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One-pot synthesis of chiral bicyclo[3.3.0]octatrienes using diphenylprolinol silyl ether-mediated ene-type reaction

Hiroaki Gotoh [a], Hiroshi Ogino [a], Hayato Ishikawa [a], Yujiro Hayashi [a,b,*]

[a] Department of Industrial Chemistry, Faculty of Engineering, Tokyo University of Science, Kagurazaka, Shinjuku-ku, Tokyo 162-8601, Japan
[b] Research Institute for Science and Technology, Tokyo University of Science Kagurazaka, Shinjuku-ku, Tokyo 162-8601, Japan

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ABSTRACT

Chiral bicyclo[3.3.0]octatrienes with excellent enantioselectivity were synthesized from the simple starting materials of α,β-unsaturated aldehyde and cyclopentadiene via one-pot operation, which consisted of a diphenylprolinol silyl ether-mediated ene-type reaction, intramolecular addition reaction of cyclopentadiene moiety with aldehyde and dehydration reaction.

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1. Introduction

One-pot reaction is one of the effective preparation methods of organic molecules. In a one-pot reaction, several transformations are performed with the formation of several bonds in a single reaction apparatus, cutting out the need for several purifications, minimizing chemical waste generation, and saving time. Recently, our group has accomplished the three one-pot synthesis of (−)-oseltamivir, a neuraminidase inhibitor used in the treatment of human influenza.[1]

Bicyclo[3.3.0]octane structure is frequently found in natural products, such as pentalene, pentalenolactone, hirsutic acid, and coriolin.[2] Bicyclo[3.3.0]octane derivatives are also a precursor of other important natural products, especially monoterpenes. Thus, the development of an efficient synthetic preparation method for the chiral bicyclo[3.3.0]octane framework is considered to be a challenge.

Our group[3] and Jørgensen and co-workers[4] have independently developed diarylprolinol silyl ether as an effective organocatalyst,[5,6] which is widely used in several asymmetric reactions. Recently, we reported on an ene-type reaction of α,β-unsaturated aldehyde and cyclopentadiene catalyzed by diphenylprolinol silyl ether **1**, affording chiral cyclopentadiene derivatives with a mixture of position isomers.[3b] To determine enantioselectivity, cyclopentadiene derivative **2** is converted into cyclopentyl derivative, which was found to possess excellent enantioselectivity (92% ee, Eq. 1). As the obtained product **2** possesses cyclopentadiene and aldehyde moieties, it would be a versatile chiral synthetic intermediate. In fact, we have converted it to the tricyclic derivative with excellent enantioselectivity via successive Wittig and Diels–Alder reactions.[3b]

It is known that β-phenyl-α,β-unsaturated ketone reacts with cyclopentadiene in the presence of pyrrolidine to afford 3-substituted 1-phenyl-1,2-dihydropentalene.[7] This is a facile process of the bicyclo[3.3.0]octane ring system, and is limited to only phenyl-substituted α,β-unsaturated ketone with only two examples. We thought that the cyclopentadienyl anion would be generated by treating a mixture of **2a** and **2b** with an appropriate base, which would react with aldehyde moiety intramolecularly to generate bicyclo[3.3.0]octatriene after a dehydration reaction (Scheme 1). In this communication we describe the successful realization of this scenario with the synthesis of chiral bicyclo[3.3.0]octatrienes in a one-pot operation.

We chose a mixture of **2a** and **2b** as a model, and examined the base. The results were summarized in Table 1. When NaOMe was used in MeOH, the desired bicyclo[3.3.0]octatriene derivative **3** was obtained in 23% yield, along with the methoxy adduct **4**, which would be generated by the overreaction of the once-generated **3** with MeOH. When **2a** and **2b** were treated with DBU, alcohol **5** was obtained in good yield (84%) with a diastereomeric mixture. On the other hand, when **2a** and **2b** were treated with *i*-Bu_2NH and *p*-nitrophenol, the desired **3** was obtained in good yield with excellent enantioselectivity (95% ee), which is higher than that

* Corresponding author. Tel.: +81 3 5228 8318; fax: +81 3 5261 4631; e-mail address: hayashi@ci.kagu.tus.ac.jp (Y. Hayashi).

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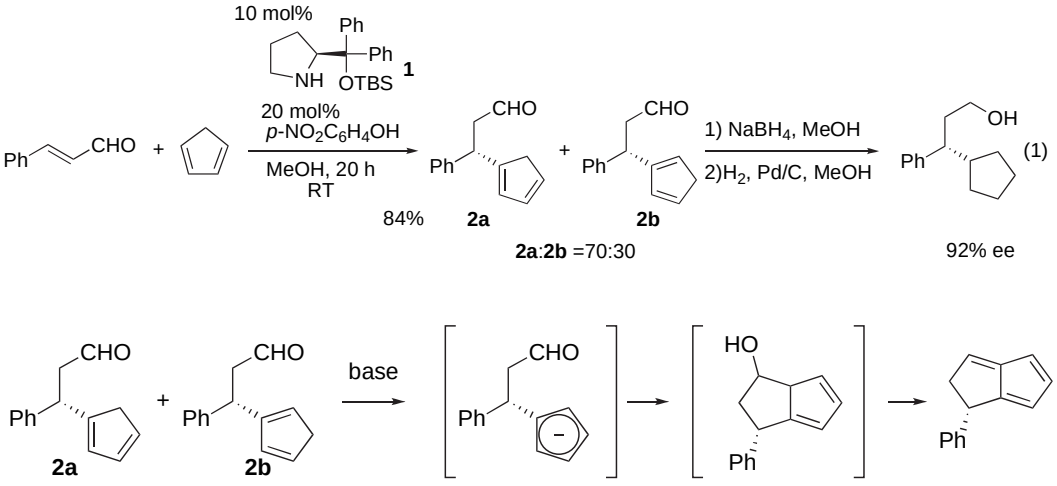
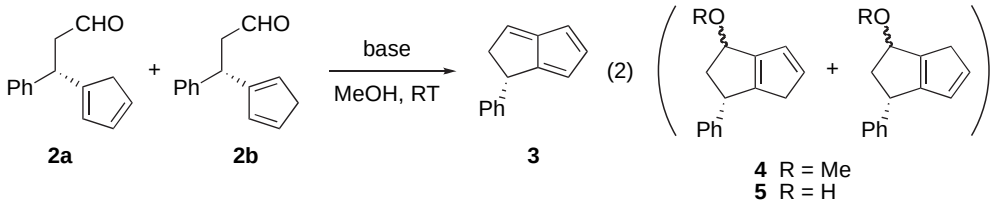


Scheme 1. The probable reaction mechanism of the formation of bicyclo[3.3.0]octatriene.

Table 1
The effect of base in the reaction of **2** to **3**[a]

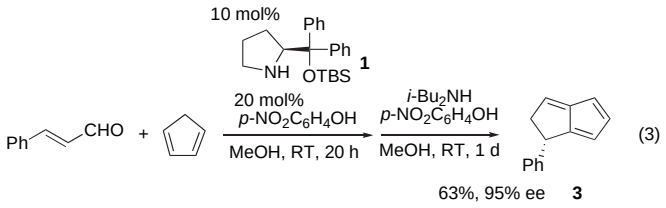


Entry	Base	Additive	Yield[b] [%]	ee [%][c]
1	NaOMe[d]	None	23[e]	nd[f]
2[g]	DBU[d]	None	0[h]	nd
3	*i*-Bu_2NH	None	0	nd
4	*i*-Bu_2NH	*p*-$NO_2C_6H_4OH$[i]	75	95

[a] Unless otherwise shown, the reaction conditions: a mixture of **2a** and **2b** (0.2 mmol), base (0.2 mmol), in MeOH (0.4 mL) at room temperature for 24 h.
[b] Isolated yield.
[c] ee was determined by HPLC analysis using chiral column.
[d] Base (0.4 mmol) was employed.
[e] Methoxy derivative **4** was obtained in 15% yield.
[f] nd=not determined.
[g] *i*-PrOH was used as a solvent.
[h] Hydroxy derivative **5** was obtained in 84% yield.
[i] *p*-$NO_2C_6H_4OH$ (0.2 mmol) was employed.

reported in the previous ene-type reaction (92% ee, vide infra). In this reaction, both *i*-Bu_2NH and *p*-nitrophenol are essential, as the reaction does not proceed in the presence of only one of these two reagents.[8]

Next, we investigated a one-pot operation for the synthesis of bicyclo[3.3.0]octatriene structure. After the treatment of cinnamaldehyde and cyclopentadiene in the presence of diphenylprolinol silyl ether **1** and *p*-nitrophenol for 20 h, *i*-Bu_2NH and *p*-nitrophenol were added to the reaction mixture. Further stirring of the reaction mixture afforded the bicyclo[3.3.0]octatriene **3** in good yield, without compromising the enantioselectivity (63%, 95% ee, Eq. 3).



After optimizing the reaction conditions, the generality of the one-pot synthesis of bicyclo[3.3.0]octatriene was investigated, and the results were summarized in Table 2. The reaction has broad substrate applicability. Not only phenyl, but also a 2-naphthyl-substituted acrolein derivative gave an excellent result (entry 2). When the substituent was electron-rich, such as 3,4-methylenedioxyphenyl or *p*-methoxyphenyl, the reaction also proceeded efficiently, generating bicyclo[3.3.0]octatrienes with excellent enantioselectivity values (entries 3 and 4). Acrolein derivatives possessing electron-deficient aromatic substituents, such as *p*-bromophenyl were also good substrates, generating an excellent result (entry 5). Not only aromatic groups, but also heteroaromatic groups, such as furyl and thienyl were suitable substituents (entries 6 and 7).

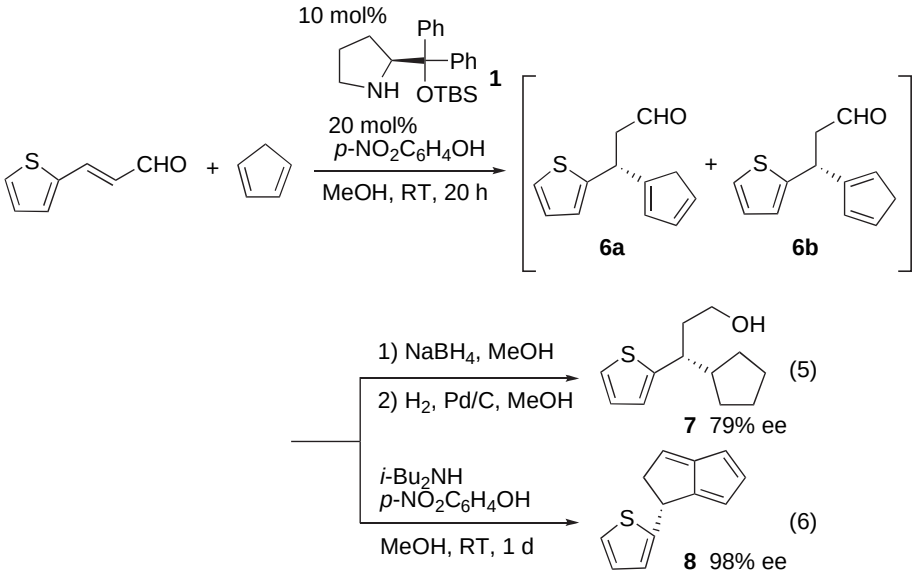
The enantiomeric excess values of the ene-type and the present reaction were found to be different, although the enantiodiscriminating step should be the same. A marked difference was observed in the reaction of 3-thienylpropenal. That is, in the cyclopentyl derivative **7**, which is prepared by an ene-type reaction followed by treatment with H_2 in presence of Pd/C (Eq. 5),[3b] only moderate enantioselectivity (79% ee) is observed, whereas in the

ene-type reaction followed by the base treatment to afford bicyclo[3.3.0]octatriene derivative **8** (Eq. 6) we obtained excellent enantioselectivity (98% ee). These data indicate that partial racemization occurs in the hydrogenation of cyclopentadiene **6**. In the previous paper,[3b] we reported the enantioselectivity of ene-type reaction based on HPLC analysis using chiral column of a cyclopentyl derivative, which was found to be inaccurate. The enantiomeric excess of the ene-type reaction should be similar to that of the present bicyclo[3.3.0]octatriene derivative, and they should be revised to have the same value in Table 2.

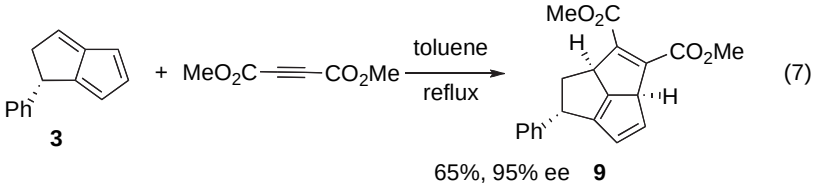
2. Experimental section

2.1. General remarks

All reactions were carried out under argon atmosphere and monitored by thin-layer chromatography using Merck 60 F_{254} precoated silica gel plates (0.25 mm thickness). FT-IR spectra were recorded on a JASCO FT/IR-410 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Brucker AM400 (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR) instrument. Data for ^{1}H NMR are reported as chemical shift (δ ppm), multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet), coupling constant (Hz), and integration. Data for ^{13}C NMR are reported as chemical shift. High-resolution mass spectral analyses (HRMS) were carried out using Bruker ESI-TOF MS and APCI-TOF MS. Preparative thin-layer chromatography was performed using Wakogel B-5F purchased from Wako Pure Chemical Industries, Tokyo, Japan. Flash chromatography was performed using silica gel 60 N of Kanto Chemical Co. Int., Tokyo, Japan. HPLC analysis was performed on a HITACHI Elite LaChrom Series HPLC, UV detection monitored at appropriate wavelength, respectively, using Chiralcel OJ-H (0.46 cm×25 cm), Chiralpak OD-H (0.46 cm×25 cm).



Although fulvenes usually react with activated alkenes to provide Diels–Alder products,[9] only in the reaction of 6-aminofulvenes, in which fulvenes are activated by amino moiety, the [6+2] cycloaddition reaction proceeds as reported by Hong and co-workers.[10] Even in activated 6-aminofulvenes, dimethyl acetylenedicarboxylate fails to react in a [6+2] cycloaddition manner. Next, bicyclo[3.3.0]octatriene was treated with alkyne. When **3** was treated with dimethyl acetylenedicarboxylate under reflux condition in toluene, the [6+2] cycloaddition reaction proceeded smoothly to provide tricyclo[5.2.1.0^{4,10}]decane derivative **9** in 65% yield without compromising the enantioselectivity (Eq. 7). This is one of the very rare successful [6+2] cycloaddition reactions of a fulvene derivative and dimethyl acetylenedicarboxylate to afford a chiral tricyclic compound.

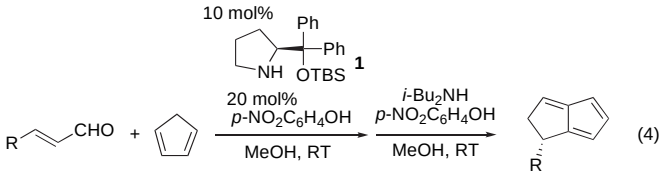


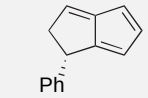
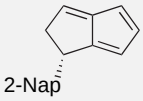
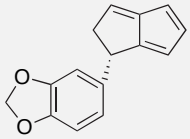
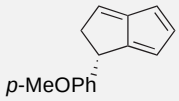
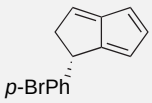
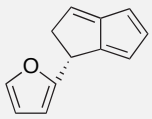
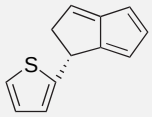
In summary, we have accomplished a one-pot synthesis of chiral bicyclo[3.3.0]octatrienes with excellent enantioselectivity via successive reactions, namely the diphenylprolinol silyl ether-mediated ene-type reaction, the intramolecular addition reaction of cyclopentadiene moiety with aldehyde, and dehydration. As the bicyclo[3.3.0]octatrienes were prepared in a one-pot operation, using only inexpensive starting materials with excellent enantioselectivity, the present method would be useful for the preparation of chiral synthetic intermediates.

2.2. The synthesis of (*S*)-1-phenyl-1,2-dihydropentalene from cinnamaldehyde and cyclopentadiene (Table 2, entry 1)

To a solution of catalyst **1** (22.1 mg, 0.06 mmol) and *p*-nitrophenol (16.7 mg, 0.12 mmol) in MeOH (1.2 mL) was added (*E*)-cinnamaldehyde (74.8 μL, 0.6 mmol) at room temperature. The solution was stirred for 1 min before the addition of cyclopentadiene (147 μL, 1.8 mmol). After stirring the reaction mixture for 20 h at room temperature, excess cyclopentadiene was

Table 2
The generality of the one-pot reaction of the formation of chiral bicyclo[3.3.0]octatriene[a]



Entry	Product	Yield[b] [%]	ee[c] [%]
1		63	95
2		79	98
3		67	99
4		66	99
5		70	99
6		51	97
7		43	98

[a] The reaction conditions: α,β-unsaturated aldehyde (0.6 mmol), cyclopentadiene (1.8 mmol), *p*-nitrophenol (0.12 mmol), and catalyst **1** (0.06 mmol) in MeOH (1.2 mL) at room temperature. After the first reaction, *i*-Bu_2NH (0.6 mmol) and *p*-nitrophenol (0.6 mmol) were added and the reaction mixture was further stirred for one day at room temperature.
[b] Isolated yield.
[c] ee was determined by HPLC analysis using chiral column.

azeotropically removed with benzene from the reaction mixture. To a solution of crude **2a**, **2b** in MeOH (1.2 mL) were added *p*-nitrophenol (83.5 mg, 0.6 mmol) and diisobutylamine (107.7 μL, 0.6 mmol) at room temperature. The solution was stirred for 24 h. The resulting mixture was quenched with pH 7.0 phosphate buffer. The organic materials were extracted with AcOEt and dried over anhydrous Na_2SO_4, then concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford compound **3** as a yellow solid (68.1 mg, 0.38 mmol, 63%).

Enantiomeric excess was determined by HPLC using a Chiralpak OD-H column (100/1 hexane/*i*-PrOH; flow rate 1.0 mL/min, t_{R1}=4.8 (major), t_{R2}=5.8 (minor) min).

^{1}H NMR ($CDCl_3$) δ 3.00 (1H, d, *J*=20.0 Hz), 3.67 (1H, ddd, *J*=2.4, 6.4, 20.0 Hz), 4.17 (1H, d, *J*=6.4 Hz), 5.91 (1H, d, *J*=1.2 Hz), 6.23 (1H, dd, *J*=4.8 Hz), 6.83 (1H, d, *J*=1.6 Hz), 6.90 (1H, d, *J*=4.4 Hz), 7.16–7.24 (3H, m), 7.25–7.32 (2H, m); ^{13}C NMR ($CDCl_3$) δ 42.1, 51.5, 112.4, 116.6, 126.2, 127.2 (2C), 128.5 (2C), 140.9, 142.2, 144.5, 153.6 (2C); IR (neat) ν 2921, 1628, 1491, 1471, 1452, 1320, 815, 698 cm^{-1}; HRMS (APCI): $[M+H]^+$ calculated for $C_{14}H_{13}$: 181.1012, found: 181.1010; $[\alpha]_D^{23}$ +18.6 (*c* 0.71, $CHCl_3$).

2.2.1. (S)-2-(1,2-Dihydropentalen-1-yl)naphthalene (Table 2, entry 2). To a solution of catalyst **1** (22.1 mg, 0.06 mmol) and *p*-nitrophenol (16.7 mg, 0.12 mmol) in MeOH (1.2 mL) was added 3-(2-naphthyl)propenal (109.3 mg, 0.6 mmol) at room temperature. The solution was stirred for 1 min before the addition of cyclopentadiene (147 μL, 1.8 mmol). After stirring the reaction mixture for 20 h at room temperature, excess cyclopentadiene was azeotropically removed with benzene from the reaction mixture. To a solution of crude mixture in MeOH (1.2 mL) were added *p*-nitrophenol (83.5 mg, 0.6 mmol) and diisobutylamine (107.7 μL, 0.6 mmol) at room temperature. The solution was stirred for 24 h. The resulting mixture was quenched with pH 7.0 phosphate buffer. The organic materials were extracted with AcOEt and dried over anhydrous Na_2SO_4, then concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford (*S*)-2-(1,2-dihydropentalen-1-yl)naphthalene (109.1 mg, 0.47 mmol, 79%) as a yellow solid.

Enantiomeric excess was determined by HPLC using a Chiralpak OJ-H column (100/1 hexane/*i*-PrOH; flow rate 1.0 mL/min, t_{R1}=14.9 (minor), t_{R2}=20.0 (major) min).

^{1}H NMR ($CDCl_3$) δ 3.00 (1H, dt, J_d=20.0 Hz, J_t=2.4 Hz), 3.63 (1H, ddd, *J*=2.8, 6.8, 20.0 Hz), 4.23 (1H, d, *J*=6.4 Hz), 5.84 (1H, d, *J*=1.6 Hz), 6.17 (1H, d, *J*=5.2 Hz), 6.76 (1H, q, *J*=2.8 Hz), 6.83 (1H, d, *J*=4.4 Hz), 7.16 (1H, dd, *J*=2.0, 8.4 Hz), 7.29–7.37 (2H, m), 7.59 (1H, d, *J*=0.8 Hz), 7.63–7.72 (3H, m); ^{13}C NMR ($CDCl_3$) δ 42.3, 51.4, 112.5, 116.8, 125.3 (2C), 125.9, 126.0, 127.6 (2C), 128.3, 132.3, 133.6, 140.9, 141.8, 142.3, 153.6, 153.7; IR (neat) ν 2926, 1715, 908, 818, 733 cm^{-1}; HRMS (APCI): $[M+H]^+$ calculated for $C_{18}H_{15}$: 231.1168, found: 231.1163; $[\alpha]_D^{25}$ +67.1 (*c* 1.8, $CHCl_3$).

2.2.2. (S)-5-(1,2-Dihydropentalen-1-yl)benzo[d][1,3]dioxole (Table 2, entry 3). To a solution of catalyst **1** (22.1 mg, 0.06 mmol) and *p*-nitrophenol (16.7 mg, 0.12 mmol) in MeOH (1.2 mL) was added 3-(3,4-methylenedioxyphenyl)propenal (105.7 mg, 0.6 mmol) at room temperature. The solution was stirred for 1 min before the addition of cyclopentadiene (147 μL, 1.8 mmol). After stirring the reaction mixture for 20 h at room temperature, excess cyclopentadiene was azeotropically removed with benzene from the reaction mixture. To a solution of crude mixture in MeOH (1.2 mL) were added *p*-nitrophenol (83.5 mg, 0.6 mmol) and diisobutylamine (107.7 μL, 0.6 mmol) at room temperature. The solution was stirred for 24 h. The resulting mixture was quenched with pH 7.0 phosphate buffer. The organic materials were extracted with AcOEt and dried over anhydrous Na_2SO_4, then concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford compound (*S*)-5-(1,2-dihydropentalen-1-yl)benzo[*d*][1,3]dioxole (90.2 mg, 0.40 mmol, 67%) as a yellow solid.

Enantiomeric excess was determined by HPLC using a Chiralpak OD-H column (100/1 hexane/*i*-PrOH; flow rate 1.0 mL/min, t_{R1}=8.0 (minor), t_{R2}=10.4 (major) min).

^{1}H NMR ($CDCl_3$) δ 2.96 (1H, d, *J*=20.0 Hz), 3.63 (1H, ddd, *J*=2.4, 6.4, 20.0 Hz), 4.09 (1H, d, *J*=6.4 Hz), 5.89–5.94 (1H, m), 5.91 (2H, s), 6.21 (1H, d, *J*=5.2 Hz), 6.63–6.75 (3H, m), 6.78–6.84 (1H, m), 6.89 (1H, d, *J*=4.8 Hz); ^{13}C NMR ($CDCl_3$) δ 41.8, 51.6, 100.8, 107.5, 108.0, 112.4, 116.6, 120.1, 138.4, 140.9, 142.1, 145.9, 147.8, 153.5 (2C); IR (neat) ν 2995, 1627, 1488, 1442, 1247, 1039, 936, 807 cm^{-1}; HRMS

(APCI): $[M+H]^+$ calculated for $C_{15}H_{13}O_2$: 225.0910, found: 225.0914; $[\alpha]_D^{24}$ +20.1 (*c* 0.22, $CHCl_3$).

2.2.3. (S)-1-(4-Methoxyphenyl)-1,2-dihydropentalene (Table 2, entry 4). To a solution of catalyst **1** (22.1 mg, 0.06 mmol) and *p*-nitrophenol (16.7 mg, 0.12 mmol) in MeOH (1.2 mL) was added 3-(4-methoxyphenyl) propenal (97.3 mg, 0.6 mmol) at room temperature. The solution was stirred for 1 min before the addition of cyclopentadiene (147 μL, 1.8 mmol). After stirring the reaction mixture for 20 h at room temperature, excess cyclopentadiene was azeotropically removed with benzene from the reaction mixture. To a solution of crude mixture in MeOH (1.2 mL) were added *p*-nitrophenol (83.5 mg, 0.6 mmol) and diisobutylamine (107.7 μL, 0.6 mmol) at room temperature. The solution was stirred for 24 h. The resulting mixture was quenched with pH 7.0 phosphate buffer. The organic materials were extracted with AcOEt and dried over anhydrous Na_2SO_4, then concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford (*S*)-1-(4-methoxyphenyl)-1,2-dihydropentalene (83.3 mg, 0.40 mmol, 66%) as a yellow solid.

Enantiomeric excess was determined by HPLC using a Chiralpak OD-H column (100/1 hexane/*i*-PrOH; flow rate 0.3 mL/min, t_{R1}=31.7 (minor), t_{R2}=34.6 (major) min).

^{1}H NMR ($CDCl_3$) δ 2.99 (1H, d, *J*=20.0 Hz), 3.66 (1H, ddd, *J*=2.8, 6.8, 20.0 Hz), 3.80 (3H, s), 4.15 (1H, d, *J*=6.4 Hz), 5.92 (1H, s), 6.24 (1H, d, *J*=4.8 Hz), 6.80–6.85 (1H, m), 6.85 (2H, d, *J*=8.8 Hz), 6.92 (1H, d, *J*=4.8 Hz), 7.14 (2H, d, *J*=8.8 Hz); ^{13}C NMR ($CDCl_3$) δ 41.4, 51.6, 55.2, 112.3, 113.9 (2C), 116.4, 128.1 (2C), 136.5, 140.9, 142.1, 153.5, 153.9, 158.1; IR (neat) ν 2906, 1511, 1248, 1177, 1036, 812 cm^{-1}; HRMS (APCI): $[M+H]^+$ calculated for $C_{15}H_{15}O$: 211.1117, found: 211.1119; $[\alpha]_D^{24}$ +20.9 (*c* 2.1, $CHCl_3$).

2.2.4. (S)-1-(4-Bromophenyl)-1,2-dihydropentalene (Table 2, entry 5). To a solution of catalyst **1** (22.1 mg, 0.06 mmol) and *p*-nitrophenol (16.7 mg, 0.12 mmol) in MeOH (1.2 mL) was added 3-(4-bromophenyl)propenal (126.6 mg, 0.6 mmol) at room temperature. The solution was stirred for 1 min before the addition of cyclopentadiene (147 μL, 1.8 mmol). After stirring the reaction mixture for 20 h at room temperature, excess cyclopentadiene was azeotropically removed with benzene from the reaction mixture. To a solution of crude mixture in MeOH (1.2 mL) were added *p*-nitrophenol (83.5 mg, 0.6 mmol) and diisobutylamine (107.7 μL, 0.6 mmol) at room temperature. The solution was stirred for 24 h. The resulting mixture was quenched with pH 7.0 phosphate buffer. The organic materials were extracted with AcOEt and dried over anhydrous Na_2SO_4, then concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford (*S*)-1-(4-bromophenyl)-1,2-dihydropentalene (108.8 mg, 0.42 mmol, 70%) as a yellow solid.

Enantiomeric excess was determined by HPLC using a Chiralpak OD-H column (100/1 hexane/*i*-PrOH; flow rate 0.3 ml/min, t_{R1}=31.7 (minor), t_{R2}=34.6 (major) min).

^{1}H NMR ($CDCl_3$) δ 2.97 (1H, d, *J*=20.0 Hz), 3.66 (1H, ddd, *J*=2.4, 6.4, 20.0 Hz), 4.12 (1H, d, *J*=6.4 Hz), 5.90 (1H, d, *J*=0.8 Hz), 6.23 (1H, d, *J*=5.2 Hz), 6.80 (1H, d, *J*=1.6 Hz), 6.89 (1H, d, *J*=4.4 Hz), 7.08 (2H, d, *J*=8.4 Hz), 7.40 (2H, d, *J*=8.4 Hz); ^{13}C NMR ($CDCl_3$) δ 41.5, 51.4, 112.6, 116.8, 119.9, 129.0 (2C), 131.5 (2C), 140.7, 142.2, 143.6, 153.0, 153.5; IR (neat) ν 1487, 1011, 808 cm^{-1}; $[\alpha]_D^{23}$ +17.4 (*c* 0.51, $CHCl_3$).

2.2.5. (R)-2-(1,2-Dihydropentalen-1-yl)furan (Table 2, entry 6). To a solution of catalyst **1** (22.1 mg, 0.06 mmol) and *p*-nitrophenol (16.7 mg, 0.12 mmol) in MeOH (1.2 mL) was added 3-furyl-propenal (73.3 mg, 0.6 mmol) at room temperature. The solution was stirred for 1 min before the addition of cyclopentadiene (147 μL, 1.8 mmol). After stirring the reaction mixture for 20 h at room temperature, excess cyclopentadiene was azeotropically removed with benzene from the reaction mixture. To a solution of crude mixture in MeOH (1.2 mL) were added *p*-nitrophenol (83.5 mg, 0.6 mmol) and diisobutylamine (107.7 μL, 0.6 mmol) at room temperature. The solution was stirred for 24 h. The resulting mixture was quenched with pH 7.0 phosphate buffer. The organic materials were extracted with AcOEt and dried over anhydrous Na_2SO_4, then concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford (*R*)-2-(1,2-dihydropentalen-1-yl)furan (52.1 mg, 0.31 mmol, 51%) as a yellow solid.

Enantiomeric excess was determined by HPLC using a Chiralpak OD-H column (100/1 hexane/*i*-PrOH; flow rate 0.3 mL/min, t_{R1}=26.4 (major), t_{R2}=30.6 (minor) min).

^{1}H NMR ($CDCl_3$) δ 3.20 (1H, dd, *J*=2.4, 20.0 Hz), 3.58 (1H, ddd, *J*=2.4, 6.4, 20.0 Hz), 4.25 (1H, d, *J*=6.4 Hz), 6.06–6.11 (2H, m), 6.24 (1H, d, *J*=4.8 Hz), 6.29 (1H, dd, *J*=1.6, 3.2 Hz), 6.79 (1H, d, *J*=1.6 Hz), 6.91 (1H, d, *J*=5.2 Hz), 7.35 (1H, s); ^{13}C NMR ($CDCl_3$) δ 35.3, 47.6, 104.4, 110.0, 112.8, 116.9, 140.4, 141.5, 142.0, 150.2, 153.0, 156.5; IR (neat) ν 2914, 1629, 1590, 1505, 1473, 1323, 1009, 815, 734 cm^{-1}; HRMS (APCI): $[M+H]^+$ calculated for $C_{12}H_{11}O$: 171.0804, found: 171.0807; $[\alpha]_D^{23}$ −19.6 (*c* 1.6, $CHCl_3$).

2.2.6. (R)-2-(1,2-Dihydropentalen-1-yl)thiophene (Table 2, entry 7). To a solution of catalyst **1** (22.1 mg, 0.06 mmol) and *p*-nitrophenol (16.7 mg, 0.12 mmol) in MeOH (1.2 mL) was added 3-thienyl-propenal (82.9 mg, 0.6 mmol) at room temperature. The solution was stirred for 1 min before the addition of cyclopentadiene (147 μL, 1.8 mmol). After stirring the reaction mixture for 20 h at room temperature, excess cyclopentadiene was azeotropically removed with benzene from the reaction mixture. To a solution of crude mixture in MeOH (1.2 mL) were added *p*-nitrophenol (83.5 mg, 0.6 mmol) and diisobutylamine (107.7 μL, 0.6 mmol) at room temperature. The solution was stirred for 24 h. The resulting mixture was quenched with pH 7.0 phosphate buffer. The organic materials were extracted with AcOEt and dried over anhydrous Na_2SO_4, then concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford (*R*)-2-(1,2-dihydropentalen-1-yl)thiophene (48.1 mg, 0.26 mmol, 43%) as a yellow solid.

Enantiomeric excess was determined by HPLC using a Chiralpak OD-H column (100/1 hexane/*i*-PrOH; flow rate 0.3 mL/min, t_{R1}=32.8 (major), t_{R2}=38.0 (minor) min).

^{1}H NMR ($CDCl_3$) δ 3.16 (1H, d, *J*=20.0 Hz), 3.71 (1H, ddd, *J*=1.6, 6.4, 20.0 Hz), 4.47 (1H, d, *J*=6.4 Hz), 6.09 (1H, s), 6.25 (1H, d, *J*=5.2 Hz), 6.79 (1H, s), 6.89–6.98 (3H, m), 7.15 (1H, d, *J*=4.8 Hz); ^{13}C NMR ($CDCl_3$) δ 37.0, 51.6, 112.7, 117.2, 123.3, 123.5, 126.6, 140.1, 142.0, 147.8, 152.5, 153.0; IR (neat) ν 2924, 1628, 1472, 1321, 813, 696 cm^{-1}; HRMS (APCI): $[M+H]^+$ calculated for $C_{12}H_{11}S$: 187.0576, found: 187.0577; $[\alpha]_D^{25}$ −15.1 (*c* 0.18, $CHCl_3$).

*2.2.7. (S)-Dimethyl-5-phenyl-2a,5,6,6a-tetrahydrocyclopenta[cd]pentalene-1,2-dicarboxylate **4**.* To a toluene solution (4.9 mL) of compound **3** (88.2 mg, 0.49 mmol) was added dimethyl acetylenedicarboxylate (89.7 μL, 0.732 mmol) at room temperature. After stirring the reaction mixture for 10 h at 130 °C, the resulting mixture was concentrated under reduced pressure at room temperature. The residue was purified by silica gel column chromatography to afford compound **4** (101.7 mg, 0.32 mmol, 65%). Enantiomeric excess was determined by HPLC using a Chiralpak IA column (20/1 hexane/*i*-PrOH; flow rate 1.0 mL/min, t_{R1}=5.6 (minor), t_{R2}=6.0 (major) min).

^{1}H NMR ($CDCl_3$) δ 2.75 (1H, ddd, *J*=2.0, 4.4, 16.4 Hz), 3.12 (1H, ddd, *J*=2.0, 9.2, 16.4 Hz), 3.77 (3H, s), 3.87 (3H, s), 3.91 (1H, dd, *J*=4.4, 9.2 Hz), 4.46 (1H, t, *J*=2.0 Hz), 4.51 (1H, d, *J*=2.8 Hz), 6.43 (1H, d, *J*=5.2 Hz), 6.80 (1H, d, *J*=2.8, 4.8 Hz), 7.20 (2H, d, *J*=7.2 Hz), 7.21–7.27 (1H, m), 7.33 (2H, t, *J*=7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 41.8, 45.4, 49.8, 52.0, 81.1, 93.7, 126.3, 128.1 (2C), 128.4 (2C), 141.2, 142.8, 143.3,

149.3, 156.3, 164.0, 165.7, 167.1; IR (neat) ν 1715, 1607, 1435, 1270, 1197 cm^{-1}; HRMS (ESI): $[M+Na]^+$ calculated for $C_{20}H_{18}O_4Na$: 345.1097, found: 345.1079; $[\alpha]_D^{23}$ −17.3 (*c* 0.37, MeOH).

Relative stereochemistry was determined by NOE experiment after reduction of ester.

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Supplementary data

Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2010.03.010.

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