Supporting Information

Rhodium-Catalyzed Diastereoselective Synthesis of Highly Substituted Morpholines from Nitrogen-Tethered Allenols

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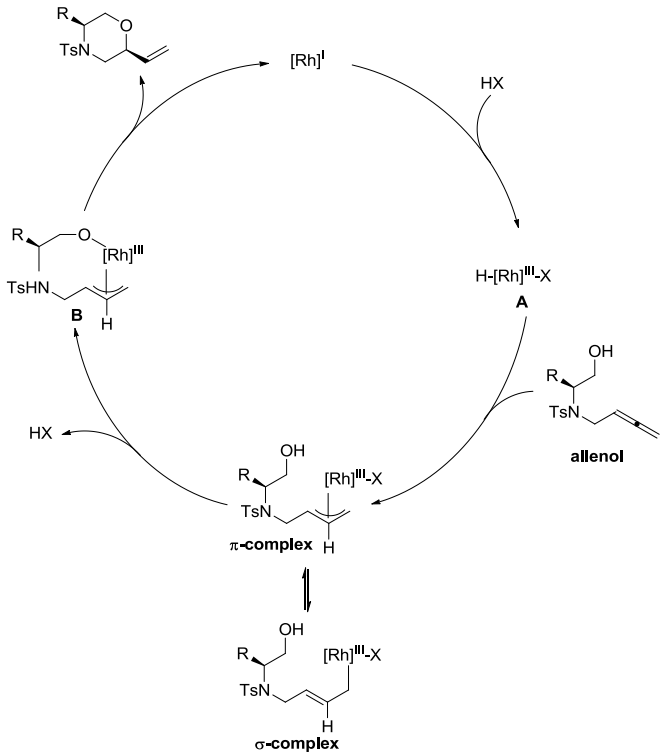
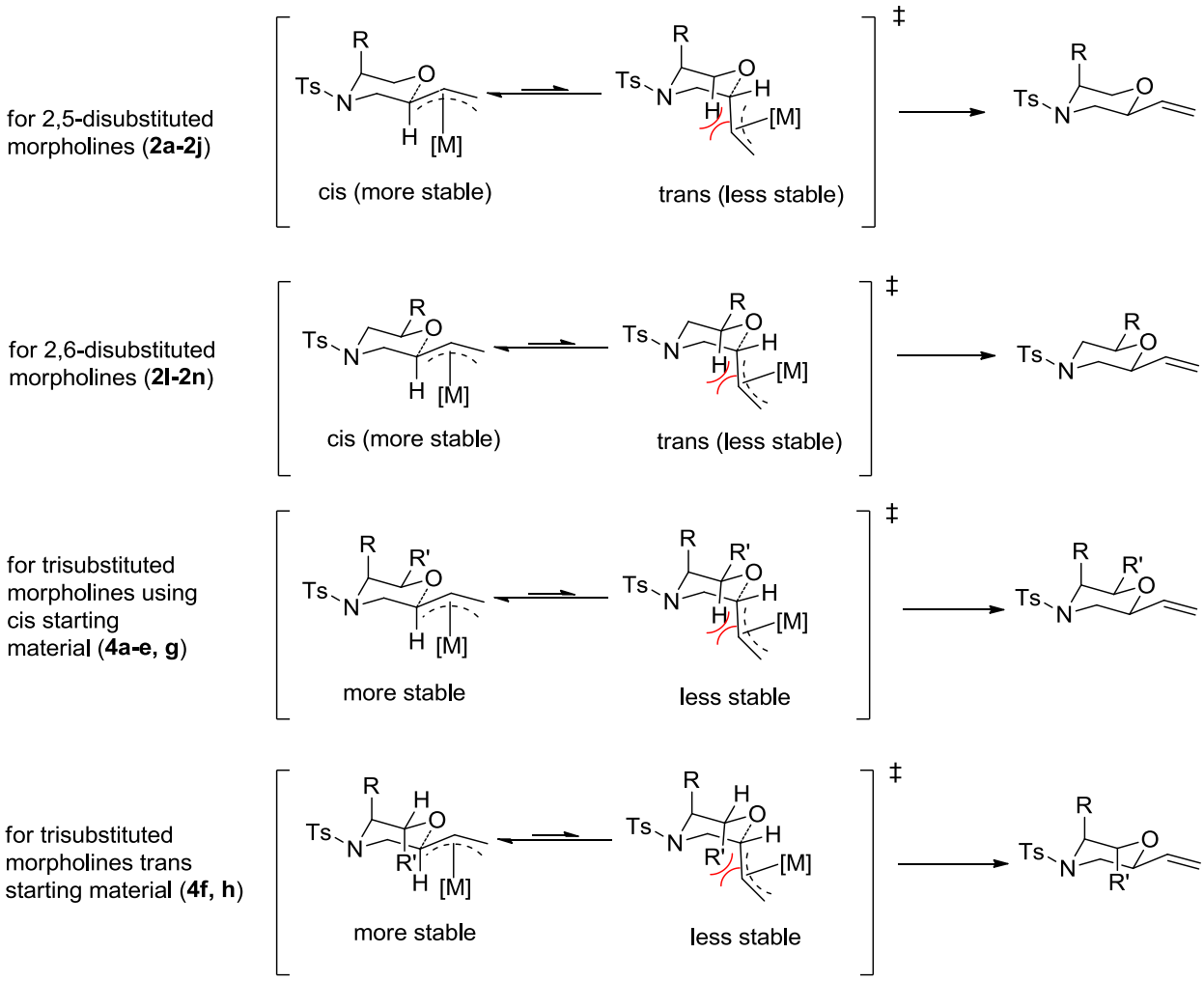
Proposed mechanism

Proposed mechanism for the synthesis of substituted morpholines by using Rhodium/ligand catalytic system in the presence of an additive is depicted in Scheme 1.



Scheme 1. Proposed mechanism for Rh-catalyzed synthesis of substituted morpholines

By considering the spatial orientation of substituents in two possible diastereomers as described in Scheme 2, it can be concluded that the *cis* diastereomer is more stable than the *trans* diastereomer due to the lack of unfavorable 1,3-diaxial interactions between the π-allyl moiety and the axial hydrogen/alkyl group at C6.



Scheme 2. Relative stability of *cis* and *trans* diastereoisomers in di- and trisubstituted morpholines

Determination of the stereochemistry of products by NOESY experiment

The structures of all final products (**2a-n**, **4a-h** and **5-8**) were determined by using ^{1}H NMR, ^{13}C NMR, DQF-COSY, edHSQC, HMBC NMR techniques and HRMS analysis. After determining the chemical shifts of carbons and hydrogens by the mentioned NMR techniques, the stereochemistry of all products was examined by the aid of NOESY experiment. The results of NOESY experiment for compound **2d** are described here as an example (selected important correlations are depicted in Figure 1). The NOESY experiment of **2d** shows space correlation of H10 (δ 5.74) with the axial hydrogen in the position 3 (δ 2.90 ppm). In addition, H_{ax} in the position 3 shows correlations with H7 and H7' (δ 1.36 ppm and 1.53 ppm). Furthermore, H2 (δ

3.74 ppm) correlates with axial hydrogen in the position 6 (δ 3.54 ppm). By considering these important correlations, it can be simply concluded that the vinyl group in the position 2 and the isobutyl group in the position 5 are in *cis* configuration (Figures 2-4).

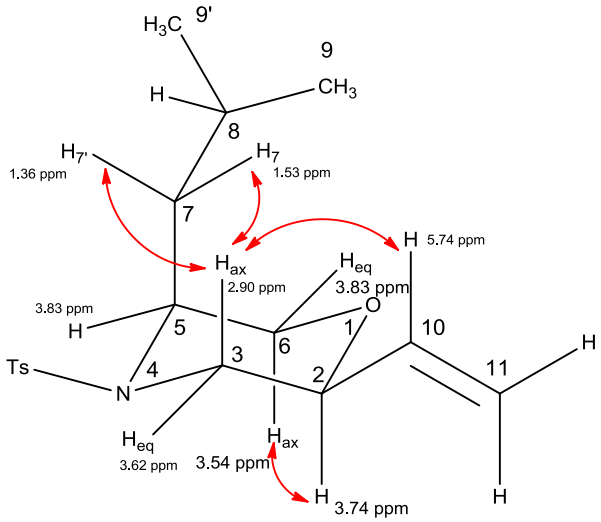


Figure 1. Selected correlations illustrations in compound **2d** by NOESY experiment

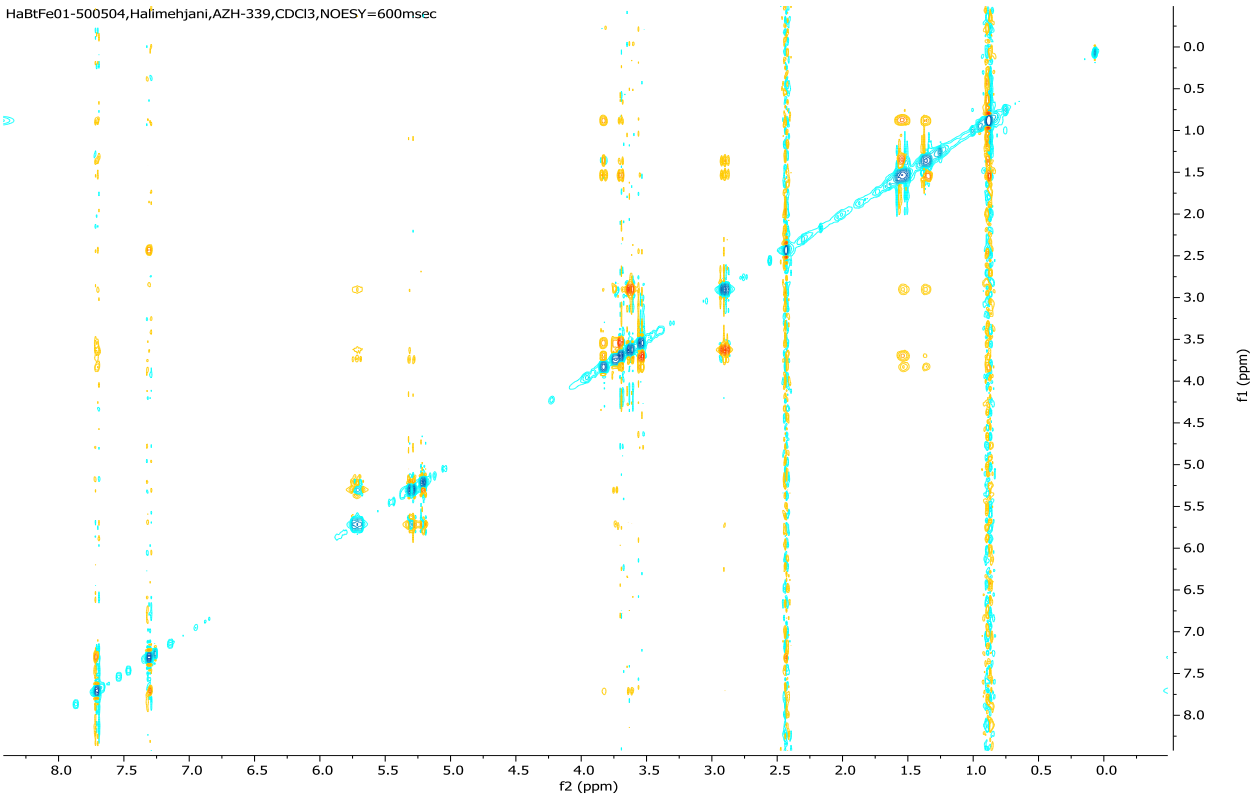


Figure 2. NOESY spectra for compound **2d**

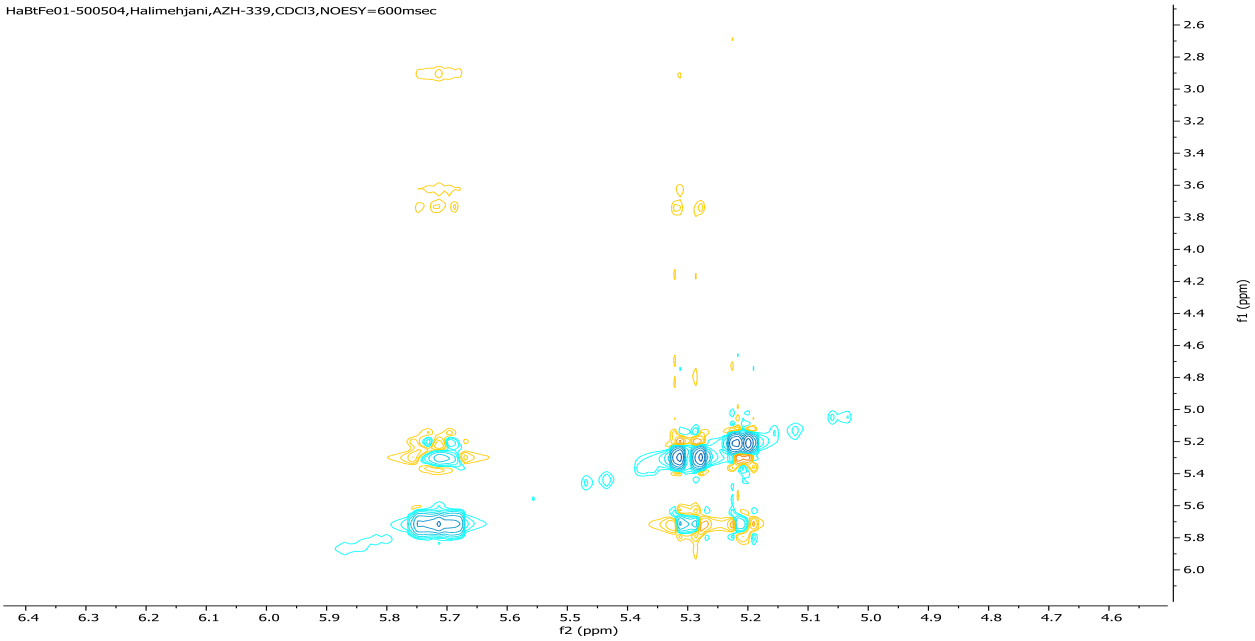


Figure 3. Expanded NOESY spectra for compound **2d**

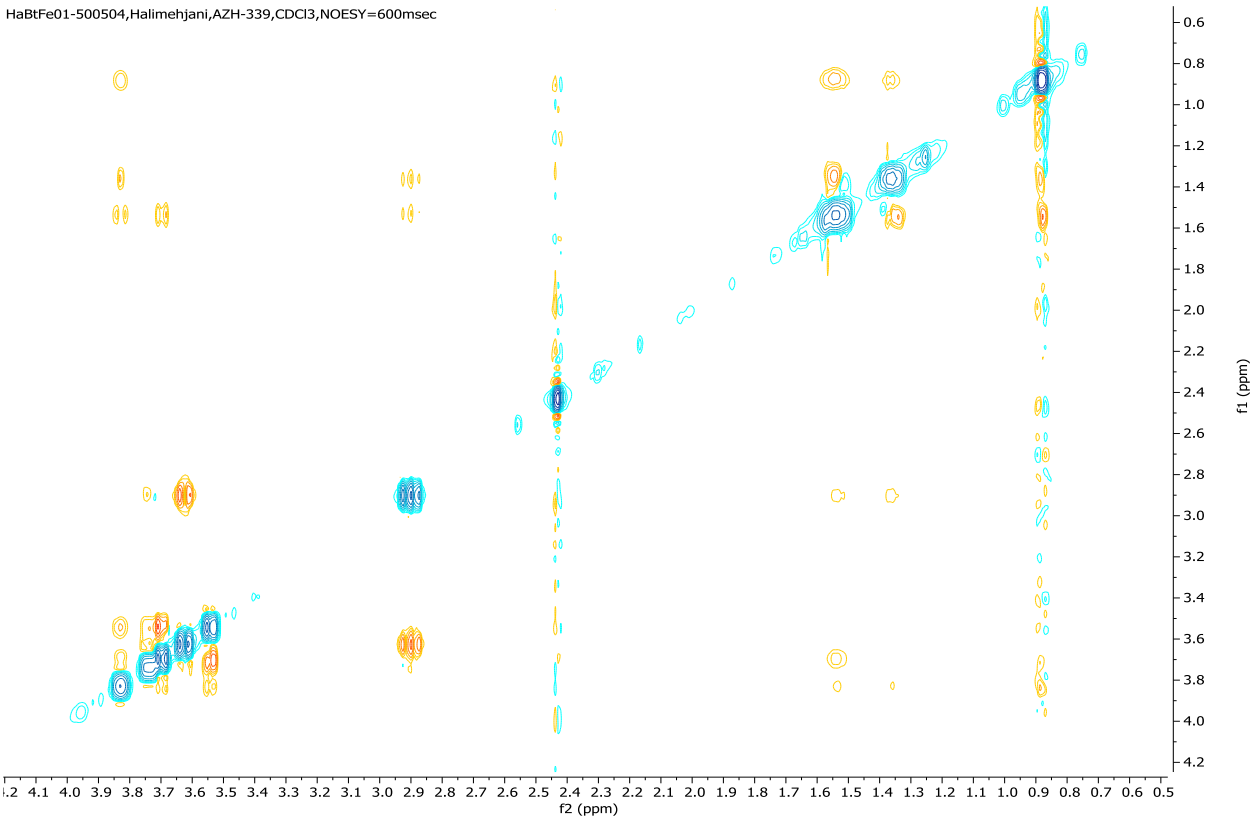


Figure 4. Expanded NOESY spectra for compound **2d**

The selected correlations in **4b** by NOESY experiment is illustrated in Figure 5. The NOESY experiment of **4b** shows space correlation of H10 (δ 5.76) with the axial hydrogen in the position 5 (δ 2.78 ppm). In addition, H_{ax} in the position 5 shows correlation with the methyl group (δ 0.92 ppm) in position 3. The methyl group in position 3 correlates with the methyne hydrogen (H8, δ 1.54 ppm). Furthermore, H6 (δ 3.88 ppm) correlates with axial hydrogen in the position 2 (δ 3.02 ppm) (Figures 6-7). By considering these important correlations, the stereochemistry of **4b** was considered as all *cis* as depicted in Figure 5.

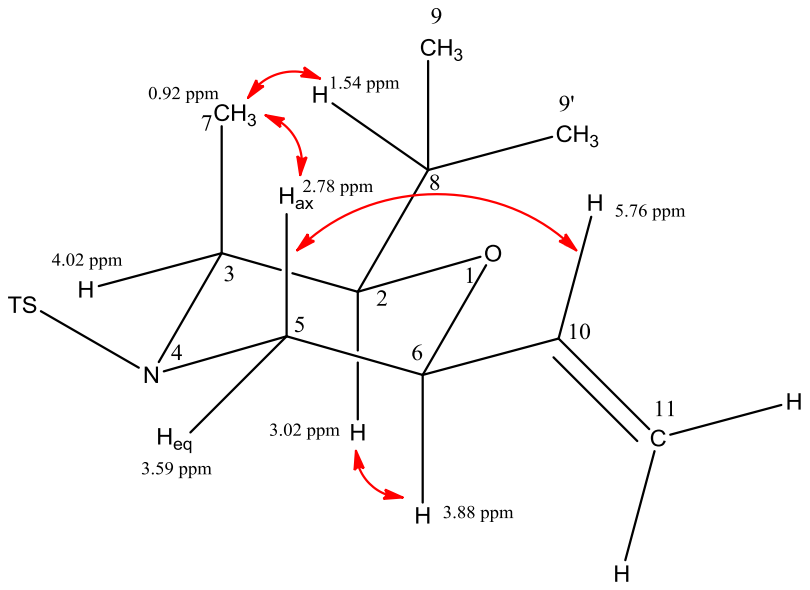


Figure 5. Selected correlations illustrations in compound **4b** by NOESY experiment

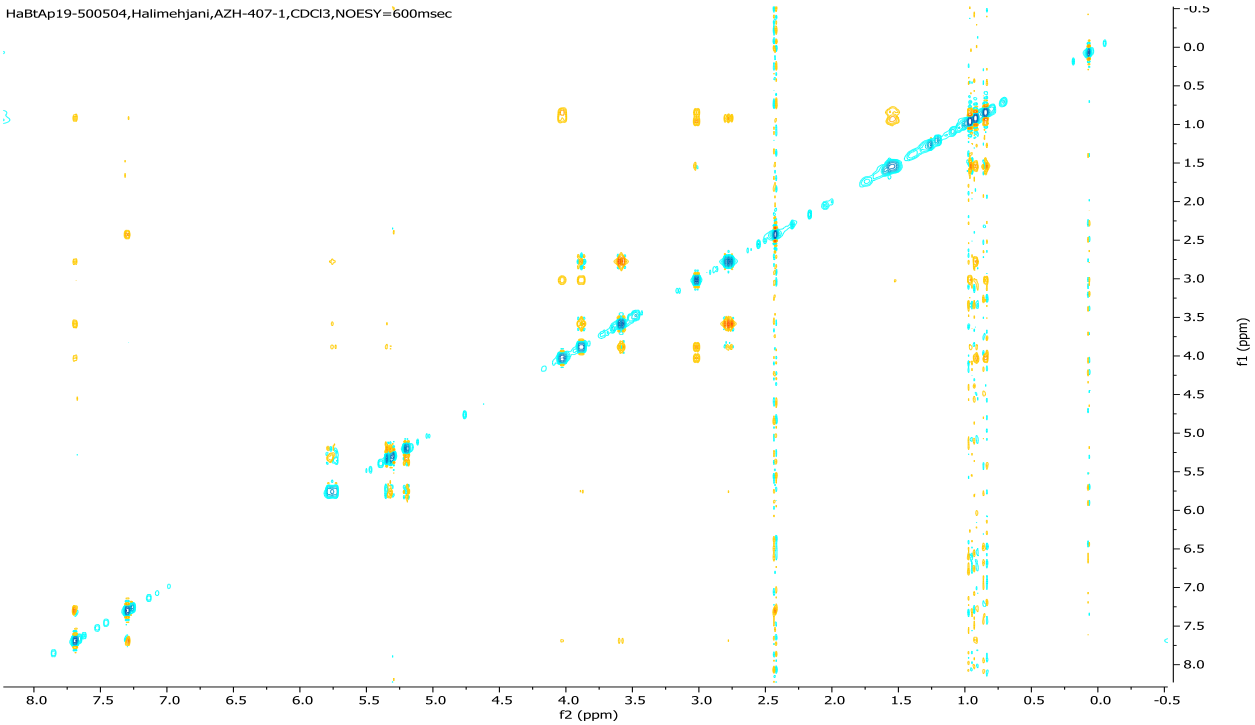


Figure 6. NOESY spectra for compound **4b**

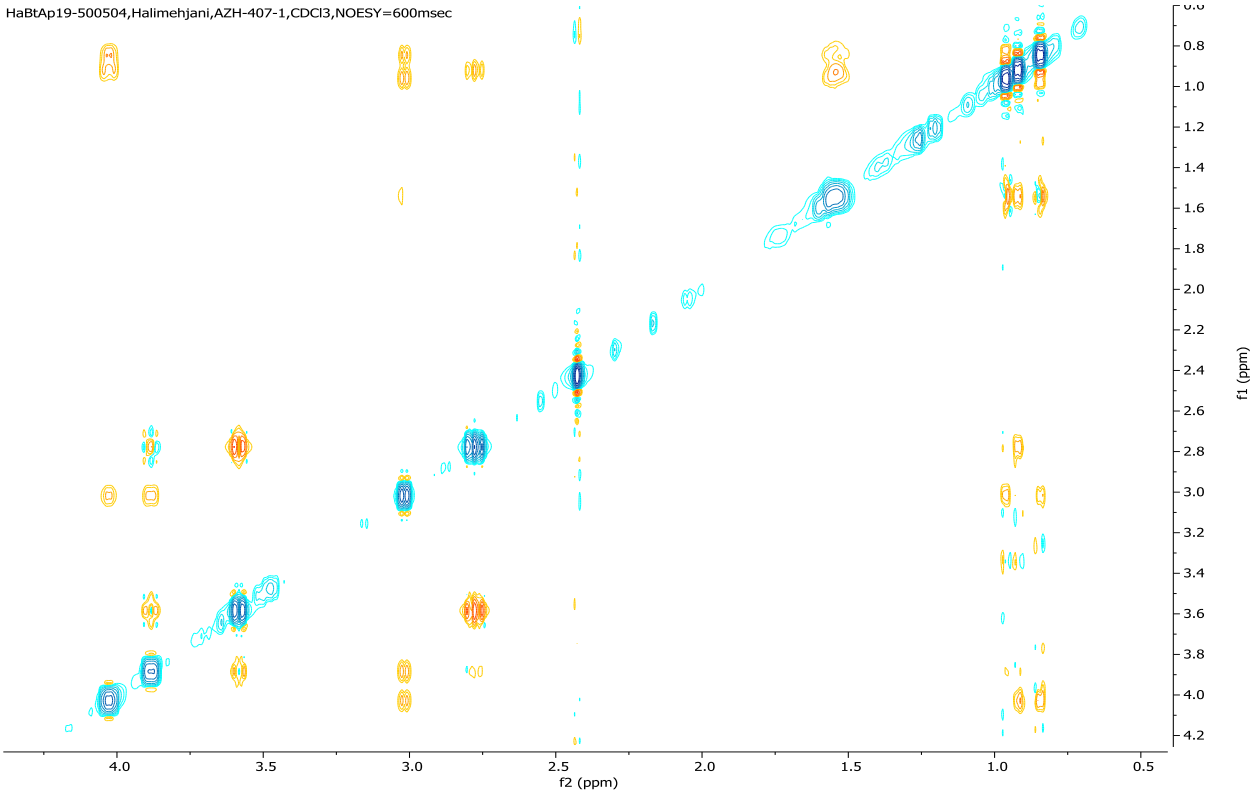


Figure 7. Expanded NOESY spectra for compound **4b**

Experimental Section: General remarks

Chemicals were purchased from commercial suppliers and used as received.

The ***reaction solvents*** were dried in the lab before use. Solvents employed for work-up and column chromatography were purchased in technical grade quality and distilled before use.

Column Chromatography was performed using silica gel 60 (0.04 - 0.063 mm, 230 - 240 mesh ASTM) from Macherey-Nagel GmbH & Co. TLC (Thin Layer Chromatography) was performed on aluminum plates pre-coated with silica gel (MERCK, 60 F254), which were visualized by UV fluorescence (λmax= 254 nm) and/or by staining with 1% w/v $KMnO_4$ in 0.5 M aqueous K_2CO_3 solution.

NMR spectra for the compounds were recorded on a Bruker Avance spectrometer (400 or 500 MHz for ^{1}H and 100.6 or 126 MHz for ^{13}C nucleus). All ^{1}H NMR spectra are reported in parts per million (ppm) downfield of TMS and were measured relative to the signals at 7.26 ppm for chloroform. All ^{13}C NMR spectra were reported in ppm relative to residual $CHCl_3$ (77.16 ppm) and were obtained with ^{1}H-decoupling. The *cis/trans* ratio was measured by evaluating the ^{1}H NMR of crude mixture. The stereochemistry of products was confirmed using NOESY analysis.

HRMS (High Resolution Mass Spectra) was measured on a THERMO SCIENTIFIC Advantage and a THERMO SCIENTIFIC Exactive instrument equipped with an APCI source in the positive-ion mode.

Chiral HPLC was performed on a MERCK HITACHI HPLC apparatus (pump: L-7100, UV detector: D-7400, oven: L-7360; columns: AD-3, L-C3 and L-C3).

Optical Rotation of chiral compounds (dissolved in CH_2Cl_2) was determined on a PERKIN-ELMER PE 241 apparatus and converted to the specific optical rotation with the following formula.

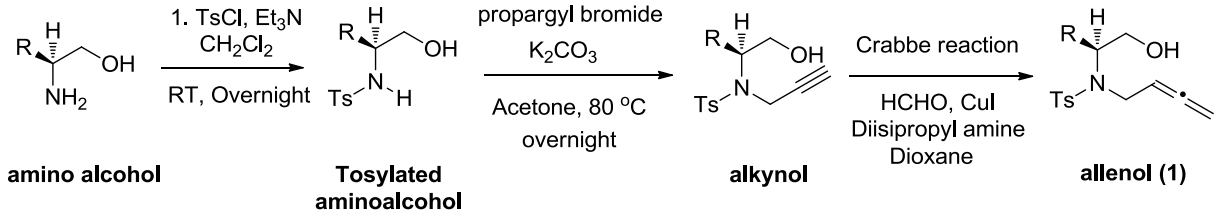
$$[\alpha]_D^T = \frac{\alpha . 100}{c.d}$$

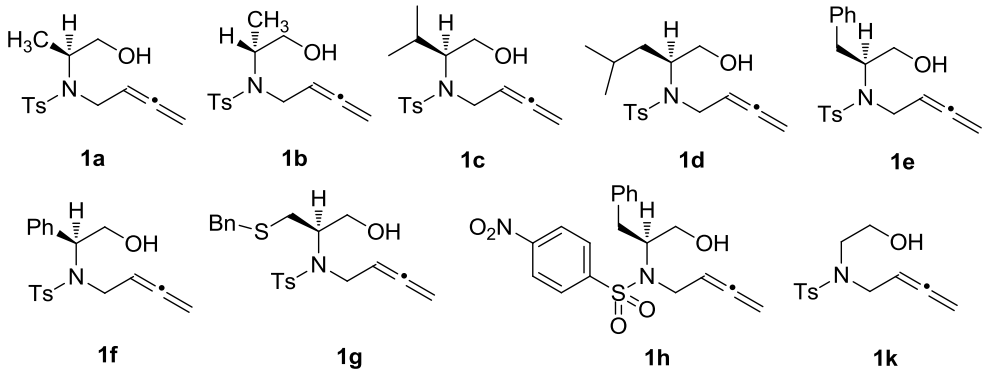
α:measured value; c: concentration in g/100 mL; d: length of the cuvette in dm; T: temperature in °C.

Synthesis of starting materials and their characterization data

Allenols

Allenols **1a-1h** and **1k** were prepared according to the general procedures 1-3 starting from the corresponding aminoalcohols, according to the following general scheme:





General procedure 1: Tosylation (Nosylation) of aminoalcohols

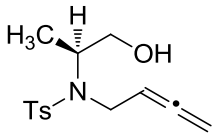
To a solution of an aminoalcohol (1.0 equiv) and a sulfonyl chloride (1.1 equiv) in dichloromethane (3 mL/mmol) at 0 °C, Et_3N (1.1 equiv) was added gradually and the mixture was allowed to warm to room temperature and further stirred for overnight. Finally, the organic phase was washed with 2M aqueous HCl solution (2 x 2.5 mL/mmol), dried over Na_2SO_4, and evaporated to give the crude product. Recrystallization of the residue from diethyl ether/*n*-pentane afforded the pure tosylated aminoalcohol.[1]

General Procedure 2: Synthesis of alkynols by propargylation reaction

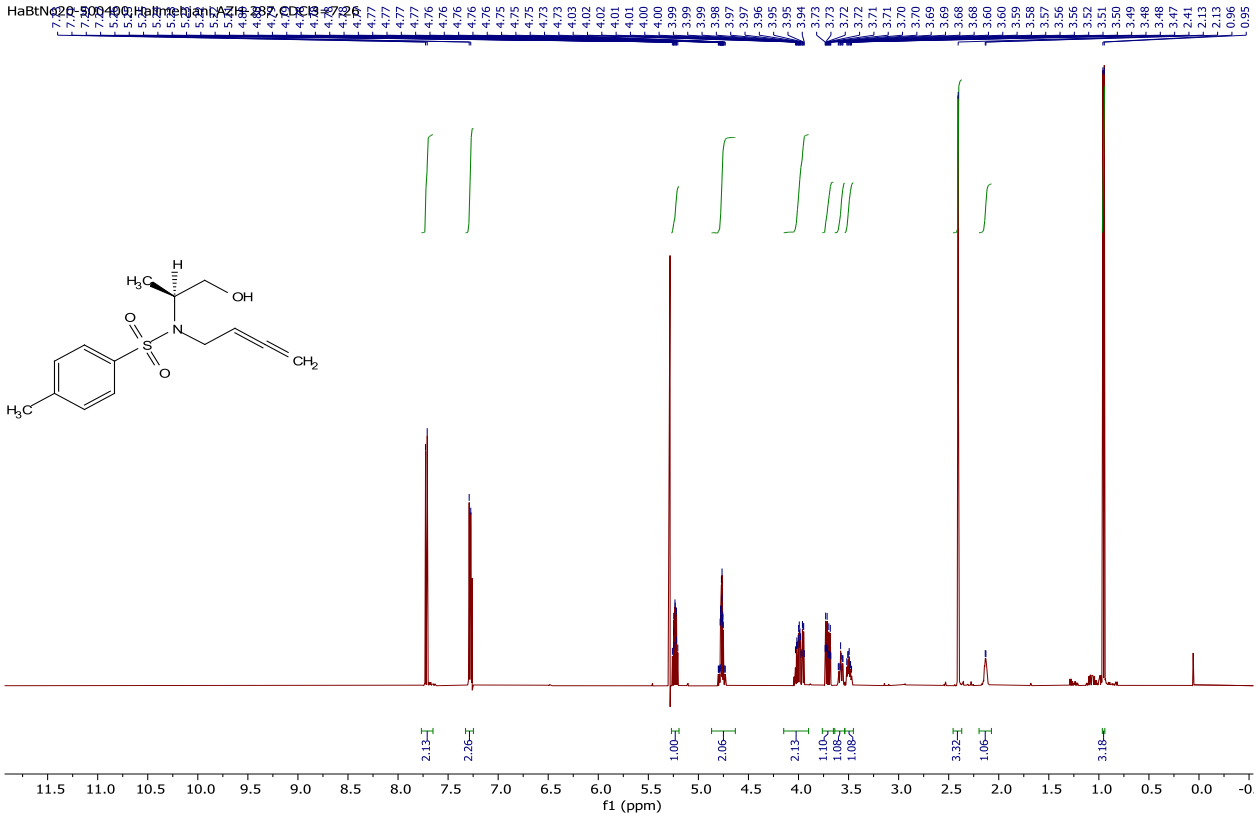
A mixture of tosylated (Nosylated) aminoalcohol **2** (1.0 equiv), propargyl bromaide (1.2 equiv), and K_2CO_3 (1.0 equiv) in acetone (2 mL/mmol) was heated to 85 °C for overnight. The mixture was filtered to remove solid and the filtrate was concentrated to afford the corresponding propargylated product.[2]

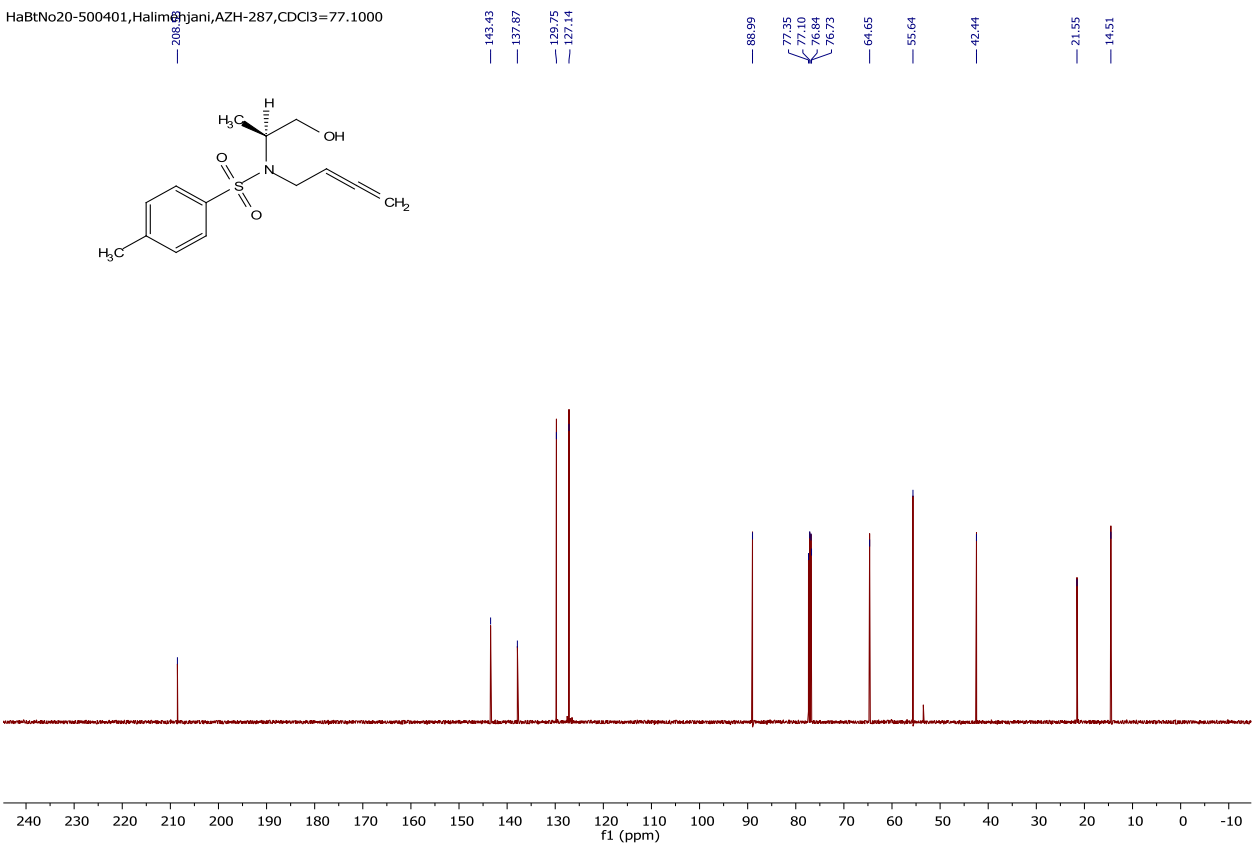
General Procedure 3: Synthesis of allenols 1a-1h and 1k from corresponding alkynol by Crabbe reaction

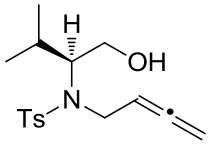
A suspension of alkynol adduct (1.0 equiv), cuprous iodide (0.5 equiv), paraformaldehyde (2.5 equiv) and diisopropylamine (2.0 equiv) in dioxane (5 mL/mmol) was gently heated at reflux and stirred for 12 h, cooled to room temperature, and filtered through a Celite pad. The dark-brown filtrate was concentrated in vacuo to afford a gummy residue. The residue was triturated with diethyl ether and filtered through the same Celite pad. This procedure was repeated 2 more times until a light yellow filtrate was obtained. Finally, the solvent was evaporated under reduced pressure to afford the crude product which was purified by column chromatography.[3]



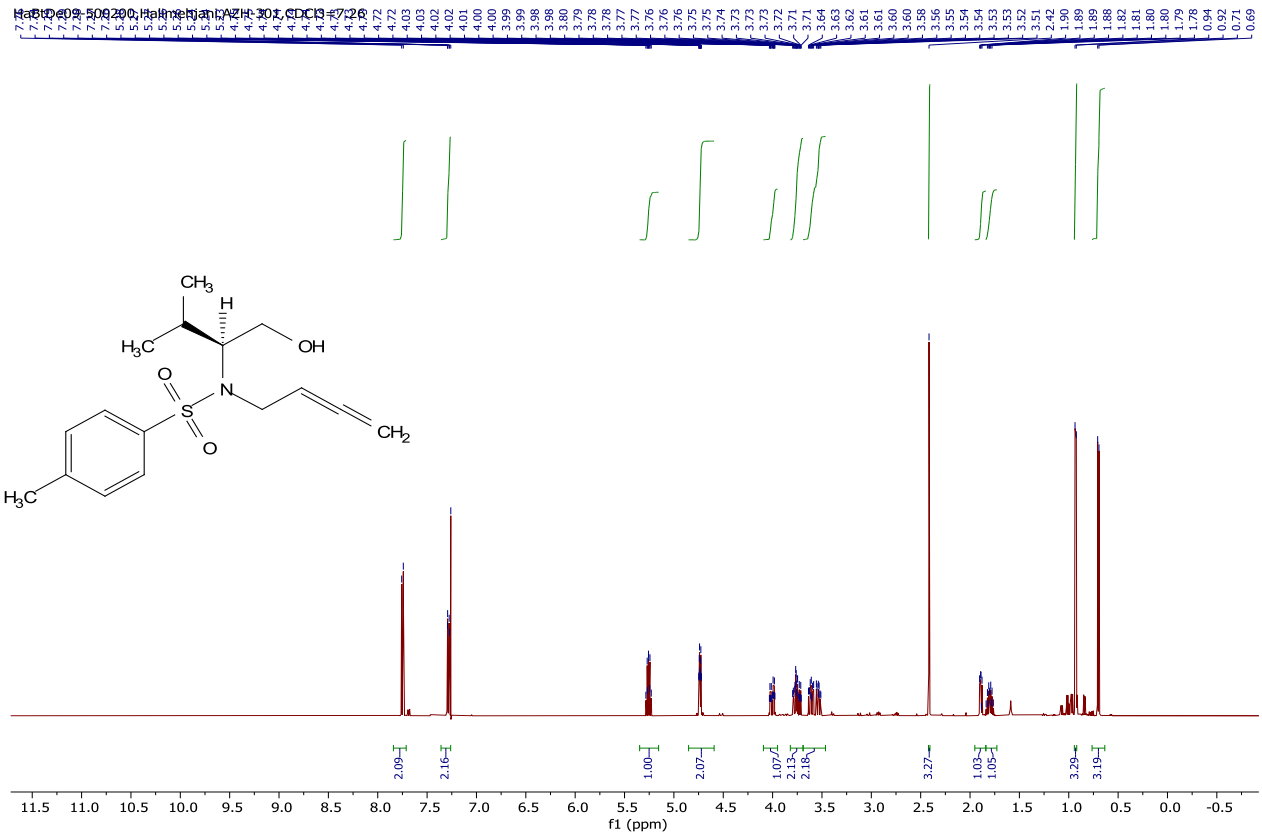
(S)-N-(buta-2,3-dien-1-yl)-N-(1-hydroxypropan-2-yl)-4-methylbenzenesulfonamide (**1a**): ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.72 (d, J = 8.3 Hz, 2H), 7.28 (d, J = 7.9 Hz, 2H), 5.27 – 5.19 (m, 1H), 4.87 – 4.63 (m, 2H), 4.15 – 3.90 (m, 2H), 3.73–3.68 (m, 1H), 3.60–3.56 (m, 1H), 3.52–3.47 (m, 1H), 2.41 (s, 3H), 2.13 (brs, 1H), 0.95 (d, J = 7.0 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 208.5, 143.4, 137.8, 129.7, 127.1, 88.9, 76.7, 64.6, 55.6, 42.4, 21.5, 14.5 ppm; HRMS (ESI) calcd for $C_{14}H_{19}NO_3S$ $[M+H]^+$: 282.1164; found: 282.1161; $[\alpha]_D^{25}$ = +63.12 (c = 0.385, CH_2Cl_2). The allenol **1b** was prepared by the same procedure.







(S)-N-(buta-2,3-dien-1-yl)-N-(1-hydroxypropan-2-yl)-4-methylbenzenesulfonamide (**1c**): ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.75 (d, J = 8.4 Hz, 2H), 7.28 (d, J = 8.6, 2H), 5.26 (m, 1H), 4.80–4.72 (m, 2H), 3.98 (m, 1H), 3.82 – 3.69 (m, 2H), 3.69 – 3.46 (m, 2H), 2.42 (s, 3H), 1.89 (dd, J = 7.0, 5.3 Hz, 1H), 1.80 (m, 1H), 0.93 (d, J = 6.6 Hz, 3H), 0.70 (d, J = 6.7 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 208.5, 143.4, 138.2, 129.6, 127.5, 88.5, 76.4, 66.6, 62.1, 43.3, 28.0, 21.6, 20.6, 20.3 ppm; HRMS (ESI) calcd for $C_{16}H_{24}NO_3S$ $[M+H]^+$: 310.1477; found: 310.1475; $[\alpha]_D^{25}$ = +7.06 (c = 1.232, CH_2Cl_2).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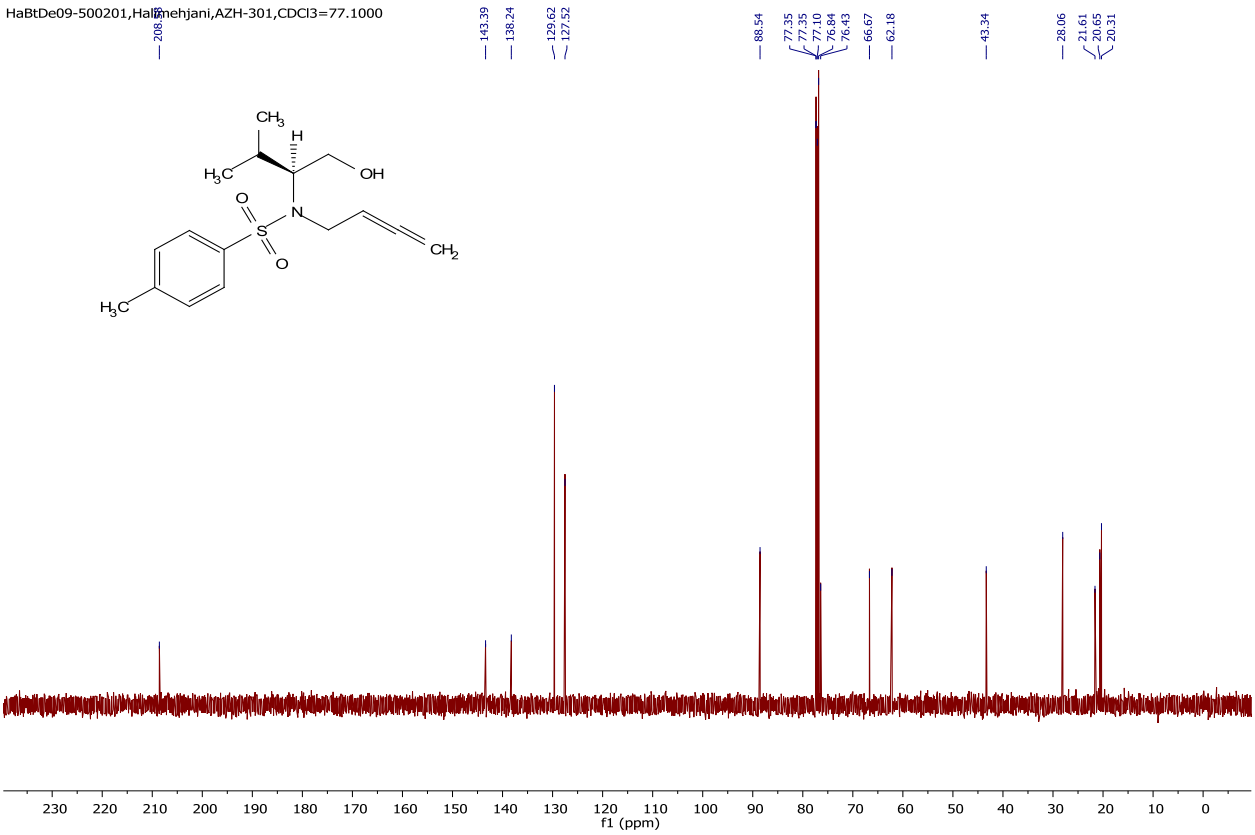
CH3
H
H3C
OH
O
N
S
O
CH2
H3C
2.09
2.16
1.00
2.07
1.07
2.13
2.18
3.27
1.03
1.05
3.29
3.19
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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129.62
127.52
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77.35
77.35
77.10
76.84
76.43
66.67
62.18
43.34
28.06
21.61
20.65
20.31
CH3
H
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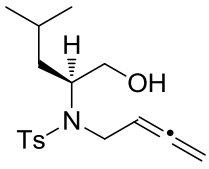
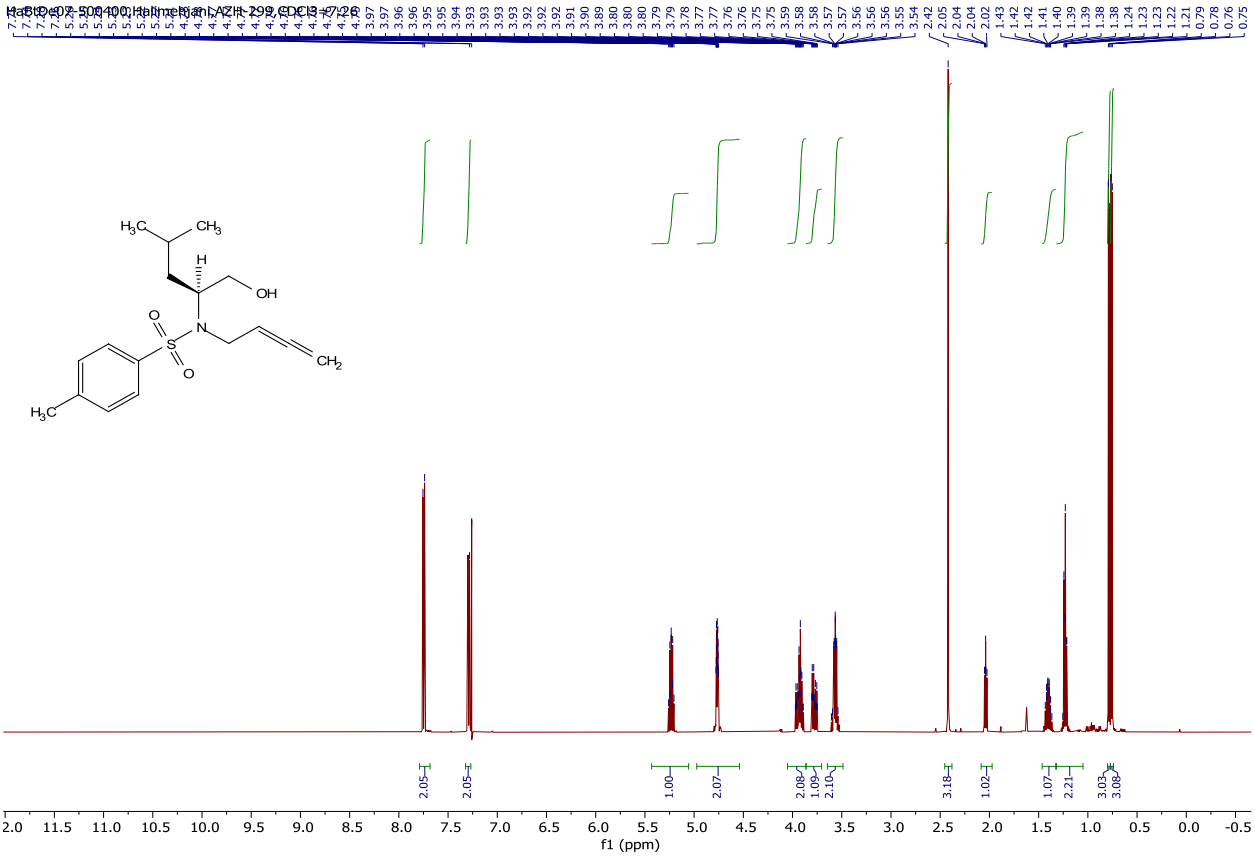
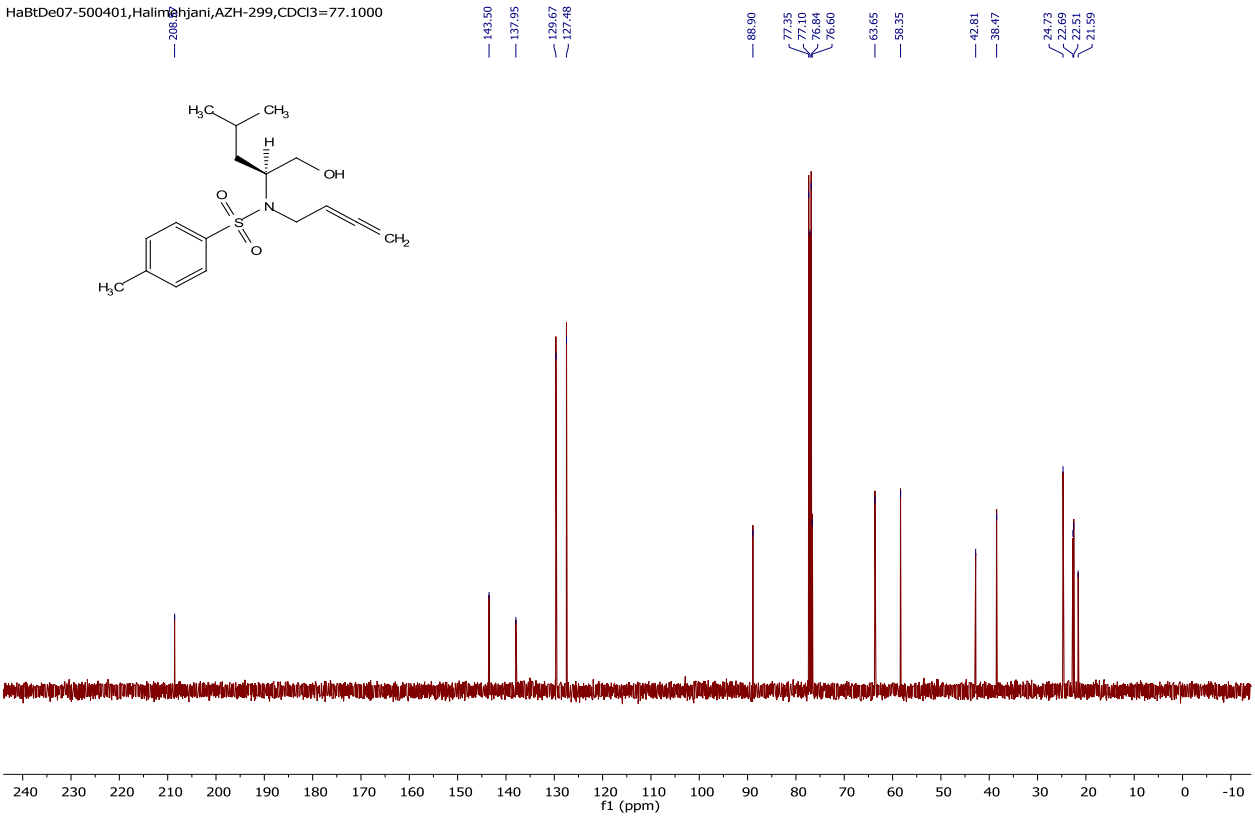
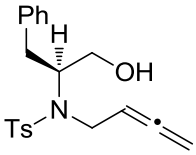
f1 (ppm)



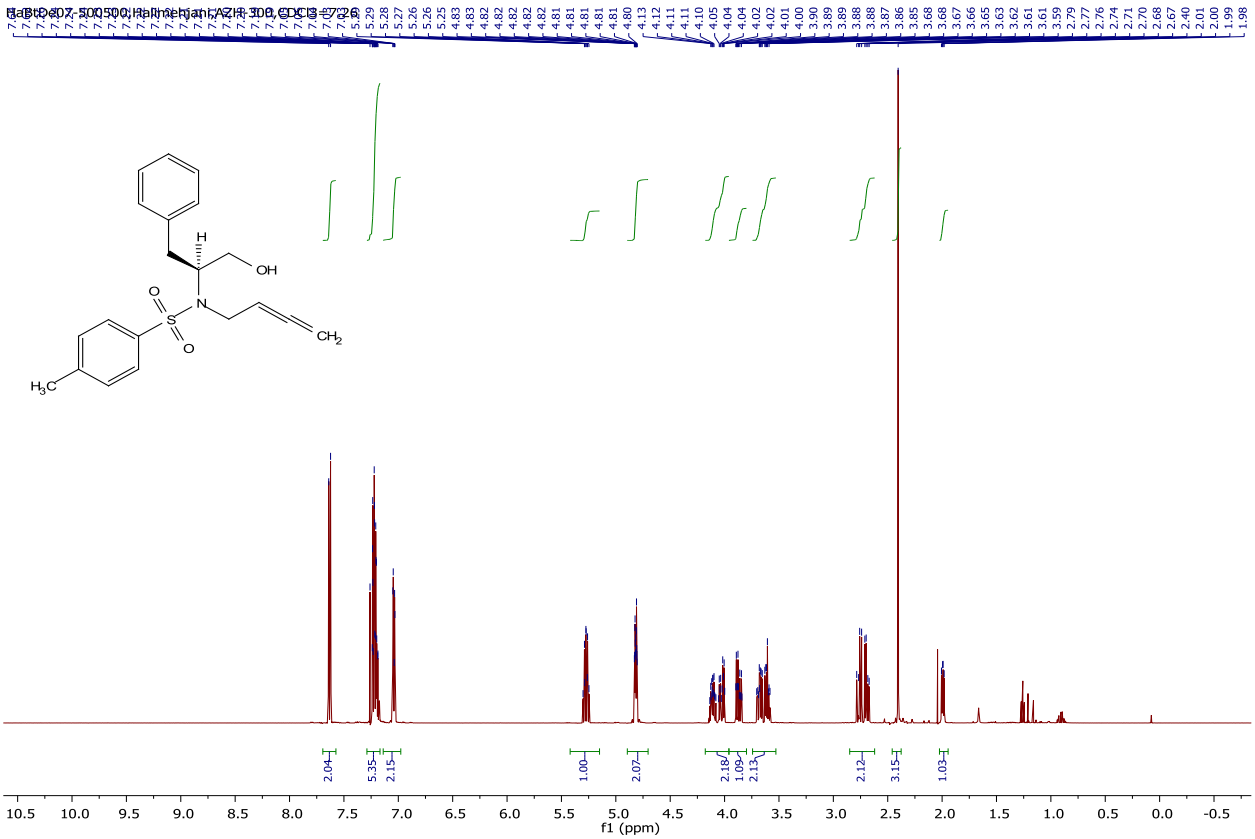
(S)-N-(buta-2,3-dien-1-yl)-N-(1-hydroxy-4-methylpentan-2-yl)-4-methylbenzenesulfonamide (**1d**): ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.75 (d, *J* = 8.3 Hz, 2H), 7.28 (d, *J* = 8.3 Hz, 2H), 5.23 (m, 1H), 4.80–4.72 (m, 2H), 4.05 – 3.86 (m, 2H), 3.78 (m, 1H), 3.65 – 3.49 (m, 2H), 2.42 (s, 3H), 2.04 (dd, *J* = 6.9, 5.5 Hz, 1H), 1.40 (m, 1H), 1.32 – 1.05 (m, 2H), 0.78 (d, *J* = 6.6 Hz, 3H), 0.76 (d, *J* = 6.5 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) *δ* 208.5, 143.5, 137.9, 129.6, 127.4, 88.9, 76.6, 63.6, 58.3, 42.8, 38.4, 24.7, 22.6, 22.5, 21.5 ppm; HRMS (ESI) calcd for $C_{17}H_{26}NO_3S$ $[M+H]^+$: 324.1633; found: 324.1628; $[\alpha]_D^{25}$ = +13.81 (c = 0.905, CH_2Cl_2).







(S)-N-(buta-2,3-dien-1-yl)-N-(1-hydroxy-3-phenylpropan-2-yl)-4-methylbenzenesulfonamide (**1e**): ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.63 (d, J = 8.4 Hz, 2H), 7.29 – 7.17 (m, 5H), 7.04 (dd, J = 7.9, 1.7 Hz, 2H), 5.27 (m, 1H), 4.84–4.80 (m, 2H), 4.18 – 3.96 (m, 2H), 3.87 (m, 1H), 3.74 – 3.53 (m, 2H), 2.85 – 2.62 (m, 2H), 2.40 (s, 3H), 1.99 (brs, 1H, OH) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 208.6, 143.4, 137.7, 137.6, 129.7, 129.0, 128.6, 127.3, 126.6, 88.8, 76.7, 62.5, 61.9, 43.5, 36.3, 21.5 ppm; HRMS (ESI) calcd for $C_{20}H_{23}NO_3S$ $[M+H]^+$: 358.1477; found: 358.1473; $[\alpha]_D^{25}$ = -35.95 (c = 1.038, CH_2Cl_2).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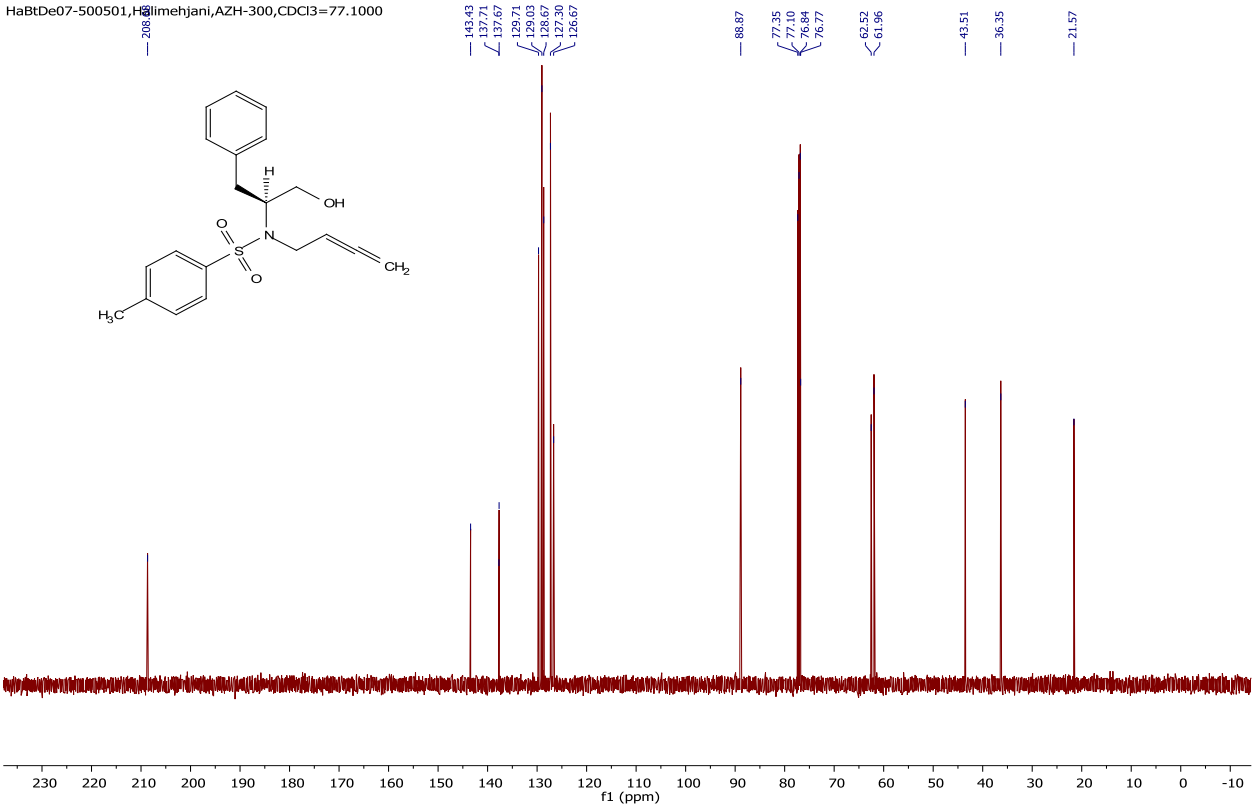
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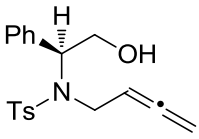
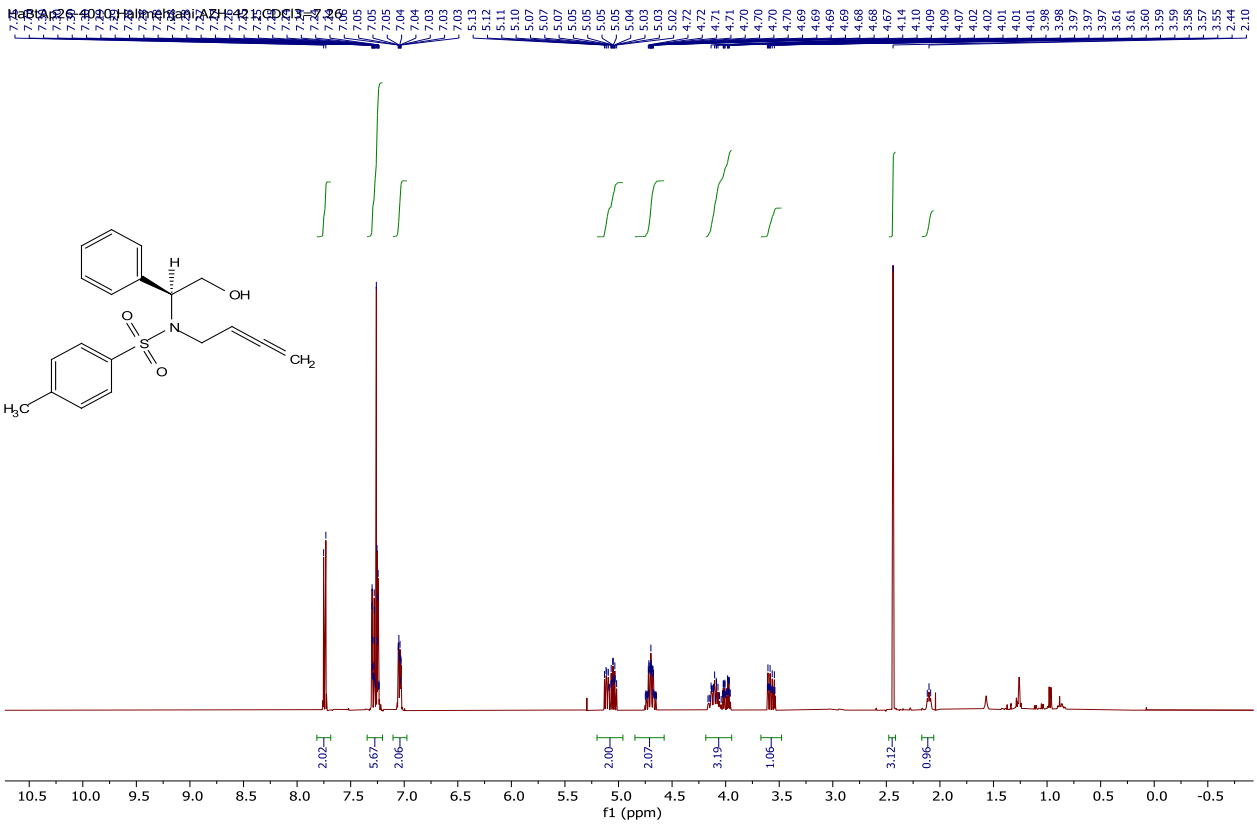
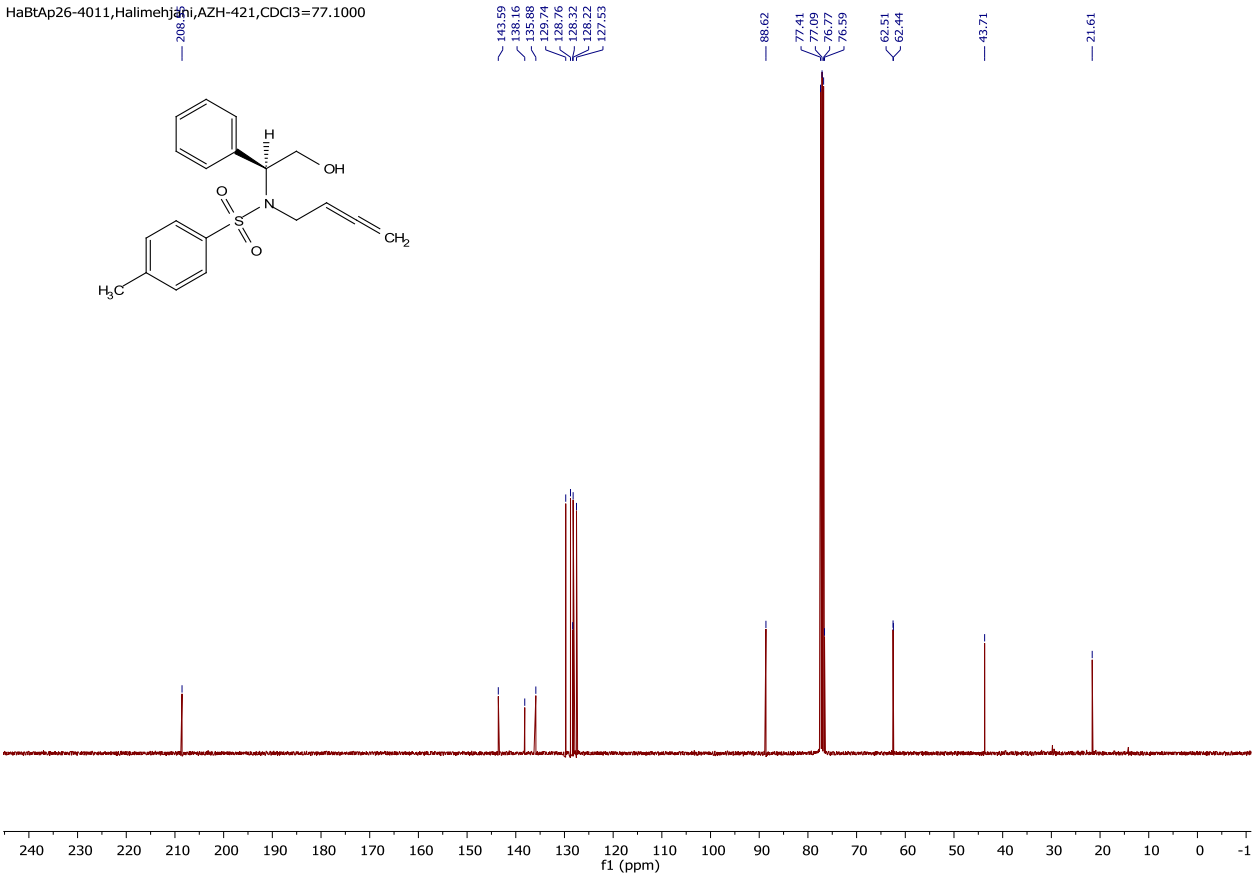
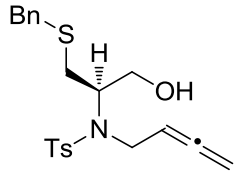
f1 (ppm)



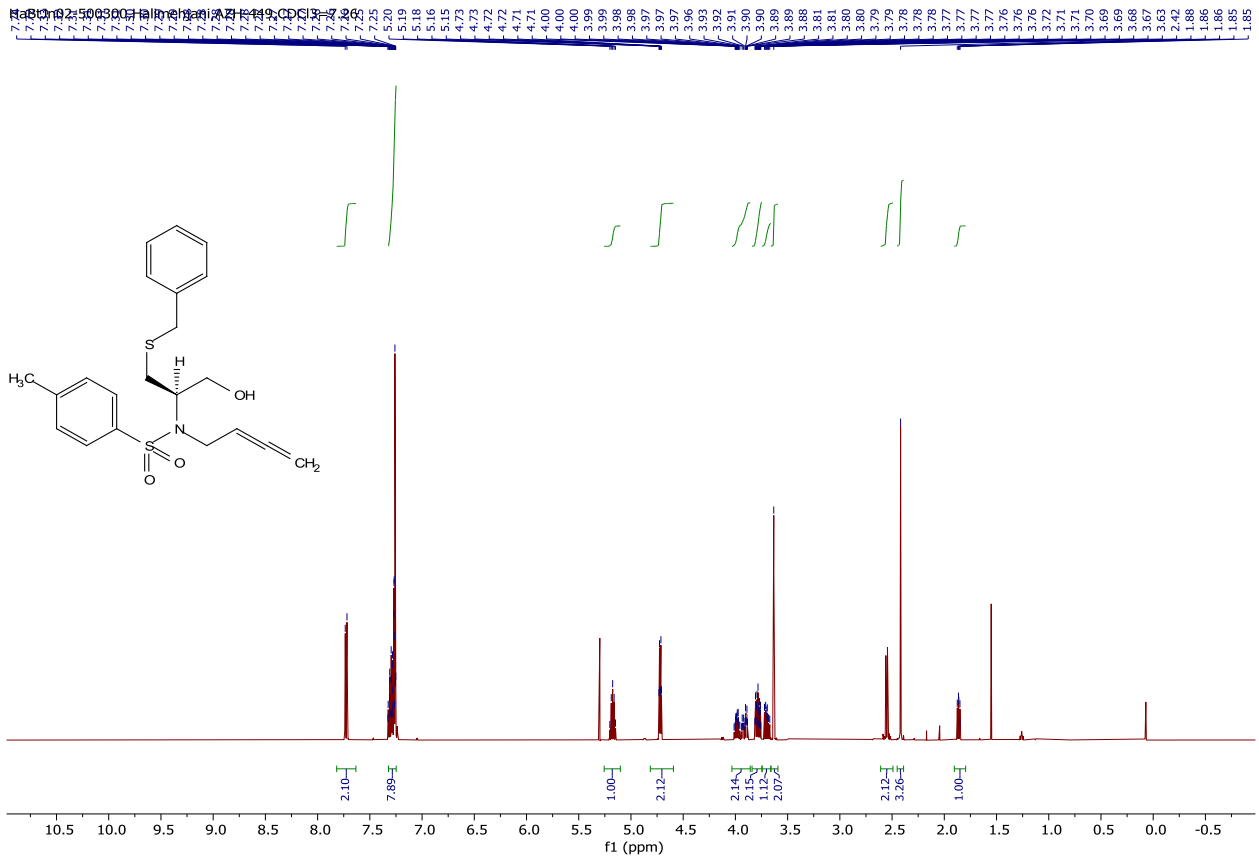
(S)-N-(buta-2,3-dien-1-yl)-N-(2-hydroxy-1-phenylethyl)-4-methylbenzenesulfonamide (**1f**): ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.74 (d, J = 8.4 Hz, 2H), 7.35 – 7.20 (m, 5H), 7.10 – 6.98 (m, 2H), 5.20 – 4.96 (m, 2H), 4.85 – 4.57 (m, 2H), 4.19 – 3.94 (m, 3H), 3.58 (m, 1H), 2.44 (s, 3H), 2.10 (t, J = 6.3 Hz, 1H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 208.5, 143.5, 138.1, 135.8, 129.7, 128.7, 128.3, 128.2, 127.5, 88.6, 76.5, 62.5, 62.4, 43.7, 21.6 ppm; HRMS (ESI) calcd for $C_{19}H_{21}NO_3S$ $[M+H]^+$: 344.1320; found: 344.1318; $[\alpha]_D^{25}$ = 77.40 (c = 0.717, CH_2Cl_2).

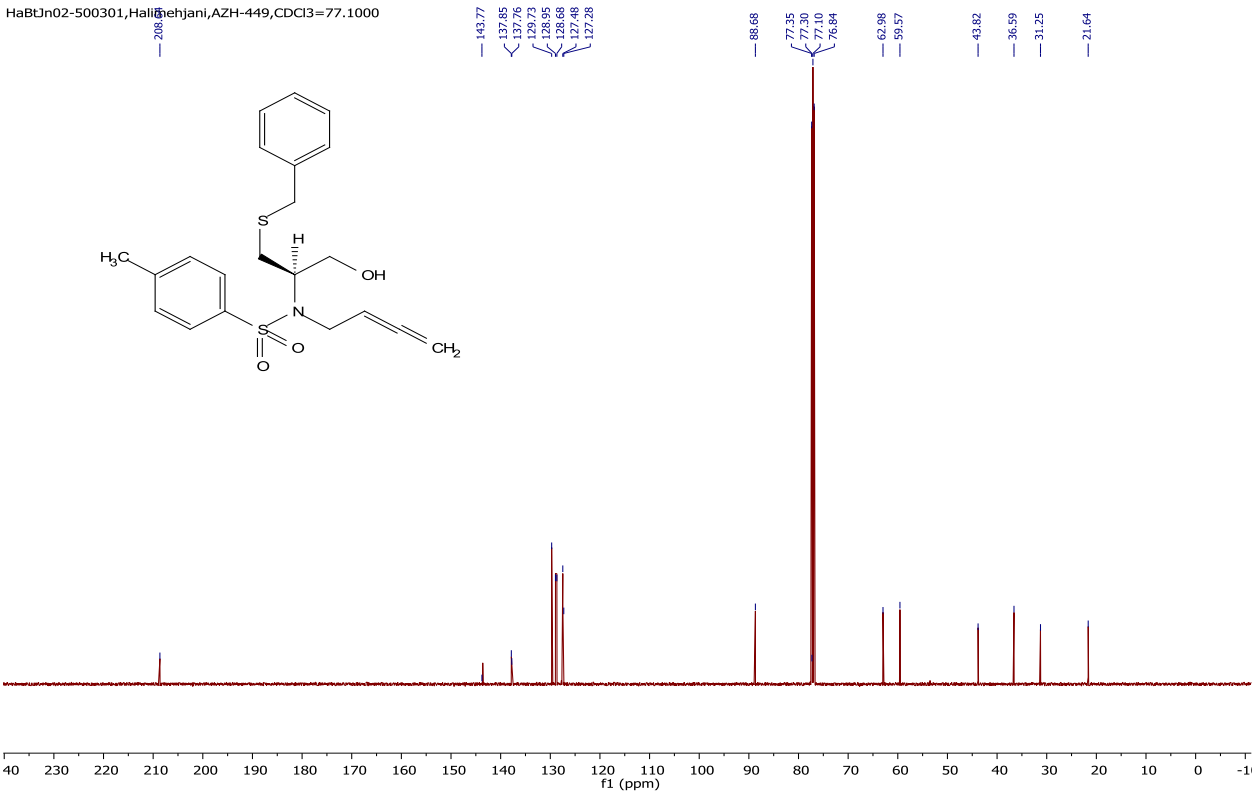


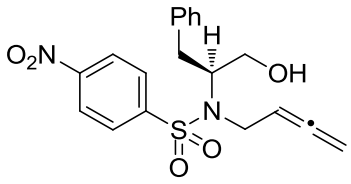




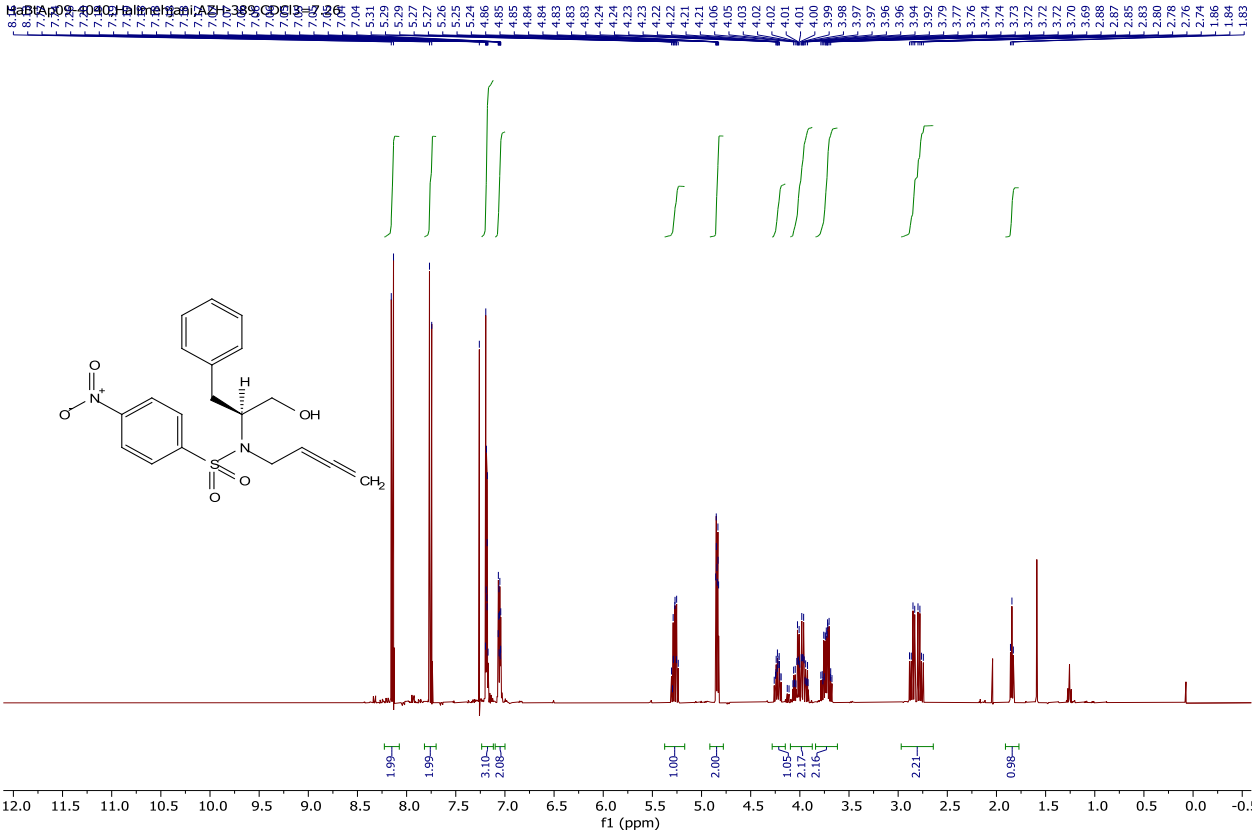
(R)-N-(1-(benzylthio)-3-hydroxypropan-2-yl)-N-(buta-2,3-dien-1-yl)-4-methylbenzenesulfonamide (**1g**): ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.73 (d, J = 8.3 Hz, 2H), 7.32 – 7.25 (m, 7H), 5.18 (m, 1H), 4.74–4.70 (m, 2H), 4.03 – 3.86 (m, 2H), 3.84 – 3.75 (m, 2H), 3.70 (m, 1H), 3.63 (s, 2H), 2.61 – 2.49 (m, 2H), 2.42 (s, 3H), 1.86 (dd, J = 7.1, 5.5 Hz, 1H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 208.6, 143.7, 137.8, 137.7, 129.7, 128.9, 128.6, 127.4, 127.2, 88.6, 76.8, 62.9, 59.5, 43.8, 36.5, 31.2, 21.6 ppm; HRMS (ESI) calcd for $C_{21}H_{25}NO_3S_2$ $[M+Na]^+$: 426.1174; found: 426.1168; $[\alpha]_D^{25}$ = +7.35 (c = 0.87, CH_2Cl_2).

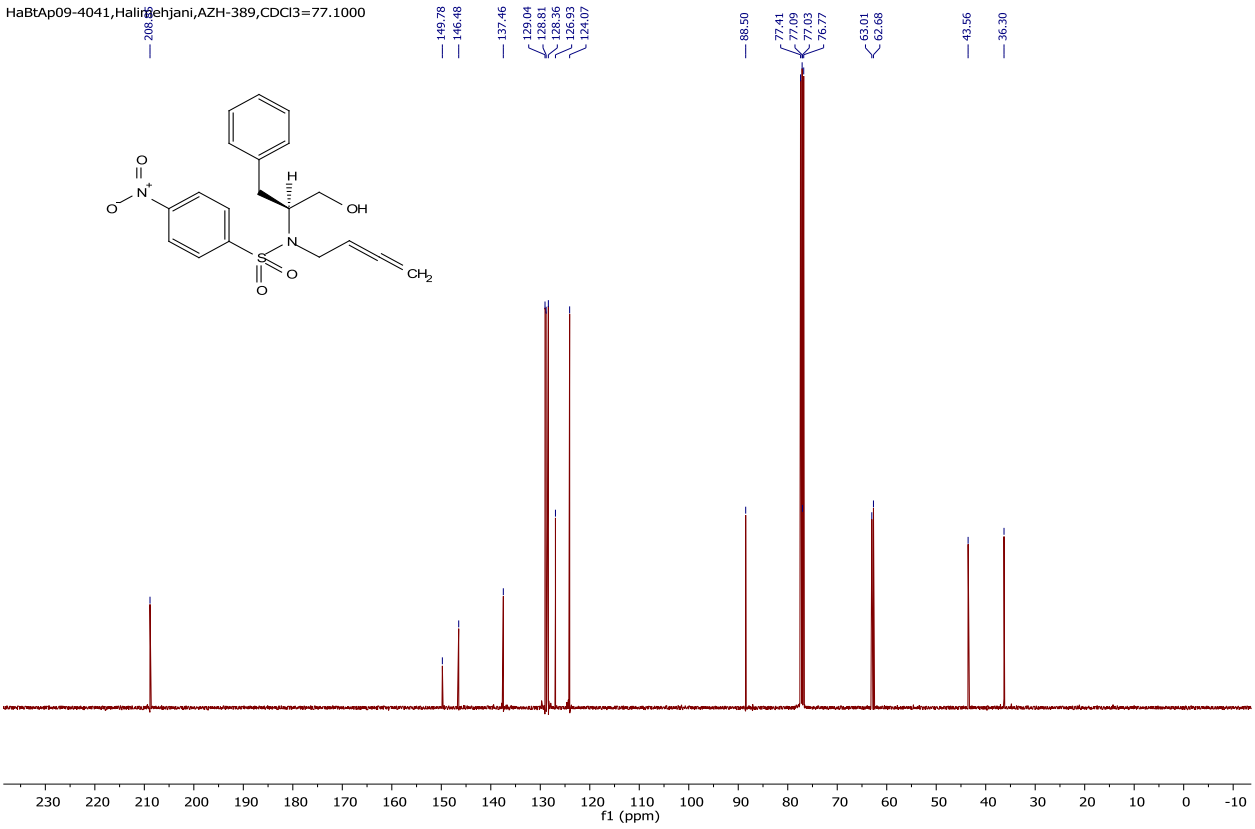

HaBtJn02-500300,Halimehjani,AZH-449,CDCl3=7.26
f1 (ppm)

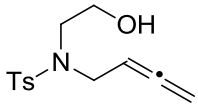

HaBtJn02-500301,Halimehjani,AZH-449,CDCl3=77.1000
f1 (ppm)



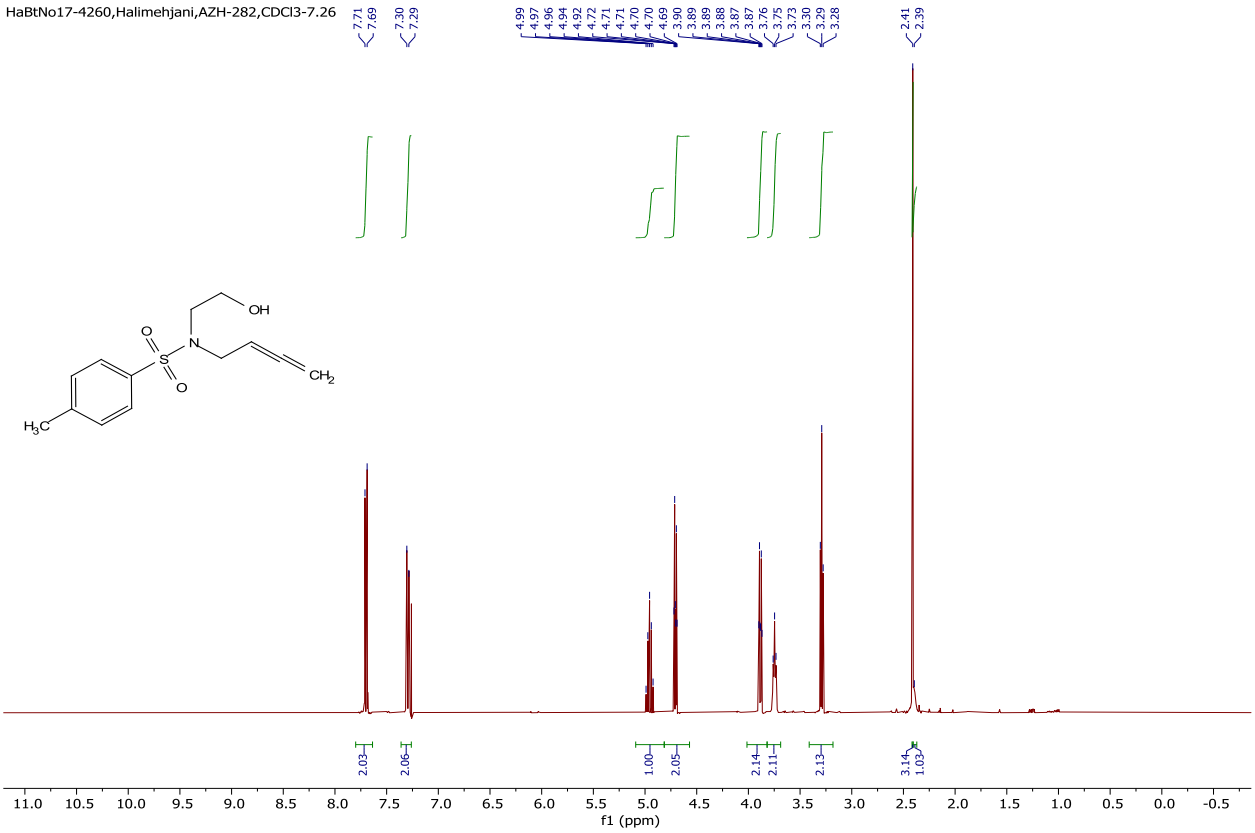
(S)-N-(buta-2,3-dien-1-yl)-N-(1-hydroxy-3-phenylpropan-2-yl)-4-nitrobenzenesulfonamide (**1h**): ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.14 (d, J = 9.0 Hz, 2H), 7.76 (d, J = 9.0 Hz, 2H), 7.24 – 7.12 (m, 3H), 7.10 – 7.00 (m, 2H), 5.27 (m, 1H), 4.86–4.80 (m, 2H), 4.23 (m, 1H), 4.10 – 3.87 (m, 2H), 3.84 – 3.62 (m, 2H), 2.97 – 2.64 (m, 2H), 1.84 (t, J = 5.8 Hz, 1H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 208.8, 149.7, 146.4, 137.4, 129.0, 128.8, 128.3, 126.9, 124.0, 88.5, 77.0, 63.0, 62.6, 43.5, 36.3 ppm; HRMS (ESI) calcd for $C_{19}H_{20}N_2O_5S$ $[M-H]^-$: 387.1015; found: 387.1021; $[\alpha]_D^{25}$ = -4.58 (c = 0.655, CH_2Cl_2).

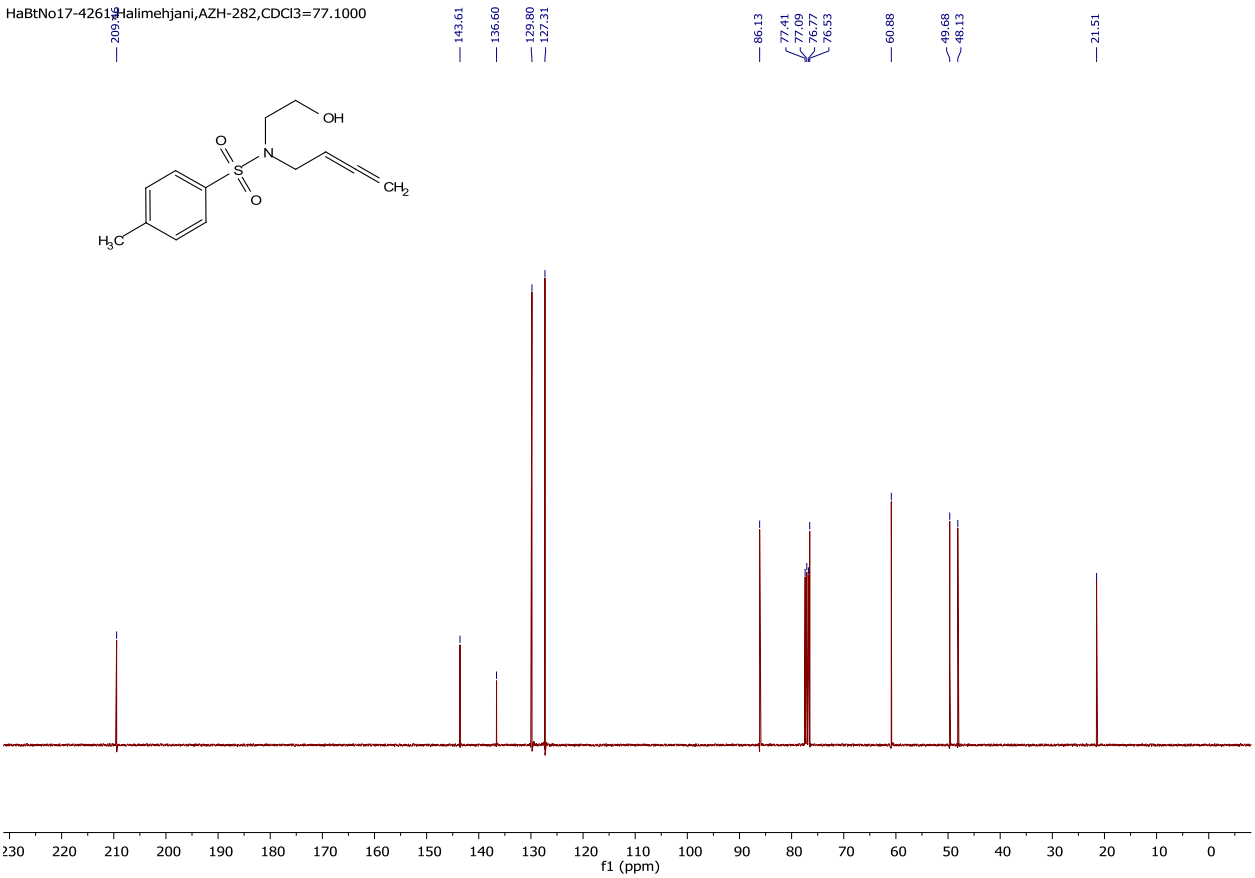






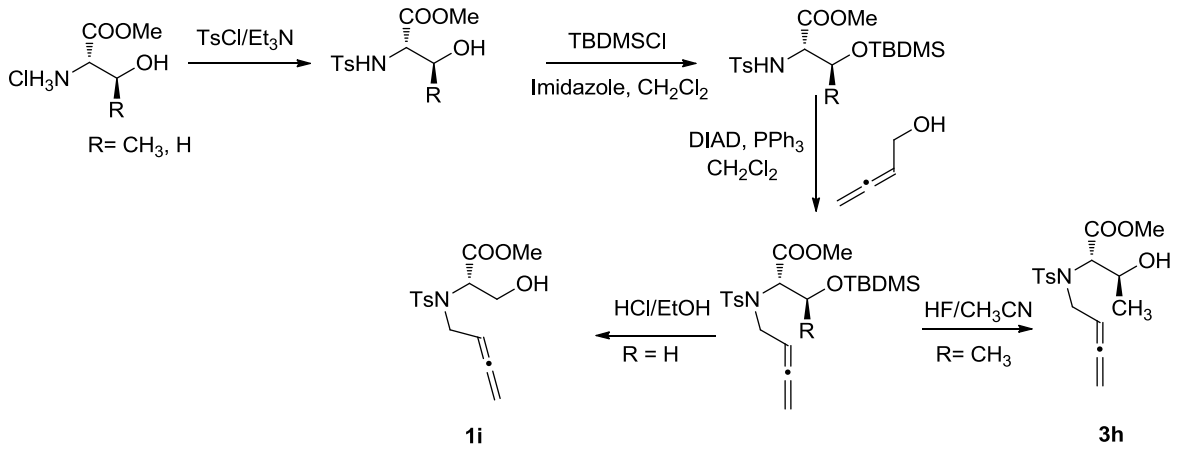
N-(buta-2,3-dien-1-yl)-N-(2-hydroxyethyl)-4-methylbenzenesulfonamide (**1k**): ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.70 (d, J = 8.4 Hz, 2H), 7.29 (d, J = 7.7 Hz, 2H), 4.96 (p, J = 6.8 Hz, 1H), 4.72–4.69 (m, 2H), 3.88 (dt, J = 7.0, 2.6 Hz, 2H), 3.75 (t, J = 5.5 Hz, 2H), 3.29 (t, J = 5.5 Hz, 2H), 2.41 (s, 3H), 2.39 (brs, 1H, OH) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 209.4, 143.6, 136.6, 129.8, 127.3, 86.1, 76.5, 60.8, 49.6, 48.1, 21.5 ppm; HRMS (ESI) calcd for $C_{13}H_{17}NO_3S$ $[M+H]^+$: 268.1007; found: 268.1002.


HaBtNo17-4260,Halimehjani,AZH-282,CDCl3-7.26
7.71
7.69
7.30
7.29
4.99
4.97
4.96
4.94
4.92
4.72
4.71
4.71
4.70
4.70
4.69
3.90
3.89
3.88
3.87
3.87
3.76
3.75
3.73
3.30
3.29
3.28
2.41
2.39
OH
O
S
N
O
CH2
H3C
2.03
2.06
1.00
2.05
2.14
2.11
2.13
3.14
1.03
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

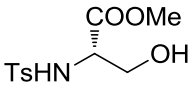

HaBtNo17-4261,Halimehjani,AZH-282,CDCl3=77.1000
209.49
143.61
136.60
129.80
127.31
86.13
77.41
77.09
76.77
76.53
60.88
49.68
48.13
21.51
OH
O
S
N
O
CH2
H3C
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

Synthesis of (L)-Serine and (L)-threonine-based allenols 1i and 3h

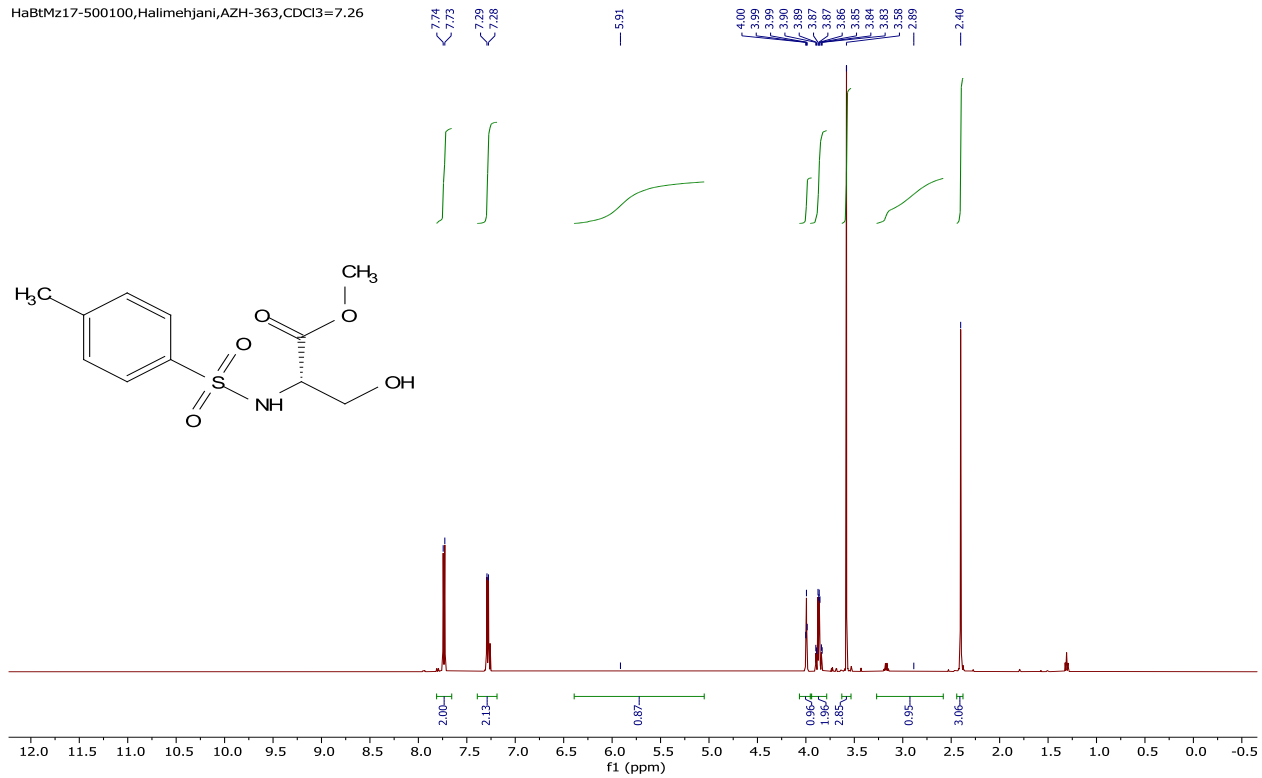
(*L*)-Serine and (*L*)-threonine-based allenols were prepared according to the following reaction Scheme:

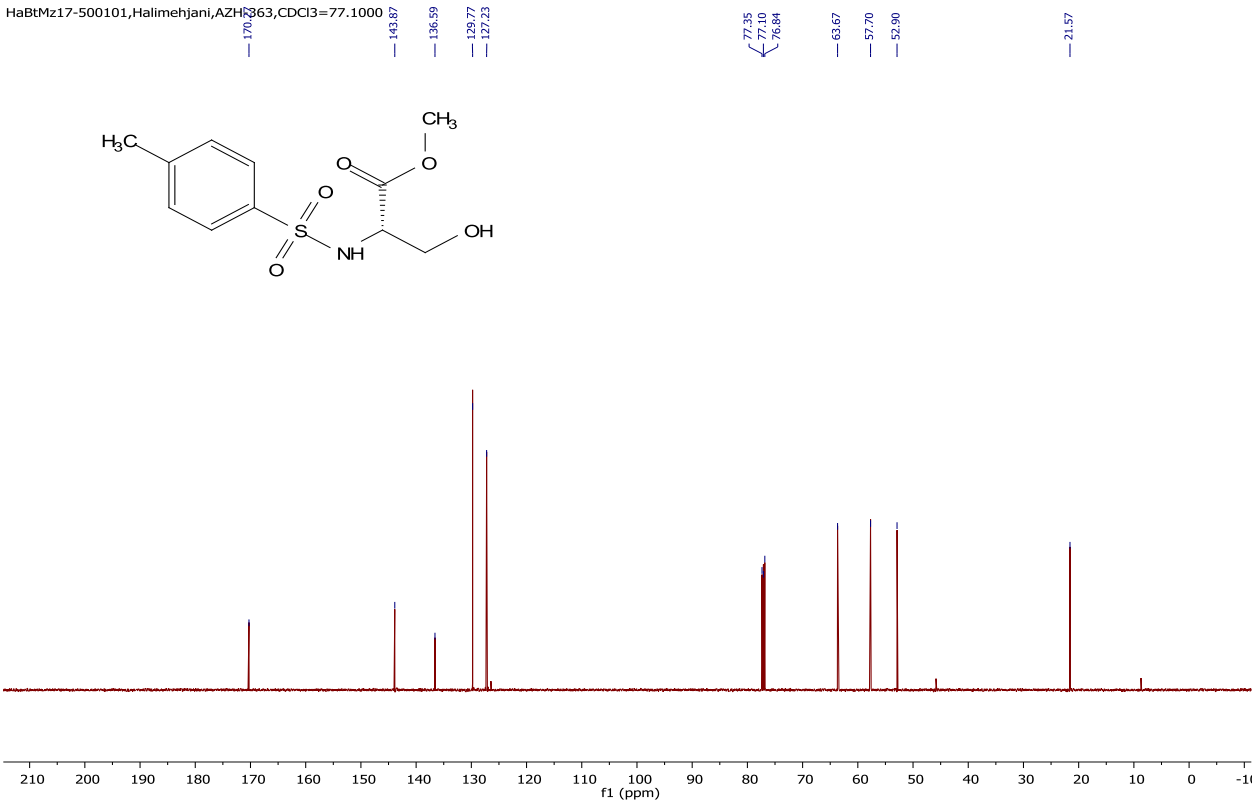


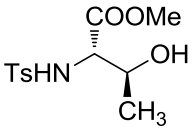
Tosylation of (L)-serine methyl ester hydrochloride and (L)-threonine methyl ester hydrochloride: (*L*)-serine methyl ester hydrochloride or (*L*)-threonine methyl ester hydrochloride (1 equiv) was dissolved in dry CH_2Cl_2 (1.8 mL/mmol), cooled to 0 °C and triethylamine (2.4 equiv) was added under argon and the reaction stirred for 5 min. Then, tosyl chloride (1.1 equiv) was added and the mixture was stirred for 2h at the same temperature. After that the reaction mixture was allowed to warm to RT and further stirred for 12 h. The reaction was quenched with water (4 mL/mmol) and extracted with CH_2Cl_2 (3 × 6 mL/mmol). The combined organic layers were washed with sat. $NaHCO_3$ (3 mL/mmol), 10% citric acid (3 mL/mmol), water (3 mL/mmol), and brine (3 mL/mmol). The organic phase was dried over Na_2SO_4, filtered, concentrated under vacuum and washed with diethyl ether to give the pure tosylated product in almost quantitative yield.



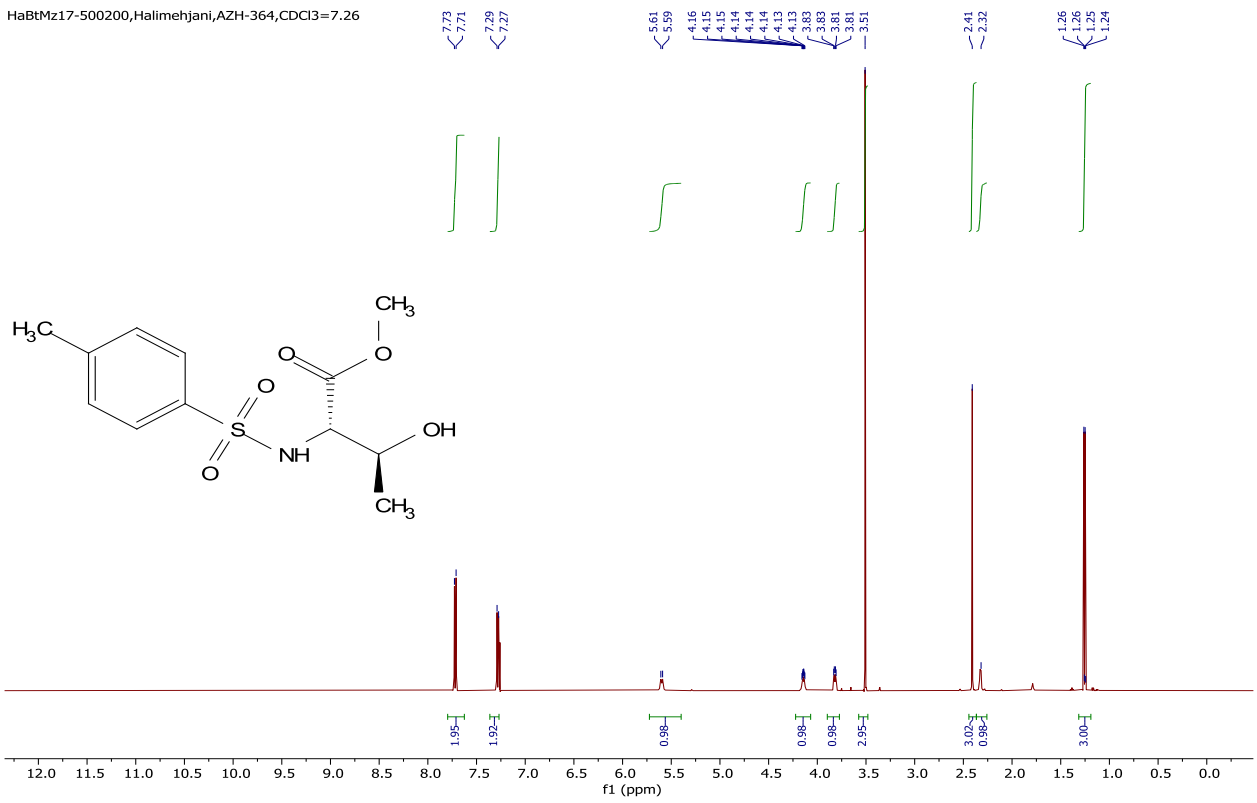
(S)-methyl 3-hydroxy-2-(4-methylphenylsulfonamido)propanoate: ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.74 (d, J = 8.4 Hz, 2H), 7.28 (d, J = 7.7 Hz, 2H), 5.91 (brs, 1H), 3.99 (t, J = 3.8 Hz, 1H), 3.95 – 3.78 (m, 2H), 3.58 (s, 3H), 2.89 (brs, 1H), 2.40 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.2, 143.8, 136.5, 129.7, 127.2, 63.6, 57.7, 52.9, 21.5 ppm; HRMS (ESI) calcd for $C_{11}H_{15}NO_5S$ $[M+H]^+$: 274.0749; found: 274.0746. $[\alpha]_D^{25}$ = -10.0 (c = 0.08, CH_2Cl_2).

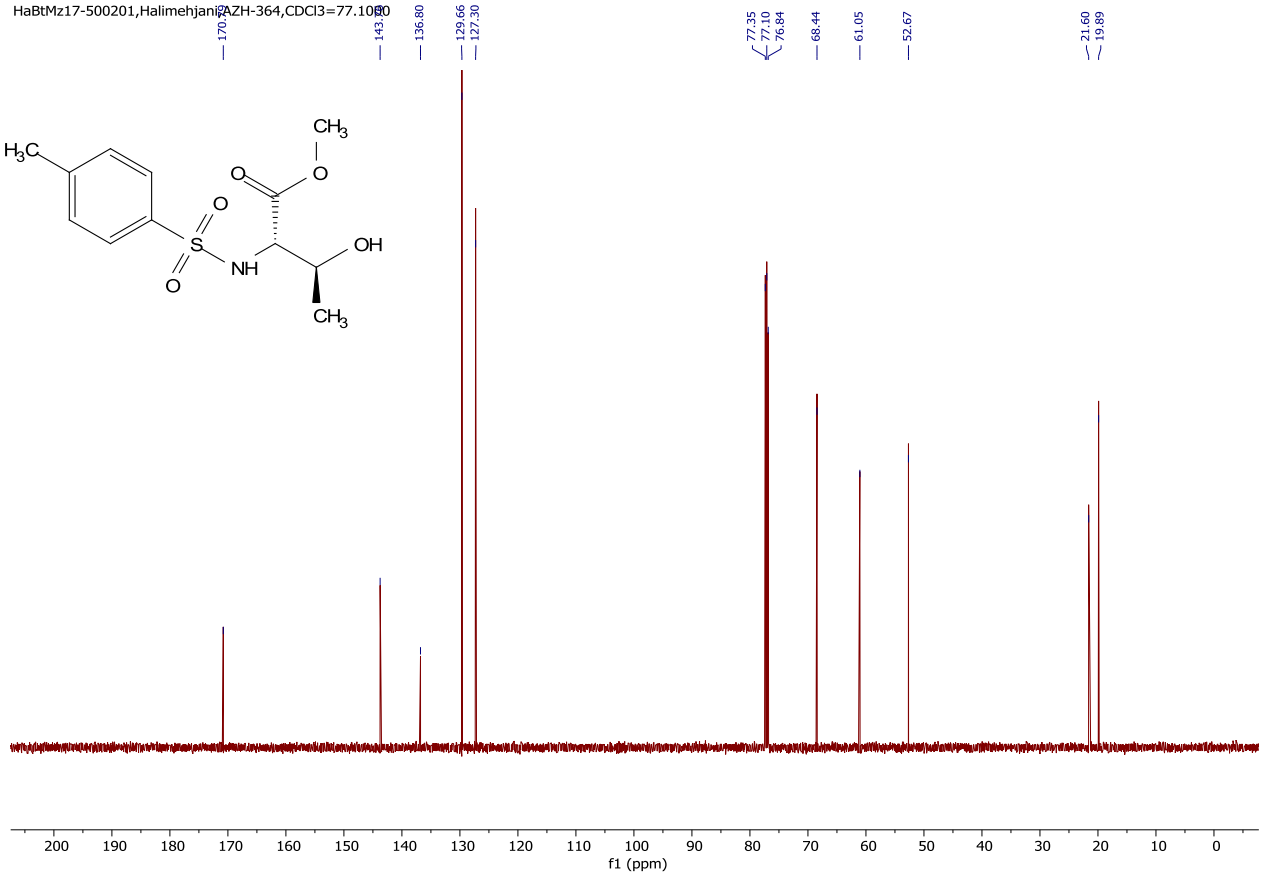

HaBtMz17-500100,Halimehjani,AZH-363,CDCl3=7.26
7.74
7.73
7.29
7.28
5.91
4.00
3.99
3.99
3.90
3.89
3.87
3.87
3.86
3.85
3.84
3.83
3.58
2.89
2.40
CH3
O
O
H3C
O
S
NH
OH
O
2.00
2.13
0.87
0.96
1.96
2.85
0.95
3.06
f1 (ppm)


HaBtMz17-500101,Halimehjani,AZH-363,CDCl3=77.1000
170.66
143.87
136.59
129.77
127.23
77.35
77.10
76.84
63.67
57.70
52.90
21.57
CH3
O
O
H3C
O
S
NH
OH
O
f1 (ppm)

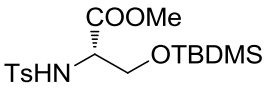


(2S,3S)-methyl 3-hydroxy-2-(4-methylphenylsulfonamido)butanoate: ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.72 (d, J = 8.4 Hz, 2H), 7.28 (d, J = 7.8 Hz, 2H), 5.60 (d, J = 8.9 Hz, 1H), 4.22 – 4.07 (m, 1H), 3.82 (dd, J = 8.9, 3.1 Hz, 1H), 3.51 (s, 3H), 2.41 (s, 3H), 2.32 (s, 1H), 1.26 (d, J = 6.4 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.7, 143.7, 136.8, 129.6, 127.3, 68.4, 61.0, 52.6, 21.6, 19.8 ppm; HRMS (ESI) calcd for $C_{12}H_{17}NO_5S$ $[M+H]^+$: 288.0898; found: 288.0906; $[\alpha]_D^{25}$ = -8.57 (c = 0.28, CH_2Cl_2).

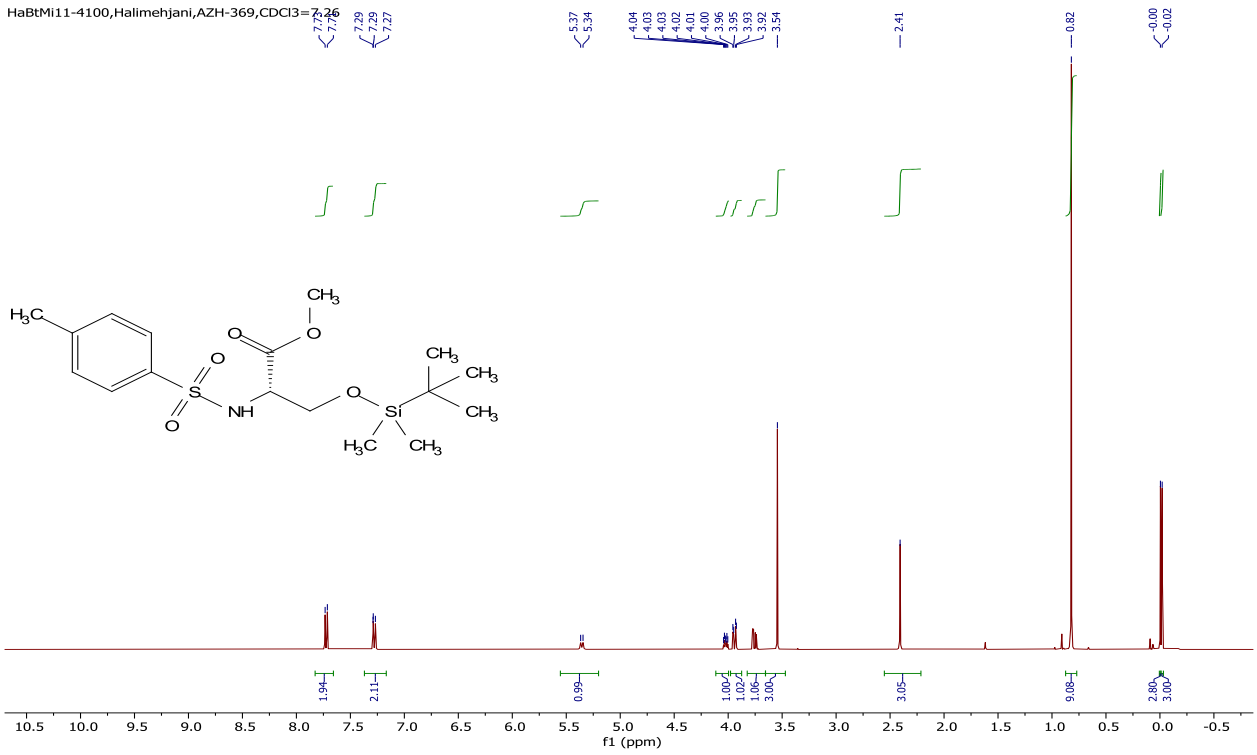


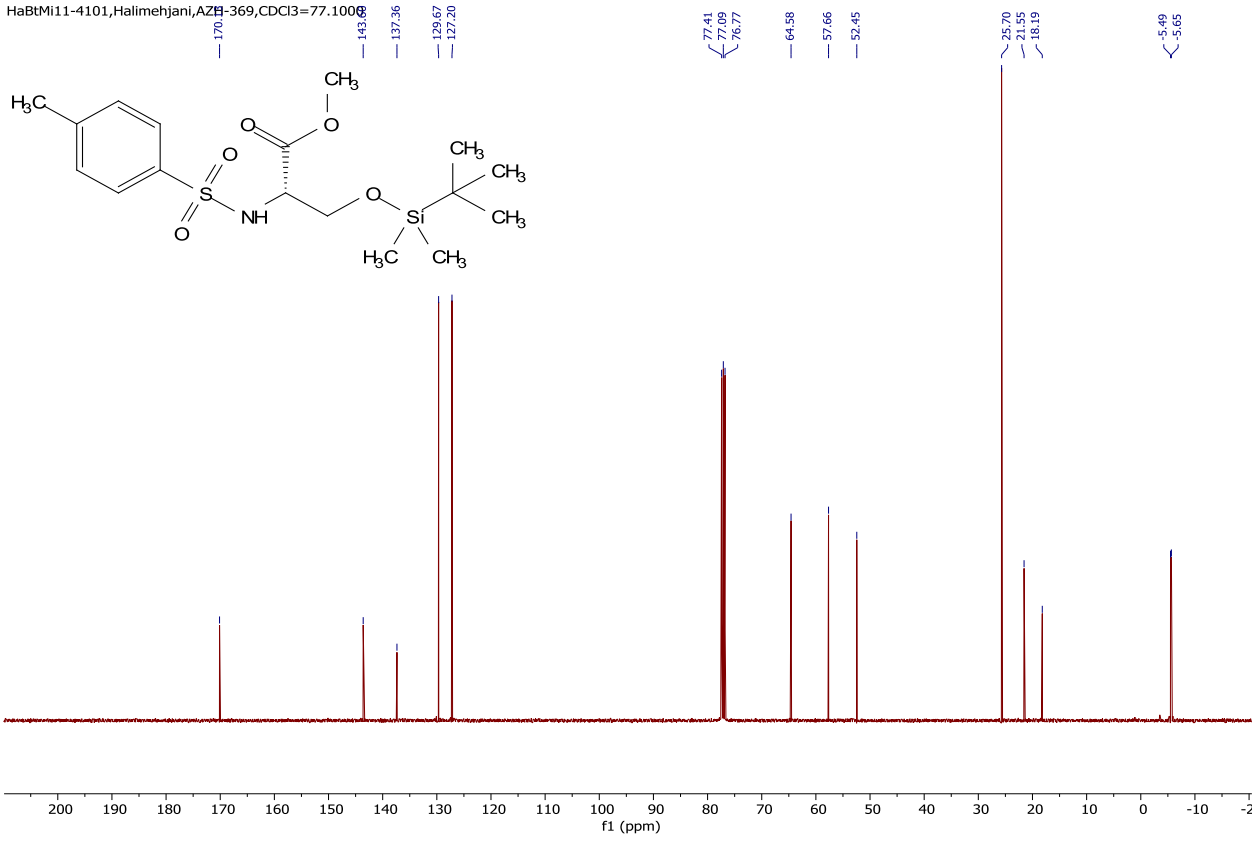


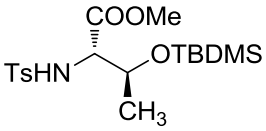
Silylation reaction: *tert*-Butyldimethylchlorosilane (1.2 equiv) was added portion wise to a solution of an alcohol and imidazole (1.2 equiv) in dichloromethane (4 mL/mmol), and the mixture was stirred at rt for 4 h. The reaction was quenched with water and the organic phase was separated. The aqueous phase was extracted two more times with CH_2Cl_2 (2 × 3 mL/mmol). The combined organic phases was dried with $MgSO_4$ and concentrated in vacuum to give the pure product.[4]



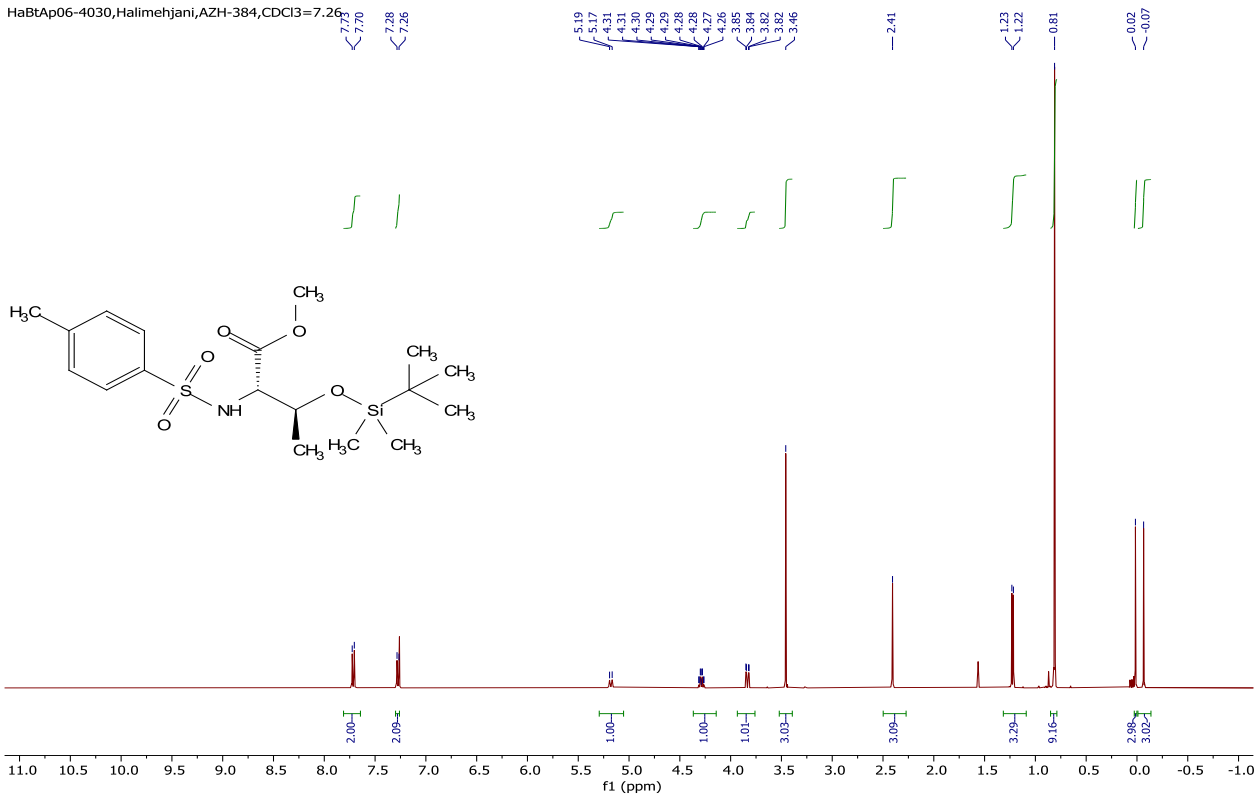
(S)-methyl 3-((tert-butyldimethylsilyl)oxy)-2-(4-methylphenylsulfonamido)propanoate: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.72 (d, J = 8.4 Hz, 2H), 7.37 – 7.17 (m, 2H), 5.36 (d, J = 8.9 Hz, 1H), 4.04–4.00 (m, 1H), 3.94 (dd, J = 10.0, 3.0 Hz, 1H), 3.76 (dd, J = 10.0, 3.5 Hz, 1H), 3.54 (s, 3H), 2.41 (s, 3H), 0.82 (s, 9H), -0.00 (s, 3H), -0.02 (s, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 143.6, 137.3, 129.6, 127.2, 64.5, 57.6, 52.4, 25.7, 21.5, 18.1, -5.4, -5.6 ppm; HRMS (ESI) calcd for $C_{17}H_{29}NO_5SSi$ $[M+H]^+$: 388.1614; found:388.1612; $[\alpha]_D^{25}$ = +6.875 (c = 0.48, CH_2Cl_2).

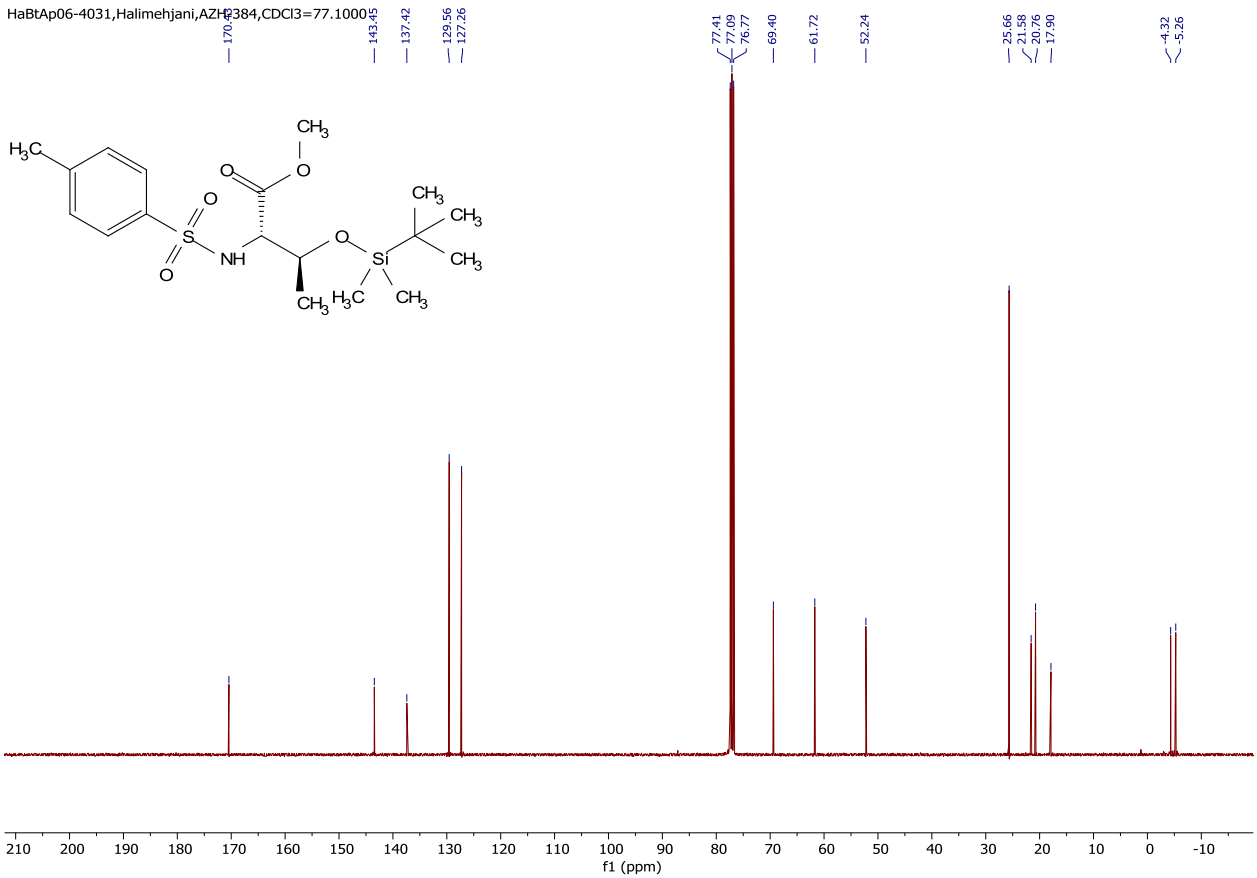

HaBtMi11-4100,Halimehjani,AZH-369,CDCl3=7.26
f1 (ppm)


HaBtMi11-4101,Halimehjani,AZH-369,CDCl3=77.1008
f1 (ppm)

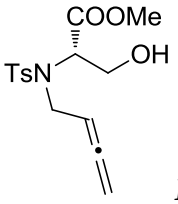


(2S,3S)-methyl 3-((tert-butyldimethylsilyl)oxy)-2-(4-methylphenylsulfonamido)butanoate: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.71 (d, J = 8.3 Hz, 2H), 7.27 (d, J = 8.4 Hz, 2H), 5.18 (d, J = 10.3 Hz, 1H), 4.29–4.26 (m, 1H), 3.83 (dd, J = 10.3, 2.1 Hz, 1H), 3.46 (s, 3H), 2.41 (s, 3H), 1.22 (d, J = 6.2 Hz, 3H), 0.81 (s, 9H), 0.02 (s, 3H), -0.07 (s, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.4, 143.4, 137.4, 129.5, 127.2, 69.4, 61.7, 52.2, 25.6, 21.5, 20.7, 17.9, -4.3, -5.2 ppm; HRMS (ESI) calcd for $C_{18}H_{31}NO_5SSi$ $[M+Na]^+$: 424.1584; found: 424.1590; $[\alpha]_D^{25}$ = -17.98 (c = 0.267, CH_2Cl_2).



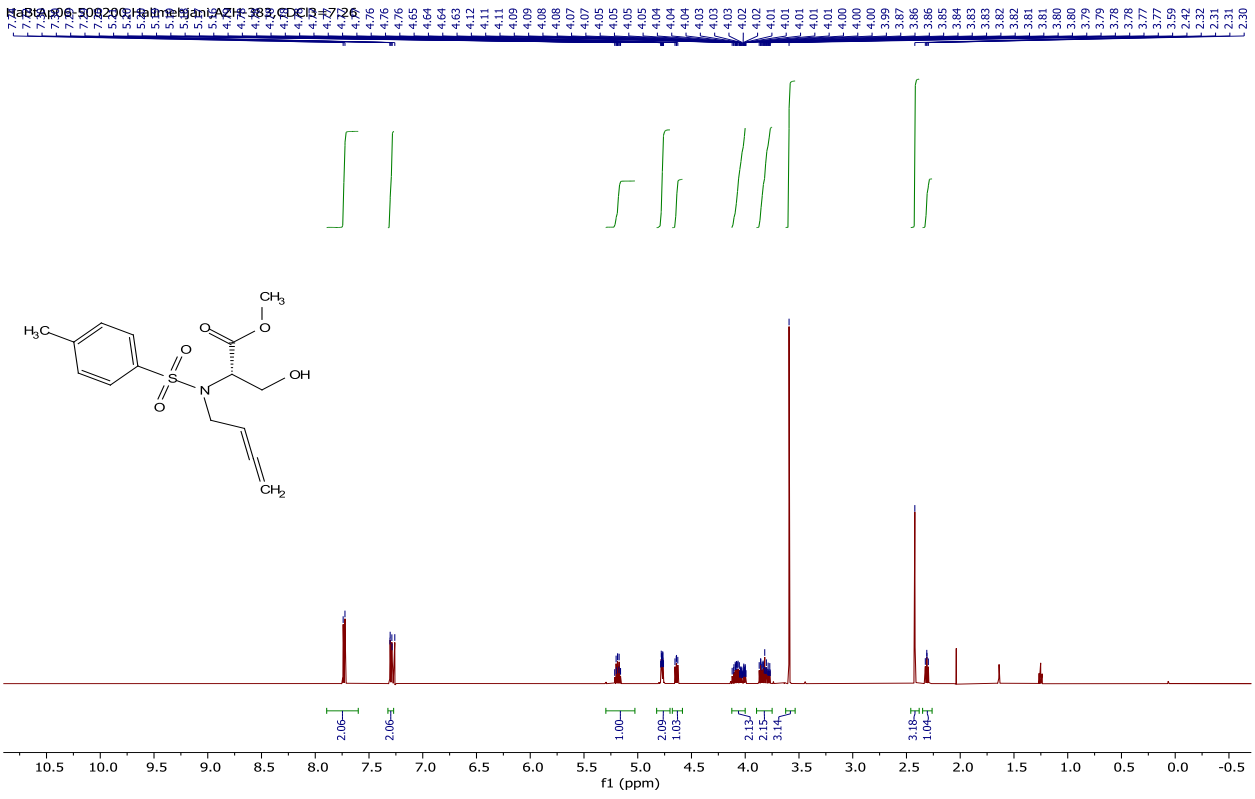


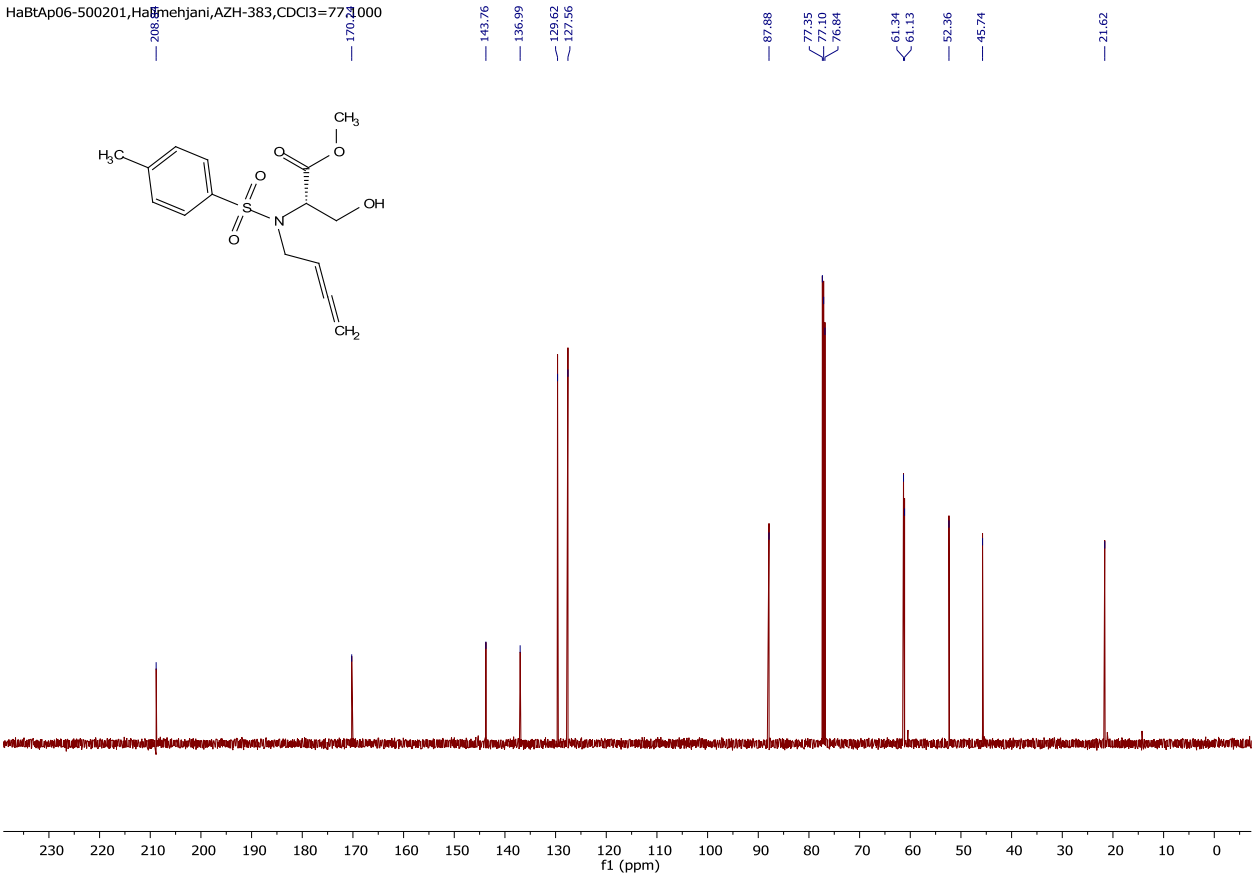
Allylation of TBDMS-protected tosylamide by Mitsunobu reaction*:* A mixture of silylated tosylamide (2 equiv), buta-2,3-dien-1-ol (1 equiv) and PPh_3 (2 equiv) in CH_2Cl_2 (6 mL/mmol of alcohol) was cooled to 0 °C. The solution of DIAD (2 equiv) in CH_2Cl_2 (6 mL/mmol) was then added dropwise at the same temperature. The mixture was allowed to warm to room temperature and further stirred for 6 hours. Finally, the reaction mixture was concentrated under reduced pressure, and the crude mixture was purified with flash column chromatography (hexane/AcOEt = 20/1) to give the pure product.[5] The products were applied directly in desilylation reactions as described below:

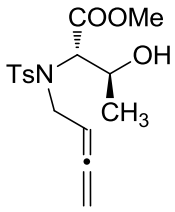


Desilylation reaction*: Synthesis of (S)-methyl 2-(N-(buta-2,3-dien-1-yl)-4-methylphenylsulfonamido)-3-hydroxypropanoate (**1i**):* The Mitsunobu adduct XXX (1 mmol) was dissolved in a 1% HCl solution in ethanol (25 mL), which was prepared from conc. HCl and

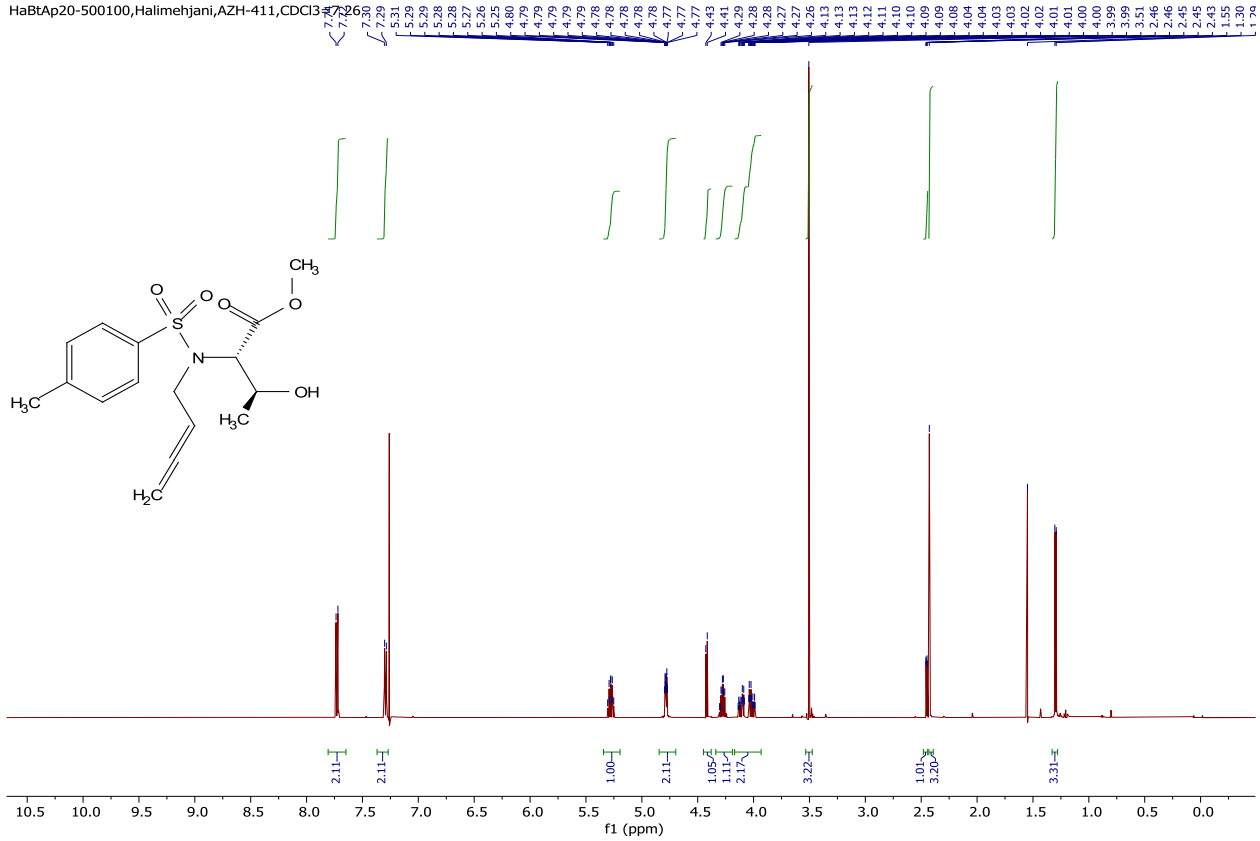
EtOH, and the mixture was stirred for 5 h at room temperature. Water was added to the mixture, and the whole was extracted with EtOAc. The extract was washed with brine and dried over $MgSO_4$. The filtrate was concentrated under reduced pressure to give an oily residue, which was purified by column chromatography over silica gel with *n*-hexane-EtOAc gradient (9:1 to 1:1) to give (*S*)-methyl 2-(N-(buta-2,3-dien-1-yl)-4-methylphenylsulfonamido)-3-hydroxypropanoate **1i** in quantitative yield.[6] ^{1}H NMR (500 MHz, Chloroform-*d*) δ ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.73 (d, J = 8.4 Hz, 2H), 7.30 (d, J = 8.7 Hz, 2H), 5.20–5.17 (m, 1H), 4.82 – 4.70 (m, 2H), 4.64 (dd, J = 7.2, 6.0 Hz, 1H), 4.12 – 4.00 (m, 2H), 3.89 – 3.75 (m, 2H), 3.59 (s, 3H), 2.42 (s, 3H), 2.31 (dd, J = 7.4, 6.7 Hz, 1H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 208.8, 170.2, 143.7, 136.9, 129.6, 127.5, 87.8, 61.3, 61.1, 52.3, 45.7, 21.6 ppm; HRMS (ESI) calcd for $C_{15}H_{19}NO_5S$ $[M+NH_4]^+$: 343.1328; found: 343.1323; $[\alpha]_D^{25}$ = -55.09 (c = 0.57, CH_2Cl_2).

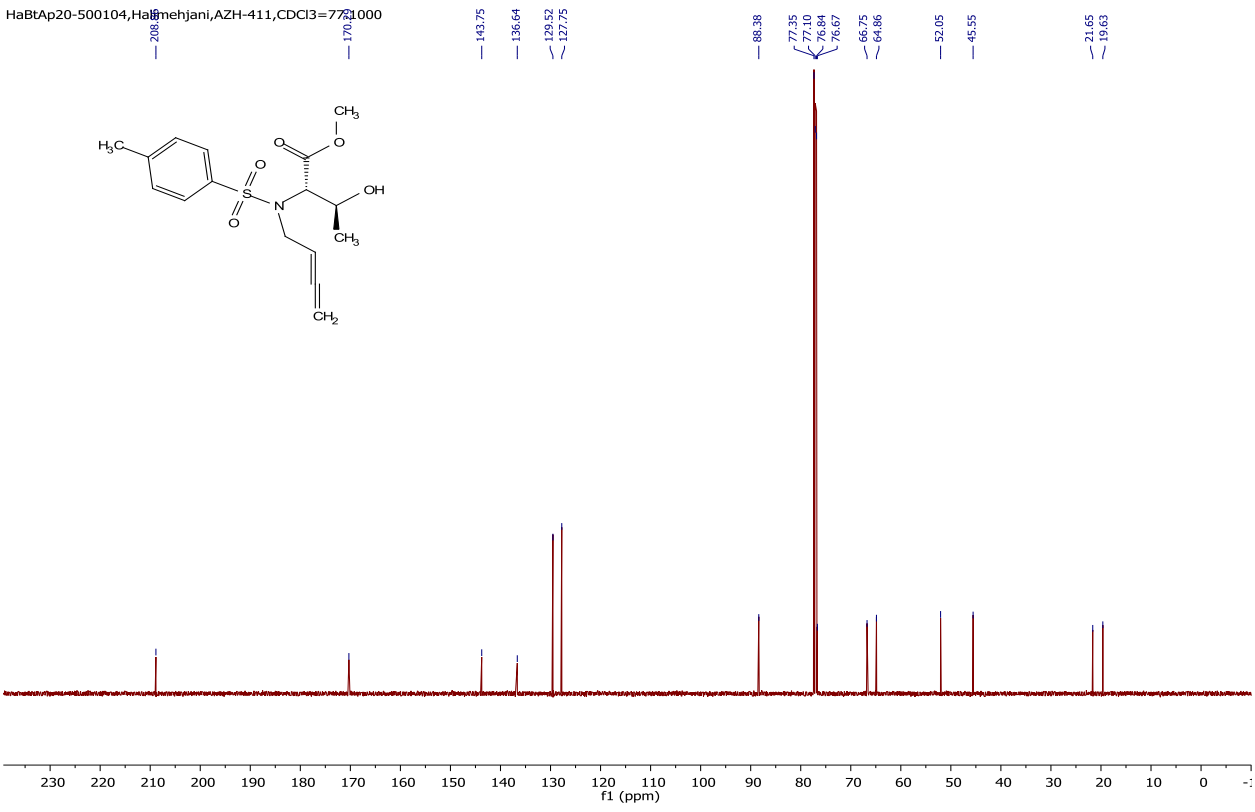






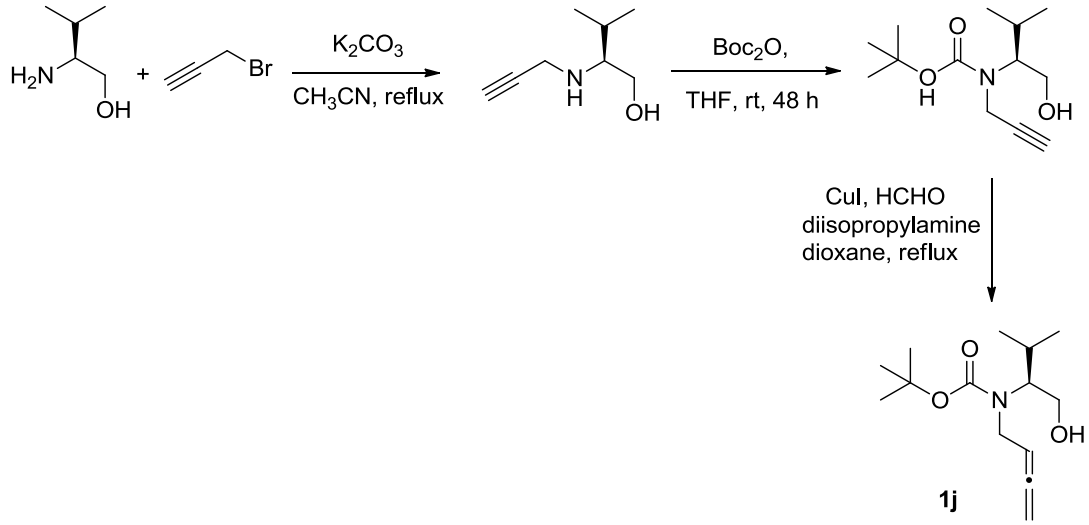
Desilylation reaction: *Synthesis of (2S,3S)-methyl 2-(N-(buta-2,3-dien-1-yl)-4-methylphenylsulfonamido)-3-hydroxybutanoate* (**3h**):Add 40 % aqueous HF solution (10 mL) rapidly to a stirred solution of Mitsunobu adduct (1 mmol) in MeCN (15 mL) at room temperature over 2-3 seconds. The reaction mixture was stirred for 2 hours and then quenched with solid $NaHCO_3$ (2.0 g) and H_2O (20 mL). The product was extracted with Et_2O (3 × 10 mL), the combined organic phases were dried over $MgSO_4$, and concentrated in vacuo. Purification was carried out using column chromatography over silica gel with *n*-hexane-EtOAc gradient (9:1 to 1:1).[7] ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.73 (d, J = 8.3 Hz, 2H), 7.29 (d, J = 7.9 Hz, 2H), 5.29–5.26 (m, 1H), 4.85 – 4.70 (m, 2H), 4.42 (d, J = 6.4 Hz, 1H), 4.29–4.26 (m, 1H), 4.17 – 3.93 (m, 2H), 3.51 (s, 3H), 2.45 (dd, J = 4.3, 0.5 Hz, 1H), 2.43 (s, 3H), 1.30 (d, J = 6.2 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 208.8, 170.2, 143.7, 136.6, 129.5, 127.7, 88.3, 76.6, 66.7, 64.8, 52.0, 45.5, 21.6, 19.6 ppm; HRMS (ESI) calcd for $C_{16}H_{21}NO_5S$ $[M+H]^+$: 340.1219; found: 340.1221; $[\alpha]_D^{25}$ = -83.88 (c = 0.335, CH_2Cl_2).

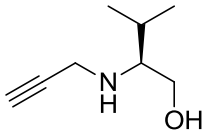

HaBtAp20-500100,Halimehjani,AZH-411,CDCl3=7.26
f1 (ppm)


HaBtAp20-500104,Halimehjani,AZH-411,CDCl3=77.1000
f1 (ppm)

Synthesis of Boc-protected allenol (1j) from (*L*)-valinol:

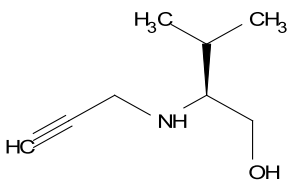
(*S*)-*tert*-butyl buta-2,3-dien-1-yl(1-hydroxy-3-methylbutan-2-yl)carbamate (**1j**) was prepared according to the following scheme:



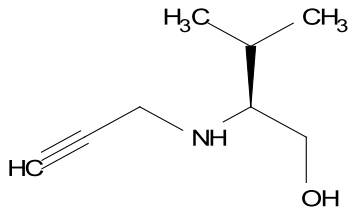


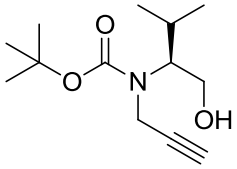
Propargylation of *L*-valinol: *Synthesis of (S)-3-methyl-2-(prop-2-yn-1-ylamino)butan-1-ol*: A mixture of *L*-valinol (1.03 g, 10 mmol), propargyl bromide (1.35 mL, 12 mmol) and potassium carbonate (3.45 g, 25 mmol) in acetonitrile (30 mL) was stirred at room temperature for overnight. The mixture was filtered and evaporated to give a crude mixture. Purification was carried out by silica gel column chromatography using EtOH:EtOAc eluent (1:9).[8] ^{1}H NMR (400 MHz, Chloroform-*d*) δ 3.64 (dd, J = 10.9, 4.0 Hz, 1H), 3.50 – 3.35 (m, 3H), 2.56 (td, J = 6.1, 4.0 Hz, 1H), 2.21 (t, J = 2.4 Hz, 1H), 2.15 – 1.33 (m, 3H, -NH, -OH and -CH), 0.97 (d, J = 6.8 Hz, 3H), 0.93 (d, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 82.5, 71.3, 63.3, 60.7, 36.3, 28.9, 19.4, 18.6 ppm; HRMS (ESI) calcd for $C_8H_{16}NO$ $[M+H]^+$: 142.1232; found: 142.1225.

HaBtAp26-4020,Halimehjani,AZH-423,CDCl3=7.26

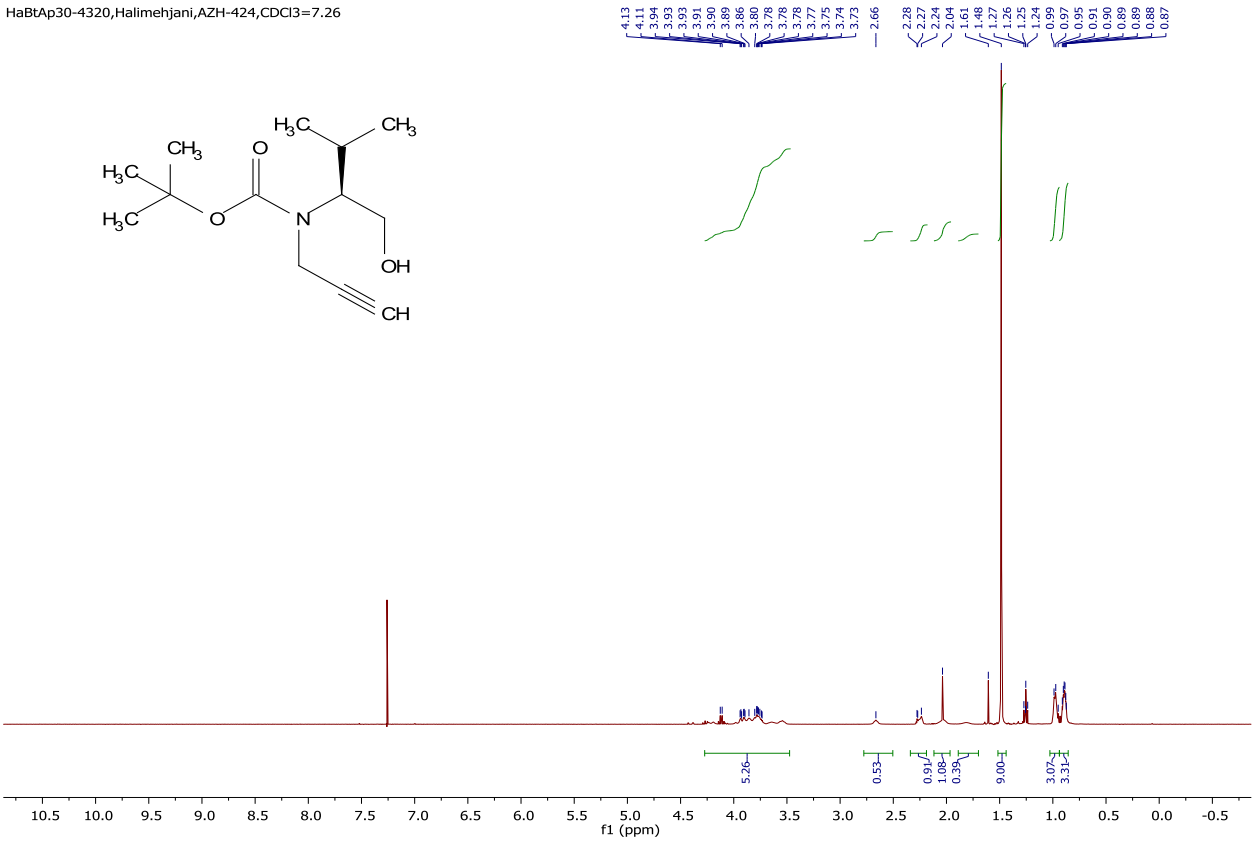


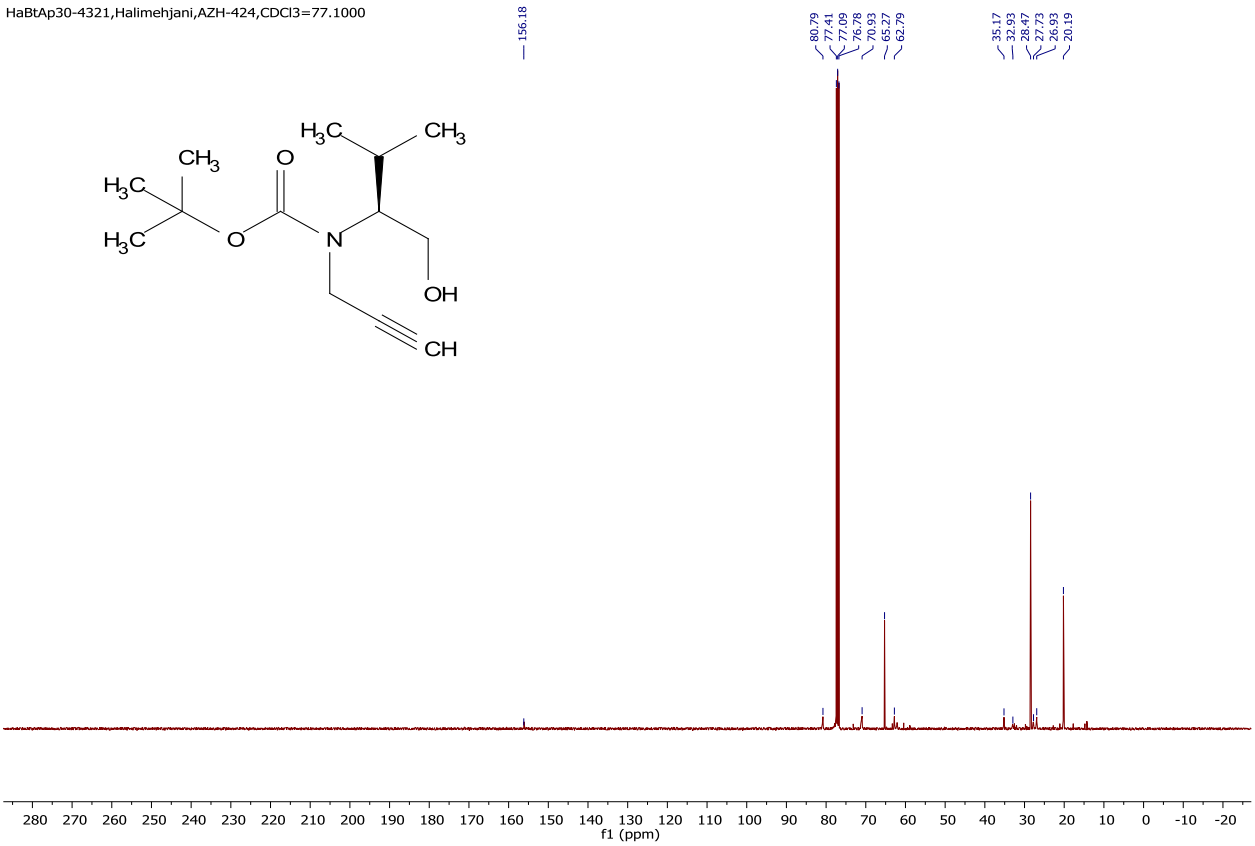
HaBtAp26-4021,Halimehjani,AZH-423,CDCl3=77.1000

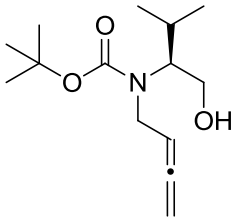




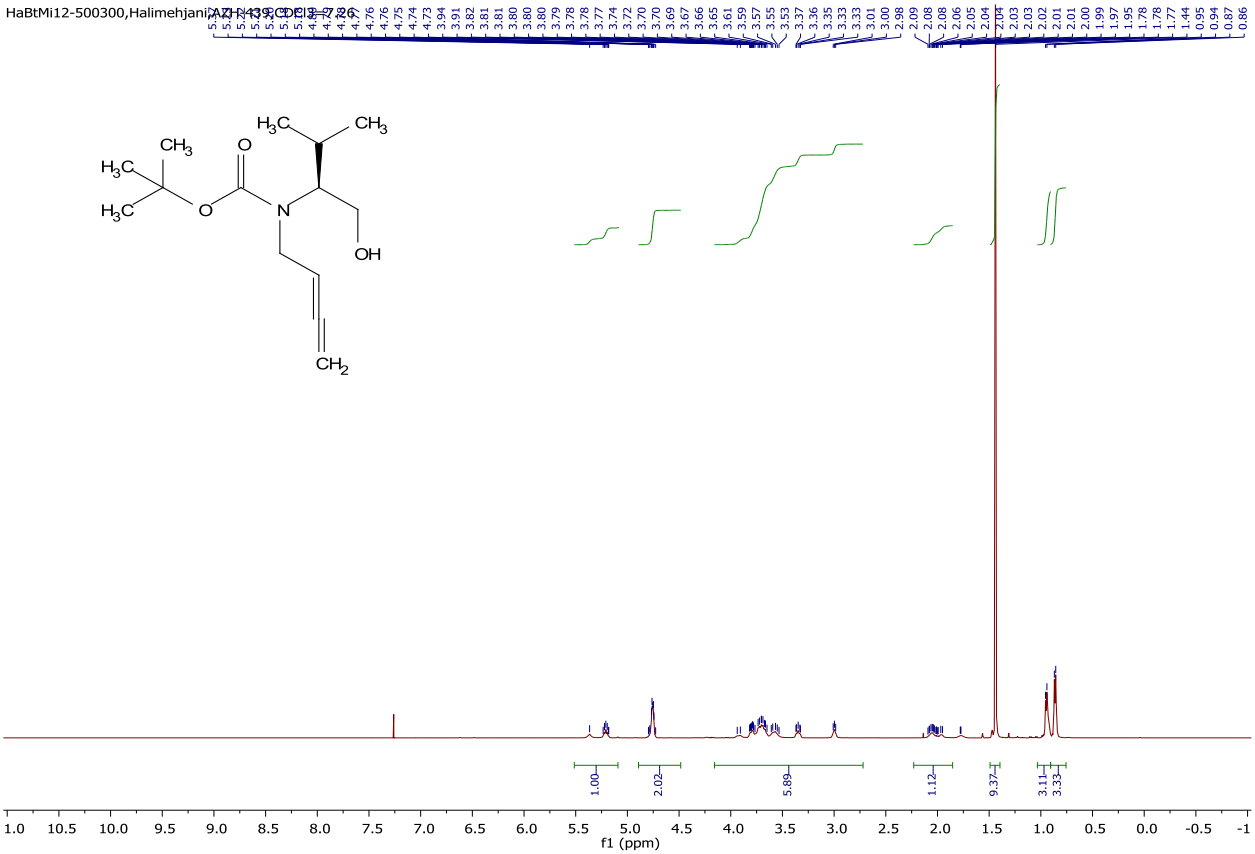
Protection reaction of N-propargyl-(L)-valinol with Boc_2O*: Synthesis of (S)-tert-butyl (1-hydroxy-3-methylbutan-2-yl)(prop-2-yn-1-yl)carbamate***:** The propargylated product (6.1 mmol) and Boc_2O (7 mmol) was dissolved in THF (20 mL) and the mixture was stirred at room temperature for 48 h. The solvent was evaporated under reduced pressure and purified by SiO_2 column chromatography (EtOAc:*n*-pentane, 3:7) to give the product in 88% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 4.27 – 3.47 (m, 5H), 2.66 (brs, 1H), 2.26 (brs, 1H), 2.04 (brs, 1H), 1.48 (s, 9H), 0.97 (t, J = 7.9 Hz, 3H), 0.90 (dd, J = 6.5, 3.3 Hz, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.1, 80.7, 70.9, 65.2, 62.7, 35.1, 32.9, 28.4, 27.7, 26.9, 20.1 ppm; HRMS (ESI) calcd for $C_{20}H_{21}NO_3S$ $[M+H]^+$: 242.1756; found: 242.1751.

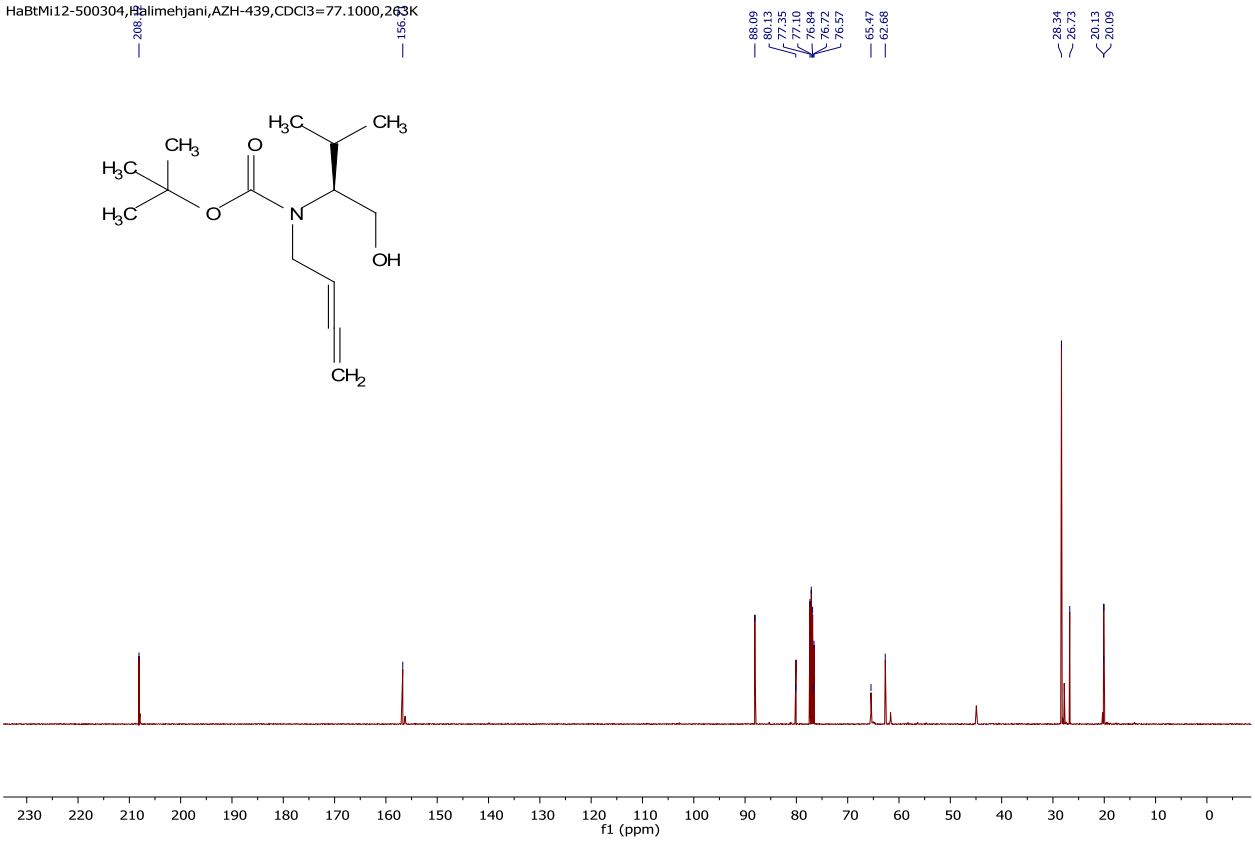






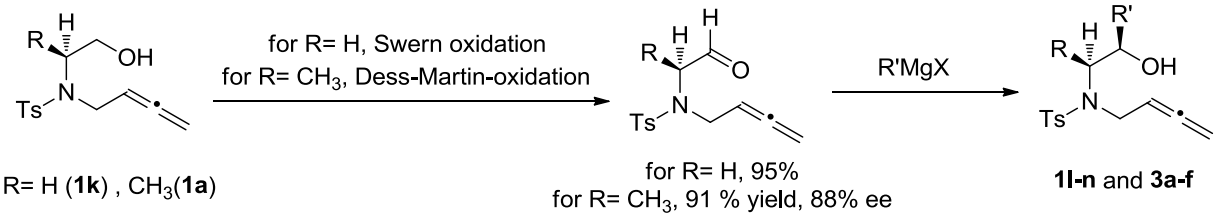
Synthesis of Boc-protected allenol (**1j**): A suspension of Boc-protected propargylated adduct (1.0 equiv), cuprous iodide (0.5 equiv), paraformaldehyde (2.5 equiv) and diisopropylamine (1.8 equiv) in dioxane (6 mL/mmol) was gently heated at reflux and stirred for overnight, cooled to room temperature, and filtered through a Celite pad. The dark-brown filtrate was concentrated in vacuo to afford a gummy residue. The residue was triturated with diethyl ether and filtered through the same Celite pad. This procedure was repeated 2 more times until a light yellow filtrate was obtained. Finally, the solvent was evaporated under reduced pressure to afford the crude product which was purified by silica gel column chromatography using EtOAc:*n*-pentane (1:10) to afford the Boc-protected allenol **1j** in 50% yield. *(S)-tert-butyl buta-2,3-dien-1-yl(1-hydroxy-3-methylbutan-2-yl)carbamate* (**1j**): ^{1}H NMR (500 MHz, Chloroform-*d*) δ 5.51 – 5.09 (m, 1H), 4.78–4.74 (m, 2H), 4.16 – 2.72 (m, 6H), 2.23 – 1.85 (m, 1H), 1.44 (s, 9H), 0.95 (d, J = 6.7 Hz, 3H), 0.86 (d, J = 6.7 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 208.1, 156.7, 88.0, 80.1, 76.7, 76.5, 65.4, 62.6, 28.3, 26.7, 20.1, 20.0 ppm; HRMS (ESI) calcd for $C_{14}H_{26}NO_3$ $[M+H]^+$: 256.1913; found: 256.1908; $[\alpha]_D^{25}$ = +24.36 (c = 0.587, CH_2Cl_2).

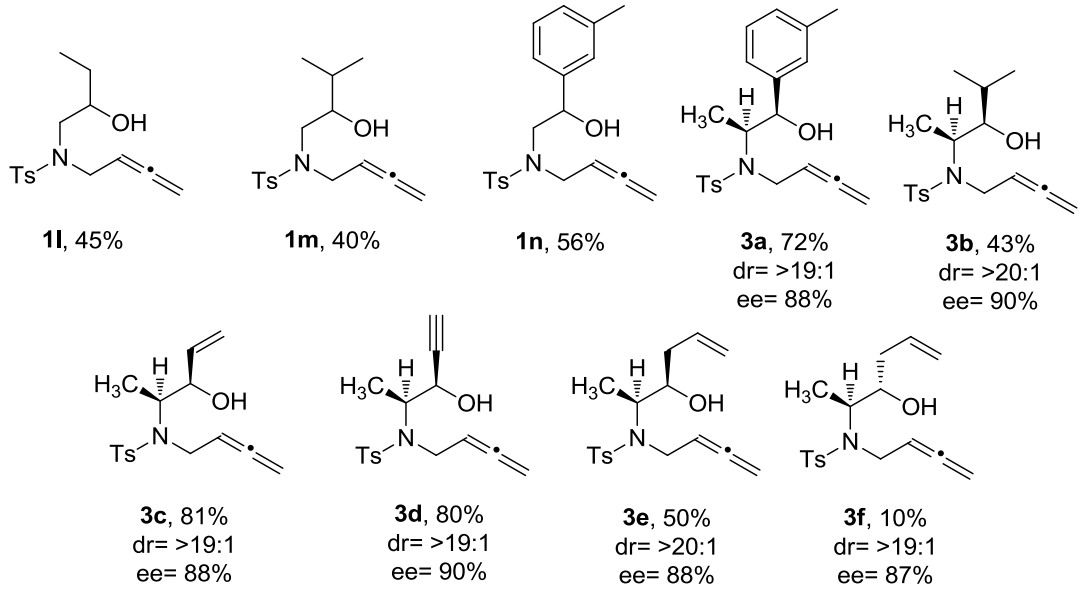

HaBtMi12-500300,Halimehjani,AZH-439,CDCl3=7.26
f1 (ppm)

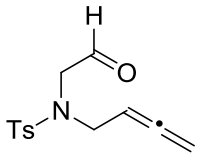

HaBtMi12-500304,Halimehjani,AZH-439,CDCl3=77.1000,263K
f1 (ppm)

Synthesis of allenols 1l-1n and 3a-3f

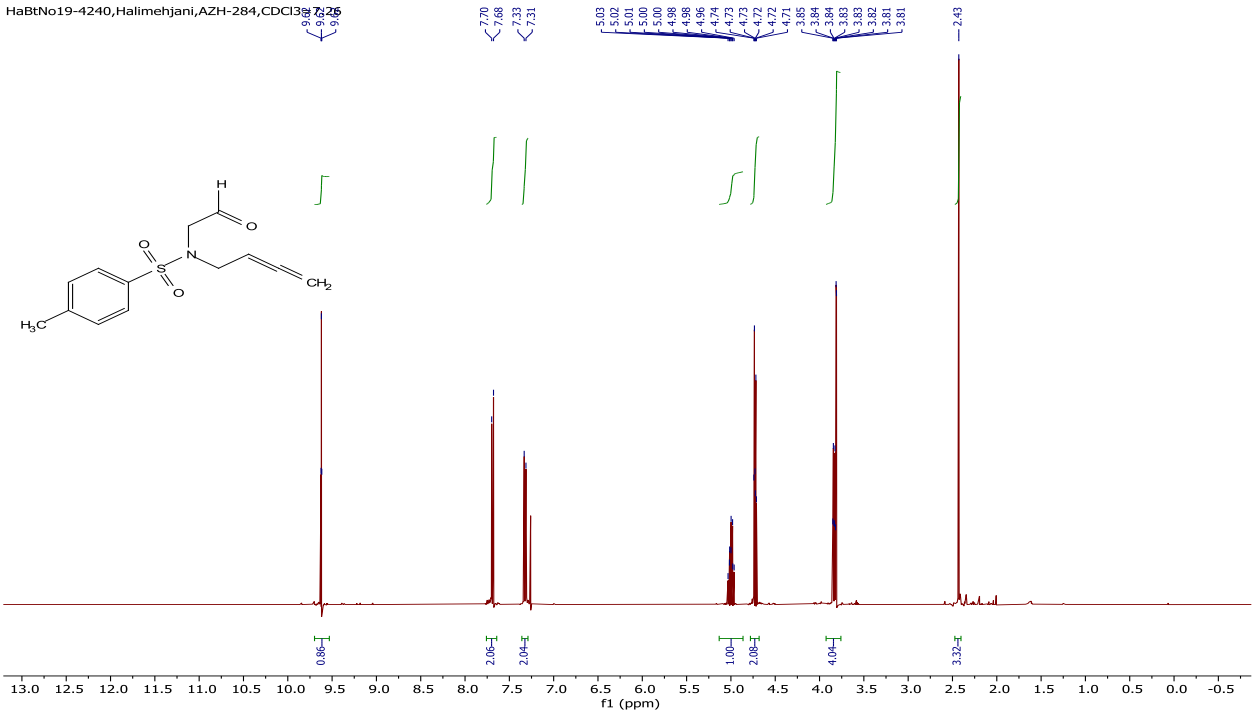
Allenols **1l-1n** and **3a-3f** were prepared from the corresponding allenols **1k** and **1a** respectively, according to the following scheme. For (R=H), Swern oxidation of allenol **1k** afforded the corresponding allenal in 95% isolated yield. For allenol **1a** (R= CH_3), Swern oxidation afforded the corresponding allenal in excellent yield, but complete epimerization was observed during the oxidation. For this purpose, various oxidation methods were screened to find an epimerization-free protocol. Finally, we found that Dess–Martin oxidation of allenol **1a** afforded the corresponding allenal in 91% yield and 88% ee. The *ee* of the allenal (R=CH_3) was determined as 88% by the borohydride reduction procedure.[9] Finally, the reaction of freshly prepared allenals with Grignard reagents afforded the final allenols with almost similar *ee* and satisfactory diastereoselectivity. In the case of **3a-3f**, purification afforded the major diastereomer with excellent dr ratio.

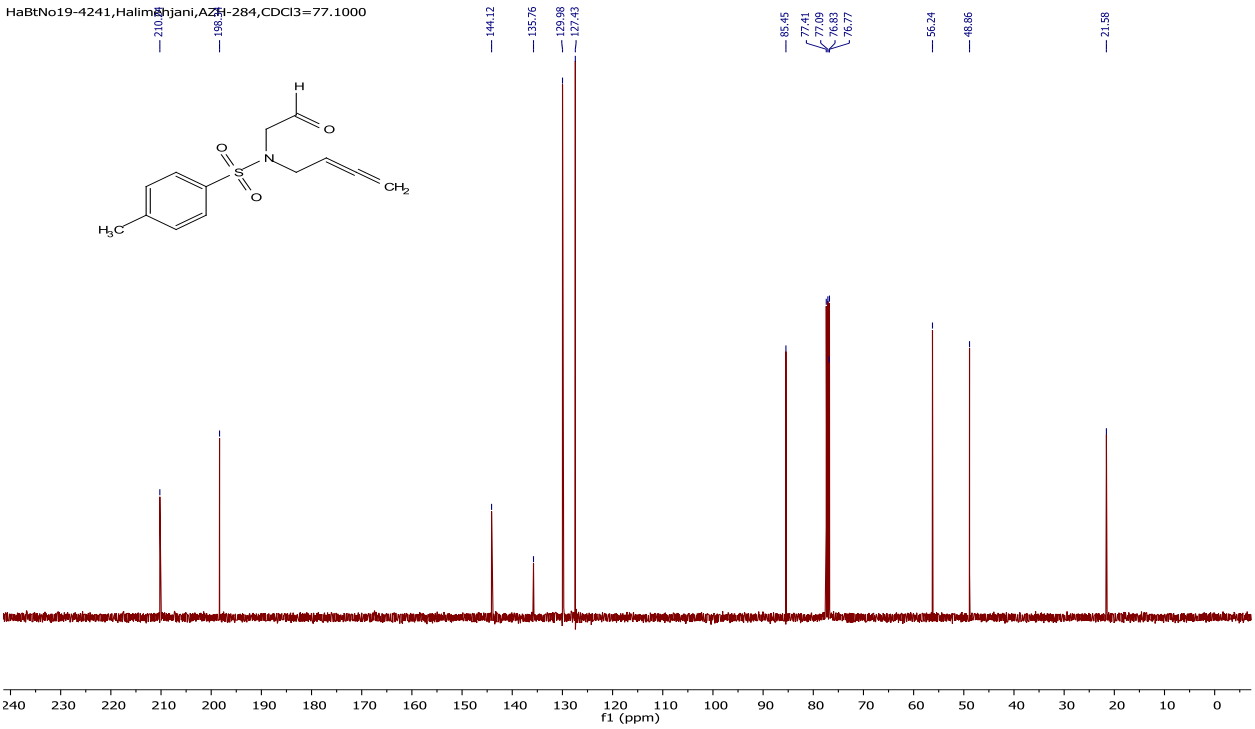


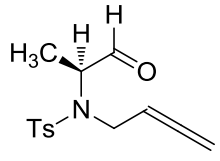




Swern Oxidation: Synthesis of N-(buta-2,3-dien-1-yl)-4-methyl-N-(2-oxoethyl)benzenesulfonamide: In a flask under argon atmosphere, Oxalyl chloride (13.5 mmol, 1.5 equiv) was dissolved in CH_2Cl_2 (36 mL) and the mixture was cooled to -78 °C. DMSO (27 mmol, 3 equiv) was added dropwise and the mixture was stirred at the same temperature for 30 minutes. Then, a solution of allenol **1k** (3 mmol, 1 equivalent) dissolved in CH_2Cl_2 (15 mL) was added dropwise to the reaction mixture and stirring was continued for 1 hour. Finally, Et_3N (18 mmol, 6 equivalents) was added to the reaction mixture and the reaction mixture was allowed to warm to room temperature (approximately 2 hours). The reaction mixture was quenched with water (50 mL) and the organic layer was separated. The aqueous phase was extracted two more times by CH_2Cl_2 and the combined organic layers were dried with $MgSO_4$ and concentrated under vacuum to afford the crude product which was purified by silica gel column chromatography using EtOAc: *n*-pentane (2:8).[10] ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.62 (t, J = 1.5 Hz, 1H), 7.69 (d, J = 8.3 Hz, 2H), 7.32 (d, J = 7.9 Hz, 2H), 5.13 – 4.86 (m, 1H), 4.73 (dt, J = 6.6, 2.4 Hz, 2H), 3.93 – 3.76 (m, 4H), 2.43 (s, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.2, 198.3, 144.1, 135.7, 129.9, 127.4, 85.4, 76.7, 56.2, 48.8, 21.5 ppm; HRMS (ESI) calcd for $C_{13}H_{15}NO_3S$ $[M+H]^+$: 266.0851; found: 266.0846.

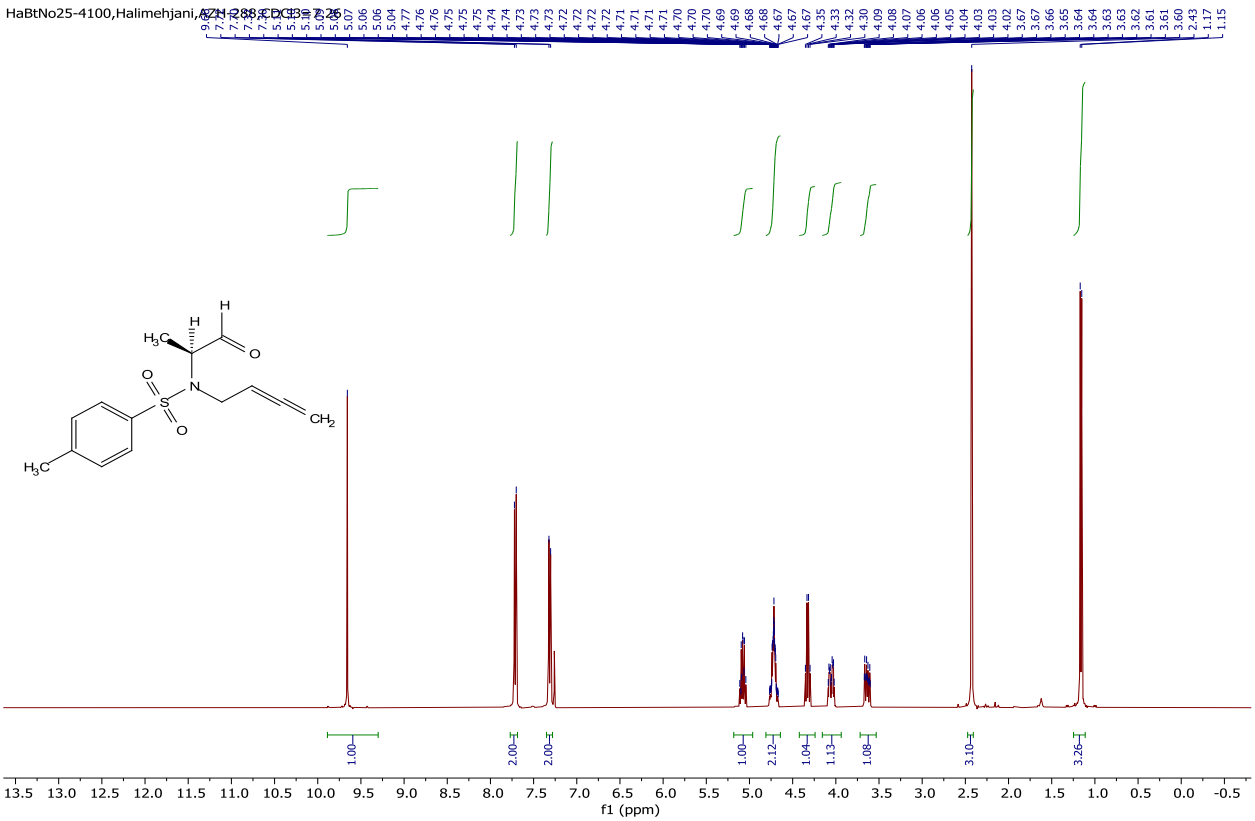






Dess-Martin Oxidation of allenol 1a: Synthesis of (S)-N-(buta-2,3-dien-1-yl)-4-methyl-N-(1-oxopropan-2-yl)benzenesulfonamide:[11] To a solution of allenol **1a** (17 mmol, 1 equiv) in water-saturated CH_2Cl_2 (60 mL) at 0 °C, Dess-Martin-Periodinane (34 mmol, 2 equiv) was added, and the mixture was allowed to warm to room temperature. Meanwhile after 15 minutes, in each 5 minutes, 6 mL of water-saturated CH_2Cl_2 was added to the reaction mixture until the TLC shows complete consumption of the starting material. Finally, the reaction mixture was diluted with CH_2Cl_2 and the organic phase was washed several times with a mixture of saturated $NaHCO_3$ (aqueous) and saturated $Na_2S_2O_3$ (aqueous). The resulting organic extract was dried over $MgSO_4$ and concentrated under reduced pressure. Purification was carried out by silica gel column chromatography using Et_2O:*n*-pentane (4:6). The prepared aldehyde is not stable for long time and the freshly prepared aldehyde must be used for the Grignard reaction. The *ee* of the prepared aldehyde was assigned by the reduction of aldehyde to the corresponding alcohol according to the method described by Myers et al.[9] ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.66 (s, 1H), 7.71 (d, J = 8.3 Hz, 2H), 7.31 (d, J = 7.7 Hz, 2H), 5.10–4.06 (m, , 1H), 4.81 – 4.64 (m, 2H), 4.33 (q, J = 7.1 Hz, 1H), 4.05 (ddt, J = 14.9, 6.0, 2.9 Hz, 1H), 3.64 (ddt, J = 14.9, 8.5, 1.8 Hz, 1H), 2.43 (s, 3H), 1.16 (d, J = 7.1 Hz, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.0, 200.0, 143.9, 137.3, 129.9, 127.2, 86.7, 76.7, 61.2, 44.5, 21.5, 11.5 ppm; HRMS (ESI) calcd for

$C_{14}H_{17}NO_3S$ $[M+NH_4]^+$: 297.1273; found: 297.1270. HPLC data for the reduced compound: (ChiralPAK AD-3, heptane/EtOH = 80:20, 0.5 mL/min) t_R = 19.39 min (minor), t_R = 28.71 min (major), 88% ee. ; $[\alpha]_D^{25}$ = 26.28 (c = 0.7, CH_2Cl_2).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1.00
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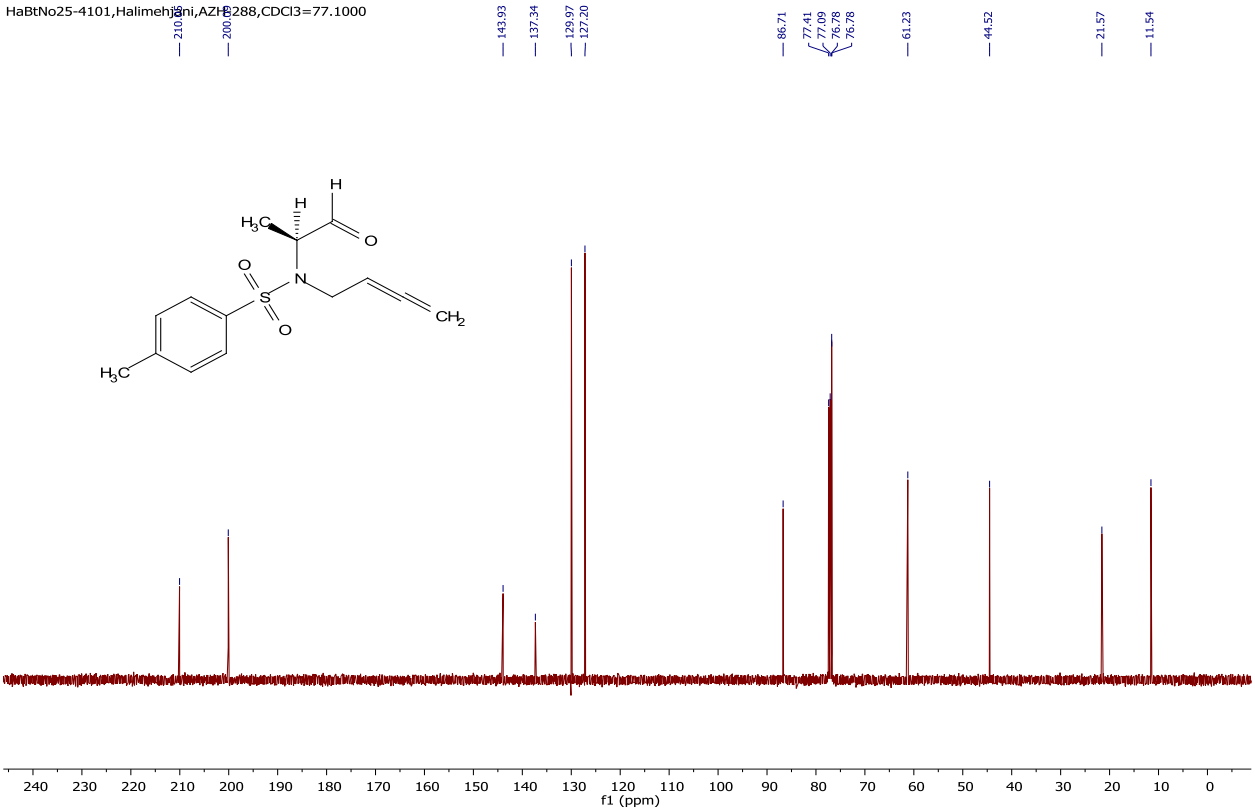
2.00
1.00
2.12
1.04
1.13
1.08
3.10
3.26
f1 (ppm)


HaBtNo25-4101,Halimehjani,AZH-288,CDCl3=77.1000
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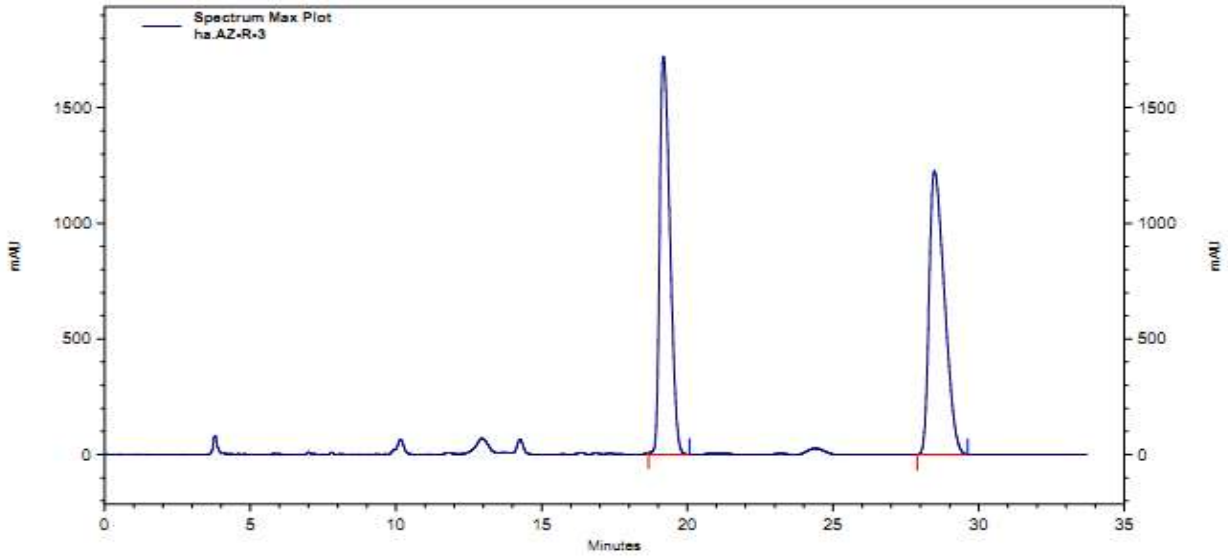
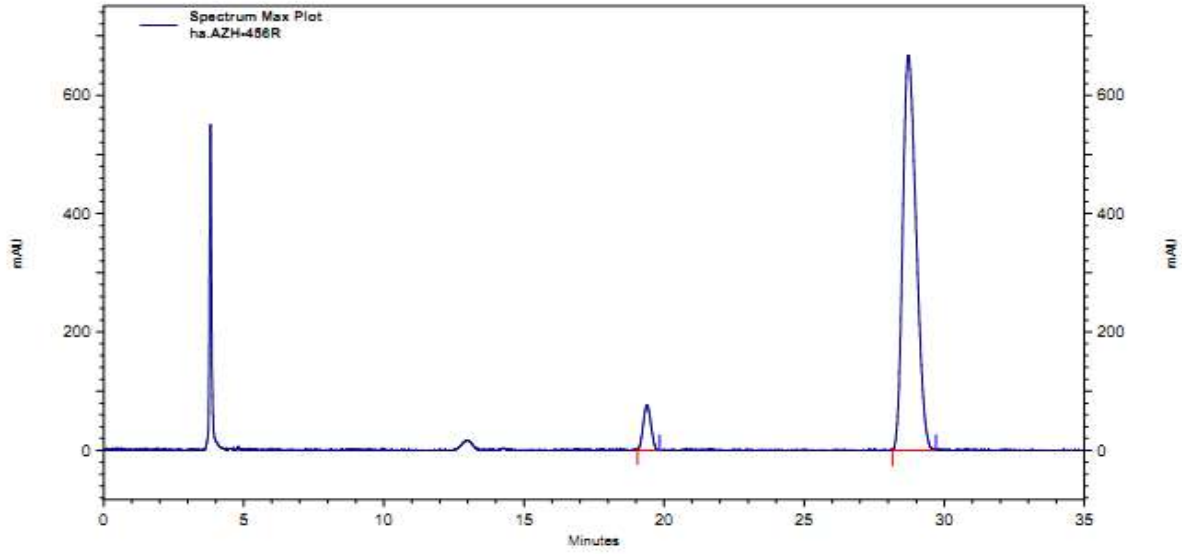
200.00
143.93
137.34
129.97
127.20
86.71
77.41
77.09
76.78
76.78
61.23
44.52
21.57
11.54
f1 (ppm)



Spectrum Max Plot
Results

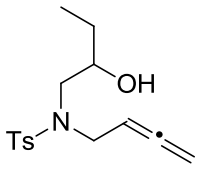
Peak Number	Retention Time	Area Percent	Area
1	19,185	48,535	5666199582
2	28,483	51,465	6008325586
Totals		100,000	11674525168



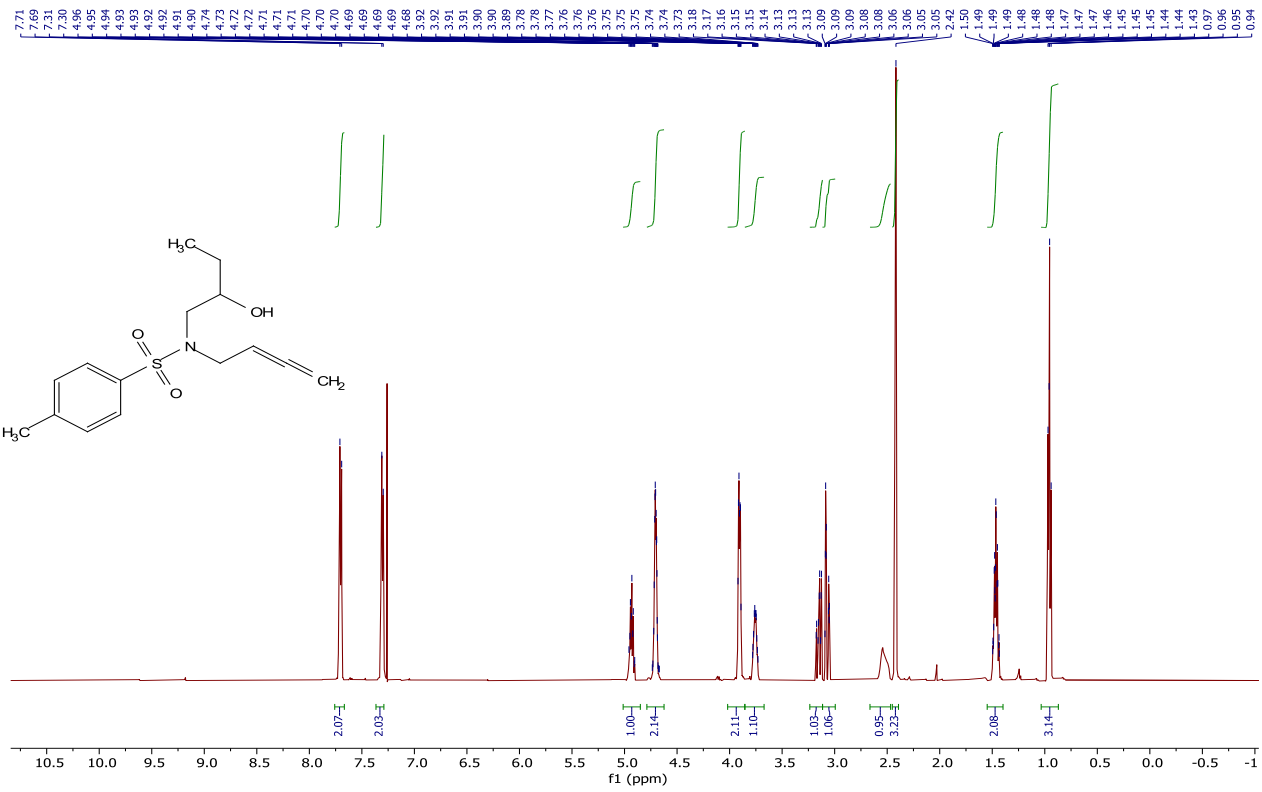
Spectrum Max Plot
Results

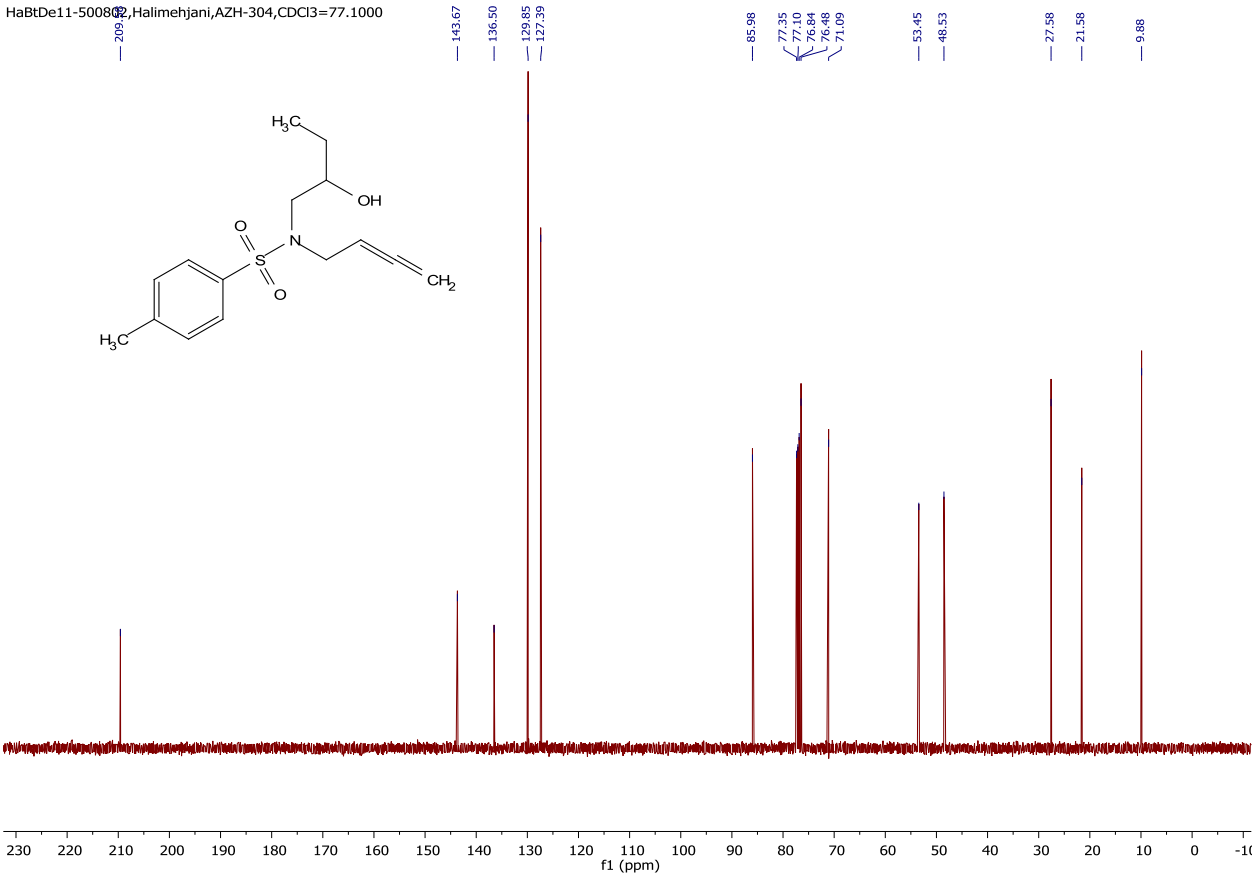
Peak Number	Retention Time	Area Percent	Area
1	19,397	6,233	197805735
2	28,708	93,767	2975662339
Totals		100,000	3173468074

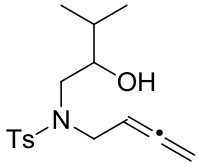
General procedure for the Grignard Reaction: To a solution of an allenal (2 mmol) in dry THF (5 mL) at 0°C, a Grignard reagent (2.5 mmol) was added dropwise for about 10 minutes and the reaction mixture was allowed to warm to room temperature (about 1 hour). The reaction was quenched with cool saturated ammonium chloride solution and extracted with ethyl acetate. The organic phase was washed with water and brine, dried over anhydrous sodium sulfate, and concentrated under vacuum to afford the crude product. Purification was carried out by silica gel column chromatography using EtOAc:*n*-pentane (1:9).[12]



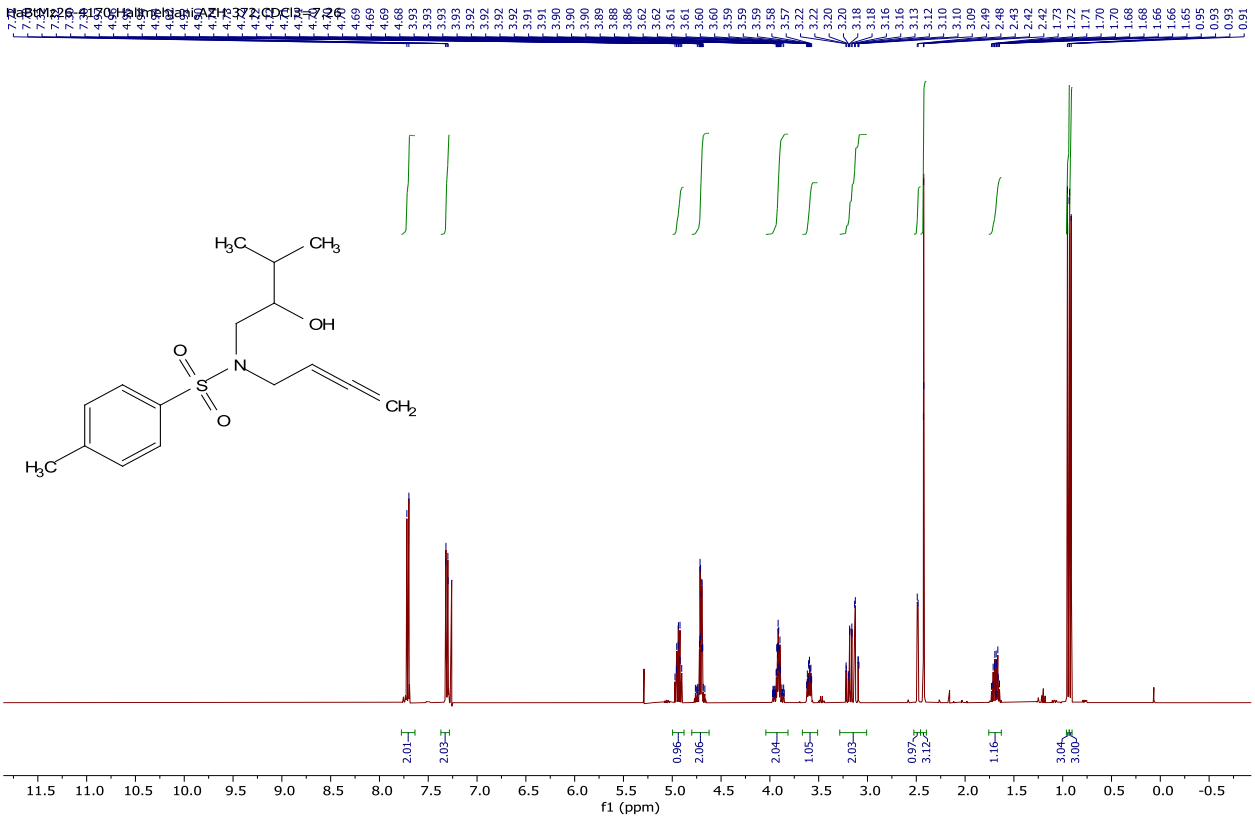
N-(buta-2,3-dien-1-yl)-N-(2-hydroxybutyl)-4-methylbenzenesulfonamide (**1l**): The reaction was carried out according to the general procedure using ethylmagnesium bromide (1M in THF): ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.70 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 8.3 Hz, 2H), 5.01 – 4.85 (m, 1H), 4.79 – 4.62 (m, 2H), 3.94–3.90 (m, 2H), 3.85 – 3.67 (m, 1H), 3.15 (ddd, *J* = 14.4, 8.6, 1.7 Hz, 1H), 3.07 (ddd, *J* = 14.6, 3.1, 1.2 Hz, 1H), 2.54 (brs, 1H), 2.42 (s, 3H), 1.55 – 1.40 (m, 2H), 1.03 – 0.87 (m, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) *δ* 209.5, 143.6, 136.5, 129.8, 127.3, 85.9, 76.4, 71.0, 53.4, 48.5, 27.5, 21.5, 9.8 ppm; HRMS (ESI) calcd for $C_{15}H_{21}NO_3S$ $[M+H]^+$: 296.1320; found: 296.1318.

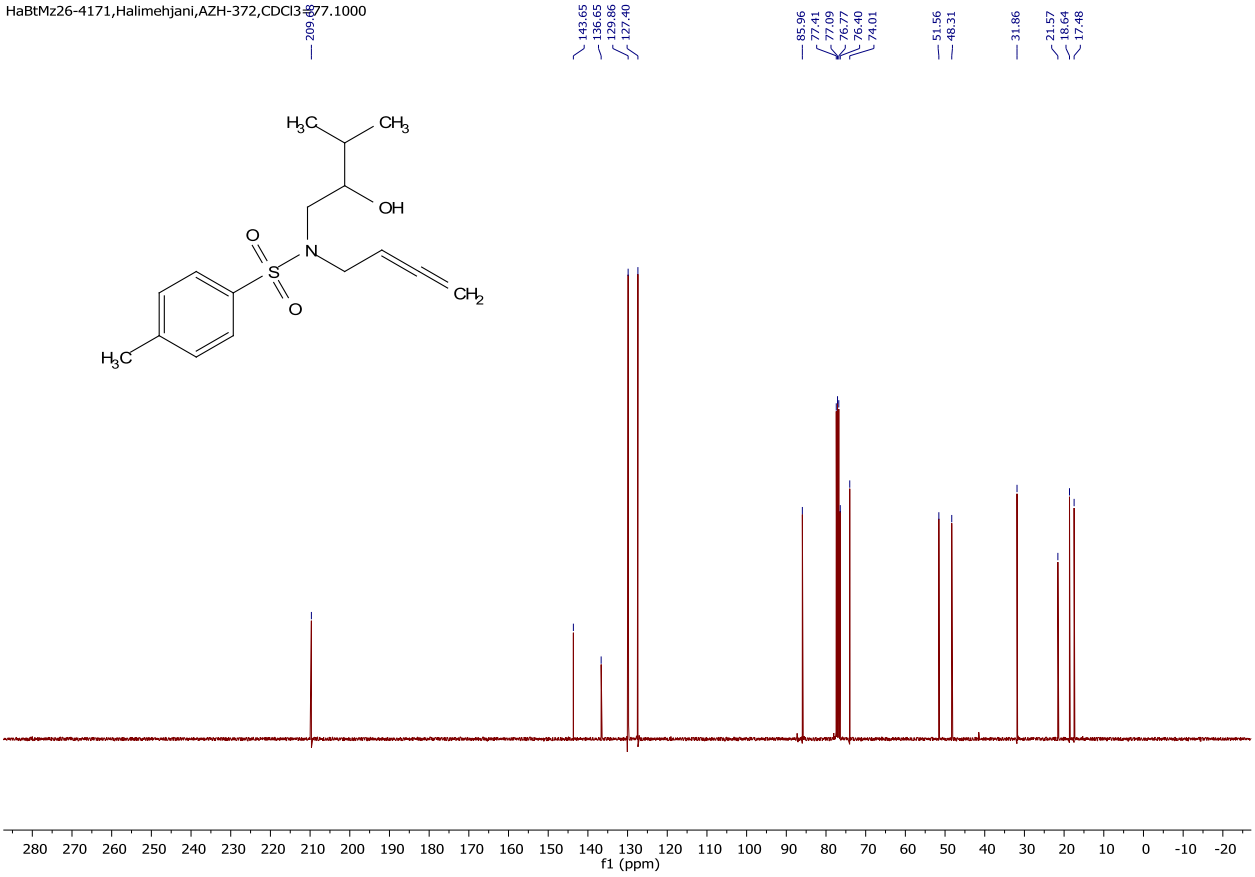


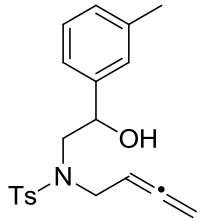




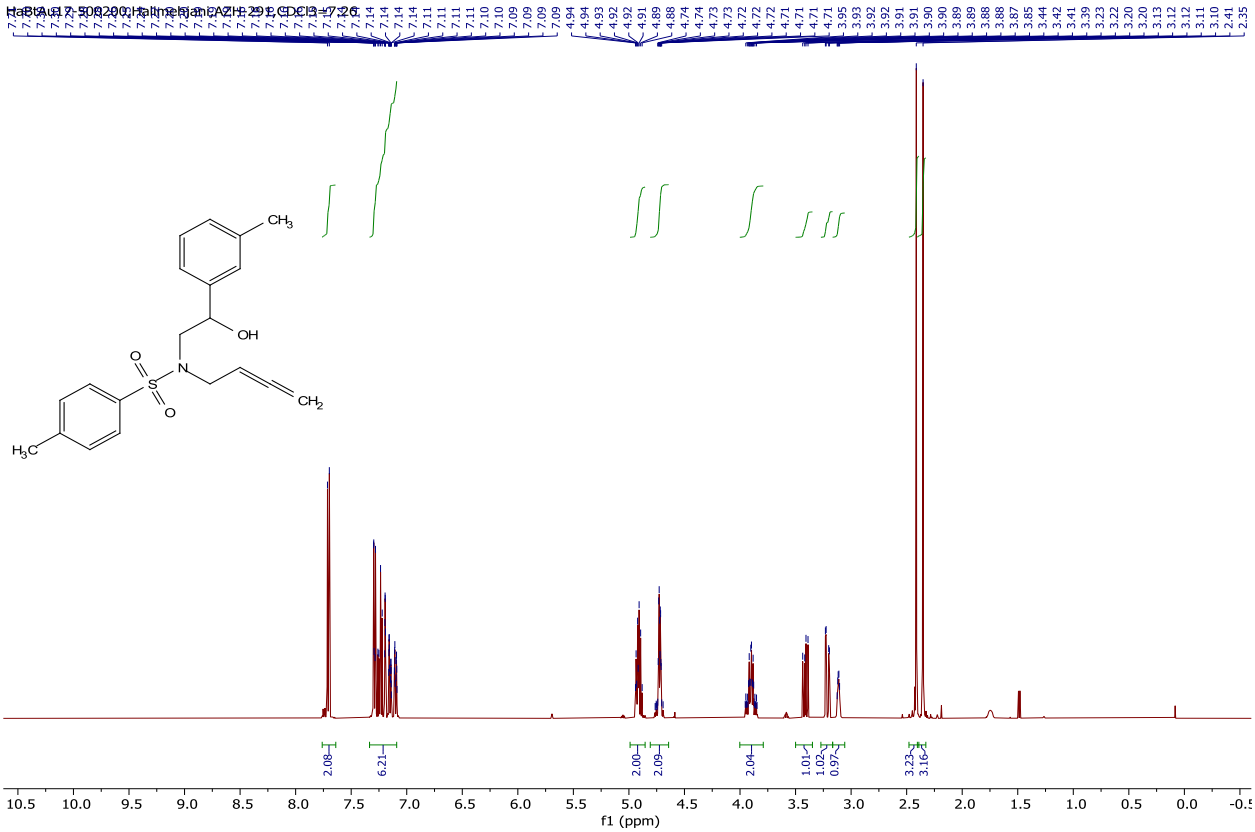
N-(buta-2,3-dien-1-yl)-N-(2-hydroxy-3-methylbutyl)-4-methylbenzenesulfonamide (**1m**): The reaction was carried out according to the general procedure using isopropylmagnesium bromide (2M in THF): ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.71 (d, J = 8.3 Hz, 2H), 7.31 (dd, J = 8.6, 0.7 Hz, 2H), 4.96–4.93 (m, 1H), 4.72–4.68 (m, 2H), 4.04 – 3.81 (m, 2H), 3.67 – 3.51 (m, 1H), 3.28 – 3.01 (m, 2H), 2.49 (d, J = 3.4 Hz, 1H), 2.42 (s, 3H), 1.70–1.67 (m, 1H), 0.94 (d, J = 6.8 Hz, 3H), 0.92 (d, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 209.6, 143.6, 136.6, 129.8, 127.4, 85.9, 76.4, 74.0, 51.5, 48.3, 31.8, 21.5, 18.6, 17.4 ppm; HRMS (ESI) calcd for $C_{16}H_{23}NO_3S$ $[M+H]^+$: 310.1477; found: 310.1473.

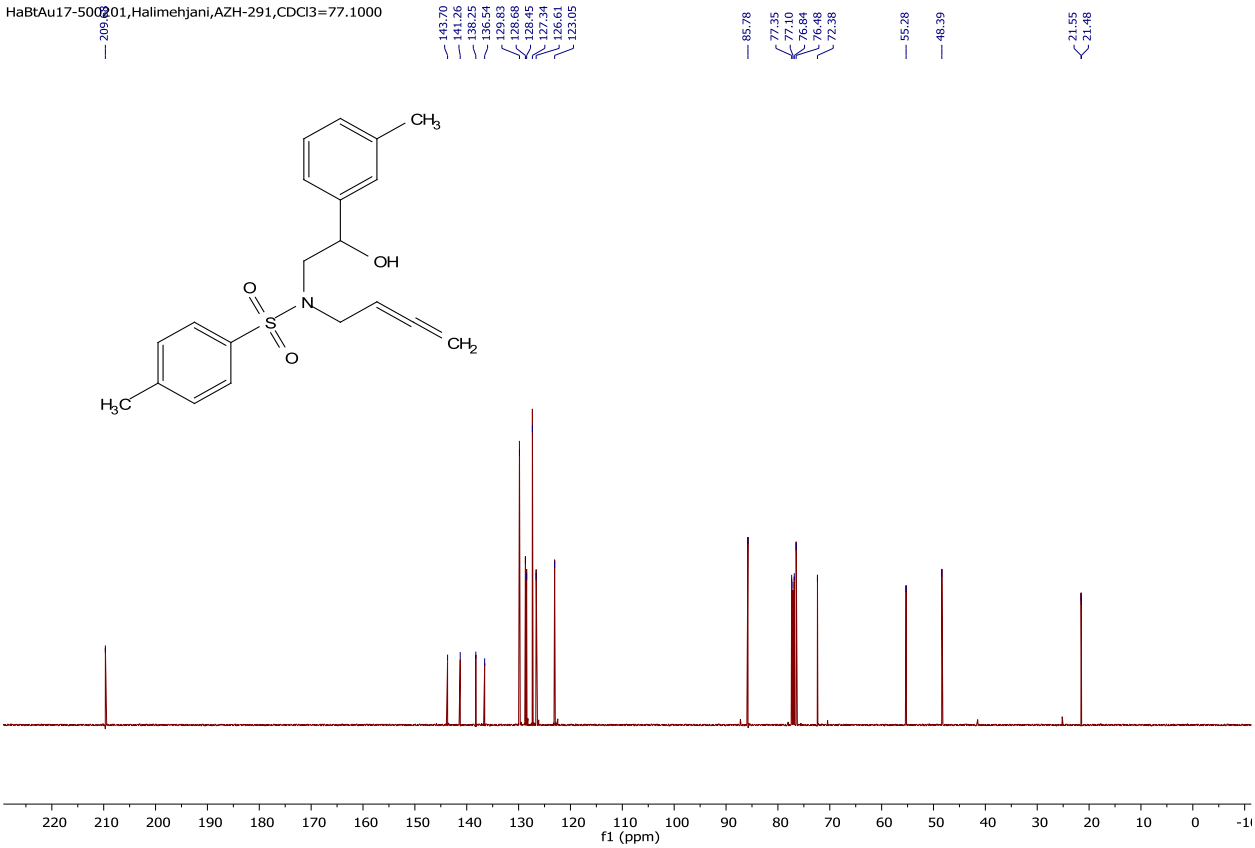

HaBtMz26-4170,Halimehjani,AZH-372,CDCl3-7.26
H3C
CH3
OH
O
N
S
O
CH2
H3C
2.01
2.03
0.96
2.06
2.04
1.05
2.03
0.97
3.12
1.16
3.04
3.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

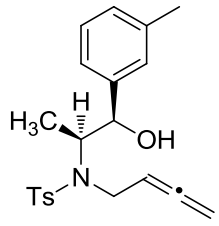

HaBtMz26-4171,Halimehjani,AZH-372,CDCl3-77.1000
209.48
143.65
136.65
129.86
127.40
85.96
77.41
77.09
76.77
76.40
74.01
51.56
48.31
31.86
21.57
18.64
17.48
H3C
CH3
OH
O
N
S
O
CH2
H3C
280 270 260 250 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)



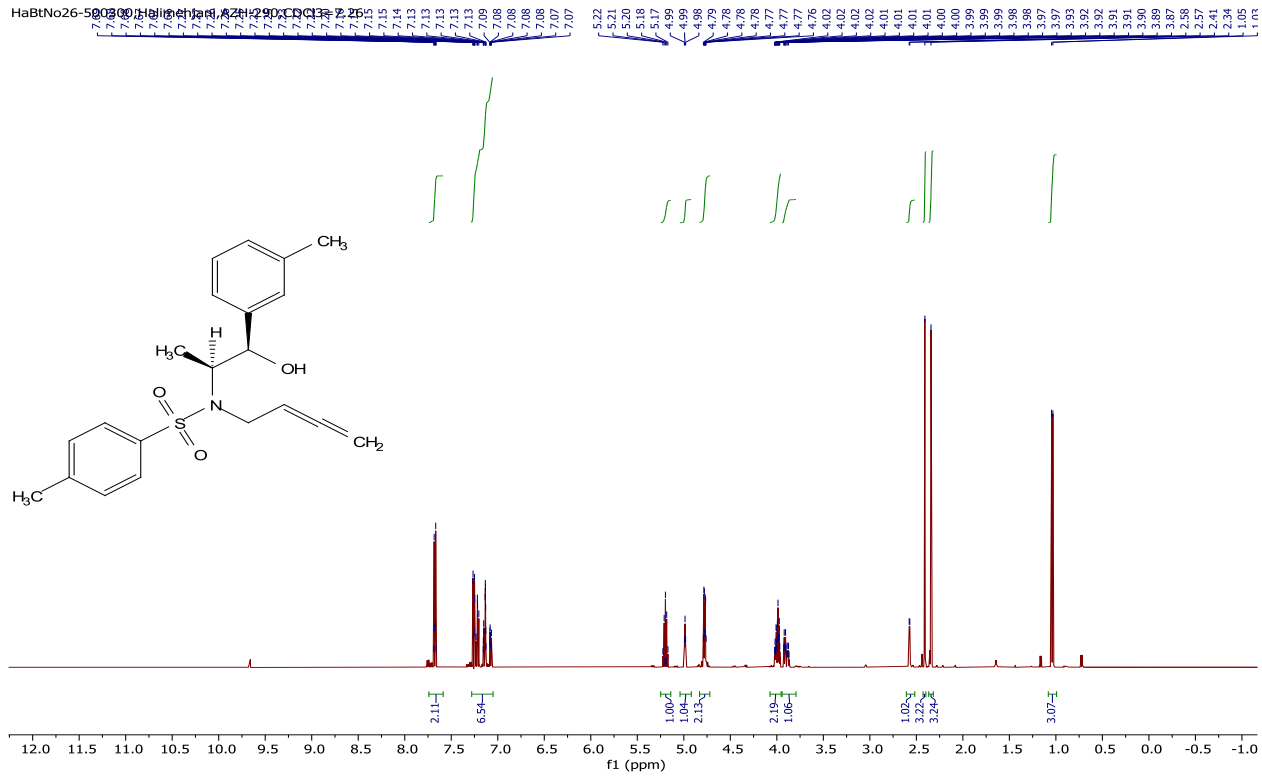
N-(buta-2,3-dien-1-yl)-N-(2-hydroxy-2-(m-tolyl)ethyl)-4-methylbenzenesulfonamide (**1n**): The reaction was carried out according to the general procedure using freshly prepared *m*-tolylmagnesium bromide: ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.70 (d, J = 8.3 Hz, 2H), 7.33 – 7.09 (m, 6H), 4.99 – 4.85 (m, 2H), 4.81 – 4.64 (m, 2H), 4.00 – 3.79 (m, 2H), 3.41 (dd, J = 14.8, 9.1 Hz, 1H), 3.21 (dd, J = 14.8, 3.2 Hz, 1H), 3.12 (brs, 1H), 2.41 (s, 3H), 2.35 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 209.6, 143.7, 141.2, 138.2, 136.5, 129.8, 128.6, 128.4, 127.3, 126.6, 123.0, 85.7, 76.4, 72.3, 55.2, 48.3, 21.5, 21.4 ppm; HRMS (ESI) calcd for $C_{20}H_{23}NO_3S$ $[M+H]^+$: 358.1477; found: 358.1472.

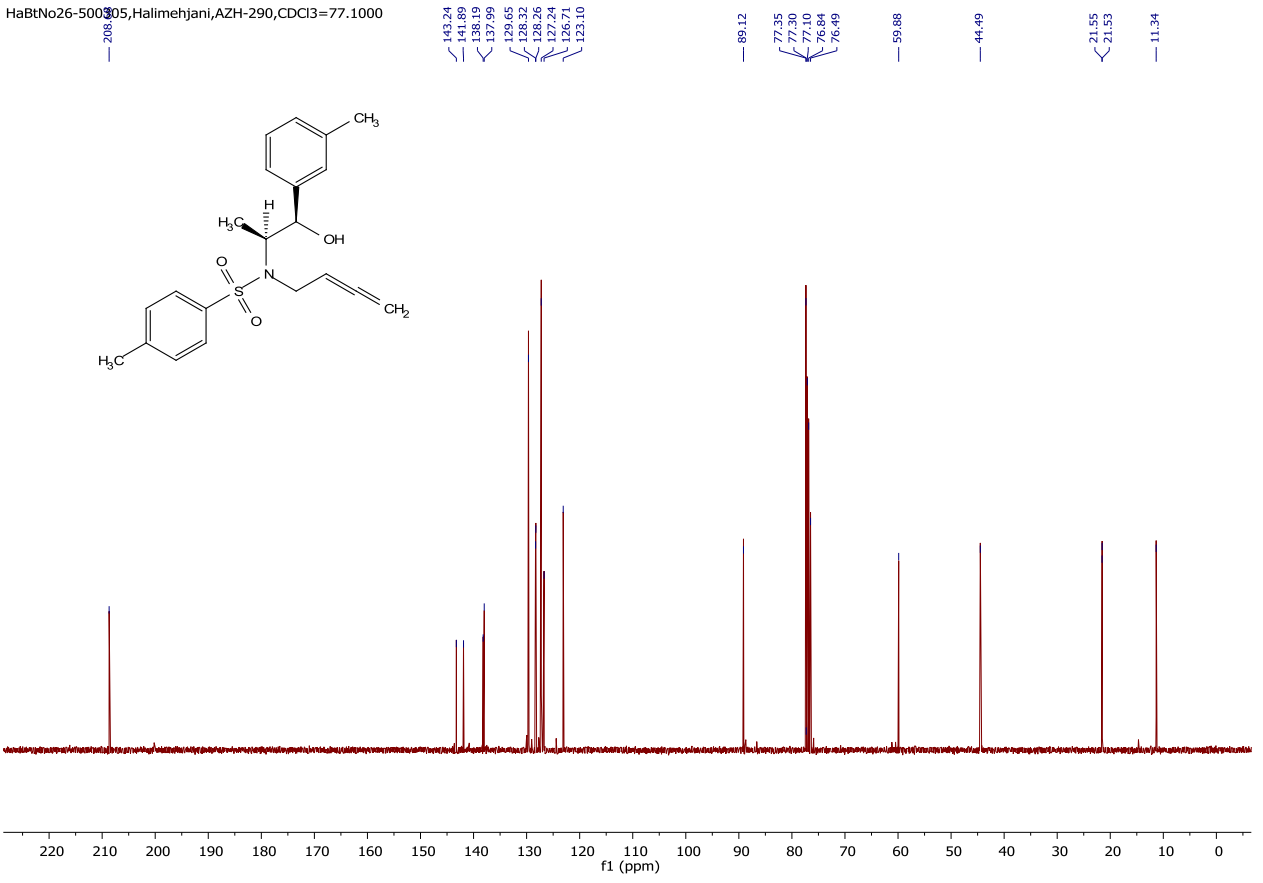


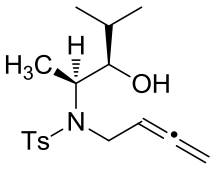




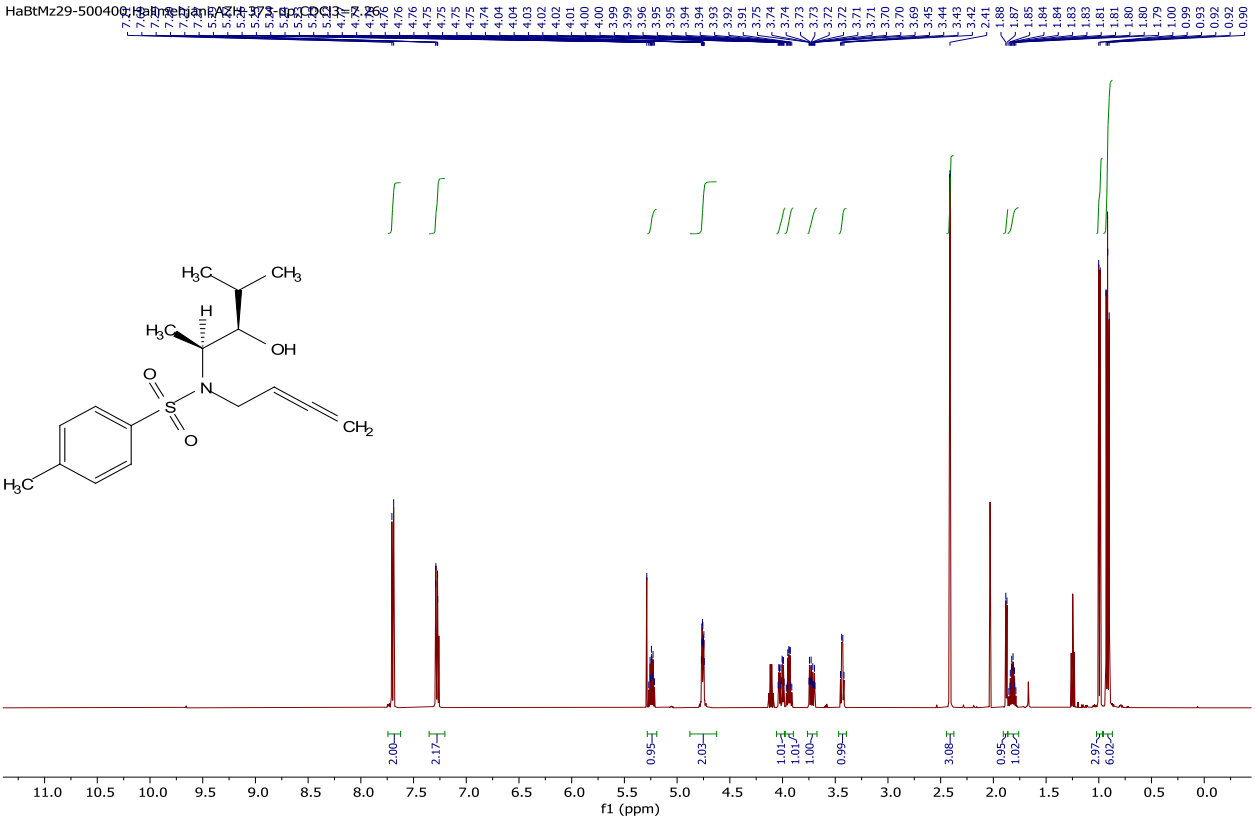
N-(buta-2,3-dien-1-yl)-N-((1R,2S)-1-hydroxy-1-(m-tolyl)propan-2-yl)-4-methylbenzenesulfonamide (**3a**): The reaction was carried out according to the general procedure using freshly prepared *m*-tolylmagnesium bromide. The crude mixture was obtained with *dr* ratio of 5.6:1. After purification, the major diastereomer **3a** was obtained in >19:1 dr ratio. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.74 – 7.59 (m, 2H), 7.28 – 7.05 (m, 6H), 5.22–5.18 (m, 1H), 4.99 (t, *J* = 3.1 Hz, 1H), 4.79–4.75 (m, 2H), 4.07 – 3.95 (m, 2H), 3.92–3.88 (m, 1H), 2.57 (d, *J* = 3.3 Hz, 1H), 2.41 (s, 3H), 2.34 (s, 3H), 1.04 (d, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 208.6, 143.2, 141.8, 138.1, 137.9, 129.6, 128.3, 128.2, 127.2, 126.7, 123.1, 89.1, 77.3, 76.49, 59.8, 44.4, 21.5, 21.5, 11.3 ppm; HRMS (ESI) calcd for $C_{21}H_{25}NO_3S$ $[M+H]^+$: 372.1633; found: 372.1629; $[\alpha]_D^{25}$ = +4.79 (c = 0.71, CH_2Cl_2).

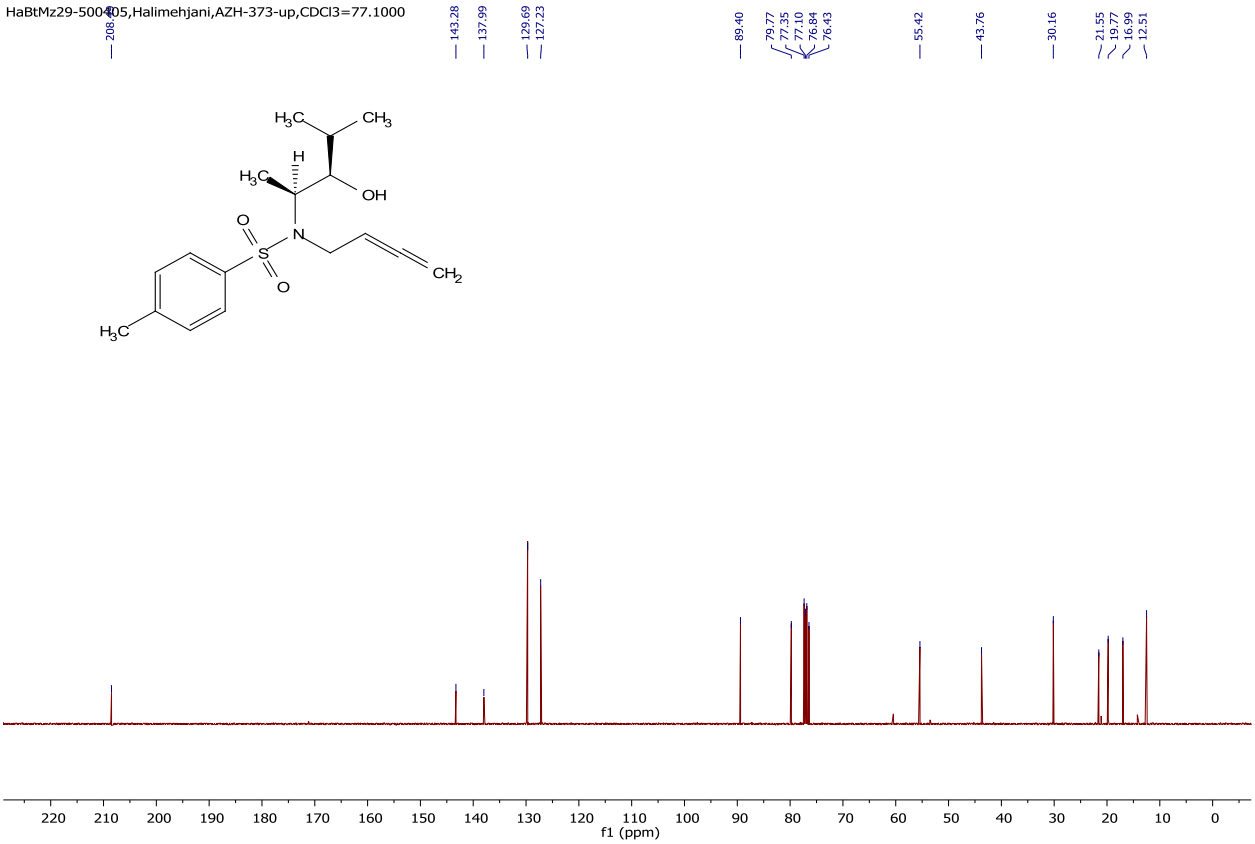

HaBtNo26-500200,Halimehjani,AZH-290,CDCl3=7.26
f1 (ppm)

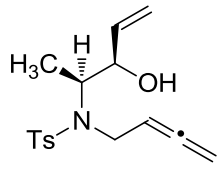

HaBtNo26-500305,Halimehjani,AZH-290,CDCl3=77.1000
f1 (ppm)



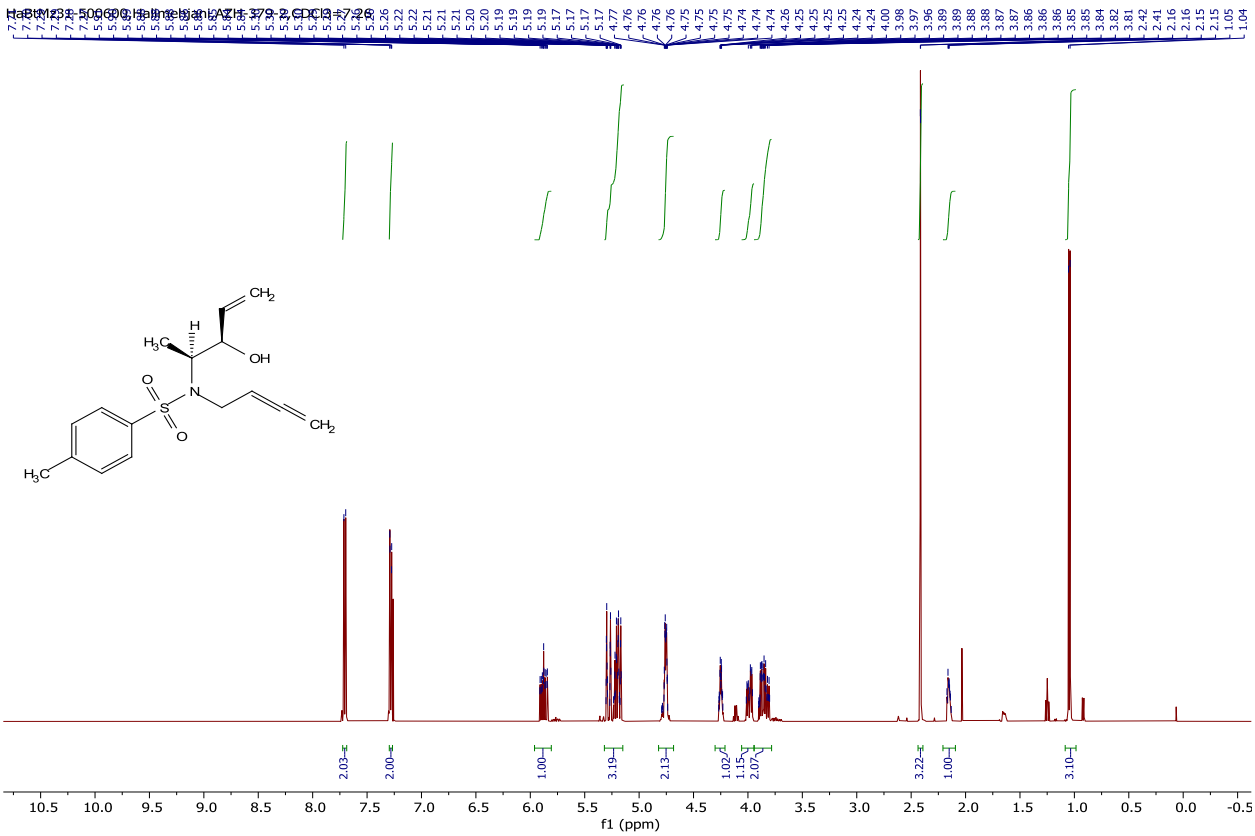
N-(buta-2,3-dien-1-yl)-N-((2S,3R)-3-hydroxy-4-methylpentan-2-yl)-4-methylbenzenesulfonamide (**3b**): The reaction was carried out according to the general procedure using isopropylmagnesium bromide (2M in THF). The crude mixture was obtained with *dr* ratio of >20:1. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.70 (d, J = 8.3 Hz, 2H), 7.35 – 7.20 (m, 2H), 5.26-5.23 (m, 1H), 4.78–4.74 (m, 2H), 4.03–3.98 (m, 1H), 3.94 (qd, J = 6.9, 5.0 Hz, 1H), 3.72 (ddt, J = 15.8, 7.8, 2.1 Hz, 1H), 3.43 (q, J = 5.5 Hz, 1H), 2.41 (s, 3H), 1.88 (d, J = 5.4 Hz, 1H), 1.84–1.80 (m, 1H), 0.99 (d, J = 7.0 Hz, 3H), 0.94–0.90 (m, 6H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 208.4, 143.2, 137.9, 129.6, 127.2, 89.4, 79.7, 76.4, 55.4, 43.7, 30.1, 21.5, 19.7, 16.9, 12.5 ppm; HRMS (ESI) calcd for $C_{17}H_{25}NO_3S$ $[M+H]^+$: 324.1633; found: 324.1628; $[\alpha]_D^{25}$ = +42.90 (c = 0.303, CH_2Cl_2).

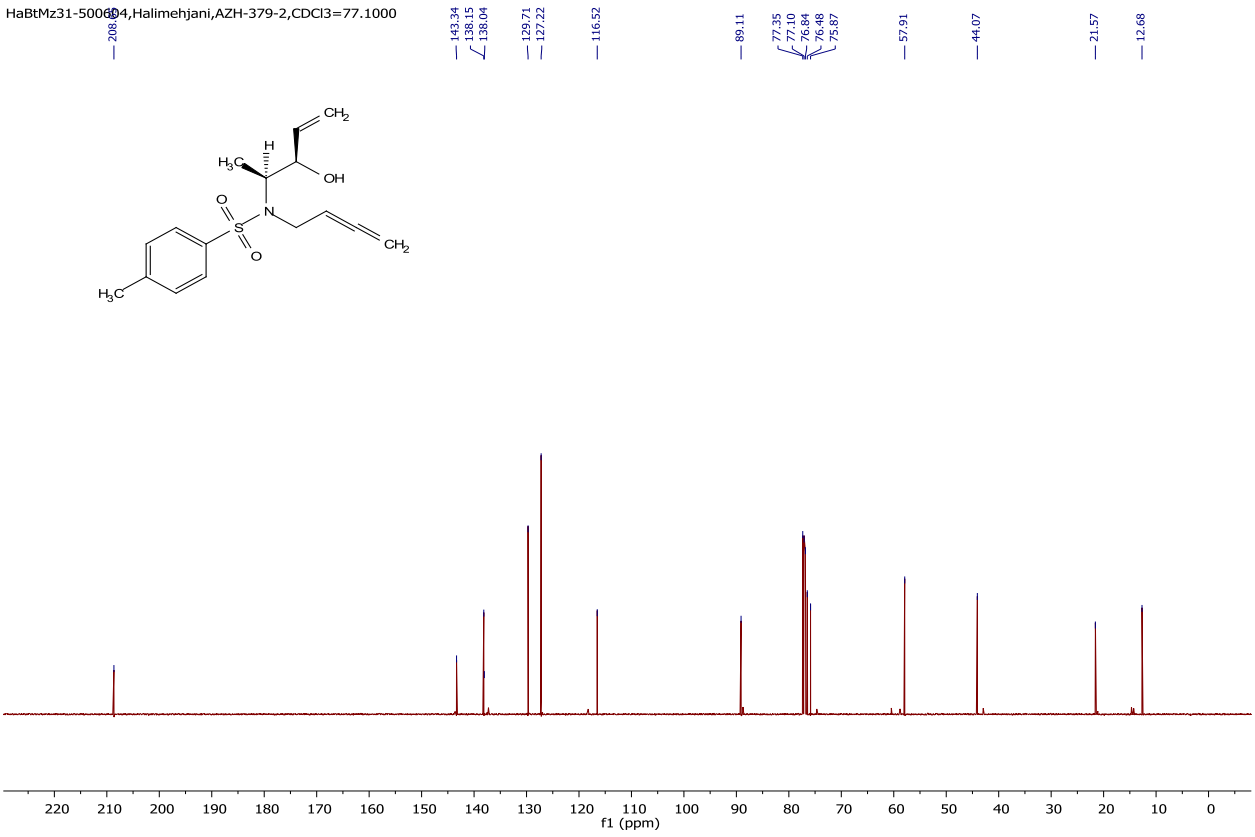


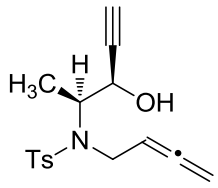




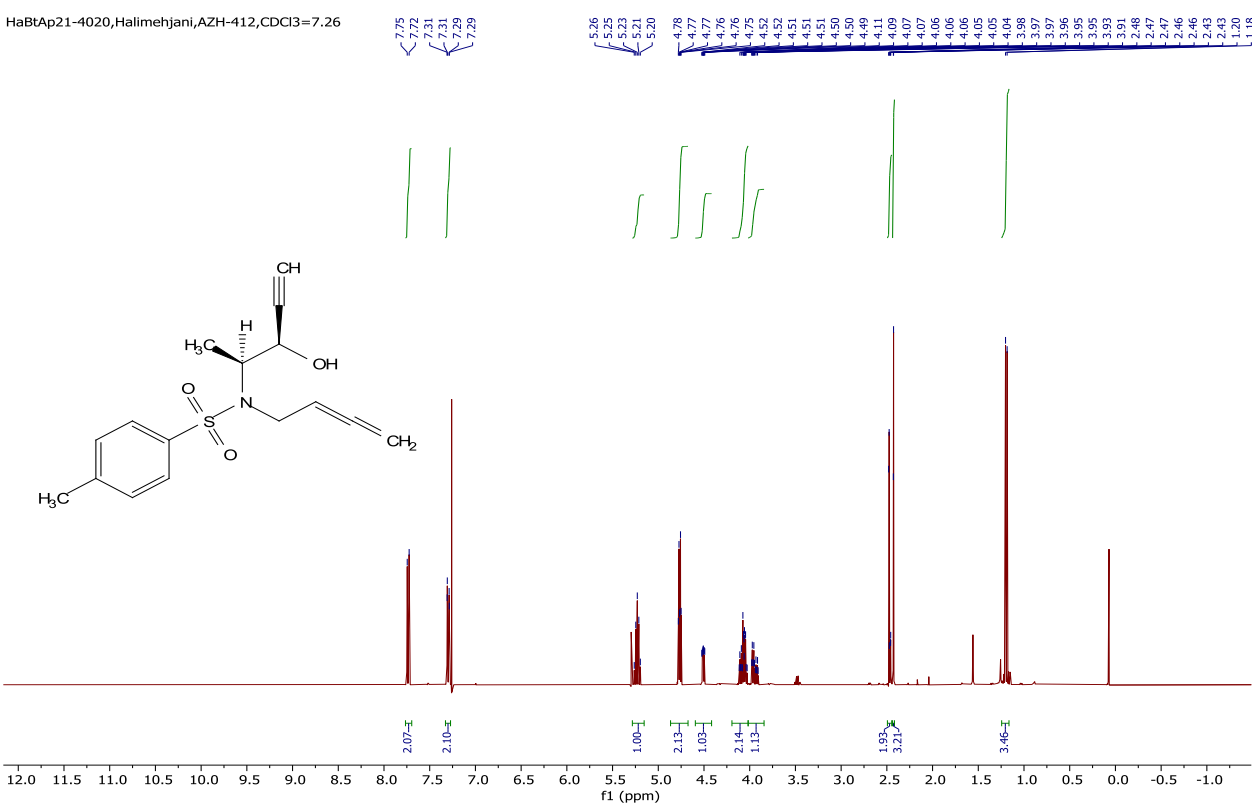
N-(buta-2,3-dien-1-yl)-N-((2S,3R)-3-hydroxypent-4-en-2-yl)-4-methylbenzenesulfonamide (**3c**): The reaction was carried out according to the general procedure using vinylmagnesium bromide (1M in THF). The crude mixture was obtained with *dr* ratio of 7.3:1. After purification, the major diastereomer **3c** was obtained in >19:1 dr ratio.^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.70 (d, J = 8.4 Hz, 2H), 7.28 (dd, J = 7.9, 0.8 Hz, 2H), 5.89–5.86 (m, 1H), 5.32 – 5.15 (m, 3H), 4.82 – 4.68 (m, 2H), 4.30 – 4.21 (m, 1H), 3.99–3.97 (m, 1H), 3.94 – 3.78 (m, 2H), 2.41 (s, 3H), 2.21 – 2.09 (m, 1H), 1.05 (d, J = 7.1 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 208.6, 143.3, 138.1, 138.0, 129.7, 127.2, 116.5, 89.1, 76.4, 75.8, 57.9, 44.0, 21.5, 12.6 ppm; HRMS (ESI) calcd for $C_{15}H_{21}NO_3S$ $[M+H]^+$: 308.1320; found: 308.1316; $[\alpha]_D^{25}$ = +45.10 (c = 0.337, CH_2Cl_2).

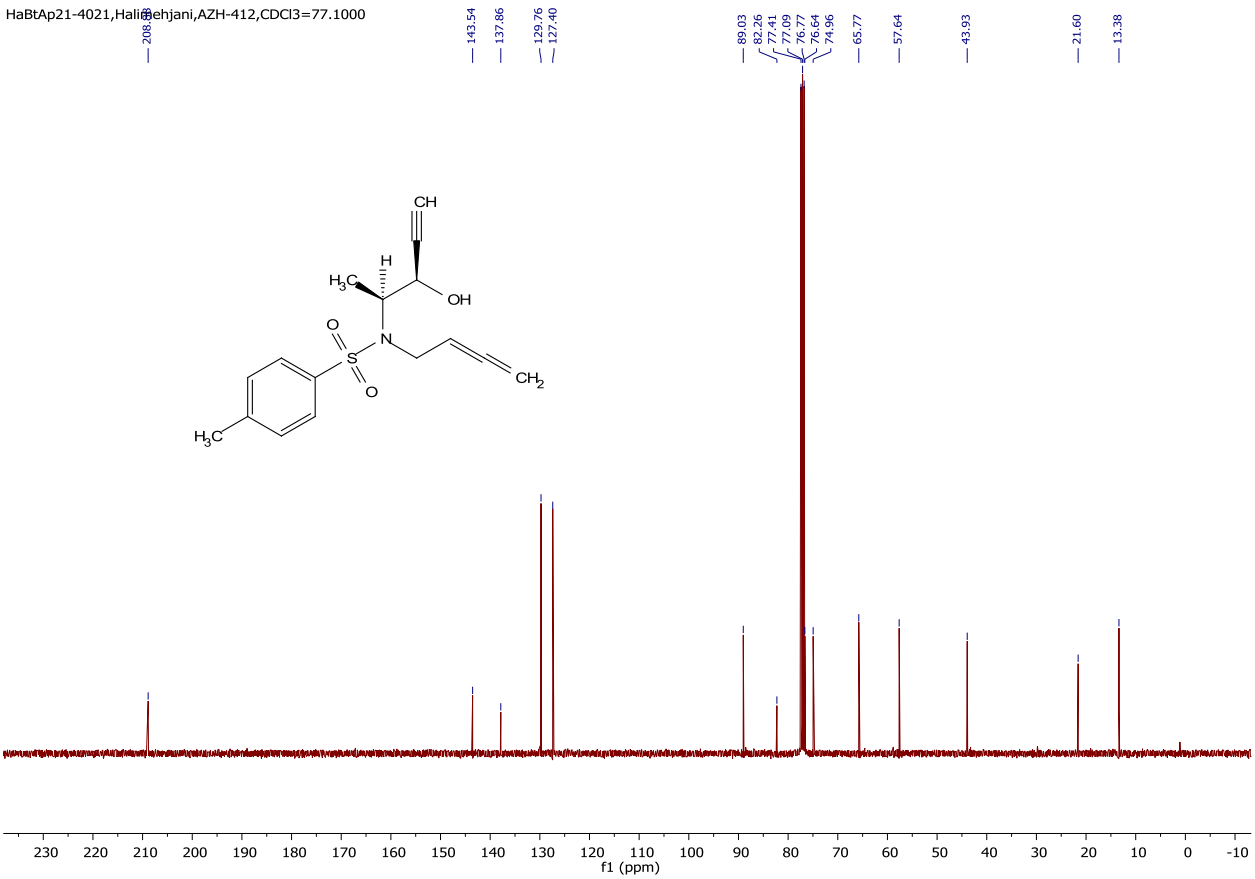

HaBtMz31-500600,Halimehjani,AZH-379-2,CDCl3=7.26
2.03
2.00
1.00
3.19
2.13
1.02
1.15
2.07
3.22
1.00
3.10
f1 (ppm)

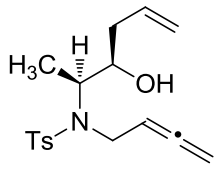

HaBtMz31-500604,Halimehjani,AZH-379-2,CDCl3=77.1000
208.61
143.34
138.15
138.04
129.71
127.22
116.52
89.11
77.35
77.10
76.84
76.48
75.87
57.91
44.07
21.57
12.68
f1 (ppm)



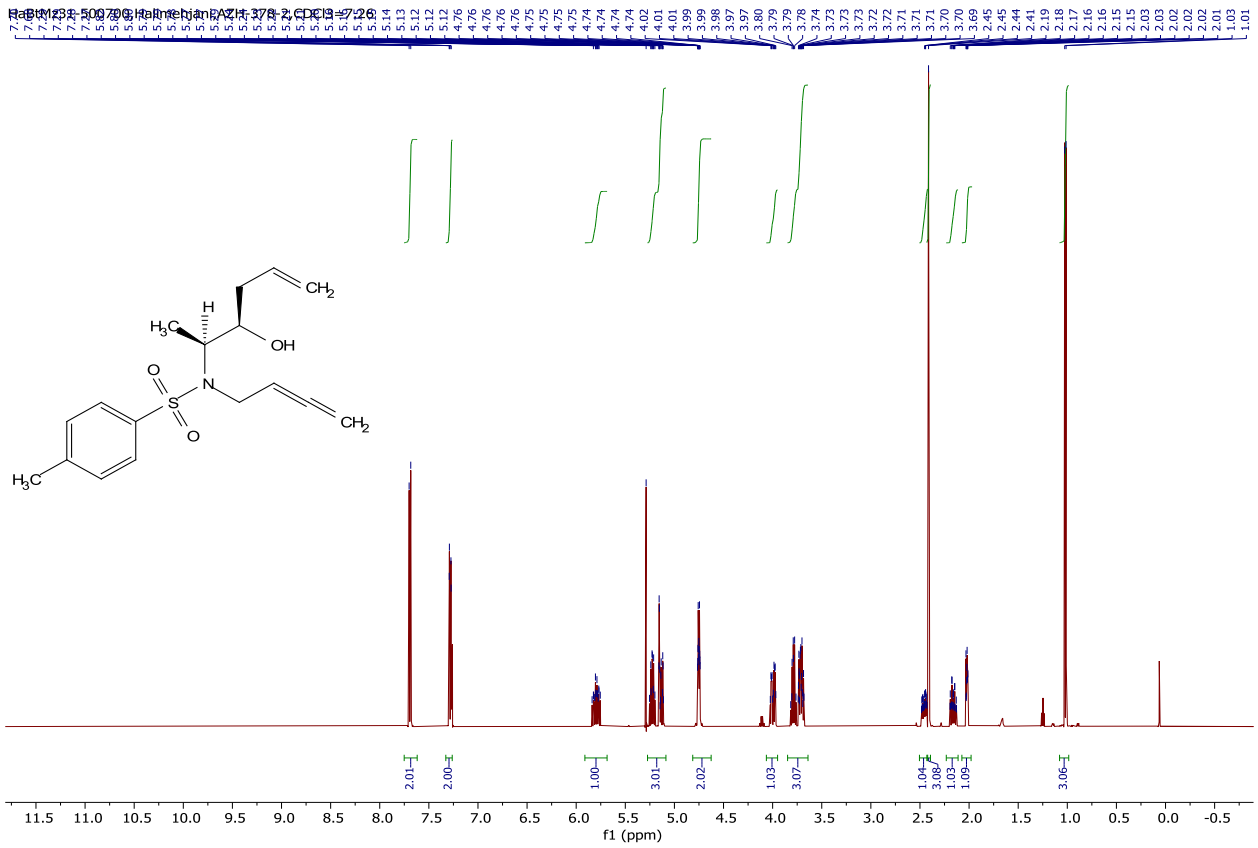
N-(buta-2,3-dien-1-yl)-N-((2S,3R)-3-hydroxypent-4-yn-2-yl)-4-methylbenzenesulfonamide (**3d**): The reaction was carried out according to the general procedure using ethynylmagnesium bromide (0.5 M in THF). The crude mixture was obtained with *dr* ratio of 9:1. After purification, the major diastereomer **3d** was obtained in >19:1 dr ratio. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.74 (d, *J* = 8.3 Hz, 2H), 7.30 (dd, *J* = 8.6, 0.7 Hz, 2H), 5.23 (p, *J* = 6.7 Hz, 1H), 4.77 (dt, *J* = 6.7, 2.7 Hz, 2H), 4.51 (ddd, *J* = 6.1, 4.6, 2.3 Hz, 1H), 4.19 – 4.02 (m, 2H), 3.94 (ddt, *J* = 16.0, 6.9, 2.6 Hz, 1H), 2.49 – 2.45 (m, 2H), 2.43 (d, *J* = 0.8 Hz, 3H), 1.19 (d, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 208.8, 143.5, 137.8, 129.7, 127.4, 89.0, 82.2, 76.6, 74.9, 65.7, 57.6, 43.9, 21.6, 13.3 ppm; HRMS (ESI) calcd for $C_{16}H_{19}NO_3S$ $[M+H]^+$: 306.1164; found: 306.1162; $[\alpha]_D^{25}$ = +37.75 (c = 0.347, CH_2Cl_2).

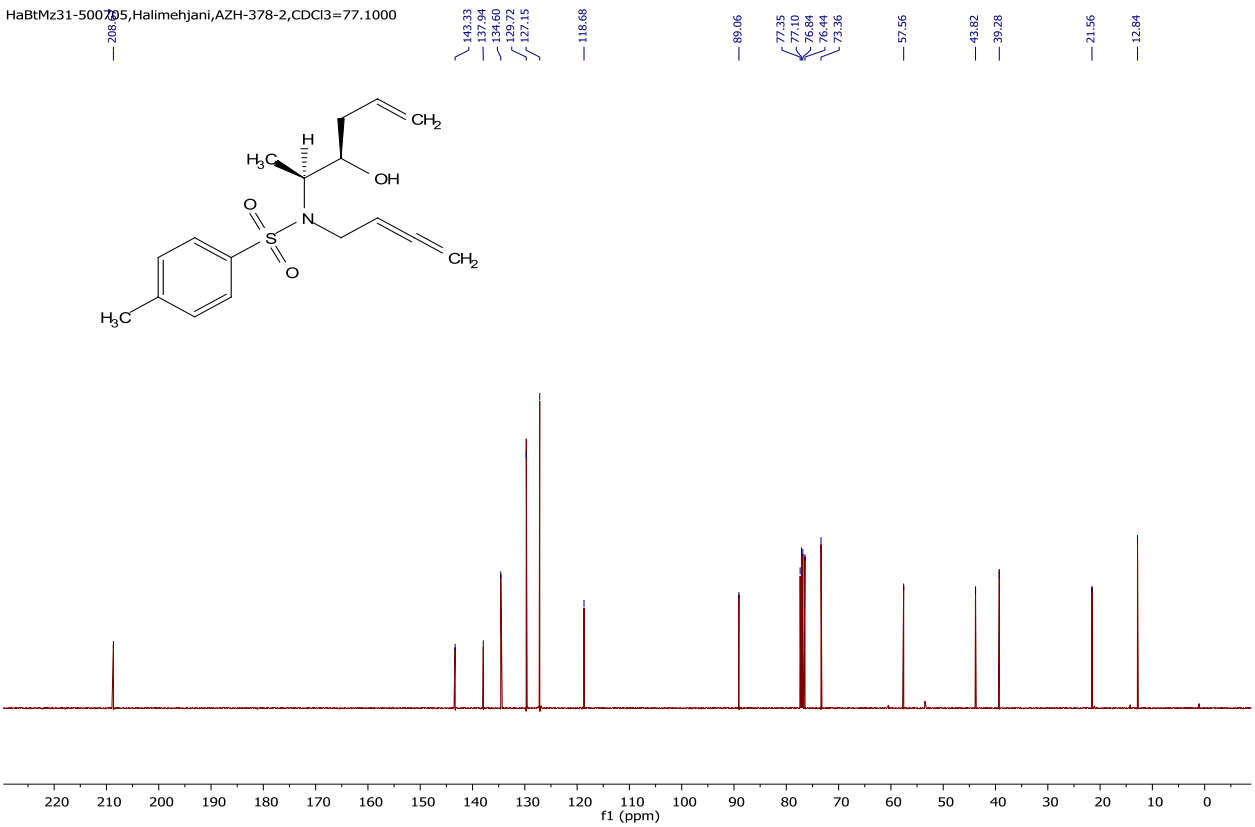


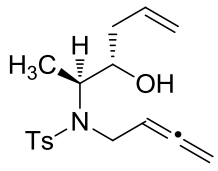




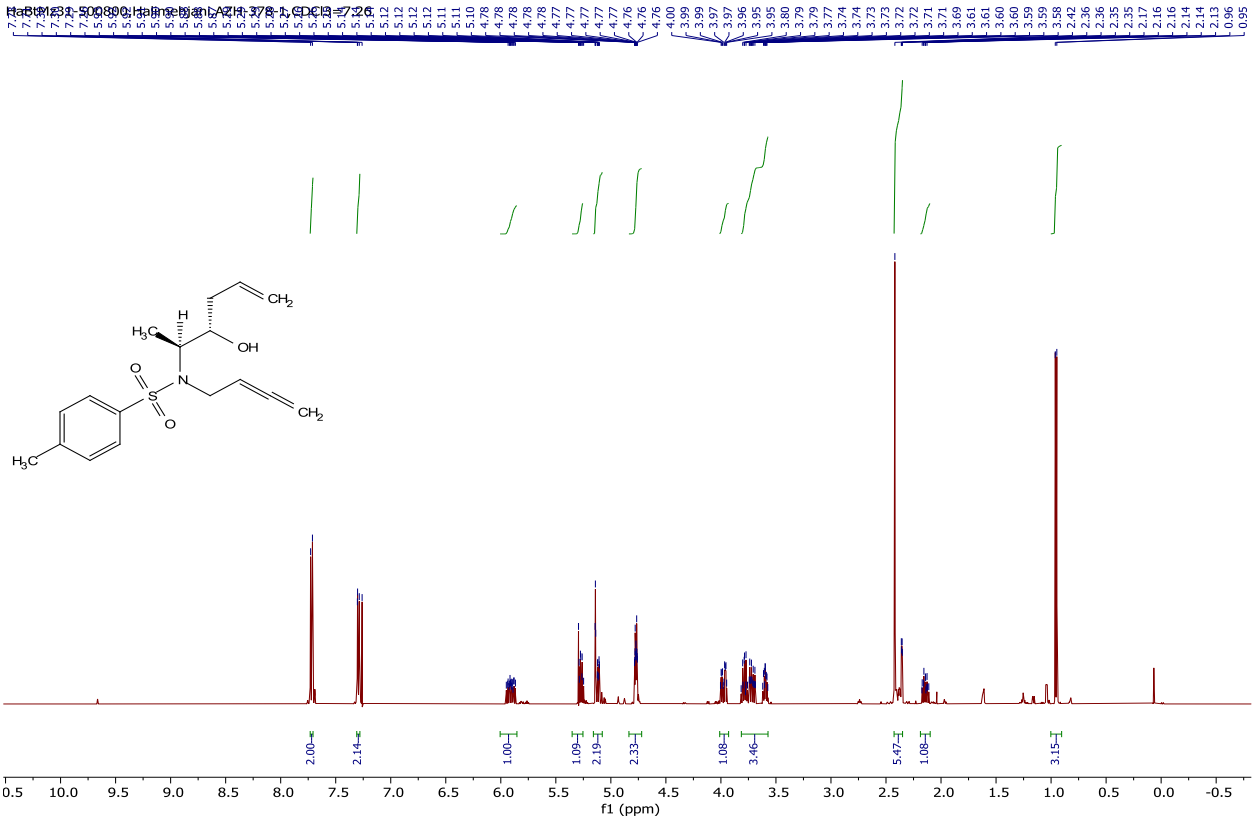
N-(buta-2,3-dien-1-yl)-N-((2S,3R)-3-hydroxyhex-5-en-2-yl)-4-methylbenzenesulfonamide (**3e**): The reaction was carried out according to the general procedure using allylmagnesium bromide (1M in THF). The crude mixture was obtained with *dr* ratio of 4:1. After purification, the major diastereomer **3e** was obtained in >20:1 dr ratio and minor disatereomer **3f** was obtained in >19:1 dr ratio. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.69 (d, J = 8.3 Hz, 2H), 7.33 – 7.26 (m, 2H), 5.82–5.78 (m, 1H), 5.27 – 5.09 (m, 3H), 4.75 (dddd, J = 6.3, 3.0, 2.0, 1.0 Hz, 2H), 4.00 (ddt, J = 15.6, 6.0, 3.0 Hz, 1H), 3.85 – 3.64 (m, 3H), 2.46 (dddt, J = 14.2, 6.7, 4.0, 1.4 Hz, 1H), 2.41 (s, 3H), 2.18–2.14 (m, 1H), 2.07 – 1.98 (m, 1H), 1.02 (d, J = 6.9 Hz, 3H) ppt; ^{13}C NMR (126 MHz, $CDCl_3$) δ 208.6, 143.3, 137.9, 134.6, 129.7, 127.1, 118.6, 89.0, 76.4, 73.3, 57.5, 43.8, 39.2, 21.5, 12.8 ppm; HRMS (ESI) calcd for $C_{17}H_{23}NO_3S$ $[M+H]^+$: 322.1477; found: 322.1473; $[\alpha]_D^{25}$ = +45.78 (c = 0.38, CH_2Cl_2).

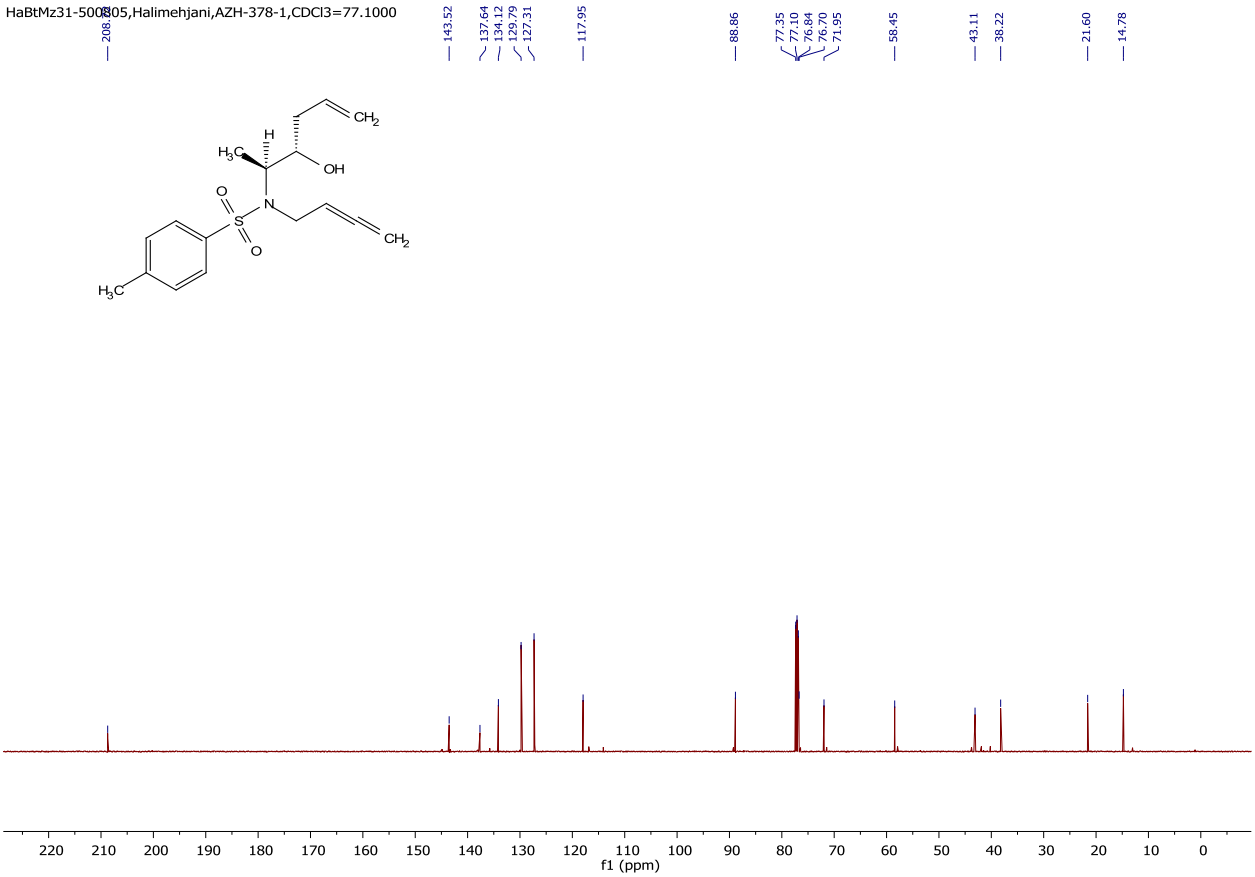

HaBtMz31-500706,Halimehjani,AZH-378-2,CDCl3=7.26
CH2
H
H3C
OH
O
N
S
O
CH2
H3C
2.01
2.00
1.00
3.01
2.02
1.03
3.07
1.04
3.08
1.03
1.09
3.06
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


HaBtMz31-500705,Halimehjani,AZH-378-2,CDCl3=77.1000
208.01
143.33
137.94
134.60
129.72
127.15
118.68
89.06
77.35
77.10
76.84
76.44
73.36
57.56
43.82
39.28
21.56
12.84
CH2
H
H3C
OH
O
N
S
O
CH2
H3C
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

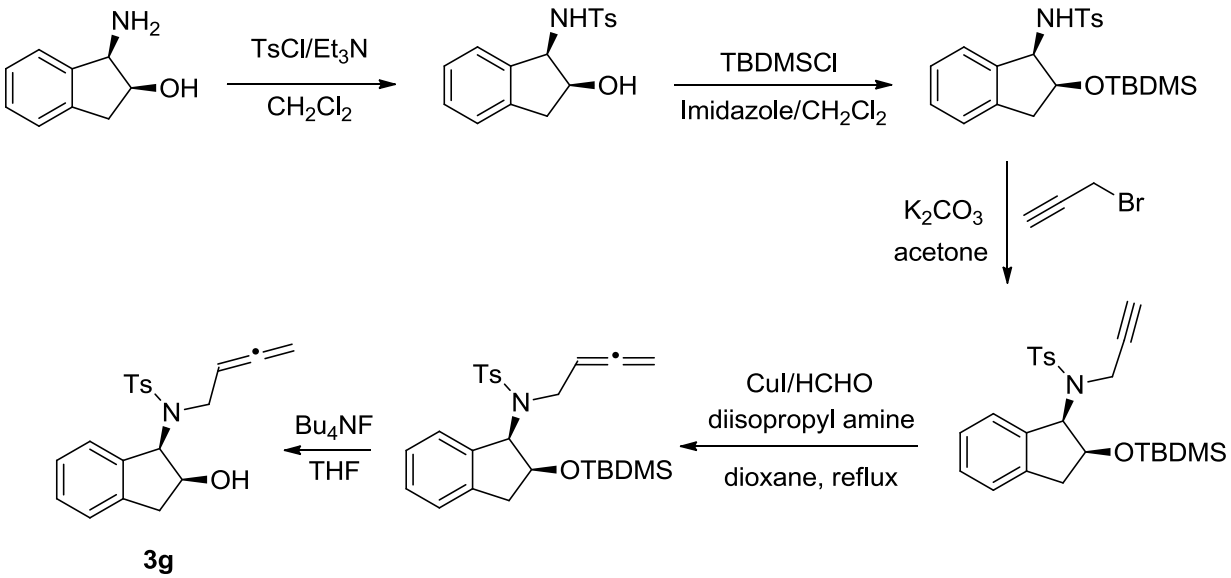


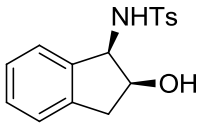
N-(buta-2,3-dien-1-yl)-N-((2S,3S)-3-hydroxyhex-5-en-2-yl)-4-methylbenzenesulfonamide (**3f**): This compound was obtained as minor diastereomer in the reaction of allylmagnesium bromide (1M in THF) with allenal. After purification, **3f** was obtained in >19:1 dr ratio. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.72 (d, J = 8.4 Hz, 2H), 7.31 – 7.28 (m, 2H), 6.01 – 5.85 (m, 1H), 5.35 – 5.25 (m, 1H), 5.16 – 5.08 (m, 2H), 4.79–4.76 (m, 2H), 3.99–3.96 (m, 1H), 3.81 – 3.57 (m, 3H), 2.43 – 2.35 (m, 5H), 2.19 – 2.10 (m, 1H), 0.95 (d, J = 6.9 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 208.7, 143.5, 137.6, 134.1, 129.7, 127.3, 117.9, 88.8, 76.7, 71.9, 58.4, 43.1, 38.2, 21.6, 14.7 ppm; HRMS (ESI) calcd for $C_{17}H_{23}NO_3S$ $[M+H]^+$: 322.1477; found: 322.1471; $[\alpha]_D^{25}$ = +57.08 (c = 0.24, CH_2Cl_2).



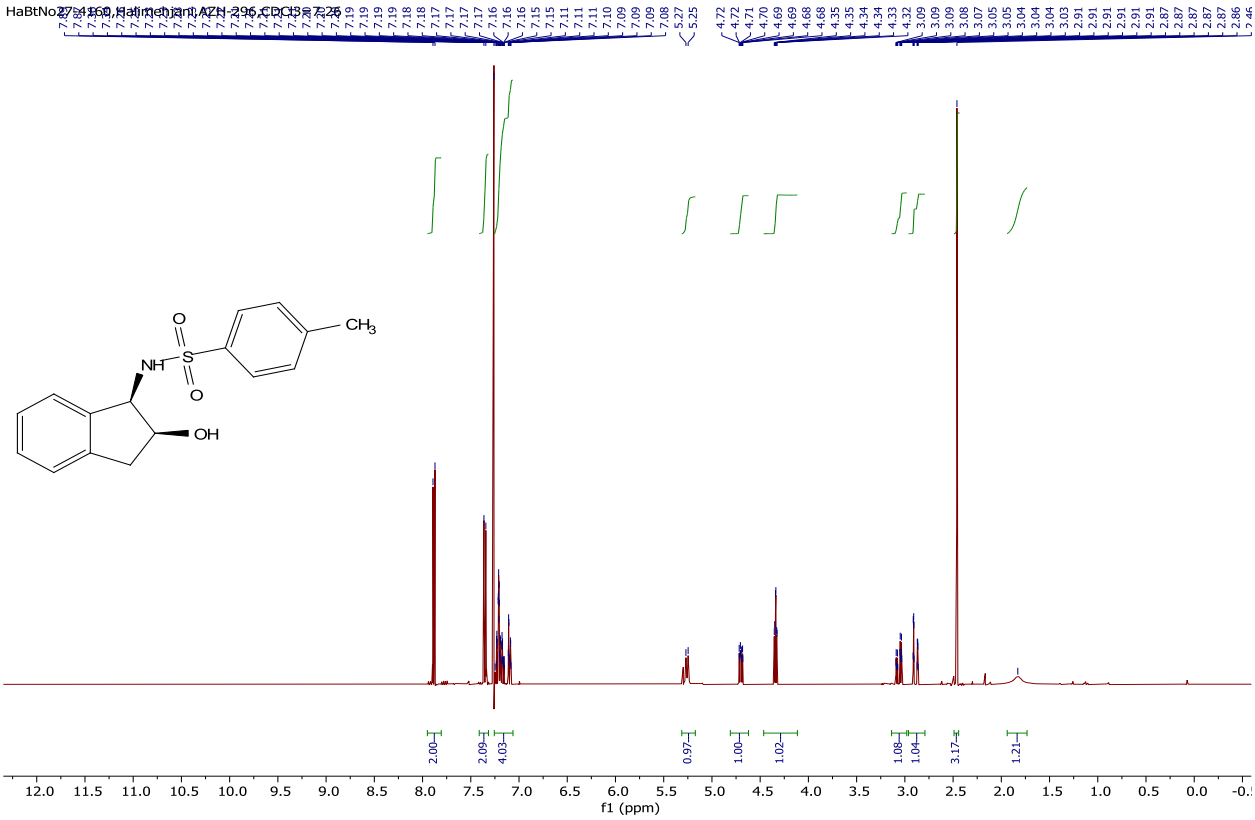


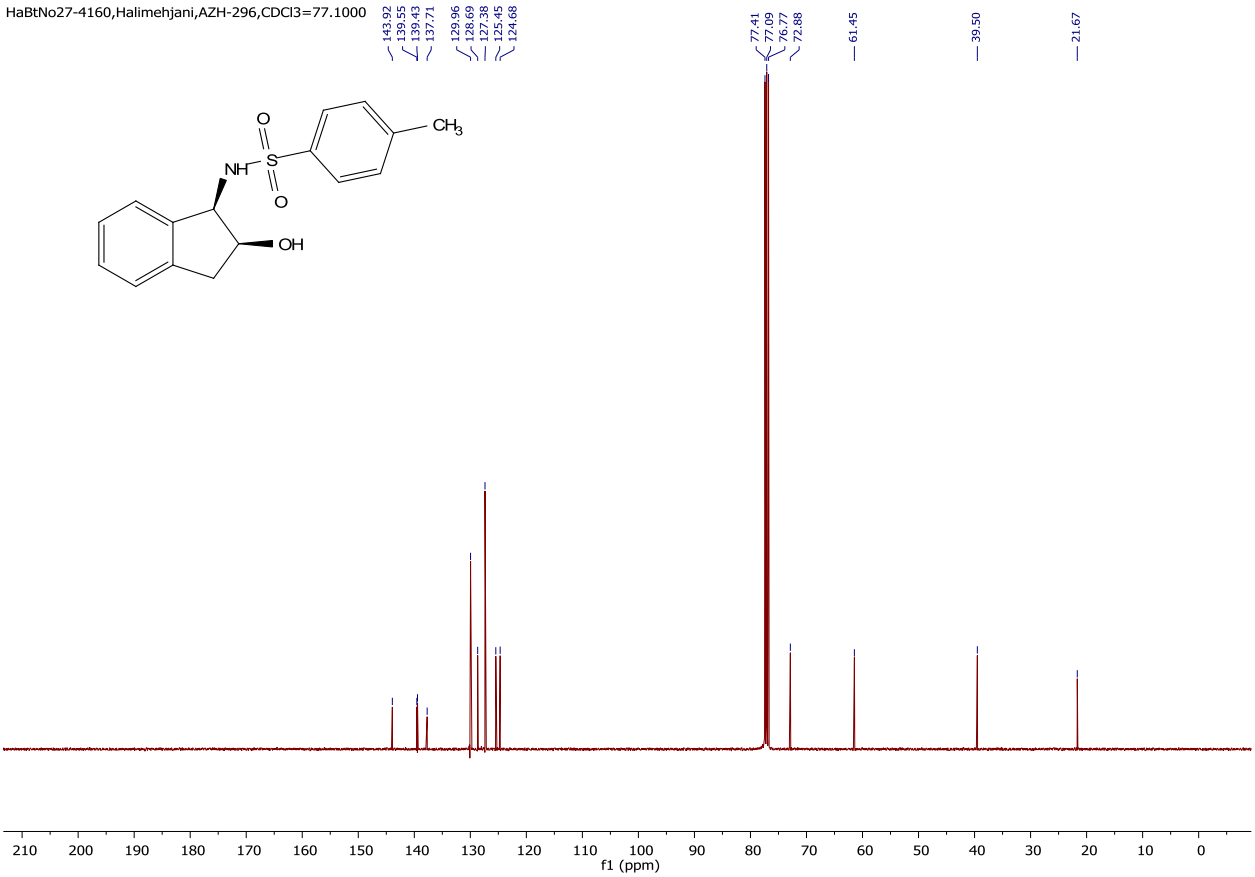
Synthesis of allenol 3g from (1*R*,2*S*)-1-amino-2,3-dihydro-1H-inden-2-ol

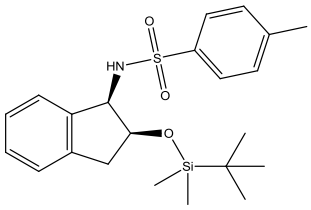




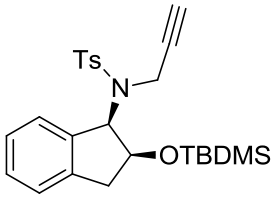
N-((1R,2S)-2-hydroxy-2,3-dihydro-1H-inden-1-yl)-4-methylbenzenesulfonamide: was prepared according to **general procedure 1** starting from (1*R*,2*S*)-1-amino-2,3-dihydro-1*H*-inden-2-ol: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.88 (d, *J* = 8.3 Hz, 2H), 7.35 (d, *J* = 7.9 Hz, 2H), 7.26 – 7.06 (m, 4H), 5.26 (d, *J* = 9.1 Hz, 1H), 4.70 (ddd, *J* = 9.2, 4.9, 1.0 Hz, 1H), 4.34 (td, *J* = 5.0, 1.7 Hz, 1H), 3.14 – 2.98 (m, 1H), 2.96 – 2.79 (m, 1H), 2.46 (s, 3H), 1.83 (s, 1H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.9, 139.5, 139.4, 137.7, 129.9, 128.6 (2C), 127.3, 125.4, 124.6, 72.8, 61.4, 39.5, 21.6 ppm; HRMS (ESI) calcd for $C_{16}H_{17}NO_3S$ $[M+NH_4]^+$: 321.1273; found: 321.1270; $[\alpha]_D^{25}$ = -8.62 (c = 0.325, CH_2Cl_2).



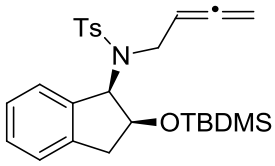




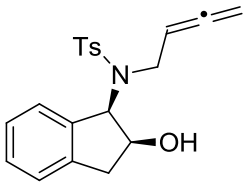
N-((1R,2S)-2-((tert-butyldimethylsilyl)oxy)-2,3-dihydro-1H-inden-1-yl)-4-methylbenzenesulfonamide: *tert*-Butyldimethylchlorosilane (1.2 equiv) was added portion wise to a solution of tosylamide (1 equiv) and imidazole (1.2 equiv) in dichloromethane (5 mL/mmol), and the mixture was stirred at rt for 4 h. The reaction was quenched with water and the organic phase was separated. The aqueous phase was extracted two more times with CH_2Cl_2 (2 × 3 mL/mmol). The combined organic phases was dried with $MgSO_4$ and concentrated in vacuum to give the crude product. The crude product was applied in the next step without further purification.



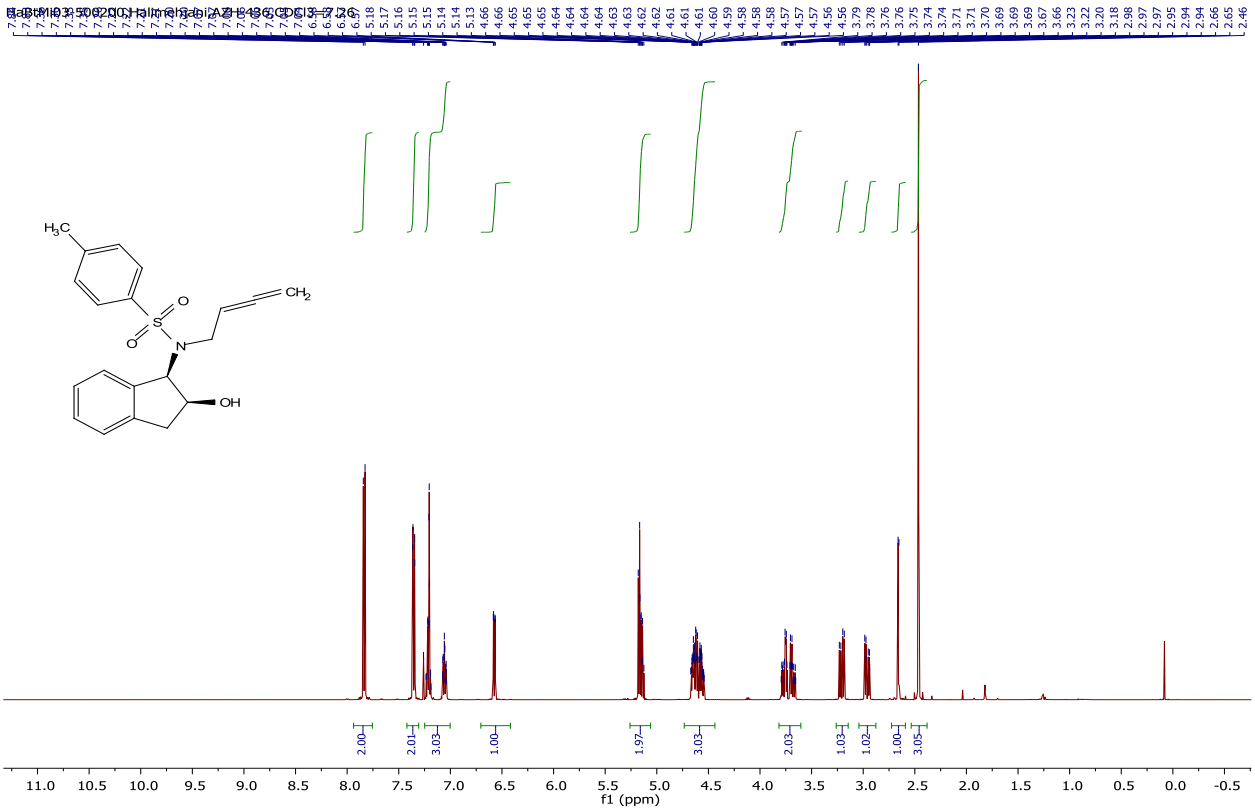
N-((1R,2S)-2-((tert-butyldimethylsilyl)oxy)-2,3-dihydro-1H-inden-1-yl)-4-methyl-N-(prop-2-yn-1-yl)benzenesulfonamide: was prepared according to general procedure 2 and was appliedin the next step without further purification.

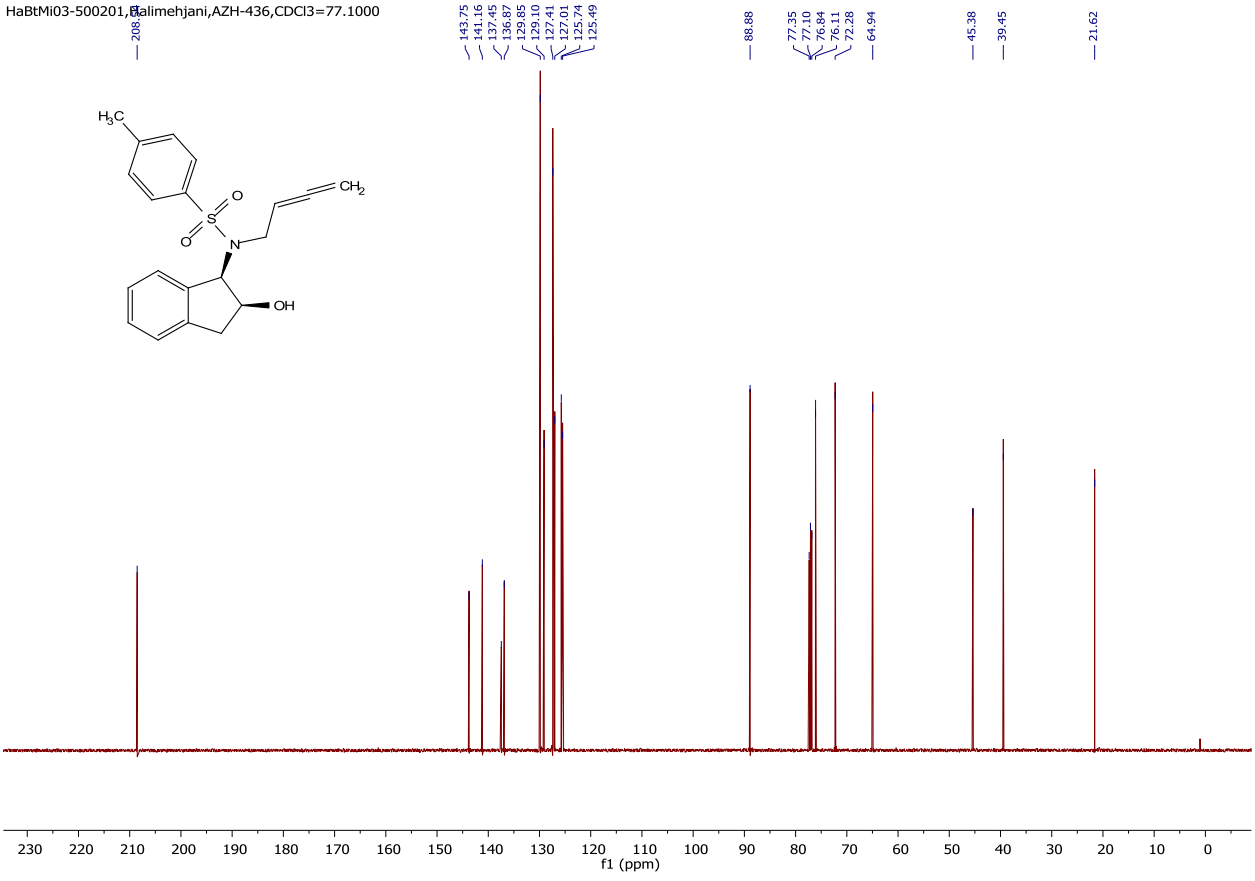


N-(buta-2,3-dien-1-yl)-N-((1R,2S)-2-((tert-butyldimethylsilyl)oxy)-2,3-dihydro-1H-inden-1-yl)-4-methylbenzenesulfonamide: was prepared according to general procedure 3 starting from the corresponding silylated alkynol and were applied directly in the desilylation reaction as described below:



N-(buta-2,3-dien-1-yl)-N-((1R,2S)-2-hydroxy-2,3-dihydro-1H-inden-1-yl)-4-methylbenzenesulfonamide (3g)*:* A stirred solution of silylated allenol (1 equiv) in THF (15 mL/mmol) was cooled to 0 °C and treated with *n*-Bu_4NF (2.5 equiv, 1 M in THF). The reaction was stirred for 1 hour at 0 °C then partitioned between H_2O and Et_2O. The layers were separated and the aqueous layer was extracted with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. Purification was carried out by silica gel chromatography using EtOAc:*n*-pentane (3:7).[13] ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.84 (d, J = 8.3 Hz, 2H), 7.42 – 7.31 (m, 2H), 7.25 – 7.00 (m, 3H), 6.57 (dd, J = 7.7, 1.0 Hz, 1H), 5.26 – 5.06 (m, 2H), 4.73 – 4.44 (m, 3H), 3.82 – 3.60 (m, 2H), 3.21 (dd, J = 16.5, 7.4 Hz, 1H), 3.04 – 2.88 (m, 1H), 2.66 (d, J = 3.9 Hz, 1H), 2.46 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 208.5, 143.7, 141.1, 137.4, 136.8, 129.8, 129.1, 127.4, 127.0, 125.7, 125.4, 88.8, 76.1, 72.2, 64.9, 45.3, 39.4, 21.6 ppm; HRMS (ESI) calcd for $C_{20}H_{21}NO_3S$ $[M+Na]^+$: 378.1140; found: 378.1137; $[\alpha]_D^{25}$ = -96.64 (c = 0.835, CH_2Cl_2).

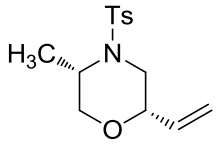

H3C
CH2
O
S
O
N
OH
2.00
2.01
3.03
1.00
1.97
3.03
2.03
1.03
1.02
1.00
3.05
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


HaBtMi03-500201,Halimehjani,AZH-436,CDCl3=77.1000
208.83
143.75
141.16
137.45
136.87
129.85
129.10
127.41
127.01
125.74
125.49
88.88
77.35
77.10
76.84
76.11
72.28
64.94
45.38
39.45
21.62
H3C
CH2
O
S
O
N
OH
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

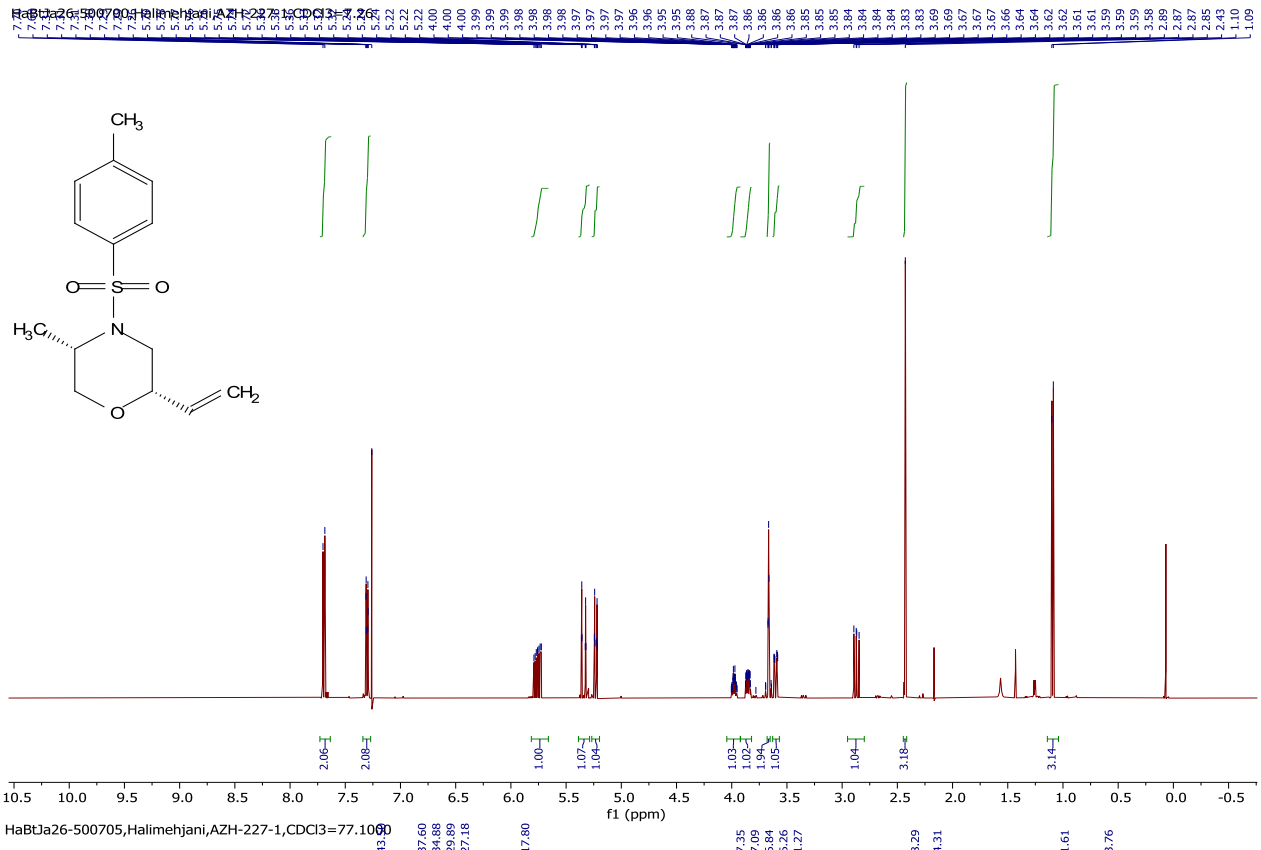
Synthesis of functionalized morpholines and their characterization data

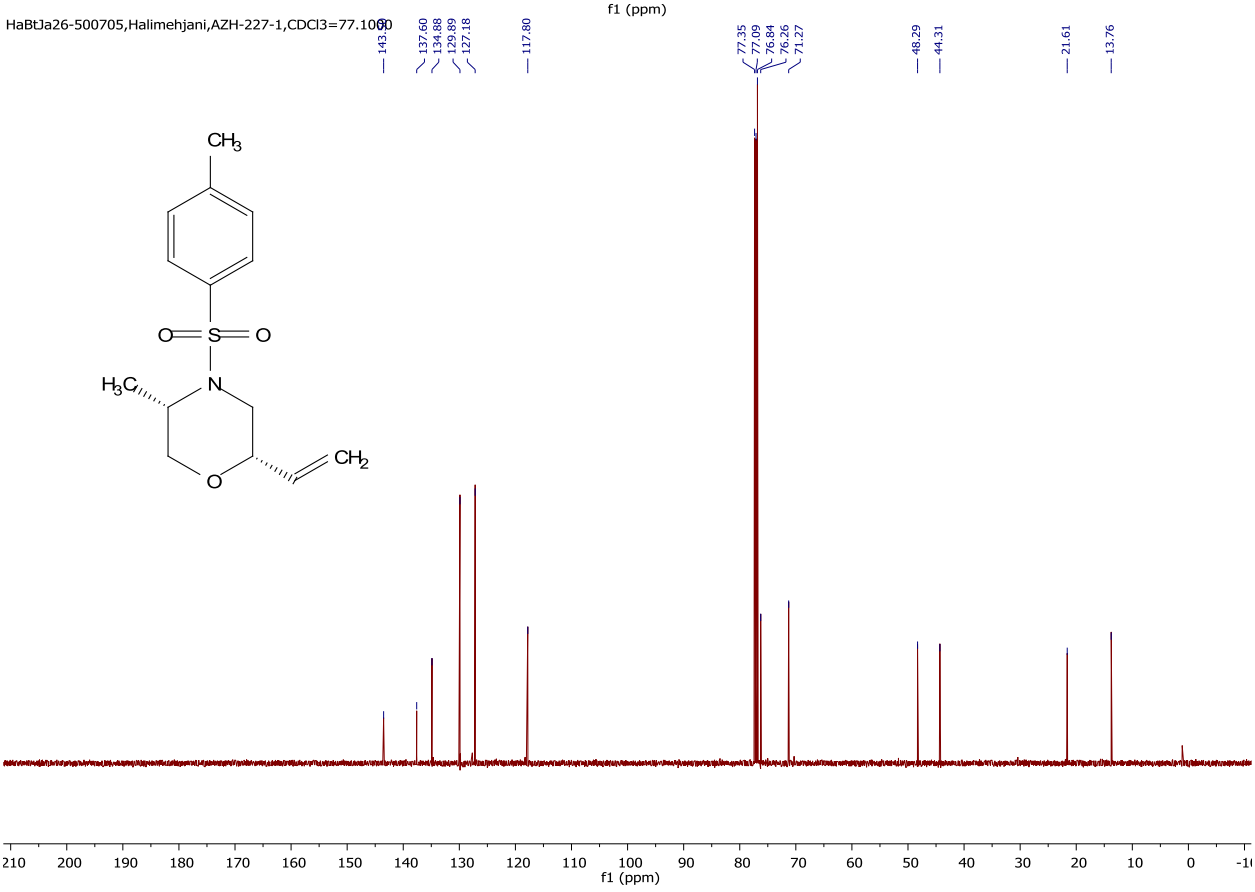
General procedure 4: ***Synthesis of morpholines 2a-n and 4a-h***

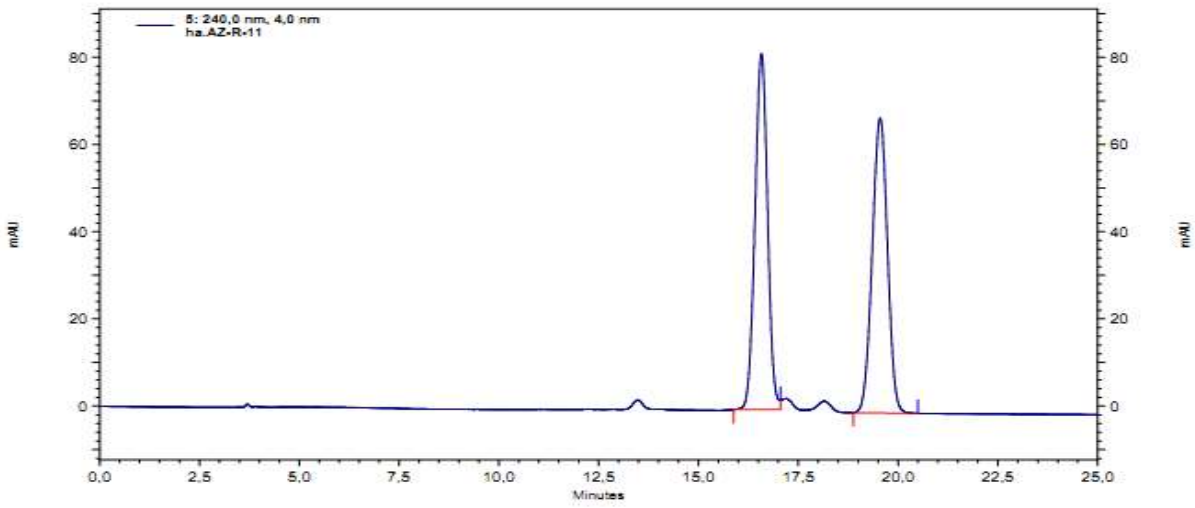
A screw-cap Schlenk tube was flame-dried under vacuum, backfilled with argon, and cooled to r.t. using a standard Schlenk line apparatus. The Schlenk tube was charged with $[Rh(COD)Cl]_2$ (1.5 mg, 0.003 mmol, 2 mol%), DPEphos (3.3 mg, 0.006 mmol, 4 mol %) and chloroacetic acid (2.8 mg, 20 mol%). The tube was placed on the Schlenk line to evacuate and backfilled with argon three times. Then, dichloroethane (0.75 mL, 0.2 M) and an allenol (0.15 mmol) were added under a flow of argon and the tube was sealed by a screw cap and the resulting mixture was stirred at 55 ^{o}C for 16 h. The solvent was removed under reduced pressure and the residue was purified by chromatography on silica gel using *n*-pentane:EtOAc (9:1).



(2S,5S)-5-methyl-4-tosyl-2-vinylmorpholine (**2a**): ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.69 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 5.76 (ddd, *J* = 17.4, 10.7, 5.5 Hz, 1H), 5.34 (dt, *J* = 17.4, 1.4 Hz, 1H), 5.23 (dt, *J* = 10.7, 1.3 Hz, 1H), 4.04 – 3.92 (m, 1H), 3.87–3.83 (m, 1H), 3.68 – 3.65 (m, 2H), 3.63–3.58 (m, 1H), 2.87 (dd, *J* = 13.0, 10.9 Hz, 1H), 2.43 (s, 3H), 1.09 (d, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.5, 137.6, 134.8, 129.8, 127.1, 117.8, 76.2, 71.2, 48.2, 44.3, 21.6, 13.7 ppm; HRMS (ESI) calcd for $C_{14}H_{19}NO_3S$ $[M+H]^+$: 282.1164; found: 282.1161; **HPLC** (L-C4 column, Heptane/Isopropanol = 90:10, 0.5 mL/min) t_R = 16.51 min (minor), t_R = 19.48 min (major), >99% ee; $[\alpha]_D^{25}$ = +26.28 (c = 0.70, CH_2Cl_2).


HaBtJa26-500701,Halimehjani,AZH-227-1,CDCl3=7.26
CH3
O
S
O
H3C
N
O
CH2
2.06
2.08
1.00
1.07
1.04
1.03
1.02
1.94
1.05
1.04
3.18
3.14
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

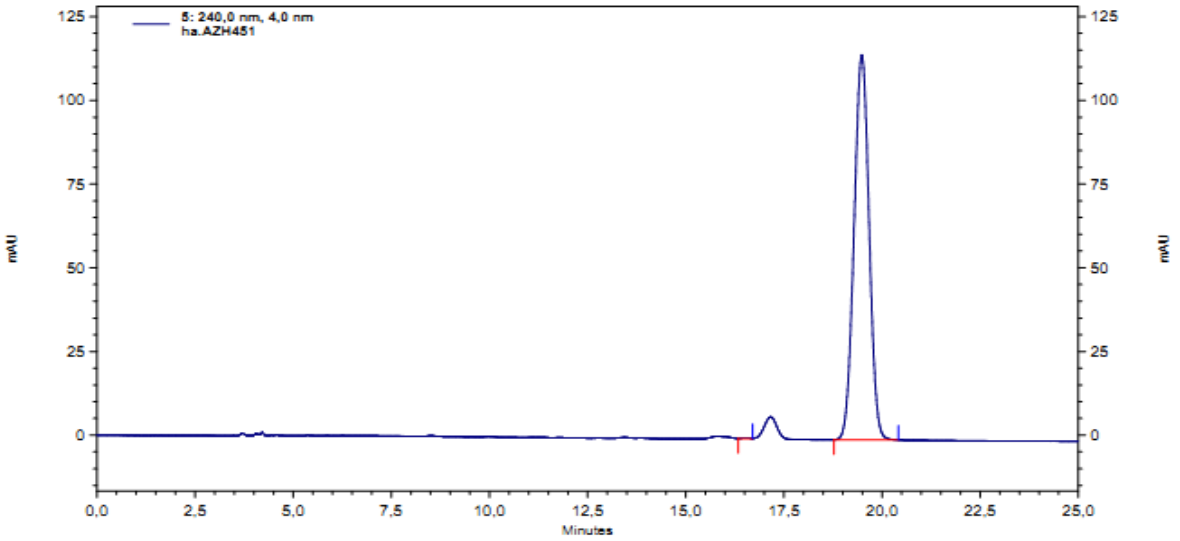

HaBtJa26-500705,Halimehjani,AZH-227-1,CDCl3=77.1060
143.60
137.60
134.88
129.89
127.18
117.80
77.35
77.09
76.84
76.26
71.27
48.29
44.31
21.61
13.76
CH3
O
S
O
H3C
N
O
CH2
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



5: 240,0 nm, 4,0 nm

Results

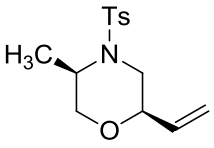
Peak Number	Retention Time	Area Percent	Area
1	16,577	49,943	240675465
2	19,548	50,057	241228141
Totals		100,000	481903606



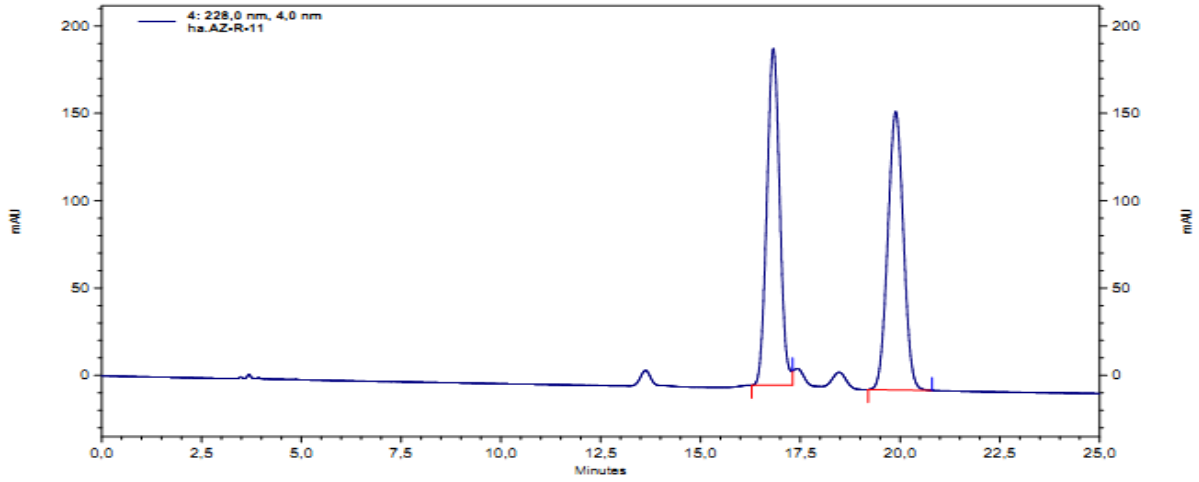
5: 240,0 nm, 4,0 nm

Results

Peak Number	Retention Time	Area Percent	Area
1	16,507	0,059	244800
2	19,483	99,941	411366221
Totals		100,000	411611021

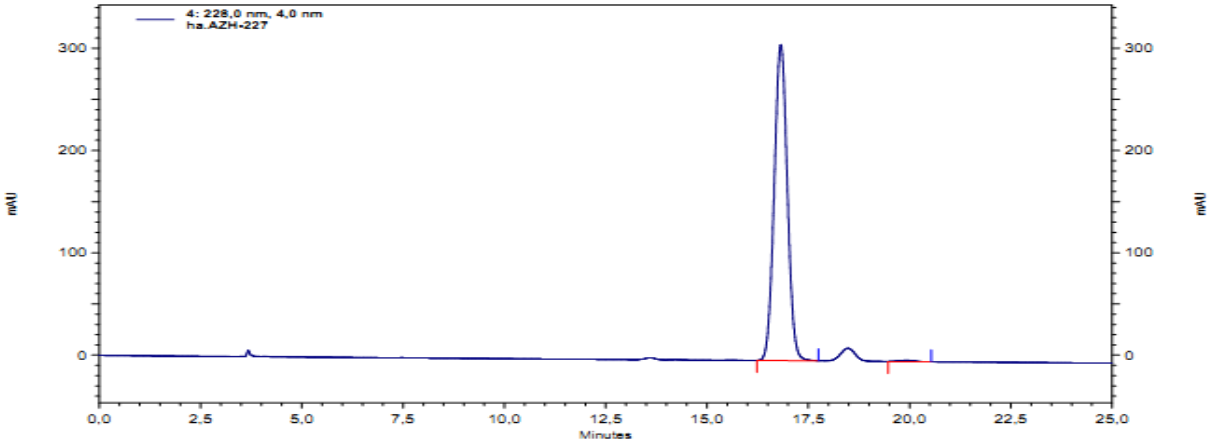


For *(2R,5R)-5-methyl-4-tosyl-2-vinylmorpholine* (**2b**): **HPLC** (L-C4 column, Heptane/Isopropanol = 90:10, 0.5 mL/min) t_R = 16.82 min (major), t_R = 19.92 min (minor), >99% ee; $[\alpha]_D^{25}$ = -26.28 (c = 0.15, CH_2Cl_2).



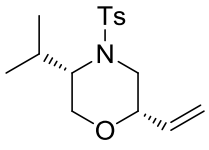
4: 228,0 nm, 4,0 nm
Results

Peak Number	Retention Time	Area Percent	Area
1	16,825	49,810	579599920
2	19,890	50,190	584023461
Totals		100,000	1163623381

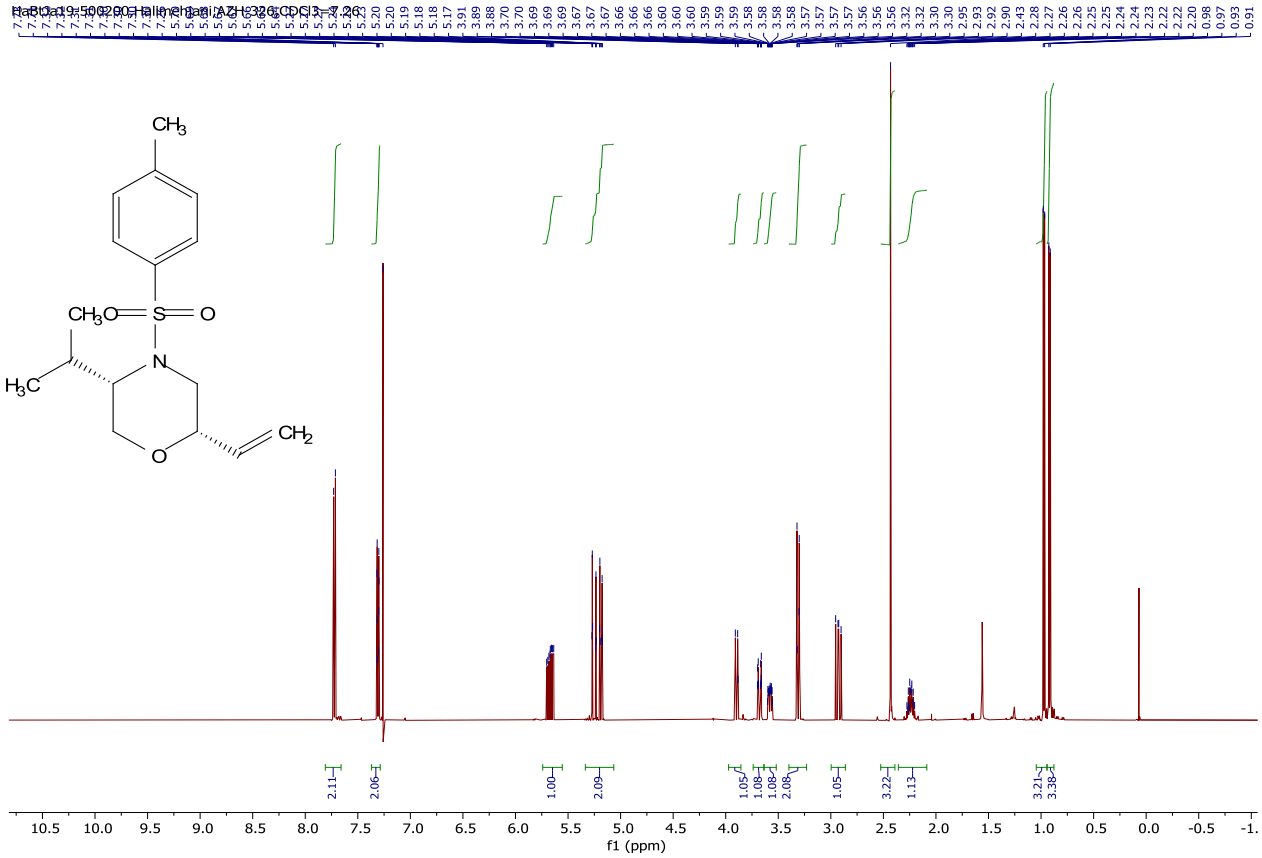


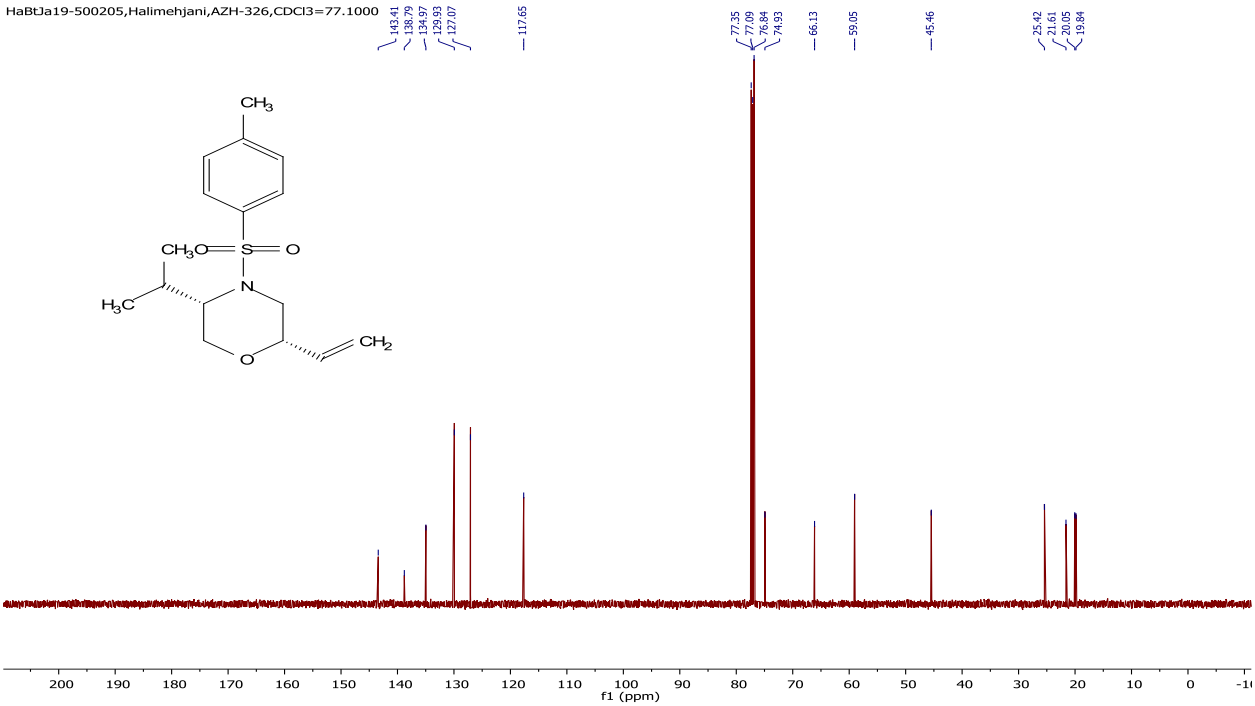
4: 228,0 nm, 4,0 nm
Results

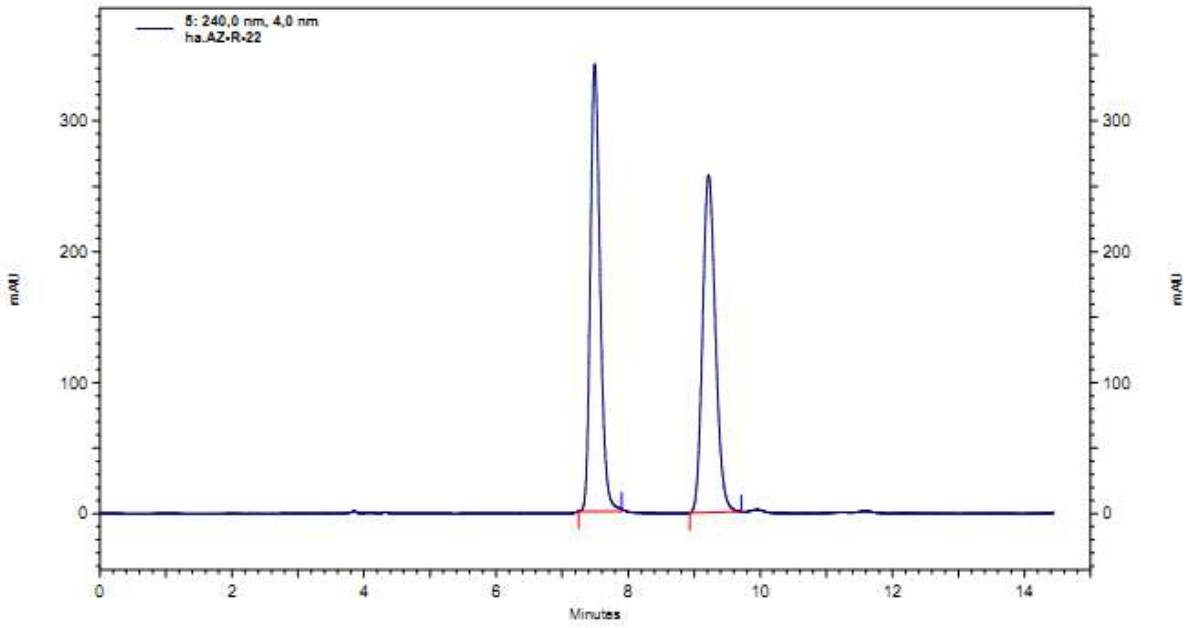
Peak Number	Retention Time	Area Percent	Area
1	16,820	99,516	933989091
2	19,922	0,484	4539395
Totals		100,000	938528486



(2S,5S)-5-isopropyl-4-tosyl-2-vinylmorpholine (**2c**): ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.72 (d, *J* = 8.3 Hz, 2H), 7.37 (d, *J* = 8.3 Hz, 2H), 5.67 (ddd, *J* = 17.4, 10.7, 5.5 Hz, 1H), 5.34 – 5.06 (m, 2H), 3.97 – 3.86 (m, 1H), 3.74 – 3.64 (m, 1H), 3.59–3.57 (m, 1H), 3.40 – 3.23 (m, 2H), 2.93 (dd, *J* = 14.6, 11.2 Hz, 1H), 2.43 (s, 3H), 2.26–2.22 (m, 1H), 0.97 (d, *J* = 6.6 Hz, 3H), 0.92 (d, *J* = 6.8 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.4, 138.7, 134.9, 129.9, 127.0, 117.6, 74.9, 66.1, 59.0, 45.4, 25.4, 21.6, 20.0, 19.8 ppm; HRMS (ESI) calcd for $C_{16}H_{23}NO_3S$ $[M+H]^+$: 310.1477; found: 310.1470; **HPLC** (LC-3 column, heptane/ethanol = 95:5, 0.5 mL/min) t_R = 7.49 min (major), t_R = 9.23min (minor), >99% ee; $[\alpha]_D^{25}$ = +5.07 (c = 0.375, CH_2Cl_2).

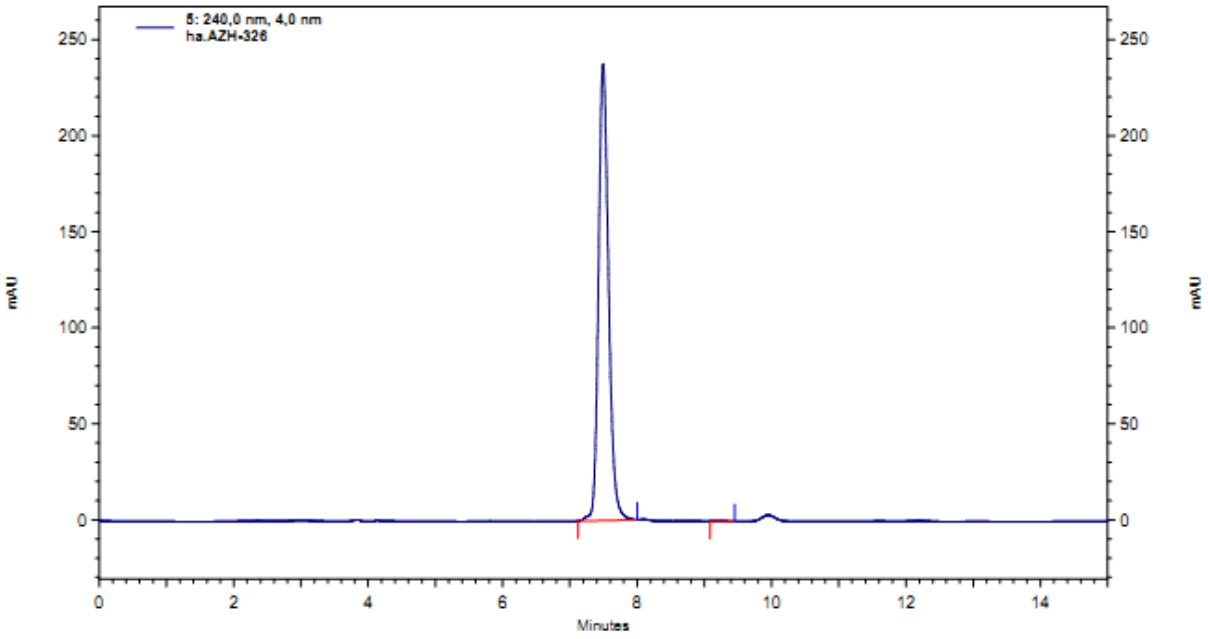






5: 240,0 nm, 4,0 nm
Results

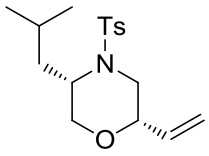
Peak Number	Retention Time	Area Percent	Area
1	7,493	49,936	467591943
2	9,217	50,064	468789513
Totals		100,000	936381456



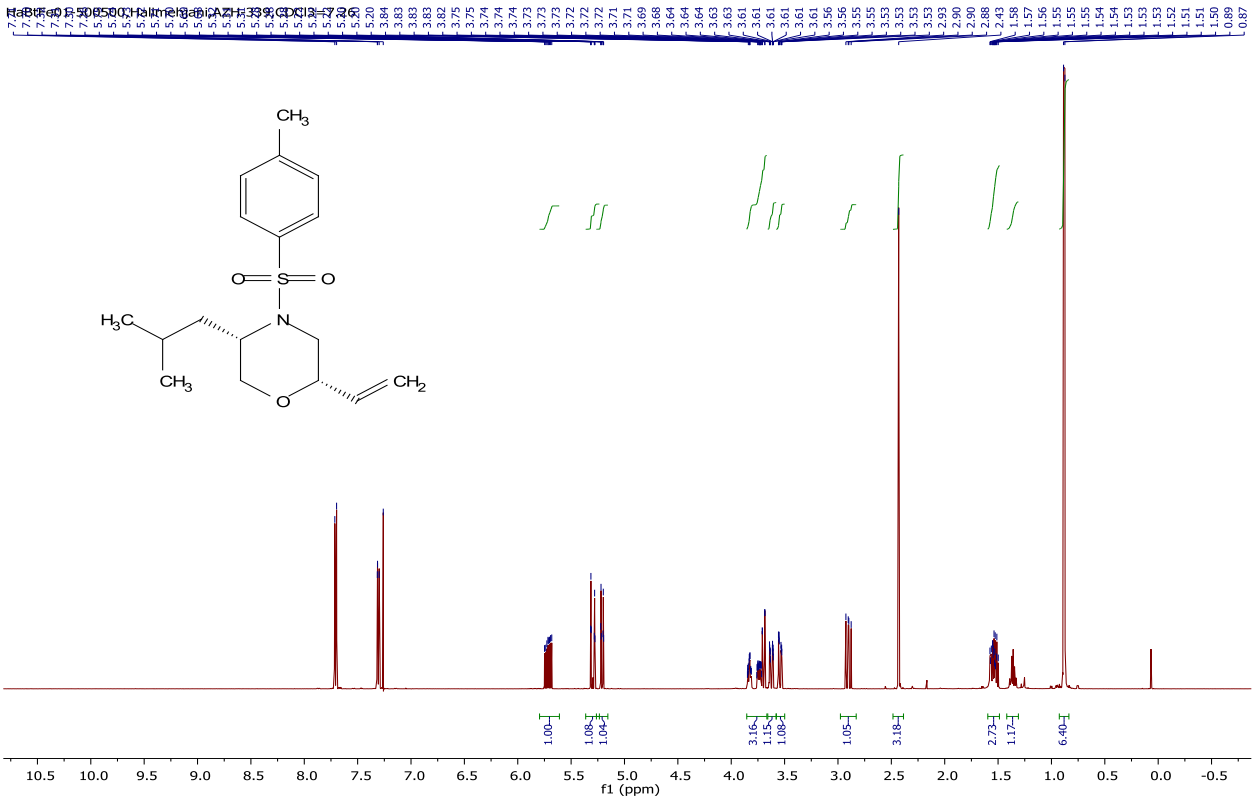
5: 240,0 nm, 4,0 nm

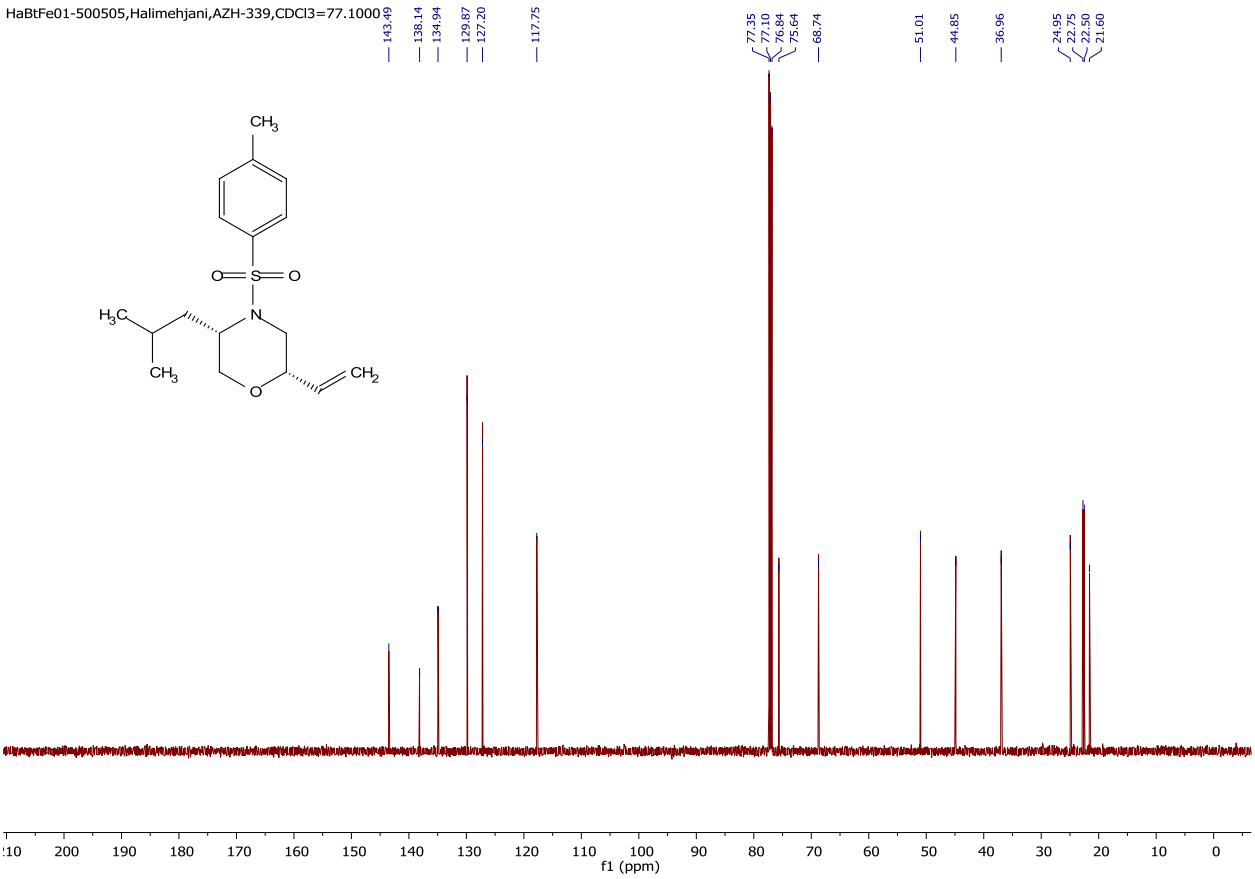
Results

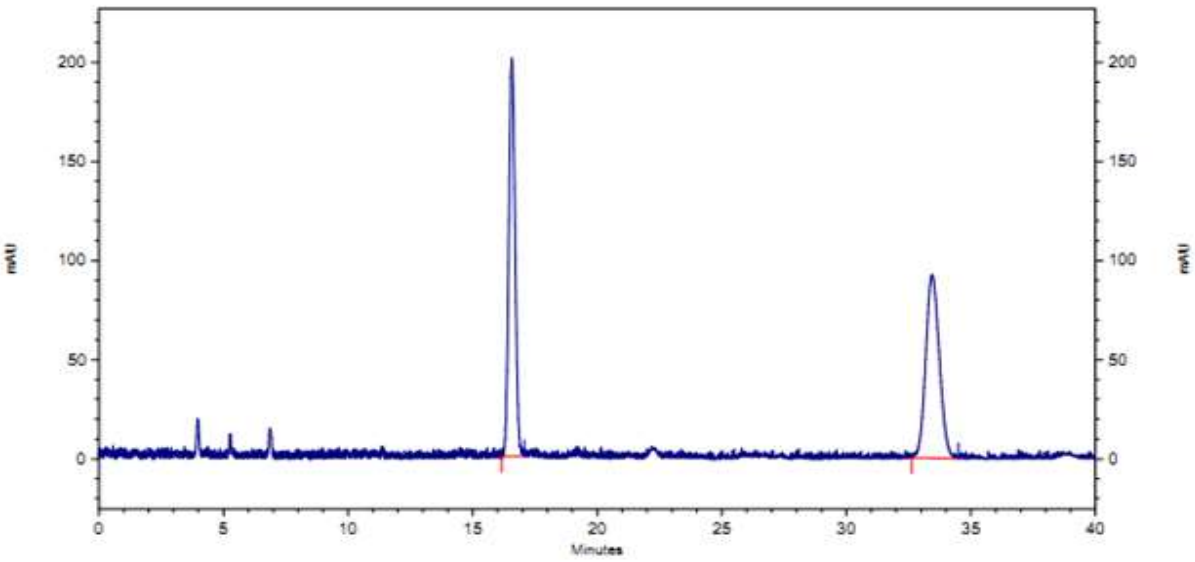
Peak Number	Retention Time	Area Percent	Area
1	7,495	99,924	332234073
2	9,227	0,076	254224
Totals		100,000	332488297



(2S,5S)-5-isobutyl-4-tosyl-2-vinylmorpholine(2S,5S)-5-isobutyl-4-tosyl-2-vinylmorpholine (**2d**): ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.71 (d, *J* = 8.3 Hz, 2H), 7.36 – 7.29 (d, *J* = 8.3 Hz, 2H), 5.72 (ddd, *J* = 17.4, 10.8, 5.6 Hz, 1H), 5.30 (dt, *J* = 17.4, 1.4 Hz, 1H), 5.21 (dt, *J* = 10.8, 1.3 Hz, 1H), 3.85 – 3.67 (m, 3H), 3.66 – 3.58 (m, 1H), 3.54 (ddd, *J* = 11.6, 3.1, 0.8 Hz, 1H), 2.90 (dd, *J* = 13.7, 11.0 Hz, 1H), 2.43 (s, 3H), 1.60 – 1.49 (m, 2H), 1.42 – 1.31 (m, 1H), 0.88 (d, *J* = 6.3 Hz, 6H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) *δ* 143.4, 138.1, 134.9, 129.8, 127.2, 117.7, 75.6, 68.7, 51.0, 44.8, 36.9, 24.9, 22.7, 22.5, 21.6 ppm; HRMS (ESI) calcd for $C_{17}H_{25}NO_3S$ $[M+H]^+$: 324.1633; found: 324.1630; **HPLC** (ChiralPAK AD-3, heptane/EtOH= 85:15, 0.5 mL/min) t_R = 16.57 min (minor), t_R = 33.44 min (major), >99% ee; $[\alpha]_D^{25}$ = +25.38 (c = 0.26, CH_2Cl_2).

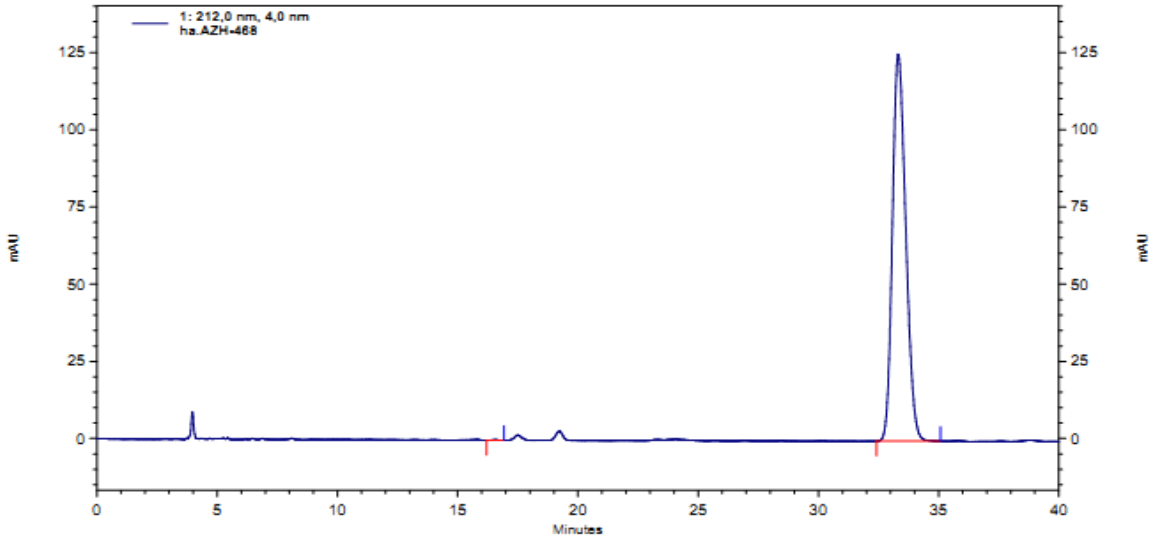

CH3
O
S
O
N
H3C
CH3
O
CH2
1.00
1.08
1.04
3.16
1.15
1.08
1.05
3.18
2.73
1.17
6.40
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


HaBtFe01-500505,Halimehjani,AZH-339,CDCl3=77.1000
143.49
138.14
134.94
129.87
127.20
117.75
77.35
77.10
76.84
75.64
68.74
51.01
44.85
36.96
24.95
22.75
22.50
21.60
CH3
O
S
O
N
H3C
CH3
O
CH2
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



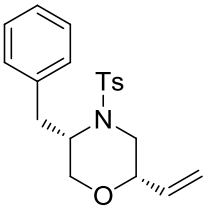
Spectrum Max Plot
Results

Peak Number	Retention Time	Area Percent	Area
1	16,577	49,909	470284661
2	33,440	50,091	471993224
Totals		100,000	942277885

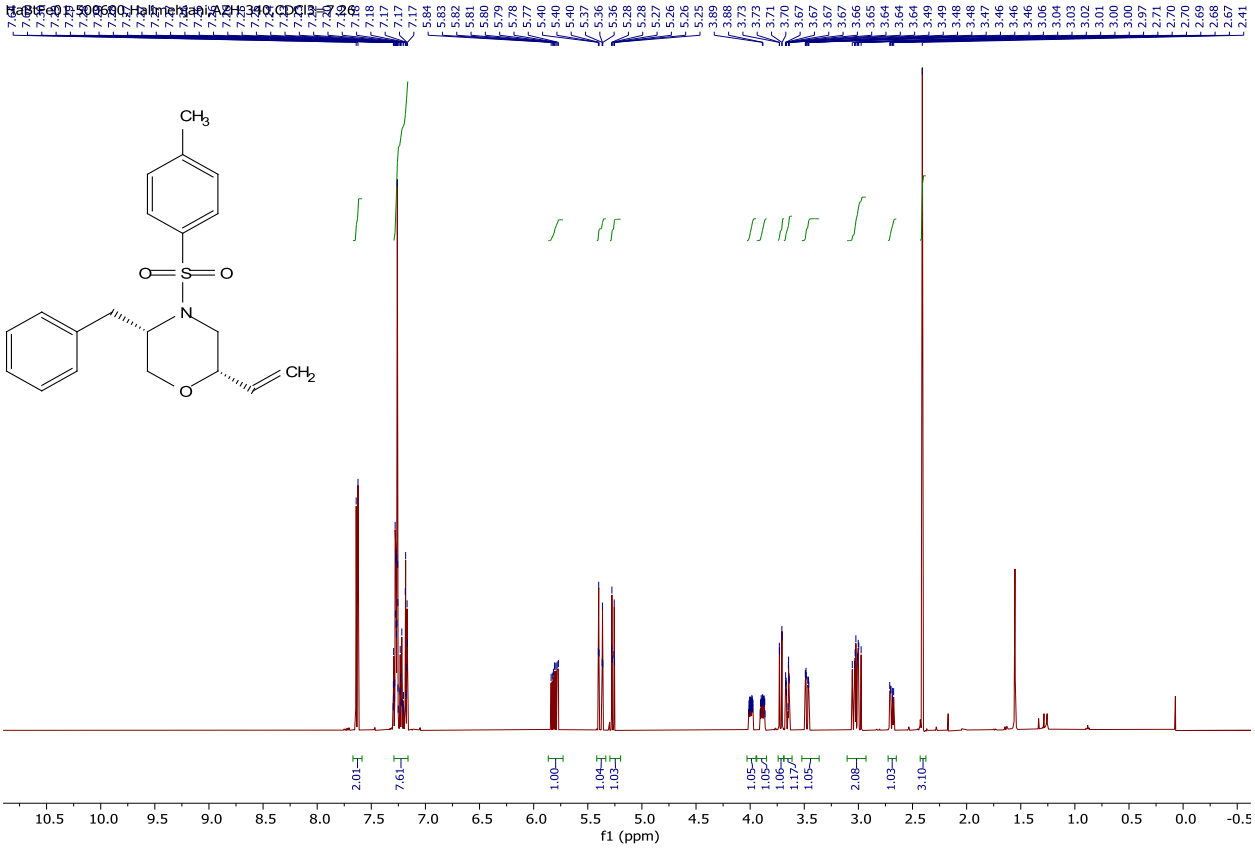


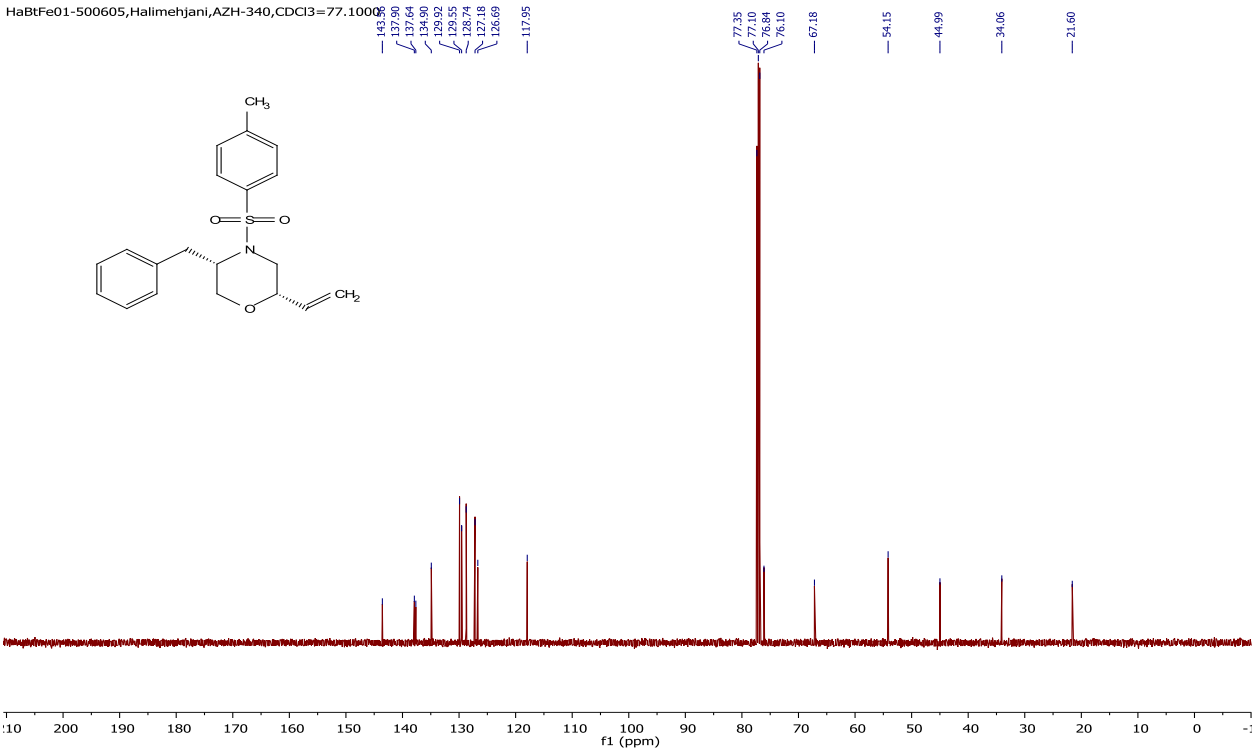
1: 212,0 nm, 4,0 nm
Results

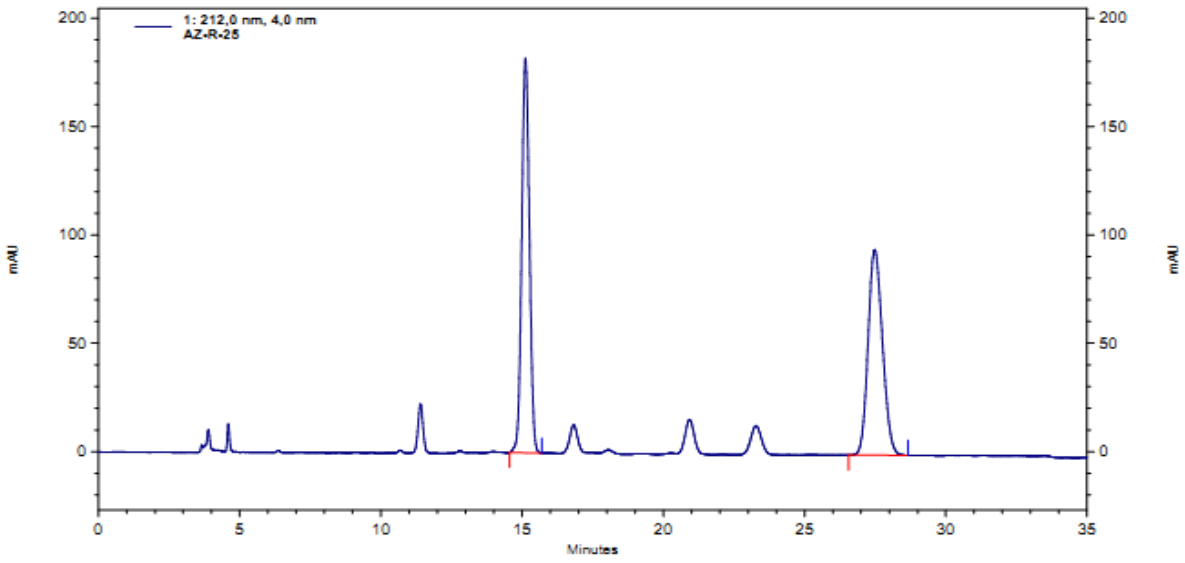
Peak Number	Retention Time	Area Percent	Area
1	16,572	0,074	480906
2	33,318	99,926	651041653
Totals		100,000	651522559



(2S,5S)-5-benzyl-4-tosyl-2-vinylmorpholine (**2e**): ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.63 (d, J = 8.4 Hz, 2H), 7.29 – 7.16 (m, 7H), 5.81 (ddd, J = 17.4, 10.7, 5.6 Hz, 1H), 5.38 (dt, J = 17.4, 1.4 Hz, 1H), 5.27 (dt, J = 10.7, 1.3 Hz, 1H), 3.99–3.96 (m, 1H), 3.89–3.87 (m, 1H), 3.72 (dd, J = 11.7, 1.0 Hz, 1H), 3.69 – 3.61 (m, 1H), 3.47 (ddd, J = 11.7, 3.1, 1.2 Hz, 1H), 3.02 (ddd, J = 17.2, 13.2, 10.7 Hz, 2H), 2.73 – 2.65 (m, 1H), 2.41 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.5, 137.9, 137.6, 134.9, 129.9, 129.5, 128.7, 127.1, 126.6, 117.9, 76.1, 67.1, 54.1, 44.9, 34.0, 21.6 ppm; HRMS (ESI) calcd for $C_{20}H_{23}NO_3S$ $[M+H]^+$: 358.1477; found: 358.1473; **HPLC** (ChiralPAK AD-3, heptane/ethanol = 85:15, 0.5 mL/min) t_R = 14.70 min (minor), t_R = 27.39 min (major), >99% ee; $[\alpha]_D^{25}$ = -19.33 (c = 0.15, CH_2Cl_2).



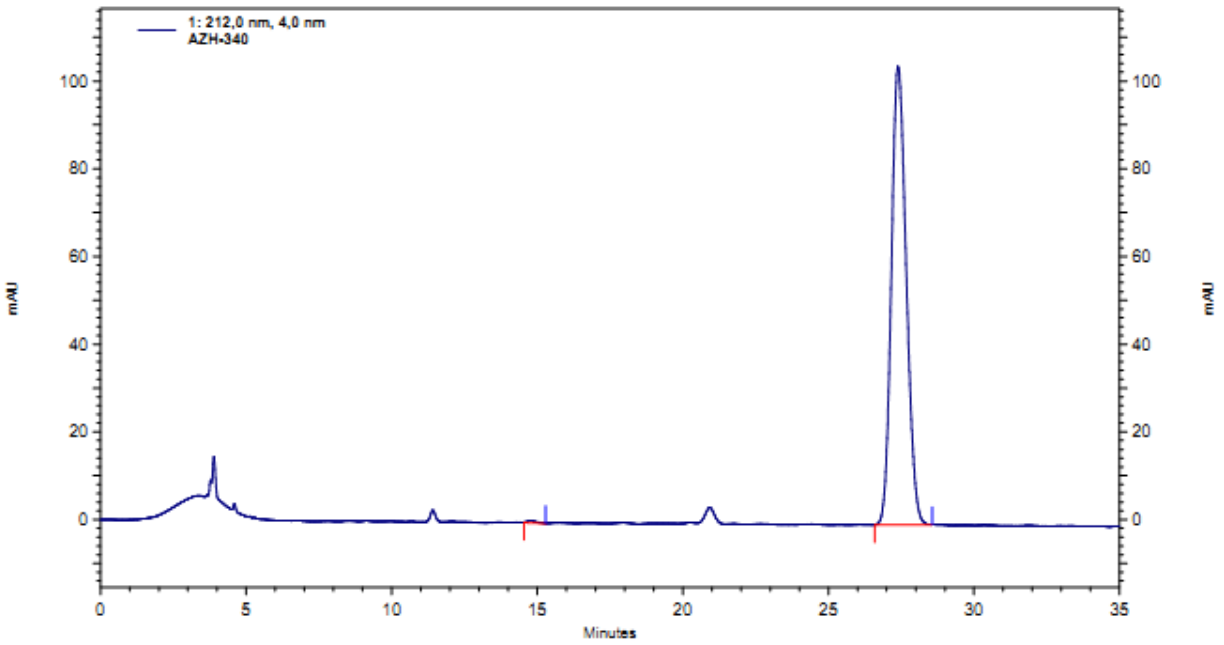




1: 212,0 nm, 4,0 nm

Results

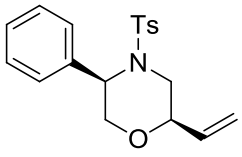
Peak Number	Retention Time	Area Percent	Area
1	15,117	50,774	465074531
2	27,482	49,226	450888215
Totals		100,000	915962746



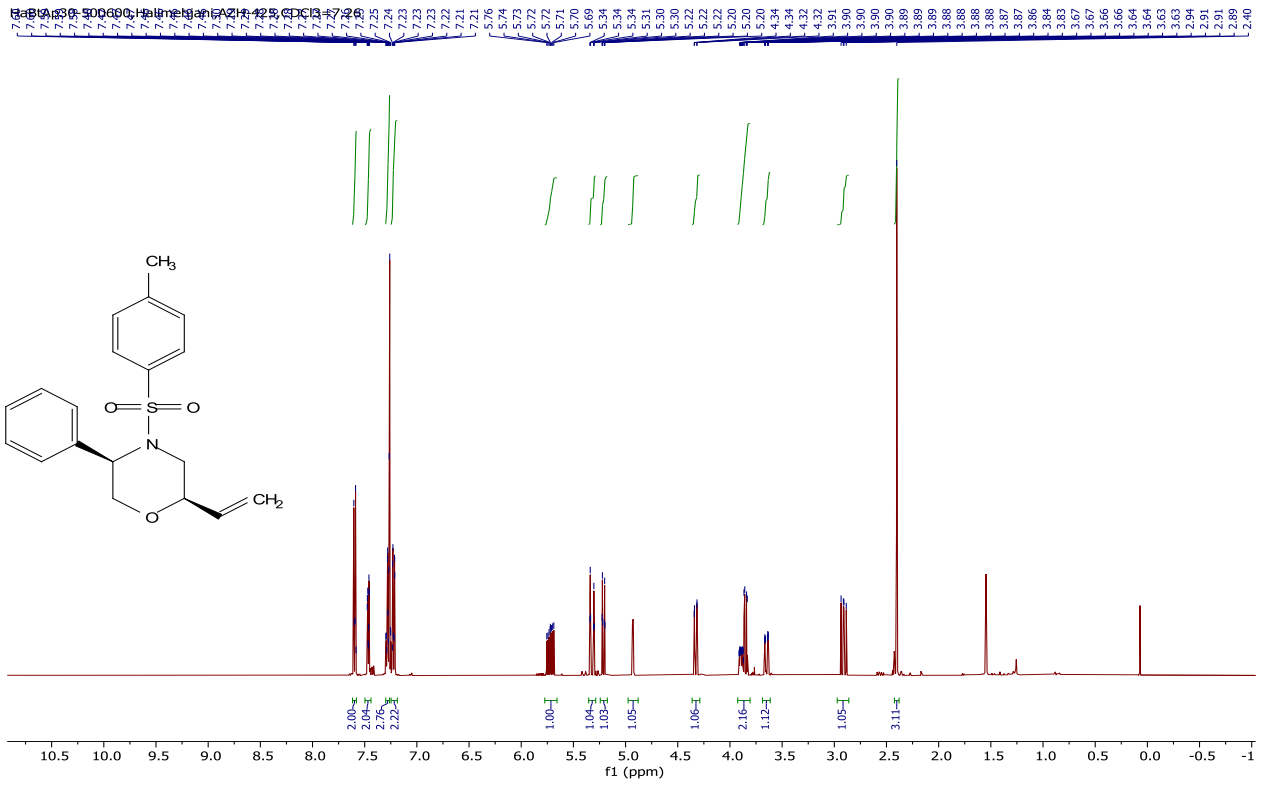
1: 212,0 nm, 4,0 nm

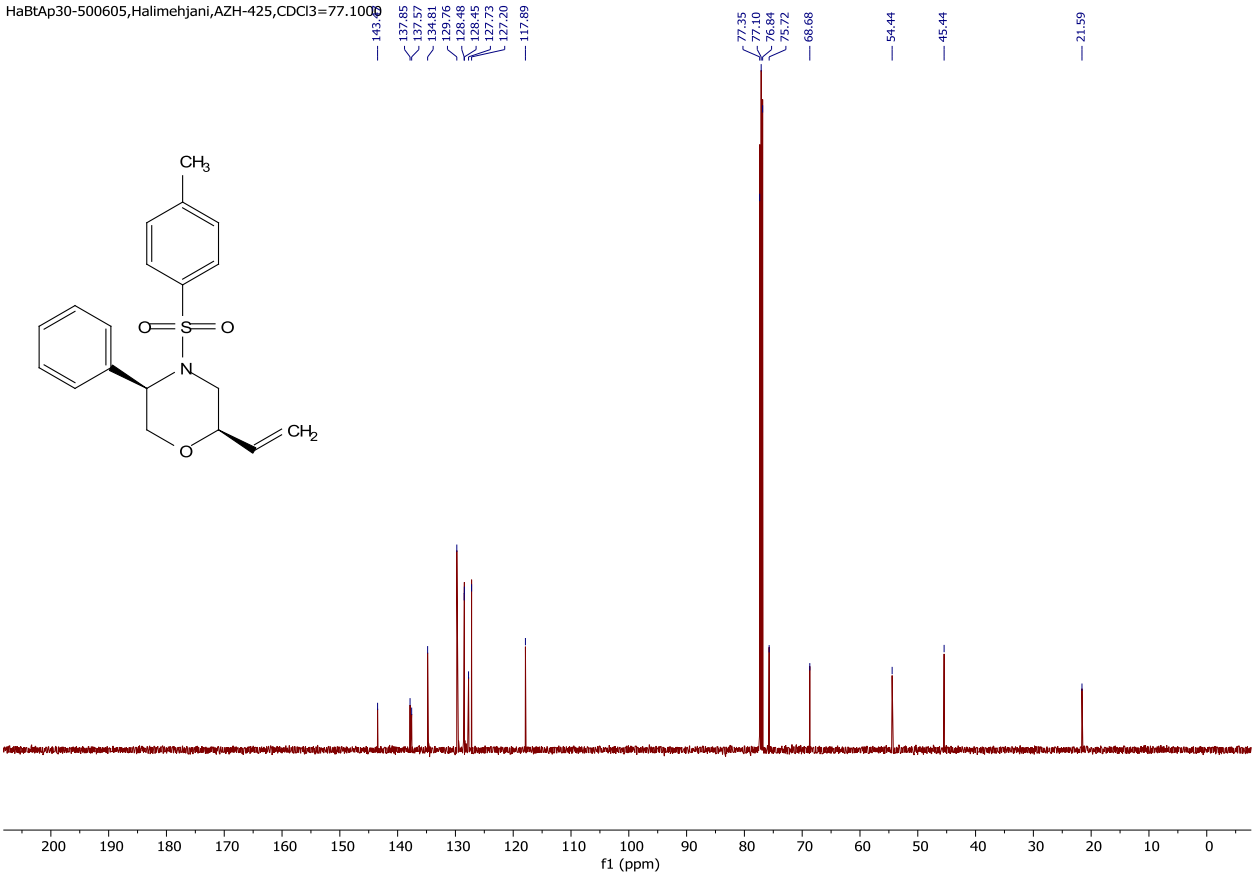
Results

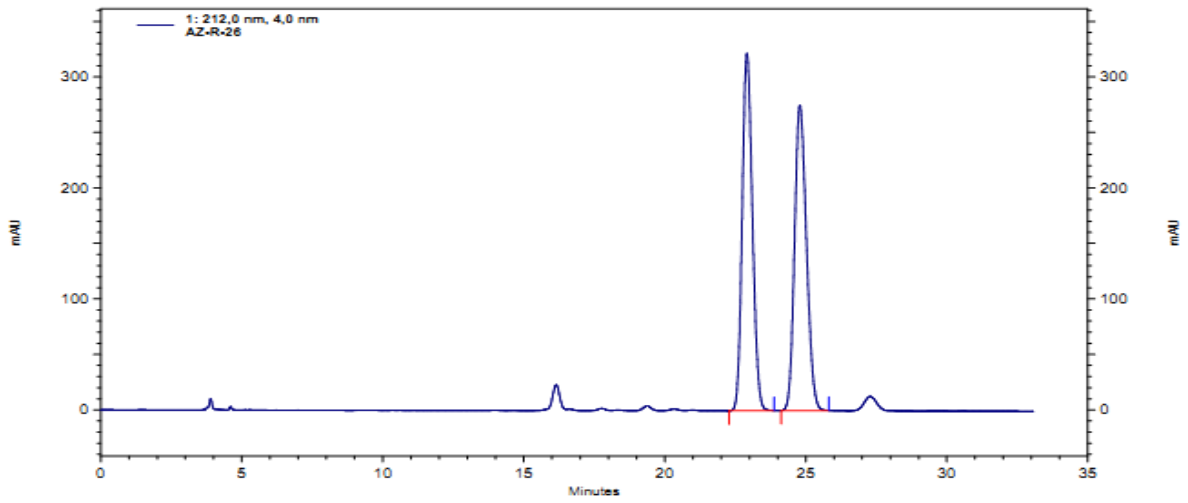
Peak Number	Retention Time	Area Percent	Area
1	14,755	0,273	1362164
2	27,390	99,727	497169124
Totals		100,000	498531288



(2R,5R)-5-phenyl-4-tosyl-2-vinylmorpholine (**2f**): ppm; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.62 – 7.58 (m, 2H), 7.50 – 7.44 (m, 2H), 7.30 – 7.26 (m, 3H), 7.25 – 7.19 (m, 2H), 5.72 (ddd, *J* = 17.4, 10.7, 5.6 Hz, 1H), 5.32 (dt, *J* = 17.4, 1.4 Hz, 1H), 5.21 (dt, *J* = 10.8, 1.3 Hz, 1H), 4.93 (d, *J* = 3.7 Hz, 1H), 4.33 (dd, *J* = 12.1, 1.0 Hz, 1H), 3.93 – 3.81 (m, 2H), 3.65 (ddd, *J* = 13.8, 3.1, 1.1 Hz, 1H), 2.91 (dd, *J* = 13.8, 11.1 Hz, 1H), 2.40 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.4, 137.8, 137.5, 134.8, 129.7, 128.4, 128.4, 127.7, 127.2, 117.8, 75.7, 68.6, 54.5, 45.4, 21.5 ppm; HRMS (ESI) calcd for $C_{19}H_{21}NO_3S$ $[M+H]^+$: 344.1320; found: 344.1318; **HPLC** (ChiralPAK AD-3, heptane/ethanol = 85:15, 0.5 mL/min) t_R = 22.66 min (minor), t_R = 24.80 min (major), >99% ee; $[\alpha]_D^{25}$ = -40.4 (c = 0.25, CH_2Cl_2).


HaBtAp30-500600,Halimehjani,AZH-425,CDCl3=7.26
CH3
O
S
O
N
O
CH2
2.00
2.04
2.76
2.22
1.00
1.04
1.03
1.05
1.06
2.16
1.12
1.05
3.11
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

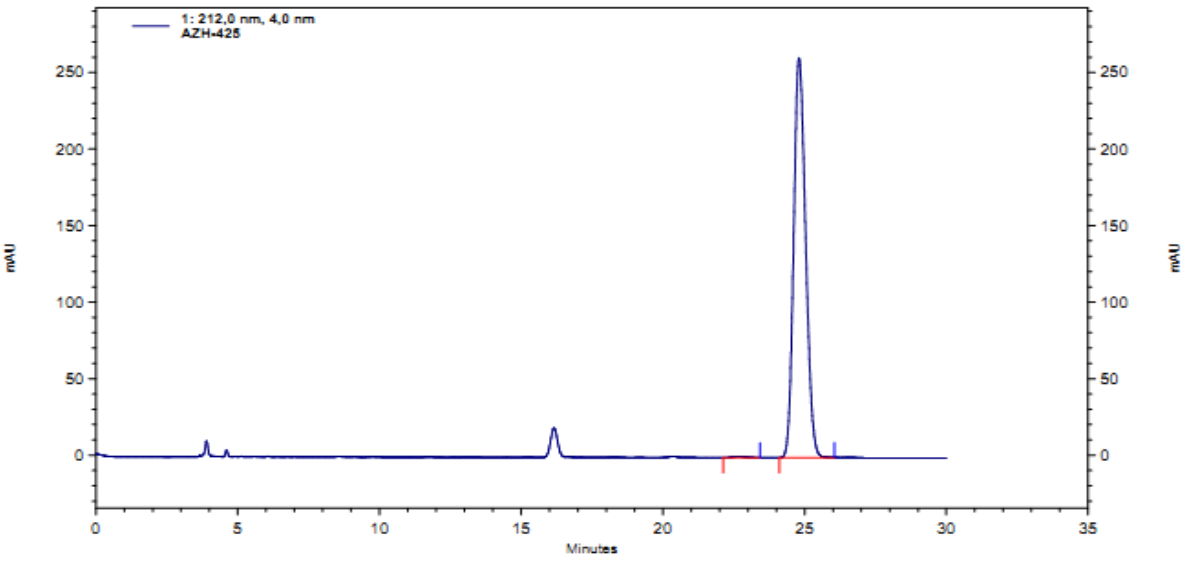

HaBtAp30-500605,Halimehjani,AZH-425,CDCl3=77.1000
143.00
137.85
137.57
134.81
129.76
128.48
128.45
127.73
127.20
117.89
77.35
77.10
76.84
75.72
68.68
54.44
45.44
21.59
CH3
O
S
O
N
O
CH2
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



1: 212,0 nm, 4,0 nm

Results

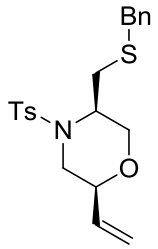
Peak Number	Retention Time	Area Percent	Area
1	22,910	50,157	1089134629
2	24,790	49,843	1082307422
Totals		100,000	2171442051



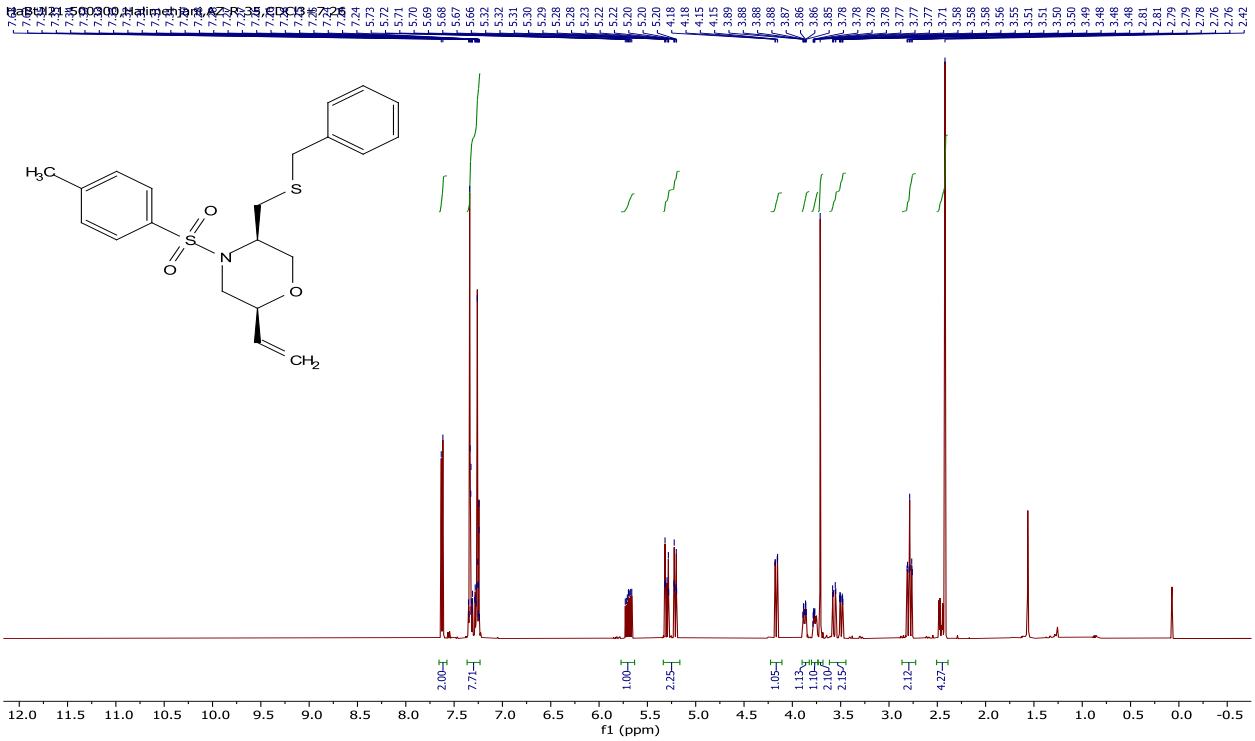
1: 212,0 nm, 4,0 nm

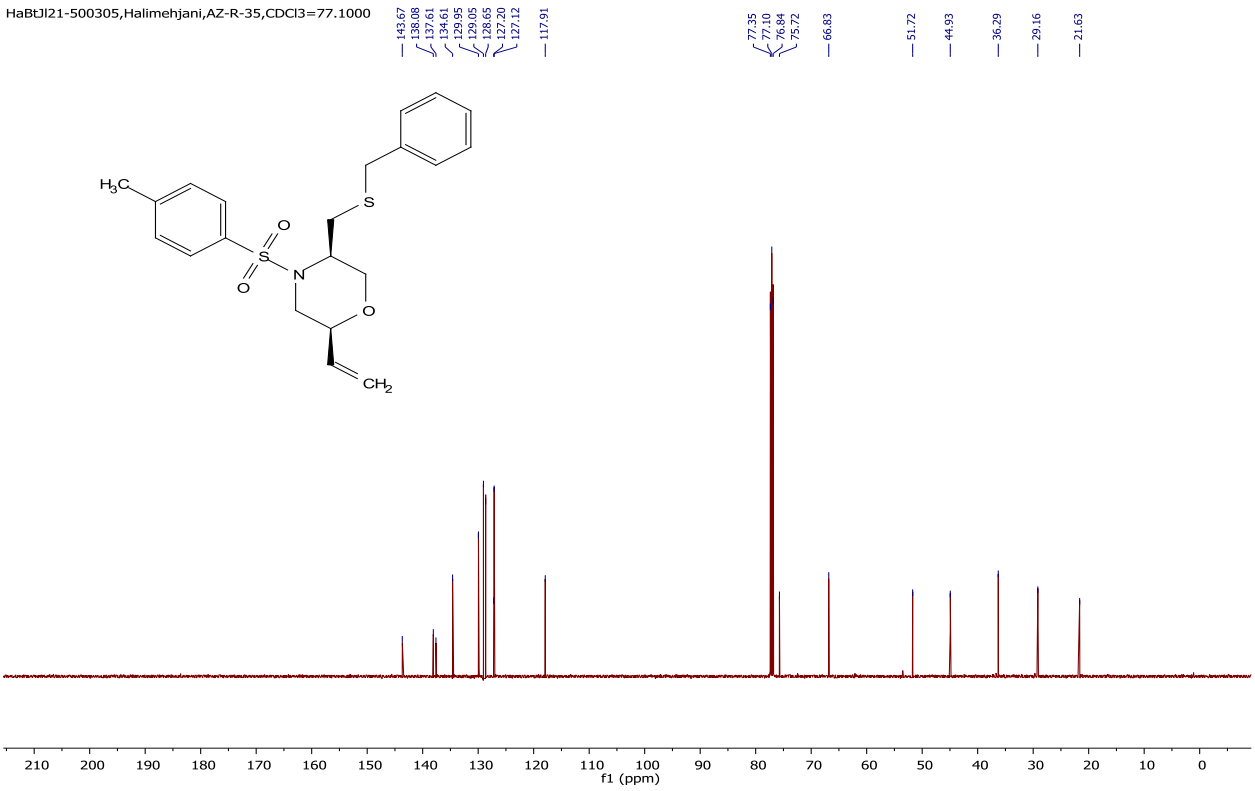
Results

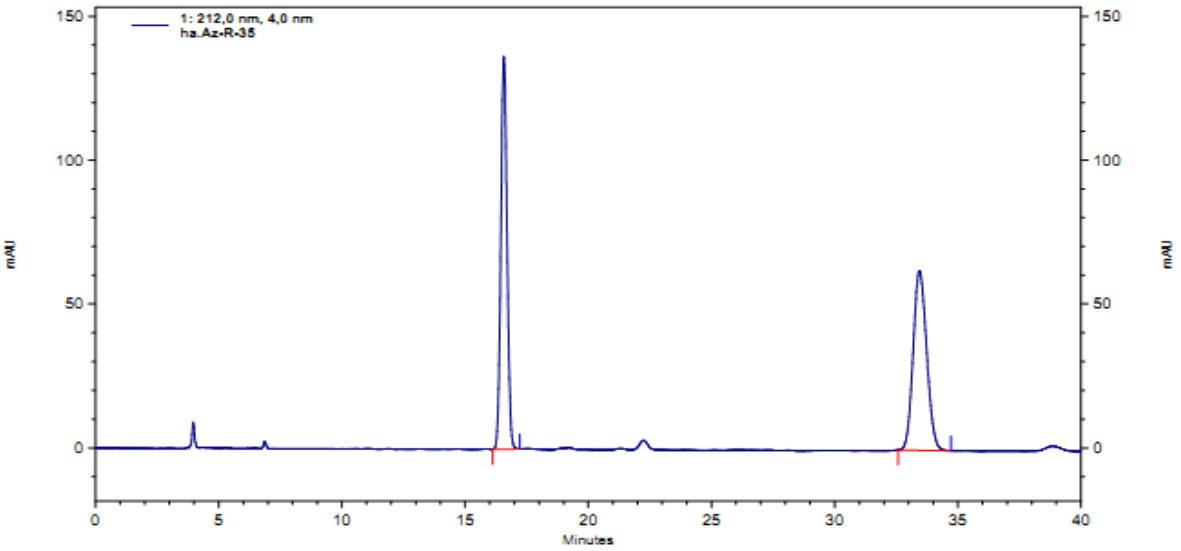
Peak Number	Retention Time	Area Percent	Area
1	22,663	0,401	4130335
2	24,802	99,599	1025933014
Totals		100,000	1030063349



(2S,5R)-5-((benzylthio)methyl)-4-tosyl-2-vinylmorpholine (**2g**): ppm; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.62 (d, *J* = 8.3 Hz, 2H), 7.37 – 7.23 (m, 7H), 5.70 (ddd, *J* = 17.3, 10.8, 5.5 Hz, 1H), 5.34 – 5.16 (m, 2H), 4.17 (dd, *J* = 11.8, 0.9 Hz, 1H), 3.87 (ddd, *J* = 10.5, 4.5, 3.2 Hz, 1H), 3.78 (ddd, *J* = 5.4, 3.0, 1.5 Hz, 1H), 3.71 (s, 2H), 3.62 – 3.45 (m, 2H), 2.79 (ddd, *J* = 13.5, 10.8, 2.7 Hz, 2H), 2.42 (s, 4H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.6, 138.0, 137.6, 134.6, 129.9, 129.0, 128.6, 127.2, 127.1, 117.9, 75.7, 66.8, 51.7, 44.9, 36.2, 29.1, 21.6 ppm; HRMS (ESI) calcd for $C_{21}H_{25}NO_3S_2$ $[M+H]^+$: 404.1354; found: 404.1352; **HPLC** (ChiralPAK AD-3, heptane/ethanol = 85:15, 0.5 mL/min) t_R = 16.57 min (minor), t_R = 33.31 min (major), >99% ee; $[\alpha]_D^{25}$ = +52.69 (c = 0.465, CH_2Cl_2).



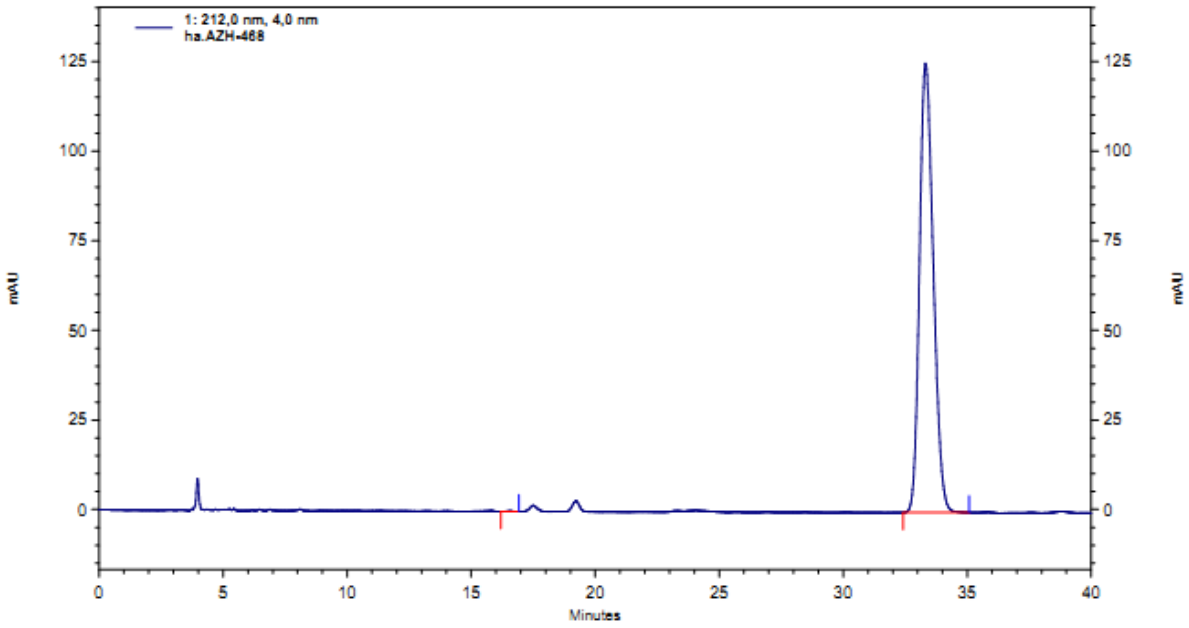




1: 212,0 nm, 4,0 nm

Results

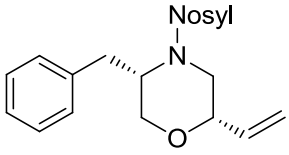
Peak Number	Retention Time	Area Percent	Area
1	16,575	50,115	320799101
2	33,442	49,885	319332750
Totals		100,000	640131851



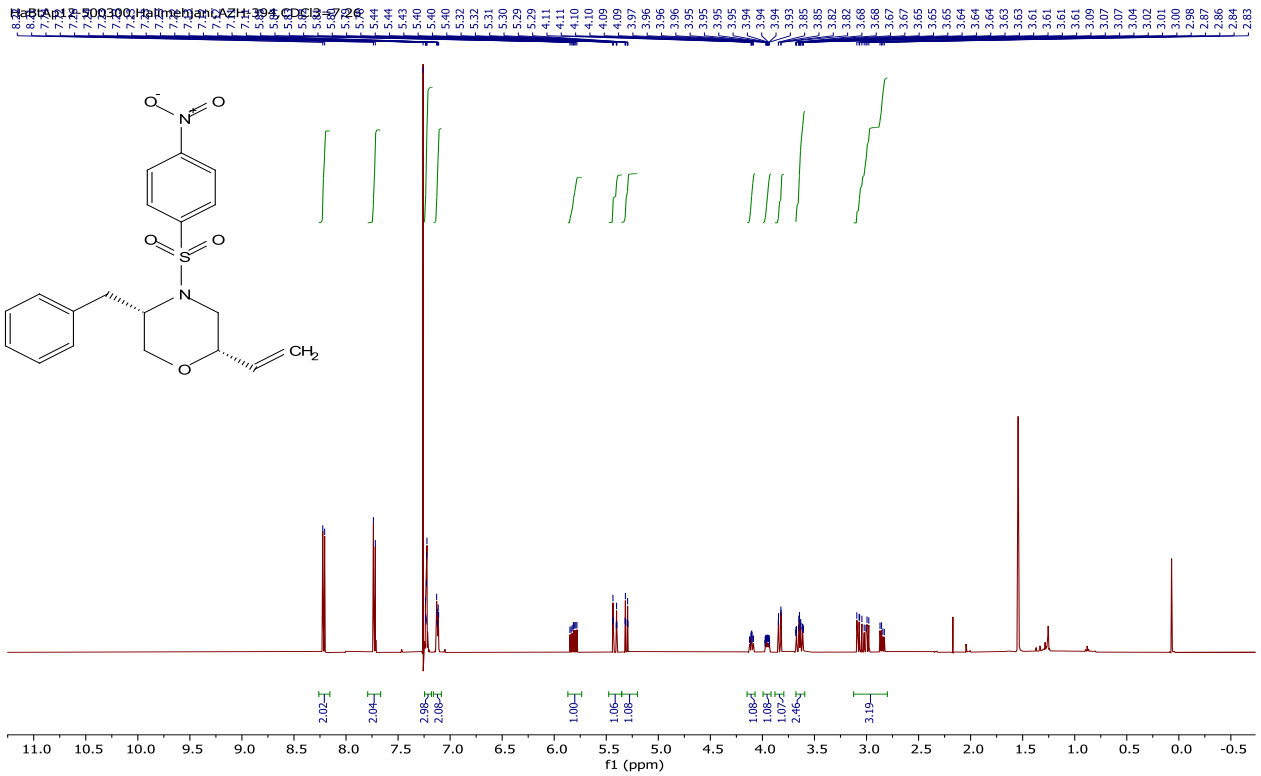
1: 212,0 nm, 4,0 nm

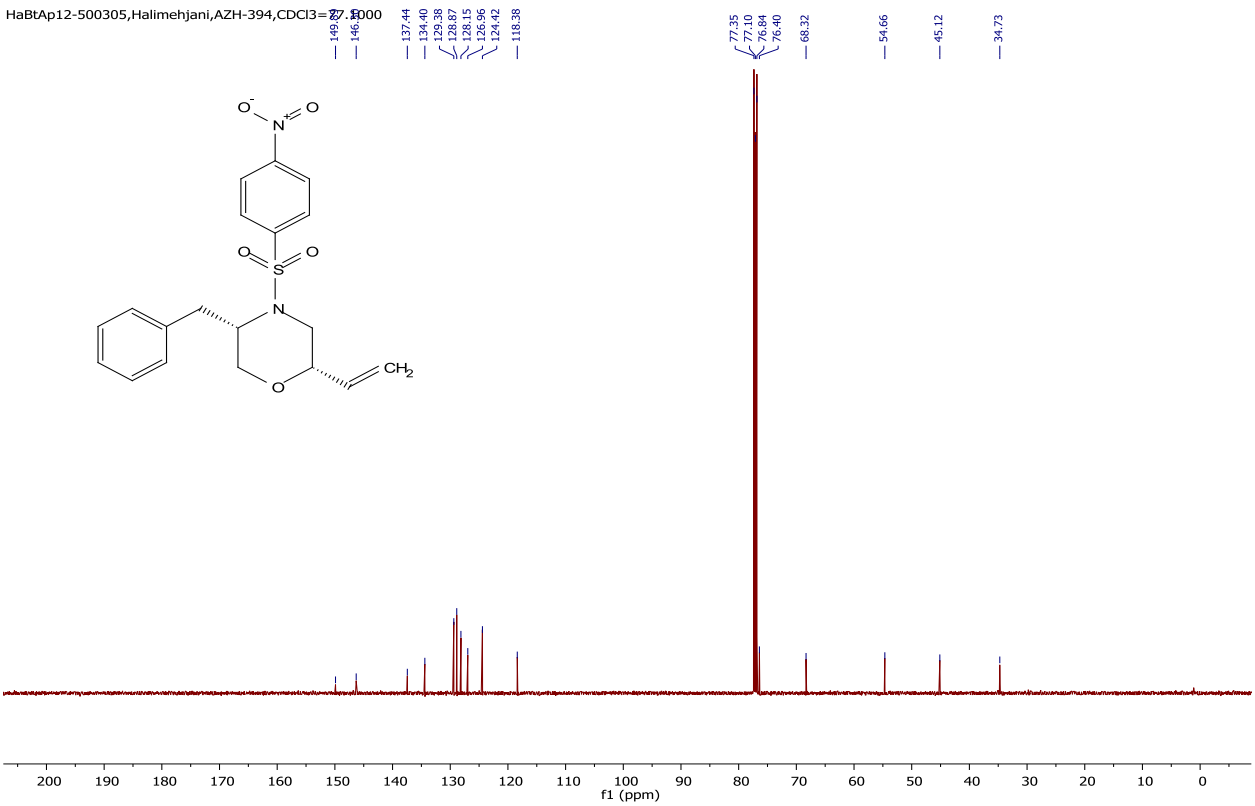
Results

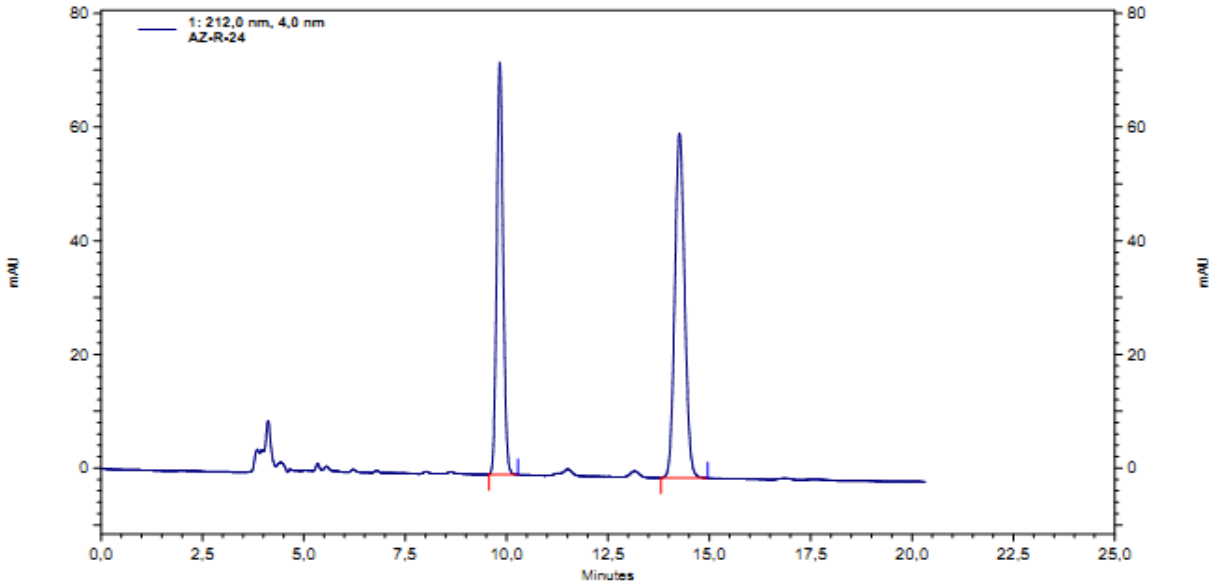
Peak Number	Retention Time	Area Percent	Area
1	16,572	0,074	480906
2	33,318	99,926	651041653
Totals		100,000	651522559



(2S,5S)-5-benzyl-4-((4-nitrophenyl)sulfonyl)-2-vinylmorpholine (**2h**): ppm; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.21 (d, J = 9.0 Hz, 2H), 7.73 (d, J = 9.1 Hz, 2H), 7.25 – 7.18 (m, 3H), 7.14–7.12 (M, 2H), 5.82 (ddd, J = 17.4, 10.8, 5.5 Hz, 1H), 5.42 (dt, J = 17.4, 1.3 Hz, 1H), 5.31 (dt, J = 10.8, 1.3 Hz, 1H), 4.15 – 4.07 (m, 1H), 3.97–3.93 (m, 1H), 3.88 – 3.79 (m, 1H), 3.68 – 3.59 (m, 2H), 3.12 – 2.80 (m, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.8, 146.3, 137.4, 134.4, 129.3, 128.8, 128.1, 126.9, 124.4, 118.3, 76.4, 68.3, 54.6, 45.1, 34.7 ppm; HRMS (ESI) calcd for $C_{19}H_{20}N_2O_5S$ $[M]^-$: 388.1093; found: 388.1107; **HPLC** (ChiralPAK AD-3, heptane/isopropanol = 70:30, 0.5 mL/min) t_R = 9.79 min (minor), t_R = 14.18 min (major), >99% ee; $[\alpha]_D^{25}$ = -16.5 (c = 0.20, CH_2Cl_2).


HaBtAp12-500300,Halimehjani,AZH-394,CDCl3=7.26
f1 (ppm)

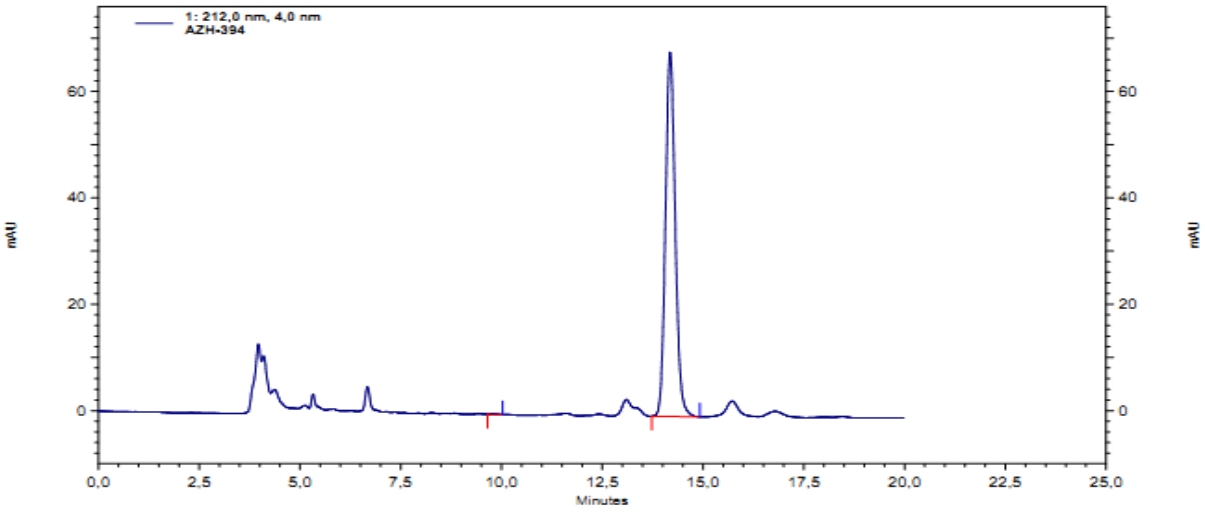

HaBtAp12-500305,Halimehjani,AZH-394,CDCl3=77.000
f1 (ppm)



1: 212,0 nm, 4,0 nm

Results

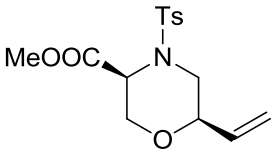
Peak Number	Retention Time	Area Percent	Area
1	9,833	43,841	107531095
2	14,267	56,159	137743815
Totals		100,000	245274910



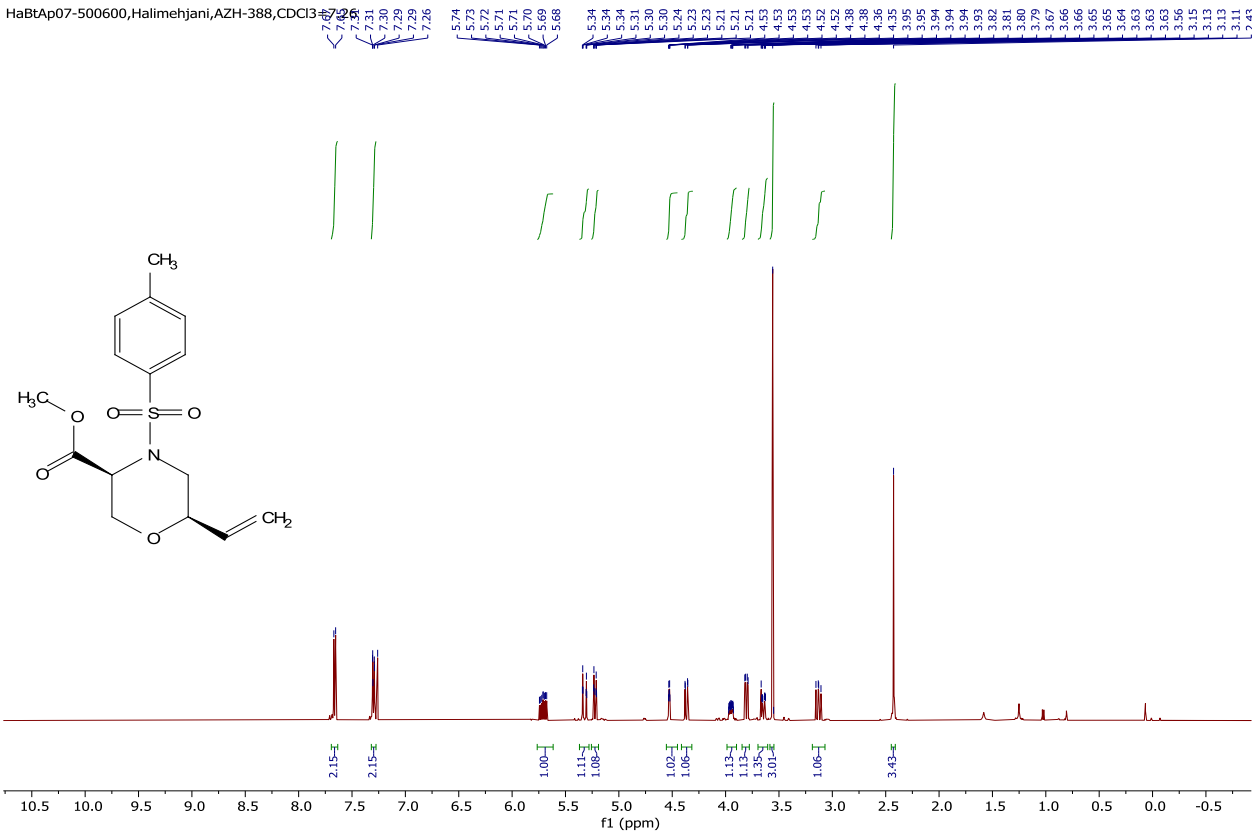
1: 212,0 nm, 4,0 nm

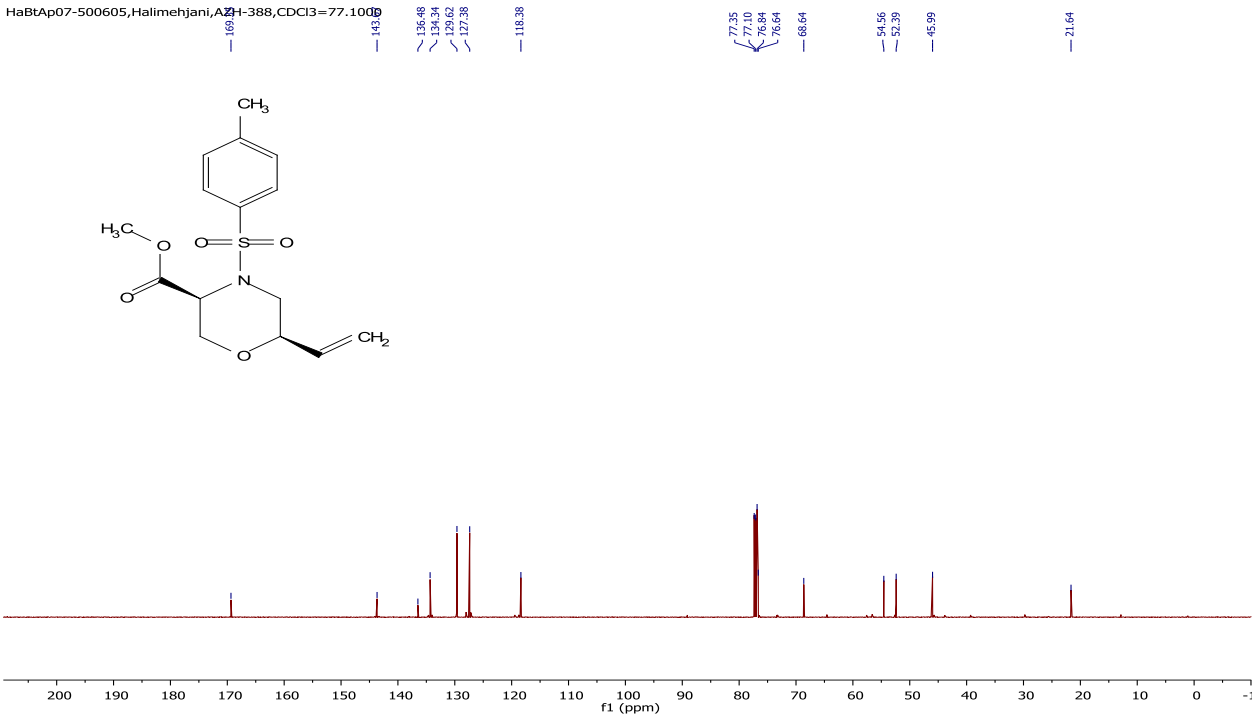
Results

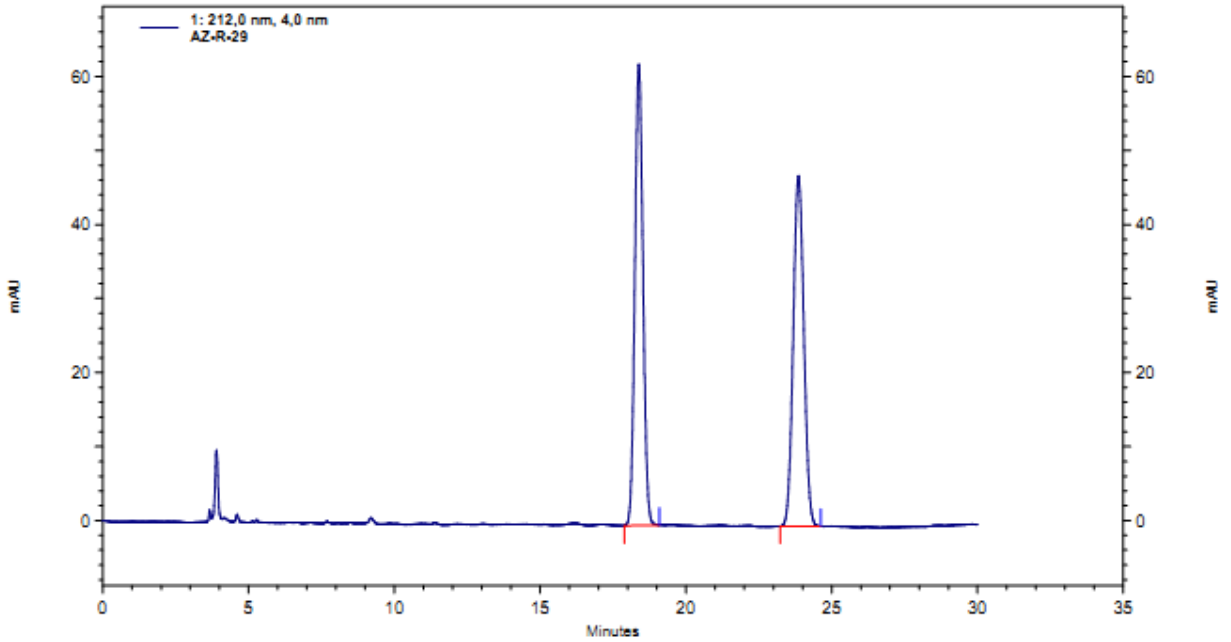
Peak Number	Retention Time	Area Percent	Area
1	9,793	0,072	112451
2	14,180	99,928	155413205
Totals		100,000	155525656



(3S,6R)-methyl 4-tosyl-6-vinylmorpholine-3-carboxylate (**2i**): ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.66 (d, J = 8.3 Hz, 2H), 7.30 (dd, J = 8.5, 0.8 Hz, 2H), 5.71 (ddd, J = 17.4, 10.7, 5.7 Hz, 1H), 5.32 (dt, J = 17.4, 1.4 Hz, 1H), 5.22 (dt, J = 10.8, 1.3 Hz, 1H), 4.53 (dt, J = 3.7, 1.2 Hz, 1H), 4.37 (dd, J = 11.6, 1.2 Hz, 1H), 3.98–3.95 (m, 1H), 3.80 (dd, J = 11.7, 3.8 Hz, 1H), 3.70 – 3.61 (m, 1H), 3.56 (s, 3H), 3.13 (dd, J = 12.6, 11.0 Hz, 1H), 2.43 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.3, 143.6, 136.4, 134.3, 129.6, 127.3, 118.3, 76.6, 68.6, 54.5, 52.3, 45.9, 21.6 ppm; HRMS (ESI) calcd for $C_{15}H_{19}NO_5S$ $[M+Na]^+$: 348.0882; found: 348.0880; **HPLC** (ChiralPAK AD-3, heptane/ethanol = 85:15, 0.5 mL/min) t_R = 18.34 min (major), t_R = 23.91 min (minor), 98.5% ee; $[\alpha]_D^{25}$ = -78.67 (c = 0.675, CH_2Cl_2).



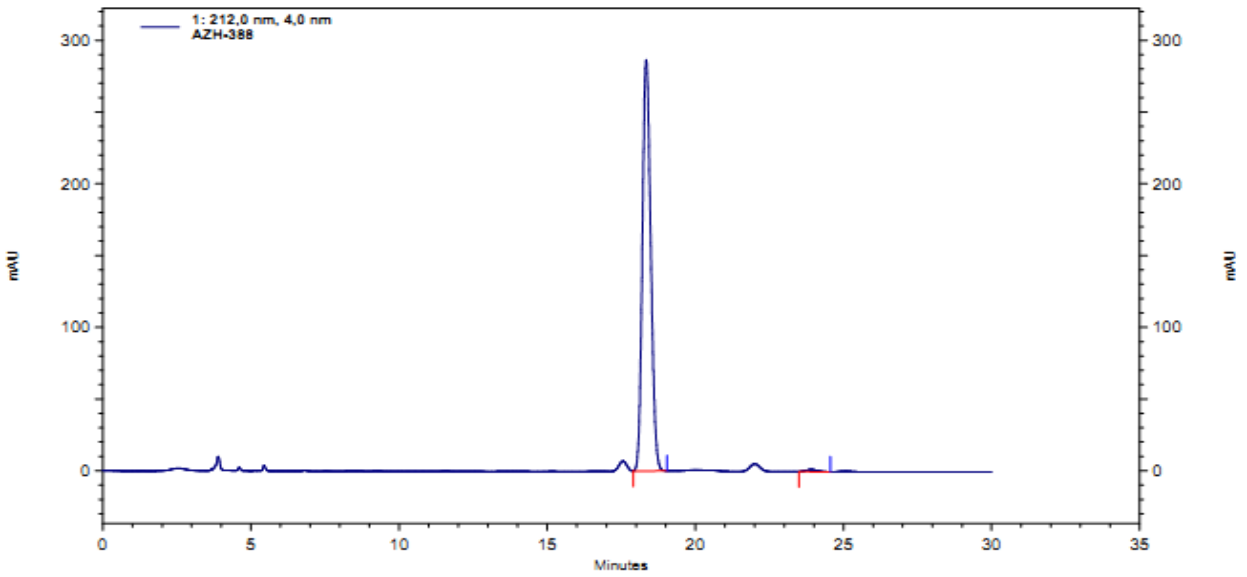




1: 212,0 nm, 4,0 nm

Results

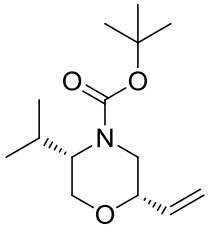
Peak Number	Retention Time	Area Percent	Area
1	18,383	50,187	162126278
2	23,860	49,813	160920440
Totals		100,000	323046718



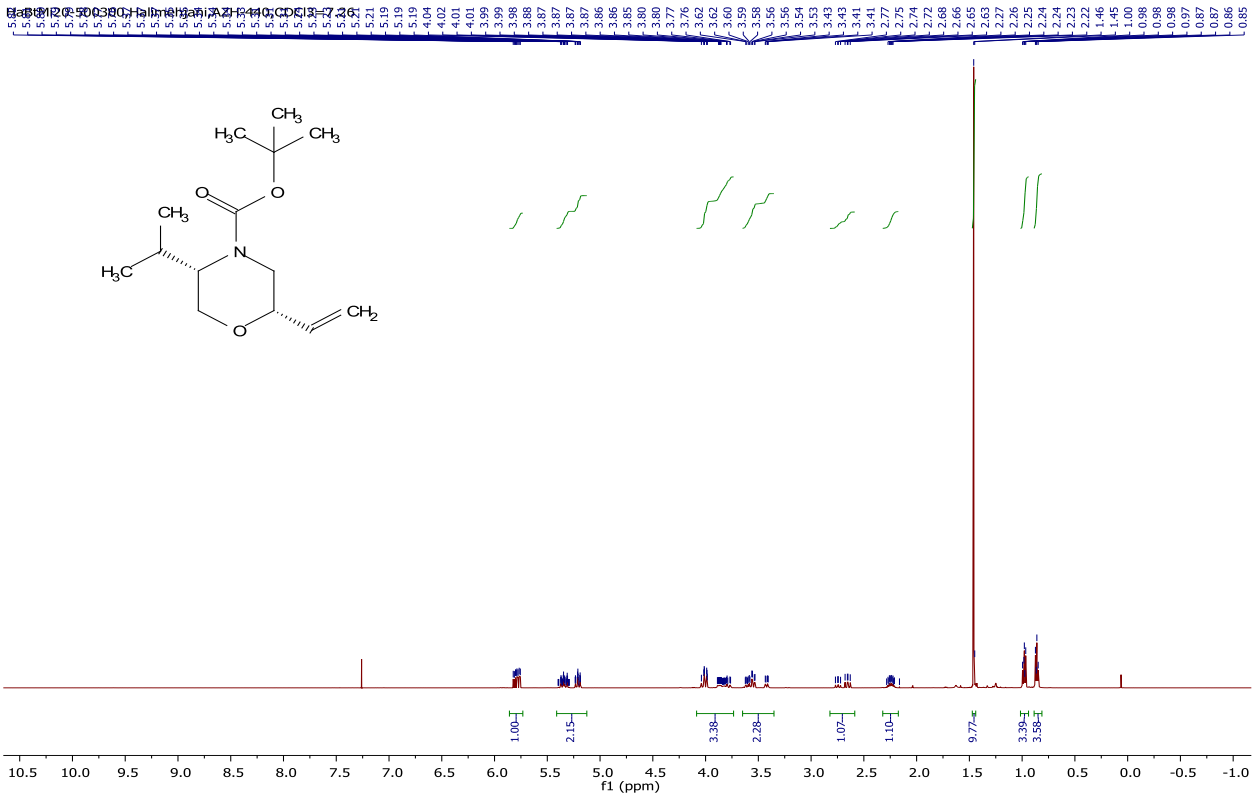
1: 212,0 nm, 4,0 nm

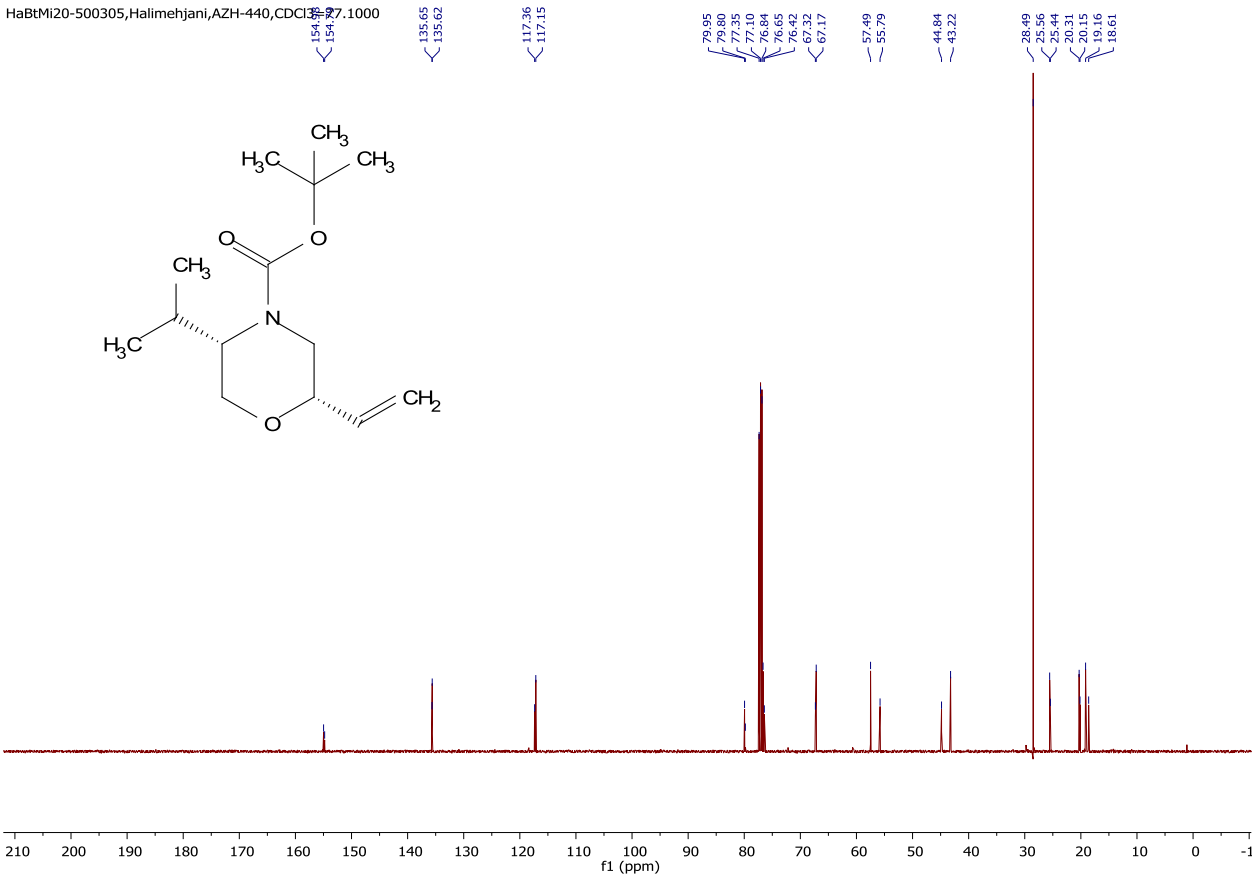
Results

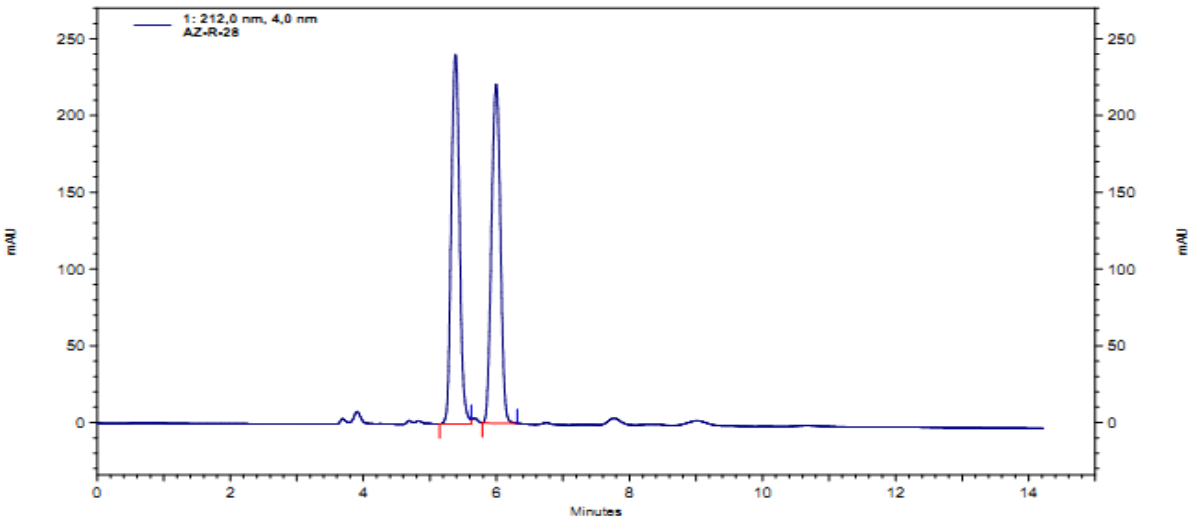
Peak Number	Retention Time	Area Percent	Area
1	18,340	99,258	755717849
2	23,913	0,742	5649032
Totals		100,000	761366881



(2S,5S)-tert-butyl 5-isopropyl-2-vinylmorpholine-4-carboxylate (**2j**): ^{1}H NMR (500 MHz, Chloroform-*d*) δ 5.79 (ddd, J = 17.4, 10.7, 5.4 Hz, 1H), 5.41 – 5.13 (m, 2H), 4.09 – 3.73 (m, 3H), 3.65 – 3.35 (m, 2H), 2.72–268 (m, 1H), 2.27–2.23 (m, 1H), 1.46 (s, 9H), 0.98 (m, 3H), 0.86 (m, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.9, 154.7, 135.6, 135.6, 117.3, 117.1, 79.9, 79.8, 76.6, 76.4, 67.3, 67.1, 57.4, 55.7, 44.8, 43.2, 28.4, 25.5, 25.4, 20.3, 20.1, 19.1, 18.6 ppm; HRMS (ESI) calcd for $C_{14}H_{25}NO_3$ $[M+H]^+$: 256.1913; found: 256.1908; **HPLC** (ChiralPAK AD-3, heptane/isopropanol = 99.5:0.5, 0.5 mL/min) t_R = 5.34 min (minor), t_R = 5.66 min (major), 95% ee; $[\alpha]_D^{25}$ = +16.47 (c = 0.212, CH_2Cl_2).


HaBtMi20-500305,Halimehjani,AZH-440,CDCl3-17.26
CH3
H3C
CH3
O
O
CH3
N
H3C
CH2
O
1.00
2.15
3.38
2.28
1.07
1.10
9.77
3.39
3.58
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

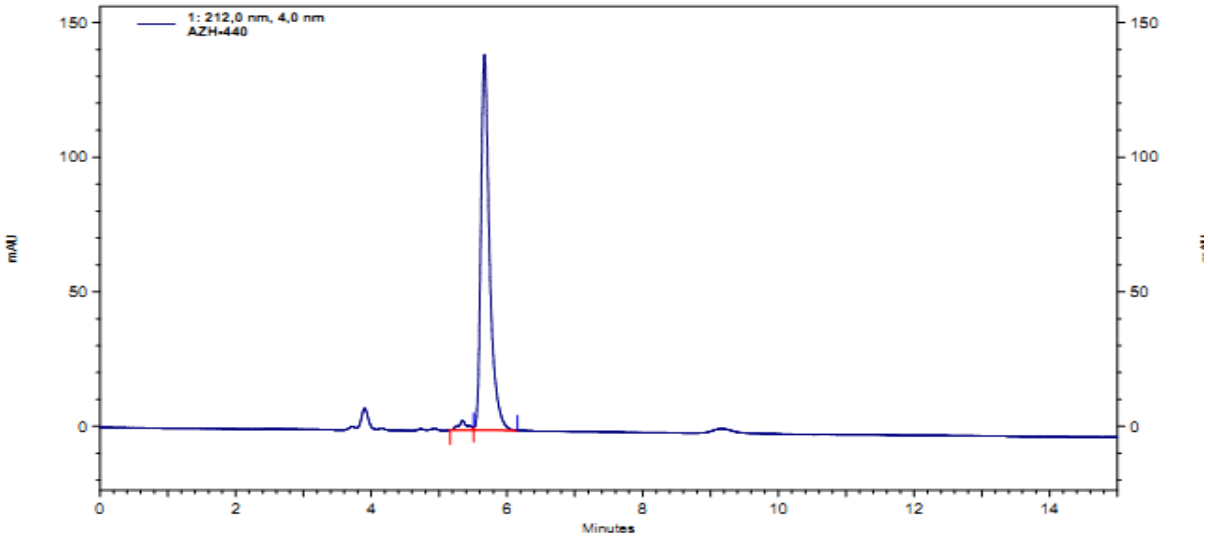

HaBtMi20-500305,Halimehjani,AZH-440,CDCl3-27.1000
154.47
154.37
135.65
135.62
117.36
117.15
79.95
79.80
77.35
77.10
76.84
76.65
76.42
67.32
67.17
57.49
55.79
44.84
43.22
28.49
25.56
25.44
20.31
20.15
19.16
18.61
CH3
H3C
CH3
O
O
CH3
N
H3C
CH2
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)



1: 212,0 nm, 4,0 nm

Results

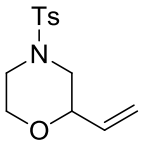
Peak Number	Retention Time	Area Percent	Area
1	5,385	50,481	280313787
2	5,995	49,519	274975389
Totals		100,000	555289176



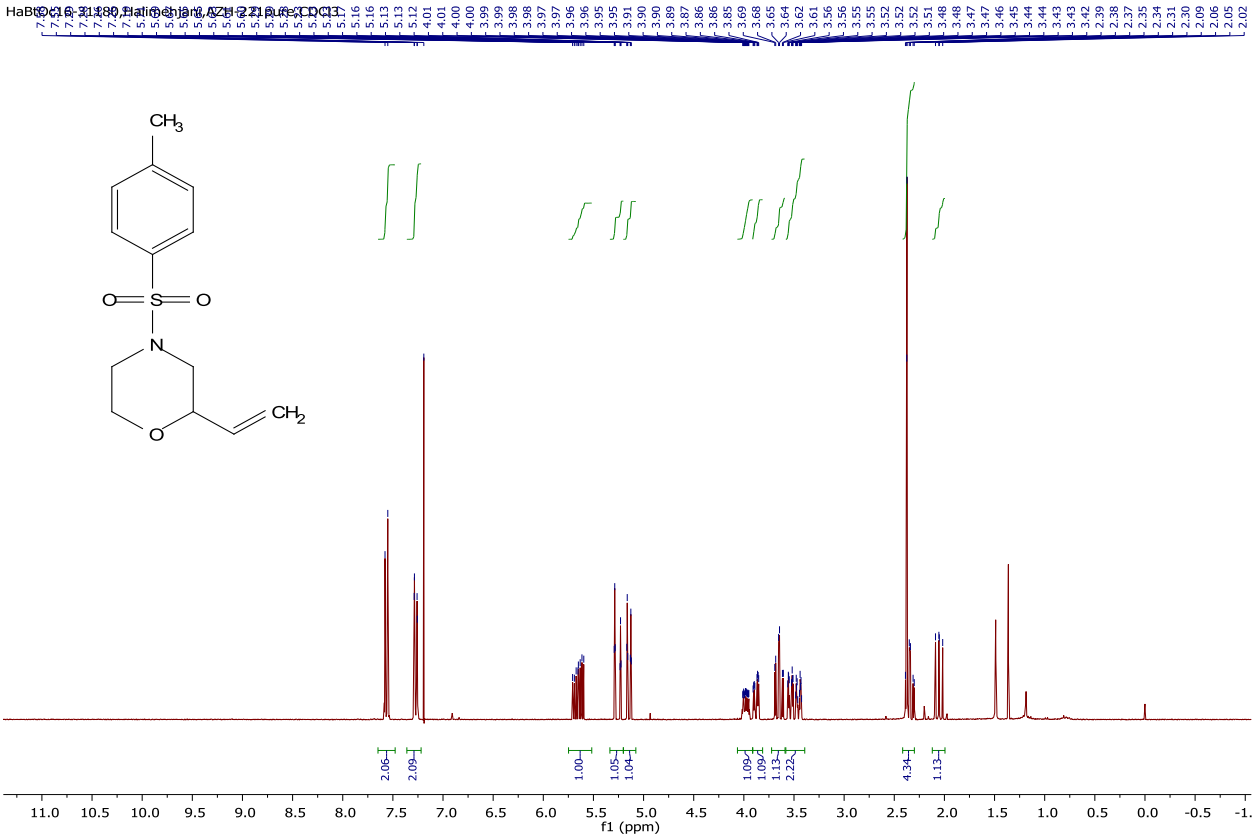
1: 212,0 nm, 4,0 nm

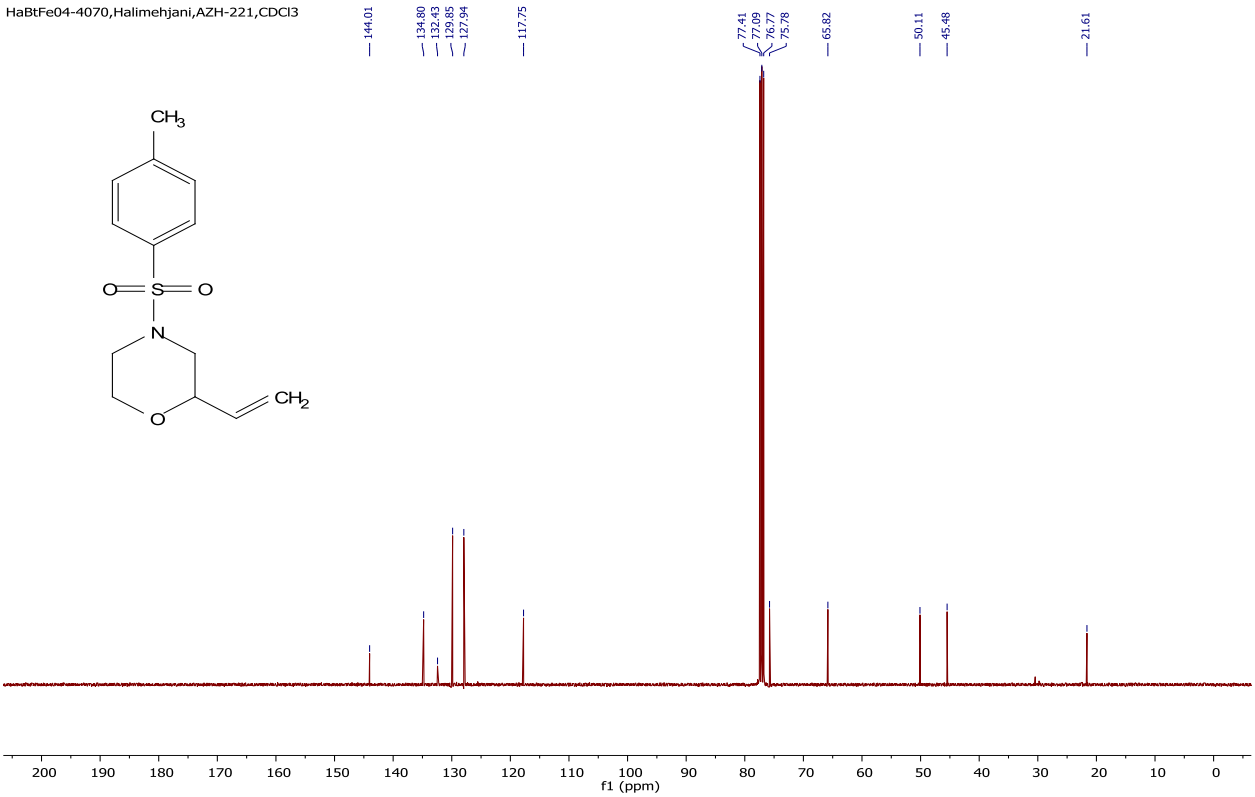
Results

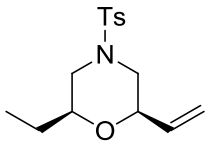
Peak Number	Retention Time	Area Percent	Area
1	5,347	2,566	4385991
2	5,667	97,434	166551997
Totals		100,000	170937988



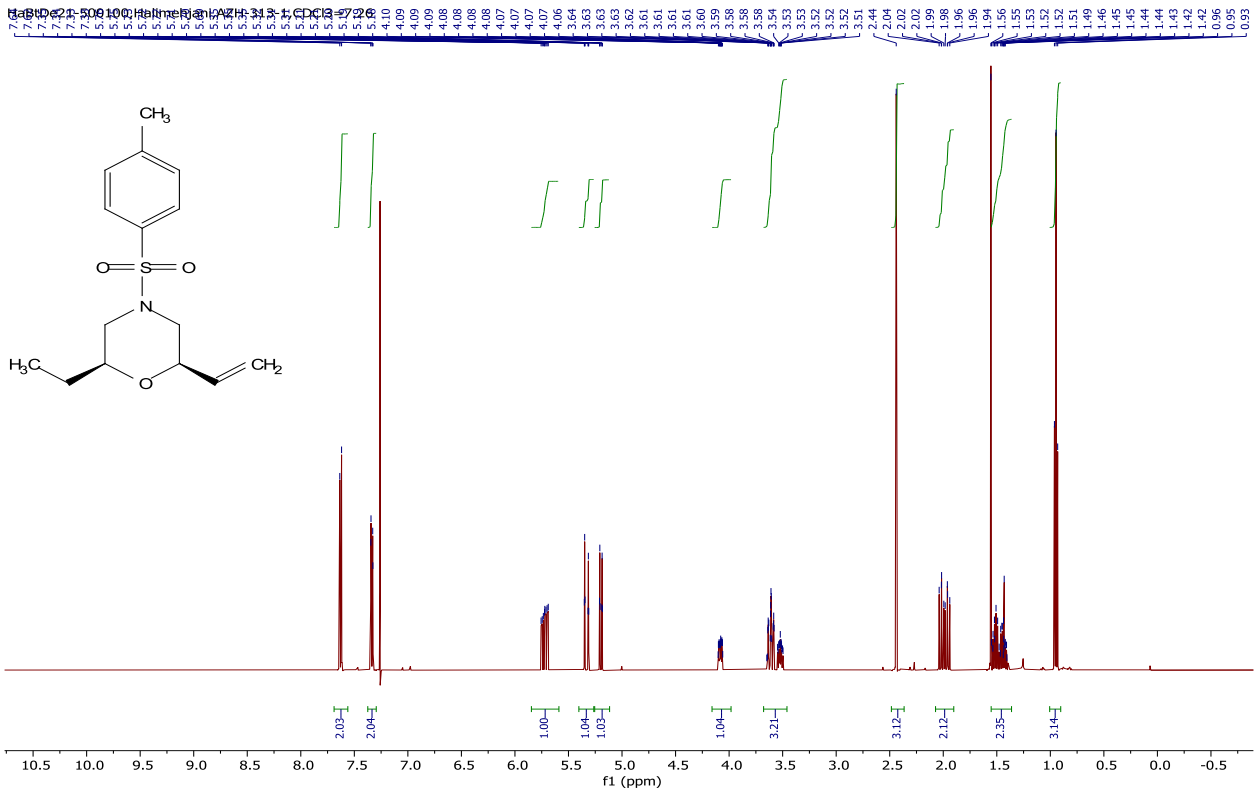
4-tosyl-2-vinylmorpholine (**2k**): (known compound) ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.56 (d, J = 8.3 Hz, 2H), 7.36 – 7.22 (m, 2H), 5.65 (ddd, J = 17.4, 10.7, 5.4 Hz, 1H), 5.26 (dt, J = 17.3, 1.4 Hz, 1H), 5.14 (dt, J = 10.7, 1.3 Hz, 1H), 4.06 – 3.91 (m, 1H), 3.88 (ddd, J = 11.6, 3.4, 1.6 Hz, 1H), 3.65 (td, J = 11.5, 2.7 Hz, 1H), 3.58 – 3.39 (m, 2H), 2.42 – 2.30 (m, 4H), 2.05 (dd, J = 11.4, 10.1 Hz, 1H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.0, 134.8, 132.4, 129.8, 127.9, 117.7, 75.7, 65.8, 50.1, 45.4, 21.6 ppm.

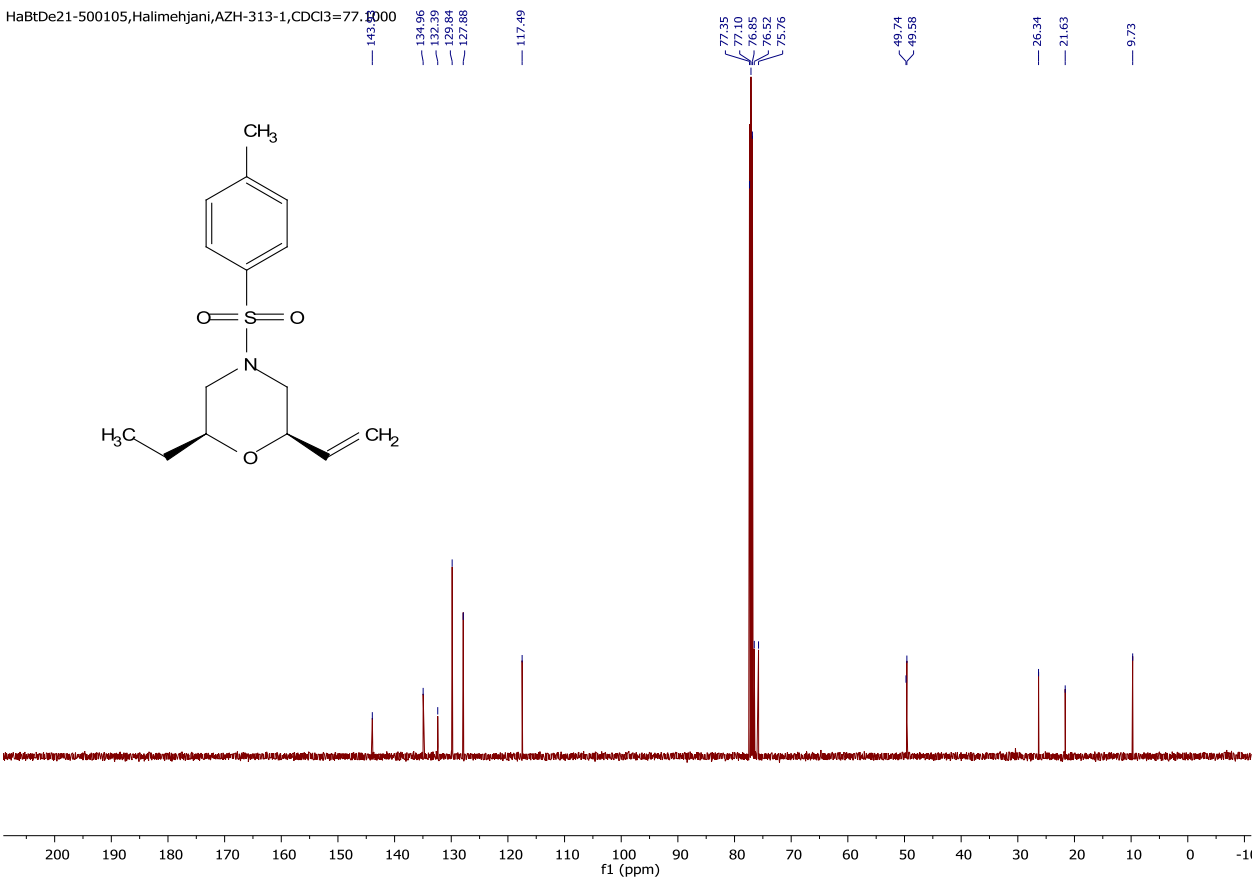


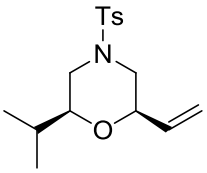




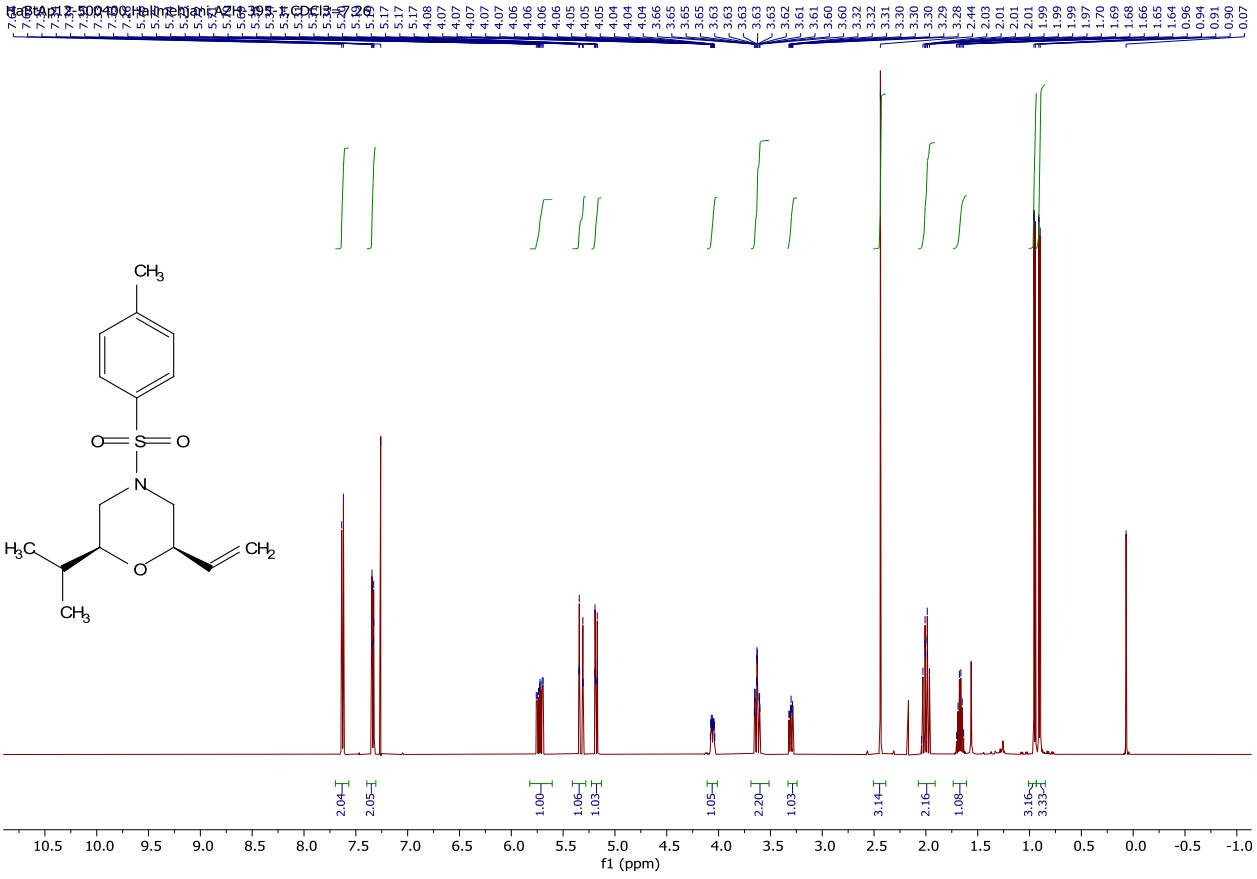
Cis-2-ethyl-4-tosyl-6-vinylmorpholine (**2l**): (major diastereomer) ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.63 (d, J = 8.3 Hz, 2H), 7.34 (dd, J = 8.7, 0.7 Hz, 2H), 5.72 (ddd, J = 17.4, 10.7, 5.5 Hz, 1H), 5.33 (dt, J = 17.4, 1.5 Hz, 1H), 5.20 (dt, J = 10.7, 1.4 Hz, 1H), 4.09–4.07 (m, 1H), 3.68 – 3.46 (m, 3H), 2.44 (s, 3H), 2.01–1.97 (m, 2H), 1.55 – 1.36 (m, 2H), 0.95 (t, J = 7.5 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.9, 134.9, 132.3, 129.8, 127.8, 117.4, 76.5, 75.7, 49.7, 49.5, 26.3, 21.6, 9.7 ppm; HRMS (ESI) calcd for $C_{15}H_{21}NO_3S$ $[M+H]^+$: 296.1320; found: 296.1316.

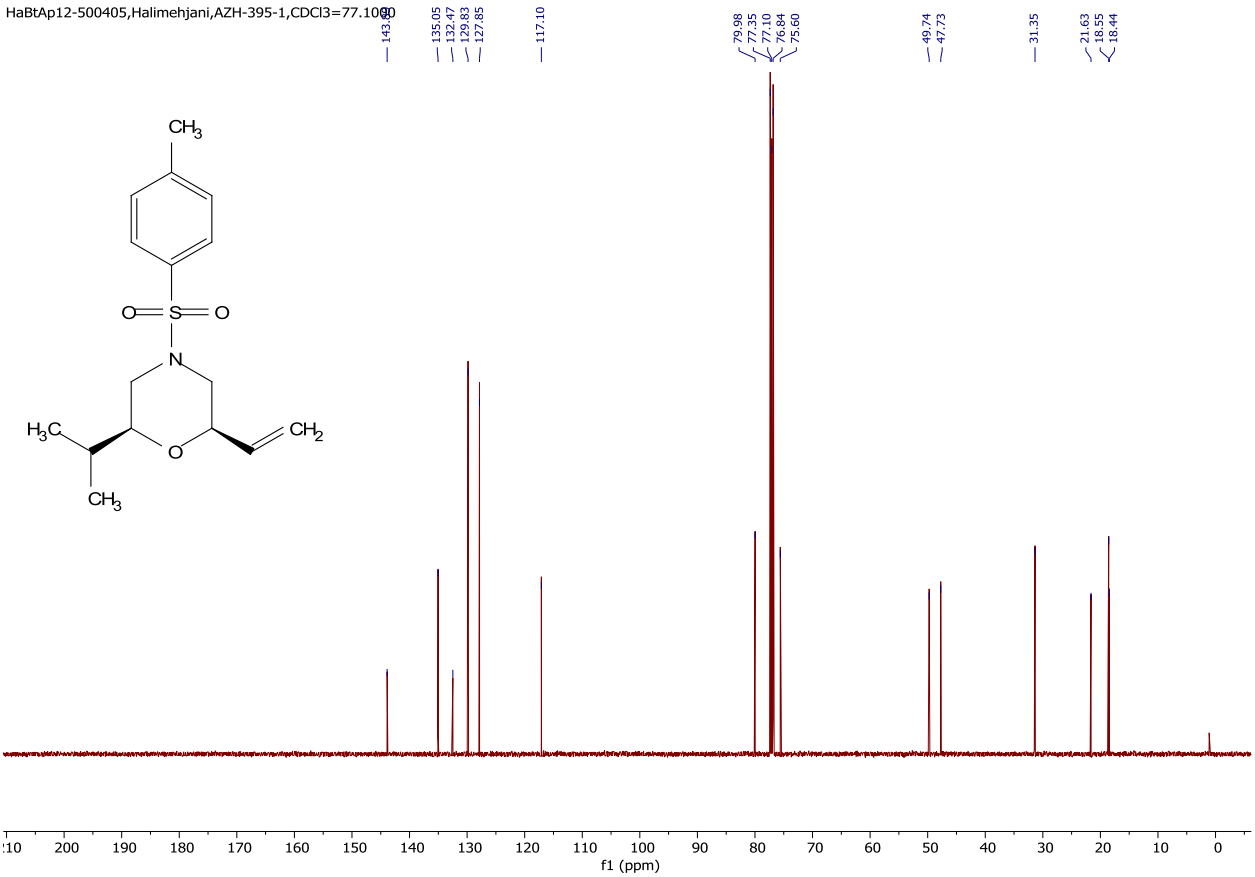

HaBtDe21-500100,Halimehjani,AZH-313-1,CDCl3=7.26
CH3
O
S
O
N
H3C
O
CH2
2.03
2.04
1.00
1.04
1.03
1.04
3.21
3.12
2.12
2.35
3.14
f1 (ppm)

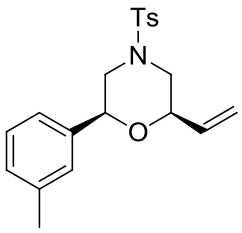

HaBtDe21-500105,Halimehjani,AZH-313-1,CDCl3=77.2000
143.
134.96
132.39
129.84
127.88
117.49
77.35
77.10
76.85
76.52
75.76
49.74
49.58
26.34
21.63
9.73
CH3
O
S
O
N
H3C
O
CH2
f1 (ppm)



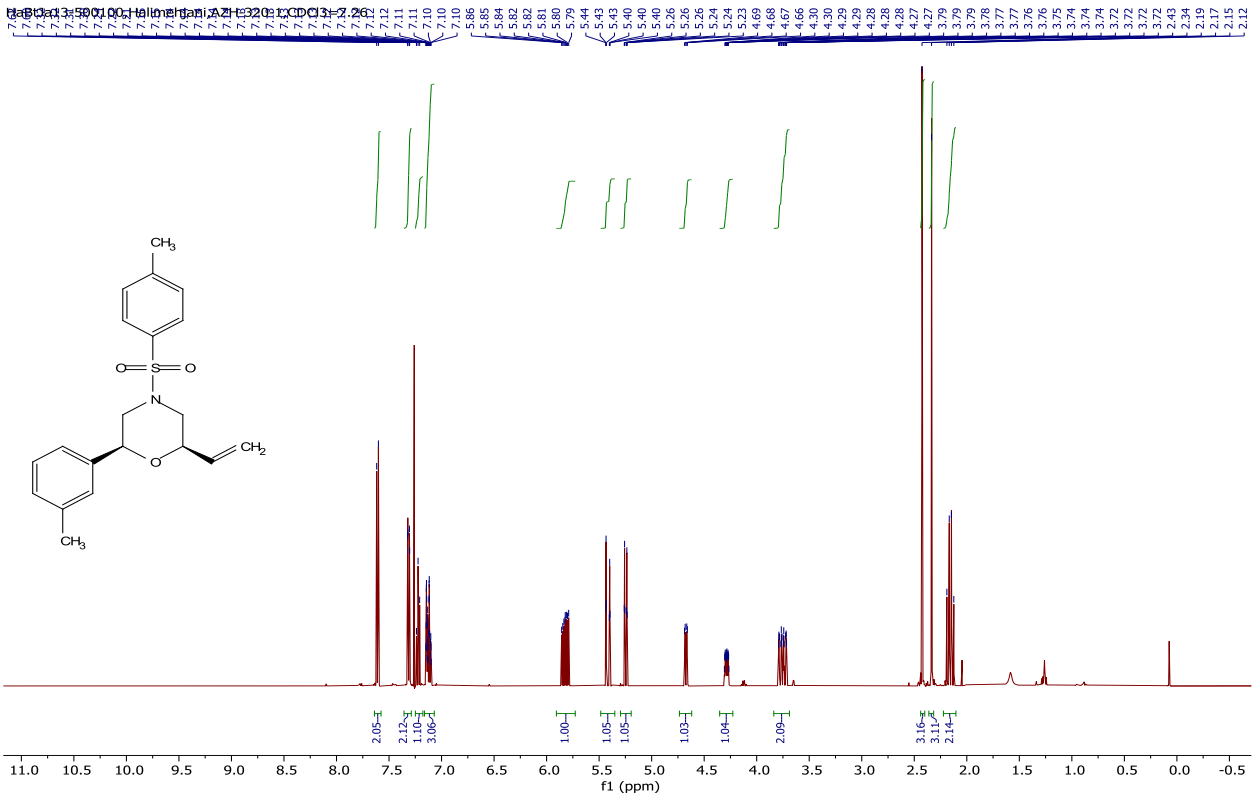
Cis-2-isopropyl-4-tosyl-6-vinylmorpholine (**2m**): (major diastereomer) ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.63 (d, J = 8.3 Hz, 2H), 7.39 – 7.31 (m, 2H), 5.73 (ddd, J = 17.4, 10.8, 5.2 Hz, 1H), 5.33 (dt, J = 17.4, 1.5 Hz, 1H), 5.18 (dt, J = 10.7, 1.5 Hz, 1H), 4.09–4.04 (m, 1H), 3.69 – 3.51 (m, 2H), 3.30 (ddd, J = 10.5, 6.8, 2.4 Hz, 1H), 2.44 (s, 3H), 2.00 (ddd, J = 11.2, 10.4, 9.7 Hz, 2H), 1.69–1.65 (m, 1H), 0.95 (d, J = 6.8 Hz, 3H), 0.90 (d, J = 6.9 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.8, 135.0, 132.4, 129.8, 127.8, 117.1, 79.9, 75.6, 49.7, 47.7, 31.3, 21.6, 18.5, 18.4 ppm; HRMS (ESI) calcd for $C_{16}H_{23}NO_3S$ $[M+H]^+$: 310.1477; found: 310.1479.

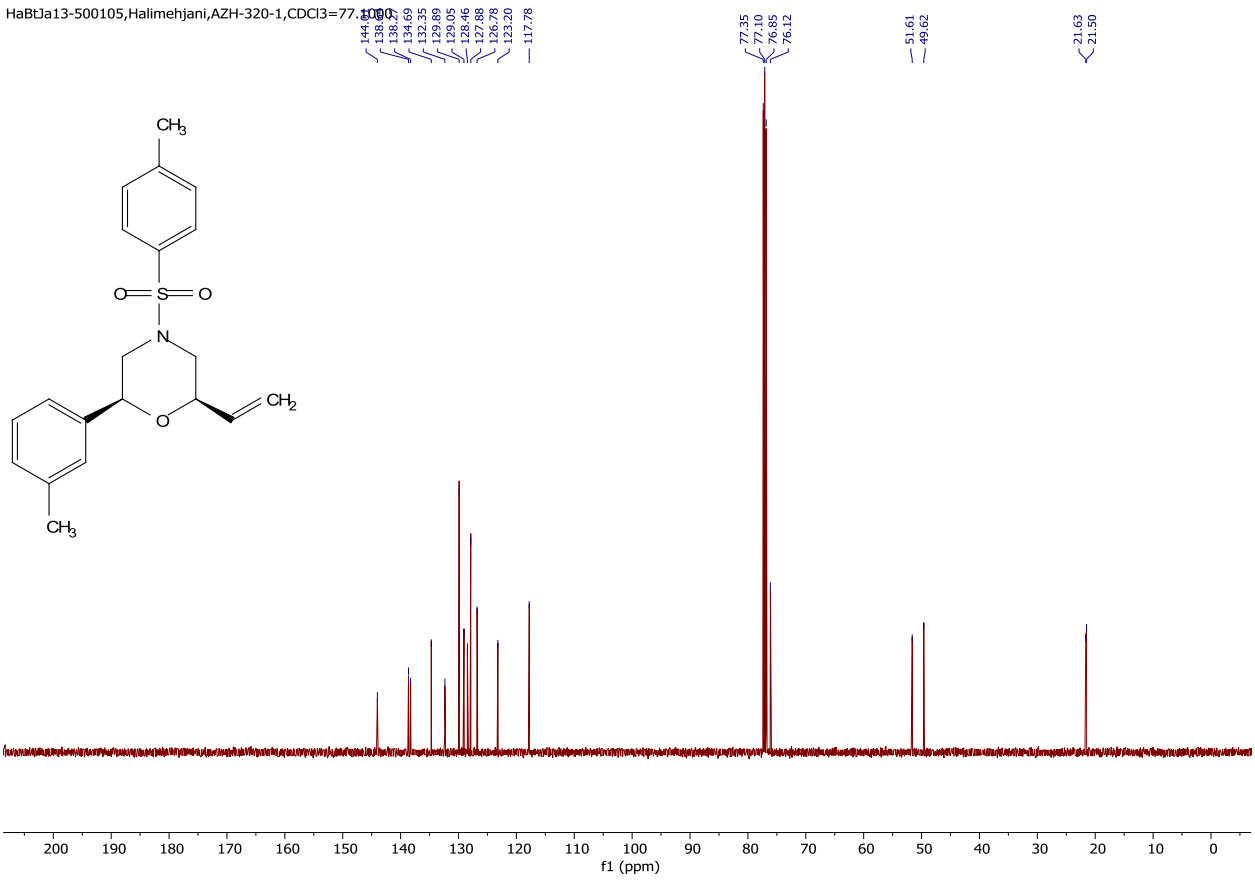


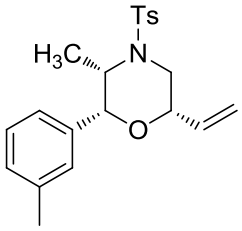




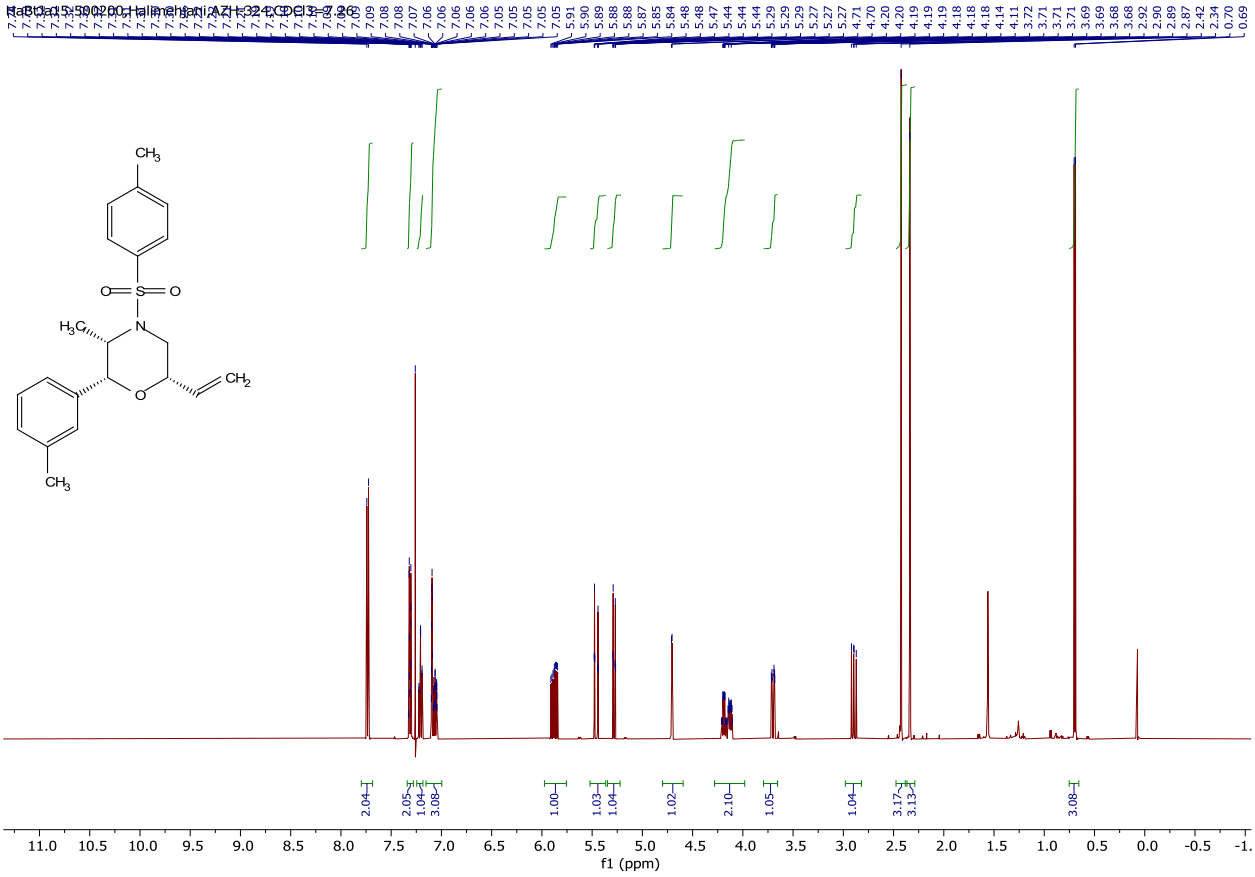
Cis-2-(m-tolyl)-4-tosyl-6-vinylmorpholine (**2n**): (major diastereomer) ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.61 (d, J = 8.3 Hz, 2H), 7.31 (dd, J = 8.5, 0.8 Hz, 2H), 7.22 (t, J = 7.5 Hz, 1H), 7.16 – 7.07 (m, 3H), 5.82 (ddd, J = 17.4, 10.7, 5.4 Hz, 1H), 5.42 (dt, J = 17.4, 1.4 Hz, 1H), 5.25 (dt, J = 10.8, 1.3 Hz, 1H), 4.67 (dd, J = 10.4, 2.7 Hz, 1H), 4.30–4.26 (m, 1H), 3.78–3.74 (m, 2H), 2.43 (s, 3H), 2.34 (s, 3H), 2.22 – 2.10 (m, 2H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.0, 138.6, 138.2, 134.6, 132.3, 129.8, 129.0, 128.4, 127.8, 126.7, 123.2, 117.7, 77.1, 76.1, 51.6, 49.6, 21.6, 21.5 ppm; HRMS (ESI) calcd for $C_{20}H_{23}NO_3S$ $[M+H]^+$: 358.1477; found: 358.1472.

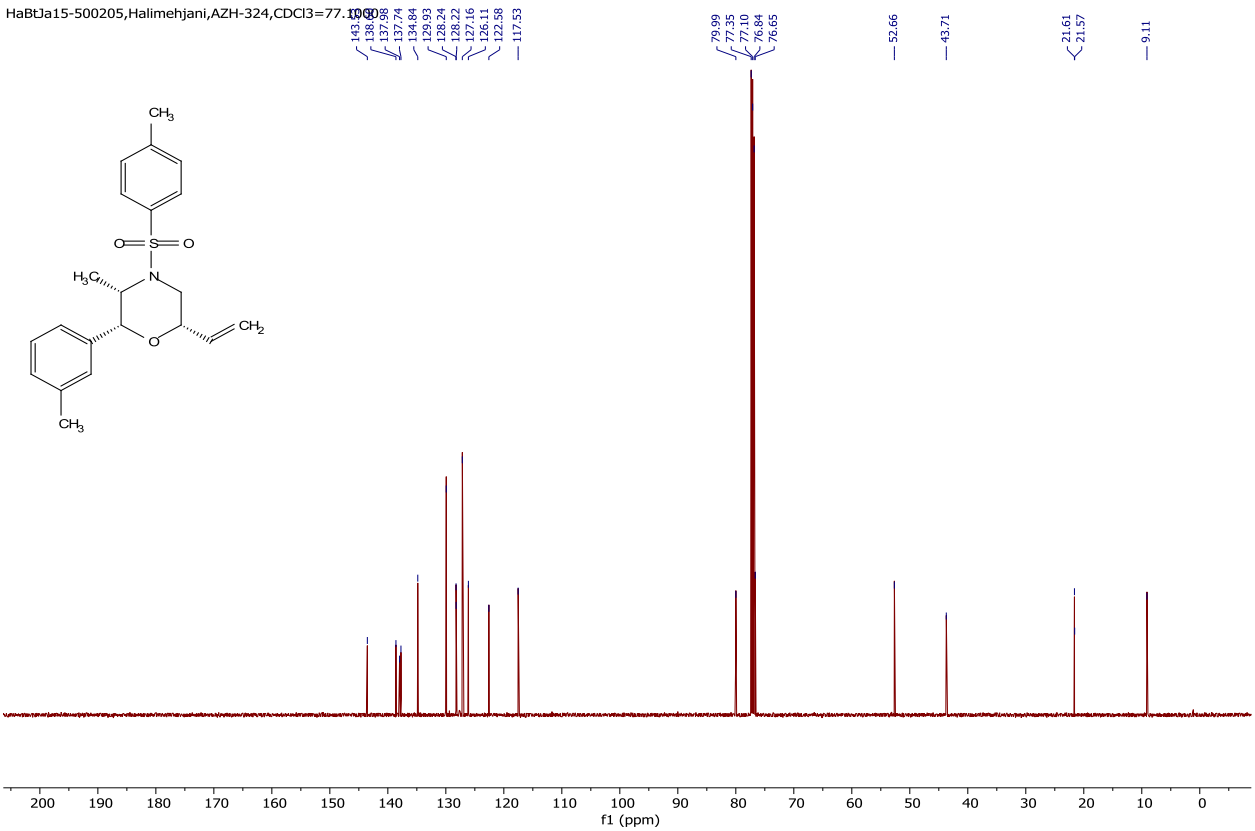

HaBtJa13-500100,Halimehjani,AZH-320-1,CDCl3=7.26
CH3
O
S
O
N
O
CH2
CH3
2.05
2.12
1.10
3.06
1.00
1.05
1.05
1.03
1.04
2.09
3.16
3.11
2.14
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

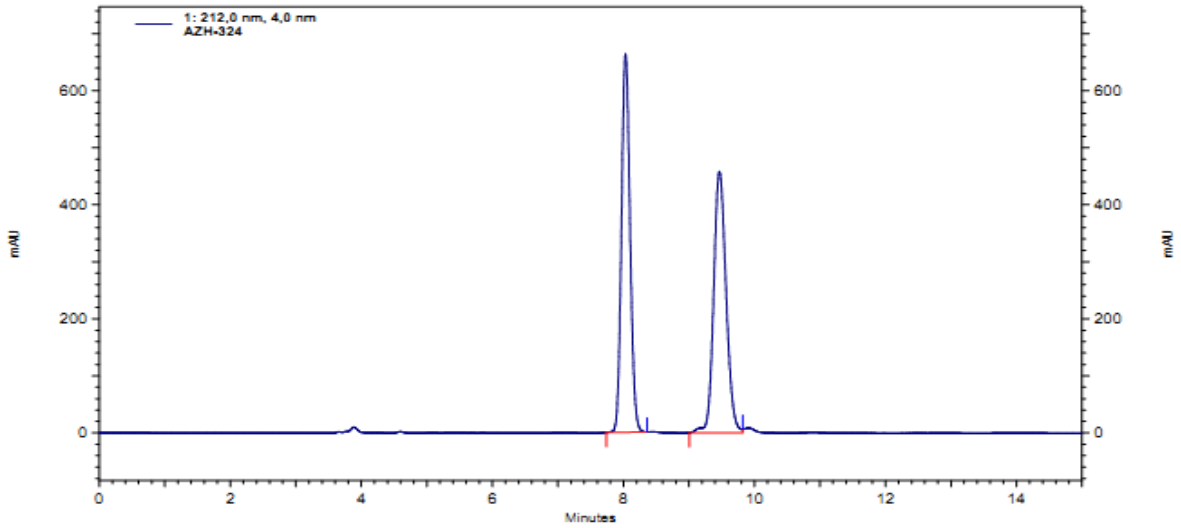

HaBtJa13-500105,Halimehjani,AZH-320-1,CDCl3=77.1000
144.09
138.22
138.22
134.69
132.35
129.89
129.05
128.46
127.88
126.78
123.20
117.78
77.35
77.10
76.85
76.12
51.61
49.62
21.63
21.50
CH3
O
S
O
N
O
CH2
CH3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



(2R,3S,6S)-3-methyl-2-(m-tolyl)-4-tosyl-6-vinylmorpholine (**4a**): ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.73 (d, J = 8.3 Hz, 2H), 7.34 – 7.28 (m, 2H), 7.23–7.20 (m, 1H), 7.15 – 7.00 (m, 3H), 5.88 (ddd, J = 17.4, 10.7, 5.2 Hz, 1H), 5.46 (dt, J = 17.4, 1.5 Hz, 1H), 5.28 (dt, J = 10.8, 1.4 Hz, 1H), 4.71 (d, J = 2.9 Hz, 1H), 4.28 – 3.98 (m, 2H), 3.70 (ddd, J = 13.0, 3.2, 0.9 Hz, 1H), 2.90 (dd, J = 13.0, 11.0 Hz, 1H), 2.42 (s, 3H), 2.34 (s, 3H), 0.70 (d, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.5, 138.6, 137.9, 137.7, 134.8, 129.9, 128.2, 128.2, 127.1, 126.1, 122.5, 117.5, 79.9, 76.6, 52.6, 43.7, 21.6, 21.5, 9.1 ppm; HRMS (ESI) calcd for $C_{21}H_{25}NO_3S$ $[M+H]^+$: 372.1633; found: 372.1626; **HPLC** (ChiralPAK AD-3, heptane/EtOH = 85:15, 0.5 mL/min) t_R = 8.02 min (major), t_R = 9.48 min (minor), 88.3% ee; $[\alpha]_D^{25}$ = -3.58 (c = 0.475, CH_2Cl_2).



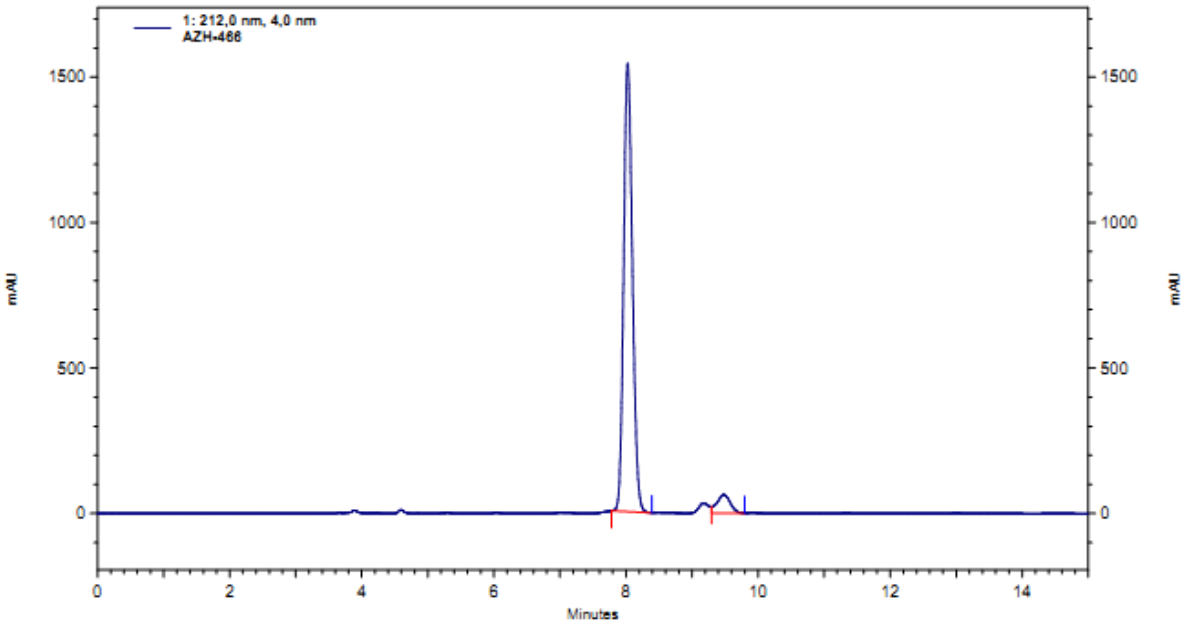




1: 212,0 nm, 4,0 nm

Results

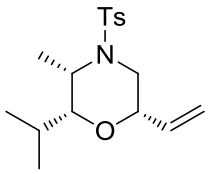
Peak Number	Retention Time	Area Percent	Area
1	8,032	49,938	809821709
2	9,465	50,062	811824830
Totals		100,000	1621646539



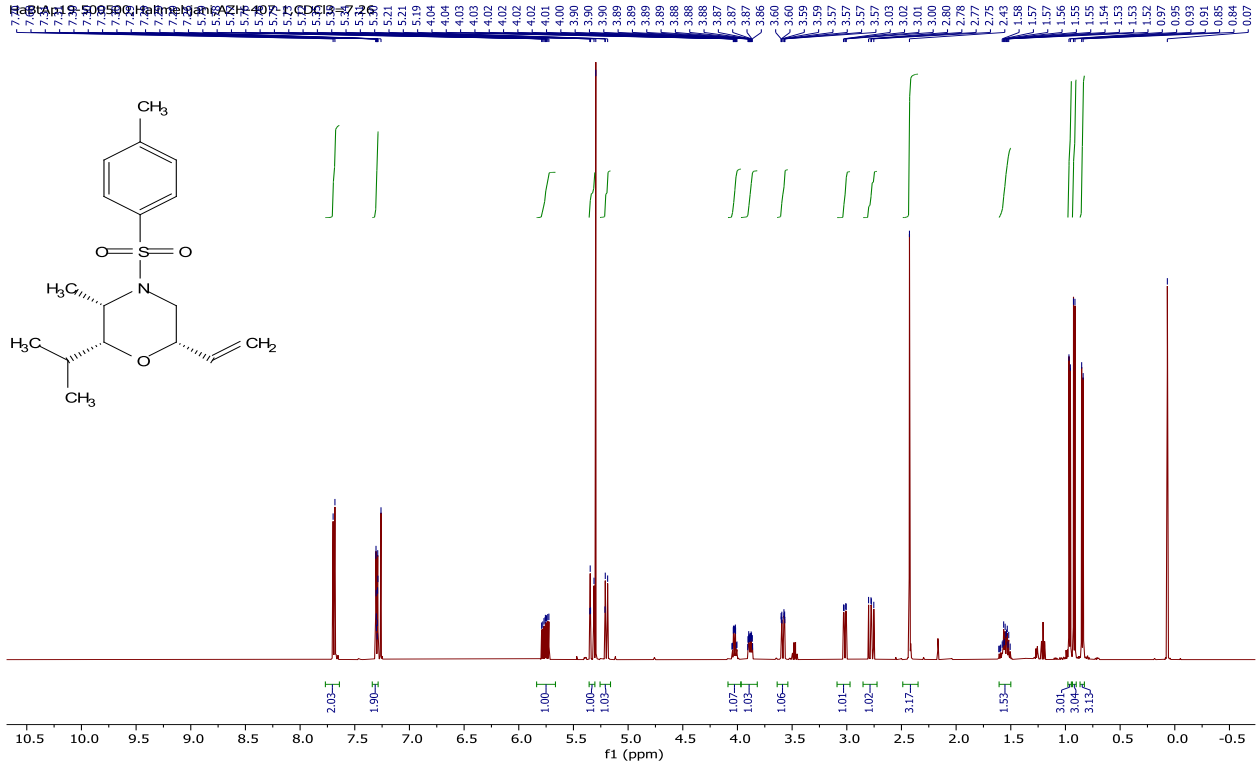
1: 212,0 nm, 4,0 nm

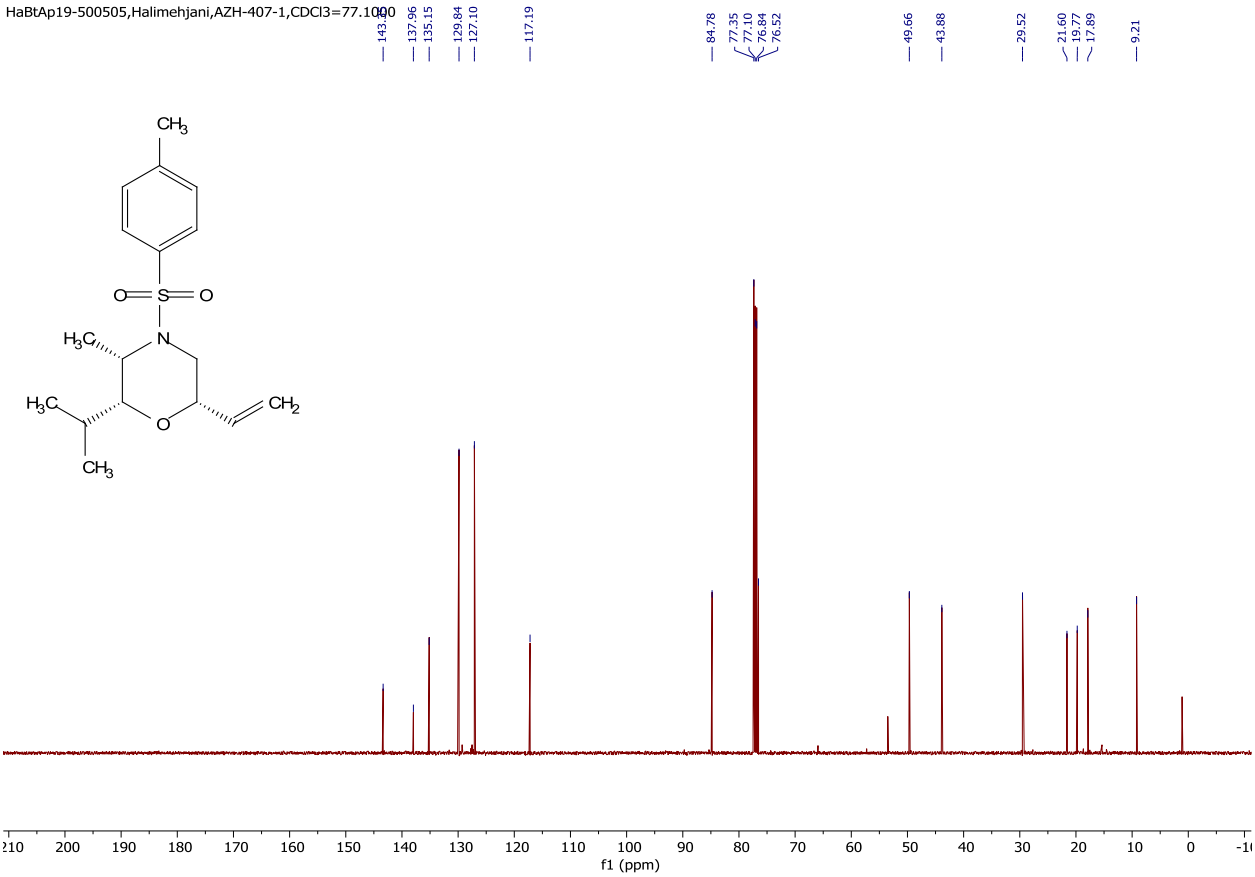
Results

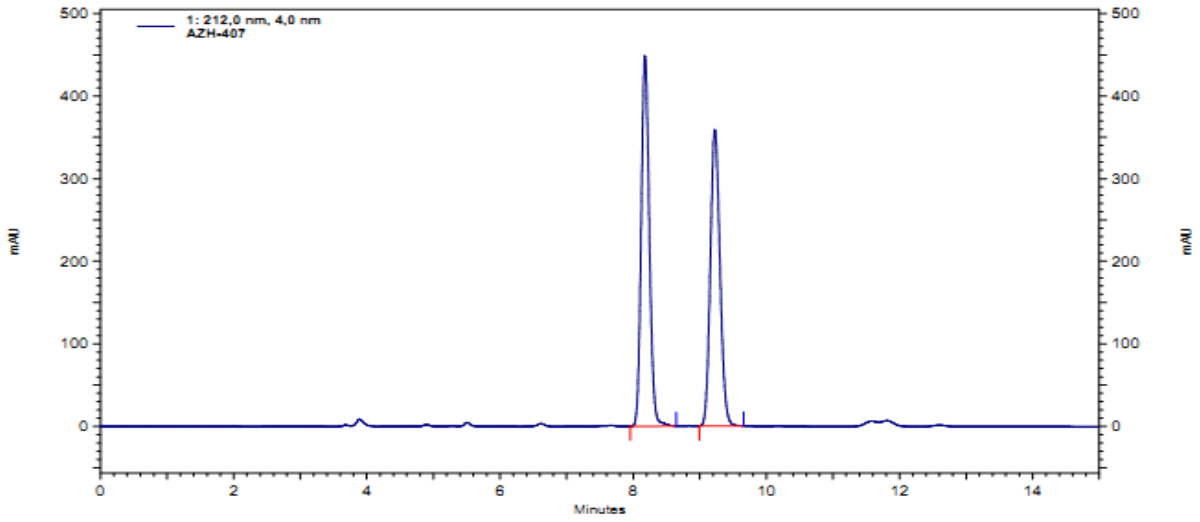
Peak Number	Retention Time	Area Percent	Area
1	8,025	94,159	1911723958
2	9,483	5,841	118587235
Totals		100,000	2030311193



(2R,3S,6S)-2-isopropyl-3-methyl-4-tosyl-6-vinylmorpholine (**4b**): ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.69 (d, J = 8.4 Hz, 2H), 7.34 – 7.29 (m, 2H), 5.76 (ddd, J = 17.4, 10.7, 5.2 Hz, 1H), 5.36 – 5.30 (m, 1H), 5.26 – 5.16 (m, 1H), 4.05–4.01 (m, 1H), 3.89–386 (m, 1H), 3.58 (ddd, J = 12.8, 3.1, 0.8 Hz, 1H), 3.02 (dd, J = 9.9, 2.5 Hz, 1H), 2.78 (dd, J = 12.8, 11.0 Hz, 1H), 2.43 (s, 3H), 1.58–1.53 (m, 2H), 0.96 (d, J = 6.5 Hz, 3H), 0.92 (d, J = 6.8 Hz, 3H), 0.85 (d, J = 6.7 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.3, 137.9, 135.1, 129.8, 127.1, 117.1, 84.7, 76.5, 49.6, 43.8, 29.5, 21.6, 19.7, 17.8, 9.2 ppm; HRMS (ESI) calcd for $C_{17}H_{25}NO_3S$ $[M+H]^+$: 324.1633; found: 324.1630; **HPLC** (ChiralPAK AD-3, heptane/EtOH = 95:5, 0.5 mL/min) t_R = 8.16 min (major), t_R = 9.24 min (minor), 90% ee; $[\alpha]_D^{25}$ = 40.83 (c = 0.6, CH_2Cl_2).


HaBtAp19-500505,Halimehjani,AZH-407-1,CDCl3=7.26
CH3
O S O
N
H3C
H3C
O
CH2
CH3
2.03
1.90
1.00
1.00
1.03
1.07
1.03
1.06
1.01
1.02
3.17
1.53
3.01
3.04
3.13
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

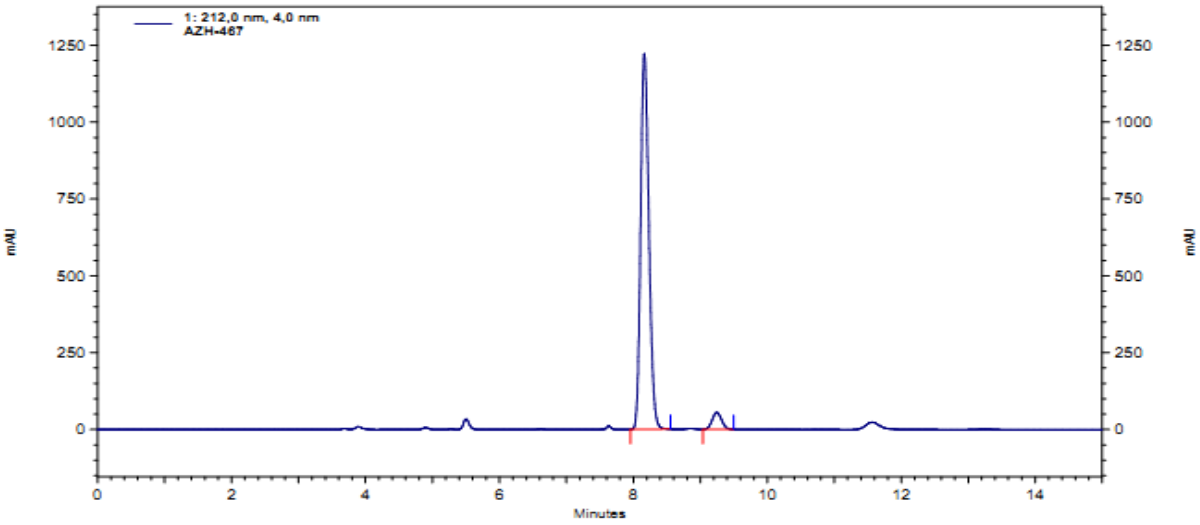

HaBtAp19-500505,Halimehjani,AZH-407-1,CDCl3=77.1000
143.88
137.96
135.15
129.84
127.10
117.19
84.78
77.35
77.10
76.84
76.52
49.66
43.88
29.52
21.60
19.77
17.89
9.21
CH3
O S O
N
H3C
H3C
O
CH2
CH3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



1: 212,0 nm, 4,0 nm

Results

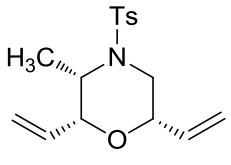
Peak Number	Retention Time	Area Percent	Area
1	8,177	51,388	511423176
2	9,227	48,612	483793879
Totals		100,000	995217055



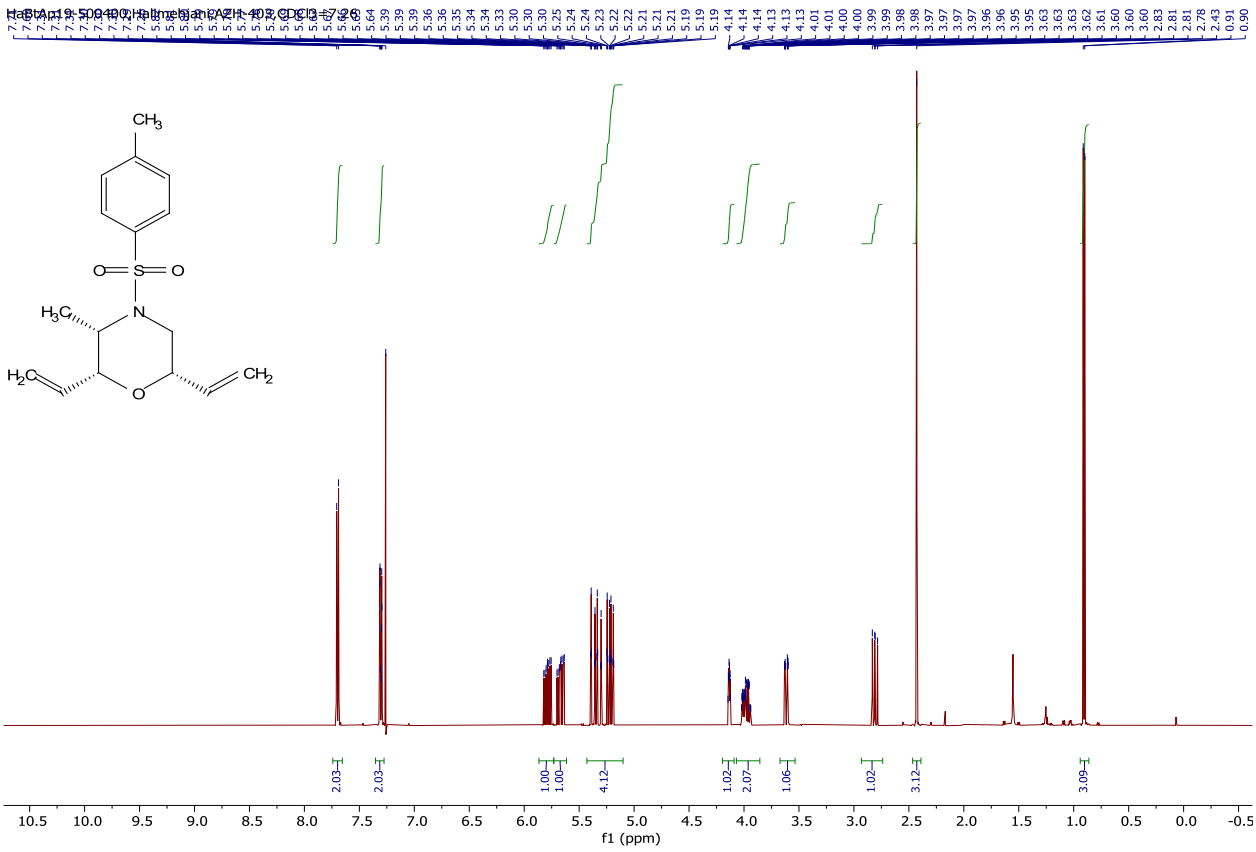
1: 212,0 nm, 4,0 nm

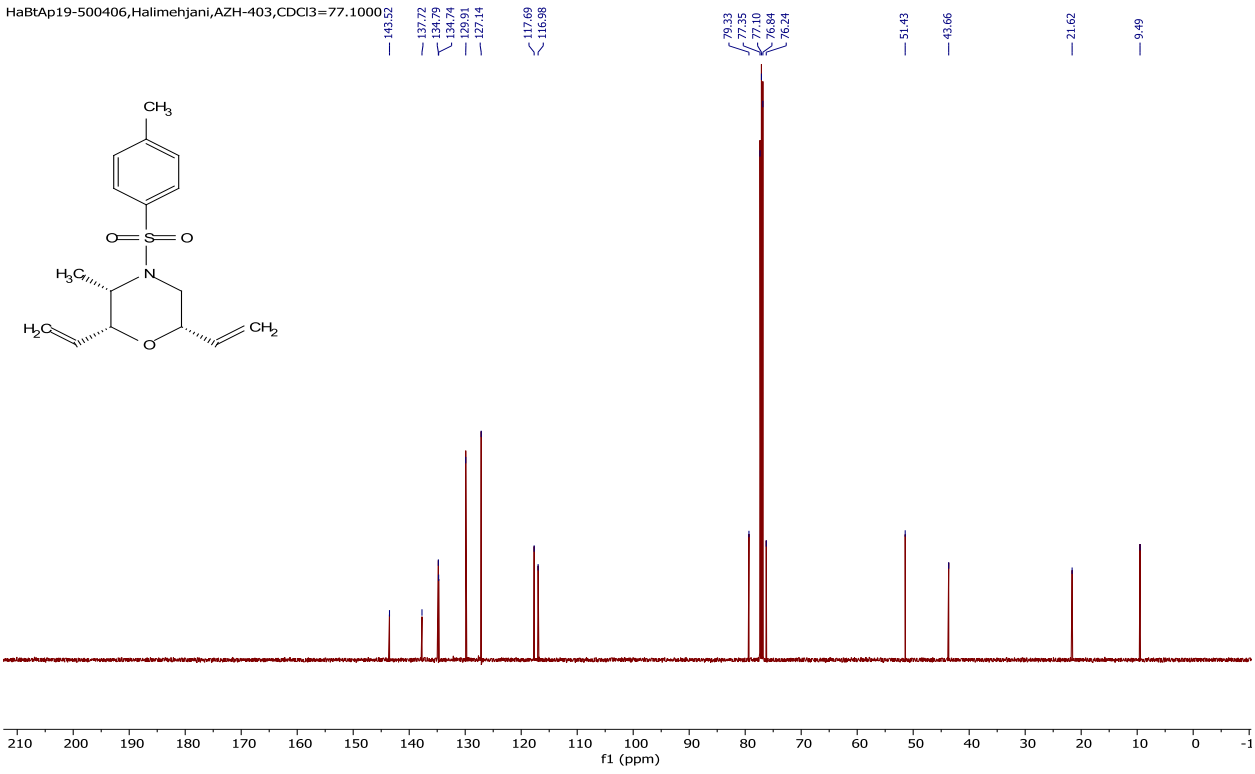
Results

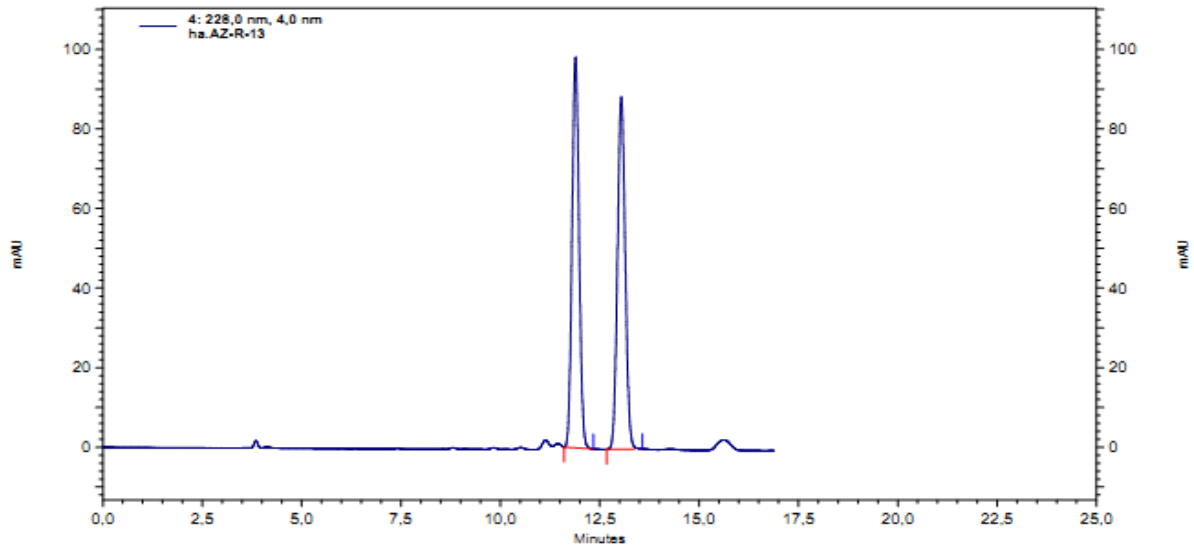
Peak Number	Retention Time	Area Percent	Area
1	8,163	95,068	1411457859
2	9,245	4,932	73224613
Totals		100,000	1484682472



(2R,3S,6S)-3-methyl-4-tosyl-2,6-divinylmorpholine (**4c**): ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.70 (d, J = 8.3 Hz, 2H), 7.35 – 7.28 (m, 2H), 5.79 (ddd, J = 17.4, 10.7, 5.5 Hz, 1H), 5.67 (ddd, J = 17.4, 10.8, 5.1 Hz, 1H), 5.43 – 5.10 (m, 4H), 4.15–4.11 (m, 1H), 4.07 – 3.86 (m, 2H), 3.61 (ddd, J = 12.9, 3.2, 0.9 Hz, 1H), 2.81 (dd, J = 12.9, 11.0 Hz, 1H), 2.43 (s, 3H), 0.91 (d, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.5, 137.7, 134.7, 134.7, 129.9, 127.1, 117.6, 116.9, 79.3, 76.2, 51.4, 43.6, 21.6, 9.4 ppm; HRMS (ESI) calcd for $C_{16}H_{21}NO_3S$ $[M+H]^+$: 308.1320; found: 308.1318; **HPLC** (ChiralPAK AD-3, heptane/isopropanol = 95:5, 0.5 mL/min) t_R = 11.88 min (minor), t_R = 13.00 min (major), 89% ee; $[\alpha]_D^{25}$ = 53.7 (c = 0.525, CH_2Cl_2).



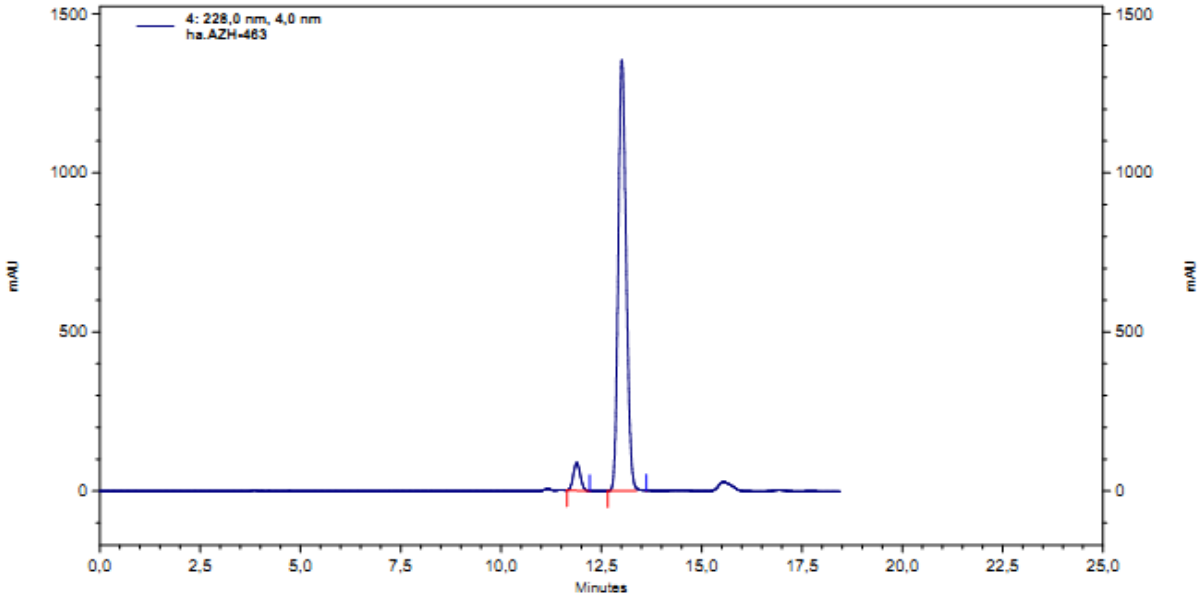




4: 228,0 nm, 4,0 nm

Results

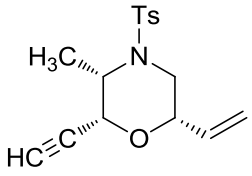
Peak Number	Retention Time	Area Percent	Area
1	11,890	49,898	161415316
2	13,042	50,102	162074809
Totals		100,000	323490125



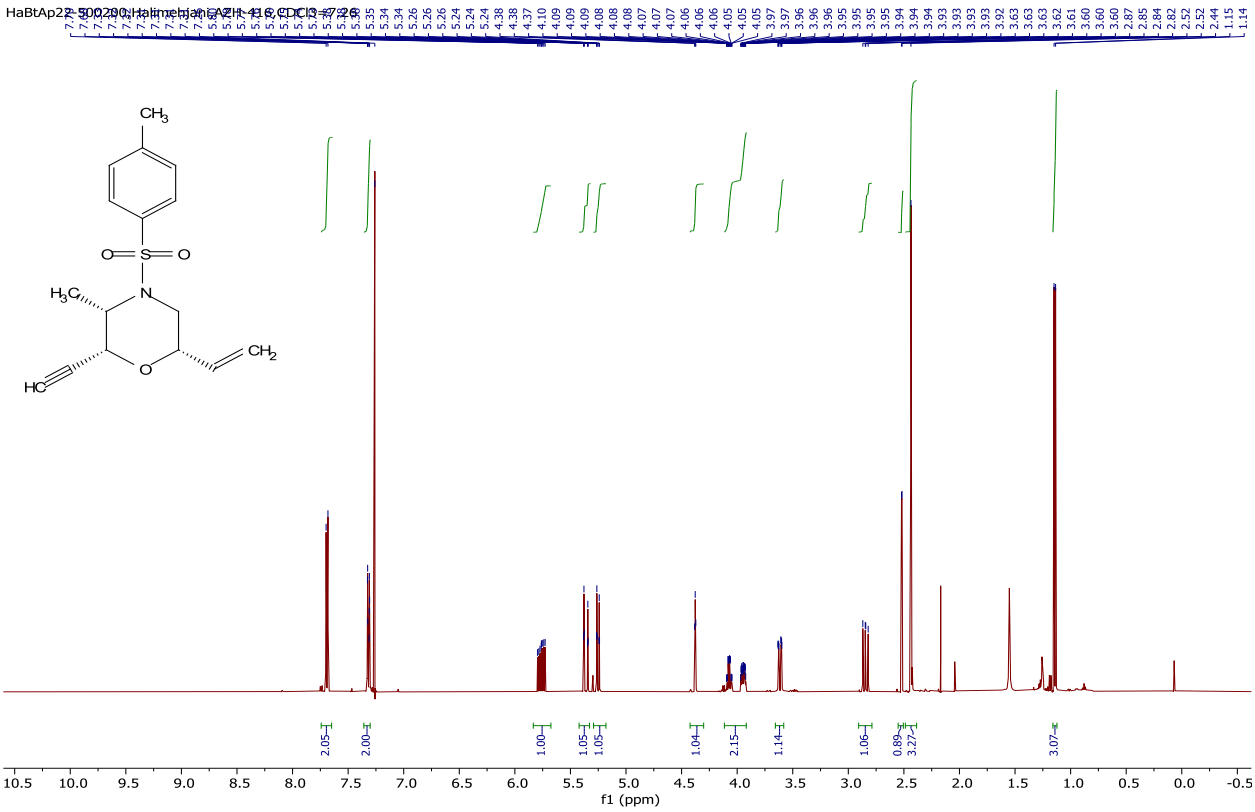
4: 228,0 nm, 4,0 nm

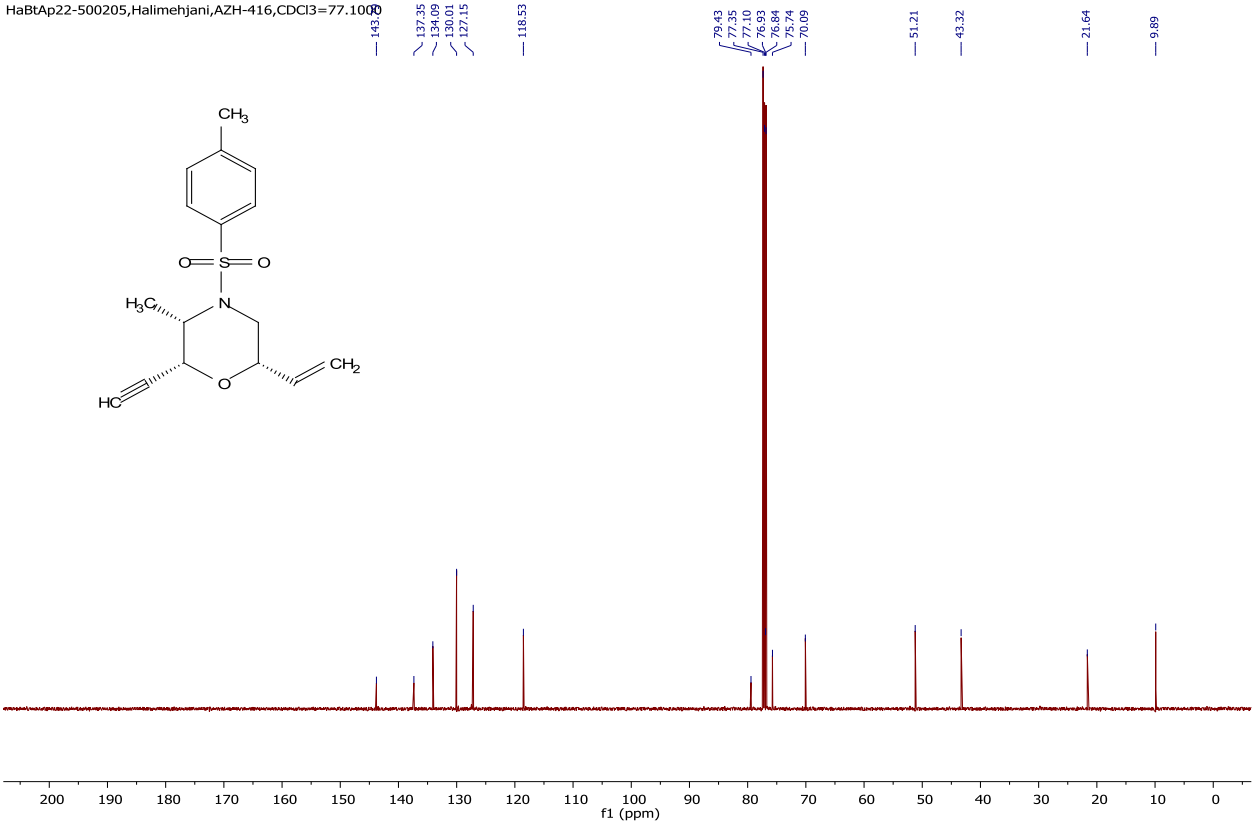
Results

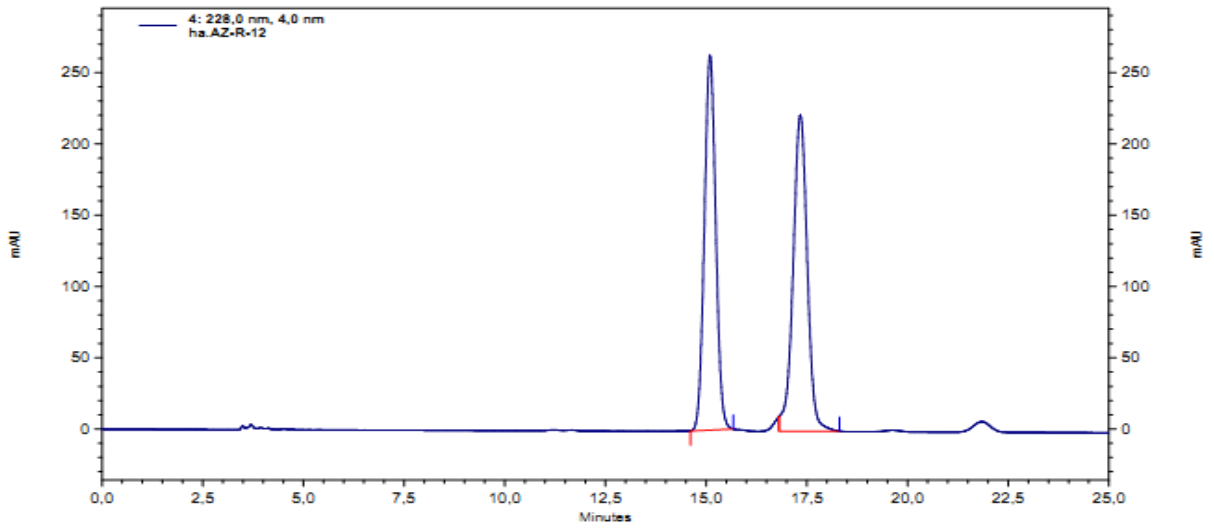
Peak Number	Retention Time	Area Percent	Area
1	11,885	5,380	143359731
2	13,008	94,620	2521452816
Totals		100,000	2664812547



(2R,3S,6S)-2-ethynyl-3-methyl-4-tosyl-6-vinylmorpholine (**4d**): ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.69 (d, J = 8.3 Hz, 2H), 7.36 – 7.30 (m, 2H), 5.76 (ddd, J = 17.4, 10.7, 5.7 Hz, 1H), 5.36 (dt, J = 17.4, 1.3 Hz, 1H), 5.25 (dt, J = 10.7, 1.2 Hz, 1H), 4.38 (t, J = 2.6 Hz, 1H), 4.11 – 3.92 (m, 2H), 3.62 (ddd, J = 13.2, 3.1, 0.9 Hz, 1H), 2.85 (dd, J = 13.2, 10.9 Hz, 1H), 2.52 (d, J = 2.3 Hz, 1H), 2.44 (s, 3H), 1.14 (d, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.7, 137.3, 134.0, 130.0, 127.1, 118.5, 79.4, 76.9, 75.7, 70.0, 51.2, 43.3, 21.6, 9.8 ppm; HRMS (ESI) calcd for $C_{16}H_{19}NO_3S$ $[M+H]^+$: 306.1164; found: 306.1161; **HPLC** (L-C4 column, heptane/isopropanol = 90:10, 0.5 mL/min) t_R = 15.1 min (minor), t_R = 17.3 min (major), 90.5% ee; $[\alpha]_D^{25}$ = 8.18 (c = 0.22, CH_2Cl_2).


HaBtAp22-500200,Halimehjani,AZH-416,CDCl3=7.26
CH3
O=S=O
H3C
N
O
CH2
HC
2.05
2.00
1.00
1.05
1.05
1.04
2.15
1.14
1.06
0.89
3.27
3.07
f1 (ppm)

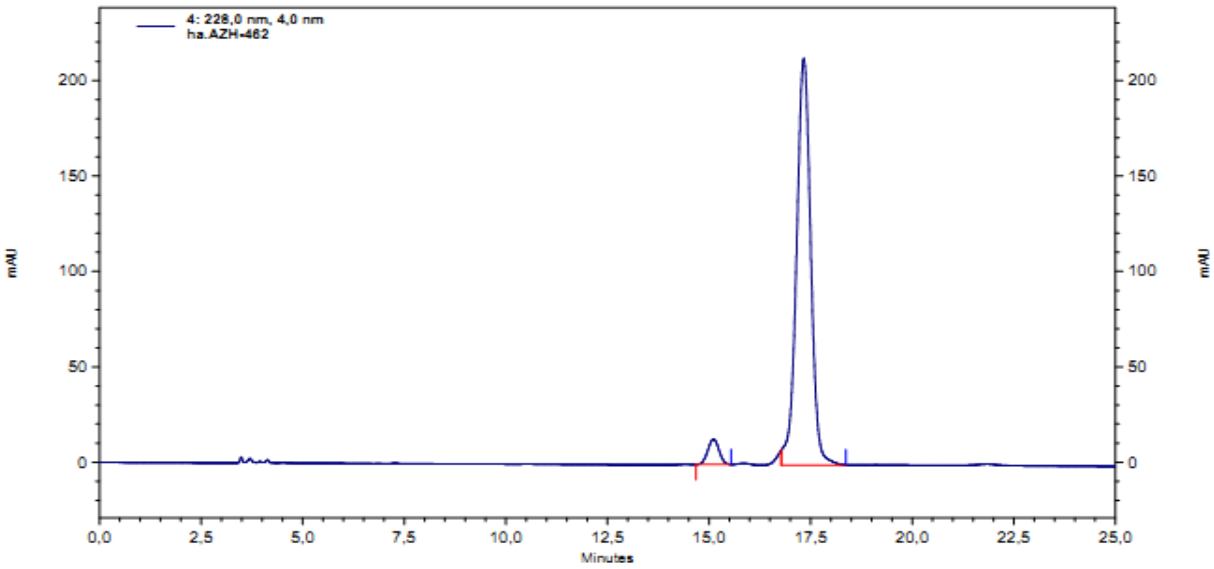

HaBtAp22-500205,Halimehjani,AZH-416,CDCl3=77.1000
143.30
137.35
134.09
130.01
127.15
118.53
79.43
77.35
77.10
76.93
76.84
75.74
70.09
51.21
43.32
21.64
9.89
CH3
O=S=O
H3C
N
O
CH2
HC
f1 (ppm)



4: 228,0 nm, 4,0 nm

Results

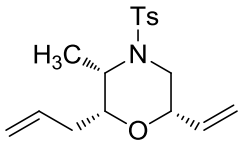
Peak Number	Retention Time	Area Percent	Area
1	15,093	48,719	691987432
2	17,337	51,281	728366542
Totals		100,000	1420353974



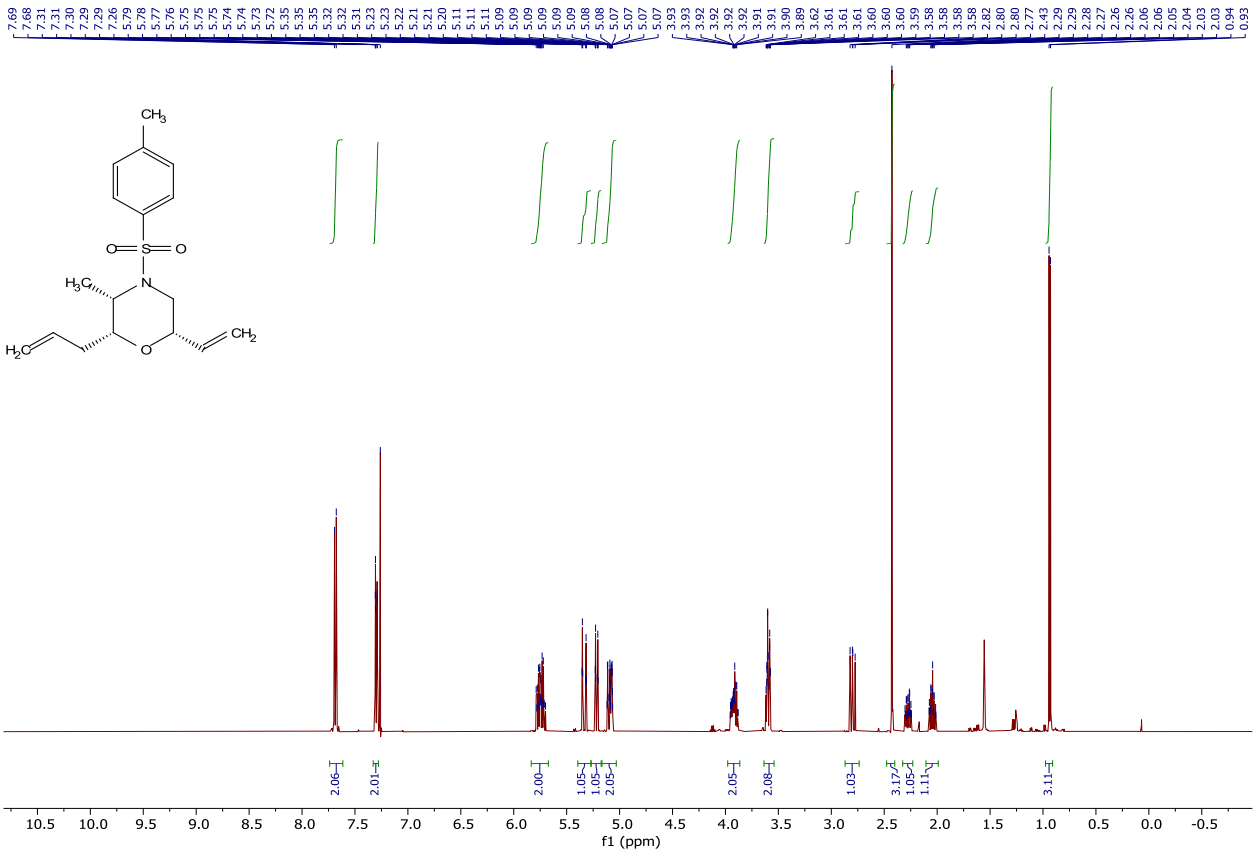
4: 228,0 nm, 4,0 nm

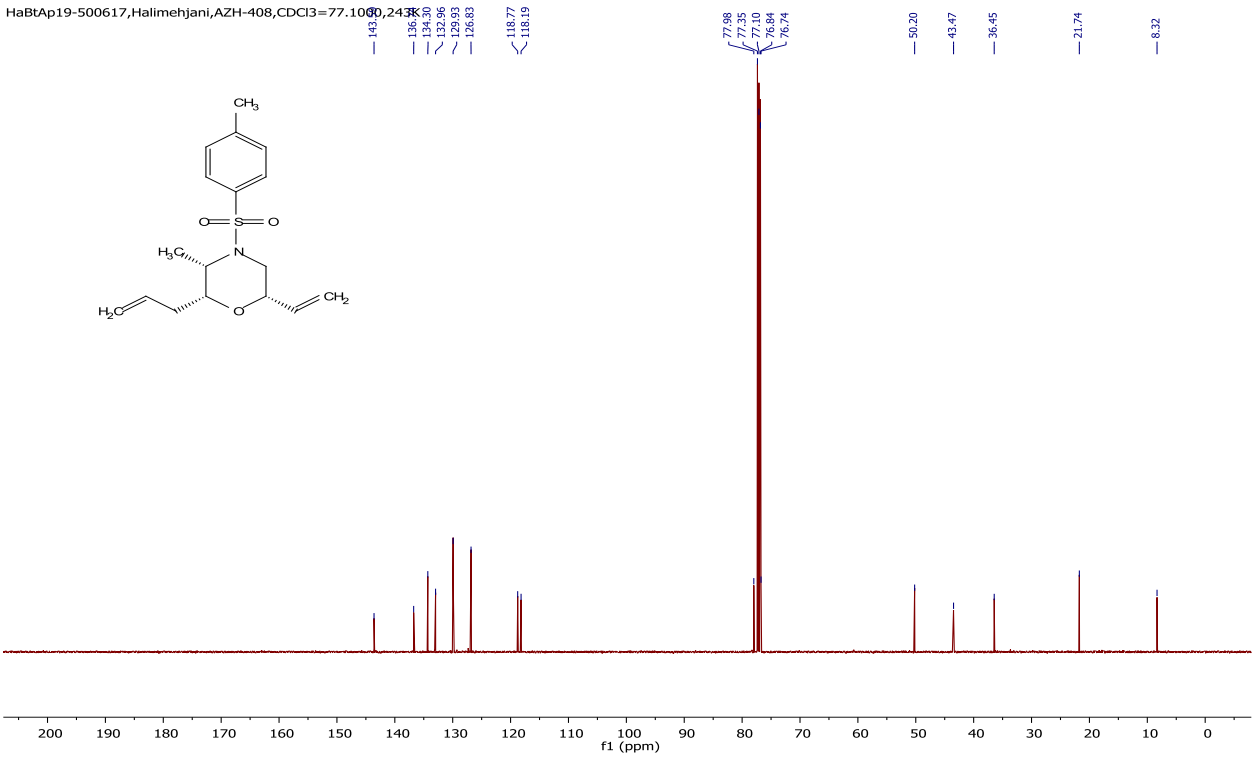
Results

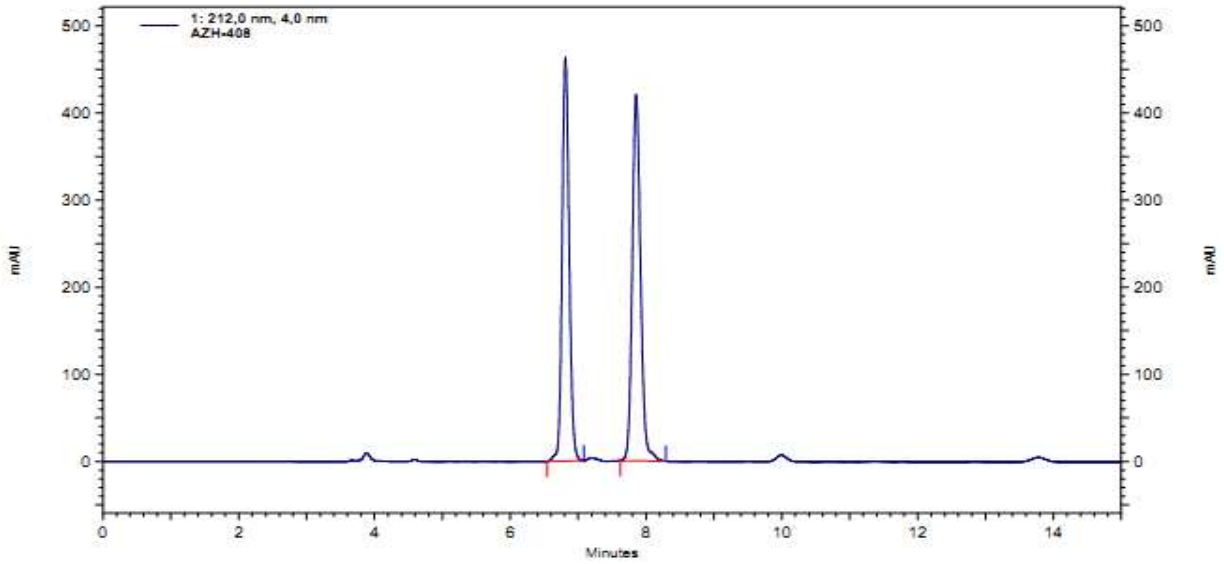
Peak Number	Retention Time	Area Percent	Area
1	15,107	4,729	34492020
2	17,328	95,271	694909296
Totals		100,000	729401316



(2R,3S,6S)-2-allyl-3-methyl-4-tosyl-6-vinylmorpholine (**4e**): ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.68 (d, J = 8.3 Hz, 2H), 7.33 – 7.28 (m, 2H), 5.83 – 5.67 (m, 2H), 5.33 (dt, J = 17.4, 1.5 Hz, 1H), 5.22 (dt, J = 10.7, 1.4 Hz, 1H), 5.17 – 5.03 (m, 2H), 3.98 – 3.86 (m, 2H), 3.64 – 3.54 (m, 2H), 2.80 (dd, J = 13.0, 11.0 Hz, 1H), 2.43 (s, 3H), 2.29–2.26 (m, 1H), 2.11 – 1.99 (m, 1H), 0.94 (d, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.5, 136.7, 134.3, 132.9, 129.9, 126.8, 118.7, 118.1, 77.9, 76.7, 50.2, 43.4, 36.4, 21.7, 8.3 ppm; HRMS (ESI) calcd for $C_{17}H_{23}NO_3S$ $[M+H]^+$: 322.1477; found: 322.1474; **HPLC** (ChiralPAK AD-3, heptane/EtOH = 85:15, 0.5 mL/min) t_R = 6.8 min (minor), t_R = 7.8 min (major), 87%; $[\alpha]_D^{25}$ = 41.71 (c = 0.35, CH_2Cl_2).



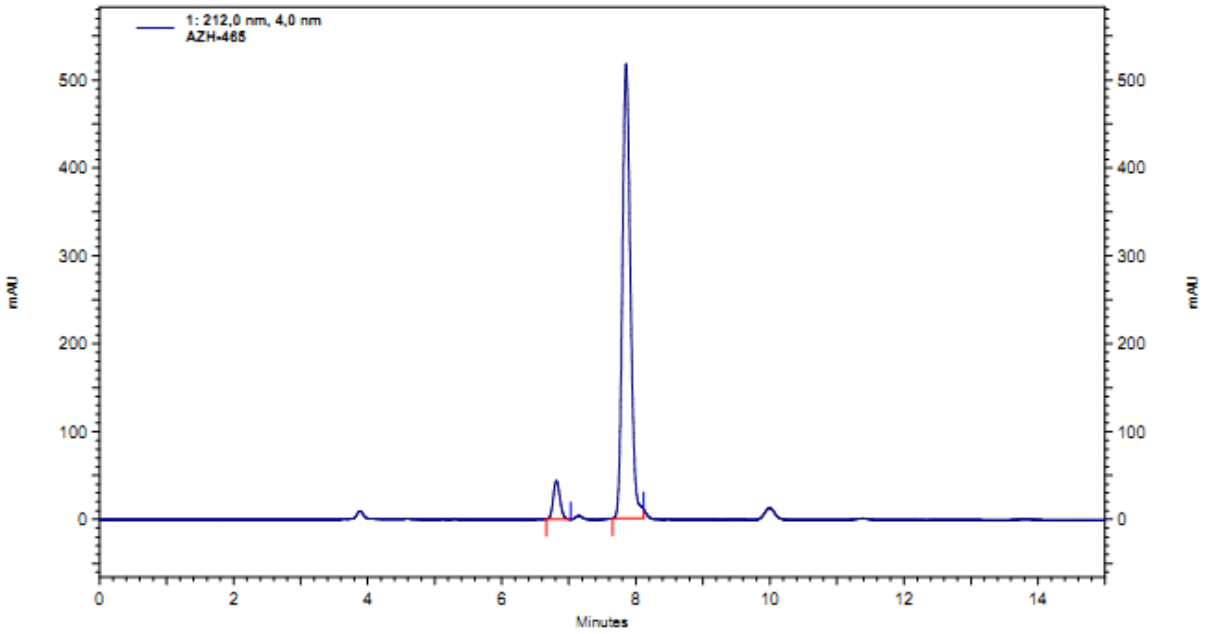




1: 212,0 nm, 4,0 nm

Results

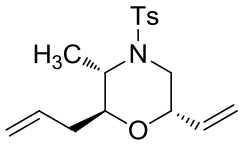
Peak Number	Retention Time	Area Percent	Area
1	6,812	48,213	446505996
2	7,853	51,787	479607490
Totals		100,000	926113486



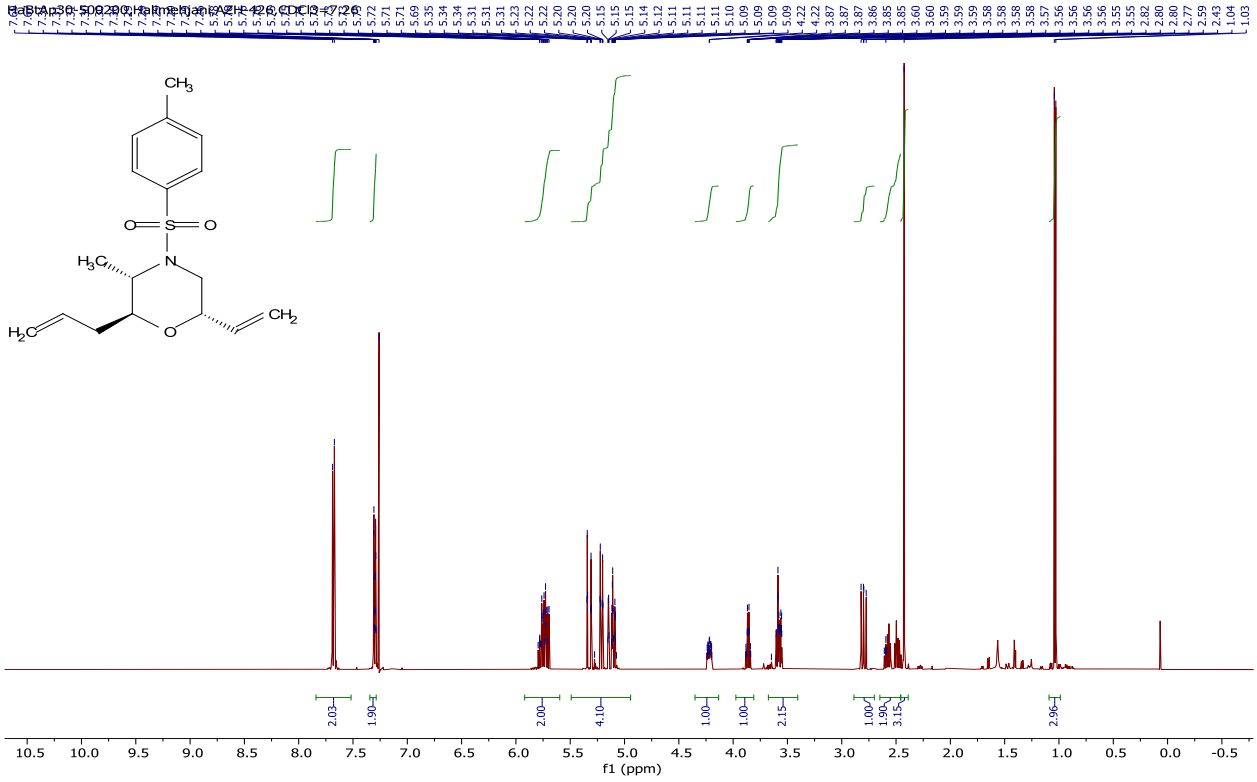
1: 212,0 nm, 4,0 nm

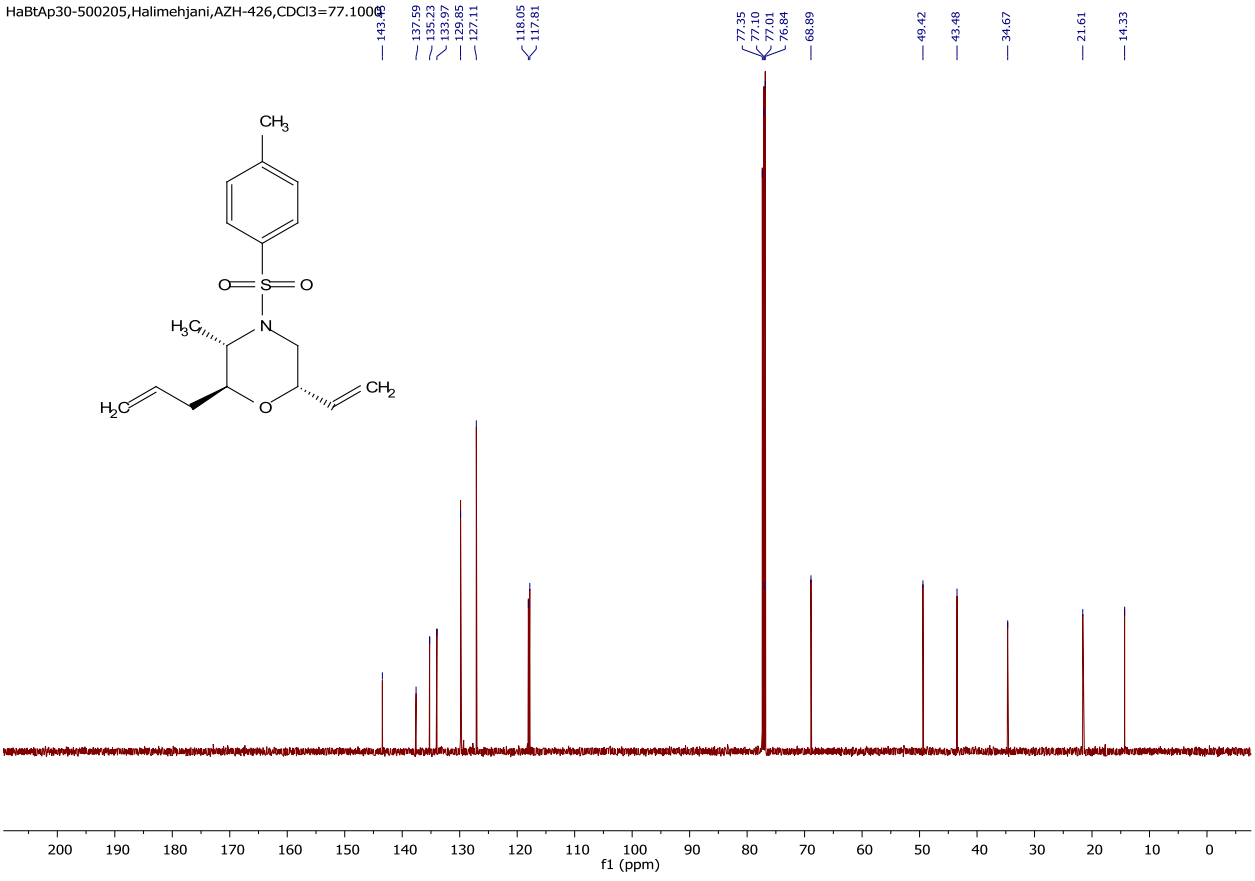
Results

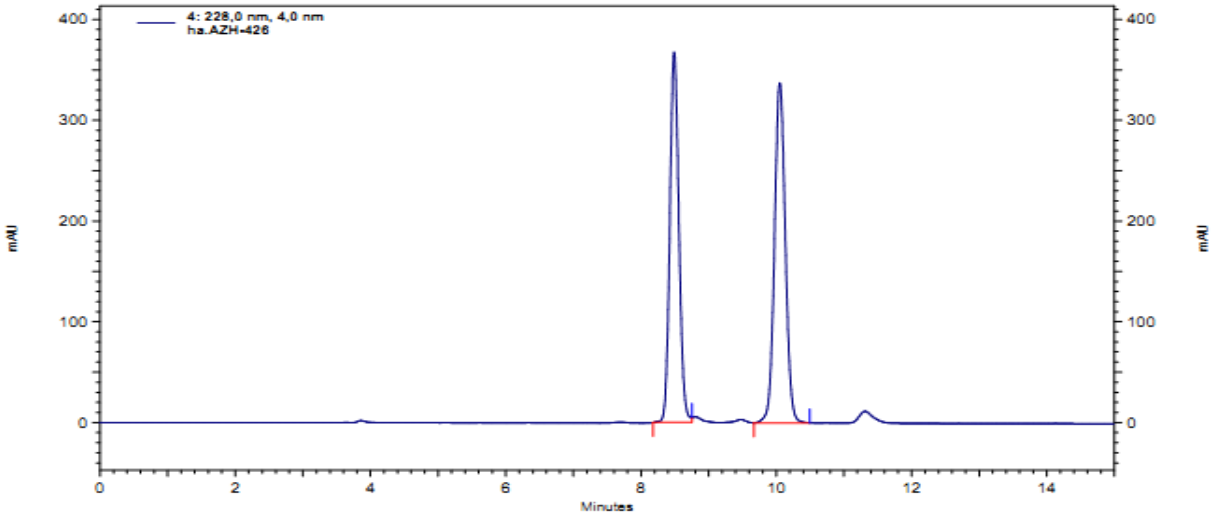
Peak Number	Retention Time	Area Percent	Area
1	6,815	6,598	40926775
2	7,855	93,402	579396913
Totals		100,000	620323688



(2S,3S,6S)-2-allyl-3-methyl-4-tosyl-6-vinylmorpholine (**4f**): ppm; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.68 (d, J = 8.3 Hz, 2H), 7.34 – 7.29 (m, 2H), 5.92 – 5.60 (m, 2H), 5.49 – 4.94 (m, 4H), 4.24–4.20 (m, 1H), 3.88–3.84 (m, 1H), 3.68 – 3.40 (m, 2H), 2.80 (dd, J = 12.5, 11.0 Hz, 1H), 2.65 – 2.46 (m, 2H), 2.43 (s, 3H), 1.04 (d, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.4, 137.5, 135.2, 133.9, 129.8, 127.1, 118.0, 117.8, 77.0, 68.8, 49.4, 43.4, 34.6, 21.6, 14.3 ppm; HRMS (ESI) calcd for $C_{17}H_{23}NO_3S$ $[M+H]^+$: 322.1477; found: 322.1476; **HPLC** (ChiralPAK AD-3, heptane/Isopropanol = 90:10, 0.5 mL/min) t_R = 8.46 min (minor), t_R = 9.97 min (major), 88.5% ee; $[\alpha]_D^{25}$ = 31.06 (c = 0.2125, CH_2Cl_2).


HaBtAp30-500200,Halimehjani,AZH-426,CDCl3=7.26
CH3
O=S=O
N
H3C
H2C
O
CH2
2.03
1.90
2.00
4.10
1.00
1.00
2.15
1.00
1.90
3.15
2.96
f1 (ppm)

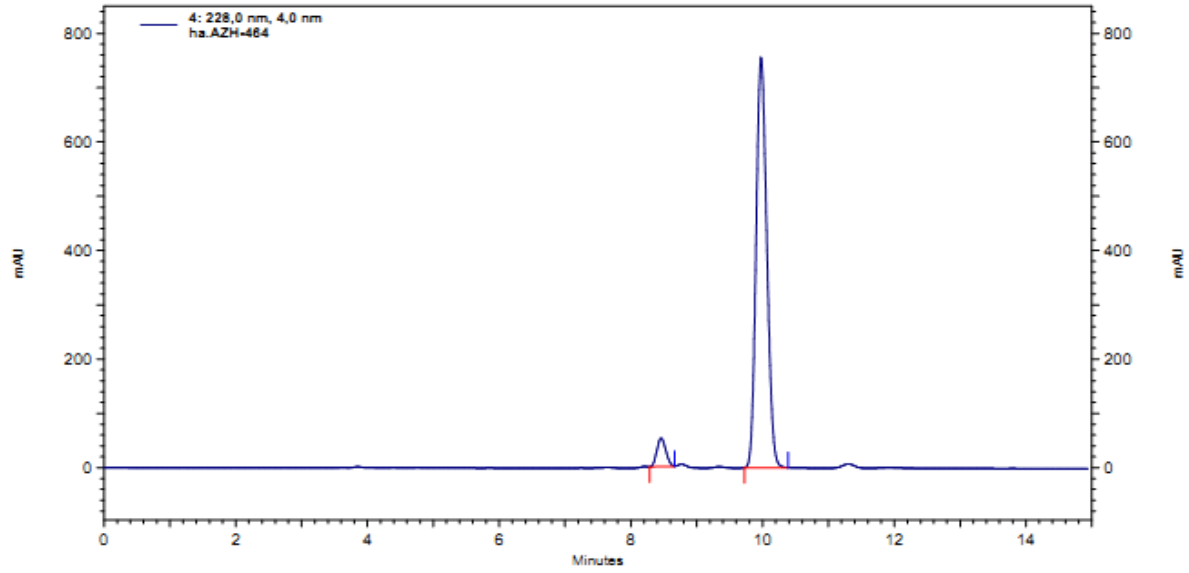

HaBtAp30-500205,Halimehjani,AZH-426,CDCl3=77.1006
143.44
137.59
135.23
133.97
129.85
127.11
118.05
117.81
77.35
77.10
77.01
76.84
68.89
49.42
43.48
34.67
21.61
14.33
CH3
O=S=O
N
H3C
H2C
O
CH2
f1 (ppm)



4: 228,0 nm, 4,0 nm

Results

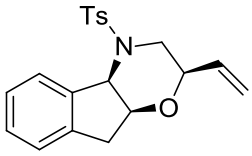
Peak Number	Retention Time	Area Percent	Area
1	8,487	47,805	461383618
2	10,053	52,195	503756321
Totals		100,000	965139939



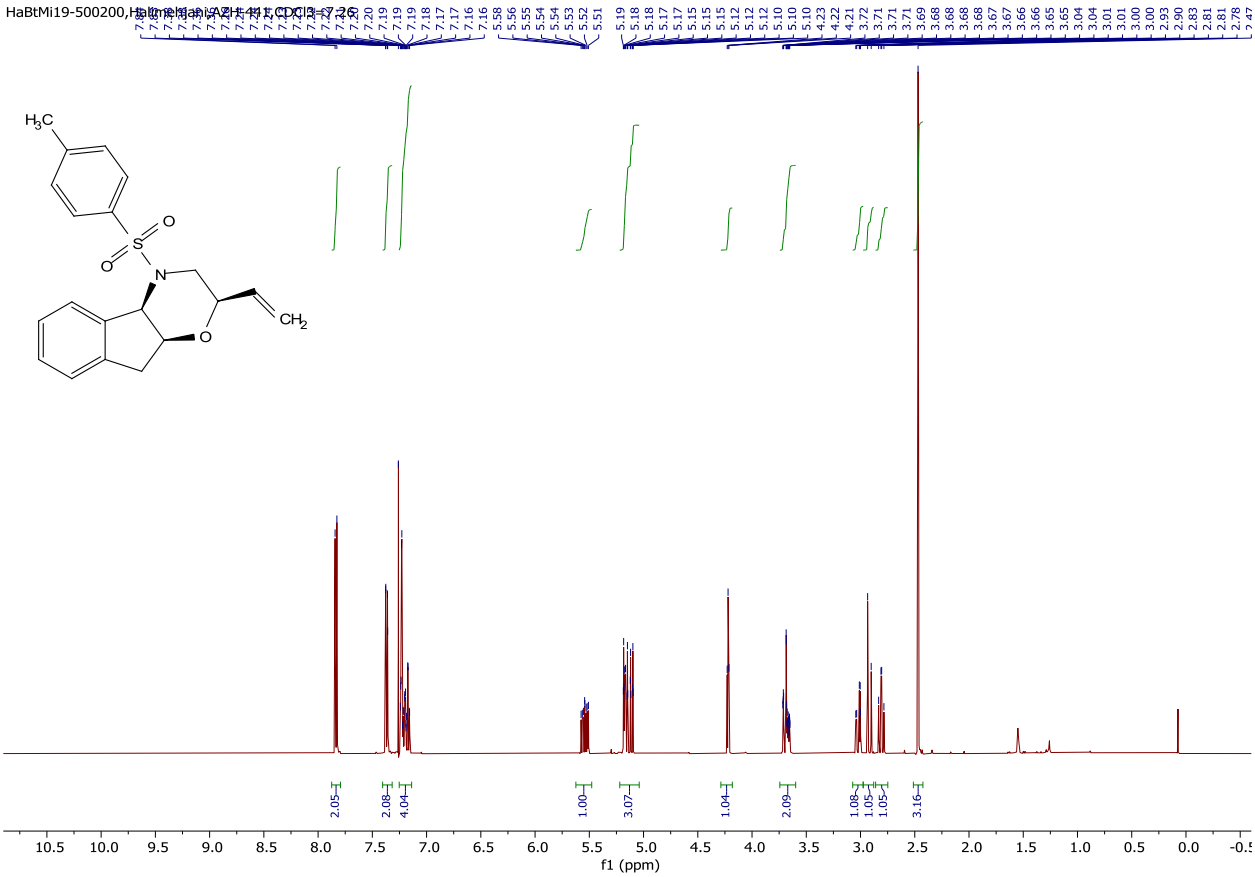
4: 228,0 nm, 4,0 nm

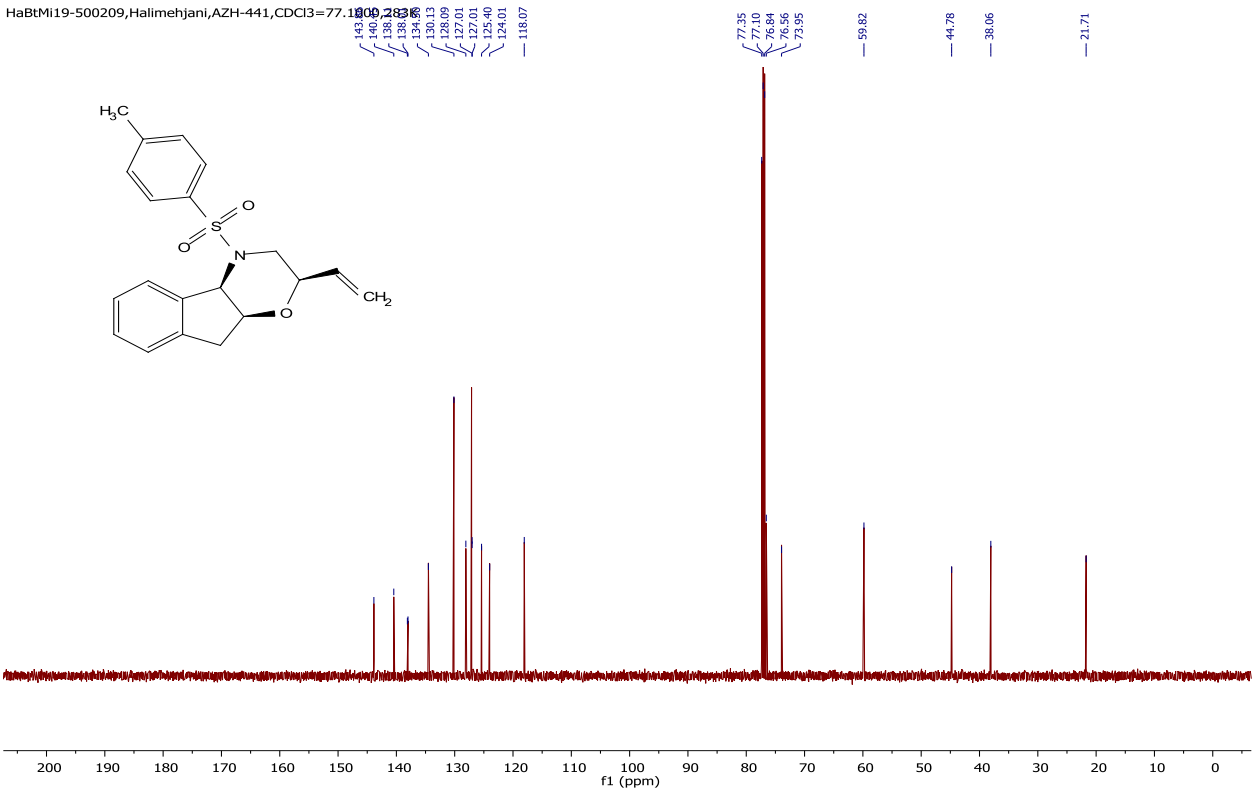
Results

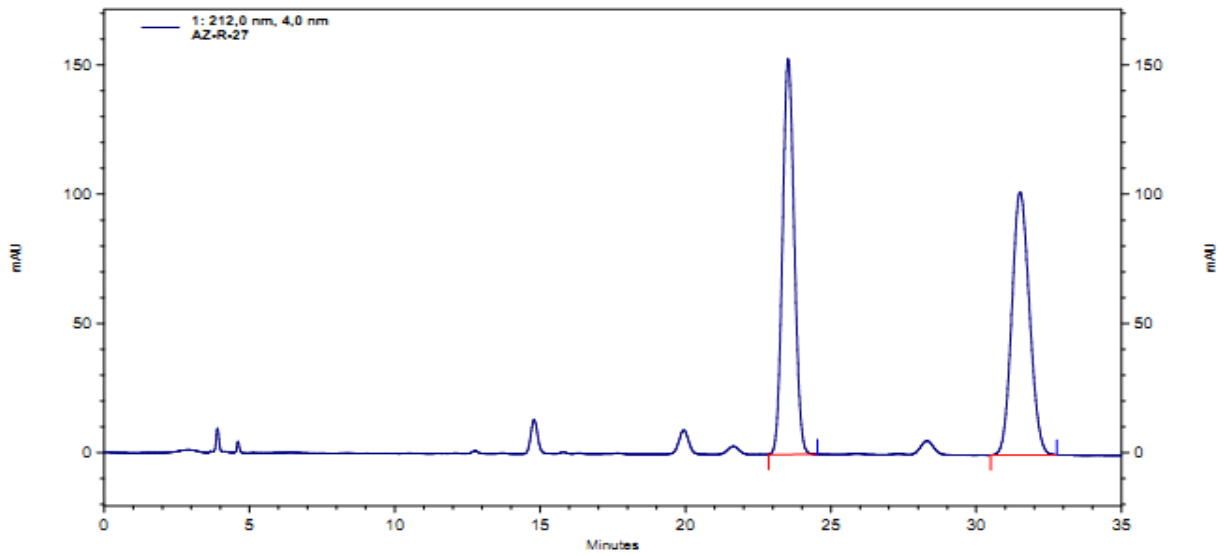
Peak Number	Retention Time	Area Percent	Area
1	8,460	5,518	66625326
2	9,973	94,482	1140831020
Totals		100,000	1207456346



(2R,4aR,9aS)-4-tosyl-2-vinyl-2,3,4,4a,9,9a-hexahydroindeno[2,1-b][1,4]oxazine (**4g**): ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.84 (d, J = 8.3 Hz, 2H), 7.41 – 7.32 (m, 2H), 7.25 – 7.14 (m, 4H), 5.54 (ddd, J = 17.4, 10.7, 5.8 Hz, 1H), 5.22 – 5.04 (m, 3H), 4.22 (t, J = 4.0 Hz, 1H), 3.74 – 3.60 (m, 2H), 3.07 – 2.98 (m, 1H), 2.92 (d, J = 16.4 Hz, 1H), 2.86 – 2.75 (m, 1H), 2.47 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.8, 140.4, 138.1, 138.0, 134.5, 130.1, 128.0, 127.0, 127.0, 125.4, 124.0, 118.0, 76.5, 73.9, 59.8, 44.7, 38.0, 21.7 ppm; HRMS (ESI) calcd for $C_{20}H_{21}NO_3S$ $[M+H]^+$: 356.1320; found: 356.1314; **HPLC** (ChiralPAK AD-3, heptane/EtOH = 85:15, 0.5 mL/min) t_R = 24.08 min (minor), t_R = 31.13 min (major), >99.9% ee; $[\alpha]_D^{25}$ = -22.85 (c = 0.7, CH_2Cl_2).



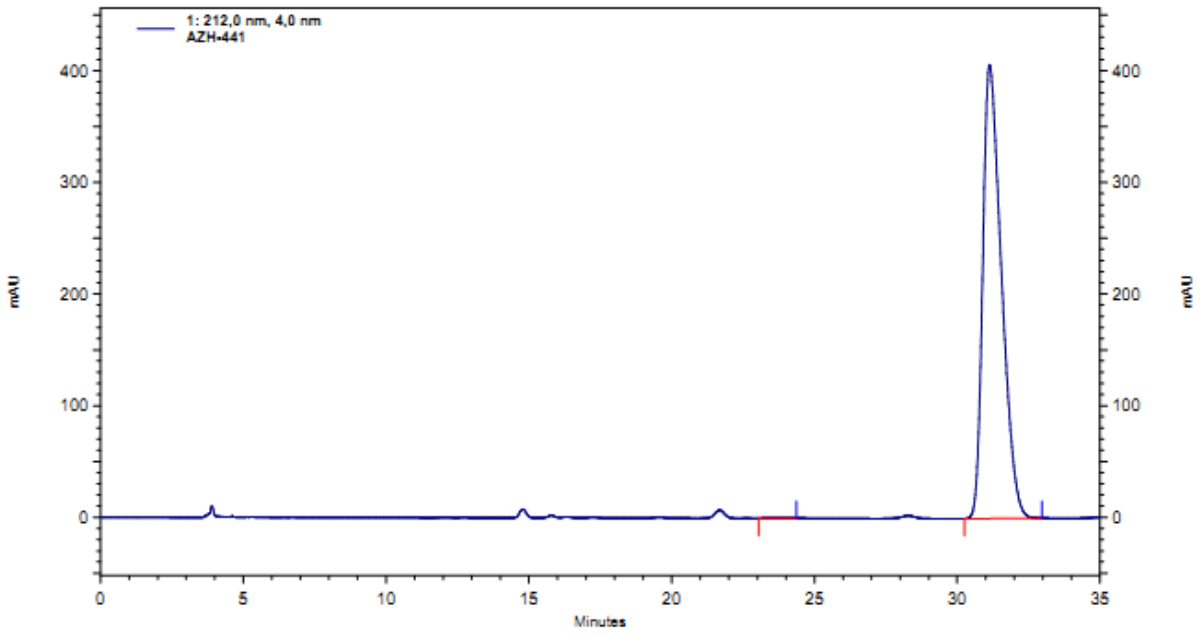




1: 212,0 nm, 4,0 nm

Results

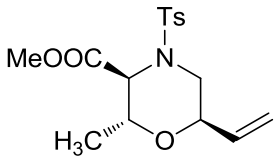
Peak Number	Retention Time	Area Percent	Area
1	23,530	49,978	575211708
2	31,508	50,022	575716402
Totals		100,000	1150928110



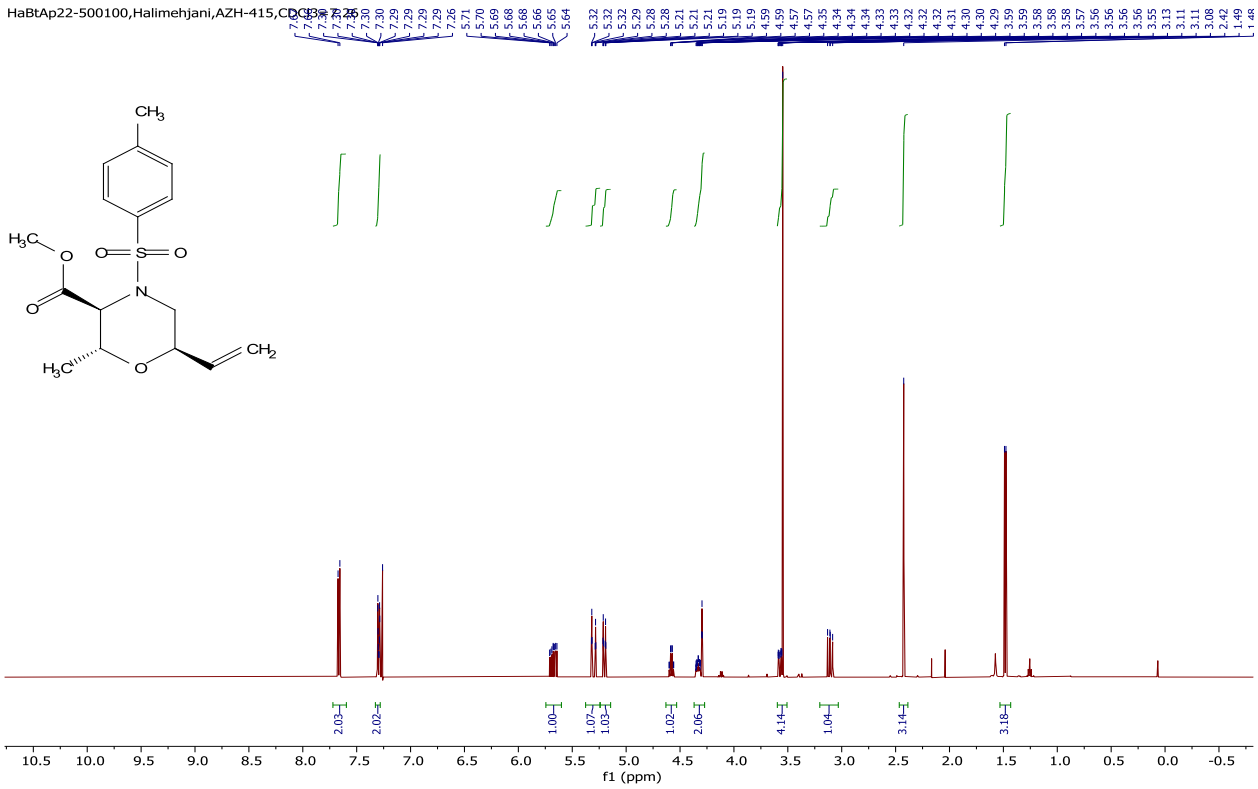
1: 212,0 nm, 4,0 nm

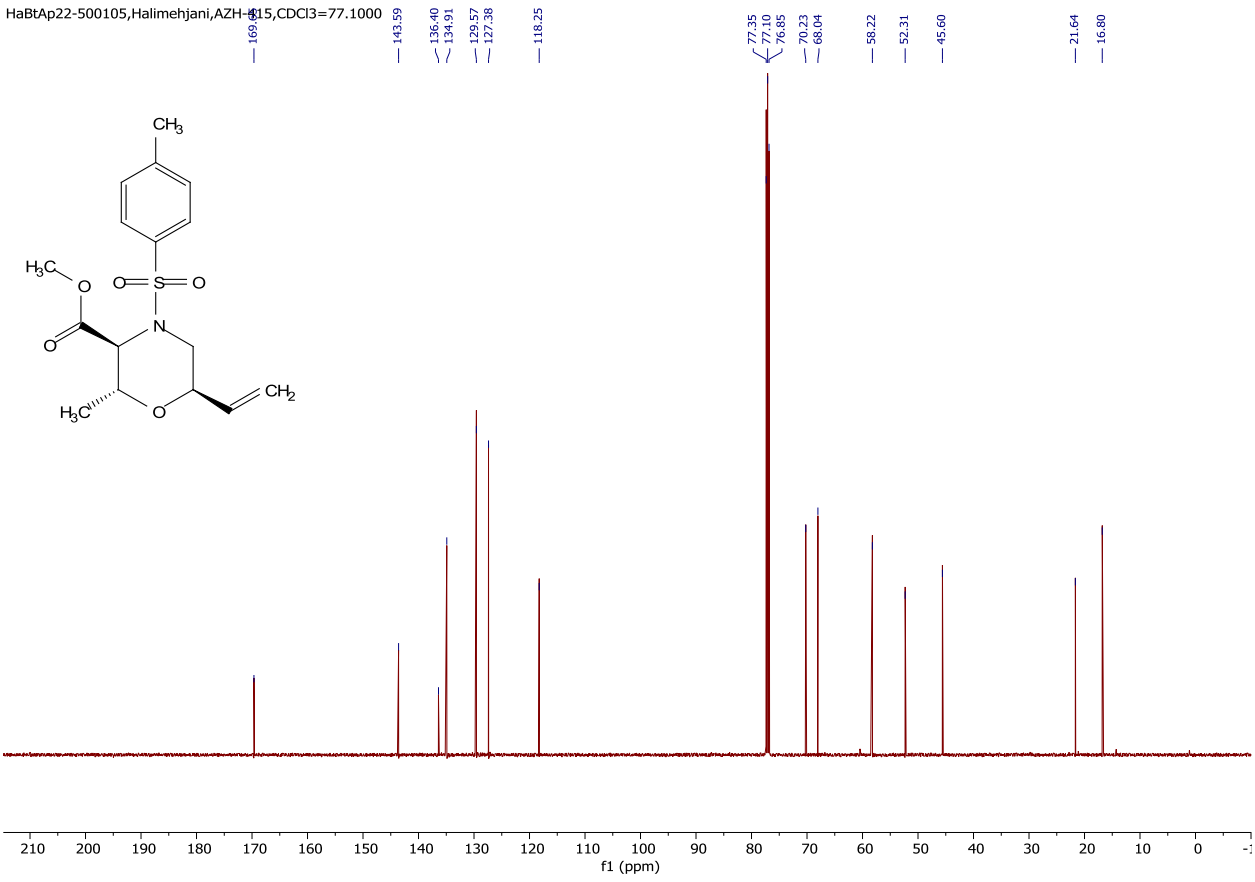
Results

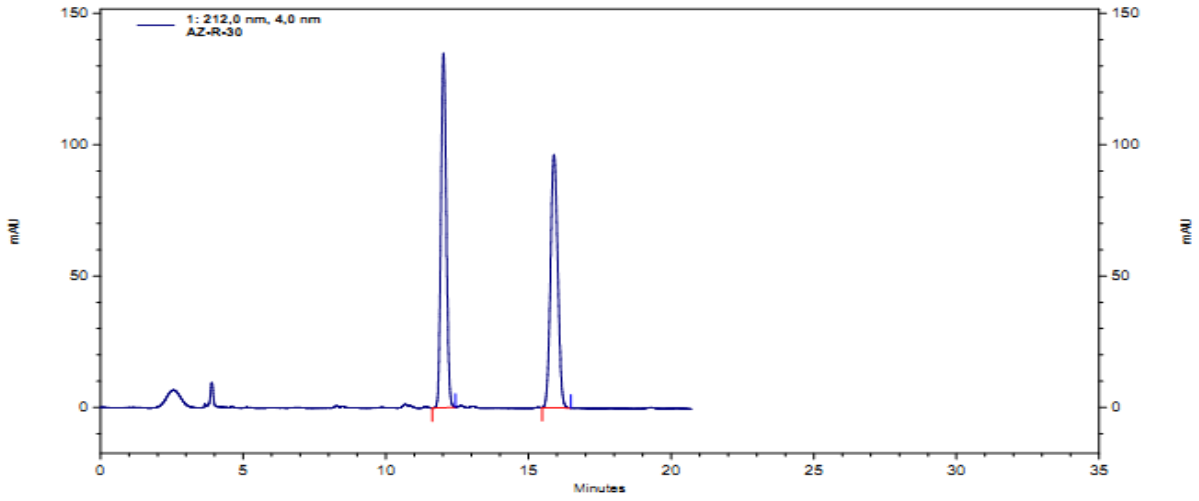
Peak Number	Retention Time	Area Percent	Area
1	24,085	0,041	1025933
2	31,133	99,959	2476899699
Totals		100,000	2477925632



(2R,3S,6R)-methyl 2-methyl-4-tosyl-6-vinylmorpholine-3-carboxylate (**4h**): ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.66 (d, *J* = 8.4 Hz, 2H), 7.33 – 7.28 (m, 2H), 5.68 (ddd, *J* = 17.3, 10.6, 5.9 Hz, 1H), 5.30 (dt, *J* = 17.4, 1.3 Hz, 1H), 5.20 (dt, *J* = 10.6, 1.2 Hz, 1H), 4.59–4.57 (m, 1H), 4.37 – 4.27 (m, 2H), 3.55 (s, 4H), 3.11 (dd, *J* = 12.6, 10.9 Hz, 1H), 2.42 (s, 3H), 1.48 (d, *J* = 6.7 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.6, 143.5, 136.4, 134.9, 129.5, 127.3, 118.2, 70.2, 68.0, 58.2, 52.3, 45.6, 21.6, 16.8ppm; HRMS (ESI) calcd for $C_{16}H_{21}NO_5S$ $[M+H]^+$: 340.1219; found: 340.1215; **HPLC** (ChiralPAK AD-3, Heptane/EtOH = 85:15, 0.5 mL/min) t_R = 11.7 min (major), t_R = 15.2 min (minor), >98% ee; $[\alpha]_D^{25}$ = -87.5 (c = 0.45, CH_2Cl_2).


HaBtAp22-500100,Halimehjani,AZH-415,CDCl3=7.26
f1 (ppm)

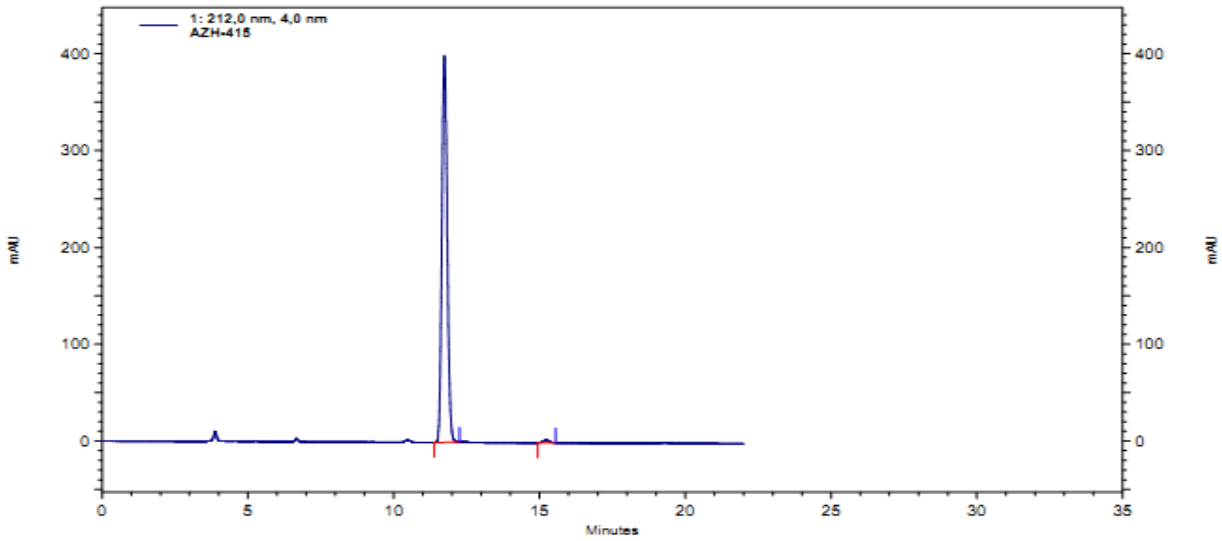

HaBtAp22-500105,Halimehjani,AZH-415,CDCl3=77.1000
f1 (ppm)



1: 212,0 nm, 4,0 nm

Results

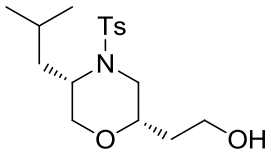
Peak Number	Retention Time	Area Percent	Area
1	12,022	50,529	233604385
2	15,895	49,471	228711137
Totals		100,000	462315522



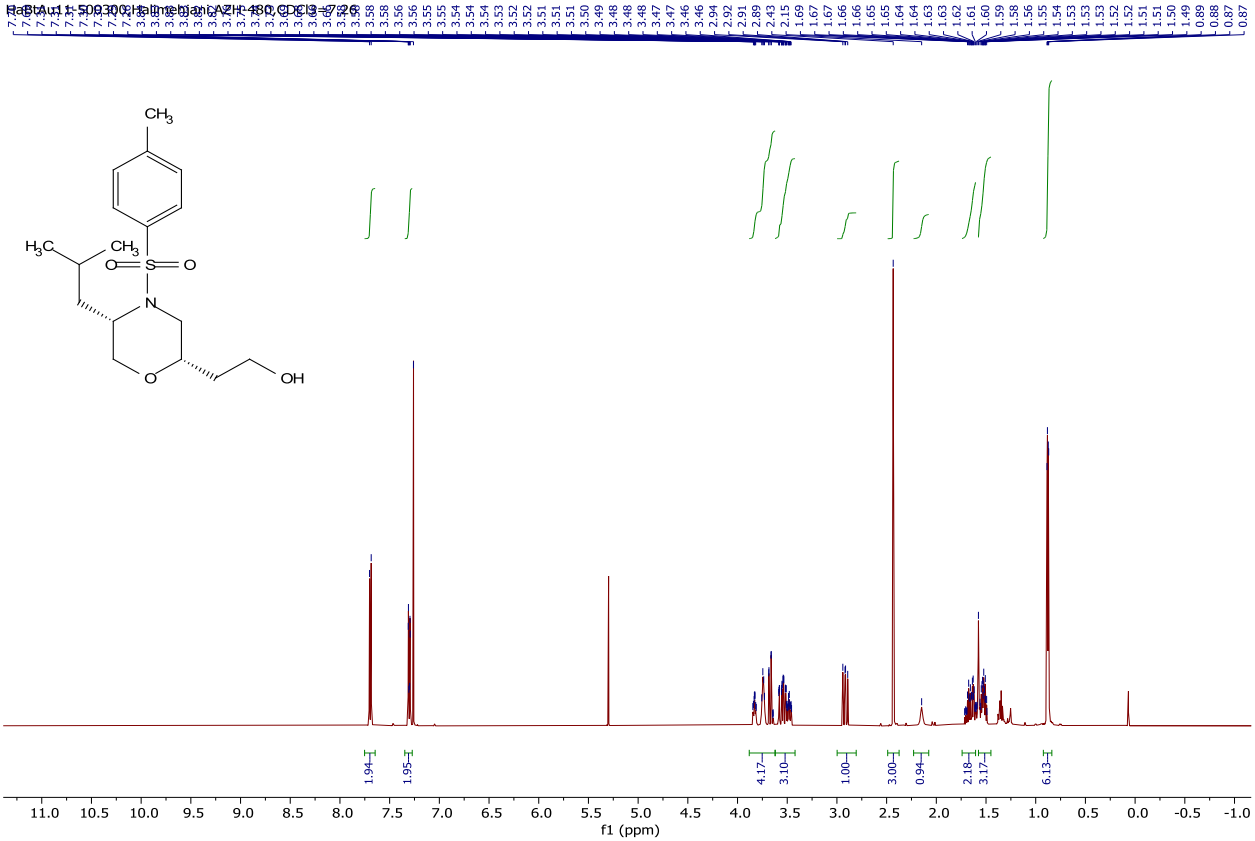
1: 212,0 nm, 4,0 nm

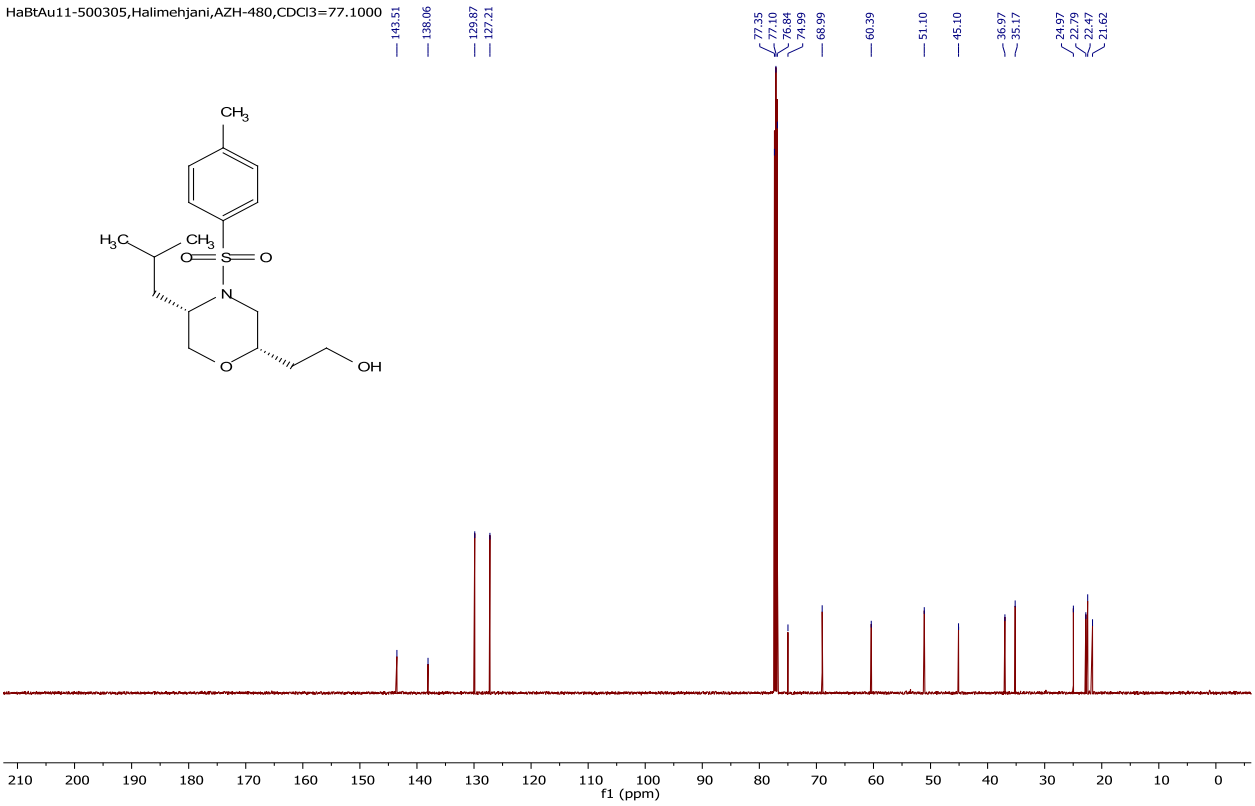
Results

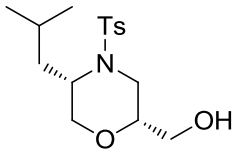
Peak Number	Retention Time	Area Percent	Area
1	11,737	99,091	679602610
2	15,225	0,909	6237056
Totals		100,000	685839666



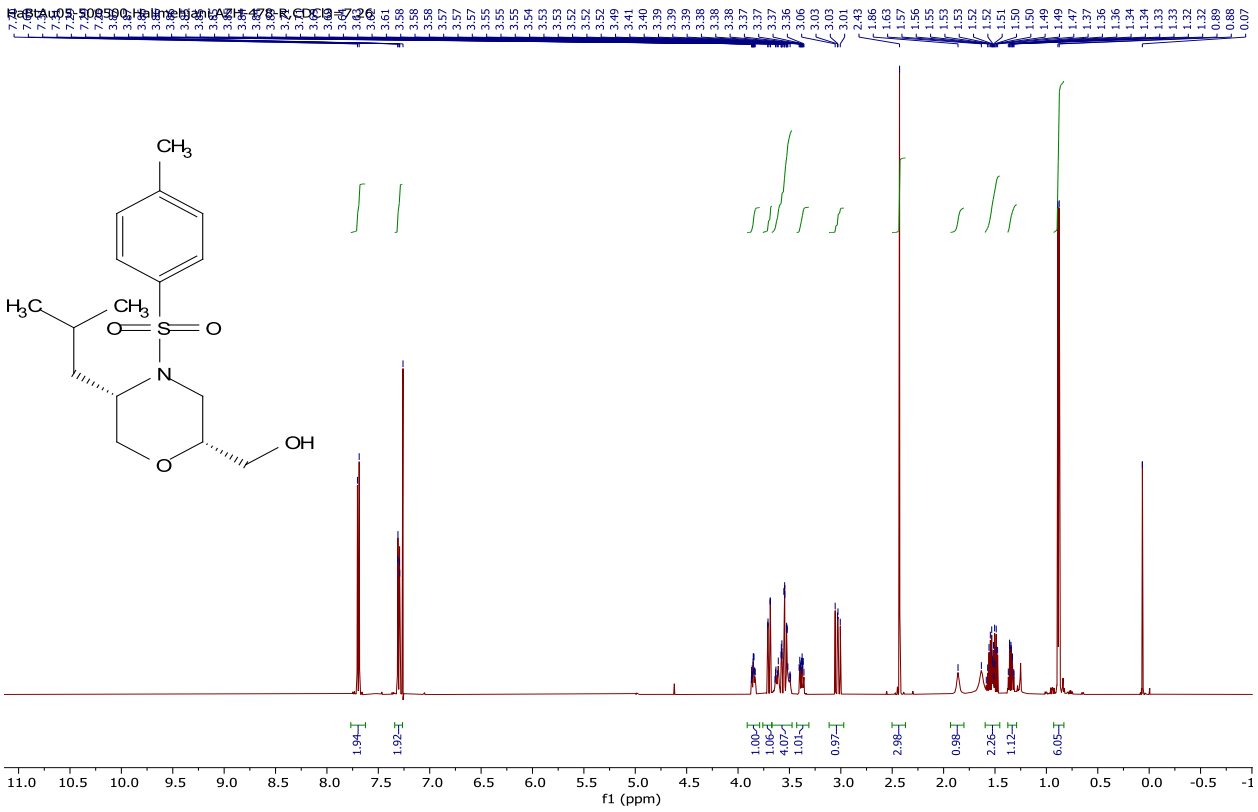
Synthesis of *2-((2S,5S)-5-isobutyl-4-tosylmorpholin-2-yl)ethanol* (5): To a stirred solution of (2S,5S)-5-isobutyl-4-tosyl-2-vinylmorpholine (**2d**) (80 mg, 0.25 mmol, 1.00 eq) in THF (0.5 mL, 0.5 M) was added 9-BBN (0.55 mL, 0.275 mmol, 0.5 M, 1.1 eq) dropwise at 0 °C. The reaction mixture was stirred at rt for 3 h until aqueous NaOH (1.1 mL, 2M) and aqueous H_2O_2 (30 w-%, 0.37 mL) were added at rt. The mixture was stirred for 50 min and quenched by the addition of aqueous $Na_2S_2O_3$ (sat., 5.0 mL). The resulting mixture was diluted with CH_2Cl_2 (20 mL) and washed with H_2O (10 mL) and brine (10 mL). The organic layer was dried over Na_2SO_4 and the solvent was evaporated under reduced pressure. The residue was purified by flash chromatography (SiO_2, *n*-pentane:AcOEt = 7:3) to afford the title compound **5** in 90% isolated yield. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.69 (d, J = 8.3 Hz, 2H), 7.35 – 7.27 (m, 2H), 3.88 – 3.62 (m, 4H), 3.62 – 3.42 (m, 3H), 2.92 (dd, J = 13.6, 11.0 Hz, 1H), 2.43 (s, 3H), 2.15 (s, 1H), 1.74 – 1.61 (m, 2H), 1.58 – 1.45 (m, 3H), 0.88 (d, J = 6.3, 6H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.5, 138.0, 129.8, 127.2, 74.9, 68.9, 60.3, 51.1, 45.1, 36.9, 35.1, 24.9, 22.7, 22.4, 21.6 ppm; HRMS (ESI) calcd for $C_{17}H_{27}NO_4S$ $[M+H]^+$: 342.1739; found: 342.1732. $[\alpha]_D^{25}$ = +56.0 (c = 0.0.0875, CH_2Cl_2).

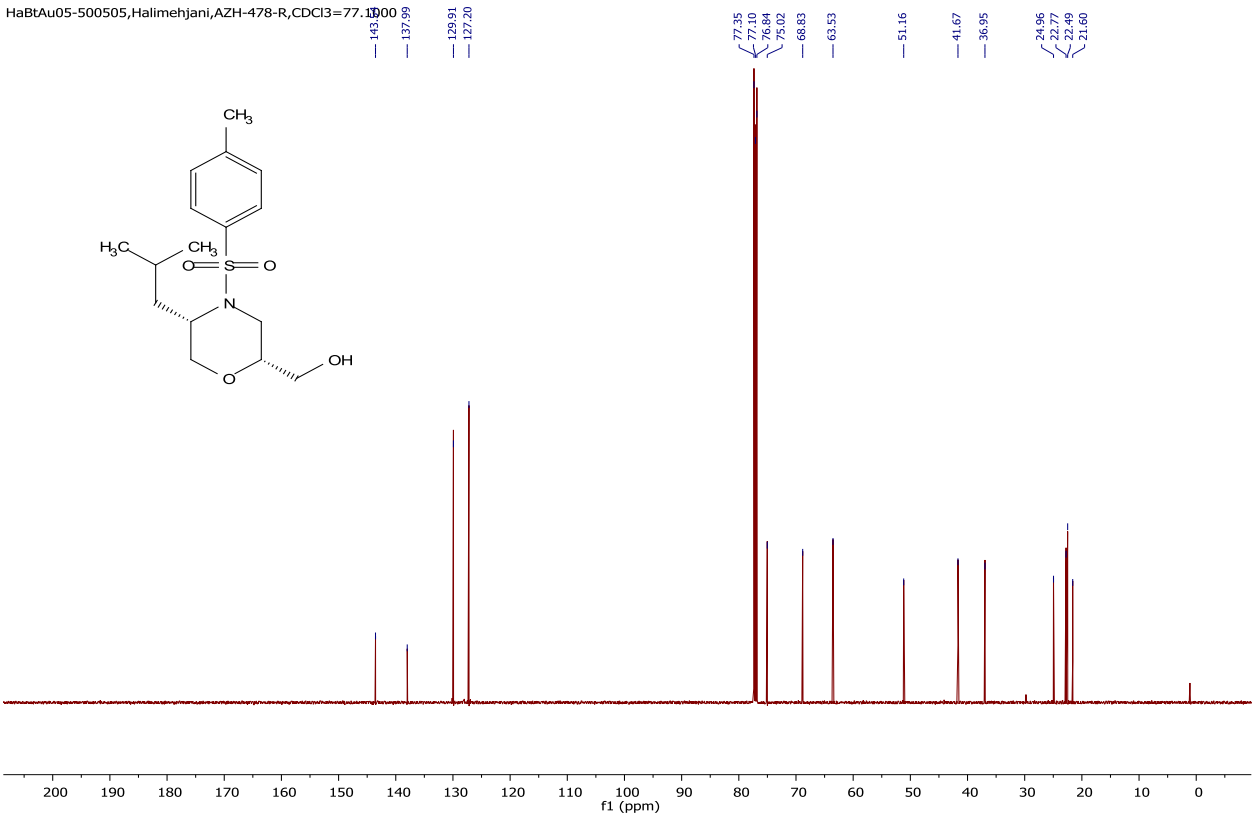


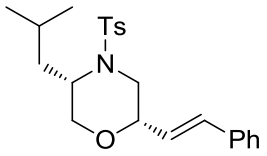




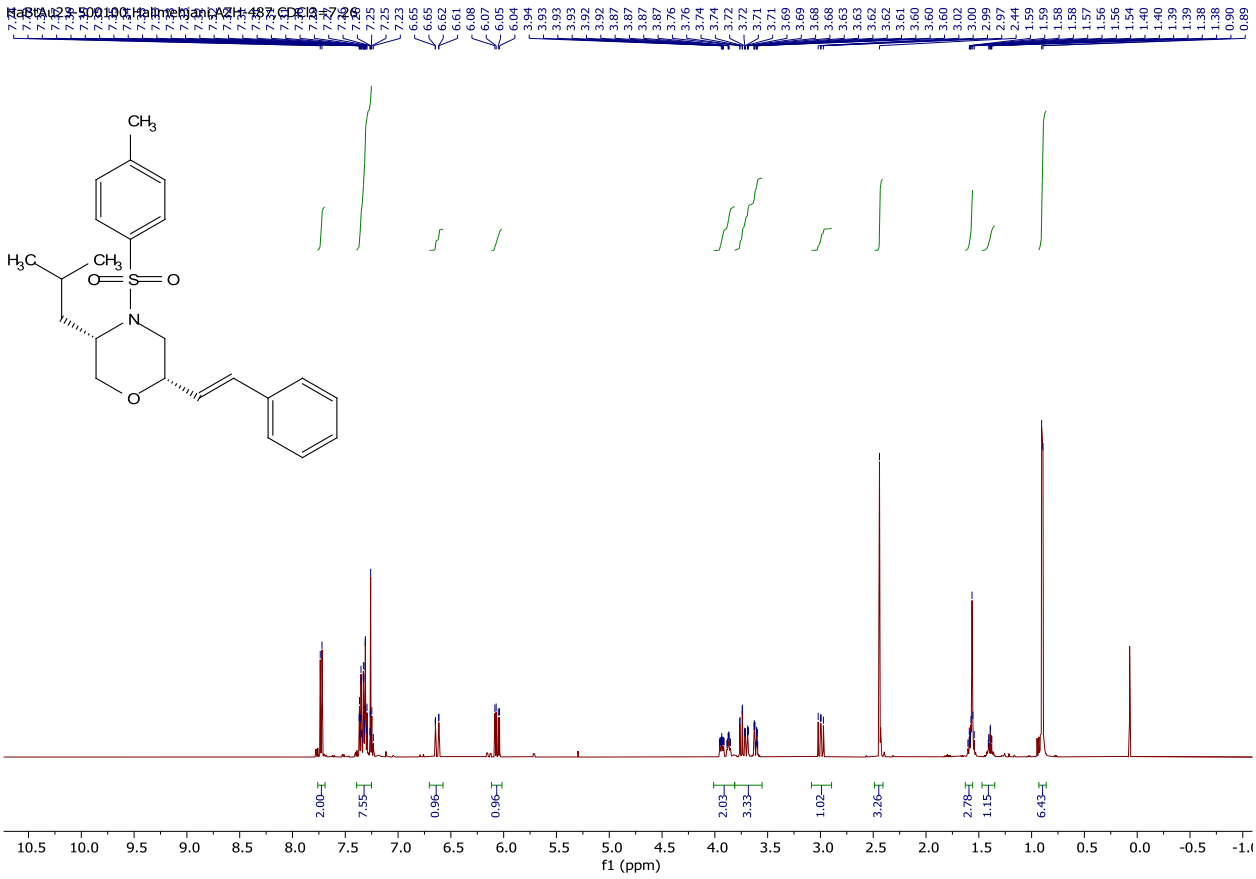
Synthesis of ((2*R*,5*S*)-5-isobutyl-4-tosylmorpholin-2-yl)methanol (6): A solution of (2*S*,5*S*)-5-isobutyl-4-tosyl-2-vinylmorpholine **2d** (90 mg, 0.28 mmol, 1.0 equiv.) in CH_2Cl_2 (5 mL) was cooled to −78 °C. Ozone was bubbled through the solution until the solution showed a blue color (approx. 15 min). Then, the reaction vessel was degassed with nitrogen until disappearance of the blue color occurred. Me_2S (50 µL) was added and the reaction mixture was allowed to warm to room temperature. The solution was concentrated under recued pressure to give a crude product. The crude mixture was dissolved in methanol (5 ml) and $NaBH_4$ (1 mmol) was added and the mixture was stirred at room temperature for 5h. Evaporation of the solvent and chromatography on silica gel (EtOAc:*n*-pentane; 2:8) afforded the pure product in 95% isolated yield. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.69 (d, J = 8.4 Hz, 2H), 7.34 – 7.26 (m, 2H), 3.87–3.82 (m, 1H), 3.70 (dd, J = 11.6, 0.9 Hz, 1H), 3.67 – 3.47 (m, 4H), 3.39–3.36 (m, 1H), 3.03 (dd, J = 13.6, 11.2 Hz, 1H), 2.43 (s, 3H), 1.86 (brs, 1H), 1.60 – 1.45 (m, 2H), 1.38 – 1.29 (m, 1H), 0.88 (d, J = 6.4 Hz, 6H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.5, 137.9, 129.9, 127.2, 75.0, 68.8, 63.5, 51.1, 41.6, 36.9, 24.9, 22.7, 22.4, 21.6 ppm; HRMS (ESI) calcd for $C_{16}H_{25}NO_4S$ $[M+Na]^+$: 350.1402; found: 350.1396; $[\alpha]_D^{25}$ = +24.71 (c = 0.392, CH_2Cl_2).

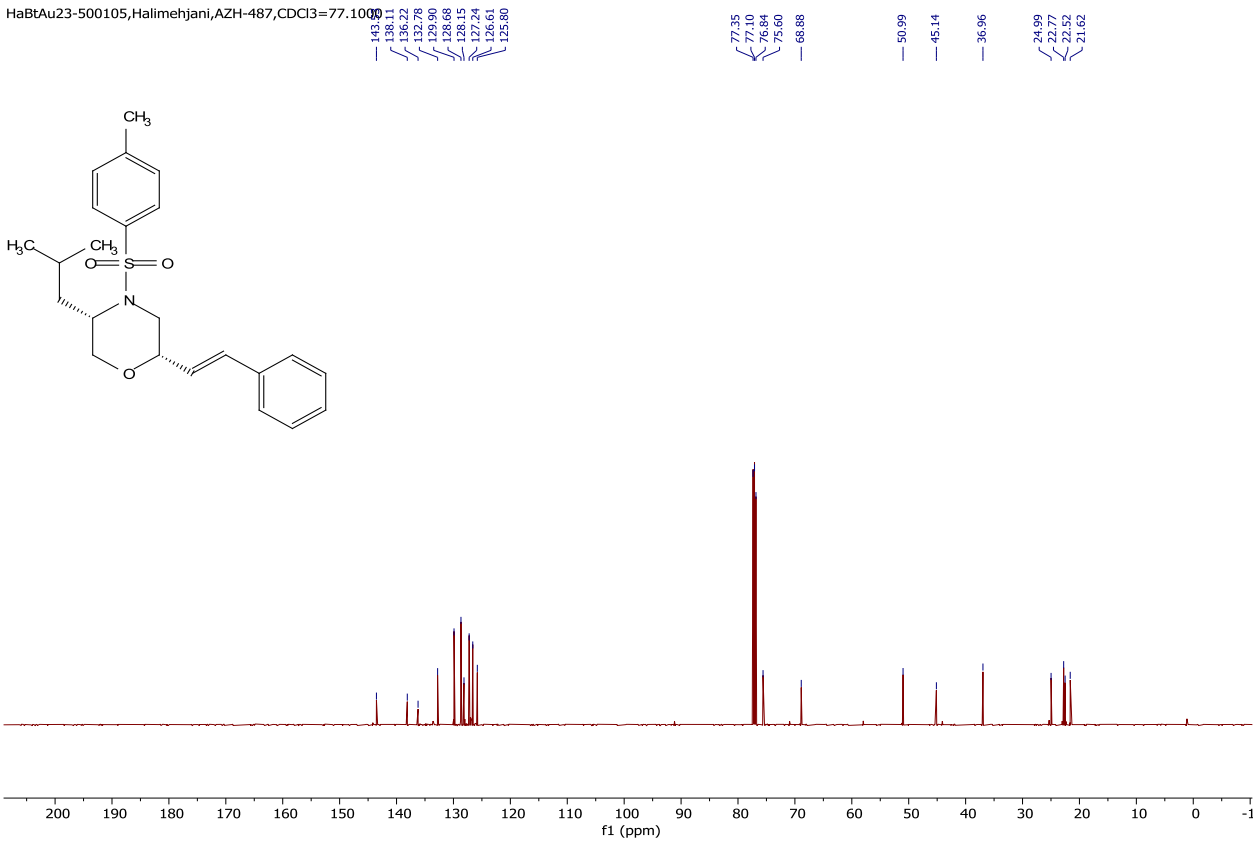

CH3
H3C
CH3
O
S
O
N
O
OH
1.94
1.92
1.00
1.06
4.07
1.01
0.97
2.98
0.98
2.26
1.12
6.05
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

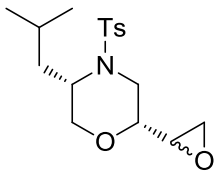

HaBtAu05-500505,Halimehjani,AZH-478-R,CDCl3=77.1
143.10
137.99
129.91
127.20
77.35
77.10
76.84
75.02
68.83
63.53
51.16
41.67
36.95
24.96
22.77
22.49
21.60
CH3
H3C
CH3
O
S
O
N
O
OH
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



Synthesis of *(2S,5S)-5-isobutyl-2-((E)-styryl)-4-tosylmorpholine* (7): A mixture of (2*S*,5*S*)-5-isobutyl-4-tosyl-2-vinylmorpholine (**2d**) (80 mg, 0.25 mmol, 1.00 eq), trans-stilbene (450 mg, 10 mmol, 10.0 eq) and Hoveyda-Grubbs II (15.6 mg, 10.0 mol%) in DCE (1.25 mL, 0.2 M) were refluxed at 80 °C for 18 h. The reaction mixture was concentrated under reduced pressure and the crude product was purified by flash column chromatography (SiO2, petroleum ether:AcOEt = 20:1 to 15:1). The title product **7** was obtained as a colourless oil in 80% isolated yield. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.73 (d, *J* = 8.3 Hz, 2H), 7.39 – 7.25 (m, 7H), 6.63 (dd, *J* = 16.2, 1.2 Hz, 1H), 6.06 (dd, *J* = 16.1, 6.0 Hz, 1H), 4.01 – 3.81 (m, 2H), 3.81 – 3.55 (m, 3H), 3.00 (dd, *J* = 13.7, 11.0 Hz, 1H), 2.44 (s, 3H), 1.63 – 1.56 (m, 2H), 1.39–1.37 (m, 1H), 0.90 (d, *J* = 6.3 Hz, 6H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.5, 138.1, 136.2, 132.7, 129.9, 128.6, 128.1, 127.2, 126.6, 125.8, 75.6, 68.8, 50.9, 45.1, 36.9, 24.9, 22.7, 22.5, 21.6 ppm; HRMS (ESI) calcd for $C_{23}H_{29}NO_3S$ $[M+H]^+$: 400.1946; found: 400.1945; $[\alpha]_D^{25}$ = -26.5 (c = 0.608, CH_2Cl_2).

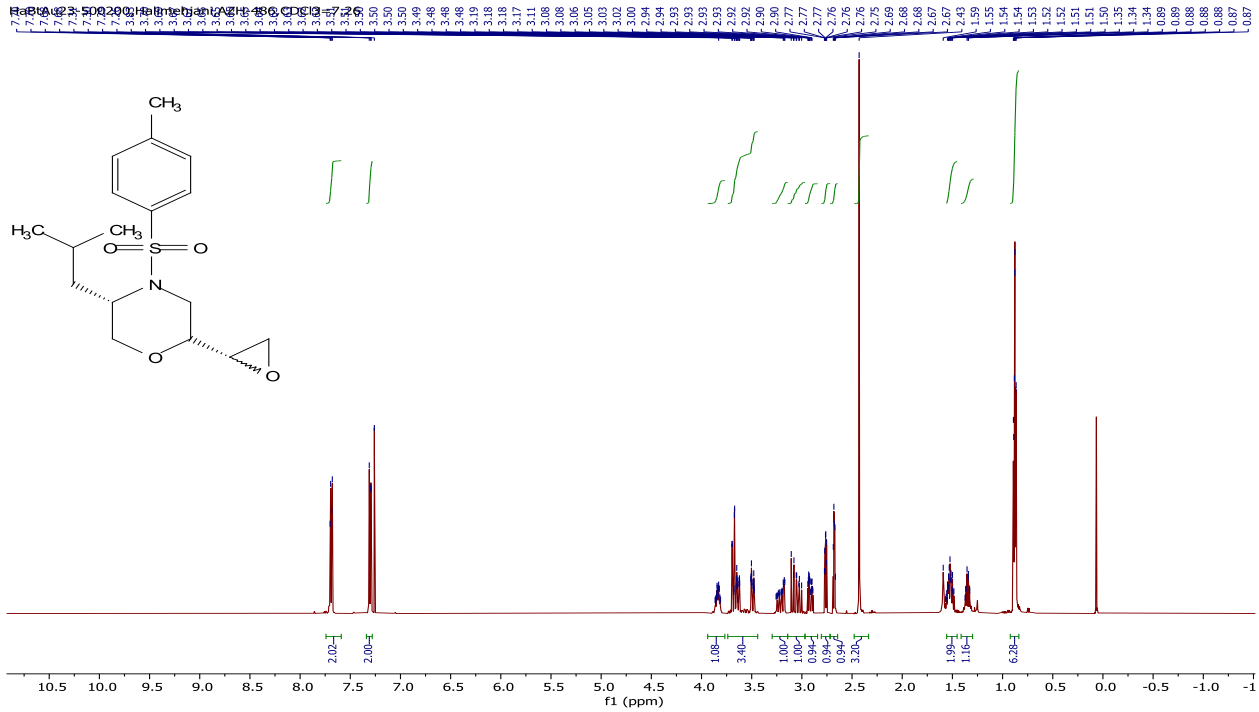


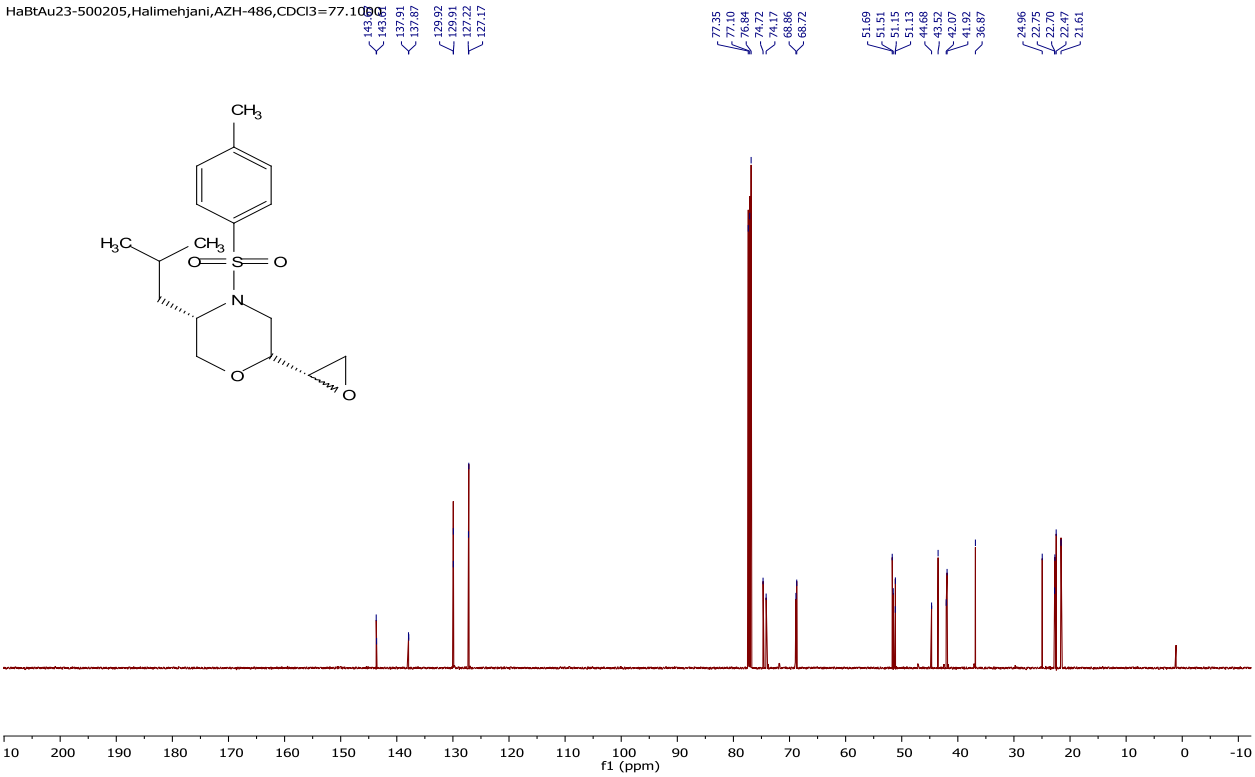




Synthesis of *(2R,5S)-5-isobutyl-2-(oxiran-2-yl)-4-tosylmorpholine* (8): (2*S*,5*S*)-5-isobutyl-4-tosyl-2-vinylmorpholine (**2d**) (80 mg, 0.25 mmol) was dissolved in DCE (0.5 ml). To this solution *m*-CPBA (115 mg, 0.5 mmol, 75%, 2.0 eq.) was added and the mixture was refluxed for 16 h. Afterwards the reaction was cooled to 0 °C and quenched with saturated Na_2SO_3 (5 ml) and $NaHCO_3$ (6 ml, 10 %). The aqueous layer was extracted with dichlormethane (3 x 10 ml) and the combined organic layers were dried over Na_2SO_4 and evaporated. The resulting crude product was purified by flash column chromatography on silica gel (*n*-penatne / EtOAc = 8:2) to afford the product as a colourless oil (90% isolated yield for both diastereomeres, *dr* ratio was determined to be 6:4 by crude ^{1}H NMR analysis). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.69 (d, *J* = 8.3 Hz, 2H), 7.34 – 7.28 (m, 2H), 3.94 – 3.77 (m, 1H), 3.74 – 3.44 (m, 3H), 3.23–3.19 (m, 1H), 3.05 (ddd, *J* = 26.9, 13.5, 11.3 Hz, 1H), 2.97 – 2.84 (m, 1H), 2.76 (ddd, *J* = 5.4, 4.1, 1.5 Hz, 1H), 2.69–2.66 (m, 1H), 2.43 (s, 3H), 1.56 – 1.45 (m, 2H), 1.41 – 1.30 (m, 1H), 0.92 – 0.84 (m, 6H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.6 and 143.6, 137.9 and 137.8, 129.9 and 129.9, 127.2 and 127.1, 74.7 and 74.1,

68.8 and 68.7, 51.6 and 51.5, 51.1 and 51.1, 44.6 and 43.5, 42.0 and 41.9, 36.8 (2C), 24.9 (2C), 22.8 and 22.7, 22.4 (2C), 21.6 (2C) ppm; HRMS (ESI) calcd for $C_{17}H_{25}NO_4S$ $[M+H]^+$: 340.1583; found: 340.1580.





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