Mechanistic Support for Intramolecular Migrative Cyclization of Propargyl Sulfones Provided by Catalytic Asymmetric Induction with a Chiral Counter Cation Strategy

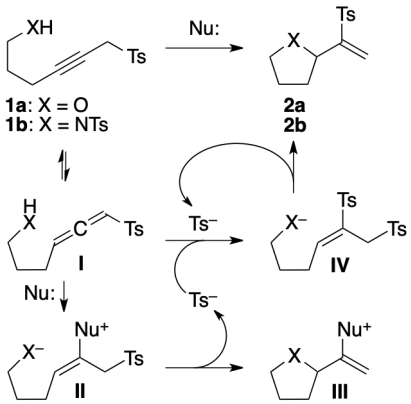
Kohta Yamasaki,[a] Akiho Yamauchi,[a] Tsubasa Inokuma,[a,b] Yasunori Miyakawa,[c] Yinli Wang,[a,c] Raphaël Oriez,[c] Yousuke Yamaoka,[c] Kiyosei Takasu,[c] Naonobu Tanaka,[a] Yoshiki Kashiwada,[a] and Ken-ichi Yamada*[a,b]

[a] K. Yamasaki, A. Yamauchi, Dr. T. Inokuma, Dr. Y. Wang, Prof. Dr. N. Tanaka, Prof. Dr. Y. Kashiwada, Prof. Dr. K. Yamada
Graduate School of Pharmaceutical Sciences
Tokushima University
Shomachi, Tokushima 770-8505, Japan
E-mail: yamak@tokushima-u.ac.jpResearch Cluster on "Innovative Chemical Sensing"
[b] Dr. T. Inokuma, Prof. Dr. K. Yamada
Tokushima University
[c] Y. Miyakawa, Dr. Y. Wang, Dr. R. Oriez, Dr. Y. Yamaoka, Prof. Dr. K. Takasu
Shomachi, Tokushima 770-8505, Japan.
Graduate School of Pharmaceutical Sciences
Kyoto University
Yoshida, Sakyo-ku, Kyoto 606-8501, Japan

ABSTRACT: We previously reported an intramolecular migrative cyclization of propargylsufones and sulfonylalkynamides giving oxa- and azacycles, respectively. To confirm the postulated reaction mechanism, the reaction was conducted with chiral nucleophiles such as N-heterocyclic carbenes, phosphines, and pyridines, or with sulfinate anions and chiral cations. As expected, migrative cyclization proceeded to give the enantiomerically enriched products. These results strongly support the postulated mechanism and provide the first example of the asymmetric version of this reaction.

Introduction

As part of our ongoing studies to develop catalytic reactions,[1] we recently reported that an oxa- and azacycle-forming reaction of sulfonylalkynols and sulfonylalkynamides was triggered by nucleophiles, such as an N-heterocyclic carbene (NHC),[2] 4-dimethylaminopyridine (DMAP), and phosphines (Scheme 1).[3] In the presence of catalytic amounts of these nucleophiles, bond formation with the internal O- or N-nucleophile occurred at the γ-position of sulfone with 1,2-sulfonyl migration.[4,5] This transformation can be regarded as an example of γ-umpolung bond formation because the latent polarity of the γ-position is negative.[6,7] We proposed the following mechanism: (1) Tautomerization of propargyl sulfone **1** occurs to generate sulfonylallene **I**.[8] (2) Conjugate addition of the nucleophilic catalysts to **I** followed by proton transfer provides allyl sulfone **II**, which undergoes an intramolecular S_N2'-type reaction to liberate *p*-toluenesulfinate anions (Ts^-) along with **III**. (3) Conjugate addition of Ts^- to **I** followed by proton transfer provides allylic sulfone **IV**, whose S_N2'-type cyclization leads to **2** and regeneration of Ts^-. According to the postulated reaction mechanism,[2,3] we envisaged that the cyclization of **IV** could enantioselectively produce **2** in the presence of chiral cations. We expected that a counter cation of cyclizing alkoxide **IV** would be cationic co-product **III** and that observation of enantioenrichment in **2** with chiral **III** would strongly support the mechanism. Here, we report the first examples of this type of cyclization reaction with asymmetric induction.[9]



Scheme 1. Migrative Cyclization of Sulfonylalkynol and Sulfonylalkynamides and the Postulated Reaction Mechanism: Nu = nucleophiles such as NHC, DMAP, and phosphines.

Results and Discussion

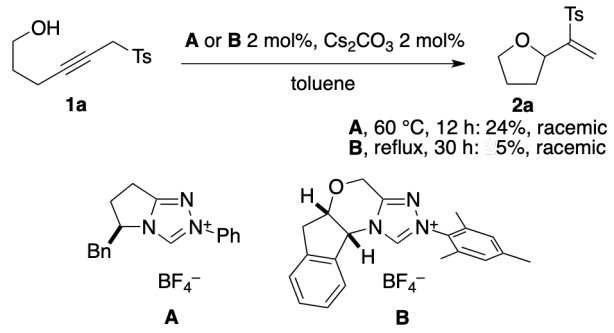
In Situ Generation of Chiral Counter Cations

First, we tested the reaction using two representative chiral NHCs as the nucleophile. According to the postulated mechanism, chiral cation **III** should be generated by the reaction of chiral NHC and sulfonylallene **I**, and act as a chiral counter

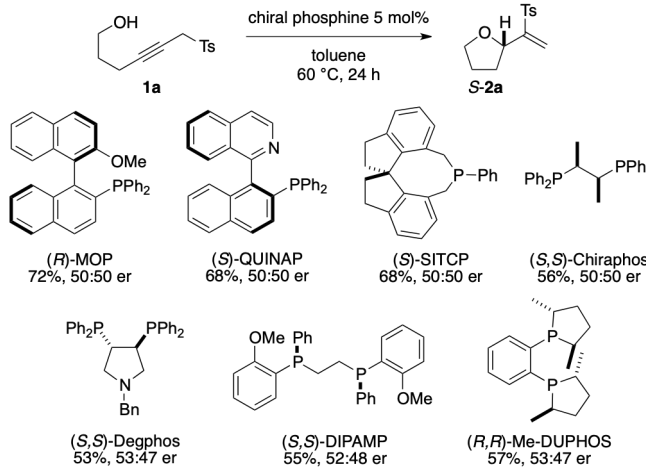
cation in the cyclization of intermediate **IV**. Thus, sulfonylalkynol **1a** was heated to 60 °C in toluene in the presence of Cs_2CO_3 and NHC precursor **A**[10] (2 mol% each); however, THF derivative **2a** was obtained as a racemic mixture in only 24% yield after 12 h (Scheme 2). The reaction with Cs_2CO_3 and precursor **B**[11] (2 mol% each) was much slower, giving racemic **2a** in 5% yield after 30 h in refluxing toluene.

Next, we utilized chiral phosphines as the nucleophile (Scheme 3).[3] Although binaphthyl-based chiral phosphines such as MOP[12] and QUINAP,[13] spiroindane-type SITCP,[14] and the chiral diphosphine Chiraphos[15] failed to induce enantioselectivity, the chiral diphosphines Degphos,[16] DIPAMP,[17] and Me-DUPHOS[18] provided slightly enantioenriched *S*-**2a** with 53:47 enantiomeric ratio (er). The absolute configuration of the major enantiomer was assigned on the basis of the electronic circular dichroism (ECD) spectrum (*vide infra*).

We also examined chiral pyridine-derived nucleophiles. We expected the hydrogen-bonding abilities of pyrrolidinylpyridine **C**[19] and binaphthyl-derived pyridine **D**[20] developed by Kawabata and Suga, respectively, to favorably affect enantiodifferentiation in the cyclization step (Scheme 4). Interestingly, the reactions with **C** and **D** proceeded at room temperature, probably because the basicity of these nucleophiles facilitated the generation of allenic tautomer **I**. A significant amount of dihydropyran **3a**, however, was produced along with tetrahydrofuran *S*-**2a**. This is probably also due to the high basicity inducing intramolecular conjugate addition of the hydroxy group, which competes with the intermolecular conjugate addition of the external nucleophiles such as **C**, **D**, and Ts^-, in sulfonylallene **I**. To avoid the undesired reaction, we utilized sulfonylalkanol **1c**, because the undesired intramolecular conjugate addition of sulfonylallene **I** is relatively slow due to the formation of a seven-membered ring. Although the reaction was rather slow, desired products **2c** were produced at 80 °C after 27 and 20 h in improved yields (43% and 19%) with **C** and **D**, respectively. It is noteworthy that the reaction of **1c** with **D** produced *R*-**2c** with significant enantioenrichment (59:41 er)[21] for the first time, providing strong support for our proposed mechanism shown in Scheme 1.



Scheme 2. Reaction of **1a** with Chiral NHC Precursors **A** and **B**.



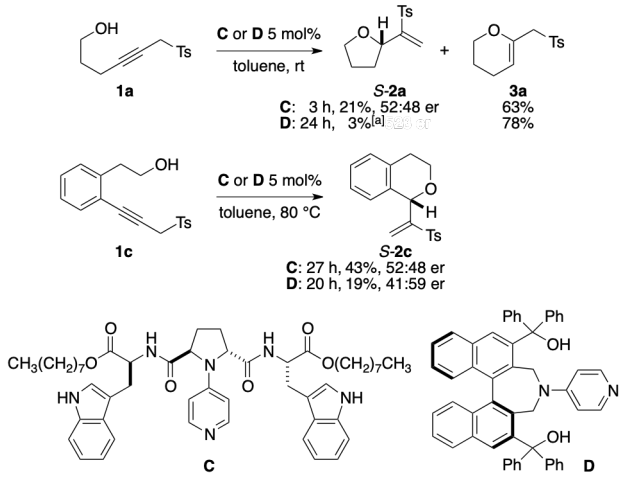
Scheme 3. Reaction of **1a** with Chiral Phosphines.[3]

External Chiral Counter Cation

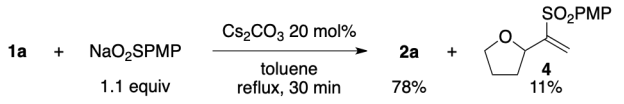
According to the postulated mechanism, addition of external sulfinate anions should promote the reaction, even in the absence of a nucleophile trigger. Indeed, in the presence of NaTs and Cs_2CO_3 (20 mol% each), the reaction of **1a** proceeded in toluene at 80 °C to give **2a** in 83% yield after 6 h (Table 1, entry 2). When sodium 4-methoxybenzenesulfinate (NaO_2SPMP) was used in place of NaTs, crossover of sulfonyl groups was observed to produce tetrahydrofuran **4** bearing a 4-methoxybenzenesulfonyl ($PMPSO_2$) group in 11% yield along with **2a** in 78% yield (Scheme 5). These results also strongly support the proposed mechanism.

It is noteworthy that the reaction failed to proceed in the absence of the base (entry 1). This may indicate that the base is necessary for the tautomerization to generate allenic intermediate **I** *in situ*, and/or that cesium cations should solubilize Ts^- as counter cations. While K_2CO_3 also promoted the reaction to give **2a** in 62% (entry 3), most of **1a** was recovered with Na_2CO_3 and Li_2CO_3, and **2a** was produced in only 4% and 15% yield, respectively (entries 4 and 5).

The result shown in entry 4 indicates that the solubility of the sodium salts of carbonate and sulfinate is too low in toluene at 80 °C to promote the reaction. Thus, we expected that



Scheme 4. Reaction of **1a** and **1c** with Chiral Pyridines **C** and **D**. [a] The er was not determined.



Scheme 5. Crossover Experiment of **1a** with NaO_2SPMP.

addition of an external chiral cation as a phase transfer catalyst should solubilize the anions forming ion pairs. This would lead to the formation of an ion pair of the chiral cation and intermediate **IV**, which would undergo cyclization in the asymmetric environment to give an enantioenriched product (Scheme 1).

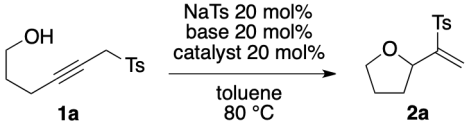
Thus, the reaction of **1a** was conducted with NaTs and Na_2CO_3 using binaphthyl-derived chiral ammonium salt **E**[22] as a catalyst. The catalyst promoted the reaction to give **2a** in 40% yield after 23 h, but enantioselectivity was not observed (entry 6). Although neither bisbinaphthyl-type **F**,[23] biphenyl-type **G**,[24] nor quinidine-derived **H**[25] realized enantioinduction (entries 7–9), the use of N-bistrifluoromethylbenzylated quinidine **J**[26] resulted in slight enantioenrichment (54:46 er, entry 10). Significant effects of an O-substituent of the cation were observed, and O-benzylated catalyst **K**[27] increased the enantioselectivity to give *S*-**2a** with 61:39 er (entry 11), while O-methylated catalyst **L**[28] provided a racemic product (entry 12). *N,*O-Bistrifluoromethylbenzylated catalyst **M** [29] further improved the enantioinduction to give *S*-**2a** with 64:36 er (entry 13). Interestingly, pseudoenantiomeric quinine-derived catalyst **N**[29] exhibited much lower asymmetric induction to provide mainly *R*-**2a** with 45:55 er (entry 14). The reaction of **1a** proceeded with reduced amounts of NaTs and Na_2CO_3 (10 and 5 mol%, respectively) at 60 °C to give *S*-**2a** with 65:35 er in 88% yield after 20 h (Table 2, entry 1).

Catalyst **M**, which was thus far best for migrative cyclization of **1a**, was then applied to the reactions of other sulfonylalkynols **1** (Table 2, entries 2–4). The cyclization of tertiary alcohol **1d** also proceeded with enantioenrichment to give 2,2,5-trisubstituted tetrahydrofuran *S*-**2d** with 57:43 er in 72% yield (entry 2). The asymmetric induction was also observed in a 6-membered ring formation of **1e** and **1c**, and dihydropyran *S*-**2e** and benzodihydropyran *S*-**2c** were produced with 55:45 and 54:46 er in 62% and 50% yields, respectively (entries 3 and 4).

The reaction with **1b** bearing an N-nucleophile was also tested. Under the same conditions, tetrahydropyridine was formed to a significant degree by cyclization of allenic intermediate **I** to give *S*-**2b** with 56:44 er and **3b** in 76% combined yield as a 67:33 mixture (entry 5). In these reactions, the catalyst showed high substrate specificity and the observed asymmetric induction was much lower in the reaction of substrates other than **1a**.

The observed substrate specificity of the catalyst encouraged us to explore a more suitable catalyst for **1b**. Catalyst **K** performed the same level of asymmetric induction (56:44 er) to give a mixture of **2b** and **3b** with a higher **2b**-content (51% vs 69%; entry 1 vs 2). Catalyst **G** promoted the reaction more **2b**-selectively, providing an 89:11 mixture of **2b** and **3b** in

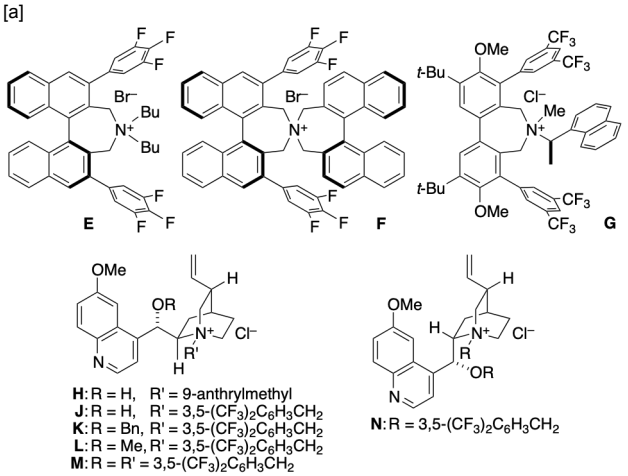
Table 1. Reaction of **1a** in the Presence of NaTs.



1a **2a**

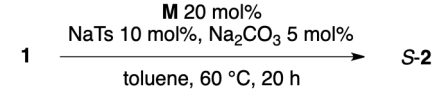
entry	base	catalyst[a]	time (h)	yield of **2a**	er[b] of **2a**
1	-	-	6	0%	-
2	Cs_2CO_3	-	6	83%	-
3	K_2CO_3	-	6	62%	-
4	Na_2CO_3	-	6	4%	-
5	Li_2CO_3	-	6	15%	-
6	Na_2CO_3	**E**	23	40%	50:50
7	Na_2CO_3	**F**	23	48%	50:50
8[c]	Na_2CO_3	**G**	2	67%	50:50
9	Na_2CO_3	**H**	23	40%	50:50
10	Na_2CO_3	**J**	23	93%	54:46
11	Na_2CO_3	**K**	23	92%	61:39
12	Na_2CO_3	**L**	23	91%	50:50
13[c]	Na_2CO_3	**M**	16.5	90%	64:36
14	Na_2CO_3	**N**	23	88%	45:55

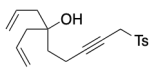
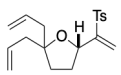
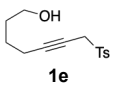
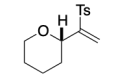
[a]



[b] Ratio of *S*- and *R*-**2a**. The absolute configuration of **2a** was assigned by the ECD spectrum (*vide infra*). [c] NaTs (10 mol%), Na_2CO_3 (5 mol%).

Table 2. Reaction of Sulfonylalkynols **1** Using **M** as a Catalyst.



entry	**1**	*S*-**2**[a]	yield	er
1	**1a**	*S*-**2a**	88	65:35
2	 **1d**	 *S*-**2d**	72	57:43
3	 **1e**	 *S*-**2e**	62	55:45
4	**1c**	*S*-**2c**	50	54:46
5	**1b**	*S*-**2b**	51[b]	56:44

[a] The absolute configuration of *S*-**2a** and *S*-**2b** was assigned by the ECD spectrum (*vide infra*), and those of **2c**–**d** were tentatively assigned by analogy. [b] **3b** was produced in 25% yield (see also Table 3, entry 1).

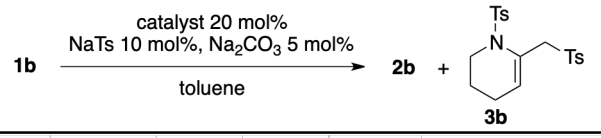
94% combined yield with 53:47 er (entry 3). While the reaction with catalyst **M** at rt was much slower, producing an 83:17 mixture of **2b** and **3b** (57:43 er) in 81% yield after 96 h (entry 4), the reaction rate with catalyst **G** was sufficient at rt, producing an 83:17 mixture of **2b** and **3b** in 98% yield after 20 h with a slightly higher enantiomeric ratio of 59:42 (entry 6). The reaction using catalyst **K** at rt produced **2b** with an improved enantiomeric ratio (61:39), but the yield (48%) and **2b**:**3b** ratio (60:40) were lower (entry 5), and a lower temperature (0 °C) did not confer additional benefit to the asymmetric induction, giving a 94:6 mixture of **2b** and **3b** with 60:40 er (entry 7). Although the reaction with catalyst **G** was also slow at 0 °C, the formation of **3b** was suppressed and the enantioselectivity was increased to provide **2b** with 62:38 er and **3b** in 41% yield with a 96:4 ratio as well as 50% recovery of **1b** (entry 8).

Assignment of the Absolute Configuration of 2a and 2b

The absolute configurations of **2a** and **2b** were assigned by the ECD method, which is widely utilized for assigning the absolute configuration of natural products.[30] First, significantly contributing conformers of **2a** were searched using the conformer analysis with the MMFF (Merck Molecular Force Field). The conformers' geometries were fully optimized at the B3LYP/6-31G* theoretical level, and the ECD spectra were calculated at the TD-B3LYP/6-31+G* theoretical level with correction of the polarizable continuum model (PCM) for MeOH. Comparison of the experimentally observed ECD spectrum of **2a** (64:36 er) in MeOH with the weighted average of the calculated spectra for *S*-**2a** based on the Bolzmann distribution revealed that the mainly produced enantiomer should be *S*-**2a** (Figure 1).

In the same way, the absolute configuration of **2b** was assigned to be an *S*-configuration as well. Figure 2 shows the experimentally observed spectrum of **2b** (62:38 er) and the calculated spectrum for *S*-**2b**.

Table 3. Reaction of Sulfonylalkynamde **1b**



entry	catalyst	temp	time	yield[a]	**2b**:**3b**	er[b] of **2b**
1[c]	**M**	60 °C	20 h	76%	67:33	56:44
2	**K**	60 °C	20 h	90%	77:23	56:44
3	**G**	60 °C	20 h	94%	89:11	53:47
4	**M**	rt	96 h	81%	83:17	57:43
5	**K**	rt	120 h	48%[d] (69%)	60:40	61:39
6	**G**	rt	20 h	98%	83:17	59:42
7	**K**	0 °C	120 h	37%[e] (50%)	94: 6	60:40
8	**G**	0 °C	72 h	41%[f] (82%)	96: 4	62:38

[a] Combined yields of **2b** and **3b**. The yields in the parentheses are based on recovered **1b**. [b] *S*:*R* [c] Data from Table 2, entry 5 for comparison. [d] With recovery of **1b** (30%). [e] With recovery of **1b** (26%). [f] With recovery of **1b** (50%).

Conclusion

The present study demonstrated that the addition of sulfinate anions allowed for migrative cyclization of sulfonylalkynols to proceed without a nucleophilic additive and that crossover of the sulfonyl groups occurred in the presence of sulfinate anions different from those leaving the substrate. Moreover, significant asymmetric induction was observed in the reactions of sulfonylalkynols and *N*-*p*-tosylsulfonylalkynamine in the presence of chiral DMAP-derivative **D**, and chiral cations **G** or **M**. Although the enantioselectivity was moderate and substrate-specific, and the reaction has room for improvement, the results strongly support the previously proposed reaction mechanism and provide the first example of an asymmetric version of this reaction.

Experimental Section

General. All melting points are uncorrected. Silica gel was used for column chromatography. NMR (400 and 100 MHz for ^{1}H and ^{13}C, respectively) was measured in DMSO-d6 unless otherwise mentioned. 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

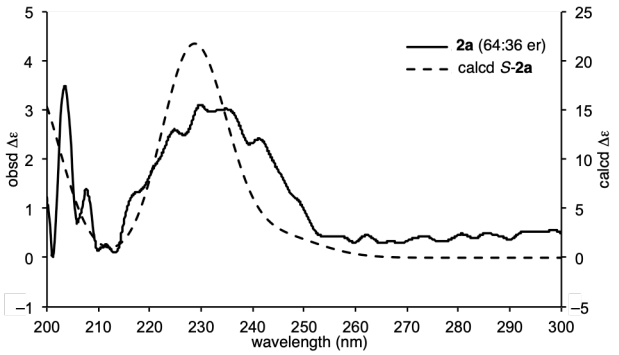


Figure 1. Experimentally Observed and Calculated ECD Spectra of **2a**. The vertical line (Δε) of the observed spectrum (left) is scaled by 20% of that of the calculated spectrum (right).

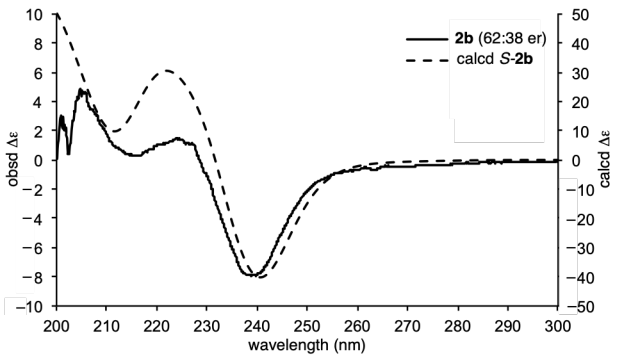


Figure 2. Experimentally Observed and Calculated ECD Spectra of **2b**. The vertical line (Δε) of the observed spectrum (left) is scaled by 20% of that of the calculated spectrum (right).

were made based on DEPT data. For IR spectroscopy, the wave numbers of maximum absorption peaks are reported in cm^{-1}. TOF mass spectrometer was used for ESI-MS. Anhydrous solvents were purchased and used without further desiccation.

Preparation of the Catalysts. The chiral phosphines and catalyst **F** were purchased and used as received. Catalysts **A**,[31] **B**,[32] **E**,[33] **H**,[29b] and **J**[34] were prepared by the reported procedures.

(*R*)-2,10-Di-*tert*-butyl-3,9-dimethoxy-6-methyl-6-(1-naphthalen-1-ylethyl)-4,8-bis(3,5-bistrifluoromethylphenyl)-6,7-dihydro-5*H*-dibenzo[c,e]-azepinium Chloride (G): To a solution of (*R*)-2,10-di-*tert*-butyl-3,9-dimethoxy-6-methyl-6-(1-naphthalen-1-ylethyl)-4,8-bis(3,5-bistrifluoromethylphenyl)-6,7-dihydro-5*H*-dibenzo[*c*,*e*]-azepinium bromide[35] (208 mg, 0.200 mmol) in CH_2Cl_2 (50 mL) and water (5 mL), was added NaCl (58 mg, 1.0 mmol). The mixture was stirred vigorously at rt for 3 h. The organic layer was separated and washed with brine, which was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo to give the title compound (173 mg, 87%) as a yellow solid of mp 114.5–116 °C with $[\alpha]_D^{28}$ +74.3 (*c* 1.00, $CHCl_3$): ^{1}H NMR: 8.32 (s, 1H), 8.08 (s, 2H), 8.03 (s, 1H), 7.92 (d, *J* = 8.5, 1H), 7.91 (d, *J* = 7.5, 1H), 7.86 (s, 1H), 7.55 (s, 2H), 7.49 (t, *J* = 7.5, 1H), 7.39–7.26 (m, 3H), 7.06 (d, *J* = 8.5, 1H), 6.81 (s, 1H), 5.45 (d, *J* = 14.5, 1H), 5.18 (q, *J* = 7.0, 1H), 4.16 (d, *J* = 14.5, 1H), 3.38 (d, *J* = 13.0, 1H), 3.20 (s, 3H), 3.01 (s, 3H), 2.91 (s, 3H), 2.82 (d, *J* = 13.0, 1H), 1.60 (s, 9H), 1.46 (s, 9H), 1.09 (d, *J* = 7.0, 3H). ^{13}C NMR: 158.1 (C), 157.9 (C), 147.7 (C), 137.7 (C), 137.5 (C),137.3 (C), 137.1 (C),135.5 (C), 134.4 (C), 134.0 (C), 132.8 (q, *J* = 30, C), 132.4 (CH), 131.9 (CH), 131.7 (C), 131.1 (q, *J* = 32, C), 130.8 (q, *J* = 32, C), 130.7 (m, CH), 130.4 (CH), 129.7 (m, CH), 129.1 (CH), 128.8 (CH), 128.2 (CH), 127.3 (C), 126.5 (CH), 126.2 (CH), 125.5 (C), 125.0 (CH), 123.6 (C), 122.8 (q, *J* = 273, C), 122.7 (q, *J* = 270, C), 122.7 (m, CH), 122.3 (q, *J* = 272, C), 121.8 (m, CH), 119.2 (CH), 62.1 (CH), 61.0 (CH_3), 60.8 (CH_3), 59.1 (CH_2), 57.7 (CH_2), 42.4 (CH_3), 35.8 (C), 35.7 (C), 30.7 (CH_3), 30.6 (CH_3), 15.5 (CH_3). IR (KBr): 2962, 1467, 1446, 1396, 1365, 1327, 1281, 1244, 1181,1139, 1083, 1055, 900, 851, 802, 717, 683. HRMS–ESI (*m*/*z*): $[M - Cl]^+$ calcd for $C_{53}H_{50}F_{12}NO_2$, 960.3644; found, 960.3667.

***O*-Benzyl-*N*-(3,5-bis(trifluoromethyl)benzyl)quinidinium Chloride (K)**: To a suspension of *O*-benzylquinidine[36] (360 mg, 0.868 mmol) in THF (4.4 mL) was added 3,5-bis(trifluoromethyl)benzyl bromide (0.18 mL, 0.96 mmol). The stirred mixture was heated under reflux for 14 h, concentrated in vacuo, and purified by flash chromatography ($MeOH/CHCl_3$ 1:10 to 1:5) to give a yellow solid. To a solution of the yellow solid (300 mg, 0.416 mmol) in CH_2Cl_2 (5 mL) and water (0.5 mL), was added NaCl (120 mg, 2.05 mmol). The resulting mixture was stirred vigorously at rt for 21 h. The organic layer was separated and washed with brine, which was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo to give the title compound (203 mg, 34%) as a yellow solid of mp 157.8–161.5 °C with $[\alpha]_D^{26}$ +99.0 (c 1.00, $CHCl_3$): ^{1}H NMR (500 MHz): 8.84 (d, *J* = 5.5, 1H), 8.53 (s, 2H), 8.37 (s, 1H), 8.05 (d, *J* = 9.5, 1H), 7.74 (br m, 1H), 7.60–7.50 (br m, 1H), 7.57 (d, *J* = 7.0, 2H), 7.52 (d, *J* = 9.5, 1H), 7.44 (t, *J* = 7.0, 2H), 7.38 (t, *J* = 7.0, 1H), 6.48 (br m, 1H), 5.92 (ddd, *J* = 17.0, 10.0, 6.5, 1H), 5.18 (br m, 1H), 5.14 (d, *J* = 10.0, 1H), 5.11 (d, *J* = 17.0, 1H), 4.96 (br d, *J* = 13.0, 1H), 4.89 (d, *J* = 11.5, 1H), 4.49 (d, *J* = 11.5, 1H), 4.27 (br m, 1H), 4.16–3.88 (m, 5H), 3.52 (br t, *J* = 10.0, 1H), 2.96 (br q, *J* = 10.0, 1H), 2.61–2.50 (m, 2H), 1.94 (br s, 1H), 1.81–1.68 (m, 2H), 1.36 (br m, 1H). ^{13}C NMR (500 MHz): 157.8 (C), 147.3 (CH), 144.1 (C), 139.3 (C), 137.1 (CH), 134.7 (CH), 131.3 (CH), 131.2 (C), 130.8 (q, *J* = 33, C), 128.5 (CH), 128.4 (CH), 128.1 (CH), 126.6 (C), 124.1 (CH), 123.2 (q, *J* = 271, C), 122.0 (CH), 116.8 (CH_2), 102.4 (CH), 72.2 (CH), 70.3 (CH_2), 67.6 (CH), 61.5 (CH_2), 55.9 (CH_2), 55.5 (CH_3), 54.5 (CH_2), 36.7 (CH), 26.5 (CH), 23.0 (CH_2), 21.1 (CH_2). IR (KBr): 2956, 1622, 1509, 1475, 1372, 1281, 1178, 1135, 1024, 903, 828, 703, 682. HRMS–ESI (*m*/*z*): $[M - Cl]^+$ calcd for $C_{36}H_{35}F_6N_2O_2$, 641.2597; found, 641.2606.

***N*-(3,5-Bis(trifluoromethyl)benzyl)-*O*-methylquinidinium Chloride (L):** To a solution of *N*-(3,5-bis(trifluoromethyl)benzyl)-*O*-methylquinidinium bromide[37] (511 mg, 0.791 mmol) in CH_2Cl_2 (30 mL) and water (3 mL), was added NaCl (229 mg, 3.96 mmol). The mixture was stirred vigorously at rt for 5 h. The organic layer was separated and washed with brine, which was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo to give the title compound (453 mg, 44%) as a yellow solid of mp 166–171 °C with $[\alpha]_D^{21}$ +155 (*c* 0.98, $CHCl_3$): ^{1}H NMR: 8.84 (d, *J* = 4.0, 1H), 8.73 (br m, 2H), 8.36 (br m, 1H), 8.03 (br m, 1H), 7.66 (br m, 1H), 7.60–7.45 (br m, 2H), 6.22 (br m, 1H), 6.01 (ddd, *J* = 17.0, 10.0, 7.0, 1H), 5.29–5.26 (br m, 3H), 5.01 (br m, 1H), 4.50–4.22 (br m, 2H), 4.09 (br s, 3H), 3.93 (br m, 1H), 3.51 (br m, 1H), 3.48 (br s, 3H), 2.95 (br m, 1H), 2.65 (br m, 1H), 2.46 (br m, 1H), 1.91 (br s, 1H), 1.80–1.70 (br m, 2H), 1.27 (br m, 1H). ^{13}C NMR: 157.7 (C), 147.1 (CH), 144.2 (C), 138.9 (C), 137.2 (CH), 134.9 (CH), 131.5 (C), 131.1 (CH), 130.6 (q, *J* = 33, C), 126.7 (C), 123.7 (CH), 123.2 (q, *J* = 271, C), 121.8 (CH), 120.2 (CH), 116.8 (CH_2), 102.3 (CH), 79.5 (CH), 67.5 (CH), 61.3 (CH_2), 56.5 (CH_3), 55.9 (CH), 55.2 (CH_2), 54.5 (CH_2), 36.7 (CH), 26.5 (CH), 23.0 (CH_2), 21.0 (CH_2). IR (KBr): 2947, 1622, 1508, 1474, 1373, 1281, 1177, 1135, 1071, 907, 755, 678. HRMS–ESI (*m*/*z*): $[M - Cl]^+$ calcd for $C_{30}H_{31}F_6N_2O_2$, 565.2284; found, 565.2314.

***N*-(3,5-Bis(trifluoromethyl)benzyl)-*O*-(3,5-bis(trifluoromethyl)-benzyl)quinidinium Chloride (M)**: To a solution of *N*-(3,5-bis(trifluoromethyl)benzyl)-*O*-(3,5-bis(trifluoromethyl)benzyl)quinidinium bromide[29b] (551 mg, 0.640 mmol) in CH_2Cl_2 (30 mL) and water (3 mL), was added NaCl (186 mg, 3.20 mmol). The mixture was stirred vigorously at rt for 20 h. The organic layer was separated and washed with brine, which was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo to give the title compound (435 mg, 85%) as a yellow solid of mp 168–171 °C with $[\alpha]_D^{20}$ +78.1 (c 1.00, $CHCl_3$): ^{1}H NMR: 8.80 (br d, *J* = 4.0, 1H), 8.57 (br m, 2H), 8.37 (br m, 1H), 8.29 (br s, 1H), 8.08 (br s, 1H), 8.04 (br d, *J* = 9.0, 1H), 7.77 (br s, 1H), 7.60–7.45 (m, 2H), 6.65 (br m, 1H), 5.97 (m, 1H), 5.40–5.05 (m, 5H), 4.69 (br d, *J* = 12.0, 1H), 4.40–3.85 (br m, 5H), 3.55 (br m, 1H), 2.97 (br m, 1H), 2.70–2.60 (m, 2H), 1.97 (br s, 1H), 1.88–1.68 (br m, 2H), 1.44 (br m, 1H). ^{13}C NMR: 158.2 (C), 147.8 (CH), 144.6 (C), 141.3 (C), 139.2 (C), 137.6 (CH), 135.1 (CH), 131.9 (CH), 131.6 (C), 131.2 (q, *J* = 33, C), 130.8 (q, *J* = 33, C), 129.3 (CH), 126.8 (C), 124.7 (CH), 123.8 (q, *J* = 271, C), 123.6 (q, *J* = 271, C), 122.1 (CH), 117.1 (CH_2), 102.9 (CH), 73.0 (CH), 69.3 (CH_2), 69.2 (CH), 62.2 (CH_2), 56.2 (CH_2), 55.1 (CH_3), 55.0 (CH_2), 37.3 (CH), 26.7 (CH), 23.4 (CH_2), 21.4 (CH_2). IR (KBr): 2955, 1623, 1509, 1464, 1373, 1280, 1178, 1135, 1032, 902, 842, 707, 682. HRMS–ESI (*m*/*z*): $[M - Cl]^+$ calcd for $C_{38}H_{33}F_{12}N_2O_2$, 777.2345; found, 777.2338.

***N*-(3,5-Bis(trifluoromethyl)benzyl)-*O*-(3,5-bis(trifluoromethyl)-benzyl)quininium Chloride (N):** To a suspension of *N*-(3,5-bis(trifluoromethyl)benzyl)quininium bromide[28b] (778 mg, 1.25 mmol) in CH_2Cl_2 (8.0 mL), were added 3,5-bis(trifluoromethyl)benzyl bromide (1.1 mL, 6.3 mmol) and 50% aqueous KOH (700 µL, 6.25 mmol). The mixture was stirred vigorously at rt for 6 h, diluted with water (5 mL), and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were dried over Na_2SO_4, concentrated in vacuo, and purified by flash chromatography ($MeOH/CHCl_3$ 1:30 to 1:8) to give a yellow solid. To a solution of the yellow solid (750 mg, 0.875 mmol) in CH_2Cl_2 (30 mL) and water (3 mL), was added NaCl (254 mg, 4.38 mmol). The mixture was stirred vigorously at rt for 2.5 h. The organic layer was separated and washed with brine, which was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo to give the title compound (633 mg, 62%) as a yellow solid of mp 166.5–170 °C with $[\alpha]_D^{21}$ –74.6 (c 1.00, $CHCl_3$): ^{1}H NMR: 8.78 (d, *J* = 4.0, 1H), 8.65 (s, 2H), 8.32 (s, 2H), 8.20 (br s, 1H), 7.98 (d, *J* = 8.0, 1H), 7.97 (s, 1H), 7.75 (br m, 1H), 7.51 (br s, 1H), 7.37 (dd, *J* = 8.0, 2.0, 1H), 7.07 (br s, 1H), 6.50 (br s, 1H), 5.75 (ddd, *J* = 16.0, 10.0, 7.0, 1H), 5.50 (d, *J* = 12.0, 1H), 5.37 (d, *J* = 12.0, 1H), 5.16 (d, *J* = 16.0, 1H), 4.99 (d, *J* = 10.0, 1H), 4.74 (d, *J* = 12.0, 1H), 4.17 (br m, 1H), 4.15–3.95 (m, 2H), 3.94 (s, 3H), 3.50–3.30 (m, 2H), 2.65 (m, 1H), 2.57 (m, 1H), 2.00–2.07 (br m, 2H), 1.80

(br m, 1H), 1.68 (br m, 1H). ^{13}C NMR: 157.6 (C), 147.2 (CH), 144.1 (C), 140.9 (C), 139.6 (C), 137.6 (CH), 134.7 (CH), 131.5 (C), 131.2 (CH), 130.6 (q, *J* = 33, C), 130.2 (q, *J* = 33, C), 129.1 (CH), 126.1 (C), 123.7 (CH), 123.2 (q, *J* = 271, C), 123.1 (q, *J* = 271, C), 121.9 (CH), 121.3 (CH), 120.0 (CH), 116.7 (CH_2), 101.6 (CH), 71.8 (CH), 69.0 (CH), 68.6 (CH_2), 61.5 (CH_2), 58.4 (CH_2), 55.5 (CH_3), 50.4 (CH_2), 37.0 (CH), 26.2 (CH), 23.9 (CH_2), 19.9 (CH_2). IR (KBr): 2976, 1623, 1509, 1474, 1374, 1281, 1179, 1136, 1072, 903, 843, 682. HRMS–ESI (*m*/*z*): [M – Cl]$^+$ calcd for $C_{38}H_{33}F_{12}N_2O_2$, 777.2345; found, 777.2344.

Preparation of Substrates. Propargyl sulfones **1a**–**1e** were prepared in the reported procedures.[2]

General Procedure for Chiral Pyridine Mediated Reactions. 1-(1-Tosylvinyl)isochromane (2c): A 10 mL flame-dried test tube with a magnetic stirring bar was charged with **1c** (31.4 mg, 100 µmol) and **D** (3.7 mg, 5.0 µmol). The tube was filled with argon by evacuate-and-refill processes. After addition of toluene (0.5 mL), the mixture was stirred at 80 °C for 36 h, cooled to rt, and concentrated. The residue was purified by column chromatography (hexane/EtOAc 2:1) to give the title compound (6.0 mg, 19%) as a yellow oil. The spectroscopic data were identical to those reported.[2] The enantiomeric ratio was determined to be 59:41 by chiral stationary phase HPLC analysis (CHIRALPAK AD–H, hexane/*i*-PrOH 10:1, 1.1 mL/min, 254 nm, t_R = 15.7 min for *R* and 21.2 min for *S*). The absolute configuration of the major enantiomer was opposite to that provided by catalysts **C** and **M**, and thus tentatively assigned to *R* by analogy to **2a**.

General Procedure for Chiral Ammonium Mediated Reactions. 2-(1-Tosylvinyl)tetrahydrofuran (2a): A 10 mL flame-dried test tube was charged with a magnetic stirring bar, **M** (16.3 mg, 20.0 µmol), NaTs (1.8 mg, 10 µmol), and Na_2CO_3 (0.5 mg, 5.0 µmol). The tube was filled with argon by evacuate-and-refill processes. After addition of toluene (0.5 mL), the mixture was stirred at 60 °C for 5 min. Then, **1a** (25.2 mg, 100 µmol) in toluene (1.0 mL) was added, and the mixture was stirred at 60 °C for 20 h, cooled to room temperature, and diluted with EtOAc (10 mL) and H_2O (5 mL). The organic layer was separated, washed with brine (10 mL), dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography (hexane/EtOAc 5:2) to give the title compound (22.1 mg, 88%) in 65:35 er as a colorless oil with $[\alpha]_D^{29}$ +2.63 (*c* 1.00, $CHCl_3$). The spectroscopic data were identical to those reported.[2] The enantiomeric ratio was determined by chiral stationary phase HPLC analysis (CHIRALPAK AD-H, hexane/*i*-PrOH 97:3, 1.0 mL/min, 254 nm, t_R = 17.4 min for *S* and 22.0 min for *R*). The absolute configuration of the major enantiomer was assigned to *S* by the ECD method (*vide infra*).

1-Tosyl-2-(1-tosylvinyl)pyrrolidine (2b) and 1-Tosyl-6-(tosylmethyl)-1,2,3,4-tetrahydropyridine (3b): The typical procedure using **G** (19.9 mg, 20.0 µmol) and **1b** (40.6 mg, 100 µmol) in place of **M** and **1a**, and purification by column chromatography (hexane/EtOAc 2:1) gave a 96:4 mixture of **2b** in 62:38 er and **3b** (16.8 mg, 40% and 2%, respectively) as a yellow oil with $[\alpha]_D^{29}$ –35 (*c* 0.46, $CHCl_3$). The spectroscopic data were identical to those reported.[2] The ratio of **2b** and **3b** was determined by the integral area of the ^{1}H NMR signals at 6.46 and 5.66 ppm. The enantiomeric ratio of **2b** was determined by chiral stationary phase HPLC analysis (CHIRALPAK 3A, hexane/*i*-PrOH 85:15, 1.0 mL/min, 254 nm, t_R = 16.1 min for *S*-**2b**, 18.3 min for *R*-**2b**, and 32.8 min for **3b**). The absolute configuration of the major enantiomer of **2b** was assigned to *S* by the ECD method (*vide infra*).

1-(1-Tosylvinyl)isochromane (2c): The typical procedure using **1c** (31.4 mg, 100 µmol) in place of **1a** and purification by column chromatography (hexane/EtOAc 2:1) gave the title compound (15.8 mg, 50%) in 54:46 er as a yellow oil with $[\alpha]_D^{20}$ +14 (*c* 0.80, $CHCl_3$). The spectroscopic data were identical to those reported.[2] The enantiomeric ratio was determined by chiral stationary phase HPLC analysis (CHIRALPAK AD–H, hexane/*i*-PrOH 10:1, 1.1 mL/min, 254 nm, t_R = 15.7 min for *R* and 21.2 min for *S*). The absolute configuration of the major enantiomer was tentatively assigned to *S* by analogy to **2a**.

2,2-Diallyl-5-(1-tosylvinyl)tetrahydrofuran (2d): The typical procedure using **1e** (33.2 mg, 100 µmol) in place of **1a** and purification by column chromatography (hexane/EtOAc 2:1) gave the title compound (24.0 mg, 72%) in 57:43 er as a yellow oil with $[\alpha]_D^{25}$ –1.94 (*c* 1.30, $CHCl_3$). The spectroscopic data were identical to those reported.[2] The enantiomeric ratio was determined by chiral stationary phase HPLC analysis (CHIRALPAK AS-3, hexane/*i*-PrOH 19:1, 1.0 mL/min, 254 nm, t_R = 17.0 min for *R* and 20.7 min for *S*). The absolute configuration of the major enantiomer was tentatively assigned to *S* by analogy to **2a**.

2-(1-Tosylvinyl)tetrahydro-2*H*-pyran (2e): The typical procedure using **1d** (26.6 mg, 100 µmol) in place of **1a** and purification by column chromatography (hexane/EtOAc 2:1) gave the title compound (16.4 mg, 62%) in 55:45 er as a yellow oil with $[\alpha]_D^{18}$ +1.01 (*c* 1.20, $CHCl_3$). The spectroscopic data were identical to those reported.[2] The enantiomeric ratio was determined by chiral stationary phase HPLC analysis (CHIRALPAK 3A, hexane/*i*-PrOH 99:1, 1.0 mL/min, 254 nm, t_R = 18.8 min for *S* and 22.2 min for *R*). The absolute configuration of the major enantiomer was tentatively assigned to *S* by analogy to **2a**.

Reaction of 1a with Sodium 4-Methoxybenzenesulfinate (Scheme 5). 2-(1-Tosylvinyl)tetrahydrofuran (2a) and 2-(1-(4-Methoxybenzenesulfonyl)vinyl)tetrahydrofuran (4): A 30 mL flame-dried round-bottom flask was charged with a magnetic stirring bar, sodium 4-methoxybenzenesulfinate (106 mg, 550 µmol),[38] and Cs_2CO_3 (30.6 mg, 100 µmol). The flask was filled with argon by evacuate-and-refill processes. After addition of toluene (6.0 mL), the mixture was heated under reflux for 30 min with continuous stirring. Then, 1a (126 mg, 500 µmol) in toluene (1.5 mL) was added, and the mixture was heated under reflux for additional 30 min, cooled to room temperature, and diluted with EtOAc (10 mL) and H_2O (10 mL). The aqueous layer was separated and extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography (hexane/EtOAc 5:1 to 2:1) to give 2a (98.5 mg, 78%) as a colorless oil and 4 (14.5 mg, 11%) as a yellow oil: ^{1}H NMR ($CDCl_3$): 7.80 (d, *J* = 9.0, 2H), 6.99 (d, *J* = 9.0, 2H), 6.32 (s, 1H), 6.02 (s, 1H), 4.51 (t, *J* = 7.0, 1H), 3.93 (td, *J* = 7.0, 6.5, 1H), 3.88 (s, 3H), 3.77 (td, *J* = 7.0, 6.5, 1H), 2.21 (m, 1H), 2.00–1.80 (m, 3H). ^{13}C NMR ($CDCl_3$): 163.6 (C), 152.9 (C), 130.9 (C), 130.4 (CH), 122.4 (CH_2), 114.4 (CH), 75.7 (CH), 68.6 (CH_2), 55.6 (CH_3), 33.0 (CH_2), 25.6 (CH_2). IR (neat): 2960, 2917, 2854, 1592, 1497, 1380, 1311, 1264, 1165, 1056, 839. HRMS–ESI (*m*/*z*): [M + Na]+ calcd for $C_{13}H_{16}O_4NaS$, 291.0667; found, 291.0679.

Assignment of the Absolute Configuration: Calculations of the ECD Spectra. The conformatinal searches of *S*-**2a** and *S*-**2b** were performed with the MMFF using Spartan 18 program.[39] The geometries of the conformers found for *S*-**2a** and *S*-**2b** with Boltzmann distributions over 1% (four and nine conformers, respectively) were further optimized at the B3LYP/6-31G(d) theoretical level using Gaussian 09 program.[40] The optimized geometries were subjected to TDDFT calculations at the B3LYP/6–31+G(d) theoretical level with the PCM correction for MeOH. The resultant rotatory strengths of the lowest 30 excited states were converted into Gaussian-type curves with half-bands of 0.2 eV using SpecDis v1.61.[41] The calculated ECD spectrum of *S*-**2a** was shifted by –10 nm.

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References and Notes

1. (a) Inokuma, T.; Sakakibara, T.; Someno, T.; Masui, K.; Shigenaga, A.; Otaka, A.; Yamada, K. *Chem. —Eur. J.* **2019**, *25*, 13829. (b) Mogi, Y.; Inanaga, K.; Tokuyama, H.; Ihara, M.; Yamaoka, Y.; Yamada, K.; Takasu, K. *Org. Lett.* **2019**, *21*, 3954. (c) Kono, M.; Harada, S.; Nozaki, T.; Hashimoto, Y.; Murata, S.; Gröger, H.; Kuroda, Y.; Yamada, K.; Takasu, K.; Hamada, Y.; Nemoto, T. *Org. Lett.* **2019**, *21*, 3750. (d) Kiyama, H.; Inokuma, T.; Kuroda, Y.; Yamaoka, Y.; Takasu, K.; Yamada, K. *Tetrahedron Lett.* **2019**, *60*, 175. (e) Jichu, T.; Inokuma, T.; Aihara, K.; Kohiki, T.; Nishida, K.; Shigenaga, A.; Yamada, K.; Otaka, A. *ChemCatChem* **2018**, *10*, 3402. (f) Inokuma, T.; Nishida, K.; Shigenaga, A.; Yamada, K.; Otaka, A. *Heterocycles* **2018**, *97*, 1269. (g) Yamaoka, Y.; Ueda, M.; Yamashita, T.; Shimoda, K.; Yamada, K.; Takasu, K. *Tetrahedron Lett.* **2017**, *58*, 2944. (h) Kang, B.; Wang, Y.; Kuwano, S.; Yamaoka, Y.; Takasu, K.; Yamada, K. *Chem. Commun.* **2017**, *53*, 4469. (i) Kuroda, Y.; Harada, S.; Oonishi, A.; Kiyama, H.; Yamaoka, Y.; Yamada, K.; Takasu, K. *Angew. Chem. Int. Ed.* **2016**, *55*, 13137. (j) Yamada, K.; Oonishi, A.; Kuroda, Y.; Harada, S.; Kiyama, H.; Yamaoka, Y.; Takasu, K. *Tetrahedron Lett.* **2016**, *57*, 4098. (k) Kuroda, Y.; Harada, S.; Oonishi, A.; Yamaoka, Y.; Yamada, K.; Takasu, K. *Angew. Chem. Int. Ed.* **2015**, *54*, 8263. (l) Fujiwara, S.; Romain, C.; Yamaoka, Y.; Takasu, K.; Yamada, K. *Eur. J. Org. Chem.* **2015**, 1264. (m) Kang, B.; Sutou, T.; Wang, Y.; Kuwano, S.; Yamaoka, Y.; Takasu, K.; Yamada, K. *Adv. Synth. Catal.* **2015**, *357*, 131. (n) Kuwano, S.; Harada, S.; Kang, B.; Oriez, R.; Yamaoka, Y.; Takasu, K.; Yamada, K. *J. Am. Chem. Soc.* **2013**, *135*, 11485. (o) Harada, S.; Kuwano, S.; Yamaoka, Y.; Yamada, K.; Takasu, K. *Angew. Chem. Int. Ed.* **2013**, *52*, 10227. (p) Kuwano, S.; Harada, S.; Oriez, R.; Yamada, K. *Chem. Commun.* **2012**, *48*, 145.
2. Wang, Y.; Oriez, R.; Kuwano, S.; Yamaoka, Y.; Takasu, K.; Yamada, K. *J. Org. Chem.* **2016**, *81*, 2652.
3. Wang, Y.; Oriez, R.; Oh, S.; Miyakawa, Y.; Yamaoka, Y.; Takasu, K.; Yamada, K. *Heterocycles* **2017**, *95*, 314.
4. Review: Flynn, A. J.; Ford, A.; Maguire, A. R. *Org. Biomol. Chem.* **2020**, *18*, 2549.
5. Recent examples of sulfonyl migration reactions: (a) Xiong, B.; Chen, L.; Xu, J.; Sun, H.; Li, X.; Li, Y.; Lian, Z. *Org. Lett.* **2020**, *22*, 9263. (b) Omer, H. M.; Liu, P.; Brummond, K. M. *J. Org. Chem.* **2020**, *85*, 7959. (c) Heo, N.; Jung, I.; Kim, D. K.; Han, S. H.; Lee, K.; Lee, P. H. *Org. Lett.* **2020**, *22*, 6562. (d) Zeng, L.; Lin, Y.; Li, J.; Sajiki, H.; Xie, H.; Cui, S. *Nat. Commun.* **2020**, *11*, 5639. (e) Martzel, T.; Lohier, J.–F.; Gaumont, A.–C.; Brière, J.–F.; Perrio, S. *Adv. Synth. Catal.* **2018**, *360*, 2696. (f) Martzel, T.; Lohier, J.–F.; Gaumont, A.–C.; Brière, J.–F.; Perrio, S. *Eur. J. Org. Chem.* **2018**, 5069. (g) Kuwano, S.; Masuda, T.; Yamaguchi, K.; Arai , T. *Heterocycles* **2017**, *95*, 232. (h) Miao, M.; Luo, Y.; Xu, H.; Chen, Z.; Xu, J.; Ren, H. *Org. Lett.* **2016**, *18*, 4292.
6. (a) Padwa, A.; Yeske, P. E. *J. Am. Chem. Soc.* **1988**, *110*, 1617. (b) Padwa, A.; Yeske, P. E. *J. Org. Chem.* **1991**, *56*, 6386.
7. Representative examples of γ-umpolung reactions: (a) Trost, B. M.; Li, C.-J. *J. Am. Chem. Soc.* **1994**, *116*, 10819. (b) Trost, B. M.; Dake, G. R. *J. Org. Chem.* **1997**, *62*, 5670.
8. (a) Stirling, C. J. M. *J. Chem. Soc.* **1964**, 5856. (b) Stirling, C. J. M. *J. Chem. Soc.* **1964**, 5863. (c) Back, T. G.; Clary, K. N.; Gao, D. *Chem. Rev.* **2010**, *110*, 4498.
9. Our preliminary results were reported in ref. 3.
10. Kerr, M. S.; Read de Alaniz, J.; Rovis, T. *J. Am. Chem. Soc.* **2002**, *124*, 10298.
11. He, M.; Struble, J. R.; Bode, J. W. *J. Am. Chem. Soc.* **2006**, *128*, 8418.
12. Uozumi, Y.; Hayashi, T. *J. Am. Chem. Soc.* **1991**, *113*, 9887.
13. Alcock, N. W.; Brown, J. M.; Hulmes, D. I. *Tetrahedron: Asymmetry* **1993**, *4*, 743.
14. Zhu, S.-F.; Yang, Y.; Wang, L.-X.; Liu, B.; Zhou, Q.-L. *Org. Lett.* **2005**, *7*, 2333.
15. Fryzuk, M. D.; Bosnich, B. *J. Am. Chem. Soc.* **1977**, *99*, 6262.
16. Nagel, U.; Kinzel, E. *Chem. Ber.* **1986**, *119*, 3326.
17. Knowles, W. S.; Sabacky, M. J.; Vineyard, B. D.; Weinkauff, D. J. *J. Am. Chem. Soc.* **1975**, *97*, 2567.
18. Burk, M. J. *J. Am. Chem. Soc.* **1991**, *113*, 8518.
19. Kawabata, T.; Muramatsu, W.; Nishio, T.; Shibata, T.; Schedel, H. *J. Am. Chem. Soc.* **2007**, *129*, 12890.
20. Mandai, H.; Fujii, K.; Yasuhara, H.; Abe, K.; Mitsudo, K.; Korenaga, T.; Suga, S. *Nat. Commun.* **2016**, *7*, 11297.
21. The absolute configuration of the major enantiomers was tentatively assigned by analogy to *S*-**2a**.
22. Kitamura, M.; Shirakawa, S.; Maruoka, K. *Angew. Chem. Int. Ed.* **2005**, *44*, 1549.
23. (a) Ooi, T.; Kameda, M.; Maruoka, K. *J. Am. Chem. Soc.* **1999**, *121*, 6519. (b) Ooi, T.; Takeuchi, M.; Kameda, M.; Maruoka, K. *J. Am. Chem. Soc.* **2000**, *122*, 5228.
24. Lygo, B.; Allbutt, B.; James, S. R. *Tetrahedron Lett.* **2003**, *44*, 5629.
25. Lygo, B.; Wainwright, P. G. *Tetrahedron Lett.* **1997**, *38*, 8595.
26. Arai, S.; Ishida, T.; Shioiri, T. *Tetrahedron Lett.* **1998**, *39*, 8299.
27. Denmark, S. E.; Weintraub, R. C. *Heterocycles* **2011**, *82*, 1527.
28. (a) Hu, X.; Wang, J.; Li, W.; Lin, L.; Liu, X.; Feng, X. *Tetrahedron Lett.* **2009**, *50*, 4378. (b) Matoba, K.; Kawai, H.; Furukawa, T.; Kusuda, A.; Tokunaga, E.; Nakamura, S.; Shiro, M.; Shibata, N. *Angew. Chem. Int. Ed.* **2010**, *49*, 5762.
29. (a) Bernardi, L.; Fini, F.; Fochi, M.; Ricci, A. *Synlett* **2008**, 1857. (b) Wu, S.; Zeng, W.; Wang, Q.; Chen, F.-X. *Org. Biomol. Chem.* **2012**, *10*, 9334.
30. Nugroho, A. E.; Morita, H. *J. Nat. Med.* **2014**, *68*, 1.
31. Kerr, M. S.; Read de Alaniz, J.; Rovis, T. *J. Org. Chem.* **2005,** *70,* 5725.
32. Kobayashi, S.; Kinoshita, T.; Uehara, H; Sudo, T. Ryu, I. *Org. Lett.* **2009**, *11*, 3934.
33. Hashimoto, T.; Sakata, K.; Tamakuni, F.; Dutton, M. J.; Maruoka, K. *Nat. Chem.* **2013**, *5*, 240.
34. Boyd, W. C.; Crimmin, M. R.; Rosebrugh, L. E.; Schomaker, J. M.; Bergman, R. G.; Toste, F. D. *J. Am. Chem. Soc.* **2010**, *132*, 16365.
35. Lygo, B.; Allbutt, B.; Beaumont, D. J.; Butt, U.; Gilks, J. A. R. *Synlett* **2009**, 675.
36. Li, H.; Wang, Y.; Tang, L.; Deng, L. *J. Am. Chem. Soc.* **2004**, *126,* 9906.
37. Matoba, K.; Kawai, H.; Furukawa, T.; Kusuda, A.; Tokunaga, E.; Nakamura, S.; Shiro, M.; Shibata, N. *Angew. Chem. Int. Ed.* **2010,** *49,* 5762.
38. Lv, F.; Guo, X.; Wu, H.; Li, H.; Tang, B.; Yu, C.; Hao, E.; Jiao, L. *Chem. Commun.* **2020**, 15577.
39. *Spartan '18*, Wavefunction Inc. Irvine, CA.
40. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; et al. *Gaussian 09, Revision C. 01*, Gaussian, Wallingford, CT, 2010.
41. Schaumloffel, T.; Hemberger, A.; Bringmann, Y. *SpecDis Version 1.61*, University of Wuerzburg, Germany, 2013.