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Efficient and Practical Method for Synthesizing Optically Active Indan-2-ols by the Ti(O-*i*-Pr)$_4$/2 *i*-PrMgCl-Mediated Metalative Reppe Reaction

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Received March 26, 2003

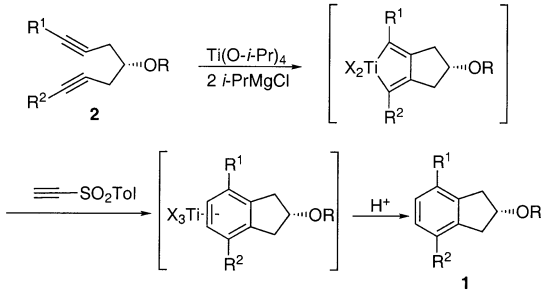
Abstract: An efficient and practical synthesis of optically active indan-2-ols **1** has been developed starting from readily accessible optically active 4-siloxy-1,6-alkadiynes **2** and ethynyl *p*-tolyl sulfone, where the metalative Reppe reaction mediated by an economical divalent titanium reagent, Ti(O-*i*-Pr)$_4$/2 *i*-PrMgCl, is a key step.

The indan-2-ol skeleton exists in a number of organic compounds and, thus, the construction of its structure is important.[1] However, its asymmetric synthesis is not necessarily an easy process. The synthetic difficulty becomes more and more marked with an increase in the number of substituents on the aromatic ring, and as far as we know, no general synthetic method is available for preparing optically active indan-2-ols having two aromatic substituents.

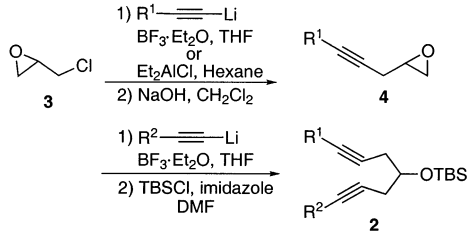
Recently, we have reported a metalative Reppe reaction mediated by an economical divalent titanium reagent, Ti(O-*i*-Pr)$_4$/2 *i*-PrMgX, which realizes the direct preparation of aryltitanium compounds from two acetylenes and ethynyl *p*-tolyl sulfone.[2,3] We anticipated that this reaction might allow the preparation of optically active 4,7-disubstituted indan-2-ols of the type **1** from optically active 4-siloxy-1,6-alkadiynes **2** and ethynyl *p*-tolyl sulfone, as shown in Scheme 1.

First, we investigated the feasibility of the transformation depicted in Scheme 1 by starting with racemic **2**. The starting **2** can be readily prepared from racemic epichlorohydrin (**3**) according to the conventional reaction sequence shown in Scheme 2. Thus, the reaction of **3** with R^1−C≡C−Li in the presence of BF_3·Et_2O[4] and/or Et_2AlCl[5]

SCHEME 1. Preparation of 4,7-Disubstituted Indan-2-ols via the Metalative Reppe Reaction



SCHEME 2. Preparation of 2 Starting from 3



and the following treatment of the resulting epoxide ring-opening product with NaOH in CH_2Cl_2 afforded **4**. The compound **4** was then converted into **2** by the treatment of R^2−C≡C−Li in the presence of BF_3·Et_2O and the silylation with TBSCl/imidazole.

The metalative Reppe reaction starting with **2** readily proceeded as we expected to provide **1** after hydrolysis. As can be seen from Table 1, which summarizes the results of the reaction, a variety of **1** having two aromatic substituents at the C-4 and C-7 positions can be prepared in high isolated yields.

As both enantiomers of **3** with more than 99% enantiometric excess (ee) are commercially available at low price and in bulk, it can be said that an efficient and practical method for preparing optically active **1** has now been opened up. And we actually prepared several optically active compounds **1**, including one that was utilized for the synthesis of biologically active compounds.

The reaction allows the preparation of both enantiomers of **1** starting from a single enantiomer of **3** by changing the order of the two acetylenes that are reacted with **3** in Scheme 2, as exemplified by the preparation of both enantiomers of **1d** (Scheme 3).

The synthesis of optically active (*S*)-4-phenyl-indan-2-ol [(*S*)-**5**] has attracted much interest because it can be used as the alcohol moiety of (*S*)-4-phenyl-2-indanyl (*Z*)-3-(2-chloro-3,3,3-trifluoro-1-propenyl)-2,2-dimethylcyclopropanecarboxylate (**6**), a highly effective pyrethroid derivative (Figure 1).[6] However, the reported synthesis of (*S*)-**5** was not so efficient; the synthetic method required multistep transformation and involved an operation for refinement of enantiomeric purity by recrys-

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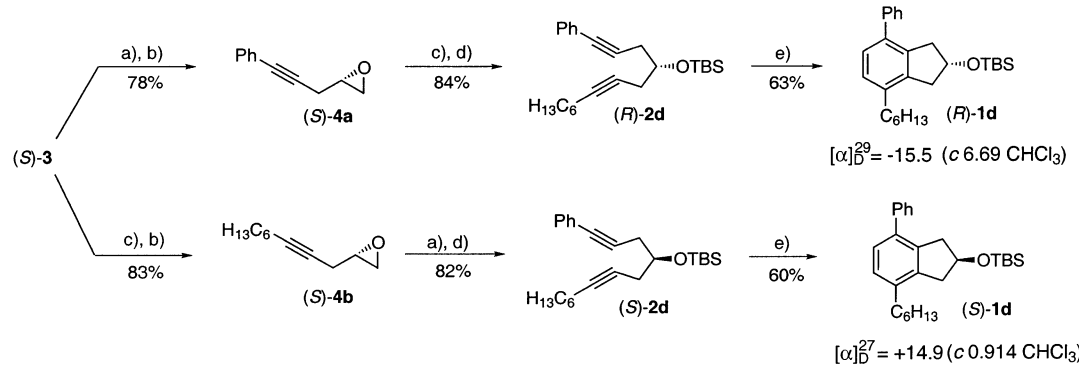
10.1021/jo034391m CCC: $25.00
Published on Web 05/10/2003

SCHEME 3. Preparation of Both Enantiomers of 1 Starting from a Single Enantiomer of 3[a]



[a] Reaction conditions: (a) PhC≡CH, *n*-BuLi, BF_3·Et_2O, THF. (b) NaOH, CH_2Cl_2. (c) $H_{13}C_6C{\equiv}CH$, *n*-BuLi, BF_3·Et_2O, THF. (d) TBSCl, imidazole, DMF. (e) Ti(O-*i*-Pr)$_4$/2 *i*-PrMgCl, Et_2O, then $TolSO_2C{\equiv}CH$.

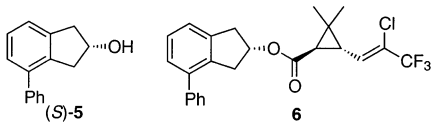
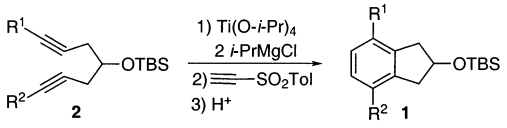


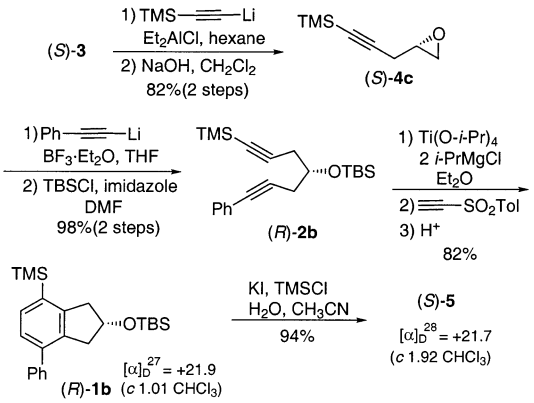
FIGURE 1. A highly effective pyrethroid derivative.

TABLE 1. Synthesis of a Variety of 1 by the Metalative Reppe Reaction



substrate	yield (%)
a: R^1 = TMS; R^2 = *n*-C_6H_{13}	76
b: R^1 = TMS; R^2 = Ph	82
c: R^1 = TMS; R^2 = O-*c*-C_6H_{11}	86
d: R^1 = Ph; R^2 = *n*-C_6H_{13}	63
e: R^1 = Ph; R^2 = O-*c*-C_6H_{11}	88
f: R^1 = *n*-C_6H_{13}; R^2 = *n*-C_4H_9	75

SCHEME 4. The Efficient Synthesis of the Alcohol Moiety of a Pyrethroid Derivative



tallization and tedious separation of byproduct(s) by column chromatography or recrystallization. As shown in Scheme 4, (*S*)-**5** can be readily synthesized by treatment of optically active (*R*)-**1b** with KI-TMSCl−H_2O[7] in 94% yield.[8] The enantiomeric excess of (*S*)-**5** thus obtained was confirmed to be >99% ee by HPLC analysis.[9]

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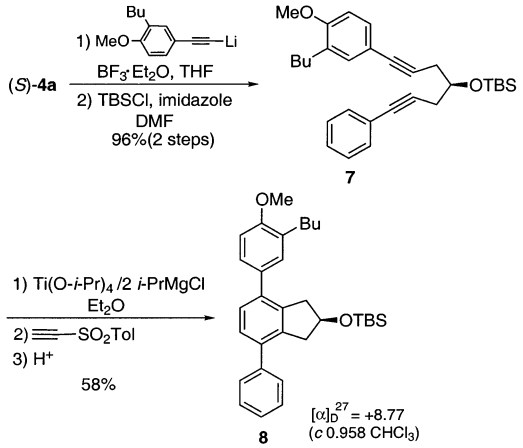
SCHEME 5. The Synthesis of Optically Active Terphenyl Derivatives



Terphenyl derivatives have attracted much interest in recent years in the field of material[10] and medicinal sciences.[11] The preparation of optically active terphenyl derivatives, however, has been scarcely reported. The present method can allow access to optically active terphenyl derivatives as exemplified by the synthesis of **8** shown in Scheme 5. The easy and practical method for synthesizing optically active terphenyl compounds developed here might find utility in the field of the sciences mentioned above.

Experimental Section

General Procedure for the Ti(II)-Mediated Metalative Reppe Reaction. As a typical example, the synthesis of (*R*)-**1d** is described as follows.

(*R*)-2-[(*tert*-Butyl)dimethylsiloxy]-4-hexyl-7-phenylindan ((*R*)-1d, Scheme 3). The titled compound was prepared according to the literature.[2] To a stirred solution of (*R*)-**2d** (0.191

(8) The metalative Reepe reaction of (*R*)-**2b** after protodesilylation did not proceed efficiently.

(9) See Supporting Information.

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g, 0.500 mmol) and Ti(O-*i*-Pr)$_4$ (0.177 mL, 0.600 mmol) in 2.50 mL of Et$_2$O was added *i*-PrMgCl (0.706 mL, 1.77 M in Et$_2$O, 1.25 mmol) at −78 °C under argon to give a yellow homogeneous solution. The solution was warmed to −50 °C over 30 min, during which period its color turned dark yellow. After the solution was stirred at −50 °C for an additional 4 h, ethynyl *p*-tolyl sulfone (0.180 g, 1.00 mmol) was added and the reaction mixture was subsequently allowed to warm to 0 °C. After being stirred for 3 h at this temperature, the reaction was terminated by the addition of H$_2$O (0.090 mL) and stirred for 10 min. After the addition of NaF (0.210 g) and Celite (0.200 g), the mixture was stirred for 10 min and filtered through a pad of Celite with Et$_2$O. The filterate was concentrated and chromatographed on silica gel (hexanes−Et$_2$O) to give (*R*)-**1d** (0.129 g, 63%) as a colorless oil. ^{1}H NMR δ 7.31−7.49 (m, 5H), 7.19 (d, J = 7.8 Hz, 1H), 7.10 (d, J = 7.8, 1H), 4.61−4.70 (m, 1H), 3.21 (dd, J = 2.7, 6.9 Hz, 1H), 3.15 (dd, J = 3.0, 6.9 Hz, 1H), 3.03 (dd, J = 6.3, 15.9 Hz, 1H), 2.91 (dd, J = 6.6, 15.9 Hz, 1H), 2.62 (dd, J = 6.6, 8.4 Hz, 2H), 1.57−1.70 (m, 2H), 1.24−1.47 (m, 6H), 0.87−0.98 (m, 3H), 0.93 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H); ^{13}C NMR δ 141.2, 139.8, 138.4, 137.6, 135.6, 128.4, 128.1, 127.1, 126.9, 126.5, 73.8, 42.5, 41.0, 33.5, 31.9, 30.3, 29.4, 26.0, 22.7, 18.3, 14.2, −4.55, −4.60; IR (neat) 3057, 3027, 2928, 1472, 1363, 1254, 1097, 896, 836, 775, 700 cm^{-1}; $[\alpha]^{29}_D$ −15.5 (*c* 6.69, CHCl$_3$). Anal. Calcd for $C_{27}H_{40}OSi$: C, 79.35; H, 9.87. Found: C, 79.67; H, 9.79.

(*S*)-2-[(*tert*-Butyl)dimethylsiloxy]-4-hexyl-7-phenylindan ((*S*)-1d, Scheme 3). (*S*)-**1d** (0.123 g, 60%) was obtained starting from (*S*)-**2d** (0.191 g, 0.500 mmol), Ti(O-*i*-Pr)$_4$ (0.177 mL, 0.600 mmol), *i*-PrMgCl (1.88 M in Et$_2$O, 0.670 mL, 1.26 mmol), and ethynyl *p*-tolyl sulfone (0.180 g, 1.00 mmol) under similar reaction conditions as described for the synthesis of (*R*)-**1d**. The spectral data (^{1}H NMR, ^{13}C NMR, IR) have been described. $[\alpha]^{27}_D$ +14.9 (*c* 0.914, CHCl$_3$).

(*R*)-2-[(*tert*-Butyl)dimethylsiloxy]-4-phenyl-7-(trimethylsilyl)indan ((*R*)-1b, Scheme 4). (*R*)-**1b** (0.163 g, 82%) was obtained starting from (*R*)-**2b** (0.185 g, 0.500 mmol), Ti(O-*i*-Pr)$_4$ (0.177 mL, 0.600 mmol), *i*-PrMgCl (1.88 M in Et$_2$O, 0.670 mL, 1.26 mmol), and ethynyl *p*-tolyl sulfone (0.180 g, 1.00 mmol) under similar reaction conditions as described for the synthesis of (*R*)-**1d**. ^{1}H NMR δ 7.35−7.52 (m, 6H), 7.24 (d, J = 7.8 Hz, 1H), 4.57−4.70 (m, 1H), 3.28 (dd, J = 6.9, 15.3 Hz, 1H), 3.16 (dd, J = 6.6, 15.9 Hz, 1H), 3.05 (dd, J = 6.6, 15.3 Hz, 1H), 3.00 (dd, J = 6.0 Hz, 15.9 Hz, 1H), 0.93 (s, 9H), 0.37 (s, 9H), 0.12 (s, 3H), 0.10 (s, 3H); ^{13}C NMR δ 147.0, 141.0, 139.0, 137.9, 134.1, 132.4, 128.4, 128.1, 126.8, 126.3, 73.8, 43.9, 41.8, 26.0, 18.3, −0.6, −4.5, −4.6; IR (neat) 3057, 2954, 1472, 1363, 1250, 1110, 910, 837, 755, 700 cm^{-1}; $[\alpha]^{27}_D$ +21.9 (*c* 1.01, CHCl$_3$). Anal. Calcd for $C_{24}H_{36}OSi_2$: C, 72.66; H, 9.15. Found: C, 72.90; H, 9.24.

(*S*)-2-[(*tert*-Butyl)dimethylsiloxy]-4-(3-butyl-4-methoxyphenyl)-7-phenylindan (8, Scheme 5). 8 (0.142 g, 58%) was obtained starting from **7** (0.230 g, 0.500 mmol), Ti(O-*i*-Pr)$_4$ (0.177 mL, 0.600 mmol), *i*-PrMgCl (1.88 M in Et$_2$O, 0.670 mL, 1.26 mmol), and ethynyl *p*-tolyl sulfone (0.180 g, 1.00 mmol) under similar reaction conditions as described for the synthesis of (*R*)-**1d**. ^{1}H NMR δ 7.43−7.51 (m, 4H), 7.28−7.39 (m, 5H), 6.94 (d, J = 8.4 Hz, 1H), 4.53−4.63 (m, 1H), 3.90 (s, 3H), 3.06−3.25 (m, 4H), 2.70 (dt, J = 2.7, 7.8 Hz, 2H), 1.59−1.70 (m, 2H), 1.36−1.49 (m, 2H), 0.97 (t, J = 7.2 Hz, 3H), 0.89 (s, 9H), 0.05 (s, 6H); ^{13}C NMR δ 156.8, 141.1, 139.3, 139.2, 137.4, 136.8, 132.9, 131.1, 130.2, 128.6, 128.4, 127.6, 127.5, 126.9, 126.8, 110.1, 74.1, 55.3, 42.5, 42.4, 31.9, 29.8, 25.8, 22.5, 18.1, 13.9, −4.9; IR (Nujol) 3052, 3022, 2926, 1464, 1374, 1248, 1146, 1083, 1038, 904, 837, 815, 769, 705 cm^{-1}; mp 89−91 °C; $[\alpha]^{27}_D$ +8.8 (*c* 0.96, CHCl$_3$). Anal. Calcd for $C_{32}H_{42}O_2Si$: C, 78.96; H, 8.70. Found: C, 79.28; H, 9.07.

(*S*)-2-(3-Phenyl-2-propynyl)oxirane ((*S*)-4a, Scheme 3). (*S*)-**4a** was prepared according to the literature.[4] To a stirred solution of ethynylbenzene (0.824 mL, 7.50 mmol) in THF (15.0 mL) was slowly added *n*-BuLi (4.75 mL, 1.58 M in hexane, 7.50 mmol) at −78 °C and the mixture was stirred for 10 min at this temperature. Then, to the mixture was added boron trifluoride etherate (0.950 mL, 7.50 mmol). After the solution was stirred for 10 min at −78 °C, freshly distilled (*S*)-**3** (0.391 mL, 5.00 mmol) was slowly added and the mixture was stirred for 1 h at the same temperature. After addition of saturated aqueous NH$_4$Cl (20 mL), the mixture was extracted with Et$_2$O (3 × 20 mL). The combined organic layers were dried over MgSO$_4$, concentrated, passed through a short silica gel column with 5% ether in hexane for removing nonpolar products such as ethynylbenzene, and then concentrated to provide a crude oil.

To a solution of the crude oil in CH$_2$Cl$_2$ (16.7 mL) was slowly added NaOH (0.400 g, 10.0 mmol) at room temperature. The mixture was stirred for 2 days. After addition of saturated aqueous NH$_4$Cl (20 mL), the mixture was extracted with CH$_2$Cl$_2$ (3 × 20 mL). The combined organic layers were dried over MgSO$_4$, concentrated, and chromatographed on silica gel (hexanes−Et$_2$O) to give (*S*)-**4a** (0.623 g, 78%) as a colorless oil. ^{1}H NMR δ 7.39−7.45 (m, 2H), 7.27−7.32 (m, 3H), 3.15−3.21 (m, 1H), 2.80−2.88 (m, 2H), 2.64−2.74 (m, 2H); ^{13}C NMR δ 131.4, 128.0, 127.8, 123.0, 84.0, 82.5, 49.9, 46.4, 23.1; IR (neat) 3060, 2996, 1598, 1490, 1442, 1406, 1071, 959, 926, 840, 756 cm^{-1}; $[\alpha]^{29}_D$ +32.4 (*c* 4.37, CHCl$_3$).

(*R*)-4-[(*tert*-Butyl)dimethylsiloxy]-1-phenyl-1,6-tridecadiyne ((*R*)-2d, Scheme 3). To a stirred solution of 1-octyne (0.885 mL, 6.00 mmol) in THF (9.0 mL) was slowly added *n*-BuLi (3.79 mL, 1.58 M in hexane, 6.00 mmol) at −78 °C and the mixture was stirred for 1 h at this temperature. Then, to the mixture was added boron trifluoride etherate (0.760 mL, 6.00 mmol). After the mixture was stirred for 1 h at −78 °C, a solution of (*S*)-**4a** (0.475 g, 3.00 mmol) in THF (4.0 mL) was added. The reaction mixture was stirred for 1 h at the same temperature and warmed to room temperature over 30 min. After addition of saturated aqueous NH$_4$Cl (20 mL), the mixture was extracted with Et$_2$O (3 × 20 mL). The combined organic layers were dried over MgSO$_4$, concentrated, passed through a short silica gel column with 5% ether in hexane for removing nonpolar products such as 1-octyne, and then concentrated to provide a crude oil.

To a mixture of the crude oil thus obtained and imidazole (0.408 g, 6.00 mmol) in DMF (6.0 mL) was added TBSCl (0.543 g, 3.60 mmol) at 0 °C. After the solution was stirred for 12 h at room temperature, the reaction was terminated by the addition of saturated aqueous NaHCO$_3$ (10 mL) at 0 °C. The mixture was extracted with Et$_2$O (3 × 10 mL). The combined organic layers were dried over MgSO$_4$, concentrated, and chromatographed on silica gel (hexanes−Et$_2$O) to give (*R*)-**2d** (0.967 g, 84%) as a colorless oil. ^{1}H NMR δ 7.39−7.43 (m, 2H), 7.26−7.31 (m, 3H), 3.95−4.04 (m, 1H), 2.75 (dd, J = 5.7, 16.5 Hz, 1H), 2.60 (dd, J = 6.3, 16.5 Hz, 1H), 2.42−2.50 (m, 2H), 2.13−2.20 (m, 2H), 1.24−1.53 (m, 8H), 0.93 (s, 9H), 0.91 (t, J = 7.2 Hz, 3H), 0.15 (s, 3H), 0.14 (s, 3H); ^{13}C NMR δ 131.4, 128.0, 127.5, 123.8, 87.4, 82.4, 82.0, 76.6, 70.7, 31.5, 29.0, 28.7, 27.9, 27.6, 25.9, 22.9, 18.9, 18.2, 14.2, −4.45, −4.50; IR (neat) 3081, 2929, 1490, 1472, 1362, 1255, 1103, 937, 837, 777, 755, 691 cm^{-1}; $[\alpha]^{28}_D$ −5.16 (*c* 2.52, CHCl$_3$). Anal. Calcd for $C_{25}H_{38}OSi$: C, 78.47; H, 10.01. Found: C, 78.68; H, 9.70.

(*S*)-2-(2-Nonynyl)oxirane ((*S*)-4b, Scheme 3). (*S*)-**4b** (1.38 g, 83%) was obtained starting from (*S*)-**3** (0.782 mL, 10.0 mmol), 1-octyne (2.95 mL, 20.0 mmol), *n*-BuLi (12.6 mL, 1.58 M in hexane, 20.0 mmol), boron trifluoride etherate (2.53 mL, 20.0 mmol), and NaOH (0.800 g, 20.0 mmol) under similar reaction conditions as described for the synthesis of (*S*)-**4a**. ^{1}H NMR δ 3.00−3.06 (m, 1H), 2.73 (dd, J = 3.9, 4.8 Hz, 1H), 2.61 (dd, J = 2.4, 4.8 Hz, 1H), 2.55 (ddt, J = 2.4, 4.5, 17.8 Hz, 1H), 2.39 (ddt, J = 2.4, 5.1, 17.8 Hz, 1H), 2.11 (tt, J = 2.4, 7.2 Hz, 2H), 1.16−1.50 (m, 8H), 0.85 (t, J = 6.9 Hz, 3H); ^{13}C NMR δ 82.7, 73.9, 50.2, 46.3, 31.3, 28.8, 28.5, 22.6, 22.5, 18.7, 14.0; IR (neat) 2930, 2858, 1466, 965, 844 cm^{-1}; $[\alpha]^{29}_D$ +20.6 (*c* 4.88, CHCl$_3$).

(*S*)-4-[(*tert*-Butyl)dimethylsiloxy]-1-phenyl-1,6-tridecadiyne ((*S*)-2d, Scheme 3). (*S*)-**2d** (0.941 g, 82%) was obtained starting from (*S*)-**4b** (0.498 g, 3.00 mmol), ethynylbenzene (0.659 mL, 6.00 mmol), *n*-BuLi (3.79 mL, 1.58 M in hexane, 6.00 mmol), boron trifluoride etherate (0.760 mL, 6.00 mmol), imidazole (0.408 g, 6.00 mmol), and TBSCl (0.543 g, 3.60 mmol) under similar reaction conditions as described for the synthesis of (*R*)-**2d**. The spectral data (^{1}H NMR, ^{13}C NMR, IR) have been described. $[\alpha]^{28}_D$ +5.24 (*c* 2.52, CHCl$_3$).

(*S*)-2-(3-Trimethylsilyl-2-propynyl)oxirane ((*S*)-4c, Scheme 4). (*S*)-**4c** was prepared according to the literature.[5,12] To a stirred solution of ethynyltrimethylsilane (65.7 mL, 465 mmol) in hexane (150 mL) was slowly added *n*-BuLi (296 mL, 1.57 M in hexane, 465 mmol) at 0 °C under argon and the mixture was stirred for 30 min. To the mixture was added Et_2AlCl (500 mL, 0.93 M in hexane, 465 mmol) at 0 °C and the mixture was stirred for 30 min. To this mixture was added freshly distilled (*S*)-**3** (30.3 mL, 387 mmol) at 0 °C and the mixture was stirring for 1.5 h. After addition of 1N HCl (500 mL) at 0 °C, the mixture was extracted with Et_2O (3 × 400 mL). The combined organic layers were dried over $MgSO_4$, concentrated, passed through a short silica gel column with 20% ether in hexane, and then concentrated to provide a crude oil.

To a solution of the crude oil in CH_2Cl_2 (500 mL) was slowly added NaOH (31 g, 775 mmol) at room temperature. The mixture was stirred for 2 days. After addition of saturated aqueous NH_4Cl (500 mL), the mixture was extracted with CH_2Cl_2 (3 × 300 mL). The combined organic layers were dried over $MgSO_4$ and concentrated and the distillation of this crude (70−72 °C, 12 mmHg) gave (*S*)-**4c** (48.7 g, 82%) as a colorless oil. ^{1}H NMR δ 3.05−3.11 (m, 1H), 2.77 (dd, J = 3.9, 5.1 Hz, 1H), 2.65 (dd, J = 4.5, 17.4 Hz, 1H), 2.64 (dd, J = 2.4, 5.1 Hz, 1H), 2.47 (dd, J = 5.4, 17.4 Hz, 1H), 0.13 (s, 9H); ^{13}C NMR δ 100.6, 87.1, 49.8, 46.5, 23.6, 0.07; IR (neat) 2960, 2900, 2179, 1406, 1250, 1027, 952, 839, 760 cm^{-1}; $[\alpha]^{27}_D$ +29.3 (*c* 1.36, $CHCl_3$).

(*R*)-4-[(*tert*-Butyl)dimethylsiloxy]-1-phenyl-7-(trimethylsilyl)-1,6-heptadiyne ((*R*)-2b, Scheme 4). (*R*)-**2b** (7.26 g, 98%) was obtained starting from (*S*)-**4c** (3.08 g, 20.0 mmol), ethynylbenzene (4.39 mL, 40.0 mmol), *n*-BuLi (25.3 mL, 1.58 M in hexane, 40.0 mmol), boron trifluoride etherate (5.07 mL, 40.0 mmol), imidazole (2.72 g, 40.0 mmol), and TBSCl (3.62 g, 24.0 mmol) under similar reaction conditions as described for the synthesis of (*R*)-**2d**. ^{1}H NMR δ 7.26−7.43 (m, 5H), 3.98−4.10 (m, 1H), 2.56−2.74 (m, 3H), 2.48 (dd, J = 6.6, 17.1 Hz, 1H), 0.93 (s, 9H), 0.17 (s, 9H), 0.15 (s, 6H); ^{13}C NMR δ 131.4, 128.1, 127.6, 123.6, 104.0, 86.9, 86.4, 82.3, 70.3, 28.7, 28.2, 25.9, 18.2, 0.2, −4.40, −4.41; IR (neat) 3057, 2957, 2178, 1491, 1472, 1250, 1107, 1036, 934, 842, 755 cm^{-1}; $[\alpha]^{27}_D$ +8.32 (*c* 1.36, $CHCl_3$); Anal. Calcd for $C_{22}H_{34}OSi_2$: C, 71.28; H, 9.25. Found: C, 71.61; H, 9.51.

(*S*)-4-Phenyl-2-indanol ((*S*)-5, Scheme 4). To a stirred solution of (*R*)-**1b** (73.7 mg, 0.186 mmol) in CH_3CN (2.80 mL) and H_2O (0.0100 mL) were added potassium iodide (92.6 mg, 0.558 mmol) and trimethylsilyl chloride (0.0710 mL, 0.560 mmol) in one portion at room temperature. After 12 h of stirring, saturated aqueous $NaHCO_3$ (4 mL) was added to the mixture. The mixture was extracted with Et_2O (3 × 4 mL). The combined organic layers were dried over $MgSO_4$, concentrated, and chromatographed on silica gel (hexanes−Et_2O) to give (*S*)-**5** (37.1 mg, 94%) as a white solid. The enantiomeric ratio was determined to be >99:<1 by HPLC analysis [CHIRALCEL OD-H column (silica gel, 0.46 ϕ × 15.25 cm), *i*-PrOH/hexane (1/20 (v/v)) at the rate of 1.5 mL/min: retention time = 8.71 min for (*S*)-**5** and 18.31 min for (*R*)-**5**].[9] ^{1}H NMR δ 7.21−7.45 (m, 8H), 4.63−4.70 (m, 1H), 3.30 (dd, J = 2.1, 6.0 Hz, 1H), 3.25 (dd, J = 1.5, 6.0 Hz, 1H), 3.00 (dd, J = 3.0, 3.0 Hz, 1H), 2.95 (dd, J = 3.0, 3.0 Hz, 1H), 1.69 (br s, 1H); ^{13}C NMR δ 141.6, 141.0, 139.0, 138.6, 128.6, 128.4, 127.3, 127.2, 127.1, 124.1, 73.0, 42.7, 42.5; IR (Nujol) 3370, 3057, 2941, 1591, 1467, 1424, 1339, 1207, 1033, 943, 789, 754, 704 cm^{-1}; mp 101−103 °C; $[\alpha]^{27}_D$ +21.7 (*c* 1.92, $CHCl_3$).

Compound 7 (Scheme 5). 7 (0.667 g, 96%) was obtained starting from (*S*)-**4a** (0.237 g, 1.50 mmol), 3-butyl-4-methoxyethynylbenzene[9] (0.564 g, 3.00 mmol), *n*-BuLi (1.92 mL, 1.56 M in hexane, 3.00 mmol), and boron trifluoride etherate (0.380 mL, 3.00 mmol) under similar reaction conditions as described for the synthesis of (*R*)-**2d**. ^{1}H NMR δ 7.40−7.45 (m, 2H), 7.21−7.33 (m, 5H), 6.75 (d, J = 8.4 Hz, 1H), 4.09−4.18 (m, 1H), 3.82 (s, 3H), 2.82 (dd, J = 6.0, 12.9 Hz, 1H), 2.77 (dd, J = 6.0, 12.9 Hz, 1H), 2.70 (dd, J = 4.8, 6.0 Hz, 1H), 2.65 (dd, J = 4.5, 6.0 Hz, 1H), 2.58 (t, J = 7.5 Hz, 2H), 1.51−1.62 (m, 2H), 1.30−1.44 (m, 2H), 0.96 (s, 9H), 0.96 (t, J = 3.6 Hz, 3H), 0.18 (s, 6H); ^{13}C NMR δ 157.3, 133.1, 131.6, 131.3, 130.4, 128.2, 127.7, 123.9, 115.4, 110.0, 87.2, 84.8, 82.5, 82.3, 70.6, 55.2, 31.7, 29.5, 28.1, 28.0, 25.7, 22.4, 18.0, 13.9, −4.7; IR (neat) 3080, 3055, 2928, 1498, 1464, 1362, 1240, 1105, 1037, 937, 837, 777, 755, 691 cm^{-1}; $[\alpha]^{26}_D$ −0.86 (*c* 0.89, $CHCl_3$); Anal. Calcd for $C_{30}H_{40}O_2Si$: C, 78.21; H, 8.75. Found: C, 78.23; H, 8.58.

Acknowledgment. T.H. would like to thank the Japan Society for the Promotion of Science for financial support. Y.T. would like to thank the Grant of the 21st Century COE Program, Ministry of Education, Culture, Sports, Science and Technology for financial support.

Supporting Information Available: Spectral data for **1a**,**c**,**e**,**f** and **2a**,**c**,**e**,**f**, and the HPLC data for (*S*)-**5**, (*R*)-**5**, and *rac*-**5**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO034391M

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