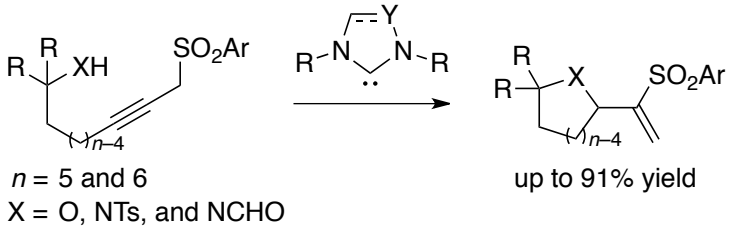
Oxa- and Azacycle-formation via Migrative Cyclization of Sulfonylalkynol and Sulfonylalkynamide with N-Heterocyclic Carbene

*Yinli Wang, Raphaël Oriez, Satoru Kuwano, Yousuke Yamaoka, Kiyosei Takasu, and Ken-ichi Yamada**

Graduate School of Pharmaceutical Sciences, Kyoto University

Yoshida, Sakyo-ku, Kyoto 606-8501, Japan.

E-mail: yamak@pharm.kyoto-u.ac.jp

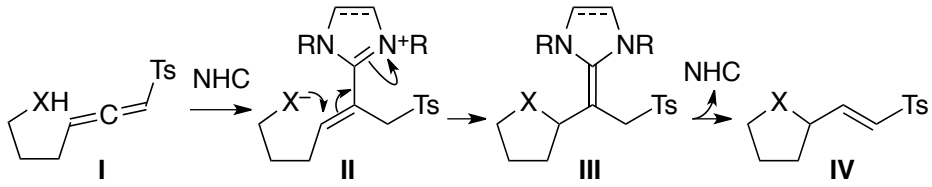


Abstract: An N-heterocyclic carbene promotes cyclization of sulfonylalkynols and sulfonylalkynamides that accompanies 1,2-migration of the sulfonyl groups. This reaction provides a novel access to oxa- and azacycles possessing a pendent vinyl sulfone functionality, which in turn is amenable for further transformations.

Oxa- and azacycles are abundant structural motifs of biologically significant compounds,[1] and therefore, construction of these heterocycles is greatly important in synthetic organic chemistry. During our continuing effort to develop new methodologies utilizing N-heterocyclic carbenes (NHC),[2,3] we envisaged that the Trost's γ-umpolung chemistry by phosphane catalysis[4] might work with NHC as

follows: the NHC would undergo intermolecular conjugate addition with allenyl sulfone **I**, and the following internal proton transfer forms **II** (Scheme 1). Intramolecular conjugate addition of **II** and the protonation at the β-position of the resulting intermediate **III** followed by the elimination of NHC would give **IV**, achieving overall umpolung bond formation between the internal nucleophile and the γ-position. Against our expectation, however, the cyclization was accompanied with 1,2-migration of the sulfonyl group (*vide infra*). The produced oxa- or aza-cycles possess a vinyl sulfone functionality, which is amenable to further transformations. In addition, medicinal and biological applications of this functional group have recently been reported.[5] Herein, we report this new type of cyclization reaction.

Scheme 1. The Initial Plan for the γ-Umpolung by NHC Catalysis



Propargyl sulfones have been used as a relatively stable and readily preparable precursor of highly reactive allenyl sulfones,[6] which are reversibly generated *in situ* under basic conditions and undergo cycloadditions[7] and radical cyclizations.[8] Therefore, we utilized propargyl sulfone **2a** as a source of allenyl sulfone **1a**, which should be generated *in situ* (eq 1). Propargyl sulfone **2a** was heated at 60 °C in the presence of SIMes·HCl (**C1**) and Cs_2CO_3 (5 mol% each) in toluene (Table 1, entry 1). After 19 h, instead of expected product **IV** (X = O), tetrahydrofuran **3a** was unexpectedly produced in 86% yield along with a small amount of dihydropyran **4a** (3%). Thus, addition of the internal nucleophile at the γ-position mainly occurred with 1,2-migration of the sulfonyl group. In the absence of **C1**, cyclization at the β-position mainly proceeded to give dihydropyran **4a** in 70% yield (entry 2). This is a usual reaction mode of allenyl sulfones bearing an internal nucleophile.[9,10]

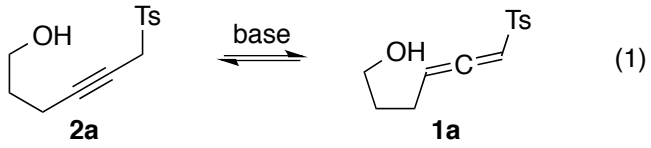
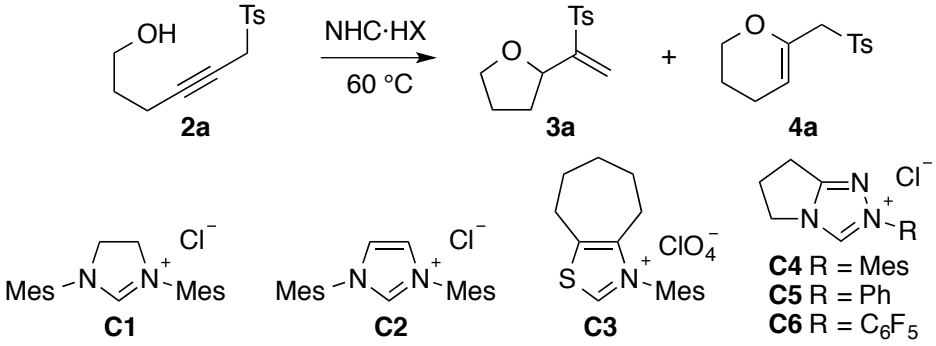


Table 1. Optimization of Conditions.

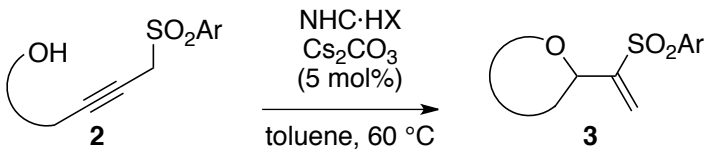


entry	NHC·HX (mol%)	base	solvent	time h	**3a** % yield	**4a** % yield	**2a** % recovery
1	**C1** (5)	Cs_2CO_3	toluene	19	86	3	0
2	–	Cs_2CO_3	toluene	12	2	70	0
3	**C1** (5)	K_2CO_3	toluene	26	0	0	89
4	**C1** (5)	Na_2CO_3	toluene	26	0	0	84
5	**C1** (5)	Et_3N	toluene	26	9	0	73
6	**C1** (5)	DBU	toluene	9	53	18	0
7	**C2** (5)	Cs_2CO_3	toluene	6	79	0	0
8	**C3** (5)	Cs_2CO_3	toluene	19	64	0	0
9	**C4** (5)	Cs_2CO_3	toluene	7.5	73	0	0
10	**C5** (5)	Cs_2CO_3	toluene	24	49	8	38
11	**C6** (5)	Cs_2CO_3	toluene	26	62	0	0
12	**C2** (5)	Cs_2CO_3	THF	26	3	0	83
13	**C2** (5)	Cs_2CO_3	$(CH_2Cl)_2$	26	40	0	55
14	**C2** (2)	Cs_2CO_3	toluene	10	91	0	0
15	**C2** (1)	Cs_2CO_3	toluene	16	74	0	0

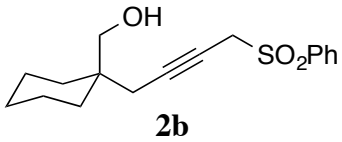
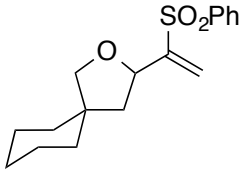
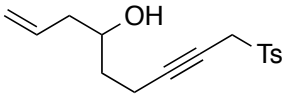
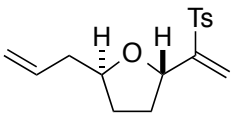
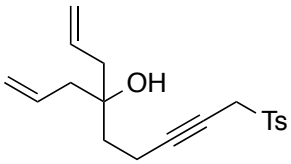
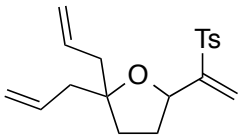
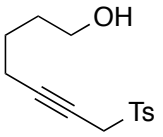
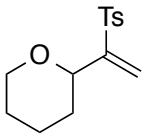
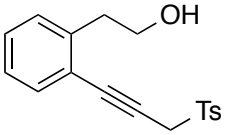
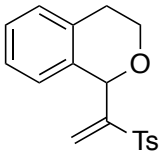
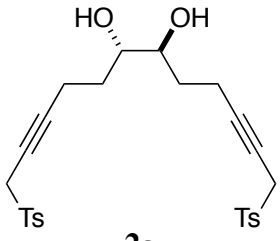
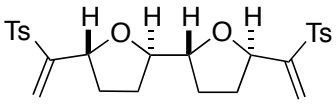
The effects of bases, azolium salts, and solvent were then investigated. Among the tested bases, Cs_2CO_3 was the best for this reaction (Table 1, entries 1 and 3–6). DBU gave usual adduct **4a** in a higher yield (18%, entry 6). Other NHC precursors **C2–C6** were tested in the reaction. The use of more acidic NHC precursors (**C2–C4** and **C6**) prevented the formation of **4a** without dramatic erosion of the yield of **3a** (entries 7–9 and 11), although the reaction with **C5** was sluggish and produced significant amount of **4a** (8%, entry 10). The reaction was much slower in THF or dichloroethane and proceeded most smoothly in toluene (entries 1, 12 and 13). The use of 2 mol% **C2** was sufficient for the reaction to give **3a** in 91% yield (entry 14), although the yield decreased to 74% with 1 mol% of **C2** (entry 15).

The reaction was applied to other ω-hydroxypropargyl sulfones (Table 2). Propargyl sulfone **2b**, bearing vicinal substituents, required 80 °C for the reaction to form spiro-tetrahydrofuran **3b** in 83% yield (entry 2). Secondary alcohol **2c** (entry 3) and tertiary alcohol **2d** (entry 4) also showed good performance in this reaction, successfully forming **3c** and **3d** in 81% and 70% yields, respectively. For the 6-membered ring formation, less acidic **C1** promoted the reaction more smoothly than **C2**. Cyclization of **2e** completed in refluxing toluene in 13 h, and tetrahydropyran **3e** was isolated in 68% yield (entry 5). Isochromane **3f** was produced in 58% yield (entry 6). The reaction of C_2-symmetric diol **2g** afforded diastereomixture of bi-THF with **3g** as a major isomer in 88% yield (entry 7). Notably, the reaction proceeded in 1.6-gram-scale without any problems to give **3a** in comparable yield (entry 1). Unfortunately, the reaction was not suitable for the formation of a 7-membered ring (*vide infra*).

Table 2. Migrative Cyclization of Sulfonylalkynols.



entry	**2**	NHC·HX	time h	**3**	yield %

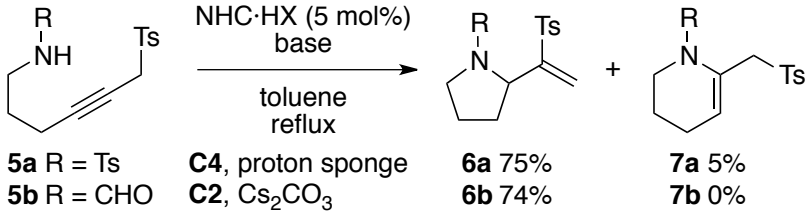
1[a]	**2a**	**C2**	10	**3a**	81
2[b]	 **2b**	**C2**	6.5	 **3b**	83
3	 **2c**	**C2**	15	 **3c**	81[c,d]
4	 **2d**	**C2**	11	 **3d**	70
5[e]	 **2e**	**C1**	13	 **3e**	68
6[e]	 **2f**	**C1**	8	 **3f**	58
7	 **2g**	**C2**	4	 **3g**	88[d,f]

[a] The reaction was performed using 1.6 g of **2a**. [b] The reaction was performed at 80 °C. [c] dr 3:2. [d] The relative configuration is based on NOESY correlations (see Experimental Section). [e] The reaction was performed in refluxing toluene. [f] dr 3:2:2.

With the successful formation of cyclic ethers, we next applied this reaction to the formation of cyclic amides (Scheme 2). Although the standard condition for alcohols (5 mol% each of **C2** and Cs_2CO_3) converted *N-p*-toluenesulfonamide **5a** into the expected product **6a** in only 7% yield and mainly

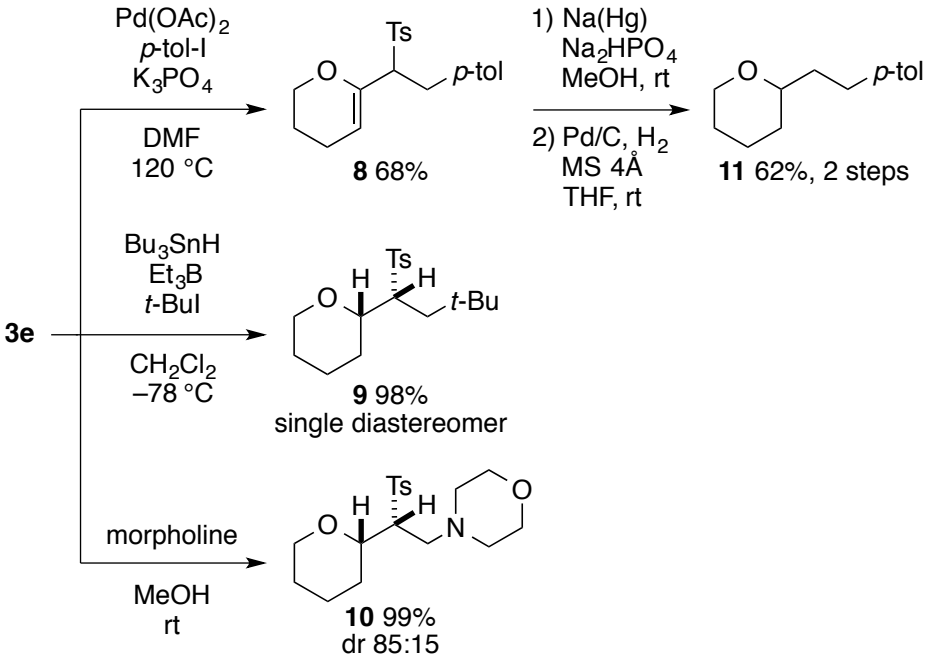
provided usual addition product **7a** in 77% yield, the use of **C4** and proton sponge successfully suppressed the generation of **7a** and improved the yield of **6a** up to 75%. In contrast, formamide **5b** was smoothly converted to **6b** in 74% yield under the standard condition for alcohols.

Scheme 2. Migrative Cyclization of Sulfonylalkynamides.



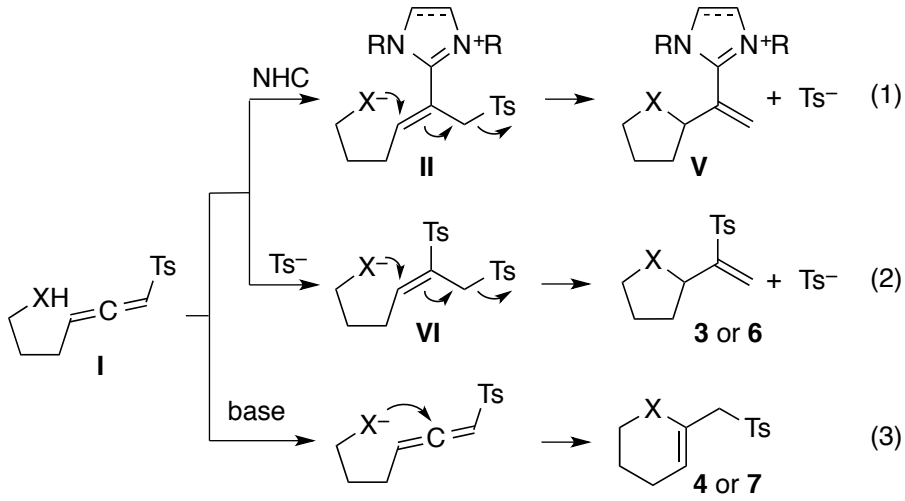
Taking the advantage of the vinyl sulfone functionality of the product, nucleophiles were introduced at the terminal carbon atom (Scheme 3). Carbonucleophiles were introduced to vinyl sulfone **3e** using the Heck reaction and a radical addition reaction, producing **8** and **9**, respectively. Introduction of N-nucleophile was also possible; conjugate addition of morpholine to **3e** quantitatively gave **10** with 85:15 diastereoselectivity. The stereochemistry of **9** and **10** was unequivocally determined by X-ray crystallography. Desulfonylation of **8** with sodium amalgam followed by hydrogenation of the dihydropyrane moiety gave **11** in 62% yield over 2 steps.

Scheme 3. Manipulation of the Vinyl Sulfone Moiety.



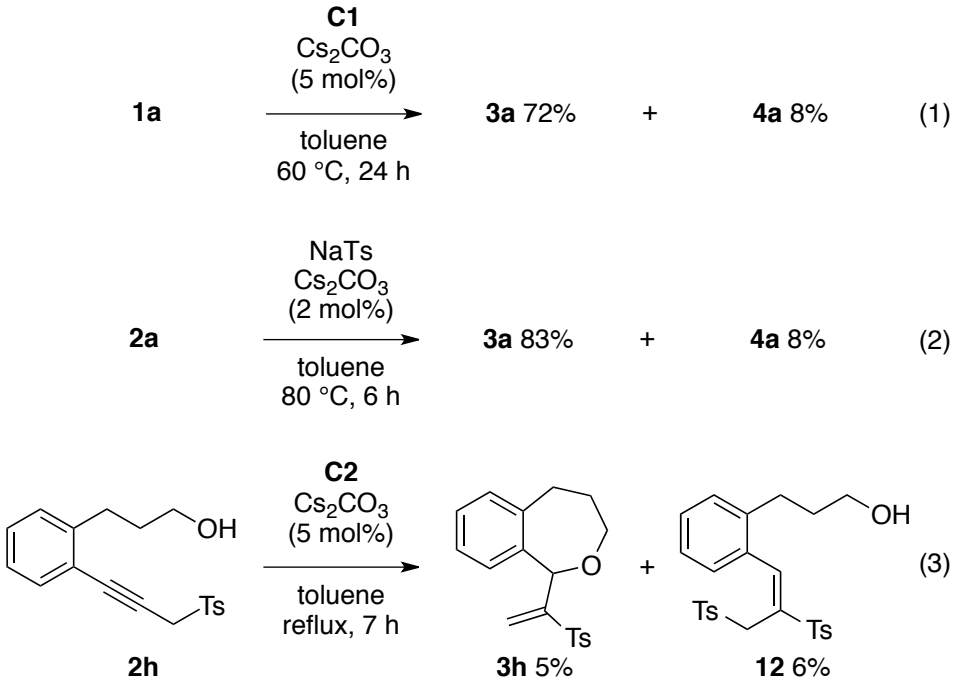
Plausible reaction pathways are shown in Scheme 4. As mentioned above, we elucidated that the reaction proceeded via allenyl sulfone intermediate **I** generated *in situ* from propargyl sulfone **2** or **5**. Conjugate addition of NHC followed by the internal proton transfer gives **II**. Then, **II** would undergo an intramolecular S_N2' reaction to give **V** and *p*-toluenesulfinate anion (Ts^-) (Scheme 4-1) rather than the initially expected conjugate addition (Scheme 1). The liberation of Ts^- triggers the productive cycle, which involves the formation of **VI** by the addition of Ts^- to **I** and the following S_N2' cyclization that results in the production of **3** or **6** and the regeneration of Ts^- (Scheme 4-2).[11] In the absence of NHC or in the reaction with an internal nucleophile of a relatively high nucleophilicity, allenyl sulfone **I** undergoes usual intramolecular conjugate addition to produce **4** or **7** (Scheme 4-3).

Scheme 4. Plausible Reaction Pathways.



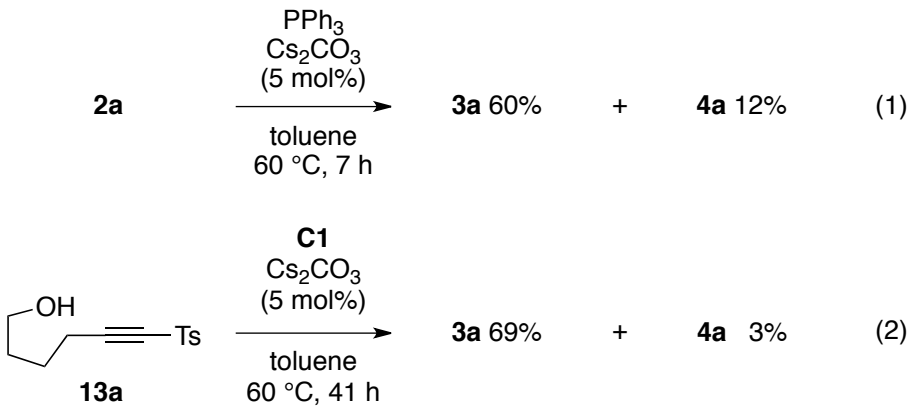
The following results support the aforementioned scenario (Scheme 5): (1) When allenyl sulfone **1a** was heated at 60 °C in toluene in the presence of **C1** and Cs_2CO_3 (5 mol% each), **3a** was produced in 72% yield. This result indicates that the allenyl sulfone could be an intermediate of this transformation. (2) In the presence of 2 mol% sodium *p*-toluenesulfinate (NaTs), the reaction proceeded smoothly in the absence of NHC and gave **3a** in 83% yield along with **4a** in 8% yield after 6 h. Thus, Ts^- actually induces the reaction as shown in Scheme 4-2. (3) When propargyl sulfone **2h** was heated for 7 h in refluxing toluene in the presence of **C2** and Cs_2CO_3 (5 mol% each), disulfone **12** was obtained in 6% yield along with 7-membered cyclic ether **3h** in 5% yield. The isolation of **12** strongly supports the existence of intermediate **VI** and therefore, the reaction pathway shown in Scheme 4-2. The efforts to detect the formation of **V** were unsuccessful as yet.

Scheme 5. Experimental Supports for the Proposed Pathways.



While the sulfonyl migration of an allyl sulfone to give a vinyl sulfone is, to the best of our knowledge, unprecedented with NHC,[12] the reaction promoted by triphenylphosphine has been reported.[13] Therefore, the performance of triphenylphosphine in this reaction was tested; triphenylphosphine also worked as a nucleophile to trigger the reaction, but the yield of **3a** was lower (60%) than that with **C1** (Table 1, entry 1; 86%), when it was heated with **2a** at 60 °C in toluene for 7 h (Scheme 6-1). In addition, we also tested **13a** in this reaction because 1-alkynyl sulfones are also known as a precursor of allenyl sulfones.[6] The reaction with **13a**, however, gave **3a** in a slightly lower yield (69%) (Scheme 6-2). Although the uses of triphenylphosphine and **13a** in lieu of **C1** and **2a**, respectively, resulted in the decreased yield of the product, the formation of **3a** under these conditions is additional support for the proposed reaction pathways shown in Scheme 4.

Scheme 6. The reactions of **2a** with Ph_3P and 1-Alkynyl Sulfone **13a** with **C1**.



In conclusion, an oxa- and azacycle-forming reaction of sulfonylakynols and sulfonylakynamides utilizing NHC was developed. Bond formation with internal O- and N-nucleophiles occurred at the γ-position of the propargyl sulfones with 1,2-sulfonyl migration, while a bond-formation mainly occurred at the β-position in the absence of NHC. To the best of our knowledge, this is the first example of this type of sulfonyl migration with NHC. Oxa- and azacycles are abundant substructures of natural products and pharmaceuticals, and the pendent vinyl sulfone functionality is useful for further bond-formation.

Experimental Section

General. All melting points are uncorrected. Silica gel was used for column chromatography. NMR (500 and 125 MHz for ^1H and ^{13}C, respectively) was measured in $CDCl_3$. Chemical shifts (δ) and coupling constants (*J*) are presented in parts per million relative to tetramethylsilane and hertz, respectively. Abbreviations are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. ^{13}C peak multiplicity assignments were made based on DEPT data. IR spectroscopy was recorded using an attenuated total reflectance FTIR, and the wave numbers of maximum absorption peaks are reported in cm^{-1}. Double-focusing magnetic sector and TOF mass spectrometers were used for FAB- and ESI-MS, respectively. Anhydrous solvents were purchased and used without further desiccation. The precursors of N-heterocyclic carbenes **C1–C6** were purchased and used as received.

Starting Materials.

6-Tosylhexa-4,5-dien-1-ol (1a): To a solution of butane-1,4-diol (25.0 g, 277 mmol) in anhydrous CH_2Cl_2 (280 mL) under argon atmosphere were added TrCl (19 g, 69 mmol), pyridine (11 mL, 0.14 mol), and MS4A (100 g), and the mixture was stirred at rt for 19 h. After dilution with CH_2Cl_2, the mixture was filtered through a pad of celite and concentrated *in vacuo*. The crude product was purified by column chromatography (hexane/EtOAc 2:1) to give 4-trityloxybutan-1-ol (**1a-1**) (23.0 g, quant) as a white solid of mp 52–58 °C: ^{1}H NMR: δ 7.44 (d, *J* = 7.5, 6H), 7.30 (t, *J* = 7.5, 6H), 7.25–7.22 (m, 3H), 3.64 (q, *J* = 5.0, 2H), 3.12 (t, *J* = 5.5, 2H), 1.71–1.65 (m, 4H). ^{13}C NMR: δ 144.1 (C), 128.5 (CH), 127.7 (CH), 126.8 (CH), 86.5 (C), 63.4 (CH_2), 62.6 (CH_2), 29.7 (CH_2), 26.4 (CH_2). IR: 3365, 2940, 1447, 1219, 1061, 907, 729; ESIMS *m/z*: 355 (M + Na). HRMS-ESI (*m/z*): $[M + Na]^+$ calcd for $C_{23}H_{24}NaO_2$, 355.1669; found, 355.1667.

To a solution of **1a-1** (12.6 g, 38.0 mmol) in anhydrous CH_2Cl_2 (190 mL), were added PCC (12 g, 57 mmol) and celite (20 g), and the mixture was stirred at rt for 1.5 h. After diluted with Et_2O, the mixture was filtered through a pad of SiO_2 and concentrated *in vacuo* to give 4-trityloxybutanal as colorless solid (12.3 g), which was used in the next reaction without further purification: ^{1}H NMR: δ 9.78 (t, *J* = 1.5, 1H), 7.42 (d, *J* = 7.0, 6H), 7.30 (t, *J* = 7.0, 6H), 7.23 (t, *J* = 7.0, 3H), 3.13 (t, *J* = 6.0, 2H), 2.54 (dd, *J* = 7.0, 1.5, 2H), 1.96 (tt, *J* = 7.0, 6.0, 2H). ^{13}C NMR: δ 202.4 (CH), 144.1 (C), 128.6 (CH), 127.8 (CH), 126.9 (CH), 86.6 (C), 62.5 (CH_2), 41.0 (CH_2), 22.8 (CH_2).

To a solution of the above aldehyde (12.3 g) in anhydrous THF (88 mL) cooled at –78 °C under argon atmosphere was added a 0.5 M THF solution of ethynylmagnesium bromide (91 mL, 46 mmol), and the mixture was stirred for 7 h. The reaction was quenched by the addition of saturated aqueous NH_4Cl, and the organic layer was separated. The aqueous layer was extracted 3 times with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 2:1) to give 6-trityloxyhex-1-yn-3-ol (**1a-2**) (9.52 g, 69% for 2 steps) as a colorless oil: ^{1}H NMR: δ 7.44 (d, *J* = 7.5, 6H), 7.30 (dd, *J* = 7.5, 7.0, 6H), 7.23 (d, *J* = 7.0, 3H), 4.39 (m, 1H), 3.15 (m, 1H), 3.10 (m, 1H), 2.47 (d, *J* = 2.0, 1H), 2.28 (d, *J* = 6.0, 1H), 1.88–1.77 (m, 4H). ^{13}C NMR: δ 144.1 (C), 128.6 (CH), 127.8 (CH), 126.9 (CH), 86.7 (C), 84.8 (C), 72.9 (CH), 63.2 (CH_2), 62.0 (CH), 34.9 (CH_2), 25.6 (CH_2). IR: 3302, 3021, 1728, 1489, 1446, 1219, 1072, 1029,

748. ESIMS *m/z*: 379 (M + Na). HRMS-ESI (*m/z*): $[M + Na]^+$ calcd for $C_{25}H_{24}NaO_2$, 379.1669; found, 379.1668.

To a solution of TsCl (1.0 g, 5.4 mmol) and Et_3N (0.84 mL, 6.0 mmol) in anhydrous CH_2Cl_2 (14 mL) under argon atmosphere were added a solution of **1a-2** (1.92 g, 5.40 mmol) and PPh_3 (1.4 g, 5.4 mmol) in anhydrous CH_2Cl_2 (14 mL) dropwise at 19 °C over 10 min. The mixture was stirred at the same temperature for 1.5 h, then filtered through a short pad of SiO_2 to remove $Et_3N{\cdot}HCl$, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 9:1) to give a 1:1 diastereomer mixture of 1-ethynyl-4-trityloxybutyl *p*-toluenesulfinate (**1a-3**) (2.31 g, 85%) as a colorless oil: ^{1}H NMR: δ 7.61 (d, *J* = 8.0, 2H), 7.44–7.38 (m, 6H), 7.32–7.25 (m, 8H), 7.25–7.20 (m, 3H), 4.92–4.86 (m, 1H), 3.10–3.07 (m, 1H), 3.06–3.03 (m, 1H), 2.65 (d, *J* = 1.0, 0.5H), 2.42 (s, 1.5H), 2.41 (s, 1.5H), 2.37 (d, *J* = 1.4, 0.5H), 1.98–1.88 (m, 2H), 1.82–1.71 (m, 2H). ^{13}C NMR: δ 144.2 (C), 142.91 (C), 142.86 (C), 142.3 (C), 141.6 (C), 129.7 (CH), 128.61 (CH), 128.59 (CH), 127.9 (CH), 127.7 (CH), 126.9 (CH), 125.3 (CH), 125.0 (CH), 106.7 (C), 86.4 (CH), 75.9 (C), 74.0 (C), 62.7 (CH_2), 33.2 (CH_2), 25.4 (CH_2), 21.5 (CH_3). IR: 1597, 1493, 1447, 1134, 1076, 748. ESIMS *m/z*: 533 (M + K). HRMS-ESI (*m/z*): $[M + K]^+$ calcd for $C_{32}H_{30}KO_3S$, 533.1547; found, 533.1547.

To $AgSbF_6$ (60 mg, 0.17 mmol) under argon atmosphere was added a solution of **1a-3** (4.20 g, 8.50 mmol) in anhydrous CH_2Cl_2 (17 mL) dropwise at rt over 10 min. The mixture was stirred for 1 h, diluted with Et_2O (5 mL), filtered through a pad of SiO_2, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 5:1) to give 1-tosyl-6-trityloxyhexa-1,2-diene (**1a-4**) (2.45 g, 57%) as a colorless oil: ^{1}H NMR: δ 7.76 (d, *J* = 8.0, 2H), 7.40 (d, *J* = 7.0, 6H), 7.31–7.27 (m, 8H), 7.23 (t, *J* = 7.0, 3H), 6.11 (dt, *J* = 5.5, 3.0, 1H), 5.82 (dt, *J* = 5.5, 7.0, 1H), 3.07 (m, 2H), 2.41 (s, 3H), 2.25 (m, 2H), 1.69 (m, 2H). ^{13}C NMR: δ 205.3 (C), 144.2 (C), 144.0 (C), 138.3 (C), 129.6 (CH), 128.5 (CH), 127.6 (CH), 127.5 (CH), 126.8 (CH), 101.5 (CH), 100.7 (CH), 86.3 (C), 62.2 (CH_2), 28.6 (CH_2), 24.6 (CH_2), 21.5 (CH_3). IR: 1956, 1597, 1446, 1319, 1146, 1084, 748. ESIMS *m/z*: 533 (M + K). HRMS-ESI (*m/z*): $[M + K]^+$ calcd for $C_{32}H_{30}KO_3S$, 533.1547; found, 533.1547.

To a solution of **1a-4** (315 mg, 0.640 mmol) in a 2:1 mixture of MeOH and toluene (6.4 mL) cooled in an ice–water bath was added TFA (0.34 mL, 4.5 mmol), and the mixture was stirred for 1 h. Then, the mixture was allowed to warm to 10 °C and stirred for 18 h. The reaction was quenched by the addition of saturated aqueous $NaHCO_3$, and the organic layer was separated. The aqueous layer was extracted 3 times with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 4:1 to 1:2) to give **1a** (70.1 mg, 43%) as a colorless oil: ^{1}H NMR: δ 7.78 (d, *J* = 8.5, 2H), 7.34 (d, *J* = 8.5, 2H)), 6.18 (dt, *J* = 5.5, 3.0, 1H), 5.89 (td, *J* = 7.5, 5.5, 1H), 3.73 (t, *J* = 4.0, 2H), 2.45 (s, 3H), 2.30 (m, 2H), 1.82 (br s, 1H), 1.74 (m, 1H), 1.68 (m, 1H). ^{13}C NMR: δ 205.5 (C), 144.5 (C), 138.4 (C), 129.8 (CH), 127.5 (CH), 101.3 (CH), 100.8 (CH), 61.4 (CH_2), 30.8 (CH_2), 24.4 (CH_2), 21.6 (CH_3). IR: 3476, 3021, 1956, 1315, 1215, 1142, 748; ESIMS *m/z*: 291 (M + K). HRMS-ESI (*m/z*): $[M + K]^+$ calcd for $C_{13}H_{16}KO_3S$, 291.0452; found, 291.0448.

6-Tosylhex-4-yn-1-ol (2a): To a solution of hex-5-yn-1-ol (2.1 mL, 20 mmol) in anhydrous THF (60 mL) cooled at –78 °C under argon atmosphere was added a 1.6 M hexane solution of BuLi (26 mL, 42 mmol), and the mixture was stirred for 15 min. A solution of *p*-ditolyl disulfide (5.9 g, 24 mmol) and MeI (1.5 mL, 24 mmol) in anhydrous THF (80 mL), which had been stirred for 1 h, was added dropwise. The cooling bath was removed, and the whole was stirred for 1 h. After addition of saturated aqueous NH_4Cl, the organic layer was separated. The aqueous layer was extracted 3 times with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane to hexane/EtOAc 4:1) to give 6-*p*-tolylthiohex-5-yn-1-ol **(2a-1)** (4.41 g, quant) as a colorless oil: ^{1}H NMR: δ 7.30 (d, *J* = 8.0, 2H), 7.14 (d, *J* = 8.0, 2H), 3.70 (q, *J* = 6.0, 2H), 2.49 (t, *J* = 6.5, 2H), 2.33 (s, 3H), 1.75–1.66 (m, 4H). ^{13}C NMR: δ 136.1 (C), 129.8 (CH), 129.7 (C), 126.1 (CH), 98.7 (C), 65.6 (C), 62.2 (CH_2), 31.7 (CH_2), 24.9 (CH_2), 20.9 (CH_3), 20.0 (CH_2). IR: 3344, 2939, 1493, 1053, 910, 802, 737. ESIMS *m/z*: 221(M +H). HRMS-ESI (*m/z*): $[M + H]^+$ calcd for $C_{13}H_{17}OS$, 221.0995; found, 221.0995.

To a solution of **2a-1** (4.41g, 20.0 mmol) in anhydrous CH_2Cl_2 (50 mL) under argon atmosphere were added TrCl (5.9 g, 21 mmol), pyridine (1.8 mL, 22 mmol), and MS4A (20 g), and the mixture was

stirred at rt for 10 h. After diluted with EtOAc, the mixture was filtered through a pad of celite and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 20:1) to give 1-*p*-tolylthio-6-trityloxyhex-1-yne (**2a-2**) (9.25 g, quant) as a yellow oil: ^{1}H NMR: δ 7.44 (d, *J* = 7.5, 6H), 7.31–7.28 (m, 8H), 7.22 (t, *J* = 7.5, 3H), 7.11 (d, *J* = 8.0, 2H), 3.09 (t, *J* = 6.0, 2H), 2.41 (t, *J* = 6.5, 2H), 2.31 (s, 3H), 1.76 (m, 2H), 1.71 (m, 2H). ^{13}C NMR: δ 144.3 (C), 136.1 (C), 129.8 (CH), 128.6 (CH), 127.9 (C), 127.7 (CH), 126.8 (CH), 126.1 (CH), 99.0 (C), 86.3 (C), 65.5 (C), 62.9 (CH_2), 29.2 (CH_2), 25.6 (CH_2), 20.9 (CH_3), 20.1 (CH_2). IR: 2940, 1493, 1447, 1076, 910, 802, 764. ESIMS *m*/*z*: 501 (M + K). HRMS-ESI (*m*/*z*): $[M + K]^+$ calcd for $C_{32}H_{30}KOS$, 501.1649; found, 501.1648.

To a solution of **2a-2** (9.24 g, 20.0 mmol) in CH_2Cl_2 (200 mL) cooled in an ice–water bath was added *m*-CPBA (12 g, 50 mmol), and the mixture was stirred for 1 h. After addition of saturated aqueous $Na_2S_2O_3$ (50 mL), the cooling bath was removed, and the mixture was stirred for 2 h. To the mixture was added saturated aqueous $NaHCO_3$, and the organic layer was separated. The aqueous layer was extracted 3 times with $CHCl_3$. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was recrystallized from hexane–EtOAc (6:1) to give 1-tosyl-6-trityloxyhex-1-yne (**2a-3**) (6.92 g, 70%) as a white solid of mp 114–117 °C: ^{1}H NMR: δ 7.87 (d, *J* = 8.0, 2H), 7.40 (d, *J* = 7.5, 6H), 7.34 (d, *J* = 8.0, 2H), 7.30–7.26 (m, 6H), 7.23 (t, *J* = 7.0, 3H), 3.04 (t, *J* = 5.5, 2H), 2.43 (s, 3H), 2.33 (t, *J* = 6.5, 2H), 1.68–1.62 (m, 4H). ^{13}C NMR: δ 145.0 (C), 144.1 (C), 139.1 (C), 129.9 (CH), 128.6 (CH), 127.7 (CH), 127.2 (CH), 126.9 (CH), 97.0 (C), 86.4 (C), 78.5 (C), 62.4 (CH_2), 28.9 (CH_2), 24.1 (CH_2), 21.7 (CH_3), 18.7 (CH_2). IR: 3024, 2936, 2199, 1447, 1327, 1157, 1088, 752. ESIMS *m*/*z*: 533 (M +K). HRMS-ESI (*m*/*z*): $[M + K]^+$ calcd for $C_{32}H_{30}KO_3S$, 533.1547; found, 533.1547.

A 1 M THF solution of *t*-BuOK (17 mL, 17 mmol) was diluted with anhydrous THF (30 mL) under argon atmosphere and cooled at –78 °C. To the solution, was added **2a-3** (3.36g, 6.80 mmol) in THF (40 mL) dropwise over 15 min, and the mixture was stirred for 5 min. The reaction was quenched by the addition of a 1 M THF solution of AcOH (15 mL), and the cooling bath was removed. After addition of saturated aqueous $NaHCO_3$, the organic layer was separated. The aqueous layer was extracted 3 times with Et_2O. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 5:1) to give 1-tosyl-6-

trityloxyhex-2-yne (**2a-4**) (3.06 g, 91%) as a light brown oil: ^{1}H NMR: δ 7.79 (d, *J* = 8.5, 2H), 7.39 (d, *J* = 8.5, 6H), 7.31–7.26 (m, 8H), 7.24–7.21 (m, 3H), 3.84 (t, *J* = 2.5, 2H), 3.07 (t, *J* = 6.0, 2H), 2.42 (s, 3H), 2.31 (tt, *J* = 7.0, 2.5, 2H), 1.71 (tt, *J* = 7.0, 6.0, 2H). ^{13}C NMR: δ 145.0 (C), 144.1 (C), 134.8 (C), 129.5 (CH), 128.8 (CH), 128.6 (CH), 127.7 (CH), 126.9 (CH), 88.2 (C), 86.3 (C), 67.8 (C), 61.7 (CH_2), 49.0 (CH_2), 28.8 (CH_2), 21.7 (CH_3), 15.9 (CH_2). IR: 1447, 1319, 1134, 1069, 748. ESIMS *m/z*: 533 (M + K). HRMS-ESI (*m/z*): $[M + K]^+$ calcd for $C_{32}H_{30}KO_3S$, 533.1547; found, 533.1547.

To a solution of **2a-4** (8.11 g, 16.4 mmol) in a 4:1 mixture of MeOH and toluene (160 mL) was added TsOH•H_2O (1.4 g, 8.2 mmol), and the mixture was stirred for 30 min at rt. To the mixture were added EtOAc and saturated aqueous $NaHCO_3$, and the organic layer was separated. The aqueous layer was extracted 3 times with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 1:1) to give **2a** (3.18 g, 77%) as a light yellow oil: ^{1}H NMR: δ 7.85 (d, *J* = 8.0, 2H), 7.37 (d, *J* = 8.0, 2H), 3.91 (br s, 2H), 3.67 (br td, *J* = 6.0, 3.5, 2H), 2.47 (s, 3H), 2.30 (br t, *J* = 7.0, 2H), 1.71 (tt, *J* = 7.0, 6.0, 2H), 1.35 (br s, 1H). ^{13}C NMR: δ 145.2 (C), 134.8 (C), 129.7 (CH), 128.7 (CH), 87.9 (C), 68.1 (C), 61.2 (CH_2), 49.0 (CH_2), 30.7 (CH_2), 21.7 (CH_3), 15.2 (CH_2). IR: 3522, 2947, 1597, 1319, 1134, 1084, 748. ESIMS *m/z*: 291 (M + K). HRMS-ESI (*m/z*): $[M + K]^+$ calcd for $C_{13}H_{16}KO_3S$, 291.0452; found, 291.0452.

1-(4-Benzenesulfonylbut-2-ynyl)cyclohexanemethanol (2b): To a solution of 1-allylcyclohexane-1-carbaldehyde[14] (4.26 g, 28.0 mmol) in MeOH (56 mL), was added $NaBH_4$ (1.1 g, 28 mmol), and the mixture was stirred at rt for 2 h. The reaction was quenched by the addition of water, and after dilution with EtOAc, the organic layer was separated. The aqueous layer was extracted 5 times with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 9:1) to give 1-allylcyclohexanemethanol (3.58 g, 83%) as a colorless oil: ^{1}H NMR: δ 5.87 (m, 1H), 5.10–5.00 (m, 2H), 3.42 (s, 2H), 2.12 (d, *J* = 7.5, 2H), 1.51–1.40 (m, 5H), 1.36–1.29 (m, 5H). ^{13}C NMR: δ 135.3 (CH), 117.0 (CH_2), 68.8 (CH_2), 40.0 (CH_2), 37.8 (C), 32.3 (CH_2), 26.3 (CH_2), 21.4 (CH_2). IR: 3383, 3075, 2924, 1636, 1454, 1385, 1030, 910. ESIMS *m/z*: 155 (M + H).

To a solution of the above alcohol (3.24 g, 21.0 mmol) in DMF (42 mL) were added DMAP (6.4 g, 53 mmol) and TrCl (12 g, 42 mmol), and the mixture was stirred for 8 h at 100 °C. After addition of water and Et_2O, and the organic layer was separated. The aqueous layer was extracted 5 times with Et_2O. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/toluene 9:1) to give 1-allyl-1-trityloxymethylcyclohexane (**2b-1**) (6.41 g, 77%) as a brown oil: ^{1}H NMR: δ 7.45 (d, *J* = 7.5, 6H), 7.29–7.26 (m, 6H), 7.23–7.19 (m, 3H), 5.53 (ddt, *J* = 16.5, 10.0, 7.5, 1H), 4.93 (dd, *J* = 16.5, 2.0, 1H), 4.86 (dd, *J* = 10.0, 2.0, 1H), 2.87 (s, 2H), 2.24 (d, *J* = 7.5, 2H), 1.40–1.21 (m, 10H). ^{13}C NMR: δ 144.4 (C), 135.1 (CH), 128.9 (CH), 127.6 (CH), 126.8 (CH), 116.7 (CH_2), 85.8 (C) 67.5 (CH_2), 40.3 (CH_2), 37.4 (CH_2), 33.2 (CH_2), 26.3 (CH_2), 21.5 (CH_2). IR: 2924, 2855, 1489, 1447, 1215, 1069, 752. ESIMS *m/z*: 435 (M + K). HRMS-ESI (*m/z*): $[M + K]^+$ calcd for $C_{29}H_{32}KO$, 435.2085; found, 435.2085.

To a solution of **2b-1** (416 mg, 1.05 mmol) in anhydrous THF (25 mL) cooled in an ice–water bath was added a 0.5 M THF solution of 9-BBN (3.4 mL, 1.7 mmol) dropwise over 1 min. The cooling bath was removed, and the mixture was stirred for 2.5 h. Then, 3 M aqueous NaOH (3.3 mL) and 30% aqueous H_2O_2 (3.3 mL) were added slowly, and the resulting solution was stirred for 4 h. After addition of water and Et_2O, the organic layer was separated. The aqueous layer was extracted 3 times with Et_2O. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/Et_2O 2:1) to give 1-trityloxymethylcyclohexanepropanol (**2b-2**) (357 mg, 82%) as a colorless oil: ^{1}H NMR: δ 7.45 (d, *J* = 7.5, 6H), 7.29 (t, *J* = 7.5, 6H), 7.22 (t, *J* = 7.5, 3H), 3.51 (t, *J* = 6.5, 2H), 2.88 (s, 2H), 1.49–1.46 (m, 2H), 1.41–1.28 (m, 10H), 1.17–1.10 (m, 2H). ^{13}C NMR: δ 144.3 (C), 128.8 (CH), 127.6 (CH), 126.8 (CH), 85.7 (C), 67.0 (CH_2), 63.9 (CH_2), 36.6 (C), 33.5 (CH_2), 27.4 (CH_2), 26.4 (CH_2), 26.2 (CH_2), 21.5 (CH_2). IR: 3352, 2924, 1447, 1215, 1065, 752. ESIMS *m/z*: 437 (M + Na). HRMS-ESI (*m/z*): $[M + Na]^+$ calcd for $C_{29}H_{34}NaO_2$, 437.2451; found, 437.2452.

To a mixture of DMSO (0.34 mL, 4.8 mmol) and anhydrous CH_2Cl_2 (7 mL) cooled at –78 °C under argon atmosphere was added a solution of $(COCl)_2$ (0.33 mL, 3.8 mmol) in anhydrous CH_2Cl_2 (5 mL) dropwise over 5 min. Then, a solution of **2b-2** (1.29 g, 3.12 mmol) in anhydrous CH_2Cl_2 (4 mL) was

added dropwise over 15 min. After 15 min, Et_3N (2.2 mL, 16 mmol) was added over 3 min with vigorous stirring. After 10 min, the cooling bath was removed, and the mixture was stirred for 30 min. After addition of saturated aqueous NH_4Cl, the organic layer was separated. The aqueous layer was extracted 3 times with $CHCl_3$. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 20:1) to give 1-trityloxymethylcyclohexanepropanal (940 mg, 73%) as a light brown oil: ^{1}H NMR: δ 9.63 (s, 1H), 7.44 (d, *J* = 7.5, 6H), 7.30 (t, *J* = 7.5, 6H), 7.23 (t, *J* = 7.5, 3H), 2.88 (s, 2H), 1.97 (t, *J* = 8.5, 2H), 1.76 (t, *J* = 8.5, 2H), 1.42–1.30 (m, 10H). ^{13}C NMR: δ 203.2 (CH), 144.0 (C), 128.7 (CH), 127.7 (CH), 126.9 (CH), 85.9 (C), 81.2 (CH_2), 38.1 (CH_2), 36.4 (C), 33.5 (CH_2), 30.0 (CH_2), 26.3 (CH_2), 21.5 (CH_2). IR: 2924, 1721, 1447, 1065, 756. ESIMS *m/z*: 413 (M + H).

To a solution of CBr_4 (2.9 g, 8.6 mmol) and PPh_3 (4.5 g, 17 mmol) in anhydrous CH_2Cl_2 (16 mL) cooled at –78 °C under argon atmosphere, were sequentially added Et_3N (4.8 mL, 35 mmol) and a solution of the above aldehyde (1.78 g, 4.30 mmol) in anhydrous CH_2Cl_2 (0.7 mL). After 1.5 h, hexane was added, and the cooling bath was removed. The mixture was filtered and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/toluene 20:1) to give 1-(4,4-dibromobut-3-enyl)-1-trityloxymethylcyclohexane (1.64 g, 67%) as a yellow oil: ^{1}H NMR: δ 7.44 (d, *J* = 7.5, 6H), 7.29 (t, *J* = 7.5, 6H), 7.24–7.21 (m, 3H), 6.31 (t, *J* = 7.2, 1H), 2.87 (s, 2H), 1.75–1.71 (m, 2H), 1.57–1.54 (m, 2H), 1.39–1.26 (m, 10H). ^{13}C NMR: δ 144.2 (C), 139.5 (CH), 128.8 (CH), 128.2 (C), 127.7 (CH), 126.9 (CH), 85.9 (C), 67.1 (CH_2), 36.9 (CH), 33.5 (CH_2), 27.1 (C), 26.3 (CH_2), 26.3 (CH_2), 21.5 (CH_2). IR: 1477, 1435, 1215, 1088, 1069, 907, 741.

To a solution of the above dibromide (1.59 g, 2.80 mmol) in anhydrous THF (17 mL) cooled at –78 °C under argon atmosphere was added a 1.6 M hexane solution of BuLi (7.0 mL, 11 mmol), and the mixture was stirred for 1.5 h. After dilution with Et_2O, the reaction was quenched by the addition of saturated aqueous NH_4Cl. The organic layer was separated, and the aqueous layer was extracted 3 times with Et_2O. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/toluene 10:1) to give 1-(but-3-ynyl)-1-trityloxymethylcyclohexane (**2b-3**) (980 mg, 86%) as a yellow oil: ^{1}H NMR: δ 7.47–7.44 (m,

6H), 7.32–7.28 (m, 6H), 7.25–7.21 (m, 3H), 2.83 (s, 2H), 1.90 (t, *J* = 2.5, 1H), 1.82–1.76 (m, 4H), 1.40–1.25 (m, 10H). ^{13}C NMR: δ 144.2 (C), 128.8 (CH), 127.7 (CH), 126.8 (CH), 85.9 (CH), 85.7 (C), 67.5 (CH_2), 66.9 (C), 36.8 (C), 34.8 (CH_2), 33.2 (CH_2), 2.6.3 (CH_2), 21.5 (CH_2), 12.5 (CH_2). IR: 2928, 1450, 1215, 1065, 748. ESIMS *m/z*: 447 (M + K). HRMS-ESI (*m/z*): $[M + K]^+$ calcd for $C_{30}H_{32}KO$, 447.2085; found, 447.2083.

To a solution of **2b-3** (172 mg, 0.420 mmol) in anhydrous THF (1.4 mL) cooled at –78 °C under argon atmosphere was added a 1.6 M hexane solution of BuLi (0.29 mL, 0.46 mmol), and the mixture was stirred for 15 min. A mixture of $(PhS)_2$ (0.11 g, 0.50 mmol) and MeI (0.03 mL, 0.5 mmol) in anhydrous THF (1.6 mL), which had been stirred for 1 h, was added dropwise, and the cooling bath was removed. After 1 h, the reaction was quenched by the addition of saturated aqueous NH_4Cl, and the organic layer was separated. The aqueous layer was extracted 3 times with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was passed through a short SiO_2 plug, which is rinsed with hexane to remove MeSPh and then with (hexane/toluene 10:1) to give crude 1-(4-phenylthiobut-3-ynyl)-1-trityloxymethylcyclohexane (210 mg), which was used in the next reaction without further purification: ^{1}H NMR: δ 7.46 (d, *J* = 8.0, 6H), 7.39 (d, *J* = 7.5, 2H), 7.30 (dd, *J* = 8.0, 7.5, 6H), 7.27 (t, *J* = 7.5, 1H), 7.23 (d, *J* = 7.5, 3H), 7.15 (t, *J* = 7.5, 2H), 2.87 (s, 2H), 2.07 (dd, *J* = 8.5, 8.0, 2H), 1.84 (dd, *J* = 8.5, 8.0, 2H), 1.44–1.25 (m, 10H).

To a solution of the crude sulfide (210 mg) in CH_2Cl_2 (4 mL) cooled in an ice–water bath was added *m*-CPBA (0.25 g, 1.1 mmol), and the mixture was stirred for 1 h. After addition of saturated aqueous $Na_2S_2O_3$ (1 mL), the cooling bath was removed. After 2 h, saturated aqueous $NaHCO_3$ was added, and the organic layer was separated. The aqueous layer was extracted 3 times with $CHCl_3$. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to give crude 1-(4-benzenesulfonylbut-3-ynyl)-1-trityloxymethylcyclohexane as a yellow oil (266 mg), which was used in the next reaction without further purification: ^{1}H NMR: δ 7.98 (d, *J* = 7.5, 2H), 7.65 (t, *J* = 7.5, 1H), 7.54 (t, *J* = 7.5, 2H), 7.39 (d, *J* = 7.5, 6H), 7.27 (t, *J* = 7.5, 1H), 7.22 (t, *J* = 7.5, 3H), 2.81 (s, 2H), 1.90 (t, *J* = 8.0, 2H), 1.70 (t, *J* = 8.0, 2H), 1.38–1.22 (m, 10H).

A 1 M THF solution of *t*-BuOK (1.0 mL, 1.0 mmol) was diluted with anhydrous THF (3 mL) under argon atmosphere. To the solution cooled at –78 °C was added a solution of the crude alkynyl sulfone (266 mg) in anhydrous THF (1 mL) dropwise over 1 min, and the mixture was stirred for 5 min. The reaction was quenched by the addition of a 1 M THF solution of AcOH (1.0 mL), and the cooling bath was removed. After addition of saturated aqueous $NaHCO_3$, and the organic layer was separated. The aqueous layer was extracted 3 times with $CHCl_3$. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 5:1) to give 1-(4-benzenesulfonylbut-2-ynyl)-1-trityloxymethylcyclohexane (**2b-4**) (131 mg, 57% for 3 steps) as a light brown oil: ^{1}H NMR: δ 7.90 (d, *J* = 7.5, 2H), 7.60 (d, *J* = 7.5, 1H), 7.49 (t, *J* = 7.5, 2H), 7.39 (d, *J* = 7.0, 6H), 7.28–7.25 (m, 6H), 7.23–7.20 (m, 3H), 3.83 (t, *J* = 2.5, 2H), 2.86 (s, 2H), 2.36 (t, *J* = 2.5, 2H), 1.30–1.15 (m, 10H). ^{13}C NMR: δ 144.1 (C), 137.8 (C), 133.9 (CH), 128.9 (CH), 128.8 (CH), 128.7 (CH), 127.6 (CH), 126.8 (CH), 86.6 (C), 85.8 (C), 69.0 (C), 66.6 (CH_2), 48.9 (CH_2), 37.7 (C), 32.5 (CH_2), 26.5 (CH_2), 26.0 (CH_2), 21.5 (CH_2). IR: 2924, 2855, 2199, 1447, 1327, 1161, 1088, 1065, 752. ESIMS *m/z*: 571 (M + Na). HRMS-ESI (*m/z*): $[M + Na]^+$ calcd for $C_{36}H_{36}NaO_3S$, 571.2277; found, 571.2276.

To a solution of **2b-4** (198 mg, 0.360 mmol) in a 4:1 mixture of MeOH and toluene (1.4 mL) was added TsOH•H_2O (31 mg, 0.18 mmol), and the mixture was stirred at rt for 30 min. After addition of EtOAc and saturated aqueous $NaHCO_3$, and the organic layer was separated. The aqueous layer was extracted with EtOAc, and the combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 5:1) to give **2b** (65.1 mg, 59%) as a light yellow oil: ^{1}H NMR: δ 7.98 (d, *J* = 8.0, 2H), 7.69 (t, *J* = 7.5, 1H), 7.59 (dd, *J* = 8.0, 7.5, 2H), 3.98 (br s, 2H), 3.42 (d, *J* = 5.0, 2H), 2.23 (br s, 2H), 1.44–1.31 (m, 10H). ^{13}C NMR: δ 137.9 (C), 134.1 (CH), 129.1 (CH), 128.7 (CH), 86.4 (C), 69.4 (C), 68.3 (CH_2), 49.0 (CH_2), 37.9 (C), 31.8 (CH_2), 29.7 (CH_2), 26.0 (CH_2), 21.5 (CH_2). IR: 3537, 2924, 1447, 1312, 1134, 1084, 744. FABMS m/z: 329 (M + Na). HMRS-FAB: m/z calculated for $C_{17}H_{22}NaO_3S$ 329.1182; found, 329.1179.

9-Tosylnon-1-en-7-yn-4-ol (2c): To a solution of **2a** (252 mg, 1.00 mmol) in anhydrous CH_2Cl_2 (5 ml) cooled in an ice–water bath was added Dess–Martin periodinane (0.51 g, 1.2 mmol), Then the

cooling bath was removed, and the whole was stirred for 17 h. The mixture was filtered, and the filtrate was washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 2:1) to give 6-tosylhex-4-ynal (225 mg, 90%) as a light yellow oil: ^{1}H NMR: δ 9.73 (s, 1H), 7.83 (d, *J* = 8.0, 2H), 7.38 (d, *J* = 8.0, 2H), 3.90 (t, *J* = 2.5, 2H), 2.62 (t, *J* = 7.0, 2H), 2.50–2.47 (m, 2H), 2.48 (s, 3H). ^{13}C NMR: δ 199.8 (CH), 145.2 (C), 134.6 (C), 129.6 (CH), 128.6 (CH), 86.3 (C), 68.6 (C), 48.7 (CH_2), 41.8 (CH_2), 21.6 (CH_3), 11.8 (CH_2). IR: 2920, 1724, 1319, 1134, 1084, 748. ESIMS *m/z*: 273 (M + Na).

To a solution of the above aldehyde (175 mg, 0.700 mmol) in anhydrous CH_2Cl_2 (7 mL) under argon atmosphere was added a 1.0 M CH_2Cl_2 solution of $TiCl_4$ (0.70 mL, 0.70 mmol), and the mixture was stirred at rt for 5 min. Then, allyltrimethylsilane (0.19 mL, 1.1 mmol) was added, and the whole was stirred at rt for 3 h. To the mixture, were added Et_2O and saturated aqueous $NaHCO_3$, and the organic layer was separated. The aqueous layer was extracted 3 times with Et_2O. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 5:1) to give **2c** (163 mg, 80%) as a light yellow oil: ^{1}H NMR: δ 7.84 (d, *J* = 8.0, 2H), 7.37 (d, *J* = 8.0, 2H), 5.80 (m, 1H), 5.17–5.13 (m, 2H), 3.92 (br s, 2H), 3.68 (m, 1H), 2.47 (s, 3H), 2.37–2.31 (m, 2H), 2.27 (m, 1H), 2.14 (m, 1H), 1.67 (m, 1H), 1.62 (m, 1H). ^{13}C NMR: δ 145.1 (C), 134.9 (C), 134.3 (CH), 129.6 (CH), 128.8 (CH), 118.4 (CH_2), 88.1 (C), 69.1 (CH), 68.1 (C), 49.0 (CH_2), 41.8 (CH_2), 34.8 (CH_2), 21.6 (CH_3), 15.3 (CH_2). IR: 3522, 2920, 1319, 1134, 1084, 748. ESIMS *m/z*: 315 (M + Na). HRMS-ESI (*m/z*): $[M + Na]^+$ calcd for $C_{16}H_{20}NaO_3S$, 315.1025; found, 315.1022.

4-Allyl-9-tosylnon-1-en-7-yn-4-ol (2d): To a solution of **2c** (84.8 mg, 0.290 mmol)) in anhydrous CH_2Cl_2 (1.4 mL) was added PCC (94 mg, 0.44 mmol) and celite (200 mg), and the mixture was stirred at rt for 7 h. After dilution with Et_2O, the mixture was filtered through a pad of SiO_2, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 5:1) to give 9-tosylnon-1-en-7-yn-4-one (**2d-1**) (73.3 mg, 87%) as a white solid of mp 55–59 °C: ^{1}H NMR: δ 7.83 (d, *J* = 8.0, 2H), 7.37 (d, *J* = 8.0, 2H), 5.90 (ddt, *J* = 17.0, 10.0, 6.5, 1H), 5.21 (d, *J* = 10.0, 1H), 5.16 (d, *J* = 17.0, 1H), 3.89 (br s, 2H), 3.17 (d, *J* = 6.5, 2H), 2.63 (t, *J* = 7.0, 2H), 2.47 (s, 3H), 2.43 (br t, *J* = 7.0, 2H). ^{13}C

NMR: δ 206.0 (C), 145.1 (C), 134.8 (C), 130.0 (CH), 129.6 (CH), 128.7 (CH), 119.2 (CH_2), 86.9 (C), 68.2 (C), 48.9 (CH_2), 47.6 (CH_2), 40.4 (CH_2), 21.6 (CH_3), 13.1 (CH_2). IR: 2913, 1713, 1319, 1134, 1084, 748. ESIMS *m/z*: 329 (M + K). HRMS-ESI (m/z): $[M + Na]^+$ calcd for $C_{16}H_{18}KO_3S$, 329.0608; found, 329.0609.

To a solution of **2d-1** (29.0 mg, 0.100 mmol) in anhydrous CH_2Cl_2 (1 mL) under argon atmosphere was added a 1.0 M CH_2Cl_2 solution of $TiCl_4$ (0.10 mL, 0.10 mmol), and the mixture was stirred at rt for 5 min. Then, allyltrimethylsilane (0.03 mL, 0.2 mmol) was added, and the whole was stirred for 1 h at rt. To the mixture were added Et_2O and saturated aqueous $NaHCO_3$, and the organic layer was separated. The aqueous layer was extracted 3 times with Et_2O. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 2:1) to give **2d** (26.6 mg, 80%) as a white solid of mp 55–59 °C: ^{1}H NMR: δ 7.84 (d, *J* = 8.0, 2H), 7.37 (d, *J* = 8.0, 2H), 5.80 (ddt, *J* = 17.0, 10.0, 7.0, 2H), 5.17 (d, *J* = 10.0, 2H), 5.13 (d, *J* = 17.0, 2H), 3.91 (br s, 2H), 2.47 (s, 3H), 2.27 (br t, *J* = 8.0, 2H), 2.19 (d, *J* = 7.0, 4H), 1.64 (t, *J* = 8.0, 2H). ^{13}C NMR: δ 145.1 (C), 134.8 (CH), 133.1 (C), 129.6 (CH), 128.8 (CH), 119.1 (CH_2), 88.6 (C), 72.7 (C), 67.8 (C), 49.0 (CH_2), 43.4 (CH_2), 37.2 (CH_2), 21.7 (CH_3), 13.1 (CH_2). IR: 2974, 1639, 1597, 1315, 1138, 1045, 752. ESIMS *m/z*: 335 (M + Na). HRMS-ESI (m/z): $[M + Na]^+$ calcd for $C_{19}H_{24}NaO_3S$, 355.1338; found, 355.1337.

7-Tosylhept-5-yn-1-ol (2e): To a solution of hept-6-yn-1-ol[15] (426 mg, 3.80 mmol) in anhydrous CH_2Cl_2 (50 mL) under argon atmosphere were added TrCl (1.1 g, 4.0 mmol), pyridine (0.34 mL, 4.2 mmol), and MS4A (6 g), and the mixture was stirred at rt for 12 h. After dilution with EtOAc, the mixture was filtered through a pad of celite and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 4:1) to give 7-trityloxyhept-1-yne (**2e-1**) (1.33 g, 99%) as a colorless solid of mp 65–70 °C: ^{1}H NMR: δ 7.44 (d, *J* = 8.5, 6H), 7.29 (dd, *J* = 8.0, 7.0, 6H), 7.23 (t, *J* = 7.0, 3H), 3.06 (t, *J* = 6.5, 2H), 2.18 (m, 2H), 1.93 (t, *J* = 2.5, 1H), 1.64 (quintet, *J* = 6.5, 2H), 1.52–1.47 (m, 4H). ^{13}C NMR: δ 144.4 (C), 128.6 (CH), 127.7 (CH), 126.8 (CH), 86.3 (C), 84.5 (C), 68.2 (CH), 63.3 (CH_2), 29.5 (CH_2), 28.3 (CH_2), 25.4 (CH_2), 18.3 (CH_2). IR: 3294, 2936, 1489, 1447, 1072, 744. ESIMS *m/z*: 393 (M + K). HRMS-ESI (*m/z*): $[M + K]^+$ calcd for $C_{26}H_{26}KO$, 393.1615; found, 393.1615.

To a solution of **2e-1** (1.77 g, 5.00 mmol) in anhydrous THF (16 mL) cooled at –78 °C under argon atmosphere was added a 1.6 M hexane solution of BuLi (6.9 mL, 11 mmol). After 15 min, a mixture of *p*-ditolyl disulfide (1.5 g, 6.0 mmol) and MeI (0.37 ml, 6.0 mmol) in anhydrous THF (20 mL), which had been stirred for 1 h, was added dropwise to the mixture. The cooling bath was removed, and the whole was stirred for 1 h. After addition of aqueous saturated NH_4Cl, the organic layer was separated. The aqueous layer was extracted 3 times with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane to hexane/EtOAc 5:1) to give 1-*p*-tolylthio-7-trityloxyhept-1-yne (**2e-2**) (2.05 g, 86%) as a colorless oil: ^{1}H NMR: δ 7.44 (d, *J* = 8.0, 6H), 7.31–7.26 (m, 8H), 7.23–7.20 (m, 3H), 7.09 (d, *J* = 8.0, 2H), 3.07 (t, *J* = 6.5, 2H), 2.42 (t, *J* = 6.5, 2H), 2.30 (s, 3H), 1.65 (quintet, *J* = 6.5, 2H), 1.57–1.51 (m, 4H). ^{13}C NMR: δ 144.4 (C), 136.0 (C), 129.8 (CH), 128.6 (CH), 127.9 (C), 127.7 (CH), 126.8 (CH), 126.0 (CH), 99.1 (C), 86.3 (C), 65.3 (C), 63.4 (CH_2), 29.5 (CH_2), 28.5 (CH_2), 25.6 (CH_2), 20.9 (CH_3), 20.2 (CH_2). IR: 2936, 1489, 1069, 802, 745. ESIMS *m/z*: 515 (M + K). HRMS-ESI (*m/z*): [M + K]$^+$ calcd for $C_{33}H_{32}KOS$, 515.1805; found, 515.1803.

To a solution of **2e-2** (1.62 g, 3.40 mmol) in CH_2Cl_2 (34 mL) cooled in an ice–water bath was added *m*-CPBA (2.0 g, 8.5 mmol), and the mixture was stirred for 1 h. After addition of saturated aqueous $Na_2S_2O_3$ (5 mL), the cooling bath was removed, and the mixture was stirred for 2 h. To the mixture, was added saturated aqueous $NaHCO_3$, and the organic layer was separated. The aqueous layer was extracted 3 times with $CHCl_3$. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (toluene/$CHCl_3$ 9:1) to give 1-tosyl-7-trityloxyhept-1-yne (**2e-3**) (1.54 g, 89%) as a white solid of mp 103–107 °C: ^{1}H NMR: δ 7.85 (d, *J* = 8.5, 2H), 7.42 (d, *J* = 7.0, 6H), 7.31–7.27 (m, 8H), 7.24–7.21 (m, 3H), 3.03 (t, *J* = 6.5, 2H), 2.42 (s, 3H), 2.32 (t, *J* = 7.0, 2H), 1.57 (m, 2H), 1.50 (m, 2H), 1.41 (m, 2H). ^{13}C NMR: δ 145.0 (C), 144.3 (C), 139.1 (C), 129.8 (CH), 128.6 (CH), 127.7 (CH), 127.2 (CH), 126.9 (CH), 97.1 (C), 86.3 (C), 78.4 (C), 63.0 (CH_2), 29.3 (CH_2), 26.8 (CH_2), 25.6 (CH_2), 21.7 (CH_3), 18.9 (CH_2). IR: 2936, 2199, 1446, 1327, 1157, 1087, 748. ESIMS *m/z*: 531 (M + Na). HRMS-ESI (*m/z*): [M + Na]$^+$ calcd for $C_{33}H_{32}NaO_3S$, 531.1964; found, 531.1965.

A 1 M THF solution of *t*-BuOK (7.0 mL, 7.0 mmol) was diluted with anhydrous THF (15 mL) under argon atmosphere and cooled at –78 °C. To the solution was added **2e-3** (1.42 g, 2.80 mmol) in anhydrous THF (13 mL) dropwise over 5 min, and the mixture was stirred for 5 min. The reaction was quenched by the addition of a 1 M THF solution of AcOH (7 mL), and the cooling bath was removed. After addition of saturate aqueous $NaHCO_3$, the organic layer was separated. The aqueous layer was extracted 3 times with Et_2O. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 5:1) to give 1-tosyl-7-trityloxyhept-2-yne (**2e-4**) (1.05 g, 74%) as a white solid of mp 113–116 °C: ^{1}H NMR: δ 7.81 (d, *J* = 8.0, 2H), 7.42 (d, *J* = 7.0, 6H), 7.31–7.28 (m, 8H), 7.23 (d, *J* = 7.0, 3H), 3.90 (br s, 2H), 3.03 (t, *J* = 6.0, 2H), 2.37 (s, 3H), 2.14 (br t, *J* = 6.5, 2H), 1.64–1.57 (m, 4H). ^{13}C NMR: δ 145.0 (C), 144.2 (C), 134.8 (C), 129.5 (CH), 128.7 (CH), 128.6 (CH), 127.7 (CH), 126.8 (CH), 88.4 (C), 86.3 (C), 67.8 (C), 62.7 (CH_2), 49.0 (CH_2), 29.0 (CH_2), 25.1 (CH_2), 21.6 (CH_3), 18.5 (CH_2). IR: 2947, 1489, 1447, 1327, 1134, 1069, 748. ESIMS *m/z*: 547 (M + K). HRMS-ESI (*m/z*): $[M + K]^+$ calcd for $C_{33}H_{32}KO_3S$, 547.1704; found, 547.1704.

To a solution of **2e-4** (916 mg, 1.80 mmol) in a 4:1 mixture of MeOH and toluene (18 mL) was added TsOH•H_2O (0.16 mg, 0.90 mmol), and the mixture was stirred at rt for 30 min. After addition of EtOAc and saturated aqueous $NaHCO_3$, and the organic layer was separated. The aqueous layer was extracted 3 times with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 1:1) to give **2e** (407 mg, 85%) as a light yellow oil: ^{1}H NMR: δ 7.84 (d, *J* = 8.0, 2H), 7.37 (d, *J* = 8.0, 2H), 3.92 (t, *J* = 2.0, 2H), 3.64 (br s, 2H), 2.47 (s, 3H), 2.21 (m, 2H), 1.61–1.53 (m, 4H). ^{13}C NMR: δ 145.1 (C), 134.7 (C), 129.6 (CH), 128.7 (CH), 88.3 (C), 67.8 (C), 61.9 (CH_2), 48.9 (CH_2), 31.5 (CH_2), 24.3 (CH_2), 21.6 (CH_3), 18.4 (CH_2). IR: 3367, 2936, 2199, 1597, 1323, 1153, 1088, 814. ESIMS *m/z*: 305 (M + K). HRMS-ESI (*m/z*): $[M + K]^+$ calcd for $C_{14}H_{18}KO_3S$, 305.0608; found, 305.0606.

2-(3-Tosylprop-1-ynyl)benzeneethanol (2f): To a solution of 2-iodobenzeneethanol (248 mg, 1.00 mmol) in Et_3N (3 mL) under argon atmosphere were added $PdCl_2(PPh_3)_2$ (21 mg, 0.030 mmol) and CuI (11 mg, 0.060 mmol), and the mixture was stirred at rt for 30 min. A solution of 3-*p*-tolylthiopropyne[16]

(0.33 g, 2.0 mmol) in Et_3N (1 mL) was added dropwise over 1 min. The mixture was stirred at 70 °C for 7 h, and then cooled to rt. After dilution with $CHCl_3$, the reaction was quenched by the addition of water, and the organic layer was separated. The aqueous layer was extracted 3 times with $CHCl_3$. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to give crude 2-(3-*p*-tolylthioprop-1-ynyl)benzeneethanol as a yellow oil (278 mg), which was used in the next reaction without further purification: ^{1}H NMR: δ 7.40 (d, *J* = 8.0, 2H), 7.36 (d, *J* = 7.5, 1H), 7.23 (d, *J* = 7.5, 1H), 7.19 (d, *J* = 7.5, 1H), 7.18–7.13 (m, 3H), 3.85 (s, 2H), 3.73 (br t, *J* = 7.5, 2H), 2.89 (t, *J* = 7.5, 2H), 2.34 (s, 3H).

To a solution of the crude sulfide (278 mg) in CH_2Cl_2 (10 mL) cooled in an ice–water bath was added *m*-CPBA (0.58 mg, 2.5 mmol), and the mixture was stirred for 30 min. After addition of saturated aqueous $Na_2S_2O_3$ (1 mL), the cooling bath was removed. After 2 h, saturated aqueous $NaHCO_3$ was added, and the organic layer was separated. The aqueous layer was extracted 3 times with $CHCl_3$. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 3:2) to give **2f** (116 mg, 37% over 2 steps) as a brown oil: ^{1}H NMR: δ 7.89 (d, *J* = 8.0, 2H), 7.39 (d, *J* = 8.0, 2H), 7.34 (d, *J* = 7.5, 1H), 7.30 (t, *J* = 7.5, 1H), 7.25 (d, *J* = 7.5, 1H), 7.18 (t, *J* = 7.5, 1H), 4.23 (s, 2H), 3.82 (t, *J* = 7.0, 2H), 3.00 (t, *J* = 7.0, 2H), 2.47 (s, 3H). ^{13}C NMR: δ 145.4 (C), 141.3 (C), 135.0 (C), 132.4 (CH), 129.9 (CH), 129.6 (CH), 129.2 (CH), 128.6 (CH), 126.3 (CH), 121.6 (C), 86.3(C), 80.0 (C), 63.0 (CH_2), 49.6 (CH_2), 38.1 (CH_2), 21.7 (CH_3). IR: 1597, 1319, 1134, 1084, 1018, 756. ESIMS *m*/*z*: 353 (M + K). HRMS-ESI (*m*/*z*): [M + K]$^+$ calcd for $C_{18}H_{18}KO_3S$, 353.0608; found, 353.0608.

(*RS*,*RS*)-1,12-Ditosyldodeca-2,10-diyne-6,7-diol (2g): To a solution of dimethyl (*E*)-hex-3-enedioate (31.8 mL, 203 mmol) in a 7:1 mixture of acetone and water (615 mL) were added *N*-methylmorpholine-N-oxide (29 g, 24 mmol) and a 4% aqueous OsO_4 (19 mL, 3.1 mmol), and the mixture was stirred at rt for 5 h. The reaction was quenched by the addition of $NaHSO_3$ (20 g), and the mixture was filtered through a pad of celite. The filtrate was acidified with 3 N HCl and concentrated *in vacuo*. The residual solids were recrystallized from hexane–EtOAc (5:1) to give dimethyl (*RS*,*RS*)-3,4-dihydroxyhexanedioate (**2g-1**) (20.3 g, 48%) as a white solid of mp 72-76 °C: ^{1}H NMR: δ 3.99 (br s,

2H), 3.73 (s, 6H), 3.15 (br s, 2H), 2.68 (dd, J = 16.5, 8.5, 2H), 2.59 (dd, J = 16.5, 3.5, 2H). ^{13}C NMR: δ 173.0 (C), 69.8 (CH_3), 52.0 (CH_3), 37.8 (CH_2). IR: 3298, 1782, 1732, 1435, 1369, 1153, 1057, 768. ESIMS *m/z*: 229 (M + Na). HRMS-ESI (*m/z*): $[M + Na]^+$ calcd for $C_8H_{14}NaO_6$, 229.0683; found, 229.0681.

To a solution of **2g-1** (20.1g, 97.6 mmol) in 2,2-dimethoxypropane (485 mL) was added TsOH•H_2O (3.4 g, 20 mmol), and the mixture was stirred at rt for 12 h. The reaction was quenched by the addition of saturated aqueous $NaHCO_3$, and the organic layer was separated. The aqueous layer was extracted 3 times with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 5:1) to give dimethyl (*RS*,*RS*)-2,2-dimethyl-1,3-dioxolane-4,5-diacetate (**2g-2**) (19.7 g, 82%) as a white solid of mp 37-41 °C: ^{1}H NMR: δ 4.18–4.14 (m, 2H), 3.71 (s, 6H), 2.69–2.63 (m, 4H), 1.40 (s, 6H). ^{13}C NMR: δ 170.9 (C), 109.1 (C), 76.6 (CH_2), 51.8 (CH_3), 37.8 (CH_3), 27.0 (CH_2). IR: 2990, 1736, 1439, 1381, 1169, 1057, 841. ESIMS *m/z*: 269 (M + Na). HRMS-ESI (*m/z*): $[M + Na]^+$ calcd for $C_{11}H_{18}NaO_6$, 269.0996; found, 269.0997.

To a suspension of $LiAlH_4$ (12 g, 0.32 mol) in anhydrous THF (270 mL) cooled in an ice-water bath was added a solution of **2g-2** (19.7 g, 79.9 mmol) in anhydrous THF (50 mL) dropwise over 20 min. The cooling bath was removed, and the mixture was stirred at rt for 3 h. Then, the mixture was cooled in an ice–water bath, and the reaction was quenched by the slow addition of saturated aqueous Rochelle salt (100 mL). After 1 h, the whole was diluted with Et_2O, and the organic layer was separated. The aqueous layer was extracted 3 times with Et_2O, and the combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 1:2) to give (*RS*,*RS*)-2,2-dimethyl-1,3-dioxolane-4,5-diethanol (**2g-3**) (9.73 g, 64%) as a colorless oil: ^{1}H NMR: δ 3.87–3.85 (m, 2H), 3.85–3.81 (m, 4H), 2.32 (br s, 2H), 1.87–1.83 (m, 2H), 1.81–1.74 (m, 2H), 1.41 (s, 6H). ^{13}C NMR: δ 108.6 (C), 79.3 (CH), 60.1 (CH_2), 34.4 (CH_2), 27.1 (CH_3). IR: 3360, 2936, 1373, 1219, 1045, 872. ESIMS *m/z*: 213 (M + Na). HRMS-ESI (*m/z*): $[M + Na]^+$ calcd for $C_9H_{18}NaO_4$ 213.1097, found 213.1098.

To a solution of **2g-3** (9.42 g, 49.6 mmol), Et_3N (28 mL, 0.20 mol), Me_3NHCl (4.7 g, 50 mmol) in anhydrous THF (165 mL) cooled in an ice-water bath was added MsCl (15 mL, 0.20 mol) dropwise over 10 min, and the mixture was stirred for 30 min. The reaction was quenched by the addition of saturated aqueous NH_4Cl, and the organic layer was separated. The aqueous layer was extracted 3 times with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to give crude (*RS*,*RS*)-4,5-bis(2-mesyloxyethyl)-2,2-dimethyl-1,3-dioxolane as a yellow oil (18.1 g), which was used in the next reaction without further purification: ^{1}H NMR: δ 4.42 (m, 2H), 4.36 (m, 2H), 3.81 (m, 2H), 3.04 (s, 6H), 2.07 (m, 2H), 1.91 (m, 2H), 1.38 (s, 6H).

To a solution of the crude mesylate (18.1 g) in anhydrous acetone (500 mL) were added NaI (89 g, 0.60 mol) and $NaHCO_3$ (13 g, 0.15 mol), and the mixture was stirred at 40 °C for 12 h. After addition of saturated aqueous $Na_2S_2O_3$ (100 mL), and the organic layer was separated. The aqueous layer was extracted 3 times with Et_2O. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to give crude (*RS*,*RS*)-4,5-bis(2-iodoethyl)-2,2-dimethyl-1,3-dioxolane as a brown oil (20.9 g), which was used in the next reaction without further purification: ^{1}H NMR: δ 3.74 (m, 2H), 3.32 (m, 2H), 3.25 (m, 2H), 2.11–2.04 (m, 4H), 1.38 (s, 6H). ^{13}C NMR: δ 108.9 (C), 79.7 (CH), 36.9 (CH_2), 27.2 (CH_3), 1.5 (CH_2).

To a solution of *tert*-butyldimethylsilyl propargyl ether[17] (42 g, 0.25 mol) and HMPA (59 mL, 0.34 mol) in anhydrous THF (81 mL) cooled at –78 °C under argon atmosphere was added a 1.6 M hexane solution of BuLi (0.16 L, 0.26 mol). After slowly warmed up to –40 °C, the mixture was stirred for 1 h. Then, the mixture was cooled to –78 °C, and a solution of the crude iodide (20.9 g) in anhydrous THF (80 mL) was added dropwise for 25 min. The cooling bath was removed, and the whole was stirred for 1 h. The reaction was quenched by the addition of saturated aqueous NH_4Cl, and the organic layer was separated. The aqueous layer was extracted 3 times with Et_2O. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was filtered through a short SiO_2 plug, which is rinsed with hexane. Concentration of the combined filtrate gave crude (*RS*,*RS*)-2,2-dimethyl-4,5-bis(5-*tert*-butyldimethylsiloxypent-3-ynyl)-1,3-dioxolane as a brown oil (61.2 g),

which was used in the next reaction without further purification: ^{1}H NMR: δ 4.30 (t, *J* = 2.0, 4H), 3.74 (m, 2H), 2.41 (m, 2H), 2.36 (m, 2H), 1.78–1.72 (m, 4H), 1.37 (s, 6H), 0.91 (s, 18H), 0.12 (s, 12H).

To a solution of the crude alkyne (61.2 g) in anhydrous THF (350 mL) was added a 1.0 M THF solution of TBAF (0.25 L, 0.25 mol), and the mixture was stirred for 3 h. The reaction was quenched by addition of saturated aqueous NH_4Cl, and the organic layer was separated. The aqueous layer was extracted 3 times with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 2:1) to give (*RS*,*RS*)-2,2-dimethyl-1,3-dioxolane-4,5-bis(pent-2-yn-1-ol) (**2g-4**) (5.11 g, 39% over 4 steps) as a colorless oil: ^{1}H NMR: δ 4.26 (t, *J* = 2.0, 4H), 3.80–3.78 (m, 2H), 2.48–2.41 (m, 2H), 2.39–2.33 (m, 2H), 1.81–1.75 (m, 4H), 1.38 (s, 6H). ^{13}C NMR: δ 108.5 (C), 85.4 (C), 79.2 (CH), 79.0 (C), 51.2 (CH_2), 31.8 (CH_2), 27.3 (CH_3), 15.5 (CH_2). IR: 3356, 2932, 1377, 1219, 1065, 1011, 864. ESIMS *m*/*z*: 289 (M + Na). HRMS-ESI (*m*/*z*): $[M + Na]^+$ calcd for $C_{15}H_{22}NaO_4$ 289.1410, found 289.1410.

To a solution of **2g-4** (4.08 g, 15.3 mmol), Et_3N (8.6 mL, 61 mmol), and Me_3NHCl (1.5 g, 15 mmol) in anhydrous THF (150 mL) cooled in an ice-water bath was added MsCl (4.8 mL, 61 mmol) dropwise over 10 min, and the mixture was stirred for 30 min. The reaction was quenched by addition of saturated aqueous NH_4Cl, and the organic layer was separated. The aqueous layer was extracted 3 times with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 2:1) to give (*RS*,*RS*)-4,5-bis(5-mesyloxypent-3-ynyl)-2,2-dimethyl-1,3-dioxolane (**2g-5**) (5.69 g, 88%) as a brown oil: ^{1}H NMR: δ 4.85 (s, 4H), 3.73–3.72 (m, 2H), 3.11 (s, 6H), 2.50–2.38 (m, 4H), 1.81–1.73 (m, 4H), 1.37 (s, 6H). ^{13}C NMR: δ 108.6 (C), 89.7 (C), 78.9 (CH), 72.8 (C), 58.2 (CH_2), 38.8 (CH_3), 31.4 (CH_2), 27.2 (CH_3), 15.5 (CH_2). IR: 3028, 1354, 1173, 934, 748. ESIMS *m*/*z*: 445 (M + Na). HRMS-ESI (*m*/*z*): $[M + Na]^+$ calcd for $C_{17}H_{26}NaO_8S_2$ 445.0961, found 445.0960.

To a solution of *p*-thiocresol (4.7 g, 38 mmol) and Et_3N (5.3 mL, 38 mmol) in anhydrous CH_2Cl_2 (100 mL) under argon atmosphere was added a solution of **2g-5** (5.66 g, 13.4 mmol) in anhydrous CH_2Cl_2 (30 mL) dropwise over 10 min. After 9 h, the solvent was removed *in vacuo* and the residue was dissolved in anhydrous CH_2Cl_2 (80 mL). To the solution cooled in an ice-water bath, was added *m*-CPBA (15 g, 67

mmol), and the mixture was stirred for 30 min. After addition of saturated aqueous $Na_2S_2O_3$ (30 mL), the cooling bath was removed, and the mixture was stirred for 2 h. To the mixture, was added saturated aqueous $NaHCO_3$, and the organic layer was separated. The aqueous layer was extracted 3 times with $CHCl_3$. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to give crude (*RS*,*RS*)-2,2-dimethyl-4,5-bis(5-tosylpent-3-ynyl)-1,3-dioxolane as a yellow oil (6.80 g), which was used in the next reaction without further purification: ^{1}H NMR: δ 7.84 (d, *J* = 8.0, 2H), 7.37 (d, *J* = 8.0, 2H), 3.92 (m, 4H), 3.67 (m, 2H), 2.46 (s, 6H), 2.40–2.25 (m, 4H), 1.70–1.65 (m, 4H), 1.37 (s, 6H).

To a solution of the crude sulfone (6.80 g) in MeOH (110 mL) was added TsOH•H_2O (0.23 g, 1.3 mmol). After heated under reflux for 5 h, the mixture was cooled to rt, and the reaction was quenched by the addition of water and saturated aqueous $NaHCO_3$. After diluted with EtOAc, the organic layer was separated. The aqueous layer was extracted 3 times with EtOAc. The combined organic layers were washed with water and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residual solids were recrystallized from hexane–EtOAc (2:1) to give **2g** (2.35 g, 35% over 3 steps) as a white solid of mp 125-128 °C: ^{1}H NMR: δ 7.84 (d, *J* = 8.0, 4H), 7.38 (d, *J* = 8.0, 4H), 3.92 (t, *J* = 2.5, 4H), 3.57–3.52 (m, 2H) 2.47 (s, 6H), 2.36 (tt, *J* = 7.0, 2.5, 4H), 2.30 (d, *J* = 5.5, 2H), 1.66 (td, *J* = 7.0, 6.0, 4H). ^{13}C NMR: δ 145.3 (C), 134.9 (C), 129.8 (CH), 128.7 (CH), 88.1 (C), 72.8 (CH), 68.3 (C), 49.0 (CH_2), 31.8 (CH_2), 21.7 (CH_3), 15.3 (CH_2). IR: 3495, 3318, 2920, 1597, 1304, 1142, 1083, 729. ESIMS *m*/*z*: 525 (M + Na). HRMS-ESI (*m*/*z*): $[M + Na]^+$ calcd for $C_{26}H_{30}NaO_6S_2$, 525.1376, found 525.1377.

2-(3-Tosylprop-1-ynyl)benznepropanol (2h): To a solution of 2-iodobenzenepropanol (262 mg, 1.00 mmol) in Et_3N (3 mL) under argon atmosphere were added $PdCl_2(PPh_3)_2$ (21 mg, 0.030 mmol), and CuI (11 mg, 0.060 mmol), and the mixture was stirred at rt for 30 min. A solution of 3-*p*-tolylthiopropyne[エラー!ブックマークが定義されていません。] (0.33 g, 2.0 mmol) in Et_3N (1 mL) was added dropwise over 1 min. The mixture was stirred at 70 °C for 14 h, and then cooled to rt. After diluted with $CHCl_3$, the reaction was quenched with water, and the organic layer was separated. The aqueous layer was extracted 3 times with $CHCl_3$. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to give crude 2-(3-*p*-tolylthioprop-1-ynyl)benzenepropanol as a yellow oil (310 mg), which was

used in the next reaction without further purification: ^{1}H NMR: δ 7.41 (d, *J* = 8.5, 2H), 7.34 (d, *J* = 7.5, 1H), 7.23 (t, *J* = 7.5, 1H), 7.19–7.12 (m, 4H), 3.85 (s, 2H), 3.57 (q, *J* = 6.0, 2H), 2.75 (t, *J* = 7.5, 3H), 2.34 (s, 3H), 1.81 (tt, *J* = 7.5, 6.0, 2H).

To a solution of the crude sulfide (310 mg) in CH_2Cl_2 (10 mL) cooled in an ice–water bath was added *m*-CPBA (0.58 g, 2.5 mmol), and the mixture was stirred for 30 min. After addition of saturated aqueous $Na_2S_2O_3$ (1 mL), the cooling bath was removed. After 2 h, saturated aqueous $NaHCO_3$ was added, and the organic layer was separated. The aqueous layer was extracted 3 times with $CHCl_3$. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 1:1) to give **2h** (148 mg, 45% over 2 steps) as a white solid of mp 88-92 °C: ^{1}H NMR: δ 7.88 (d, *J* = 8.0, 2H), 7.37 (d, *J* = 8.0, 2H), 7.32 (d, *J* = 7.5, 1H), 7.29 (dd, *J* = 7.5, 6.5, 1H), 7.21 (d, *J* = 6.5, 1H), 7.15 (t, *J* = 7.5, 1H), 4.22 (s, 2H), 3.67 (t, *J* = 6.0, 2H), 2.83 (t, *J* = 8.0, 2H), 2.47 (s, 3H), 1.86 (tt, *J* = 8.0, 6.0, 2H). ^{13}C NMR: δ 145.4 (C), 144.9 (C), 134.9 (C), 132.4 (CH), 129.8 (CH), 129.2 (CH), 128.9 (CH), 128.6 (CH), 125.8 (CH), 121.0 (C), 86.3 (C), 79.9 (C), 62.1 (CH_2), 49.6 (CH_2), 33.8 (CH_2), 30.9 (CH_2), 21.6 (CH_3). IR: 3526, 2936, 1597, 1315, 1134, 1084, 752. ESIMS *m/z*: 351 (M + Na). HRMS-ESI (*m/z*): $[M + Na]^+$ calcd for $C_{19}H_{20}NaO_3S$, 351.1025; found, 351.1025.

4-Methyl-N-(6-tosylhex-4-yn-1-yl)benzenesulfonamide (5a): To a solution of **2a-1** (375 mg, 1.70 mmol), Et_3N (0.47 mL, 3.4 mmol), and Me_3NHCl (0.16 g, 1.7 mmol) in anhydrous toluene (1.7 mL) cooled in an ice-water bath, was added MsCl (0.20 mL, 2.5 mmol) dropwise over 1 min. After 30 min, the reaction was quenched by the addition of saturated aqueous NH_4Cl, and the organic layer was separated. The aqueous layer was extracted 3 times with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (toluene/$CHCl_3$ 1:1) to give 6-*p*-tolylthiohex-5-ynyl methanesulfonate (**5a-1**) (477 mg, 94%) as a brown oil: ^{1}H NMR: δ 7.29 (d, *J* = 8.0, 2H), 7.14 (d, *J* = 8.0, 2H), 4.28 (t, *J* = 6.5, 2H), 3.01 (s, 3H), 2.51 (t, *J* = 7.0, 2H), 2.33 (s, 3H), 1.91 (m, 2H), 1.72 (m, 2H). ^{13}C NMR: δ 136.3 (C), 129.9 (CH), 129.5 (C), 126.2 (CH), 97.7 (C), 69.3 (CH_2), 66.5 (C), 37.4 (CH_3), 28.2 (CH_2), 24.5 (CH_2), 20.9 (CH_3), 19.7 (CH_2). IR: 2959, 1493, 1350, 1173, 930, 806, 733. ESIMS *m/z*: 321 (M + Na). HRMS-ESI (*m/z*):

$[M + Na]^+$ calcd for $C_{14}H_{18}NaO_3S_2$, 321.0590, found 321.0582.

To a solution of **5a-1** (95.4 mg, 0.320 mmol) in anhydrous MeCN (16 mL) were added K_2CO_3 (54 mg, 0.39 mmol) and BocTsNH (0.11 g, 0.39 mmol). After heated under reflux for 48 h, the mixture was cooled to rt. The reaction was quenched by the addition of water, and the organic layer was separated. The aqueous layer was extracted 3 times with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 10:1) to give *tert*-butyl (6-*p*-tolylthiohex-5-ynyl)tosylcarbamate (**5a-2**) (1.45 g, 96%) as a yellow oil: ^{1}H NMR: δ 7.78 (d, J = 8.5, 2H), 7.31–7.28 (m, 4H), 7.13 (d, J = 8.0, 2H), 3.87 (t, J = 7.5, 2H), 2.51 (t, J = 7.0, 2H), 2.43 (s, 3H), 2.31 (s, 3H), 1.91 (m, 2H), 1.66 (m, 2H), 1.33 (s, 9H). ^{13}C NMR: δ 150.9 (C), 144.0 (C), 137.4 (C), 136.1 (C), 129.9 (CH), 129.7 (C), 129.2 (CH), 127.8 (CH), 126.1 (CH), 98.5 (C), 84.2(C), 65.9 (C), 46.5 (CH_2), 29.4 (CH_2), 27.8 (CH_3), 25.8 (CH_2), 21.6 (CH_3), 21.0 (CH_3), 20.0 (CH_2). IR: 3291, 2920, 1493, 1408, 1231, 1092, 1018, 806, 733. ESIMS *m/z*: 496 (M + Na). HRMS-ESI (*m/z*): $[M + Na]^+$ calcd for $C_{25}H_{31}NNaO_4S_2$, 496.1587; found, 496.1588.

To a solution of **5a-2** (5.02 g, 10.6 mmol) in CH_2Cl_2 (100 mL) cooled in an ice–water bath, was added *m*-CPBA (6.1 g, 27 mmol), and the mixture was stirred for 30 min. After addition of saturated aqueous $Na_2S_2O_3$ (25 mL), the cooling bath was removed, and the mixture was stirred for 2 h. To the mixture, was added saturated aqueous $NaHCO_3$, and the organic layer was separated. The aqueous layer was extracted 3 times with $CHCl_3$. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 5:1) to give *tert*-butyl tosyl(6-tosylhex-5-ynyl)carbamate (**5a-3**) (5.09 g, 95%) as a yellow oil: ^{1}H NMR: δ 7.88 (d, J = 8.5, 2H), 7.76 (d, J = 8.5, 2H), 7.36 (d, J = 8.0, 2H), 7.32 (d, J = 8.0, 2H), 3.81 (t, J = 7.5, 2H), 2.45 (s, 3H), 2.44 (s, 3H), 1.81 (m, 2H), 1.63 (m, 2H), 1.33 (s, 9H). ^{13}C NMR: δ 150.8 (C), 145.1 (C), 144.2 (C), 138.9 (C), 137.1 (C), 129.9 (CH), 129.3 (CH), 127.7 (CH), 127.2 (CH), 96.3 (C), 84.3 (C), 78.7 (C), 46.1 (CH_2), 29.2 (CH_2), 27.8 (CH_3), 24.1 (CH_2), 21.7 (CH_3), 21.6 (CH_3), 18.6 (CH_2). IR: 2978, 2199, 1724, 1331, 1153, 1088, 999, 813, 756. ESIMS *m/z*: 528 (M +Na). HRMS-ESI (*m/z*): $[M + Na]^+$ calcd for $C_{25}H_{31}NNaO_6S_2$, 528.1485; found, 528.1487.

A 1 M THF solution of *t*-BuOK (25 mL, 25 mmol) was diluted with anhydrous THF (50 mL) under

argon atmosphere and cooled at –78 °C. To the solution was added **5a-3** (5.05 g, 10.0 mmol) in THF (50 mL) dropwise over 20 min, and the mixture was stirred for 5 min. The reaction was quenched by the addition of a 1 M THF solution of AcOH (18 mL), and the cooling bath was removed. After addition of saturate aqueous $NaHCO_3$, the organic layer was separated. The aqueous layer was extracted twice with Et_2O. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to give crude *tert*-butyl tosyl(6-tosylhex-4-ynyl)carbamate as a brown amorphous solid (5.17 g), which was used in the next reaction without further purification.

To a solution of the crude propargyl sulfone (5.17 g) in CH_2Cl_2 (10 mL) was added TFA (0.5 mL, 5 mmol), and the mixture was stirred at rt for 10 h. The reaction was quenched by addition of saturate aqueous $NaHCO_3$, and the organic layer was separated. The aqueous layer was extracted 3 times with Et_2O. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 3:2) to give **5a** (3.12 g, 77% over 2 steps) as a white solid of mp 91-96 °C: ^{1}H NMR: δ 7.82 (d, *J* = 8.5, 2H), 7.75 (d, *J* = 7.5, 2H), 7.37 (d, *J* = 8.5, 2H), 7.32 (d, *J* = 7.5, 2H), 4.50 (br m, 1H), 3.88 (t, *J* = 2.5, 2H), 3.00 (q, *J* = 6.5, 2H), 2.47 (s, 3H), 2.43 (s, 3H), 2.23 (tt, *J* = 6.5, 2.5, 2H), 1.64 (quintet, *J* = 6.5, 2H). ^{13}C NMR: δ 145.3 (C), 143.4 (C), 136.8 (C), 134.8 (C), 129.74 (CH), 129.72 (CH), 128.7 (CH), 127.0 (CH), 87.0 (C), 68.8 (C), 48.9 (CH_2), 41.9 (CH_2), 28.0 (CH_2), 21.7 (CH_3), 21.5 (CH_3), 16.0 (CH_2). IR: 3283, 2951, 1597, 1319, 1157, 1087, 752. ESIMS *m/z*: 444 (M + K). HRMS-ESI (*m/z*): $[M + K]^+$ calcd for $C_{20}H_{23}KNO_4S_2$, 444.0700; found, 444.0701.

***N*-(6-Tosylhex-4-ynyl)formamide (5b):** To a solution of **5a-1** (1.22 g, 4.10 mmol) in anhydrous DMSO (21 mL) were added Cs_2CO_3 (3.2 g, 9.8 mmol) and Boc_2NH (0.98 g, 4.5 mmol). After heated under reflux for 4 h, the mixture was cooled to rt, and water was added. The organic layer was separated, and the aqueous layer was extracted 3 times with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 10:1) to give *N,N*-bis(*tert*-butoxycarbonyl)-6-*p*-tolylthiohex-5-ynamine (**5b-1**) (1.65 g, 96%) as a yellow oil: ^{1}H NMR: δ 7.28 (d, *J* = 8.0, 2H), 7.13 (d, *J* = 8.0, 2H), 3.60 (t, *J* = 8.0, 2H), 2.47 (t, *J* = 7.5, 2H), 2.32 (s, 3H), 1.72 (m, 2H), 1.60 (m, 2H), 1.501 (s, 9H), 1.498 (s, 9H). ^{13}C

NMR: δ 152.4 (C), 135.8 (C), 129.7 (CH), 129.6 (C), 125.9 (CH), 98.4 (C), 81.9 (C), 65.5 (C), 45.6 (CH_2), 28.1 (CH_2), 27.8 (CH_3), 25.8 (CH_2), 20.7 (CH_3), 19.9 (CH_2). IR: 2978, 1744, 1694, 1366, 1250, 1134, 1111, 856, 802. ESIMS *m/z*: 442 (M + Na). HRMS-ESI (*m/z*): $[M + Na]^+$ calcd for $C_{23}H_{33}NNaO_4S$, 442.2023; found, 442.2025.

To a solution of **5b-1** (1.42 g, 3.40 mmol) in CH_2Cl_2 (34 mL) cooled in an ice–water bath was added *m*-CPBA (2.0 g, 8.5 mmol), and the mixture was stirred for 30 min. After addition of saturated aqueous $Na_2S_2O_3$ (5 mL), the cooling bath was removed, and the mixture was stirred for 2 h. To the mixture, was added saturated aqueous $NaHCO_3$, and the organic layer was separated. The aqueous layer was extracted 3 times with $CHCl_3$. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 5:1) to give *N,N*-bis(*tert*-butoxycarbonyl)-6-*p*-tosylhex-5-ynamine (**5b-2**) (1.45 g, 94%) as a yellow oil: ^{1}H NMR: δ 7.87 (d, *J* = 8.0, 2H), 7.36 (d, *J* = 8.0, 2H), 3.54 (t, *J* = 7.0, 2H), 2.46 (s, 3H), 2.39 (t, *J* = 7.0, 2H), 1.62 (m, 2H), 1.56 (m, 2H), 1.49 (s, 18H). ^{13}C NMR: δ 152.6 (C), 145.1 (C), 139.0 (C), 129.9 (CH), 127.3 (CH), 96.5 (C), 82.4 (C), 78.6 (C), 45.3 (CH_2), 28.2 (CH_2), 28.0 (CH_3), 24.3 (CH_2), 21.7 (CH_3), 18.7 (CH_2). IR: 2203, 1732, 1694, 1366, 1331, 1134, 752. ESIMS *m/z*: 474 (M + Na). HRMS-ESI (*m/z*): $[M + Na]^+$ calcd for $C_{23}H_{33}NNaO_6S$, 474.1921; found, 474.1921.

A 1 M THF solution of *t*-BuOK (5.8 mL, 5.8 mmol) was diluted with anhydrous THF (10 mL) under argon atmosphere and cooled at –78 °C. To the solution was added **5b-2** (1.04 g, 2.30 mmol) in THF (13 mL) dropwise over 25 min, and the mixture was stirred for 5 min. The reaction was quenched by the addition of a 1 M THF solution of AcOH (5 mL), and the cooling bath was removed. After addition of saturate aqueous $NaHCO_3$, the organic layer was separated. The aqueous layer was extracted twice with Et_2O. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 3:1) to give *N,N*-bis(*tert*-butoxycarbonyl)-6-*p*-tosylhex-4-ynamine (**5b-3**) (430 mg, 43%) as a brown oil: ^{1}H NMR: δ 7.84 (d, *J* = 8.0, 2H), 7.36 (d, *J* = 8.0, 2H), 3.90 (br s, 2H), 3.56 (t, *J* = 7.0, 2H), 2.46 (s, 3H), 2.19 (br t, *J* = 7.0, 2H), 1.72 (quintet, *J* = 7.0, 2H), 1.50 (s, 18H). ^{13}C NMR: δ 152.5 (C), 145.1 (C), 134.9 (C), 129.7 (CH), 128.8 (CH), 87.6 (C), 82.3 (C), 68.0 (C), 49.0 (CH_2), 45.5 (CH_2), 28.0 (CH_3), 27.6 (CH_2), 21.7 (CH_3),

16.5 (CH_2). IR: 3021, 2978, 1694, 1366, 1323, 1134, 748. ESIMS *m/z*: 407 (M + Na). HRMS-ESI (*m/z*): $[M + Na]^+$ calcd for $C_{23}H_{33}NNaO_6S$, 474.1921; found, 474.1925.

To a solution of **5b-3** (452 mg, 1.00 mmol) in anhydrous CH_2Cl_2 (3 mL) was added TFA (0.15 mL, 2.0 mmol), and the mixture was stirred at rt for 10 min, and concentrated *in vacuo*. The residue was dissolved in $CHCl_3$ and washed with saturated aqueous $NaHCO_3$, and the organic layer was separated. The aqueous layer was extracted 3 times with $CHCl_3$. The combined organic layers were washed with brine, dried over Na_2SO_4, concentrated *in vacuo*. The residue was dissolved in ethyl formate (2.2 mL, 25 mmol), and the mixture was heated under reflux for 22 h. After evaporation of ethyl formate *in vacuo*, the residue was purified by column chromatography (hexane/EtOAc 1:3) to give **5b** (111 mg, 40% over 2 steps) as a brown oil: ^{1}H NMR: δ 8.20 (s, 1H), 7.83 (d, *J* = 8.0, 2H), 7.39 (d, *J* = 8.0, 2H), 5.99 (br m, 1H), 3.92 (br s, 2H), 3.38 (q, *J* = 6.5, 2H), 2.48 (s, 3H), 2.28 (t, *J* = 6.5, 2H), 1.74 (quintet, *J* = 6.5, 2H). ^{13}C NMR: δ 161.6 (CH), 145.4 (C), 134.9 (C), 129.8 (CH), 128.5 (CH), 87.6 (C), 68.6 (C), 49.0 (CH_2), 37.4 (CH_2), 27.6 (CH_2), 21.7 (CH_3), 16.6 (CH_2). IR: 3375, 3279, 2947, 1663, 1528, 1385, 1319, 1134, 1084, 748. ESIMS *m/z*: 302 (M + Na). HRMS-ESI (*m/z*): $[M + Na]^+$ calcd for $C_{14}H_{17}NNaO_3S$, 302.0821; found, 302.0821.

6-Tosylhex-5-yn-1-ol (13a): To a solution of **2a-1** (220 mg, 1.00 mmol) in CH_2Cl_2 (10 mL) cooled in an ice–water bath was added *m*-CPBA (0.57 g, 2.5 mmol), and the mixture was stirred for 30 min. After addition of saturated aqueous $Na_2S_2O_3$ (25 mL), the cooling bath was removed, and the mixture was stirred for 2 h. To the mixture, was added saturated aqueous $NaHCO_3$, and the organic layer was separated. The aqueous layer was extracted 3 times with $CHCl_3$. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 2:1) to give the title compound (209 mg, 83%) as a colorless oil: ^{1}H NMR: δ 7.88 (d, *J* = 8.5, 2H), 7.37 (d, *J* = 8.5, 2H)), 3.64 (t, *J* = 6.0, 2H), 2.47 (s, 3H), 2.42 (t, *J* = 7.0, 2H), 1.70–1.59 (m, 4H). ^{13}C NMR: δ 145.2 (C), 138.9 (C), 129.9 (CH), 127.2 (CH), 96.9 (C), 78.4 (C), 61.7 (CH_2), 31.4 (CH_2), 23.4 (CH_2), 21.6 (CH_3), 18.7 (CH_2). IR: 3557, 2199, 1323, 1153, 1088, 814. ESIMS *m/z*: 253 (M + H). HRMS-ESI (*m/z*): $[M + H]^+$ calcd for $C_{13}H_{17}O_3S$, 253.0893; found, 253.0893.

Migrative Cyclization (Table 2 and Scheme 2).

General Procedure A. 2-(1-Tosylvinyl)tetrahydrofuran (3a): A 10 mL flame-dried test tube with a magnetic stirring bar was charged with **C2** (3.4 mg, 0.010 mmol) and Cs_2CO_3 (3.3 mg, 0.010 mmol). The test tube was filled with argon by the evacuation–refill process. After addition of toluene (0.6 mL), the mixture was stirred at 60 °C for 30 min. After the reaction mixture was allowed to cool to rt, a solution of **2a** (50.4 mg, 0.200 mmol) in toluene (0.4 mL) was added *via* cannula. The mixture was then stirred at 60 °C until TLC monitoring showed that **2a** was completely consumed. After diluted with EtOAc (2 mL), the organic layer was washed sequentially with aqueous 10% HCl, saturated aqueous $NaHCO_3$, and brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography (hexane/EtOAc 5:2) to give the title compound (40.0 mg, 79%) as a colorless oil: ^{1}H NMR: δ 7.76 (d, *J* = 8.0, 2H), 7.33 (d, *J* = 8.0, 2H), 6.35 (d, *J* = 1.5, 1H), 6.05 (d, *J* = 1.5, 1H), 4.50 (t, *J* = 6.5, 1H), 3.92 (q, *J* = 8.0, 1H), 3.76 (q, *J* = 8.0, 1H), 2.44 (s, 3H), 2.21 (m, 1H), 1.92–1.83 (m, 3H). ^{13}C NMR: δ 152.7 (C), 144.5 (C), 136.5 (C), 129.8 (CH), 128.1 (CH), 122.9 (CH_2), 75.6 (CH), 68.6 (CH_2), 32.9 (CH_2), 25.6 (CH_2), 21.6 (CH_3). ^{1}H and ^{13} C NMR, IR, and MS were in good agreement with those reported.[18]

3-(1-(Benzenesulfonyl)vinyl)-2-oxaspiro[4.5]decane (3b): Procedure A, using **2b** (61.3 mg, 0.200 mmol) in place of **2a**, and purification by column chromatography (hexane/toluene 10:1) gave the title compound (50.9 mg, 83%) as a colorless oil: ^{1}H NMR: δ 7.88 (d, *J* = 7.5, 2H), 7.63 (t, *J* = 7.5, 1H), 7.54 (t, *J* = 7.5, 2H), 6.35 (s, 1H), 6.14 (s, 1H), 4.55 (t, *J* = 8.0, 1H), 3.61 (d, *J* = 8.5, 1H), 3.57 (d, *J* = 8.5, 1H), 2.15 (dd, *J* = 13.0, 7.0, 1H), 1.56 (m, 1H), 1.42–1.40 (m, 10H). ^{13}C NMR: δ 152.8 (C), 139.7 (C), 133.5 (CH), 129.2 (CH), 128.1 (CH), 123.0 (CH_2) 75.4 (CH_2), 44.5 (CH), 36.2 (CH_2), 35.0 (CH_2), 25.9 (C), 23.9 (CH_2), 23.3 (CH_2). IR: 2920, 2851, 1447, 1308, 1142, 1057, 748. ESIMS *m/z*: 345 (M + K). HRMS-ESI (*m/z*): $[M + K]^+$ calcd for $C_{17}H_{22}KO_3S$, 345.0921; found, 345.0921.

***trans*- and *cis*-2-Allyl-5-(1-tosylvinyl)tetrahydrofuran (3c)**: Procedure A, using **2c** (29.2 mg, 0.100 mmol) in place of **2a**, and purified by column chromatography (hexane/EtOAc 9:1) gave a 3:2 mixture of the title compounds (23.7 mg, 81%) as a colorless oil: ^{1}H NMR: *trans* δ 7.74 (d, *J* = 8.0, 2H), 7.71 (d, *J* = 8.0, 2H), 6.34 (s, 1H), 6.05 (s, 1H), 5.81–5.70 (m, 1H), 5.10-5.02 (m, 2H), 4.62 (t, *J* = 7.0, 1H), 4.09 (quintet, *J* = 6.5, 1H), 2.43 (s, 3H), 2.31–2.25 (m, 2H), 2.23–2.16 (m, 1H), 2.05–1.99 (m, 1H), 1.89–1.81

(m, 1H), 1.63–1.56 (m, 1H); *cis* δ 7.74 (d, *J* = 8.0, 2H), 7.71 (d, *J* = 8.0, 2H), 6.36 (br s, 1H), 6.13 (br s, 1H), 5.81–5.70 (m, 1H), 5.10–5.02 (m, 2H), 4.48 (t, *J* = 7.0, 1H), 3.92 (quintet, *J* = 6.5, 1H), 2.43 (s, 3H), 2.38–2.31 (m, 1H), 2.31–2.25 (m, 2H), 2.23–2.16 (m, 1H), 1.99–1.94 (m, 1H), 1.63–1.56 (m, 1H). ^{13}C NMR: *trans* δ 152.74 (C), 144.48 (C), 136.7 (CH), 134.4 (C), 129.76 (CH), 128.2 (CH), 122.7 (CH_2), 117.1 (CH_2), 79.30 (CH), 75.8 (CH), 39.9 (CH_2), 33.2 (CH_2), 31.1 (CH_2), 21.6 (CH_3); *cis* δ 152.70 (C), 144.53 (C), 136.5 (CH), 134.4 (C), 129.79 (CH), 128.2 (CH), 123.1 (CH_2), 117.2 (CH_2), 7925 (CH), 75.6 (CH), 39.9 (CH_2), 32.8 (CH_2), 30.3 (CH_2), 21.6 (CH_3). IR: 2978, 2932, 1697, 1636, 1435. ESIMS m/z: 315 (M + Na). HRMS-ESI (m/z): $[M + Na]^+$ calcd for $C_{16}H_{20}NaO_3S$, 315.1025; found, 315.1025. The relative configuration was determined by NOESY correlation between the signals of the methine proton at the 5-position (4.62 ppm) and the allylic proton (2.31-2.25 ppm) for *trans*, and those of the methine protons at the 2- and 5-position (3.92 and 4.48 ppm, respectively) for *cis*. The diastereomeric ratio was determined based on the integration area of ^{1}H NMR signals at 4.62 and 4.48 ppm.

2,2-Diallyl-5-(1-tosylvinyl)tetrahydrofuran (3d): Procedure A, using **2d** (33.2 mg, 0.100 mmol) in place of **2a**, and purification by column chromatography (hexane/EtOAc 9:1) gave the title compound (23.3 mg, 70%) as a colorless oil: ^{1}H NMR: δ 7.74 (d, *J* = 8.0, 2H), 7.32 (d, *J* = 8.0, 2H), 6.34 (s, 1H), 6.18 (s, 1H), 5.74 (m, 2H), 5.09–5.02 (m, 4H), 4.54 (t, *J* = 7.0, 1H), 2.44 (s, 3H), 2.27–2.23 (m, 5H), 1.82–1.71 (m, 3H). ^{13}C NMR: δ 152.6 (C), 144.5 (C), 136.5 (C), 133.9 (CH), 133.2 (CH), 129.8 (CH), 128.2 (CH), 122.9 (CH_2), 118.22 (CH_2), 118.17 (CH_2), 85.0 (C), 75.5 (CH), 44.0 (CH_2), 43.3 (CH_2), 34.2 (CH_2), 33.7 (CH_2), 21.6 (CH_3). IR: 2974, 1639, 1597, 1315, 1138, 1045, 752. ESIMS *m/z*: 355 (M + Na). HRMS-ESI (*m/z*): $[M + Na]^+$ calcd for $C_{19}H_{24}NaO_3S$, 355.1338; found, 355.1335.

2-(1-Tosylvinyl)tetrahydro-2*H*-pyran (3e): Procedure A, using **2e** (53.3 mg, 0.200 mmol) and **C1** (3.4 mg, 0.010 mmol) in place of **2a** and **C2**, and purification by column chromatography (hexane/EtOAc 3:1) gave the title compound (36.2 mg, 68%) as a colorless oil: ^{13}C NMR: δ 152.4 (C), 144.4 (C), 136.6 (C), 129.7 (CH), 128.2 (CH), 124.5 (CH_2), 74.3 (C), 69.0 (C), 32.5 (CH_2), 25.4 (CH_2), 23.4 (CH_2), 21.6 (CH_3). ^{1}H and ^{13}C NMR, IR, and MS were in good agreement with those reported.[エラー! ブックマークが定義されていません。]

1-(1-Tosylvinyl)isochromane (3f): Procedure A, using **2f** (62.8 mg, 0.200 mmol) and **C1** (3.4 mg, 0.010 mmol) in place of **2a** and **C2**, and purification by column chromatography (hexane/EtOAc 5:1) gave the title compound (36.5 mg, 58%) as a colorless oil: ^{1}H NMR: δ 7.85 (d, *J* = 8.0, 2H), 7.33 (d, *J* = 8.0, 2H), 7.19 (t, *J* = 7.5, 1H), 7.14 (t, *J* = 7.5, 1H), 7.09 (d, *J* = 7.5, 1H), 6.89 (d, *J* = 7.5, 1H), 6.67 (s, 1H), 5.81 (s, 1H), 5.55 (s, 1H), 3.44–3.36 (m, 2H), 2.85 (m, 1H), 2.61 (td, *J* = 3.5, 16.5, 1H), 2.45 (s, 3H). ^{13}C NMR: δ 151.8 (C), 144.2 (C), 137.1 (C), 133.9 (C), 132.9 (C), 129.7 (CH_2), 129.5 (CH), 129.0 (CH), 128.5 (CH), 127.4 (CH), 126.8 (CH), 126.0 (CH), 72.2 (CH), 59.6 (CH_2), 27.7 (CH_2), 21.6 (CH_3). IR: 3021, 1315, 1215, 1134, 1080, 756. ESIMS *m/z*: 353 (M + K). HRMS-ESI (*m/z*): $[M + K]^+$ calcd for $C_{18}H_{18}KO_3S$, 353.0608; found, 353.0609.

General Procedure B. *cis,trans*-, *trans,trans*-, and *cis,cis*-5,5'-Bis(1-tosylvinyl)octahydro-2,2'-bifuran (3g): A 10 mL flame-dried test tube with a magnetic stir bar was charged with **C2** (3.4 mg, 0.010 mmol), Cs_2CO_3 (3.3 mg, 0.010 mmol), and **2g** (101 mg, 0.200 mmol). The flask was filled with argon by the evacuate–refill process. After addition of toluene (1.0 mL), and the mixture was stirred at 60 °C until TLC monitoring showed the complete consumption of **2g**. After addition of EtOAc (2 mL), the organic layer was washed sequentially with 10% aqueous HCl, saturated aqueous $NaHCO_3$, and brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography (toluene/Et_2O 2:1) to give a 3:2:2 mixture of the title compounds (89.1 mg, 88%) as a yellow oil: ^{1}H NMR: δ 7.71 (d, *J* = 8.0, 4H), 7.29 (d, *J* = 8.0, 4H), 6.34 (s, 3/7H, *cis,trans*), 6.32 (s, 8/7H, *trans,trans* and *cis,cis*), 6.28 (s, 3/7H, *cis,trans*), 6.07 (s, 10/7H, *cis,trans* and *trans,trans*), 6.03 (s, 4/7H, *cis,cis*), 4.58–4.46 (m, 2H), 4.03 (q, J = 7.0, 3/7H, *cis,trans*), 3.93 (m, 4/7H, *trans,trans*), 3.81 (m, 4/7H, *cis,cis*), 3.71 (q, J = 7.0, 3/7H, *cis,trans*), 2.33–2.15 (m, 4H), 2.03–1.80 (m, 4H). ^{13}C NMR: δ 152.33 (C), 152.29 (C), 152.22 (C), 152.20 (C), 144.61 (C), 144.57 (C), 144.55 (C), 136.5 (C), 136.3 (C), 129.79 (CH), 129.76 (CH), 128.17 (CH), 128.14 (CH), 123.4 (CH_2), 123.3 (CH_2), 123.1 (CH_2), 82.1 (CH), 81.9 (CH), 81.6 (CH), 76.6 (CH), 76.4 (CH), 75.9 (CH), 75.8 (CH), 33.7 (CH_2), 33.4 (CH_2), 32.7 (CH_2), 32.6 (CH_2), 28.7 (CH_2), 28.2 (CH_2), 27.6 (CH_2), 27.5 (CH_2), 21.6 (CH_3). IR: 1597, 1300, 1138, 1053, 752. ESIMS *m/z*: 525 (M + H). HRMS-ESI (*m/z*): $[M + H]^+$ calcd for $C_{26}H_{30}NaO_6S_2$, 525.1376; found, 525.1375. The relative configuration was determined by NOESY correlation between the signals of the methine protons

at the 2- and 5-position (4.03 and 4.48 ppm, respectively) for *cis,trans,* and those of the methine protons at the 2,2'- and 5,5'-positions (3.81 and 4.51 ppm, respectively) for *cis,cis*. The diastereomeric ratio of **3h** was determined based on the integration area of ^{1}H NMR signals at 4.03 (*cis,trans*), 3.96-3.91 (*trans,trans*), and 3.83-3.78 ppm (*cis,cis*).

1-(1-Tosylvinyl)-1,3,4,5-tetrahydrobenzo[*c*]oxepine (3h) and (*E*)-2-(2,3-Ditosylprop-1-enyl)benzenepropanol (12): Procedure B, using **2h** (65.7 mg, 0.200 mmol) and **C1** (3.4 mg, 0.010 mmol) in place of **2g** and **C2**, and purification by column chromatography (hexane/EtOAc 3:1) gave the title compounds as a colorless oil (3.3 mg, 5%) and a yellow oil (5.8 mg, 6%), respectively.

3h: ^{1}H NMR: δ 7.74 (d, *J* = 8.5, 2H), 7.28 (d, *J* = 8.5, 2H), 7.16–7.11 (m, 2H), 7.01 (dd, *J* = 7.5, 7.0, 1H), 6.90 (d, *J* = 7.5, 1H), 6.69 (s, 1H), 6.03 (s, 1H), 5.55 (s, 1H), 3.94 (dt, *J* = 12.5, 4.0, 1H), 3.58 (ddd, *J* = 12.5, 10.0, 3.5, 1H), 2.98 (m, 1H), 2.91 (m, 1H), 2.42 (s, 3H), 1.83–1.71 (m, 2H). ^{13}C NMR: δ 150.9 (C), 144.5 (C), 141.4 (C), 138.4 (C), 136.3 (C), 129.7 (CH_2), 129.6 (CH), 128.5 (CH), 128.14 (CH), 128.12 (CH), 127.5 (CH), 126.1 (CH), 78.3 (CH), 72.1 (CH_2), 34.0 (CH_2), 29.3 (CH_2), 21.6 (CH_3). IR: 2928, 1674, 1489, 1315, 1134, 1084, 756. ESIMS *m/z*: 367 (M + K). HRMS-ESI (*m/z*): $[M + K]^+$ calcd for $C_{19}H_{20}KO_3S$, 367.0765; found, 367.0766.

12: ^{1}H NMR: δ 8.31 (s, 1H), 7.87 (d, *J* = 8.5, 2H), 7.51 (d, *J* = 8.5, 2H), 7.42 (d, *J* = 7.5, 1H), 7.37 (d, *J* = 8.5, 2H), 7.33 (d, *J* = 7.5, 1H), 7.27–7.22 (m, 4H), 4.42 (s, 2H), 3.63 (br m, 2H), 2.67 (t, *J* = 7.5, 2H), 2.46 (s, 3H), 2.41 (s, 3H), 1.79 (tt, *J* = 7.5, 6.5, 2H). ^{13}C NMR: δ 146.5 (CH), 144.84 (C), 144.75 (C), 141.4 (C), 136.9 (C), 136.1 (C), 133.4 (C), 131.6 (C), 130.1 (CH), 129.72 (CH), 129.67 (CH), 129.6 (CH), 128.7 (CH), 127.8 (CH), 127.6 (CH), 126.4 (CH), 61.6 (CH_2), 54.3 (CH_2), 33.1 (CH_2), 29.7 (CH_2), 21.64 (CH_3), 21.56 (CH_3). IR: 3534, 1597, 1304, 1146, 1084, 756. ESIMS *m/z*: 523 (M + K). HRMS-ESI (*m/z*): $[M + K]^+$ calcd for $C_{26}H_{28}KO_5S_2$, 523.1010; found, 523.1010. The *E*-geometry was determined on the basis of the NOESY correlation between the protons at the 3-position of the benzenepropanol (7.42 ppm) and the allylic position (4.42 ppm).

The Reaction in the Absence of NHC (Table 1, entry 2). 6-(Tosylmethyl)-3,4-dihydro-2H-pyran (4a): To a suspension of Cs_2CO_3 (3.3 mg, 0.010 mmol) in anhydrous toluene (0.6 mL), was added a

solution of **2a** (50.4 mg, 0.200 mmol) in toluene (0.4 mL) *via* cannula. The mixture was then stirred at 60 °C for 12 h. After dilution with EtOAc (2 mL), the organic layer was washed sequentially with aqueous 10% HCl, saturated aqueous $NaHCO_3$, and brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography (hexane/EtOAc 5:2) to give a 1:35 mixture of **3a** and the title compound as a colorless oil (36.3 mg, 2% and 70%, respectively). The ^{1}H and ^{13}C NMR were identical to those reported.[19]

1-Tosyl-2-(1-tosylvinyl)pyrrolidine (6a) and 1-Tosyl-6-(tosylmethyl)-1,2,3,4-tetrahydropyridine (7a): Procedure A, using **5a** (81.1 mg, 0.200 mmol), **C4** (3.3 mg, 0.010 mmol), and proton sponge (4.3 mg, 0.020 mmol) under reflux, instead of **2a**, **C2**, and Cs_2CO_3 at 60 °C, and purification by column chromatography (hexane/Et_2O 2:3) gave a 15:1 mixture of the title compounds (66 mg, 75% and 5%, respectively) as a yellow oil: ^{1}H NMR: **6a** δ 7.83 (d, *J* = 8.0, 2H), 7.44 (d, *J* = 8.0, 2H), 7.22–7.18 (m, 4H), 6.46 (s, 1H), 6.20 (s, 1H), 4.04 (dd, *J* = 7.5, 2.5, 1H), 3.58 (ddd, *J* = 9.5, 6.5, 3.5, 1H), 3.12 (td, *J* 9.5, 6.5, 1H), 2.51 (s, 3H), 2.42 (s, 3H), 2.03 (m, 1H), 1.81–1.77 (m, 2H), 1.61 (m, 1H); **7a** δ 7.77 (d, *J* = 8.5, 2H), 7.63 (d, *J* = 8.5, 2H), 7.34 (d, *J* = 7.5, 2H), 7.29 (d, *J* = 7.5, 2H), 5.66 (t, *J* = 3.5, 1H), 4.45 (s, 2H), 3.22–3.20 (m, 2H), 2.46 (s, 3H), 2.43 (s, 3H), 1.96–1.94 (m, 2H), 1.31–1.29 (m, 2H). ^{13}C NMR: **6a** δ 151.4 (C), 144.8 (C), 143.8 (C), 135.7 (C), 133.1 (C), 129.8 (CH), 129.59 (CH), 128.6 (CH), 127.3 (CH), 125.0 (CH_2), 58.1 (CH), 49.5 (CH_2), 33.5 (CH_2), 23.3 (CH_2), 21.7 (CH_3), 21.50 (CH_3); **7a** δ 144.6 (C), 143.9 (C), 136.1 (C), 135.8 (C), 129.7 (CH), 129.56 (CH), 128.4 (CH), 127.4 (CH), 126.9 (C), 126.2 (CH), 61.7 (CH_2), 46.3 (CH_2), 22.6 (CH_2), 21.6 (CH_3), 21.55 (CH_3), 19.1 (CH_2). IR: 2766, 2441, 1691, 1304, 1121, 756. ESIMS *m/z*: 406 (M + H). HRMS-ESI (*m/z*): $[M + H]^+$ calcd for $C_{20}H_{24}NO_4S_2$, 406.1141; found, 406.1140. ^{13}C NMR of **6a** was identical to that reported.[エラー! ブックマークが定義されていません。]

The chemical shifts of the aromatic protons of **6a** were slightly different from the reported values (doublets of 2H each at 7.43, 7.44, 7.82, and 7.83 ppm), which may have been incorrectly reported. The ratio of **6a** and **7a** was determined based on the integration area of ^{1}H NMR signals at 6.46 and 5.66 ppm.

2-(1-Tosylvinyl)pyrrolidine-1-carbaldehyde (6b): Procedure A, using **5b** (55.9 mg, 0.200 mmol) under reflux, instead of **2a** at 60 °C, and purification by column chromatography (hexane/ EtOAc 10:1) gave the title compound (41.4 mg, 74%) as a light yellow oil. The two rotamers (ratio 2:1) were

observed in ^{1}H and ^{13}C NMR: ^{1}H NMR: major δ 7.78 (d, *J* = 8.0, 2H), 7.76 (s, 1H), 7.37 (d, *J* = 8.0, 2H), 6.43 (s, 1H), 5.78 (s, 1H), 4.57 (dd, *J* = 8.5, 2.5, 1H), 3.50 (t, *J* = 7.0, 2H), 2.46 (s, 3H), 2.21–2.15 (m, 1H), 2.01–1.96 (m, 1H), 1.93–1.86 (m, 2H); minor δ 8.11 (s, 1H), 7.80 (d, *J* = 7.5, 2H), 7.35 (d, *J* = 7.5, 2H), 6.37 (s, 1H), 5.73 (s, 1H), 4.54 (m, 1H), 3.60–3.56 (m, 2H), 2.44 (s, 3H), 2.33–2.24 (m, 1H), 2.21–2.15 (m, 1H), 2.01–1.96 (m, 1H), 1.93–1.86 (m, 2H). ^{13}C NMR: major δ 161.4 (CH), 153.3 (C), 145.3 (C), 135.4 (C), 130.2 (CH), 128.2 (CH), 124.1 (CH_2), 56.1 (CH), 44.0 (CH_2), 32.4 (CH_2), 22.0 (CH_2), 21.6 (CH_3); minor δ 160.4 (CH), 149.9 (C), 144.6 (C), 135.9 (C), 129.7 (CH), 128.1 (CH), 123.1 (CH_2), 54.8 (CH), 46.6 (CH_2), 32.2 (CH_2), 23.4 (CH_2), 21.6 (CH_3). IR: 1670, 1377, 1304, 1130, 1080, 814, 733. ESIMS *m/z*: 302 (M + Na). HRMS-ESI (*m/z*): $[M + Na]^+$ calcd for $C_{14}H_{17}NNaO_3S$, 302.0821; found, 302.0821.

Transformation of Vinyl Sulfone into Other Functional Groups (Scheme 3).

6-(2-*p*-Tolyl-1-tosylethyl)-3,4-dihydro-2*H*-pyran (8): To a solution of **2e** (613 mg, 2.30 mmol) in anhydrous DMF (15 mL) under argon atmosphere were added $Pd(OAc)_2$ (52 mg, 0.23 mmol), 4-iodotoluene (1.3 g, 5.8 mmol), and K_3PO_4 (1.5 g, 6.9 mmol). After heated at 120 °C for 24 h, the mixture was cooled to rt and diluted with EtOAc. After addition of water, the organic layer was separated. The aqueous layer was extracted 5 times with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 3:1 and then hexane/toluene/Et_2O = 5:3:2) to give the title compound (558 mg, 68%) as a yellow oil: ^{1}H NMR: δ 7.78 (d, *J* = 8.0, 2H), 7.32 (d, *J* = 8.0, 2H), 7.06–7.02 (m, 4H), 4.49 (t, *J* = 3.5, 1H), 3.83 (td, *J* = 10.0, 3.0, 1H), 3.73 (td, *J* = 10.0, 3.0, 1H), 3.61 (dd, *J* = 12.0, 3.0, 1H), 3.31 (dd, *J* = 13.5, 3.0, 1H), 3.13 (dd, *J* = 13.5, 12.0, 1H), 2.45 (s, 3H), 2.29 (s, 3H), 1.84–1.79 (m, 2H), 1.68–1.59 (m, 2H). ^{13}C NMR: δ 144.9 (C), 144.3 (C), 135.9 (C), 134.7 (C), 133.8 (C), 129.1 (CH), 129.0 (CH), 128.9 (CH), 128.7 (CH), 105.3 (CH), 72.6 (CH), 66.1 (CH_2), 30.5 (CH_2), 21.47 (CH_2), 21.45 (CH_3), 20.9 (CH_2), 20.1 (CH_2). IR: 1597, 1516, 1296, 1142, 1065, 748. ESIMS *m/z*: 395 (M + K). HRMS-ESI (*m/z*): $[M + K]^+$ calcd for $C_{21}H_{24}KO_3S$, 395.1078; found, 395.1079.

(*RS,SR*)-2-(3,3-Dimethyl-1-tosylbutyl)tetrahydro-2*H*-pyran (9): To a solution of **2e** (40.2 mg, 0.150 mmol) in anhydrous CH_2Cl_2 (15 mL) cooled at –78 °C under argon atmosphere were added *t*-BuI

(0.06 mL, 0.5 mmol), Et_3B (0.47 mL, 0.46 mmol), and Bu_3SnH (0.13 mL, 0.46 mmol), and the mixture was stirred for 6 h. Then, the mixture was poured into saturated aqueous NaH_2PO_4, and the organic layer was separated. The aqueous layer was extracted 3 times with Et_2O. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane to hexane/EtOAc 9:1) to give the title compound (47.7 mg, 98%) as a white solid of mp 88–89 °C (hexane/EtOAc): ^{1}H NMR: δ 7.77 (d, *J* = 8.5, 2H), 7.31 (d, *J* = 8.5, 2H), 3.86 (d, *J* = 11.0, 1H), 3.71 (dd, *J* = 11.0, 3.0, 1H), 3.23 (td, *J* = 11.0, 3.0, 1H), 2.96 (m, 1H), 2.43 (s, 3H), 1.86 (m, 1H), 1.81 (dd, *J* = 15.5, 4.0, 1H), 1.71 (dd, *J* = 15.5, 4.0, 1H), 1.52–1.42 (m, 5H), 0.89 (s, 9H). ^{13}C NMR: δ 144.2 (C), 136.3 (C), 129.6 (CH), 129.2 (CH), 76.8 (CH), 68.5 (CH_2), 67.5 (CH), 36.1 (CH_2), 30.5 (C), 29.8 (CH_3), 29.4 (CH_2), 25.3 (CH_2), 23.7 (CH_2), 21.6 (CH_3). IR: 2951, 1288, 1130, 1084, 1045, 814, 756. ESIMS *m*/*z*: 347 (M + Na). HRMS-ESI (*m*/*z*): $[M + Na]^+$ calcd for $C_{18}H_{28}NaO_3S$, 347.1651; found, 347.1653. Recrystallization of **9** from hexane–EtOAc (5:1) gave colorless needles of mp 88–89 °C suitable for X-ray diffraction to determine the structure shown in Scheme 3. The cif file is available as a separate file in the supporting information.

***(RS,SR)*- and (*RS,RS*)-4-(2-(Tetrahydro-2*H*-pyran-2-yl)-2-tosylethyl)morpholine (10):** To a solution of **2e** (26.7 mg 0.100 mmol) in MeOH (2 mL) under argon atmosphere was added morpholine (0.10 mL, 0.10 mmol), and the mixture was stirred at rt for 10 h. Then, the mixture was concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 2:1) to give an 85:15 mixture of the title compounds (35.0 mg, 99%) as a white solid of mp 82–85 °C: ^{1}H NMR: major δ 7.79 (d, *J* = 8.5, 2H), 7.30 (d, *J* = 8.5, 2H), 4.22 (d, *J* = 11.0, 1H), 3.90 (dd, *J* = 11.5, 1.5, 1H), 3.50–3.41 (m, 5H), 3.06 (br t, *J* = 5.0, 1H), 2.78 (dd, *J* = 14.0, 7.0, 1H), 2.72 (dd, *J* = 14.0, 5.0, 1H), 2.44 (s, 3H), 2.35–2.20 (m, 4H), 1.87 (m, 1H), 1.68 (ddd, *J* = 13.0, 11.0, 3.5, 1H), 1.45–1.52 (m, 4H); minor δ 7.78 (d, *J* = 8.5, 2H), 7.30 (d, *J* = 8.5, 2H), 4.10 (m, 1H), 3.90 (m, 1H), 3.40–3.39 (m, 2H), 3.36–3.32 (m, 2H), 3.31–3.17 (m, 2H), 2.97 (dd, *J* = 13.5, 9.0, 1H), 2.66 (dd, *J* = 13.5, 3.5, 1H), 2.44 (s, 3H), 2.35–2.20 (m, 4H), 1.90–1.85 (m, 1H), 1.72–1.64 (m, 1H), 1.57–1.54 (m, 4H). ^{13}C NMR: major δ 144.1 (C), 136.9 (C), 129.1 (CH), 128.99 (CH), 74.4 (CH), 68.4 (CH_2), 66.9 (CH), 66.6 (CH_2), 53.2 (CH_2), 53.1 (CH_2), 29.5 (CH_2), 25.3 (CH_2), 23.6 (CH_2), 21.5 (CH_3); minor δ 143.9 (C), 138.7 (C), 129.04 (CH), 128.4 (CH), 74.5

(CH), 69.1 (CH_2), 66.6 (CH), 66.4 (CH_2), 53.9 (CH_2), 53.0 (CH_2), 27.5 (CH_2), 25.7 (CH_2), 23.1 (CH_2), 21.5 (CH_3). IR: 2940, 2851, 1454, 1142, 1115, 1084, 752. ESIMS *m/z*: 354 (M + H). HRMS-ESI (*m/z*): $[M + H]^+$ calcd for $C_{18}H_{28}NO_4S$ 354.1734, found 354.1734. Anal. Calcd for $C_{18}H_{27}NO_4S$: C, 61.16; H, 7.70; N, 3.96. Found: C, 61.03; H, 7.59; N, 3.90. The major *(RS,SR)*-isomer was isolated by recrystallization from hexane–EtOAc (10:1). Another recrystallization of the major diastereomer from hexane–EtOAc (2:1) gave colorless needles of mp 87-88 °C suitable for X-ray diffraction to determine the structure shown in Scheme 3. The cif file is available as a separate file in the supporting information.

2-(2-*p*-tolylethyl)tetrahydro-2*H*-pyran (11): To a suspension of 10% Na(Hg) (2.3 g, 10 mmol) and Na_2HPO_4 (0.57 mg, 4.0 mmol) in anhydrous MeOH (10 mL) cooled in an ice-water bath was added a solution of **10** (357 mg, 1.00 mmol) in anhydrous MeOH (3 mL), and the mixture was stirred at rt for 17 h. After addition of water and Et_2O, and the organic layer was separated. The aqueous layer was extracted 3 times with Et_2O. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. To the residue, were added Pd/C (40 mg), MS4A (300 mg), and anhydrous THF (10 mL), and the mixture was stirred under H_2 atmosphere at rt for 20 h. The mixture was filtered through a pad of celite, which was washed successively with Et_2O. The combined filtrate was concentrated *in vacuo*, and the residue was purified by column chromatography (pentane/Et_2O 20:1) to give the title compound (127 mg, 62% over 2 steps) as a colorless oil: ^{1}H NMR: δ 7.09 (s, 4H), 4.00 (ddd, *J* = 11.0, 2.5, 2.0, 1H), 3.42 (td, *J* = 11.5, 2.0, 1H), 3.24 (m, 1H), 2.72 (ddd, *J* = 13.5, 10.0, 5.5, 1H), 2.62 (ddd, *J* = 13.5, 9.5, 7.0, 1H), 2.32 (s, 3H), 1.83–1.76 (m, 2H), 1.69–1.62 (m, 1H), 1.60 (m, 1H), 1.57–1.53 (m, 1H), 1.51–1.47 (m, 2H), 1.29 (qd, *J* = 12.5, 2.0, 1H). ^{13}C NMR: δ 139.2 (C), 134.9 (C), 128.9 (CH), 128.3 (CH), 76.8 (CH), 68.4 (CH_2), 38.4 (CH_2), 31.9 (CH_2), 31.2 (CH_2), 26.1 (CH_2), 23.5 (CH_2), 20.9 (CH_3). IR: 2932, 2843, 1516, 1088, 1045, 810, 733. ESIMS *m/z*: 227 (M + Na). HRMS-ESI (*m/z*): $[M + Na]^+$ calcd for $C_{14}H_{20}NaO$, 227.1406; found, 227.1392.

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Supporting Information. NMR spectra of new compounds and crystallographic information of **9** and **10**. These materials are available free of charge via the Internet at http://pubs.acs.org.

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