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Cp_2TiCl-Promoted Isomerization of Trisubstituted Epoxides to *exo*-Methylene Allylic Alcohols on Carvone Derivatives

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The ring-opening reaction of trisubstituted epoxides promoted by Cp_2TiCl led to *exo*-methylene allylic alcohols as major compounds when 0.5 M solutions of the epoxides were added to 0.1 M solutions of the reagent at room temperature in THF. In most cases, the allylic alcohols were contaminated with saturated alcohols. Normal and reverse addition modes led to the alternate product being favored. The different stereochemical outcome of *cis*- and *trans*-epoxy acetates is rationalized in terms of mechanistically biased elimination processes.

Introduction

Radicals generated upon treating epoxides with paramagnetic bis(cyclopentadienyl)titanium(III) chloride (Cp_2TiCl) have been described as intermediates in processes of high synthetic value: they can participate in both intramolecular (hex-5-enyl cyclization)[1] and intermolecular addition reactions.[2] The radicals generated this way can also serve as intermediates in the overall reduction or deoxygenation of the epoxide.[3] Depending on the reactivity of the acceptor, the initially formed radical can participate in addition processes or can be reduced further by Ti(III) to the corresponding carbanion. In the absence of an H-atom donor or an olefin, the resulting β-oxido-Ti organometallic species undergoes facile elimination to give an olefin. The reaction conditions are remarkably mild and are applicable to very sensitive substrates.[4]

The generation of exocyclic olefins has been reported in the course of radical cyclizations of epoxy alkenes leading to drimanes,[5] eudesmanolides,[6] and different ring synthons of paclitaxel.[7] In these cases, termination of the radical cyclization is not reductive; rather, it involves β-hydrogen elimination providing an alkene function. Furthermore, the titanocene-promoted isomerization of trisubstituted epoxides to *exo*-methylene allylic alcohols has been recently reported as a side reaction in the intramolecular addition of radicals to carbonyl compounds. The inability of certain intermediate radical species to cyclize led to the isolation of the isomeric allylic alcohols via formation of titanoxyorganotitanium intermediates followed by exocyclic β-hydrogen elimination.[8]

It seemed reasonable to us to study the Cp_2TiCl-promoted isomerization of trisubstituted epoxides to *exo*-methylene allylic alcohols in order to evaluate the scope of this particular transformation.[9]

Results and Discussion

To investigate this conjecture, several trisubstituted epoxides were synthesized from (*R*)-(−)- and (*S*)-(+)-carvone and treated with Cp_2TiCl in an attempt to elucidate the possible stereochemical implications of the isomerization process.

The low-valent titanium(III) complex was readily prepared by the in situ reduction of 2.5 equiv of Cp_2TiCl_2 with 5 equiv of powdered zinc in THF for 45 min at room temperature. The reaction took place either by addition via cannula of a 0.1 M solution of the Cp_2TiCl reagent in THF to a 0.5 M solution of the epoxide in the same solvent (method A) or in the reverse fashion (method B) (Table 1).

The epoxides were prepared by known procedures from (*S*)-(+)-carvone (**1a**−**5a**, **11a**, and **12a**) or (*R*)-(−)-carvone

(1) Nugent, W. A.; RajanBabu, T. V. *J. Am. Chem. Soc.* **1988**, *110*, 8562−8564.
(2) RajanBabu, T. V.; Nugent, W. A. *J. Am. Chem. Soc.* **1989**, *111*, 4525−4527.
(3) RajanBabu, T. V.; Nugent, W. A.; Beattie, M. S. *J. Am. Chem. Soc.* **1990**, *112*, 6408−6409.
(4) (a) RajanBabu T. V.; Nugent, W. A. *J. Am. Chem. Soc.* **1994**, *116*, 986−997. (b) Gansäuer, A.; Rinker, B. In *Titanium and Zirconium in Organic Synthesis*; Marek, I., Ed.; Wiley-VCH: Weinheim, 2002; Chapter 12, pp 435−440. (c) Gansäuer, A.; Pierobon, M. In *Radicals in Organic Synthesis*; Renaud, P., Sibi, M. P., Eds; Wiley-VCH: Weinheim, 2001; Vol. 2, Chapter 3.3, pp 207−220.
(5) (a) Barrero A. F.; Cuerva, J. M.; Alvarez-Manzaneda, E. J.; Oltra, J. E.; Chahboun, R. *Tetrahedron Lett.* **2002**, *43*, 2793−2796. (b) Barrero A. F.; Cuerva, J. M.; Herrador, M. M.; Valdivia, M. V. *J. Org. Chem.* **2001**, *66*, 4074−4078.
(6) Barrero, A. F.; Olatra, J. E.; Cuerva J. M.; Rosales, A. *J. Org. Chem.* **2202**, *67*, 2566−2571.
(7) Nakai, K.; Kamoshita, M.; Doi, T.; Yamada, H.; Takahashi, T. *Tetrahedron Lett.* **2001**, *42*, 7855−7857.
(8) Fernández-Mateos, A.; Martín de la Nava, E.; Pascual Coca, G.; Ramos Silvo, A.; Rubio González, R. *Org. Lett.* **1999**, *1*, 607−609.
(9) A highly selective and efficient isomerization of the epoxide moiety of a dieneoxide (*E*)-ester to the corresponding *exo*-methylene allylic dieneol using palladium catalysis has been recently described with occasion of the synthesis of vitamin D fluoro analogues: (a) Kabat, M. M.; Garofalo, L. M.; Daniewski, A. R.; Hutchings, S. D.; Liu, W.; Okabe, M.; Radinov, R.; Zhou, T. *J. Org. Chem.* **2001**, *66*, 6141−6150. (b) Daniewski A. R.; Garofalo, L. M.; Hutchings, S. D.; Kabat, M. M.; Liu, W.; Okabe, M.; Radinov, R.; Yiannikouros, G. P. *J. Org. Chem.* **2002**, *67*, 1580−1587.

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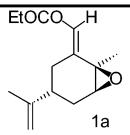
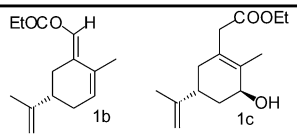
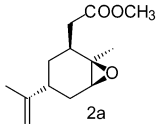
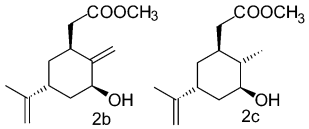
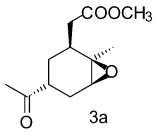
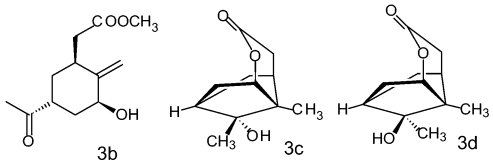
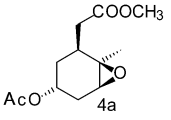
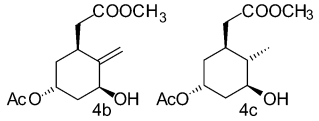
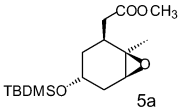
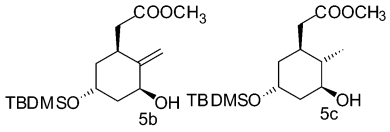
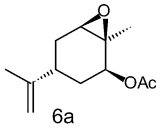
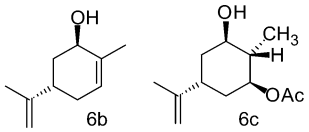
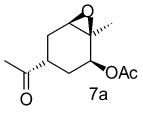
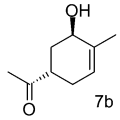
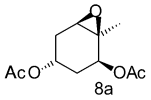
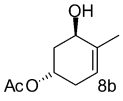
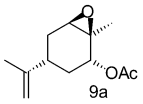
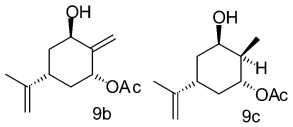
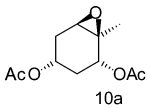
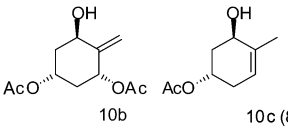
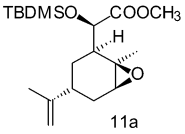
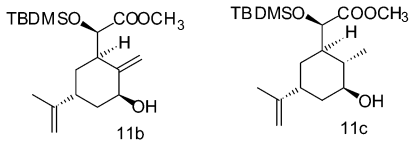
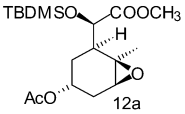
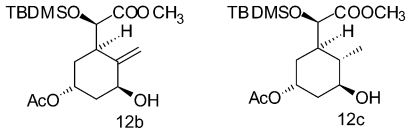
TABLE 1. Ring-Opening Reactions of Epoxide Derivatives of (*R*)-(−)- and (*S*)-(+)-Carvone Promoted by Cp_2TiCl

Entry	Epoxide	Products	ratio	yield[a]
1	 1a	 1b 1c	A) 1b: 1c= 1:1	63%
2	 2a	 2b 2c	A) 2b: 2c= 1: 3.5	68%
			B) 2b: 2c= 4: 1	70%
3	 3a	 3b 3c 3d	A) 3b: 3c: 3d= 1: 8: 4	66%
			B) 3b: 3c: 3d = 2.5: 20: 10	67%
4	 4a	 4b 4c	A) 4b: 4c= 1: 1.5	62%
			B) 4b: 4c= 1.5: 1	65%
5	 5a	 5b 5c	A) 5c	65%
			B) 5b: 5c= 6: 1	60%
6	 6a	 6b 6c	A) 6b: 6c= 1: 5	65%
			B) 6b: 6c= 5: 1	75%
7	 7a	 7b	A) 7b	65%
			B) 7b	72%
8	 8a	 8b	A) 8b	66%
			B) 8b	70%
9	 9a	 9b 9c	A) 9b: 9c= 1: 1.5	75%
			B) 9b: 9c= 3: 1	87%
10	 10a	 10b 10c (8b)	A) 10b: 8b= 1: 1.5	62%
			B) 10b: 8b= 3: 1	65%
11	 11a	 11b 11c	A) 11b: 11c= 1: 1.7	65%
			B) 11b: 11c= 3: 1	67%
12	 12a	 12b 12c	A) 12b: 12c= 3: 1	72%
			B) 12b	75%

[a] Isolated yields obtained by flash chromatography.

(**6a**−**10a**). In most cases, the overall yields of the desired *exo*-methylene allylic alcohols were acceptable, although they were always contaminated with the saturated alcohols. The chromatographic resolution of the resulting products, however, proved satisfactory in most cases.

Vinyl oxirane **1a**[10] led to a 1:1 mixture of the deoxygenated product **1b** and the allylic alcohol **1c**. Formation of the hydroxy compound **1c** may arise by formation of the allylic radical, further reduction to the titanium enolate, and hydrolysis during the workup. This result is similar to that obtained by Molander and co-workers[11] upon reducing vinyl oxiranes of the enantiomeric series with samarium diiodide.

Starting from (−)-*trans*-carveol,[12] the homologated epoxide **2a** was obtained by application of a four-step synthetic sequence with 52% overall yield: ortho ester Claisen rearrangement, saponification, bromolactonization, and methanolysis. The oxidative degradation of the isopropenyl chain allowed us to prepare the epoxides **3a**−**5a** by sequential ozonolysis, Baeyer−Villiger oxidation, saponification, and either acetylation or silyl protection processes.[13]

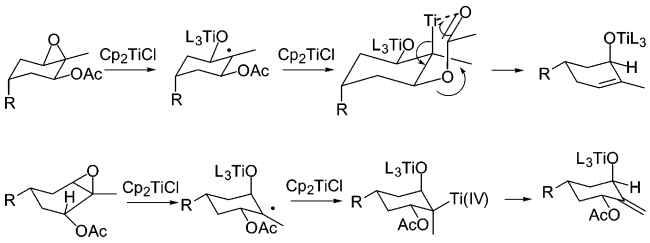
Under Cp_2TiCl promotion, the epoxy esters **2a**−**5a** undergo epoxide ring opening to yield the desired allylic alcohols **2b**−**5b** with the exocyclic double bond in all cases. These products are major components of the reaction mixture obtained by addition of the epoxide solution to the reagent solution (method B) except for **3a**. Normal addition led to the saturated products **2c**−**5c** as major products (method A).

It is known that under an excess of the reagent (method B) the reduction of alkoxytitanium radicals to alkoxytitanium carbanions takes place, after which these species undergo β-hydrogen elimination to yield the allylic alcohols. At low Ti(III) concentrations, however, the radicals are not reduced to carbanions but instead abstract hydrogens atoms from the solvent (THF) leading to the formation of the saturated alcohols (method A).

The stereochemistry of the saturated alcohols **2c**, **4c**, and **5c** was demonstrated by spectroscopic analysis including ^{1}HNMR NOE studies. Thus, in all cases there are sizable NOE effects (5−8%) at the secondary methyl groups upon irradiation at the vicinal methine protons of the corresponding secondary alcohols.[14]

In the case of the epoxide **3a**, the addition of the radical species to the carbonyl functionality takes place. Both methods (A and B) yielded the tricyclic lactone **3c**, mp 125−127 °C, as the major product. A single crystal for X-ray analysis was grown from diisopropyl ether, and the correct stereochemistry of **3c** was established. We assume that, first, radical addition to the carbonyl takes place and then the alkoxytitanium species promotes lactonization. Both methods afforded the allylic alcohol **3b** as the minor component of the reaction mixture.

SCHEME 1. Ring-Opening Reactions of *cis*- and *trans*-Epoxy Acetates under Cp_2TiCl Promotion



The *cis*-epoxy acetate **6a** was easily prepared from (*R*)-(−)-carvone by alkaline hydrogen peroxide epoxidation followed by L-Selectride reduction[15] and further alcohol protection. Again, the oxidative degradation of the unsaturated chain allowed us to sequentially isolate the epoxides **7a** and **8a** following the above-mentioned procedure. The *trans*-epoxy acetates **9a** and **10a** were prepared from (*R*)-(−)-carvone by epoxidation followed by triisobutylaluminum reduction,[16] acetylation, and oxidative degradation of the isopropenyl chain.

When method B was applied, the *cis*-epoxy acetates **6a**, **7a**, and **8a** yielded the β-elimination products **6b**, **7b**, and **8b**, respectively. Only in the case of **6a** was the presence of saturated acetate **6c** detected as a major product by normal addition (method A).

However, the *trans*-epoxy acetates **9a** and **10a** yielded the allylic alcohols **9b** and **10b**, respectively, as major components when method B was used. In addition, the saturated hydroxy derivative **9c** or the β-elimination product **8b** were isolated as minor components of the reaction mixture. These two latter products were obtained as major components of the reaction mixture when method A was applied.

To explain the different chemical behavior of the *cis*- and *trans*-epoxy acetates, in the cis case the reductive opening of the epoxide takes place by cleavage of the axial CO bond of the most likely starting conformation (Scheme 1). We assume that the oxyanionic group would be coordinated with the titanocene that attacks the radical and that the ring Ti thus ends up on the same side as the acetate group. The elimination can then easily be envisioned as a concerted cis-elimination via a six-membered ring transition state with minimum charge development.

In the trans case, the titanocene chloride attacks the radical from the same side as the oxyanionic group; the ring Ti is thus on the opposite side from the acetate group, thus precluding a concerted cis elimination involv-

(10) (a) Baggiolini, E. G.; Iacobelli, J. A.; Hennessy, B. M.; Uskokovic, M. R. *J. Am. Chem. Soc.* **1982**, *104*, 2945−2948. (b) Baggiolini, E. G.; Iacobelli, J. A.; Hennessy, B. M.; Batcho, A. D.; Sereno, J. F.; Uskokovic, M. R. *J. Org. Chem.* **1986**, *51*, 3098−3108.

(11) Molander, G. A.; La Belle, B. E.; Hahn, G. *J. Org. Chem.* **1986**, *51*, 5259−5264.

(12) (a) Johnston, R. G.; Read, J. *J. Chem. Soc.* **1934**, 233−237 (b) Klein, E.; Ohloff, G. *Tetrahedron.* **1963**, *19*, 1091−1099 (c) Schroeter, S. *Liebigs Ann.* **1964**, 118−121 (d) Schroeter, S.; Eliel, E. L. *J. Org. Chem.* **1965**, *30*, 1−7.

(13) Experimental procedures for the preparation of **2a**−**5a**, **11a**, and **12a** are provided in the Supporting Information. Similar transformations have been reported in the enantiomeric series starting from (*R*)-(−)-carvone: (a) Bermejo, F.; Rico-Ferreira, R.; Bamidele-Sanni, S.; García-Granda, S. *J. Org. Chem.* **2001**, *66*, 8257−8260. (b) Rico, R.; Zapico, J.; Bermejo, F. *Tetrahedron: Asymmetry* **1998**, *9*, 293−303.

(14) In case of the epoxy ester **2a**, the isolation of the saturated alcohol **2c** was more easily achieved by treatment of the reaction mixture with MnO_2 and fractionation of the reaction mixture by flash chromatography.

(15) Hatakeyama, S.; Numata, H.; Shimada, J.; Osanai, K.; Takano, S. *J. Org. Chem.* **1989**, *54*, 3515−3517.

(16) (a) Roberts, M. R.; Parsons, W. H.; Schlessinger, R. H. *J. Org. Chem.* **1978**, *43*, 3970−3972. (b) Gemal, A. L.; Luche, J.-L. *J. Am. Chem. Soc.* **1981**, *103*, 5454−5459. (c) Kirsch, S.; Bach, T. *Synthesis* **2003**, 1827−1836.

ing minimum charge development. Instead, β-hydride elimination occurs, presumably in a cis mode.[17]

Silyl-protected epoxy esters **11a** and **12a** were available by anionic [2,3]-Wittig rearrangement[18] of (−)-*trans*-carvyloxyacetic acid and subsequent transformations similar to those described for the preparation of **2a**−**4a**.

The epoxide opening of epoxides **11a** and **12a** led to the allylic alcohols **11b** and **12b**, respectively, which were contaminated with the saturated alcohols **11c** and **12c** when method A was used; however, optimal conversion of **12a** into **12b** was achieved when we made use of the reverse addition (method B).

Conclusions

The ring-opening reaction of trisubstituted epoxides promoted by Cp_2TiCl yielded the isomeric *exo*-methylene allylic alcohols with good yields. In most cases, the allylic alcohols were contaminated with the saturated alcohols although they can be separated by flash chromatography. Different modes of reactant addition led to the alternate product being favored. The different stereochemical outcome of the ring-opening reaction of *cis*- and *trans*-epoxy acetates is rationalized in terms of mechanistically biased processes: β-acetate elimination (*cis*-epoxy acetates) or β-hydride elimination (*trans*-epoxy acetates).

Experimental Section

General Procedure for Reductive Opening of Epoxides 1a−12a.[19] **Solution a.** Titanocene dichloride Cp_2TiCl_2 (548 mg, 2.2 mmol) and powdered Zn (431 mg, 6.6 mmol) were placed in a two-necked 50 mL round-bottomed flask under an argon atmosphere. Anhydrous fresh distilled and deoxygenated THF (2.2 mL) was added, and stirring was maintained for 1 h at room temperature (deep green color appeared after 15−30 min).

Solution b. The epoxide (1 mmol) was placed in a two-necked round-bottomed flask, and anhydrous freshly distilled and deoxygenated THF (10 mL) was added under an argon atmosphere.

Method A. Solution a was added dropwise via cannula to solution b under argon at room temperature. The reaction mixture was stirred at room temperature for 3−5 h.

Method B. Solution b was added dropwise via cannula to solution a at room temperature under an argon atmosphere. The reaction mixture was stirred at room temperature for 3−5 h.

Workup. When the reaction mixture turned from deep green to red saturated solutions of $NaPO_4H_2$ (5 mL) and NaCl (5 mL) were added. Stirring was maintained for 1 h, and the reaction mixture was then diluted with ether and filtered. The filtrate was extracted with ether (3 × 25 mL), washed with a saturated NaCl solution, and dried over Na_2SO_4. Evaporation of the solvent at reduced pressure led to the isolation of the reaction product. Isolation of the reaction products was successfully achieved by flash chromatography on silica gel.[20]

Cp_2TiCl-Promoted Ring-Opening Reaction of Epoxide 1a. Ethyl (*E*)-[(5*S*)-2-methyl-5-(2-propenyl)cyclohex-2-en-1-ylidene]acetate 1b: R_f = 0.4 (hexane/EtOAc 98:2); $[\alpha_D]^{20}_D$ +99.5 (*c* 0.9, $CHCl_3$); IR (neat) ν 2972, 1711, 1607, 1167, 1042, 887 cm^{-1}; MS (EI) *m*/*z* 220 (M^+, 15), 205 (5), 191 (10), 175 (20), 147 (40), 119 (40), 105 (100), 91 (70), 77 (60), 55 (50); ^1H NMR ($CDCl_3$) δ 1.25 (t, J = 7 Hz, 3H), 1.73 (s, 3H), 1.82 (s, 3H), 2.1−2.4 (m, 4H), 3.71 (m, 1H), 4.13 (q, J = 7 Hz, 2H), 4.74 (s, 2H), 5.71 (s, 1H), 6.04 (t, J = 4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.3 (CH_3), 19.5 (CH_3), 20.6 (CH_3), 31.3 (CH_2), 31.6 (CH_2), 41.2 (CH), 59.5 (CH_2), 109.6 (CH_2), 112.2 (CH), 132.6 (C), 135.1 (CH), 148.3 (C), 154.8 (C), 167.2 (*C*O). Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15. Found: C, 76.41; H, 9.19.

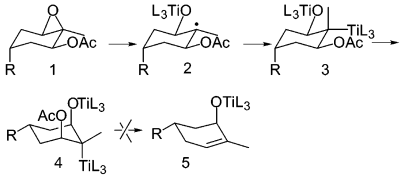
Ethyl [(3*S*,5*R*)-3-hydroxy-2-methyl-5-(2-propenyl)-1-cyclohexenyl]acetate 1c: R_f = 0.3 (hexane/EtOAc 98:2); $[\alpha_D]^{20}_D$ −130.6 (*c* 0.9, $CHCl_3$); IR (neat) ν 3461, 2980, 2936, 1732, 1645, 1443, 1370, 1167, 1030, 889 cm^{-1}; MS (*EI*) *m*/*z* 238 (M^+, 10), 220 (60), 121 (100), 105 (70), 91 (50), 77 (45); ^1H NMR (Cl_3CD) δ 1.23 (t, J = 7 Hz, 3H), 1.72 (s, 3H), 1.79 (s, 3H), 1.4−2.5 (m, 5H), 3.04 (s, 2H), 4.02 (m, 1H), 4.11 (q, J = 7 Hz, 2H), 4.72 (s, 2H); ^{13}C NMR (Cl_3CD) δ 14.4 (CH_3), 17.1 (CH_3), 21.0 (CH_3), 35.9 (CH), 36.2 (CH_2), 36.7 (CH_2), 39.2 (CH_2), 60.8 (CH_2), 69.9 (CH), 109.3 (CH_2), 128.0 (C), 131.5 (C), 149.8 (C), 171.7 (*C*O). Anal. Calcd for $C_{14}H_{22}O_3$ C: 70.56; H, 9.30. Found: C, 70.63; H, 9.34.

Cp_2TiCl-Promoted Ring-Opening Reaction of Epoxide 2a. Methyl [(1*S*,3*S*,5*R*)-3-hydroxy-2-methylene-5-(2-propenyl)cyclohexyl]acetate 2b: R_f = 0.3 (hexane/EtOAc 8:2); $[\alpha]^{20}_D$ −6.9 (*c* 1.4 $CHCl_3$); IR (neat) ν 3461, 2951, 1738, 1439, 1024, 897 cm^{-1}; MS (*EI*) *m*/*z* 224 (M^+, 1), 206 (10), 191 (20), 146 (30), 132 (100), 117 (40), 105 (65), 91 (60), 67 (50), 55 (70); ^1H NMR ($CDCl_3$) δ 1.5−1.7 (m, 4H), 1.72 (s, 3H), 1.93 (m, 1H), 2.51 (m, 2H), 2.86 (m, 1H), 3.65 (s, 3H), 4.36 (t, J = 4 Hz, 1H), 4.75 (s, 2H), 4.78 (1s, 1H), 4.94 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 21.1 (CH_3), 33.7 (CH), 36.5 (CH_2), 38.2 (CH), 38.8 (CH_2), 39.7 (CH_2), 51.4 (CH_3), 72.1 (CH), 109.4 (CH_2), 111.5 (CH_2), 148.0 (C), 150.1 (C), 173.6 (*C*O); HRMS (*EI*) calcd for $C_{13}H_{20}O_3$ (M^+) 224.1412, found 224.1423.

Methyl [(1*S*,2*S*,3*S*,5*R*)-3-hydroxy-2-methyl-5-(2-propenyl)cyclohexyl]acetate 2c: R_f = 0.2 (hexane/EtOAc 8:2); $[\alpha]^{20}_D$ −23.0 (*c* 0.9 $CHCl_3$); IR (neat) ν 3503, 2934, 1738, 1437, 1260, 1165, 1024, 889 cm^{-1}; MS (EI) *m*/*z* 226 (M^+, 2), 208 (10), 135 (15), 168 (10), 154 (20), 134 (75), 119 (65), 105 (30), 93 (50), 74 (100); ^1H NMR ($CDCl_3$) δ 0.97 (d, J = 7 Hz, 3H), 1.35−1.71 (m, 4H), 1.72 (s, 3H), 1.73 (m, 1H), 2.24 (m, 1H), 2.40 (m, 1H), 2.51−2.54 (m, 2H), 3.66 (s, 3H), 3.91 (m, 1H), 4.76 (s, 1H), 4.80 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 13.0 (CH_3), 21.3 (CH_3), 33.7 (CH_2), 34.0 (CH), 34.4 (CH), 35.2 (CH_2), 37.1 (CH_2), 37.9 (CH), 51.3 (CH_3), 70.9 (CH), 109.2 (CH_2), 148.9 (C), 174.5 (*C*O); HRMS (EI) calcd for $C_{13}H_{22}O_3$ (M^+) 226.1569, found 226.1574.

Cp_2TiCl-Promoted Ring-Opening Reaction of Epoxide 3a. Methyl (1*S*,3*S*,5*R*)-5-acetyl-3-hydroxy-2-methylenecyclohexyl acetate 3b: R_f = 0.4 (hexane/EtOAc 1:1); $[\alpha]^{20}_D$ −6.5 (*c* 0.4 $CHCl_3$); IR (neat) ν 3445, 2928, 1738, 1715, 1653, 1437, 1362, 1262, 1167, 909 cm^{-1}; MS (*EI*) *m*/*z* 226 (M^+, 15), 210 (20), 183 (55), 152 (95), 109 (95), 98 (85), 71 (100), 59 (90); ^1H NMR ($CDCl_3$) δ 1.5−1.9 (m, 4H), 2.20 (s, 3H), 2.4−2.6 (m, 3H), 3.02 (m, 1H), 3.67 (s, 3H), 4.37 (t, J = 5.3 Hz, 1H), 4.79 (s, 1H), 5.00 (s, 1H); ^{13}C NMR($CDCl_3$) δ 28.4 (CH_3), 33.7 (CH_2), 36.1 (CH_2), 37.5 (CH), 39.4 (CH_2), 42.5 (CH), 51.9 (CH_3), 71.3

(17) If the titanium chloride attacks the radical (2) from the trans side, the resulting product has the Ti ring group and the acetate in a trans diequatorial conformation (3) that cannot lead to elimination. In order for the latter to occur, the ring would have to flip to a conformation with three axial groups, two of which are strongly eclipsed (4). It is likely that elimination in the direction of the methyl will occur instead in clear contradiction with our results. We are greatly indebted to the reviewer who suggested the cis elimination pathway to us prior to publication of this paper.



(18) Nakai, T.; Mikami, K. In *Organic Reactions*; Paquette, L. A., Ed.; John Wiley & Sons, Inc.: New York, 1994; Vol. 46, p 105.

(19) See the Supporting Information for experimental details on the preparation of epoxides **1a**−**12a** (Table 1).

(20) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923−2925.

(CH), 110.8 (CH_2), 149.5 (C), 175.8 (CO), 211.5 (*C*O); HRMS (EI) calcd for $C_{12}H_{18}O_4$ (M^+) 226.1205, found 226.1193.

(1*S*,5*S*,7*R*,8*R*,9*S*)-8,9-Dimethyl-3-oxo-2-oxatricyclo-[5.2.1.0^{5,9}]decan-8-ol 3c: R_f = 0.3 (hexane/EtOAc 1:1); mp 125−127 °C (diisopropyl ether); $[\alpha]^{20}_D$ +19.3 (*c* 1.29, $CHCl_3$); IR (KBr) ν 3466, 2957, 1703, 1378, 1235, 1026, 941, 814 cm^{-1}; MS (*EI*) *m*/*z* 196 (M^+, 2), 178 (5), 152 (100), 109 (20), 94 (25), 71 (15); ^{1}H NMR ($CDCl_3$) δ 1.05 (s, 3H), 1.22 (s, 3H), 1.29 (dd, J_1 = 14.4 Hz, J_2 = 2.7 Hz, 1H), 1.57 (m, 1H), 1.90 (t, J = 4.4 Hz, 1H), 2.28 (m, 1H), 2.45 (m, 2H), 2.58 (m, 2H), 4.47 (dt, J_1 = 10 Hz, J_2 = 2.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 11.3 (CH_3), 19.0 (CH_3), 31.3 (CH_2), 34.6 (CH), 35.4 (CH_2), 37.7 (CH_2), 42.9 (CH), 44.9 (C), 84.5 (C), 84.7 (CH), 169.9 (*C*O); HRMS (EI) calcd for $C_{11}H_{16}O_3$ (M^+) 196.1099, found 196.1112.

X-ray Data. The X-ray data have been deposited at the Cambridge Crystallographic Data Centre (deposition no. CCDC 223320). An ORTEP diagram and crystallographic information in CIF format are available as Supporting Information.

(1*S*,5*S*,7*R*,8*S*,9*S*)-8,9-Dimethyl-3-oxo-2-oxatricyclo-[5.2.1.0^{5,9}]decan-8-ol 3d: R_f = 0.3 (hexane/EtOAc 1:1); $[\alpha]^{20}_D$ +23.9 (*c* 0.30 $CHCl_3$); IR (neat) ν 3447, 2963, 1701, 1456, 1389, 1231, 1109, 1059, 1028, 937 cm^{-1}; MS (*EI*) *m*/*z* 196 (M^+, 8), 178 (17), 152 (100), 109 (35), 94 (35), 71 (25); ^{1}H NMR ($CDCl_3$) δ 1.06 (s, 3H), 1.26 (s, 3H), 1.28 (m, 1H), 1.9 (t, J = 4.4 Hz, 1H), 2.0−2.2 (m, 2H), 2.4−2.7 (m, 4H), 4.77 (dt, J_1 = 10 Hz, J_2 = 2.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 11.3 (CH_3), 18.6 (3H, s, CH_3), 31.7 (CH_2), 34.2 (CH), 34.6 (CH_2), 38.0 (CH_2), 42.8 (CH), 44.5 (C), 85.8 (C), 86.5 (CH), 169.8 (*C*O); HRMS (EI) calcd for $C_{11}H_{16}O_3$ (M^+) 196.1099, found 196.1104.

Cp_2TiCl-Promoted Ring-Opening Reaction of Epoxide 4a. Methyl (1*S*,3*S*,5*R*)-5-acetoxy-3-hydroxy-2-methylenecyclohexyl acetate 4b: R_f = 0.4 (hexane/EtOAc 1:1); $[\alpha]^{20}_D$ −42.9 (*c* 0.6 $CHCl_3$); IR (neat) ν 3495, 2955, 1734, 1437, 1375, 1260, 1020, 903, 804 cm^{-1}; MS (*EI*) *m*/*z* 242 (M^+, 4), 224 (4), 182 (18), 108 (100), 77(45); ^{1}H NMR ($CDCl_3$) δ 1.40 (dt, J_1 = 14 Hz, J_2 = 2.8 Hz, 1H), 1.59 (dt, J_1 = 14 Hz, J_2 = 2.8 Hz, 1H), 1.95 (dt, J_1 = 14 Hz, J_2 = 1.5 Hz, 1H), 2.08 (s, 3H), 2.23 (dt, J_1 = 14 Hz, J_2 = 1.5 Hz, 1H), 2.37 (dd, J_1 = 15 Hz, J_2 = 7 Hz, 1H), 2.69 (dd, J_1 = 15 Hz, J_2 = 7 Hz, 1H), 2.87 (m, 1H), 3.68 (s, 3H), 4.40 (dd, J_1 = 10.5 Hz, J_2 = 4.4 Hz, 1H), 4.75 (s, 1H), 5.09 (s, 1H), 5.23 (m, 1H); ^{13}C NMR ($CDCl_3$) δ: 21.3 (CH_3), 34.0 (CH), 37.2 (CH_2), 37.6 (CH_2), 40.5 (CH_2), 51.6 (CH_3), 68.8 (CH), 69.3 (CH), 103.7 (CH_2), 152.3 (C), 170.3 (CO), 172.8 (CO); HRMS (EI) calcd for $C_{12}H_{18}O_5$ (M^+) 242.1154, found 242.1159.

Methyl (1*S*,2*S*,3*S*,5*R*)-5-acetoxy-3-hydroxy-2-methylcyclohexyl acetate 4c: R_f = 0.3 (hexane/EtOAc 1:1); $[\alpha]^{20}_D$ −21.45 (*c* 0.42 $CHCl_3$); IR (neat) ν 3447, 2957, 1734, 1717, 1437, 1373, 1262, 1022, 909, 801 cm^{-1}; MS (EI) *m*/*z* 244 (M^+, 4), 184 (18), 166 (25), 111 (100), 93 (55), 74 (100); ^{1}H NMR ($CDCl_3$) δ 0.83 (d, J = 7 Hz, 3H), 1.45 (dt, J_1 = 14 Hz, J_2 = 2.8 Hz, 1H), 1.55 (m, 3H), 1.85 (m 1H), 2.04 (s, 3H), 2.1−2.4 (m, 3H), 3.68 (s, 3H), 4.08 (m, 1H), 5.13 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 5.1 (CH_3), 21.2 (CH_3), 30.1 (CH_2), 31.7 (CH), 33.1 (CH_2), 37.5 (CH), 37.6 (CH_2), 51.5 (CH_3), 68.7 (CH), 69.4 (CH), 170.2 (CO), 173.0 (CO); HRMS (*EI*) calcd for $C_{12}H_{20}O_5$ (M^+) 244.1311, found 244.1298.

Cp_2TiCl-Promoted Ring-Opening Reaction of Epoxide 5a. Methyl (1*S*,3*S*,5*R*)-5-*tert*-butyldimethylsilyloxy-3-hydroxy-2-methylenecyclohexyl acetate 5b: R_f = 0.5 (hexane/EtOAc 1:1); $[\alpha]^{20}_D$ −20.0 (*c* 0.27 $CHCl_3$); IR (neat) ν 3252, 2926, 2857, 1740, 1437, 1252, 1086, 1028, 835, 775, 694 cm^{-1}; MS (EI) *m*/*z* 314 (M^+, 12), 293 (5), 257 (100), 225 (35), 181(28), 105 (85), 91(29), 75(95). ^{1}H NMR ($CDCl_3$) δ 0.06 (s, 3H), 0.07 (s, 3H), 0.90 (s, 9H), 1.31 (m, 1H), 1.46 (dt, J_1 = 13.2 Hz, J_2 = 2.4 Hz, 1H), 1.77 (m, 1H), 2.09 (m, 1H), 2.33 (dd, J_1 = 15 Hz, J_2 = 6.5 Hz, 1H), 2.69 (dd, J_1 = 15 Hz, J_2 = 6.5 Hz, 1H), 2.97 (m, 1H), 3.67 (s, 3H), 4.19 (m, 1H), 4.48 (dd, J_1 = 10.5 Hz, J_2 = 4.4 Hz, 1H), 4.68 (s, 1H), 5.02 (s, 1H); ^{13}C NMR ($CDCl_3$) δ −5.0 (CH_3), −4.9 (*C*H$_3$), 17.9 (C), 25.7 (3CH$_3$), 33.3 (CH), 37.5 (CH_2), 41.3 (CH_2), 44.4 (CH_2), 51.5 (CH_3), 66.3 (CH), 69.2 (CH), 102.1 (CH_2), 153.9 (C), 170.0 (CO). Anal. Calcd for $C_{16}H_{30}O_4Si$: C, 61.11; H, 9.61. Found: C, 61.49; H, 9.65.

Methyl (1*S*,2*S*,3*S*,5*R*)-5-*tert*-butyldimethylsilyloxy-3-hydroxy-2-methylcyclohexyl acetate 5c: R_f = 0.3 (hexane/EtOAc 1:1); $[\alpha]^{20}_D$ −7.1 (*c* 1.43 $CHCl_3$); IR (neat) ν 3437, 2930, 2857, 1742, 1472, 1437, 1256, 1051, 835, 775 cm^{-1}; MS (*EI*) *m*/*z* 316 (M^+, 4), 259 (100), 227 (20), 183 (30), 153 (20), 107 (35), 93 (85), 75 (62); ^{1}H NMR ($CDCl_3$) δ 0.02 (s, 3H), 0.05 (s, 3H), 0.78 (d, J = 7 Hz, 3H), 0.87 (s, 9H), 1.36 (m, 1H), 1.52 (m, 1H), 1.65 (m, 2H), 2.00 (m, 1H), 2.24 (ddd, J_1 = 15 Hz, J_2 = 8.5 Hz, J_3 = 6.8 Hz, 2H), 2.49 (m, 1H), 3.64 (s, 3H), 4.08 (dt, J_1 = 3.2 Hz, J_2 = 6.5 Hz 1H), 4.14 (m, 1H); ^{13}C NMR ($CDCl_3$) δ: -4.9 (2*C*H$_3$), 5.1 (CH_3), 17.9 (C) 25.7 (3CH_3), 31.1 (CH), 33.5 (CH_2), 36.7 (CH_2), 38.2 (CH), 38.3 (CH_2), 51.3 (CH_3), 60.8 (CH), 68.6 (CH), 173.3 (CO). Anal. Calcd for $C_{16}H_{32}O_4Si$: C, 60.72; H, 10.19. Found: C, 60.82; H, 10.28.

Cp_2TiCl-Promoted Ring-Opening Reaction of Epoxide 6a. The spectroscopic properties obtained for **6b** are identical to those described for (+)-*trans*-carveol.[12a,b,d,21] **(1*R*,2*S*,3*S*,5*R*)-3-Acetoxy-2-methyl-5-(2-propenyl)cyclohexanol 6c:** R_f = 0.5 (hexane/EtOAc 8:2) 0.5; $[\alpha]^{20}_D$ +32.5 (*c* 0.4 $CHCl_3$). IR (neat) ν 3592, 3470, 2936, 1645, 1449, 1375, 1256, 1063, 1020, 889 cm^{-1}; MS (*EI*) *m*/*z* 212 (M^+, 4), 181 (5), 152 (35), 134 (100), 119 (65), 105 (20), 93 (35), 79 (25); ^{1}H NMR ($CDCl_3$) δ 1.08 (d, J = 7 Hz, 3H), 1.37−1.49 (m, 2H), 1.72 (s, 3H), 1.73 (m, 1H), 2.01 (m, 1H), 2.05 (m, 1H), 2.10 (s, 3H), 2.42 (tt, J_1 = 12.8 Hz, J_2 = 3.2 Hz, 1H), 3.85 (m, 1H), 4.71 (s, 1H), 4.75 (s, 1H), 5.17 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 14.2 (CH_3), 20.9 (CH_3), 21.2 (CH_3), 32.1 (CH), 35.1 (CH_2), 37.4 (CH), 38.7 (CH_2), 71.2 (CH), 74.9 (CH), 109.4 (CH_2), 148.5 (C), 169.7 (CO); HRMS (EI) calcd for $C_{12}H_{20}O_3$ (M^+) 212.1412, found 212.1418.

Cp_2TiCl-Promoted Ring-Opening Reaction of Epoxide 7a. (1*R*,5*S*)-5-Acetyl-2-methylcyclohex-2-en-1-ol 7b: R_f = 0.4 (hexane/EtOAc 7:3); $[\alpha]^{20}_D$ +186.2 (*c* 1.2 $CHCl_3$); IR (neat) ν 3414, 2918, 1709, 1443, 1356, 1244, 1173, 1057, 1034, 808 cm^{-1}; MS *(EI) m*/*z* 154 (M^+, 6), 136 (15), 121 (24), 111 (100), 93 (42), 77 (28); ^{1}H NMR ($CDCl_3$) δ 1.61 (dt, J_1 = 13.2 Hz, J_2 = 4 Hz, 2H), 1.76 (s, 3H), 2.01−2.24 (m, 2H), 2.16 (s, 3H), 2.80 (m, 1H) 4.01 (s, 1H), 5.52 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 20.7 (CH_3), 27.1 (CH_2), 28.1 (CH_3), 33.6 (CH_2), 42.0 (CH), 67.3 (CH), 123.7 (CH), 134.4 (C), 211.4 (CO). Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.21; H, 9.12.

Cp_2TiCl-Promoted Ring-Opening Reaction of Epoxide 8a. (1*R*,5*S*)-5-Acetoxy-2-methylcyclohex-2-en-1-ol 8b: R_f = 0.4 (hexane/EtOAc 8:2); $[\alpha]^{20}_D$ +92.7 (*c* 0.56 $CHCl_3$); IR (neat) ν 3453, 2961, 1738, 1437, 1370, 1244, 1036, 795 cm^{-1}; MS (FAB) *m*/*z* 171 (M^+ + 1, 5), 154 (35), 111 (40), 93 (70), 73 (100); ^{1}H NMR ($CDCl_3$) δ 1.79 (s, 3H), 1.81−1.99 (m, 2H), 2.03 (s, 3H), 2.39 (m, 2H), 4.14 (s, 1H), 5.10 (m, 1H), 5.40 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 20.0 (CH_3), 21.3 (CH_3), 31.1 (CH_2), 37.0 (CH_2), 67.1 (CH), 68.5 (CH), 121.6 (CH), 135.4 (C), 170.6 (CO); HRMS (FAB) calcd for $C_9H_{14}O_3$ (M^+ + 1) 171.0943, found 171.0951.

Cp_2TiCl-Promoted Ring-Opening Reaction of Epoxide 9a. (1*R*,3*R*,5*R*)-3-Acetoxy-2-methylene-5-(2-propenyl)cyclohexanol 9b: R_f = 0.5 (hexane/EtOAc 1:1); $[\alpha]^{20}_D$ −91.6 (*c* 1.40 $CHCl_3$); IR (film) ν 3461, 2940, 1738, 1645, 1435, 1375, 1248, 1099, 1053, 1028, 891 cm^{-1}; MS (EI) *m*/*z* 210 (M^+, 2), 150 (82), 132 (85), 108 (100), 91 (50), 77 (65), 67 (45); ^{1}H NMR ($CDCl_3$) δ 1.17−1.50 (m, 2H), 1.71 (s, 3H), 1.97−2.82 (m, 3H), 2.15 (s, 3H), 4.53 (t, J = 2.8 Hz, 1H), 4.71 (s, 2H), 4.87 (s, 1H), 4.96 (s, 1H), 5.61 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 20.7 (CH_3), 21.0 (CH_3), 37.2 (CH), 38.3 (CH_2), 38.5 (CH_2), 71.0 (CH), 73.3 (CH), 107.6 (CH_2), 109.5 (CH_2), 147.8 (C), 170.1 (CO); HRMS (EI) calcd for $C_{12}H_{18}O_3$ (M^+) 210.1256, found 210.1271.

(1*R*,2*R*,3*R*,5*R*)-3-Acetoxy-2-methyl-5-(2-propenyl)cyclohexanol 9c: R_f = 0.5 (hexane/EtOAc 1:1); $[\alpha]^{20}_D$ −83.2 (*c* 1.4 $CHCl_3$); IR (neat) ν 3488, 2934, 1734, 1645, 1456, 1373, 1244, 1026, 891 cm^{-1}; MS (EI) *m*/*z* 212 (M^+, 2), 194 (5), 152 (53), 124 (100), 119 (68), 105 (15), 93 (10); ^{1}H NMR ($CDCl_3$) δ 1.01 (d, J = 7 Hz, 2H), 1.2 (m, 1H), 1.42 (ddd, J_1 = 14 Hz, J_2 =

(21) (a) Naves, Y. R. Helv. Chim. Acta, **1964**, *47*, 1617−1621 (b) Barton, D. H. R.; Motherwell, R. S. H.; Motherwell W. B. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2363−2367 (c) Yasui, K.; Fugami, K; Tanaka, S.; Tamaru, Y. *J. Org. Chem.* **1995**, *60*, 1365−1380.

12.8 Hz, J_3 = 2.5 Hz, 1H), 1.6 (m, 1H), 1.72 (s, 3H), 1.9 (m, 1H), 2.05 (s, 3H), 2.1 (m, 1H), 2.53 (tt, J_1 = 12.8 Hz, J_2 = 2.5 Hz, 1H), 4.03 (m, 1H), 4.70 (s, 1H), 4.72 (s, 1H), 4.90 (dt, J_1 = 11.2 Hz, J_2 = 4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.1 (CH_3), 20.8 (CH_3), 21.2 (CH_3), 36.8 (CH_2), 36.8 (CH), 38.0 (CH_2), 40.9 (CH), 71.6 (CH), 73.9 (CH), 109.2 (CH_2), 148.4 (C), 170.7 (CO); HRMS (EI) calcd for $C_{12}H_{20}O_3$ (M^+) 212.1412, found 212.1398.

Cp_2TiCl-Promoted Ring-Opening Reaction of Epoxide 10a. (1R,3R,5R)-3,5-bisacetoxy-2-methylenecyclohexanol 10b: R_f = 0.3 (hexane/EtOAc 8:2); $[\alpha]^{20}_D$ −32.2 (*c* 1.60 $CHCl_3$); IR (neat) ν_{max} 3482, 2936, 1748, 1723, 1653, 1437, 1260, 1063, 1026, 982, 918 cm^{-1}; MS (*EI*) *m*/*z* 228 (M^+, 4), 211 (10), 129 (12), 109 (60), 91 (72), 81 (48), 69 (72); ^{1}H NMR ($CDCl_3$) δ 1.6−2.4 (m, 4H), 2.01 (s, 3H), 2.07 (s, 3H), 4.57 (t, J = 4.3 Hz, 1H), 4.93 (s, 1H), 5.06 (s, 1H), 5.28 (m, 1H), 5.57 (dd, J_1 = 9.6 Hz, J_2 = 4.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 20.9 (CH_3), 21.1 (CH_3), 37.2 (CH_2), 38.9 (CH_2), 67.8 (CH), 69.9 (CH), 70.1 (CH), 109.1 (CH_2), 146.4 (C), 169.8 (*C*O), 170.1 (*C*O); HRMS (EI) calcd for $C_{11}H_{16}O_5$ (M^+) 228.0998, found 228.1013.

10c. The spectroscopic properties obtained for **10c** are identical to those described for **8b**.

Cp_2TiCl-Promoted Ring-Opening Reaction of Epoxide 11a. (2*R,1′*R**,3′*S**,5′*R**)-2-*tert*-Butyldimethyldimethylsilyloxy-2-[3′-hydroxy-2′-methylene-5′-(2-propenyl)cyclohexyl]acetic acid methyl ester 11b:** R_f = 0.4 (hexane/EtOAc 8:2); IR (neat) ν 3461, 2951, 2859, 1740, 1647, 1474, 1437, 1258, 1119, 839, 781 cm^{-1}; MS (EI) *m*/*z* 354 (M^+, 3), 295 (10), 239 (35), 205 (75), 133 (80), 73 (100); ^{1}H NMR ($CDCl_3$) δ 0.08 (s, 3H), 0.11 (s, 3H), 0.96 (s, 9H), 1.37 (dt, J_1 = 13.2 Hz, J_2 = 2.8 Hz, 1H), 1.68 (m, 1H), 1.70 (s, 3H), 1.76 (m, 1H), 1.99 (dq, J_1 = 13.2 Hz, J_2 = 2.4 Hz, 1H), 2.78 (tt, J_1 = 13.2 Hz, J_2 = 3.6 Hz, 1H), 2.97 (t, J = 5 Hz, 1H), 3.69 (s, 3H), 4.23 (t, J_2 = 2.4 Hz, 1H), 4.49 (d, J = 5 Hz, 1H), 4.69 (s, 1H), 4.72 (s, 1H), 4.80 (s, 1H), 5.0 (s, 1H); ^{13}C NMR ($CDCl_3$) δ −5.5 (CH_3), −5.4 (CH_3), 18.0 (C), 20.7 (CH_3), 25.6 ($3CH_3$), 34.0 (CH), 34.5 (CH_2), 39.5 (CH_2), 44.7 (CH), 51.6 (CH_3), 71.1 (CH), 77.9 (CH), 109.1 (CH_2), 116.3 (CH_2), 146.0 (C), 149.2 (C), 172.2 (*C*O); HRMS (EI) calcd for $C_{19}H_{34}O_4Si$ (M^+) 354.2226, found 354.2216.

(2*R,1′*R**,2′*S**,3′*S**,5′*R**)-2-*tert*-Butyldimethyldimethylsilyloxy-2-[3′-hydroxy-2′-methyl-5′-(2-propenyl)cyclohexyl]acetic acid methyl ester 11c:** R_f = 0.3 (hexane/EtOAc 8:2); IR (neat) ν 3422, 2951, 2859, 1740, 1458, 1260, 1105, 839, 779 cm^{-1}; MS (*EI*) *m*/*z* 356 (M^+, 2), 323 (6), 297 (12), 281 (92), 207 (62), 147 (70), 107 (40), 75 (100); ^{1}H NMR ($CDCl_3$) δ 0.04 (s, 3H), 0.08 (s, 3H), 0.90 (d, J = 7 Hz, 3H), 0.92 (s, 9H), 1.48 (m, 1H), 1.54 (m, 1H), 1.70 (s, 3H), 1.72 (m, 1H), 2.15 (m, 1H), 2.32 (m, 1H), 2.50 (t, J = 5 Hz, 1H), 3.71 (s, 3H), 3.82 (m, 1H), 4.13 (d, J = 6.7 Hz, 1H), 4.75 (s, 1H), 4.83 (s, 1H); ^{13}C NMR ($CDCl_3$) δ −5.4 (CH_3), −5.2 (*C*H_3), 8.5 (CH_3), 18.1 (C), 21.9 (CH_3), 25.7 ($3CH_3$), 29.3 (CH_2), 29.6 (CH_2), 36.0 (CH), 36.2 (CH), 36.9 (CH), 39.9 (CH), 51.6 (CH_3), 69.2 (CH), 75.2 (CH), 110.2 (CH_2), 147.2 (C), 173.8 (CO); HRMS (EI) calcd for $C_{19}H_{36}O_4Si$ (M^+) 356.2383, found 356.2371.

Cp_2TiCl-Promoted Ring-Opening Reaction of Epoxide 12a. (2*R,1′*R**,3′*S**,5′*R**)-2-(5′-Acetoxy-3′-hydroxy-2′-methylenecyclohexyl)-2-*tert*-butyldimethyldimethylsilyloxyacetic acid methyl ester 12b:** R_f = 0.5 (hexane/EtOAc 1:1); IR (neat) ν 2953, 2859, 1738, 1439, 1373, 1246, 1157, 1022, 841, 779, 706 cm^{-1}; MS (EI) *m*/*z* 372 (M^+, 3), 315 (5), 237 (17), 195 (75), 163 (100), 121 (200), 75 (70); ^{1}H NMR ($CDCl_3$) δ 0.07 (s, 3H), 0.12 (s, 3H), 0.93 (s, 9H), 1.74 (m, 1H), 1.86 (m, 3H), 2.03 (s, 3H), 2.97 (m, 1H), 3.68 (s, 3H), 4.27 (t, J = 5.2 Hz, 1H), 4.36 (d, J = 3.8 Hz, 1H), 4.99 (s, 1H), 5.09 (s, 1H), 5.35 (m, 1H); ^{13}C NMR ($CDCl_3$) δ −5.5 (CH_3), −5.3 (CH_3), 18.2 (C), 21.2 (CH_3), 25.6 ($3CH_3$), 34.9 (CH_2), 40.1 (CH_2), 43.1 (CH), 51.7 (CH_3), 67.9 (CH), 69.9 (CH), 75.8 (CH), 111.5 (CH_2), 146.1 (C), 170.2 (CO), 172.5 (CO). Anal. Calcd for $C_{18}H_{32}O_6Si$: C, 58.03; H, 8.66. Found: C, 58.22; H, 8.81.

(2*R,1′*R**,2′*S**,3′*S**,5′*R**)-2-(5′-Acetoxy-3′-hydroxy-2′-methylcyclohexyl)-2-*tert*-butyldimethyldimethylsilyloxyacetic acid methyl ester 12c:** R_f = 0.3 (hexane/EtOAc 3:1); IR (neat) ν 3478, 2953, 2859, 1738, 1250, 839, 779 cm^{-1}; MS (*EI*) *m*/*z* 374 (M^+, 2), 315 (15), 299 (40), 239 (70), 165 (90), 133 (35), 75 (100); ^{1}H NMR ($CDCl_3$) δ 0.03 (s, 3H), 0.05 (s, 3H), 0.90 (d, J = 7 Hz, 3H), 0.91 (s, 9H), 1.36 (m, 1H), 1.57−1.65 (m, 2H), 1.84 (m, 1H), 2.02 (s, 3H), 2.23 (m, 2H), 3.72 (s, 3H), 4.00 (m, 1H), 4.08 (d, J = 7 Hz, 1H), 5.15 (m, 1H); ^{13}C NMR ($CDCl_3$) δ −5.4 (CH_3), −5.1 (CH_3), 5.0 (CH_3), 18.1 (C), 21.2 (CH_3), 25.6 ($3CH_3$), 26.3 (CH_2), 32.6 (CH_2), 34.8 (CH), 38.6 (CH), 51.7 (CH_3), 68.5 (CH), 69.5 (CH), 74.5 (CH), 170.2 (CO), 173.5 (CO). Anal. Calcd for $C_{18}H_{34}O_6Si$: C, 57.72; H, 9.15. Found: C, 57.98; H, 9.27.

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Supporting Information Available: Experimental procedures for the preparation of the epoxides **2a**−**5a**, **11a**, and **12a** and the intermediates **13**−**16**, **17a**,**b**, **18**, **20**, and **21**; spectroscopic data (^{1}H NMR and ^{13}C NMR) of compounds **1a**−**12a**, **1b**−**12b**, **1c**−**6c**, **9c**, **11c**, and **12c**, and intermediates **13**−**21**; NOE or ROESY experiments for **2c**, **4c**, **5c**, **6c**, **9c**, **11c**, **12c**, and **20**; ORTEP diagram and tables of the crystal data, bond lengths, angles, atomic coordinates, and anisotropic thermal parameters obtained for the tricyclic lactone **3c**. This material is available free of charge via the Internet at http://pubs.acs.org.

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