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Synthesis of 5,6- and 7-membered 1,3- and 1,4-heterocyclic compounds *via* intramolecular hydroalkoxylation/hydrothio-alkoxylation of alkenols/ thioalkenols

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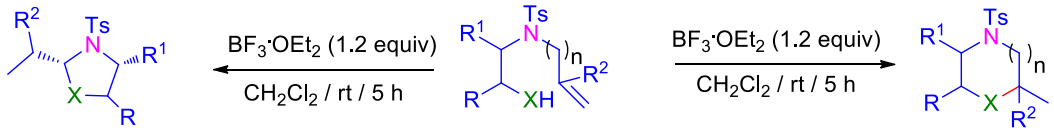


X = S; n = 1
R = H; R^1 = CO_2Me, CH_2OAc, CH_2OH
R^2 = Me, Ph
Yields up to 74%
4 examples

X = S, O; n = 1 or 2
R = H, aryl; R^1 = H, alkyl, aryl, CO_2Me
R^2 = Me, Ph
Yields up to 93%
18 examples

ABSTRACT: Intramolecular hydroalkoxylation/hydrothioalkoxylation of nitrogen tethered alkenes and alcohols/thiols mediated by boron trifluoride etherate leads to 5-membered thiazolidine, 6-membered 1,4-oxazines (morpholines) and tetrahydro-2*H*-1,4-thiazine (thiomorpholines) and 7-membered 1,4-oxazepanes in good yields.

INTRODUCTION

Substituted 1,4-oxazines, tetrahydro-2*H*-1,4-thiazines and 1,4-oxazepanes are widely distributed in many naturally occurring and biologically active molecules.[1] For example,

reboxetine (**1**), a morpholine containing compound shows antidepressant properties.[2] Similarly, the compounds **2** and **3** possess anti-inflammatory and $GABA_B$ receptor-antagonist properties.[3] 1,4-Oxazepane unit is found in naturally occurring alkaloid batrachotoxin (**4**), which acts as ligand for CC chemokine receptors, such as CCRl (Figure 1).[1d-e,4] These heterocyclic scaffolds are versatile synthetic units in organic synthesis particularly for the construction of agrochemicals, fungicides and bactericides.[5] 1,4-Oxazines are also used as chiral auxiliary.[6] On the other hand, thiazolines are known as flavouring agent and are found in fruits and vegetables.[7] They are also known to possess biological activities such as anti-cancer,[8] antimicrobial,[9] anti-hypertensive[10] activity and are used as building blocks in peptide synthesis.[11]

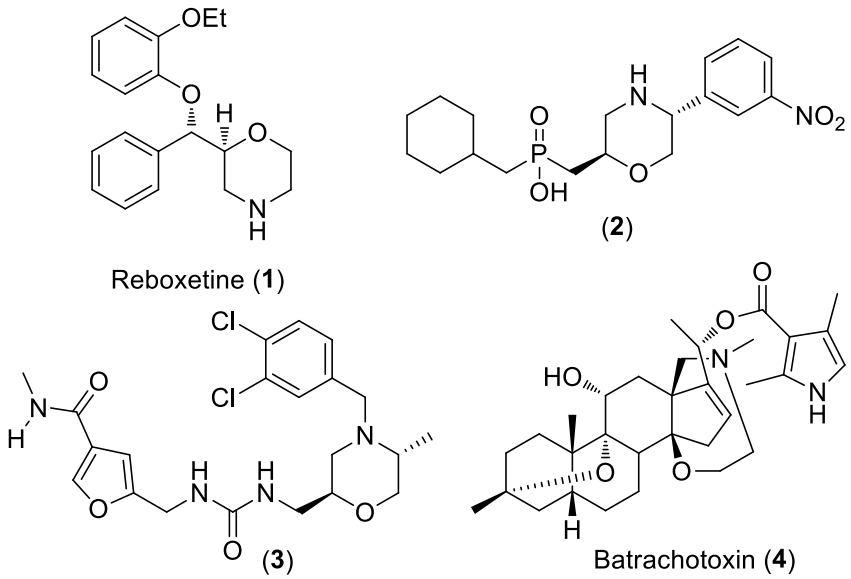


Figure 1. Biologically important morpholine and 1,4-oxazepane derivatives

Numerous synthetic approaches have been developed for the preparation of 1,4-oxazines and 1,4-oxazepanes such as ring closure of amino diols,[12] amino alcohols and bromosulphonium salts,[13] double allylic substitution by amino alcohols,[14] cyclization of *N*-tethered haloalcohols,[15] reductive amination of diketones,[16] reductive etherification of *N*-tethered ketoalcohols,[17] cyclization of *O*-protected amino alcohols,[18] oxirane ring opening by

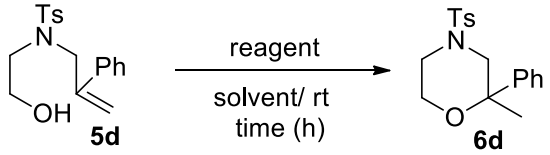
tosylamide and subsequent cyclization[19] and ring opening of aziridines.[20] Recently, Chemler and co-workers have reported the synthesis of 1,4-oxazines *via* intramolecular cyclization of *N*-tethered alkene-alkanol mediated by copper.[21] The thiazolidines are synthesized by Asinger method, a multicomponent reaction between an α-mercaptoketone, an aldehyde and ammonia.[22] Another method is condensation of cysteine and aldehydes.[23] These methods have their own merits and demerits but some of them suffer from serious problems such as lack of selectivity,[23a,c] low yields[15c,16,19] and harsh reaction conditions.[21] Moreover, intramolecular hydroalkoxylation/ hydrothio-alkoxylation reactions are currently of great interest for the synthesis of five and six membered cyclic ethers and thioethers using γ-and δ-hydroxy/ thio olefins in the presence of transition metal and lanthanide catalysts such as $[PtCl_2(H_2C{=}CH_2)]_2$, AgOTf, $Ph_3PAuOTf$, Au nanocluster (Au:PVP), $CeCl_3{\cdot}7H_2O{-}NaI$, $Ln(OTf)_3$, $In(OTf)_3$ and $Yb(OTf)_3$.[24] Similarly, $BF_3{\cdot}OEt_2$ has been used for the synthesis of tetrahydrocannabinols, cannabinoid derivatives and in total synthesis of quinone and hydroquinone sesquiterpenes via intermolecular addition of phenol to alkene.[25] But, the use of $BF_3{\cdot}OEt_2$ in intramolecular hydroalkoxylation/ hydrothio-alkoxylation reaction for the synthesis of 5,6- and 7-membered 1,3- and 1,4-heterocyclic compounds has not been reported so far. We now present a general and transition metal free methodology for the synthesis of 1,4-oxazines, 1,4-oxazepanes and thiazolidines using intramolecular hydroalkoxylation/ hydrothioalkoxylation of alkenols/ thioalkenols mediated by boron trifluoride etherate at ambient temperature in moderate to good yields.

RESULTS AND DISCUSSION

In continuation of our interest in oxygen and nitrogen heterocycles,[26] we were in search of synthesizing heterocyclic frameworks having two heteroatoms. To start with alkenol **5d** was treated with 1.2 equivalents of boron trifluoride etherate in dichloromethane at room temperature for 5 h and 2-methyl-2-phenyl-4-tosylmorpholine **6d** was obtained in 90% yield.

The reaction was also performed in different Lewis and Brønsted acidic conditions and the results are shown in Table 1. The reaction with 0.5 equivalents of $BF_3{\cdot}OEt_2$ furnished only 38% yield over 12 h. Metal triflates such as zinc, copper, indium and silver triflates were also screened for the reaction. Out of these, only zinc and indium triflates gave 5% and 30%

Table 1. Optimization of the reaction condition[a]



entry	reagent (mmol)	solvent	time/h	conversion (%)[b]	yield (%)[c]
1	**$BF_3{\cdot}OEt_2$ (1.2)**	**CH_2Cl_2**	**5**	**100**	**90**
2	$BF_3{\cdot}OEt_2$ (0.5)	CH_2Cl_2	12	44	38
3	$Zn(OTf)_2$ (0.2)	CH_2Cl_2	24	9	5
4	$Cu(OTf)_2$ (0.2)	CH_2Cl_2	24	0	–[d]
5	$In(OTf)_3$ (0.2)	CH_2Cl_2	24	36	30
6	$Ag(OTf)_2$ (0.2)	CH_2Cl_2	24	0	–[d]
7	$InCl_3$ (0.2)	CH_2Cl_2	24	0	–[d]
8	$CeCl_3.7H_2O$ (1.2)	CH_2Cl_2	24	0	–[d]
9	$FeCl_3$ (1.2)	CH_2Cl_2	24	0	–[d]
10	TsOH (1.2)	CH_2Cl_2	24	22	19
11	CSA (1.2)	CH_2Cl_2	24	34	26
12	TfOH (1.2)	CH_2Cl_2	24	63	52
13	HF (1.2)	CH_2Cl_2	24	0	–[d]
14	$BF_3{\cdot}OEt_2$ (1.2)	toluene	12	79	72
15	$BF_3{\cdot}OEt_2$ (1.2)	CH_3CN	12	35	26
16	$BF_3{\cdot}OEt_2$ (1.2)	THF	12	61	53

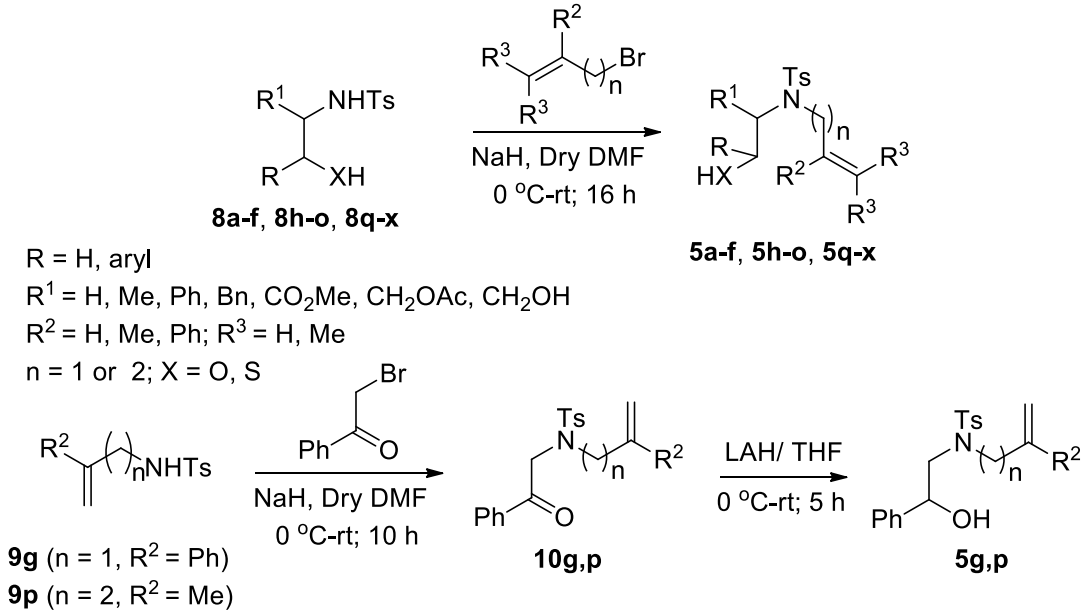
[a]Reaction conditions: alkenol (1.0 mmol), solvent (5 mL) [b]Determined by ^1H NMR.
[c]Yield refers to isolated yield. [d]No reaction, starting material was recovered.

yields, respectively. Similarly, metal salts $InCl_3$, $CeCl_3{\cdot}7H_2O$ and $FeCl_3$ failed to give the desired product, but starting material was recovered in 98% yield. Brønsted acids such as

toluene sulfonic acid (TsOH), camphorsulfonic acid (CSA) and triflic acid (TfOH) gave 19%, 26% and 52% yields, respectively, whereas HF did not work. The reaction was also screened in other solvents such as toluene (entry 14), acetonitrile (entry 15) and THF (entry 16), and gave 72%, 26% and 53% yields, respectively. Therefore, $BF_3 \cdot Et_2O$ in CH_2Cl_2 at room temperature was found to be the best conditions for this reaction.

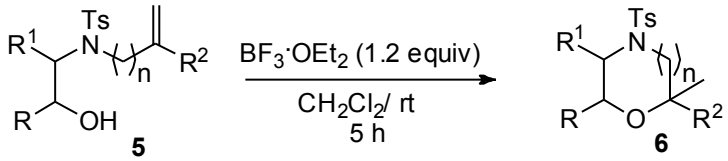
Having obtained the optimized conditions, we further examined the scope of the reaction with a variety of substrates, which were synthesized according to the literature methods either by allylation of *N*-tosyl amino alcohols/ thiols or substitution reaction between phenyl acetyl bromide and allyl/homoallyl tosylamide followed by the reduction of ketone (Scheme 1).[27]

Scheme 1. Synthesis of starting materials



It was observed from the Table 2 that, primary and secondary alkenols, having alkyl and aryl substituted olefinic groups, **5a-5l** (entries 1-12) gave the desired 1,4-oxazines in good yields. In case of secondary alkenols, the substrates having electron-withdrawing aromatic substituents (entries 7-11) gave good yields, whereas electron-donating aromatic substituted alkenol **5l** decomposed under these reaction conditions (entry 12). The chiral substrates **5e** and **5f** (entries 5 and 6) gave single diastereomers with 2-alkyl and 5-phenyl groups *cis* to

Table 2. Synthesis of 1,4- oxazines and 1,4-oxazepanes



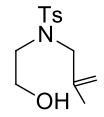
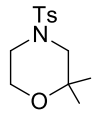
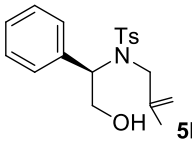
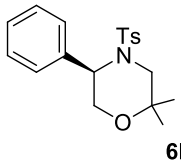
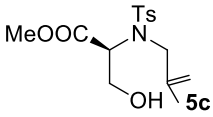
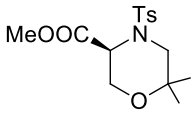
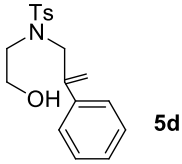
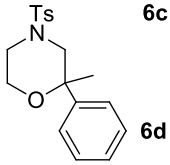
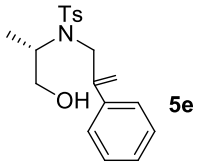
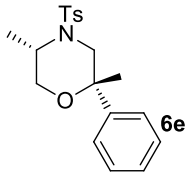
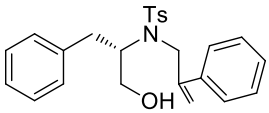
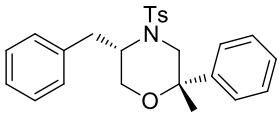
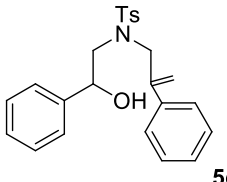
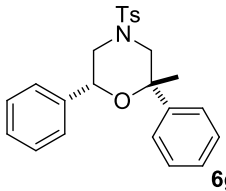
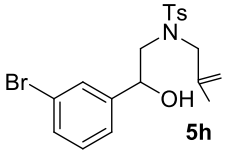
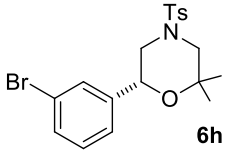
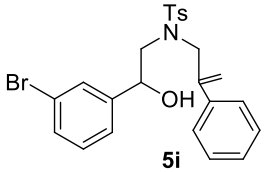
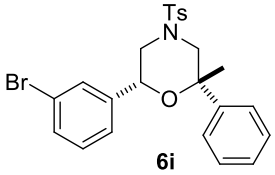
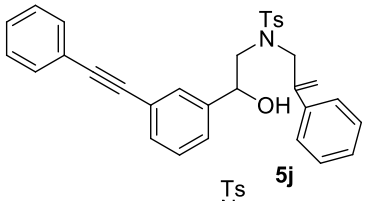
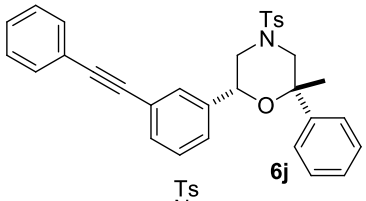
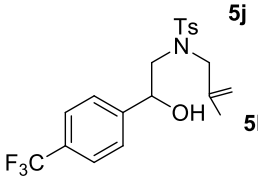
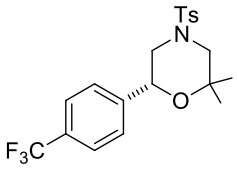
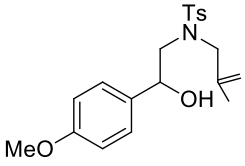
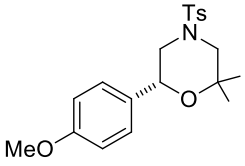
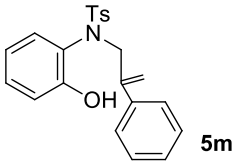
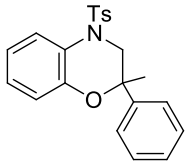
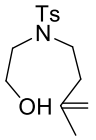
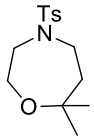
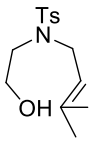
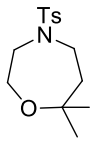
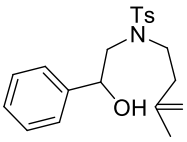
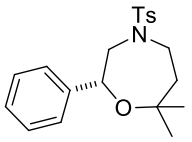
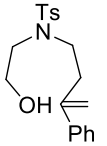
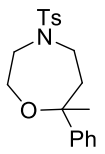
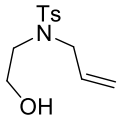
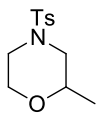
Entry	Substrate **5**	Product **6**	Yield (%) [a]
1	 **5a**	 **6a**	83
2	 **5b**	 **6b**	71
3	 **5c**	 **6c**	86
4	 **5d**	 **6d**	90
5	 **5e**	 **6e**	74
6	 **5f**	 **6f**	63
7	 **5g**	 **6g**	79
8	 **5h**	 **6h**	81
9	 **5i**	 **6i**	86

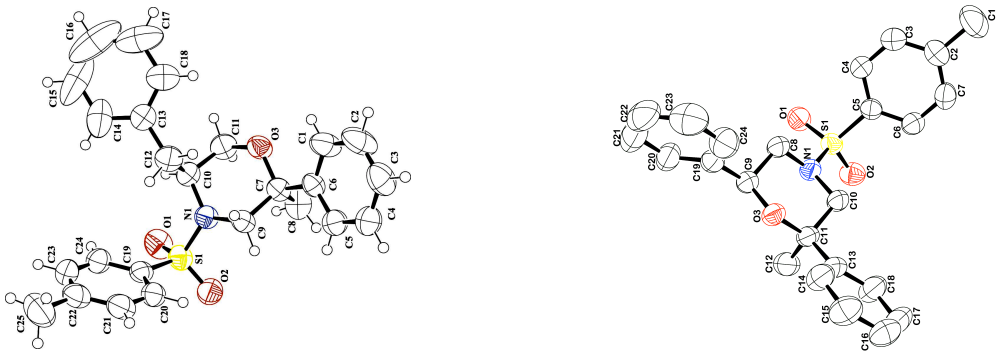
Table 2. continued

Entry	Substrate **5**	Product **6**	Yield (%)[a]
10	 **5j**	 **6j**	73
11	 **5k**	 **6k**	92
12	 **5l**	 **6l**	0
13	 **5m**	 **6m**	68
14	 **5n**	 **6n**	93
15	 **5o**	 **6n**	88
16	 **5p**	 **6p**	72
17	 **5q**	 **6q**	75
18	 **5r**	 **6r**	0

[a]Yields refer to isolated yield. The compounds were characterized by IR, NMR and Mass spectrometry.

each other. Similarly, the secondary alkenols **5g**, **5i** and **5j** also produced exclusively single diastereomers having a *cis* relationship between the phenyl groups at 2,6-positions. The *cis* stereochemistry was confirmed by X-ray crystallographic structures of **6f,g** (Figure 2).[28]

This method also worked well for the phenolic compound **5m** (entry 13) and gave 2-methyl-2-phenyl-4-tosyl-3,4-dihydro-2*H*-benzo[*b*]-[1,4]-oxazine **6m** in 68% yield. Similarly, alkenols **5n-5q** (entries 14-17) gave the corresponding 1,4-oxazepanes **6n-q** in good yields. The isomeric alkenols **5n** and **5o** gave same product **6n**. On the other hand, substrate having terminal alkene **5r** (entry 18) was unreactive under the same reaction conditions and starting material was recovered in 98%.



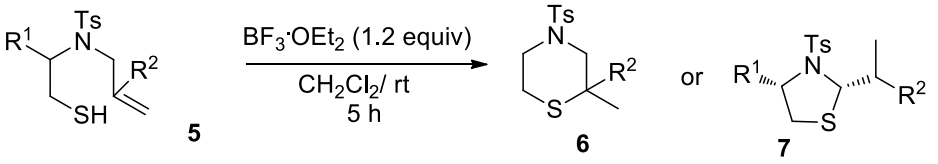
6f **6g**

Figure 2. ORTEP Diagram of compounds **6f** and **6g**

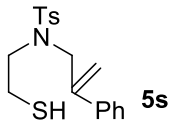
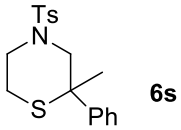
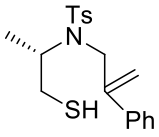
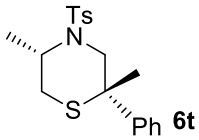
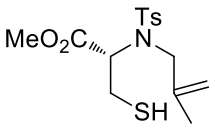
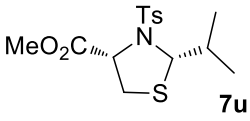
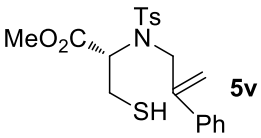
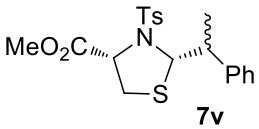
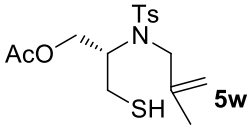
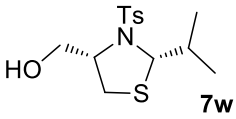
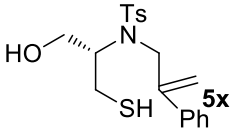
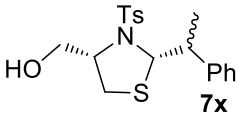
After successful study of this methodology to the synthesis of 1,4-oxazines and oxazepanes, its application to the synthesis of 1,4-thiaoxazines and thiazepanes was explored. The starting material thioalkene **5s-t** (Table 3, entries 1 and 2) when treated with boron trifluoride etherate under the same reaction conditions gave 2-methyl-2-phenyl-4-tosylthiaoxazine **6s** and 2-(prop-1-en-2-yl)-4-tosylthiomorpholine **6t** in 70% and 73% yields, respectively. On the other hand, substrates **5u-x** (Table 3, entries 3-6) having substitution at the α-position to *N*-tosyl group gave thiazolidines **7u-x** (Table 3) in 66%, 71%, 59% and 74% yields, respectively.

Substrate **5v** and **5x** (entries 4 and 6) gave two inseparable diastereomers **7v** and **7x** in 71% and 74% overall yield, respectively. The substrate **5w** gave hydrolyzed product **7w** under this reaction conditions. On the other hand, **5x** having hydroxyl and thiol groups gave thiazolidine **7x** selectively, without formation of any morpholine products. The stereochemistry of the

Table 3. Synthesis of tetrahydro-2*H*-1,4-thiazine and thiazolidine



R^1 = Me, CO_2Me, CH_2OAc, CH_2OH
R^2 = H, Me, Ph

Entry	Substrate **5**	Product **6** / **7**	Yield (%) [a]
1	 **5s**	 **6s**	70[b]
2	 **5t**	 **6t**	86
3	 **5u**	 **7u**	66
4	 **5v**	 **7v**	71[c]
5	 **5w**	 **7w**	59
6	 **5x**	 **7x**	74[d]

[a]Yield refers to isolated yield. All the products were characterized by ^1H,^{13}C NMR and Mass spectrometry. [b]Reaction took 12 h. [c,d]Inseperable mixture of diastereomers with a ratio 7:3 and 3:2, respectively. Ratio is determined by ^1H NMR.

thiazolidine was determined by ^{1}H and nOe experiment of **7u** (Figure 3). There is a strong nOe between protons at C-2 and C-4 of **7u**, which confirms that they are *cis* to each other.

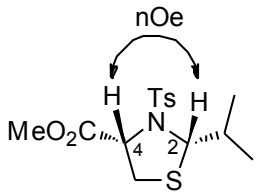
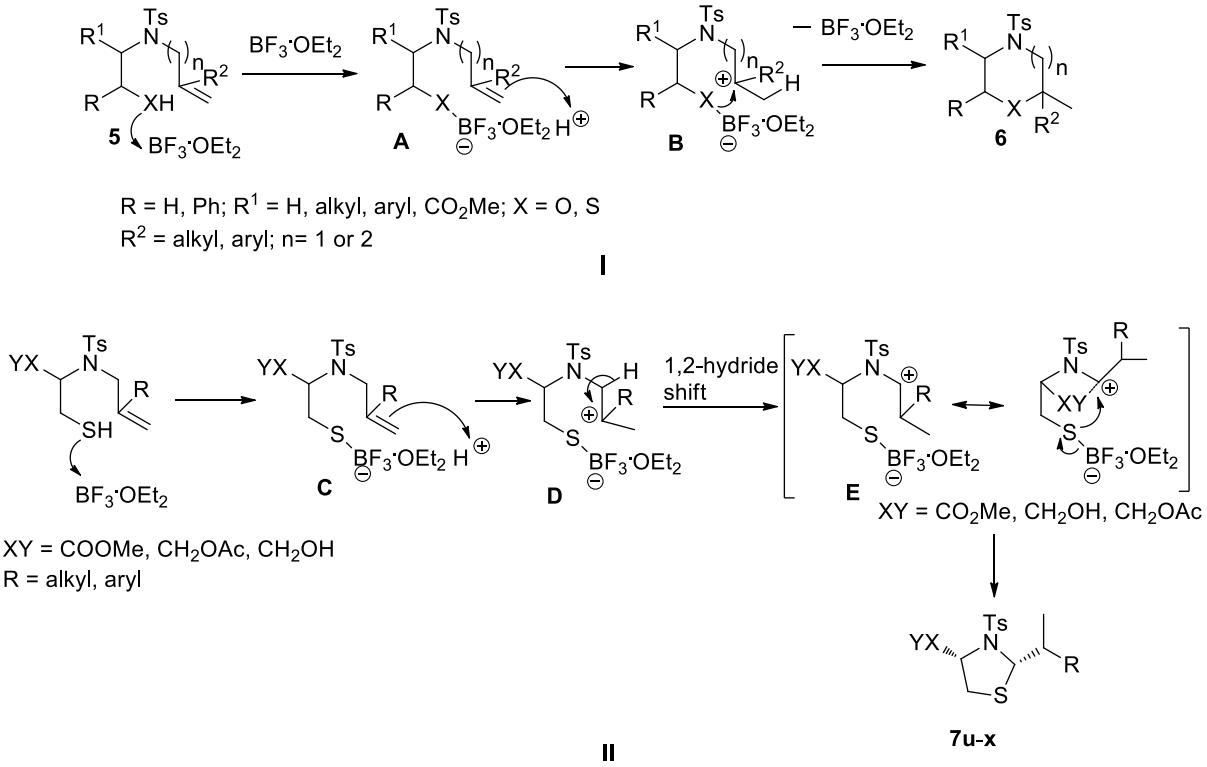


Figure 3. nOe diagram of compound **7u**

The exact mechanism of formation of 1,4-oxazines and 1,4-oxazepanes or their sulfur analogues *via* intramolecular hydroalkoxylation/hydrothioalkoxylation of alkenols/thioalkenols mediated by boron trifluoride etherate is not known. But mechanisms for the hydroalkoxylation of alkenols promoted by transition metal or lanthanide reagents are proposed by different groups, where metal forms a coordinated complex with alcohols and olefinic groups.[21] The same mechanism cannot be applied in this case as boron cannot form such type of complex. An alternative mechanism is proposed which can be explained as follows. The alkenol/thioalkenols **5** reacts with boron trifluoride etherate to form intermediate **A**, an ion pair, of which the proton adds to the double bond to give more stable carbocation **B**. The carbocation **B** is then attacked by alkoxide/ ion to form 1,4-oxazines, 1,4-oxazepanes and thiazine (Scheme 2, I). This explains the incapability of formation of product by the substrate **5r**, where the carbocation **B** is not stable. On the other hand, the mechanism for the formation of thiazolidine products **7u-x** can be explained as follows. First thiol reacts with boron trifluoride etherate to form intermediate **C,** an ion pair, of which the proton adds to the double bond to give carbocation **D**, which is similar to intermediate **B**. This intermediate **D** undergoes 1,2 hydride shift to give rearranged carbocation **E**, which is stabilized by ester or hydroxyl groups present at position 2. Finally, the thiol group attacks the carbocation **E** to give more stable five membered compounds **7u-x (**Scheme 2, II).[24k] The presence of ester and

hydroxyl groups at 2-position are crucial for the formation of five membered ring, which can be exemplified by the fact that the compound **5t** having methyl group at 2-position gave six membered ring **6t**.

Scheme 2. Plausible mechanism of the reaction



CONCLUSIONS

In conclusion, we have developed a mild and efficient general method for the synthesis of substituted 1,4-oxazines, 1,4-oxazepanes and thiazolidines *via* intramolecular cyclization reaction of alkenols/thioalkenols in good yields and excellent diastereoselectivity. The reaction is highly atom economic and compatible to a wide range of functional groups such as ester, hydroxy, -CF_3, bromo and alkyne. Furthermore, *N*-tethered alkenthiol having substituents at the α-position to nitrogen provides an excellent access to a diverse array of thiazolidine derivatives with 2,4-*cis* relationship.

EXPERIMENTAL SECTION

General Information: All the reagents were of reagent grade (AR grade) and were used as purchased without further purification. Silica gel (60-120 mesh size) was used for column chromatography. Reactions were monitored by TLC on silica gel GF_{254} (0.25 mm). Melting points were recorded in an open capillary tube and are uncorrected. Fourier transform-infra red (FT-IR) spectra were recorded as neat liquid or KBr pellets. NMR spectra were recorded in $CDCl_3$ with tetramethylsilane as the internal standard for ^1H (600 MHz, 400 MHz) or ^{13}C (150 MHz, 100 MHz) NMR. Chemical shifts (δ) are reported in ppm and spin-spin coupling constants (*J*) are given in Hz. HRMS spectra were recorded using Q-TOF mass spectrometer.

Synthesis of starting materials

General procedure for the synthesis of starting materials 5a-f, 5h-o and 5q-x: Amino alcohol or thiol (**8a-f**, **8h-o** and **8q-x**) (1.0 equiv) in anhydrous DMF was added to the stirred solution of sodium hydride (1.2 equiv) in dry DMF under inert atmosphere at 0 °C. After complete evolution of hydrogen gas, substituted allyl bromide (1.0 equiv) in DMF was added drop wise for 10 min and the reaction was stirred at room temperature for 16 h. After completion of the reaction, brine solution was added to the reaction mixture and extracted with ethylacetate. The organic layer was further washed with brine solution for 2-3 times. The combined organic layers were dried over Na_2SO_4 and concentrated in rotary evoparator. The obtained crude was subjected to column chromatography over silica gel giving corresponding products (**5a-f**, **5h-o** and **5q-x**).

General procedure for the synthesis of starting materials 5g,p: Tosyl amide **9g**,**p** (1.0 equiv) in anhydrous DMF was added to the stirred solution of sodium hydride (1.2 equiv) in dry DMF under inert atmosphere at 0 °C. After complete evolution of hydrogen gas, bromoacetophenone (1.0 equiv) in DMF was added drop wise for 10 min and the reaction

was stirred at room temperature for 10 h. After completion of the reaction, brine solution was added to the reaction mixture and extracted with ethyl acetate. The organic layer was further washed with brine solution (2x15 mL). The combined organic layers were dried over Na_2SO_4 and concentrated in rotary evaporator. The crude was subjected to column chromatography over silica gel giving corresponding products **10g**,**p**.

10g,**p** (1.0 equiv) in dry THF was added to a stirred suspension of LAH (1.0 equiv) in THF at 0 °C. The reaction mixture was stirred at room temperature for 5 h, after that the reaction mixture was quenched with 2 N NaOH and passed through celite pad and washed with ethyl acetate. The mixture was treated with brine, extracted with EtOAc and the combined organic extracts were dried over anhydrous Na_2SO_4, filtered and concentrated invacuo. The crude product was purified using column chromatography to give resulted compounds **5g**,**p**.

*N-(2-Hydroxyethyl)-4-methyl-N-(2-methylallyl)benzene-sulfonamide (**5a**):*

White solid; mp 74-76 ^oC; R_f (hexane/ EtOAc 7:3) 0.47; yield 393 mg, 73%; ^1H NMR (400 MHz, $CDCl_3$) δ 1.70 (s, 3 H), 2.40 (s, 3 H), 3.15 (t, *J* = 5.6 Hz, 2 H), 3.65 (t, *J* = 5.6 Hz, 2 H), 3.68 (s, 2 H), 4.84 (s, 1 H), 4.88 (s, 1 H), 7.28 (d, *J* = 7.6 Hz, 2 H), 7.68 (d, *J* = 8.8 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.0, 21.7, 50.6, 56.4, 61.2, 115.0, 127.5, 129.9, 136.0, 141.0, 143.8; IR (KBr, neat) 3440, 2924, 1334, 1159, 1020, 708 cm^{-1}; HRMS (ESI) calcd. for $C_{13}H_{20}NO_3S$ $(M + H)^+$ 270.1158, found 270.1157.

*(R)-N-(2-Hydroxy-1-phenylethyl)-4-methyl-N-(2-methy-lallyl)benzenesulfonamide (**5b**):*

Colourless gum; R_f (hexane/ EtOAc 7:3) 0.54; yield 566 mg, 82%; $[\alpha]_D^{25}$ = - 81.0 (c = 0.15, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 1.68 (s, 3 H), 2.45 (s, 3 H), 3.32 (d, *J* = 16.0 Hz, 1 H), 3.93 (d, *J* = 16.0 Hz, 1 H), 4.02 (dd, *J* = 11.2 and 6.0 Hz, 1 H), 4.16 (dd, *J* = 11.2 and 8.8 Hz, 1 H), 4.82 (s, 1 H), 4.87 (s, 1 H), 4.95 (dd, *J* = 8.8 and 6.4 Hz, 1 H), 6.83 (d, *J* = 7.6 Hz, 2 H), 7.16-7.27 (m, 3 H), 7.29 (d, *J* = 8.0 Hz, 2 H), 7.71 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (100

MHz, $CDCl_3$) δ 20.0, 21.7, 51.3, 62.8, 62.9, 114.0, 127.5, 128.5, 128.6, 128.8, 129.9, 135.2, 138.0, 142.6, 143.7; IR (KBr, neat) 3532, 2953, 2925, 1742, 1658, 1439, 1339, 1159, 1093, 816, 709 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{24}NO_3S$ $(M + H)^+$ 346.1471, found 346.1477.

*(S)-Methyl 3-hydroxy-2-(4-methyl-N-(2-methylallyl)phenyl-sulfonamido)propanoate (**5c**):*

Pale yellow oil; R_f (hexane/ EtOAc 7:3) 0.46; yield 432 mg, 66%; $[\alpha]_D^{25}$ = - 29.0 (c = 0.1, CH_2Cl_2). ^1H NMR (600 MHz, $CDCl_3$) δ 1.67 (s, 3 H), 2.43 (s, 3 H), 3.59 (s, 3 H), 3.75 (d, *J* = 16.2 Hz, 1 H), 3.82 (dd, *J* = 11.4 and 6.0 Hz, 1 H), 3.92 (d, *J* = 15.6 Hz, 1 H), 4.10-4.14 (m, 1 H), 4.41 (t, *J* = 6.6 Hz, 1 H), 4.94 (s, 1 H), 5.00 (s, 1 H), 7.30 (d, *J* = 7.8 Hz, 2 H), 7.73 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 20.0, 21.7, 52.3, 53.5, 61.0, 61.7, 114.9, 127.8, 129.7, 136.8, 141.6, 143.9, 170.4; IR (KBr, neat) 3528, 2924, 2855, 1598, 1496, 1330, 1159, 1020, 898, 701 cm^{-1}; HRMS (ESI) calcd. for $C_{15}H_{22}NO_5S$ $(M + H)^+$ 328.1213, found 328.1219.

*N-(2-Hydroxyethyl)-4-methyl-N-(2-phenylallyl)benzene-sulfonamide (**5d**):*

Colourless solid, mp 83-85 °C; R_f (hexane/ EtOAc 7:3) 0.48; yield 596 mg, 90%; ^1H NMR (600 MHz, $CDCl_3$) δ 2.44 (s, 3 H), 3.16 (t, *J* = 5.4 Hz, 2 H), 3.56 (t, *J* = 5.4 Hz, 2 H), 4.24 (s, 2 H), 5.23 (s, 1 H), 5.50 (s, 1 H), 7.26-7.36 (m, 5 H), 7.46 (d, *J* = 7.8 Hz, 2 H), 7.67 (d, *J* = 7.8 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.7, 50.3, 53.9, 61.2, 117.0, 126.7, 127.7, 128.5, 128.8, 130.0, 135.4, 138.0, 143.2, 143.9; IR (KBr, neat) 3527, 2925, 1598, 1495, 1334, 1185, 1016, 916, 709 cm^{-1}; HRMS (ESI) calcd. for $C_{18}H_{22}NO_3S$ $(M + H)^+$ 332.1315, found 332.1318.

*(S)-N-(1-Hydroxypropan-2-yl)-4-methyl-N-(2-phenylallyl)-benzenesulfonamide (**5e**):*

Pale yellow gum; R_f (hexane/ EtOAc 7:3) 0.53; yield 449 mg, 65%; $[\alpha]_D^{25}$ = + 26.0 (c = 0.14, CH_2Cl_2). ^1H NMR (600 MHz, $CDCl_3$) δ 0.86 (d, *J* = 6.6 Hz, 3 H), 2.43 (s, 3 H), 3.35 (dd, *J* =

11.4 and 4.8 Hz,1 H), 3.48 (dd, *J* = 12.0 and 9.0 Hz, 1 H), 3.91-3.97 (m, 1 H), 4.04 (d, *J* = 15.6 Hz, 1 H), 4.62 (d, *J* = 16.2 Hz, 1 H), 5.39 (s, 1 H), 5.45 (s, 1 H), 7.25-7.40 (m, 5 H), 7.46 (t, *J* = 7.2 Hz, 2 H), 7.69 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 13.6, 21.7, 48.3, 56.2, 65.0, 115.9, 126.9, 127.5, 128.5, 128.8, 130.0, 137.5, 138.6, 143.7, 145.5; IR (KBr, neat) 3538, 2925, 1598, 1495, 1334, 1155, 1026, 912, 738 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{24}NO_3S$ $(M + H)^+$ 346.1471, found 346.1469.

*(S)-N-(1-Hydroxy-3-phenylpropan-2-yl)-4-methyl-N-(2-phenylallyl)benzenesulfonamide (**5f**):*

Pale yellow oil; R_f (hexane/ EtOAc 4:1) 0.55; yield 598 mg, 71%; $[\alpha]_D^{25}$ = - 26.0 (c = 0.1, CH_2Cl_2). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.43 (s, 3 H), 2.54 (dd, *J* = 13.8 and 4.2 Hz, 1 H), 2.73 (dd, *J* = 13.2 and 10.8 Hz, 1 H), 3.44 (dd, *J* = 11.4 and 3.0 Hz, 1 H), 3.57 (dd, *J* = 12.0 and 9.0 Hz, 1 H), 3.88-3.94 (m, 1 H), 4.31 (d, *J* = 16.2 Hz, 1 H), 4.57 (d, *J* = 16.2 Hz, 1 H), 5.44 (s, 1 H), 5.49 (s, 1 H), 6.93 (d, *J* = 6.6 Hz, 2 H), 7.16-7.21 (m, 2 H), 7.29 (d, *J* = 7.8 Hz, 2 H), 7.32-7.36 (m, 4 H), 7.43 (d, *J* = 8.4 Hz, 2 H), 7.71 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.7, 36.0, 49.5, 62.2, 62.4, 116.3, 126.8, 126.9, 127.8, 128.5, 128.8, 128.83, 129.2, 130.0, 137.5, 138.0, 138.6, 143.9, 145.4; IR (KBr, neat) 3479, 2926, 1494, 1331, 1157, 1041, 814, 701 cm^{-1}; HRMS (ESI) calcd. for $C_{25}H_{28}NO_3S$ $(M + H)^+$ 422.1784, found 422.1781.

*N-(2-Hydroxy-2-phenylethyl)-4-methyl-N-(2-phenylallyl)-benzenesulfonamide (**5g**):*

Colourless gum; R_f (hexane/ EtOAc 4:1) 0.50; yield 459 mg, 56%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41 (s, 3 H), 3.05 (dd, *J* = 15.2 and 2.4 Hz, 1 H), 3.25 (dd, *J* = 15.2 and 9.6 Hz, 1 H), 4.16 (d, *J* = 14.8 Hz, 1 H), 4.46 (d, *J* = 14.8 Hz, 1 H), 4.79 (dd, *J* = 10.0 and 2.4 Hz, 1 H), 5.23 (s, 1 H), 5.54 (s, 1 H), 7.22-7.37 (m, 10 H), 7.45-7.49 (m, 2 H), 7.65 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.4, 53.8, 56.1, 72.1, 117.1, 125.7, 126.0, 126.4, 127.2, 127.4, 127.7, 128.3, 128.6, 129.6, 129.7, 137.8, 142.9, 143.7; IR (KBr, neat) 3538, 2925,

1598, 1495, 1334, 1155, 1026, 912, 738 cm^{-1}; HRMS (ESI) calcd. for $C_{24}H_{25}NNaO_3S$ $(M + Na)^+$ 430.1447, found 430.1456.

*N-(2-(3-Bromophenyl)-2-hydroxyethyl)-4-methyl-N-(2-methylallyl)benzenesulfonamide (**5h**):*

White solid, mp 89-91 ^oC; R_f (hexane/ EtOAc 9:1) 0.39; yield 711 mg, 84%; ^1H NMR (600 MHz, $CDCl_3$) δ 1.70 (s, 3 H), 2.42 (s, 3 H), 3.04 (dd, *J* = 15.0 and 3.0 Hz, 1 H), 3.31 (dd, *J* = 15.0 and 9.6 Hz, 1 H), 3.43 (brs, 1 H), 3.58 (d, *J* = 14.4 Hz, 1 H), 3.92 (d, *J* = 15.0 Hz, 1 H), 4.86 (d, *J* = 9.0 Hz, 1 H), 4.89 (s, 1 H), 4.97 (s, 1 H), 7.18 (t, *J* = 7.8 Hz, 1 H), 7.23 (d, *J* = 7.8 Hz, 1 H), 7.30 (d, *J* = 7.8 Hz, 2 H), 7.38 (d, *J* = 7.8 Hz, 1 H), 7.47 (s, 1 H), 7.70 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.0, 21.7, 56.4, 56.9, 72.0, 115.7, 122.8, 124.8, 127.5, 129.2, 130.0, 130.2, 131.0, 135.9, 140.8, 144.0, 144.1; IR (KBr, neat) 3482, 2923, 1597, 1427, 1333, 1155, 1091, 922, 655 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{23}BrNO_3S$ $(M + H)^+$ 424.0577, found 424.0574.

*N-(2-(3-Bromophenyl)-2-hydroxyethyl)-4-methyl-N-(2-phenylallyl)benzenesulfonamide (**5i**):*

Pale yellow gum, R_f (hexane/ EtOAc 4:1) 0.50; yield 757 mg, 78%; ^1H NMR (600 MHz, $CDCl_3$) δ 2.42 (s, 3 H), 3.01-3.07 (m, 2 H), 3.21 (dd, *J* = 15.0 and 9.0 Hz, 1 H), 4.12 (d, *J* = 14.4 Hz, 1 H), 4.46 (d, *J* = 14.4 Hz, 1 H), 4.73 (d, *J* = 9.6 Hz, 1 H), 5.23 (s, 1 H), 5.56 (s, 1 H), 7.16 (t, *J* = 7.2 Hz, 2 H), 7.29 (d, *J* = 7.8 Hz, 2 H), 7.32-7.38 (m, 4 H), 7.40 (s 1 H), 7.48 (d, *J* = 7.8 Hz, 2 H), 7.65 (d, *J* = 7.8 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.7, 54.4, 56.3, 71.8, 117.6, 122.8, 124.7, 126.7, 127.7, 128.7, 128.9, 129.1, 130.1, 130.2, 131.0, 135.2, 137.8, 143.1, 143.9, 144.2; IR (KBr, neat) 3501, 2923, 1597, 1449, 1334, 1157, 1093, 911, 696 cm^{-1}; HRMS (ESI) calcd. for $C_{24}H_{25}BrNO_3S$ $(M + H)^+$ 486.0733, found 486.0730.

*N-(2-Hydroxy-2-(3-(phenylethynyl)phenyl)ethyl)-4-methyl-N-(2-phenylallyl)-benzenesulfonamide (**5j**):*

Plae yellow gum; R_f (hexane/ EtOAc 4:1) 0.40; yield 720 mg, 71%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.41 (s, 3 H), 3.02-3.08 (m, 2 H), 3.26 (dd, *J* = 15.0 and 9.6 Hz, 1 H), 4.15 (d, *J* = 14.4 Hz, 1 H), 4.47 (d, *J* = 14.4 Hz, 1 H), 4.79 (d, *J* = 9.0 Hz, 1 H), 5.25 (s, 1 H), 5.56 (s, 1 H), 7.23 (d, *J* = 7.8 Hz, 1 H), 7.26-7.36 (m, 9 H), 7.43 (d, *J* = 7.8 Hz, 2 H), 7.50 (d, *J* = 7.8 Hz, 2 H), 7.53 (d, *J* = 7.8 Hz, 2 H), 7.66 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.7, 54.3, 56.3, 72.0, 89.4, 89.8, 117.5, 123.4, 123.6, 126.0, 126.7, 127.7, 128.5, 128.57, 128.6, 128.7, 128.9, 129.2, 130.0, 131.1, 131.8, 135.4, 138.0, 141.9, 143.1, 144.1; IR (KBr, neat) 3497, 2923, 1599, 1493, 1444, 1334, 1157, 1093, 912, 812, 696 cm^{-1}; HRMS (ESI) calcd. for $C_{32}H_{30}NO_3S$ $(M + H)^+$ 508.1941, found 508.1939.

*N-(2-Hydroxy-2-(4-(trifluoromethyl)phenyl)ethyl)-4-methyl-N-(2-methylallyl)benzene-sulfonamide (**5k**):*

Colorless gum; R_f (hexane/ EtOAc 9:1) 0.50; yield 653 mg, 79%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.72 (s, 3 H), 2.42 (s, 3 H), 3.05 (d, *J* = 15.2, 1 H), 3.31 (dd, *J* = 15.2 and 9.6 Hz, 1 H), 3.58 (d, *J* = 15.2 Hz, 2 H), 3.95 (d, *J* = 14.4 Hz, 1 H), 4.90 (s, 1 H), 4.95-4.99 (m, 2 H), 7.31 (d, *J* = 8.0 Hz, 2 H), 7.46 (d, *J* = 8.0 Hz, 2 H), 7.58 (d, *J* = 8.0 Hz, 2 H), 7.70 (d, *J* = 8.0 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 20.0, 21.7, 56.5, 57.0, 72.3, 115.8, 124.3 (q, *J* = 270.0 Hz), 125.6, 126.5, 127.5, 130.1, 130.2 (q, *J* = 31.5 Hz), 135.9, 140.9, 144.1, 145.8; ^{19}F NMR (376 MHz, C_6F_6/$CDCl_3$): 99.22; IR (KBr, neat) 3502, 2925, 1598, 1417, 1326, 1158, 1123, 1067, 921, 815, 777 cm^{-1}; HRMS (ESI) calcd. for $C_{20}H_{23}F_3NO_3S$ $(M + H)^+$ 414.1345, found 414.1359.

*N-(2-Hydroxy-2-(4-methoxyphenyl)ethyl)-4-methyl-N-(2-methylallyl)benzenesulfonamide (**5l**):*

Pale yellow gum; R_f (hexane/ EtOAc 4:1) 0.48; yield 503 mg, 67%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.71 (s, 3 H), 2.41 (s, 3 H), 3.03 (dd, *J* = 15.6 and 3.0 Hz, 1 H), 3.16 (brs, 1 H),

3.35 (dd, *J* = 15.6 and 9.6 Hz, 1 H), 3.61 (d, *J* = 14.4 Hz, 1 H), 3.79 (s, 3 H), 3.90 (d, *J* = 15.0 Hz, 1 H), 4.85 (d, *J* = 9.0 Hz, 1 H), 4.88 (s, 1 H), 4.96 (s, 1 H), 6.86 (d, *J* = 9.0 Hz, 2 H), 7.24 (d, *J* = 9.0 Hz, 2 H), 7.29 (d, *J* = 7.8 Hz, 2 H), 7.71 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 20.1, 21.7, 55.5, 56.6, 56.7, 72.2, 114.1, 115.5, 127.3, 127.5, 130.0, 133.9, 136.3, 141.0, 143.9, 159.5; IR (KBr, neat) 3508, 2924, 1612, 1514, 1444, 1334, 1156, 1033, 919, 656 cm^{-1}; Anal. calcd. for $C_{20}H_{26}NO_4S$: C 63.97, H 6.71, N 3.73, found C 64.05, H 6.76, N 3.64.

*N-(2-Hydroxyphenyl)-4-methyl-N-(2-phenylallyl)-benzenesulfonamide (**5m**):*

Pale yellow gum; R_f (hexane/ EtOAc 7:3) 0.57; yield 570 mg, 75%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.45 (s, 3 H), 4.94 (s, 1 H), 5.26 (s, 1 H), 5.68 (s, 1 H), 6.32 (d, *J* = 8.4 Hz, 1 H), 6.50 (t, *J* = 8.6 Hz, 1 H), 6.87 (d, *J* = 8.4 Hz, 1 H), 7.13 (t, *J* = 7.6 Hz, 1 H), 7.26-7.45 (m, 8 H), 7.52 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.9, 55.6, 117.4, 117.8, 120.1, 124.9, 126.8, 127.5, 128.5, 128.6, 128.9, 129.8, 130.1, 133.7, 137.7, 142.2, 144.6, 155.3; IR (KBr, neat) 3508, 2852, 1597, 1493, 1344, 1161, 1091, 814, 704 cm^{-1}; HRMS (ESI) calcd. for $C_{22}H_{22}NO_3S$ $(M + H)^+$ 380.1315, found 380.1323.

*N-(2-Hydroxyethyl)-4-methyl-N-(3-methylbut-3-en-1-yl)-benzenesulfonamide (**5n**):*

Colourless oil; R_f (hexane/ EtOAc 7:3) 0.40; yield 490 mg, 90%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.70 (s, 3 H), 2.24 (t, *J* = 7.8 Hz, 2 H), 2.41 (s, 3 H), 2.57 (brs, 1 H), 3.23 (t, *J* = 5.4 Hz, 2 H), 3.26 (t, *J* = 7.8 Hz, 2 H), 3.74 (t, *J* = 4.8 Hz, 2 H), 4.67 (s, 1 H), 4.76 (s, 1 H), 7.30 (d, *J* = 7.8 Hz, 2 H), 7.69 (d, *J* = 7.8 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 22.6, 37.0, 48.6, 51.0, 61.4, 112.4, 127.4, 129.9, 136.1, 142.3, 143.7; IR (KBr, neat) 3517, 2931, 1598, 1454, 1378, 1158, 1088, 815, 734 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{21}NNaO_3S$ $(M + Na)^+$ 306.1134, found 306.1133.

*N-(2-Hydroxyethyl)-4-methyl-N-(3-methylbut-2-en-1-yl)-benzenesulfonamide (**5o**):*

Pale yellow oil; R_f (hexane/ EtOAc 7:3) 0.40; yield 496 mg, 81%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.62 (s, 3 H), 1.67 (s, 3 H), 2.43 (s, 3 H), 3.20 (t, *J* = 5.6 Hz, 2 H), 3.72 (t, *J* = 4.8 Hz, 2 H), 3.84 (d, *J* = 7.2 Hz, 2 H), 5.02 (dt, *J* = 6.8 and 1.6 Hz, 1 H), 7.31 (d, *J* = 8.4 Hz, 2 H), 7.70 (d, *J* = 7.6 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.0, 21.7, 25.9, 47.1, 49.9, 61.4, 119.0, 127.5, 129.9, 136.6, 137.7, 143.6; IR (KBr, neat) 3524, 2926, 1598, 1448, 1336, 1158, 1090, 816, 702 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{21}NaNO_3S$ $(M + Na)^+$ 306.1134, found 306.1136.

*N-(2-Hydroxy-2-phenylethyl)-4-methyl-N-(3-methylbut-3-en-1-yl)benzenesulfonamide (**5p**):*

Pale yellow gum; R_f (hexane/ EtOAc 7:3) 0.60; yield 470 mg, 66%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.71 (s, 3 H), 2.14 (t, *J* = 7.2 Hz, 2 H), 2.41 (s, 3 H), 3.05 (dd, *J* = 13.2 and 6.6 Hz, 2 H), 3.26-3.35 (m, 2 H), 4.68 (s, 1 H), 4.78 (s, 1 H), 4.95 (dd, *J* = 9.0 and 3.6 Hz, 1 H), 7.28-7.39 (m, 7 H), 7.71 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.7, 22.7, 37.4, 49.1, 57.1, 73.0, 112.5, 126.1, 127.3, 127.5, 128.8, 129.9, 130.0, 141.6, 142.4, 143.8; IR (KBr, neat) 3504, 2924, 1494, 1454, 1329, 1157, 1092, 814, 700 cm^{-1}; HRMS (ESI) calcd. for $C_{20}H_{26}NO_3S$ $(M + H)^+$ 360.1628, found 360.1635.

*N-(2-Hydroxyethyl)-4-methyl-N-(3-phenylbut-3-en-1-yl)benzenesulfonamide (**5q**):*

Pale yellow gum; R_f (hexane/ EtOAc 7:3) 0.45; yield 492 mg, 67%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.41 (s, 3 H), 2.82 (t, *J* = 7.2 Hz, 2 H), 3.23-3.27 (m, 4 H), 3.73 (t, *J* = 5.4 Hz, 2 H), 5.01 (s, 1 H), 5.36 (s, 1 H), 7.28 (d, *J* = 8.4 Hz, 2 H), 7.33 (t, *J* = 7.2 Hz, 3 H), 7.38 (d, *J* = 7.8 Hz, 2 H), 7.68 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.7, 35.4, 49.5, 51.6, 61.5, 114.6, 126.1, 127.5, 128.0, 128.7, 130.0, 136.3, 140.1, 143.7, 145.0; IR (KBr, neat) 3427, 2923, 2853, 1494, 1463, 1261, 1154, 1089, 1020, 801, 705 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{23}NNaO_3S$ $(M + Na)^+$ 368.1291, found 368.1300.

*N-(2-Mercaptoethyl)-4-methyl-N-(2-phenylallyl)benzene-sulfonamide (**5s**):*

Pale yellow gum; R_f (hexane/ EtOAc 7.3) 0.60; yield 638 mg, 92%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.43 (s, 3 H), 2.49 (dd, *J* = 8.8 and 5.6 Hz, 2 H), 3.21 (dd, *J* = 10.8 and 8.0 Hz, 2 H), 4.18 (s, 2 H), 5.18 (s, 1 H), 5.46 (s, 1 H), 7.26-7.33 (m, 5 H), 7.41-7.46 (m, 2 H), 7.66 (d, *J* = 8.0 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.7, 35.9, 47.4, 53.2, 117.3, 126.6, 127.5, 128.4, 128.7, 130.0, 135.7, 137.8, 142.7, 143.8; IR (KBr, neat) 3058, 2924, 1597, 1445, 1339, 1159, 1090, 914, 818, 658 cm^{-1}; HRMS (ESI) calcd. for $C_{18}H_{22}NO_2S_2$ $(M + H)^+$ 348.1086, found 348.1078.

*N-(1-Mercaptopropan-2-yl)-4-methyl-N-(2-phenylallyl)benzenesulfonamide (**5t**):*

Pale yellow gum; R_f (hexane/ EtOAc 19:1) 0.30; yield 267 mg, 74%; $[\alpha]_D^{25}$ = + 8.0 (c = 0.1, CH_2Cl_2). ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.07 (d, *J* = 6.6 Hz, 3 H), 2.36-2.41 (m, 1 H), 2.43 (s, 3 H), 2.54-2.59 (m, 1 H), 3.81-3.87 (m, 1 H), 4.07 (d, *J* = 16.2 Hz, 1 H), 4.49 (d, *J* = 16.2 Hz, 1 H), 5.36 (s, 1 H), 5.46 (s, 1 H), 7.28-7.32 (m, 3 H), 7.34 (t, *J* = 7.8 Hz, 2 H), 7.42 (d, *J* = 7.2 Hz, 2 H), 7.69 (d, *J* = 7.8 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 16.3, 21.7, 30.0, 48.5, 57.8, 116.3, 126.8, 127.5, 128.3, 128.7, 129.9, 137.6, 138.7, 143.6, 145.1; IR (KBr, neat) 3464, 2925, 2855, 1598, 1495, 1448, 1334, 1154, 1090, 998, 701 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{24}NO_2S_2$ $(M + H)^+$ 362.1243, found 362.1245.

*(S)-Methyl 3-mercapto-2-(4-methyl-N-(2-methylallyl)phenyl-sulfonamido)propanoate (**5u**):*

Pale yellow gum; R_f (hexane/ EtOAc 7:3) 0.58; yield 453 mg, 66%; $[\alpha]_D^{25}$ = +33.0 (c = 0.1, CH_2Cl_2). ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.76 (s, 3 H), 2.42 (s, 3 H), 2.78 (d, *J* = 5.4 Hz, 2 H), 3.05 (d, *J* = 10.2 Hz, 2 H), 3.57 (s, 3 H), 4.10-4.14 (m, 1 H), 4.81 (s, 1 H), 4.86 (s, 1 H), 5.40 (d, *J* = 8.4 Hz, 1 H), 7.29 (d, *J* = 8.4 Hz, 2 H), 7.73 (d, *J* = 7.8 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 20.6, 21.7, 33.9, 39.9, 52.8, 55.5, 114.7, 127.4, 129.8, 136.9, 140.6, 143.9, 170.8; IR (KBr, neat) 3277, 2923, 2854, 1744, 1598, 1436, 1341, 1160, 1090, 815, 662 cm^{-1}; HRMS (ESI) calcd. for $C_{15}H_{22}NO_4S_2$ $(M + H)^+$ 344.0985, found 344.0989.

*(S)-Methyl 3-mercapto-2-(4-methyl-N-(2-phenylallyl)phenyl-sulfonamido)propanoate (**5v**):*

Pale yellow gum; R_f (hexane/ EtOAc 7:3) 0.60; yield 494 mg, 61%; $[\alpha]_D^{25}$ = +10.0 (c =0.05, CH_2Cl_2). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.41 (s, 3 H), 2.83 (d, *J* = 5.4 Hz, 2 H), 3.53 (s, 3 H), 3.57 (s, 2 H), 4.11-4.16 (m, 1 H), 5.21 (s, 1 H), 5.46 (s, 1 H), 7.26-7.30 (m, 3 H), 7.34 (t, *J* = 7.2 Hz, 2 H), 7.41 (d, *J* = 7.2 Hz, 2 H), 7.72 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.7, 34.3, 37.1, 52.9, 55.6, 116.2, 126.5, 127.4, 128.1, 128.6, 129.9, 136.9, 139.0, 143.1, 144.0, 170.7; IR (KBr, neat) 3447, 2924, 1742, 1626, 1494, 1444, 1341, 1161, 1092, 908, 779 cm^{-1}; HRMS (ESI) calcd. for $C_{20}H_{24}NO_4S_2$ $(M + H)^+$ 406.1141, found 406.1141.

*(S)-3-Mercapto-2-(4-methyl-N-(2-methylallyl)phenyl-sulfonamido)propyl acetate (**5w**):*

Pale yellow oil; R_f (hexane/ EtOAc 7:3) 0.42; yield 607 mg, 85%; $[\alpha]_D^{25}$ = +15.0 (c = 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.75 (s, 3 H), 1.94 (s, 3 H), 2.43 (s, 3 H), 2.54 (d, *J* = 10.8 Hz, 1 H), 2.56 (d, *J* = 9.2 Hz, 1 H), 2.93 (d, *J* = 7.2 Hz, 2 H), 3.58 (dt, *J* = 12.8 and 5.6 Hz, 1 H), 3.99 (dd, *J* = 12.0 and 4.4 Hz, 1 H), 4.18 (dd, *J* = 11.2 and 5.6 Hz, 1 H), 4.73 (s, 1 H), 4.82 (s, 1 H), 5.01 (d, *J* = 7.6 Hz, 1 H), 7.31 (d, *J* = 8.4 Hz, 2 H), 7.77 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.6, 20.8, 21.7, 33.0, 39.8, 51.9, 64.7, 114.5, 127.3, 129.9, 137.7, 140.7, 143.8, 170.9; IR (KBr, neat) 3450, 2932, 1728, 1616, 1503, 1449, 1350, 1149, 1093, 909, 777 cm^{-1}; HRMS (ESI) calcd. for $C_{16}H_{24}NO_4S_2$ $(M + H)^+$ 358.1141, found 358.1140.

*N-(1-Hydroxy-3-mercaptopropan-2-yl)-4-methyl-N-(2-phenylallyl)benzenesulfonamide (**5x**):*

Pale yellow oil; R_f (hexane/ EtOAc 3:2) 0.49; yield 566 mg, 75%; $[\alpha]_D^{25}$ = - 9.0 (c = 0.4, CH_2Cl_2). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.41 (s, 3 H), 2.55 (dd, *J* = 6.6 and 2.4 Hz, 2 H), 3.29-3.34 (m, 2 H), 3.40 (d, *J* = 13.8 Hz, 1 H), 3.60 (s, 2 H), 5.07 (s, 1 H), 5.32 (brs, 1 H), 5.37 (s, 1 H), 7.26-7.37 (m, 7 H), 7.75(d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.7, 33.0, 36.8, 54.1, 63.6, 115.8, 126.4, 127.4, 128.2, 128.6, 130.0, 137.2, 139.0, 143.2,

143.9; IR (KBr, neat) 3504, 3279, 2924, 1598, 1494, 1444, 1327, 1157, 1092, 1036, 814, 702 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{24}NO_3S_2$ $(M + H)^+$ 378.1192, found 378.1193.

General Procedure for the Synthesis of 6a-t & 7u-x: To a stirred solution of compound **5a-x** (1 mmol.) in dichloromethane (5 mL), 1.2 equivalents of borontrifluoride etherate under nitrogen atmosphere was added at room temperature. Then it was continuously stirred for 5 h. After completion of the reaction, the reaction mixture was quenched by addition of saturated sodium bicarbonate solution (5 mL). The aqueous layer was extracted with dichloromethane (3 X 10 mL) and the organic layer was dried over anhydrous Na_2SO_4. After concentration under vacuum, the crude product was purified using column chromatography on silica gel with ethylacetate and hexane as eluents.

*2,2-Dimethyl-4-tosylmorpholine (**6a**):*

White solid, mp 92-94 ^oC; R_f (hexane/ EtOAc 4:1) 0.47; yield 223 mg, 83%; ^1H NMR (600 MHz, $CDCl_3$) δ 1.26 (s, 6 H), 2.44 (s, 3 H), 2.72 (s, 2 H), 2.91 (t, *J* = 4.8 Hz, 2 H), 3.77 (t, *J* = 4.8 Hz, 2 H), 7.33 (d, *J* = 7.8 Hz, 2 H), 7.61 (t, *J* = 8.4 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) 21.7 (2C), 24.6, 45.9, 54.9, 60.4, 71.2, 128.0, 129.9, 132.6, 144.0; IR (KBr, neat) 2978, 2877, 1598, 1351, 1166, 1099, 759 cm^{-1}; HRMS (ESI) calcd. for $C_{13}H_{20}NO_3S$ $(M + H)^+$ 270.1158 found 270.1157.

*(R)-2,2-Dimethyl-5-phenyl-4-tosylmorpholine (**6b**):*

Pale yellow solid, mp 77-79 ^oC; R_f (hexane/ EtOAc 4:1) 0.47; yield 245 mg, 71%; $[\alpha]_D^{25}$ = -68.5 (c = 0.33, CH_2Cl_2). ^1H NMR (600 MHz, $CDCl_3$) δ 1.24 (s, 3 H), 1.25 (s, 3 H), 2.37 (s, 3 H), 3.11 (d, *J* = 13.2 Hz, 1 H), 3.23 (d, *J* = 12.6 Hz, 1 H), 3.99 (dd, *J* = 12.0 and 2.4 Hz, 1 H), 4.10 (dd, *J* = 12.0 and 4.2 Hz, 1 H), 4.71 (t, *J* = 3.0 Hz, 1 H), 7.16 (d, *J* = 8.4 Hz, 2 H), 7.21-7.23 (m, 3 H), 7.36-7.38 (m, 2 H), 7.47 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) 21.6, 22.4, 26.7, 50.6, 55.8, 64.7, 71.4, 127.5, 127.9, 128.4, 128.7, 129.5, 137.1,

137.8, 143.3; IR (KBr, neat) 2975, 2872, 1599, 1495, 1340, 1164, 1026, 705 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{24}NO_3S$ $(M + H)^+$ 346.1471 found 346.1471.

*(S)-Methyl 6,6-dimethyl-4-tosylmorpholine-3-carboxylate (**6c**):*

Pale yellow gum; R_f (hexane/ EtOAc 4:1) 0.50; yield 281 mg, 86%; $[\alpha]_D^{25}$ = - 70.0 (c = 0.1, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 1.14 (s, 3 H), 1.26 (s, 3 H), 2.40 (s, 3 H), 3.12 (d, *J* = 12.4 Hz, 1 H), 3.32 (d, *J* = 12. 8 Hz, 1 H), 3.52 (s, 3 H), 4.00-4.10 (m, 2 H), 4.44 (d, *J* = 3.6 Hz, 1 H), 7.26 (d, *J* = 8.0 Hz, 2 H), 7.62 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) 20.8, 21.7, 27.5, 50.6, 52.5, 54.5, 62.5, 71.2, 127.5, 129.6, 136.6, 143.6, 169.7; IR (KBr, neat) 2981, 1339, 1154, 1091, 1049, 905, 815, 741 cm^{-1}; HRMS (ESI) calcd. for $C_{15}H_{22}NO_5S$ $(M + H)^+$ 328.1213 found 328.1225.

*2-Methyl-2-phenyl-4-tosylmorpholine (**6d**):*

Pale yellow solid, mp 126-128 ^oC; R_f (hexane/ EtOAc 4:1) 0.50; yield 298 mg, 90%; ^1H NMR (600 MHz, $CDCl_3$) δ 1.44 (s, 3 H), 2.45 (s, 3 H), 2.71-2.78 (m, 2 H), 3.13 (d, *J* = 11.4 Hz, 1 H), 3.62-3.68 (m, 1 H), 3.72-3.79 (m, 2 H), 7.28 (d, *J* = 7.8 Hz, 1 H), 7.34-7.39 (m, 4 H), 7.47 (d, *J* = 7.8 Hz, 2 H), 7.65 (d, *J* = 7.8 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) 21.6, 28.1, 45.7, 52.7, 60.7, 75.1, 126.1, 127.3, 127.9, 128.6, 129.9, 132.1, 142.7, 144.0; IR (KBr, neat) 2977, 2853, 1599, 1458, 1351, 1168, 1093, 802, 701 cm^{-1}; HRMS (ESI) calcd. for $C_{18}H_{22}NO_3S$ $(M + H)^+$ 332.1315 found 332.1318.

*(2S,5S)-2,5-Dimethyl-2-phenyl-4-tosylmorpholine (**6e**):*

Pale yellow oil; R_f (hexane/ EtOAc 4:1) 0.60; yield 255 mg, 74%; $[\alpha]_D^{25}$ = + 48.0 (c = 0.1, CH_2Cl_2). ^1H NMR (600 MHz, $CDCl_3$) δ 1.02 (d, *J* = 6.6 Hz, 3 H), 1.58 (s, 3 H), 2.41 (s, 3 H), 3.26 (d, *J* = 12.6 Hz, 1 H), 3.52 (d, *J* = 11.4 and 2.4 Hz, 2 H), 3.84-3.88 (m, 1 H), 4.07-4.10 (m, 1 H), 7.26-7.30 (m, 3 H), 7.37 (t, *J* = 7.2 Hz, 2 H), 7.47 (d, *J* = 7.2 Hz, 2 H), 7.68 (d, *J* =

7.8 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) 13.5, 21.7, 22.6, 49.0, 49.5, 65.9, 74.7, 124.9, 127.3, 127.5, 128.6, 129.9, 137.1, 143.6, 144.9; IR (KBr, neat) 2978, 2874, 1590, 1447, 1338, 1152, 1021, 800, 701 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{24}NO_3S$ $(M + H)^+$ 346.1471 found 346.1471.

*(2S,5S)-5-Benzyl-2-methyl-2-phenyl-4-tosylmorpholine (**6f**):*

Pale yellow solid, mp 95-97 °C; R_f (hexane/ EtOAc 4:1) 0.65; yield 265 mg, 63%; $[\alpha]_D^{25}$ = + 26.0 (c = 0.1, CH_2Cl_2). ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.60 (s, 3 H), 2.41 (s, 3 H), 2.44 (dd, *J* = 13.2 and 3.0 Hz, 1 H), 3.03 (dd, *J* = 13.2 and 10.8 Hz, 1 H), 3.19 (d, *J* = 12.6 Hz, 1 H), 3.64 (d, *J* = 12.0 Hz, 1 H), 3.77 (d, *J* = 12.6 Hz, 1 H), 3.93-3.99 (m, 2 H), 7.14 (d, *J* = 7.2 Hz, 2 H), 7.21 (t, *J* = 7.2 Hz, 1 H), 7.27-7.33 (m, 5 H), 7.40 (t, *J* = 7.8 Hz, 2 H), 7.53 (d, *J* = 7.8 Hz, 2 H), 7.71 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) 21.5, 21.7, 32.3, 49.7, 54.4, 61.1, 74.2, 124.7, 126.8, 127.2, 127.6, 128.7, 128.9, 129.7, 130.1, 137.8, 138.0, 143.7, 145.4; IR (KBr, neat) 2924, 2872, 1599, 1448, 1339, 1165, 1052, 814, 702 cm^{-1}; HRMS (ESI) calcd. for $C_{25}H_{28}NO_3S$ $(M + H)^+$ 422.1784 found 422.1782.

(2S,6R*)-2-Methyl-2,6-diphenyl-4-tosylmorpholine (**6g**):*

Pale yellow solid, mp 191-193 °C; R_f (hexane/ EtOAc 4:1) 0.70; yield 180 mg, 79%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.83 (s, 3 H), 2.14 (t, *J* = 10.8 Hz, 1 H), 2.29 (d, *J* = 11.4 Hz, 1 H), 2.37 (s, 3 H), 3.87 (dd, *J* = 10.8 and 2.4 Hz, 1 H), 5.18 (dd, *J* = 10.2 and 3.0 Hz, 1 H), 7.24 (d, *J* = 7.2 Hz, 2 H), 7.27-7.45 (m, 8 H), 7.52 (d, *J* = 7.8 Hz, 1 H), 7.55 (d, *J* = 7.8 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 22.3, 52.5, 54.8, 71.4, 75.4, 124.7, 126.5, 127.6, 127.9, 128.4, 128.6, 128.8, 130.0, 132.6, 139.5, 144.1, 145.3; IR (KBr, neat) 2928, 1558, 1447, 1351, 1168, 1091, 999, 699 cm^{-1}; HRMS (ESI) calcd. for $C_{24}H_{26}NO_3S$ $(M + H)^+$ 408.1628 found 408.1644.

(2S,6R*)-6-(3-Bromophenyl)-2,2-dimethyl-4-tosylmorpholine (**6h**):*

White solid, mp 150-152 ^{o}C; R_f (hexane/ EtOAc 9:1) 0.65; yield 343 mg, 81%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.27 (s, 3 H), 1.47 (s, 3 H), 1.99 (t, *J* = 10.8 Hz, 1 H), 2.14 (d, *J* = 11.4 Hz, 1 H), 2.42 (s, 3 H), 3.47 (dd, *J* = 10.8 and 1.2 Hz, 1 H), 3.73 (dd, *J* = 9.6 and 1.8 Hz, 1 H), 4.87 (dd, *J* = 10.8 and 3.0 Hz, 1 H), 7.19 (t, *J* = 7.8 Hz, 1 H), 7.22 (t, *J* = 7.2 Hz, 1 H), 7.31 (d, *J* = 7.8 Hz, 2 H), 7.40 (d, *J* = 7.8 Hz, 1 H), 7.48 (s, 1 H), 7.58 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.7, 21.8, 28.0, 52.0, 54.4, 70.8, 72.3, 122.8, 125.1, 127.9, 129.4, 130.0, 130.2, 131.4, 132.6, 141.7, 144.1; IR (KBr, neat) 2978, 1597, 1453, 1352, 1165, 1093, 998, 694 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{23}BrNO_3S$ $(M + H)^+$ 424.0577, found 424.0576.

(2S,6R*)-6-(3-Bromophenyl)-2-methyl-2-phenyl-4-tosylmorpholine (**6i**):*

White solid, mp 134-136 ^{o}C; R_f (hexane/ EtOAc 9:1) 0.48; yield 417 mg, 86%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.82 (s, 3 H), 2.10 (t, *J* = 11.4 Hz, 1 H), 2.29 (d, *J* = 11.4 Hz, 1 H), 2.38 (s, 3 H), 3.85 (d, *J* = 11.4 Hz, 2 H), 5.14 (dd, *J* = 10.2 and 2.4 Hz, 1 H), 7.23-7.28 (m, 3 H), 7.30 (t, *J* = 7.8 Hz, 1 H), 7.34-7.40 (m, 4 H), 7.50 (d, *J* = 7.8 Hz, 2 H), 7.57 (d, *J* = 8.4 Hz, 2 H), 7.60 (s, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.7, 22.3, 52.3, 54.7, 70.9, 75.7, 122.9, 124.6, 125.1, 127.7, 127.9, 128.7, 129.5, 130.1, 130.3, 131.6, 132.6, 141.8, 144.2, 145.0; IR (KBr, neat) 2984, 1597, 1449, 1344, 1164, 1091, 999, 756, 694 cm^{-1}; HRMS (ESI) calcd. for $C_{24}H_{25}BrNO_3S$ $(M + H)^+$ 486.0733, found 486.0731.

(2S,6R*)-2-Methyl-2-phenyl-6-(3-(phenylethynyl)phenyl)-4-tosylmorpholine (**6j**):*

Colourless gum; R_f (hexane/ EtOAc 9:1) 0.38; yield 370 mg, 73%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.84 (s, 3 H), 2.14 (t, *J* = 11.4 Hz, 1 H), 2.31 (d, *J* = 11.4 Hz, 1 H), 2.38 (s, 3 H), 3.87 (d, *J* = 9.6 Hz, 2 H), 5.18 (dd, *J* = 10.8 and 3.0 Hz, 1 H), 7.31 (d, *J* = 7.2 Hz, 2 H), 7.35-7.41 (m, 7 H), 7.50 (d, *J* = 7.8 Hz, 2 H), 7.52-7.55 (m, 4 H), 7.57 (d, *J* = 8.4 Hz, 2 H), 7.61 (s, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.7, 22.4, 52.4, 54.8, 71.2, 75.6, 89.2, 90.0, 123.3, 123.8, 124.7, 125.1, 126.4, 127.7, 127.9, 128.6, 128.63, 128.8, 129.6, 130.1, 131.6, 131.9,

132.6, 139.8, 144.1, 145.2; IR (KBr, neat) 2924, 1600, 1493, 1450, 1348, 1165, 1094, 1002, 909, 697 cm^{-1}; HRMS (ESI) calcd. for $C_{32}H_{30}NO_3S$ $(M + H)^+$ 508.1941, found 508.1947.

(2S,6R*)-2,2-Dimethyl-4-tosyl-6-(4-(trifluoromethyl)phenyl)morpholine (**6k**):*

Colorless solid, mp 141-143 ^oC; R_f (hexane/ EtOAc 9:1) 0.65; yield 380 mg, 92%; ^1H NMR (600 MHz, $CDCl_3$) δ 1.29 (s, 3 H), 1.49 (s, 3 H), 2.00 (t, *J* = 10.8 Hz, 1 H), 2.16 (d, *J* = 11.4 Hz, 1 H), 2.43 (s, 3 H), 3.49 (dd, *J* = 11.4 and 1.2 Hz, 1 H), 3.78 (dt, *J* = 10.8 and 1.2 Hz, 1 H), 4.96 (dd, *J* = 10.8 and 3.0 Hz, 1 H), 7.31 (d, *J* = 8.4 Hz, 2 H), 7.44 (d, *J* = 8.4 Hz, 2 H), 7.57-7.60 (m, 4 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.7, 21.8, 28.0, 52.0, 54.5, 71.0, 72.4, 124.2 (q, *J* = 270.0 Hz), 125.6, 126.8, 127.9, 130.1, 130.5 (q, *J* = 33.0 Hz), 132.6, 143.4, 144.2; ^{19}F NMR (376 MHz, $C_6F_6/CDCl_3$): 99.12; IR (KBr, neat) 2926, 1599, 1454, 1325, 1165, 1093, 1029, 941, 667 cm^{-1}; HRMS (ESI) calcd. for $C_{20}H_{23}F_3NO_3S$ $(M + H)^+$ 414.1345, found 414.1343.

*2-Methyl-2-phenyl-4-tosyl-3,4-dihydro-2H-benzo[b][1,4]-oxazine (**6m**):*

Colourless solid, mp 119-121 ^oC; R_f (hexane/ EtOAc 4:1) 0.73; yield 258 mg, 68%; ^1H NMR (600 MHz, $CDCl_3$) δ 1.67 (s, 3 H), 2.34 (s, 3 H), 3.97 (d, *J* = 12.6 Hz, 1 H), 4.14 (d, *J* = 12.6 Hz, 1 H), 6.77-6.80 (m, 1 H), 6.95-6.98 (m, 1 H), 7.02 (dd, *J* = 7.8 and 1.2 Hz, 1 H), 7.15 (d, *J* = 7.8 Hz, 1 H), 7.32 (t, *J* = 7.2 Hz, 1 H), 7.36 (t, *J* = 7.2 Hz, 2 H), 7.44-7.50 (m, 6 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.7, 26.0, 53.0, 77.5, 118.2, 119.0, 120.9, 124.5, 124.6, 125.3, 127.4, 127.9, 128.9, 129.9, 136.7, 142.6, 144.1, 144.7; IR (KBr, neat) 2927, 2869, 1598, 1493, 1352, 1165, 1090, 813, 700 cm^{-1}; HRMS (ESI) calcd. for $C_{22}H_{22}NO_3S$ $(M + H)^+$ 380.1315 found 380.1316.

*7,7-Dimethyl-4-tosyl-1,4-oxazepane (**6n**):*

Colourless solid, mp 62-64 ^{o}C; R_f (hexane/ EtOAc 4:1) 0.50; yield 263 mg, 93%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.13 (s, 6 H), 1.91 (t, *J* = 4.8 Hz, 2 H), 2.42 (s, 3 H), 3.20-3.23 (m, 4 H), 3.70 (t, *J* = 4.2 Hz, 2 H), 7.31 (d, *J* = 7.8 Hz, 2 H), 7.64 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 27.7 (2C), 41.3, 43.8, 51.3, 62.6, 76.9, 127.3, 129.7, 134.8, 143.4; IR (KBr, neat) 2973, 2870, 1598, 1452, 1385, 1163, 1034, 862, 718 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{22}NO_3S$ $(M + H)^+$ 284.1315 found 284.1316.

*7,7-Dimethyl-2-phenyl-4-tosyl-1,4-oxazepane (**6p**):*

Yellow solid, mp 137-139 ^{o}C; R_f (hexane/ EtOAc 4:1) 0.68; yield 258 mg, 72%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.20 (s, 3 H), 1.21 (s, 3 H), 1.96 (dd, *J* = 15.6 and 7.2 Hz, 1 H), 2.13 (dd, *J* = 15.6 and 9.6 Hz,1 H), 2.42 (s, 3 H), 2.66 (dd, *J* = 12.6 and 9.6 Hz, 1 H), 2.83 (dd, *J* = 13.8 and 10.2 Hz, 1 H), 3.88 (dd, *J* = 13.2 and 7.8 Hz, 1 H), 3.98 (d, *J* = 12.6 Hz, 1 H), 4.84 (d, *J* = 9.6 Hz, 1 H), 7.26-7.35 (m, 7 H), 7.63 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.7, 26.5, 29.5, 42.3, 44.0, 57.0, 73.9, 75.2, 126.1, 127.4, 127.7, 128.5, 129.9, 135.5, 141.0, 143.5; IR (KBr, neat) 2972, 2927, 1598, 1449, 1339, 1162, 1026, 890, 724 cm^{-1}; HRMS (ESI) calcd. for $C_{20}H_{26}NO_3S$ $(M + H)^+$ 360.1628 found 360.1631.

*7-Methyl-7-phenyl-4-tosyl-1,4-oxazepane (**6q**):*

Colourless gum; R_f (hexane/ EtOAc 7:3) 0.58; yield 275 mg, 75%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.44 (s, 3 H), 2.45 (s, 3 H), 2.72 (d, *J* = 12.0 Hz, 1 H), 2.76 (d, *J* = 8.4 Hz,1 H), 3.12 (d, *J* = 11.4 Hz, 1 H), 3.62-3.67 (m, 2 H), 3.73-3.79 (m, 3 H), 7.28 (t, *J* = 7.2 Hz, 1 H), 7.35 (d, *J* = 7.8 Hz, 2 H), 7.38 (t, *J* = 7.8 Hz, 2 H), 7.47 (d, *J* = 8.4 Hz, 2 H), 7.64 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.8, 28.3, 29.9, 45.9, 52.8, 60.9, 75.3, 126.3, 127.5, 128.1, 128.9, 130.0, 132.4, 142.8, 144.1; IR (KBr, neat) 2923, 2853, 1530, 1453, 1349, 1165, 1092, 761, 660 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{23}NNaO_3S$ $(M + Na)^+$ 368.1291 found 368.1288.

*2-Methyl-2-phenyl-4-tosylthiomorpholine (**6s**):*

Pale yellow solid, mp 121-123 ^{o}C; R_f (hexane/ EtOAc 4:1) 0.70; yield 243 mg, 70%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.65 (s, 3 H), 2.44 (s, 3 H), 2.56-2.64 (m, 1 H), 2.75-2.82 (m, 1 H), 3.18-3.30 (m, 2 H), 3.32-3.39 (m, 1 H), 3.87 (d, *J* = 11.6 Hz, 1 H), 7.26 (t, *J* = 7.6 Hz, 1 H), 7.31-7.38 (m, 4 H), 7.62 (d, *J* = 8.4 Hz, 2 H), 7.67 (d, *J* = 8.0 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 26.2, 46.5, 47.5 (2C), 57.6, 127.0, 127.4, 127.7, 128.7, 130.0, 133.8, 143.3, 144.0; IR (KBr, neat) 2922, 2853, 1597, 1494, 1454, 1338, 1285, 1164, 1089, 899, 762 cm^{-1}; HRMS (ESI) calcd. for $C_{18}H_{22}NO_2S_2$ $(M + H)^+$ 348.1086, found 348.1080.

2,5-Dimethyl-2-phenyl-4-tosylthiomorpholine (6t):

Pale yellow gum; R_f (hexane/ EtOAc 19:1) 0.30; yield 311 mg, 86%; $[\alpha]_D^{25}$ = +42.83 (c = 0.6, CH_2Cl_2). ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.12 (d, *J* = 6.6 Hz, 3 H), 1.85 (s, 3 H), 2.35 (d, *J* = 13.2 Hz, 1 H), 2.42 (s, 3 H), 3.44-3.50 (m, 1 H), 3.85 (d, *J* = 13.2 Hz, 1 H), 4.48 (bs, 1 H), 7.27-7.31 (m, 3 H), 7.38 (t, *J* = 7.8 Hz, 2 H), 7.60 (d, *J* = 7.8 Hz, 2 H), 7.66 (d, *J* = 7.8 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 13.5, 21.7, 24.0, 32.2, 45.4, 46.8, 51.2, 126.4, 127.1, 127.8, ,129.9, 137.9, 143.4, 143.7; IR (KBr, neat) 2924, 2855, 1598, 1495, 1446, 1337, 1167, 1029, 995, 697 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{24}NO_2S_2$ $(M + H)^+$ 362.1243, found 362.1248.

*(2S,4S)-Methyl 2-isopropyl-3-tosylthiazolidine-4-carboxylate (7**u**):*

Yellow gum; R_f (hexane/ EtOAc 4:1) 0.56; yield 226 mg, 66%; $[\alpha]_D^{25}$ = - 2.0 (c = 0.06, CH_2Cl_2). ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.98 (d, *J* = 6.6 Hz, 3 H), 1.11 (d, *J* = 6.6 Hz, 3 H),1.88-1.95 (m, 1 H), 2.44 (s, 3 H), 2.82 (dd, *J* = 11.4 and 7.8 Hz, 1 H), 3.23 (dd, *J* = 11.4 and 6.0 Hz, 1 H), 3.78 (s, 3 H), 4.61 (t, *J* = 6.6 Hz, 1 H), 4.71 (d, *J* = 8.4 Hz, 1 H), 7.33 (d, *J* = 8.4 Hz, 2 H), 7.74 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.3, 20.5, 21.8, 33.9, 36.1, 53.1, 65.3, 74.9, 128.1, 130.1, 134.5, 144.6, 170.8; IR (KBr, neat) 2959, 2924,

1742, 1438, 1350, 1164, 1090, 1009, 815, 661 cm^{-1}; HRMS (ESI) calcd. for $C_{15}H_{22}NO_4S_2$ $(M + H)^+$ 344.0985 found 344.0984.

*(2S,4S)-Methyl 2-(1-phenylethyl)-3-tosylthiazolidine-4-carboxylate (**7v**, two diastereomers with a ratio of 7:3):*

Pale yellow gum; R_f (hexane/ EtOAc 4:1) 0.50; yield 288 mg, 71%; $[\alpha]_D^{25}$ = - 5.0 (c = 0.08, CH_2Cl_2). ^1H NMR (600 MHz, $CDCl_3$) δ 1.43 (d, *J* = 7.2 Hz, 3 H, minor), 1.54 (d, *J* = 7.2 Hz, 3 H, major), 2.41 (s, 3 H, minor), 2.43 (s, 3 H, major), 2.72 (dd, *J* = 11.4 and 7.8 Hz, 1 H, major), 2.92 (dd, *J* = 11.4 and 7.8 Hz, 1 H, minor), 3.00-3.06 (m, 2 H, major), 3.30 (dd, *J* = 11.4 and 6.6 Hz, 1 H, minor), 3.49 (dd, *J* = 11.4 and 6.0 Hz, 1 H, minor), 3.78 (s, 3 H, minor), 3.80 (s, 3 H, major), 4.57-4.62 (m, 2 H, major, minor), 5.15 (d, *J* = 9.6 Hz, 1 H, major), 5.18 (d, *J* = 6.6 Hz, 1 H, minor), 7.22-7.34 (m, 14 H, major, minor), 7.59 (d, *J* = 7.8 Hz, 2 H, minor), 7.77 (d, *J* = 8.4 Hz, 2 H, major); ^{13}C NMR (150 MHz, $CDCl_3$) δ 20.3, 21.7, 21.8, 22.9, 33.9, 34.0, 46.2, 48.0, 53.0, 53.1, 65.6, 66.2, 74.0, 74.1, 127.1, 127.2, 128.1, 128.2, 128.3, 128.5, 128.6, 130.0, 130.2, 134.1, 134.4, 142.8, 142.9, 144.6, 144.8, 170.5, 170.7; IR (KBr, neat) 2924, 2853, 1747, 1597, 1494, 1453, 1352, 1165, 1091, 815, 701 cm^{-1}; HRMS (ESI) calcd. for $C_{20}H_{24}NO_4S_2$ $(M + H)^+$ 406.1141 found 406.1143.

*((2S,4S)-2-Isopropyl-3-tosylthiazolidin-4-yl)methanol (**7w**):*

Yellow oil; R_f (hexane/ EtOAc 7:3) 0.30; yield 186 mg, 59%; $[\alpha]_D^{25}$ = - 40.0 (c = 0.1, CH_2Cl_2). ^1H NMR (600 MHz, $CDCl_3$) δ 1.01 (d, *J* = 6.6 Hz, 3 H), 1.13 (d, *J* = 6.6 Hz, 3 H), 1.93-1.99 (m, 1 H), 2.45 (s, 3 H), 2.66 (dd, *J* = 12.0 and 7.2 Hz, 1 H), 2.80 (dd, *J* = 12.0 and 6.0 Hz, 1 H), 3.74 (d, *J* = 6.0 Hz, 2 H), 4.01-4.06 (m, 1 H), 4.72 (d, *J* = 9.0 Hz, 1 H), 7.34 (d, *J* = 7.8 Hz, 2 H), 7.73 (d, *J* = 7.8 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 19.6, 20.8, 21.8, 33.2, 36.1, 65.2, 66.3, 75.3, 128.3, 130.1, 134.3, 144.6; IR (KBr, neat) 3412, 2924, 2854,

1712, 1637, 1462, 1344, 1161, 1090, 1037, 812, 661, 584, 550 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{22}NO_3S_2$ $(M + H)^+$ 316.1036 found 316.1035.

*((2S,4S)-2-(1-Phenylethyl)-3-tosylthiazolidin-4-yl)methanol (**7x,** diastereomeric mixture 3:2):*

Pale yellow gum; R_f (hexane/ EtOAc 3:2) 0.75; yield 279 mg, 74%; $[\alpha]_D^{25}$ = + 32.0 (c = 0.3, CH_2Cl_2). ^1H NMR (600 MHz, $CDCl_3$) δ 1.42 (d, *J* = 6.6 Hz, 3 H, minor), 1.46 (d, *J* = 7.2 Hz, 3 H, major), 2.33 (brs, 1 H), 2.42 (s, 3 H, minor), 2.44 (s, 3 H, major), 2.49 (d, *J* = 6.0 Hz, 2 H, major), 2.60 (dd, *J* = 12.0 and 7.2 Hz, 1 H, minor), 2.80 (dd, *J* = 12.0 and 4.8 Hz, 1 H, minor), 3.28 (pentet, *J* = 7.2Hz, 1 H, major), 3.35 (dd, *J* = 10.8 and 5.4 Hz, 1 H, major), 3.40 (dd, *J* = 11.4 and 6.6 Hz, 1 H, major), 3.48 (pentet, *J* = 6.6 Hz, 1 H, minor), 3.74 (dd, *J* = 10.8 and 6.0 Hz, 1 H, minor), 3.80 (dd, *J* = 11.4 and 6.6 Hz, 1 H, minor), 3.96 (pentet, *J* = 6.6 Hz, 1 H, major), 4.06 (pentet, *J* = 6.6 Hz, 1 H, minor), 5.15 (d, *J* = 7.8 Hz, 1 H, major), 5.21 (d, *J* = 6.6 Hz, 1 H, minor), 7.25-7.36 (m, 7 H), 7.62 (d, *J* = 8.4 Hz, 2 H, minor), 7.76 (d, *J* = 8.4 Hz, 2 H, major); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.3, 14.4, 19.9, 21.3, 21.8, 22.9, 32.1, 33.1, 46.6, 47.2, 64.5, 64.7, 74.2, 74.3, 127.3, 127.5, 128.2, 128.3, 128.5, 128.7, 129.2, 130.1, 130.2, 134.1, 142.0, 142.7, 144.6, 144.7; IR (KBr, neat) 3421, 2926, 1598, 1454, 1346, 1162, 1091, 1035, 813, 661 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{24}NO_3S_2$ $(M + H)^+$ 378.1192 found 378.1191.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra of all new compounds, crystal parameters and ORTEP diagram of compounds **6f,g** are included. This material is available free of charge *via* the Internet at http://pubs.acs.org.

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28 The crystallographic data for compounds **6f,g** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC 1051766 and 1041712, respectively.