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Synthesis of Five-, Six-, and Seven-Membered 1,3- and 1,4-Heterocyclic Compounds via Intramolecular Hydroalkoxylation/Hydrothioalkoxylation of Alkenols/Thioalkenols

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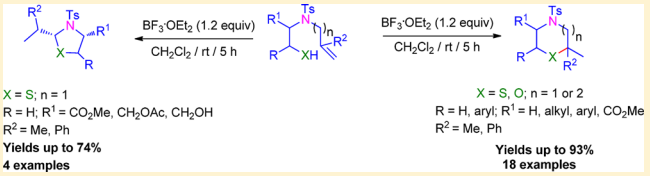
Supporting Information

ABSTRACT: Intramolecular hydroalkoxylation/hydrothioalkoxylation of nitrogen-tethered alkenes and alcohols/thiols mediated by boron trifluoride etherate leads to five-membered thiazolidine, six-membered 1,4-oxazines (morpholines) and tetrahydro-2*H*-1,4-thiazines (thiomorpholines), and seven-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, compounds **2** and **3** possess anti-inflammatory and $GABA_B$ receptor-antagonist properties.[3] The 1,4-oxazepane unit is found in naturally occurring alkaloid batrachotoxin (**4**), which acts as a ligand for CC chemokine receptors, such as CCRl (Figure 1).[1d,e,4] These heterocyclic

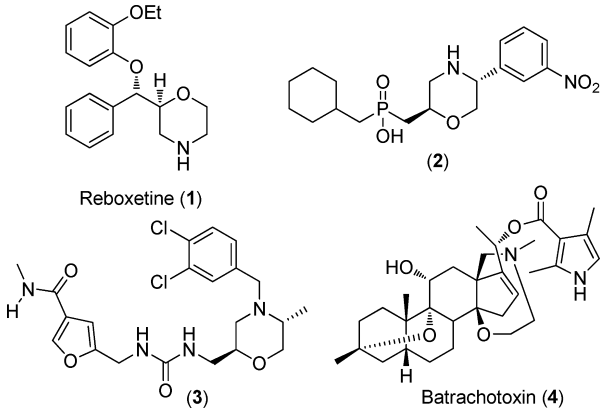


Figure 1. Biologically important morpholine and 1,4-oxazepane derivatives.

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 auxiliaries.[6] On the other hand, thiazolines are known as flavouring agents and are found in fruits and vegetables.[7] They are also known to possess biological activities such as anticancer,[8] antimicrobial,[9] and antihypertensive[10] activity and are used as building blocks in peptide synthesis.[11]

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 bromosulfonium salts,[13] double allylic substitution by amino alcohols,[14] cyclization of *N*-tethered halo alcohols,[15] reductive amination of diketones,[16] reductive etherification of *N*-tethered keto alcohols,[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 the Asinger method, a multicomponent reaction between an α-mercapto ketone, 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/hydrothioalkoxylation 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 and cannabinoid derivatives and in the total synthesis of quinone and hydroquinone sesquiterpenes via intermolecular addition of phenol to alkene.[25] However, the use of $BF_3{\cdot}OEt_2$ in intramolecular hydroalkoxylation/hydrothioalkoxylation reaction for the synthesis of five-, six-, and seven-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

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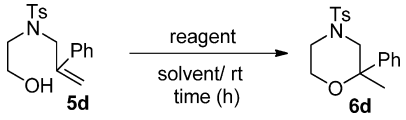
mediated by boron trifluoride etherate at ambient temperature in moderate to good yields.

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 equiv 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

Table 1. Optimization of the Reaction Conditions[a]



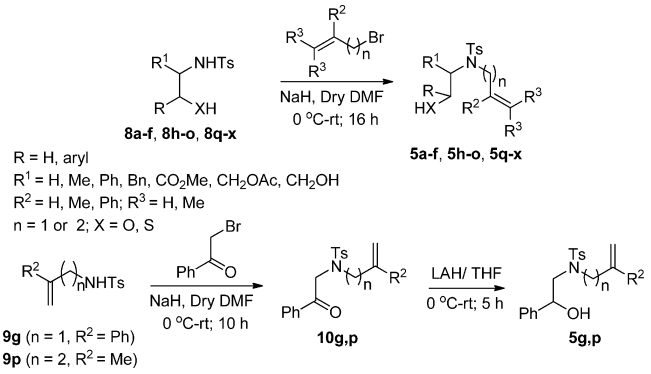
entry	reagent (amt, mmol)	solvent	time (h)	conversion[b] (%)	yield[c] (%)
1	$BF_3{\cdot}OEt_2$ (1.2)	CH_2Cl_2	5	100	90
2	$BF_3{\cdot}OEt_2$ (0.5)	CH_2Cl_2	12	44	38
3	$Zn(OTf)_2$ (0.2)	CH_2Cl_2	24	g	5
4	$Cu(OTf)_2$ (0.2)	CH_2Cl_2	24	0	*d*
5	$In(OTf)_3$ (0.2)	CH_2Cl_2	24	36	30
6	$Ag(OTf)_2$ (0.2)	CH_2Cl_2	24	0	*d*
7	$InCl_3$ (0.2)	CH_2Cl_2	24	0	*d*
8	$CeCl_3{\cdot}7H_2O$ (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	70	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 ^{1}H NMR. [c]Yield refers to isolated yield. [d]No reaction; starting material was recovered.

reaction with 0.5 equiv 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% 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 toluenesulfonic 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*-tosylamino alcohols/thiols or by substitution reaction between phenylacetyl bromide and *N*-allyl/homoallyltosylamide followed by the reduction of the ketone (Scheme 1).[27]

Scheme 1. Synthesis of Starting Materials



It was observed from Table 2 that primary and secondary alkenols **5a−5l** (entries 1−12) having alkyl- and aryl-substituted olefinic groups gave the desired 1,4-oxazines in good yields. In the 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 each other. Similarly, the secondary alkenols **5g**, **5i**, and **5j** also produced exclusively single diastereomers having a *cis* relationship between the phenyl groups at the 2- and 6-positions. The *cis* stereochemistry was confirmed by the 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*-benz[*b*][1,4]oxazine (**6m**) in 68% yield. Similarly, alkenols **5n−5q** (entries 14−17) gave the corresponding 1,4-oxazepanes **6n−6q** in good yields. The isomeric alkenols **5n** and **5o** gave the same product, **6n**. On the other hand, a substrate having a terminal alkene, **5r** (entry 18), was unreactive under the same reaction conditions, and starting material was recovered in 98%.

After successful study of this methodology for the synthesis of 1,4-oxazines and oxazepanes, its application to the synthesis of 1,4-thiazines and thiazepanes was explored. The starting material thioalkenes **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-tosylthiomorpholine (**6s**) and 2,5-dimethyl-2-phenyl-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 the *N*-tosyl group gave thiazolidines **7u−x** (Table 3) in 66%, 71%, 59%, and 74% yields, respectively. Substrates **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 these 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 thiazolidine was determined by ^{1}H NMR and NOE experiments 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.

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

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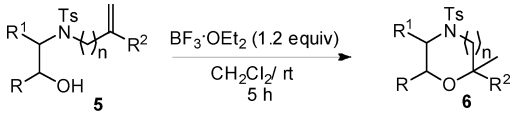
Table 2. Synthesis of 1,4-Oxazines and 1,4-Oxazepanes



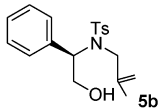
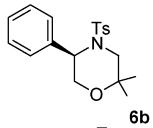
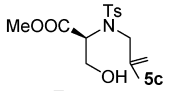
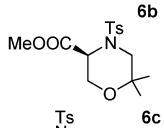
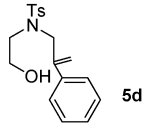
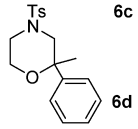
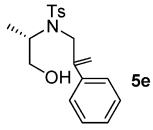
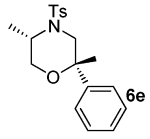
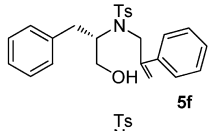
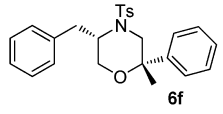
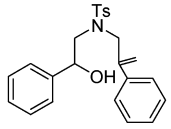
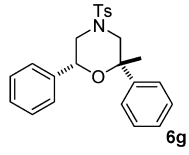
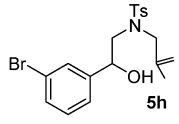
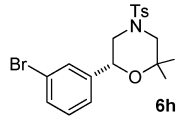
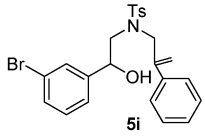
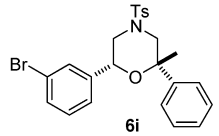
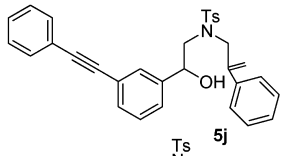
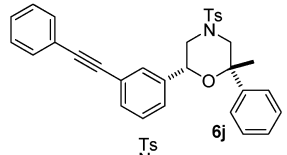
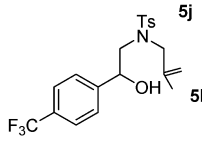
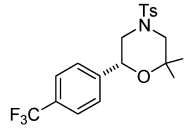
Entry	Substrate **5**	Product **6**	Yield (%) [a]
1	 **5a**	 **6a**	83
2	 **5b**	 **6b**	71
3	 **5c**	 **6c**	86
4	 **5d**	 **6d**	90
5	 **5e**	 **6e**	74
6	 **5f**	 **6f**	63
7	 **5g**	 **6g**	79
8	 **5h**	 **6h**	81
9	 **5i**	 **6i**	86
10	 **5j**	 **6j**	73
11	 **5k**	 **6k**	92

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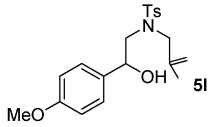
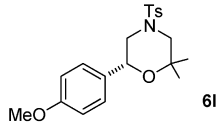
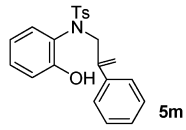
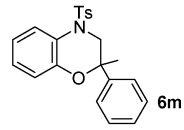
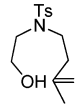
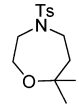
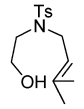
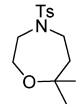
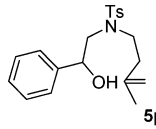
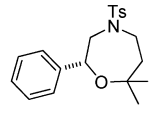
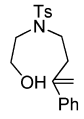
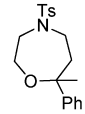
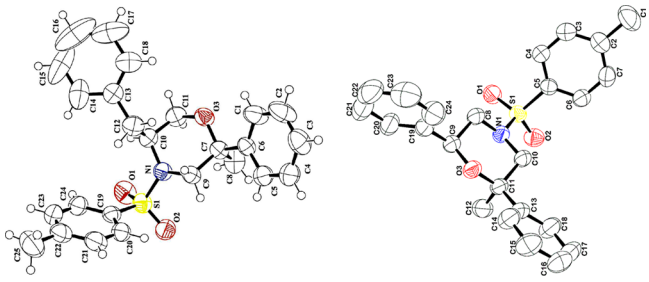
Table 2. continued

Entry	Substrate **5**	Product **6**	Yield (%)[a]
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 the isolated yield. The compounds were characterized by IR, NMR, and mass spectrometry.



6f **6g**

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

different groups, where the 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 a type of complex. An alternative mechanism is proposed which can be explained as follows. The alkenols/thioalkenols **5** react with boron trifluoride etherate to form intermediate **A**, an ion pair, the proton of which 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 thiazines (Scheme 2, mechanism 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, the proton of which adds to the double bond to give carbocation **D**, which is similar to intermediate **B**. This intermediate **D** undergoes a 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, mechanism II).[24k] The presence of ester and hydroxyl groups at the 2-position is crucial for the formation of the five-membered ring, which can be exemplified by the fact that compound **5t** having a methyl group at the 2-position gave six-membered ring **6t**.

■ CONCLUSIONS

In conclusion, we have developed a mild and efficient general method for the synthesis of substituted 1,4-oxazines, 1,4-oxazepanes, 1,4-thiazines and thiazolidines via intramolecular cyclization reaction of alkenols/thioalkenols in good yields and excellent diastereoselectivity. The reaction is highly atom economic and compatible with 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 excellent access to a diverse array of thiazolidine derivatives with a 2,4-*cis* relationship.

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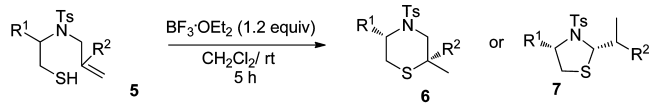
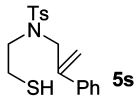
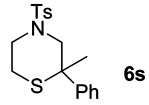
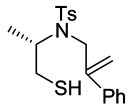
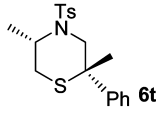
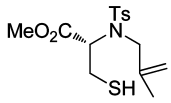
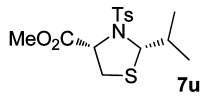
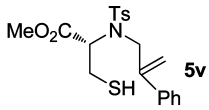
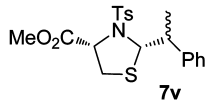
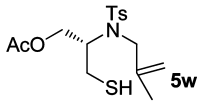
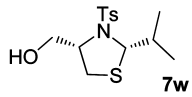
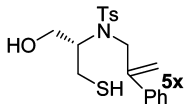
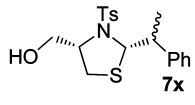
Table 3. Synthesis of Tetrahydro-2*H*-1,4-thiazines and Thiazolidines



R1 = Me, CO2Me, CH2OAc, CH2OH
R2 = 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 the isolated yield. All the products were characterized by ^{1}H and ^{13}C NMR and mass spectrometry. [b]The reaction took 12 h. [c]Inseperable mixture of diastereomers with a ratio of 7:3. The ratio is determined by ^{1}H NMR. [d]Inseperable mixture of diastereomers with a ratio of 3:2. The ratio is determined by ^{1}H NMR.

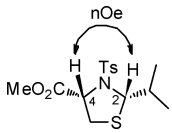


Figure 3. NOE diagram of compound **7u**.

EXPERIMENTAL SECTION

General Information. All the reagents were of analytical reagent (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 infrared (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 ^{1}H (600 MHz, 400 MHz) and ^{13}C (150 MHz, 100 MHz) NMR. Chemical shifts (δ) are reported in parts per million, and spin−spin coupling constants (J) are given in hertz. HRMS spectra were recorded using a Q-TOF mass spectrometer.

Synthesis of Starting Materials. *General Procedure for the Synthesis of Starting Materials **5a−f, 5h−o, and 5q−x**.* Amino alcohols and thiols **8a−f**, **8h−o**, and **8q−x** (1.0 equiv) in anhydrous DMF were added to a stirred solution of sodium hydride (1.2 equiv) in dry DMF under an inert atmosphere at 0 °C. After complete evolution of hydrogen gas, substituted allyl bromide (1.0 equiv) in DMF was added dropwise 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 the reaction mixture was extracted with ethyl acetate. The organic layer was further washed with brine solution 2−3 times. The combined organic layers were dried over Na_2SO_4 and concentrated in a 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 amides **9g,p** (1.0 equiv) in anhydrous DMF were added to a stirred solution of sodium hydride (1.2 equiv) in dry DMF under an inert atmosphere at 0 °C. After complete evolution of hydrogen gas, bromoacetophenone (1.0 equiv) in DMF was added dropwise 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 the reaction mixture was extracted with ethyl acetate. The organic layer was further washed with brine solution (2 × 15 mL). The combined organic layers were dried over Na_2SO_4 and concentrated in a 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 which the reaction mixture was quenched with 2 N NaOH, passed through a Celite pad, and washed with ethyl acetate. The mixture was treated with brine and extracted with EtOAc, and the combined organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The crude

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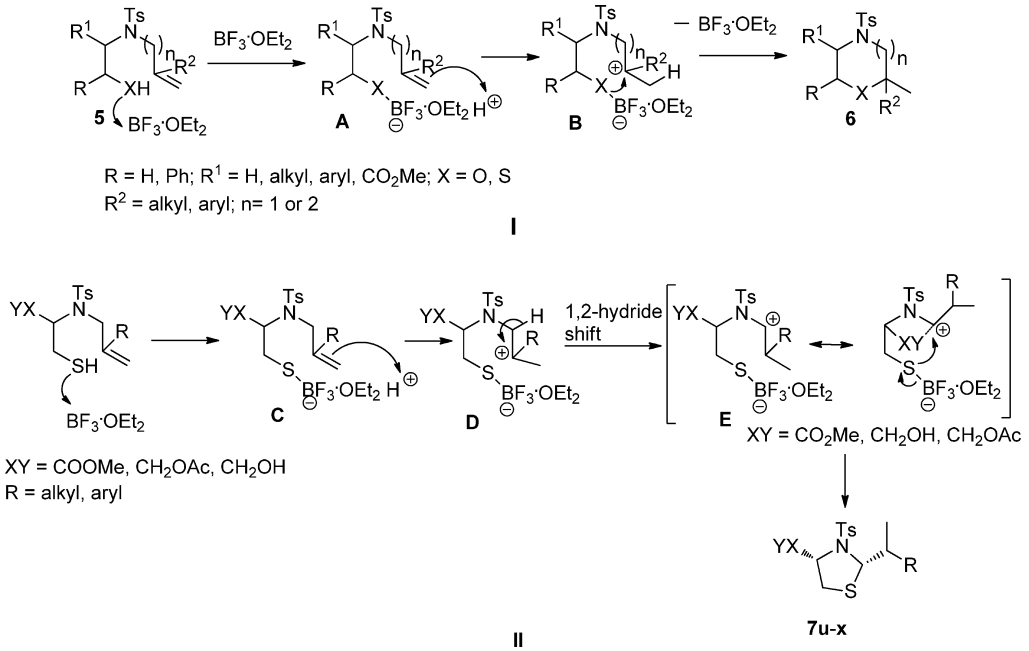
Scheme 2. Plausible Mechanism of the Reaction



product was purified using column chromatography to give compounds **5g**,**p**.

*Data for N-(2-hydroxyethyl)-4-methyl-N-(2-methylallyl)-benzenesulfonamide (**5a**):* white solid; mp 74−76 °C; R_f (hexane/EtOAc, 7:3) 0.47; yield 393 mg, 73%; ^{1}H 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) m/z calcd for $C_{13}H_{20}NO_3S$ (M + H)$^+$ 270.1158, found 270.1157.

*Data for (R)-N-(2-hydroxy-1-phenylethyl)-4-methyl-N-(2-methylallyl)benzenesulfonamide (**5b**):* colorless gum; R_f (hexane/EtOAc, 7:3) 0.54; yield 566 mg, 82%; $[\alpha]_D^{25}$ = −81.0 (c = 0.15, CH_2Cl_2); ^{1}H 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) m/z calcd for $C_{19}H_{24}NO_3S$ (M + H)$^+$ 346.1471, found 346.1477.

*Data for (S)-methyl 3-hydroxy-2-(4-methyl-N-(2-methylallyl)-benzenesulfonamido)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); ^{1}H 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) m/z calcd for $C_{15}H_{22}NO_5S$ (M + H)$^+$ 328.1213, found 328.1219.

*Data for N-(2-hydroxyethyl)-4-methyl-N-(2-phenylallyl)-benzenesulfonamide (**5d**):* colorless solid; mp 83−85 °C; R_f (hexane/EtOAc, 7:3) 0.48; yield 596 mg, 90%; ^{1}H 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) m/z calcd for $C_{18}H_{22}NO_3S$ (M + H)$^+$ 332.1315, found 332.1318.

*Data for (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); ^{1}H 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) m/z calcd for $C_{19}H_{24}NO_3S$ (M + H)$^+$ 346.1471, found 346.1469.

*Data for (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) m/z calcd for $C_{25}H_{28}NO_3S$ (M + H)$^+$ 422.1784, found 422.1781.

*Data for N-(2-hydroxy-2-phenylethyl)-4-methyl-N-(2-phenylallyl)benzenesulfonamide (**5g**):* colorless 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) m/z calcd for $C_{24}H_{25}NNaO_3S$ (M + Na)$^+$ 430.1447, found 430.1456.

*Data for N-(2-(3-bromophenyl)-2-hydroxyethyl)-4-methyl-N-(2-methylallyl)benzenesulfonamide (**5h**):* white solid; mp 89−91 °C; R_f

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(hexane/EtOAc, 9:1) 0.39; yield 711 mg, 84%; ^{1}H 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 (br s, 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) m/z calcd for $C_{19}H_{23}BrNO_3S$ (M + H)$^+$ 424.0577, found 424.0574.

*Data for 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%; ^{1}H 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) m/z calcd for $C_{24}H_{25}BrNO_3S$ (M + H)$^+$ 486.0733, found 486.0730.

*Data for N-(2-hydroxy-2-(3-(phenylethynyl)phenyl)ethyl)-4-methyl-N-(2-phenylallyl)benzenesulfonamide (**5j**):* pale 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) m/z calcd for $C_{32}H_{30}NO_3S$ (M + H)$^+$ 508.1941, found 508.1939.

*Data for N-(2-hydroxy-2-(4-(trifluoromethyl)phenyl)ethyl)-4-methyl-N-(2-methylallyl)benzenesulfonamide (**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) m/z calcd for $C_{20}H_{23}F_3NO_3S$ (M + H)$^+$ 414.1345, found 414.1359.

*Data for 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 (br s, 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.

*Data for 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) m/z calcd for $C_{22}H_{22}NO_3S$ (M + H)$^+$ 380.1315, found 380.1323.

*Data for N-(2-hydroxyethyl)-4-methyl-N-(3-methylbut-3-en-1-yl)-benzenesulfonamide (**5n**):* colorless 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 (br s, 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) m/z calcd for $C_{14}H_{21}NNaO_3S$ (M + Na)$^+$ 306.1134, found 306.1133.

*Data for 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) m/z calcd for $C_{14}H_{21}NNaO_3S$ (M + Na)$^+$ 306.1134, found 306.1136.

*Data for 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) m/z calcd for $C_{20}H_{26}NO_3S$ (M + H)$^+$ 360.1628, found 360.1635.

*Data for 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) m/z calcd for $C_{19}H_{23}NNaO_3S$ (M + Na)$^+$ 368.1291, found 368.1300.

*Data for N-(2-mercaptoethyl)-4-methyl-N-(2-phenylallyl)-benzenesulfonamide (**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) m/z calcd for $C_{18}H_{22}NO_2S_2$ (M + H)$^+$ 348.1086, found 348.1078.

*Data for 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) m/z calcd for $C_{19}H_{24}NO_2S_2$ (M + H)$^+$ 362.1243, found 362.1245.

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*Data for (S)-methyl 3-mercapto-2-(4-methyl-N-(2-methylallyl)-benzenesulfonamido)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) m/z calcd for $C_{15}H_{22}NO_4S_2$ (M + H)$^+$ 344.0985, found 344.0989.

*Data for (S)-methyl 3-mercapto-2-(4-methyl-N-(2-phenylallyl)-benzenesulfonamido)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) m/z calcd for $C_{20}H_{24}NO_4S_2$ (M + H)$^+$ 406.1141, found 406.1141.

*Data for (S)-3-mercapto-2-(4-methyl-N-(2-methylallyl)-benzenesulfonamido)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) m/z calcd for $C_{16}H_{24}NO_4S_2$ (M + H)$^+$ 358.1141, found 358.1140.

*Data for 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 (br s, 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) m/z calcd for $C_{19}H_{24}NO_3S_2$ (M + H)$^+$ 378.1192, found 378.1193.

General Procedure for the Synthesis of 6a−t and 7u−x. To a stirred solution of compounds **5a−x** (1 mmol) in dichloromethane (5 mL) was added 1.2 equiv of borontrifluoride etherate under a nitrogen atmosphere at room temperature. The resulting solution 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 × 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 ethyl acetate and hexane as eluents.

*Data for 2,2-dimethyl-4-tosylmorpholine (**6a**):* white solid; mp 92−94 °C; R_f (hexane/EtOAc, 4:1) 0.47; yield 223 mg, 83%; ^{1}H 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) m/z calcd for $C_{13}H_{20}NO_3S$ (M + H)$^+$ 270.1158 found 270.1157.

*Data for (R)-2,2-dimethyl-5-phenyl-4-tosylmorpholine (**6b**):* pale yellow solid; mp 77−79 °C; R_f (hexane/EtOAc, 4:1) 0.47; yield 245 mg, 71%; $[\alpha]_D^{25}$ = −68.5 (c = 0.33, CH_2Cl_2); ^{1}H 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) m/z calcd for $C_{19}H_{24}NO_3S$ (M + H)$^+$ 346.1471 found 346.1471.

*Data for (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); ^{1}H 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) m/z calcd for $C_{15}H_{22}NO_5S$ (M + H)$^+$ 328.1213 found 328.1225.

*Data for 2-methyl-2-phenyl-4-tosylmorpholine (**6d**):* pale yellow solid; mp 126−128 °C; R_f (hexane/EtOAc, 4:1) 0.50; yield 298 mg, 90%; ^{1}H 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) m/z calcd for $C_{18}H_{22}NO_3S$ (M + H)$^+$ 332.1315 found 332.1318.

*Data for (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); ^{1}H 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) m/z calcd for $C_{19}H_{24}NO_3S$ (M + H)$^+$ 346.1471 found 346.1471.

*Data for (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) m/z calcd for $C_{25}H_{28}NO_3S$ (M + H)$^+$ 422.1784 found 422.1782.

Data for (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) m/z calcd for $C_{24}H_{26}NO_3S$ (M + H)$^+$ 408.1628 found 408.1644.

Data for (2S,6R*)-6-(3-bromophenyl)-2,2-dimethyl-4-tosylmorpholine (**6h**):* white solid; mp 150−152 °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

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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) m/z calcd for $C_{19}H_{23}BrNO_3S$ (M + H)$^+$ 424.0577, found 424.0576.

Data for (2S,6R*)-6-(3-bromophenyl)-2-methyl-2-phenyl-4-tosylmorpholine (**6i**):* white solid; mp 134−136 °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) m/z calcd for $C_{24}H_{25}BrNO_3S$ (M + H)$^+$ 486.0733, found 486.0731.

Data for (2S,6R*)-2-methyl-2-phenyl-6-(3-(phenylethynyl)-phenyl)-4-tosylmorpholine (**6j**):* colorless 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) m/z calcd for $C_{32}H_{30}NO_3S$ (M + H)$^+$ 508.1941, found 508.1947.

Data for (2S,6R*)-2,2-dimethyl-4-tosyl-6-(4-(trifluoromethyl)-phenyl)morpholine (**6k**):* colorless solid; mp 141−143 °C; R_f (hexane/EtOAc, 9:1) 0.65; yield 380 mg, 92%; ^{1}H 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) m/z calcd for $C_{20}H_{23}F_3NO_3S$ (M + H)$^+$ 414.1345, found 414.1343.

*Data for 2-methyl-2-phenyl-4-tosyl-3,4-dihydro-2H-benz[b][1,4]-oxazine (**6m**):* colorless solid; mp 119−121 °C; R_f (hexane/EtOAc, 4:1) 0.73; yield 258 mg, 68%; ^{1}H 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) m/z calcd for $C_{22}H_{22}NO_3S$ (M + H)$^+$ 380.1315 found 380.1316.

*Data for 7,7-dimethyl-4-tosyl-1,4-oxazepane (**6n**):* colorless solid; mp 62−64 °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) m/z calcd for $C_{14}H_{22}NO_3S$ (M + H)$^+$ 284.1315 found 284.1316.

*Data for 7,7-dimethyl-2-phenyl-4-tosyl-1,4-oxazepane (**6p**):* yellow solid; mp 137−139 °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) m/z calcd for $C_{20}H_{26}NO_3S$ (M + H)$^+$ 360.1628 found 360.1631.

*Data for 7-methyl-7-phenyl-4-tosyl-1,4-oxazepane (**6q**):* colorless 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) m/z calcd for $C_{19}H_{23}NNaO_3S$ (M + Na)$^+$ 368.1291 found 368.1288.

*Data for 2-methyl-2-phenyl-4-tosylthiomorpholine (**6s**):* pale yellow solid; mp 121−123 °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) m/z calcd for $C_{18}H_{22}NO_2S_2$ (M + H)$^+$ 348.1086, found 348.1080.

*Data for 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 (br s, 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) m/z calcd for $C_{19}H_{24}NO_2S_2$ (M + H)$^+$ 362.1243, found 362.1248.

*Data for (2S,4S)-methyl 2-isopropyl-3-tosylthiazolidine-4-carboxylate (**7u**):* 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) m/z calcd for $C_{15}H_{22}NO_4S_2$ (M + H)$^+$ 344.0985 found 344.0984.

*Data for (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); ^{1}H 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) m/z calcd for $C_{20}H_{24}NO_4S_2$ (M + H)$^+$ 406.1141 found 406.1143.

*Data for ((2S,4S)-2-isopropyl-3-tosylthiazolidin-4-yl)methanol (**7w**):* yellow oil; R_f (hexane/EtOAc, 7:3) 0.30; yield 186 mg, 59%;

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$[\alpha]_D^{25}$ = −40.0 (*c* = 0.1, CH_2Cl_2); ^{1}H 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) *m*/*z* calcd for $C_{14}H_{22}NO_3S_2$ $(M + H)^+$ 316.1036 found 316.1035.

*Data for ((2S,4S)-2-(1-phenylethyl)-3-tosylthiazolidin-4-yl)-methanol (**7x**, diastereomeric mixture with a ratio of 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); ^{1}H 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 (br s, 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* = 7.2 Hz, 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) *m*/*z* calcd for $C_{19}H_{24}NO_3S_2$ $(M + H)^+$ 378.1192 found 378.1191.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR and HRMS spectra of all new compounds, NOE spectra of compound **7u**, and crystal parameters, ORTEP diagrams, and crystallographic data in CIF format for compounds **6f,g**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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