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Desymmetrization and Switching of Stereoselectivity in Direct Organocatalytic Michael Addition of Ketones to 1,1-Bis(phenylsulfonyl)ethylene

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The organocatalytic desymmetrization was demonstrated for 4-substituted cyclohexanones by treatment with a vinyl sulfone in the presence of an organocatalyst. The desired Michael adducts were typically obtained in high chemical yields and high to excellent stereoselectivities (up to 97 % yield, 93 % *ee*). An efficient desymmetrization method was developed for the synthesis of enantiomeric products by using either camphor-derived pyrrolidine **V** or cinchonidine-derived primary amine **VII** as a catalyst. The absolute stereochemistry of the (2*R*,4*R*)-2-[2,2-bis(phenylsulfonyl)ethyl]-4-methylcyclohexanone (**3a**) and (2*R*,4*R*)-2-[2,2-bis(phenylsulfonyl)ethyl]-4-*tert*-butylcyclohexanone (**3b**) was confirmed by single-crystal X-ray structure analyses.

Introduction

Recently, the use of small organic molecules to catalyze organic reactions has been recognized as a powerful protocol for asymmetric synthesis, complemented by the use of enzymes and transition-metal complexes.[1] In the emerging field of organocatalysis, the conjugate addition of carbon nucleophiles to electron-deficient Michael acceptors has become one of the most efficient and reliable carbon–carbon bond-forming reactions.[2] The sulfonyl group is a valuable functionality that can be used in organic reactions for numerous chemical transformations.[3] The use of vinyl sulfones as Michael acceptors in the presence of organocatalysts to form enantiomerically enriched products has been previously studied by Alexakis.[4] Considerable efforts have been directed to the development of the enantioselective catalysis of vinyl sulfones.[5] In recent years, desymmetrization has attracted much attention for the synthesis of chiral non-racemic molecules.[6] The desymmetrization process results in the loss of one or more symmetry elements and converts prochiral/*meso* molecules into optically active products. The use of catalytic desymmetrization represents a convenient protocol for the preparation of synthetically useful intermediates. Transition-metal-mediated[7] and metal-free[8] enantioselective desymmetrizations have been documented. Additionally, the development of organocatalytic protocols for the asymmetric synthesis of both enantiomeric products is synthetically practical and worth pursuing.[9]

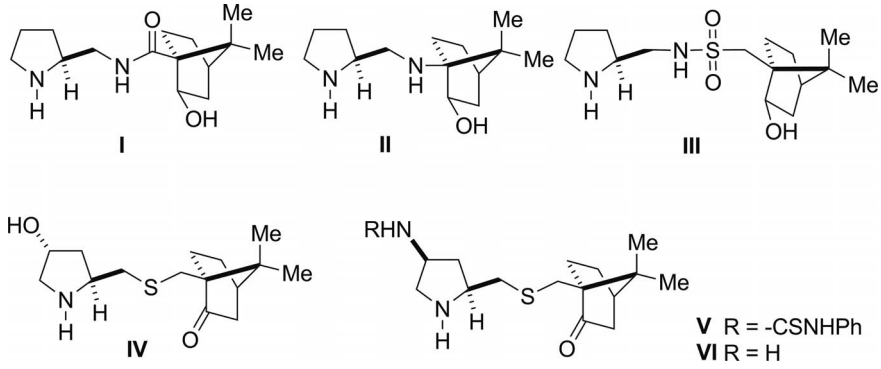

Figure 1. Chemical structures of various organocatalysts.

In our continued effort to develop new organocatalysts, we envision that the well-defined, rigid, bicyclic camphor scaffold can serve as an efficient element of stereocontrol.[10] The assembly of a pyrrolidine and camphor framework with an appropriate linker can yield a new class of bifunctional organocatalysts (see Figure 1).

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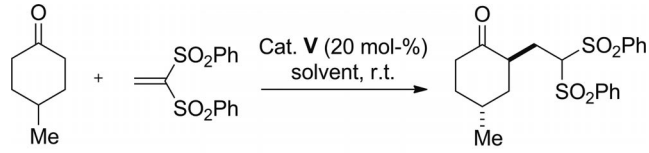
In addition to the linker moiety, the pyrrolidine C-4 and the C-2 atom in the camphor moiety can be functionalized to enhance hydrogen-bonding interactions in the transition state. The installation of a thiourea moiety at the C-4 position of the pyrrolidine would provide an interesting influence on an organocatalytic reaction. In this context, we report the synthesis of a camphor-derived pyrrolidine that contains a thiourea group at the C-4 position (i.e., **V**). The direct desymmetrization of 4-substituted cyclohexanone through an asymmetric Michael addition to 1,1-bis(phenylsulfonyl)ethylene was examined. Both enantiomeric Michael products were obtained with high stereoselectivities in reactions that were catalyzed by **V** or the cinchonidine-derived catalyst **VII**, respectively.

Results and Discussion

The design and synthesis of readily accessible, highly stereoselective, and tunable asymmetric catalysts are always desirable. We expect that organocatalyst **V** could be prepared from the known L-proline-derived *N*-Boc-protected tosylate **4** and (1*S*)-1-(mercaptomethyl)-7,7-dimethylbicyclo[2.2.1]heptan-2-one (**5**) as illustrated in Scheme 1. Ketone sulfide **6** was obtained in 88% yield by treating the *N*-Boc-protected tosyl prolinol **4** with **5** in the presence of NaH as a base. The amino ketone sulfide **7** was obtained through a three-step procedure with a favorable overall chemical yield. By using a standard procedure, the thiourea functionality was incorporated followed by a subsequent deprotection to give **V**. The structure of organocatalyst **V** was fully characterized by IR, HRMS, and ^{1}H and ^{13}C NMR spectroscopy and then further verified by single-crystal X-ray structure analysis.[11,12]

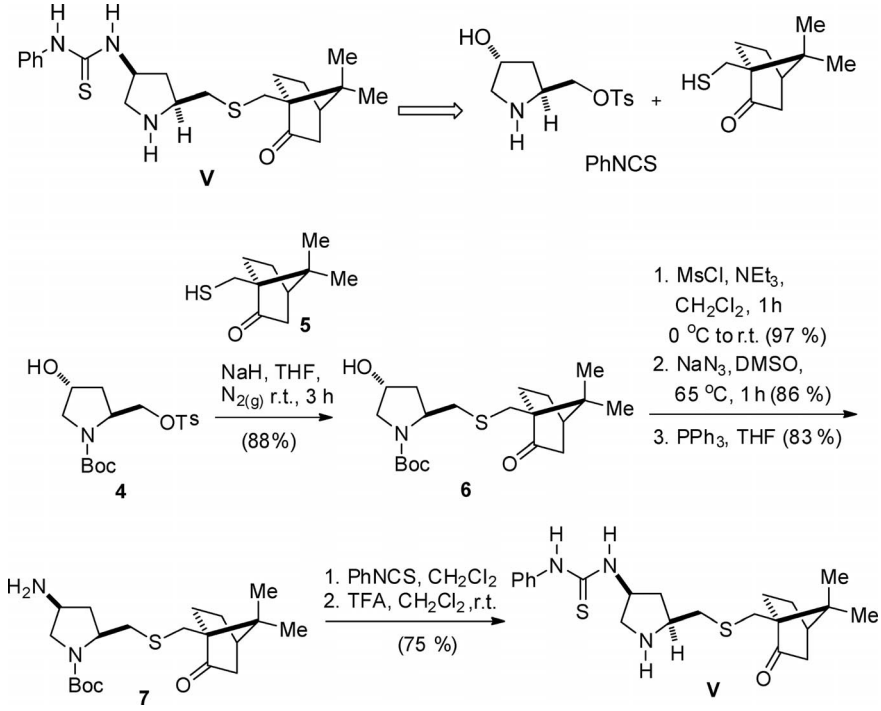
After the success of synthesizing organocatalyst **V**, its efficacy in the Michael addition reaction was examined (see Table 1). 1,1-Bis(phenylsulfonyl)ethylene (**2**) and 4-methyl-

Table 1. Optimization of the Michael reaction of 4-methylcyclohexanone (**1a**) with 1,1-bis(phenylsulfonyl)ethylene (**2**).[a]



Entry	Catalyst	Solvent	*t* [d]	% Yield[b]	*dr*[c]	% *ee*[c]
1	**V**	hexane	2	N.R.	–	–
2	**V**	toluene	2	54	3:1	89
3	**V**	$CHCl_3$	2	75	3:1	88
4	**V**	CH_2Cl_2	2	41	4:1	90
5	**V**	EA	2	28	5:1	90
6	**V**	ether	2	32	4:1	87
7	**V**	MeCN	2	20	6:1	80
8	**V**	MeOH	2	40	7:1	17
9	**I**	$CHCl_3$	3	17	7:1	54
10	**II**	$CHCl_3$	3	40	1:1	53[d]
11	**III**	$CHCl_3$	3	<10	–	–
12	**IV**	$CHCl_3$	3	35	5:1	77
13	**VI**	$CHCl_3$	2	50	2:1	40

[a] All reactions were carried out with 4-methylcyclohexanone (**1a**, 2.0 equiv.) and 1,1-bis(phenylsulfonyl)ethylene (**2**, 1.0 equiv.) with the organocatalyst (20 mol-%) at ambient temperature. [b] Isolated yield. [c] Determined by chiral AS-H HPLC analysis. [d] The major diastereomer.

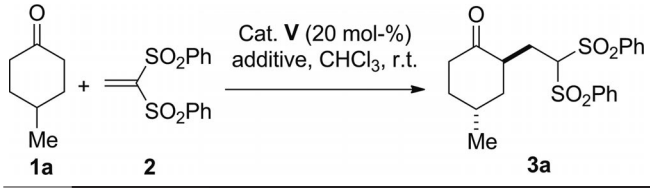


Scheme 1. Synthesis of camphor-derived pyrrolidine containing the thiourea functionality (i.e., organocatalyst **V**).

cyclohexanone (**1a**) were used as model substrates in the Michael reaction that was catalyzed by **V** (20 mol-%) at ambient temperature. Screening the solvents revealed that chloroform was the best option for the reaction. No reaction (N.R.) occurred when nonpolar hexane was used (see Table 1, Entry 1). The reactivity was slightly higher when toluene was used (see Table 1, Entry 2). To our delight, the desired product **3a** was obtained with high enantioselectivity (90% *ee*) in halogenated solvents (see Table 1, Entries 3 and 4). The reactivities were lower when polar solvents such as ethyl acetate (EA), ether, and MeCN were used (see Table 1, Entries 5–7). Both the chemical yield and the enantioselectivity were reduced when the reaction was performed in methanol (see Table 1, Entry 8). The disruption of the hydrogen-bonding interactions might account for this result. Next, the organocatalysts were screened. In CH_2Cl_2, catalysts **I**, **II**, and **IV** yielded the desired product with modest enantioselectivity and chemical yield (see Table 1, Entries 9, 10, and 12), but sulfonamide catalyst **III** yielded only a trace amount of the Michael adduct (see Table 1, Entry 11). A drop in stereoselectivity was observed when catalyst **VI**, with the C-4 amino group, was utilized (see Table 1, Entry 13), which indicates the importance of the thiourea functionality in the asymmetric Michael reaction. Two diastereomeric products were obtained, but they were inseparable by flash column chromatography. The diastereomeric ratios and enantioselectivity of the stereoisomers were determined by ^{1}H NMR and HPLC analyses.

Various acidic and basic additives were then investigated to improve the reaction further. Comparable results with improved reactivities were obtained when the reaction was carried out in the presence of $PhCO_2H$, acetic acid, and *para*-toluenesulfonic acid (*p*-TsOH, see Table 2, Entries 2–4). The reactivity decreased when trifluoroacetic acid (TFA)

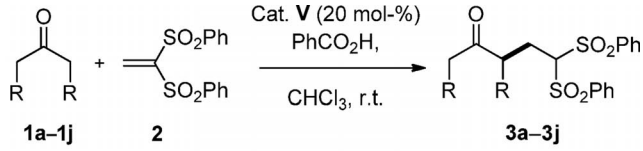
Table 2. Screening of additives in the asymmetric Michael addition reaction.[a]

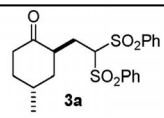
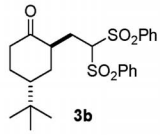
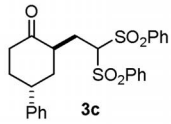
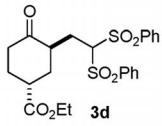
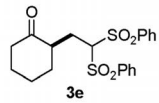
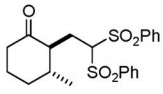
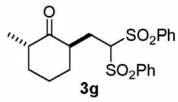
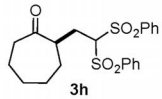
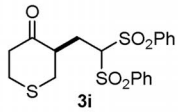
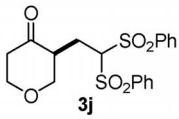


Entry	Additive	*t* [d]	% Yield[b]	*dr*[c]	% *ee*[c,d]
1	–	2	75	3:1	88
2	$PhCO_2H$	1	95	3:1	88
3	acetic acid	1	87	3:1	89
4	*p*-TsOH	1	82	5:1	87
5	TFA	1	17	2:1	15
6	NEt_3	1	trace	–	–
7	imidazole	1	62	3:1	89
8[e]	$PhCO_2H$	1	89	3:1	90

[a] All reactions were carried out with 4-methylcyclohexanone (**1a**, 2.0 equiv.) and 1,1-bis(phenylsulfonyl)ethylene (**2**, 1.0 equiv.), additive (20 mol-%), and organocatalyst **V** (20 mol-%) at ambient temperature. [b] Isolated yield. [c] Determined by chiral HPLC analysis. [d] The *ee* value reported corresponds to the major diastereomer. [e] The reaction was carried out from 0 °C to ambient temperature.

Table 3. Screening various cyclohexanones for Michael addition with vinyl sulfone **2** catalyzed by **V**.[a]



Entry	Product	Yield (%)[b]	*dr*[c]	% *ee*[c,d]
1	 **3a**	95	3:1	88
2	 **3b**	85	2:1	86
3	 **3c**	75	3:1	88
4	 **3d**	55	2:1	86
5	 **3e**	73	–	81
6	 **3f**	72	2:1.3:0.4	78[e]
7	 **3g**	trace	–	–
8	 **3h**	50	–	51
9	 **3i**	78	–	86
10	 **3j**	97	–	88

[a] All reactions were carried out with cyclohexanones **1a**–**1j** (2.0 equiv.) and 1,1-bis(phenylsulfonyl)ethylene (**2**, 1.0 equiv.) with organocatalyst **V** (20 mol-%) at ambient temperature. [b] Isolated yield. [c] Determined by chiral HPLC analysis. [d] The *ee* value reported corresponds to the major diastereomer. [e] The major diastereomer.

was used as an acidic additive. This is perhaps caused by the protonation of the secondary amine, which then hampers the enamine formation (see Table 2, Entry 5). The use of a basic additive failed to improve the reaction results (see Table 2, Entries 6 and 7).

Under the optimized reaction conditions, the scope of the methodology was investigated with 4-alkyl- or 4-aryl-substituted cyclohexanones **1** and 1,1-bis(phenylsulfonyl)-ethylene (**2**) in the presence of 20 mol-% of catalyst **V** in $CHCl_3$ at ambient temperature (see Table 3). A broad range of cyclohexanones **1a**–**1j** were investigated to evaluate the general utility of this asymmetric transformation. As presented in Table 3, the asymmetric desymmetrization process proceeded smoothly when 4-substituted cyclohexanones **1a**–**1d** were used to form the corresponding Michael adducts in high chemical yields and with high enantioselectivities (see Table 3, Entries 1–4). The use of 3-methylcyclohexanone (**1f**) provided the product with moderate selectivity (see Table 3, Entry 6). The two major diastereomers (2:1.3) were believed to be the 2,3- and 2,5-regioisomer with the two substituents located in the equatorial position. The use of a 2-methyl-substituted cyclohexanone gave trace amounts of the product (see Table 3, Entry 7). Moderate yields were obtained when cycloheptanone was employed (see Table 3, Entry 8). However, high chemical yields and high enantioselectivities were obtained when tetrahydrothiopyran-4-one and tetrahydropyran-4-one were used (see Table 3, Entries 9 and 10). The structures of the Michael products were determined by the analysis of the IR, HRMS, and ^1H and ^{13}C NMR spectroscopic data. The absolute stereochemistry of the two products (2*R*,4*R*)-**3a** and (2*R*,4*R*)-**3b** was further confirmed by single-crystal X-ray structure analyses (space groups are *P* 21/*n* and *P* 21/*c*, respectively).[12]

The enantioselective Michael addition of 4-methylcyclohexanone (**1a**, 10 equiv.) to 1,1-bis(phenylsulfonyl)ethylene (**2**, 1 equiv.) catalyzed by cinchonidine-derived primary amine **VII** has been reported.[13] However, careful examination of the HPLC chromatography results from this study reveals that a different stereoisomer was obtained when organocatalyst **VII** was used. To clarify this discrepancy, our protocol was expanded, and various quinine and cinchonidine-derived organocatalysts (i.e., **VII**–**X**) were systematically screened (see Figure 2).

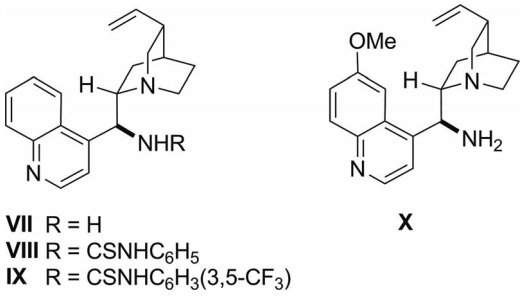
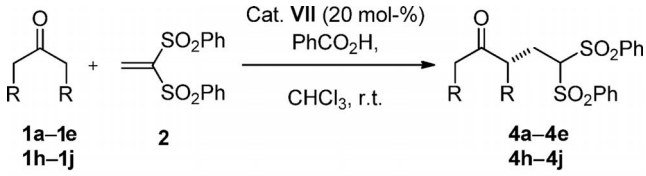
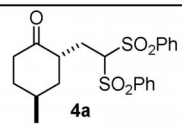
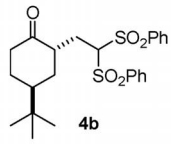
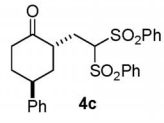
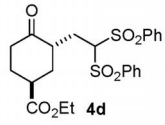
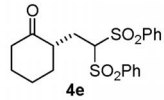
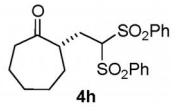
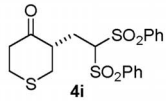
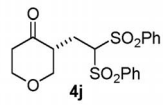


Figure 2. Chemical structures of organocatalysts **VII**–**X**.

The addition of 4-methylcyclohexanone (**1a**) and 1,1-bis(phenylsulfonyl)ethylene (**2**) in $CHCl_3$ was first conducted with cinchonidine-derived catalyst **VII** at ambient temperature. The product was obtained in good chemical yield with the high enantioselectivity of 92%*ee*. This result is comparable to that previously reported. However, the absolute stereochemistry of the major product was determined to have the (2*S*,4*S*) configuration, which is the enantiomer of the product obtained when organocatalyst **V** was used. The use of structurally related catalysts resulted in low reactivity (**VIII** afforded <10% chemical yield) or low stereoselectivi-

Table 4. Screening various cyclohexanones for Michael addition to 1,1-bis(phenylsulfonyl)ethylene (**2**) catalyzed by **VII**.[a]

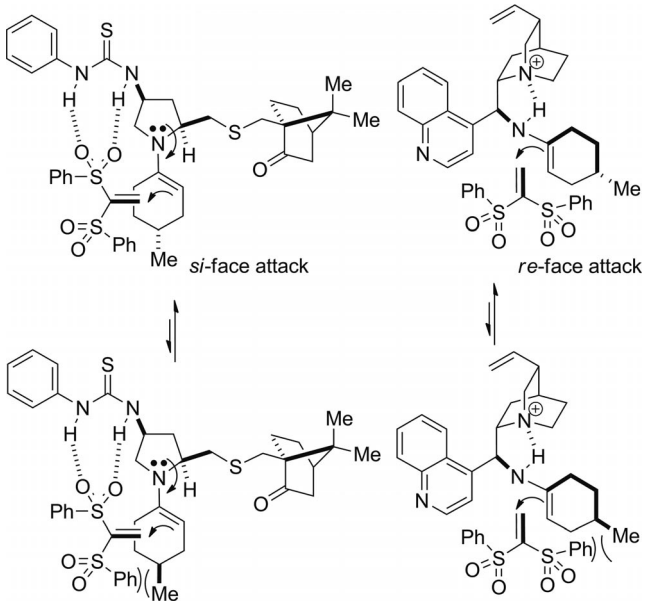


Entry	Product	Yield (%)[b]	*dr*[c]	% *ee*[c,d]
1	 **4a**	73	4:1	92
2	 **4b**	86	1:2	91
3	 **4c**	88	2:1	94
4	 **4d**	96	2:1	80
5	 **4e**	89	–	85
6	 **4h**	56	–	66
7	 **4i**	90	–	93
8	 **4j**	92	–	77

[a] All reactions were carried out with cyclohexanones **1a**–**1e** and **1h**–**1j** (2.0 equiv.) and 1,1-bis(phenylsulfonyl)ethylene (**2**, 1.0 equiv.) with organocatalyst **VII** (20 mol-%) at ambient temperature. [b] Isolated yield. [c] Determined by chiral HPLC analysis. [d] The *ee* value reported corresponds to the major diastereomer.

ties (**IX** afforded 39% yield, *dr* 6:1, 61%*ee*; **X** afforded 40% yield, *dr* 1:1, 40%*ee*). Therefore, catalyst **VII** was used for the asymmetric Michael additions to produce enantiomerically enriched ketosulfones (see Table 4). A series of cyclohexanones were employed, and comparable chemical yields and stereoselectivities were typically obtained (up to 96% chemical yield, 94%*ee*). The diastereomeric ratios in Entries 1–4 of Tables 3 and 4 ranged from 4:1 to 1:2. This may indicate that the 2,4-substituents are located in the axial and equatorial positions, respectively.

Although the mechanisms for the reactions in this study remain to be defined, two reaction modes are proposed and described in Scheme 2. The initial reaction of the camphor-derived pyrrolidine catalyst **V** with 4-methylcyclohexanone gave the nucleophilic enamine, as the vinyl sulfone, acting as the Michael acceptor, was activated by the thiourea moiety through a hydrogen-bonding interaction. This activation was followed by the addition of the nucleophilic enamine from the *si* face to the electrophilic component to generate the desired product **3a**. On the other hand, catalysis of the reaction by the cinchonidine-derived primary amine catalyst **VII** may also involve hydrogen-bonding interactions. The favored enamine was formed from the primary amino group of the catalyst and 4-methylcyclohexanone with the methyl group away from the 1,1-bis(phenylsulfonyl)ethylene (**2**). The bicyclic moiety selectively shielded the approach of the Michael acceptor. The conjugate addition occurred from the *re* face of the nucleophile to give the observed stereochemistry of Michael adduct **4a**.



Scheme 2. Plausible reaction mechanisms.

Conclusions

In summary, a new camphor-derived pyrrolidine organocatalyst that contains a thiourea group at the C-4 position was successfully synthesized. This study demonstrated that organocatalyst **V** effectively catalyzed the Michael reaction between cyclohexanones **1a**–**1j** and 1,1-bis(phenylsulfonyl)-ethylene (**2**). The enantiomeric products were obtained with high to excellent levels of stereoselectivity when the cinchonidine-derived catalyst **VII** was used. This methodology has proven to be effective for the purpose of asymmetric desymmetrization in the preparation of nonracemic chiral molecules. The asymmetric desymmetrization protocol is actively under investigation in our laboratory.

Experimental Section

General Remarks: Chemicals and solvents were purchased from commercial suppliers and used as received. The cyclohexanones and 1,1-bis(phenylsulfonyl)ethylene were purchased from Sigma–Aldrich and used as received. IR spectra were recorded with a Perkin–Elmer 500 spectrometer. The ^{1}H and ^{13}C NMR spectroscopic data were recorded with a Bruker Avance 400 (400 MHz) or Bruker Avance 500 (500 MHz) spectrometer. Chemical shifts are reported in δ (ppm) and referenced to TMS as an internal standard for ^{1}H NMR spectroscopy and to deuterated chloroform (δ = 77.0 ppm) as an internal standard for ^{13}C NMR spectroscopy. The abbreviations for the multiplicities of the NMR spectra are s (singlet), d (doublet), t (triplet), q (quartet), m (multiple), dd (doublet of doublet), and br. s (broad singlet). The coupling constants are reported in Hertz (Hz). All high resolution mass spectra were obtained with a Finnigan/MAT 95XL-T spectrometer. The X-ray diffraction measurements were carried out at 200 K with a KAPPA APEX II CCD area detector system equipped with a graphite monochromator and a Mo-K_α fine-focus sealed tube (k = 0.71073 Å). Merck precoated TLC plates (Merck 60 F254) were used for thin layer chromatography, and compounds were visualized under UV light at 254 nm. Solutions were evaporated to dryness under reduced pressure with a rotary evaporator, and the residues were purified by flash column chromatography on silica gel (230–400 mesh) with the indicated eluents. The enantiomeric excess value for a product was determined by chiral-phase HPLC analysis.

Synthesis of Catalyst V

***tert*-Butyl (2*S*,4*R*)-2-[({[(1*S*,4*S*)-7,7-Dimethyl-2-oxobicyclo[2.2.1]-heptan-1-yl]methyl}thio)methyl]-4-hydroxypyrrolidine-1-carboxylate (6):** To a solution of NaH (2.69 g, 67.30 mmol) were added sequentially a solution of **4** (5.00 g, 13.46 mmol) in tetrahydrofuran (THF, 20 mL) and **5** (2.98 g, 16.51 mmol) dropwise at ambient temperature. The reaction mixture was stirred for 3 h and then quenched with H_2O (10 mL). The mixture was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were washed with brine, dried with anhydrous $MgSO_4$, and filtered. Purification by flash column chromatography (hexanes/EtOAc, 2:1) gave the coupled product (88% yield) as a viscous liquid. $[\alpha]_D^{20}$ = –18.0 (c = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.45–4.41 (m, 1 H), 4.19–4.11 (m, 1 H), 3.61–3.43 (m, 2 H), 2.92 (d, J = 12.8 Hz, 1 H), 2.87 (d, J = 12.8 Hz, 1 H), 2.72–2.67 (m, 1 H), 2.57 (d, J = 12.0 Hz, 1 H), 2.36 (dq, J = 4.7, 2.6 Hz, 1 H), 2.15–1.95 (m, 6 H), 1.86 (d, J = 18.3 Hz, 1 H), 1.84–1.51 (m, 1 H), 1.39 (s, 9 H), 1.04 (s, 3 H), 0.90 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 216.9, 154.3, 79.5, 68.4, 60.5, 55.4, 54.6, 47.4, 43.1, 42.7, 38.7, 37.7, 29.7, 28.1, 26.4, 26.3, 19.9, 19.8 ppm. IR (CH_2Cl_2): $\tilde{\nu}$ = 3424, 3055, 2959, 2878, 1742, 1668, 1407 cm^{-1}. HRMS (EI): calcd. for $C_{20}H_{33}NO_4S$ 383.2130; found 383.2138.

***tert*-Butyl (2*S*,4*R*)-2-[({[(1*S*,4*S*)-7,7-Dimethyl-2-oxobicyclo[2.2.1]-heptan-1-yl]methyl}thio)methyl]-4-[(methylsulfonyl)oxy]pyrrolidine-**

1-carboxylate: To a solution of ketosulfide **6** (2.50 g, 6.50 mmol) in CH_2Cl_2 (10 mL) were added Et_3N (1.8 mL, 13 mmol) and methanesulfonyl chloride (MsCl, 0.75 mL, 9.77 mmol) dropwise at 0 °C. After stirring for 1 h, the reaction mixture was quenched with H_2O (5.0 mL), and the resulting solution was adjusted to pH = 9–10 with an aqueous solution of $NaHCO_3$ (1.0 M). The reaction mixture was then extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were washed with brine, dried with anhydrous $MgSO_4$, and filtered. Purification by flash column chromatography (hexanes/EtOAc, 2:1) gave the product (97% yield) as a viscous liquid. $[\alpha]_D^{20}$ = –17.8 (*c* = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.19 (s, 1 H), 4.30–4.10 (m, 1 H), 4.02–3.78 (m, 1 H), 3.64–3.49 (m, 1 H), 3.03 (s, 3 H), 2.95–2.75 (m, 2 H), 2.83 (d, *J* = 12.8 Hz, 1 H), 2.62–2.30 (m, 3 H), 2.30–2.18 (m, 1 H), 2.10–1.90 (m, 3 H), 1.84 (d, *J* = 18.4 Hz, 1 H), 1.55–1.40 (m, 1 H), 1.45 (s, 9 H), 1.40–1.30 (m, 1 H), 0.98 (s, 3 H), 0.85 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 217.0, 154.0, 80.4, 78.8, 60.8, 55.4, 52.5, 47.7, 43.4, 43.0, 38.6, 38.0, 36.7, 31.5, 30.2, 28.3, 26.7, 20.1, 20.0 ppm. IR (CH_2Cl_2): $\tilde{\nu}$ = 2968, 2887, 1741, 1693, 1479, 1398 cm^{-1}. HRMS (EI): calcd. for $C_{21}H_{35}NO_6S_2$ 461.1906; found 461.1908.

***tert*-Butyl (2*S*,4*S*)-4-Azido-2-[({[(1*S*,4*S*)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl]methyl}thio)methyl]pyrrolidine-1-carboxylate:** To a solution of the previously prepared mesylate compound (2.58 g, 5.59 mmol) in dimethyl sulfoxide (DMSO, 10 mL) was added NaN_3 (1.80 g, 28 mmol). The resulting mixture was heated to 65 °C for 1 h. The reaction mixture was quenched with H_2O, and the resulting solution was then extracted with diethyl ether. The combined organic layers were washed with brine, dried with anhydrous $MgSO_4$, and filtered. Purification by flash column chromatography (hexanes/EtOAc, 5:1) gave the product (86% yield) as a viscous liquid. $[\alpha]_D^{20}$ = –7.5 (*c* = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.18–3.95 (m, 2 H), 3.75–3.60 (m, 1 H), 3.40–3.25 (m, 1 H), 3.10–2.85 (m, 1 H), 2.89 (d, *J* = 12.8 Hz, 1 H), 2.70 (dd, *J* = 10.2, 13.2 Hz, 1 H), 2.60–2.50 (m, 1 H), 2.40–2.22 (m, 2 H), 2.22–2.13 (m, 1 H), 2.08–1.92 (m, 3 H), 1.84 (d, *J* = 18.3 Hz, 1 H), 1.55–1.40 (m, 1 H), 1.46 (s, 9 H), 1.40–1.33 (m, 1 H), 1.03 (s, 3 H), 0.88 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 216.8, 153.8, 80.1, 60.7, 58.8, 56.2, 51.7, 47.6, 43.3, 42.9, 38.2, 35.1, 29.6, 28.3, 26.7, 26.5, 20.1 (2×) ppm. IR (CH_2Cl_2): $\tilde{\nu}$ = 2965, 2889, 2103, 1742, 1694, 1477, 1366 cm^{-1}. HRMS (EI) *m*/*z*: calcd. for $C_{20}H_{32}N_4O_3S$ 408.2195; found 408.2203.

***tert*-Butyl (2*S*,4*S*)-4-Amino-2-[({[(1*S*,4*S*)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl]methyl}thio)methyl]pyrrolidine-1-carboxylate (7):** To a solution of the previously prepared azido compound (1.7 g, 4.16 mmol) in THF (10 mL) was added PPh_3 (1.2 g, 4.58 mmol) portionwise. The reaction mixture was heated at reflux for 4 h and then was quenched with H_2O. To the resulting solution was added aqueous HCl (1.2 N solution, 25.0 mL), and the pH was adjusted with an aqueous solution of NaOH (1.0 M, 30.0 mL) to pH = 8–9. The reaction mixture was then extracted with EtOAc. The combined organic layers were washed with brine, dried with anhydrous $MgSO_4$, and filtered. Purification by flash column chromatography (hexanes/EtOAc, 5:1) gave compound **7** (83% yield) as a viscous liquid. $[\alpha]_D^{20}$ = –6.5 (*c* = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.10–3.90 (m, 1 H), 3.90–3.62 (m, 1 H), 3.55–3.47 (m, 1 H), 3.20–2.80 (m, 5 H), 2.88 (d, *J* = 12.8 Hz, 1 H), 2.65–2.53 (m, 2 H), 2.45–2.30 (m, 2 H), 2.10–1.93 (m, 2 H), 1.86 (d, *J* = 18.3 Hz, 1 H), 1.77–1.69 (m, 1 H), 1.47 (s, 9 H), 1.43–1.32 (m, 1 H), 1.04 (s, 3 H), 0.90 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 217.1, 154.3, 79.6, 60.9, 56.8, 55.0, 50.0, 47.8, 43.5, 43.1, 39.5, 38.6, 30.0, 28.5, 26.9, 26.8, 20.2 (2×) ppm. IR (CH_2Cl_2): $\tilde{\nu}$ = 3431, 2966, 2888, 2096, 1738, 1679, 1477, 1400 cm^{-1}. HRMS (EI): calcd. for $C_{20}H_{34}N_2O_3S$ 382.2290; found 382.2292.

***tert*-Butyl (2*S*,4*S*)-2-[({[(1*S*,4*S*)-7,7-Dimethyl-2-oxobicyclo[2.2.1]-heptan-1-yl]methyl}thio)methyl-]-4-(3-phenylthioureido)pyrrolidine-1-carboxylate:** A solution of compound **7** (1.0 g, 2.6 mmol) in CH_2Cl_2 (10 mL) was treated with PhNCS (0.34 mL, 2.88 mmol) dropwise at ambient temperature. After stirring for 2 h, the reaction mixture was quenched with H_2O, and the resulting solution was adjusted to pH = 9–10 with an aqueous solution of $NaHCO_3$ (1.0 M). The reaction mixture was then extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried with anhydrous $MgSO_4$, and filtered. Purification by flash column chromatography (hexanes/EtOAc, 2:1) gave the product (76% yield) as a viscous liquid. $[\alpha]_D^{20}$ = –11.9 (*c* = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.50 (br. s, 1 H, NH), 7.43–7.35 (m, 2 H), 7.35–7.23 (m, 3 H), 7.30 (br. s, 1 H, NH), 5.07–4.97 (m, 1 H), 4.15–3.94 (m, 2 H), 3.35–3.00 (m, 2 H), 2.80–2.70 (m, 2 H), 2.65–2.45 (m, 2 H), 2.34 (ddd, *J* = 2.9, 4.5, 18.4 Hz, 1 H), 2.06 (t, *J* = 4.3 Hz, 1 H), 2.02–1.93 (m, 1 H), 1.93–1.78 (m, 3 H), 1.50–1.40 (m, 1 H), 1.45 (s, 9 H), 1.40–1.30 (m, 1 H), 0.98 (s, 3 H), 0.88 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 217.6, 180.5, 154.2, 136.9, 129.7, 126.6, 124.8, 79.9, 61.0, 56.4, 52.9, 47.8, 43.5, 43.1, 38.4, 35.5, 30.3, 28.4, 27.2, 26.7, 25.3, 20.4, 19.8 ppm. IR (CH_2Cl_2): $\tilde{\nu}$ = 3461, 3336, 2967, 2885, 2081, 1738, 1661, 1531, 1476, 1392 cm^{-1}. HRMS (FAB+): calcd. for $C_{27}H_{40}O_3N_3S_2$ $[MH]^+$ 518.2511; found 518.2507.

1-{(3*S*,5*S*)-5-[({[(1*S*,4*S*)-7,7-Dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl]methyl}thio)methyl]pyrolidin-3-yl}-3-phenylthiourea (V): To a solution of the C-4-substituted thiourea ketosulfide (0.5 g, 0.97 mmol) in CH_2Cl_2 (5 mL) was added TFA (1.8 mL, 24.23 mmol) dropwise at ambient temperature. After stirring for 6 h, the reaction mixture was quenched with H_2O, and the resulting solution was adjusted to pH = 9–10 with an aqueous solution of $NaHCO_3$ (1.0 M). The reaction mixture was then extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried with anhydrous $MgSO_4$, and filtered. Purification by flash column chromatography (hexanes/EtOAc, 2:1) gave **V** (99% yield) as a white solid; m.p. 81.6–82.5 °C. $[\alpha]_D^{20}$ = +1.8 (*c* = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.57 (br. s, 1 H), 7.41–7.36 (m, 2 H), 7.31–7.28 (m, 2 H), 7.22 (t, *J* = 7.1 Hz, 1 H), 7.07–6.96 (m, 1 H), 4.90 (br. s, 1 H), 3.40–3.29 (m, 1 H), 3.11 (dd, *J* = 10.9, 6.0 Hz, 1 H), 3.07–2.97 (m, 1 H), 2.80 (dd, *J* = 4.4, 13.5 Hz, 1 H), 2.76 (d, *J* = 12.9 Hz, 1 H), 2.58 (dd, *J* = 13.3, 6.9 Hz, 1 H), 2.60–2.45 (m, 1 H), 2.48 (d, *J* = 13.1 Hz, 1 H), 2.45–2.30 (m, 2 H), 2.06 (t, *J* = 3.7 Hz, 1 H), 2.03–1.84 (m, 2 H), 1.84 (d, *J* = 18.4 Hz, 1 H), 1.52–1.22 (m, 4 H), 0.99 (s, 3 H), 0.87 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 218.9, 180.9, 137.5, 129.2, 126.2, 124.6, 61.2, 59.1, 53.6, 51.6, 48.0, 43.6, 43.1, 36.4, 32.1, 29.2, 27.4, 26.8, 20.2, 19.6 ppm. IR (CH_2Cl_2): $\tilde{\nu}$ = 3424, 3055, 2959, 2089, 1735, 1676, 1616, 1543, 1498, 1318, 1200 cm^{-1}. HRMS (FAB+): calcd. for $C_{22}H_{32}ON_3S_2$ $[MH]^+$ 418.1987; found 418.1984.

Crystal Structure Data of V at 200(2) K: $C_{44}H_{64}Cl_2O_2N_6S_4$, *M* = 908.15 g mol^{-1}, monoclinic, *C2*, *a* = 31.545(6) Å, *b* = 8.3641(18) Å, *c* = 19.695(4) Å, α = 90.00°, β = 110.966(9)°, γ = 90.00°, *V* = 4852.4(17) Å^3, *F*(000) = 1936, λ (Mo-K_α) = 0.71073 Å, *Z* = 4, *D* = 1.243 g cm^{-3}, 15677 reflections, 1 restraint, 523 parameters, *R* = 0.2356, wR_2 = 0.1786 for all data.[12]

General Procedure: To a mixture of 1-{(3*S*,5*S*)-5-[({[(1*S*,4*S*)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl]methyl}thio)methyl]pyrrolidin-3-yl}-3-phenylthiourea (**V**, 5.4 mg, 0.01 mmol), benzoic acid (1.6 mg, 0.01 mmol), and 1,1-bis(phenylsulfonyl)ethylene (**2**, 20 mg, 0.06 mmol) in anhydrous chloroform (0.04 mL) in a vial at ambient temperature was added cyclohexanone **1** (14.8 μL, 0.12 mmol). The vial was then sealed, and the reaction mixture was stirred at ambi-

ent temperature for 24 h. To the reaction mixture was added EtOAc/H_2O. The organic layer was separated, dried with anhydrous Na_2SO_4, filtered, and concentrated in vacuo. Purification by flash column chromatography (ethyl acetate/hexanes, 1:2) afforded the desired adducts **3a**–**3j** and the desired adducts **4a**–**4e** and **4h**–**4j**.

2-[2,2-Bis(phenylsulfonyl)ethyl]-4-methylcyclohexanone [(2*R*,4*R*)-3a]: White solid (95% yield, 88%*ee*); m.p. 183.5–185.1 °C. $[\alpha]_D^{20}$ = –16.0 (c = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$, mixture): δ = 0.97 (d, J = 5.2 Hz, 1.2 H, minor), 1.12 (d, J = 6.8 Hz, 1.8 H, major), 1.58–1.64 (m, 3 H), 1.98–2.28 (m, 3 H), 2.35–2.60 (m, 3 H), 2.96–3.02 (m, 0.64 H, major), 3.11–3.18 (m, 0.36 H, minor), 4.85–4.87 (m, 0.62 H, major), 4.98–5.00 (m, 0.38 H, minor), 7.54–7.59 (m, 4 H), 7.66–7.71 (m, 2 H), 7.89–7.96 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, mixture): δ = 18.89 (major), 21.04 (minor), 26.47 (major), 26.73 (minor), 31.81 (minor), 33.27 (major), 35.70 (minor), 37.62 (major), 40.04 (major), 41.31 (minor), 42.76 (minor), 43.89 (major), 46.25 (minor), 80.52 (major), 80.71 (minor), 129.0, 129.08, 129.10, 129.26, 129.34, 129.54, 129.74, 134.39, 134.43, 134.56, 137.98 (minor), 138.01 (major), 212.04 (minor), 213.07 (major) ppm. HRMS (ESI): calcd. for $C_{21}H_{24}O_5S_2$ [M + Na]$^+$ 443.0963; found 443.0977. HPLC analysis (Chiralcel AS-H, λ = 220 nm, 15% *i*PrOH/hexanes, flow rate: 1.0 mL min^{-1}): t_R (major) = 51.1 min (major), t_R = 38.5 min (minor).

Crystal Structure Data of 3a at 200(2) K: $C_{21}H_{24}O_5S_2$, M = 420.52 g mol^{-1}, monoclinic, $P\,21/n$, a = 10.6461(11) Å, b = 18.590(2) Å, c = 11.3438(12) Å, α = 90.00°, β = 116.380(7)°, γ = 90.00°, V = 2011.3(4) Å^3, F(000) = 888, λ (Mo-K_α) = 0.71073 Å, Z = 4, D = 1.389 g cm^{-3}, 13321 reflections, 0 restraints, 253 parameters, R = 0.2067; wR_2 = 0.3423 for all data.[12]

(2*S*,4*S*)-4a: Viscous liquid (73% yield, 92%*ee*). $[\alpha]_D^{20}$ = +16.7 (c = 1.00, $CHCl_3$). HRMS (ESI): calcd. for $C_{21}H_{24}O_5S_2$ [M + Na]$^+$ 443.0963; found 443.0974. HPLC analysis (Chiralcel AS-H, λ = 220 nm, 15% *i*PrOH/hexanes, flow rate: 1.0 mL min^{-1}): t_R = 35.7 min (major), t_R = 47.93 min (minor).

2-[2,2-Bis(phenylsulfonyl)ethyl]-4-(*tert*-butyl)-cyclohexanone [(2*R*,4*R*)-3b]: White solid (85% yield, 86%*ee*); m.p. 127.2–128.1 °C. ^{1}H NMR (500 MHz, $CDCl_3$, mixture): δ = 0.91 (s, 3 H), 0.93 (s, 6 H), 1.27–1.55 (m, 3 H), 1.64–1.67 (m, 2 H), 1.93–1.95 (m, 1 H), 2.23–2.36 (m, 2 H), 2.62–2.67 (m, 1 H), 2.74–2.80 (m, 0.66 H, major), 3.09–3.14 (m, 0.34 H, minor) 4.78–4.80 (m, 0.67 H, major), 5.05–5.07 (m, 0.33 H, minor), 7.54–7.56 (m, 4 H), 7.67–7.72 (m, 2 H), 7.86–7.97 (m, 4 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, mixture): δ = 25.01, 26.77 (minor), 26.88 (major), 27.23 (minor), 27.57 (minor), 28.61 (major), 31.27 (major), 32.57 (minor), 35.90 (major), 38.57 (major), 41.39 (minor), 41.76 (major), 45.71 (major), 46.79 (minor), 80.59 (major), 80.72 (minor), 129.02, 129.10, 129.13, 129.14, 129.28, 129.39, 129.40, 129.69, 130.15, 133.62, 134.40, 134.48, 134.54, 137.57, 138.06 (minor), 138.18 (major), 212.75 (minor), 214.53 (major) ppm. HRMS (ESI): calcd. for $C_{24}H_{30}O_5S_2$ [M + Na]$^+$ 485.1432; found 485.1446. HPLC analysis (Chiralcel AS-H, λ = 220 nm, 15% *i*PrOH/hexanes, flow rate: 1.0 mL min^{-1}): t_R = 51.2 min (major), t_R = 22.0 min (minor).

Crystal Structure Data of 3b at 200(2) K: $C_{24}H_{30}O_5S_2$, M = 462.60 g mol^{-1}; monoclinic, $P\,21/c$, a = 13.0368(17) Å, b = 15.1059(19) Å, c = 12.1816(13) Å, α = 90.00°, β = 102.527(5)°, γ = 90.00°, V = 2341.8(5) Å^3, F(000) = 984, λ (Mo-K_α) = 0.71073 Å, Z = 4, D = 1.312 g cm^{-3}, 14519 reflections, 1 restraint, 270 parameters, R = 0.2277, wR_2 = 0.4544 for all data.[12]

(2*S*,4*S*)-4b: Viscous liquid (86% yield, 91%*ee*). HRMS (ESI): calcd. for $C_{24}H_{30}O_5S_2$ [M + Na]$^+$ 485.1432; found 485.1446; HPLC analysis (Chiralcel AS-H, λ = 220 nm, 15% *i*PrOH/hexanes, flow rate: 1.0 mL min^{-1}): t_R = 21.5 min (major), t_R = 52.8 min (minor).

2-[2,2-Bis(phenylsulfonyl)ethyl]-4-phenylcyclohexanone [(2*R*,4*R*)-3c]: Viscous liquid (75% yield, 88%*ee*). ^{1}H NMR (400 MHz, $CDCl_3$, mixture): δ = 1.88–2.13 (m, 2 H), 2.16–2.21 (m, 4 H), 2.39–2.43 (m, 2 H), 2.78–2.83 (m, 1 H), 3.11–3.14 (m, 0.75 H, major), 3.32–3.38 (m, 0.25 H, minor), 4.77 (dd, J = 7.7, 2.8 Hz, 0.72 H, major), 5.01 (dd, J = 9.3, 3.8 Hz, 0.28 H, minor),7.18–7.39 (m, 5 H), 7.49–7.69 (m, 6 H), 7.84–7.96 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.47, 26.75, 31.79, 34.80, 37.04, 38.26, 38.38, 41.59, 41.72, 43.07, 45.61, 46.66, 80.35, 80.67, 126.62, 126.69, 126.82, 128.47, 128.68, 128.78, 129.14, 129.31, 129.41, 129.48, 129.78, 130.14, 134.46, 134.51, 134.56, 134.62, 137.77, 137.93, 143.36, 212.61 ppm. HRMS (ESI): calcd. for $C_{26}H_{26}O_5S_2$ [M + Na]$^+$ 505.1120; found 505.1135. HPLC analysis (Chiralcel AS-H, λ = 220 nm, 15% *i*PrOH/hexanes, flow rate: 1.0 mL min^{-1}): t_R = 81.7 min (major), t_R = 61.8 min (minor).

(2*S*,4*S*)-4c: Viscous liquid (88% yield, 94%*ee*). HRMS (ESI): calcd. for $C_{26}H_{26}O_5S_2$ [M + Na]$^+$ 505.1120; found 505.1134. HPLC analysis (Chiralcel AS-H, λ = 220 nm, 15% *i*PrOH/hexanes, flow rate: 1.0 mL min^{-1}): t_R = 66.1 min (major), t_R = 87.2 min (minor).

Ethyl 3-[2,2-Bis(phenylsulfonyl)ethyl]-4-oxocyclohexanecarboxylate [(1*R*,3*R*)-3d]: Viscous liquid (55% yield, 86%*ee*). ^{1}H NMR (500 MHz, $CDCl_3$, mixture): δ = 1.27 (t, J = 7.0 Hz, 1.27 H, minor), 1.33 (t, J = 7.0 Hz, 1.73 H, major), 1.46–1.59 (m, 1 H), 1.74–2.01 (m, 3 H), 2.38–2.45 (m, 5 H), 2.77–2.82 (m, 0.7 H, major), 3.19–3.26 (m, 0.3 H, minor), 4.14–4.15 (m, 0.6 H, minor), 4.24–4.27 (m, 1.4 H, major), 4.89–4.91 (m, 0.72 H, major), 5.01–5.03 (m, 0.28 H, minor), 7.55–7.60 (m, 4 H), 7.67–7.71 (m, 2 H), 7.88–7.98 (m, 4 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, mixture): δ = 14.41, 14.25, 26.05 (major), 26.44 (minor), 28.29 (major), 29.68 (minor), 34.73 (major), 36.21 (minor), 38.44 (major), 38.71 (major), 40.37 (minor), 41.80 (minor), 44.07 (major), 45.59 (minor), 60.88 (minor), 61.15 (major), 79.01 (minor), 80.68 (major), 128.43, 129.03, 129.08, 129.13, 129.18, 129.27, 129.73 129.88, 130.08, 134.38, 134.49, 134.60, 134.67, 137.38, 137.81, 137.88, 138.23, 173.42, 210.44 (minor), 211.22 (major) ppm. HRMS (ESI): calcd. for $C_{23}H_{26}O_7S_2$ [M + Na]$^+$ 501.1018; found 501.1032. HPLC analysis (Chiralcel AS-H, λ = 220 nm, 15% *i*PrOH/hexanes, flow rate: 1.0 mL min^{-1}): t_R = 69.7 min (major), t_R = 59.1 min (minor).

(1*S*,3*S*)-4d: Viscous liquid (96% yield, 80%*ee*). HRMS (ESI): calcd. for $C_{23}H_{26}O_7S_2$ [M + Na]$^+$ 501.1018; found 501.1028. HPLC analysis (Chiralcel AS-H, λ = 220 nm, 15% *i*PrOH/hexanes, flow rate: 1.0 mL min^{-1}): t_R = 60.0 min (major), t_R = 72.0 min (minor).

2-[2,2-Bis(phenylsulfonyl)ethyl]cyclohexanone [(*R*)-3e]: Viscous liquid (73% yield, 81%*ee*). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.25–1.30 (m, 2 H), 1.60–1.86 (m, 3 H), 1.93–2.11 (m, 2 H), 2.29–2.34 (m, 2 H), 2.50–2.52 (m, 1 H), 3.07–3.10 (m, 1 H), 4.98 (q, J = 4.0 Hz, 1 H), 7.54–7.58 (m, 4 H), 7.66–7.71 (m, 2 H), 7.89–7.95 (m, 4 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 24.94, 26.46, 27.75, 34.73, 41.97, 47.31, 80.70, 128.99, 129.06, 129.23, 129.69, 134.37, 134.55, 137.98, 138.04, 212.26 ppm. HRMS (ESI): calcd. for $C_{20}H_{22}O_5S_2$ [M + Na]$^+$ 429.0801; found 429.0818. HPLC analysis (Chiralcel AS-H, λ = 220 nm, 30% *i*PrOH/hexanes, flow rate: 1.0 mL min^{-1}): t_R = 28.0 min (major), t_R = 21.3 min (minor).

(*S*)-4e: Viscous liquid (89% yield, 85%*ee*). HRMS (ESI): calcd. for $C_{20}H_{22}O_5S_2$ [M + Na]$^+$ 429.0801; found 429.0820. HPLC analysis (Chiralcel AS-H, λ = 220 nm, 30% *i*PrOH/hexanes, flow rate: 1.0 mL min^{-1}): t_R = 27.4 min (major), t_R = 36.7 min (minor).

(2*S*,3*R*)-2-[2,2-Bis(phenylsulfonyl)ethyl]-3-methylcyclohexanone (3f): Viscous liquid (72% yield, 78%*ee*). ^{1}H NMR (400 MHz, $CDCl_3$,

mixture): δ = 0.94 (d, J = 7.04 Hz, 1.56 H, major), 1.01 (d, J = 6.32 Hz, 1.13 H, minor), 1.07–1.09 (d, J = 5.76 Hz, 0.31 H, minor), 1.53–1.58 (m, 3 H), 1.92–2.32 (m, 4 H), 2.44–2.49 (m, 2 H), 2.58–2.96 (m, 1 H), 4.88 (dd, J = 5.2, 3.6 Hz, 0.6 H, major), 4.90 (dd, J = 5.6, 3.6 Hz, 0.32 H, minor), 4.97 (dd, J = 8.0, 2.8 Hz, 0.08 H, minor), 7.54–7.58 (m, 4 H), 7.67–7.69 (m, 2 H), 7.87–7.95 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, mixture): δ = 19.22, 22.22, 26.41, 29.73, 30.14, 32.23, 33.65, 33.70, 35.63, 46.50, 47.05, 47.98, 50.21, 80.72 (major), 80.85 (minor), 81.31 (minor), 128.93, 129.00, 129.04, 129.10, 129.29, 129.33, 129.68, 129.77, 129.89, 134.39, 134.53, 138.10, 138.17, 212.62 (minor), 212.42 (major) ppm. HRMS (ESI): calcd. for $C_{21}H_{24}O_5S_2$ [M + Na]$^+$ 443.0963; found 443.0977. HPLC analysis (Chiralcel AD-H, λ = 220 nm, 8% *i*PrOH/hexanes, flow rate: 1.0 mL min^{-1}): t_R = 59.2 min (major), t_R = 64.5 min (minor).

2-[2,2-Bis(phenylsulfonyl)ethyl]cycloheptanone [(*R*)-3h]: Viscous liquid (50% yield, 51% *ee*). $[\alpha]_D^{20}$ = –6.6 (c = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.20–1.29 (m, 2 H), 1.44–1.55 (m, 2 H), 1.62–1.73 (m, 4 H), 1.74–2.16 (m, 1 H), 2.38–2.48 (m, 3 H), 3.17–3.21 (m, 1 H), 4.79–4.82 (m, 1 H), 7.52–7.58 (m, 4 H), 7.66–7.71 (m, 2 H), 7.69–7.95 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.75, 27.91, 28.61, 29.01, 32.16, 42.96, 48.58, 80.50, 129.05, 129.12, 129.25, 129.66, 134.38, 134.56, 138.02, 138.24, 214.86 ppm. HRMS (ESI): calcd. for $C_{21}H_{24}O_5S_2$ [M + Na]$^+$ 443.0963; found 443.0966. HPLC analysis (Chiralcel AD-H, λ = 220 nm, 15% *i*PrOH/hexanes, flow rate: 1.0 mL min^{-1}): t_R = 44.6 min (major), t_R = 39.8 min (minor).

(*S*)-4h: Viscous liquid (56% yield, 66% *ee*). $[\alpha]_D^{20}$ = +6.9 (c = 1.00, $CHCl_3$). HRMS (ESI): calcd. for $C_{21}H_{24}O_5S_2$ [M + Na]$^+$ 443.0963; found 443.0956. HPLC analysis (Chiralcel AD-H, λ = 220 nm, 15% *i*PrOH/hexanes, flow rate: 1.0 mL min^{-1}): t_R = 42.3 min (major), t_R = 47.3 min (minor).

3-[2,2-Bis(phenylsulfonyl)ethyl]dihydro-2*H*-thiopyran-4(3*H*)-one [(*R*)-3i]: Viscous liquid (78% yield, 86% *ee*). $[\alpha]_D^{20}$ = –11.3 (c = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.01–2.07 (m, 1 H), 2.61–2.73 (m, 4 H), 2.90–2.93 (m, 3 H), 3.38–3.43 (m, 1 H), 4.83–4.86 (m, 1 H), 7.55–7.59 (m, 4 H), 7.66–7.70 (m, 2 H), 7.87–7.95 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.21, 30.84, 36.25, 44.06, 49.87, 80.47, 129.11, 129.15, 129.32, 129.67, 134.51, 134.70, 137.82, 209.42 ppm. HRMS (ESI): calcd. for $C_{19}H_{20}O_5S_3$ [M + Na]$^+$ 447.0371; found 447.0378. HPLC analysis (Chiralcel AS-H, λ = 220 nm, 40% *i*PrOH/hexanes, flow rate: 1.0 mL min^{-1}): t_R = 46.5 min (major), t_R = 32.1 min (minor).

(*S*)-4i: Viscous liquid (90% yield, 93% *ee*). $[\alpha]_D^{20}$ = –11.7 (c = 1.00, $CHCl_3$). HRMS (ESI): calcd. for $C_{19}H_{20}O_5S_3$ [M + Na]$^+$ 447.0371; found 447.0370. HPLC analysis (Chiralcel AS-H, λ = 220 nm, 40% *i*PrOH/hexanes, flow rate: 1.0 mL min^{-1}): t_R = 33.6 min (major), t_R = 49.2 min (minor).

3-[2,2-Bis(phenylsulfonyl)ethyl]dihydro-2*H*-pyran-4(3*H*)-one [(*S*)-3j]: Viscous liquid (97% yield, 88% *ee*). $[\alpha]_D^{20}$ = –17.4 (c = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.89–1.93 (m, 1 H), 2.30–2.35 (m, 1 H), 2.47–2.60 (m, 2 H), 3.25–3.33 (m, 2 H), 3.66–3.99 (m, 1 H), 4.13–4.20 (m, 2 H), 4.93–4.97 (m, 1 H), 7.54–7.59 (m, 4 H), 7.66–7.68 (m, 2 H), 7.70–7.95 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.19, 42.22, 42.77, 48.23, 67.70, 68.49, 72.32, 80.29, 129.06, 129.10, 129.28, 129.35, 129.57, 134.49, 134.66, 137.64, 137.69, 207.61 ppm. HRMS (ESI): calcd. for $C_{19}H_{20}O_6S_2$ [M + Na]$^+$ 431.0599; found 431.0602. HPLC analysis (Chiralcel AS-H, λ = 220 nm, 40% *i*PrOH/hexanes, flow rate: 1.0 mL min^{-1}): t_R = 39.2 min (major), t_R = 26.2 min (minor).

(*R*)-4j: Viscous liquid (92% yield, 77% *ee*). $[\alpha]_D^{20}$ = +16.5 (c = 1.00, $CHCl_3$). HRMS (ESI): calcd. for $C_{19}H_{20}O_6S_2$ [M + Na]$^+$ 431.0599; found 431.0598. HPLC analysis (Chiralcel AS-H, λ = 220 nm, 40% *i*PrOH/hexanes, flow rate: 1.0 mL min^{-1}): t_R = 26.5 min (major), t_R = 39.9 min (minor).

Supporting Information (see footnote on the first page of this article): Copies of the HPLC chromatograms of all products and ^{1}H and ^{13}C NMR spectra of **6**, **7** and **V**.

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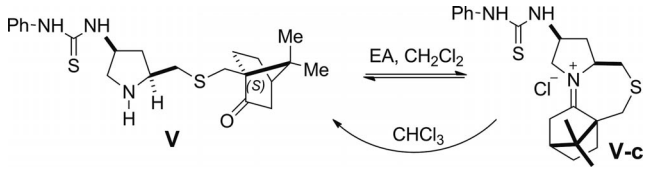
[11] Interestingly, the cyclized iminium salt **V-c** was cocrystallized with **V** in EA/CH_2Cl_2 and shifted completely to **V** in $CHCl_3$.



[12] CCDC-902857 (for **V**), -900954 (for **3a**), and -900955 (for **3b**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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