# Asymmetric Dihydroxylation of a *Meso*-Symmetric Cyclic Diene Using AD-Mix Reagents: A New Enantiocontrolled Route to Conduritol E

Seiichi Takano,* Takehiko Yoshimitsu, and Kunio Ogasawara

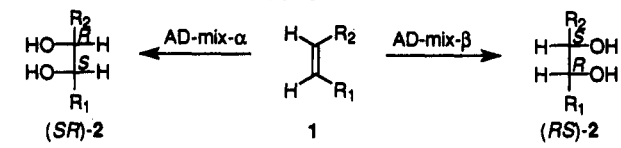
*Pharmaceutical Institute, Tohoku University, Aobayama, Sendai 980, Japan*

*Received September 13, 1993*•

The asymmetric dihydroxylation of two symmetric cyclohexa-1,3-diene derivatives, including a *meso*-symmetric substrate, has been investigated for the first time using the Sharpless AD-mix reagents. Although cyclohexa-1,3-diene itself showed unsatisfactory enantioselectivity, *meso*-symmetric 1,2-*O*-benzylidene-*cis*-cyclohexa-3,5-diene-1,2-diol showed a practical level of enantioselectivity and furnished the optically active diol in good yield. The diol obtained could be transformed into optically pure (+)-conduritol E in good yield, after a single recrystallization. The stereochemical outcome of the dihydroxylation was in harmony with the observations so far reported.

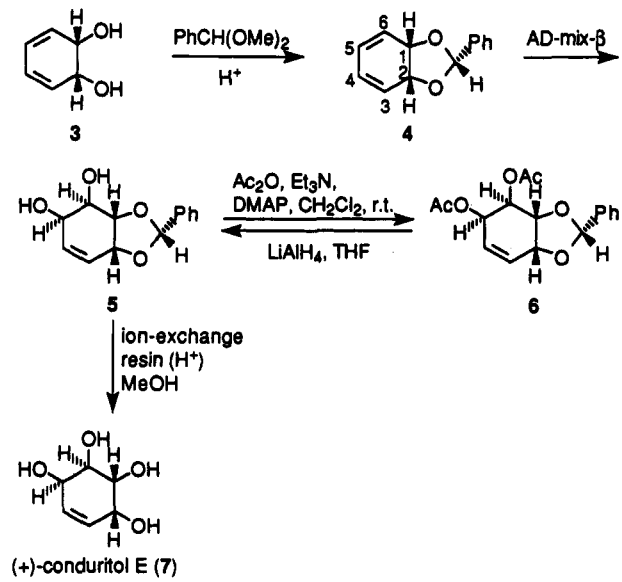
The Sharpless AD-mix reagents offer high levels of enantioselectivity and practicality in introducing chiral 1,2-glycol functionality into olefinic substrates.[1] Although limited examples of *cis*-olefinic compounds have been reported,[2,3] the enantiofacial selectivity of the AD-mix reagents (1) may be expressed as shown in Scheme 1 by using a Fischer projection wherein $R_1$ is the directing group if $R_1$ is larger than $R_2$ or is a polar group such as aryl, alkenyl, ester, or amide. Alkoxy and silyloxy functionalities are found to be weaker directors.[3] Since we were interested in knowing the directing effect of the functional groups in *meso*-symmetric substrates, as well as the stereochemical outcome of the reaction in *meso*-symmetric substrates, we investigated asymmetric dihydroxylation of two cyclohexa-1,3-diene substrates, **3** and **8**, having symmetric structures, one of which led to a new enantiocontrolled synthesis of optically pure conduritol E[4,5] (**7**).

**Scheme 1**




$R_1 > R_2$ ($R_1$, $R_2$=alkyl, alkenyl, aryl, $CO_2R'$, CONR'R", CONR'(OR"), $R_2$=H, OMe, OTBS)

**Scheme 2**




## Results and Discussion

We first investigated the dihydroxylation of *meso*-1,2-*O*-benzylidene-*cis*-cyclohexa-3,5-diene-1,2-diol (**4**) using AD-mix-$\alpha$ and AD-mix-$\beta$ reagents (Scheme 2, Table 1). Reaction of *meso*-symmetric *cis*-cyclohexa-3,5-diene-1,2-diol[4b] (**3**) with benzaldehyde dimethyl acetal in dichloromethane in the presence of pyridinium *p*-toluenesulfonate[6] (PPTS) proceeded at room temperature to give the *meso*-acetal **4** in 72% yield as a single isomer. The stereochemistry of **4** was determined to be the all-*cis*-1,3-dioxolane structure by an NOE experiment that showed significant interaction between the benzylidene proton and both of the allylic protons. Under standard conditions[1a] in the presence of an equimolar amount of AD-mix reagent, asymmetric dihydroxylation of **4** occurred in a diastereoselective manner from the less-hindered face of the molecule to give the dihydroxylation product **5** in more than 85% ee when either AD-mix-$\alpha$ or AD-mix-$\beta$ was used. Although no significant improvement in the asymmetric induction was observed, the reaction was apparently accelerated by the addition of methanesulfonamide.[1a] It was interesting to note that neither diastereomeric diol nor double dihydroxylation product formed under the conditions employed. Since direct isolation of the dihydroxylation product **5** was found to be difficult due to persistent contamination of a minor

• Abstract published in *Advance ACS Abstracts*, December 1, 1993.

(1) (a) Sharpless, K. B.; Bennani, Y. L.; Crispino, G. A.; Hartung, J.; Jeong, K.-S.; Kwong, H.-L.; Morikawa, K.; Wang, Z.-M.; Xu, D.; Zhang, X.-L. *J. Org. Chem.* **1992**, *57*, 2768 and refs cited therein. (b) Amberg, W.; Bennani, Y. L.; Chadha, R. K.; Crispino, G. A.; Davis, W. B.; Hartung, J.; Jeong, K.-S.; Ogino, Y.; Shibata, T.; Sharpless, K. B. *J. Org. Chem.* **1993**, *58*, 844 and refs cited therein.

(2) (a) Wang, L.; Sharpless, K. B. *J. Am. Chem. Soc.* **1992**, *114*, 7568. (b) Xu, D.; Crispino, G. A.; Sharpless, K. B. *J. Am. Chem. Soc.* **1992**, *114*, 7570. (c) Jeong, K.-S.; Sjö, P.; Sharpless, K. B. *Tetrahedron Lett.* **1992**, *33*, 3833. (d) Ko, S. Y.; Malik, M. *Tetrahedron Lett.* **1993**, *34*, 4675.

(3) Hashiyama, T.; Morikawa, K.; Sharpless, K. B. *J. Org. Chem.* **1992**, *57*, 5067.

(4) Reviews: (a) Balci, M.; Sutbeyaz, Y.; Secen, H. *Tetrahedron* **1990**, *46*, 3715. (b) Carless, H. A. J. *Tetrahedron: Asymmetry* **1992**, *3*, 795.

(5) Chiral synthesis: Hudlicky, T.; Price, J. D.; Olivo, H. *Synlett* **1991**, 645.

(6) Miyashita, M.; Yoshikoshi, A.; Grieco, P. A. *J. Org. Chem.* **1977**, *42*, 3772.

0022-3263/94/1959-0054$04.50/0 

**Table 1. Dihydroxylation of the *Meso*-Diene 4 with AD-Mix Reagents[a]**

| | | 6 | | | 5 | | |
|---|---|---|---|---|---|---|---|
| entry | conditions | yield[b] (%) | $[\alpha]^{30}_D$ ($CHCl_3$) | (% ee)[c] | yield[d] (%) | $[\alpha]^{30}_D$ ($CHCl_3$) | (% ee)[c] |
| 1 | AD-mix-$\alpha$ $MeSO_2NH$ (1 equiv) 0 °C, 38 h | 81[e] | −256° (*c* 1.32) | ~87 | 86 | −206° (*c* 0.39) mp 83–85 °C | >99 |
| 2 | AD-mix-$\beta$ no additive 0 °C, 137 h | 67[f] | +258° (*c* 1.08) | ~84 | | | |
| 3 | AD-mix-$\beta$ $MeSO_2NH_2$ (1 equiv) 0 °C, 60 h | 85[g] | +258° (*c* 1.56) | ~85 | 71 | +207° (*c* 0.57) mp 83–85 °C | >99 |

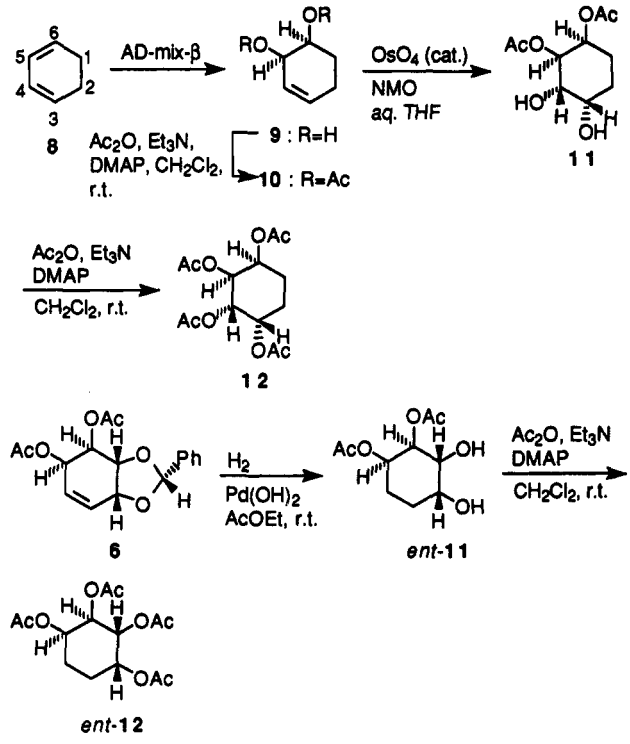
[a] AD-mix reagents were purchased from Aldrich and used without further purification. [b] Isolated yield after diacetylation. [c] Determined by HPLC using a chiral column (Chiralcel OD elution with 10% v/v 2-propanol–hexane). [d] Purified yield after recrystallization from $CCl_4$–$CH_2Cl_2$. [e] Unreacted starting material was recovered in 10% yield. [f] Unreacted starting material was recovered in 25% yield. [g] Unreacted starting material was recovered in 14% yield.

amount of impurities, the product was isolated after conversion to the diacetate **6**. Optically pure diol **5** could be obtained from **6** by reductive deacylation by lithium aluminum hydride, followed by a single recrystallization of the resulting optically enriched **5**. Overall yield of optically pure **5** from **4** *via* **6** was 55–65%.

In order to determine its absolute structure, the optically pure diol (+)-**5**, obtained by the reaction of **4** with AD-mix-$\beta$, was treated with methanol in the presence of ion-exchange resin ($H^+$ form) to remove the benzylidene group and yield optically pure (+)-conduritol E (**7**), mp 192–194 °C, $[\alpha]^{30}_D$ +327° (*c* 0.22, $H_2O$). Its physical and spectral data were identical with those reported for (+)-conduritol E [mp 192–193 °C, $[\alpha]^{20}_D$ +330° (*c* 4.5, $H_2O$)[5,7] ]. This indicated that the dihydroxylation occurred selectively at the 5,6-double bond of **4** from the less-hindered $\beta$-face to give the *anti-cis*-diol **5**. This also represents a new enantiocontrolled entry into both enantiomers of a cyclitol, conduritol E (**7**).[4,5] The observed stereochemical outcome may be explainable if the 3,4-double bond has a stronger directing effect in the dihydroxylation reaction than the 1-alkyloxy-substituted functionality, this being consistent with the empirical observations so far reported for *cis*-olefinic substrates.[2,3]

Having established the stereochemistry of the dihydroxylation of the *meso*-diene **4**, we next examined the same asymmetric dihydroxylation of 1,2-dihydrobenzene (**8**) using AD-mix-$\beta$ to confirm the empirical rule. We anticipated that selective dihydroxylation would occur at the 5,6-double bond from the $\beta$-face to afford the optically active diol **9** if the 3,4-olefinic functionality exerts stronger directing effect than the 1-methylene functionality. The diene **8** was treated with an equimolar amount of AD-mix-$\beta$ under standard conditions. The reaction terminated at the monodihydroxylation stage to give rise to the optically active diol **9** in 72% yield. Although its optical purity estimated by the Mosher method[8] (500-MHz $^1H$ NMR) was found to be disappointingly low (~33% ee), the stereochemical outcome was in harmony with that anticipated (Scheme 3). Namely, the diol **9** obtained was first transformed into the (+)-diacetate **10** which then was dihydroxylated diastereoselectively by osmate reagent from the less hindered face to give (−)-diacetoxydihydroconduritol E (**11**), $[\alpha]^{30}_D$ −29.4° (*c* 0.82, $CHCl_3$). This compound as well as its peracetate (**12**), $[\alpha]^{28}_D$ −25.5° (*c* 0.93, $CHCl_3$), were identical in all respects except for their

**Scheme 3**




signs of optical rotation with those of the products, *ent*-**11**, $[\alpha]^{30}_D$ +55.4° (*c* 1.09, $CHCl_3$) and *ent*-**12**, $[\alpha]^{30}_D$ +50.2° (*c* 1.13, $CHCl_3$), generated from the aforementioned (+)-diacetate **6** by concomitant hydrogenation–hydrogenolysis followed by acetylation of the resulting (+)-diol (*ent*-**11**). This clarified that the dihydroxylation of **8** occurred at the 5,6-double bond preferentially from the $\beta$-face by virtue of the stronger directing effect of the 3,4-double bond relative to the 1-methylene functionality.

In conclusion, we have demonstrated the first instance of asymmetrization of a *meso*-symmetric cyclic diene having *cis*-olefin configuration with a practical level of enantioselectivity, accomplished in a predictable manner by the enantioselective discrimination between two *cis*-diene double bonds in the molecule, using AD-mix reagents. This led to a simple, enantiocontrolled synthesis of both enantiomers of conduritol E (**7**) from a readily available common cyclic diene (**3**). Further studies on the application of the present strategy to the asymmetrization of acyclic *meso*-substrates are in progress.

## Experimental Section

Melting points are uncorrected. IR spectral were recorded on a JASCO-IR-700 spectrometer. $^1H$ NMR spectra were recorded

(7) Abraham, R. J.; Gottschalk, H.; Thomas, W. A. *J. Chem. Soc.* **1965**, 6268.
(8) Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512.

on Hitachi R-3000 (300 MHz) and JEOL-JNM-GX500 (500 MHz) spectrometers. Mass spectra were measured on a JEOL JMS-DX303 instrument. Optical rotations were measured with a JASCO-DIP-370 digital polarimeter. Optical purities were determined on a Gilson Model-307 instrument equipped with a chiral column.

***meso-cis-O*-Benzylidene-1,2-dihydroxy-3,5-cyclohexadiene (4).** A mixture of *cis*-1,2-dihydroxy-3,5-cyclohexadiene (3) (247 mg, 2.21 mmol), benzaldehyde dimethyl acetal (1.0 mL, 6.63 mmol), and pyridinium *p*-toluenesulfonate (55 mg, 0.22 mmol) in $CH_2Cl_2$ (10 mL) was stirred at room temperature for 18 h. The mixture was washed with 5% aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, evaporated under reduced pressure, and chromatographed on a silica gel column (30 g, elution with 1:8 v/v $Et_2O$–hexane) to give the acetal 4 (317 mg, 72%) as a colorless oil: IR (neat) $\nu$ 3044, 2882, 1457, 1401 $cm^{-1}$; $^1H$-NMR (500 MHz) ($CDCl_3$) $\delta$ 7.52–7.45 (m, 2H), 7.38–7.31 (m, 3H), 6.08–6.05 (m, 2H), 6.02–5.96 (m, 2H), 5.67 (s, 1H), 4.69 (dd, 2H, $J$ = 1.83, 1.83 Hz); $^{13}C$-NMR (75 MHz) ($CDCl_3$) $\delta$ 136.7, 129.5, 128.3, 127.0, 124.3, 124.0, 98.3, 71.1; MS $m/z$ 200 ($M^+$), 105 (100%); HRMS calcd for $C_{13}H_{12}O_2$ 200.0837, found 200.0872.

**Reaction of 4 with AD-mix Reagents.** (a) Reaction of 4 with AD-mix-$\alpha$ (with additive). A mixture of 4 (261 mg, 1.31 mmol), AD-mix-$\alpha$ (1.8 g), and $MeSO_2NH_2$ (125 mg, 1.31 mmol) in 50% aqueous *tert*-BuOH (13.2 mL) was stirred at 0 °C for 38 h. To the mixture was added $Na_2SO_3$ (1.97 g) and KOH (720 mg) and the stirring was continued for 1 h at room temperature. The mixture was diluted with AcOEt and the organic layer was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure to leave the crude diol 5 (383 mg) as a colorless oil. This was then stirred with $Ac_2O$ (0.37 mL, 3.93 mmol), $Et_3N$ (0.64 mL, 4.59 mmol), and 4-(*N*,*N*-dimethylamino)pyridine (DMAP) (16 mg, 0.13 mmol) in $CH_2Cl_2$ (10 mL) at room temperature for 10 min. The mixture was washed with brine, dried over $MgSO_4$, evaporated under reduced pressure, and chromatographed on a silica gel column (20 g, elution with 1:2 v/v $Et_2O$–hexane) to give the unreacted 4 (25 mg, 10%) and (1*R*,2*R*,3*R*,4*R*)-3,4-*O*-diacetyl-1,2-*O*-benzylideneconduritol E (6) (336 mg, 81%) as a colorless oil: $[\alpha]^{30}_D$ −256° (*c* 1.32, $CHCl_3$) (87% ee by HPLC using a chiral column, Chiralcel OD, elution with 1:9 v/v *i*-PrOH–hexane); IR (neat) $\nu$ 1745 $cm^{-1}$; $^1H$ NMR (500 MHz) ($CDCl_3$) $\delta$ 7.47–7.45 (m, 2H), 7.39-7.36 (m, 3H), 6.17 (dd, 1H, $J$ = 9.76, 3.66 Hz), 6.03 (ddd, 1H, $J$ = 9.77, 5.49, 1.22 Hz), 5.90 (s, 1H), 5.55 (dd, 1H, $J$ = 5.49, 3.66 Hz), 5.27 (dd, 1H, $J$ = 8.54, 3.66 Hz), 4.81 (ddd, 1H, $J$ = 9.16, 3.67, 1.22 Hz), 4.57 (dd, 1H, $J$ = 8.55, 6.71 Hz), 2.09 (s, 3H), 2.08 (s, 3H); MS $m/z$ 319 ($M^+$ + 1), 318 ($M^+$), 43 (100%). Anal. Calcd for $C_{17}H_{18}O_6$: C, 64.14; H, 5.70. Found: C, 64.27; H, 5.60.

(b) Reactiom of 4 with AD-mix-$\beta$ (without additive). A mixture of 4 (70.3 mg, 0.352 mmol) and AD-mix-$\beta$ (492 mg) in 50% aqueous *tert*-BuOH (3.6 mL) was stirred at 0 °C for 137 h. To the mixture was added $Na_2SO_3$ (530 mg) and the stirring was continued for 1 h at room temperature. The mixture was diluted with AcOEt and the organic layer was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure to leave the crude diol 5 (75 mg) as a colorless oil. This was then stirred with $Ac_2O$ (0.2 mL, 2.08 mmol), $Et_3N$ (0.27 mL, 1.93 mmol), and DMAP (4 mg, 0.03 mmol) in $CH_2Cl_2$ (4 mL) at room temperature for 30 min. The mixture was diluted with $Et_2O$, washed with brine, dried over $MgSO_4$, evaporated under reduced pressure, and chromatographed on a silica gel column (10 g, elution with 1:3 v/v $Et_2O$–hexane) to give the unreacted 4 (18.4 mg, 25%) and (1*S*,2*S*,3*S*,4*S*)-3,4-*O*-diacetyl-1,2-*O*-benzylideneconduritol E (6) (69.0 mg, 67%) as a colorless oil: $[\alpha]^{28}_D$ +258° (*c* 1.08, $CHCl_3$) (84% ee by HPLC using a chiral column, Chiralcel OD, elution with 1:9 v/v *i*-PrOH–hexane). Spectral data were identical all respects with those of the enantiomer above.

(c) Reaction of 4 with AD-mix-$\beta$ (with additive). A mixture of 4 (311 mg, 1.56 mmol), AD-mix-$\beta$ (2.18 g), and $MeSO_2NH_2$ (148 mg, 1.56 mmol) in 50% aqueous *tert*-BuOH (16 mL) was stirred at 0 °C for 60 h. To the mixture was added $Na_2SO_3$ (2.4 g) and KOH (880 mg) and the stirring was continued for 30 min at room temperature. The mixture was diluted with AcOEt and the organic layer was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure to leave the crude diol 5 (470 mg) as a colorless oil. This was then stirred with $Ac_2O$ (0.44 mL, 4.68 mmol), $Et_3N$ (0.72 mL, 5.15 mmol), and DMAP (19.5 mg, 0.16 mmol) in $CH_2Cl_2$ (10 mL) at room temperature for 10 min. The mixture was diluted with $Et_2O$, washed with brine, dried over $MgSO_4$, evaporated under reduced pressure, and chromatographed on a silica gel column (40 g, elution with 1:1 v/v $Et_2O$–hexane) to give the unreacted 4 (45 mg, 14.4%) and (1*R*,2*R*,3*R*,4*R*)-3,4-*O*-diacetyl-1,2-*O*-benzylideneconduritol E (6) (423 mg, 85%) as a colorless oil: $[\alpha]^{30}_D$ +258° (*c* 1.56, $CHCl_3$) (85% ee by HPLC using a chiral column, Chiralcel OD, elution with 1:9 v/v *i*-PrOH–hexane). Spectral data were identical all respects with those of the above samples.

**Reductive Removal of the Diacetyl Groups from 6.** (a) Generation of (1*S*,2*S*,3*S*,4*S*)-1,2-*O*-Benzylideneconduritol E (5). To a stirred solution of (1*S*,2*S*,3*S*,4*S*)-diacetate 6 (the product by AD-mix-$\alpha$) (104 mg, 0.327 mmol) in THF (5 mL) was added $LiAlH_4$ (25 mg, 0.65 mmol) at 0 °C and the stirring was continued for 10 min at room temperature. The reaction was quenched by addition of an appropriate amount of 28% aqueous $NH_4OH$ and the mixture was stirred with a small amount of Celite for 3 h. The mixture was diluted with AcOEt and filtered through a Celite pad. Evaporation of the filtrate left (1*S*,2*S*,3*S*,4*S*)-1,2-*O*-benzylideneconduritol E (5) (70 mg, 91.0%) as colorless crystals which on recrystallization from $CCl_4$–$CH_2Cl_2$ gave optically pure 5 (66 mg, 86%) as colorless fibrous crystals: mp 83–85 °C, $[\alpha]^{30}_D$ −206° (*c* 0.39, $CHCl_3$) (~100% ee by HPLC using a chiral column as above determined after reconversion into 6); IR (KBr) $\nu$ 3420 $cm^{-1}$; $^1H$ NMR (500 MHz) ($CDCl_3$) $\delta$ 7.46–7.45 (m, 2H), 7.39-7.37 (m, 3H), 6.08–5.99 (m, 2H), 5.90 (s, 1H), 4.74 (dd, 1H, $J$ = 6.72, 3.66 Hz), 4.46 (dd, 1H, $J$ = 6.72, 6.71 Hz), 4.31 (d, 1H, $J$ = 3.05 Hz), 4.02 (dd, 1H, $J$ = 6.71, 3.66 Hz), 2.71 (d, 1H, $J$ = 3.05 Hz), 2.54 (d, 1H, $J$ = 4.27 Hz); MS $m/z$ 235 ($M^+$ + 1), 234 ($M^+$); HRMS calcd for $C_{13}H_{14}O_4$ 234.0892, found 234.0860. Anal. Calcd for $C_{13}H_{14}O_4$: C, 66.66; H, 6.02. Found: C, 66.73; H, 5.97.

(b) Generation of (1*R*,2*R*,3*R*,4*R*)-1,2-*O*-Benzylideneconduritol E (5). To a stirred solution of (1*R*,2*R*,3*R*,4*R*)-diacetate (the product by AD-mix-$\beta$) (269 mg, 0.846 mmol) in THF (8 mL) was added $LiAlH_4$ (51 mg, 1.35 mmol) at 0 °C and the stirring was continued for 20 min at 0 °C and for 20 min at room temperature. The reaction was quenched by addition of an appropriate amount of 28% aqueous $NH_4OH$, and the mixture was stirred with a small amount of Celite for 3 h. The mixture was diluted with AcOEt and filtered through a Celite pad. Evaporation of the filtrate left (1*R*,2*R*,3*R*,4*R*)-1,2-*O*-benzylideneconduritol E (5) (165 mg, 83.3%) as colorless crystals which on recrystallization from $CCl_4$–$CH_2Cl_2$ gave optically pure 5 (140 mg, 71%) as colorless fibrous crystals: mp 83–85 °C, $[\alpha]^{30}_D$ +207° (*c* 0.57, $CHCl_3$) (~100% ee by HPLC using a chiral column as above determined after reconversion into 6). Spectral data were identical in all respects with those of the enantiomer.

**Reconversion of Optically Pure Diol 5 into Optically Pure Diacetate 6.** To a stirred solution of the optically pure (1*R*,2*R*,3*R*,4*R*)-5 (19 mg, 0.08 mmol) in $CH_2Cl_2$ (3 mL) were added $Ac_2O$ (0.02 mL, 0.244 mmol), $Et_3N$ (0.037 mL, 0.264 mmol), and DMAP (1 mg, 0.008 mmol) at room temperature and the stirring was continued for 40 min at the same temperature. The mixture was diluted with $Et_2O$, washed with brine, dried over $MgSO_4$, evaporated under reduced pressure, and chromatographed on a silica gel column (8 g, elution with 2:1 v/v $Et_2O$–hexane) to give the optically pure diacetate 6 (24.5 mg, 93.4%) as a colorless oil: $[\alpha]^{27}_D$ +308° (*c* 1.12, $CHCl_3$) (~100% ee by HPLC using a chiral column, Chiralcel OD, elution with 1:9 v/v *i*-PrOH–hexane). Spectral data were identical in all respects with those of the optically enriched material above.

**(1*R*,2*R*,3*R*,4*R*)-Conduritol E (7).** Optically pure (1*R*,2*R*,-3*R*,4*R*)-1,2-*O*-benzylideneconduritol E (5) (60 mg, 0.256 mmol) in MeOH (3 mL) was stirred with Dowex-50W-X8 ($H^+$ form) (6 mg) for 5 h at room temperature. The mixture was filtered through a Celite pad and the filtrate was evaporated under reduced pressure to leave a colorless crystalline mass (36 mg) which on recrystallization from MeOH gave (+)-conduritol E (7) (28 mg, 75%) as colorless pillars: mp 192–194 °C (lit.[5] mp 192–193 °C), $[\alpha]^{30}_D$ +327 (*c* 0.22, $H_2O$) (lit.[5] $[\alpha]^{20}_D$ +330° (*c* 4.5, $H_2O$)); IR (KBr) $\nu$ 3400 $cm^{-1}$; $^1H$ NMR (500 MHz) ($D_2O$) $\delta$ 5.89 (dd, 2H, $J$=2.44, 1.22 Hz), 4.33 (m, 2H), 3.94 (m, 2H); MS $m/z$ 128 ($M^+$ − 18), 86 (100%); HRMS calcd for $C_6H_8O_3$ ($M^+ - H_2O$) 128.0473; found 128.0449.

**(1*R*,2*R*,3*R*,4*R*)-1,2-Di-*O*-acetyldihydroconduritol E (11) [*ent*-11] from 6.** A suspension of the optically enriched (1*R*,2*R*,3*R*,4*R*)-diacetate (6) (85% ee) (140 mg, 0.44 mmol) and $Pd(OH)_2$ (20% on carbon) (14 mg) in AcOEt (5 mL) was stirred under atmosphere of hydrogen (1 atm) at room temperature for 2 h. After removal of the catalyst by filtration, the solvent was evaporated under reduced pressure to leave a colorless oil (100 mg) which was chromatographed on a silica gel column (10 g, elution with 2:1 v/v AcOEt-hexane) to give (+)-diol (11) [*ent*-11] (96.6 mg, 95%) as a colorless oil: $[\alpha]^{30}_D$ +55.4° (*c* 1.09, $CHCl_3$); IR (neat) $\nu$ 3442, 1743 $cm^{-1}$; $^1H$ NMR (500 MHz) ($CDCl_3$) $\delta$ 5.37–5.35 (m, 1H), 5.11–5.08 (dd, 1H, $J$ = 9.76, 3.05 Hz), 4.15 (br s, 1H), 3.95–3.92 (m, 1H), 2.52 (d, 1H, $J$ = 4.88 Hz), 2.37 (br s, 1H), 2.08 (s, 3H), 2.06 (s, 3H), 2.06–1.94 (m, 1H), 1.86–1.78 (m, 2H), 1.76–1.68 (m, 1H); MS *m/z* 233 ($M^+$ + 1), 43 (100%); HRMS calcd for $C_{10}H_{17}O_6$ 233.1025, found 233.1029.

**(1*R*,2*R*,3*R*,4*R*)-1,2,3,4-Tetra-*O*-acetyldihydroconduritol E (12) [*ent*-12].** A mixturte of (+)-diol (11) [*ent*-11] (33.5 mg, 0.144 mmol), $Ac_2O$ (0.04 mL, 0.433 mmol), $Et_3N$ (0.07 mL, 0.477 mmol), and DMAP (1.7 mg, 0.014 mmol) in $CH_2Cl_2$ (3 mL) was stirred at room temperature for 1.5 h. The mixture was diluted with AcOEt and evaporated under reduced pressure to leave a colorless oil which on purification by silica gel column chromatography (10 g, elution with 2:1 v/v $Et_2O$–hexane) afforded the tetraacetate (12) [*ent*-12] (43 mg, 94%) as colorless needles ($Et_2O$): mp 82–84 °C; $[\alpha]^{30}_D$ +50.2° (*c* 1.13, $CHCl_3$); IR (neat) $\nu$ 2966, 1740 $cm^{-1}$; $^1H$ NMR (500 MHz) ($CDCl_3$) $\delta$ 5.40 (br s, 2H), 5.23 (br s, 2H), 2.09 (s, 6H), 2.02 (s, 6H), 1.99–1.77 (m, 4H); MS *m/z* 317 ($M^+$ + 1), 43 (100%); HRMS calcd for $C_{14}H_{21}O_8$ ($M^+$ + H) 317.1237, found 317.1234. Anal. Calcd for $C_{14}H_{20}O_8$: C, 53.15; H, 6.38. Found: C, 53.13; H, 6.34.

**Reaction of Cyclohexa-1,3-diene with AD-mix-$\beta$.** A mixture of cyclohexa-1,3-diene (8) (80 mg, 1 mmol) and AD-mix-$\beta$ (2.8 g) in 50% aqueous *tert*-BuOH (20 mL) was stirred at 0 °C for 35 h. After addition of $Na_2SO_3$ (3.0 g) at 0 °C, the stirring was continued for 1 h. The mixture, after being diluted with AcOEt, was washed with brine, dried over $MgSO_4$, evaporated under reduced pressure, and chromatographed on a silica gel column (15 g, elution with 1:1 v/v AcOEt–hexane) to give the diol 9 (81.8 mg, 72%) as a colorless oil: $[\alpha]^{30}_D$ +62.1° (*c* 0.76, $CHCl_3$) [~33% ee by $^1H$ NMR (500 MHz) analysis of MTPA [(*R*)- and (*S*)-esters]: IR (neat) $\nu$ 3368 $cm^{-1}$; $^1H$ NMR (90 MHz) ($CDCl_3$) $\delta$ 6.00–5.60 (m, 2H), 4.30-4.00 (br s, 1H), 4.00–3.70 (m, 1H), 3.03–2.85 (m, 2H), 2.40–1.65 (m, 4H); MS *m/z* 114 ($M^+$), 70 (100%); HRMS calcd for $C_6H_{10}O_2$ 114.0681, found 114.0657.

***cis*-3,4-Diacetoxycyclohexene (10).** A mixturte of the diol 9 (107 mg, 0.94 mmol), $Ac_2O$ (0.27 mL, 2.82 mmol), $Et_3N$ (0.43 mL, 3.10 mmol), and DMAP (11 mg, 0.09 mmol) in $CH_2Cl_2$ (5 mL) was stirred at room temperature for 20 min. The mixture was diluted with $Et_2O$ and was washed with brine, dried over $MgSO_4$, evaporated under reduced pressure, and chromatographed on a silica gel column (10 g, elution with 1:1 v/v $Et_2O$–hexane) to give the diacetate 10 (167 mg, 90%) as a colorless oil: $[\alpha]^{27}_D$ +74.8° (*c* 1.39, $CHCl_3$); IR (neat) $\nu$ 1743, 1251 $cm^{-1}$; $^1H$ NMR (500 MHz) ($CDCl_3$) $\delta$ 6.01–5.95 (m, 1H), 5.70–5.63 (m, 1H), 5.45 (br s, 1H), 5.12–5.07 (m, 1H), 2.35–2.12 (m, 2H), 2.08 (s, 3H), 2.05 (s, 3H), 2.05–1.93 (m, 1H), 1.84–1.75 (m, 1H); MS *m/z* 199 ($M^+$), 43 (100%); HRMS calcd for $C_8H_{11}O_3$ ($M^+$ – $CH_3CO$) 155.1740, found 155.0747.

**(1*S*,2*S*,3*S*,4*S*)-1,2-Di-*O*-acetyldihydroconduritol E (11).** To a stirred mixture of the diacetate 10 (100 mg, 0.505 mmol) and morpholine 1-oxide (NMO) (89 mg, 0.758 mmol) in 50% aqueous THF (6 mL) was added $OsO_4$ (0.11 M in THF, 0.05 mL, 0.005 mmol) at room temperature and the stirring was continued for 21 h. The reaction was quenched by addition of $Na_2SO_3$ (630 mg) at the same temperature. The mixture was extracted with AcOEt, washed with brine, dried over $MgSO_4$, evaporated under reduced pressure, and chromatographed on a silica gel column (30 g, elution with AcOEt) to give the unreacted 10 (11%) and the diol 11 (41 mg, 35%) as a colorless oil: $[\alpha]^{30}_D$ –29.4° (*c* 0.82, $CHCl_3$). Spectral data were identical in all respects with those of the enantiomeric (+)-11. Moreover, diastereomeric diol, presumed to be an acyl-migrated product, was obtained in 43 mg (36%) as colorless crystals which afforded the same tetraacetate 12 on acetylation.

**(1*S*,2*S*,3*S*,4*S*)-1,2,3,4-Tetra-O-acetyldihydroconduritol E (12).** A mixture of the (–)-diol (11) (16 mg), $Ac_2O$ (0.02 mL, 0.21 mmol), $Et_3N$ (0.03 mL, 0.23 mmol), and DMAP (1 mg, 0.01 mmol) in $CH_2Cl_2$ (3 mL) was stirred at room temperature for 40 min. The mixture was evaporated under reduced pressure and the residue was chromatographed on a silica gel column (6 g, elution with 1:1 v/v $Et_2O$–hexane) to give the (–)-tetraacetate 12 (18.5 mg, 84%) as colorless needles ($Et_2O$): mp 82–84 °C; $[\alpha]^{28}_D$ –25.5° (*c* 0.93, $CHCl_3$). Spectral data were identical in all respects with those of the enantiomer above.

**Acknowledgment.** We thank Mr. K. Kawamura, Miss M. Inada, and Mrs. A. Sato of this Institute for spectral measurement and microanalyses.

**Supplementary Material Available:** Copies of $^1H$ NMR spectra of all new compounds and HPLC traces of racemic and optically active acetates (11 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.