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Chiral sulfideoxathiane ligands for palladium-catalyzed asymmetric allylic alkylation

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Abstract—Easily prepared, chiral sulfideoxathiane ligands are described, which give excellent enantioselectivities (up to 99% ee) in the Pd-catalyzed allylic alkylation of 1,3-diphenyl-2-propenyl acetate with a range of alkyl malonate nucleophiles.

1. Introduction

Palladium-catalyzed allylation is one of the most important methods for forming carbon–carbon bonds in synthetic organic chemistry.[1] As such, the asymmetric version using a chiral ligand has also been studied extensively over the last decade.[1] Generally, the combination of a donor atom and a rigid backbone in the ligand is very important for realizing high levels of asymmetric induction in the reaction. There are many efficient homo- and heterodonor chiral ligands, such as N–N,[2] P–P,[3] N–P,[4] and S–P[5] ligands, but S–S[6] type ligands are inefficient, despite having advantages such as lower cost, toxicity, and oxidation potential. To the best of our knowledge, Gomez et al.[6a] have reported the only allylic alkylation using C_2-symmetric S–S type ligands, but this only afforded modest asymmetric induction (up to 81% ee) as the donor sites are insufficiently different for discriminating between both terminal allylic carbons in the intermediate. We attempted to synthesize asymmetric S–S type ligands with a borneol backbone because the ligand can be prepared easily from the reactions of mercaptoisoborneol or mercaptoborneol with phenylthio- or naphthylthiobenzaldehydes and because the lack of C_2-symmetry in the ligand may give rise to more than one intermediate complex whose reactivities determine the enantioselection. Herein, we report that the easily prepared S–S type sulfideoxathiane (SOT) ligands **7a–f** and **8a** and **b** showed dramatic reactivity and enantioselectivity (up to 99% ee) in all cases of the Pd-catalyzed allylic alkylation of 1,3-diphenyl-2-propenyl acetate with dimethyl and dialkyl methylmalonate nucleophiles.[7]

2. Results and discussion

2.1. Synthesis of chiral sulfideoxathiane ligands

Chiral sulfideoxathiane (SOT) ligands **7a–f** and **8a** and **b** were synthesized easily (Scheme 1). The 2-phenylthio- **4a–d** and 2-naphthylthiobenzaldehydes **4e** and **f** were prepared from the reactions of commercially available 2-chlorobenzaldehyde **1** with benzenethiols **2a–d** or naphthalenethiols **3a** and **b**, respectively, as reported elsewhere.[8] The desired SOT ligands **7a–d** and **8a** and **b**, were synthesized easily from the condensation reactions of commercially available (1*S*)-(−)-mercaptoisoborneol **5** or (1*S*)-(−)-mercaptoborneol **6** with 2-phenylthiobenzaldehydes **4a–d**. Furthermore, ligands **7e** or **7f** were obtained from the reactions of **5** with aldehydes **4e** or **4f**, respectively. Consequently, the simplest ligand **7a** with a fused isoborneol skeleton was obtained in 94% yield. Bulkier **7b**,**c**, and **7d**, which contain linking 2,6-dimethylmethylthio, 2-ethylphenylthio, or 2-*tert*-butylphenylthio moieties, were prepared in 97%, 98%, and 83% yields, respectively. The bulkiest ligands, **7e** and **7f**, containing linking 1-naphthylthio or 2-naphthylthio moieties, were both obtained in moderate yields (**7e**: 63%, **7f**: 65%). The stereochemical outcomes of **7a–f** and **8a** and **b** were determined using NOE difference spectra (NOEDS).[5c] NOE enhancement was observed between the hydrogens at the 3- and 5-positions when either the 3- or 5-position was irradiated, respectively.

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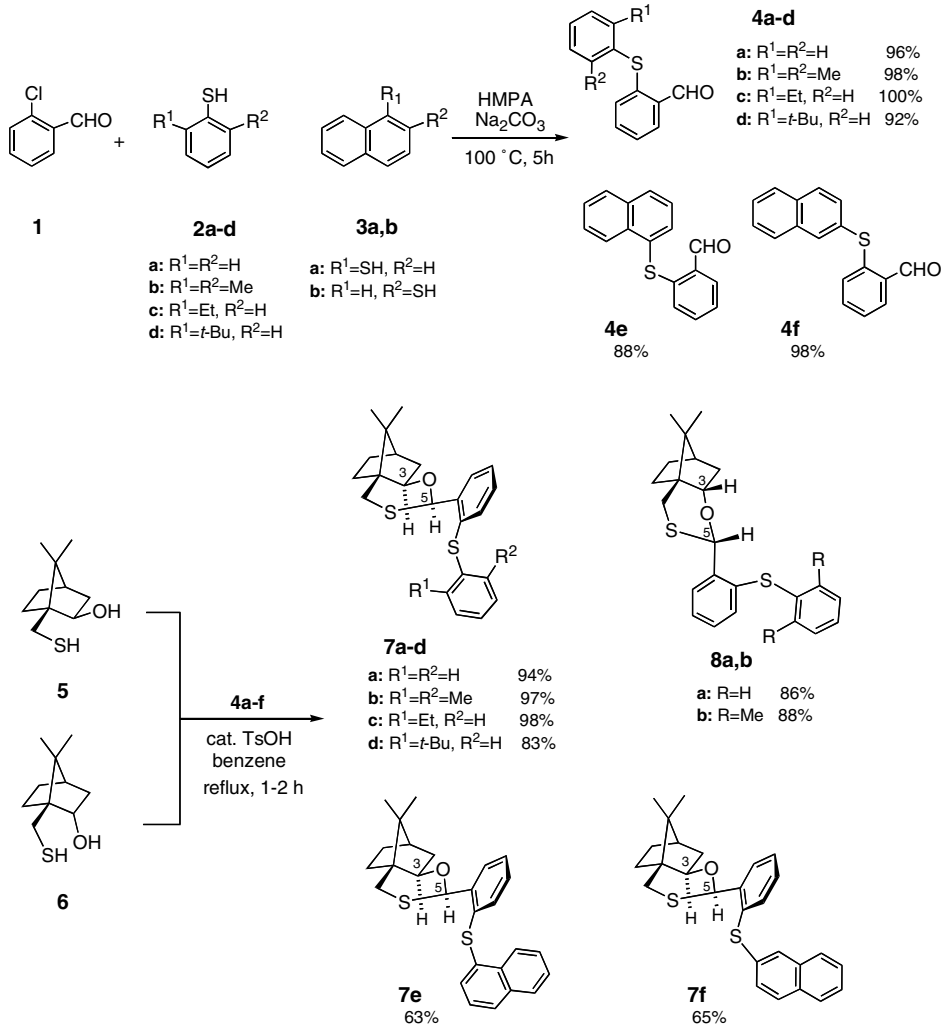


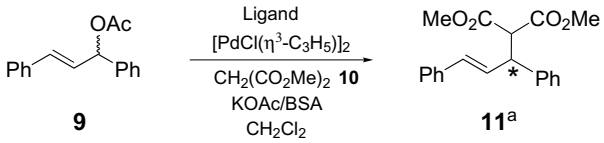
Scheme 1.

2.2. Palladium-catalyzed asymmetric allylic alkylation

The catalytic efficiency of the ligands was examined with the Pd-catalyzed asymmetric allylic alkylation of 1,3-diphenyl-2-propenyl acetate **9** with dimethyl malonate **10** in the presence of $[PdCl((\eta^3\text{-}C_3H_5)]_2$ and *N*,*O*-bis(trimethylsilyl)acetamide (BSA)[9] to give the allylation product **11** (Table 1). Initially, chiral ligands **7a**–**f** were tested. The simplest ligand, **7a**, showed excellent reactivity, but the enantioselectivity was moderate (57% ee) (entry 1). Ligand **7b** underwent a high degree of asymmetric induction (94% ee) (entry 2), while the reaction at 0 °C improved the enantioselectivity to 98% ee (entry 3). Next, ligands **7c** and **7d** were also tested at 0 °C (entries 4 and 5). Both ligands showed high reactivities and good enantioselectivities, but the results did not reach those of **7b**. On the other hand, ligands **7e** and **7f**, which incorporated a bulkier linked 1- or 2-naphthylthio moiety, gave the contrasted result. Thus, ligand **7e** showed moderate reactivity and good enantioselectivity. Inversely, **7f** showed excellent yield and moderate enatioselectivity (entries 6 and 7). Similarly, the catalytic activities of ligands **8a** and **8b**, with the fused borneol skeleton, were also examined. Although both ligands showed excellent reactivity, they did not give high enantiomeric excess (entries 8–10). From these results, SOT ligand **7b** was the most effective ligand in this reaction. These results indicated that the reactivity and enantioselectivity might depend greatly on the existence of a substituent group at the 2-position on the phenylthio group in STO ligand.

To optimize the reaction conditions using ligand **7b**, we next examined the effects of the molar ratio of ligand **7b**, the palladium source, and the solvent (Table 1). The use of 5 mol % of ligand **7b** caused a slight decrease in enantioselectivity (93% ee) (entry 11), and, at lower catalytic loadings (1 and 0.5 mol %), the reactions retained good enantioselectivity (1 mol %: 94% ee and 0.5 mol %: 92% ee), albeit in low chemical yields (entries 12 and 13). Furthermore, the effective combination of Pd-source and solvent was also examined using $[PdCl(\eta^3\text{-}C_3H_5)]_2$, $(dba)_3Pd_2CHCl_3$, $(dba)_3Pd_2$, and $PdCl_2(PhCN)_2$ as Pd-sources and CH_2Cl_2 or THF as solvents (Table 2, entries 1–8). The results showed that the combination of $[PdCl(\eta^3\text{-}C_3H_5)]_2$ and CH_2Cl_2 was better than any other Pd-source and solvent combination (entry 1). From these results, the most effective set of reaction conditions

Table 1. Asymmetric Pd-catalyzed allylic alkylation of acetate **9**[a]

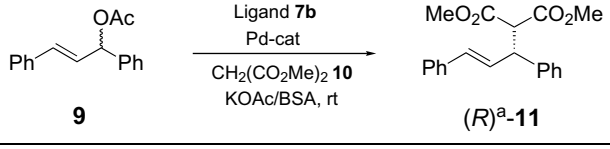


9 **11**[a]

Entry	Ligand	Ligand (mol %)	Temperature (°C)	Time (h)	Yield[d] (%)	ee[e] (%)
1[b]	**7a**	2	rt	12	100	57 (*R*)
2	**7b**	2	rt	15	100	94 (*R*)
3	**7b**	2	0	48	92	98 (*R*)
4	**7c**	2	0	72	83	93 (*R*)
5	**7d**	2	0	64	92	92 (*R*)
6	**7e**	2	0	66	56	86 (*R*)
7	**7f**	2	0	58	97	69 (*R*)
8	**8a**	2	rt	9	100	49 (*S*)
9	**8b**	2	rt	13	100	75 (*S*)
10	**8b**	2	0	48	86	86 (*S*)
11[c]	**7b**	5	0	48	100	93 (*R*)
12	**7b**	1	0	120	40	94 (*R*)
13	**7b**	0.5	0	144	38	92 (*R*)

[a] (*R*)-Configurations based on the specific rotation with literature data.[5c]
[b] Molar ratio for entries 1–10: $[PdCl(\eta^3\text{-}C_3H_5)]_2$ (0.01 equiv), dimethyl malonate (3 equiv), *N*,*O*-bis(trimethylsilyl)acetamide (BSA) (3 equiv), potassium acetate (0.02 equiv), **9** (1 equiv), ligands **7a**–**f** and **8a** and **8b** (0.02 equiv).
[c] Molar ratio for entries 11–13: $[PdCl(\eta^3\text{-}C_3H_5)]_2$ (5 mol %: 0.025 equiv, 0.1 mol %: 0.005 equiv, 0.5 mol %: 0.0025 equiv), dimethyl malonate (3 equiv), BSA (3 equiv), potassium acetate (0.02 equiv), **9** (1 equiv), ligand **7b** (5 mol %: 0.05 equiv, 1 mol %: 0.0105 equiv, 0.5 mol %: 0.005 equiv).
[d] Isolated yields.
[e] Determined by HPLC analysis using a DAICEL Chiralcel OD-H.

Table 2. Effect of the palladium precursor on the asymmetric allylic alkylation of acetate **9**[a]



9 (*R*)[a]-**11**

Entry[b]	Pd-catalyzed	Solvent	Time (h)	Yield[c] (%)	ee[d] (%)
1	$[PdCl(\eta^3\text{-}C_3H_5)]_2$	CH_2Cl_2	15	100	94
2	$[PdCl(\eta^3\text{-}C_3H_5)]_2$	THF	24	59	94
3	$(dba)_3Pd_2CHCl_3$	CH_2Cl_2	48	83	93
4	$(dba)_3Pd_2CHCl_3$	THF	72	54	94
5	$(dba)_3Pd_2$	CH_2Cl_2	48	82	92
6	$(dba)_3Pd_2$	THF	48	62	94
7	$PdCl_2(PhCN)_2$	CH_2Cl_2	144	26	90
8	$PdCl_2(PhCN)_2$	THF	144	16	90

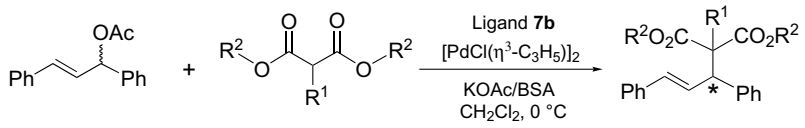
[a] (*R*)-Configurations based on the specific rotation with literature data.[5c]
[b] Molar ratio for entries 1–8: [Pd-cat. (0.01 equiv), dimethyl malonate (3 equiv), *N*,*O*-bis(trimethylsilyl)acetamide (BSA) (3 equiv), potassium acetate (0.02 equiv).
[c] Isolated yields.
[d] Determined by HPLC analysis using a DAICEL Chiralcel OD-H.

involved using 2 mol % of ligand **7b** with $[PdCl(\eta^3\text{-}C_3H_5)]_2$ in CH_2Cl_2 at 0 °C.

We also examined the reactions of acetate **9** with the bulkier diethyl malonate **12a** and dimethyl or diethyl methylmalonates **12b** and **c** as nucleophiles under the optimized reaction conditions using SOT ligand **7b** (Table 3). The reaction with **12a** proceeded in good chemical yield and enantioselectivity to give product **13a** (entry 1). Additionally, the use of malonates **12b** and **12c** afforded the corresponding products **13b** and **13c** with a stereogenic quaternary carbon center, in excellent chemical yield and enantioselectivity (entries 2 and 3). In particular, nucleophile **13c** achieved near complete stereocontrol with quantitative yield.

A superior SOT ligand **7b** was applied to the reactions of 3-acetoxycyclohexene **14** with nucleophiles **10** or **12a** in the presence of $[PdCl(\eta^3\text{-}C_3H_5)]_2$ and *N*,*O*-bis(trimethylsilyl)acetamide (BSA)[9] to give the corresponding allylation products **15a**[10] or **15b**[11] (Scheme 2). However, both reactions only afforded low enantioselectivities

Table 3. Pd-catalyzed asymmetric allylic alkylation of acetate **9** with dialkylmalonates **12a–c**[a]

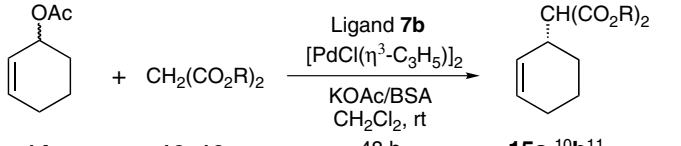


9 **12a-c** **13a-c**[a]

a: R^1=H, R^2=Et
b: R^1=Me, R^2=Me
c: R^1=Me, R^2=Et

Entry[b]	12a–c		Yield[c] (%)	ee[d] (%)
	R^1	R^2		
1	H	Et	96	93 (*R*)
2	Me	Me	100	96 (*S*)
3	Me	Et	100	99 (*S*)

[a] R Configuration based on the specific rotation with the literature data.[1e]
[b] Molar ratio for entries 1–3: $[PdCl(\eta^3\text{-}C_3H_5)]_2$ (0.01 equiv), dimethyl malonate (3 equiv), *N*,*O*-bis(trimethylsilyl)acetamide (BSA) (3 equiv), potassium acetate (0.02 equiv).
[c] Isolated yields.
[d] Determined by HPLC analysis using a DAICEL Chiralcel OJ-H or OD-H.



14 **10, 12a** **15a,**[10]**b**[11]

10: R=Me
12a: R=Et

a: R=Me, 78%, 35% ee
b: R=Et, 74%, 33% ee

Scheme 2.

(**10**: 35% ee, **12a**: 33% ee), although the chemical yields were good.

3. Conclusion

In conclusion, we have easily prepared a novel class of chiral sulfideoxathiane ligands (**7a–f** and **8a** and **b**) in two steps and applied it to Pd-catalyzed asymmetric allylic alkylation. As a result, SOT ligand **7b**, containing a linking 2,6-dimethylphenylthio moiety, had excellent activity and enantioselectivity for the reactions of acetate **9** with three kinds of malonate (96–99% ee). One advantage is that the developed SOT ligands are very stable in air and may be superior to ligands containing the phosphorus atom for practical use. This is a superlative result for an allylic alkylation. The SOT ligand has a characteristic structure and should prove useful not just for other allylations but also for other asymmetric processes.

4. Experimental

4.1. General methods

IR spectra were measured with a Perkin–Elmer 1725X spectrophotometer. ^{1}H NMR spectra were recorded on a JEOL JNM-GSX 270 and a JEOL JNM-LA 600 spectrometers with TMS as an internal standard. MS was taken on a JEOL JNM-DX 303 spectrometers. Optical rotations were measured with a JASCO-DPI-370 digital polarimeter.

4.2. General procedure for preparations of 4a–f

A mixture of 2-chlorobenzaldehyde **1** (1.0 g, 7.11 mmol), benzenethiol **2a–d**, or naphthalenethiol **3a** and **b** (7.82 mmol), sodium carbonate (1.51 g, 14.22 mmol) and HMPA (2 mL) was heated at 100 °C for 5 h with stirring. After cooling, the reaction mixture was poured into water and extracted with ether. The organic layer was washed with water and dried over anhydrous $MgSO_4$. Removal of the solvent under a reduced presser afforded **4a–f**, respectively.

4.2.1. 2-(2-Phenylthio)benzaldehyde 4a.[8a] Obtained (1.49 g, 98%) as a light yellow oil.

4.2.2. 2-(2,6-Dimethylphenylthio)benzaldehyde 4b. Obtained (1.69 g, 98%) as a white solid, mp 43–45 °C (hexane). IR (KBr) cm^{-1}: 1695, 1583, 844, 751. ^{1}H NMR ($CDCl_3$): δ 10.35 (s, 1H), 7.83 (d, $J = 6.9$ Hz, 1H), 7.18–7.30 (m, 5H), 6.55 (d, $J = 7.8$ Hz, 1H), 2.40 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 191.22, 144.05, 142.75, 133.91, 133.54, 132.22, 129.79, 129.27, 128.68, 125.23, 124.22, 21.59. MS *m*/*z*: 242 (M^+). HRMS calcd for $C_{15}H_{14}OS$: 242.0766, found: 242.0777.

4.2.3. 2-(2-Ethylphenylthio)benzaldehyde 4c. Obtained (1.70 g, 99%) as a light yellow oil. IR (film) cm^{-1}: 1695, 1587, 1558, 845, 755, 655. ^1H NMR ($CDCl_3$): δ 10.34 (s, 1H). 7.83 (dd, $J = 1.7$, 7.5 Hz, 1H), 7.18–7.38 (m, 6H), 6.84 (d, $J = 7.6$ Hz, 1H), 2.78 (dd, $J = 7.6$, 15.0 Hz, 2H), 1.18 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 191.18, 147.26, 142.40, 135.34, 133.84, 133.02, 132.31, 130.77, 129.39, 129.30, 128.68, 127.14, 125.35, 27.22, 15.18. MS m/z: 242 (M^+). HRMS calcd for $C_{15}H_{14}OS$: 242.0766, found: 242.0777.

4.2.4. 2-(2-*tert*-Butylphenylthio)benzaldehyde 4d. Obtained (1.77 g, 92%) as a light yellow oil. IR (film) cm^{-1}: 1693, 1588, 1558, 845, 656. ^1H NMR ($CDCl_3$): δ 10.36 (s, 1H), 7.84 (dd, $J = 1.7$, 7.5 Hz, 1H), 7.54 (d, $J = 8.2$ Hz, 1H), 7.16–7.38 (m, 5H), 6.80 (d, $J = 7.9$ Hz, 1H), 1.52 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 191.08, 152.62, 144.00, 138.27, 133.80, 133.03, 131.92, 131.57, 129.42, 128.78, 127.23, 127.16, 125.13, 36.73, 30.79×3. MS m/z: 270 (M^+). HRMS calcd for $C_{17}H_{18}OS$: 270.1078, found: 270.1058.

4.2.5. 2-(1-Naphthylthio)benzaldehyde 4e. Obtained (1.65 g, 88%) as a white solid, mp 83–84 °C (hexane). IR (KBr) cm^{-1}: 1673, 1588, 846, 759. ^1H NMR ($CDCl_3$): δ 10.40 (s, 1H), 8.27 (m, 1H), 7.75–7.96 (m, 4H), 7.46–7.56 (m, 3H), 7.14–7.25 (m, 2H), 6.67 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 191.24, 142.25, 134.46, 134.17, 133.90, 133.75, 132.88, 132.59, 130.31, 128.85, 128.60, 128.32, 127.27, 126.56, 125.95, 125.44, 125.08. MS m/z: 264 (M^+). HRMS calcd $C_{17}H_{12}OS$: 264.0609, found: 264.0574.

4.2.6. 2-(2-Naphthylthio)benzaldehyde 4f.[8b] Obtained as a white solid (1.84 g, 98%).

4.3. General procedure for preparations of chiral ligands 7a–f and 8a and b

(1*S*)-(−)-10-Mercaptoisoborneol **1** (100 mg, 0.54 mmol) or (1*S*)-(−)-10-mercaptoborneol **2** (100 mg, 0.54 mmol), 2-phenylthiobenzaldehyde **4a**–**d** (0.60 mmol) or 2-naphthylthiobenzaldehyde **4e**,**f** (0.60 mmol), *p*-toluenesulfonic acid monohydrate (20 mg, 0.11 mmol), and benzene (8 mL), were placed in a flask equipped with a Dean-Stark trap. The mixture was refluxed for 1–2 h. The solvent was evaporated under a reduced pressure and the residue purified by preparative TLC (hexane–ether = 10:1) to give the corresponding products **7a**–**f** and **8a** and **b**.

4.3.1. (1*R*,3*R*,5*R*,8*S*)-11,11-Dimethyl-4-oxa-5-(2-phenylthio)phenyl-6-thiatricyclo[6.2.1.0]undecane 7a. Obtained (194 mg, 94%) as a colorless oil. $[\alpha]_D^{24} = -55.2$ (*c* 1.74, $CHCl_3$). IR (film) cm^{-1}: 1583, 691, 656. ^1H NMR ($CDCl_3$): δ 7.69 (d, $J = 7.8$ Hz, 1H), 7.16–7.43 (m, 8H), 6.20 (s, 1H), 3.75 (dd, $J = 3.1$, 8.1 Hz, 1H), 3.29 (d, $J = 14.3$ Hz, 1H), 2.79 (d, $J = 14.2$ Hz, 1H), 2.01 (m, 1H), 1.68–1.78 (m, 3H), 1.54 (m, 1H), 1.50 (s, 3H), 1.00–1.02 (m, 2H), 0.96 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 140.45, 136.13, 132.74, 132.03, 130.10, 128.89, 128.76, 128.15, 127.97, 127.54, 126.46, 126.19, 85.67, 80.28, 46.77, 45.56, 41.94, 37.91, 34.30, 29.95, 27.24, 23.41, 20.45. MS m/z: 382 (M^+). HRMS calcd for $C_{23}H_{26}OS_2$: 382.1425, found: 382.1443.

4.3.2. (1*R*,3*R*,5*R*,8*S*)-11,11-Dimethyl-5-(2,6-dimethylphenylthio)phenyl-4-oxa-6-thiatricyclo[6.2.1.0]undecane 7b. Obtained (215 mg, 97%) as a white solid, mp 117–118 °C (hexane–ether). $[\alpha]_D^{24} = -10.0$ (*c* 2.20, $CHCl_3$). IR (KBr) cm^{-1}: 1580, 768, 750. ^1H NMR ($CDCl_3$): δ 7.59 (d, $J = 7.7$ Hz, 1H), 7.08–7.24 (m, 4H), 6.99 (t, $J = 7.6$ Hz, 1H), 6.46 (d, $J = 7.9$ Hz, 1H), 6.21 (s, 1H), 3.89 (dd, $J = 3.1$ Hz, 7.9 Hz, 1H), 3.38 (d, $J = 14.2$ Hz, 1H), 2.84 (d, $J = 14.2$ Hz, 1H), 2.39 (s, 6H), 2.06 (m, 1H), 1.72–1.84 (m, 3H), 1.58 (m, 1H), 1.51 (s, 3H), 1.03–1.13 (m, 2H), 0.98 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 143.90, 136.75, 134.91, 130.93, 129.19, 128.64, 128.48, 127.09, 125.55, 125.26, 85.98, 79.67, 46.89, 45.63, 42.16, 38.06, 34.43, 29.93, 27.35, 23.49, 21.90, 20.51. MS m/z: 410 (M^+). HRMS calcd for $C_{25}H_{30}OS_2$: 410.1738, found: 410.1711.

4.3.3. (1*R*,3*R*,5*R*,8*S*)-11,11-Dimethyl-5-(2-ethylphenylthio)phenyl-4-oxa-6-thiatricyclo[6.2.1.0]undecane 7c. Obtained (217 mg, 98%) as a white solid, mp 70–72 °C (hexane–ether). $[\alpha]_D^{22} = -27.95$ (*c* 1.86, $CHCl_3$). IR (KBr) cm^{-1}: 1586, 748, 706. ^1H NMR ($CDCl_3$): δ 7.66 (d, $J = 7.8$ Hz, 1H), 7.05–7.28 (m, 6H), 7.01 (d, $J = 7.8$ Hz, 1H), 6.17 (s, 1H), 3.76 (dd, $J = 3.0$, 7.9 Hz, 1H), 3.29 (d, $J = 14.3$ Hz, 1H), 2.76–2.85 (m, 3H), 1.99 (m, 1H), 1.70–1.78 (m, 3H), 1.51 (m, 1H), 1.50 (s, 3H), 1.24 (t, $J = 7.5$ Hz, 3H), 1.00–1.09 (m, 2H), 0.95 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 144.84, 139.60 133.84, 133.19, 132.63, 131.28, 128.74, 128.65, 127.53, 127.48, 127.25, 126.61, 85.80, 80.24, 46.85, 45.61, 42.07, 38.03, 34.41, 30.05, 27.35, 27.12, 23.52, 20.55, 14.88. MS m/z: 410 (M^+). HRMS calcd for $C_{25}H_{30}OS_2$: 410.1738, found: 410.1729.

4.3.4. (1*R*,3*R*,5*R*,8*S*)-5-(2-*tert*-Butylphenylthio)phenyl-11,11-dimethyl-4-oxa-6-thiatricyclo[6.2.1.0]undecane 7d. Obtained (196 mg, 83%) as a white solid, mp 100–102 °C (hexane–ether). $[\alpha]_D^{22} = -39.45$ (*c* 1.47, $CHCl_3$). IR (KBr) cm^{-1}: 1587, 759, 692. ^1H NMR ($CDCl_3$): δ 7.65 (dd, $J = 1.6$, 7.7 Hz, 1H), 7.43 (dd, $J = 1.4$, 8.0 Hz, 1H), 7.11–7.35 (m, 4H), 7.03 (t, $J = 7.3$ Hz, 2H), 6.16 (s, 1H), 3.72 (dd, $J = 3.1$, 7.9 Hz, 1H), 3.28 (d, $J = 14.2$ Hz, 1H), 2.78 (d, $J = 14.2$ Hz, 1H), 1.99 (m, 1H), 1.69–1.77 (m, 3H), 1.58 (s, 9H), 1.15 (m, 1H), 1.50 (s, 3H), 0.96 (s, 3H), 0.92–1.11 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 150.18, 139.67, 135.32, 135.03, 134.87, 131.99, 128.84, 127.52, 127.24, 126.93, 126.74, 126.46, 85.80, 80.38, 46.87, 45.63, 42.07, 38.04, 36.61, 34.44, 30.68×3, 30.04, 27.37, 23.52, 20.57. MS m/z: 438 (M^+). HRMS calcd for $C_{27}H_{34}OS_2$: 438.2051, found: 438.2061.

4.3.5. (1*R*,3*R*,5*R*,8*S*)-11,11-Dimethyl-5-(1-naphthylthio)phenyl-4-oxa-6-thiatricyclo[6.2.1.0]undecane 7e. Obtained (147 mg, 63%) as a white solid, mp 128–130 °C (hexane–ether). $[\alpha]_D^{22} = -57.6$ (*c* 1.18, $CHCl_3$).

IR (KBr) cm^{-1}: 1587, 793, 766, 697. ^1H NMR ($CDCl_3$): δ 8.35 (m, 1H), 7.79–7.87 (m, 2H), 7.68 (d, $J = 6.8$ Hz, 1H), 7.48–7.54 (m, 3H), 7.38 (t, $J = 7.8$ Hz, 1H), 7.23 (t, $J = 7.1$ Hz, 1H), 7.05 (t, $J = 7.6$ Hz, 1H), 6.91 (d, $J = 7.9$ Hz, 1H), 6.29 (s, 1H), 3.77 (dd, $J = 3.1$, 7.8 Hz, 1H), 3.28 (d, $J = 14.2$ Hz, 1H), 2.79 (d, $J = 14.2$ Hz, 1H), 2.03 (m, 1H), 1.67–1.79 (m, 3H), 1.51 (s, 3H), 1.48 (m, 1H), 0.95 (s, 3H), 0.92–1.10 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 139.16, 134.12, 133.27, 133.06, 131.87, 131.67, 130.74, 128.88, 128.62, 128.51, 127.59, 127.25, 126.85, 126.34, 125.86, 125.43, 85.86, 80.22, 46.83, 45.57, 42.03, 37.98, 34.29, 29.95, 27.27, 23.47, 20.47. MS *m/z*: 432 (M^+). HRMS calcd for $C_{27}H_{28}OS_2$: 432.1582, found: 432.1595.

4.3.6. (1*R*,3*R*,5*R*,8*S*)-11,11-Dimethyl-5-(2-naphthylthio)-phenyl-4-oxa-6-thiatricyclo[6.2.1.0]undecane 7f. Obtained (152 mg, 65%) as a white solid, mp 138–140 °C (hexane–ether). $[\alpha]_D^{22} = -12.0$ (*c* 1.50, $CHCl_3$). IR (KBr) cm^{-1}: 1587, 806, 742, 699. ^1H NMR ($CDCl_3$): δ 7.71–7.80 (m, 5H), 7.19–7.46 (m, 6H), 6.25 (s, 1H), 3.74 (dd, $J = 3.1$, 7.9 Hz, 1H), 3.30 (d, $J = 14.2$ Hz, 1H), 2.79 (d, $J = 14.2$ Hz, 1H), 2.00 (m, 1H), 1.66–1.74 (m, 3H), 1.51 (m, 1H), 1.50 (s, 3H), 0.90–1.04 (m, 2H), 0.95 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 140.57, 132.86, 132.18, 132.01, 128.93, 128.69, 128.13, 128.04, 127.70, 127.61, 127.27, 126.47, 125.95, 85.83, 80.44, 46.90, 45.64, 42.07, 38.02, 34.42, 30.08, 27.36, 23.54, 20.58. MS *m/z*: 432 (M^+). HRMS calcd for $C_{27}H_{28}OS_2$: 432.1582, found: 432.1556.

4.3.7. (1*R*,3*S*,5*S*,8*S*)-11,11-Dimethyl-4-oxa-5-(2-phenylthio)phenyl-6-thiatricyclo[6.2.1.0]undecane 8a. Obtained (177 mg, 86%) as a white solid, mp 98–99 °C (hexane–ether). $[\alpha]_D^{24} = -26.7$ (*c* 1.50, $CHCl_3$). IR (KBr) cm^{-1}: 1580, 741, 689. ^1H NMR ($CDCl_3$): δ 7.86 (d, $J = 7.5$ Hz, 1H), 7.35 (m, 1H), 7.17–7.28 (m, 7H), 6.35 (s, 1H), 3.93 (m, 1H), 3.25 (d, $J = 12.2$ Hz, 1H), 2.77 (m, 1H), 2.50 (d, $J = 12.2$ Hz, 1H), 2.22 (m, 1H), 1.71–1.77 (m, 2H), 1.26–1.48 (m, 2H), 1.15 (dd, $J = 4.7$ Hz, 13.6 Hz, 1H), 0.95 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 139.92, 136.18, 132.80, 132.23, 130.13, 128.99, 128.89, 128.06, 127.94, 126.47, 84.37, 82.16, 47.06, 44.73, 44.25, 34.47, 33.31, 27.92, 25.92, 19.61, 18.66. MS *m/z*: 382 (M^+). HRMS calcd for $C_{23}H_{26}OS_2$: 382.1425, found: 382.1400.

4.3.8. (1*R*,3*S*,5*S*,8*S*)-11,11-Dimethyl-5-(2-dimethylphenylthio)phenyl-4-oxa-6-thiatricyclo[6.2.1.0]undecane 8b. Obtained (195 mg, 88%) as a white solid, mp 154–156 °C (hexane–ether). $[\alpha]_D^{24} = -60.6$ (*c* 1.60, $CHCl_3$). IR (KBr) cm^{-1}: 1589, 770, 747, 697. ^1H NMR ($CDCl_3$): δ 7.75 (d, $J = 7.7$ Hz, 1H), 7.11–7.23 (m, 4H), 7.01 (m, 1H), 6.46 (d, $J = 8.0$ Hz, 1H), 6.35 (s, 1H), 4.05 (m, 1H), 3.32 (d, $J = 12.2$ Hz, 1H), 2.93 (m, 1H), 2.55 (d, $J = 12.4$ Hz, 1H), 2.39 (s, 6H), 2.30 (m, 1H), 1.73–1.78 (m, 2H), 1.33–1.50 (m, 2H), 1.15 (dd, $J = 4.8$ Hz, 13.5 Hz, 1H), 0.98 (d, $J = 6.1$ Hz, 6H). ^{13}C NMR ($CDCl_3$): δ 143.79, 136.07, 134.99, 130.71, 129.10, 128.75, 128.37, 127.42, 125.38, 125.21, 84.63, 81.57, 47.22, 44.87, 44.51, 34.69, 33.33, 28.06, 26.08, 21.99, 19.78, 18.83. MS *m/z*: 410 (M^+). HRMS calcd for $C_{25}H_{30}OS_2$: 410.1738, found: 410.1722.

4.4. Typical procedure of Pd-catalyzed asymmetric allylic alkylations of 1,3-diphenyl-2-propenyl acetate 9 with malonates 10 and 12a–c

A mixture of the ligands **7a–f** and **8a** and **8b** (0.008 mmol) and $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (1.46 mg, 0.004 mmol) in dry dichloromethane (1 mL) was stirred at room temperature for 1 h, and the resulting yellow solution added to a mixture of acetate **9** (100 mg, 0.40 mmol) and potassium acetate (0.8 mg, 0.008 mmol) in dry dichloromethane (1 mL), followed by the addition of malonates **10**, **12a–c** (1.2 mmol), and BSA (240 mg, 1.2 mmol). The mixture was stirred at rt or 0 °C, diluted with ether, and quenched with satd NH_4Cl. The organic layer was washed with brine and dried over $MgSO_4$. The solvent was evaporated under a reduced pressure, and the residue was purified by preparative TLC (hexane–ether = 6:1) to give pure products **11** and **13a–c**, respectively. The enantiomeric excess was determined by HPLC (**10**: Chiralcel OD-H, 0.5 mL/min, hexane–2-propanol = 98–2, **13a**: Chiralcel OJ-H, 0.5 mL/min, hexane–2-propanol = 95:5, **13b,c**: Chiralcel OD-H + OD-H, 0.5 mL/min, hexane–2-propanol = 199:1). The absolute configuration was determined by the specific rotation.[1d,e]

4.5. Typical procedure of Pd-catalyzed asymmetric allylic alkylations of 3-acetoxycyclohexene 14 with malonates 10 and 12a

A mixture of ligand **7b** (23.4 mg, 0.057 mmol) and $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (10.4 mg, 0.0285 mmol) in dry dichloromethane (1 mL) was stirred at room temperature for 1 h, and the resulting yellow solution added to a mixture of acetate **14** (80 mg, 0.57 mmol) and potassium acetate (1.1 mg, 0.011 mmol) in dry dichloromethane (1 mL), followed by the addition of malonates **10** or **12a** (1.71 mmol) and BSA (348 mg, 1.71 mmol). The mixture was stirred at rt, diluted with ether, and quenched with satd NH_4Cl. The organic layer was washed with brine and dried over $MgSO_4$. The solvent was evaporated under a reduced pressure, and the residue was purified by preparative TLC (hexane–ether = 10:1) to give a pure products **15a** and **15b**, respectively. The enantiomeric excess of **15a**[10] was determined by ^1H NMR with $Eu(hfc)_3$ and of **15b**[11] was determined by the specific rotation. The absolute configuration of **15a**[10] and **15b**[11] were determined by the specific rotation.

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