Selective Allylation of Two Aldehydes with Allyltrifluorosilane/Catechol/Triethylamine Systems. To a CH_2Cl_2 (4 mL) solution of catechol (220 mg, 2.0 mmol) and triethylamine (405 mg, 4.0 mmol) was added an allyltrifluorosilane (2.0 mmol) at 0 °C, and then the mixture was stirred for 30 min. After addition of a mixture of a linear (1.0 mmol) and an α-branched alkanal (1.0 mmol), the solution was stirred for 20 h at ambient temperature. The reaction was quenched by 1 M HCl, and the organic layer was washed with 1 M NaOH. The yields of homoallyl alcohols and recovered aldehydes were determined by GLC.

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Enantiocontrolled Synthesis of Quaternary Carbon Centers via Anionic Oxy-Cope Rearrangement: An Efficient Synthesis of (+)-Dihydromayurone

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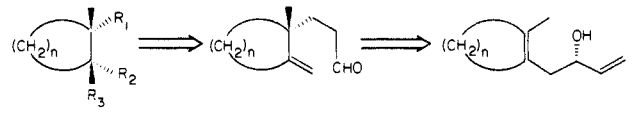
Abstract: (+)-Dihydromayurone (**1**) was enantioselectively synthesized from β-cyclocitral (**7**). The key step in the synthesis involved anionic oxy-Cope rearrangement of allylic alcohol **6** to aldehyde **5**. Efficient transfer of chirality from the secondary allylic alcohol center to the quaternary carbon center was observed via chairlike transition state with the equatorial oxyanionic bond.

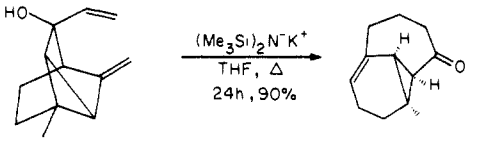
Creation of asymmetric quaternary carbon centers is one of the most important problems for the enantioselective syntheses of natural products such as steroids, terpenoids, and alkaloids. A number of methods have been reported recently[1] for the highly enantioselective construction of quaternary carbon centers in various molecular frames.

Our own interest in the subject led us to consider the possibility of constructing a chiral quaternary carbon center via chirality transfer from a secondary carbinol center using anionic oxy-Cope rearrangement[2] (Scheme I). Optically active allylic alcohols are accessible by a number of standard procedures, for example, asymmetric vinyl or acetylenic addition to aldehydes,[3] asymmetric reduction of corresponding ketones,[4] or allylic transposition of primary allylic alcohols using Sharpless asymmetric epoxidation reaction as the crucial step.[5]

Scheme I



Scheme II



For the transfer of chirality in the types of reactions represented in Scheme I, the relative equatorial/axial preference of the oxyanionic bond ($C-O^-$) is of paramount importance. Inasmuch as the anionic oxy-Cope rearrangement was used frequently in syntheses of complex natural products,[6] we were surprised to realize that this fundamental facet of the reaction had not yet been addressed properly in the literature. The situation is quite different from the case of Claisen rearrangement,[6] which was exhaustively studied in the context of specific chirality transfers in many natural product syntheses.

In many recent cases, anionic oxy-Cope rearrangement is forced to proceed through bridged tricyclic transition states. For example, the crucial step in Paquette's synthesis of cerorubenic acid III ring system involves anionic oxy-Cope rearrangement with a rigid, predetermined transition state[7] (Scheme II).

In more flexible systems, chairlike transition states are generally favored, which then coax the oxyanionic bond to assume either

(1) For some leading references on the construction of chiral quaternary carbon centers, see: (a) Tomioka, K.; Seo, W.; Ando, K.; Koga, K. *Tetrahedron Lett.* **1987**, *28*, 6637-6640. (b) Stork, G.; Saccomano, N. A. *Tetrahedron Lett.* **1987**, *28*, 2087-2090. (c) Greene, A. E.; Charbonnier, F.; Luch, M. J.; Moyano, A. *J. Am. Chem. Soc.* **1987**, *109*, 4752-4753. (d) Hiroi, K.; Nakamura, H.; Anzai, T. *J. Am. Chem. Soc.* **1987**, *109*, 1249-1250. (e) Fuji, K.; Node, M.; Nagasawa, H.; Naniwa, Y.; Terada, S. *J. Am. Chem. Soc.* **1986**, *108*, 3855-3856. (f) Hanamoto, T.; Katsuki, T.; Yamaguchi, M. *Tetrahedron Lett.* **1986**, *27*, 2463-2464. (g) Hua, D. H.; Sinai-Zingde, G.; Venkataraman, S. *J. Am. Chem. Soc.* **1985**, *107*, 4088-4090. (h) Pfau, M.; Revial, G.; Guingant, A.; d'Angelo, J. *J. Am. Chem. Soc.* **1985**, *107*, 273-274. (i) Posner, G. H.; Kogan, T. P.; Hulce, M. *Tetrahedron Lett.* **1984**, *25*, 383-386. (j) Johnson, W. S.; Elliott, J. D.; Hanson, G. J. *J. Am. Chem. Soc.* **1984**, *106*, 1138-1139. (k) Meyers, A. I.; Harre, M.; Garland, R. *J. Am. Chem. Soc.* **1984**, *106*, 1146-1148. (l) Yamamoto, K.; Iijima, M.; Ogimura, Y.; Tsuji, J. *Tetrahedron Lett.* **1984**, *25*, 2813-2816. (m) Tomioka, K.; Masumi, F.; Yamashita, T.; Koga, K. *Tetrahedron Lett.* **1984**, *25*, 333-336. (n) Trost, B. M.; Curran, D. P. *Tetrahedron Lett.* **1981**, *22*, 4929-4932. (o) Shimizu, I.; Naito, V.; Tsuji, J. *Tetrahedron Lett.* **1980**, *21*, 487-490. (p) For earlier examples, see: Martin, S. F. *Tetrahedron* **1980**, *36*, 419.

(2) (a) Evans, D. A.; Golob, A. M. *J. Am. Chem. Soc.* **1975**, *97*, 4765-4766. (b) Evans, D. A.; Baillargeon, D. J.; Nelson, J. V. *J. Am. Chem. Soc.* **1978**, *100*, 2242-2244.

(3) For a review on the asymmetric addition to aldehydes and ketones, see: Solladie, G. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1983; Vol. 2, pp 157-199.

(4) For a review on the reduction with chiral boron reagents, see: Midland, M. M. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1983; Vol. 2, pp 45-69.

(5) (a) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974-5976. (b) Finn, M. G.; Sharpless, K. B. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1985; Vol. 5, pp 247-308.

(6) (a) Desimoni, G.; Tacconi, G.; Barco, A.; Pollini, G. P. *Natural Product Synthesis Through Pericyclic Reactions*; ACS Monograph Series 180; American Chemical Society: Washington, DC, 1983; pp 267-338. (b) Hill, R. K. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1984; Vol. 3, pp 503-572.

(7) Paquette, L. A.; Poupart, M. A. *Tetrahedron Lett.* **1988**, *29*, 273-276.

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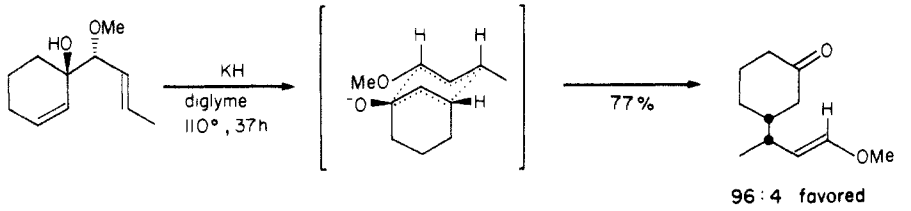
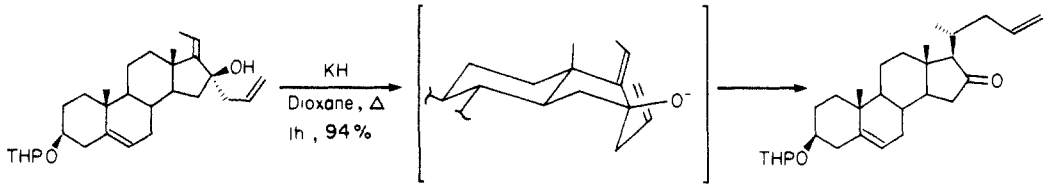
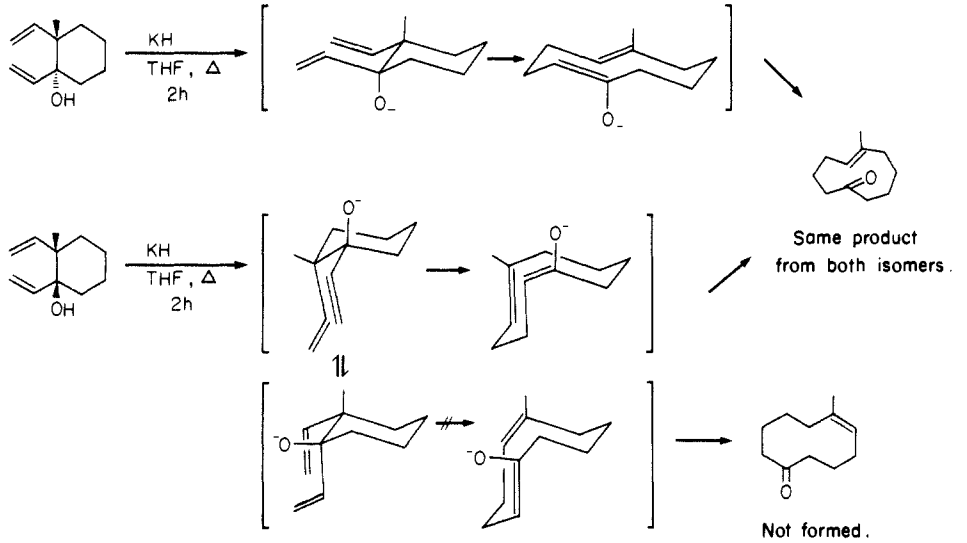
Scheme III



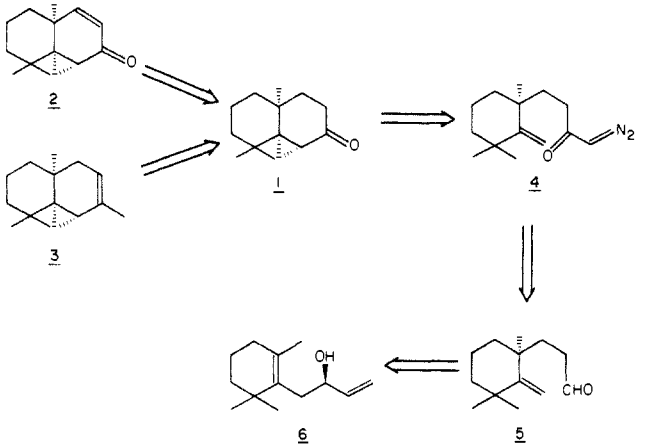
Scheme IV



Scheme V



Scheme VI



equatorial or axial position. In juvabione synthesis,[8] Evans found that chairlike transition state was favored with the requisite equatorial oxyanionic bond (Scheme III). On the other hand, Koreeda successfully introduced the steroid side chain via anionic oxy-Cope rearrangement that must proceed through chairlike transition state with the oxyanionic bond assuming axial position[9] (Scheme IV).

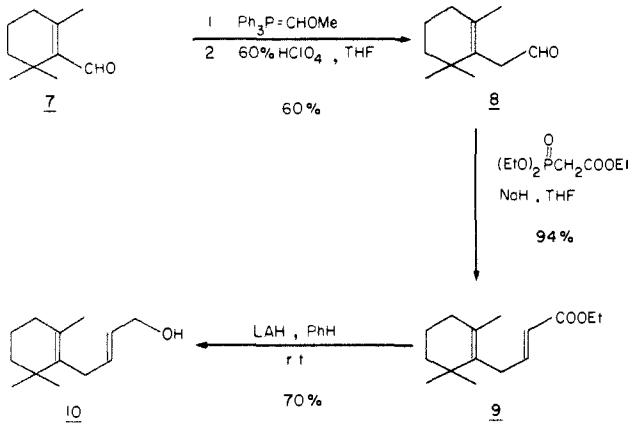
1,2-Divinylcyclohexanol systems used in many cyclodecenone syntheses call for more careful analysis. With the *trans*-divinyl derivatives, the chairlike transition state for the oxy-Cope reaction requires axial oxyanionic bond arrangement and the product is invariably (*E*)-cyclodecenone. However, when the vinyl groups are in a cis relationship, the stereochemistry of the product is conformation dependent. If the oxyanionic bond assumes an equatorial position in the transition state (which is incidentally an axial position in regard to the cyclohexane ring), (*E*)-cyclodecenone will again result; if the oxyanionic bond lies axial in the transition state, (*Z*)-cyclodecenone will form instead.

Clive and Wender independently found that clean conversion to (*E*)-6-methyl-5-cyclodecenone was achieved when either *trans*- or *cis*-1,2-divinyl-2-methylcyclohexanol was subjected to the normal anionic oxy-Cope rearrangement conditions[10] (Scheme V). Therefore it appears that there is a marked conformational preference of an equatorial oxyanionic bond when two similar

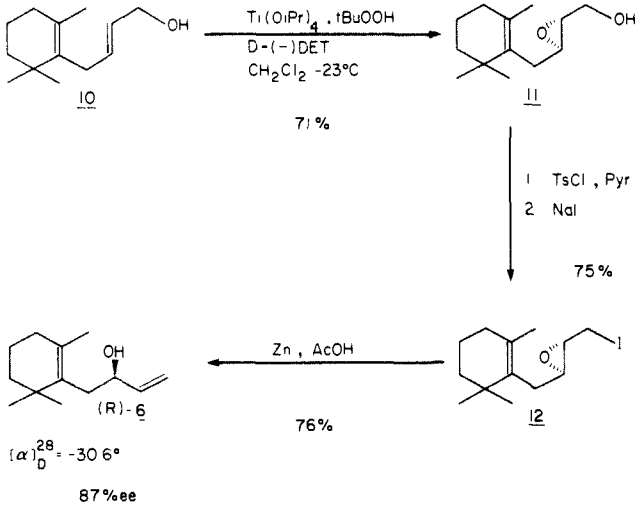
(8) Evans, D. A.; Nelson, J. V. *J. Am. Chem. Soc.* **1980**, *102*, 774–782.
(9) Koreeda, M.; Tanaka, Y.; Schwartz, A. *J. Org. Chem.* **1980**, *45*, 1172–1174.

(10) (a) Clive, D. L. J.; Russell, C. G.; Suri, S. C. *J. Org. Chem.* **1982**, *47*, 1632–1641. (b) See also: Feliu, A. Ph.D. Thesis, Harvard University, Cambridge, MA, 1981, pp 44–50. We thank Professor P. A. Wender of Stanford University for this valuable information. (c) It is interesting to note that thermal oxy-Cope rearrangement of *cis*-1,2-divinylcyclohexanol is known to produce both (*E*)- and (*Z*)-5-cyclodecenone in a 3:2 ratio. See: Marvell, E. N.; Whalley, W. *Tetrahedron Lett.* **1970**, 509–512. This is an example of thermal oxy-Cope rearrangement that proceeded with little stereoselectivity. There is evidence that *erythro*-4-methyl-1,5-hexadien-3-ol was transformed into *trans*-5-heptenal via chairlike transition state with the axial hydroxyl substitutent in vapor-phase thermal oxy-Cope rearrangement. See: Viola, A.; Iorio, E. J.; Chen, K. K.; Glover, G. M.; Nayak, U.; Kocienski, P. J. *J. Am. Chem. Soc.* **1967**, *89*, 3462–3470. However, the stereoselectivity of anionic oxy-Cope rearrangement should be explained under different context.

Scheme VII



Scheme VIII



chairlike transition states are possible in the rearrangement.

In the present research, we hoped to address this fundamental problem in a more general, nonbiased system as represented in Scheme I, which should at the same time provide a useful alternative in the synthesis of chiral quaternary carbon centers.

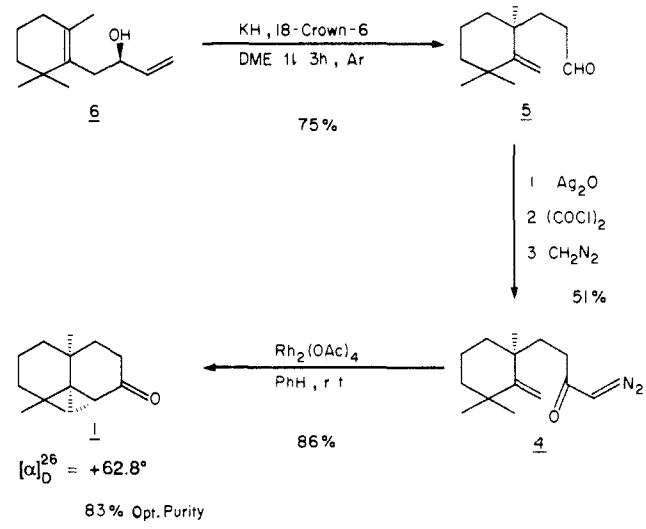
Results and Discussion

Dihydromayurone (**1**) is a pivotal intermediate in syntheses[11] of mayurone (**2**) and thujopsene (**3**). Our strategy was to prepare (+)-dihydromayurone (**1**) from optically active diazo ketone **4**, a known intermediate as a racemate in Smith's synthesis.[11a] The scheme then calls for aldehyde (*S*)-**5**, which would require allylic alcohol (*R*)-**6** assuming equatorial disposition of the oxyanionic bond in the chairlike transition state of the rearrangement (Scheme VI).

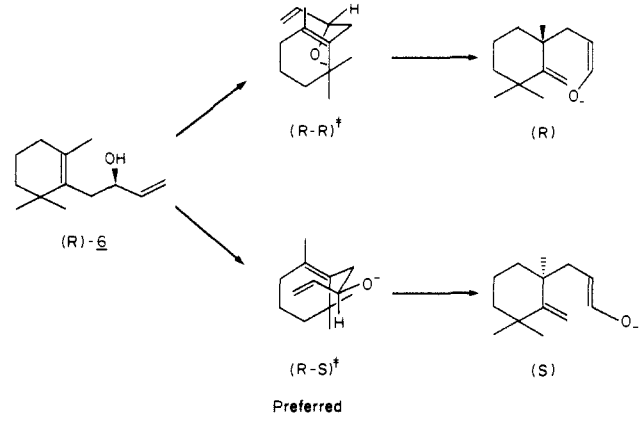
In the event, asymmetric synthesis of (*R*)-**6** was achieved most reliably via primary allylic alcohol **10**, which was prepared in conventional ways from β-cyclocitral (**7**)[12] (Scheme VII).

Primary allylic alcohol **10** was converted to optically active epoxy alcohol **11** when it was exposed to Sharpless asymmetric epoxidation conditions in the presence of (−)-diethyl D-tartrate.[5] Epoxy alchol **11** was then transformed to epoxy iodide **12** via tosylation and iodide displacement reaction. When epoxy iodide **12** was treated with zinc dust in acetic acid,[13] the desired (*R*)-(−)-**6** was obtained in satisfactory yield (Scheme VIII). The absolute stereochemical assignment was based primarily on the known stereochemical features of Sharpless asymmetric epoxidation.[5] The

Scheme IX



Scheme X



optical yield was determined to be 87% ee by comparing relative areas of the two methoxy peaks in the ^{1}H NMR spectrum of the ester derived from (*R*)-**6** and (*S*)-(MTPA)Cl. Detailed analysis of the MTPA ester ^{1}H NMR spectrum confirmed the assignment of the absolute configuration of (*R*)-(−)-**6**.[14]

Alternatively, (*R*)-(−)-**6** could be obtained by lithium acetylide addition to aldehyde **8**, Jones oxidation to acetylenic ketone, reduction with lithium aluminum hydride–Darvon alcohol complex, and partial hydrogenation. But the optical yield was unsatisfactory (40% ee).[15]

The crucial anionic oxy-Cope rearrangement of (*R*)-(−)-**6** was carried out under the standard conditions described by Evans[2] to produce a satisfactory yield of aldehyde **5**. To check the efficiency of the chirality transfer process, aldehyde **5** was reduced to the corresponding alcohol and the alcohol was derivatized with (*S*)-(MTPA)Cl. In the ^{1}H NMR spectrum of the resultant MTPA ester, one of the three methyl signals exhibited chemical

(11) (a) Branca, S. J.; Lock, R. L.; Smith, A. B., III. *J. Org. Chem.* **1977**, *42*, 3165–3168. (b) Johnson, C. R.; Barbachyn, M. R. *J. Am. Chem. Soc.* **1982**, *104*, 4290–4291.

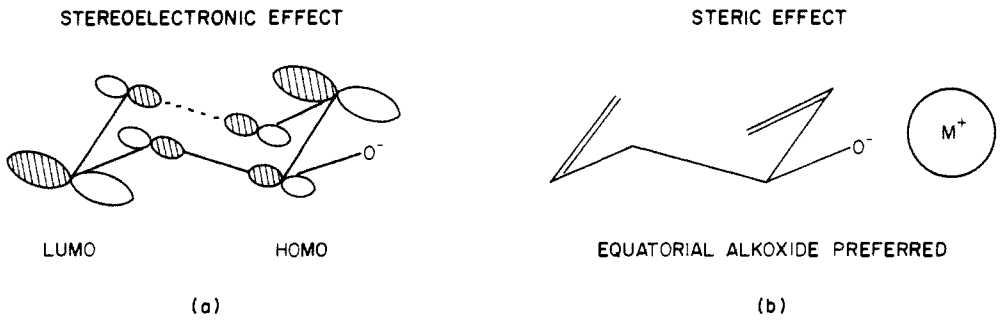
(12) Gedye, R. N.; Arora, P. C.; Deck, K. *Can. J. Chem.* **1971**, *49*, 1764–1766.

(13) Mori, K.; Ueda, H. *Tetrahedron* **1981**, *37*, 2581–2583.

(14) The methoxymethyl signal at lower field (δ 3.58) was predominant over the one at higher field (δ 3.53). These were used to determine optical purity. To assist configurational assignment, other characteristic peaks were studied. For example, two methyl signals at higher field (δ 0.98 and 0.94) were predominant over the peaks at lower field (δ 1.02 and 1.01). On the contrary, the vinyl signals at lower field were predominant over those at higher field. This provides an independent confirmation of the absolute stereochemical assignment of the optically active allylic alcohol as (*R*)-**6**. For detailed Dale-Mosher NMR configurational correlation scheme, see: Yamaguchi, S. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1983; Vol. 1, pp 130–131. Note that (*R*)-(+)-MTPA acid is converted to (*S*)-(MTPA)Cl, which is used for the synthesis of (*R*)-MTPA esters.

(15) (*R*)-Alcohols are known to be produced when acetylenic ketones are reduced by LAH–Darvon alcohol complex. See: Brinkmeyer, R. S.; Kapoor, V. M. *J. Am. Chem. Soc.* **1977**, *99*, 8339. This also confirms the configurational assignment.

Chart I



shift nonequivalence. Comparison of the relative heights of these close, but split, signals indicated very high efficiency of the chirality transfer reaction.[16]

Aldehyde **5** was then oxidized to the corresponding carboxylic acid, which was in turn converted to diazo ketone **4** via derivatization to acid chloride and treatment with diazomethane. Diazo ketone **4** was smoothly transformed to (+)-dihydromayurone (**1**) when treated with catalytic amount of rhodium acetate in benzene (Scheme IX). The specific rotation of **1** thus synthesized was determined to be +62.8° (lit.[17] $[\alpha]_D$ +75.4°), and the optical purity is calculated to be 83%. This constitutes formal total syntheses of (+)-mayurone (**2**) and (−)-thujopsene (**3**) as the conversion of **1** to **2** and **3** is already known.[11]

The results also show that, in the anionic oxy-Cope rearrangement of substrates like **6**, equatorial oxyanionic bond is heavily favored (>95:5) over the axial bond in the chairlike transition state (Scheme X). Chirality transfer is thus quite efficient.[18]

Preference of equatorial oxyanionic bond in the transition state may be explained on stereoelectronic grounds. In the frontier orbital theory, the transition state of [3,3] sigmatropic rearrangement is approached by two interacting allylic radicals. Here, SOMO–SOMO interaction is important, but the overlapping of HOMO–LUMO is also known to play a significant role.[19] The equatorial oxyanionic bond is better aligned to channel the surplus oxygen-bound electron to the allylic radical system through conjugation,[20] thus causing destabilization of HOMO. This will result in a more efficient overlapping of HOMO and LUMO and should lead to the more stable transition state[21] (Chart Ia).

The equatorial oxyanionic bond also makes more sense on steric grounds. Depending on the conditions adopted, ion-pair formation[22] or tighter solvation should render the anionic oxygen atom quite large in size and the oxyanionic bond will prefer to assume the equatorial position (Chart Ib).

The generality of this type of chirality transfer is being tested in these laboratories, and the results will be reported in conjunction with asymmetric syntheses of other classes of compounds.

(16) The signal at δ 1.03 was predominant over the one at δ 1.04. However, assignment of the absolute configuration was impossible at this stage.
(17) Dev, S.; Chetty, G. L. *Tetrahedron Lett.* **1965**, 3773–3776.
(18) Use of (+)-diethyl L-tartrate in the Sharpless epoxidation step eventually led to the synthesis of (*S*)-(+)-**6** (83% ee). It was converted to (−)-dihydromayurone (**1**) ($[\alpha]_D^{21}$ = −61.0°, optical purity 81%), confirming the efficiency in chirality transfer via anionic oxy-Cope rearrangement.
(19) Fukui, K. *Theory of Orientation and Stereoselection*; Springer-Verlag: Berlin, 1975; pp 62–63.
(20) In the chair conformation of the substrate, the equatorial oxyanionic bond lies almost in-plane with the vinyl group, whereas the axial oxyanionic bond can be considered to be gauche to the vinyl double bond. Thus, they are not identical in the substrate and should exert different influence on the transition state.
(21) The transition state may also be approached by acrolein and allyl anion. For this kind of transition state, the more stable *s-trans*-acrolein can be reached with little skeletal rearrangement from the substrate with equatorial oxyanionic bond. For related anionic rearrangements, see: Paquette, L. A.; Pierre, F.; Cottrell, C. E. *J. Am. Chem. Soc.* **1987**, *109*, 5731–5740.
(22) The rate acceleration of anionic oxy-Cope rearrangement was attributed to the ion-pair dissociation. (See ref 2a.) However, it is difficult to imagine full dissociation of ions in solvents like THF and DME. The rate acceleration can instead be explained by the increased ionic character of the alkoxide substrates that may remain associated as ion pairs.

Experimental Section

NMR spectra were recorded on Varian EM-360A, Varian XL-100, Varian XL-200, Bruker 80 MHz, and Bruker 300 MHz spectrometers with tetramethylsilane as an internal standard. Chemical shift values were recorded as parts per million and coupling constants as hertz. IR spectra were recorded on a Perkin-Elmer Model 782 spectrometer. Mass spectra were recorded on a JMS-DX300 spectrometer with JMA5000 data system. Optical rotation data were recorded on a Jasco DIP360 polarimeter with the Na D line. Melting points were determined on a Fisher-Johns apparatus and are uncorrected.

Titanium(IV) isopropoxide, (−)-diethyl D-tartrate, and (+)-diethyl L-tartrate were purchased from Aldrich. Aqueous *tert*-butyl hydroperoxide (70%) was obtained from Aldrich and used as a solution in isooctane after azeotropic removal of water. 2,6,6-Trimethyl-1-cyclohexeneacetaldehyde (**8**) could also be purchased from Aldrich. Crude products were purified by silica gel column chromatography (Merck 7734, Kieselgel 60).

2,6,6-Trimethyl-1-cyclohexeneacetaldehyde (8). Triphenyl(methoxymethyl)phosphonium chloride (1.47 g, 3.95 mmol; mp 191–193 °C) was placed in a three-neck flask under nitrogen and suspended in 40 mL of THF. *n*-Butyllithium (0.56 mL of a 7.1 M hexane solution) was slowly added with a syringe at 0 °C. After 10 min, β-cyclocitral (**7**; 0.5 g, 3.29 mmol) was added to the mixture. The mixture was further stirred for 1 h at room temperature, quenched with water, and worked up in ether. The crude product was purified by column chromatography to give a mixture of cis and trans enol ether: 0.36 g (61% yield); ^{1}H NMR ($CDCl_3$) δ 0.95 (s, 6 H, 6,6-dimethyl), 1.1–2.1 (m, 6 H, 3-H, 4-H, and 5-H), 1.50 (m, 3 H, 2-methyl), 3.53 (s, 3 H, OCH_3), 4.3–6.3 (m, J_{cis} = 7 Hz, J_{trans} = 13 Hz, olefinic).

Perchloric acid (3 mL, 60%) was added to the enol ether (0.13 g, 0.7 mmol) in THF (5 mL) at room temperature. After 30 min, the reaction mixture was poured into water and worked up with ether to give the crude product **8**, which was pure enough for the next step. For analysis, the crude product was purified by flash chromatography to give aldehyde **8**: 0.12 g (94% yield); ^{1}H NMR ($CDCl_3$) δ 0.97 (s, 6 H, 6,6-dimethyl), 1.60 (s, 3 H, 2-methyl), 1.1–2.1 (m, 6 H, 3-H, 4-H and 5-H), 3.03 (br s, 2 H, CH_2CH=O), 9.45 (br t, 1 H, CH=O).

Ethyl 4-(2′,6′,6′-Trimethyl-1′-cyclohexenyl)-2-butenoate (9). Triethyl phosphonoacetate (8 g, 36 mmol) was added to a slurry of NaH (36 mmol) in THF (10 mL). After the solution was stirred for 1 h, aldehyde **8** (2.9 g, 18 mmol) in THF (2 mL) was added dropwise while the temperature was kept below 30 °C. After 45 min, it was quenched by NH_4Cl solution and worked up with ether. The crude product was purified on a silica gel column to give **9**: 4.0 g (94% yield); ^{1}H NMR (CCl_4) δ 1.00 (s, 6 H, 6′,6′-dimethyl), 1.26 (t, 3 H, OCH_2CH_3), 1.5–1.8 (m, 4 H, 4′-H and 5′-H), 1.58 (s, 3 H, 2′-methyl), 1.95 (m, 2 H, 3′-H), 2.94 (d, 2 H, 4-H), 4.16 (q, 2 H, OCH_2CH_3), 5.68 (m, 1 H, *J* = 16 Hz, 2 -H), 6.9 (m, 1 H, 3-H); ^{13}C NMR (20.15 MHz, $CDCl_3$) δ 166.77, 148.51, 132.62, 130.13, 121.01, 59.89, 39.48, 34.78, 32.68, 31.14, 28.21, 19.89, 19.32, 14.15 (one carbon overlap); MS, *m/z* (EI, relative intensity) 236 (M^+, 99), 221 (95), 205 (20), 191 (64), 175 (91), 163 (25), 147 (100), 133 (55), 123 (95), 107 (75), 93 (24), 81 (21); HRMS for $C_{15}H_{24}O_2$, calcd 236.1777, found 236.1771.

4-(2′,6′,6′-Trimethyl-1′-cyclohexenyl)-2-butenol (10). To ester **9** (4.2 g, 17.8 mmol) in dry benzene (12 mL) was added dropwise LAH solution in THF (19.6 mmol) under nitrogen at room temperature. After the solution was stirred for 1 h, water was added dropwise and the mixture was washed with 1 N aqueous HCl, saturated aqueous $NaHCO_3$, and brine, and then dried over $MgSO_4$. The solvent was removed in vacuo to give the crude product, which was purified by column chromatography to give **10**: 2.4 g (70% yield); ^{1}H NMR ($CDCl_3$) δ 1.00 (s, 6 H, 6′,6′-dimethyl), 1.2–1.5 (m, 4 H, 4′-H and 5′-H), 1.58 (s, 3 H, 2′-methyl), 1.94 (m, 2 H, 3′-H), 2.75 (m, 2 H, 4-H), 4.00 (m, 2 H, 1-H), 5.57 (m, 2 H, 2-H and 3-H); ^{13}C NMR (20.15 MHz, $CDCl_3$) δ 134.51, 132.25, 128.70,

128.58, 63.48, 39.66, 34.65, 32.72, 31.01, 28.33, 19.78, 19.42 (one carbon overlap); IR (Nujol, $CHCl_3$) 670, 760, 1090, 1470, 1663, 2940, 3430, 3600 cm^{-1}; MS, *m/z* (EI, relative intensity) 194 (M^+, 99), 179 (94), 161 (62), 149 (18), 133 (36), 123 (100), 119 (40), 105 (50), 93 (40), 81 (56), 67 (24); HRMS for $C_{13}H_{22}O$, calcd 194.1671, found 194.1693.

Epoxy Alcohol 11. A 250-mL round-bottom flask was charged with 72 mL of dry CH_2Cl_2 and cooled to −23 °C (CCl_4–dry ice bath). Then titanium(IV) isopropoxide (2.1 mL, 7.2 mmol) and (−)-diethyl D-tartrate (1.5 mL, 8.6 mmol) were sequentially added to the flask with continuous stirring at −23 °C. The mixture was further stirred 20 min, and allylic alcohol **10** (1.4 g, 7.2 mmol) in 5 mL of CH_2Cl_2 was added to the mixture. After the mixture was stirred for 20 min, 2.3 mL of 6.3 M *tert*-butyl hydroperoxide solution in isooctane was added. The resulting homogeneous solution was then stored overnight in a sealed reaction vessel in the freezer at −20 °C. Then the flask was placed in a −23 °C bath, and 20 mL of 10% aqueous tartaric acid solution was added to it. The mixture was stirred for 30 min at −23 °C and stirred at room temperature for 1 h until the aqueous layer became clear. The organic layer was washed with water, dried over Na_2SO_4, and evaporated. The residue diluted with 60 mL of ether was mixed with 24 mL of 1 N NaOH solution. The mixture was stirred at 0 °C for 0.5 h, washed with brine, dried over Na_2SO_4, and evaporated to give the crude product. It was purified by flash chromatography to give **11**: 1.1 g (71% yield); ^1H NMR (CCl_4) δ 1.00 (s, 6 H, 6′,6′-dimethyl), 1.2–1.6 (m, 4 H, 4′-H and 5′-H), 1.68 (s, 3 H, 2′-methyl), 1.95 (m, 2 H, 3′-H), 2.30 (m, 2 H, 4-H), 2.83 (m, 2 H, 2-H and 3-H), 3.69 (m, 2 H, 1-H); ^{13}C NMR (20.15 MHz, $CDCl_3$) δ 133.01, 129.95, 61.76, 60.29, 56.25, 39.55, 34.37, 32.78, 30.18, 28.55, 28.15, 20.23, 19.33; MS, *m/z* (EI, relative intensity) 210 (M^+, 67), 195 (16), 179 (62), 159 (53), 149 (67), 135 (75), 123 (100), 107 (85), 93 (73), 81 (58), 69 (41), 55 (38), 41 (40); HRMS for $C_{13}H_{22}O_2$, calcd 210.1620, found 210.1641.

Epoxy Iodide 12. *p*-Toluenesulfonyl chloride (755 mg, 3.9 mmol) was added portionwise to a stirred and ice-cooled solution of **11** (610 mg, 3 mmol) in 6 mL of dry pyridine. The mixture was allowed to stand overnight at 0–5 °C, then poured into ice water, and extracted with ether. The ether extract was washed with water, aqueous $CuSO_4$, aqueous $NaHCO_3$, and brine, dried over $MgSO_4$, and concentrated to give the crude product that was pure enough for the next step. To the crude product in 15 mL of dry acetone was added NaI (1.38 g, 9.2 mmol) solution in acetone (3 mL), and the mixture was stirred and heated under reflux for 1.5 h. The reaction mixture was concentrated, diluted with water, and extracted with ether. The ether solution was washed with water, aqueous $Na_2S_2O_3$, aqueous $NaHCO_3$, and brine, dried over $MgSO_4$, and concentrated. The residue was purified on a silica gel column to give **12**: 720 mg (75% yield); ^1H NMR ($CDCl_3$) δ 1.00 (s, 6 H, 6′,6′-dimethyl), 1.2–1.6 (m, 4 H, 4′-H and 5′-H), 1.68 (s, 3 H, 2′-methyl), 1.96 (m, 2 H, 3′-H), 2.40 (m, 2 H, 2-H and 3-H), 2.7–3.5 (m, 4 H, 1-H and 4-H).

4-(2′,6′,6′-Trimethyl-1′-cyclohexenyl)-1-buten-3-ol (6). To epoxy iodide **12** (0.5 g, 1.6 mmol) in AcOH (2.5 mL) was added portionwise 1 g of activated Zn powder. After 2 h, wet ether was added and the reaction mixture was filtered through a sintered glass funnel; the ether solution was washed with water, aqueous $Na_2S_2O_3$, aqueous $NaHCO_3$, and brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified on a silica gel column to give **6**: 230 mg (76% yield); ^1H NMR ($CDCl_3$) δ 1.00 (s, 6 H, 6′,6′-dimethyl), 1.66 (s, 3 H, 2′-methyl) 1.2–1.8 (m, 4 H, 4′-H and 5′-H), 1.95 (m, 2 H, 3′-H), 2.23 (d, 2 H, 4-H), 4.23 (q, 1 H, 3-H), 4.8–5.5 (m, 2 H, 1-H), 5.6–6.3 (m, 1 H, 2-H); ^{13}C NMR (20.15 MHz, $CDCl_3$) δ 141.19, 133.10, 131.09, 113.55, 72.40, 39.93, 36.20, 34.66, 32.94, 29.07, 28.72, 21.02, 19.23; IR (Nujol, $CHCl_3$) 920, 1030, 1110, 1370, 1460, 1642, 2950, 3400 cm^{-1}; MS, *m/z* (EI, relative intensity) 194 (M^+, 5), 183 (5), 165 (6), 137 (56), 123 (100), 107 (40), 95 (63), 91 (21), 81 (50), 69 (20), 55 (22), 41 (31); HRMS for $C_{13}H_{22}O$, calcd 194.1671, found 194.1754; $[\alpha]^{28}_D = -30.6°$ (*c* = 0.77, EtOH).

Allylic alcohol **6** (30 mg, 0.15 mmol) was converted to the MTPA ester with (*S*)-(MTPA)Cl as described below. To (*R*)-(+)-MTPA acid (80 mg) in thionyl chloride (10 mL) was added small amount of NaCl salt, and the mixture was heated under reflux for 2 days. Excess thionyl chloride was removed in vacuo to give (*S*)-(MTPA)Cl quantitatively. Dry pyridine (0.5 mL) was placed in a 3-mL round-bottom flask, and (*S*)-(MTPA)Cl (50 mg, 0.21 mmol) in CCl_4 (0.5 mL) and allylic alcohol **6** (0.15 mmol) were added sequentially. The reaction mixture was stirred for 2 h at room temperature. 3-(Dimethylamino)-1-propylamine (0.36 mL, 0.30 mmol) was added, and the mixture was allowed to stand for 5 min. It was then diluted with ether, washed with cold dilute HCl, cold saturated Na_2CO_3, and brine, dried over $MgSO_4$, and concentrated. The residue was purified on a silica gel column to give the pure MTPA ester of **6**. The optical yield was determined to be 87% ee by comparing relative areas of the methoxy peaks of the MTPA moiety (δ 3.53 (6.5%), 3.58 (93.5%)) in the ^1H NMR spectrum (300 MHz).

Aldehyde 5. Excess KH in mineral oil was washed three times with dry DME under argon and suspended in 40 mL of DME. Allylic alcohol **6** (370 mg, 1.9 mmol) in DME (10 mL) was added dropwise. A catalytic amount of 18-crown-6 in DME (1 mL) was added. The mixture was heated under reflux for 3 h and quenched by water. The ethereal extract was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. This compound was relatively unstable and sensitive to heat. The crude product was directly used in the next step. For analysis, it was purified on a short silica gel column to give **5**: 277 mg (75% yield); ^1H NMR (CCl_4) δ 0.97 (s, 3 H, methyl), 1.10 (s, 6 H, two methyl), 1.2–2.6 (m, 10 H), 4.79 and 5.05 (s and s, 2 H, C=CH_2), 9.7 (br s, 1 H, CH=O); ^{13}C NMR (20.15 MHz, $CDCl_3$) δ 202.41, 159.36, 109.23, 41.16, 40.14, 38.68, 36.24, 32.44, 31.67, 31.48, 29.57, 29.50, 16.34.

To check the efficiency of the chirality transfer, aldehyde **5** was reduced with sodium borohydride in methanol at 0 °C to give the corresponding primary alcohol, which was converted to the MTPA ester with (*S*)-(MTPA)Cl as described above. In the ^1H NMR (300 MHz) spectrum of the resultant MTPA ester, one of the three methyl signals exhibited chemical shift nonequivalence (δ 1.04 (major), 1.03 (minor)). Comparison of the relative heights of these close, but split, signals indicated very high efficiency of the chirality transfer reaction.

Diazo Ketone 4. Crude aldehyde **5** obtained from allylic alcohol **6** (160 mg, 0.82 mmol) was diluted with EtOH (5.7 mL), and $AgNO_3$ (420 mg, 1.5 equiv) in distilled water (0.57 mL) was added slowly for 1 h under nitrogen. After the mixture was stirred for 4 h, it was filtered, washed with ether twice, acidified with 2 N HCl, and extracted with $CHCl_3$. The solvent was removed in vacuo to give the crude acid: ^1H NMR ($CDCl_3$) δ 1.03 (s, 3 H, methyl), 1.12 (s, 6 H, two methyl), 1.3–2.5 (m, 10 H), 4.76 and 5.02 (s and s, 2 H, C=CH_2), 8.9–9.7 (br, 1 H, COOH); IR (Nujol, $CHCl_3$) 900, 1220, 1300, 1450, 1710, 2925, 2500–3300 cm^{-1}; MS, *m/z* (EI, relative intensity) 210 (M^+, 8), 195 (12), 167 (15), 154 (13), 137 (100), 123 (39), 109 (26), 95 (87), 81 (73), 67 (32), 55 (40), 41 (48); HRMS for $C_{13}H_{22}O_2$, calcd 210.1620, found 210.1659.

Oxalyl chloride (ca. 2 equiv) was added to the crude acid in dry benzene (0.5 mL). After the solution was stirred for 7 h at room temperature, benzene and excess oxalyl chloride were removed in vacuo. The residue was diluted with dry ether (5 mL), and the ether solution was added dropwise to ethereal CH_2N_2 solution at 0 °C. After the reaction mixture was stirred for 2 h at 0 °C, excess CH_2N_2 was removed by nitrogen bubbling. The residue was concentrated and separated on a silica gel column to give **4**: 84 mg (overall 58% yield from **5**); ^1H NMR ($CDCl_3$) δ 1.03 (s, 6 H, two methyl), 1.12 (s, 3 H, methyl), 1.3–2.7 (m, 10 H), 4.80 and 5.07 (s and s, 2 H, C=CH_2), 5.23 (s, 1 H, CH=N_2); IR (Nujol, $CHCl_3$) 900, 1355, 1645, 2100, 2960, 3100 cm^{-1}.

(+)-Dihydromayurone (1). To diazo ketone **4** (84 mg, 0.34 mmol) in dry benzene (55 mL) was added a catalytic amount of $Rh_2(OAc)_4$, and the reaction was stirred overnight at room temperature. Then, benzene was evaporated and the residue was purified on a silica gel column to give **1**: 64 mg (86% yield); ^1H NMR ($CDCl_3$) δ 0.63 (s, 3 H, methyl), 1.16 (s, 3 H, methyl), 1.25 (s, 3 H, methyl), 0.9–2.5 (m, 13 H); ^{13}C NMR (50.31 MHz, $CDCl_3$) δ 210.19, 39.96, 38.91, 34.98, 34.60, 33.60, 32.88, 32.67, 32.39, 28.28, 28.20, 27.07, 18.66, 13.14; IR (Nujol, $CHCl_3$) 870, 915, 1100, 1275, 1470, 1682, 2870, 2930, 3005, 3075 cm^{-1}; MS, *m/z* (EI, relative intensity) 206 (M^+, 17), 191 (14), 178 (11), 163 (10), 149 (10), 135 (13), 123 (100), 107 (17), 93 (25), 79 (23), 69 (16), 55 (27), 41 (24); HRMS for $C_{14}H_{22}O$, calcd 206.1671, found 206.1661; $[\alpha]^{26}_D = +62.8°$ (*c* = 1.2, $CHCl_3$), 83% optical purity; mp 98–99 °C.

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