Two-Directional Synthesis of Polycyclopropanes. An Approach to the Quinquecyclopropane Fragment of U-106305

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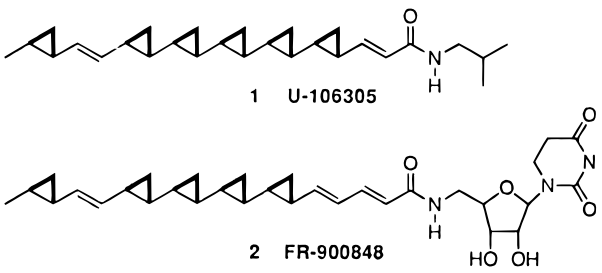
The stereoselective preparation of three stereoisomeric tercyclopropanes and a quinquecyclopropane was investigated. Two of the tercyclopropanes were C_2-symmetric and were prepared efficiently through the two-directional application of Charette's reagent-stereocontrolled cyclopropanation methodology. The nonsymmetric tercyclopropane was prepared by an iterative one-directional application of the same reagent-mediated cyclopropanation method. It was shown that the reagent-controlled transformations are far more effective for the stereoselective preparation of the tercyclopropanes than are the reactions which rely upon the influence of the substrate stereocenters. A C_2-symmetric quinquecyclopropane, which possesses the repeating trans-syn stereochemistry, was prepared by iterative application of the two-directional strategy.

Interest in the preparation of polycyclopropanes has been stimulated by the recent isolation and structure determination of two unprecedented natural products. While the amide functionalities of the cholesteryl ester transfer protein inhibitor U-106305 (**1**)[1] and the antifungal antibiotic FR-900848 (**2**)[2] demonstrate nature's diversity, the fatty acid side chains of **1** and **2** are remarkably similar. The presence of an additional methylene unit bridging the γ,δ-position of the fatty amide backbone of U-106305 appears to be the only difference between the two side chains. Studies by Barrett and Falck have determined that the polycyclopropane fragment of FR-900848 (**2**) possesses a repeating trans-syn-trans relationship both between and within the vinylogous and contiguous cyclopropanes.[3] Numerous efforts directed toward the preparation of FR-900848 have been reported, including a recent total syntheses.[4] The similar structure of U-106305 suggested that its quinquecyclopropane fragment possessed the same stereochemical relationship. Synthetic approaches directed at U-106305 have been reported, including two recent total syntheses.[5]



Since the possibility exists that the quinquecyclopropane fragment of U-106305 (**1**) is C_2-symmetric, an attractive synthetic approach would utilize a two-directional strategy.[6] Two-directional synthetic approaches have found use in preparative chemistry because they promote the rapid increase in complexity while the number of reactions being performed is minimized. We recently described our efforts to develop an iterative strategy for polycyclopropane preparation in which every possible stereoisomeric combination of cyclopropanes can be synthesized.[7] There is no question that application of this iterative approach to the two-directional synthesis of polycyclopropanes will allow the more rapid preparation of polycyclopropanes.

A similar two-directional strategy was used in the synthetic approach to FR-900848 (**2**) in which an enantiomerically pure bicyclopropane was prepared and homologated in two directions to provide diastereomeric quatercyclopropanes.[5] The relevant two-directional disconnections proposed for our study of U-106305 (**1**) are illustrated in Scheme 1. We anticipated that the C_2-symmetric quinquecyclopropane **3** would be derived from the corresponding tercyclopropane **4**, which in turn would come from the monocyclopropane **5**. The efficiency of this synthetic approach would depend upon the ability to control the stereochemistry in both directions. Previous reports from our laboratory have detailed the unsuccessful stereoselective preparation of polycyclopropanes through one-dimensional substrate-stereocontrolled reactions;[7] thus we anticipated this same difficulty in a two-directional reaction which relied upon substrate-mediated stereocontrol. Although we believed that use of an efficient reagent-mediated stereoselective process would

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(4) (a) Barrett, A. G. M.; Kasdorf, K.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1994**, 1781. (b) Barrett, A. G. M.; Doubleday, W. W.; Tustin, G. J.; White, A. J. P.; Williams, D. J. *Chem. Soc., Chem. Commun.* **1994**, 1783. (c) Armstrong, R. W.; Maurer, K. W. *Tetrahedron Lett.* **1995**, *36*, 357. (d) Barrett, A. G. M.; Tustin, G. J. *J. Chem. Soc., Chem. Commun.* **1995**, 357. (e) Barrett, A. G. M.; Doubleday, W. W.; Kasdorf, K.; Tustin, G. J.; White, A. J. P.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1995**, 407. (f) Barrett, A. G. M.; Kasdorf, K.; White, A. J. P.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1995**, 649. (g) Barrett, A. G. M.; Kasdorf, K. *J. Chem. Soc., Chem. Commun.* **1996**, 325. (h) Barrett, A. G. M.; Kasdorf, K. *J. Am. Chem. Soc.* **1996**, *118*, 11030.

(5) (a) Barrett, A. G. M.; Hamprecht, D.; White, A. J. P.; Williams, D. J. *J. Am. Chem. Soc.* **1996**, *118*, 7863. (b) Charette, A.; Lebel, H. *J. Am. Chem. Soc.* **1996**, *118*, 10327.

(6) (a) Schreiber, S. L. *Chem. Scr.* **1987**, *27*, 563. (b) Poss, C. S.; Schreiber, S. L. *Acc. Chem. Res.* **1994**, *27*, 9.

(7) (a) Theberge, C. R.; Zercher, C. K. *Tetrahedron Lett.* **1994**, *35*, 9181. (b) Theberge, C. R.; Zercher, C. K. *Tetrahedron Lett.* **1995**, *36*, 5495.

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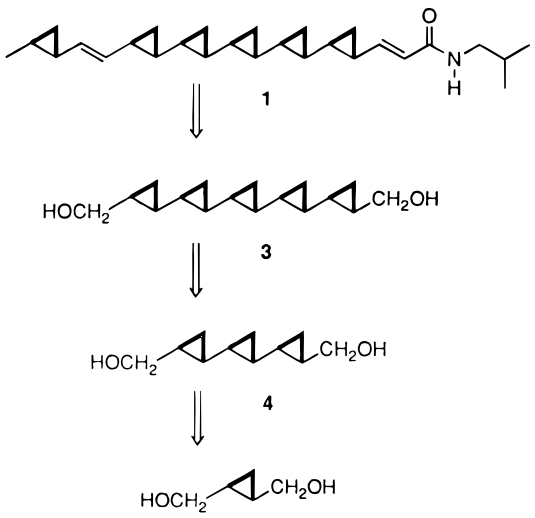
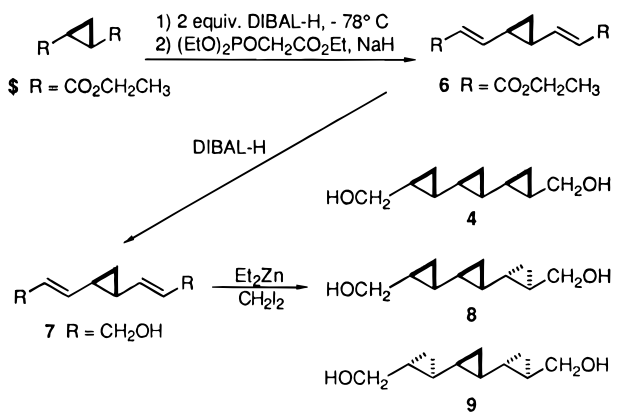
Scheme 1



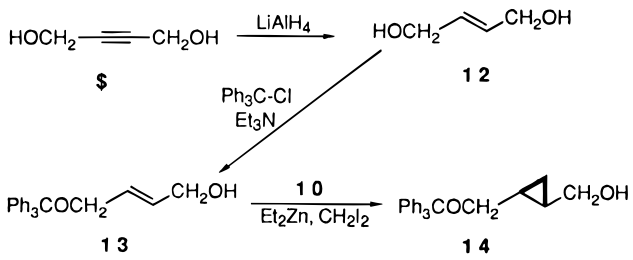
Scheme 2



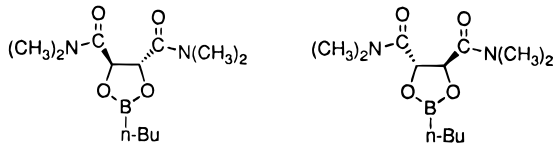
be necessary, we desired to explore the substrate-mediated stereoselectivity of the two-directional process.

Commercially available diethyl *trans*-cyclopropanedicarboxylate was converted to divinylcyclopropane **6** in a one-pot procedure in modest overall yields[8] (Scheme 2). Reduction of the diester to the bis(allylic alcohol) **7** with DIBAL-H proceeded without difficulty and provided the substrate necessary to study the bis-cyclopropanation reaction. Exposure of the bis(allylic alcohol) to diethyl zinc and methylene iodide[9] resulted in the efficient preparation of a mixture of tercyclopropanes **4**, **8**, and **9**.[10] Although the ^{1}H NMR spectrum was quite complicated, it was easy to elucidate from the ^{13}C NMR spectrum that multiple isomers were present. This mixture of products was not totally unexpected and confirmed the expectation that substrate-mediated stereocontrol in the two-directional cyclopropanation reaction would be inefficient.[7] Nevertheless, we learned that stable polycyclopropanes could be prepared in high yield through a two-directional strategy. We turned our attention to the two-directional application of a reagent-mediated stereocontrolled strategy.

Scheme 3



Application of a reagent-controlled two-directional cyclopropanation strategy required access to the optically active monocyclopropane **5** and was anticipated to allow the preparation of the two C_2-symmetric tercyclopropanes **4** and **9**. We anticipated that Charette's enantioselective cyclopropanation methodology,[11] which utilizes stoichiometric amounts of the tartrate-derived chiral dioxaboralanes **10** and **11**, would allow efficient preparation of



the desired optically active monocyclopropane. Although the enantioselective cyclopropanation of diol **12** was expected to proceed efficiently, we protected this diol for a number of reasons. First and foremost, appropriate monoprotection of the diol **12** would decrease water solubility of the corresponding monocyclopropane. Since removal of dioxaboralane **10** or **11** from a primary alcohol requires extensive exposure to aqueous sodium hydroxide, it was expected that the water soluble diol **5**, obtained by direct cyclopropanation of **12**,[12] would be difficult to isolate from the sodium hydroxide solution. Second, monoprotection of **12** would allow us to generate the optically enriched cyclopropane with the expenditure of just 1 equiv of the expensive dioxaboralane. We chose to use the triphenylmethyl (trityl) protecting group due to its hydrophobicity and ability to promote crystallinity. The sensitivity of the triphenylmethyl protecting group to Lewis acidic conditions was a source of diminished yields later in the sequence; however, the overall performance of this protecting group was satisfactory.[13] A single triphenylmethyl group was incorporated, although in low yield, through the use of 1 equiv of triphenylmethyl chloride (Scheme 3). Application of Charette's cyclopropanation methodology resulted in the formation of monocyclopropane **14**[14] which, after recrystallization, was determined to be optically pure by ^{13}C NMR analysis of the Mosher ester.[15]

The triphenylmethyl group was removed with HCl in methanol to provide the optically pure diol **5** (Scheme 4).

(8) Takacs, J. M.; Helle, M. A.; Seely, F. L. *Tetrahedron Lett.* **1986**, *27*, 1257.

(9) (a) Furakawa, J.; Kawabata, N.; Nishimusa, J. *Tetrahedron Lett.* **1966**, 3353. (b) Furukawa, J.; Kawabata, N.; Nishimura, J. *Tetrahedron* **1968**, *24*, 53.

(10) The structures were assigned by comparison to the NMR spectra of **4**, **8**, and **9** prepared subsequently.

(11) (a) Charette, A. B.; Juteau, H. *J. Am. Chem. Soc.* **1994**, *116*, 2651. (b) Charette, A. B.; Prescott, S.; Brochu, C. *J. Org. Chem.* **1995**, *60*, 1081.

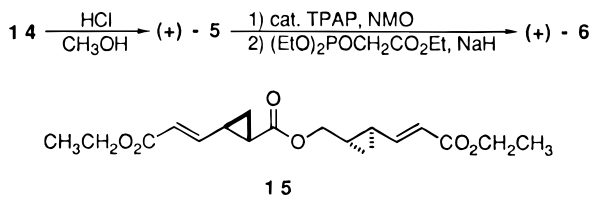
(12) Baumann, H.; Duthaler, R. O. *Helv. Chim. Acta* **1988**, *71*, 1025.

(13) The TBDMS group was also shown to be an effective protecting group, with no difference in ee observed in the cyclopropanation reaction.

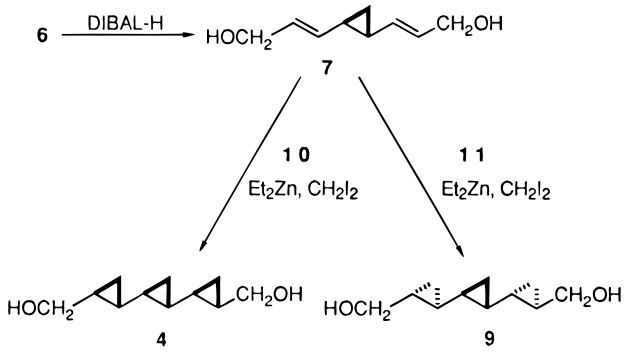
(14) Takahashi, H.; Yoshioka, M.; Ohno, M.; Kobayashi, S. *Tetrahedron Lett.* **1992**, *33*, 2575.

(15) (a) Dale, J. A.; Dull, L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543. (b) Dale, A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512. No signal separation of racemic material was observed in ^{19}F or ^{1}H NMR spectra; however the ^{13}C resonances for two of three cyclopropyl carbons showed base line resolution.

Scheme 4



Scheme 5



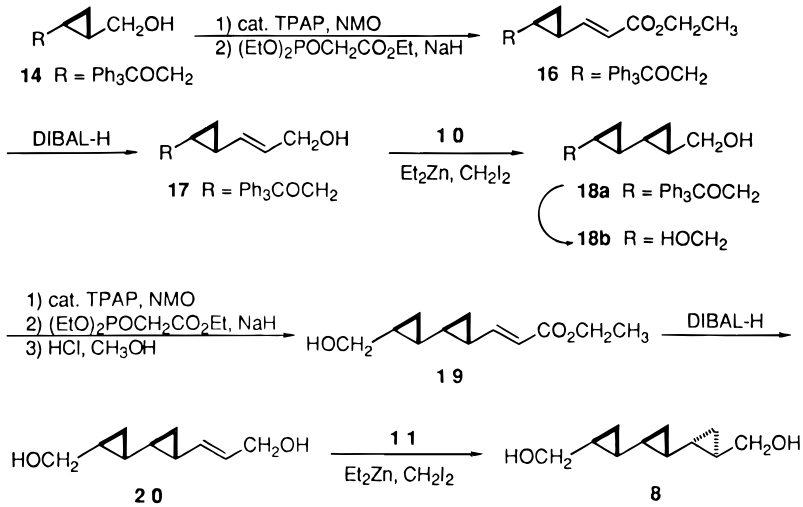
Since it was anticipated that the analogous dialdehyde might be difficult to handle, we decided to couple the oxidation and Horner−Emmons reactions. Diol **5** was exposed to catalytic tetrapropylammonium perruthenate (TPAP) and stoichiometric *N*-methylmorpholine *N*-oxide (NMO).[16] After filtration and evaporation of the solvent, a preformed phosphonate anion was added by cannula. When the Horner−Emmons reaction was quenched within an hour, the overall yield of this two-step two-directional transformation was >75%. If, however, the Horner−Emmons reaction was allowed to stir overnight, the yields were significantly diminished. Decomposition of the purified product **6** upon exposure to catalytic triethylamine demonstrated the base sensitivity of the product.[17] It should also be pointed out that the TPAP oxidation component of the two-part reaction was sensitive to the concentration of diol. When the concentration of **5** was greater than 0.2 M, the coupled reaction sequence resulted in significant amounts of **15**. This byproduct could be eliminated by reducing the concentration of the TPAP oxidation or separated from the target **6** by careful chromatography.

The conversion of the optically active bis α,β-unsaturated ester **6** to the bis(allylic alcohol) **7** was accomplished by treatment with DIBAL-H (Scheme 5). Treatment of **7** with 2 equiv of the L-tartrate-derived dioxaboralane **10** and excess zinc carbenoid resulted in the formation of the syn-syn tercyclopropane **4**. Utilization of the enantiomeric dioxaboralane **11** resulted in the formation of the isomeric anti-anti tercyclopropane **9**. Inspection of the representative ^{13}C NMR spectra indicated that both **4** and **9** were C_2-symmetric; however confirmation of the stereochemistry necessitated correlation with a symmetric tercyclopropane prepared through a one-directional approach (vida infra).

In order to assign with confidence the stereoselectivity of the substrate-stereocontrolled reaction (Scheme 1), the preparation of the third tercyclopropane isomer **8** was necessary. We felt the challenge of preparing the non-C_2-symmetric tercyclopropane **8** provided a forum for testing our iterative cyclopropanation strategy. The monocyclopropane **14** was oxidized with TPAP/NMO and upon immediate exposure to Horner−Emmons reaction conditions resulted in the production of **16** (Scheme 6). Reduction with DIBAL-H followed by a cyclopropanation reaction mediated by the L-tartrate-derived dioxaboralane **10** provided the bicyclopropane **18**. The diastereoselectivity of this cyclopropanation reaction was often not as efficient;[18] however the presence of the minor (anti) diastereomer in this reaction was not expected to affect the diastereoselective formation of **8**.[19] Application of the one-vessel TPAP/NMO oxidation and Horner−Emmons reaction protocol followed by removal of the triphenylmethyl group with HCl/methanol provided the α,β-unsaturated ester **19**. Reduction of the ester with DIBAL-H generated the cyclopropanation precursor **20**. The non-C_2-symmetric tercyclopropane **8** was generated by exposure of **20** to 2 equiv of dioxaboralane **11** and excess zinc carbenoid. The impressive selectivity observed in the formation of **8**, as demonstrated in the ^{13}C NMR spectrum, indicated that the third cyclopropanation reaction proceeded with outstanding facial selectivity.

Comparison of the ^{13}C NMR spectra of the individually prepared tercyclopropanes **4**, **8**, and **9** indicated that efficient formation of symmetric and nonsymmetric tercyclopropanes through either two-directional or one-directional cyclopropanation procedures was possible (Figure 1). The prediction of stereochemistry in the symmetric tercyclopropanes **4** and **9** relied upon application of the Charette model; however this does not constitute a stereochemical proof. The successful prepa-

Scheme 6



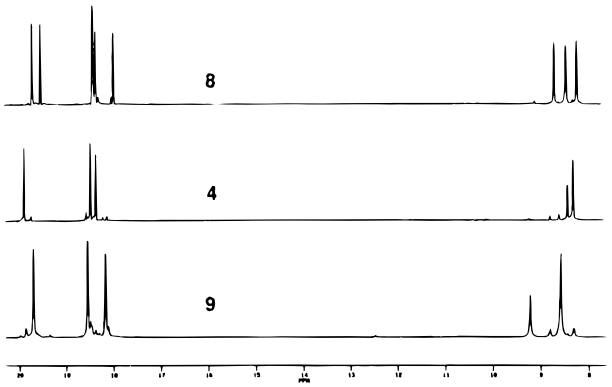
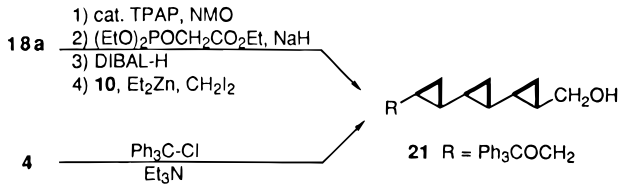


Figure 1. ^{13}C NMR spectral comparison of the cyclopropane region of tercyclopropane isomers **4**, **8**, and **9**.

Scheme 7

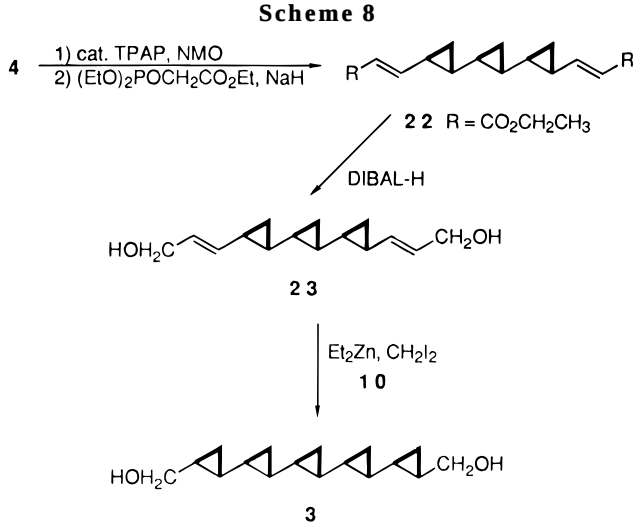


ration of the syn-syn tercyclopropane **4** through a one-directional process confirmed the stereochemical assignment. Pure **18a** was deprotected to provide the *optically active* bicyclopropane **18b**. Whereas the antiisomer would be meso, the enantiomerically pure compound could be assigned the syn stereochemistry. Compound **18a** was homologated, reduced, and converted to a tercyclopropane (**21**) in the presence of dioxaboralane **10** (Scheme 7). This trityl-protected tercyclopropane was identical in all respects to the mono-protection product of the C_2-symmetric tercyclopropane **4**. Therefore, it can be deduced that compound **4** possesses a syn-syn stereochemical relationship.

Furthermore, we were able to compare the ^{13}C NMR spectra of the individual tercyclopropane isomers, **4**, **8**, and **9**, with the ^{13}C NMR spectrum obtained from the nonselective substrate-stereocontrolled two-directional process. Even though we were unable to determine the precise diastereomeric ratios within the reaction mixture due to overlapping ^{13}C NMR resonances, addition of optically active **8** to the mixture of tercyclopropane isomers allowed us to identify that the nonsymmetric isomer **8** was present in the highest concentration. This result was consistent with that found in our previous study where one-directional zinc carbenoid cyclopropanation of vinyl-*trans*-cyclopropanes was unselective (syn:anti 1.0:1.3).[7]

The conversion of C_2-symmetric tercyclopropane **4** into quinquecyclopropane **3** appeared to be possible through application of the same reagent-mediated approach. We exposed **4** to the one-vessel TPAP/NMO oxidation/Horner−Emmons reaction conditions and isolated the bis-

Scheme 8



α,β-unsaturated ester **22** (Scheme 8). The quinquecyclopropane **3** was prepared by DIBAL-H reduction of the diester **22** and a dioxaboralane-mediated two-directional cyclopropanation reaction. The stereoselectivity of this two-directional cyclopropanation reaction, as reflected in the diastereomeric purity of **3**, was further compromised by the presence of slight diastereomeric impurities in the starting tercyclopropane **4**. This result serves as an example of an iterative strategy's limitations, in that stereoselective elaboration of polycyclopropane chains will be inefficient when the starting material is not enantiomerically or diastereomerically pure. We have been unable to effect the separation of the tercyclopropanes **4**, **8**, and **9** by chromatographic methods, including HPLC. Therefore, the preparation of stereoisomerically pure **3** will require the identification of an appropriate purification methodology.[20]

We have successfully demonstrated that two-directional stereoselective cyclopropanation is efficient for the preparation of the symmetric tercyclopropanes. Furthermore, the iterative application of a one-directional cyclopropanation strategy was successful for the diastereoselective preparation of a nonsymmetric tercyclopropane. Further elaboration of these tercyclopropanes to quinquecyclopropanes will require the development of an efficient method for the separation of the stereoisomeric impurities. Efforts directed toward the further elaboration of the tercyclopropanes and the preparation of polycyclopropanated natural products **1** and **2** are presently underway.

Experimental Section

General Methods. Melting points are uncorrected. Unless indicated otherwise, all reagents were commercially available and used without further purification. Tetrahydrofuran (THF), dimethoxyethane (DME), and diethyl ether (Et_2O) were distilled from sodium/benzophenone. Methylene chloride (CH_2Cl_2) was distilled from phosphorus pentoxide, dimethyl formamide (DMF) from calcium hydride, and dimethyl sulfoxide (DMSO) from calcium hydride and stored over 4 Å sieves. All reactions were performed under a nitrogen atmosphere using magnetic stirrers unless indicated otherwise. Thin layer chromatography (TLC) plates supplied by EM (Merck) of silica gel 60 F_{254} at 250 μm thickness were used and were visualized with short-wave UV and anisaldehyde stain. Flash chromatography was conducted according to the procedure of Still and

(16) Ley, S. V.; Norman, J.; Griffith, W. P.; Marsden, S. P. *Synthesis* **1994**, 639.

(17) It is believed that decomposition of **6** was due to the presence of *N*-methylmorpholine, a byproduct of the TPAP/NMO oxidation reaction.

(18) Determined by integration of cyclopropane ^{13}C resonances.

(19) This is based upon the assumption that the third cyclopropanation reaction will proceed efficiently. Even though the diastereoselective formation of the nonsymmetric tercyclopropane isomer **8** would not be negatively affected, the enantiomeric excess of **8** would be reduced.

(20) Subsequent to our work, the successful purification of compounds **3** and **4** through crystallization has been reported. See ref 5.

co-workers[21] using Baker 40 μm flash chromatography silica gel. The term "concentrated under reduced pressure" refers to the use of a rotary evaporator equipped with a water aspirator. All optical rotations were conducted in chloroform solution (unless indicated otherwise) and concentrations are given in g/mL. Low-resolution mass spectrometry was performed by the UNH Instrumentation Center. High-resolution mass spectrometry was performed by the University of California at Riverside Mass Spectrometry Facility.

(±)-*trans*-1,2-Bis[(*E*)-2-(ethoxycarbonyl)ethenyl]cyclopropane (6). Diethyl *trans*-1,2-cyclopropanedicarboxylate (10.0 g, 53.7 mmol) and toluene (50 mL) were cooled to −78 °C under nitrogen. A solution of DIBAL-H (72 mL, 1.5 M in hexanes) was added slowly via syringe pump at a rate of 0.4 mL/min. After the addition was complete, the solution was allowed to stir at −78 °C for an additional 2 h. The triethylphosphonoacetate (29.1 g, 130 mmol) was activated by slowly adding it to an ice-cold suspension of NaH (6.8 g, 50% oil dispersion) in 10 mL of dimethoxyethane. The activated phosphonoacetate was transferred via cannula to the cold solution of reduced cyclopropane. The mixture was stirred at room temperature for 1 h, cooled in an ice bath, and quenched by the slow sequential addition of water, 2 N NaOH solution, and water. Celite was added to the reaction mixture and the solution filtered. The solid residue was washed with ether and ethyl acetate, and the solvents were removed under reduced pressure to provide 12 g of a crude yellow oil. The product was purified by chromatography on silica (3:1 hexanes:ethyl acetate) to give 8.76 g of a white solid (69%). The solid **6** was recrystallized from hot hexane to provide white plates: mp = 72.5−73.5 °C; ^{1}H NMR ($CDCl_3$) δ 6.45 (dd, J = 15.6, 9.3 Hz, 2H), 5.90 (d, J = 15.6 Hz, 2H), 4.15 (q, J = 7.1 Hz, 4H), 1.85 (m, 2H), 1.25 (m, 8H); ^{13}C NMR ($CDCl_3$) δ 166.3, 149.5, 119.9, 60.2, 25.1, 19.0, 14.3. Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.59; H, 7.88.

(±)-*trans*-1,2-Bis[(E)-3-hydroxypropenyl]cyclopropane (7). A solution of (±)-**6** (7.0 g, 30 mmol) in 75 mL of THF was cooled to −78 °C, and DIBAL-H (80 mL, 1.5 M in hexanes) was added dropwise. The mixture was allowed to warm to room temperature and was stirred for 7 h. Celite was added to the mixture, followed by the sequential addition of water (15 mL), 2 N NaOH (15 mL), and water (15 mL). The aluminum salts were removed by filtration and the solvent removed under reduced pressure to give a yellow oil. The oil was purified by chromatography on silica using ethyl acetate as the eluent to give 4.0 g (87%) of a colorless oil: ^{1}H NMR ($CDCl_3$) δ 5.71 (dt, J = 15.3, 6.1 Hz, 2H), 5.28 (dd, J = 15.3, 8.4 Hz, 2H), 4.08 (d, J = 6.1 Hz, 4H), 1.45 (m, 2H), 1.29 (s, 2H), 0.87 (dd, J = 6.8 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 135.1, 127.6, 63.8, 23.5, 15.3; HRMS (CI-NH_3) calcd for $C_9H_{18}O_2N$ (M + NH_4^+) 172.1338, obsd 172.1345.

Mixture of (±)-1,9-Bis(hydroxymethyl)tercyclopropanes 4, 8, and 9. To a solution of Et_2Zn (1.05 mL, 1.05 mmol, 1.0 M in hexanes) in dry CH_2Cl_2 (15 mL) at −5 °C was added CH_2I_2 (0.17 mL, 2.1 mmol) at a rate of 0.2 mL/min, and the solution was allowed to stir at −5 °C for an additional 5 min. At this time 25 mL of an anhydrous CH_2Cl_2 solution containing the bis(allylic alcohol) **7** (65 mg, 0.42 mmol) was added in one portion. The resulting mixture was stirred at room temperature for 2 h. Saturated aqueous NH_4Cl (20 mL) was added, and the product was extracted with Et_2O. The organic extract was stirred over 5 N KOH for 2 h, dried over $MgSO_4$, concentrated under reduced pressure, and purified by flash chromatography using ethyl acetate as the eluent to yield 50 mg (66%) of a mixture of **4**, **8**, and **9** as a clear oil: ^{1}H NMR ($CDCl_3$) δ 3.39 (m, 4H), 1.90 (s, 2H), 0.84 (m, 2H), 0.70 (m, 2H), 0.57 (m, 2H), 0.29 (m, 4H), 0.15 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 67.14, 19.99, 19.85, 19.83, 18.64, 18.52, 18.38, 18.31, 18.17, 9.22, 8.85, 8.70, 8.69, 8.58, 8.40, 8.39.

***(E)*-2-Butene-1,4-diol (12).**[12] A suspension of $LiAlH_4$ (19.4 g, 510 mmol) in THF (380 mL) was cooled to 0 °C in an ice bath. A solution of 2-butyne-1,4-diol (20.0 g, 232 mmol) in THF (20 mL) was added dropwise, and the resulting suspension was refluxed for 18 h. The mixture was cooled, Celite (5 g) was added, and the mixture was carefully hydrolyzed by the addition of a saturated $(NH_4)_2SO_4$ solution (25 mL). Removal of the salts by filtration, washing of the filter cake with Et_2O, and evaporation of the solvent were performed to yield a yellow oil. The oil was purified by vacuum distillation at 111 °C/5 mm (lit. 104 °C/2 mm)[22] (132 °C/13 mm)[23]) to yield 18 g (90%) of **12** as a clear oil: ^{1}H NMR (DMSO-d_6) δ 5.65 (t, J = 1.0 Hz, 2H), 4.65 (t, J = 5.5 Hz, 2H), 3.90 (m, 4H); ^{13}C NMR (DMSO-d_6) δ 129.9, 61.1 ppm.

(E)-1-Hydroxy-4-(triphenylmethoxy)-2-butene (13).[24] A solution of **12** (6.9 g, 78 mmol), triphenylmethyl chloride (19.6 g, 70 mmol), triethylamine (15 mL), and DMAP (0.48 g, 4 mmol) in 50 mL of DMF was stirred at room temperature under nitrogen. After 12 h the yellow cloudy solution was poured into ice−water and extracted with CH_2Cl_2 (3 × 250 mL). The combined organic extracts were washed with saturated aqueous NH_4Cl and water and dried over $MgSO_4$. After removal of the solvent under reduced pressure, the resulting orange oil was purified using flash chromatography on silica (3:1 hexane:EtOAc). Subsequent recrystallization from hot hexane/EtOAc provided 8.5 g (37% yield) of a white crystalline solid identified as **13**: mp = 61−62 °C; ^{1}H NMR ($CDCl_3$) δ 7.66 (m, 6H), 7.30 (m, 6H), 7.22 (m, 3H), 6.01 (dt, J = 15.5, 4.9 Hz, 1H), 5.81 (dt, J = 15.5, 4.6 Hz, 1H), 4.17 (m, 2H), 3.64 (d, J = 4.6 Hz, 2H), 1.39 (3, 1H); ^{13}C NMR ($CDCl_3$) δ 144.1, 130.0, 128.6, 127.8, 127.0, 86.9, 64.0, 63.4 ppm. Anal. Calcd for $C_{23}H_{22}O_2$: C, 83.60; H, 6.71. Found: C, 83.71; H, 6.78.

(+)-(1*S*,3*S*)-1-(Hydroxymethyl)-3-[(triphenylmethoxy)-methyl]cyclopropane (14).[14] To a solution of Et_2Zn (151.3 mL, 151 mmol, 1.0 M in hexane) in anhydrous CH_2Cl_2 (500 mL) at −5 °C was added CH_2I_2 (24.4 mL, 302 mmol) at a rate of 0.2 mL/min during which time a white precipitate formed. A solution of the L-tartrate-derived dioxaboralane **10** (18.0 g, 66 mmol) and **13** (20.0 g, 60 mmol) in anhydrous CH_2Cl_2 (100 mL) was added to the zinc carbenoid in one portion. The resulting mixture was stirred at room temperature for 2 h. Saturated aqueous NH_4Cl (200 mL) was added, and the solution was extracted with Et_2O (2 × 200 mL). The organic extract was stirred over 5 N KOH (200 mL) for 2 h, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was recrystallized from hot hexane to yield 15.9 g (76%) of **14** as colorless needles. A second crop from the mother liquor yielded an additional 2.5 g. Both crops were combined for a total overall yield of 89%: mp = 101−102 C; $[\alpha]^{25}_D$ = +11.8 (c 2.19, $CHCl_3$), lit. enantiomer $[\alpha]^{25}_D$ = −7.4 (reported[14] as 80% ee); ^{1}H NMR ($CDCl_3$) δ 7.45 (m, 6H), 7.25 (m, 9H), 3.50 (m, 2H), 3.05 (dd, J = 9.7, 5.6 Hz, 1H), 2.88 (dd, J = 9.7, 6.4 Hz, 1H), 1.64 (s, 1H), 0.95 (m, 2H), 0.45 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 144.3, 128.7, 127.8, 126.8, 86.4, 66.5, 31.0, 19.6, 17.0, 8.13. Anal. Calcd for $C_{24}H_{24}O_2$: C, 83.69; H, 7.02. Found: C, 83.59; H, 7.04.

(+)-(1*S*,3*S*)-1,3-Bis(hydroxymethyl)cyclopropane (5).[14] In a 250 mL round-bottom flask equipped with a magnetic stirrer, compound **14** (2.5 g, 7.2 mmol) was treated with 20 mL of 1.0 N HCl/MeOH. After the solution was stirred at room temperature for 30 min, the solvent was removed under reduced pressure. The residue was purified using flash chromatography on silica (300:60:1 CH_3OH:$CHCl_3$:AcOH) to yield 615 mg (97%) of **5** as a colorless oil: $[\alpha]^{25}_D$ = +16.1 (c 0.010, EtOH), lit. enantiomer $[\alpha]^{25}_D$ = −12.9 (reported[14] as 80% ee), ^{1}H NMR (DMSO-d_6) δ 4.40 (t, J = 5.6, 2H), 3.25 (m, 2H), 3.19 (m, 2H), 0.79 (m, 2H), 0.29 (dd, J = 6.8, 2H); ^{13}C NMR (DMSO-d_6) δ 64.0, 18.9, 7.7.

(+)-(1*S*,2*S*)-*trans*-1,2-Bis[(E)-2-(ethoxycarbonyl)ethenyl]-cyclopropane (6). A dried three-neck flask was charged with CH_2Cl_2 (80 mL), 4 Å molecular sieves (10 g), compound **5** (1.62 g, 20.6 mmol), and *N*-methylmorpholine *N*-oxide (NMO) (7.30 g, 62.0 mmol). The solution was cooled to 0 °C, and tetrapro-

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pylammonium perruthenate (TPAP) (0.36 g, 1.0 mmol) was added in one portion. The reaction mixture was warmed to room temperature and stirred for 2 h. The reaction was monitored to completion by TLC, and the mixture was filtered through a short pad of silica with CH_2Cl_2. The filtrate was evaporated, and the residual dialdehyde was diluted with THF (40 mL) and stirred under nitrogen. In a separate dry three-neck flask was stirred NaH (60% oil dispersion) (1.81 g, 45.3 mmol) in THF (60 mL). The NaH suspension was cooled to 0 °C, triethyl phosphonoacetate (8.90 mL, 45.3 mmol) was added dropwise, and the solution was allowed to stir for 5 min. The suspension of activated triethyl phosphonoacetate was added in one portion to the dialdehyde. Analysis by TLC indicated that the reaction was complete in less than 5 min. The reaction was immediately quenched with NH_4Cl (100 mL), and the aqueous layer was extracted with ethyl acetate (2 × 50 mL). The combined organic layers were washed with water and brine, dried with $MgSO_4$, filtered, and concentrated. Chromatography on silica (3:1 hexane:EtOAc) and subsequent recrystallization yielded 2.2 g (58%) of **6** as a white solid: mp = 73−74 °C; $[\alpha]^{25}_D = +298$ (*c* 3.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 6.45 (dd, J = 15.6, 9.3 Hz, 2H), 5.90 (d, J = 15.6 Hz, 2H), 4.15 (q, J = 7.1 Hz, 4H), 1.85 (m, 2H), 1.25 (m, 8H); ^{13}C NMR ($CDCl_3$) δ 166.3, 149.5, 119.9, 60.2, 25.1, 19.0, 14.3. Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.16; H, 7.45.

Byproduct from the Coupled TPAP Oxidation/Horner−Emmons Reaction on Compound 5. A minor product (<10%) was isolated from the reaction mixture and was identified as **15**: ^{1}H NMR ($CDCl_3$) δ 6.43 (m, 2H), 5.96 (d, J = 15.4 Hz, 1H), 5.88 (d, J = 15.4 Hz, 1H), 4.18 (q, J = 7.1 Hz, 4H), 4.05 (m, 1H), 3.94 (m, 1H), 2.13 (m, 1H), 1.85 (m, 1H), 1.54 (m, 2H), 1.43 (m, 1H), 1.28 (dd, J = 7.0 Hz, 6H), 1.17 (m, 1H), 0.94 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 172.6, 166.6, 166.3, 151.1, 148.4, 121.3, 119.4, 67.5, 60.5, 60.3, 24.6, 22.9, 21.0, 20.5, 16.7, 14.4, 13.6; EIMS *m*/*z* 336 (M^+), 152, 95, 79, 29.

(+)-(1*S*,2*S*)-*trans*-1,2-Bis[(*E*)-3-hydroxypropenyl]cyclopropane (7). In a dry three-neck flask equipped with a septum and nitrogen inlet was stirred a solution of the diester **6** (1.6 g, 6.8 mmol) in THF (100 mL). The solution was cooled to 0 °C, and DIBAL-H (22.5 mL, 26.5 mmol, 1.5 M in toluene) was added. The reaction mixture was stirred at room temperature for 2 h. Celite was added to the reaction mixture in order to aid filtration, and the mixture was quenched by sequential addition of H_2O (5 mL), 2 N NaOH (10 mL), and H_2O (5 mL). The resulting salts were removed by filtration through Celite, and the solvent was removed under reduced pressure. Chromatography on silica was performed with ethyl acetate as the eluent and yielded 722 mg (69% yield) of **7** as a clear oil: $[\alpha]^{25}_D = +220$ (*c* 0.20, $CHCl_3$); ^{1}H ($CDCl_3$) δ 5.71 (dt, J = 15.3, 6.1 Hz, 2H), 5.28 (dd, J = 15.3, 8.4 Hz, 2H), 4.08 (m, 4H), 1.45 (m, 2H), 1.32 (m, 2H), 0.87 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 135.1, 127.6, 63.8, 23.5, 15.3; CI-MS *m*/*e* 154, 137, 119, 109, 93; HRMS (CI-NH_3) calcd for $C_9H_{18}O_2N$ ($M + NH_4^+$) 172.1338, obsd 172.1345.

(1*S*,3*R*,4*S*,6*S*,7*R*,9*S*)-1,9-Bis(hydroxymethyl)tercyclopropane (4). To a solution of Et_2Zn (23.4 mL, 23.4 mmol, 1.0 M in hexanes) in 500 mL of dry CH_2Cl_2 at −5 °C was added CH_2I_2 (3.8 mL, 46.8 mmol) at a rate of 0.2 mL/min. The solution was stirred at −5 °C, and an anhydrous CH_2Cl_2 solution (50 mL) which contains the L-tartrate-derived dioxaboralane **10** (2.8 g, 10.3 mmol) and the bis(allylic alcohol) **7** (0.72 g, 4.7 mmol) was added in one portion. The resulting mixture was stirred at room temperature for 2 h. Saturated aqueous NH_4Cl (250 mL) was added, and the product was extracted with Et_2O. The organic extract was stirred over 5 N KOH for 2 h, dried over $MgSO_4$, concentrated under reduced pressure, and purified by flash chromatography on silica using ethyl acetate as the eluent to yield 708 mg (83% yield) of **4** as a clear oil: $[\alpha]^{25}_D = +191.7$ (*c* 0.65, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 3.40 (d, J = 6.8 Hz, 4H), 1.49 (s, 2H), 0.83 (m, 2H), 0.72 (m, 2H), 0.60 (m, 2H), 0.28 (m, 4H), 0.15 (dd, J = 6.8 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 66.98, 19.88, 18.48, 18.38, 8.45, 8.32; CIMS (NH_3) *m*/*e* 165, 147, 133, 123; HRMS (CI-NH_3) calcd for $C_{11}H_{22}O_2N$ ($M + NH_4^+$) 200.1650, obsd 200.1659.

(1*R*,3*S*,4*S*,6*S*,7*S*,9*R*)-1,9-Bis(hydroxymethyl)tercyclopropane (9). To a solution of Et_2Zn (4.53 mL, 4.5 mmol, 1.0 M in hexanes) in 75 mL of dry CH_2Cl_2 at −5 °C was added CH_2I_2 (0.73 mL, 9.1 mmol) at a rate of 0.2 mL/min. After the mixture was stirred for an additional 5 min, 35 mL of an anhydrous CH_2Cl_2 solution which contained the D-tartrate-derived dioxaboralane **11** (0.49 g, 1.8 mmol) and the bis(allylic alcohol) **7** (65 mg, 0.82 mmol) was added in one portion. The resulting mixture was stirred at room temperature for 2 h. Saturated aqueous NH_4Cl (50 mL) was added, and the product was extracted with Et_2O. The organic extract was stirred over 5 N KOH for 2 h, dried over $MgSO_4$, and concentrated under reduced pressure. Purification of the oil by chromatography on silica using ethyl acetate as the eluent yielded 42 mg (65% yield) of **9** as a clear oil: $[\alpha]^{25}_D = +113.2$ (*c* 0.042, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 3.39 (d, J = 6.9 Hz, 4H), 1.90 (s, 2H), 0.84 (m, 2H), 0.70 (m, 2H), 0.57 (m, 2H), 0.29 (m, 4H), 0.15 (dd, J = 4.9 Hz, 2H); ^{13}C ($CDCl_3$) δ 66.93, 19.70, 18.55, 18.17, 9.22, 8.58 (major isomer); CIMS (NH_3) *m*/*e* 165, 147, 133, 123, 105, 99; HRMS (CI-NH_3) calcd for $C_{11}H_{22}O_2N$ ($M + NH_4^+$) 200.1650, obsd 200.1646.

(+)-(1*R*,2*S*)-1-[(2-Ethoxycarbonyl)ethenyl]-2-[(triphenylmethoxy)methyl]cyclopropane (16). A dry three-neck round-bottom flask was charged with CH_2Cl_2 (100 mL), oven-dried molecular sieves (30 g), **14** (4.6 g, 14 mmol), and NMO (1.74 g, 15 mmol). The solution was cooled to 0 °C, and a catalytic amount of TPAP (0.24 g, 0.67 mmol) was added. The reaction mixture was stirred at room temperature for 2 h. The reaction mixture was filtered through a short pad of silica with CH_2Cl_2. The filtrate was evaporated, and the residual aldehyde was diluted with THF (50 mL) and stirred under nitrogen. In a separate dry three-neck flask equipped with a septum and nitrogen inlet was stirred NaH (0.89 g, 15 mmol, 60% dispersion) in 50 mL of THF. The suspension was cooled to 0 °C, triethyl phosphonoacetate (2.94 mL, 15 mmol) was added dropwise, and the solution was allowed to stir for 5 min. The suspension of activated triethyl phosphonoacetate was added in one portion to the aldehyde. Analysis by TLC indicated that the reaction was complete within 5 min. The reaction was immediately quenched with saturated aqueous NH_4Cl (50 mL), and the aqueous layer was extracted with EtOAc (2 × 100 mL). The combined organic solutions were washed successively with water and brine, dried with $MgSO_4$, filtered, and concentrated. Chromatography on silica (3:1 hexane:EtOAc) afforded 4.15 g (75% yield) of **16** as a colorless semisolid: $[\alpha]^{25}_D = +88$ (*c* 0.40, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.44 (m, 6H), 7.27 (m, 9H), 6.50 (dd, J = 15.4, 9.9 Hz, 1H), 5.85 (d, J = 15.4 Hz, 1H), 4.17 (q, J = 7.1 Hz, 2H), 3.03 (m, 2H), 1.44 (m, 1H), 1.39 (m, 1H), 1.29 (t, J = 7.1 Hz, 3H), 0.86 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 166.7, 152.5, 144.1, 128.6, 127.7, 126.9, 118.4, 86.4, 65.9, 60.0, 22.5, 20.0, 14.3, 13.5; MS (FAB) *m*/*e* 413, 387, 271, 255, 243, 176, 165; HRMS (FAB-MNa^+) calcd for $C_{28}H_{29}O_3$ ($M + H^+$) 413.2117, obsd 413.2105. Anal. Calcd for $C_{28}H_{28}O_3$: C, 81.52; H, 6.84. Found: C, 81.21; H, 7.11.

(+)-(1*R*,2*S*)-1-[(*E*)-3-Hydroxypropenyl]-2-[(triphenylmethoxy)methyl]cyclopropane (17). A dried three-neck flask was charged with THF (50 mL) and ester **16** (4.05 g, 10 mmol). The solution was cooled in an ice bath, DIBAL-H (13.76 mL, 21 mmol, 1.5 M in hexane) was added slowly, and the solution was allowed to stir at room temperature for 4 h. The reaction mixture was quenched by sequential addition of H_2O (0.5 mL), 2 N NaOH (1.0 mL), and H_2O (0.5 mL). The inorganic salts were removed by filtration through Celite. The resulting filtrate was concentrated under reduced pressure, and the resultant oil was purified by chromatography on silica (3:1 hexane:EtOAc) to afford 2.5 g (70% yield) of **17** as a colorless oil: $[\alpha]^{25}_D = +47.2$ (*c* 0.57, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.44 (m, 6H), 7.27 (m, 9H), 5.69 (dt, J = 15.3, 6.1 Hz, 1H), 5.31 (dd, J = 15.3, 8.7 Hz, 1H), 4.10 (m, 2H), 3.02 (m, 1H), 2.97 (m, 1H), 1.55 (s, 1H), 1.24 (m, 1H), 1.15 (m, 1H), 0.65 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 153.2, 144.3, 135.9, 128.6, 127.7, 126.9, 86.2, 66.6, 63.6, 20.6, 19.1, 11.9; MS (FAB) *m*/*e* 293, 259, 243, 215, 183, 165; HRMS (FAB-MNa^+) calcd for $C_{26}H_{22}O_2Na$ ($M + Na^+$) 393.1830, obsd 393.1833.

(1*S*,3*R*,4*R*,6*S*)-1-(Hydroxymethyl)-6-[(triphenylmethoxy)methyl]bicyclopropane (18a). To a solution of Et_2Zn (12.4 mL, 12.4 mmol, 1.0 M in hexane) in dry CH_2Cl_2 (50 mL) at −5 °C was added CH_2I_2 (2.0 mL, 24.8 mmol) at a rate of 0.2 mL/min. The mixture was stirred an additional 5 min. A solution of the L-tartrate-derived dioxaboralane **10** (1.6 g, 6.0 mmol) and allylic alcohol **17** (1.84 g, 5.0 mmol) in anhydrous CH_2Cl_2 (25 mL) was added in one portion. The resulting mixture was stirred at room temperature for 2 h. Saturated aqueous NH_4Cl (50 mL) was added, and the mixture was extracted with Et_2O (2 × 50 mL). The organic extract was stirred over 5 N KOH (50 mL) for 2 h, dried over $MgSO_4$, and concentrated under reduced pressure. Chromatography on silica (3:1 hexane:EtOAc) afforded 1.49 g (78% yield) of **18a** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.44 (m, 6H), 7.27 (m, 9H), 3.41 (m, 2H), 2.93 (dd, J = 9.6, 6.3 Hz, 1H), 2.87 (dd, J = 9.6, 6.9 Hz, 1H), 0.76 (m, 4H), 0.30 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 144.3, 128.6, 127.6, 126.8, 86.0, 67.3, 66.5, 19.6, 18.2, 17.8, 17.0, 8.24, 8.17 (major isomer); MS (FAB) *m/e* 329, 259, 243, 183, 176, 165; HRMS (FAB-MNa$^+$) calcd for $C_{27}H_{28}O_2Na$ (M + Na$^+$) 407.1987, obsd 407.1996.

(1*S*,3*R*,4*R*,6*S*)-1,6-Bis(hydroxymethyl)bicyclopropane (18b). The triphenylmethyl group was removed by dissolving the oil in a saturated solution of HCl in MeOH. The methanol was removed under reduced pressure, and the residue was filtered through a plug of silica to yield 283 mg of a colorless oil (**18**): $[\alpha]^{25}_D$ = +55.4 (*c* 0.007, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 3.49 (m, 2H), 3.37 (m, 2H), 2.45 (bs, 2H), 0.92 (m, 2H), 0.73 (m, 2H), 0.33 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 66.8, 19.9, 18.3, 8.32.

(1*S*,3*S*,4*R*,6*S*)-1-[(E)-2-(Ethoxycarbonyl)ethenyl]-6-(hydroxymethyl)bicyclopropane (19). A dry three-neck flask was charged with CH_2Cl_2 (50 mL), oven-dried molecular sieves (10 g), compound **18** (1.45 g, 3.8 mmol), and NMO (0.45 g, 3.8 mmol). The solution was cooled to 0 °C, and TPAP (67 mg, 0.19 mmol) was added in one portion. The reaction mixture was warmed to room temperature and stirred for 2 h. The reaction mixture was filtered through a short pad of silica with CH_2Cl_2, and the filtrate was evaporated. The residual aldehyde was diluted with THF (50 mL) and stirred under nitrogen. In a separate dry three-neck flask equipped with septum and nitrogen inlet was stirred NaH (0.23 g, 3.8 mmol, 60% dispersion) in THF (25 mL). The suspension was cooled to 0 °C, and triethyl phosphonoacetate (0.75 mL, 3.8 mmol) was added dropwise. After the solution was allowed to stir for 5 min, the suspension of activated triethyl phosphonoacetate was added in one portion to the aldehyde. Analysis by TLC indicated that the reaction was complete in less than 5 min. The reaction was immediately quenched with saturated aqueous NH_4Cl (25 mL) and the aqueous layer extracted with EtOAc (2 × 50 mL). The combined organic layers were washed sequentially with water and brine, dried with $MgSO_4$, filtered, and concentrated. Chromatography on silica (3:1 hexane: EtOAc) afforded 1.2 g (72% yield) of an oil believed to be the triphenylmethyl-protected bicyclopropane. The triphenylmethyl group was removed by dissolving the oil in a saturated solution of HCl in MeOH. The methanol was removed under reduced pressure, and the residue was filtered through a plug of silica to yield 283 mg of a colorless oil (**19**): ^{1}H NMR ($CDCl_3$) δ 6.47 (dd, J = 15.4, 10.0 Hz, 1H), 5.84 (d, J = 15.4 Hz, 1H), 4.18 (q, J = 7.2 Hz, 2H), 3.45 (m, 2H), 1.59 (s, 1H), 1.32 (m, 1H), 1.26 (t, J = 7.2 Hz, 3H), 1.16 (m, 1H), 0.92 (m, 1H), 0.83 (m, 1H), 0.76 (m, 2H), 0.39 (dd, J = 6.4, 7.4 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 167.0, 153.0, 118.2, 66.8, 60.3, 24.3, 20.8, 20.1, 18.0, 14.5, 14.0, 7.9.

(1*S*,3*R*,4*S*,6*S*)-1-(Hydroxymethyl)-6-(3-hydroxypropenyl)bicyclopropane (20). A dry three-neck flask was charged with THF (50 mL) and the α,β-unsaturated ester **19** (283 mg, 1.4 mmol). The solution was cooled in an ice bath, and DIBAL-H (1.79 mL, 2.7 mmol, 1.5 M in hexane) was added slowly. The solution was allowed to stir at room temperature for 4 h at which time the reaction mixture was quenched by sequential addition of H_2O (0.2 mL), 2 N NaOH (0.4 mL), and H_2O (0.2 mL). The inorganic salts were removed by filtration over Celite. The filtrate was concentrated under reduced pressure, and the resulting oil was purified using chromatography on silica with ethyl acetate to afford 123 mg (60% yield) of **20** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 5.66 (dt, J = 15.1, 6.1 Hz, 1H), 5.24 (dd, J = 15.1, 8.8 Hz, 1H), 4.06 (d, J = 6.1 Hz, 2H), 3.43 (m, 2H), 1.57 (s, 2H), 1.19 (m, 1H), 0.90 (m, 2H), 0.79 (m, 1H), 0.51 (m, 2H), 0.35 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 136.3, 126.3, 66.7, 63.6, 21.9, 20.02, 19.97, 18.0, 11.8, 7.8.

(1*S*,3*R*,4*S*,6*S*,7*S*,9*R*)-1,9-Bis(hydroxymethyl)tercyclopropane (8). To a solution of Et_2Zn (7.34 mL, 7.3 mmol, 1.0 M in hexane) in dry CH_2Cl_2 (50 mL) at −5 °C was added CH_2I_2 (1.2 mL, 14.6 mmol) at a rate of 0.2 mL/min. The mixture was stirred at −5 °C for an additional 5 min. A solution of the D-tartrate-derived dioxaboralane **11** (475 mg, 1.8 mmol) and allylic alcohol **20** (1.84 g, 5.0 mmol) in 25 mL of anhydrous CH_2Cl_2 was added in one portion. The resulting mixture was stirred at room temperature for 2 h. Saturated aqueous NH_4Cl (25 mL) was added, and the product was extracted with diethyl ether. The organic extract was stirred over 5 N KOH (50 mL) for 2 h, dried over $MgSO_4$, and concentrated under reduced pressure. Chromatography on silica with ethyl acetate afforded 85 mg (70% yield) of **8** as a colorless oil: $[\alpha]^{25}_D$ = +58.8 (*c* 0.025, $CHCl_3$) (estimated from 75% diastereomeric excess of **18** to be 75% ee); ^{1}H NMR ($CDCl_3$) δ 3.40 (m, 4H), 2.6 (s, 2H), 0.85 (m, 2H), 0.73 (m, 2H), 0.69 (m, 2H), 0.28 (m, 4H), 0.18 (m, 2H): ^{13}C NMR ($CDCl_3$) δ 66.69, 19.73, 19.55, 18.44, 18.38, 17.99, 8.72, 8.48, 8.25 (major isomer); CIMS (NH_3) *m/e* 165, 147, 133, 123; HRMS (CI-NH_3^+) calcd for $C_{11}H_{22}O_2N$ (M + NH_4^+) 200.1650, obsd 200.1647.

(1*S*,3*R*,4*S*,6*S*,7*R*,9*S*)-1-[(Triphenylmethoxy)methyl]-9-(hydroxymethyl)tercyclopropane (21). To a CH_2Cl_2 solution of compound **18a** (600 mg, 1.56 mmol) were added NMO (550 mg, 4.68 mmol), molecular sieves (750 mg), and a catalytic portion of TPAP. After stirring under nitrogen for 2 h, the solution was filtered through silica and evaporated to give a crude oil. The oil was dissolved in THF and added to a THF solution of NaH (138 mg, 3.43 mmol) and triethyl phosphonoacetate (0.62 mL, 3.12 mmol). After 1 h the reaction was quenched with aqueous ammonium chloride, dried with $MgSO_4$, and evaporated to dryness. Column chromatography on silica (10:1 hexane:ethyl acetate) provided 463 mg of a oily product which was immediately dissolved in THF. The solution was cooled to 0 °C, DIBAL-H (3.2 mL of a 1.0 M solution, 3.2 mmol) added dropwise, and the solution stirred for 3 h. The reaction was quenched with water and aqueous NaOH and stirred overnight. The organic solution was separated, dried over $MgSO_4$, and purified on silica (1:1 hexane:ethyl ether). The product (340 mg) isolated from this silica column and compound **10** (450 mg, 1.66 mmol) were dissolved in 10 mL of CH_2Cl_2. Into a separate vessel which contained a solution of Et_2Zn (1.7 mL, 1.7 mmol, 1.0 M in hexanes) and 10 mL of dry CH_2Cl_2 at −5 °C was added CH_2I_2 (0.27 mL, 3.31 mmol) at a rate of 0.2 mL/min. The solution was stirred at −5 °C, and the anhydrous CH_2Cl_2 solution which contained compound **10** and the allylic alcohol was added in one portion. The resulting mixture was stirred at room temperature for 2 h. Saturated aqueous NH_4Cl was added, and the product was extracted with Et_2O. The organic extract was stirred with 5 N KOH overnight, dried with $MgSO_4$, and concentrated under reduced pressure. Purification by chromatography on silica provided 151 mg of **21** as a clear oil: $[\alpha]^{25}_D$ = +191.7 (*c* 0.65, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.46 (m, 6H), 7.30 (m, 9H), 3.44 (m, 2H), 2.94 (m, 1H), 2.84 (m, 1H), 1.22 (bs, 1H), 0.50−0.90 (m, 6H), 0.20 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 144.5, 128.7, 127.7, 126.8, 86.0, 67.4, 67.0, 19.8, 18.41, 18.39, 18.30, 18.05, 16.96, 8.43, 8.32, 8.26.

(1*S*,3*R*,4*S*,6*S*,7*R*,9*S*)-1-[(Triphenylmethoxy)methyl]-9-(hydroxymethyl)tercyclopropane (21) from 4. Compound **4** (8.0 mg) was dissolved in 5 mL of dry pyridine. Excess triphenylmethyl chloride was added in small portions and the reaction monitored by TLC. When all of the starting material had been consumed, the solution was diluted with ethyl ether and washed with aqueous sodium bicarbonate. The organic layer was dried with $MgSO_4$ and evaporated to dryness. The monoprotected tercyclopropane **21** was isolated by column chromatography on silica (1:1 hexane:ether). Spectroscopic data were identical to those reported above.

(1*S*,3*R*,4*S*,6*S*,7*R*,9*S*)-1,9-Bis[(*E*)-2-(ethoxycarbonyl)ethenyl]tercyclopropane (22). A dried three-neck flask was charged with CH_2Cl_2 (20 mL), molecular sieves (2 g), compound **4** (708 mg, 3.9 mmol), and NMO (1.37 g, 12 mmol). The solution was cooled to 0 °C, and TPAP (68 mg, 0.2 mmol) was added in one portion. The reaction mixture was warmed to room temperature and stirred for 2 h. The reaction was monitored by TLC and upon apparent completion of the reaction the mixture was filtered through a short pad of silica with CH_2Cl_2. The filtrate was evaporated, and the residual dialdehyde was diluted with THF (10 mL) and stirred under nitrogen. In a separate dry three-neck flask was stirred NaH (340 mg, 8.6 mmol, 60% oil dispersion) in 10 mL of THF. The NaH suspension was cooled to 0 °C, triethyl phosphonoacetate (1.7 mL, 8.6 mmol) was added dropwise, and the solution was allowed to stir for 5 min. The suspension of activated triethyl phosphonoacetate was added in one portion to the dialdehyde. Analysis by TLC indicated that the reaction was complete in less than 5 min. The reaction was quenched with NH_4Cl (20 mL), and the aqueous layer was extracted with EtOAc (2 × 20 mL). The combined organic layers were washed with water and brine, dried with $MgSO_4$, filtered, and concentrated. Chromatography on silica (3:1 hexane:EtOAc) yielded 868 mg (70%) of **22** as a colorless oil: $[\alpha]^{25}_D = +358$ (*c* 0.012, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 6.43 (dd, J = 15.4, 10.0 Hz, 2H), 5.80 (d, J = 15.4 Hz, 2H), 4.14 (q, J = 7.2 Hz, 4H), 1.25 (m, 4H), 1.20 (t, J = 7.2 Hz, 6H), 0.98 (m, 2H), 0.70 (m, 4H), 0.19 (dd, 2H); ^{13}C NMR ($CDCl_3$) δ 153.2, 147.1, 118.0, 60.2, 24.7, 21.3, 19.0, 14.5, 13.9, 7.5; CI-MS *m/e* 319, 290, 273, 243, 234, 159, 112; HRMS (DCI-NH_3) calcd for $C_{19}H_{27}O_4$ (M + H^+) 319.1909, obsd 319.1913.

(1*S*,3*R*,4*S*,6*S*,7*R*,9*S*)-1,9-Bis[(*E*)-3-hydroxypropenyl]tercyclopropane (23). In a dry three-neck flask equipped with a septum and nitrogen inlet was stirred a solution of the diester **22** (862 mg, 2.7 mmol) in 50 mL of THF. The solution was cooled to 0 °C, and DIBAL-H (9.02 mL, 10.8 mmol, 1.5 M in toluene) was added. The reaction mixture was warmed to room temperature and stirred for 2 h. The mixture was quenched by sequential addition of H_2O (5 mL), 2 N NaOH (10 mL), and H_2O (5 mL). The resulting salts were removed by filtration through Celite, and the solvent was removed under reduced pressure. Chromatography on silica was performed with ethyl acetate as the eluent and yielded 600 mg (95% yield) of **23** as a clear oil: $[\alpha]^{25}_D = +200.6$ (*c* 0.24, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 5.65 (dt, J = 15.2, 6.2 Hz, 2H), 5.23 (dd, J = 15.2, 8.8 Hz, 2H), 4.05 (d, J = 6.2 Hz, 4H), 1.26 (br s, 2H), 1.15 (m, 2H), 0.84 (m, 2H), 0.65 (m, 2H), 0.45 (m, 4H), 0.12 (dd, J = 6.9 Hz, 2H); ^{13}C NMR δ 136.94, 136.92, 63.94, 22.43, 20.12, 18.57, 12.01, 7.54; LRMS (EI) 234 (M^+), 203, 155.

(1*S*,3*R*,4*S*,6*R*,7*S*,9*S*,10*R*,12*S*,13*R*,15*S*)-1,15-Bis(hydroxymethyl)quinquecyclopropane (3). To a solution of Et_2Zn (1.06 mL, 1.06 mmol, 1.0 M in hexanes) in dry CH_2Cl_2 (15 mL) at −5 °C was added CH_2I_2 (0.17 mL, 2.13 mmol), and the mixture was stirred at −5 °C for an additional 5 min. At this time 15 mL of an anhydrous CH_2Cl_2 solution which contains the chiral L-tartrate-derived dioxaboralane **10** (254 mg, 0.94 mmol) and the bis(allylic alcohol) **23** (50 mg, 0.21 mmol) was added in one portion. The resulting mixture was stirred at room temperature for 2 h. Saturated aqueous NH_4Cl (15 mL) was added, and the product was extracted with Et_2O (2 × 10 mL). The organic extract was stirred over 5 N KOH (50 mL) for 2 h, dried over $MgSO_4$, and concentrated under reduced pressure. Chromatography on silica using EtOAc as the eluent yielded 45 mg (80%) of a clear oil in which the C_2-symmetric isomer **3** was the major product: $[\alpha]^{25}_D = +208$ (*c* 0.045, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 3.40 (m, 4H), 1.28 (s, 2H), 0.81 (m, 2H), 0.69 (m, 2H), 0.51 (m, 6H), 0.26 (m, 4H), 0.07 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 67.13, 19.92, 18.71, 18.56, 18.48, 18.06, 8.41, 8.37, 8.31; CI-MS *m/e* 255, 221, 173, 136; HRMS (CI-NH_3) calcd for $C_{17}H_{30}NO_2$ (M + NH_4^+) 280.2277, obsd 280.2282.

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Supporting Information Available: ^{1}H NMR spectra of **3**, **4**, **5**, **6**, **7**, **8**, **9**, **14**, **15**, **16**, **17**, **18a**, **18b**, **20**, **21**, **22**, and **23** and ^{13}C NMR spectra of **3**, **4**, **5**, **6**, **7**, **8**, **9**, **14**, **15**, **16**, **17**, **18a**, **18b**, **19**, **20**, **21**, and **23** (34 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of this journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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