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Oxidative Intramolecular Bromo-Amination of *N*-Alkenyl Sulfonamides via Umpolung of Alkali Metal Bromides

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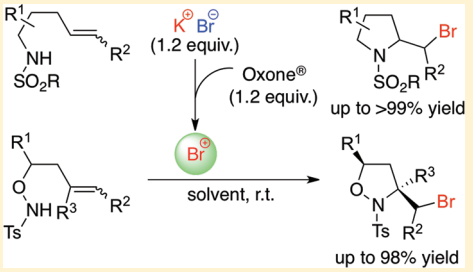
Supporting Information

ABSTRACT: The oxidative intramolecular bromo-amination of various *N*-alkenyl sulfonamides and *N*-alkenoxyl sulfonamides via umpolung of alkali metal bromides occurred *exo*-selectively to generate cyclic bromoamides in high yields with good diastereoselectivities. This method provided the desired products without elaborating the stoichiometric amount of corresponding organic waste.

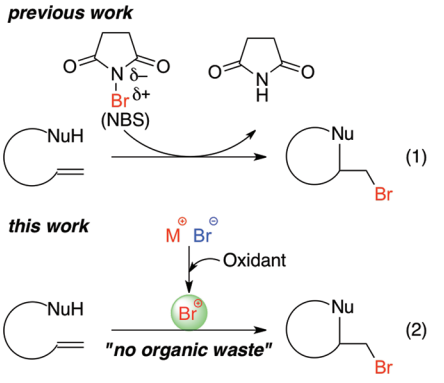


Intramolecular halo-amination[1] is an important tool for the synthesis of nitrogen-containing heterocycles, which are useful building blocks of biologically active natural products and pharmacological products.[2] In particular, some bromo compounds have also been noted in the biosynthesis of halogenated marine natural products[3] and medicinal plants.[3a,4] As for the bromo-amination of alkenes by both intermolecular and intramolecular reactions with *N*-protected amines, straightforward methods using transition metal catalysts and stoichiometric amounts of brominating reagents have been developed. However, those methods present a disadvantage in that toxic heavy metals (Os,[5] Mn,[6] V,[6] Cu,[6,7] or Pd[7,8]) are required. On the other hand, such organic brominating reagents as *N*-bromosuccinimide (NBS),[9] 1,3-dibromo-5,5-dimethylhydantoin (DBDMH),[10] 2,4,4,6-tetrabromocyclohexa-2,5-dienone (TBCO),[11] and bromodiethylsulfonium bromopentachloroantimonate (BDSB)[12] have been used as active bromo sources for chemoselective bromo-cyclization reactions. However, they present a particular problem in that the stoichiometric amount of the corresponding organic waste is increased (Scheme 1, eq 1). To overcome this problem, it is very important to develop a bromo cyclization using nonorganic bromo reagents under heavy-metal-free conditions. Therefore, we focused on the oxidative bromo-cyclization via umpolung of alkali metal bromides, which can oxidize bromide ion (Br^-) (inorganic bromide) to activate bromonium-like species (Br^+) using various kinds of oxidants (Scheme 1, eq 2).[13]

In the past, the *exo*-selective intramolecular bromo-amination was developed. However, the reaction required NBS as the bromo reagent.[14] We report here an *exo*-selective intramolecular bromo-amination of *N*-alkenyl sulfonamides and *N*-alkenoxyl sulfonamides via umpolung of inorganic bromides.

First, we screened a series of bromo reagents and oxidants for the intramolecular bromo-amination with **1a** (Table 1). The use of Br_2 as bromo reagent for intramolecular bromo-amination was

Scheme 1. Intramolecular Bromo-Cyclization of Alkenes



not suitable to give **2a** in moderate yield together with many byproducts (entry 1). In contrast, the use of NBS gave **2a** in 90% yield (entry 2). When **1a** was treated with KBr as the bromo reagent and *m*-CPBA or Oxone as the oxidant in CH_2Cl_2, **2a** was obtained in low yields (entries 3 and 4). Then, solvent effects on the intramolecular bromo-amination using KBr/Oxone were investigated (entries 5−7). Whereas the treatment of **1a** in THF and AcOEt gave **2a** in 70% and 92% yields, respectively (entries 5 and 6), the reaction in MeCN gave **2a** in >99% yield as the best result (entry 7). Use of other oxidants, such as *m*-CPBA, H_2O_2, $PhI(OAc)_2$, or *t*-BuOCl, in this reaction with **1a** decreased the yield of **2a** (entries 8−11). Furthermore, use of NaBr instead of KBr also decreased the yield of **2a** (entry 12) and the use of KBr alone was totally ineffective for the transformation of **1a** into **2a** (entry 13).

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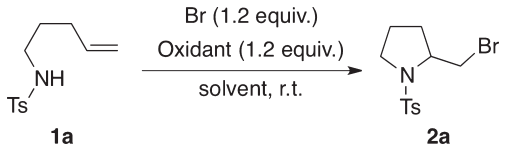
Table 1. Screening of Intramolecular Bromo-amination with 1a[a]



1a **2a**

entry	Br	oxidant	solvent	time (h)	conv. (%)	yield of **2a** (%)[b]
1	Br_2		MeCN	1	>99	57
2	NBS		MeCN	3	>99	90
3	KBr	*m*-CPBA	CH_2Cl_2	2	>99	37
4	KBr	Oxone	CH_2Cl_2	20	>99	19
5	KBr	Oxone	THF	8	>99	70
6	KBr	Oxone	AcOEt	24	>99	92
7	KBr	Oxone	MeCN	2	>99	>99
8	KBr	*m*-CPBA	MeCN	2	>99	32
9	KBr	H_2O_2	MeCN	64	0	0
10	KBr	$PhI(OAc)_2$	MeCN	12	>99	75
11	KBr	*t*-BuOCl	MeCN	24	>99	82
12	NaBr	Oxone	MeCN	3	>99	60
13	KBr		MeCN	64	0	0

[a] Reaction of **1a** (0.25 mmol) was carried out with Br source (1.2 equiv) and oxidant (1.2 equiv) in solvent (1 mL). [b] Isolated yield.

Next, we investigated the scope of the intramolecular bromo-amination of *N*-alkenyl sulfonamides **1** via the umpolung reaction of KBr under optimized reaction conditions (Table 2). The reaction of *N*-alkenyl sulfonamides bearing other sufonyl groups, such as benzenesulfonyl (**1b**), 1-naphthalenesulfonyl (**1c**), 4-fluorobenzenesulfonyl (**1d**), *n*-butanesulfonyl (**1e**), and (1*S*)-camphorsulfonyl (**1f**), also gave the corresponding products in excellent yields (Table 2, entries 1−5). A variety of substituted alkenes underwent the intramolecular bromo-amination to give the intramolecular bromo-amination to give the corresponding amino-bromides. When *N*-(2,2-dialkyl substituted) and *N*-(1,2-dialkyl substituted) 4-penten-1-yl sulfonamides **1g**, **1h**, **1i**, and **1j** were used, cyclization products **2g**, **2h**, **2i**, and **2j** were obtained in >99%, 97%, >99%, and 96% yields, respectively (entries 6−9). *N*-Alkenyl sulfonamides with cyclic alkene **1k** and internal alkenes (*E*)-**1l** and (*Z*)-**1m** were efficiently converted into corresponding products **2k**, **2l**, and **2m** in high yields (89−91%) with good diastereoselectivities (dr = 77:23 to >99:<1) (entries 10−12). Disubstituted terminal alkene **1n** could be also used and corresponding product **2n** with a quaternary carbon center was obtained in 90% yield (entry 13). Moreover, the same treatment of the chiral *N*-alkenyl sulfonamides (**1o** and **1p**) derived from α-amino acids also provided corresponding products **2o** and **2p** in excellent yields with moderate diastereoselectivities (>99% and 93% yields, dr = 77:23 and 57:43), respectively (entries 14 and 15).

The present method for the oxidative intramolecular bromo-amination of *N*-alkenyl sulfonamides was applied to the synthesis of bromo isoxazolidines from *N*-alkenoxyl sulfonamide derivatives. Isoxazolidines are useful for the synthesis of biologically active compounds.[15] They also serve as precursors to *β*-amino alcohols,[16] *β*-amino ketones,[17] *β*-amino acids,[18] and 3-isoxazolidines.[19] Isoxazolidines have been synthesized via the 1,3-dipolar cycloaddition reaction of nitrones with alkenes[16a,20] and the Pd-catalyzed cyclization of *N*- or *O*-homoallyl hydroxylamines.[21] To the best of our knowledge, however, there has been no report of the synthesis of bromo isoxazolidines. We report here the first synthesis of bromo isoxazolidines via the oxidative intramolecular bromo-amination of *N*-alkenoxyl sulfonamide derivatives **3** (Scheme 2). Treatment of **3a** ($R^1 = R^2 = R^3 = H$) with KBr and Oxone in a 4:1 mixture of MeCN and toluene gave **4a** in 93% yield. The same treatment of 2-aryl substituted *N*-alkenoxyl sulfonamides bearing H, MeO, and CF_3 at aryl group **3b**, **3c**, and **3d** (R^1 = Ph, 4-MeO-C_6H_4, and 4-CF_3−C_6H_4, $R^2 = R^3 = H$) also provided corresponding products **4b**, **4c**, and **4d** in excellent yields (90−97%) with moderate diastereoselectivities (dr = 4:1). Use of disubstituted internal alkene **3e** (R^1 = 1-naphthyl, R^2 = Me, $R^3 = H$) and terminal alkene **3f** (R^1 = 4−Cl-C_6H_4, $R^2 = H$, R^3 = Me) provided corresponding products **4e** and **4f** in 91% and 95% yields, respectively. Moreover, treatment of 2-thienyl substituted *N*-alkenoxyl sulfonamides **3g** (R^1 = 2-thienyl, $R^2 = R^3 = H$) and 2-butyl substituted *N*-alkenoxyl sulfonamides **3h** (R^1 = *n*-butyl, $R^2 = R^3 = H$) also gave desired products **4g** and **4h** in 82% and 98% yields, respectively.

The proposed reaction mechanism is depicted in Scheme 3. The key step is the generation of the activated bromonium-like species (Br^+), but not Br_2, via oxidative umpolung of KBr with Oxone in MeCN at room temperature (Table 1, entries 1 vs 7). We speculate that there are two pathways for the bromo-amination of *N*-alkenyl sulfonamides **1** with Br^+. First, the reaction may occur via intermolecular bromination of the olefin moiety, and then, the bromonium cation intermediate may be intramolecularly attacked by the sulfonamide to form cyclization products **2** (path A). Alternatively, sulfonamides may undergo direct bromination to form *N*-bromo sulfonamides, followed by intramolecular bromonium ion transfer to the olefin moiety, and the cyclization of bromonium cation intermediate proceeds to afford desired products **2** (path B). Some of the mechanistic approaches to the intramolecular bromo-amination indicate that the activated bromonium-like species first brominate the olefin moiety of the substrates (path A) (see Experimental Section).[22]

In conclusion, we have developed an oxidative intramolecular bromo-amination that involves *N*-alkenyl sulfonamides and *N*-alkenoxyl sulfonamides using the umpolung of alkali metal bromides with Oxone. This reaction provides the desired products without elaborating the stoichiometric amount of the corresponding organic waste, thus contributing to green sustainable chemistry. We expect that activated bromonium-like species (Br^+) would be further applicable to fine organic synthesis, such as enantioselective reactions or catalyst-mediated reactions.

EXPERIMENTAL SECTION

General Procedure for the Intramolecular Bromo-amination of *N*-Alkenyl Sulfonamides with a Metal Bromide/Oxone System (Table 1, entry 7). To a solution of **1a** (59.8 mg, 0.25 mmol) and Oxone (184.4 mg, 0.30 mmol) in acetonitrile (1 mL) was added KBr (35.7 mg, 0.30 mmol) under argon atmosphere. The solution was stirred at room temperature for 3 h. Saturated $NaHCO_3$ aqueous solution (10 mL) was added to the reaction mixture, and the product was extracted with AcOEt (15 mL × 3). The combined extracts were washed by brine (10 mL) and dried over Na_2SO_4. The organic phase was concentrated under reduced pressure and the crude product was purified by silica gel column chromatography (eluent: hexane/AcOEt = 5/1), to give the desired product **2a** (79.2 mg, >99% yield).

2-(Bromomethyl)-1-tosylpyrrolidine (***2a***): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.51−1.61 (m, 1H), 1.69−1.80 (m, 1H), 1.81−1.89 (m, 1H), 1.90−1.98 (m, 1H), 2.44 (s, 3H), 3.15 (dt, *J* = 10.1, 7.1 Hz, 1H),

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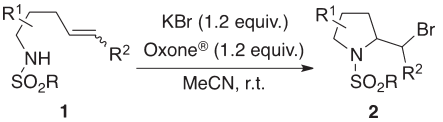
Table 2. *Exo*-selective Intramolecular Bromo-amination of Various *N*-Alkenylsulfonamides[a]



1 **2**

entry	substrate	product	time (h)	yield[b] (%)
1[c]	R = Ph (**1b**)	**2b**	2	95
2[d]	R = 1-Naphthyl (**1c**)	**2c**	16	96
3[d]	R = 4-F-C_6H_4 (**1d**)	**2d**	17	93
4[d]	R = *n*-Bu (**1e**)	**2e**	12	>99
5[e]	R = **1f**	**2f**	3 (dr = 64:36)	98
6[c]	**1g**	**2g**	1	>99
7[c]	**1h**	**2h**	3	97
8[d]	*cis*-**1i**	**2i**	8 (dr = 68:32)	>99
9[d]	*trans*-**1j**	**2j**	5 (dr = 84:16)	96
10[c]	**1k**	**2k**	8 (dr = >99:<1)	91
11[d]	(*E*)-**1l**	**2l**	24 (dr = 77:23)	89
12[d]	(*Z*)-**1m**	**2m**	20 (dr = >99:<1)	90
13	**1n**	**2n**	2	90
14	R = Me (**1o**)	**2o**	8 (dr = 77:23)	>99
15	R = *i*-Pr (**1p**)	**2p**	1 (dr = 57:43)	93

[a] Reaction of **1** (0.25 mmol) was carried out with KBr (1.2 equiv) and Oxone (1.2 equiv) in MeCN (1 mL). [b] Isolated yield. [c] Reaction was carried out in MeCN (2 mL). [d] Reaction was carried out under dark conditions. [e] Reaction was carried out with Oxone (2.0 equiv) in a mixture of MeCN and toluene (4:1) (1 mL).

3.36 (t, J = 9.7 Hz, 1H), 3.51−3.44 (m, 1H), 3.74−3.79 (m, 1H), 3.80−3.87 (m, 1H), 7.34 (d, J = 8.2 Hz, 2H), 7.73 (d, J = 8.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 23.7, 30.2, 36.0, 49.8, 60.3, 127.5 (2C), 129.8 (2C), 134.0, 143.8. IR (neat) 1338, 1161, 1091, 1034, 986 cm^{-1}. MS (ESI) calcd for $C_{12}H_{17}BrNO_2S$ $[M + H]^+$ 318.0158, found 318.0151. Anal. calcd for $C_{12}H_{16}BrNO_2S$: C, 45.29; H, 5.07; N, 4.40%. Found: C, 45.60; H, 5.16; N, 4.27%.

2-(Bromomethyl)-1-(phenylsulfonyl)pyrrolidine (***2b***): yield 95%, 72.2 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.51−1.61 (m, 1H), 1.68−1.80 (m, 1H), 1.80−1.90 (m, 1H), 1.91−2.00 (m, 1H), 3.17 (dt, J = 10.1, 7.5 Hz, 1H), 3.37 (t, J = 9.8 Hz, 1H), 3.46−3.53 (m, 1H), 3.78 (dd, J = 10.1, 3.3 Hz, 1H), 3.81−3.89 (m, 1H), 7.56 (t, J = 7.6 Hz, 2H), 7.60−7.66 (m, 1H), 7.86 (d, J = 7.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.7, 30.1, 35.9, 49.7, 60.3, 127.3 (2C), 129.1 (2C), 132.9, 136.7. IR (KBr) 1337, 1199, 1162, 1092, 1030 cm^{-1}. MS (ESI) calcd for $C_{11}H_{15}BrNO_2S$ $[M + H]^+$ 304.0001, found 304.0005.

2-(Bromomethyl)-1-(naphthalen-1-ylsulfonyl)pyrrolidine (***2c***): yield 96%, 85.0 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.63−1.73 (m, 1H), 1.82−1.92 (m, 2H), 1.93−2.04 (m, 1H), 3.36 (t, J = 9.7 Hz, 1H), 3.30−3.43 (m, 2H), 3.68 (dd, J = 10.1, 3.2 Hz, 1H), 4.12−4.20 (m, 1H), 7.52−7.64 (m, 2H), 7.64−7.71 (m, 1H), 7.93 (d, J = 8.2 Hz, 1H), 8.09 (d, J = 8.5 Hz, 1H), 8.25 (d, J = 7.6 Hz, 1H), 8.86 (d, J = 8.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.0, 30.4, 35.6, 49.5, 59.7, 124.2, 125.1, 126.9, 128.2, 128.9, 129.0, 130.0, 133.5, 134.3, 134.6. IR (neat) 1347, 1159, 1133, 1029, 989 cm^{-1}. MS (ESI) calcd for $C_{15}H_{17}BrNO_2S$ $[M + H]^+$ 354.0158, found 354.0152.

2-(Bromomethyl)-1-((4-fluorophenyl)sulfonyl)pyrrolidine (***2d***): yield 93%, 74.9 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.52−1.65 (m, 1H), 1.71−1.82 (m, 1H), 1.82−1.93 (m, 1H), 1.93−2.02 (m, 1H), 3.15 (dt, J = 10.1, 7.3 Hz, 1H), 3.37 (t, J = 9.8 Hz, 1H), 3.44−3.52 (m, 1H), 3.76 (dd, J = 9.8, 3.1 Hz, 1H), 3.79−3.87 (m, 1H), 7.23 (t, J = 8.7 Hz, 2H), 7.84−7.91 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.8, 30.2, 35.8, 49.8, 60.4, 116.5 (d, J = 22.0 Hz, 2C) 130.1 (d, J = 8.6 Hz, 2C), 133.2, 165.3 (d, J = 256.8 Hz). IR (KBr) 1343, 1231, 1169, 1093, 1057 cm^{-1}. MS (ESI) calcd for $C_{11}H_{14}BrFNNaO_2S$ $[M + Na]^+$ 343.9727, found 343.9722.

2-(Bromomethyl)-1-(butylsulfonyl)pyrrolidine (***2e***): yield >99%, 71.1 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96 (t, J = 7.5 Hz, 3H), 1.47 (sext, J = 7.5 Hz, 2H), 1.75−2.18 (m, 6H), 2.95−3.02 (m, 2H), 3.35−3.48 (m, 3H), 3.64 (dd, J = 10.3, 3.2 Hz, 1H), 4.04−4.12 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$)

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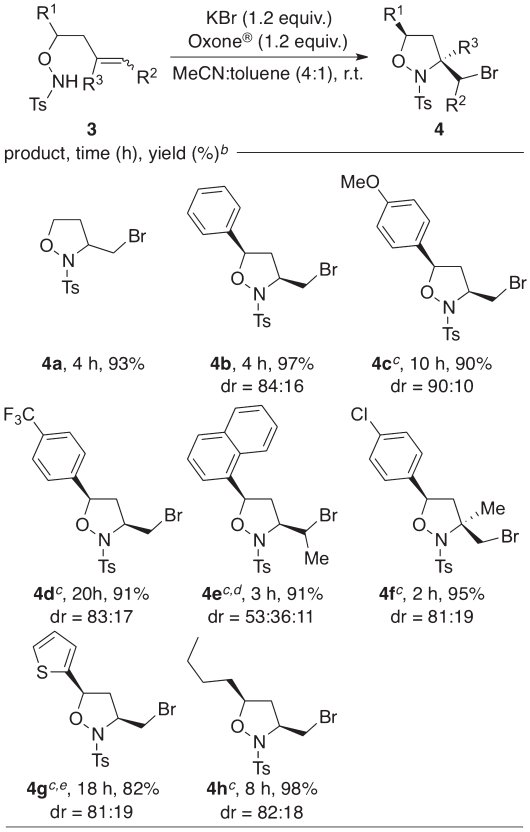
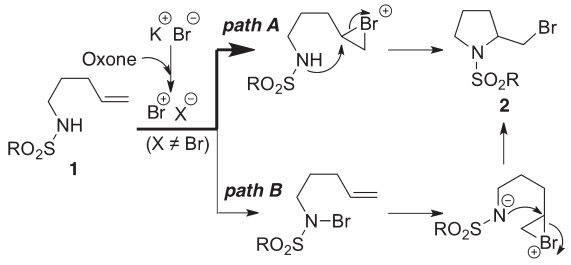
Scheme 2. *Exo*-selective Intramolecular Bromo-amination of Various *N*-Alkenoxyl Sulfonamides



[a] Reaction of **3** (0.25 mmol) was carried out with KBr (1.2 equiv) and Oxone (1.2 equiv) in MeCN (1 mL). The relative configuration of **4** was determined by NOE experiments. [b] Isolated yield. [c] Reaction was carried out under dark conditions. [d] Starting materials with a 2:1 mixture of *E*/*Z* isomers were used. [e] Reaction was carried out in a mixture of MeCN and toluene (1:1) (1 mL).

Scheme 3. Plausible Reaction Mechanism



δ 13.6, 21.7, 24.6, 25.2, 30.4, 36.2, 49.4, 50.2, 59.7. IR (KBr) 1334, 1142, 1067, 1035, 989 cm^{-1}. MS (ESI) calcd for $C_9H_{18}BrNNaO_2S$ $[M + Na]^+$ 306.0134, found 306.0133.

*2-(Bromomethyl)-1-((1S)-10-Camphorsulfonyl)pyrrolidine (**2f**, Diastereomer Mixtures):* yield 98%, 92.7 mg. Major-diastereomer: ^1H NMR (400 MHz, $CDCl_3$) δ 0.90 (s, 3H), 1.14 (s, 3H), 1.39−1.48 (m, 1H), 1.62−1.71 (m, 1H), 1.88−2.22 (m, 7H), 2.34−2.45 (m, 1H), 2.47−2.58 (m, 1H), 2.88 (d, *J* = 14.9 Hz, 1H), 3.33−3.43 (m, 2H), 3.43−3.54 (m, 2H), 3.67 (dd, *J* = 10.3, 3.3 Hz, 1H), 4.02−4.11 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.8, 20.0, 24.3, 25.2, 26.9, 30.4, 36.1, 42.6, 42.8, 45.8, 47.9, 49.4, 58.3, 60.1, 215.5. Minor-diastereomer: ^1H NMR (400 MHz, $CDCl_3$) δ 0.90 (s, 3H), 1.15 (s, 3H), 1.39−1.48 (m, 1H), 1.62−1.71 (m, 1H), 1.88−2.22 (m, 7H), 2.34−2.45 (m, 1H), 2.47−2.58 (m, 1H), 2.84 (d, *J* = 14.6 Hz, 1H), 3.33−3.43 (m, 2H), 3.43−3.54 (m, 2H), 3.70 (dd, *J* = 10.1, 3.2 Hz, 1H), 3.99−4.08 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.8, 20.0, 24.2, 25.1, 26.9, 30.5, 35.9, 42.6, 42.8, 45.1, 47.9, 49.6, 58.2, 60.1, 215.3. IR (KBr) 1745, 1341, 1200, 1146, 1037 cm^{-1}. MS (ESI) calcd for $C_{15}H_{24}BrNNaO_3S$ $[M + Na]^+$ 400.0552, found 400.0550.

*2-(Bromomethyl)-4,4-dimethyl-1-tosylpyrrolidine (**2g**):* yield >99%, 86.5 mg. ^1H NMR (400 MHz, $CDCl_3$) δ 0.53 (s, 3H), 1.05 (s, 3H), 1.70 (dd, *J* = 13.0, 8.5 Hz, 1H), 1.88 (dd, *J* = 13.0, 7.6 Hz, 1H), 2.44 (s, 3H), 3.14 (d, *J* = 10.8 Hz, 1H), 3.19 (d, *J* = 10.8 Hz, 1H), 3.52 (t, *J* = 9.6 Hz, 1H), 3.82−3.91 (m, 1H), 3.94 (dd, *J* = 9.6, 3.0 Hz, 1H), 7.33 (d, *J* = 7.8 Hz, 2H), 7.74 (d, *J* = 7.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 25.7, 26.0, 37.4, 37.5, 45.8, 60.0, 61.8, 127.5 (2C), 129.7 (2C), 134.8, 143.7. IR (KBr) 1345, 1157, 1092, 1043, 1024 cm^{-1}. MS (ESI) calcd for $C_{14}H_{21}BrNO_2S$ $[M + H]^+$ 346.0471, found 346.0463.

*3-(Bromomethyl)-2-tosyl-2-azaspiro[4.5]decane (**2h**):* yield 97%, 93.7 mg. ^1H NMR (400 MHz, $CDCl_3$) δ 0.59−0.69 (m, 1H), 0.74−0.84 (m, 1H), 1.05−1.50 (m, 8H), 1.63 (dd, *J* = 13.3, 8.5 Hz, 1H), 1.95 (dd, *J* = 13.3, 7.5 Hz, 1H), 2.43 (s, 3H), 3.15 (d, *J* = 11.0 Hz, 1H), 3.35 (d, *J* = 11.0 Hz, 1H), 3.50 (dd, *J* = 9.8, 9.0 Hz, 1H), 3.75−3.84 (m, 1H), 3.94 (dd, *J* = 9.8, 3.0 Hz, 1H), 7.33 (d, *J* = 8.6 Hz, 2H), 7.74 (d, *J* = 8.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 22.7, 23.6, 25.7, 33.9, 36.1, 37.7, 41.4, 44.0, 59.0, 59.2, 127.4 (2C), 129.7 (2C), 134.6, 143.7. IR (KBr) 1350, 1220, 1160, 1090, 1031 cm^{-1}. MS (ESI) calcd for $C_{17}H_{25}BrNO_2S$ $[M + H]^+$ 386.0784, found 386.0776. Anal. calcd for $C_{17}H_{24}BrNO_2S$: C, 52.85; H, 6.26; N, 3.63%. Found: C, 52.81; H, 6.27; N, 3.55%.

*cis-2-(Bromomethyl)-1-tosyloctahydro-1H-indole (**2i**, Diastereomer Mixtures):* yield >99%, 93.0 mg. Major-diastereomer: ^1H NMR (400 MHz, $CDCl_3$) δ 0.99−1.31 (m, 2H), 1.32−1.48 (m, 2H), 1.48−1.74 (m, 4H), 1.80−2.04 (m, 2H), 2.07−2.18 (m, 1H), 2.44 (s, 3H), 3.41 (t, *J* = 9.8 Hz, 1H), 3.62−3.71 (m, 1H), 3.71−3.78 (m, 1H), 4.00 (dd, *J* = 9.8, 3.6 Hz, 1H), 7.33 (d, *J* = 8.2 Hz, 2H), 7.74 (d, *J* = 8.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.1, 21.6, 24.3, 25.7, 31.1, 34.1, 36.2, 37.8, 60.7, 61.4, 127.4 (2C), 129.8 (2C), 134.7, 143.6. Minor-diastereomer: ^1H NMR (400 MHz, $CDCl_3$) δ 0.85−0.99 (m, 1H), 0.99−1.31 (m, 2H), 1.32−1.48 (m, 2H), 1.48−1.74 (m, 4H), 1.80−2.04 (m, 2H), 2.43 (s, 3H), 3.28 (t, *J* = 10.8 Hz, 1H), 3.82−3.89 (m, 1H), 3.92−4.02 (m, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 7.74 (d, *J* = 8.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.0, 21.5, 23.5, 25.6, 27.9, 31.6, 34.5, 35.5, 59.0, 61.6, 127.3 (2C), 129.6 (2C), 138.4, 143.2. IR (KBr) 1345, 1162, 1096, 1032, 1004 cm^{-1}. MS (ESI) calcd for $C_{16}H_{23}BrNO_2S$ $[M + H]^+$ 372.0627, found 372.0624.

*trans-2-(Bromomethyl)-1-tosyloctahydro-1H-indole (**2j**, Diastereomer Mixtures):* yield 96%, 89.4 mg. Major-diastereomer: ^1H NMR (400 MHz, $CDCl_3$) δ 0.98−1.48 (m, 6H), 1.55−1.73 (m, 1H), 1.73−1.88 (m, 2H), 2.25−2.34 (m, 2H), 2.43 (s, 3H), 2.90 (dt, *J* = 10.8, 3.2 Hz, 1H), 3.60 (dd, *J* = 9.8, 8.2 Hz, 1H), 3.88 (dd, *J* = 9.8, 3.2 Hz, 1H), 4.27 (dq, *J* = 8.2, 3.2 Hz, 1H), 7.29 (d, *J* = 8.2 Hz, 2H), 7.74 (d, *J* = 8.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 25.0 (2C), 29.3, 29.6, 36.4, 38.4, 45.3, 60.2, 66.3, 127.0 (2C), 129.6 (2C), 139.6, 143.0. Minor-diastereomer: ^1H NMR (400 MHz, $CDCl_3$) δ 0.98−1.48 (m, 6H), 1.55−1.88 (m, 3H), 1.99 (dd, *J* = 12.6, 5.5 Hz, 1H), 2.25−2.34 (m, 1H), 2.46 (s, 3H), 2.46−2.52 (m,1H), 3.29 (dd, *J* = 11.4, 10.6 Hz, 1H), 3.76−3.84 (m, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 7.70 (d, *J* = 8.1 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 24.5, 25.2, 29.4, 32.4, 33.1, 35.8, 42.7, 61.3, 67.3, 127.8 (2C), 129.7 (2C), 133.0, 143.8. IR (KBr) 1333, 1148, 1118, 1088, 1035 cm^{-1}. MS (ESI) calcd for $C_{16}H_{23}BrNNaO_2S$ $[M + Na]^+$ 394.0447, found 394.0443.

*cis-6-Bromo-1-tosyloctahydrocyclopenta[b]pyrrole (**2k**):* yield 91%, 78.3 mg. ^1H NMR (400 MHz, $CDCl_3$) δ 1.45−1.54 (m, 2H), 1.67−1.76 (m, 1H), 2.00−2.07 (m, 1H), 2.13−2.28 (m, 2H), 2.45 (s, 3H), 2.74−2.82 (m, 1H), 3.01 (td, *J* = 10.1, 7.3 Hz, 1H), 3.45 (td, *J* = 10.1, 6.1 Hz, 1H), 3.89 (d, *J* = 7.6 Hz, 1H), 4.77 (d, *J* = 3.9 Hz, 1H), 7.35 (d, *J* = 8.5 Hz,

2H), 7.73 (d, J = 8.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 29.8, 30.7, 33.9, 41.9, 50.0, 57.6, 73.3, 127.9 (2C), 129.8 (2C), 132.8, 143.9. IR (KBr) 1345, 1157, 1094, 1026 cm^{-1}. MS (ESI) calcd for $C_{14}H_{18}BrNNaO_2S$ $[M + Na]^+$ 366.0134, found 366.0126. Anal. calcd for $C_{14}H_{18}BrNO_2S$: C, 48.84; H, 5.27; N, 4.07%. Found: C, 48.96; H, 5.20; N, 4.02%.

*syn-2-(1-Bromomethyl)-1-tosylpyrrolidine (**2l**):* yield 89%, 73.9 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.40 (dt, J = 12.1, 7.6 Hz, 1H), 1.68 (d, J = 7.1 Hz, 1H), 1.68−1.80 (m, 1H), 1.82−1.92 (m, 1H), 1.95−2.03 (m, 1H), 2.43 (s, 3H), 3.34 (dd, J = 7.6, 5.9 Hz, 2H), 3.69 (dt, J = 8.2, 4.7 Hz, 1H), 4.61 (dq, J = 7.1, 4.7 Hz, 1H), 7.32 (d, J = 8.2 Hz, 2H), 7.73 (d, J = 8.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 23.1, 24.5, 27.9, 49.4, 55.1, 65.0, 127.5 (2C), 129.7 (2C), 135.1, 143.6. IR (KBr) 1343, 1156, 1092, 1044, 996 cm^{-1}. MS (ESI) calcd for $C_{13}H_{19}BrNO_2S$ $[M + H]^+$ 332.0314, found 332.0314.

*anti-2-(1-Bromomethyl)-1-tosylpyrrolidine (**2m**):* yield 90%, 74.8 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37−1.49 (m, 1H), 1.66 (d, J = 7.1 Hz, 3H), 1.71−1.83 (m, 2H), 1.95−2.05 (m, 1H), 2.45 (s, 3H), 3.26 (dt, J = 10.7, 7.1 Hz, 1H), 3.47 (dt, J = 10.7, 6.2 Hz, 1H), 3.93 (dt, J = 8.0, 4.1 Hz, 1H), 4.68 (dq, J = 7.1, 4.1 Hz, 1H), 7.34 (d, J = 8.1 Hz, 2H), 7.73 (d, J = 8.1 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.6, 21.5, 24.5, 27.0, 50.8, 51.0, 64.1, 127.6 (2C), 129.8 (2C), 133.6, 143.8. IR (KBr) 1341, 1160, 1087, 1004, 978 cm^{-1}. MS (ESI) calcd for $C_{13}H_{19}BrNO_2S$ $[M + H]^+$ 332.0314, found 332.0307.

*2-(Bromomethyl)-2-methyl-1-tosylpyrrolidine (**2n**):* yield 90%, 74.8 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.57 (s, 3H), 1.67−1.92 (m, 3H), 2.25−2.33 (m, 1H), 2.42 (s, 3H), 3.31−3.39 (m, 1H), 3.39−3.46 (m, 1H), 3.76 (d, J = 10.3 Hz, 1H), 3.86 (d, J = 10.3 Hz, 1H), 7.29 (d, J = 8.3 Hz, 2H), 7.76 (d, J = 8.3 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 22.5, 24.0, 39.3, 41.0, 49.8, 67.3, 127.3 (2C), 129.5 (2C), 137.8, 143.1. IR (KBr) 1338, 1155, 1120, 1064, 1005 cm^{-1}. MS (ESI) calcd for $C_{13}H_{19}BrNO_2S$ $[M + H]^+$ 332.0314, found 332.0309.

*(5S)-2-(Bromomethyl)-5-methyl-1-tosylpyrrolidine (**2o**, Diastereomer Mixtures):* yield >99%, 83.0 mg. Major-diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.14 (d, J = 6.4 Hz, 3H), 1.50−1.57 (m, 2H), 2.07−2.12 (m, 2H), 2.43 (s, 3H), 3.23 (t, J = 10.1 Hz, 1H), 3.90 (dd, J = 9.8, 3.3 Hz, 1H), 4.02−4.16 (m, 2H), 7.30 (d, J = 8.1 Hz, 2H), 7.75 (d, J = 8.1 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.5, 21.6, 27.8, 30.9, 34.6, 57.4, 60.6, 127.1 (2C), 129.7 (2C), 138.9, 143.3. Minor-diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (d, J = 6.4 Hz, 3H), 1.58−1.74 (m, 2H), 2.02−2.20 (m, 2H), 2.44 (s, 3H), 3.33 (t, J = 10.8 Hz, 1H), 3.71 (q, J = 6.4 Hz, 1H), 3.80 (dd, J = 9.6, 3.2 Hz, 1H), 3.79−3.87 (m, 1H), 7.33 (d, J = 8.2 Hz, 2H), 7.73 (d, J = 8.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 23.2, 28.9, 31.8, 36.4, 58.3, 62.1, 127.6 (2C), 129.9 (2C), 134.4, 143.8. IR (neat) 1340, 1157, 1095, 1040 cm^{-1}. MS (ESI) calcd for $C_{13}H_{18}BrNNaO_2S$ $[M + Na]^+$ 354.0134, found 354.0125.

*(5R)-2-(Bromomethyl)-5-isopropyl-1-tosylpyrrolidine (**2p**, Diastereomer Mixtures):* yield 93%, 83.8 mg. Major-diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.40 (d, J = 6.9 Hz, 3H), 0.81 (d, J = 6.9 Hz, 3H), 1.23−1.34 (m, 1H), 1.60−1.72 (m, 1H), 1.72−1.85 (m, 1H), 1.85−2.00 (m, 1H), 2.00−2.10 (m, 1H), 2.42 (s, 3H), 3.28 (t, J = 10.0 Hz, 1H), 3.85−3.89 (m, 1H), 4.03 (dd, J = 9.7, 2.2 Hz, 1H), 4.15−4.21 (m, 1H), 7.29 (d, J = 8.1 Hz, 2H), 7.73 (d, J = 8.1 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.2, 19.8, 21.5, 22.9, 29.3, 31.2, 34.6, 61.9, 65.7, 126.8 (2C), 129.5 (2C), 138.9, 143.1. Minor-diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (d, J = 7.0 Hz, 3H), 0.99 (d, J = 7.0 Hz, 3H), 1.60−1.72 (m, 1H), 1.72−1.85 (m, 1H), 1.85−2.00 (m, 1H), 2.00−2.10 (m, 1H), 2.30−2.41 (m, 1H), 2.44 (s, 3H), 3.25 (t, J = 11.2 Hz, 1H), 3.41−3.47 (m, 1H), 3.76−3.84 (m, 2H), 7.34 (d, J = 8.1 Hz, 2H), 7.72 (d, J = 8.1 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.4, 20.0, 21.5, 25.2, 28.9, 29.3, 35.9, 62.0, 68.1, 127.6 (2C), 129.8 (2C), 134.3, 143.7. IR (KBr) 1330, 1214, 1154, 1096, 989 cm^{-1}. MS (ESI) calcd for $C_{15}H_{23}BrNO_2S$ $[M + H]^+$ 360.0627, found 360.0620.

*3-(Bromomethyl)-2-tosylisoxazolidine (**4a**):* yield 93%, 74.7 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.17−2.30 (m, 1H), 2.46 (s, 3H), 2.43−2.53 (m, 1H), 3.35 (t, J = 9.7 Hz, 1H), 3.66 (dd, J = 10.2, 4.9 Hz, 1H), 3.94−4.06 (m, 2H), 4.44−4.53 (m, 1H), 7.36 (d, J = 8.0 Hz, 2H), 7.86 (d, J = 8.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 34.2, 34.3, 59.9, 70.2, 129.2 (2C), 129.8 (2C), 132.5, 145.3. IR (KBr) 1349, 1308, 1169, 1088, 1011 cm^{-1}. MS (ESI) calcd for $C_{11}H_{15}BrNO_3S$ $[M + H]^+$ 319.9951, found 319.9944. Anal. calcd for $C_{11}H_{14}BrNO_3S$: C, 41.26; H, 4.41; N, 4.37%. Found: C, 41.57; H, 4.22; N, 4.29%.

*3-(Bromomethyl)-5-phenyl-2-tosylisoxazolidine (**4b**, Diastereomer Mixtures):* yield 97%, 96.1 mg. Data are for the major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.25 (ddd, J = 12.6, 10.8, 7.8 Hz, 1H), 2.45 (s, 3H), 2.90 (ddd, J = 12.6, 7.8, 6.0 Hz, 1H), 3.51 (t, J = 10.1 Hz, 1H), 3.79 (dd, J = 10.1, 4.8 Hz, 1H), 4.58−4.68 (m, 1H), 5.14 (dd, J = 10.8, 6.0 Hz, 1H), 7.23−7.39 (m, 7H), 7.89 (d, J = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 34.8, 42.5, 60.9, 83.7, 126.9 (2C), 128.7 (2C), 129.0, 129.3 (2C), 129.8 (2C), 132.5, 135.9, 145.4. IR (KBr) 1358, 1172, 1087, 1027, 1006 cm^{-1}. MS (ESI) calcd for $C_{17}H_{18}BrNNaO_3S$ $[M + Na]^+$ 418.0083, found 418.0071. Anal. calcd for $C_{17}H_{18}BrNO_3S$: C, 51.52; H, 4.58; N, 3.53%. Found: C, 51.66; H, 4.54; N, 3.36%.

*3-(Bromomethyl)-5-(4-methoxyphenyl)-2-tosylisoxazolidine (**4c**, Diastereomer Mixtures):* yield 90%, 95.9 mg. Data are for the major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.24 (ddd, J = 12.8, 10.8, 8.0 Hz, 1H), 2.45 (s, 3H), 2.84 (ddd, J = 12.8, 7.8, 5.5 Hz, 1H), 3.52 (t, J = 10.4 Hz, 1H), 3.78 (s, 3H), 3.79 (dd, J = 10.4, 4.6 Hz, 1H), 4.57−4.68 (m, 1H), 5.06 (dd, J = 10.8, 5.5 Hz, 1H), 6.86 (d, J = 8.8 Hz, 2H), 7.22 (d, J = 8.8 Hz, 2H), 7.35 (d, J = 8.2 Hz, 2H), 7.88 (d, J = 8.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 34.9, 42.2, 55.3, 61.0, 83.5, 114.0 (2C), 127.4, 128.5 (2C), 129.3 (2C), 129.8 (2C), 132.5, 145.3, 160.2. IR (KBr) 1517, 1356, 1254, 1166, 1030 cm^{-1}. MS (ESI) calcd for $C_{18}H_{21}BrNO_4S$ $[M + H]^+$ 426.0369, found 426.0356.

*3-(Bromomethyl)-2-tosyl-5-(4-(trifluoromethyl)phenyl)isoxazolidine (**4d**, Diastereomer Mixtures):* yield 91%, 105.6 mg. Data are for the major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.22 (ddd, J = 12.8, 10.2, 8.9 Hz, 1H), 2.46 (s, 3H), 2.97 (ddd, J = 12.8, 8.0, 6.1 Hz, 1H), 3.49 (dd, J = 10.2, 8.9 Hz, 1H), 3.76 (dd, J = 10.2, 4.6 Hz, 1H), 4.64−4.74 (m, 1H), 5.28 (dd, J = 10.5, 6.1 Hz, 1H), 7.37 (d, J = 8.2 Hz, 2H), 7.42 (d, J = 8.2 Hz, 2H), 7.60 (d, J = 8.2 Hz, 2H), 7.88 (d, J = 8.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 34.7, 42.7, 60.7, 82.7, 125.6 (d, J = 3.8 Hz, 2C), 127.0 (2C), 127.3, 129.3 (2C), 129.7 (d, J = 15.3 Hz), 129.9 (2C), 132.3, 140.3, 145.6. IR (KBr) 1363, 1332, 1168, 1124, 1036 cm^{-1}. MS (ESI) calcd for $C_{18}H_{18}BrF_3NO_3S$ $[M + H]^+$ 464.0137, found 464.0127.

*3-(1-Bromoethyl)-5-(naphthalen-1-yl)-2-tosylisoxazolidine (**4e**, Diastereomer Mixtures):* yield 91%, 104.73 mg. Major-diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.66 (d, J = 7.3 Hz, 3H), 2.44 (s, 3H), 3.16−3.26 (m, 1H), 3.49 (dd, J = 11.4, 10.1 Hz, 1H), 3.96 (dd, J = 10.1, 4.5 Hz, 1H), 4.52−4.60 (m, 1H), 5.53 (d, J = 4.5 Hz, 1H), 7.36 (d, J = 8.3 Hz, 2H), 7.40−7.53 (m, 4H), 7.56 (d, J = 7.3 Hz, 1H), 7.80 (d, J = 8.2 Hz, 1H), 7.87 (d, J = 8.4 Hz, 1H), 7.91 (d, J = 8.3 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.2, 21.7, 29.8, 41.8, 65.5, 82.0, 121.9, 123.8, 125.1, 125.7, 126.3, 128.4, 129.0, 129.6 (3C), 129.8, 129.9 (2C), 131.3, 133.3, 145.5. Minor-diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.23 (d, J = 6.6 Hz, 3H), 2.43 (s, 3H), 2.88−2.99 (m, 1H), 3.73- 3.88 (m, 2H), 4.32 (dt, J = 7.5, 4.1 Hz, 1H), 5.57 (d, J = 10.3 Hz, 1H), 7.33 (d, J = 8.0 Hz, 2H), 7.42−7.58 (m, 3H), 7.85 (t, J = 7.6 Hz, 2H), 7.93 (d, J = 8.4 Hz, 2H), 8.03 (d, J = 8.5 Hz, 1H), 8.11 (d, J = 8.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.0, 21.7, 34.5, 48.1, 66.1, 85.9, 123.3, 125.1, 125.2, 125.9, 126.5, 128.8, 129.2 (2C), 129.8 (3C), 129.9, 131.9, 132.9, 133.8, 145.2. IR (KBr) 1362, 1334, 1168, 1091, 1038 cm^{-1}. MS (ESI) calcd for $C_{22}H_{23}BrNO_3S$ $[M + H]^+$ 460.0577, found 460.0563.

*3-(Bromomethyl)-5-(4-chlorophenyl)-3-methyl-2-tosylisoxazolidine (**4f**, Diastereomer Mixtures):* yield 95%, 105.6 mg. Data are for the major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.99 (s, 3H), 2.43 (s, 3H), 2.63 (dq, J = 12.8, 7.3 Hz, 2H), 3.61 (d, J = 10.5 Hz, 1H), 3.74 (d, J = 10.5 Hz,

1H), 5.55 (t, J = 8.0 Hz, 1H), 7.21 (d, J = 8.6 Hz, 2H), 7.26−7.34 (m, 4H), 7.85 (d, J = 8.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 21.9, 41.4, 48.8, 70.8, 81.7, 128.0 (2C), 128.8 (4C), 129.5 (2C), 134.5, 135.1, 135.5, 144.8. IR (neat) 1494, 1333, 1161, 1092 cm^{-1}. MS (ESI) calcd for $C_{18}H_{20}BrClNO_3S$ $[M + H]^+$ 444.0030, found 444.0018.

*3-(Bromomethyl)-5-(thiophen-2-yl)-2-tosylisoxazolidine (**4g**, Diastereomer Mixtures):* yield 82%, 82.5 mg. Data are for the major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.36 (ddd, J = 12.8, 9.8, 7.1 Hz, 1H), 2.45 (s, 3H), 2.97 (ddd, J = 12.8, 7.8, 6.3 Hz, 1H), 3.51 (t, J = 10.1 Hz, 1H), 3.77 (dd, J = 10.1, 4.9 Hz, 1H), 4.64−4.74 (m, 1H), 5.50 (dd, J = 9.8, 6.3 Hz, 1H), 6.97 (dd, J = 5.0, 3.6 Hz, 1H), 7.04−7.08 (m, 1H), 7.32 (dd, J = 5.0, 1.1 Hz, 1H), 7.36 (d, J = 8.1 Hz, 2H), 7.89 (d, J = 8.1 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 34.5, 42.4, 60.9, 79.4, 126.8, 126.9, 127.5, 129.3 (2C), 129.8 (2C), 132.4, 138.3, 145.4. IR (KBr) 1354, 1326, 1169, 1092, 1032 cm^{-1}. MS (ESI) calcd for $C_{15}H_{17}BrNO_3S_2$ $[M + H]^+$ 401.9828, found 401.9817.

*3-(Bromomethyl)-5-butyl-2-tosylisoxazolidine (**4h**, Diastereomer Mixtures):* yield 98%, 92.2 mg. Data are for the major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (t, J = 7.0 Hz, 3H), 1.16−1.37 (m, 4H), 1.41−1.69 (m, 2H), 1.79 (ddd, J = 12.5, 10.2, 7.8 Hz, 1H), 2.46 (s, 3H), 2.59 (ddd, J = 12.5, 7.8, 5.5 Hz, 1H), 3.38 (t, J = 9.7 Hz, 1H), 3.71 (dd, J = 10.2, 4.6 Hz, 1H), 3.98−4.07 (m, 1H), 4.37−4.48 (m, 1H), 7.36 (d, J = 8.5 Hz, 2H), 7.85 (d, J = 8.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 21.7, 22.4, 28.1, 32.2, 34.9, 40.4, 60.7, 82.4, 129.2 (2C), 129.8 (2C), 132.5, 145.2. IR (neat) 1454, 1360, 1167, 1091, 1017 cm^{-1}. MS (ESI) calcd for $C_{15}H_{23}BrNO_3S$ $[M + H]^+$ 376.0577, found 376.0565.

Mechanical Study for Oxidative Intramolecular Bromo-amination of *N*-Alkenyl Sulfonamides via Umpolung of Alkali Metal Bromides (Scheme 3).[22] *N-Bromination of N-pentyl-tosylamide (**5**) via Oxidative Umpolung of KBr (eq 1):* To a solution of **5** (60.3 mg, 0.25 mmol) and Oxone (184.4 mg, 0.30 mmol) in acetonitrile (1 mL) was added KBr (35.7 mg, 0.30 mmol) under argon atmosphere. The solution was stirred at room temperature for 15 h. Saturated $NaHCO_3$ aqueous solution (10 mL) was poured into the reaction mixture, and the product was extracted with AcOEt (15 mL × 3). The combined extracts were washed by brine (10 mL) and dried over Na_2SO_4. The organic phase was concentrated under reduced pressure, and the residue was the pure desired product **6** (70.7 mg, 88% yield) without further purification.

*N-Pentyl-tosylamide (**5**):* ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (t, J = 6.9 Hz, 3H), 1.18−1.28 (m, 4H), 1.41−1.49 (m, 2H), 2.43 (s, 3H), 2.91 (q, J = 6.9 Hz, 2H), 4.71 (brd, J = 5.0 Hz, 1H), 7.31 (d, J = 8.2 Hz, 2H), 7.76 (d, J = 8.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 21.5, 22.1, 28.6, 29.1, 43.1, 127.0 (2C), 129.6 (2C), 136.9, 143.3. IR (neat) 3281, 1425, 1325, 1160, 1094 cm^{-1}. MS (ESI) calcd for $C_{12}H_{20}NO_2S$ $[M + H]^+$ 242.1209, found 242.1201.

*N-Bromo-N-pentyl-tosylamide (**6**):* ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90 (t, J = 7.1 Hz, 3H), 1.28−1.37 (m, 4H), 1.58−1.68 (m, 2H), 2.47 (s, 3H), 3.14 (t, J = 7.1 Hz, 2H), 7.38 (d, J = 8.2 Hz, 2H), 7.83 (d, J = 8.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 21.7, 22.1, 27.8, 28.0, 57.8, 129.4 (2C), 129.5 (2C), 130.6, 144.9. IR (neat) 1441, 1354, 1166, 1089 cm^{-1}. MS (ESI) calcd for $C_{12}H_{19}BrNO_2S$ $[M + H]^+$ 320.0314, found 320.0304.

General Procedure for the Competitive Bromination of N-Sulfonamides (eq 2): To a solution of **5** (60.3 mg, 0.25 mmol), **7** (63.3 mg, 0.25 mmol) and Oxone (184.4 mg, 0.30 mmol) in acetonitrile (1 mL) was added KBr (35.7 mg, 0.30 mmol) under argon atmosphere. The solution was stirred at room temperature for 15 h. Saturated $NaHCO_3$ aqueous solution (10 mL) was poured into the reaction mixture, and the product was extracted with AcOEt (15 mL × 3). The combined extracts were washed by brine (10 mL) and dried over Na_2SO_4. The organic phase was concentrated under reduced pressure, and the residue was a mixture of products **5** (48.5 mg, 80% yield), **7** (1.4 mg, 2% yield), and unknown products, yield (%) of which was estimated by ^{1}H NMR analysis.

*N-Methyl-N-(4-penten-1-yl)-tosylamide (**7**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.58−1.68 (m, 2H), 2.06−2.14 (m, 2H), 2.43 (s, 3H), 2.71 (s, 3H), 2.99 (t, J = 7.3 Hz, 2H), 4.96−5.08 (m, 2H), 5.80 (ddt, J = 17.2, 10.4, 6.6 Hz, 1H), 7.32 (d, J = 8.1 Hz, 2H), 7.66 (d, J = 8.1 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 26.8, 30.6, 34.7, 49.6, 115.3, 127.4 (2C), 129.6 (2C), 134.4, 137.5, 143.2. IR (neat) 1460, 1341, 1160, 1091 cm^{-1}. MS (ESI) calcd for $C_{13}H_{20}NO_2S$ $[M + H]^+$ 254.1209, found 254.1201.

■ ASSOCIATED CONTENT

Supporting Information. ^{1}H and ^{13}C NMR spectra of products in the intramolecular bromo-amination and in a mechanical study for intramolecular bromo-amination. This material is available free of charge via the Internet at http://pubs.acs.org.

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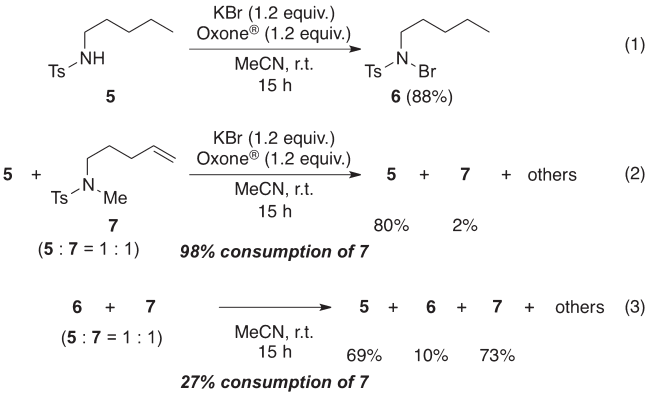
(22) To explain the reaction mechanism for oxidative intramolecular bromo-amination of *N*-alkenyl sulfonamides via umpolung of alkali metal bromides with Oxone, we investigated the competitive bromination of sulfonamides. First, the treatment of *N*-pentyl-tosylamide (**5**) with KBr and Oxone gave *N*-bromo-*N*-pentyl-tosylamide (**6**) in 88% yield (eq 1). When a mixture of **5** and *N*-methyl-*N*-(4-penten-1-yl)-tosylamide (**7**) were treated with KBr and Oxone in MeCN, **7** was predominantly converted into some of unknown products (20% consumption of **5** and 98% consumption of **7**) (eq 2). Moreover, the brominative conversion of **7** with **6** was much less effective than the reaction in eq 2 with KBr and Oxone (27% consumption of **7**) (eq 2 vs eq 3). These results indicate indirectly that the oxidative bromination preferentially occurs in the olefin moiety not in the sulfonamide nitrogen of substrate.



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