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Enantioselective Synthesis of (Thiolan-2-yl)diphenylmethanol and Its Application in Asymmetric, Catalytic Sulfur Ylide-Mediated Epoxidation

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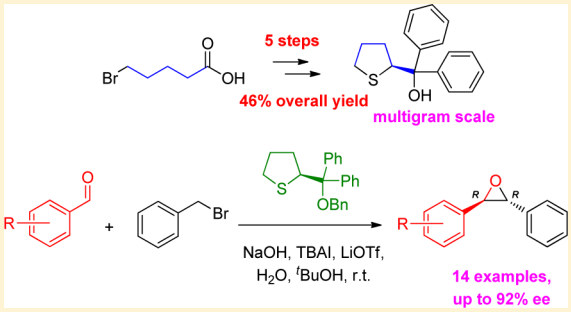
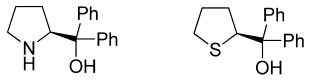
Supporting Information

ABSTRACT: This work describes an expeditious and efficient preparation of enantiopure (thiolan-2-yl)diphenylmethanol (**2**) featuring a double nucleophilic substitution and Shi epoxidation as key steps. One of the applications of its benzyl ether derivative to asymmetric sulfur ylide-mediated epoxidation with up to 92% ee (14 examples) was also demonstrated herein.



The parent diphenyl-2-pyrrolidinemethanol (**1**, *α*,*α*-diphenyl prolinol) and its ether derivatives have been proved to be very useful ligands for a wide range of asymmetric transformations.[1] **1** was first reported in 1934[2] and the interest in them was largely catalyzed by the work initiated by E. J. Corey on the asymmetric reduction of ketones[3] and the preparation of asymmetric super Lewis acid catalyst using CBS catalyst and Brønsted acid for asymmetric Diels–Alder reaction.[4] All these reactions mediated by **1** proceeded in high yields with excellent enantioselectivities. Subsequently, further contributions in 2005 based on organocatalysts with a similar motif, *α*,*α*-diphenylprolinol ethers, have also marked another milestone in practical applications of an enantioselective *α*-sulfenylation of aldehydes,[5] an asymmetric Michael addition of aldehydes to nitroolefins,[6] and a variety of C–C, C–N, C–F, and C–Br bonds formations.[7]



1 **2**

Comparatively, the sulfur analogue thiolanyl diphenylmethanol (**2**)[8] possesses different chemical character with stereotopology similar to that of **1**, yet attracts the least attention in the synthetic community. Inspired by the particular reactivity of an organic catalyst containing a sulfur atom in a myriad of biochemical processes, chiral thioethers have become one of the major catalyst sources in asymmetric transformations for accessing optically active natural products.[9] For example, the use of thiolanyl diphenylmethanol (**2**) for mediating enantioselective alkylation of an aldehyde by diethylzinc reagent is reported.[10] Regrettably, the difficulty of the preparation of **2** is attributed to having to use the highly toxic and expensive alkaloid brucine for the optical resolution of the key intermediate tetrahydro-2-thiophancarboxylic acid[11] (Figure 1, upper panel). Therefore, it is desirable to develop a more concise and accessible process to synthesize **2**, which

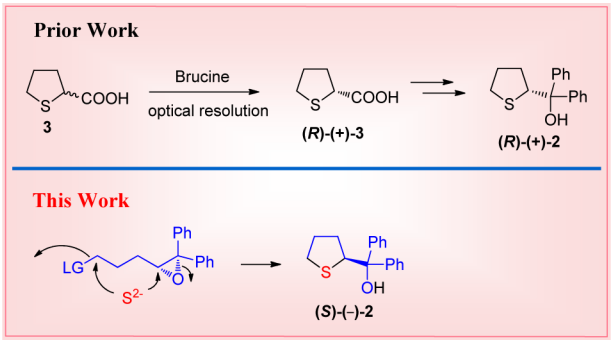


Figure 1. Synthesis of enantiopure (thiolan-2-yl)diphenylmethanol (**2**).

will have further implications in organo- and organometallic catalysis. Herein we report an efficient route to prepare compound **2** with an optically pure form in gram scale. We also examined the use of **2** to conduct the catalytic and asymmetric epoxidations based on benzaldehydes with benzyl bromide.[12]

As depicted in Figure 1 (lower panel), we anticipated that deployment of a double nucleophilic substitution by a sulfide dianion at asymmetric 2,2-diphenyl-3-propyloxirane bearing a leaving group at the terminal carbon atom would be a viable way to thiophane **2**. More importantly, the chirality of the oxirane would be fully transferred. On the basis of this rationale, commercially available 5-bromovaleric acid (**4**) was selected, and the corresponding acid chloride was reacted with phenylmagnesium bromide to afford diphenylalcohol **5** (Scheme 1 in Supporting Information). In the presence of PTSA in hot toluene solution, compound **5** was readily converted to diphenylethylene **6**

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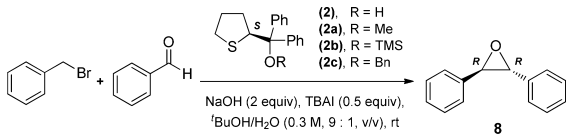
in 82% yield. With considerable optimization, we were pleased to find that Shi epoxidation protocol[13] is a suitable protocol for making epoxide product **7** in high yield (96%) with excellent (96%) ee. As expected, when epoxide **7** was subjected to the treatment of a suspension of Na_2S in ethanol solution (an ultrasonicator bath), bromide was substituted by sulfide dianion followed by a second internal nucleophilic attack of sulfide on the epoxide ring to form the cyclized compound ((*S*)-(−)-thiolan-2-yl)diphenylmethanol (**2**) in 86% yield without the loss of ee. The ee of **2** was further improved to >99% by the recrystallization of **2** in hot hexane solution. The absolute configuration of **2** was confirmed by single-crystal X-ray diffraction. Vice versa, its optical isomer (*R*)-(+)-**2** could also be synthesized through the same way with the exception that the Shi pyranose catalyst prepared from L-fructose was used in this synthetic route. It is important to note that these procedures are reliable and could be easily carried out in multigram scale.[14]

With **2** in hand, we were posed to study its application in asymmetric sulfur ylide-mediated epoxidations. Thiolane **2** (50 mol %), benzyl bromide (2 equiv), and benzaldehyde (1 equiv) were mixed together at room temperature in basic medium.[12f] Through the *in situ* formation of sulfonium salt and then the corresponding ylide, *trans*- and *cis*-stilbene oxides were obtained in a ratio of 4:1. Unfortunately, 0% ee was observed for the *trans*-isomer accompanied with the decomposition of catalyst **2**. To preserve active species **2** in the catalytic cycle for the asymmetric induction, methyl ether **2a**, trimethylsilyl (TMS) ether **2b**, and benzyl ether **2c** were synthesized and subjected to the same reaction conditions. To our delight, benzyl ether **2c** (Table 1, entry 4) showed the best enantioselectivity (84% ee)

Table 1. Catalyst Screening for Asymmetric Epoxidation



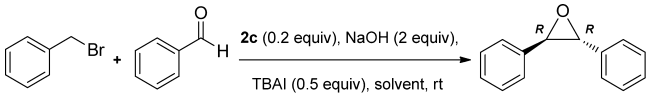
entry	catalyst (equiv)	time (h)	yield (%)	*trans*/*cis*[a]	ee[b] (%)
1	**2** (0.5)	24	23	79/21	0
2	**2a** (0.5)	48	82	77/23	83
3	**2b** (0.5)	12	61	74/26	67
4	**2c** (0.5)	36	89	78/22	84
5	**2c** (0.2)	48	72	75/25	84
6	**2c** (0.1)	48	57	73/27	82

[a]*trans*/*cis* ratio was determined by ^{1}H NMR spectroscopy. [b]Ee of the *trans* product was determined by HPLC analysis with a Chiralcel OD column.

with lower catalyst loading (20 mol %, Table 1, entry 5), while still keeping good selectivity in *trans*/*cis* ratio.

Encouraged by the outcome of using benzyl ether **2c** as a sulfur ylide source, we next examined for the optimized conditions for this transformation. As shown in Table 2, all aprotic solvents (entries 2, 3, 7, 8, and 9) mediated the reaction with higher diastereoselectivity but lower enantioselectivity. In contrast, protic solvents (entries 1, 4, and 10) showed a reversed effect in selectivity. Combining acetonitrile and *tert*-butanol (entry 6) did not seem to bring any beneficial effect on the stereoselectivity of the reaction. Among the protic solvents we screened, *tert*-butanol provided the best ee with a decent *trans*/*cis* ratio, yet the reaction proceeded slowly, as 75% of the benzaldehyde was left untouched after a day. We were pleased to find that LiOTf

Table 2. Optimization of the 2c-Mediated Asymmetric Epoxidation



entry	solvent	additive (equiv)	time (h)	yield[a] (%)	*trans*/*cis*[b]	ee of *trans*[c] (%)
1	^{t}BuOH/H_2O (9/1)	none	48	72	75/25	84
2	MeCN	none	48	85	90/10	75
3	THF	none	24	5	91/9	71
4	MeOH/H_2O (1/1)	none	24	48	75/25	84
5	EtOH	none	24	5	67/33	80
6	MeCN/ ^{t}BuOH (15/1)	none	24	52	87/13	78
7	DCE	none	24	30	90/10	75
8	toluene	none	24	1	89/11	74
9	CH_2Cl_2	none	24	54	92/8	73
10	^{t}BuOH	none	24	27	78/22	86
11	^{t}BuOH	LiOTf (0.2)	24	47	78/22	86
12	^{t}BuOH	LiOTf (0.5)	24	51	77/23	87
13	^{t}BuOH	LiOTf (1)	10	75	75/25	85
14	^{t}BuOH	LiOTf (0.2), H_2O (5)	24	92	77/23	86
15	^{t}BuOH	LiOTf (1), H_2O (5)	24	95	71/29	85

[a]GC yield, using 2,6-di-*tert*-butyl-4-methylphenol as an internal standard. [b]*trans*/*cis* ratio was determined by ^{1}H NMR spectroscopy. [c]Ee of *trans* product was determined by HPLC analysis with a Chiralcel OD column.

additive significantly accelerated the reaction rate (entries 11−13). In fact, a trace amount of water with catalytic LiOTf assisted the completion of the reaction within 24 h without having any adverse effect on stereoselectivity (entry 14).[15]

The scope of this asymmetric epoxidation process was then assessed through variation of the aldehyde components under the optimized conditions. We first examined the electronic effect on the reactivity of aldehyde toward stilbene oxide (Table 3). Benzaldehydes bearing an electron-withdrawing group such as CF_3 (entry 2), Cl (entry 3), and F (entry 4) at the para position afforded the corresponding *trans*-stilbene oxides **9**, **10**, and **11** in good yields with good to excellent enantiocontrol. On the other hand, benzyl bromide was converted slowly into *trans*-oxide **12**, **13**, and **15** when it reacted with benzaldehydes bearing one (entries 14, 15) or two (entry 17) electron-donating groups. Ortho substitution deteriorated the enantioselectivity (entries 7, 11, 12) and diastereoselectivity (entry 7), albeit with good yield. Finally, 2-naphthaldehyde (entry 13) and cinnamaldehyde (entry 14) gave epoxides **20** and **21** in good stereocontrol manner.

To provide a mechanistic rationale for the high asymmetric induction observed in the epoxidation involving sulfide **2c**, the catalytic cycle is proposed in Figure 2. The sulfide is initially transformed to sulfonium salts **22**, which then subsequently turned into the corresponding ylide **23** under basic conditions. In this juncture, the ylide can adopt either conformations **23a** or **23b** in which the filled orbital on the ylide carbons is perpendicular to the lone pair electron on sulfur.[12c,16] Intermediate **23b** should be favored as the phenyl group is located away from the bulky substituent α to the sulfur. In addition, minimization

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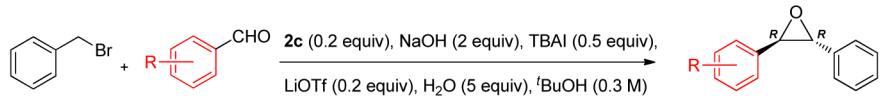
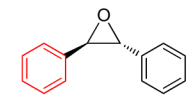
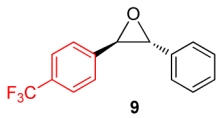
Table 3. Substrate Scope of Catalytic Sulfur Ylide-Mediated Epoxidation



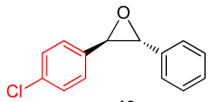
(entry), yield, *trans*/*cis*[a], ee[b], reaction time



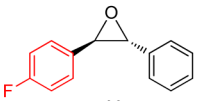
8
(1), 92%, *77/23*, 86%, 24h



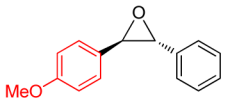
9
(2), 80%, *61/39*, 78%, 26h



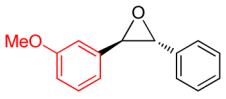
10
(3)[c], 97%, *74/26*, 92%, 24h



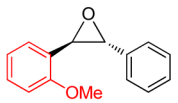
11
(4), 90%, *76/24*, 84%, 42h



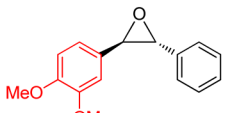
12
(5), 85%, *83/17*, 87%, 4.5d



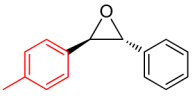
13
(6), 86%, *76/24*, 85%, 3.5d



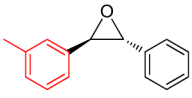
14
(7), 90%, *55/45*, 62%, 3.5d



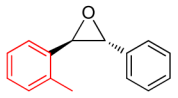
15
(8), 85%, *82/18*, 82%, 4.5d



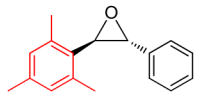
16
(9), 94%, *79/21*, 87%, 42h



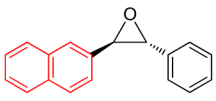
17
(10), 95%, *80/20*, 87%, 40h



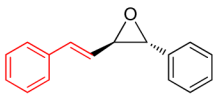
18
(11), 90%, *85/15*, 66%, 48h



19
(12), 77%, *70/30*, 20%, 2.5d



20
(13), 88%, *79/21*, 87%, 24h



21
(14), 75%, *80/20*, 79%, 24h

[a]*trans*/*cis* ratio was determined by ^{1}H NMR spectroscopy. [b]Ee of *trans* product was determined by HPLC analysis with chiralcel-OD or chiralpak-AD column. [c]0.5 equiv of **2c** was used.

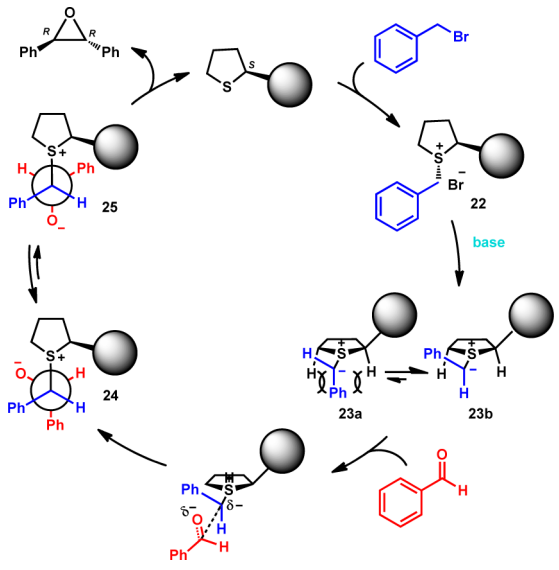


Figure 2. Thiolane-catalyzed asymmetric epoxidation (arrows may be considered equilibria).

of steric energy is achieved with the phenyl group pointing at the equatorial position. As a result, the orientation of the bulky substituent in **23a** would block the *Si* face of the ylide carbon, forcing addition of the aldehyde to the *Re* face to give the (*R*,*R*)-epoxide.

In conclusion, a new and efficient method for the synthesis of enantiopure (thiolan-2-yl)diphenylmethanol (**2**) and its application in the asymmetric sulfide-catalyzed epoxidation are reported. These chiral thioethers have high potential for other asymmetric organocatalysis and are good donor ligands[17] for the development of chiral organometallic catalysts.

EXPERIMENTAL SECTION

5-Bromo-1,1-diphenylpentan-1-ol (5). To a stirred solution of 5-bromovaleric acid (**4**) (9 g, 50 mmol) in CH_2Cl_2 (15 mL) at room temperature was slowly added thionyl chloride (7.2 mL, 99 mmol) in a period of 10 min through a droping funnel. DMF (a few drops) was added to the reaction mixture, which was then heated to reflux for 2 h. The reaction mixture was concentrated in vacuo (to remove excess $SOCl_2$ and DMF), and the resulting acid chloride was directly used for the following Grignard reaction.

To a solution of magnesium powder (1.7 g, 73 mmol) and a small piece of iodine in THF (50 mL) was added phenyl bromide (1 mL, 9.5 mmol) at room temperature. After the color of iodine disappeared, the rest of phenyl bromide (6.9 mL, 65.5 mmol) was slowly added by a syringe pump in a period of 1 h. The mixture was stirred for another 30 min after the exothermic reaction ceased. When the magnesium disappeared, the mixture was stirred for another 1 h, and 5-bromopentanoyl chloride (4.95 g, 25 mmol) in dry THF (15 mL) was added dropwise to the above mixture at 0 °C. After stirring for 12 h at room temperature, the reaction mixture was quenched with sat. NH_4Cl (10 mL) at 0 °C and extracted with EtOAc (30 mL × 3). The combined organic layers were washed with sat. $NaHCO_3$ (20 mL × 2) and brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by flash column chromatography (EtOAc/hexanes, 1:9)

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to give 5-bromo-1,1-diphenylpentan-1-ol as a colorless oil (5.4 g, 68% yield). IR (neat) 3472, 3058, 2948, 2867, 1493, 1446, 1263, 1059, 963, 753, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.48−7.26 (10H, m), 3.36 (2H, t, J = 7.0 Hz), 2.42 (1H, s), 2.35−2.31 (2H, m), 1.91 (2H, dt, J = 14.5, 7.1 Hz), 1.52−1.44 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.7, 128.0, 126.7, 125.9, 77.9, 40.8, 33.3, 32.9, 22.4; HRMS (ESI$^+$, TOF) calcd for $C_{17}H_{19}BrO$ [$(M + H - H_2O)^+$] 301.0602, found 301.0592.

5,5-Diphenyl-4-pentenyl Bromide (6). A stirred solution of 5-bromo-1,1-diphenylpentan-1-ol (**5**) (5.1 g, 16 mmol) and *p*-TsOH (255 mg, 1.5 mmol) in toluene (63 mL) was heated to 70 °C for 3 h. After cooling down to room temperature, the reaction mixture was diluted with DI water (10 mL), extracted with EtOAc (10 mL × 3), dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by flash column chromatography (EtOAc/hexanes, 3:97) to give 5,5-diphenyl-4-pentenyl bromide as a colorless oil (4.2 g, 82% yield). IR (neat) 3054, 2959, 1633, 1243, 759, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39−7.16 (10H, m), 6.04 (1H, t, J = 7.4 Hz), 3.37 (2H, t, J = 6.9 Hz), 2.26 (2H, dd, J = 14.7, 7.4 Hz), 2.03−1.95 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.0, 142.4, 139.8, 129.8, 128.2, 128.1, 127.5, 127.2, 127.0, 33.1, 33.0, 28.4; HRMS (FAB$^+$, magnetic sector) calcd for $C_{17}H_{17}Br$ (M^+) 300.0514, found 300.0518.

(*R*)-(+)-3-(3-Bromopropyl)-2,2-diphenyloxirane (7). A combined solution of 5,5-diphenyl-4-pentenyl bromide (**6**) (2.4 g, 8.0 mmol) in CH_3CN/DMM (1:2, v/v, 60 mL), and $Na_2B_4O_7{\cdot}10H_2O$ (1.5 g, 4.0 mmol), tetrabutylammonium hydrogen sulfate (108 mg, 0.32 mmol), and Shi catalyst (1.03 g, 4.0 mmol) in a buffer solution (4×10^{-4} M aqueous Na_2(EDTA), 40 mL) was cooled to −5 °C with mechanical stirring in an ice bath. A solution of Oxone (12.28 g, 20 mmol) in aqueous Na_2(EDTA) (4×10^{-4} M, 50 mL) and a solution of K_2CO_3 (12.3 g, 89.2 mmol) in DI water (50 mL) were respectively added dropwise through two separate addition funnels over a period of 3 h at −5 °C. Upon completion of the additions, the reaction was stirred for another 1 h at the same temperature. After dilution with DI water (100 mL), the resulting mixture was extracted with hexanes (100 mL × 2), dried over Na_2SO_4, and concentrated to afford the crude product which was purified by flash column chromatography (EtOAc/hexanes, 1:40 to 1:25) to afford (*R*)-(+)-3-(3-bromopropyl)-2,2-diphenyloxirane as a colorless oil. (2.41 g, 95% yield, 96% ee). $[\alpha]^{28}_D$ = +37.0 (*c* 1.0, $CHCl_3$); IR (neat) 3059, 3028, 2963, 2853, 1494, 1277, 762, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.40−7.23 (10H, m), 3.44−3.30 (3H, m), 2.13−1.94 (2H, m), 1.69 (1H, ddd, J = 14.0, 9.8, 5.3 Hz), 1.33 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.7, 137.2, 128.2, 128.1, 127.9, 127.8, 127.6, 126.9, 66.1, 65.4, 32.9, 29.6, 28.2; HRMS (FAB$^+$, magnetic sector) calcd for $C_{17}H_{18}BrO$ [$(M + H)^+$] 317.0534, found 317.0541; enantioselectivity was determined by HPLC analysis (Chiralcel-OJ, 1.0 mL/min, 220 nm, hexanes/*i*-PrOH, 4:1); retention time: 19.4 min (enantiomer) and 35.8 min (major).

1,2:4,5-Di-*O*-isopropylidene-D-erythro-2,3-hexodiuro-2,6-pyranose (Shi Catalyst).[13] To a stirred solution of D-fructose (3.68 g, 20.5 mmol) and 2,2- dimethoxypropane (1.48 mL, 12 mmol) in acetone (74 mL) at 0 °C was slowly added perchloric acid (70%, 860 μL) dropwise. After stirring for 6 h at 0 °C, the reaction mixture was quenched with 28% NH_4OH (2 mL) at 0 °C (adjust to pH 7−8). Upon removal of acetone, the residue was diluted with DI water (50 mL) and CH_2Cl_2 (50 mL). The aqueous layer was extracted with CH_2Cl_2 (10 mL × 2). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated to get the crude product which was recrystallized from hexanes/CH_2Cl_2 (4:1 v/v) to give 1,2;4,5-di-*O*-isopropylidene-β-D-fructopyranose as white needles (2.1 g, 40%). ^1H NMR (400 MHz, $CDCl_3$) δ 4.19 (1H, ddd, J = 5.8, 2.5, 0.7 Hz), 4.16 (1H, d, J = 8.8 Hz), 4.13−4.08 (2H, m), 4.00−3.95 (2H, m), 3.65 (1H, dd, J = 8.2, 6.9 Hz), 1.99 (1H, d, J = 8.2 Hz), 1.51 (3H, s), 1.49 (3H, s), 1.42 (3H, s), 1.35 (3H, s).

To a stirred solution of 1,2;4,5-di-*O*-isopropylidene-β-D-fructopyranose (3.9 g, 15 mmol) and powdered 3 Å molecular sieves (37 g, activated at 180−200 °C under high vacuum) in CH_2Cl_2 (112 mL) was added PCC (8.76 g, 40.5 mmol) portionwise over 30 min. After stirring for 3 h under nitrogen, the reaction mixture was filtered through Celite-cotton-silica gel and washed carefully with ether-hexanes (2:1, 400 mL). The filtrate was concentrated to afford 1,2;4,5-Di-*O*-isopropylidene-D-erythro-2,3-hexodiuro-2,6-pyranose as white needles (3.76 g, 97%). ^1H NMR (400 MHz, $CDCl_3$) δ 4.70 (1H, d, J = 5.6 Hz), 4.59 (1H, d, J = 9.5 Hz), 4.52 (1H, dd, J = 5.6, 1.5 Hz), 4.36 (1H, dd, J = 13.5, 2.2 Hz), 4. 09 (1H, d, J = 13.5 Hz), 3.97 (1H, d, J = 9.5 Hz), 1.53 (3H, s), 1.44 (3H, s), 1.37 (6H, s).

((*S*)-(−)-Thiolan-2-yl)diphenylmethanol (2). A mixture of the (*R*)-(+)-3-(3-bromopropyl)-2,2-diphenyloxirane (**7**) (3.06 g, 9.7 mmol) and $Na_2S{\cdot}9H_2O$ (4.64 g, 19.3 mmol) in 95% ethanol (33 mL) was sonicated at 10−25 °C for 34 h (conversion is monitored by the crude ^1H NMR). Upon removal of ethanol, the crude residue was diluted with DI water (40 mL) and CH_2Cl_2 (40 mL). The aqueous layer was extracted with CH_2Cl_2 (25 mL × 2). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated to afford the crude product which was purified by flash column chromatography (EtOAc/hexanes, 1:99 to 1:20) to afford ((*S*)-(−)-thiolan-2-yl)-diphenylmethanol as a white solid. (2.24 g, 86% yield, 93% ee). The solid ((*S*)-(−)-thiolan-2-yl)diphenylmethanol was recrystallized from hexanes to give white needles with >99% ee. Mp 72−75 °C; $[\alpha]^{28}_D$ = −120.4 (*c* 1.0, $CHCl_3$); IR (neat) 3471, 3056, 2934, 1596, 1491, 1447, 1353, 1167, 754, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.54−7.51 (2H, m), 7.44−7.41 (2H, m), 7.30−7.22 (4H, m), 7.21−7.12 (2H, m), 4.66 (1H, dd, J = 8.4, 6.8 Hz), 3.53 (1H, s), 2.86−2.83 (2H, m), 2.16 (1H, m), 1.87−1.73 (2H, m), 1.62 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.0, 145.0, 128.2, 128.0, 127.1, 126.5, 126.1, 125.4, 77.9, 59.5, 33.4, 31.7; HRMS (FAB$^+$, magnetic sector) calcd for $C_{17}H_{19}OS$ [$(M + H)^+$] 271.1157, found 271.1150; enantioselectivity was determined by HPLC analysis (Chiralpak-AD, 1.0 mL/min, 220 nm, hexanes/*i*-PrOH, 19/1); retention time 6.0 min (enantiomer) and 8.5 min (major).

(*S*)-(+)-2-(Methoxydiphenylmethyl)tetrahydrothiophene (2a). To a stirred solution of ((*S*)-(−)-thiolan-2-yl)diphenylmethanol (**2**) (135 mg, 0.5 mmol) in DMF (2 mL) at 0 °C was added sodium hydride (40 mg, 1.0 mmol). The reaction mixture was warmed to room temperature and stirred for 1 h. Methyl iodide (37 μL, 0.6 mmol) was then slowly added to the reaction mixture. After 2 h stirring at room temperature, the reaction mixture was quenched with sat. NH_4Cl (1 mL) at 0 °C, extracted with Et_2O (2 mL × 3), dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by flash column chromatography (EtOAc/hexanes, 1:49) to give (*S*)-(+)-2-(methoxydiphenylmethyl)tetrahydrothiophene as a colorless oil (132 mg, 92% yield). $[\alpha]^{31}_D$ = +93.2 (*c* 1.0, $CHCl_3$); IR (neat) 3056, 2934, 1491, 1444, 1073, 755, 701, 645 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.50 (2H, dd, J = 7.9, 1.7 Hz), 7.37 (2H, dd, J = 8.1, 1.6 Hz), 7.31−7.23 (6H, m), 4.59 (1H, t, J = 7.04 Hz), 3.06 (3H, s), 2.65 (1H, dt, J = 11.4, 5.8 Hz), 2.34 (2H, ddd, J = 10.1, 7.5, 6.2 Hz), 2.01 (1H, td, J = 12.7, 5.9 Hz), 1.81−1.63 (2H, m), 1.31 (1H, qd, J = 10.2, 4.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.7, 141.3, 129.5, 129.2, 127.4, 127.3, 127.1, 127.0, 85.9, 53.6, 51.6, 32.6, 31.6, 30.3; HRMS (ESI$^+$, TOF) calcd for $C_{18}H_{21}OS$ [$(M + H)^+$] 285.1313, found 285.1307.

(*S*)-(+)-(Diphenyl(tetrahydrothiophen-2-yl)methoxy)-trimethylsilane (2b). To a stirred solution of ((*S*)-(−)-thiolan-2-yl)diphenylmethanol (**2**) (135 mg, 0.5 mmol) in CH_2Cl_2 (0.5 mL) at 0 °C was slowly added imidazole (102 mg, 1.5 mmol) followed by TMSCl (90 μL, 1.0 mmol). The reaction mixture was warmed to room temperature and stirred overnight. The reaction mixture was quenched with sat. NH_4Cl (2 mL) at 0 °C, extracted with CH_2Cl_2 (3 mL × 3), dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by flash column chromatography (EtOAc/hexanes, 1:49) to give (*S*)-(+)-(diphenyl(tetrahydrothiophen-2-yl)methoxy)trimethylsilane as a colorless oil (165 mg, 96% yield). Mp 47−50 °C; $[\alpha]^{29}_D$ = +15.1 (*c* 1.0, $CHCl_3$); IR (neat) 2953, 2929, 2859, 1446, 1245, 1123, 834, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (2H, dd, J = 6.6, 1.3 Hz), 7.31−7.15 (8H, m), 4.39 (1H, t, J = 6.8 Hz), 2.77 (1H, dt, J = 9.3, 4.5 Hz), 2.56 (1H, m), 1.71−1.59 (4H, m), −0.10 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.4, 145.5, 128.5, 127.6, 127.3, 127.2, 127.0, 126.8, 83.8, 57.5, 33.5, 32.3, 30.2, 2.1; HRMS (FAB$^+$, magnetic sector) calcd for $C_{20}H_{25}OSiS$ [$(M - H)^+$] 341.1395, found 341.1389.

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(*S*)-(+)-2-((Benzyloxy)diphenylmethyl)tetrahydrothiophene (2c). To a stirred solution of ((*S*)-(−)-thiolan-2-yl)diphenylmethanol (**2**) (0.5 g, 1.9 mmol) in DMF (3.7 mL) at 0 °C was added sodium hydride (148 mg, 3.7 mmol). The reaction mixture was warmed to room temperature and stirred for 1 h. Benzyl bromide (270 μL, 2.2 mmol) was then slowly added to the reaction mixture. After 16 h stirring at room temperature, the reaction mixture was quenched with sat. NH_4Cl (1 mL) at 0 °C, extracted with Et_2O (5 mL × 3), dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by flash column chromatography (EtOAc/hexanes, 1:49) to give (*S*)-(+)-2-((benzyloxy)diphenylmethyl)tetrahydrothiophene as a pale-yellow solid (615 mg, 92% yield). Mp 62−65 °C; $[\alpha]^{29}_D$ = +63.6 (*c* 1.0, $CHCl_3$); IR (neat) 3059, 2930, 1494, 1444, 1063, 758, 701, 651 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.57−7.55 (2H, m), 7.44 (1H, d, *J* = 7.2 Hz), 7.34−7.16 (11H, m), 4.66 (1H, t, *J* = 7.2 Hz), 4.38 (1H, d, *J* = 11.6 Hz), 4.21 (1H, d, *J* = 11.52 Hz), 2.63 (1H, m), 2.32 (1H, ddd, *J* = 10.1, 8.2, 6.1 Hz), 1.98 (1H, td, *J* = 12.7, 6.0 Hz), 1.84 (1H, m), 1.64 (1H, m), 1.34 (1H, tt, *J* = 11.9, 5.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 129.3, 128.8, 128.0, 127.4, 127.2, 127.1, 127.0, 126.9, 126.9, 85.9, 65.5, 53.8, 32.6, 31.6, 30.2.; HRMS (FAB^+, magnetic sector) calcd for $C_{24}H_{25}OS$ [$(M + H)^+$] 361.1626, found 361.1618.

General Procedure for Sulfur Ylide-Mediated Epoxidations. To a stirred solution of (*S*)-(+)-2-((benzyloxy)diphenylmethyl)tetrahydrothiophene (**2c**) (20 mg, 0.06 mmol), TBAI (52 mg, 0.14 mmol), powdered NaOH (22 mg, 0.57 mmol), LiOTf (9 mg, 0.06 mmol), and DI water (25 μL, 1.41 mmol) in *tert*-butanol (0.9 mL) was slowly added benzyl bromide (67 μL, 0.57 mmol) and the corresponding aldehyde (0.28 mmol) sequentially. The resulting reaction mixture was stirred at room temperature for the corresponding reaction time (Table 3). The final mixture was diluted with DI water, extracted with CH_2Cl_2, dried over Na_2SO_4, and concentrated to furnish the crude product for column chromatography. The isolated yields, *trans*/*cis* ratios, and ee of *trans* isomers are listed in Table 3.

(2*R*,3*R*)-2,3-Diphenyloxirane (8)[18]: ^1H NMR (400 MHz, $CDCl_3$) δ 7.39−7.30 (10H, m), 3.85 (2H, s); enantioselectivity was determined by HPLC analysis (Chiralcel-OD, 1.0 mL/min, 228 nm, hexanes/*i*-PrOH, 19:1); retention times: 5.8 min (enantiomer) and 8.0 min (major).

(2*R*,3*R*)-2-Phenyl-3-(4-(trifluoromethyl)phenyl)oxirane (9)[19]: ^1H NMR (400 MHz, $CDCl_3$) δ 7.62 (2H, d, *J* = 8.1 Hz), 7.45 (2H, d, *J* = 8.1 Hz), 7.40−7.31 (5H, m), 3.91 (1H, d, *J* = 1.6 Hz), 3.82 (1H, d, *J* = 1.7 Hz); enantioselectivity was determined by HPLC analysis (Chiralpak-AD, 1.0 mL/min, 231 nm, hexanes/*i*-PrOH, 19:1); retention times: 5.6 min (major) and 10.3 min (enantiomer).

(2*R*,3*R*)-2-(4-Chlorophenyl)-3-phenyloxirane (10)[18]: ^1H NMR (400 MHz, $CDCl_3$) δ 7.39−7.25 (9H, m), 3.83 (1H, d, *J* = 1.8 Hz), 3.80 (1H, d, *J* = 1.8 Hz); enantioselectivity was determined by HPLC analysis (Chiralcel-OD, 1.0 mL/min, 234 nm, hexanes/*i*-PrOH, 99:1); retention times: 9.0 min (enantiomer) and 10.4 min (major).

(2*R*,3*R*)-2-(4-Fluorophenyl)-3-phenyloxirane (11)[18]: ^1H NMR (400 MHz, $CDCl_3$) δ 7.39−7.28 (7H, m), 7.07−7.03 (2H, m), 3.83 (1H, d, *J* = 1.3 Hz), 3.81 (1H, d, *J* = 1.5 Hz); enantioselectivity was determined by HPLC analysis (Chiralcel-OD, 1.0 mL/min, 220 nm, hexanes/*i*-PrOH, 19:1); retention times: 6.4 min (enantiomer) and 7.8 min (major).

(2*R*,3*R*)-2-(4-Methoxyphenyl)-3-phenyloxirane (12)[18]: ^1H NMR (400 MHz, $CDCl_3$) δ 7.38−7.29 (5H, m), 7.27 (1H, m), 7.25 (1H, m), 6.91 (1H, m), 6.89 (1H, m), 3.84 (1H, d, *J* = 1.9 Hz), 3.80 (3H, s), 3.80 (1H, d, *J* = 1.9 Hz); enantioselectivity was determined by HPLC analysis (Chiralpak-AD, 1.0 mL/min, 234 nm, hexanes/*i*-PrOH, 17:3); retention times: 6.8 min (major) and 13.8 min (enantiomer).

(2*R*,3*R*)-2-(3-Methoxyphenyl)-3-phenyloxirane (13)[20]: ^1H NMR (400 MHz, $CDCl_3$) δ 7.41−7.25 (6H, m), 6.93 (1H, d, *J* = 7.6, 1.1 Hz), 6.89−6.83 (2H, m), 3.83 (2H, s), 3.81 (3H, s); enantioselectivity was determined by HPLC analysis (Chiralpak-AD, 1.0 mL/min, 220 nm, hexanes/*i*-PrOH, 9:1); retention times: 6.9 min (major) and 14.4 min (enantiomer).

(2*R*,3*R*)-2-(2-Methoxyphenyl)-3-phenyloxirane (14)[21]: ^1H NMR (400 MHz, $CDCl_3$) δ 7.41−7.24 (7H, m), 6.97 (1H, t, *J* = 7.6 Hz), 6.87 (1H, d, *J* = 7.9 Hz), 4.23 (1H, d, *J* = 1.7 Hz), 3.80 (3H, s), 3.77 (1H, d, *J* = 1.9 Hz); enantioselectivity was determined by HPLC analysis (Chiralpak-AD, 1.0 mL/min, 234 nm, hexanes/*i*-PrOH, 19:1); retention times: 6.8 min (major) and 11.0 min (enantiomer).

(2*R*,3*R*)-2-(3,4-Dimethoxyphenyl)-3-phenyloxirane (15)[22]: ^1H NMR (400 MHz, $CDCl_3$) δ 7.40−7.28 (5H, m), 6.92 (1H, dd, *J* = 8.2, 1.9 Hz), 6.86 (1H, d, *J* = 8.2 Hz), 6.83 (1H, d, *J* = 1.9 Hz), 3.89 (3H, s), 3.88 (3H, s), 3.83 (1H, d, *J* = 1.9 Hz), 3.81 (1H, d, *J* = 1.9 Hz); enantioselectivity was determined by HPLC analysis (Chiralpak-AD, 1.0 mL/min, 231 nm, hexanes/*i*-PrOH, 9:1); retention times: 9.9 min (major) and 20.0 min (enantiomer).

(2*R*,3*R*)-2-Phenyl-3-(*p*-tolyl)oxirane (16)[18]: ^1H NMR (400 MHz, $CDCl_3$) δ 7.39−7.16 (9H, m), 3.84 (1H, d, *J* = 1.9 Hz), 3.81 (1H, d, *J* = 1.9 Hz), 2.35 (3H, s); enantioselectivity was determined by HPLC analysis (Chiralcel-OD, 1.0 mL/min, 231 nm, hexanes/*i*-PrOH, 19:1); retention times: 5.4 min (enantiomer) and 6.4 min (major).

(2*R*,3*R*)-2-Phenyl-3-(*m*-tolyl)oxirane (17)[20]: ^1H NMR (400 MHz, $CDCl_3$) δ 7.42−7.24 (6H, m), 7.14 (2H, s), 7.12 (1H, s), 3.84 (1H, d, *J* = 1.9 Hz), 3.82 (1H, d, *J* = 1.9 Hz), 2.35 (3H, s); enantioselectivity was determined by HPLC analysis (Chiralpak-AD, 1.0 mL/min, 231 nm, hexanes/*i*-PrOH, 19:1); retention times: 5.4 min (major) and 12.3 min (enantiomer).

(2*R*,3*R*)-2-Phenyl-3-(*o*-tolyl)oxirane (18)[20]: ^1H NMR (400 MHz, $CDCl_3$) δ 7.45−7.26 (5H, m), 7.24−7.08 (4H, m), 3.98 (1H, d, *J* = 1.8 Hz), 3.75 (1H, d, *J* = 1.9 Hz), 2.33 (3H, s); enantioselectivity was determined by HPLC analysis (Chiralpak-AD, 1.0 mL/min, 228 nm, hexanes/*i*-PrOH, 99:1); retention times: 6.9 min (major) and 8.9 min (enantiomer).

(2*R*,3*R*)-2-Mesityl-3-phenyloxirane (19)[23]: ^1H NMR (400 MHz, $CDCl_3$) δ 7.41−7.31 (5H, m), 6.84 (2H, s), 3.88 (1H, s), 3.79 (1H, d, *J* = 2.2 Hz), 2.38 (6H, s), 2.27 (3H, s); enantioselectivity was determined by HPLC analysis (Chiralpak-AD, 1.0 mL/min, 228 nm, hexanes/*i*-PrOH, 49:1); retention times: 5.2 min (major) and 5.9 min (enantiomer).

(2*R*,3*R*)-2-(Naphthalen-2-yl)-3-phenyloxirane (20)[22]: ^1H NMR (400 MHz, $CDCl_3$) δ 7.86−7.81 (4H, m), 7.55−7.44 (2H, m), 7.44−7.24 (6H, m), 4.02 (1H, d, *J* = 1.8 Hz), 3.95 (1H, d, *J* = 1.8 Hz); enantioselectivity was determined by HPLC analysis (Chiralpak-AD, 1.0 mL/min, 231 nm, hexanes/*i*-PrOH, 9:1); retention times: 7.2 min (major) and 12.9 min (enantiomer).

(2*R*,3*R*)-2-Phenyl-3-((*E*)-styryl)oxirane (21)[18]: ^1H NMR (400 MHz, $CDCl_3$) δ 7.47−7.22 (9H, m), 6.80 (1H, d, *J* = 16.0 Hz), 6.06 (1H, dd, *J* = 16.0, 7.7 Hz), 3.87 (1H, s), 3.51 (1H, d, *J* = 7.6 Hz); enantioselectivity was determined by HPLC analysis (Chiralcel-OD, 1.0 mL/min, 220 nm, hexanes/*i*-PrOH, 99:1); retention times: 12.5 min (enantiomer) and 13.7 min (major).

■ ASSOCIATED CONTENT

Supporting Information

Experimental details, characterization data, and crystallographic data (CIF) of (*S*)-(−)-**2**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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