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PAPER

Iridium-catalyzed asymmetric allylation of sodium triisopropylsilanethiolate: A new way to form chiral thiols†

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The iridium phosphoramidite complex-promoted regio- and enantioselective reaction of allylic carbonates with sodium triisopropylsilanethiolate produced allylic sulfides in 40–77% yields with up to 97 : 3 (branched : linear) and 89% ee, which were readily transformed into chiral thiol in 68% yield with 87% ee or disulfides with two chiral C–S bond centers in 40–73% yields with up to 90 : 10 dr and 99% ee.

Introduction

Iridium-catalyzed allylation methods for enantioselective formation of carbon–sulfur bonds[1] are less developed than those for constructing carbon–carbon,[2] carbon–nitrogen,[3] and carbon–oxygen linkages[4] because the sulfur nucleophile may poison transition metal catalysts.[5] More recently, iridium-catalyzed enantioselective allylic alkylation of sulfur compounds with various allylic substrates has drawn considerable attention due to the importance of chiral thiols and organosulfur compounds in organic chemistry and chemical biology.[6] Traditionally, an enantio-enriched thiol could be prepared from the corresponding alcohol; however, this makes one reliant on the availability of the desired alcohol in an enantiopure form. To date, few reports regarding the preparation of thiols have been disclosed.[6b,7] In connection with our research interests on carbon–sulfur bond formation, we have been searching to expand the scope of sulfur nucleophiles that can be directly utilized for the synthesis of allylic thiols. In this context, we note that the use of sulfur–heteroatom compounds (*e.g.*, sodium triisopropylsilanethiolate, an SH equivalent) as nucleophiles in iridium-catalyzed enantioselective allylation has not been explored yet. The reaction of this type mainly forms a branched allylation product,[1d,1e] which could undergo useful transformations such as (1) metathesis to give an unsymmetrical 1,3-disubstituted allylic sulfide[1d,8] that could occur by 1,3-chirality transfer through [2,3]-sigmatropic rearrangement,[9] (2) cleavage of TIPS to provide a thiol[10] or disulfide, and (3) hydrogenation to furnish an ethyl-substituted sulfide. In particular, chiral disulfides are of great importance to natural products,[11] bioactive molecules,[12] versatile building blocks,[13] and ligands.[14] Herein, we first report the highly efficient iridium-catalyzed allylation of sodium triisopropylsilanethiolate with various allylic substrates, which proceeds with both excellent regio- and enantioselectivity, and its applications in the preparation of thiols and disulfides.

Results and discussion

Initially, the experimental conditions were set identical with those used for the allylic alkylation with sodium cyclohexanethiolate,[1e] that is an iridacycle complex[1–4] made from 1 mol% of $[Ir(COD)Cl]_2$ and 2 mol% of **L1**,[15,16] methyl allyl carbonate, and dichloromethane (DCM) at 15 °C (Table 1). Triisopropylsilanethiol[17] was first tested as a nucleophile, however, this reaction failed to proceed. Notably, potassium triethylsilanolate, a hard nucleophile, was successfully employed in the iridium complex-catalyzed enantioselective allylation for the preparation of allylic alcohols.[4b] Encouraged by these results, sodium triisopropylsilanethiolate (**3**),[18] a soft nucleophile, was examined and 75% yield of the branched product **4a** with 93 : 7 regioselectivity and 66% ee[19] was achieved. In fact, the cleavage of **4a** with TBAF was carried out and the allylic disulfides instead of thiol were unexpectedly obtained, these results attracted our attention to investigate the transformation of **4a** into disulfides. In addition, the hydrogenation of **4a** catalyzed by Pd/C was conducted but it failed to proceed since sulfur compounds can poison the palladium catalyst. Furthermore, *o*-nitrobenzenesulfonylhydrazide (NBSH) is an efficient reagent for the reduction of terminal olefins.[20] As a result, a tandem reduction of **4a** with NBSH, followed by treating with TBAF, was performed and it readily produced the corresponding disulfide **6a**[14a,21] in two steps 47% yield with 72 : 28 dr and 92% ee (entry 1). In order to further optimize the allylation reaction conditions, cesium fluoride (CsF) was used as an additive in this reaction, it appeared that 77% of **4a** with 93 : 7 (**4a** : **5a**) and 87% ee[19] was attained. Similarly, the transformation of **4a** into **6a** occurred in two steps and 46% yield with 88 : 12 dr and 99% ee (entry 2). These outcomes indicate that CsF has a considerable effect on efficiency and enantioselectivity (entry 1 *vs.* entry 2), which are consistent with those of the iridium-catalyzed allylation of sodium thiophenoxide as well.[1d] A further survey was performed on the chiral phosphoramidite ligands including **L2**,[15] **L3**,[16] **L4**,[22] **L5**,[23] and PHOX ligand **L6**[24] (Fig. 1)

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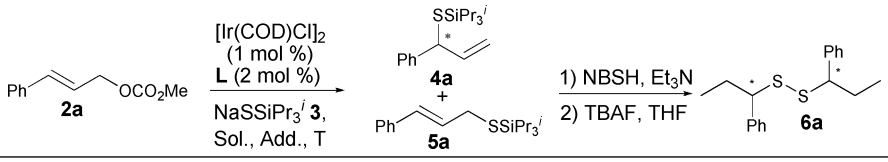
† Electronic supplementary information (ESI) available: NMR and HPLC spectra of the compounds. See DOI: 10.1039/c1ob06332d

Table 1 Reaction conditions optimization of Ir-catalyzed asymmetric allylation of **3**[a]



Entry	L	Sol.	Add.[b]	*T* (°C)	Yield of **4a** (%)[c]	**4a** : **5a**[d]	ee of **4a** (%)[e]	Yield of **6a** (%)[f]	DL : *meso*[g]	ee of **6a** (%)[g]
1	**L1**	DCM	none	15	75	93 : 7	66	47	72 : 28	92
2	**L1**	DCM	CsF	15	77	93 : 7	87	46	88 : 12	99
3	**L2**	DCM	CsF	15	55	72 : 28	—	—	—	—
4	**L3**	DCM	CsF	15	*Trace*	—	—	—	—	—
5	**L4**	DCM	CsF	15	45	88 : 12	—	—	—	—
6	**L5**	DCM	CsF	15	80	93 : 7	57	45	69 : 31	83
7	**L6**	DCM	CsF	15	*Trace*	—	—	—	—	—
8	**L1**	DCM	CsCl	15	74	96 : 4	81	52	84 : 16	97
9	**L1**	DCM	LiCl	15	80	90 : 10	72	42	77 : 23	93
10	**L1**	DCM	CsF	0	26	97 : 3	—	—	—	—
11	**L1**	DCM	CsF	–25	23	99 : 1	—	—	—	—
12	**L1**	THF	CsF	15	*Trace*	—	—	—	—	—
13	**L1**	Toluene	CsF	15	22	85 : 15	—	—	—	—

[a] Reaction conditions: 1 mol% of $[Ir(COD)Cl]_2$, 2 mol% of **L**, 110 mol% of **2a**, and 100 mol% of **3** at –25 to 15 °C. [b] 300 mol% of additive was used in entries 2–13. [c] Isolated yield based on **3**. [d] Determined by GC-MS of the crude reaction mixture. [e] The ee value was calculated on the basis of both DL : *meso* and ee of **6a** as shown in ref. 19. [f] Isolated yield based on **4a**. [g] Determined by a chiral HPLC analysis of **6a**.

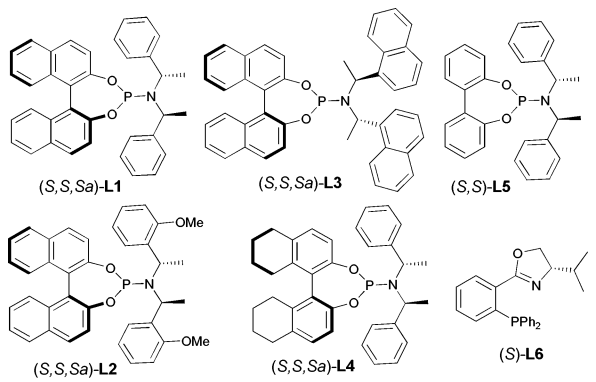


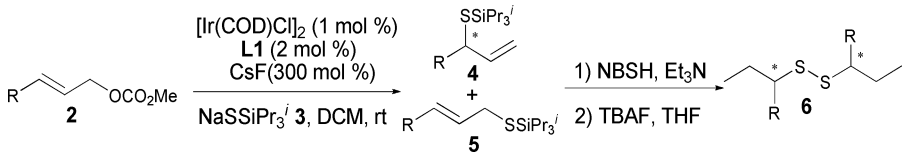
Fig. 1 Chiral ligands **L1–L6**.

to identify how the structural variation of the ligands may affect regio- and enantioselectivity. **L1** gave the best results (77% yield, 93 : 7 **4a** : **5a**, and 87% ee) in favor of the branched product **4a** (entry 2). Both **L2** and **L4** led to the formation of the desired product **4a** in only 45–55% yields with a slightly lower regioselectivity (72 : 28 to 88 : 12) (entry 3 *vs.* entry 5). **L5** gave rise to the highest yield (80%) of **4a** but with a somewhat low enantioselectivity (57% ee, entry 6). The iridium complex generated from either **L3** or **L6** failed to promote this allylation reaction (entry 4 *vs.* entry 7). Finally, the first ligand we tested, **L1**, appeared to be the best compromise between high regio- and enantioselectivity. The effect of additive, solvent, and temperature on this reaction was also investigated. The utilization of additives including CsF, CsCl, and LiCl had considerable influences on efficiency, regio- and enantioselectivity (entries 2, 8 and 9). Adjusting the temperature had a dramatic effect on the efficiency as well (entries 2, 10 and 11). The survey of solvents revealed that DCM is the optimal solvent (entry 2). Other solvents such as THF and toluene were not effective (entries 12 and 13). Thus, the reaction conditions shown in entry 2 of Table 1 were chosen as the optimal conditions for further study.

Using this optimized procedure, iridium-catalyzed enantioselective allylation of **3** with a diversity of methyl allylic carbonates was surveyed (Table 2). The reaction of phenyl- and aromatic allylic methyl carbonates **2a–2d** with an electron-rich group (*e.g.*, *p*-CH_3, *p*-CH_3O, and *m*-CH_3O) on the phenyl ring occurred in 62–77% yields with excellent regioselectivity (92 : 8 to 97 : 3) and 74–87% ee,[19] and the transformation of **4a–4d** into **6a–6d** proceeded in two steps giving 46–73% yields with 76 : 24 to 88 : 12 dr and 95–99% ee (entries 1–4). Moreover, the reaction of hetero- and aromatic allylic carbonates **4e–4g** with an electron-deficient group (*e.g.*, *p*-Cl and *p*-Br) on the phenyl ring took place in 41–72% yields and 80–85% ee,[19] although the regioselectivity was slightly lower (89 : 11 to 94 : 6); in the same manner, **6e–6g** were generated from **4e–4g** in two steps giving 40–51% yields with 82 : 18 to 87 : 13 dr and 97–99% ee (entries 5–7). It is noted that a small amount of iridium catalyst (0.5 mol% of $[Ir(COD)Cl]_2$ and 1 mol% of **L1**) was required for an allylation of (*E*)-methyl 3-(thiophen-2-yl)allyl carbonate. Otherwise, a mixture of **4g** : **5g** (52 : 48) was obtained under the optimized conditions (entry 7). We are currently studying the reason for this reaction. The reaction also worked well with the aliphatic allylic carbonate **2h** but with poor regioselectivity (57 : 43, entry 8). This deterioration in regioselectivity may stem from the influence of the bulky group of $NaSSiPr_3^i$ on this allylation reaction. A similar result was observed in the iridium complex-catalyzed allylation using NaOTIPS as a nucleophile because of the hindered effect of TIPS.[4b] The higher ee of **6** with two chiral C–S bond centers made from the corresponding **4** may result from the preferential kinetic resolution in the oxidative coupling reaction.

Further proving the value of this synthetic method, a chiral secondary thiol was prepared in this way, demonstrated in eqn (1). A tandem reduction of **4a** with NBSH, followed by reaction with a solution of HCl in Et_2O in the presence of $AlCl_3$ under argon atmosphere, provided the thiol **7a**[25] in two steps in 68% yield and 87% ee,[26] and its absolute configuration was determined as *S* by means of comparing with those of the known (*R*)- or

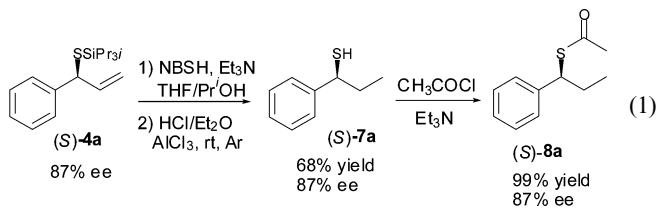
Table 2 Ir-catalyzed asymmetric allylation of allyl methyl carbonates with **3**[a]



Entry	R	Product	Yield of **4** (%)[b]	**4** : **5**[c]	ee of **4** (%)[d]	Yield of **6** (%)[e]	DL : *meso* (%)[f]	ee of **6** (%)[f]
1	C_6H_5	**4a**	77	93 : 7	87	46	88 : 12	99
2	3-$MeOC_6H_4$	**4b**	76	92 : 8	74	44	76 : 24	96
3	4-$MeOC_6H_4$	**4c**	72	97 : 3	83	69	84 : 16	97
4	4-MeC_6H_4	**4d**	62	93 : 7	82	73	86 : 14	95
5	4-ClC_6H_4	**4e**	69	94 : 6	84	51	84 : 16	99
6	4-BrC_6H_4	**4f**	72	90 : 10[g]	80	49	82 : 18	97
7[h]	2-thienyl	**4g**	41	89 : 11	85	40	87 : 13	97
8	$PhCH_2CH_2$	**4h**	40	57 : 43	89	55	90 : 10	99

[a] Reaction conditions: 1 mol% of $[Ir(COD)Cl]_2$, 2 mol% of **L1**, 300 mol% of CsF, 110 mol% of **2** and 100 mol% of **3** in DCM at 15 °C. [b] Isolated yield based on **3**. [c] Determined by GC-MS of the crude reaction mixture. [d] The ee value was calculated on the basis of both DL : *meso* and ee of **6** as shown in ref. 19. [e] Isolated yield based on **4**. [f] Determined by a chiral HPLC analysis of **6**. [g] Determined by ^1H NMR of the crude reaction mixture. [h] 0.5 mol% of $[Ir(COD)Cl]_2$ and 1 mol% of **L1** was used in this case.

(*S*)-1-phenylpropane-1-thiol.[6b,25] To the best of our knowledge, this is the first report regarding transition metal-catalyzed allylation method for the synthesis of chiral thiols.



(1)

Conclusions

In conclusion, we have developed a practical method for iridium-catalyzed regio- and enantioselective transformation of allylic carbonates into branched allylic sulfides which are converted to bisulfur compounds with two chiral carbon–sulfur bond centers. Using this method for the preparation of a chiral secondary thiol is also discussed.

Experimental section

General experimental details

All manipulations were carried out under an argon atmosphere using standard Schlenk techniques. All glassware was oven or flame dried immediately prior to use. All solvents were purified and dried according to standard methods prior to use, unless stated otherwise.

All reagents were obtained from commercial sources and used without further purification. ^1H NMR spectra were obtained at 300 MHz or 400 MHz and recorded relative to the tetramethylsilane signal (0 ppm) or residual protio-solvent. ^{13}C NMR spectra were obtained at 100 MHz, and chemical shifts were recorded relative to the solvent resonance ($CDCl_3$, 77.0 ppm). Data for ^1H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet or unresolved, br = broad singlet, coupling constant(s) in Hz, integration). Data for ^{13}C NMR are reported in terms of chemical shift (δ, ppm).

General procedure for the iridium-catalyzed enantioselective allylic alkylation of $NaSSiPr_3^i$

$[Ir(COD)Cl]_2$ (0.0020 mmol, 1.0 mol%), phosphoramidite ligand **L1** [*O*,*O*′-(S)-(1,1′-dinaphthyl-2,2′-diyl)-*N*,*N*′-di-(S,S)-[phenylethylphosphoramidite] (0.0040 mmol, 2.0 mol%) were dissolved in THF (0.5 mL) and propylamine (0.2 mL) in a dry Schlenk tube filled with argon. The reaction mixture was heated at 50 °C for 30 min and then the volatile solvents were removed under vacuum to give a yellow solid. After that, allylic carbonate **2** (0.22 mmol, 110 mol%), sodium triisopropylsilanethiolate **3** (0.20 mmol, 100 mol%), cesium fluoride (0.60 mmol, 300 mol%), and dichloromethylene (2.0 mL) were added. The reaction mixture was stirred at room temperature until the mixture became clear. Then the crude reaction mixture was filtered through celite and the solvent was removed under reduced pressure. The ratio of regioisomers (branched to linear) was determined by ^1H NMR or GC-MS of the crude reaction mixture. The crude residue was purified by flash column chromatography to give the desired product.

(*S*)-Triisopropyl(1-phenylallylthio)silane (4a). GC-MS of the crude mixture showed a ratio of branched : linear in 93 : 7. The mixture was purified by flash column chromatography (100% petroleum ether) to give **4a** as a colorless liquid in 77% yield. Calculated ee = 87%. $[\alpha]_D^{20}$ −164.0 (*c* 0.7, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ = 7.39–7.20 (m, 5H), 6.13 (ddd, *J* = 16.8, 9.9, 7.5 Hz, 1H), 5.03 (dd, *J* = 15.9, 9.3 Hz, 2H), 4.58 (d, *J* = 7.2 Hz, 1H), 1.25 (tt, *J* = 7.2, 6.9 Hz, 3H), 1.10 (d, *J* = 6.9 Hz, 9H), 1.04 (d, *J* = 6.9 Hz, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.7, 141.9, 128.3, 127.7, 126.8, 113.7, 47.3, 18.6, 18.5, 12.9. MS (EI+, *m*/*z*, rel. intensity): 117 (100), 307 (M^+). HRMS (EI+, *m*/*z*): calcd. for $C_{18}H_{30}SSi$ $[M]^+$: 306.1838, found: 306.1845. IR (KBr): ν_{max} (cm^{-1}) = 2941, 2864, 2357, 2338, 1650, 1557, 1455, 990, 880, 699, 668, 647.

(*S*)-Triisopropyl(1-(3-methoxyphenyl)allylthio)silane (4b). GC-MS of the crude mixture showed a ratio of branched : linear in

92 : 8. The mixture was purified by flash column chromatography (petroleum ether : ethyl acetate = 40 : 1) to give **4b** as a colorless liquid in 76% yield. Calculated ee = 74%. $[\alpha]_D^{20}$ −193.7 (*c* 0.7, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.21 (dd, *J* = 8.0, 8.4 Hz, 1H), 6.96–6.95 (m, 2H), 6.75 (dd, *J* = 8.0, 1.6 Hz, 1H), 6.11 (ddd, *J* = 17.2, 10.0, 7.6 Hz, 1H), 5.07 (d, *J* = 16.8 Hz, 1H), 5.01 (d, *J* = 10.0 Hz, 1H), 4.55 (d, *J* = 7.6 Hz, 1H), 3.80 (s, 3H), 1.25 (tt, *J* = 7.6, 7.2 Hz, 3H), 1.10 (d, *J* = 7.2 Hz, 9H) 1.05 (d, *J* = 7.2 Hz, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 159.6, 145.3, 141.7, 129.3, 120.0, 113.8, 113.7, 113.3, 112.4, 55.2, 47.4, 18.6, 18.5, 12.9. MS (EI+, *m*/*z*, rel. intensity): 147 (100), 337 (M^+). HRMS (EI+, *m*/*z*): calcd. for $C_{19}H_{32}OSSi$ [M^+]: 336.1943, found: 336.1945. IR (KBr): ν_{max} (cm^{-1}) = 2943, 2864, 2356, 2339, 1681, 1556, 1259, 915, 751, 669.

(*S*)-Triisopropyl(1-(4-methoxyphenyl)allylthio)silane (4c). GC-MS of the crude mixture showed a 97 : 3 branched : linear ratio. The mixture was purified by flash column chromatography (petroleum ether : ethyl acetate = 40 : 1) to give **4c** as a colorless liquid in 72% yield. Calculated ee = 83%. $[\alpha]_D^{20}$ −153.2 (*c* 0.9, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ = 7.29 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 8.4 Hz, 2H), 6.11 (ddd, *J* = 17.2, 9.6, 7.6 Hz, 1H), 5.02 (d, *J* = 17.2 Hz, 1H), 4.99 (d, *J* = 10.0 Hz, 1H), 4.56 (d, *J* = 7.6 Hz, 1H), 3.79 (s, 1 H), 1.25 (tt, *J* = 7.6, 7.2 Hz, 3H), 1.10 (d, *J* = 7.2 Hz, 9 H), 1.04 (d, *J* = 7.6 Hz, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.4, 142.1, 135.9, 128.6, 113.7, 113.4, 55.2, 46.8, 18.6, 18.5, 12.9. MS (EI+, *m*/*z*, rel. intensity): 147 (100), 337 (M^+). HRMS (EI+, *m*/*z*): calcd. for $C_{19}H_{32}OSSi$ [M]$^+$: 336.1943, found: 336.1946. IR (KBr): ν_{max} (cm^{-1}) = 2944, 2865, 1609, 1508, 1462, 1429, 1175, 1040, 883, 825, 738, 674, 646, 591.

(*S*)-Triisopropyl(1-*p*-tolylallylthio)silane (4d). GC-MS of the crude mixture showed a 93 : 7 branched : linear ratio. The mixture was purified by flash column chromatography (100% petroleum ether) to give **4d** as a colorless liquid in 62% yield. Calculated ee = 82%. $[\alpha]_D^{20}$ −229.2 (*c* 0.5, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ = 7.25 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 6.12 (ddd, *J* = 17.2, 9.6, 7.6 Hz, 1H), 5.04 (d, *J* = 16.8 Hz, 1H), 4.99 (d, *J* = 10.0 Hz, 1H), 4.55 (d, *J* = 7.6 Hz, 1H), 2.31 (s, 3H), 1.26 (tt, *J* = 7.2, 7.2 Hz, 3 H), 1.10 (d, *J* = 7.2 Hz, 9 H), 1.04 (d, *J* = 7.2 Hz, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 142.0, 140.8, 136.4, 129.0, 127.4, 113.4, 47.1, 21.0, 18.6, 18.5, 12.9. MS (EI+, *m*/*z*, rel. intensity): 131 (100), 320 (M^+). HRMS (EI+, *m*/*z*): calcd. for $C_{19}H_{32}SSi$ [M]$^+$: 320.1994, found: 320.1998. IR (KBr): ν_{max} (cm^{-1}) = 2944.6, 2865, 1511, 1462, 1382, 988, 920, 877, 815.

(*S*)-(1-(4-Chlorophenyl)allylthio)triisopropylsilane (4e). GC-MS of the crude mixture showed a 94 : 6 branched : linear ratio. The mixture was purified by flash column chromatography (100% petroleum ether) to give **4e** as a colorless liquid in 69% yield. Calculated ee = 84%. $[\alpha]_D^{20}$ −170.6 (*c* 0.7, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ = 7.31 (d, *J* = 8.8 Hz, 2H) 7.26 (d, *J* = 8.0 Hz, 2H), 6.08 (ddd, *J* = 17.2, 10.0, 7.2 Hz, 1H), 5.02 (dd, *J* = 16.8, 10.0 Hz, 2H), 4.55 (d, *J* = 7.2 Hz, 1H), 1.25 (tt, *J* = 7.6, 7.2 Hz, 3H), 1.10 (d, *J* = 7.6 Hz, 9H), 1.04 (d, *J* = 7.2 Hz, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 142.3, 141.5, 132.5, 129.1, 128.5, 114.1, 46.6, 18.6, 18.5, 12.9. MS (EI+, *m*/*z*, rel. intensity): 151 (100), 340 (M^+). HRMS (EI+, *m*/*z*): calcd. for $C_{18}H_{29}ClSSi$ [M]$^+$: 340.144, found: 340.1447. IR (KBr): ν_{max} (cm^{-1}) = 2948, 2868, 2360, 2338, 1649, 1563, 1258, 1092, 1012, 914, 880, 751, 668.

(*S*)-(1-(4-Bromophenyl)allylthio)triisopropylsilane (4f). ^1H NMR of the crude mixture showed a 90 : 10 branched : linear ratio. The mixture was purified by flash column chromatography (100% petroleum ether) to give **4f** as a colorless liquid in 72% yield. Calculated ee = 80%. $[\alpha]_D^{20}$ −135.7 (*c* 0.6, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ = 7.42 (d, *J* = 8.7 Hz, 2H), 7.26 (d, *J* = 8.4 Hz, 2H), 6.07 (ddd, *J* = 17.1, 9.9, 7.5 Hz), 5.02 (dd, *J* = 15.6, 10.2 Hz, 2H), 4.53 (d, *J* = 7.5 Hz, 1H), 1.25 (tt, *J* = 7.5, 7.2 Hz, 3H), 1.09 (d, *J* = 7.2 Hz, 9H), 1.03 (d, *J* = 7.2 Hz, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 142.8, 141.4, 131.4, 129.4, 120.6, 114.1, 46.6, 18.6, 18.5, 12.9. MS (EI+, *m*/*z*, rel. intensity): 116 (100), 384 (M^+). HRMS (EI+, *m*/*z*): calcd. for $C_{18}H_{29}BrSSi$ [M]$^+$: 384.0943, found: 384.0948. IR (KBr): ν_{max} (cm^{-1}) = 2941, 2865, 1631, 1483, 1462, 1397, 1074, 1009, 991, 917, 877, 840, 815, 745, 671.

(*S*)-Triisopropyl(1-(thiophen-2-yl)allylthio)silane (4g). GC-MS of the crude mixture showed a 89 : 11 branched : linear ratio. The mixture was purified by flash column chromatography (petroleum ether : DCM = 20 : 1) to give **4g** as a colorless liquid in 41% yield. Calculated ee = 85%. $[\alpha]_D^{20}$ −192.2 (*c* 0.1, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ = 7.18 (dd, *J* = 5.2, 1.2 Hz, 1H), 6.98 (d, *J* = 3.6 Hz, 1H), 6.91 (dd, *J* = 5.2, 3.6 Hz, 1H), 6.10 (ddd, *J* = 17.2, 10.0, 8.0 Hz, 1H), 5.11 (d, *J* = 17.2 Hz, 1H), 5.05 (d, *J* = 10.0 Hz, 1H), 4.82 (d, *J* = 8.0 Hz, 1H), 1.28 (tt, *J* = 7.6, 7.2 Hz, 3H), 1.12 (d, *J* = 7.2 Hz, 9H), 1.09 (d, *J* = 7.0 Hz, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 148.3, 141.4, 126.5, 124.7, 124.6, 113.9, 42.3, 18.6, 12.9. MS (EI+, *m*/*z*, rel. intensity): 123 (100), 313 (M^+). HRMS (EI+, *m*/*z*): calcd. for $C_{16}H_{28}S_2Si$ [M]$^+$: 312.1402, found: 312.1409. IR (KBr): ν_{max} (cm^{-1}) = 2923, 2865, 1742, 1458, 1271, 920, 877, 698.

(*S*)-Triisopropyl(5-phenylpent-1-en-3-ylthio)silane (4h). GC-MS of the crude mixture showed a 57 : 43 branched : linear ratio. The mixture was purified by flash column chromatography (petroleum ether : DCM = 20 : 1) to give **4h** as a colorless liquid in 40% yield. Calculated ee = 89%. $[\alpha]_D^{20}$ −187.9 (*c* 0.4, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ = 7.27 (t, *J* = 7.6 Hz, 2H), 7.18 (t, *J* = 7.6 Hz, 3H), 5.80 (ddd, *J* = 17.2, 9.6, 7.6 Hz, 1H), 5.03 (dd, *J* = 17.6, 9.6 Hz, 2H), 3.60 (dt, *J* = 8.4, 8.8 Hz, 1H), 2.73 (m, 1H), 2.63 (m, 1H), 2.00 (m, 2H), 1.19 (tt, *J* = 7.6, 7.2 Hz, 3H), 1.07 (d, *J* = 7.2 Hz, 18H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 142.0, 141.6, 128.5, 128.3, 125.8, 113.7, 42.8, 41.0, 33.4, 18.64, 18.60, 12.9. MS (EI+, *m*/*z*, rel. intensity): 147 (100), 334 (M^+). HRMS (EI+, *m*/*z*): calcd. for $C_{20}H_{34}SSi$ [M]$^+$: 334.2150, found: 334.2153. IR (KBr): ν_{max} (cm^{-1}) = 2945, 2865, 1462, 1071, 991, 914, 880, 745, 698.

(*E*)-Triisopropyl(5-phenylpent-2-enylthio)silane (5h). The mixture was purified by flash column chromatography (petroleum ether : DCM = 20 : 1) to give **5h** as a colorless liquid in 30% yield. ^1H NMR (400 MHz, $CDCl_3$) δ = 7.28 (t, *J* = 7.6 Hz, 2H), 7.18 (t, *J* = 7.6 Hz, 3H), 5.60 (m, 2H), 3.15 (d, *J* = 6.4 Hz, 2H), 2.68 (t, *J* = 7.6 Hz, 2H), 2.33 (dt, *J* = 6.8, 6.4 Hz, 2H) 1.26 (tt, *J* = 7.6, 7.2 Hz, 3H), 1.11 (d, *J* = 7.2 Hz, 18H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 141.9, 131.3, 129.2, 128.4, 128.3, 125.8, 35.7, 34.1, 27.9, 18.6, 12.7. MS (EI+, *m*/*z*, rel. intensity): 147 (100), 334 (M^+). HRMS (EI+, *m*/*z*): calcd. for $C_{20}H_{34}SSi$ [M]$^+$: 334.2150, found: 334.2151. IR (KBr): ν_{max} (cm^{-1}) = 2944, 2865, 2360, 2338, 1458, 1385, 877, 674.

General procedure for the preparation of disulfides (6)

To a solution of the triisopropylsilicane sulfide **4** (0.20 mmol, 100 mol%) in THF (2 mL) and *i*-PrOH (2 mL) was added *o*-nitrobenzenesulfonylhydrazide (0.40 mmol, 200 mol%) and triethylamine (0.80 mmol, 400 mol%) at 30 °C. The reaction was carried out overnight. After the addition the mixture was cooled to 0 °C and treated with a solution of TBAF (0.40 mmol, 200 mol%) in THF (2 mL). The mixture was stirred at room temperature for 2 h, and then partitioned between H_2O (5 mL) and DCM (5 mL), separated and the water layer was re-extracted with DCM (3 × 5 mL). The combined organic layer was dried with anhydrous Na_2SO_4, concentrated and purified by flash column chromatography to give the desired product.

1,2-Bis(1-phenylpropyl)disulfane (6a)[27]. The mixture was purified by flash column chromatography (100% petroleum ether) to give **6a** as a colorless liquid in 46% yield, ee = 99%, DL : *meso* = 88 : 12 [CHIRALCEL OJ-H (0.46 cm × 25 cm), hexane : 2-propanol = 90 : 10, 1.0 mL min^{-1}, λ = 214 nm, *t* (major) = 5.988 min, *t* (minor) = 4.702 min, *t* (*meso*) = 6.569 min]. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.33–7.24 (m, 6H), 7.15 (d, *J* = 8.4 Hz, 4H), 3.16 (dd, *J* = 9.6, 5.6 Hz, 2H), 2.05 (dq, *J* = 7.6, 5.6 Hz, 2H), 1.78 (dq, *J* = 9.6, 7.2 Hz, 2H), 0.77 (t, *J* = 7.2 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 141.2, 128.3, 127.4, 56.8, 27.7, 12.2.

1,2-Bis(1-(3-methoxyphenyl)propyl)disulfane (6b). The mixture was purified by flash column chromatography (100% petroleum ether) to give **6b** as a colorless liquid in 44% yield. ee = 96%, DL : *meso* = 76 : 24 [CHIRALCEL OJ-H (0.46 cm × 25 cm), hexane : 2-propanol = 90 : 10, 1.0 mL min^{-1}, λ = 214 nm, *t* (major) = 7.307 min, *t* (minor) = 7.919 min, *t* (*meso*) = 9.852 min]. $[\alpha]_D^{20}$ −87.0 (*c* 0.6, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.23 (dd, *J* = 8.0, 7.6 Hz, 2H), 6.83 (d, *J* = 8.4 Hz, 2H), 6.75 (d, *J* = 7.6 Hz, 2H), 6.70 (s, 2H), 3.80 (s, 6H), 3.14 (dd, *J* = 9.6, 5.6 Hz, 2H). 2.02 (dq, *J* = 7.6, 6.4 Hz, 2H), 1.77 (dq, *J* = 7.6, 6.8 Hz, 2H), 0.78 (t, *J* = 7.6 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 159.6, 142.9, 129.3, 120.6, 113.9, 112.8, 56.9, 55.1, 27.7, 12.2. HRMS (EI+, *m*/*z*): calcd. for $C_{20}H_{26}O_2S_2$ [M]$^+$: 362.1374, found: 362.1376. IR (KBr): ν_{max} (cm^{-1}) = 2960, 2360, 2338, 1652, 1560, 1258, 911, 748.

1,2-Bis(1-(4-methoxyphenyl)propyl)disulfane (6c). The mixture was purified by flash column chromatography (100% petroleum ether) to give **6c** as a pale yellow solid (mp: 91–97 °C) in 69% yield. ee = 98%, DL : *meso* = 84 : 16 [CHIRALCEL OJ-H (0.46 cm × 25 cm), hexane : 2-propanol = 90 : 10, 1.0 mL min^{-1}, λ = 214 nm, *t* (major) = 9.512 min, *t* (minor) = 14.193 min, *t* (*meso*) = 17.431 min]. $[\alpha]_D^{20}$ −173.3 (*c* 0.6, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.09 (d, *J* = 8.8 Hz, 4H), 6.84 (d, *J* = 8.8 Hz, 4H), 3.81 (s, 6H), 3.17 (dd, *J* = 9.6, 5.2 Hz, 2H), 2.03 (dq, *J* = 7.2, 5.6 Hz, 2H), 1.75 (dq, *J* = 7.2, 6.4 Hz, 2H), 0.78 (t, *J* = 7.6 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 159.0, 133.1, 129.3, 113.7, 56.2, 55.3, 27.7, 12.2. HRMS (EI+, *m*/*z*): calcd. for $C_{20}H_{26}O_2S_2$ [M]$^+$: 362.1374, found: 362.1360. IR (KBr): ν_{max} (cm^{-1}) = 2963, 2929, 1726, 1609, 1511, 1458, 1385, 1302, 1246, 1172, 1117, 1034, 828, 797, 763, 732, 698.

1,2-Bis(1-*p*-tolylpropyl)disulfane (6d). The mixture was purified by flash column chromatography (100% petroleum ether) to give **6d** as a white solid (mp: 67–77 °C) in 73% yield. ee = 95%, DL : *meso* = 86 : 14 [CHIRALCEL OJ-H (0.46 cm × 25 cm), hexane : 2-propanol = 100 : 1, 0.7 mL min^{-1}, λ = 214 nm, *t* (major) = 8.727 min, *t* (minor) = 11.477 min, *t* (*meso*) = 15.075 min]. $[\alpha]_D^{20}$ −70.5 (*c* 0.4, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.11 (d, *J* = 8.0 Hz, 4H), 7.04 (d, *J* = 8.0 Hz, 4H), 3.17 (dd, *J* = 9.6, 5.2 Hz, 2H), 2.34 (s, 6H), 2.02 (dq, *J* = 8.0, 7.2 Hz, 2H), 1.76 (dq, *J* = 7.6, 7.2 Hz, 2H), 0.77 (t, *J* = 7.2 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 138.1, 137.0, 129.0, 128.2, 56.6, 27.7, 21.1, 12.2. HRMS (EI+, *m*/*z*): calcd. for $C_{20}H_{26}S_2$ [M]$^+$: 330.1476, found: 330.1472. IR (KBr): ν_{max} (cm^{-1}) = 2960, 2923, 2868, 1511, 1458, 1385, 1261, 1185, 1114, 1080, 815, 797, 748.

1,2-Bis(1-(4-chlorophenyl)propyl)disulfane (6e). The mixture was purified by flash column chromatography (100% petroleum ether) to give **6e** as a colorless liquid in 51% yield. ee = 99%, DL : *meso* = 84 : 16 [CHIRALCEL OJ-H (0.46 cm × 25 cm), hexane : 2-propanol = 90 : 10, 1.0 mL min^{-1}, λ = 214 nm, *t* (major) = 4.597 min, *t* (minor) = 4.997 min, *t* (*meso*) = 5.487 min]. $[\alpha]_D^{20}$ −317.3 (*c* 0.3, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.27 (d, *J* = 8.4 Hz, 4H), 7.08 (d, *J* = 8.4 Hz, 4H), 3.17 (dd, *J* = 9.6, 5.6 Hz, 2H), 2.05 (dq, *J* = 7.6, 5.6 Hz, 2H), 1.78 (dq, *J* = 9.6, 7.2 Hz, 2H), 0.77 (t, *J* = 7.2 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 139.7, 133.2, 129.5, 128.5, 56.4, 27.8, 12.1. HRMS (EI+, *m*/*z*): calcd. for $C_{18}H_{20}Cl_2S_2$[M]$^+$: 370.0383, found: 370.0387. IR (KBr): ν_{max} (cm^{-1}) = 2960, 2929, 2868, 1895, 1489, 1455, 1403, 1375, 1286, 1178, 1092, 1012, 911, 825, 742, 520.

1,2-Bis(1-(4-bromophenyl)propyl)disulfane (6f). The mixture was purified by flash column chromatography (100% petroleum ether) to give **6f** as a colorless liquid in 49% yield. ee = 97%, DL : *meso* = 82 : 18 [CHIRALCEL OJ-H (0.46 cm × 25 cm), hexane : 2-propanol = 98 : 2, 0.3 mL min^{-1}, λ = 214 nm, *t* (major) = 22.325 min, *t* (minor) = 26.313 min, *t* (*meso*) = 27.774 min]. $[\alpha]_D^{20}$ −504.0 (*c* 0.2, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.44 (d, *J* = 8.4 Hz, 4H), 7.01 (d, *J* = 8.4 Hz, 4H), 3.15 (dd, *J* = 6.0, 5.6 Hz, 2H), 1.99 (dq, *J* = 7.2, 6.4 Hz, 2H), 1.74 (dq, *J* = 7.6, 6.8 Hz, 2H), 0.79 (t, *J* = 7.6 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 140.2, 131.5, 129.9, 56.5, 27.8, 12.2. HRMS (EI+, *m*/*z*): calcd. for $C_{18}H_{20}Br_2S_2$ [M]$^+$: 457.9373, found: 457.9377. IR (KBr): ν_{max} (cm^{-1}) = 3480, 2963, 1649, 1483, 1452, 1403, 1262, 1077, 1071, 803, 738, 702, 523.

1,2-Bis(1-(thiophen-2-yl)propyl)disulfane (6g). The mixture was purified by flash column chromatography (100% petroleum ether) to give **6g** as a colorless liquid in 40% yield. ee = 97%, DL : *meso* = 87 : 13 [CHIRALCEL OJ-H (0.46 cm × 25 cm), hexane : 2-propanol = 90 : 10, 1.0 mL min^{-1}, λ = 254 nm, *t* (major) = 8.195 min, *t* (minor) = 9.315 min, *t* (*meso*) = 10.938 min]. $[\alpha]_D^{20}$ −252 (*c* 0.25, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.25 (d, *J* = 5.6 Hz, 2H), 6.96 (dd, *J* = 4.8, 3.6 Hz, 2H), 6.90 (d, *J* = 3.2 Hz, 2H), 3.49 (dd, *J* = 5.6, 5.6 Hz, 2H), 2.09 (dq, *J* = 7.2, 6.4 Hz, 2H), 1.83 (dq, *J* = 7.2, 6.8 Hz, 2H), 0.89 (t, *J* = 7.2 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.9, 126.6, 126.1, 124.9, 52.2, 29.2, 12.2. HRMS (EI+, *m*/*z*): calcd. for $C_{14}H_{18}S_4$ [M]$^+$: 314.0291, found: 314.0277. IR (KBr): ν_{max} (cm^{-1}) = 2960, 2926, 2846, 1723, 1452, 1385, 1252, 1077, 800, 695.

1,2-Bis(1-phenylpentan-3-yl)disulfane (6h). The mixture was purified by flash column chromatography (100% petroleum ether) to give **6h** as a colorless liquid in 55% yield. ee = 99%, DL : *meso* = 90 : 10 [CHIRALCEL OJ-H (0.46 cm × 25 cm), hexane : 2-propanol = 100 : 1, 0.7 mL min^{-1}, λ = 214 nm, *t*

(major) = 28.718 min, *t* (minor) = 20.552 min, *t* (*meso*) = 23.817 min]. $[\alpha]_D^{20}$ −129.7 (*c* 0.35, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.27 (dd, *J* = 7.6, 6.8 Hz, 4H), 7.18 (dd, *J* = 6.8, 6.4 Hz, 6H), 2.74 (dd, *J* = 8.0, 7.2 Hz, 4H), 2.59 (tt, *J* = 6.8, 6.4 Hz, 2H), 1.92 (dt, *J* = 7.2, 6.8 Hz), 1.68 (dq, *J* = 7.2, 6.8 Hz, 4H), 0.97 (t, *J* = 7.2 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 141.8, 128.4, 128.4, 125.9, 53.2, 35.3, 33.0, 26.9, 11.1. HRMS (EI+, *m*/*z*): calcd for $C_{22}H_{30}S_2$ $[M]^+$: 358.1789, Found: 358.1791. IR (KBr): ν_{max} (cm^{-1}) = 2951, 2363, 2338, 1557, 1523, 1268, 917, 745, 702.

Synthesis of (*S*)-1-phenylpropane-1-thiol (7a)

To a solution of the triisopropylsilane sulfide **4a** (77 mg, 0.25 mmol) in THF (2 mL) and *i*-PrOH (2 mL) were added *o*-nitrobenzenesulfonylhydrazide (109 mg, 0.50 mmol) and triethylamine (101 mg, 1.00 mmol) at 30 °C. The reaction was carried out overnight with TLC-followed. After the addition the mixture was quenched by sat. $NaHCO_3$ and extracted by hexane (3 × 5 mL). The organic layer was washed by sat. NaCl (aq.), dried by Na_2SO_4 and then concentrated. Under Ar atmosphere, the crude product was dissolved in HCl/Et_2O (4.5 M, 5 mL) with anhydrous $AlCl_3$ (200 mg, 1.5 mmol). The mixture was stirred overnight, and then partitioned between H_2O (5 mL) and Et_2O (5 mL), separated and the water layer was re-extracted with Et_2O (3 × 5 mL). The combined organic layer was dried with anhydrous Na_2SO_4, concentrated and purified by flash column chromatography (petroleum ether) to give **7a** (26 mg, 68% yield). $[\alpha]_D^{20}$ −86 (*c* 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.32 (d, *J* = 4.0 Hz, 4H), 7.23 (t, *J* = 4.4 Hz, 1H), 3.89 (dt, *J* = 5.6, 7.2 Hz, 1H), 1.97 (dq, *J* = 7.2, 7.6 Hz, 2H), 1.91(d, *J* = 5.2 Hz, 1H), 0.93 (t, *J* = 7.6 Hz, 3H). MS (EI+, *m*/*z*, rel. intensity): 119 (100), 152 (M^+).

Acetylation of (*S*)-1-phenylpropane-1-thiol (7a)

To a solution of (*S*)-1-phenylpropane-1-thiol **7a** (26 mg, 0.17 mmol) in DCM (3 mL), acetyl chloride (0.1 mL) and triethylamine (0.1 mL) were added. The mixture was stirred at room temperature for 1h. After the addition the mixture was quenched by water, and separated. The water layer was re-extracted by DCM (2 mL × 3). The organic layer was combined, washed with saturated NaCl (aq.) and then dried by anhydrous Na_2SO_4. Concentrated and the residue was treated by flash column chromatography (petroleum ether : DCM = 3 : 1) to give **8a**[6a,23] (32 mg, 99% yield) with 87% ee [CHIRALCEL OD-H (0.46 cm × 25 cm), hexane : 2-propanol = 100 : 1, 0.5 mL min^{-1}, λ = 214 nm, *t* (major) = 10.214 min, *t* (minor) = 13.580 min]. $[\alpha]_D^{20}$ −260 (*c* 0.2, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.27–7.31 (m, 4H), 7.25–7.23 (m, 1H), 4.49 (t, *J* = 7.6 Hz, 1H), 2.30 (s, 3H), 1.96 (dq, *J* = 7.6, 7.2 Hz, 2H), 0.91 (t, *J* = 7.2 Hz, 3H). MS (EI+, *m*/*z*, rel. intensity): 119 (100), 194 (M^+).

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