol) was added to freshly prepared **1*S*** on a 3 mmol scale, and the mixture was stirred at -78 ^{o}C for 4 h and allowed to slowly reach 25 ^{o}C for a total of 16 h. The reaction mixture was cooled to 0 ^{o}C, then NaOH (3 ml, 9 mmol, 3M) and H_2O_2 (0.61 mL, 6 mmols, 30 wt. %) were added dropwise, the mixture was allowed to slowly reach 25 ^{o}C. The round bottom flask was equipped with a refluxing condensor and the solution mixture was refluxed for 2 h. Diethyl ether was added to the mixture and the organic phase was extracted with water (2 X 10 mL) and brine (2 X 10 mL). All of the volatiles of the organic phase were removed under reduced pressure (0.1 mmHg). A silica gel column chromatography with a 98:2 to 95:5 mixture of hexane:ethyl acetate was used to purify all tertiary alcohols. Yield, 78%; Crude 98% de, Isolated 98% de; $[\alpha]_D^{20}$ +7.7 (*c* 1.6, $CHCl_3$), 97% ee; FTIR (CH_2Cl_2, cm^{-1}): 3467, 3061, 3025, 2983, 2934, 2824, 1603, 1495, 1420, 1373, 1356, 1306, 1187, 1082, 976, 927, 698; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.46 (s, 3H), 2.97 (s br, 1H), 3.27 (s, 3H), 3.69 (d, *J* = 7.8 Hz, 1H), 5.17 (ddd, *J* = 0.8, 1.7, 17.2 Hz, 1H), 5.32 (dd, *J* = 1.6, 10.4 Hz, 1H), 5.70 (ddd, *J* = 7.8, 10.4, 17.3 Hz, 1H), 7.36 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.3, 56.7, 75.6, 89.5, 119.9, 125.5, 126.6,

127.6, 133.7, 145.3; Alexakis derivative: ^{31}P NMR (121.5 MHz, $CDCl_3$) δ 137.2 (98.5%), 138.1 (1.5%); HRMS (FAB) [*M* + H]$^+$ calculated for $C_{12}H_{17}O_2$: 193.1223, found: 193.1221. (Figures 6, 7)





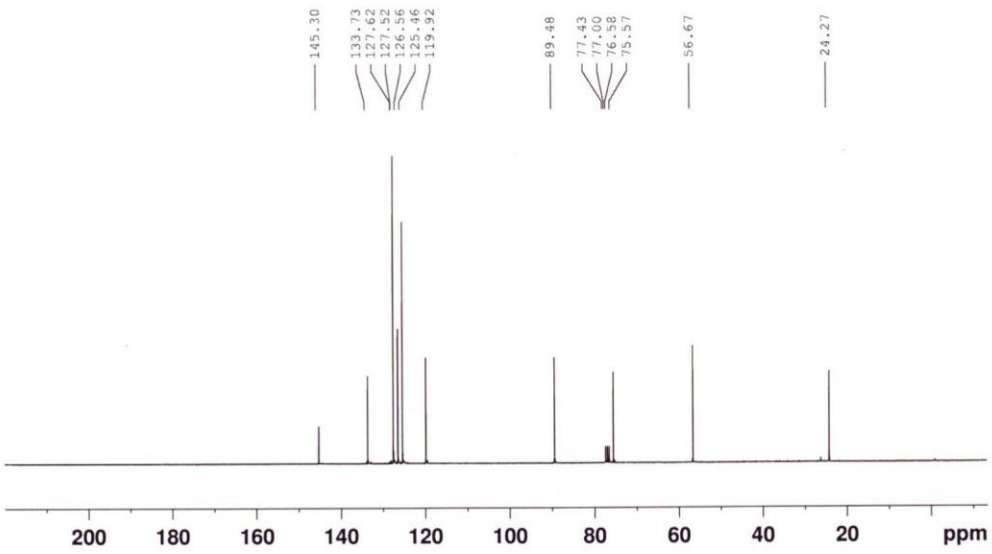


Figure 6. IR, ^{1}H and ^{13}C NMR of **10a*RR***.

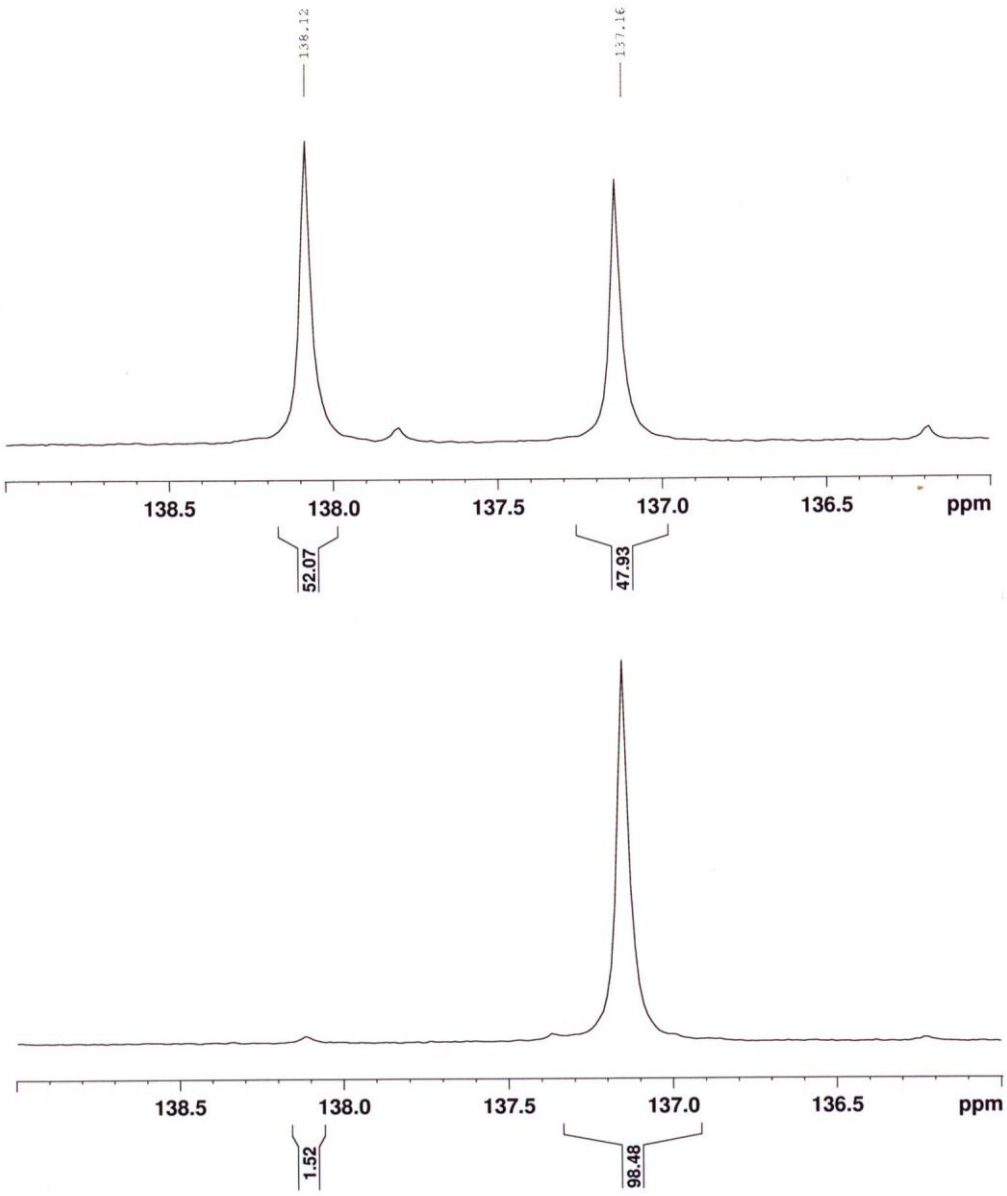
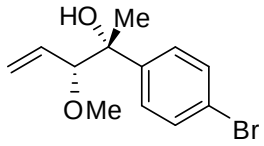
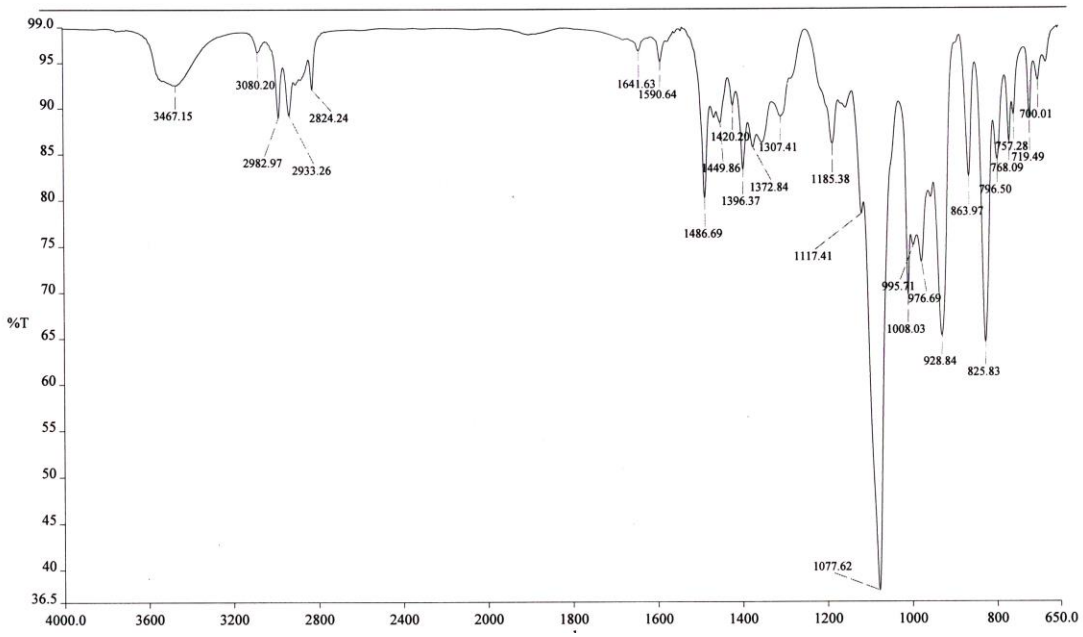


Figure 7. ^{31}P NMR of CDA derivative of **10a**.



(2*R*,3*R*)-2-(4-Bromophenyl)-3-methoxypent-4-en-2-ol (10b*RR*). From **1*S*** and *p*-bromoacetophenone (**8b**), for 16 h, yield 88%; Crude 98% de, Isolated 98% de; $[\alpha]_D^{20}$ +24.4 (*c* 1.3, $CHCl_3$), 98% ee. FTIR (CH_2Cl_2, cm^{-1}): 3467, 3080, 2983, 2933, 2824, 1642, 1591, 1487, 1396, 1185, 1078, 1008, 929, 826; ^1H NMR (300 MHz, $CDCl_3$) δ 1.41 (s, 3H), 3.22 (s, 4H), 3.59 (d, *J* = 7.9 Hz, 1H), 5.15 (d, *J* = 17.3 Hz, 1H), 5.30 (d, J = 10.4 Hz, 1H), 5.65 (m, 1H), 7.32 (d, *J* = 8.6 Hz, 2H), 7.43 (d, *J* = 8.5, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.4, 56.7, 75.4, 89.3, 120.6, 120.6, 127.5, 130.7, 133.4, 144.5; ^{31}P NMR (121.5 MHz, $CDCl_3$) δ 137.4 (99%), 138.4 (1%); HRMS (FAB) $[M + H - H_2O]^+$ calculated for $C_{12}H_{14}O^{79}Br$: 253.0222, found: 253.0220. (Figures 8, 9)



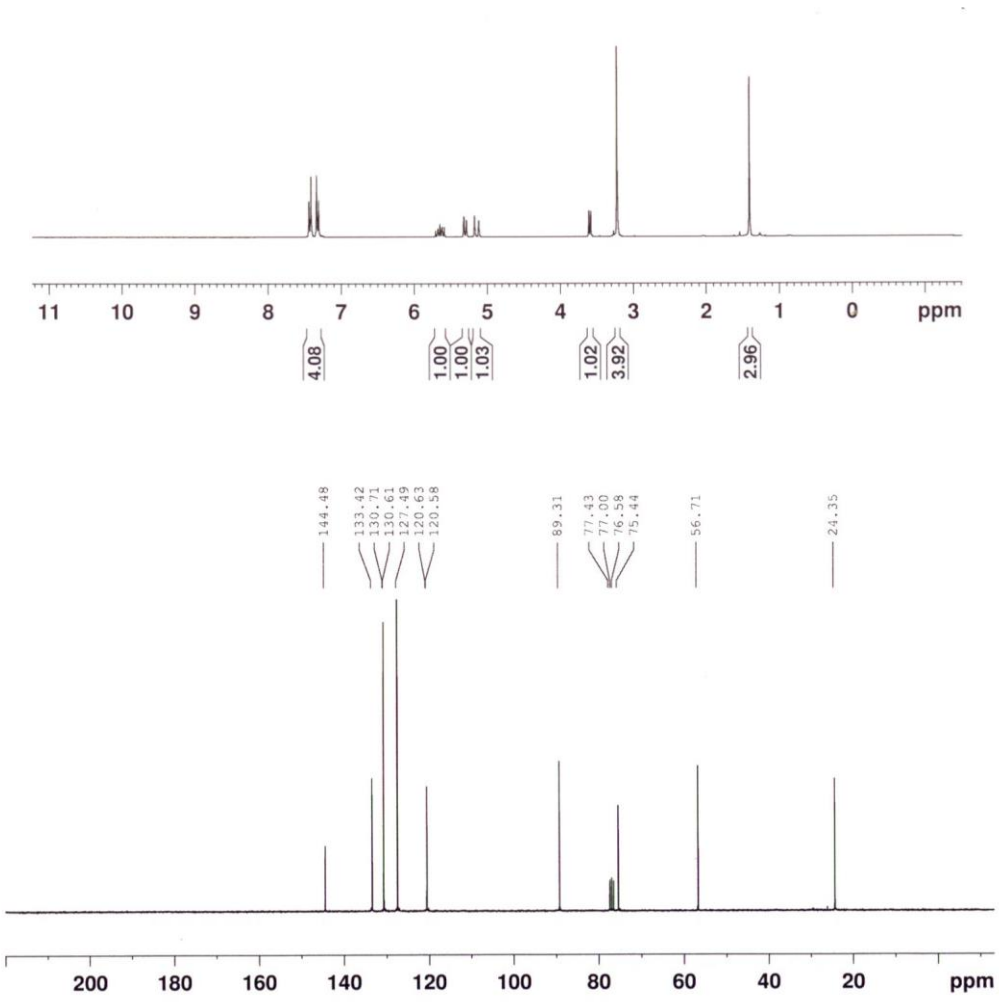


Figure 8. FTIR, ^{1}H and ^{13}C NMR of **10b*RR***.

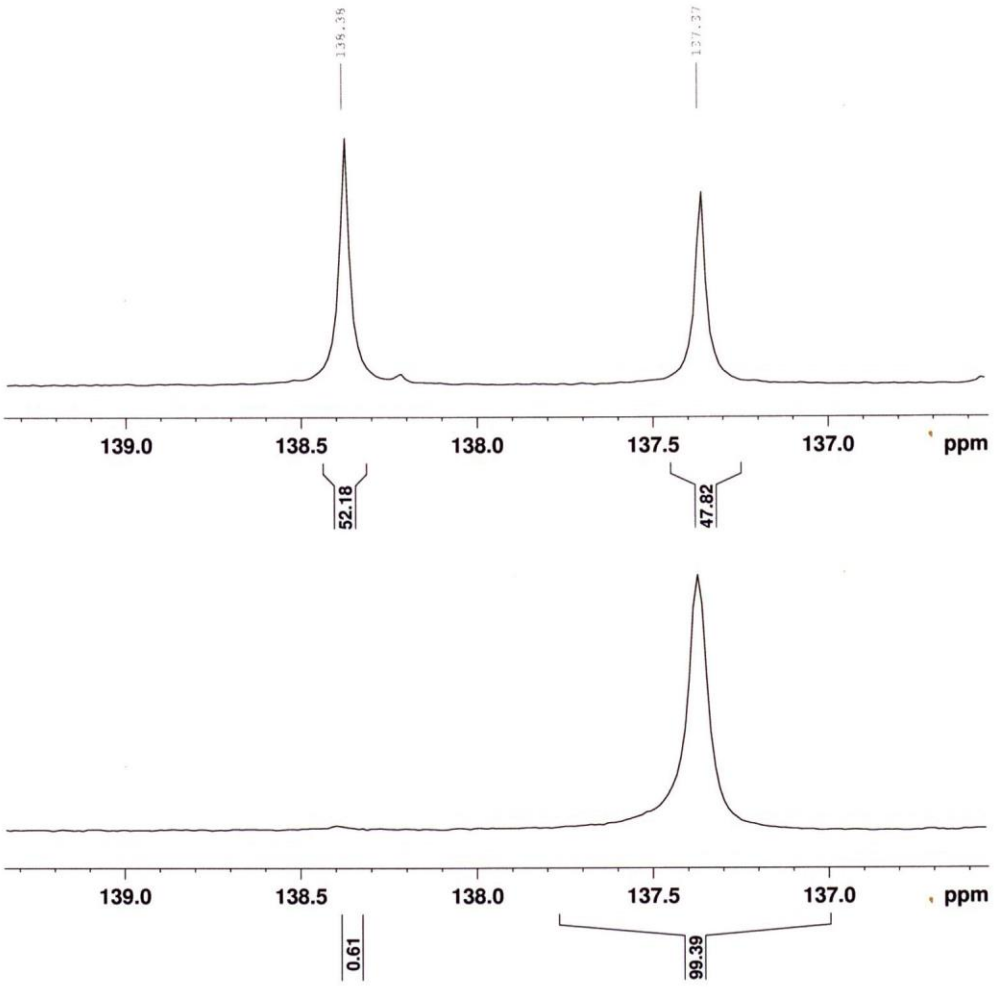
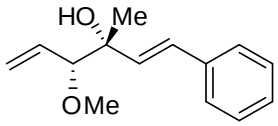
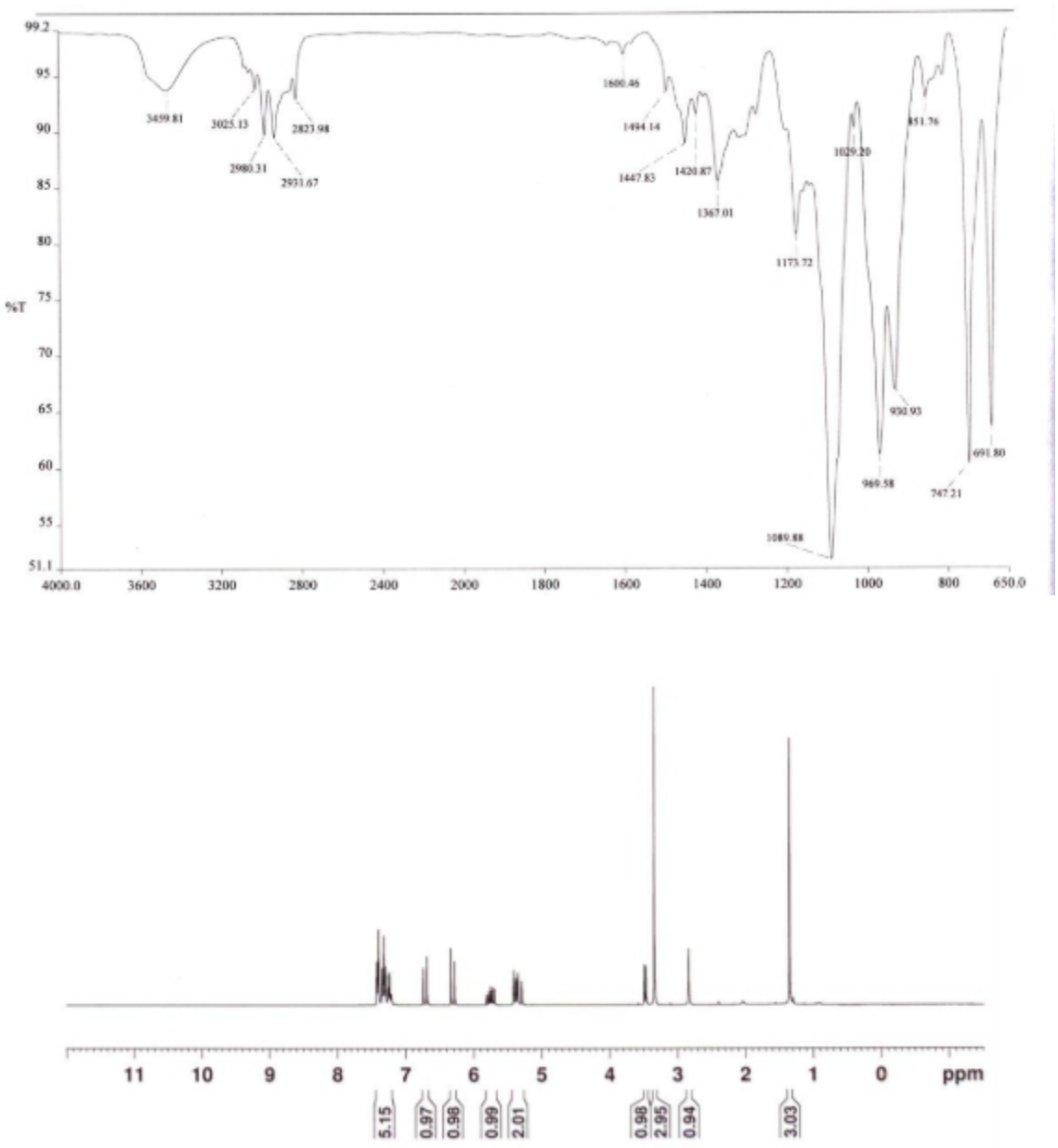


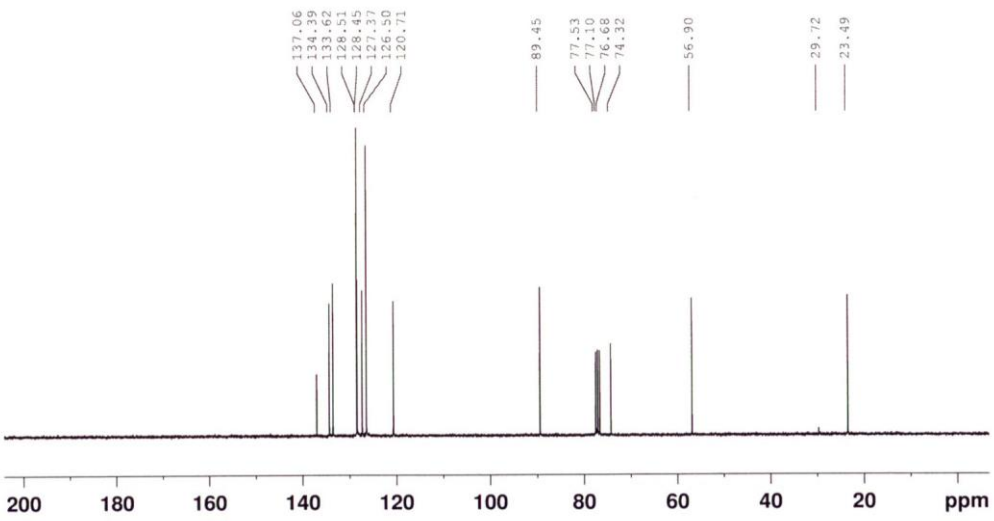
Figure 9. ^{31}P NMR of CDA derivative of **10b**.



(*E*)-(3*R*,4*R*)-4-Methoxy-3-methyl-1-phenylhexa-1,5-dien-3-ol (10c*RR*). From **1*S*** and (*E*)-4-phenylbut-3-en-2-one (**8c**) for 16 h, yield 65%; Crude 94% de, Isolated 96% de; $[\alpha]_D^{20}$ +14.5 (*c* 1.5, $CHCl_3$), 84% ee; FTIR (CH_2Cl_2, cm^{-1}): 3460, 3025, 2980, 2932, 2824, 1600, 1494, 1448, 1367, 1174, 1090, 970, 931, 747, 692; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35 (s, 3H), 2.84 (s, 1H), 3.34 (s, 3H), 3.48 (d,

J = 8.1 Hz, 1H), 5.32 (d, *J* = 17.2 Hz, 1H), 5.40 (dd, *J* = 1.7, 10.4 Hz, 1H), 5.76 (ddd, *J* = 8.1, 10.4, 17.2 Hz, 1H), 6.31 (d, *J* = 16.1 Hz, 1H), 6.72 (d, *J* = 16.1 Hz, 1H), 7.32 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.7, 56.9, 74.4, 89.5, 120.6, 126.5, 127.4, 128.5, 128.6, 133.8, 134.5, 137.2; ^{31}P NMR (121.5 MHz, $CDCl_3$) δ 137.6 (8%), 137.4 (92%); HRMS (FAB) $[M + H - H_2O]^+$ calcd for $C_{14}H_{17}O$: 201.1274, found: 201.1273 (Figure 10).





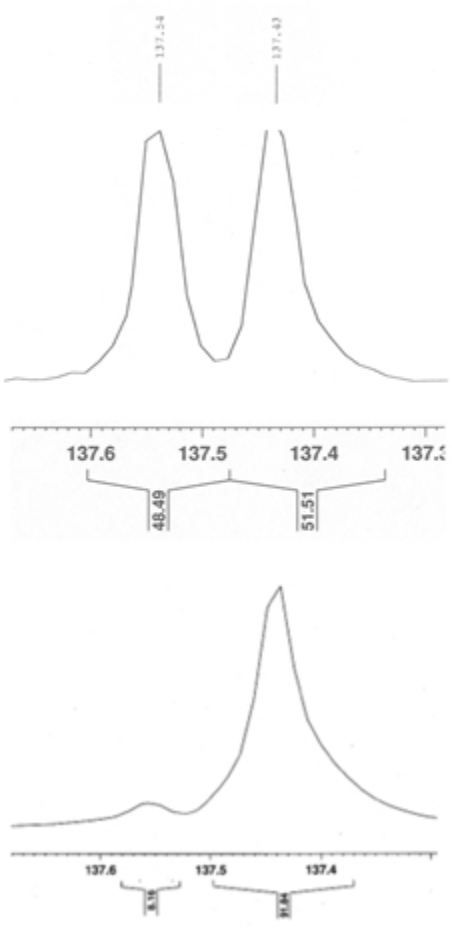
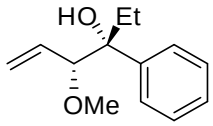
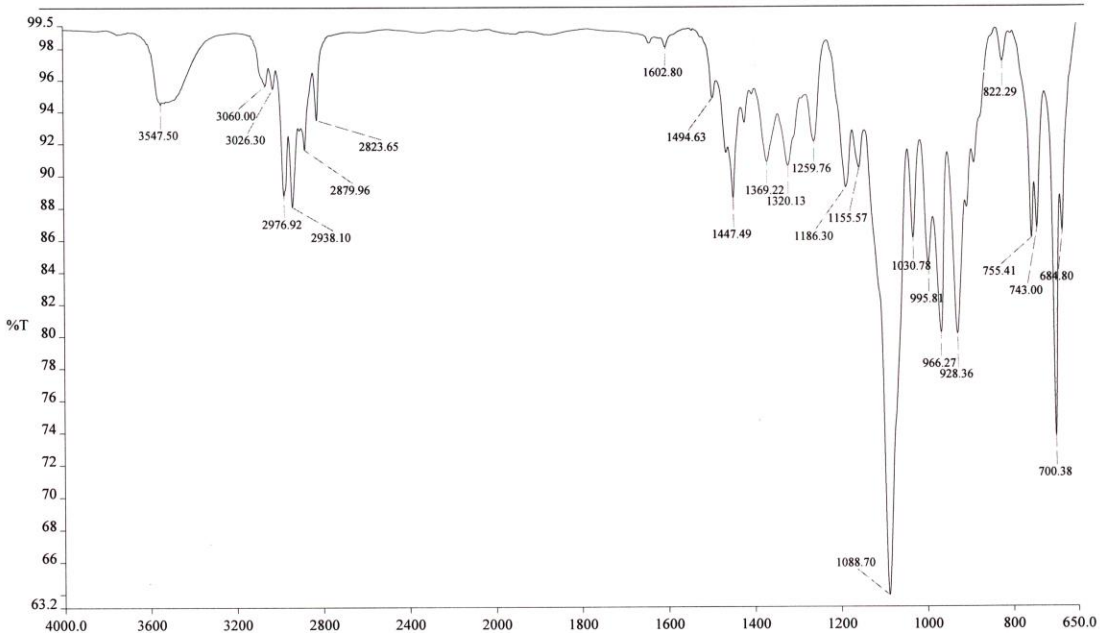


Figure 10. FTIR, ^{1}H, ^{13}C and ^{31}P (CDA derivative) NMR of **10c**.



(3*R*,4*R*)-4-Methoxy-3-phenylhex-5-en-3-ol (10d*RR*). From **1*S*** and propiophenone (**8d**), 4 h at -78 ^{o}C then slowly warmed to 25 ^{o}C for 20 h. Yield 68%; Crude 70% de, Isolated 86% de; $[\alpha]_D^{20}$ +22.7 (*c* 1.3, $CHCl_3$), 84% ee; FTIR (CH_2Cl_2, cm^{-1}): 3548, 3060, 3026, 2977, 2938, 2880, 2824, 1603, 1447, 1369, 1320, 1260, 1186, 1156, 1089, 966, 928, 700; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.70 (t, *J* = 7.4 Hz, 3H), 1.81 (q, *J* = 7.4 Hz, 2H), 2.85 (br s, 1H), 3.21 (s, 3H), 3.69 (d, *J* = 8.2 Hz, 1H), 5.22 (d, *J* = 17.3 Hz, 1H), 5.35 (d, *J* = 10.4 Hz, 1H), 5.75 (ddd, *J* = 8.2, 10.3, 17.3 Hz, 1H), 7.35 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 7.0, 26.6, 29.5, 56.3, 78.0, 89.1, 119.8, 125.9, 126.1, 127.4, 133.8, 143.4; ^{31}P NMR (121.5 MHz, $CDCl_3$) δ 137.3 (8%), 137.9 (92%); HRMS (FAB) $[M + H - H_2O]^+$ calculated for $C_{13}H_{17}O$: 189.1274, found: 189.1272. (Figures 11, 12)



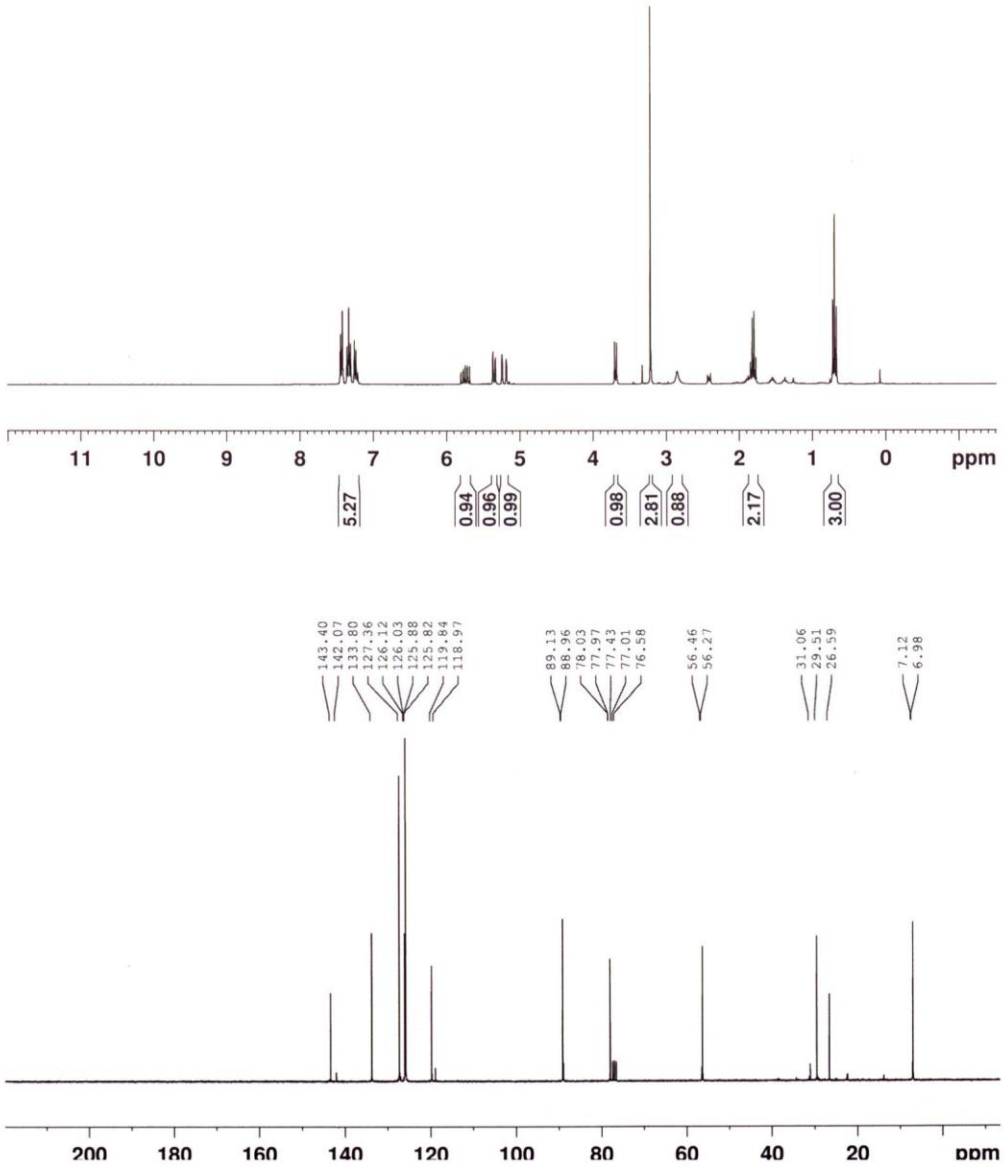


Figure 11. FTIR, ^{1}H and ^{13}C NMR of **10d*RR***.

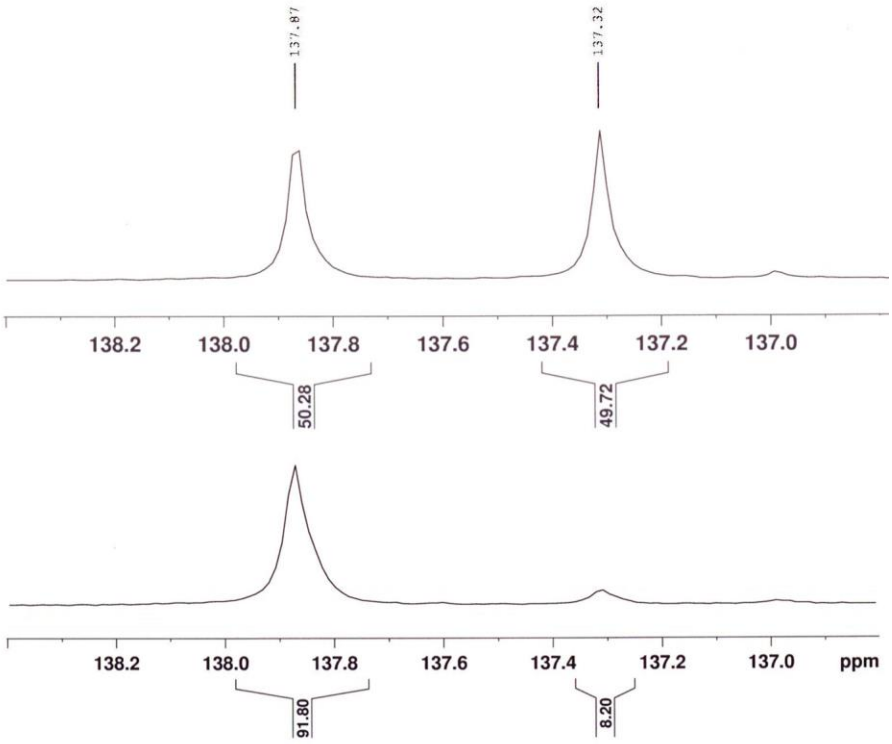
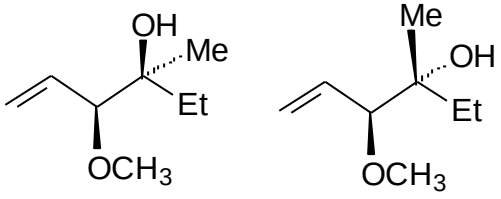
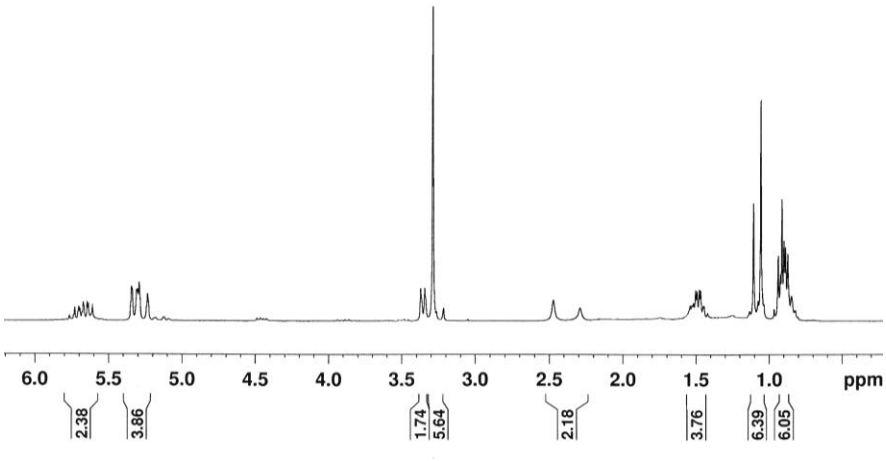


Figure 12. ^{31}P NMR of CDA derivative of **10d**.



(3*S*,4*S*)-4-Methoxy-3-methoxy-3-methylhex-5-en-3-ol and (3*S*,4*R*)-4-Methoxy-3-methylhex-5-en-3-ol mixture (10e*SS*) and (10e*SR*). From **1*R*** and methyl ethyl ketone (**8e**) for 36 h, yield 60%; Crude 48% de (major isomer is the *syn*); Isolated 56% de; $[\alpha]_D^{20}$ -4.3 (*c* 1.1, CH_2Cl_2); 70% ee; ^{1}H NMR (300 MHz, $CDCl_{3)}$ δ 0.91 (m, 6H), 1.06 (major) and 1.11 (minor) (two singlets, 6H), 1.49 (m, 4H), 2.29 (minor) and 2.48 (major) (two singlets, 2H), 3.29 (s, 6H), 3.35 (two

overlapped doublets, *J* = 8.3, 2H), 5.29 (m, 4H), 5.71 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 7.4 (minor), 7.5 (major), 21.4 (major), 22.5 (minor), 29.3 (major), 31.1 (minor), 56.6 (major), 56.8 (minor), 73.8 (single peak), 88.5 (major), 89.8 (minor), 119.4 (minor), 119.9 (major), 134.6 (single peak); ^{31}P NMR (121.5 MHz, $CDCl_3$) δ 138.2 (85%), 138.8 (15%) (major isomer). ^{13}C NMR (75 MHz, $CDCl_3$) δ 7.4 (minor), 7.5 (major), 21.4 (major), 22.5 (minor), 29.3 (major), 31.1 (minor), 56.6 (major), 56.8 (minor), 73.8 (single peak), 88.5 (major), 89.8 (minor), 119.4 (minor), 119.9 (major), 134.6 (single peak); ^{31}P NMR (121.5 MHz, $CDCl_3$) δ 138.2 (85%), 138.8 (15%) (major isomer). HRMS (APCI) [M + H - H2O]+ calcd for C8H15O : 127.1123, found 127.1127. (Figures 13, 14)



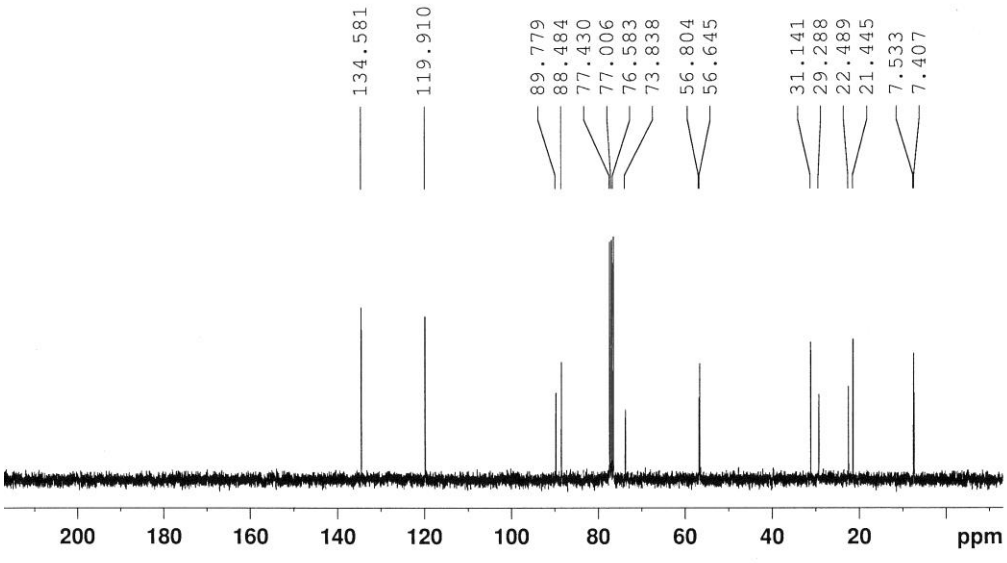


Figure13. ^{1}H and ^{13}C of **10e.**

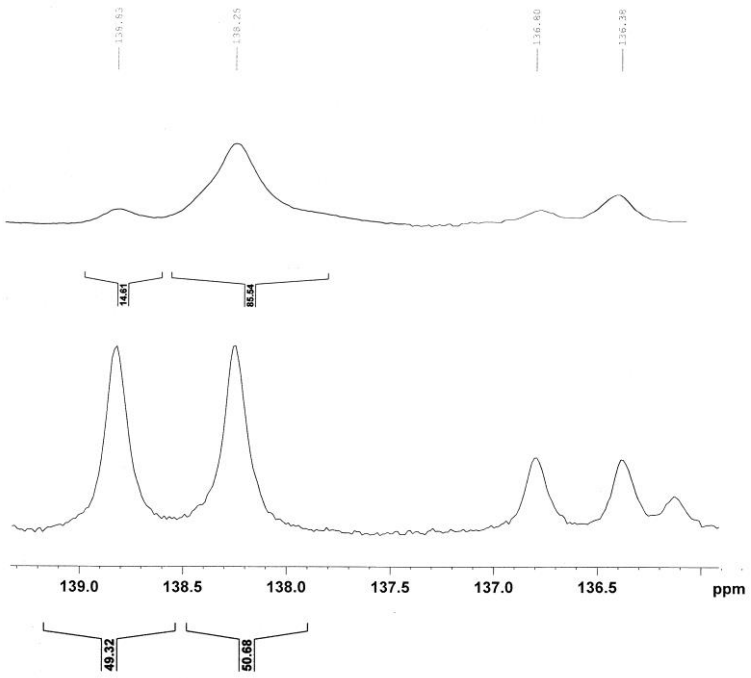
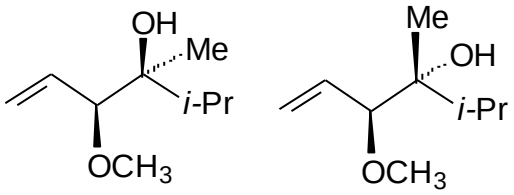
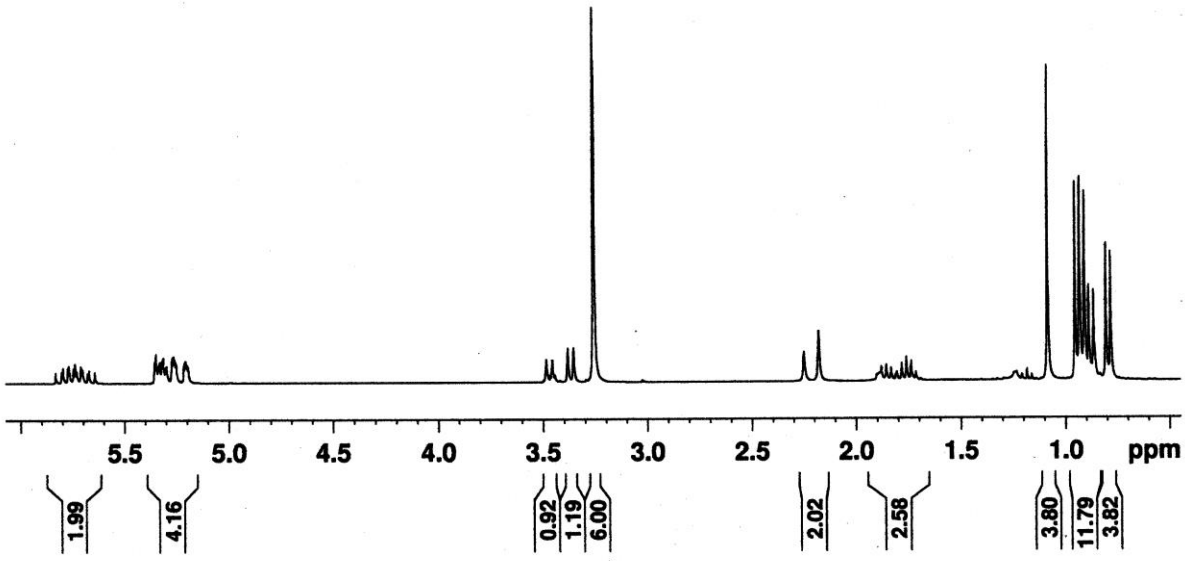


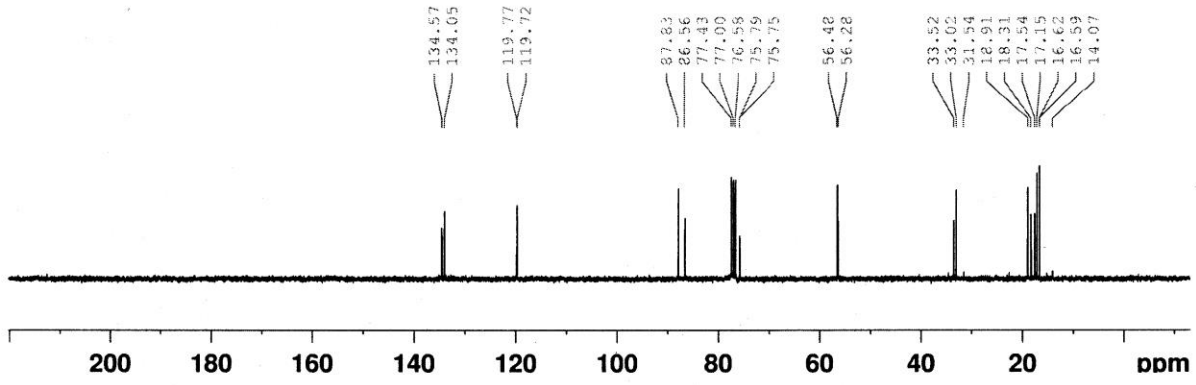
Figure 14. ^{31}P (CDA derivative) NMR of **10e**. The ^{31}P NMR shows the major (*syn*) isomer peaks at the left (as two enantiomers) and the minor (*anti*) isomer peaks at the right (as two enantiomers).



(3*S*,4*S*)-4-Methoxy-2,3-dimethylhex-5-en-3-ol (10f*SS*) and (3*S*,4*R*)-4-Methoxy-2,3-dimethyl-5-en-3-ol (10f*SR*). From **1*R*** and 3-methyl-2-butanone (**8f**), for 36 h, yield 54%; Crude 12% de, Isolated 22% de (enriched in the minor component present in the crude (the isolated sample has more of the *anti* isomer,

and the crude sample has more of the *syn* isomer)); $[\alpha]_D^{20}$ -9.7 (*c* 1.0, CH_2Cl_2); 68% ee (both isomers); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.78 (d, *J* = 6.9 Hz , 3H), 0.91 (m, 12H), 1.09 (s, 3H), 1.81 (m, 2H), 2.18 (s, 1H), 2.25 (s, 1H), 3.26 (m, 6H) (two partially overlapped singlets), 3.37 (d, *J* = 8.4, 1H), 3.47 (d, *J* = 8.4, 1H), 5.27 (m, 4H), 5.74 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.6 (minor), 16.6 (major), 17.2 (major), 17.5 (minor), 18.3 (major), 18.9 (major), 33.0 (major), 33.5 (minor), 56.3 (minor), 56.5 (major), 75.7 (minor), 75.8 (major), 86.6 (minor), 87.8 (major), 119.7 (major), 119.8 (minor), 134.0 (major), 134.6 (minor); ^{31}P NMR (121.5 MHz, $CDCl_3$) δ 139.2 (16%), 138.6 (84%) (major isomer, both peaks are the enantiomers of the *syn* isomer, as this was taken from the crude mixture), 136. 5 (16%), 136.8 (84%) (minor isomer, both peaks are the enantiomers of the *anti* isomer, as this was taken from the crude mixture).HRMS (APCI) [M + H - H2O]+ calculated for C9H17O: 141.1279, found 141.1273. (**Figure 15**).





The ^{31}P NMR spectra below shows the major (*syn*) isomer peaks at the left (as two enantiomers) and the minor (*anti*) isomer peaks at the right (as two enantiomers), this sample was taken from the crude to show the original diastereomeric composition (56 *syn*:44 *anti*).

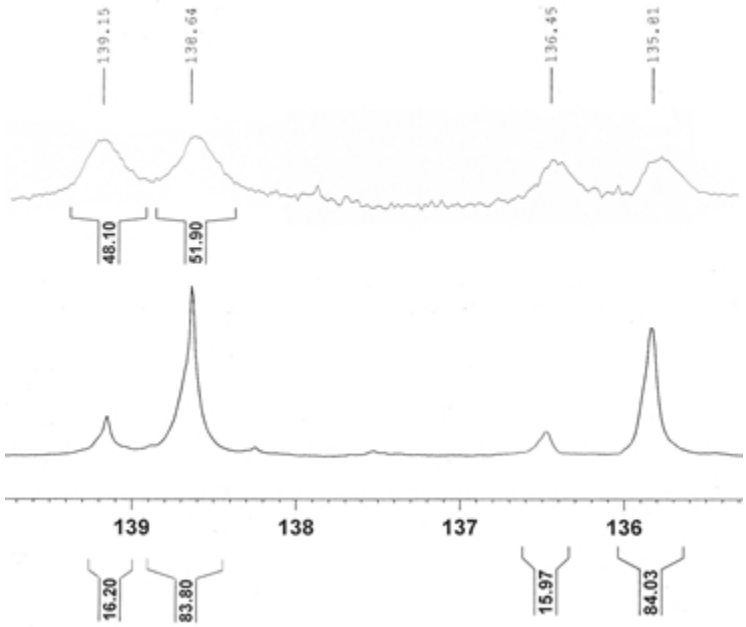
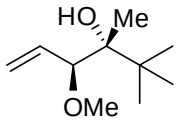
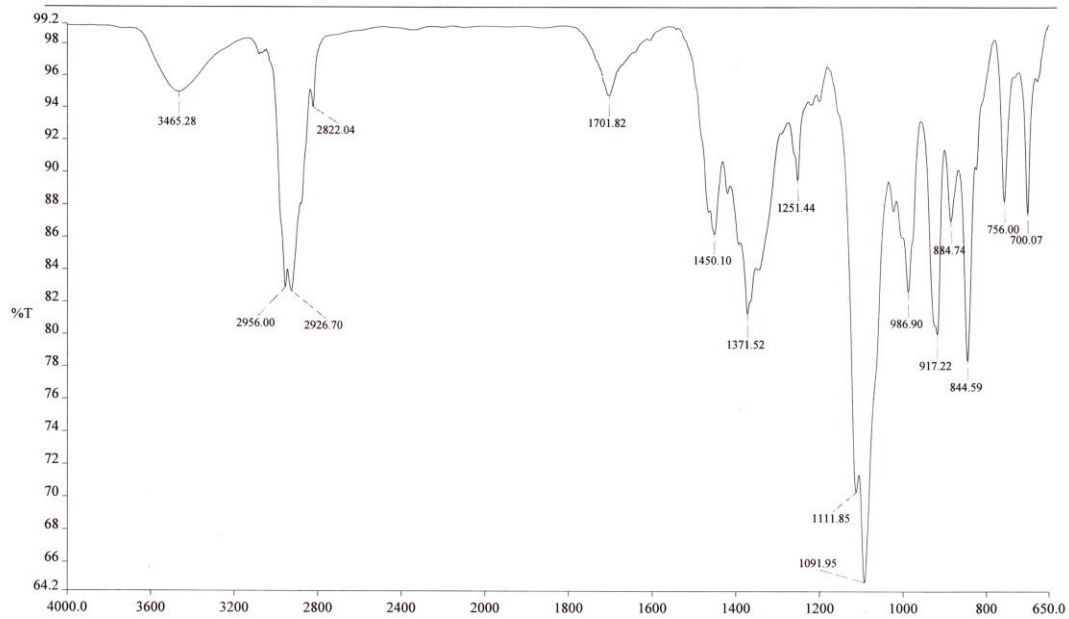


Figure 15. ^{1}H, ^{13}C and ^{31}P (CDA derivative) NMR of **10f**.



(3*R*,4*S*)-4-Methoxy-2,2,3-trimethylhex-5-en-3-ol (10g*RS*). From **1*S*** (isomerizes to **7*S***) and 3,3-dimethylbutan-2-one (**8g**), 4 h at -78 ^{o}C then slowly warmed to 25 ^{o}C for 36 h. Yield 45%; Crude 98% de, Isolated 98% de; $[\alpha]_D^{20}$ +14.5 (*c* 1.5, $CHCl_3$), 92% ee; FTIR (CH_2Cl_2, cm^{-1}): 3465, 2956, 2927, 2822, 1702, 1450, 1372, 1251, 1112, 1092, 987, 917, 845, 756, 700; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.98 (s, 9H), 1.13 (s, 3H), 1.52 (s, 1H), 3.22 (s, 3H), 3.61 (d, *J* = 7.9 Hz, 1H), 5.27 (d, *J* = 17.3 Hz, 1H), 5.36 (d, *J* = 10.4 Hz, 1H), 5.82 (ddd, *J* = 7.9, 10.4, 17.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.8, 26.3, 37.8, 56.2, 76.4, 87.3, 119.8, 135.9; ^{31}P NMR (121.5 MHz, $CDCl_3$) δ 136.0 (4%), 136.7 (96%); HRMS (FAB) $[M + H]^+$ calculated for $C_{10}H_{21}O_2$: 173.1536, found: 173.1535. (**Figures 16, 17** and **18**).



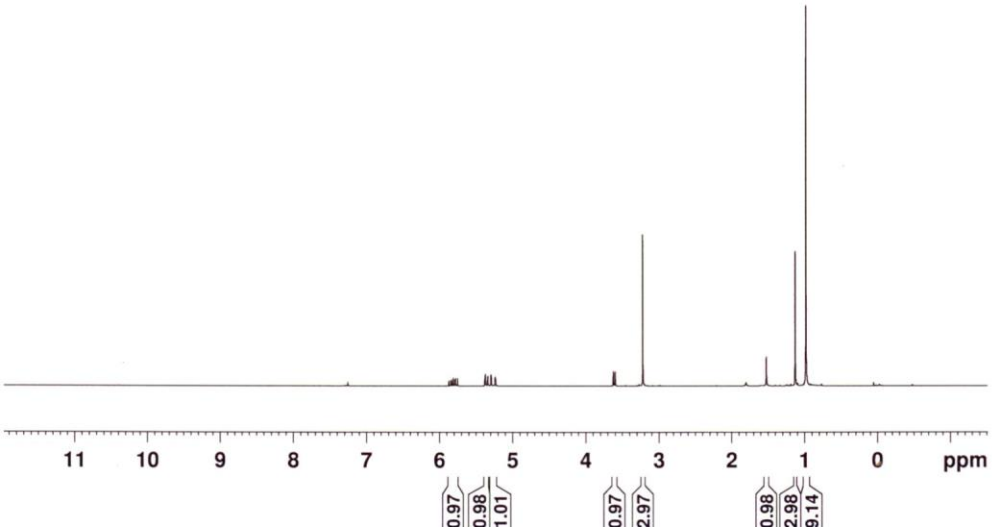


Figure 16. FTIR and ^{1}H NMR of **10g*RS***.

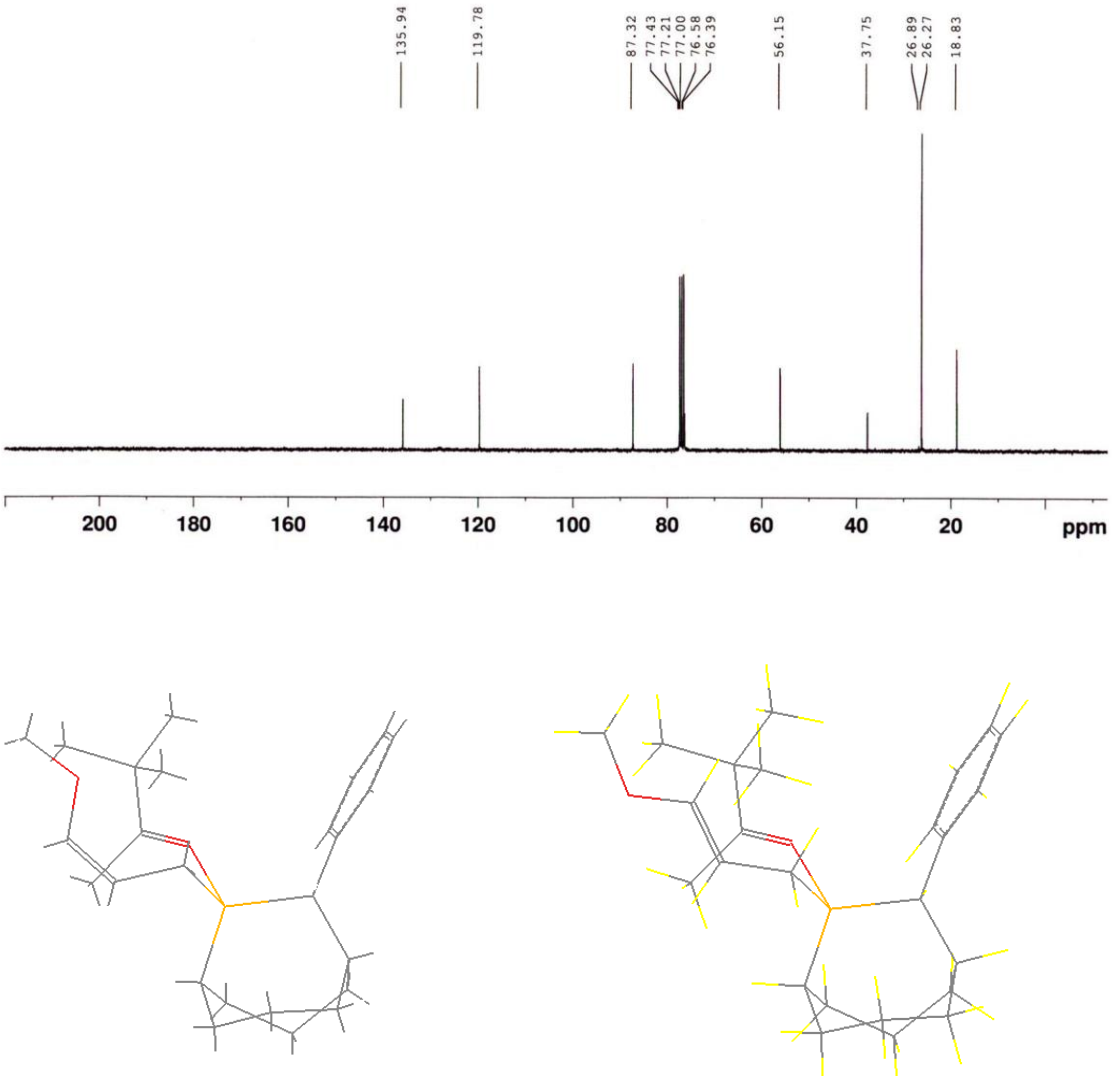


Figure 17. ^{13}C NMR of **10g*RS*** and MM (Spartan 06) structures for ***Z*–18** *vs* more stable ***E*–18** (ΔE ~2 kcal/mol).

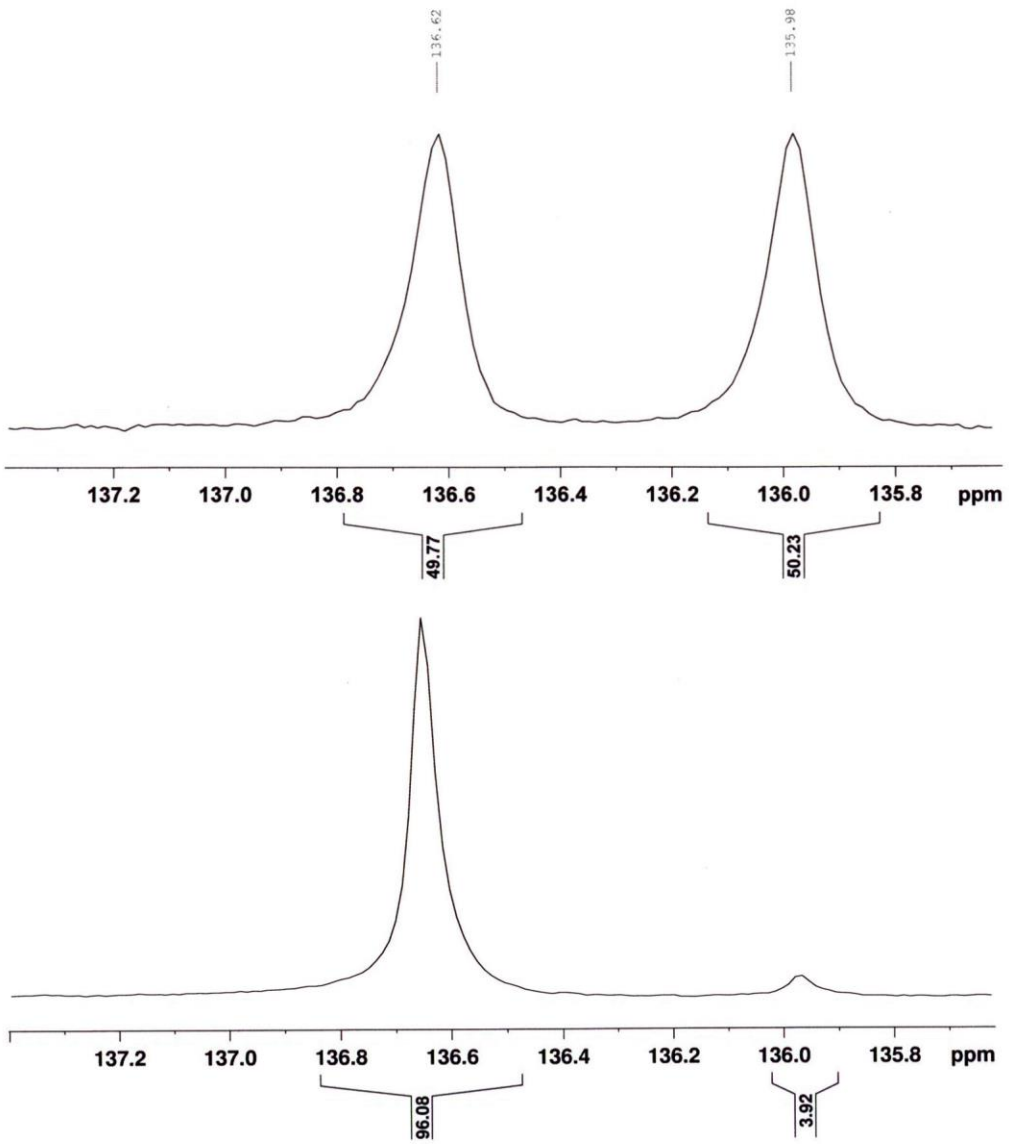
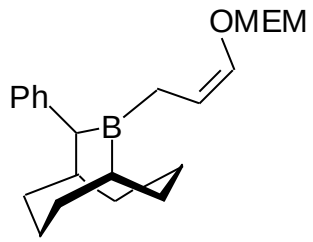
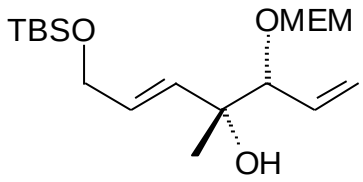


Figure 18. ^{31}P NMR of CDA derivative of **10g**.

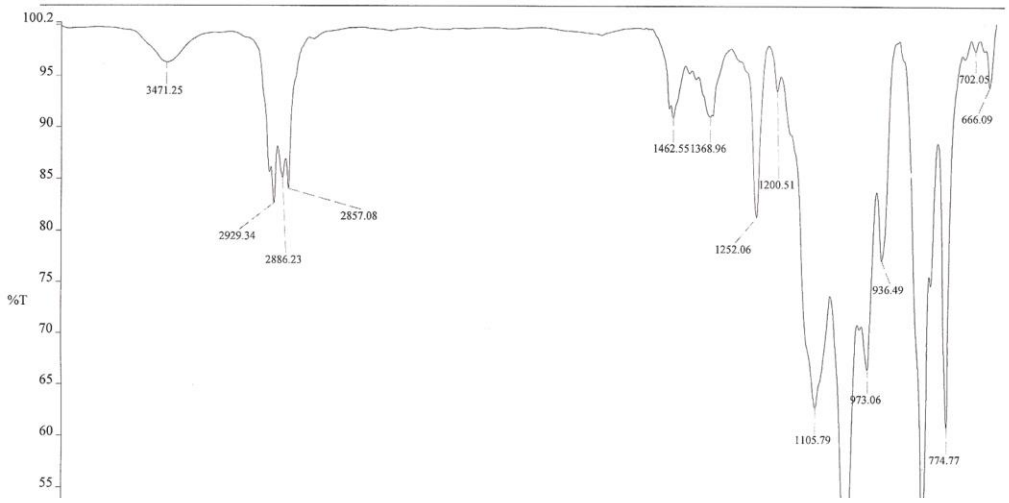


(10*S*)-*B*-[(*Z*)-γ-[(2-Methoxyethoxy)methoxyallyl]-10-phenyl-9-borabicyclo-[3.3.2]decane (22*S*). To a stirred solution of 3-[(2-methoxyethoxy)methoxy]prop-1-ene[3] (0.658 g, 4.5 mmol) in THF (2 mL) was added *sec*-butyllithium in cyclohexane (2.7 mL, 1.48 M, 4 mmol) at -78 ^{o}C, dropwise. The mixture was stirred at -78 ^{o}C for 30 min and to it was added via cannula **4*S*** in 1 mL of THF (0.727 g, 3 mmol). After the reaction mixture was stirred at -78 ^{o}C for 2 h, TMSCl (0.57 mL, 4.5 mmol) in 0.5 mL of THF was added via cannula at -78 ^{o}C. After 30 min at -78 ^{o}C, the resultant solution was immediately used without purification. The **22*R*** can be prepared by the same procedure starting with **4*R***.



(3*R*,4*R*)-5*E*-7-(*tert*-butyldimethylsilanyloxy)-3-(2-methoxyethoxymethoxy)-4-methylhepta-1,5-dien-4-ol (23). From **22*S*** and **21**[4] for 16 h, yield 81%; 94% de;

$[\alpha]_D^{20}$ -26.1 (*c* 1.8, C_6D_6), 82% ee; FTIR (CH_2Cl_2, cm^{-1}): 3471, 2929, 2886, 2857, 1463, 1370, 1252, 1106, 1025, 973, 936, 833, 775; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.05 (s, 6H), 0.90 (s, 9H), 1.22 (s, 3H), 2.64 (s, 1H), 3.39 (s, 3H), 3.54 (m, 2H), 3.62 (m, 1H), 3.84 (m, 1H), 3.88 (d, *J* = 8.0 Hz, 1H), 4.19 (d, *J* = 4.4 Hz, 2H), 4.68 (d, *J* = 6.9 Hz, 1H), 4.76 (d, J = 6.9 Hz, 1H), 5.30 (m, 2H), 5.76 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ -5.5 (2 carbons), 18.1, 23.2, 25.7 (3 carbons), 58.6, 63.0, 66.9, 71.5, 73.4, 83.5, 92.6, 120.1, 128.0, 133.7, 133.8; ^{31}P NMR (121.5 MHz, $CDCl_3$) δ 137.2 (9%), 136.7 (91%). ESI-MS: 383 (Na adduct) lit.[3] ESI-MS: 383 (Na adduct) (**Figures 19, 20**)



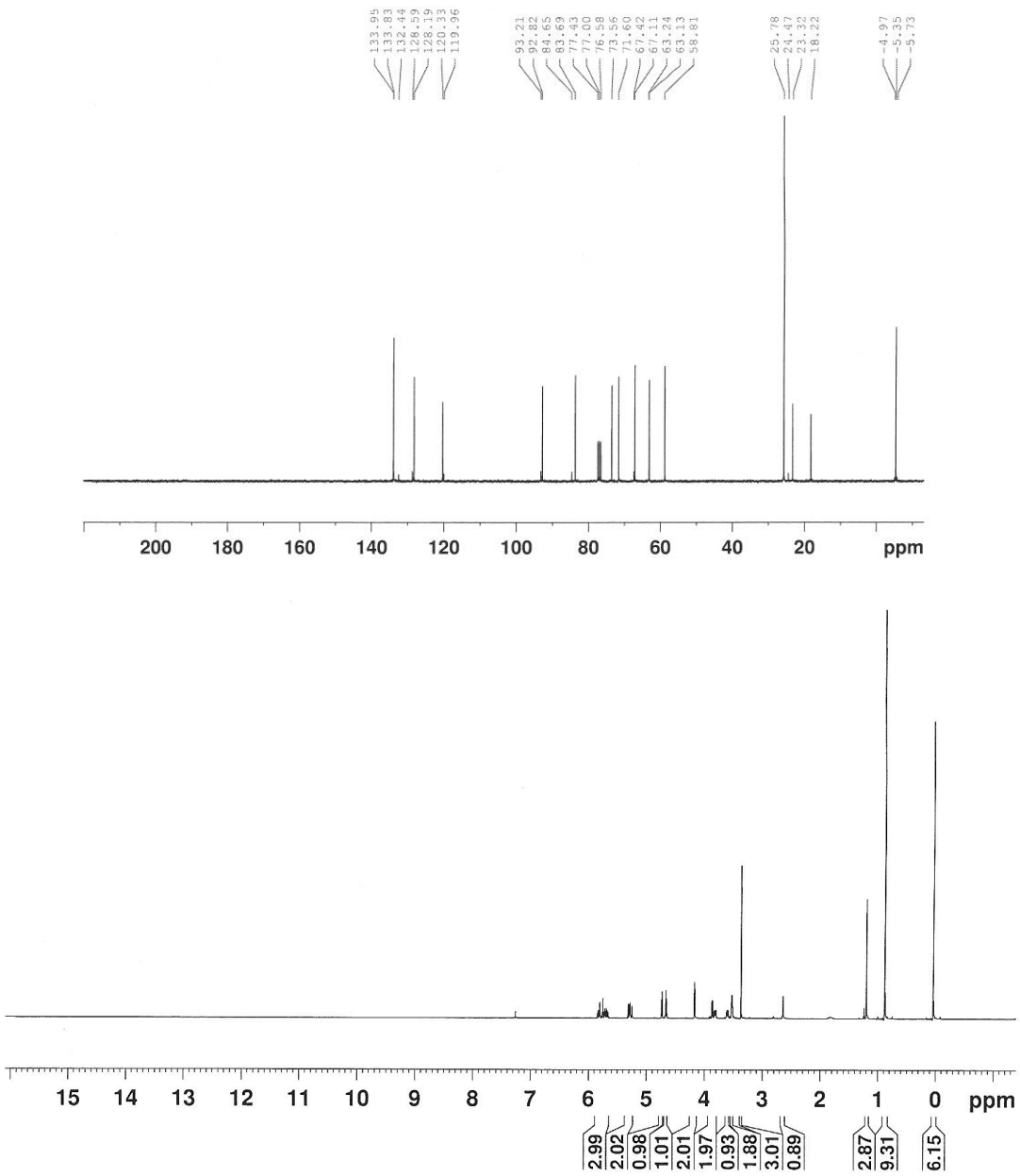


Figure 19. FTIR, ^{13}C and ^{1}H NMR of **23**.

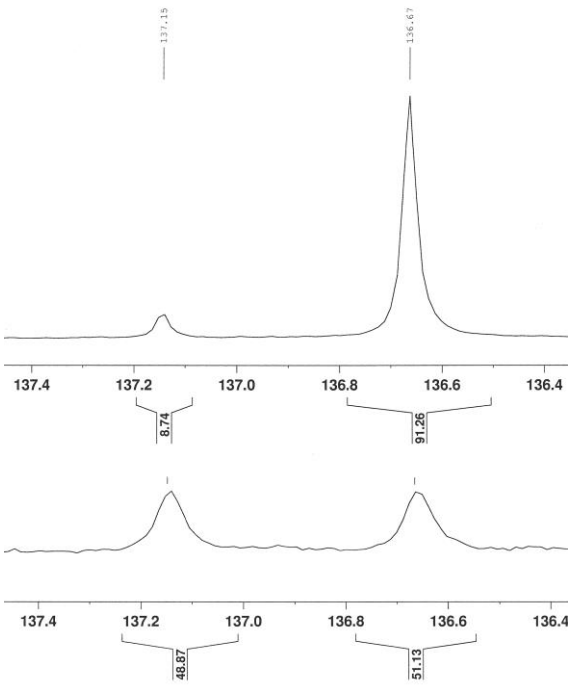
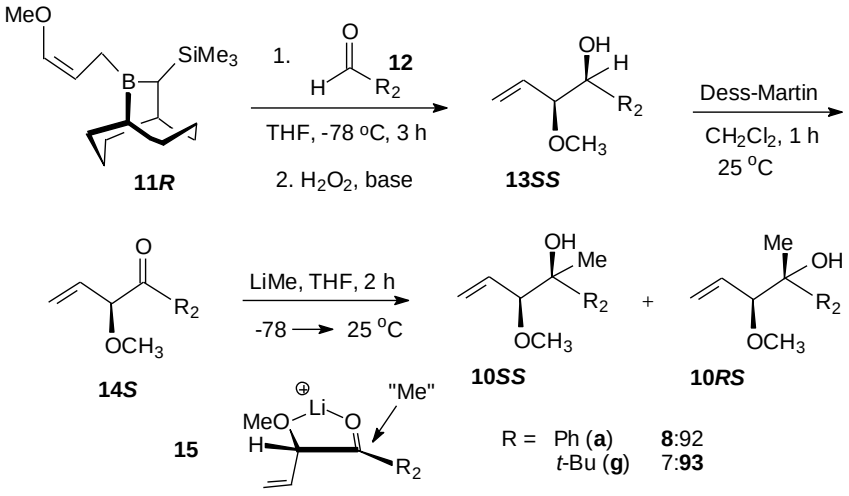


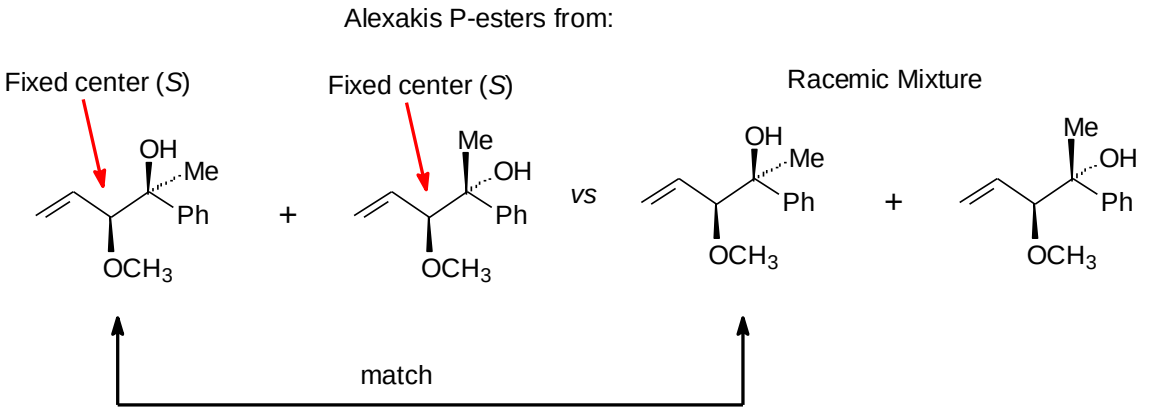
Figure 20. ^{31}P NMR of CDA derivative of **23**.

Determination of the absolute configuration of tertiary alcohols



Scheme 1. Synthesis of diastereomers **10a*SS*** and **10a*RS*** *via* nucleophilic addition to determine the absolute configuration of **10**.

One of the diastereomers formed from the sequence above had to match the absolute stereochemistry of either **10a*SS*** or **10a*RR*** in the racemic mixture/optically active sample (**1*S*** was used for the optically active sample, we expect **10a*RR*** as the major peak and **10a*SS*** as the minor peak for the Alexakis esters in the ^{31}P NMR) and thus confirm the absolute stereochemistry predicted by our model (**Schemes 1, 2 and Figure 21**).



Scheme 2. Fixed asymmetric centers after oxidation/nucleophilic addition protocol vs racemic mixture of the alkoxyallylboration of ketones.

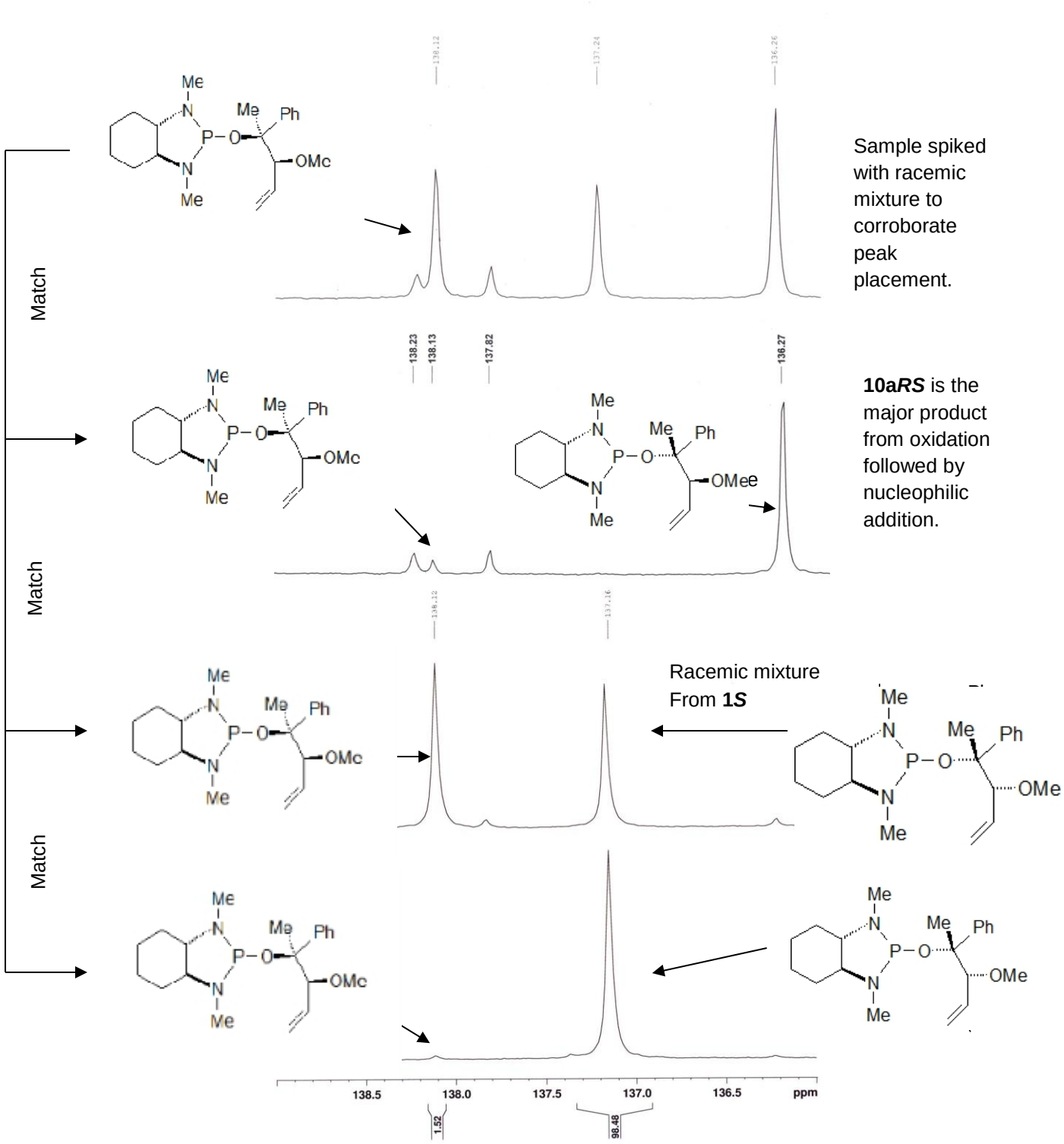


Figure 21. ^{31}P NMR analysis to determine absolute configuration of alcohol **10a*RR*** from **1*S***.

(2*R*,3*S*)-3-Methoxy-2-phenylpent-4-en-2-ol (10a*RS*) and (2*S*,3*S*)-3-methoxy-2-phenylpent-4-en-2-ol (10a*SS*) mixture. A solution of **13a*SS***[2] (0.1589 g, 0.89 mmol) in anhydrous CH_2Cl_2 (2 mL) was treated with Dess-Martin periodinane (0.5089 g, 1.2 mmol). The mixture was allowed to stir at 25 ºC for 30 min, then 5 mL of 10% aqueous $Na_2S_2O_3$ and 1.5 mL saturated aqueous $NaHCO_3$ were added. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). The organic layers were combined and dried (Na_2SO_4), filtered and solvents were removed under vacuum. The ketone product (*S*)-2-methoxy-1-phenylbut-3-en-1-one (**14a*S***) was used on the next step without further purification. Yield (crude), 90%; $[\alpha]_D^{20}$ -25.430 (*c* 5.8, CH_2Cl_2), ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.37 (s, 3H), 4.89 (d, *J* = 6.4, 1H), 5.32 (d, *J* = 10.6, 1H), 5.47 (d, *J* = 17.3 Hz, 1H), (ddd, *J* = 6.4, 10.6, 17.3 Hz, 1H), 7.45 (m, 3H), 7.99 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 56.9, 85.8, 119.8, 128.5, 128.8, 133.1, 133.3, 134.6, 197.3. (**Figures 22, 23**)

A solution of **14a*SS*** (0.0810 g, 0.46 mmol) in THF (0.5 mL) was added to a solution of MeLi (1.6 M in diethyl ether, 0.31 mL, 0.50 mmol) in anhydrous THF (0.5 mL) at -78 ^{o}C. After stirring at -78 ^{o}C for 2 h, 4 mL of a saturated solution of NH_4Cl was added *via* syringe. The layers were diluted with ether and separated, the aqueous layer was extracted with ether (2 x 5 mL); the organic layers were combined and dried (Na_2SO_4). The product diastereomeric tertiary alcohols showed a NMR spectra where the mixture could be identified as 8:92 *syn:anti* and was directly used in the ^{31}P NMR Alexakis CDA reagent analysis (**Figure 24**).

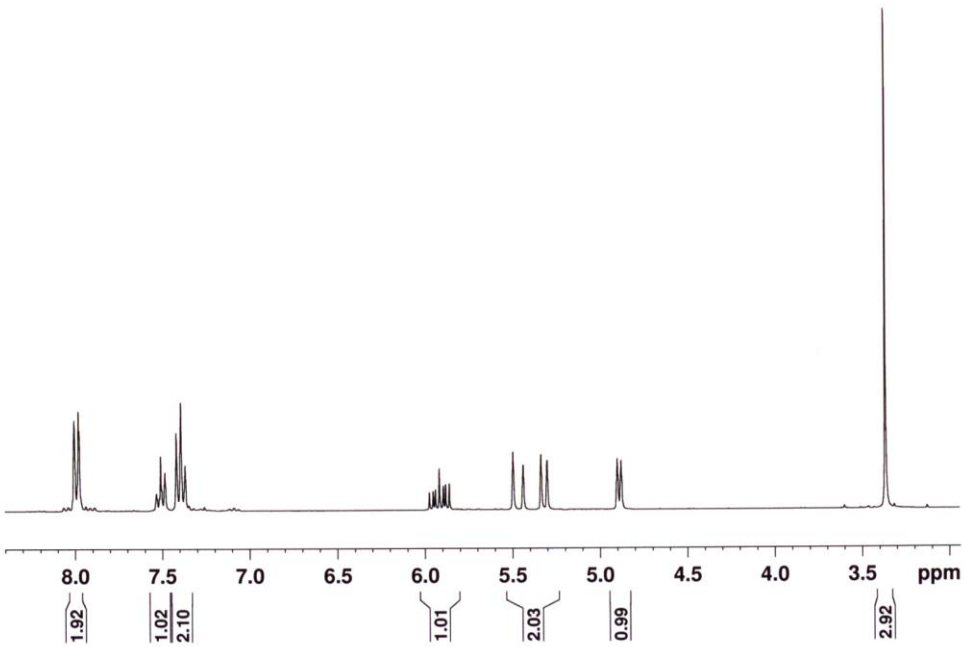


Figure 22. ^{1}H NMR of crude **14a*SS***.

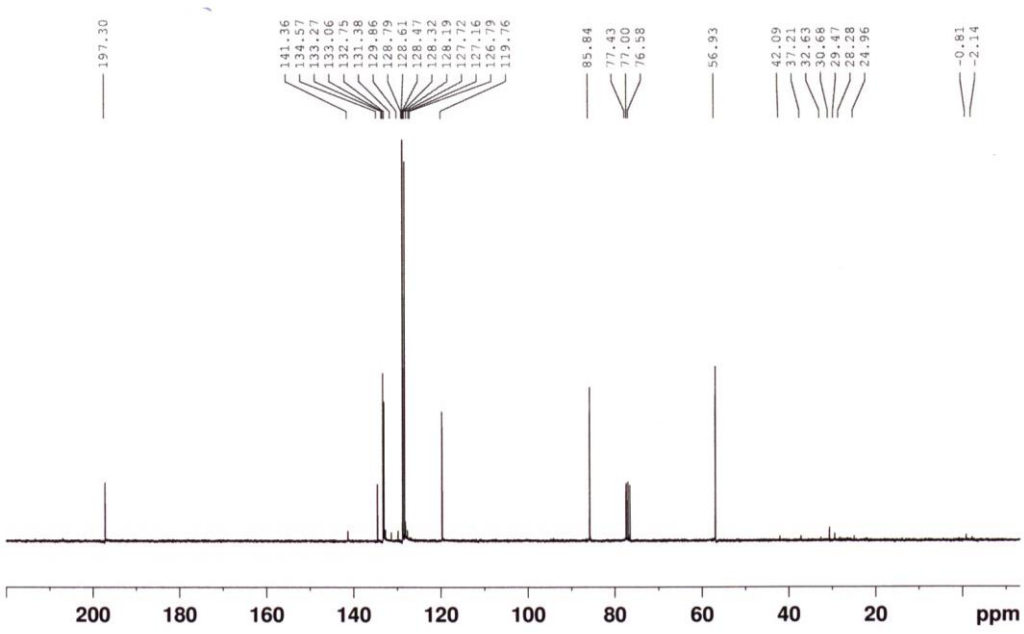


Figure 23. ^{13}C NMR of crude **14a*SS***.

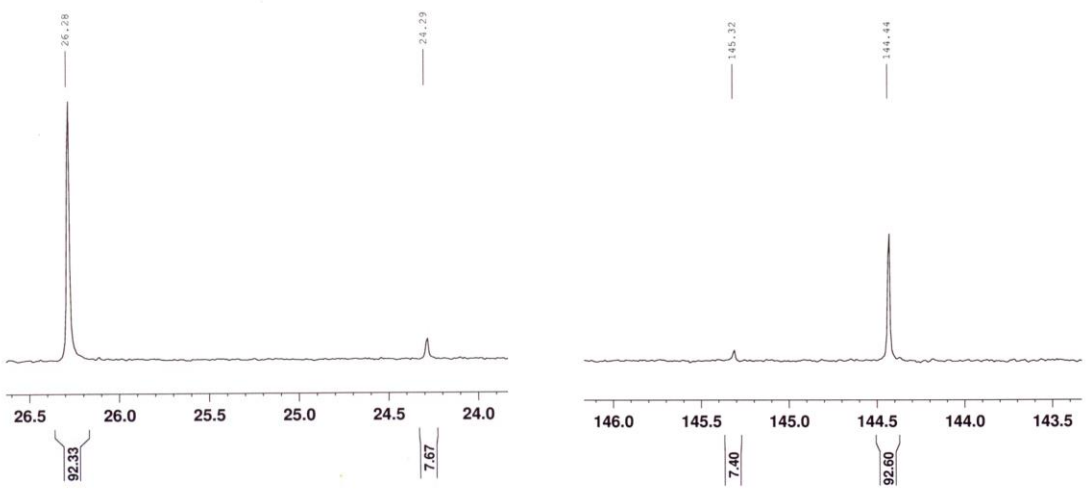


Figure 24. Selected ^{13}C NMR spectra expansions of the *anti*/*syn* mixture of **10a*RS*** and **10a*SS*** exhibiting 92% *anti*, 8% *syn*.

After careful examination of the ^{13}C NMR signals of the *syn*/*anti* diastereomeric mixture, we concluded that the signals in our **10g** (R_2 = *t*-Bu) product matched the ones on the major (*anti*) signals in the mixture obtained by the oxidation/nucleophilic addition protocol (**Scheme 1**) (**Figure 25**).

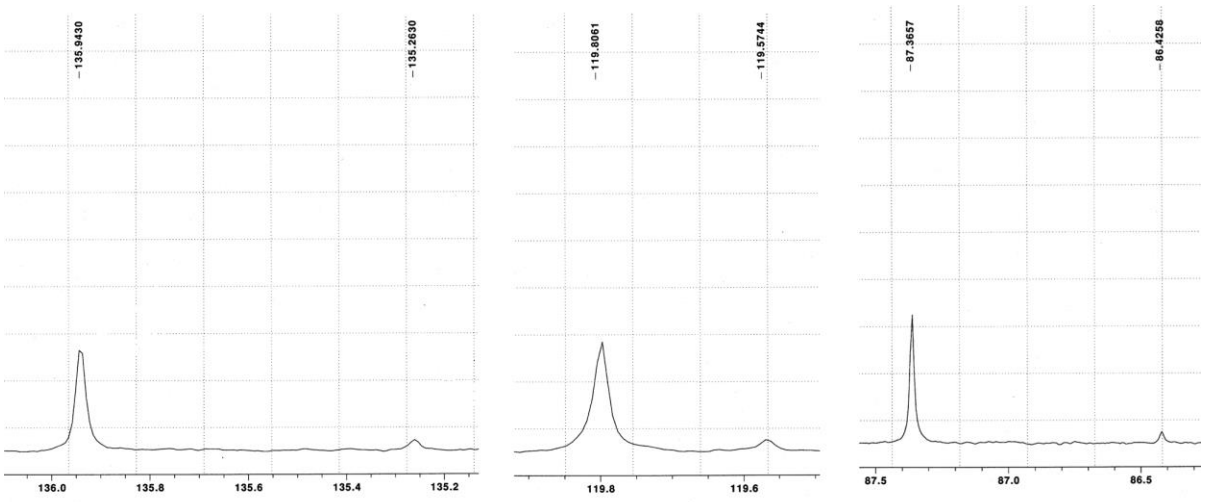
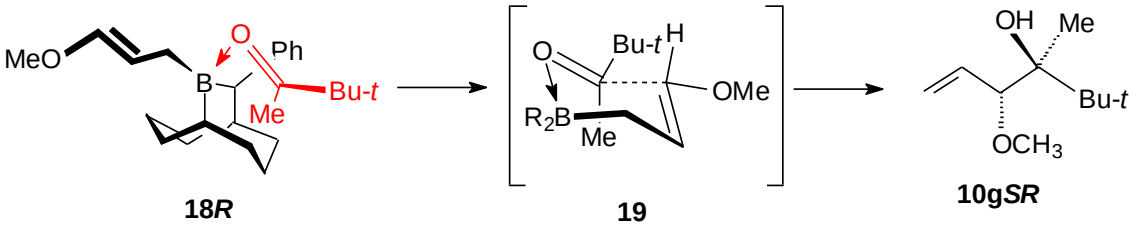


Figure 25. Selected expansions of ^{13}C NMR spectra of the *syn*/*anti* mixture of **10g*R**R*** and **10g*R**S***, 7% *syn*, 93% *anti*.

This confirms our prediction about the *anti* diastereomer coming from **7**. (**Scheme 3**).



Scheme 3. Model predicts that **18*R*** affords **10g*SR***.

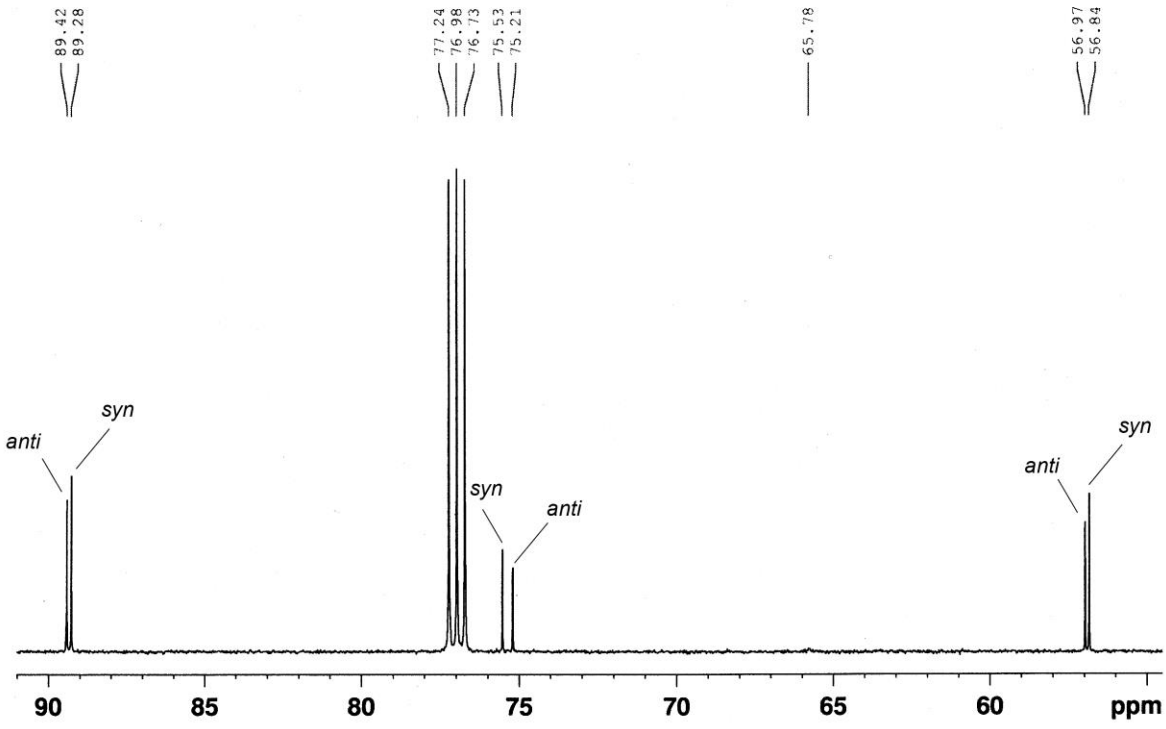
Racemic 4-methoxy-2,2,3-trimethylhex-5-en-3-ol (10g*RR* and 10g*R**S*) mixture.** A solution of **11g**[2] (0.1090 g, 0.69 mmol) in anhydrous CH_2Cl_2 (2 mL) was treated with Dess-Martin periodinane (0.4242 g, 1.0 mmols). The mixture was allowed to stir at 25 ºC for 30 min, then 5 mL of 10% aqueous $Na_2S_2O_3$ and 1.5 mL of saturated aqueous $NaHCO_3$ were added. The layers were separated

and the aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). The organic layers were combined and dried (Na_2SO_4), filtered and solvents were removed under vacuum. The ketone product **14g** was used on the next step without further purification. Yield (crude), 91%; ^{13}C NMR (75 MHz, C_6D_6) δ 26.3, 44.0, 56.3, 84.3, 119.3, 134.5, 210.2.

A solution of crude ketone **14g** (0.0702 g, 0.45 mmol) in THF (0.5 mL) was added to a solution of MeLi (1.6 M in diethyl ether, 0.31 mL, 0.50 mmol) in anhydrous THF (0.5 mL) at -78 ^oC. After stirring at -78 ^oC for 2 h, 4 mL of a saturated solution of NH_4Cl was added *via* syringe. The layers were diluted with ether and separated, the aqueous layer was extracted with ether (2 x 5 mL); the organic layers were combined and dried (Na_2SO_4). The product diastereomeric tertiary alcohols showed a NMR spectra where the mixture could be identified as 7:93 *syn:anti* and was directly used in the ^{13}C NMR analysis (**Figure 25**).

Addition of *p*-bromoacetophenone (8b) to (±)-1/7 to obtain a *syn*/*anti* mixture. After the results for **10g** (R = *t*-Bu), in which the *anti* alcohol was obtained as the major product, this would confirm that in fact other ketones would react with both **1** and **7**. Ketone **8b** was added to a 46:54 (*trans*:*cis*) mixture of **1/7** which was allowed to stand at 25 ^oC for 24 h. After a careful examination of the ^{13}C NMR of this mixture, it was noted that both *cis* and *trans* trialkylboranes reacted to give a mixture of **10b*R*R**** and **10bR*S***. (^{13}C NMR (75 MHz, $CDCl_3$) δ

24.5 (*syn*), 26.2 (*anti*), 56.8 (*syn*), 57.0 (*anti*), 75.2 (*anti*), 75.5 (*syn*), 89.3 (*syn*), 89.4 (*anti*), 120.3 (*anti*), 120.7 (*syn*), 120.8 (*syn*/*anti*), 127.6 (*syn*), 127.6 (*anti*), 130.7 (*anti*), 130.8 (*syn*), 130.5 (*syn*), 133.8 (*anti*), 143.6 (*anti*), 144.5 (*syn*)). Selected expansions of the ^{13}C NMR are shown in **Figure 26**.



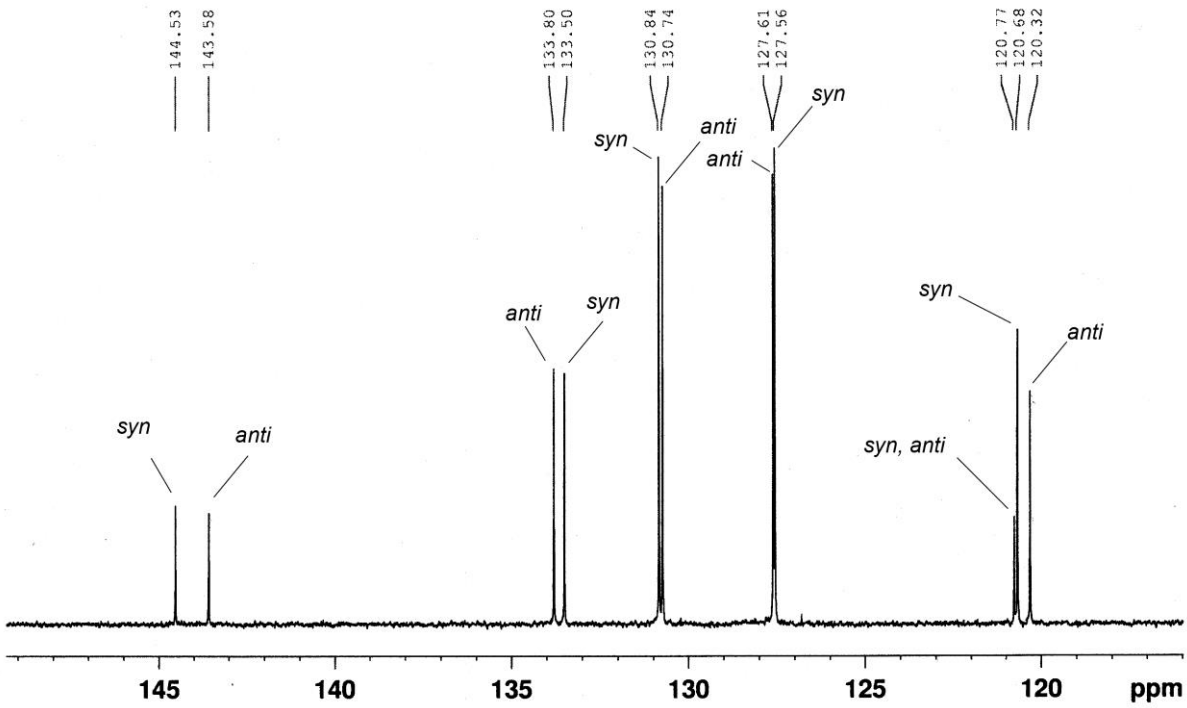


Figure 26. Selected expansions of ^{13}C NMR of the *syn*/*anti* mixture of racemic **10b**.

Competitive Experiment: Addition of of acetophenone (8a) and pinacolone (8g) to 0.5 equiv of *B*-[(*Z*)-γ-methoxyallyl]-10-phenyl-9-borabicyclo[3.3.2]decane (1).

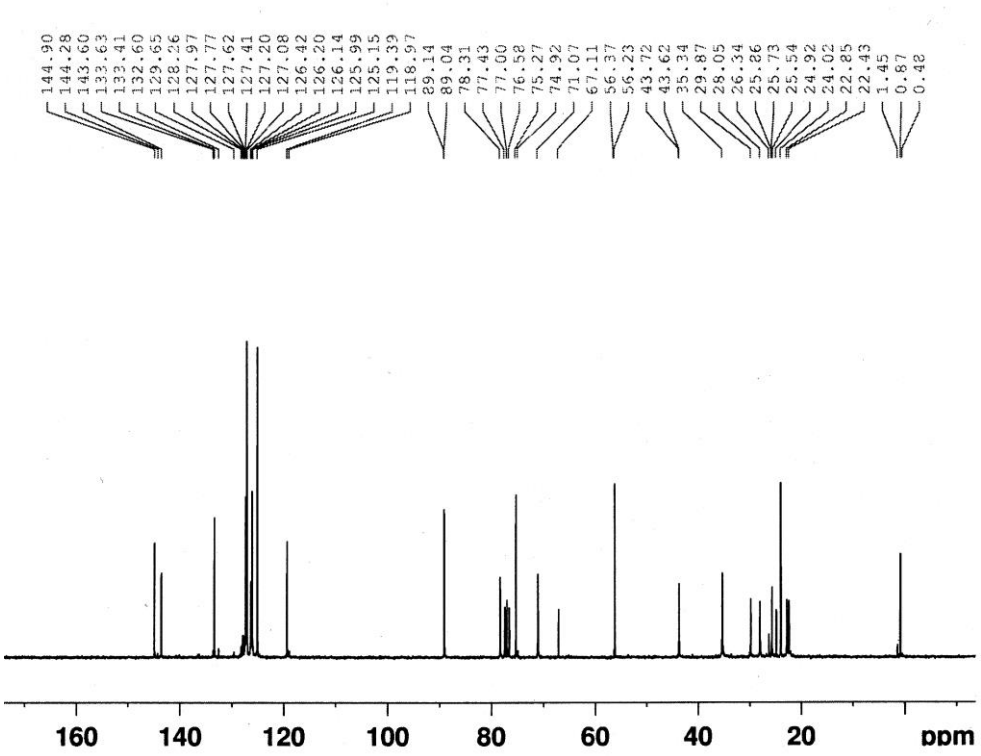


Figure 27. Crude ^{13}C NMR spectra showing only **10a** (R = Ph) as a product from the **8a** vs **8g** competitive experiment.

Ketones **8a** (0.35 mL, 3 mmol) and **8g** (0.30 mL, 3 mmol) were simultaneously added to freshly prepared **1** on a 3 mmol scale, the mixture was stirred at -78 ^{o}C for 8 h and allowed to reach 25 ^{o}C for a total of 16 h. The reaction mixture was cooled to 0 ^{o}C, then NaOH (3 ml, 9 mmol, 3M) and H_2O_2 (0.61 mL, 6 mmol, 30 wt. %) were added dropwise, the mixture was allowed to slowly reach 25 ^{o}C. The round bottom flask was equipped with a refluxing condensor and the solution mixture was refluxed for 2 h. Diethyl ether was added to the mixture and the organic phase was extracted with water (2 X 10 mL) and brine (2 X 10 mL). All of the volatiles of the organic phase were removed under reduced pressure (0.1 mmHg). The crude ^{13}C NMR spectrum was used to compare it to those of the

relevant pure tertiary alcohols **10a** and **10g** and analyze the competitive experimental results. Only the tertiary alcohol derived from **8a** (**10a**) was found in the mixture. (**Figure 27**).

Addition to *N*-TMS-Ketimines

(2*R*,3*R*)-3-((2-Methoxyethoxy)methoxy)-2-phenylpent-4-en-2-amine (26*RR*). A mixture of *N*-TMS-ketimines/enamine from benzonitrile on a 10 mmol scale (Rochow's procedure,[5] was refluxed in dry THF (40 mL) for 3 d to increase the enamine to 62%, after 3 d, all solvents were removed by vacuum) was added to freshly prepared (10*S*)-*B*-[(*Z*)-γ-methoxyethoxymethoxyallyl]-10-phenyl-9-borabicyclo[3.3.2]decane **(18*S*)** on a 3 mmol scale, the mixture was stirred at -78 ^{o}C for 8 h and allowed to slowly reach 25 ^{o}C for a total of 16 h. The reaction mixture was cooled to 0 ^{o}C, NaOH (3 ml, 9 mmol, 3M) and H_2O_2 (0.61 mL, 6 mmols, 30 wt. %) were added dropwise, the mixture was allowed to slowly reach 25 ^{o}C. The round bottom flask was equipped with a refluxing condensor and the solution mixture was refluxed for 2 h. Diethyl ether was added to the mixture and the organic phase was extracted with water (2 X 10 mL) and brine (2 X 10 mL). All of the volatiles of the organic phase were removed under reduced pressure (0.1 mmHg). A neutral alumina column chromatography with a 1:10:89 to 1:30:69 mixture of triethylamine:ethyl ether:hexane was used to purify the tertiary amine (**26*RR***) (**Figure 28**). Absolute configuration was determined by vibrational circular dichroism (VCD) in a collaboration with Dr. Rina K. Dukor from BioTools

in Jupiter, Florida. Yield, 57%; Crude 98% de, Isolated 98% de; $[\alpha]_D^{20}$ -64.8 (*c* 4.2, C_6D_6), 94% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.22 (s, 3H), 1.67 (s br, 2H), 2.74 (ddd, *J* = 4.9, 3.0, 10.7 Hz, 1H), 3.07 (m, 6H), 4.04 (d, *J* = 7.5 Hz, 1H), 4.26 (d, *J* = 7.0 Hz, 1H), 4.47 (d, *J* = 7.0 Hz, 1H), 5.11 (dd, *J* = 0.7, 17.3, 1H), 5.17 (dd, *J* = 1.7, 10.5, 1H), 5.57 (ddd, *J* = 7.6, 10.5, 17.3, 1H), 7.17 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.0, 57.6, 58.8, 66.5, 71.6, 84.1, 92.4, 120.1, 125.9, 126.1, 127.7, 134.0, 147.2; Mosher amide derivative: ^{1}H NMR (500 MHz, C_6D_6) δ 1.93 (3%), 2.02 (97%). An additional experiment was done by adding an equivalent of dry MeOH to the **18*S*** solution, followed by the ketimine/enamime mixture at -78 ^{o}C. The resulting mixture was stirred at -78 ^{o}C for 4 h and then slowly allowed to reach 25 ^{o}C for 16 h. Yield, 62%; Crude 97% de, Isolated 97% de, 94% ee. The same configuration as without added methanol was obtained which was confirmed by the sign of the the optical rotation $[\alpha]_D^{20}$ -64.7 (*c* 4.0, C_6D_6). The Mosher amide derivative showed no loss in the ee of the reaction. **26*RR*** HRMS (ESI) [M + H]+ calcd for C15H24NO3: 266.1743, found 266.1756. (**Figure 29**).

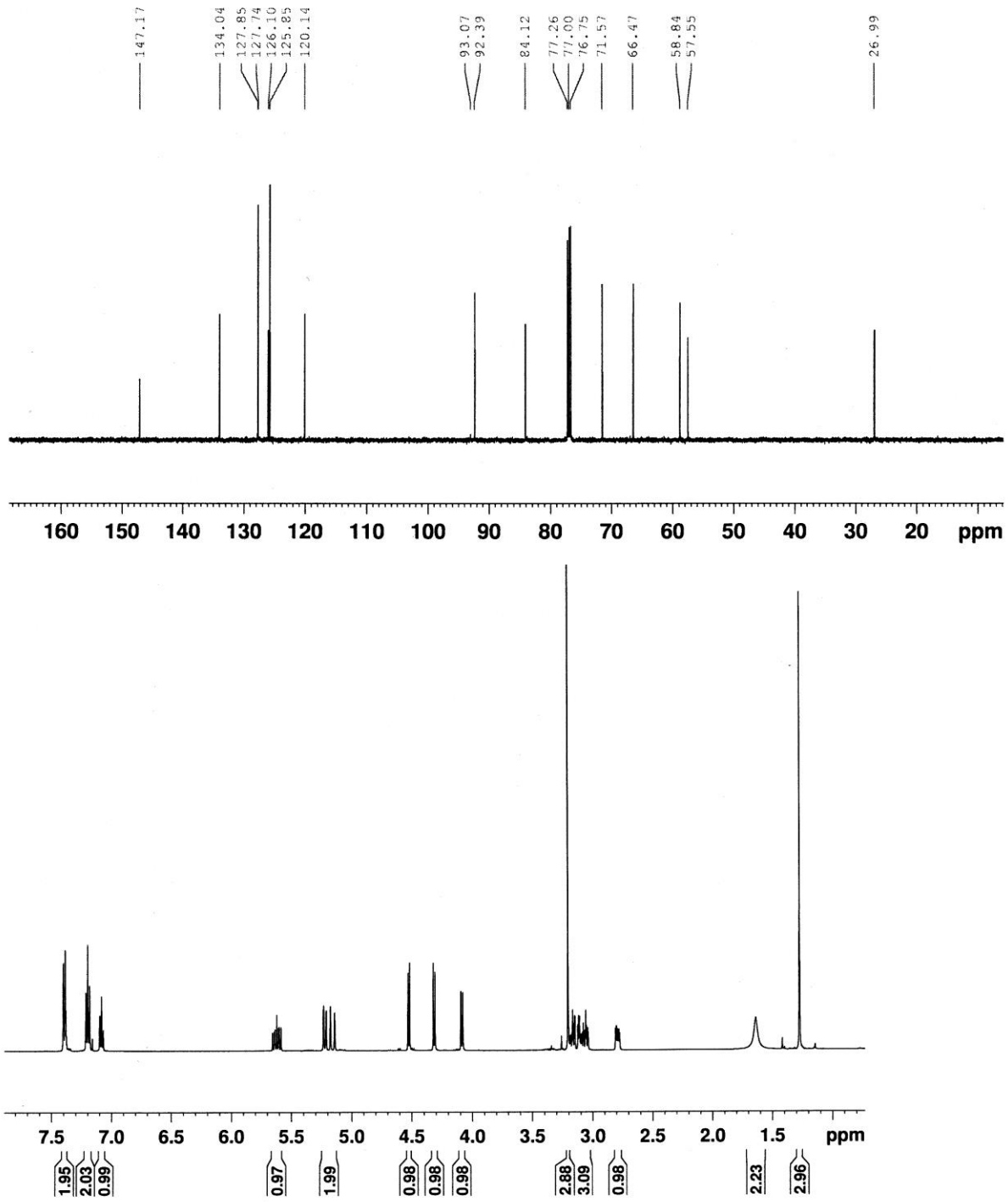


Figure 28. ^{1}H and ^{13}C NMR of **26*RR***.

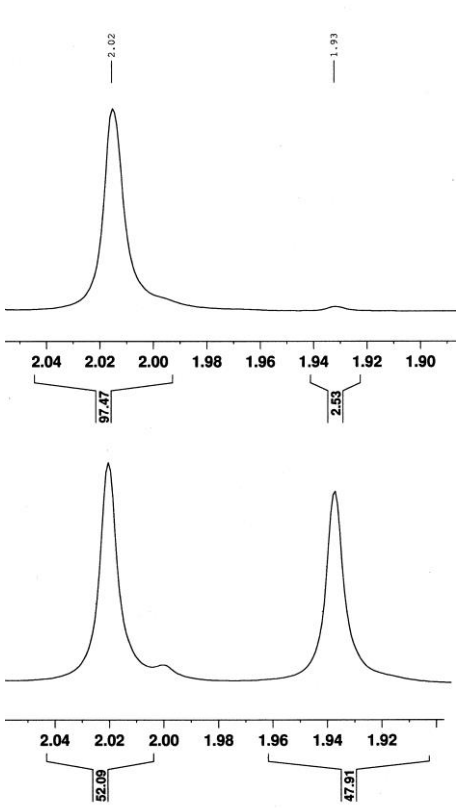


Figure 29. ^{1}H NMR of Mosher amide derivative of **26**.

(2*R*,3*R*)-2-Amino-3-methoxy-2-phenyl-4-pentene (27*RR*)). A mixture of *N*-TMS-ketimines/enamine from benzonitrile on a 10 mmol scale (Rochow's procedure)[5] was refluxed in dry THF (40 mL) for 3 d to increase the enamine content to 62%. All the solvents were removed by vacuum and the residual liquid was added to freshly prepared (10*S*)-*B*-[(*Z*)-γ-methoxy]-10-phenyl-9-borabicyclo[3.3.2]decane (**1*S***) on a 3 mmol scale and diluted with additional THF (5 mL). Adding more THF increases the reaction time which would decrease the de so that the *syn:anti* isomers could be easily identified. The mixture was stirred at -78 ^{o}C for 4 h and allowed to slowly reach 25 ^{o}C over a total of 20 h. The

reaction mixture was oxidized through cooling to 0 ^{o}C, followed by addition of NaOH (3 ml, 9 mmol, 3M) and H_2O_2 (0.61 mL, 6 mmols, 30 wt. %) dropwise. The mixture was allowed to slowly reach 25 ^{o}C. The round bottomed flask was equipped with a refluxing condensor and the mixture was refluxed for 2 h. Diethyl ether was added and the organic phase was extracted with water (2 X 10 mL) followed by brine (2 X 10 mL). The organic phase was concentrated under reduced pressure (0.1 mmHg). Neutral alumina column chromatography was performed with a 1:10:89 to 1:30:69 mixture of triethylamine:ethyl ether:hexane to purify the tertiary amine (**27*RR***). Yield, 64%; Crude 80% de, Isolated 80% de; $[\alpha]_D^{20}$ -18.4 (*c* 1.1, $CHCl_3$), 92% ee, lit[6] $[\alpha]_D^{20}$ -2.7 (*c* 1.0, $CHCl_3$), 90% de, 20% ee; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.41 (s, 3H), 2.19 (s br, 2H), 3.21 (s, 1H), 3.67 (d, *J* = 7.3 Hz, 1H), 5.16 (dd, *J* = 1.9 ,17.2 Hz, 1H), 5.26 (dd, *J* = 1.9 ,10.5 Hz, 1H), 5.58 (ddd, *J* = 7.3, 10.5, 17.2 Hz, 1H), 7.36 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.7 (*syn*), 27.0 (*anti*), 56.9 (*syn*), 57.1 (*anti*), 57.4 (*anti*), 57.6 (*syn*), 89.5 (*anti*), 90.0 (*syn*), 118.7 (*anti*), 119.2 (*syn*), 125.7 (*anti*), 125.8 (*syn*), 126.2 (*syn*), 127.6 (*syn*), 127.7 (*anti*), 134.1 (*anti*), 134.2 (*syn*), 145.4 (*anti*), 146.1 (*syn*); Mosher amide derivative: ^{1}H NMR (500 MHz, C_6D_6) δ 3.37 (96%), 3.48 (4%); HRMS (ESI) [M + Na]+ calcd for C12H17NONa: 214.1204, found 214.1208. (**Figures 30, 31**).

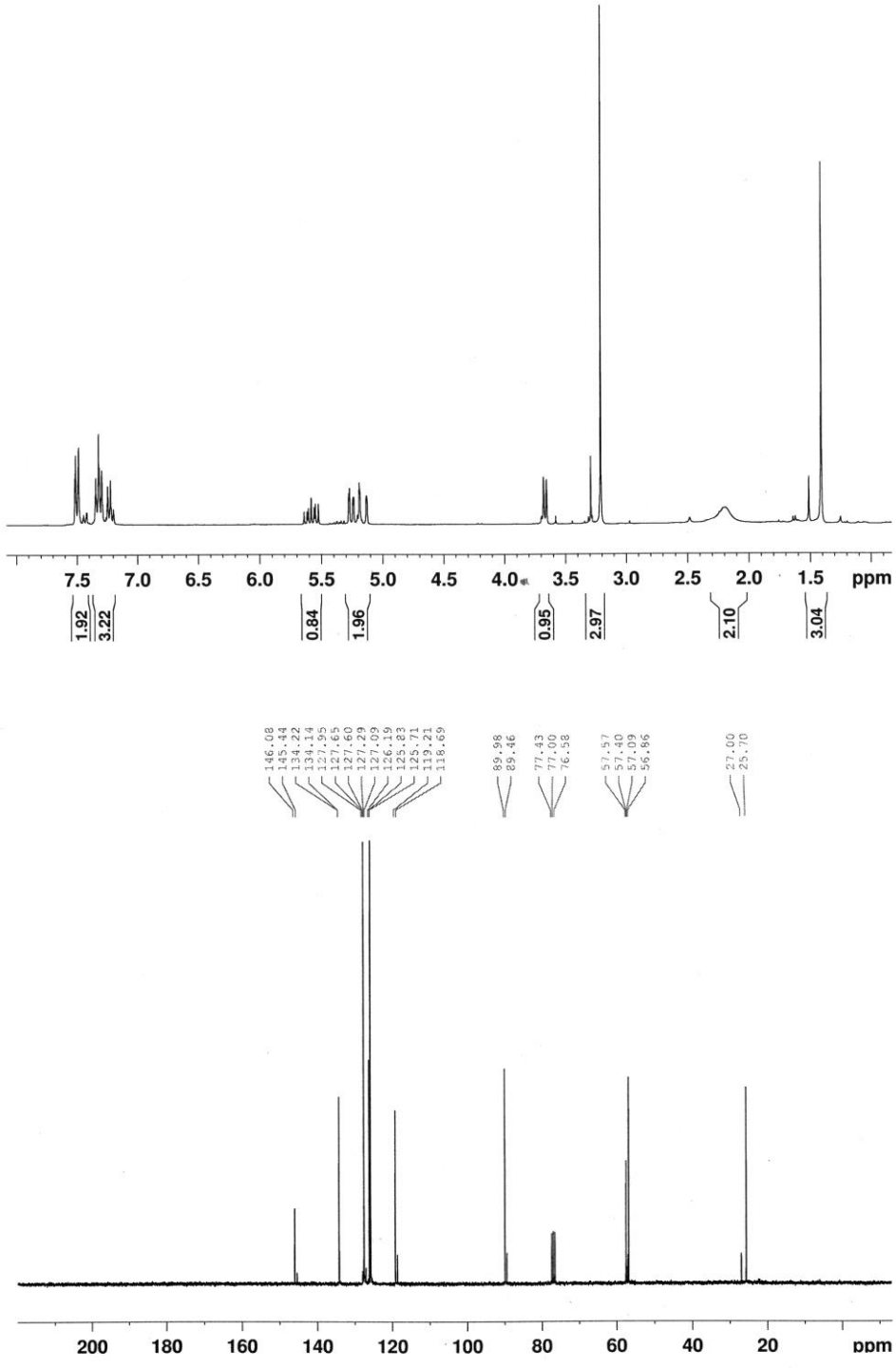


Figure 30. ^{1}H and ^{13}C NMR of **27*RR*.**

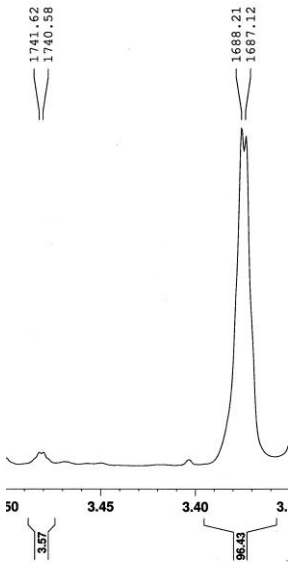


Figure 31. [1]H NMR of Mosher amide derivative of **27*RR***.

[1] Burgos, C. H.; Canales, E.; Matos, K.; Soderquist, J. A. *J. Am. Chem. Soc.* **2005**, *127*, 8044.

[2] Muñoz-Hernández, L.; Soderquist, J. A. *Org. Lett.*, **2009**, *11*, 2571.

[3] Ramachandran, P. V.; Liu, H.; Reddy, V. R.; Brown, H.C. *Org. Lett.* **2003**, *5*, 3755.

[4] Parsons, P.J.; Lacrouts, P.; Buss, A. D. *J. Chem. Soc., Chem. Commun.* **1995**, 437.

[5] Chan, L.-H.; Rochow, E. G. *J. Organometal. Chem.* **1967**, *9*, 231.

[6] Li, F.; Li, Z.-M.; Yang, H.; Jäger, V. Z. *Naturforsch.* **2008**, *63b*, 431.

APPENDIX: VCD Report

Absolute Configuration Determination Report

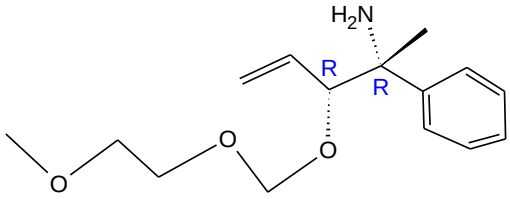
GENERAL INFORMATION	
Customer	Univ. Puerto Rico
Sales Order Number	2014.21
Sample code (Our ref.)	**Lorell's sample**
Sample description (Your ref.)	**Lorell's sample**
VCD-spectrometer	ChiralIR w/ Dual*PEM*
Report prepared by	Bo Wang
Report validated and signed by	Rina K Dukor
Date	Apr. 18, 2014
RESULTS	
Absolute Configuration of Lorell's sample **is (R,R).**	Confidence Level: **100 %**
MEASUREMENT PARAMETERS	
Concentration	5.5 mg/0.15mL
Solvent	CDCl3
Resolution	4 cm^{-1}
PEM setting	1400 cm^{-1}
Number of scans/Measurement time	12 hours
Sample cell	BaF_2
Path length	100 µm
CALCULATION DETAILS	

Gaussian version	Gaussian 09
Total low-energy conformer used for Boltzmann sum	24
Methodology and basis set for DFT calculations	B3LYP/6-31G(d)
Enantiomer used for calculation	365
Total calculated conformers	365
Number of low-energy conformations shown in report	24

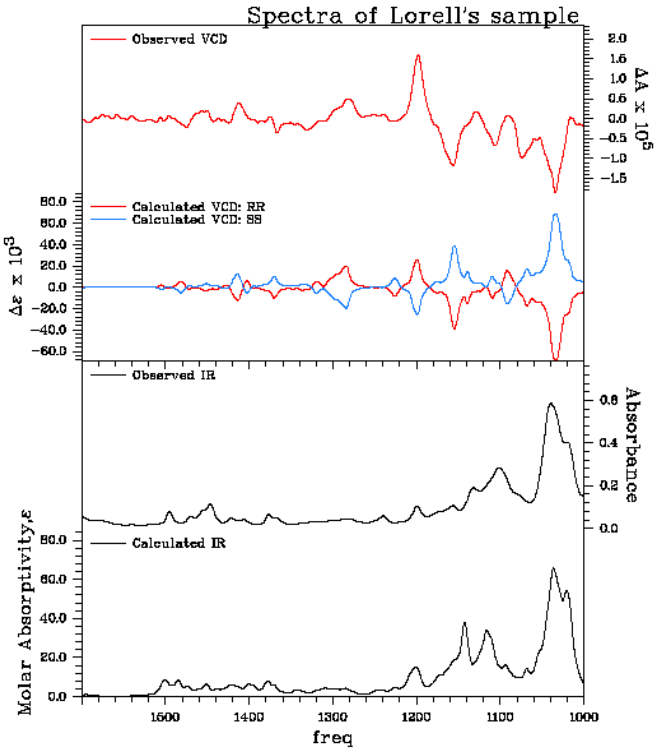
COMMENTS

Customer provided the relative configuration of the two centers as syn. Therefore calculations were performed for (R,R) and (S, S) only.

Structure of Lorell's sample:



CompareVOA results:



Scale= 0.972
TNS(IR)=96.7 TNS(VCD)= 86.3
SNS(RR)= 87.2 SNS(SS)= 4.8 ESI= 82.4

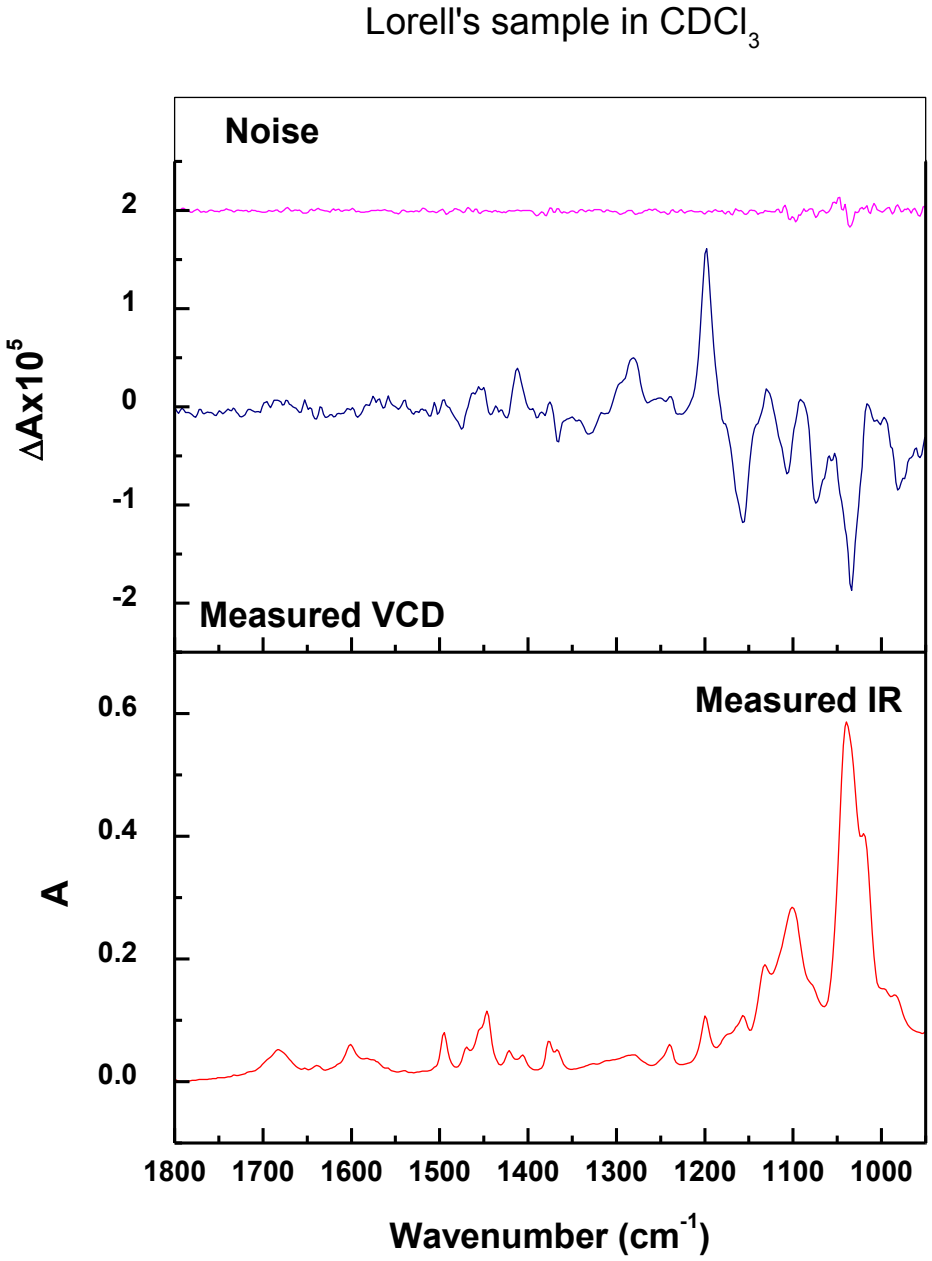
The absolute configuration of Lorell's sample is RR
The Confidence level is 100%

Table 1. Numerical comparison describing the similarity in the range of 1000-1600 cm^{-1} between the calculated IR and VCD spectra for the (**R, R**) enantiomer at the B3LYP/6-31G(d) level and the observed IR and VCD spectra for **Lorell's sample**.

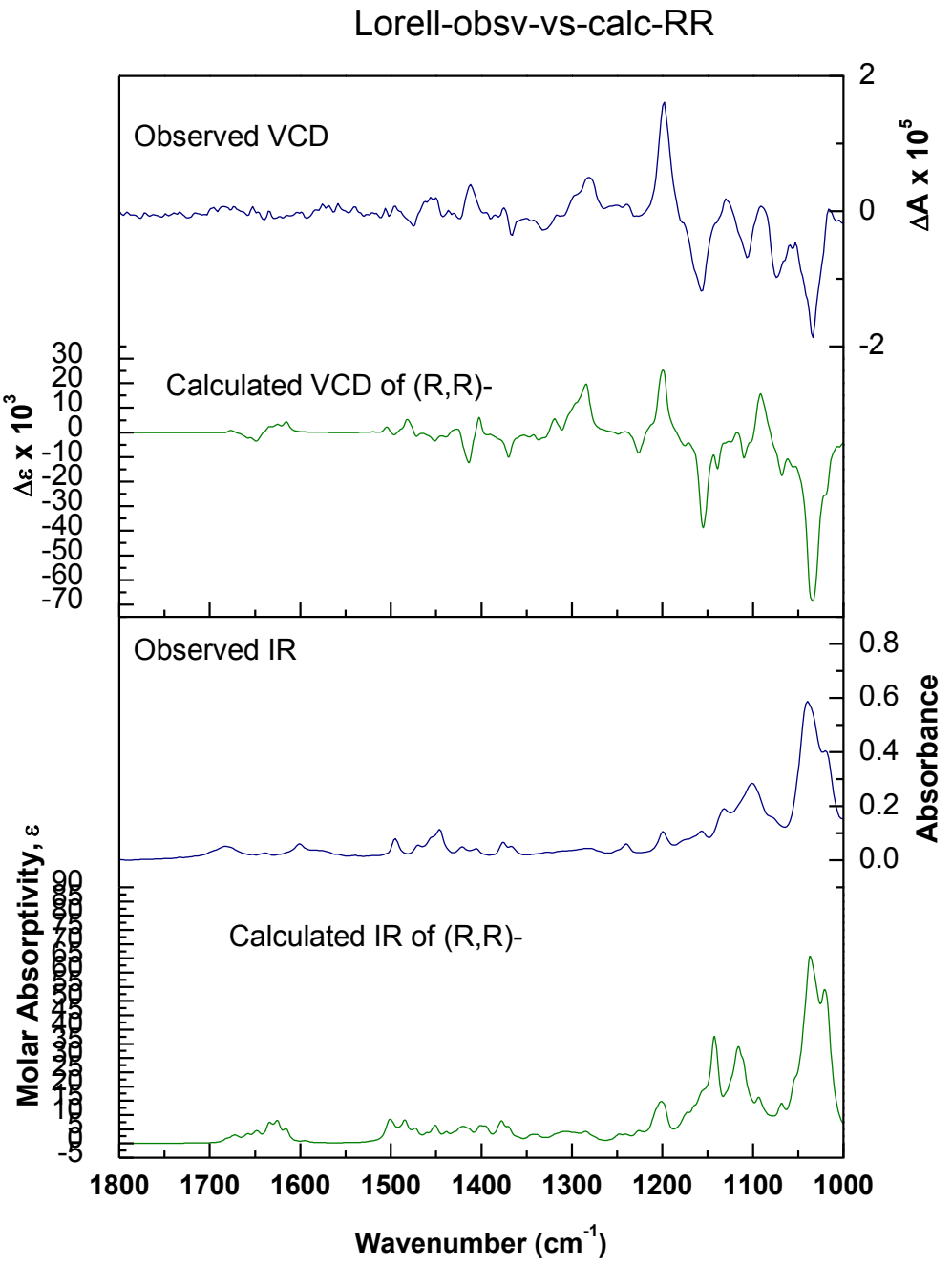
Cal. (1000-1600 cm^{-1})	Numerical comparison	Observed
		Lorell's sample
(***R,R***)	scaling factor	0.972
	IR similarity (%)	96.7
	$^{a}\sum$ (%)	87.2
	$^{b}\Delta$ (%)	82.4
	Confidence Level (%)	100

$^{a}\sum$: single VCD similarity, gives the similarity between the calculated and observed VCD spectra.

$^{b}\Delta$: enantiomeric similarity index, gives the difference between the values of $\sum$ for both enantiomers of a given diastereoisomer.

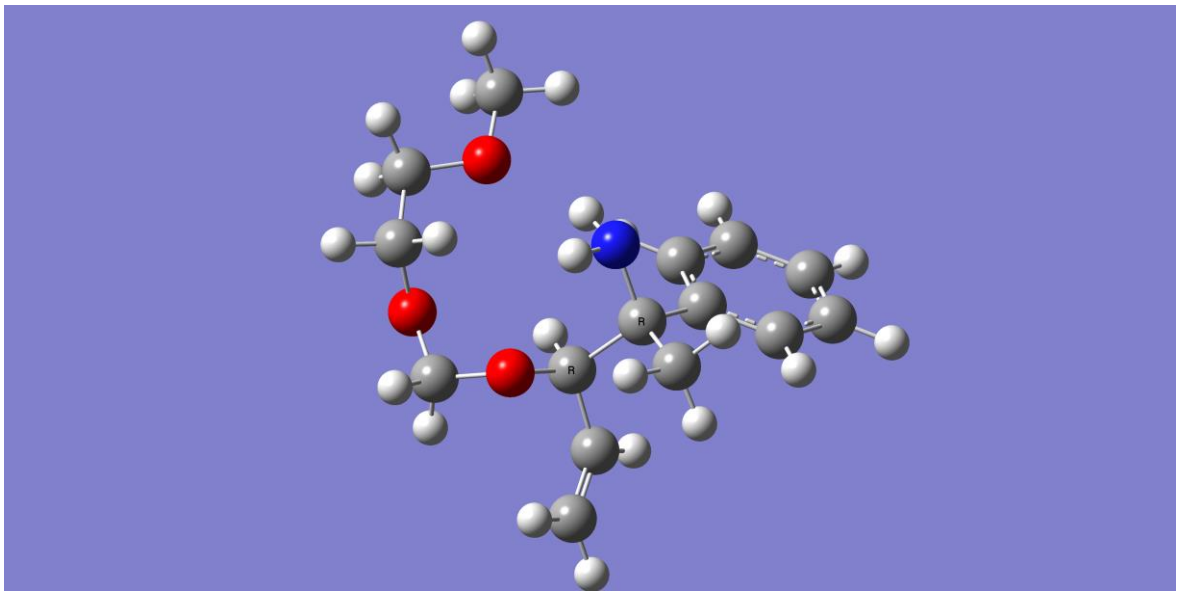


IR (lower frame) and VCD (upper frame) spectra of **Lorell's sample** in $CDCl_3$ (5.5mg/0.15mL); 0.1mm path-length cell with BaF_2 windows; 12 h collection for samples and solvent; instrument optimized at 1400 cm^{-1}. Solvent-subtracted IR and VCD spectra are shown. Uppermost trace is the VCD noise spectra.

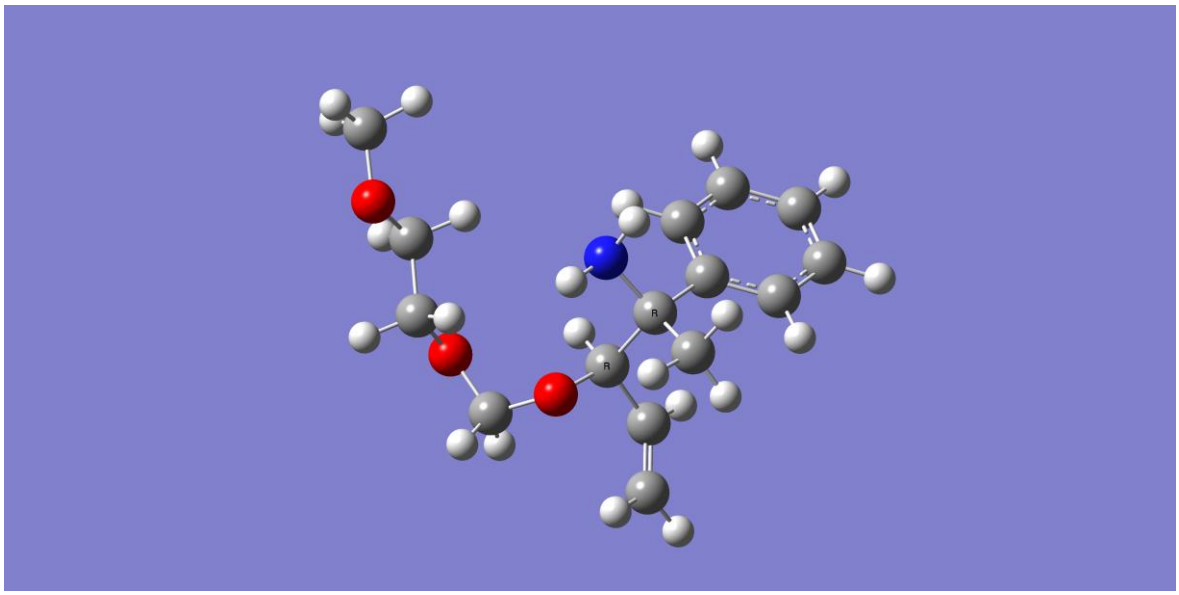


IR (lower frame) and VCD (upper frame) spectra observed for **Lorell's sample** (right axes) compared with calculated Boltzmann-averaged spectra of the calculated conformations for the (R,R)- configuration, (left axes).

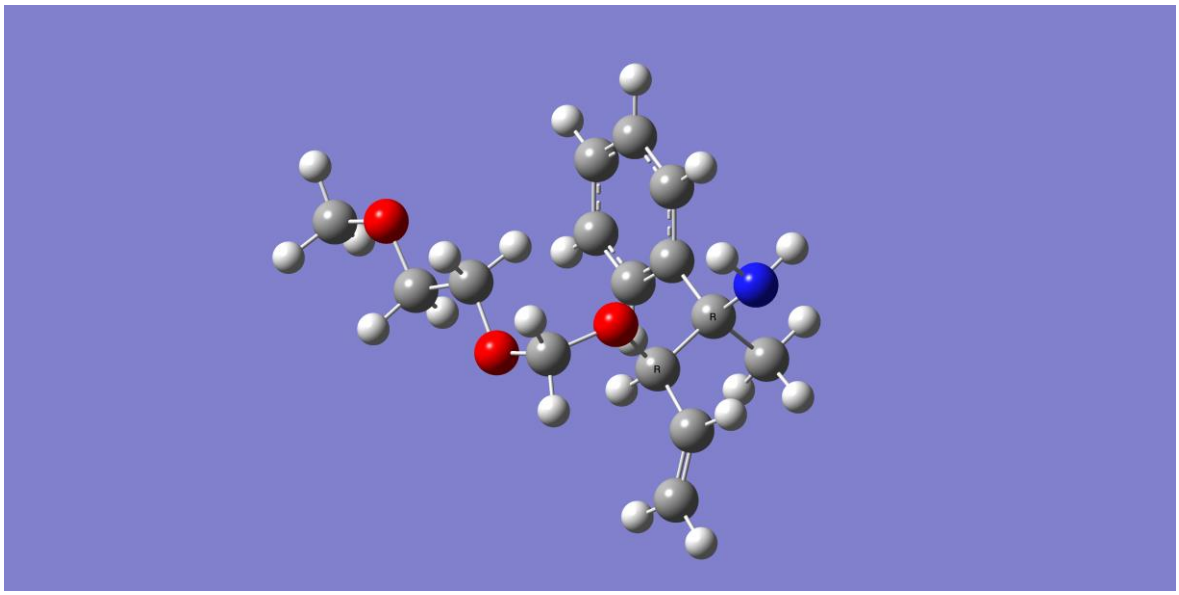
SOME OF THE LOWEST ENERGY CONFORMERS:



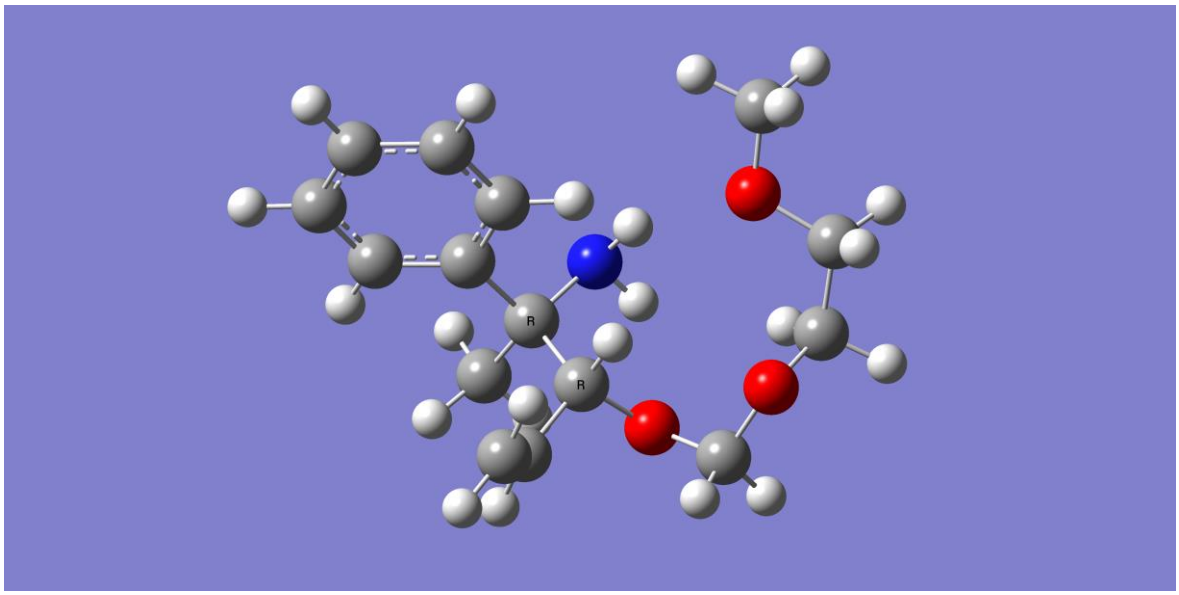
c1, 2.9%



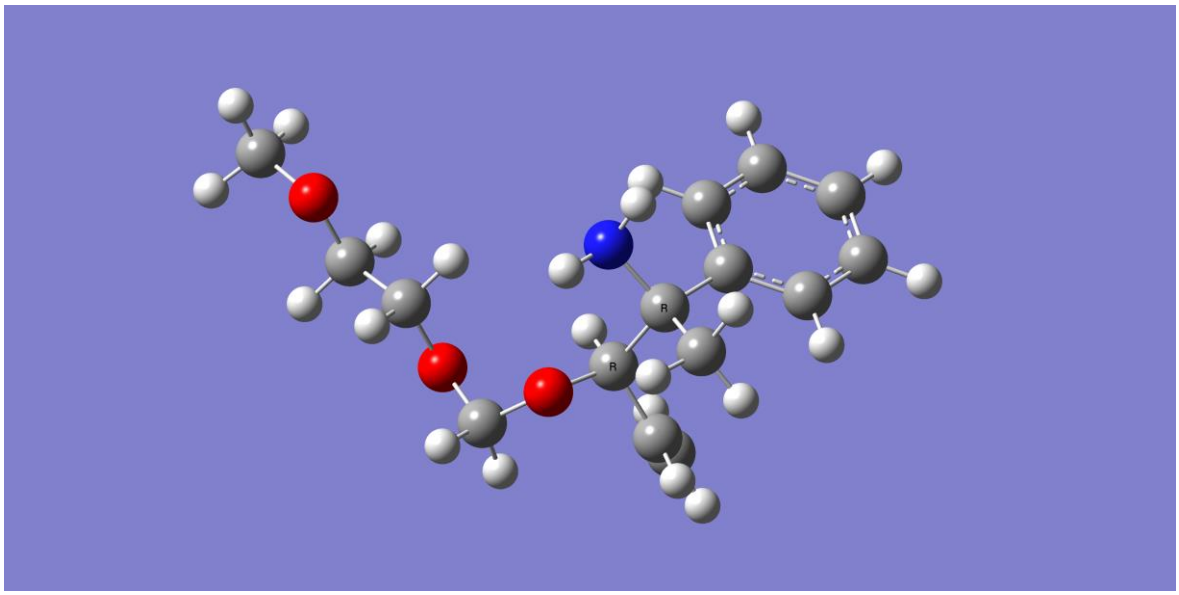
c3, 3.2%



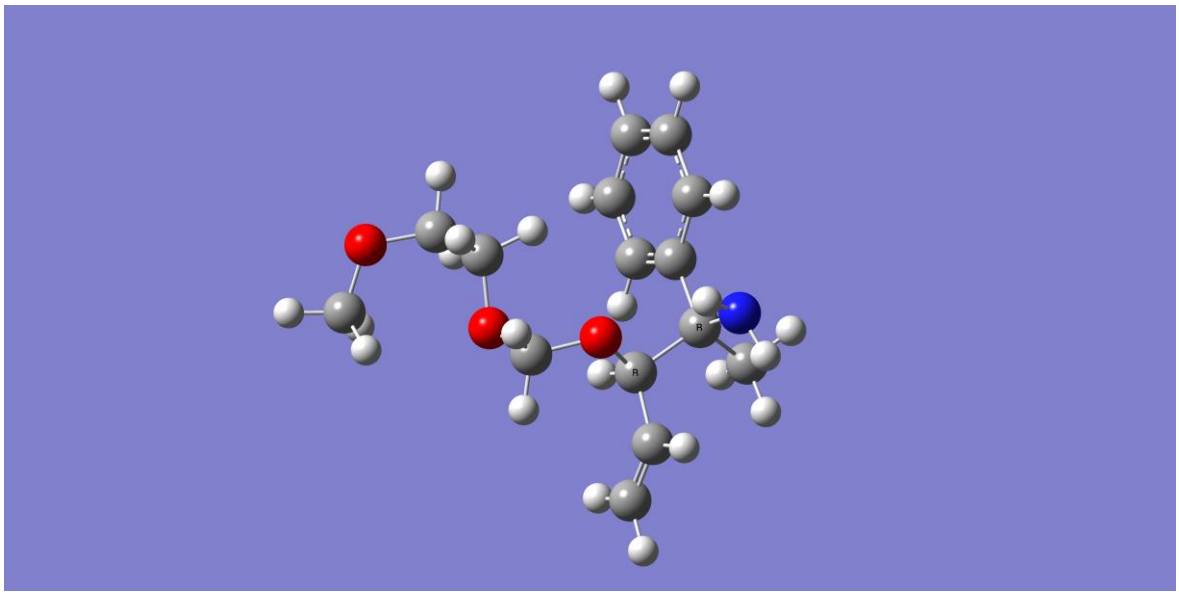
c4, 3.4%



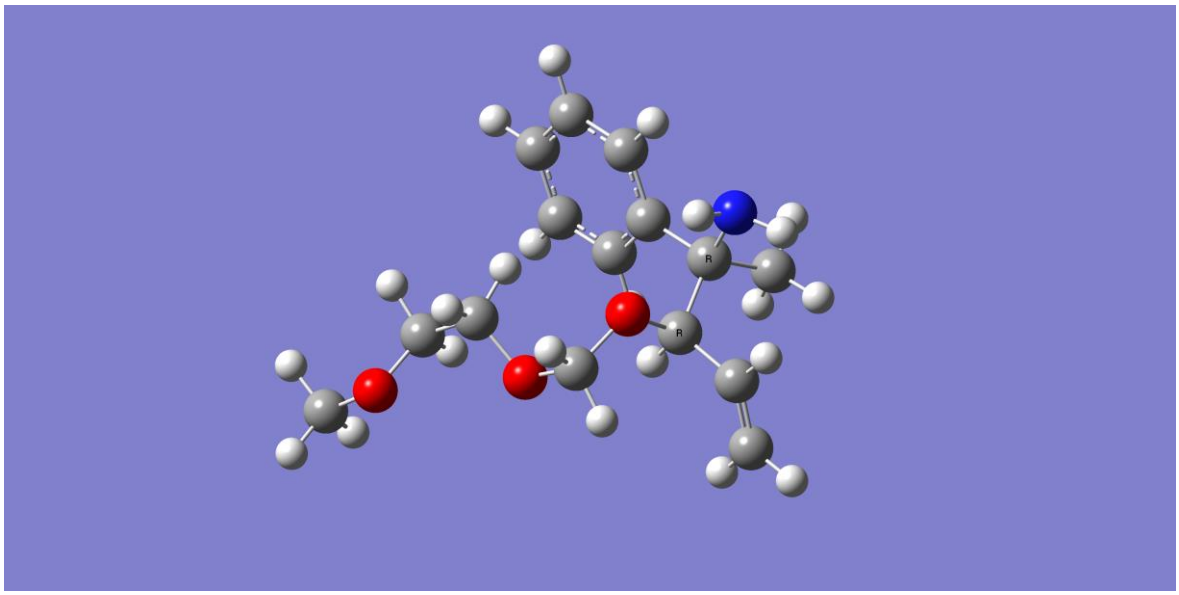
c8, 2.2%



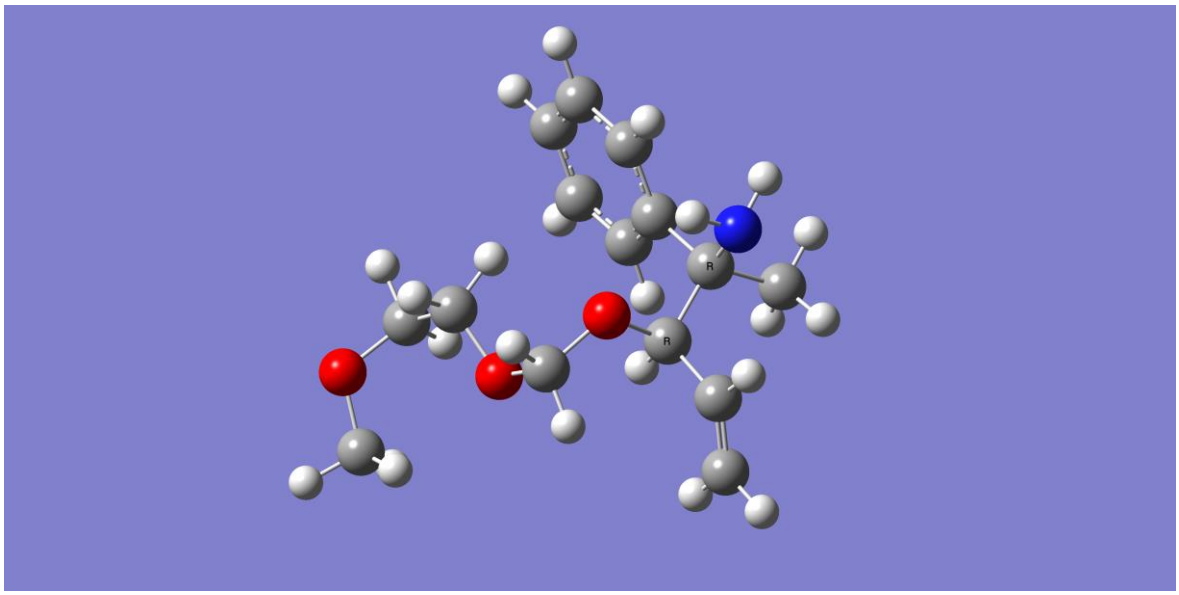
c10, 2.2%



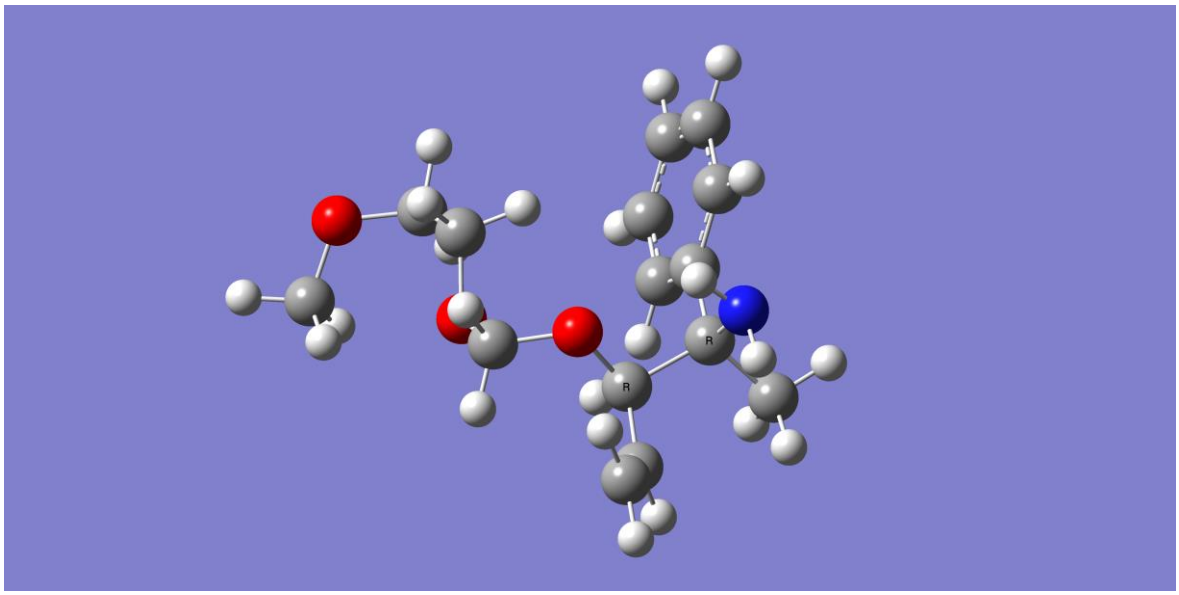
c15, 2.3%



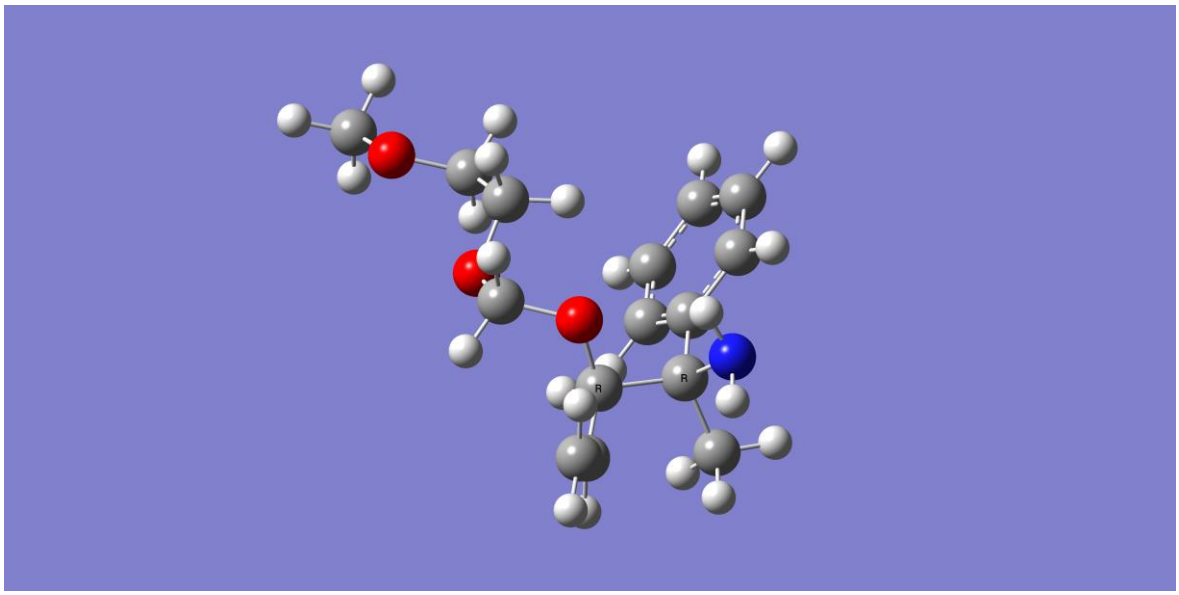
c23, 3.0%



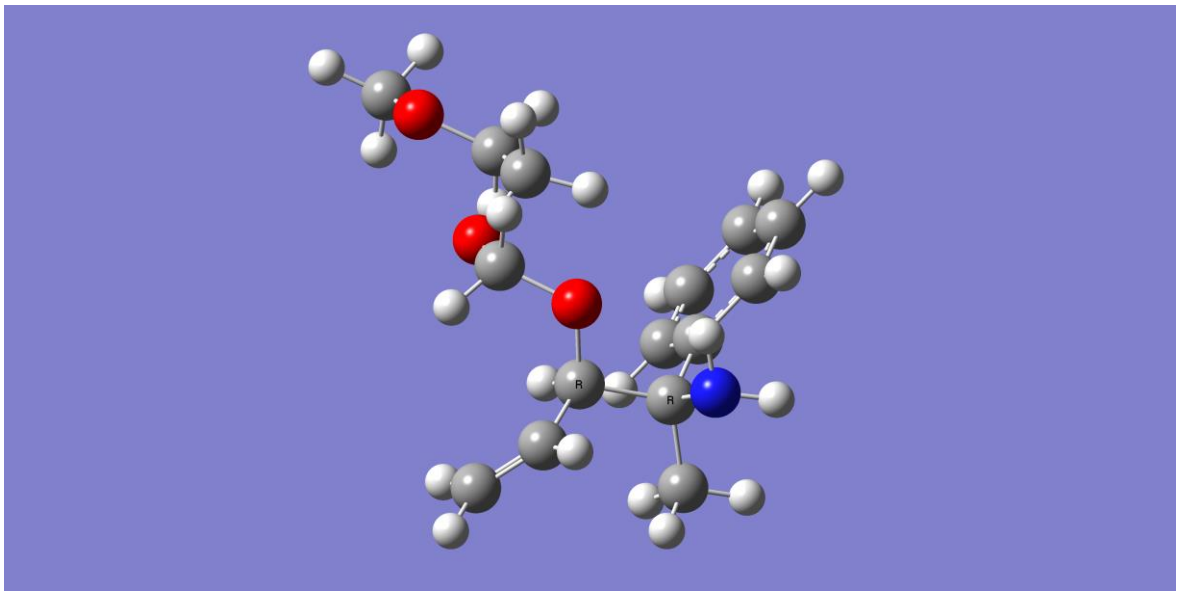
c24, 3.9%



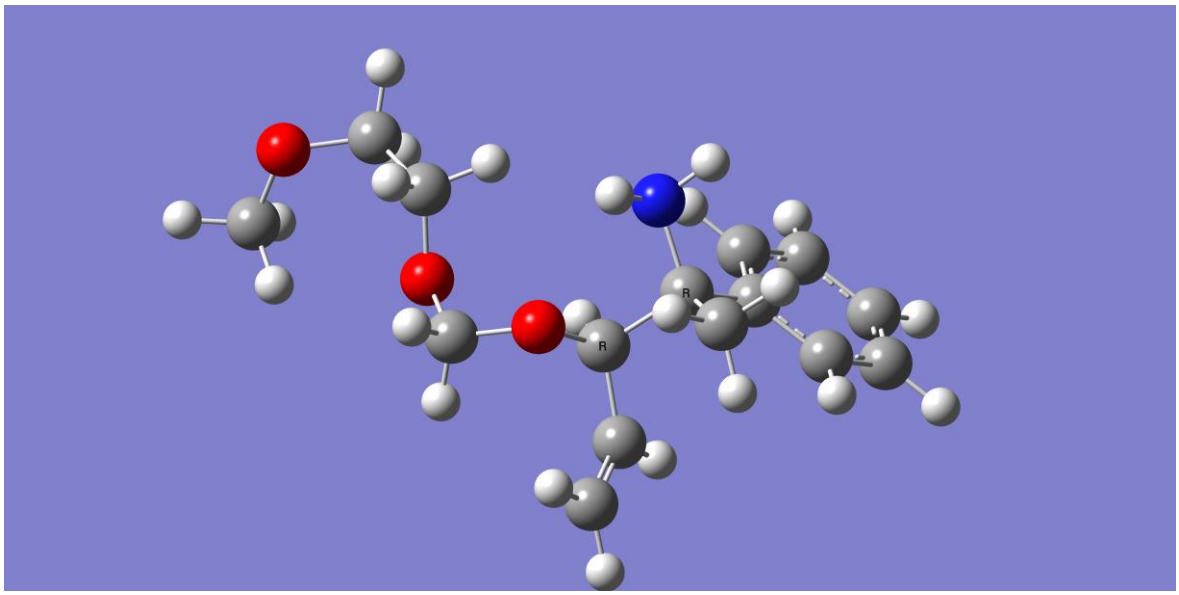
c29, 2.4%



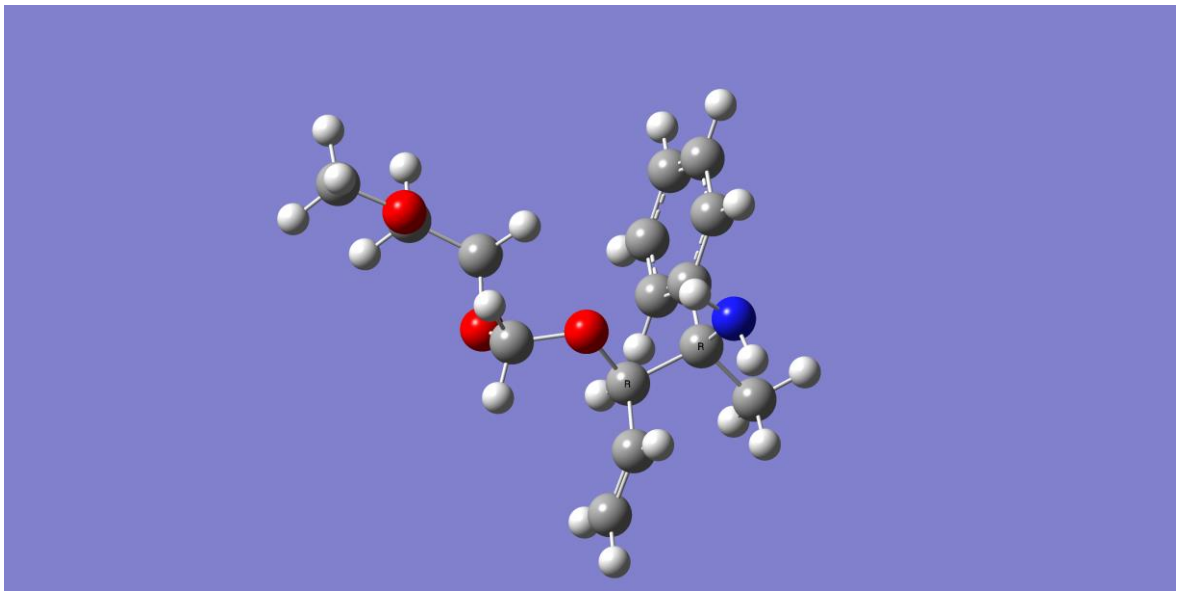
c37, 3.2%



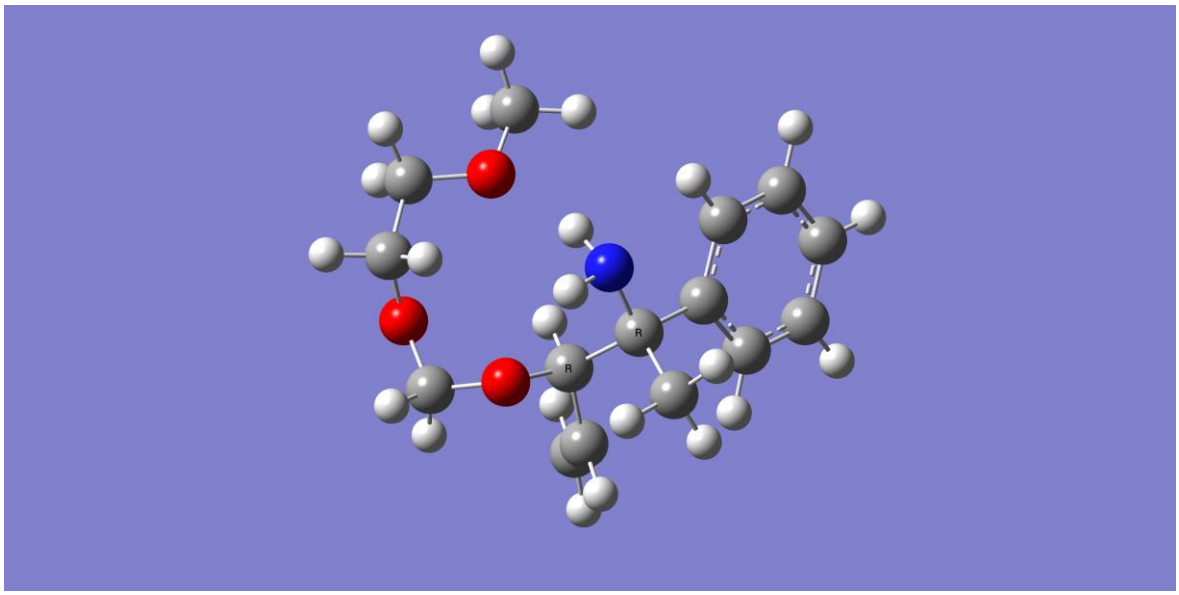
c49, 4.4%



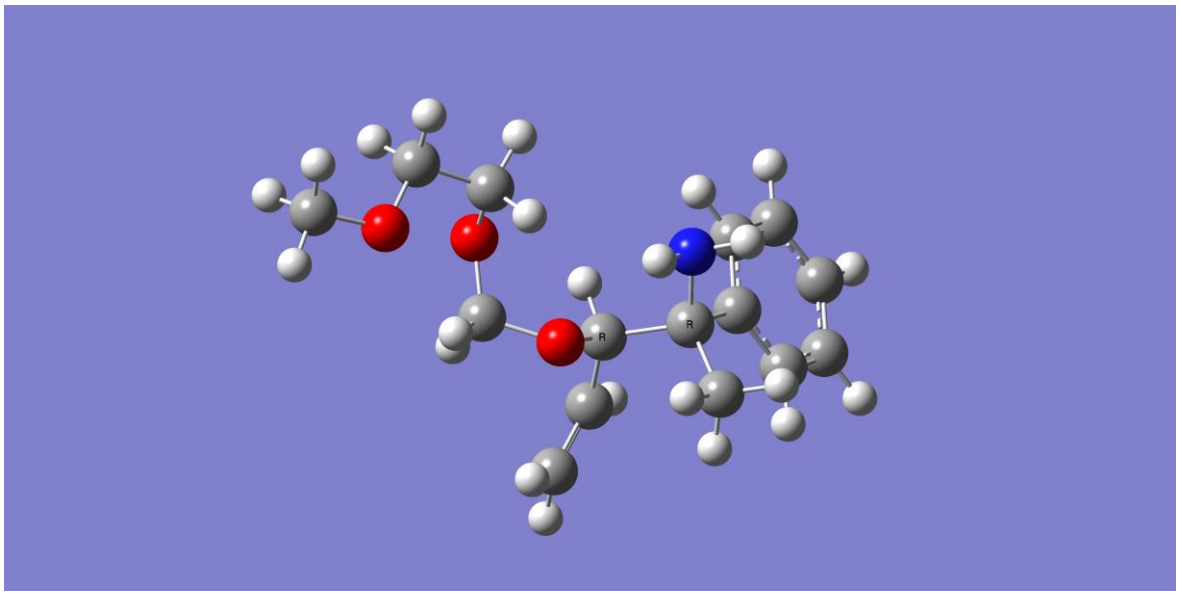
c55, 3.0%



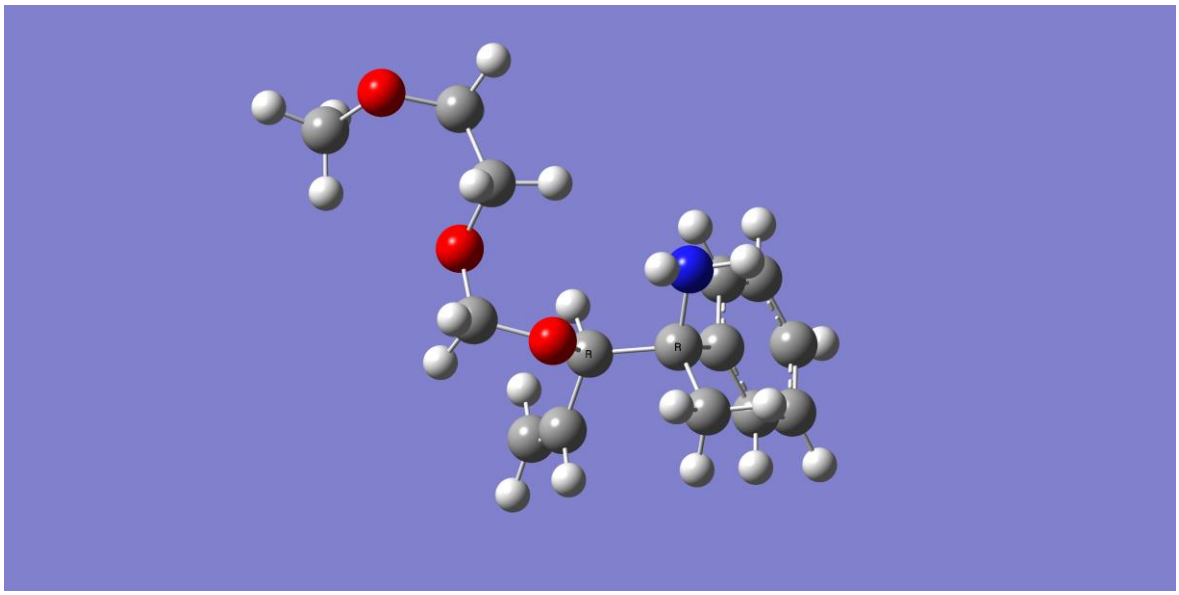
c66, 6.1%



c76, 5.9%



c84, 4.4%



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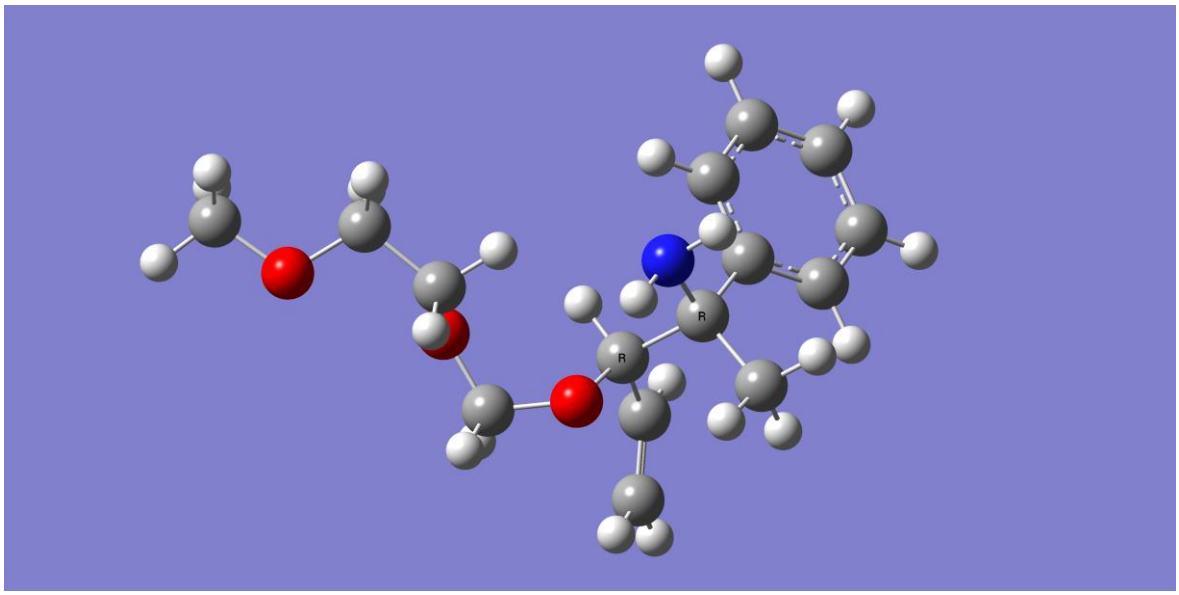
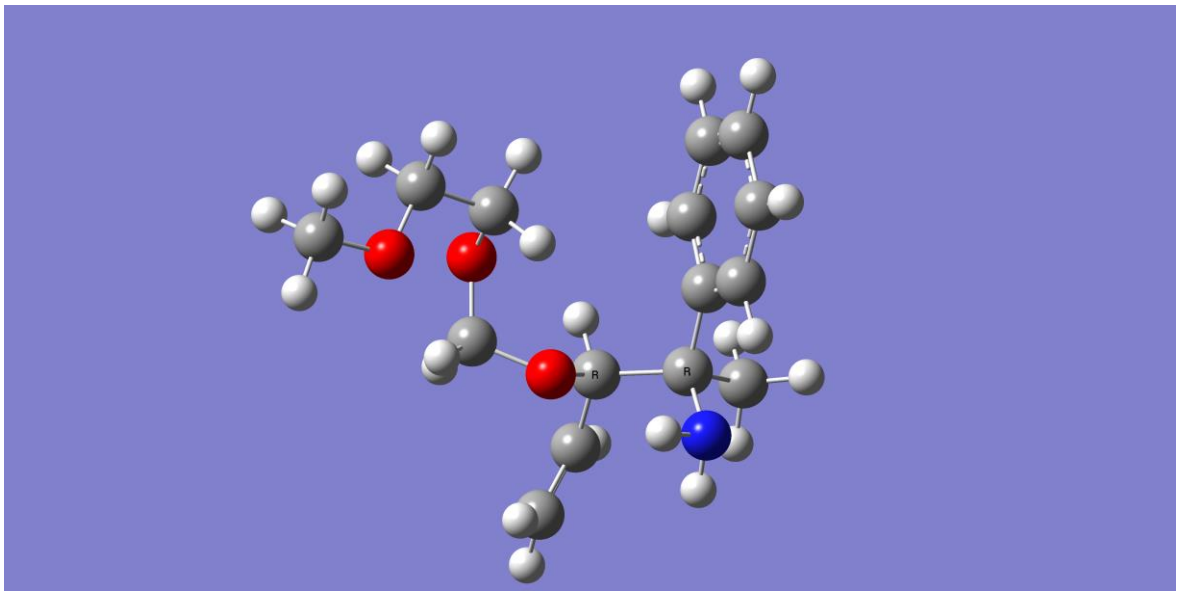
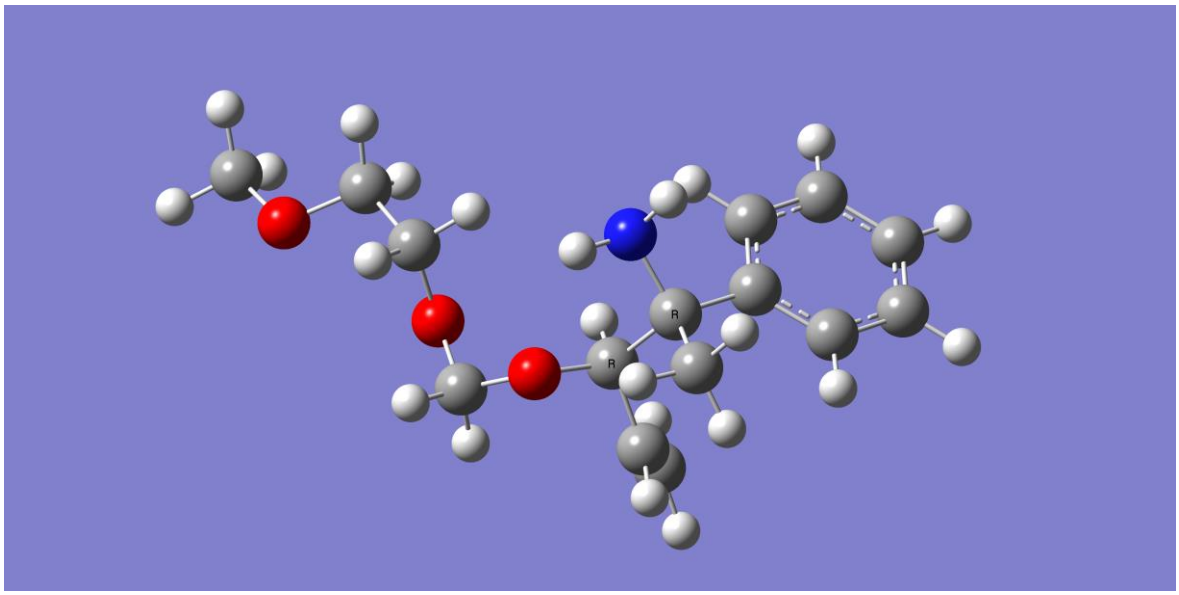


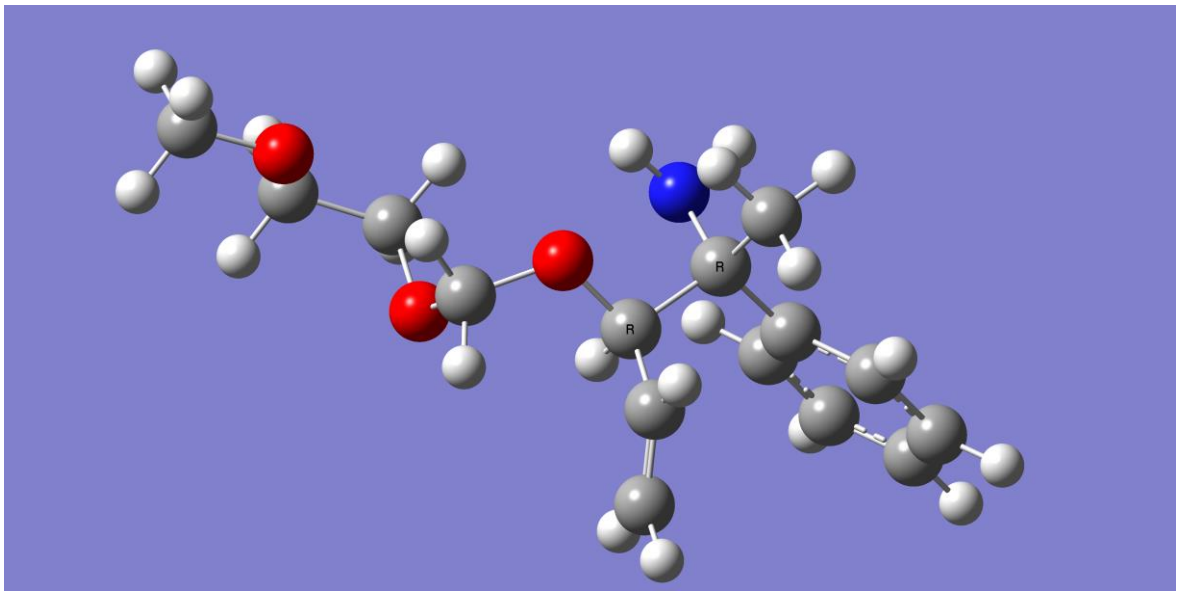
c90, 4.9%



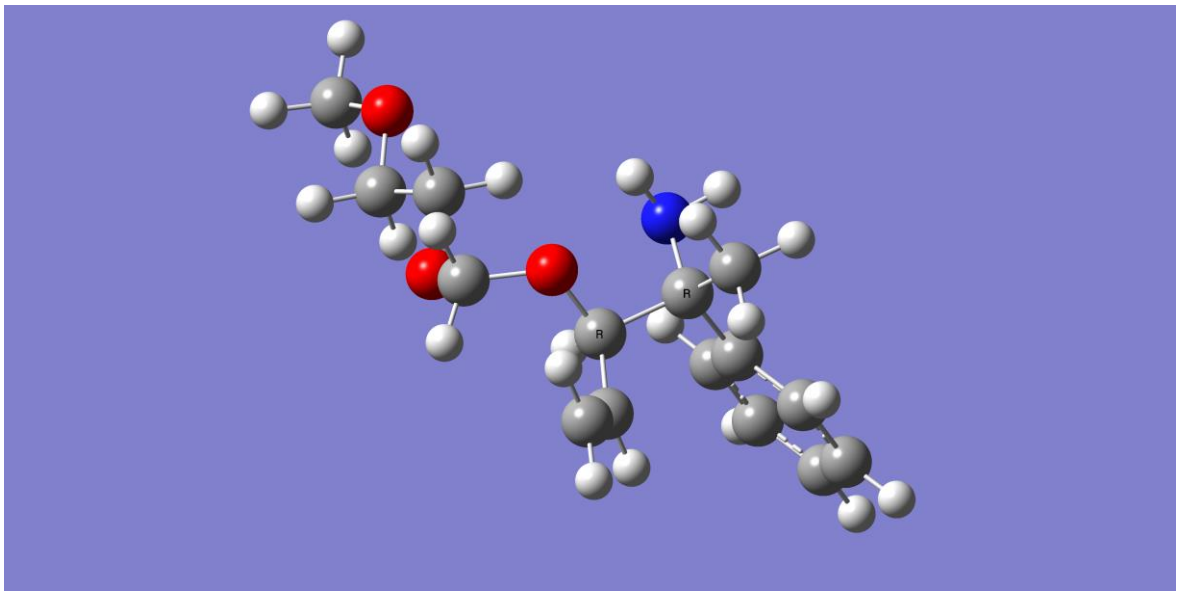
c99, 6.8%



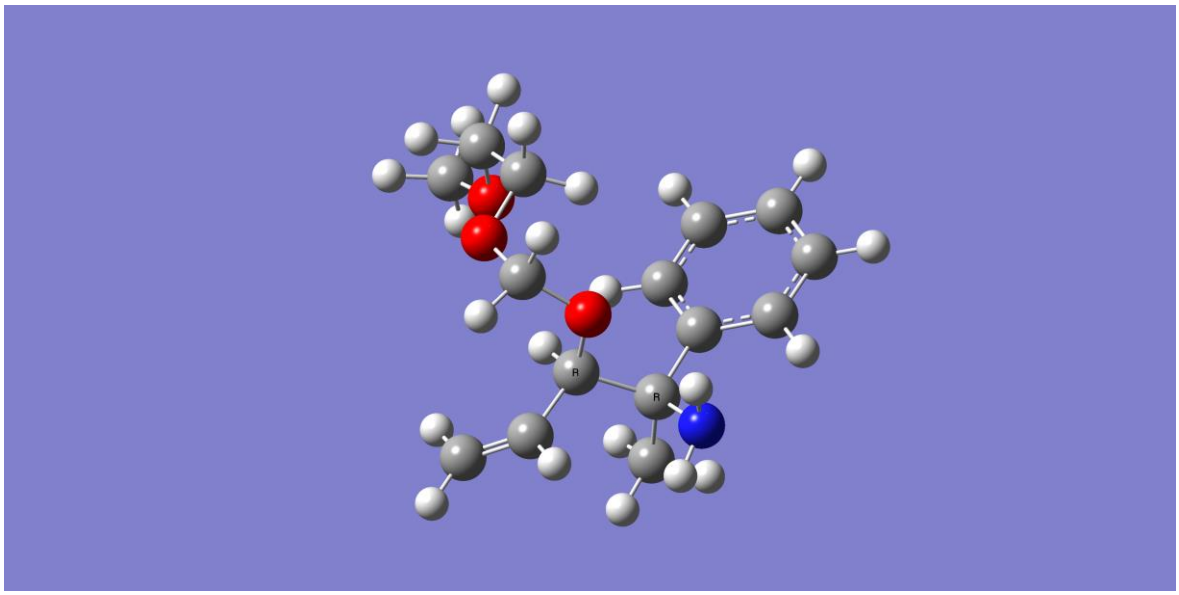
c135, 3.9%



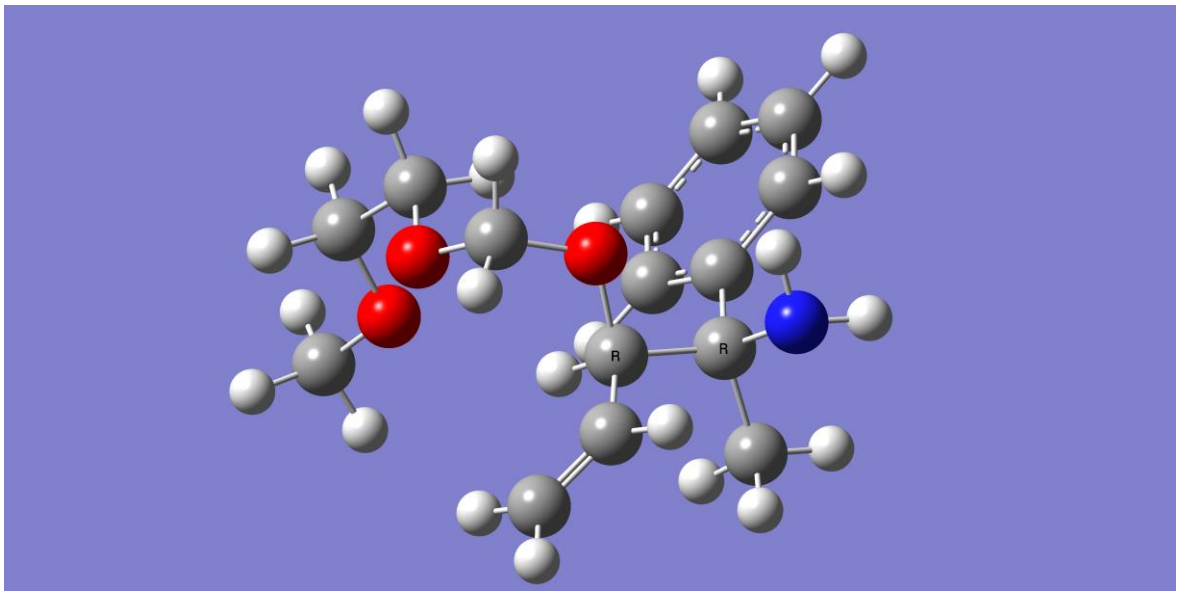
c141, 3.1%



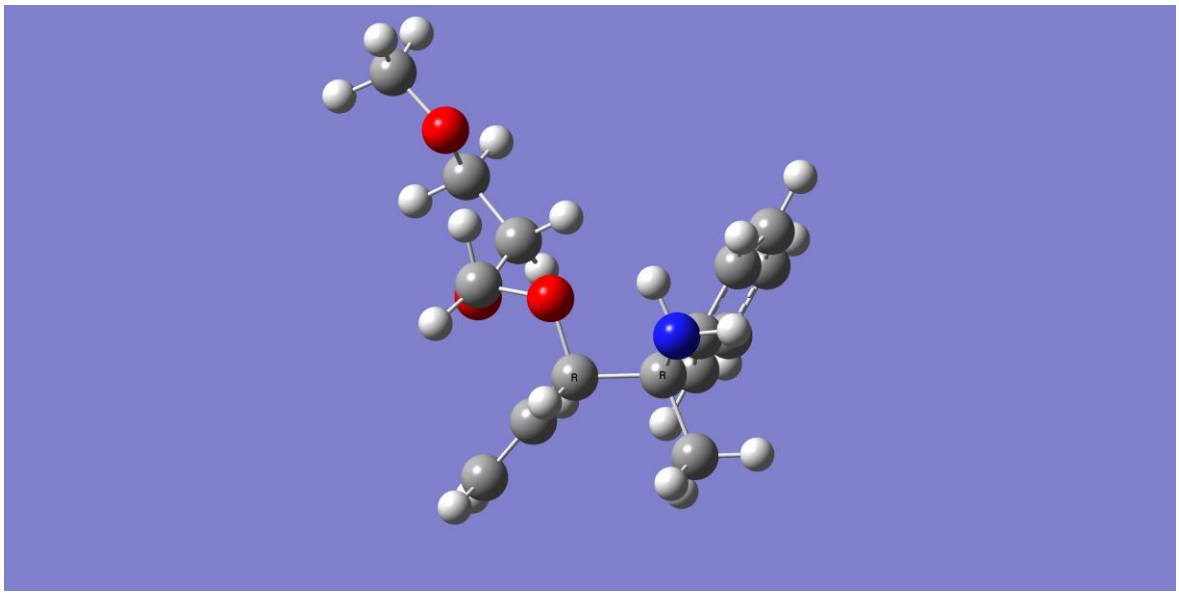
c176, 4.5%



c207, 5.1%

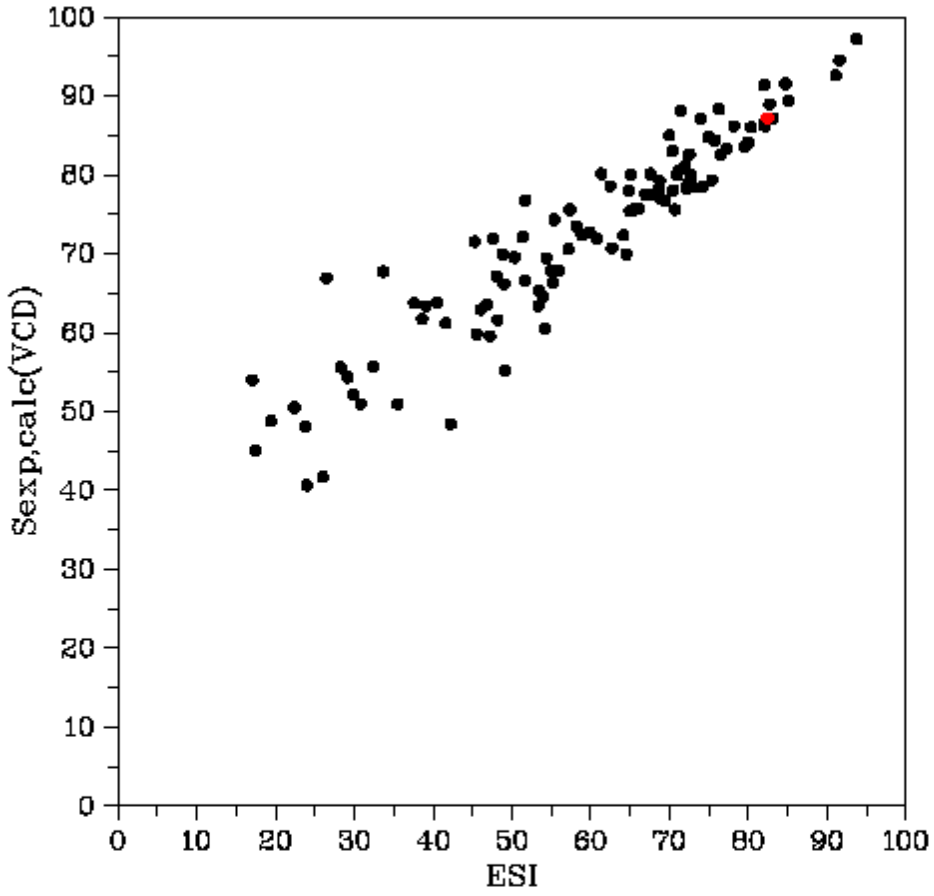


c263, 5.8%



c338, 8.7%

106 correct VCD assignments of Absolute Configuration



● Lorell's sample

The new ESI–value lies in the 92th percentile
of the database for correct assignments