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Harmony of CdI_2 with CuBr for the one-pot synthesis of optically active α-allenols†

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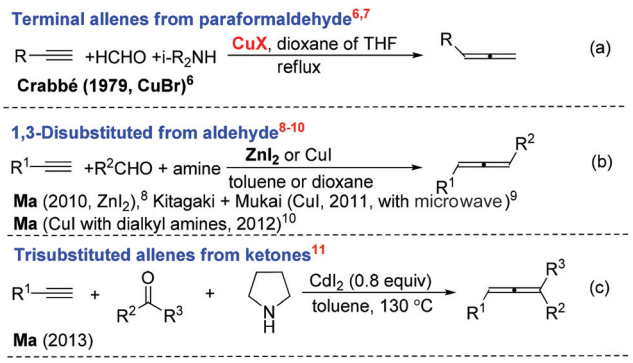
A highly efficient one-pot synthesis of chiral α-allenols from propargylic alcohols, aldehydes and pyrrolidine induced by CuBr and (*R*,R_a)-*N*-PINAP or (*R*,S_a)-*N*-PINAP and CdI_2 has been developed. Both the yields and enantioselectivities of the allenols of this one-pot procedure are practical. Comparison with ZnI_2 control experiments revealed that CdI_2 can convert propargylic amine to allene in the presence of CuBr efficiently.

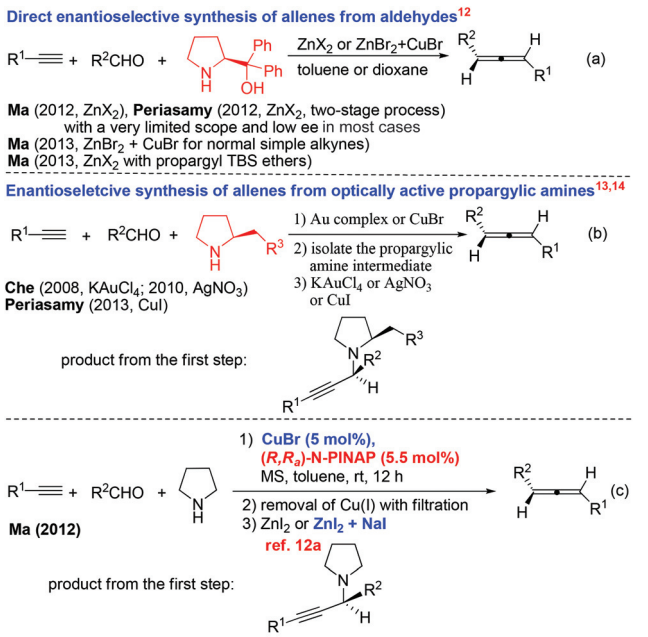
Introduction

Allenes are becoming more and more important in organic synthesis.[1,2] Allene units have also been identified in some biologically active natural products and drugs.[3] Furthermore, the potential of their axial-to-central chirality transfer would provide a very appealing and unique route to chiral products.[4] Thus, the development of highly efficient approaches to different types of allenes, especially optically active ones, is of current interest with urgency.[5] One of the methods that has been attracting our attention is the allenylation of terminal alkynes (ATA), pioneered by Crabbé originally using paraformaldehyde (the Crabbé reaction) (Scheme 1).[6–11]



Scheme 1 The evolution of allenylation of terminal alkynes.

Enantioselective syntheses of chiral allenes from terminal alkynes and aldehydes have also been developed in a one-pot or two-pot manner using chiral amines (Scheme 2).[12–14] In 2012, we also developed a two-step approach by using a catalytic amount of chiral *N*-PINAP/CuBr and ZnI_2 (or ZnI_2 together with NaI) (reaction c in Scheme 2).[12a] Although much progress has been made in allene synthesis, the synthesis of chiral allenols is still fairly complicated.[15] We are especially interested in developing one-pot approaches to the chiral allenes with a catalytic amount of a chiral ligand. In reaction c[12a] of Scheme 2, although the ee is practical, ZnI_2 is not able to convert



Scheme 2 The evolution of syntheses of axially chiral 1,3-disubstituted allenes from terminal alkynes and aldehydes.

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†Electronic supplementary information (ESI) available: The experimental procedures, characterization data, and copies of ^1H and ^{13}C NMR spectra for all products. See DOI: 10.1039/c4ob02673j

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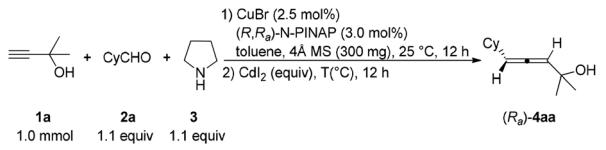
propargylic amine to allene *efficiently* in the presence of CuBr. In this paper, we wish to report our recent observation on the realization of a one-pot efficient synthesis of optically active α-allenols by an enantioselective ATA (allenylation of terminal alkynes) reaction of terminal propargylic alcohols, in which CdI_2 (ref. 11) may work in the presence of CuBr to convert the propargylic amine intermediate to allene efficiently.

Results and discussion

With 2-methyl-3-butyn-2-ol, cyclohexanal and pyrrolidine as the starting point based on our previous report,[12a] interestingly we observed that CdI_2 [11] may work in harmony with the presence of 2.5 mol% CuBr to produce (R_a)-**4aa** in practical ee with one-pot operation. After screening some parameters for the second step, we observed that the amount of CdI_2 is important to the yields of (R_a)-allenol (entries 1–3, Table 1). The reaction temperature is also critical to the yields (entries 4–6, Table 1). Neither the loading of CdI_2 nor the reaction temperature has an obvious effect on the enantioselectivity. Therefore, the standard conditions have been defined as follows (entry 7): a mixture of 2.5 mol% CuBr, 3.0 mol% (R,R_a)-*N*-PINAP, 1.0 mmol propargylic alcohol, 1.1 mmol aldehyde and 1.1 mmol pyrrolidine was heated in toluene with stirring; after the first step was complete, CdI_2 and toluene were added sequentially to the original Schlenk tube without filtration, which was then placed in an oil bath at 90 °C to execute the next step.

Table 1 Optimization of the reaction conditions[a]

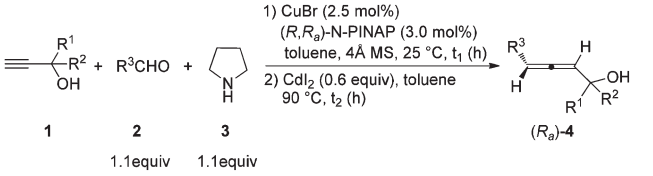


Entry	CdI_2 (equiv.)	T (°C)	(Ra)-4aa Yield[b] (%)	(Ra)-4aa ee[c] (%)
1	0.8	90	41	95
2	0.6	90	53	95
3	0.4	90	45	97
4[d]	0.6	90	66	95
5[d]	0.6	100	45	94
6[d]	0.6	80	44	95
7[e]	0.6	90	68	97

[a] The reactions were carried out with **1a** (1.0 mmol), **2a** (1.1 mmol), and **3** (1.1 mmol) in 2 mL of toluene, then CdI_2 was added to convert propargylic amine to allene. [b] Isolated yields. [c] Determined by chiral HPLC analysis. [d] After CdI_2 was added, an additional 2 mL of toluene were added. [e] The reaction time for the second step was 2 h.

With the optimized reaction conditions in hand, the generality of the reaction was investigated. Tertiary propargylic alcohols were firstly chosen to react with cyclohexanal and pyrrolidine. Tertiary propargylic alcohols were able to afford the corresponding allenols in moderate to good yields with over 90% ee (entries 1–9, Table 2). The scope of the aldehydes is also quite general: secondary alkyl (entries 1–7, Table 2), normal alkyl (entry 8, Table 2) and aromatic aldehydes (entry 9, Table 2) were all able to be used to afford the products with moderate to good yields and decent enantioselectivities. For the enantioselectivity, in general, the (R,R_a)-*N*-PINAP ligand (entries 2, 4 and 9, Table 2) is better than (R,S_a)-*N*-PINAP (entries 10–12, Table 2), which may be caused by the low solubility of the complex formed from CuBr and (R,S_a)-N-PINAP.[16] Most of the results are comparable to those of the ZnI_2-mediated two-pot approach,[12a] and some of them are even better in terms of yields and enantioselectivities.

Table 2 One-pot synthesis of optically active α-allenenols from terminal propargylic alcohols, aldehydes, and pyrrolidine with (R,R_a)-*N*-PINAP or (R,S_a)-*N*-PINAP as the chiral ligand[a]



Entry	1: R^1, R^2	2: R^3	t_1/t_2	4: Yield[b]	4: ee[c] (%)
1	Me, Me (**1a**)	Cy (**2a**)	12/2	68 (R_a-**4aa**)	97
2	Et, Et (**1b**)	Cy (**2a**)	12/12	84 (R_a-**4ba**)	93
3	–$(CH_2)_4$– (**1c**)	Cy (**2a**)	12/12	56 (R_a-**4ca**)	93
4	–$(CH_2)_5$– (**1d**)	Cy (**2a**)	12/4.5	68 (R_a-**4da**)	93
5[d]	–$(CH_2)_5$– (**1d**)	Cy (**2a**)	12/12	67 (R_a-**4da**)	94
6	–$(CH_2)_5$– (**1d**)	i-Pr (**2b**)	21.5/6	50 (R_a-**4db**)	91
7	–$(CH_2)_5$– (**1d**)	i-Bu (**2c**)	13/4	48 (R_a-**4dc**)	93
8	–$(CH_2)_5$– (**1d**)	*n*-C_7H_{15} (**2d**)	23/3	53 (R_a-**4dd**)	92
9	–$(CH_2)_5$– (**1d**)	Ph (**2e**)	19/5.5	88 (R_a-**4de**)	95
10[e]	Et, Et (**1b**)	Cy (**2a**)	12/12	80 (S_a-**4ba**)	92
11[e]	–$(CH_2)_5$– (**1d**)	Cy (**2a**)	12/4.5	70 (S_a-**4da**)	90
12[e]	–$(CH_2)_5$– (**1d**)	Ph (**2e**)	19/4.5	82 (S_a-**4de**)	93

[a] The reactions were carried out on a 1.0 mmol scale of **1** in toluene unless otherwise noted. [b] Isolated yield. [c] Determined by HPLC analysis. [d] 10.0 mmol of **1d** were used in this reaction. [e] (R,S_a)-*N*-PINAP was used as the ligand.

Control experiments showed that in the ZnI_2-mediated reaction, removal of the CuBr complex by filtration has no obvious effect on the enantioselectivity; however, it greatly improves the yield (eqn (1) and (2), Scheme 3). Interestingly, in the CdI_2-mediated reaction, there is no obvious effect on either yield or enantioselectivity, indicating the harmony of CdI_2 with CuBr and the ligand for allene formation (entry 4 in Table 2 and eqn (5) in Scheme 3). Although CuBr, the ligand and CdI_2 could together promote this reaction in one pot at room temperature yielding propargylic amines in 80% yield, the ee is very low (16%) (eqn (3) in Scheme 3), and the same reaction at 90 °C afforded the allene in 66% yield and 8% ee (eqn (4) in Scheme 3), indicating that CdI_2 could promote the formation of propargylic amine in the absence of the ligand.

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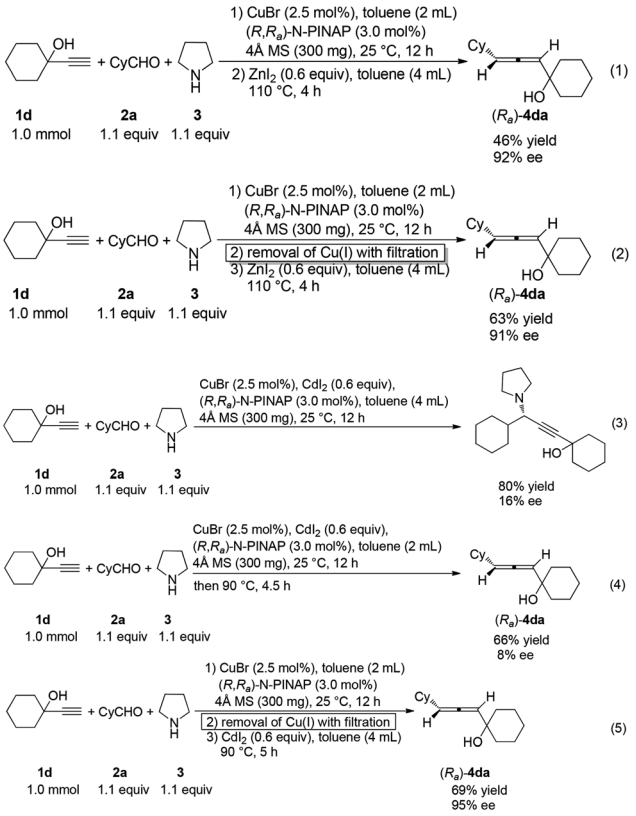
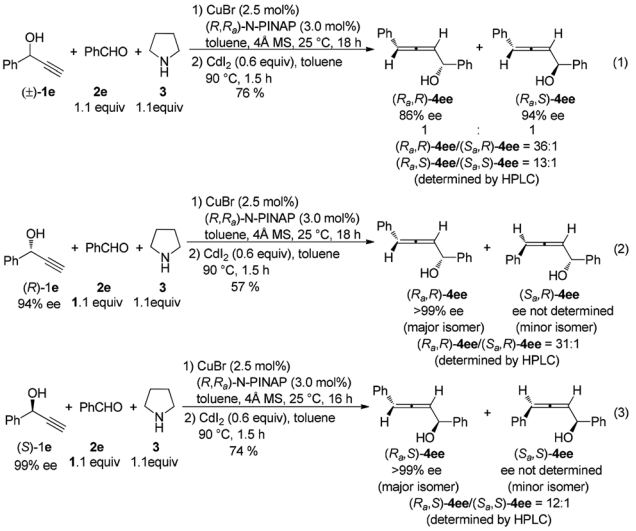
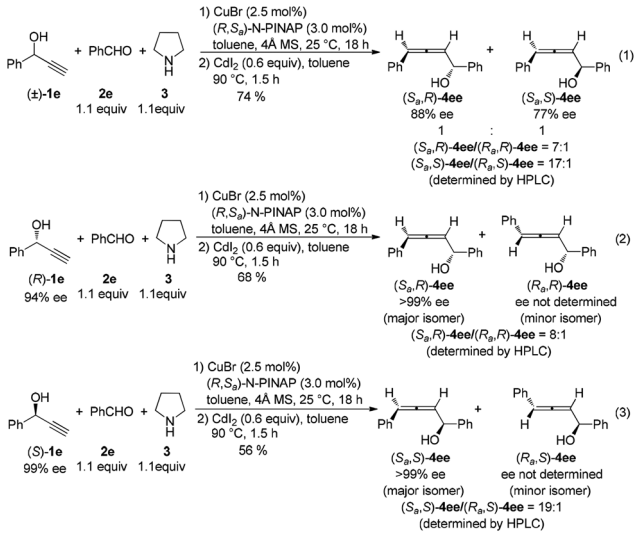


Scheme 3 Control experiments.

Next, by using optically active (*R*)- or (*S*)-1-phenyl-2-propyn-1-ol, (R_a,*R*)-**4ee** and (R_a,*S*)-**4ee** could be prepared by using (*R*,R_a)-*N*-PINAP as the ligand (eqn (1)–(3) in Scheme 4). Similarly, (S_a,*R*)-**4ee** and (S_a,*R*)-**4ee** were also prepared *via* the reactions with (*R*,S_a)-*N*-PINAP as the ligand (eqn (1)–(3) in Scheme 5).

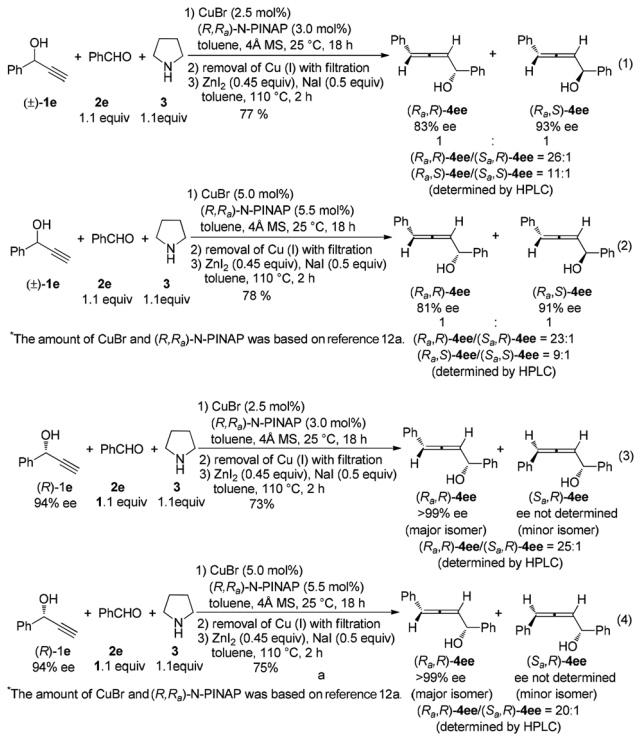


Scheme 4 The one-pot approach for the reaction of **1e**, benzaldehyde and pyrrolidine with (*R*,R_a)-*N*-PINAP as the ligand.



Scheme 5 The one-pot approach for the reaction of **1e**, benzaldehyde and pyrrolidine with (*R*,S_a)-*N*-PINAP as the ligand.

Results of the control experiments involving the ZnI_2-mediated reactions of *rac*- or (*R*)-1-phenyl-2-propyn-1-ol, cyclohexanal and pyrrolidine[12a] further show that the results of the current protocol are comparable (eqn (1)–(4) in Scheme 6).



Scheme 6 Two-pot approach for the reaction of **1e**, benzaldehyde and pyrrolidine with ZnI_2.

The absolute configurations of the allenols were assigned based on our previous study[12a] and the Lowe-Brewster rule.[17] A model to predict the absolute configuration of the allenols is shown in Scheme 7.

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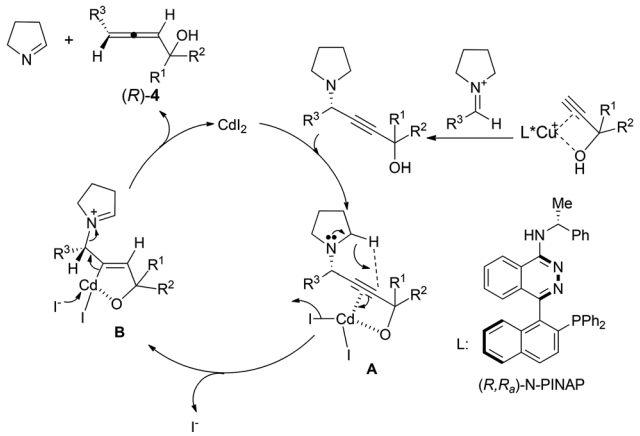

Scheme 7 Proposed mechanism and prediction of the absolute configuration of the axial chirality in allenols.

Conclusions

In conclusion, we have observed that CdI_2 can work in harmony with CuBr to transform terminal propargylic alcohols and aldehydes to allenols with high yields and enantioselectivities. The difference between ZnI_2 and CdI_2 is striking since ZnI_2 fails to convert the intermediates, propargylic amines, to allenes in high efficiency in the presence of CuBr and the chiral ligand. Due to the fact that the starting materials are commercially available, this protocol with simple operation avoiding filtration will be of great interest to the scientific community. Further studies on the substrate scope, mechanism of the weak interaction and applications of allenols are being carried out in our lab.

Experimental

General information

All reactions were carried out in oven-dried Schlenk tubes. All ^{1}H NMR experiments were referenced relative to the signal of tetramethylsilane (0 ppm) in $CDCl_3$ and ^{13}C NMR experiments were referenced with the signal of residual chloroform (77.00 ppm) in $CDCl_3$. IR spectra were recorded on a Bruker Tensor 27 infrared spectrometer. CuBr (98%) was purchased from Acros and CdI_2 (99.9%) was purchased from Aladdin and kept in a glove box; ZnI_2 was purchased from Alfa Aesar and kept in a glove box; (*R*,R_a)-*N*-PINAP (97%) and (*R*,S_a)-*N*-PINAP (97%) were purchased from Strem Chemicals and kept in a glove box; 4 Å molecular sieves were purchased from Alfa Aesar and kept in a glove box after activation (heated at 450 °C for 10 h in a Muffle furnace, taken out after cooling to 200 °C and then kept in a glove box and allowed to cool to room temperature). Aldehydes were distilled immediately before use. 2-Methyl-3-butyn-2-ol (**1a**) and pyrrolidine (**3**) were redistilled. (*R*)-1-Phenyl-2-propyn-1-ol and (*S*)-1-phenyl-2-propyn-1-ol were prepared according to the previous report.[18] Toluene was dried over sodium wire with benzophenone as the indicator and distilled freshly before use. Other reagents were used without further treatment. All temperatures refer to the temperature of the oil bath used. Petroleum ether (60–90 °C) for chromatography was distilled before use.

Typical procedure I

(1) Preparation of (R_a)-5-cyclohexyl-2-methyl-3,4-pentadien-2-ol ((R_a)-4aa). To a flame-dried Schlenk tube were added CuBr (3.7 mg, 0.025 mmol), (*R*,R_a)-*N*-PINAP (17.6 mg, 0.03 mmol), and toluene (2 mL) under an argon atmosphere. The mixture was stirred at room temperature for 30 min. 4 Å Molecular sieves (302.0 mg), **1a** (84.7 mg, 1.0 mmol), **2a** (123.2 mg, 1.1 mmol), and pyrrolidine (79.2 mg, 1.1 mmol) were then added sequentially under an argon atmosphere. The mixture was then stirred at 25 °C until completion of the reaction as monitored by TLC (12 h). CdI_2 (221.6 mg, 0.6 mmol) and an additional 2 mL of toluene were added to this Schlenk tube sequentially under an argon atmosphere. The Schlenk tube was then equipped with a condenser and placed in a preheated oil bath at 90 °C with stirring. After 2 h, the reaction was complete as monitored by TLC, and the crude reaction mixture was filtered through a pad of silica gel eluted with diethyl ether (30 mL). After evaporation, the residue was purified by chromatography on silica gel (eluent: petroleum ether–ethyl acetate = 10 : 1) to afford (R_a)-**4aa** (122.8 mg, 68%) as a low-melting point white solid:[12a] 97% ee (HPLC conditions: Chiralcel AD-H column, hexane/i-PrOH = 95/5, 0.6 mL min^{-1}, λ = 214 nm, t_R(major) = 10.4 min, t_R (minor) = 11.9 min); $[\alpha]_D^{27}$ = −99.0 (*c* = 1.02, $CHCl_3$) (reported value: 97% ee; $[\alpha]_D^{20}$ = −99.5 (*c* = 1.15, $CHCl_3$)); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.35 (dd, J_1 = 6.2 Hz, J_2 = 3.0 Hz, 1 H, one proton from CH═C═CH), 5.30 (t, *J* = 6.0 Hz, 1 H, one proton from CH═C═CH), 2.06–1.92 (m, 2 H, OH and CH from Cy), 1.82–1.59 (m, 5 H, protons from Cy), 1.34 (s, 6 H, 2 × CH_3), 1.31–1.01 (m, 5 H, protons from Cy); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 199.1, 102.0, 101.0, 69.5, 37.2, 33.02, 32.99, 30.0, 29.9, 26.04, 26.01, 25.99; MS (EI) *m*/*z* (%): 180 (M^+, 11.45), 91 (100); IR (neat): ν = 3347, 2973, 2923, 2850, 1963, 1446, 1402, 1363, 1153 cm^{-1}, HRMS calcd for $C_{12}H_{20}O$ [M^+]: 180.1514, found: 180.1518.

The following compounds (R_a)-**4ba** – (R_a)-**4de** in Table 2 were prepared according to this **Typical Procedure I**. All the racemic products were also prepared according to this procedure in the absence of the chiral ligand.

(2) Preparation of (R_a)-6-cyclohexyl-3-ethyl-4,5-hexadien-3-ol ((R_a)-4ba). The reaction of CuBr (3.8 mg, 0.025 mmol), (*R*,R_a)-*N*-PINAP (17.6 mg, 0.03 mmol), 4 Å molecular sieves (300.7 mg), **1b** (114.5 mg, 1.0 mmol), **2a** (123.7 mg, 1.1 mmol), pyrrolidine (80.2 mg, 1.1 mmol), and CdI_2 (219.6 mg, 0.6 mmol) afforded (R_a)-**4ba** (175.7 mg, 84%) (eluent: petroleum ether–ethyl acetate = 12 : 1) as an oil:[12a] 93% ee (HPLC conditions: Chiralcel AD-H column, hexane/i-PrOH = 95/5, 0.7 mL min^{-1}, λ = 214 nm, t_R(major) = 7.5 min, t_R(minor) = 8.1 min); $[\alpha]_D^{24}$ = −108.5 (*c* = 1.03, $CHCl_3$) (reported value: 96% ee; $[\alpha]_D^{20}$ = −85.9 (*c* = 1.03, $CHCl_3$)); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.35 (t, *J* = 6.2 Hz, 1 H, one proton from CH═C═CH), 5.16 (dd, J_1 = 6.2 Hz, J_2 = 3.0 Hz, 1 H, one proton

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from CH═C═CH), 2.06–1.94 (m, 1 H, CH from Cy), 1.81–1.68 (m, 5 H, protons from Cy and C═C═CC(OH)$(CH_2CH_3)_2$), 1.68–1.47 (m, 5 H, protons from Cy and C═C═CC(OH)$(CH_2CH_3)_2$), 1.35–1.03 (m, 5 H, protons from Cy and C═C═CC(OH)$(CH_2CH_3)_2$), 0.91 (t, J = 7.4 Hz, 3 H, CH_3), 0.89 (t, J = 7.6 Hz, 3 H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 199.6, 101.6, 99.6, 73.7, 37.3, 33.10, 33.07, 33.0, 32.9, 26.02, 26.01, 25.98, 8.1, 8.0; MS (EI) m/z (%): 208 (M^+, 1.20), 87 (100); IR (neat): ν = 3039, 2925, 2851, 1960, 1449, 1350, 1293, 1129, 1024 cm^{-1}.

(3) Preparation of (R_a)-1-(3-cyclohexylpropa-1,2-dienyl)-cyclopentanol ((R_a)-4ca). The reaction of CuBr (3.7 mg, 0.025 mmol), (R,R_a)-*N*-PINAP (17.7 mg, 0.03 mmol), 4 Å molecular sieves (301.0 mg), **1c** (113.3 mg, 1.0 mmol), **2a** (122.8 mg, 1.1 mmol), pyrrolidine (80.1 mg, 1.1 mmol), and CdI_2 (220.7 mg, 0.6 mmol) afforded (R_a)-**4ca** (115.7 mg, 56%) (eluent: petroleum ether–ethyl acetate = 12 : 1) as an oil:[12a] 93% ee (HPLC conditions: Chiralcel AD-H column, hexane/i-PrOH = 95/5, 0.7 mL min^{-1}, λ = 214 nm, t_R(major) = 9.5 min, t_R(minor) = 10.2 min); $[\alpha]_D^{23}$ = −90.8 (c = 1.00, $CHCl_3$) (reported value: 95% ee; $[\alpha]_D^{20}$ = −101.8 (c = 0.68, $CHCl_3$)); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.41 (dd, J_1 = 6.2 Hz, J_2 = 3.0 Hz, 1 H, one proton from CH═C═CH), 5.31 (t, J = 6.2 Hz, 1 H, one proton from CH═C═CH), 2.05–1.94 (m, 1 H, CH from Cy), 1.92–1.58 (m, 14 H, protons from Cy and C═C═CC(OH)$(CH_2)_4$), 1.35–1.01 (m, 5 H, protons from Cy and C═C═CC(OH)$(CH_2)_4$); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 199.3, 100.9, 100.2, 79.9, 40.32, 40.26, 37.2, 33.02, 33.00, 26.02, 25.98, 25.96, 23.6; MS (EI) m/z (%): 206 (M^+, 3.57), 85 (100); IR (neat): ν = 3345, 2923, 2851, 1960, 1446, 1384, 1318, 1292, 1186, 1072 cm^{-1}.

(4) Preparation of (R_a)-1-(3-cyclohexylpropa-1,2-dienyl)-cyclohexanol ((R_a)-4da). The reaction of CuBr (3.7 mg, 0.025 mmol), (R,R_a)-*N*-PINAP (17.6 mg, 0.03 mmol), 4 Å molecular sieves (301.0 mg), **1d** (126.1 mg, 1.0 mmol), **2a** (124.4 mg, 1.1 mmol), pyrrolidine (79.5 mg, 1.1 mmol), and CdI_2 (221.2 mg, 0.6 mmol) afforded (R_a)-**4da** (148.2 mg, 68%) (eluent: petroleum ether–ethyl acetate = 10 : 1) as a white solid (m.p.: 47–49 °C, we were not able to obtain the crystal from the solvent tested, the m.p. was determined by using the solid after evaporation of the eluent):[12a] 93% ee (HPLC conditions: Chiralcel AD-H column, hexane/i-PrOH = 95/5, 0.6 mL min^{-1}, λ = 214 nm, t_R(major) = 11.1 min, t_R(minor) = 11.8 min); $[\alpha]_D^{28}$ = −99.4 (c = 1.02, $CHCl_3$) (reported value: 96% ee; $[\alpha]_D^{20}$ = −108.6 (c = 0.98, $CHCl_3$)); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.33–5.29 (m, 2 H, CH═C═CH), 2.05–1.93 (m, 1 H, CH from Cy), 1.80–1.43 (m, 15 H, protons from Cy and C═C═CC(OH)$(CH_2)_5$), 1.38–1.02 (m, 6 H, protons from Cy and C═C═CC(OH)$(CH_2)_5$); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 199.9, 101.3, 100.7, 70.4, 38.3, 38.2, 37.2, 33.05, 32.97, 25.97, 25.95, 25.5, 22.42, 22.41; MS (EI) m/z (%): 220 (M^+, 1.36), 99 (100); IR (neat): ν = 3310, 2921, 2848, 1961, 1444, 1398, 1352, 1267, 1248, 1141, 1061, 1034 cm^{-1}.

Preparation of (R_a)-4da on a one-gram scale. The reaction of CuBr (37.7 mg, 0.25 mmol), (R,R_a)-*N*-PINAP (174.3 mg, 0.3 mmol), 4 Å molecular sieves (3004.0 mg), **1d** (1267.7 mg, 10 mmol), **2a** (1236.1 mg, 11 mmol), pyrrolidine (790.1 mg, 11 mmol), and CdI_2 (2211.0 mg, 6 mmol) afforded (R_a)-**4da** (1483.3 mg, 67%) (eluent: petroleum ether–ethyl acetate = 10 : 1) as a white solid:[12a] 94% ee (HPLC conditions: Chiralcel AD-H column, hexane/i-PrOH = 95/5, 0.6 mL min^{-1}, λ = 214 nm, t_R(major) = 10.7 min, t_R(minor) = 11.4 min); $[\alpha]_D^{27}$ = −105.5 (c = 1.01, $CHCl_3$) (reported value: 96% ee; $[\alpha]_D^{20}$ = −108.6 (c = 0.98, $CHCl_3$)); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.35–5.25 (m, 2 H, CH═C═CH), 2.10–1.92 (m, 1 H, CH from Cy), 1.84–1.40 (m, 15 H, protons from Cy and C═C═CC(OH)$(CH_2)_5$), 1.38–1.01 (m, 6 H, protons from Cy and C═C═CC(OH)-$(CH_2)_5$); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 199.9, 101.2, 100.7, 70.4, 38.3, 38.1, 37.2, 33.03, 32.95, 25.96, 25.93, 25.4, 22.39, 22.38; MS (EI) m/z (%): 220 (M^+, 1.38), 99 (100); IR (neat): ν = 3308, 2921, 2848, 1961, 1443, 1398, 1351, 1267, 1252, 1140, 1061, 1034 cm^{-1}.

(5) Preparation of (R_a)-1-(4-methylpenta-1,2-dienyl)cyclohexanol ((R_a)-4db). The reaction of CuBr (3.7 mg, 0.025 mmol), (R,R_a)-*N*-PINAP (17.5 mg, 0.03 mmol), 4 Å molecular sieves (300.6 mg), **1d** (126.0 mg, 1.0 mmol), **2b** (79.3 mg, 1.1 mmol), pyrrolidine (79.3 mg, 1.1 mmol), and CdI_2 (221.0 mg, 0.6 mmol) afforded (R_a)-**4db** (90.1 mg, 50%) (eluent: petroleum ether–ethyl acetate = 25 : 1) as a liquid:[12a] 91% ee (HPLC conditions: Chiralcel AD-H column, hexane/i-PrOH = 95/5, 0.7 mL min^{-1}, λ = 214 nm, t_R(major) = 8.2 min, t_R(minor) = 8.9 min); $[\alpha]_D^{26}$ = −87.6 (c = 1.03, $CHCl_3$) (reported value: 95% ee; $[\alpha]_D^{20}$ = −79.7 (c = 0.52, $CHCl_3$)); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.36–5.30 (m, J = 4.8 Hz, 2 H, CH═C═CH), 2.40–2.26 (m, 1 H, CH from ^{i}Pr), 1.74–1.24 (m, 11 H, protons from C═C═CC(OH)$(CH_2)_5$), 1.03 (d, J = 6.8 Hz, 3 H, CH_3), 1.025 (d, J = 6.8 Hz, 3 H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 199.6, 102.1, 101.6, 70.5, 38.3, 38.2, 27.9, 25.5, 22.47, 22.43, 22.39; MS (EI) m/z (%): 180 (M^+, 3.22), 99 (100); IR (neat): ν = 3344, 2959, 2928, 2860, 1961, 1462, 1445, 1410, 1381, 1359, 1346, 1318, 1296, 1245, 1192, 1145, 1057 cm^{-1}.

(6) Preparation of (R_a)-1-(4-methylpenta-1,2-dienyl)-cyclohexanol ((R_a)-4dc). The reaction of CuBr (3.7 mg, 0.025 mmol), (R,R_a)-*N*-PINAP (17.5 mg, 0.03 mmol), 4 Å molecular sieves (300.7 mg), **1d** (126.9 mg, 1.0 mmol), **2c** (94.6 mg, 1.1 mmol), pyrrolidine (78.0 mg, 1.1 mmol), and CdI_2 (221.4 mg, 0.6 mmol) afforded (R_a)-**4dc** (93.6 mg, 48%) (eluent: petroleum ether–ethyl acetate = 12 : 1) as a liquid:[12a] 93% ee (HPLC conditions: Chiralcel AD-H column, hexane/i-PrOH = 100/1, 0.7 mL min^{-1}, λ = 214 nm, t_R(major) = 16.3 min, t_R(minor) = 17.8 min); $[\alpha]_D^{28}$ = −76.1 (c = 1.04, $CHCl_3$) (reported value: 90% ee; $[\alpha]_D^{20}$ = −82.1 (c = 1.04, $CHCl_3$)); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.30–5.21 (m, 2 H, CH═C═CH), 2.02–1.87 (m, 2 H, CH_2C═C═C), 1.74–1.30 (m, 12 H, protons from ^{i}Bu and C═C═CC(OH)$(CH_2)_5$, 0.93 (d, J = 6.8 Hz, 6 H, 2 × CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 201.8, 99.5, 93.2, 70.7, 38.4, 38.32, 38.30, 28.5, 25.5, 22.60, 22.55, 22.22, 22.18; MS (EI) m/z (%): 194 (M^+, 13.66), 99 (100); IR (neat): ν = 3358, 2929, 1962, 1463, 1448, 1383, 1367, 1343, 1247, 1146, 1056, 1035 cm^{-1}, HRMS calcd for $C_{13}H_{22}O$ [M^+]: 194.1671, found: 194.1676.

(7) Preparation of (R_a)-1-(4-methylpenta-1,2-dienyl)cyclohexanol ((R_a)-4dd). The reaction of CuBr (3.8 mg, 0.025 mmol),

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(R,R_a)-*N*-PINAP (17.4 mg, 0.03 mmol), 4 Å molecular sieves (300.8 mg), **1d** (126.6 mg, 1.0 mmol), **2d** (141.7 mg, 1.1 mmol), pyrrolidine (77.9 mg, 1.1 mmol), and CdI_2 (220.3 mg, 0.6 mmol) afforded (R_a)-**4dd** (125.2 mg, 53%) (eluent: petroleum ether–ethyl acetate = 100 : 3) as an oil:[12a] 92% ee (HPLC conditions: Chiralcel AD-H column, hexane/i-PrOH = 200/1, 1.0 mL min^{-1}, λ = 214 nm, t_R(major) = 15.6 min, t_R(minor) = 16.9 min); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.34–5.21 (m, 2 H, CH═C═CH), 2.08–1.97 (m, 2 H, CH_2C═C═CH), 1.76 (s, 1 H, OH), 1.72–1.20 (m, 20 H, 10 CH_2), 0.88 (t, J = 7.0 Hz, 3 H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 201.3, 100.2, 94.6, 70.6, 38.28, 38.25, 31.8, 29.2, 29.05, 29.03, 28.8, 25.5, 22.6, 22.5, 22.49, 14.0; MS (EI) m/z (%): 236 (M^+, 4.36), 99 (100); IR (neat): ν = 3353, 2925, 2853, 1962, 1448, 1379, 1346, 1316, 1247, 1184, 1147, 1056 cm^{-1}.

(8) Preparation of (R_a)-1-(3-phenylpropa-1,2-dienyl)cyclohexanol ((R_a)-4de). The reaction of CuBr (3.7 mg, 0.025 mmol), (R,R_a)-*N*-PINAP (17.3 mg, 0.03 mmol), 4 Å molecular sieves (300.9 mg), **1d** (126.5 mg, 1.0 mmol), **2e** (116.1 mg, 1.1 mmol), pyrrolidine (79.1 mg, 1.1 mmol), and CdI_2 (219.9 mg, 0.6 mmol) afforded (R_a)-**4de** (188.5 mg, 88%) (eluent: petroleum ether–ethyl acetate = 10 : 1) as a white solid (m.p.: 49–51 °C, we were not able to obtain the crystal from the solvent tested, the m.p. was determined by using the solid after evaporation of the eluent):[12a] 95% ee (HPLC conditions: Chiralcel OD-H column, hexane/i-PrOH = 95/5, 1.0 mL min^{-1}, λ = 214 nm, t_R(major) = 6.9 min, t_R(minor) = 15.3 min); $[\alpha]_D^{28}$ = −346.3 (c = 1.01, $CHCl_3$) (reported value: 93% ee; $[\alpha]_D^{20}$ = −341.4 (c = 1.00, $CHCl_3$)); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.33–7.25 (m, 4 H, Ar–H), 7.23–7.15 (m, 1 H, Ar–H), 6.30 (d, J = 6.0 Hz, 1 H, one proton from CH═C═CH), 5.72 (d, J = 6.4 Hz, 1 H, one proton from CH═C═CH), 1.89 (s, 1 H, OH), 1.72–1.58 (m, 6 H, protons from Cy), 1.57–1.42 (m, 3 H, protons from Cy), 1.40–1.27 (m, 1 H, one proton from Cy); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 202.8, 134.0, 128.6, 127.0, 126.6, 104.3, 97.6, 71.4, 38.33, 38.26, 25.4, 22.40, 22.38; MS (EI) m/z (%): 214 (M^+, 2.81), 116 (100); IR (neat): ν = 3327, 2929, 2859, 1948, 1599, 1492, 1444, 1407, 1346, 1318, 1291, 1244, 1185, 1145, 1113, 1057, 1033 cm^{-1}.

The following compounds (S_a)-**4ba**, (S_a)-**4da**, (S_a)-**4de** in Table 2 were also prepared according to the **Typical Procedure I** with the (R,S_a)-*N*-PINAP as the chiral ligand.

(9) Preparation of (S_a)-6-cyclohexyl-3-ethyl-4,5-hexadien-3-ol ((S_a)-4ba). The reaction of CuBr (3.7 mg, 0.025 mmol), (R,S_a)-*N*-PINAP (17.5 mg, 0.03 mmol), 4 Å molecular sieves (300.7 mg), **1b** (114.3 mg, 1.0 mmol), **2a** (122.9 mg, 1.1 mmol), pyrrolidine (80.1 mg, 1.1 mmol), and CdI_2 (220.5 mg, 0.6 mmol) afforded (S_a)-**4ba** (167.8 mg, 80%) (eluent: petroleum ether–ethyl acetate = 10 : 1) as an oil: 92% ee (HPLC conditions: Chiralcel AD-H column, hexane/i-PrOH = 98/2, 1.0 mL min^{-1}, λ = 214 nm, t_R(minor) = 6.0 min, t_R(major) = 7.0 min); $[\alpha]_D^{26}$ = +103.6 (c = 1.02, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.34 (t, J = 6.2 Hz, 1 H, one proton from CH═C═CH), 5.16 (dd, J_1 = 6.2 Hz, J_2 = 3.0 Hz, 1 H, one proton from CH═C═CH), 2.06–1.93 (m, 1 H, CH from Cy), 1.82–1.64 (m, 5 H, protons from Cy and C═C═CC(OH)(CH_2CH_3)$_2$), 1.63–1.46 (m, 5 H, protons from Cy and C═C═CC(OH)(CH_2CH_3)$_2$), 1.35–1.03 (m, 5 H, protons from Cy and C═C═C(CH_2CH_3)$_2$COH), 0.89 (t, J = 7.2 Hz, 3 H, CH_3), 0.87 (t, J = 5.4 Hz, 3 H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 199.6, 101.3, 99.6, 73.6, 37.3, 33.05, 32.98, 32.9, 32.8, 26.0, 25.94, 25.92, 8.0, 7.9; MS (EI) m/z (%): 208 (M^+, 2.11), 87 (100); IR (neat): ν = 3430, 2966, 2923, 2851, 1961, 1448, 1377, 1349, 1324, 1257, 1180, 1129 cm^{-1}, HRMS calcd for $C_{14}H_{24}O$ [M^+]: 208.1827, found: 208.1824.

(10) Preparation of (S_a)-1-(3-cyclohexylpropa-1,2-dienyl)-cyclohexanol ((S_a)-4da). The reaction of CuBr (3.8 mg, 0.025 mmol), (R,S_a)-*N*-PINAP (17.6 mg, 0.03 mmol), 4 Å molecular sieves (301.0 mg), **1d** (126.8 mg, 1.0 mmol), **2a** (123.3 mg, 1.1 mmol), pyrrolidine (78.9 mg, 1.1 mmol), and CdI_2 (221.4 mg, 0.6 mmol) afforded (S_a)-**4da** (154.7 mg, 70%) (eluent: petroleum ether–ethyl acetate = 10 : 1) as a white solid (m.p.: 45–47 °C, we were not able to obtain the crystal from the solvent tested, the m.p. was determined by using the solid after evaporation of the eluent):[12a] 90% ee (HPLC conditions: Chiralcel AD-H column, hexane/i-PrOH = 95/5, 0.6 mL min^{-1}, λ = 214 nm, t_R (minor) = 11.2 min, t_R(major) = 12.0 min); $[\alpha]_D^{27}$ = +90.3 (c = 1.00, $CHCl_3$) (reported value: 93% ee; $[\alpha]_D^{20}$ = +102.3 (c = 1.00, $CHCl_3$)); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.34–5.26 (m, 2 H, CH═C═CH), 2.05–1.95 (m, 1 H, CH from Cy), 1.80–1.40 (m, 15 H, protons from Cy and C═C═CC(OH)(CH_2)$_5$), 1.37–1.02 (m, 6 H, protons from Cy and C═C═CC(OH)(CH_2)$_5$); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 199.9, 101.3, 100.7, 70.4, 38.3, 38.2, 37.2, 33.03, 32.97, 25.97, 25.94, 25.44, 22.41, 22.39; MS (EI) m/z (%): 220 (M^+, 1.27), 99 (100); IR (neat): ν = 3310, 2921, 2848, 1961, 1444, 1398, 1351, 1267, 1249, 1185, 1140, 1098, 1060, 1034 cm^{-1}; HRMS calcd for $C_{15}H_{24}O$ [M^+]: 220.1827, found: 220.1830.

(11) Preparation of (S_a)-1-(3-phenylpropa-1,2-dienyl)cyclohexanol ((S_a)-4de). The reaction of CuBr (3.7 mg, 0.025 mmol), (R,S_a)-*N*-PINAP (17.2 mg, 0.03 mmol), 4 Å molecular sieves (300.0 mg), **1d** (127.4 mg, 1.0 mmol), **2e** (118.0 mg, 1.1 mmol), pyrrolidine (79.9 mg, 1.1 mmol), and CdI_2 (220.6 mg, 0.6 mmol) afforded (S_a)-**4de** (176.1 mg, 82%) (eluent: petroleum ether–ethyl acetate = 10 : 1) as a white solid: 93% ee (HPLC conditions: Chiralcel OD-H column, hexane/i-PrOH = 90/10, 0.9 mL min^{-1}, λ = 214 nm, t_R(minor) = 6.0 min, t_R(major) = 9.2 min); $[\alpha]_D^{26}$ = +322.3 (c = 1.02, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.33–7.25 (m, 4 H, Ar–H), 7.24–7.16 (m, 1 H, Ar–H), 6.31 (d, J = 6.4 Hz, 1 H, one proton from CH═C═CH), 5.73 (d, J = 6.4 Hz, 1 H, one proton from CH═C═CH), 1.79 (s, 1 H, OH), 1.72–1.59 (m, 6 H, protons from Cy), 1.57–1.41 (m, 3 H, protons from Cy), 1.44–1.29 (m, 1 H, one proton from Cy); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 202.8, 134.0, 128.6, 127.0, 126.6, 104.3, 97.6, 71.5, 38.4, 38.3, 25.4, 22.42, 22.40; MS (EI) m/z (%): 214 (M^+, 4.45), 116 (100); IR (neat): ν = 3327, 3069, 3031, 2928, 2855, 1947, 1598, 1492, 1447, 1407, 1349, 1245, 1185, 1144, 1057 cm^{-1}; HRMS calcd for $C_{15}H_{18}O$ [M^+]: 214.1358, found: 214.1362.

The following compounds (R_a,R)-**4ee**, (R_a,S)-**4ee**, (S_a,R)-**4ee**, (S_a,R)-**4ee** in Scheme 3 and 4 were also prepared according to the **Typical Procedure I** with (R,R_a)-*N*-PINAP or (R,S_a)-*N*-PINAP as the chiral ligand.

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(12) Preparation of (R_a,*R*)-1,4-diphenyl-2,3-butadien-1-ol ((R_a,*R*)-4ee) and (R_a,*S*)-1,4-diphenyl-2,3-butadien-1-ol ((R_a,*S*)-4ee). The reaction of CuBr (3.7 mg, 0.025 mmol), (*R*,R_a)-*N*-PINAP (17.3 mg, 0.03 mmol), 4 Å molecular sieves (301.0 mg), *rac*-**1e** (134.1 mg, 1.0 mmol), **2e** (116.8 mg, 1.1 mmol), pyrrolidine (78.5 mg, 1.1 mmol), and CdI_2 (220.8 mg, 0.6 mmol) afforded a mixture of (R_a,*R*)-**4ee** and (R_a,*S*)-**4ee** (168.7 mg, 76%) (eluent: hexane–ethyl acetate = 13 : 1) as a yellow oil: 86% ee for (R_a,*R*)-**4ee** and 94% ee for (R_a,*S*)-**4ee**; (R_a,*R*)-**4ee**/(S_a,*R*)-**4ee** = 36 : 1; (R_a,*S*)-**4ee**/(S_a,*S*)-**4ee** = 13 : 1; (determined by HPLC) (HPLC conditions: Chiralcel OD column, hexane/i-PrOH = 96/4, 1.0 mL min^{-1}, λ = 214 nm, t_R(minor) = 18.4 min, t_R(major) = 19.9 min, t_R(major) = 25.1 min, t_R(minor) = 33.6 min); $[\alpha]_D^{28}$ = −184.7 (*c* = 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.41–7.11 (m, 10 H, Ar–H), 6.29 (dd, J_1 = 6.4 Hz, J_2 = 2.0 Hz, 1 H, one proton from CH═C═CH), 5.79 (dd, J_1 = 11.6 Hz, J_2 = 6.4 Hz, 1 H, one proton from CH═C═CH), 5.27 (dd, J_1 = 14.8 Hz, J_2 = 6.4 Hz, 1 H, CH), 2.73 (s, 1 H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) (R_a*,*R**)-**4ee**: δ = 203.5, 142.7, 133.58, 128.6, 128.4, 127.71, 127.20, 126.80, 126.0, 99.9, 97.8, 72.1; (R_a*,*S**)-**4ee**: δ = 203.8, 142.8, 133.57, 128.5, 128.4, 127.69, 127.16, 126.75, 125.9, 99.8, 97.5, 72.3; MS (EI) *m*/*z* (%): 222 (M^+, 13.03), 116 (100); IR (neat): ν = 3317, 3083, 3061, 3029, 1951, 1883, 1809, 1694, 1599, 1584, 1493, 1453, 1390, 1193, 1157, 1099, 1072, 1029 cm^{-1}; HRMS calcd for $C_{16}H_{14}O$ [M^+]: 222.1045, found: 222.1047 and 222.1042.

(13) Preparation of (R_a,*R*)-1,4-diphenyl-2,3-butadien-1-ol ((R_a,*R*)-4ee) and (S_a,*R*)-1,4-diphenyl-2,3-butadien-1-ol ((S_a,*R*)-4ee). The reaction of CuBr (3.7 mg, 0.025 mmol), (*R*,R_a)-*N*-PINAP (17.7 mg, 0.03 mmol), 4 Å molecular sieves (302.0 mg), (*R*)-**1e** (133.1 mg, 1.0 mmol), **2e** (116.0 mg, 1.1 mmol), pyrrolidine (79.2 mg, 1.1 mmol), and CdI_2 (221.7 mg, 0.6 mmol) afforded a mixture of (R_a,*R*)-**4ee** as the major product and (S_a,*R*)-**4ee** as the minor product (126.5 mg, 57%) (eluent: hexane–ethyl acetate = 13 : 1) as a yellow oil: 99% ee for (R_a,*R*)-**4ee**; (R_a,*R*)-**4ee**/(S_a,*R*)-**4ee** = 31 : 1 (determined by HPLC) (HPLC conditions: Chiralcel OD column, hexane/i-PrOH = 96/4, 1.0 mL min^{-1}, λ = 214 nm, t_R(minor) = 19.9 min, t_R(major) = 21.7 min, t_R(minor) = 29.1 min, t_R(minor) = 40.0 min); $[\alpha]_D^{28}$ = −205.3 (*c* = 1.025, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.42–7.15 (m, 10 H, Ar–H), 6.32 (dd, J_1 = 6.4 Hz, J_2 = 2.4 Hz, 1 H, one proton from CH═C═CH), 5.82 (t, *J* = 6.2 Hz, 1 H, one proton from CH═C═CH), 5.28 (dd, J_1 = 6.4 Hz, J_2 = 2.4 Hz, 1 H, CH), 2.54 (s, 1 H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 203.5, 142.7, 133.6, 128.61, 128.5, 127.78, 127.3, 126.83, 126.0, 100.0, 97.9, 72.1; MS (EI) *m*/*z* (%): 222 (M^+, 9.90), 116 (100); IR (neat): ν = 3306, 3083, 3061, 3029, 2891, 1951, 1881, 1809, 1693, 1599, 1494, 1454, 1194, 1001 cm^{-1}; HRMS calcd for $C_{16}H_{14}O$ [M^+]: 222.1045, found: 222.1042.

The following signals are discernible for (S_a*,*R**)-**4ee**: ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.31 (d, *J* = 6.8 Hz 1 H, CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 128.58, 127.75, 127.2, 126.79, 125.9, 99.8, 97.6, 72.3.

(14) Preparation of (R_a,*S*)-1,4-diphenyl-2,3-butadien-1-ol ((R_a,*S*)-4ee) and (S_a,*S*)-1,4-diphenyl-2,3-butadien-1-ol ((S_a,*S*)-4ee). The reaction of CuBr (3.7 mg, 0.025 mmol), (*R*,R_a)-*N*-PINAP (17.6 mg, 0.03 mmol), 4 Å molecular sieves (300.4 mg), (*S*)-**1e** (134.3 mg, 1.0 mmol), **2e** (116.8 mg, 1.1 mmol), pyrrolidine (78.2 mg, 1.1 mmol), and CdI_2 (221.2 mg, 0.6 mmol) afforded a mixture of (R_a,*S*)-**4ee** as the major product and (S_a,*S*)-**4ee** as the minor product (167.5 mg, 74%) (eluent: petroleum ether–ethyl acetate = 14 : 1) as a yellow solid: 99% ee for (R_a,*S*)-**4ee**; (R_a,*S*)-**4ee**/(S_a,*S*)-**4ee** = 12 : 1 (determined by HPLC) (HPLC conditions: Chiralcel OD column, hexane/i-PrOH = 96/4, 1.0 mL min^{-1}, λ = 214 nm, t_R(minor) = 22.9 min, t_R(major) = 31.0 min, t_R(minor) = 42.5 min); $[\alpha]_D^{28}$ = −187.9 (*c* = 1.03, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.40–7.10 (m, 10 H, Ar–H), 6.28 (dd, J_1 = 6.0 Hz, J_2 = 2.0 Hz, 1 H, one proton from CH═C═CH), 5.78 (t, *J* = 6.6 Hz, 1 H, one proton from CH═C═CH), 5.27 (dd, J_1 = 6.6 Hz, J_2 = 1.8 Hz, 1 H, CH), 2.92 (s, 1 H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 203.8, 142.8, 133.6, 128.5, 128.4, 127.6, 127.1, 126.7, 125.87, 99.7, 97.4, 72.3; MS (EI) *m*/*z* (%): 222 (M^+, 13.38), 116 (100); IR (neat): ν = 3273, 3084, 3027, 2985, 1952, 1882, 1811, 1758, 1688, 1599, 1550, 1495, 1452, 1400, 1332, 1250, 1192, 1118, 1000 cm^{-1}; HRMS calcd for $C_{16}H_{14}O$ [M^+]: 222.1045, found: 222.1044.

The following signals are discernible for (S_a*,*S**)-**4ee**: ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.23 (dd, J_1 = 6.4 Hz, J_2 = 2.4 Hz, 1 H, CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 203.5, 142.7, 127.2, 126.8, 125.9, 99.8, 97.7, 72.0.

(15) Preparation of (R_a,*S*)-1,4-diphenyl-2,3-butadien-1-ol ((R_a,*S*)-4ee) and (S_a,*S*)-1,4-diphenyl-2,3-butadien-1-ol ((S_a,*S*)-4ee). The reaction of CuBr (3.7 mg, 0.025 mmol), (*R*,S_a)-*N*-PINAP (17.5 mg, 0.03 mmol), 4 Å molecular sieves (302.0 mg), *rac*-**1e** (134.8 mg, 1.0 mmol), **2e** (117.4 mg, 1.1 mmol), pyrrolidine (79.2 mg, 1.1 mmol), and CdI_2 (221.4 mg, 0.6 mmol) afforded a mixture of (S_a,*R*)-**4ee** and (S_a,*S*)-**4ee** (163.8 mg, 74%) (eluent: hexane–ethyl acetate = 14 : 1) as a yellow oil: 88% ee for (S_a,*R*)-**4ee** and 77% ee (S_a,*S*)-**4ee**; (S_a,*R*)-**4ee**/(R_a,*R*)-**4ee** = 7 : 1; (S_a,*S*)-**4ee**/(R_a,*S*)-**4ee** = 17 : 1; (determined by HPLC) (HPLC conditions: Chiralcel OD column, hexane/i-PrOH = 96/4, 1.0 mL min^{-1}, λ = 214 nm, t_R(major) = 19.3 min, t_R(minor) = 21.2 min, t_R(minor) = 27.9 min, t_R(major) = 37.7 min); $[\alpha]_D^{28}$ = +187.5 (*c* = 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.42–7.13 (m, 10 H, Ar–H), 6.31 (dd, J_1 = 6.4 Hz, J_2 = 2.4 Hz, 1 H, one proton from CH═C═CH), 5.81 (dd, J_1 = 11.4 Hz, J_2 = 6.2 Hz, 1 H, one proton from CH═C═CH), [5.31 (dd, J_1 = 6.6 Hz, J_2 = 1.8 Hz), 5.27 (dd, J_1 = 7.2 Hz, J_2 = 2.4 Hz), 1 H, CH], 2.65 (s, 1 H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) (S_a*,*R**)-**4ee**: δ = 203.8, 142.8, 128.57, 128.46, 127.72, 127.18, 126.77, 125.9, 99.8, 97.6, 72.3; (S_a*,*S**)-**4ee**: δ = 203.5, 142.7, 128.58, 128.46, 127.75, 127.23, 126.81, 126.0, 99.9, 97.9, 72.1; MS (EI) *m*/*z* (%): 222 (M^+, 12.57), 116 (100); IR (neat): ν = 3332, 3083, 3061, 3029, 1950, 1882, 1809, 1699, 1598, 1494, 1456, 1193, 1157, 1100, 1072, 1027 cm^{-1}; HRMS calcd for $C_{16}H_{14}O$ [M^+]: 222.1045, found: 222.1041 and 222.1048.

(16) Preparation of (S_a,*R*)-1,4-diphenyl-2,3-butadien-1-ol ((S_a,*R*)-4ee) and (R_a,*R*)-1,4-diphenyl-2,3-butadien-1-ol ((R_a,*R*)-4ee). The reaction of CuBr (3.7 mg, 0.025 mmol), (*R*,S_a)-*N*-PINAP (17.4 mg, 0.03 mmol), 4 Å molecular sieves (302.0 mg), (*R*)-**1e** (132.5 mg, 1.0 mmol), **2e** (117.6 mg, 1.1 mmol),

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pyrrolidine (79.1 mg, 1.1 mmol), and CdI_2 (220.9 mg, 0.6 mmol) afforded a mixture of (S_a,*R*)-**4ee** and (R_a,*R*)-**4ee** (151.8 mg, 68%) (eluent: hexane–ethyl acetate = 14 : 1) as a yellow solid: 99% ee for (S_a,*R*)-**4ee**; (S_a,*R*)-**4ee**/(R_a,*R*)-**4ee** = 8 : 1 (determined by HPLC) (HPLC conditions: Chiralcel OD column, hexane/i-PrOH = 96/4, 1.0 mL min^{-1}, λ = 214 nm, t_R(major) = 19.1 min, t_R(minor) = 21.0 min, t_R(minor) = 27.4 min, t_R(minor) = 36.7 min); $[\alpha]_D^{27}$ = +168.6 (*c* = 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.43–7.12 (m, 10 H, Ar–H), 6.31 (dd, J_1 = 6.4 Hz, J_2 = 2.0 Hz, 1 H, one proton from CH═C═CH), 5.81 (t, 1 H, *J* = 6.4 Hz, one proton from CH═C═CH), 5.31 (dd, J_1 = 6.8 Hz, J_2 = 1.6 Hz, 1 H, CH), 2.68 (s, 1 H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 203.8, 142.8, 133.57, 128.57, 128.5, 127.7, 127.19, 126.77, 125.9, 99.8, 97.6, 72.3; MS (EI) *m*/*z* (%): 222 (M^+, 12.90), 116 (100); IR (neat): ν = 3458, 3085, 3061, 3027, 1953, 1882, 1812, 1758, 1691, 1599, 1585, 1550, 1496, 1455, 1387, 1332, 1251, 1192, 1161, 1120, 1072, 1001 cm^{-1}; HRMS calcd for $C_{16}H_{14}O$ [M^+]: 222.1045, found: 222.1050.

The following signals are discernible for (R_a*,*R**)-**4ee**: ^{1}H NMR (400 MHz, $CDCl_3$), 5.27 (dd, J_1 = 6.2 Hz, J_2 = 2.2 Hz, 1 H, CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 203.5, 142.7, 133.58, 128.60, 127.8, 127.23, 126.81, 126.0, 99.9, 97.9, 72.1.

(17) Preparation of (S_a,*S*)-1,4-diphenyl-2,3-butadien-1-ol ((S_a,*S*)-4ee) and (R_a,*S*)-1,4-diphenyl-2,3-butadien-1-ol ((R_a,*S*)-4ee). The reaction of CuBr (3.8 mg, 0.025 mmol), (*R*,S_a)-*N*-PINAP (17.4 mg, 0.03 mmol), 4 Å molecular sieves (302.0 mg), (*S*)-**1e** (132.2 mg, 1.0 mmol), **2e** (116.5 mg, 1.1 mmol), pyrrolidine (78.6 mg, 1.1 mmol), and CdI_2 (221.2 mg, 0.6 mmol) afforded a mixture of (S_a,*S*)-**4ee** and (R_a,*S*)-**4ee** (124.3 mg, 56%) (eluent: hexane–ethyl acetate = 14 : 1) as a yellow oil: 99% ee for (S_a,*S*)-**4ee**; (S_a,*S*)-**4ee**/(R_a,*S*)-**4ee** = 19 (determined by HPLC) (HPLC conditions: Chiralcel OD column, hexane/i-PrOH = 96/4, 1.0 mL min^{-1}, λ = 214 nm, t_R(minor) = 19.1 min, t_R(minor) = 20.8 min, t_R(minor) = 26.9 min, t_R(minor) = 35.7 min); $[\alpha]_D^{27}$ = +201.3 (*c* = 1.04, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.45–7.16 (m, 10 H, Ar–H), 6.33 (dd, J_1 = 6.4 Hz, J_2 = 2.8 Hz, 1 H, one proton from CH═C═CH), 5.83 (t, *J* = 6.0 Hz, 1 H, one proton from CH═C═CH), 5.29 (dd, J_1 = 6.0 Hz, J_2 = 2.4 Hz, 1 H, CH), 2.52 (s, 1 H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 203.5, 142.7, 133.6, 128.6, 128.5, 127.8, 127.3, 126.83, 126.0, 100.0, 98.0, 72.1; MS (EI) *m*/*z* (%): 222 (M^+, 11.03), 116 (100); IR (neat): ν = 3373, 3083, 3061, 3029, 1951, 1883, 1809, 1700, 1599, 1494, 1455, 1389, 1194, 1157, 1111, 1073, 1001 cm^{-1}; HRMS calcd for $C_{16}H_{14}O$ [M^+]: 222.1045, found: 222.1043.

The following signals are discernible for (R_a*,*S**)-**4ee**: ^{13}C NMR (100 MHz, $CDCl_3$) δ = 128.59, 127.78, 127.23, 126.8, 125.9, 99.9, 72.3.

Typical procedure II

(18) Two-pot procedure for preparation of (R_a,*R*)-1,4-diphenyl-2,3-butadien-1-ol ((R_a,*R*)-4ee) and (R_a,*S*)-1,4-di-phenyl-2,3-butadien-1-ol ((R_a,*S*)-4ee). To a flame-dried Schlenk tube were added CuBr (3.8 mg, 0.025 mmol), (*R*,R_a)-*N*-PINAP (17.7 mg, 0.03 mmol) and toluene (2 mL) under an argon atmosphere. The mixture was stirred at room temperature for 30 min. 4 Å Molecular sieves (302.0 mg), *rac*-**1e** (135.5 mg, 1.0 mmol), **2e** (117.5 mg, 1.1 mmol), and pyrrolidine (79.7 mg, 1.1 mmol) were then added sequentially under an argon atmosphere. The mixture was then stirred at 25 °C until completion of the reaction as monitored by TLC (18 h). The crude reaction mixture was filtered through a pad of silica gel eluted with diethyl ether (30 mL). After evaporation, the crude product was used in the next step without further treatment. To another Schlenk tube were added ZnI_2 (147.1 mg, 0.45 mmol), and NaI (77.1 mg, 0.5 mmol) inside a glove box. The Schlenk tube was then taken out and dried under vacuum with a heat gun. The above crude product was then dissolved in toluene (5 mL) and transferred to the Schlenk tube *via* a syringe under an argon atmosphere. The Schlenk tube was then equipped with a condenser and placed in a pre-heated oil bath at 110 °C with stirring. After 2 h, the reaction was complete as monitored by TLC, and the crude reaction mixture was filtered through a pad of silica gel loaded with a sand-funnel unit eluted with diethyl ether (30 mL). After evaporation, the residue was purified by chromatography on silica gel (eluent: hexane–ethyl acetate = 14 : 1) to afford a mixture of (R_a,*R*)-**4ee** and (R_a,*S*)-**4ee** (171.1 mg, 77%) as a yellow oil: 83% ee for (R_a,*R*)-**4ee** and 93% ee for (R_a,*S*)-**4ee**; (R_a,*R*)-**4ee**/(S_a,*R*)-**4ee** = 26 : 1; (R_a,*S*)-**4ee**/(S_a,*S*)-**4ee** = 11 : 1; (determined by HPLC) (HPLC conditions: Chiralcel OD-H column, hexane/i-PrOH = 96/4, 1.0 mL min^{-1}, λ = 214 nm, t_R(minor) = 17.9 min, t_R(major) = 20.0 min, t_R(major) = 25.6 min, t_R(minor) = 35.6 min); $[\alpha]_D^{23}$ = −167.5 (*c* = 1.03, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.50–7.10 (m, 10 H, Ar–H), 6.33–6.28 (m, 1 H, one proton from CH═C═CH), 5.80 (dd, J_1 = 11.8 Hz, J_2 = 5.8 Hz, 1 H, one proton from CH═C═CH), 5.28 (dd, J_1 = 14.0 Hz, J_2 = 6.0 Hz, 1 H, CH), 2.69 (s, 1 H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) (R_a*,*R**)-**4ee**: δ = 203.5, 142.7, 133.57, 128.58, 128.444, 127.74, 127.22, 126.80, 125.98, 99.9, 97.8, 72.1; (R_a*,*S**)-**4ee**: δ = 203.7, 142.8, 133.56, 128.55, 128.436, 127.71, 127.18, 126.76, 125.90, 99.8, 97.5, 72.3; MS (EI) *m*/*z* (%): 222 (M^+, 27.67), 204 (100); IR (neat): ν = 3450, 3062, 3029, 2924, 2852, 1950, 1598, 1492, 1450, 1256, 1189, 1025 cm^{-1}.

Two-pot procedure for preparation of ((R_a,*R*)-4ee) and ((R_a,*S*)-4ee) with the same loading of CuBr and ligand of the literature.[12a] (Following typical procedure II). The reaction of CuBr (7.3 mg, 0.05 mmol), (*R*,R_a)-*N*-PINAP (31.8 mg, 0.055 mmol), 4 Å molecular sieves (301.0 mg), *rac*-**1e** (134.8 mg, 1.0 mmol), **2e** (117.1 mg, 1.1 mmol), pyrrolidine (78.7 mg, 1.1 mmol), ZnI_2 (146.7 mg, 0.45 mmol), and NaI (76.2, 0.5 mmol) afforded a mixture of (R_a,*R*)-**4ee** and (R_a,*S*)-**4ee** (173.0 mg, 78%) (eluent: petroleum ether–ethyl acetate = 14 : 1) as a yellow oil: 81% ee for (R_a,*R*)-**4ee** and 91% ee for (R_a,*S*)-**4ee**; (R_a,*R*)-**4ee**/(S_a,*R*)-**4ee** = 23 : 1; (R_a,*S*)-**4ee**/(S_a,*S*)-**4ee** = 9 : 1; (determined by HPLC) (HPLC conditions: Chiralcel OD-H column, hexane/i-PrOH = 96/4, 1.0 mL min^{-1}, λ = 214 nm, t_R(minor) = 18.6 min, t_R(major) = 20.1 min, t_R(major) = 25.9 min, t_R(minor) = 34.1 min); $[\alpha]_D^{28}$ = −188.7 (*c* = 1.02, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.43–7.11 (m, 10 H, Ar–H), 6.32 (dd, J_1 = 6.4 Hz, J_2 = 2.4 Hz, 1 H, one proton from CH═C═CH), 5.84–5.79 (m, 1 H, one proton from

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CH═C═CH), [5.32 (dd, J_1 = 6.4 Hz, J_2 = 2.0 Hz), 5.28 (dd, J_1 = 6.4 Hz, J_2 = 2.4 Hz), 1 H, CH], 2.56 (s, 1 H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) (R_a*,*R**)-**4ee**: δ = 203.5, 142.7, 133.60, 128.61, 128.48, 127.78, 127.3, 126.83, 126.0, 99.9, 97.9, 72.1; (R_a*,*S**)-**4ee**: δ = 203.8, 142.8, 133.59, 128.58, 128.47, 127.75, 127.2, 126.78, 125.9, 99.8, 97.6, 72.3.

(19) Two-pot procedure for preparation of (R_a,*R*)-1,4-diphenyl-2,3-butadien-1-ol ((R_a,*R*)-4ee) and (S_a,*R*)-1,4-diphenyl-2,3-butadien-1-ol ((S_a,*R*)-4ee). (Following typical procedure II). The reaction of CuBr (3.8 mg, 0.025 mmol), (*R*,R_a)-*N*-PINAP (17.8 mg, 0.03 mmol), 4 Å molecular sieves (301.0 mg), (*R*)-**1e** (132.4 mg, 1.0 mmol), **2e** (117.5 mg, 1.1 mmol), pyrrolidine (79.2 mg, 1.1 mmol), ZnI_2 (146.6 mg, 0.45 mmol), and NaI (77.1, 0.5 mmol) afforded a mixture of (R_a,*R*)-**4ee** as the major product and (S_a,*R*)-**4ee** as the minor product (162.5 mg, 73%) (eluent: hexane–ethyl acetate = 14 : 1) as a yellow oil: 99% ee for (R_a,*R*)-**4ee**; (R_a,*R*)-**4ee**/(S_a,*R*)-**4ee** = 25 : 1 (based on HPLC) (HPLC conditions: Chiralcel OD-H column, hexane/i-PrOH = 96/4, 1.0 mL min^{-1}, λ = 214 nm, t_R(minor) = 17.7 min, t_R(major) = 19.7 min, t_R(minor) = 25.0 min, t_R(minor) = 35.6 min); $[\alpha]_D^{24}$ = −198.0 (*c* = 0.995, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.42–7.10 (m, 10 H, Ar–H), 6.30–6.25 (m, 1 H, one proton from CH═C═CH), 5.78 (t, *J* = 6.2 Hz, 1 H, one proton from CH═C═CH), 5.23 (d, *J* = 6.0 Hz, 1 H, CH), 2.83 (s, 1 H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 203.5, 142.7, 133.6, 128.54, 128.4, 127.7, 127.2, 126.8, 126.0, 99.8, 97.7, 72.0; MS (EI) *m*/*z* (%): 222 (M^+, 22.71), 131 (100); HRMS calcd for $C_{16}H_{14}O$ [M^+]: 222.1045, found: 222.1046.

The following signals are discernible for (R_a*,*S**)-**4ee**: ^{13}C NMR (100 MHz, $CDCl_3$) δ = 203.8, 142.8, 128.51, 127.6, 127.1, 126.7, 125.9, 99.7, 97.4, 72.3.

Two-pot procedure for preparation of (R_a,*R*)-4ee and (S_a,*R*)-4ee with the same loading of CuBr and ligand of the literature.[12a] (Following typical procedure II). The reaction of CuBr (7.3 mg, 0.025 mmol), (*R*,R_a)-*N*-PINAP (32.1 mg, 0.03 mmol), 4 Å molecular sieves (300.6 mg), (*R*)-**1e** (132.3 mg, 1.0 mmol), **2e** (116.8 mg, 1.1 mmol), pyrrolidine (78.7 mg, 1.1 mmol), ZnI_2 (148.9 mg, 0.45 mmol), and NaI (77.8, 0.5 mmol) afforded a mixture of (R_a,*R*)-**4ee** as the major product and (S_a,*R*)-**4ee** as the minor product (167.0 mg, 75%) (eluent: hexane–ethyl acetate = 14 : 1) as a yellow oil: 99% ee for (R_a,*R*)-**4ee**; (R_a,*R*)-**4ee**/(S_a,*R*)-**4ee** = 20 : 1 (based on HPLC) (HPLC conditions: Chiralcel OD-H column, hexane/i-PrOH = 96/4, 1.0 mL min^{-1}, λ = 214 nm, t_R(minor) = 19.6 min, t_R(major) = 21.2 min, t_R(minor) = 27.7 min, t_R(minor) = 36.5 min; $[\alpha]_D^{24}$ = −181.0 (*c* = 1.02, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.54–7.00 (m, 10 H, Ar–H), 6.31 (dd, J_1 = 6.4 Hz, J_2 = 2.4 Hz, 1 H, one proton from CH═C═CH), 5.81 (t, *J* = 6.4 Hz, 1 H, one proton from CH═C═CH), 5.27 (dd, J_1 = 6.4 Hz, J_2 = 2.4 Hz, 1 H, CH), 2.26 (s, 1 H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 203.5, 142.7, 133.6, 128.59, 128.5, 127.75, 127.23, 126.82, 125.99, 99.9, 97.9, 72.1.

The following signals are discernible for (R_a*,*S**)-**4ee**: ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.32–5.29 (m, 1 H, CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 128.57, 127.72, 127.18, 126.77, 125.92, 99.8, 97.6, 72.3.

(20) Two-pot procedure for preparation of (R_a)-1-(3-cyclohexylpropa-1,2-dienyl) cyclohexanol ((R_a)-4da). To a flame-dried Schlenk tube were added CuBr (3.7 mg, 0.025 mmol), (*R*,R_a)-*N*-PINAP (17.4 mg, 0.03 mmol) and toluene (2 mL) under an argon atmosphere. The mixture was stirred at room temperature for 30 min. 4 Å Molecular sieves (302.0 mg), **1d** (127.4 mg, 1.0 mmol), **2a** (124.7 mg, 1.1 mmol), and pyrrolidine (79.2 mg, 1.1 mmol) were then added sequentially under an argon atmosphere. The mixture was then stirred at 25 °C until completion of the reaction as monitored by TLC (12 h). The crude reaction mixture was filtered through a pad of silica gel eluted with diethyl ether (30 mL). After evaporation, the crude product was used in the next step without further treatment. To another Schlenk tube was added CdI_2 (221.2 mg, 0.6 mmol). The above crude product was then dissolved in toluene (4 mL) and transferred to the Schlenk tube *via* a syringe under an argon atmosphere. The Schlenk tube was then equipped with a condenser and placed in a pre-heated oil bath at 90 °C with stirring. After 5 h, the reaction was complete as monitored by TLC, the crude reaction mixture was filtered through a pad of silica gel eluted with diethyl ether (30 mL). After evaporation, the residue was purified by chromatography on silica gel (eluent: petroleum ether–ethyl acetate = 10 : 1) to afford (R_a)-**4da** (153.9 mg, 69%) as a white solid[12a]: 95% ee (HPLC conditions: Chiralcel AD-H column, hexane/i-PrOH = 95/5, 0.6 mL min^{-1}, λ = 214 nm, t_R(major) = 9.9 min, t_R (minor) = 10.6 min; $[\alpha]_D^{25}$ = −107.1 (*c* = 1.02, $CHCl_3$) (reported value: 96% ee; $[\alpha]_D^{20}$ = −108.6 (*c* = 0.98, $CHCl_3$)); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.35–5.25 (m, 2 H, CH═C═CH), 2.05–1.90 (m, 1 H, CH from Cy), 1.80–1.42 (m, 15 H, protons from Cy and C═C═CC(OH)$(CH_2)_5$), 1.39–1.02 (m, 6 H, protons from Cy and C═C═CC(OH)$(CH_2)_5$); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 199.9, 101.3, 100.7, 70.4, 38.3, 38.2, 37.2, 33.1, 33.0, 25.98, 25.96, 25.5, 22.43, 22.41; IR (neat): ν = 3310, 2921, 2848, 1961, 1444, 1398, 1351, 1265, 1140, 1061; MS (EI) *m*/*z* (%): 220 (M^+, 20.5), 99 (100).

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