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Asymmetric Synthesis of Bicyclopropane Derivatives

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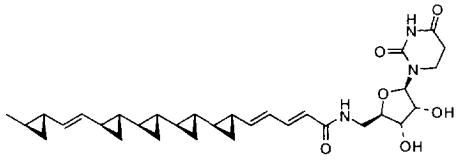
Abstract: Both *syn*- and *anti*-bicyclopropane derivatives have been efficiently prepared with good relative and absolute stereocontrol using reagent controlled asymmetric cyclopropanation reactions. Double Simmons-Smith cyclopropanation of 2,4-dien-1-ols stereoselectively gave the corresponding *anti*-bicyclopropane derivatives. Copyright © 1996 Elsevier Science Ltd

In 1990 Yoshida and coworkers at Fujisawa reported the isolation of FR-900848 from the fermentation broth of *Streptoverticillium fervens*.[1] The structure of this new natural product was established, by extensive NMR spectroscopy and partial degradation, to be the structurally remarkable pentacyclopropane nucleoside **1**. However, the full stereochemistry of FR-900848 (**1**) was only established by the synthesis of model multiple cyclopropane arrays,[2] degradation studies[3] and total synthesis[4] carried in our own laboratories. Falck and coworkers have also recently reported a second total synthesis of FR-900848 (**1**).[5] FR-900848 (**1**) shows potent, selective activity against filamentous fungi such as *Aspergillus niger*, *Mucor rouxianus, Aureobasidium pullulans,* and various *Trichophyton* sp. etc. In contrast it is essentially inactive against non-filamentous fungi including *Candida albicans* and Gram -positive and -negative bacteria. It shows activity *in-vivo* and is not appreciably toxic.[6] FR-900848 (**1**) is closely related to the cholesteryl ester transfer protein inhibitor U-106305 (**2**) from the fermentation broth of *Streptomyces* sp. UC 11136.[7] We have recently fully assigned the stereochemistry of this remarkable fatty amide by total synthesis.[8]



1

2

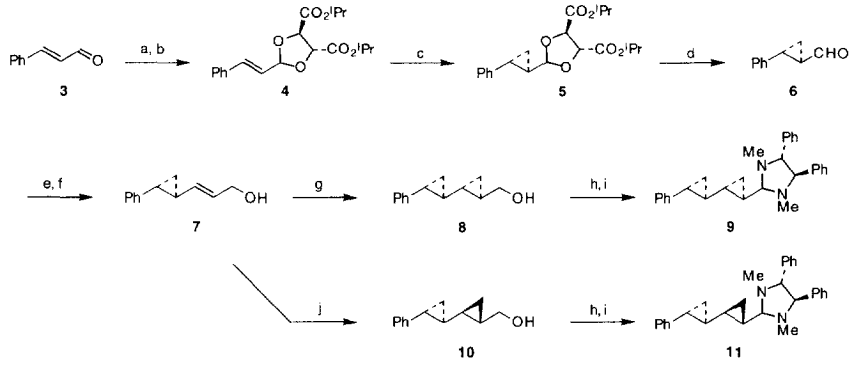
There is an extensive literature on the synthesis and reactions of bicyclopropane arrays. For example, Buchert and Reissig[9] have reported the synthesis of highly substituted bicyclopropanes. In addition, Nijveldt and Vos have carried out an X-ray crystallographic study of bicyclopropane.[10] Prior to the discovery of FR-900848 (**1**), little attention was paid to issues of stereochemistry in bicyclopropane chemistry. Recently, ourselves[11-13] and the Zercher[14,15] and Armstrong[16] groups have independently reported stereoselective methods for the preparation of bicyclopropane systems relevant to the total synthesis of FR-900848 (**1**). All of these approaches have applied known asymmetric Simmons-Smith reactions to control all four stereocentres in the assembly of 1,6-disubstituted bicyclopropanes. Herein we report full experimental

details of the stereoselective synthesis of *syn*- and *anti*- bicyclopropane arrays using Yamamoto[17] and Fujisawa[18] asymmetric cyclopropanation reactions.

Results and Discussion

trans-Cinnamaldehyde **3** was converted, *via* the chiral acetal **4** and Yamamoto asymmetric Simmons-Smith cyclopropanation, into the phenyl-substituted cyclopropyl acetal **5**[17] in good diastereoisomeric excess (>85 %). Separation of the acetal diastereoisomers by chromatography and acid mediated hydrolysis of the major isomer gave the enantiomerically pure cyclopropanecarboxaldehyde derivative **6**. Horner-Emmons homologation and DIBAL-H reduction gave the corresponding *trans*-allylic alcohol **7**. Reaction of allylic alcohol **7** with diethylzinc and diiodomethane in the presence of L(+)-diethyl tartrate according to the Fujisawa protocol[18] afforded both the *syn*- and *anti*- bicyclopropyl derivatives **8** and **10** (72%, 6 : 1) (Scheme 1) as an inseparable mixture of isomers. Alternatively, reaction of allylic alcohol **7** with diethylzinc and diiodomethane in the presence of D(-)-diethyl tartrate gave both bicyclopropanes **8** and **10** (84%, 1 : 6).

SCHEME 1

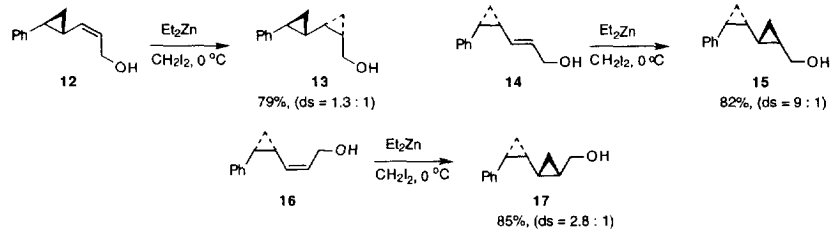


Reagents and conditions: (a) $(EtO)_3CH$, NH_4NO_3, EtOH, 25 °C; (b) L(+)-diisopropyl tartrate, TsOH, PhH, 80 °C; (c) Et_2Zn, CH_2I_2, PhMe, -20 °C; (d) TsOH, H_2O, THF, 60 °C; (e) $(EtO)_2P(O)CH_2CO_2Et$, NaH, THF, 0 °C; (f) DIBAL-H, CH_2Cl_2, -78 °C; (g) L(+)-diethyl tartrate, Et_2Zn, CH_2I_2, $ClCH_2CH_2Cl$, -12 °C; (h) PCC, NaOAc, SiO_2, CH_2Cl_2, 0 °C; (i) (1*R*,2*R*)-*N*,*N*'-dimethyl-1,2-diphenylethanediamine, Et_2O, 4Å sieves, 25 °C; (j) D(-) diethyl tartrate, Et_2Zn, CH_2I_2, $ClCH_2CH_2Cl$, -12 °C.

Again, the mixture of *syn*- **8** and *anti*- **10** isomers could not be separated. Treatment of allylic alcohol **7** with diethylzinc and diiodomethane with the absence of tartrate esters generated compounds **8** and **10** (90%, ~1 : 1) in 82 % yield. All of these experiments were carried out in parallel in the enantiomeric series of bicyclopropanes. In each case the ratio of diastereoisomers **8** and **10** were determined by ^{13}C nmr spectroscopy,[19] HPLC analysis and derivatisation (*vide infra*). It is clear that from these observations the pre-existing cyclopropane ring in alkene **7** has little or no influence on the stereochemical outcome of the second cyclopropanation reaction. Thus, *syn*- or *anti*-bicyclopropanes can be prepared *via* reagent control of stereochemistry. Zercher has observed[14] comparable stereochemical results on the generation of the bicyclopropanes **8** and **10** using Charette asymmetric cyclopropanation reactions.[20,21] In addition, this group has used double Charette asymmetric cyclopropanation chemistry to elaborate various bicyclopropanes with

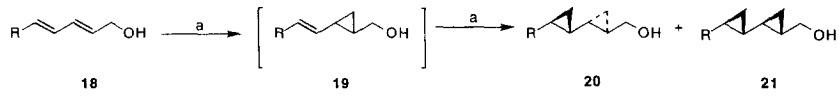
the *cis-trans-* and *cis-cis* ring stereochemistries. During these studies this group noted, in some cases, that the pre-existing cyclopropane ring dramatically influenced the stereochemistry of the second cyclopropanation reaction and representative examples of this chemistry are outlined in Scheme 2.

SCHEME 2



The structural assignments of the *syn-* and *anti-*bicyclopropanes **8** and **10** were established by derivatisation and an X-ray crystallographic study. Thus, PCC oxidation of the mixture of alcohols **8** and **10** (6 : 1) and subsequent condensation with (1*R*,2*R*)-*N*,*N'*-dimethyl-1,2-diphenylethanediamine[22,23] led to the formation of the imidazolidines **9** and **11** (90%, 6 : 1). The ratio of isomers was determined by ^{1}H nmr spectroscopy (500 MHz) and integration of the signals for the *N*-methyl substituents. The major isomer **9** was isolated by fractional recrystallisation from acetone and water and this gave material suitable for single crystal *X*-Ray analysis. The crystal structure of imidazolidine **9**[11] enabled us to determine the relative and absolute stereochemistry of all cyclopropane derivatives in Scheme 1. It is clear from this analysis that, reagent control *via* Fujisawa[18] asymmetric cyclopropanation can be used to prepare the bicyclopropane stereoisomers **8** and **10** selectively.

SCHEME 3



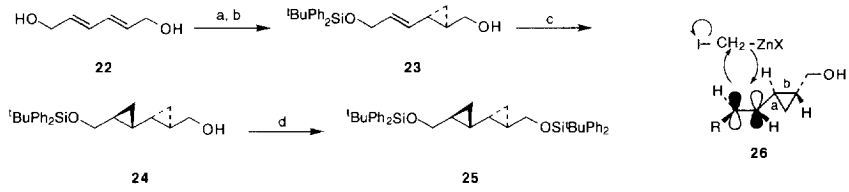
* Structures refer to racemic modifications

Reagents and conditions: (a) Et_2Zn, CH_2I_2, $ClCH_2CH_2Cl$, -20 °C

We next sought to examine the stereochemistry of cyclopropanation of 2-alkenyl-1-cyclopropanemethanol derivatives **19**. In these substrates the hydroxyl group is remote from the alkene residue and such compounds are better probes for any stereoelectronic bias of pre-existing cyclopropane rings on further cyclopropanation reactions. We therefore sought to examine the double cyclopropantion of dienols **18** since hydroxyl direction[24] should result in fast cyclopropanation of Δ^2 and subsequent slower cyclopropanation of Δ^4. The 2,4-dienols **18** were prepared from reaction of the corresponding (*E*)-α,β-unsaturated aldehydes (RCH=CHCHO)[25] with ethyl (diethoxyphosphono)acetate[26] in the presence of sodium hydride and subsequent DIBAL-H reduction.[27] 5-Phenyl-2*E*,4*E*-pentadien-1-ol (**18**, R = Ph) was allowed to react with diethylzinc and diiodomethane in 1,2-dichloroethane at -20 °C to generate the corresponding bicyclopropane derivatives **20** and **21** (Scheme 3). Much to our delight the reaction was shown to proceed in high yield (80%) and with good diastereoselectivity favouring the racemic *anti-*bicyclopropane derivative **20**. The selectivity of the reaction was determined by ^{13}C NMR spectroscopy[19]

and this was consistent with an *anti*- **20** (R = Ph) : *syn*- **21** (R = Ph) isomer ratio of 5 : 1. The cyclopropanation reaction was extended to four further 2,4-dienols **18** (Scheme 3). In each case double cyclopropanation of the 2,4-dienols **18** gave the corresponding racemic bicyclopropanemethanols **20** and **21** in good yields (61-78%). Additionally in each case, the reaction led to the predominant formation of the *anti*-diastereoisomer **20** [**20** : **21** = 5 : 1 (R = Me), 6 : 1 (R = ^{iso}Pr), 7 : 1 (R = c-C_6H_{11}), >95 : 5 (R = ^{t}BuPh$_2$SiOCH$_2$)]. In each case diastereoselectivity of reaction was determined by ^{13}C NMR spectroscopy.[19] In all four cases structural assignment of the major isomer **20** rests on analogy with bicyclopropane **20** (R = Ph). However, in one case **20** (R = ^{t}BuMe$_2$SiOCH$_2$), the assignment of *anti*-stereochemistry was further substantiated by an alternative synthesis and chiroptical analysis (Scheme 4). Thus the mono-cyclopropane derivative **23** ([α]$_D$ = -12.7°) was prepared from diethyl muconate[28] *via* DIBAL-H reduction to (*E,E*)-2,4-hexadiene-1,6-diol, mono-protection (47 %) and asymmetric monocyclopropanation in the presence of L(+)-diethyl tartrate (67 %).[18] Subsequent cyclopropanation of **23** gave the corresponding bicyclopropyl alcohol derivative **24** (79 %; [α]$_D$ = -9.2°). In this experiment, the major non-racemic product **24** was spectroscopically identical with the product derived from the direct double cyclopropanation of dienol **18** (R = ^{t}BuMe$_2$SiOCH$_2$). Finally, t-butyldiphenylsilylation of the alcohol **24** gave the corresponding disilyl ether **25** (82 %; [α]$_D$ = -0.2°). The low optical rotation of this substance is fully in agreement with an assignment of *meso*-stereochemistry.

SCHEME 4



Reagents: (a) t-BuPh$_2$SiCl, imidazole, DMF; (b) Et$_2$Zn, CH$_2$I$_2$, ClCH$_2$CH$_2$Cl, L(+) diethyl tartrate, -20 °C; (c) Et$_2$Zn, CH$_2$I$_2$, ClCH$_2$CH$_2$Cl, -20 °C; (d) t-BuPh$_2$SiCl, imidazole, DMF.

It is necessary to briefly comment on the origin of stereocontrol of the double cyclopropanation reactions in Scheme 3. It is known that cyclopropanation of allylic alcohols proceeds much faster than those of isolated alkenes due to precoordination of the zinc carbenoid to the hydroxyl group prior to methylene transfer.[24] On this basis, it is reasonable to propose that the conversion of the 2,4-dienols **18** into adducts **20** and **21** proceeded *via* the intermediacy of the racemic mono-cyclopropane **19** only. Indeed in several cases the monocyclopropane **19** (R = Ph) was observed in the ^{1}H and ^{13}C nmr spectra of incomplete double cyclopropanation reaction mixtures. Secondly, the monocyclopropanation of the unsaturated allylic ether **23** is fully consistent with the results obtained on the double cyclopropanation of 2,4-dienols **18** (R = ^{t}BuMe$_2$SiOCH$_2$) further supporting the intermediacy of alkene **19** (R = ^{t}BuMe$_2$SiOCH$_2$). It is reasonable to speculate that the alkenes **19** are subject to both steric and stereoelectronic control of the second cyclopropanation step (see diagram **26**). In this analysis, overlap of the most electron rich cyclopropane σ-bond (bond a not bond b) with the alkene π-system should enhance its nucleophilicity and favour *anti*-delivery of the zinc carbenoid electrophile. Additionally, the cyclopropane ring in **26** should shield one face of the π-system thereby biasing the direction of methylene transfer. Fortunately, both these effects are

complimentary. This analysis is also consistent with the enhanced *anti*-stereoselectivity seen with alkene **18** (R = $^{t}BuMe_2SiOCH_2$). In this case, the electron withdrawing ether group should deactivate the alkene thereby emphasising $\sigma \rightarrow \pi^*$ delocalisation.

It is clear from these results that the presence of a cyclopropane ring system has a significant effect upon adjacent cyclopropanation reactions. However this stereoelectronic control may be overwhelmed if the second ring is introduced at a double bond adjacent to a hydroxymethyl substituent.

EXPERIMENTAL

General Methods. All reactions were carried out in an atmosphere of dry nitrogen at room temperature unless otherwise stated. Hexanes refers to bp 40-60 °C redistilled petroleum ether (petrol). The following reaction solvents were purified by distillation: 1,2-dichloroethane ($ClCH_2CH_2Cl$) (CaH_2, N_2), diethyl ether (Et_2O) (Ph_2CO/Na, N_2), water (H_2O), tetrahydrofuran (THF) (Ph_2CO/K, N_2), and toluene (PhMe) (P_2O_5, N_2). The following organic reagents were purified by distillation: diiodomethane (CH_2I_2) (Cu powder, 2 mm Hg), pyridine (CaH_2, 12 mm Hg), triethylamine (Et_3N) (CaH_2, N_2), and all aldehydes. All other organic solvents and reagents were obtained from commercial sources and used without further purification. Organic extracts were dried over magnesium sulfate. Flash chromatography[29] was carried out on Merck or BDH silica gel 60, 230-400 mesh ASTM with eluants given in parenthesis. Involatile oils and solids were vacuum dried at < 2 mm Hg. Analytical thin-layer chromatography (TLC) was performed on Merck precoated silica gel 60 F_{254} plates. Optical rotations were carried out at room temperature in chloroform solution.

Ethyl 3*E*-[(1*S*,2*R*)-2-Phenyl-1-cyclopropyl]prop-1-enoate. Hexane (10 mL) washed NaH (60 % disp.) (600 mg, 14 mmol) and THF (25 mL) were cooled to 0 °C and $(EtO)_2P(O)CH_2CO_2Et$ (3.10 g, 14 mmol) was added dropwise and the mixture was stirred for 1 h. After cooling to -78 °C, aldehyde **6** (2.05 g, 14.0 mmol) in THF (5 mL) was added and the mixture was warmed up to room temperature and quenched with saturated aqueous NH_4Cl (20 mL) and diluted with H_2O (50 mL). The mixture was extracted with Et_2O (2 x 50 mL) and the organic phase washed with H_2O (2 x 50 mL) and brine (2 x 50 mL), dried and filtered. Rotary evaporation and chromatography (hexanes : EtOAc 9 : 1) gave ethyl 3*E*-[(1*S*,2*R*)-2-phenyl-1-cyclopropyl]-prop-1-enoate (2.76 g, 91 %) as a colorless oil: R_f 0.70 (hexanes : EtOAc; 4 : 1); $[\alpha]_D$ -294° (c = 1.0); IR (film) 1713, 1645, 1258 and 1146 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 7.27 (m, 3H), 7.12 (m, 2H), 6.60 (dd, 1H, *J* 15.4, 9.8 Hz), 5.90 (d, 1H, *J* 15.6 Hz), 4.21 (q, 2H, *J* 7.2 Hz), 2.16 (m, 1H), 1.82 (m, 1H), 1.43 (m, 1H), 1.30 (m, 1H), 1.28 (t, 3H, *J* 7.2 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 166.6, 151.5, 140.7, 128.5, 126.2, 125.9, 118.8, 60.1, 26.8, 26.7, 17.7, 14.3; MS (EI) m/z 216 ($M^{+\cdot}$), 143, 97. Anal. calc for $C_{14}H_{16}O_2$: C, 77.70; H, 7.46. Found: C, 77.89; H, 7.17%. Ethyl 3*E*-[(1*R*, 2*S*)-2-phenyl-1-cyclopropyl]-prop-1-enoate (2.56 g, 87 %) was prepared in exactly the same way from the enantiomer of aldehyde **6**: $[\alpha]_D$ +295° (c = 1.0); Found: C, 78.03; H, 7.32%.

3*E*-[(1*S*,2*R*)-2-Phenyl-1-cyclopropyl]-2-propen-1-ol (7). DIBAL-H (1.0 M solution in hexanes) (22.7 mL, 22.7 mmol) was added dropwise to ethyl 3*E*-[(1*S*,2*R*)-2-phenyl-1-cyclopropyl]prop-1-enoate (2.23 g, 10

mmol) in CH_2Cl_2 (20 mL) at -78 °C. After stirring at -78 °C for 1h, the mixture was quenched with saturated aqueous Na_2SO_4 (10 mL), warmed up to room temperature, filtered through Celite (CH_2Cl_2). Rotary evaporation and chromatography (hexanes : EtOAc 4 : 1) gave **7** (1.50 g, 84 %) as a colorless oil: (R_f 0.15 (hexanes : EtOAc 4 : 1) $[\alpha]_D$ -265° (c = 1.83); IR (film) 3360, 1668, 1605, 963 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 7.27-7.01 (m, 5H), 5.70 (1H, dt, *J* 15.4, 5.9 Hz), 5.37 (1H, dd, *J* 15.4, 8.5 Hz), 4.05 (2H, d, *J* 6.0 Hz), 2.07 (1H, br s), 1.93-1.86 (1H, m), 1.69-1.61 (1H, m), 1.18 (1H, dt, *J* 8.5, 5.1 Hz), 1.07 (1H, dt, *J* 8.5, 5.4 Hz); ^{13}C NMR ($CDCl_3$, 75.1 MHz) δ 142.1, 135.0, 128.3, 127.4, 125.6, 63.3, 26.1, 25.2, 16.7; MS (CI, NH_3) *m/z* 192 $(M+NH_4)^+$, 174 $(M+H)^+$, 157, 143, 91; HRMS calc for $C_{12}H_{14}O$: $(M^{+\cdot})$, 174.1045, found: $(M^{+\cdot})$ 174.1045. 3*E*-[(1*R*, 2*S*)-2-Phenyl-1-cyclopropyl]-2-propen-1-ol (1.59 g, 91%) was prepared in exactly the same way from the corresponding ester: $[\alpha]_D$ +245° (c = 1.8); HRMS found: $(M^{+\cdot})$, 174.1014. Anal. calc for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.59; H, 7.98%.

(1R,3*S*,4*S*,6*R*)-1-Hydroxymethyl-6-phenylbicyclopropane (8). Et_2Zn in hexanes (1.0 M; 0.48 mL, 0.48 mmol) was added dropwise with stirring to the allylic alcohol **7** (75 mg, 0.43 mmol) in $ClCH_2CH_2Cl$ (3 mL) at 0 °C. After 0.5 h, *L*(+)-diethyl tartrate (99 mg, 0.48 mmol) in $ClCH_2CH_2Cl$ (1 mL) was added and the reaction mixture was stirred for 1 h, cooled to -12 °C and Et_2Zn (0.89 mL, 0.89 mmol) was added. After 1 h, CH_2I_2 (0.46 g, 0.15 mL, 1.75 mmol) was added and the resulting solution stirred at -12 °C for 12 h, quenched with saturated aqueous NH_4Cl (5 mL), and extracted with Et_2O (2 x 15 mL). The organic phase was washed with 10 % NH_4Cl (15 mL), H_2O (2 x 15 mL), and brine (2 x 15 mL), dried and filtered. Rotary evaporation and chromatography (hexanes : EtOAc 4 : 1) gave **8** admixed with **10** (6 : 1; 58 mg, 72 %) as a colorless oil: R_f 0.20 (hexanes : EtOAc 4 : 1); IR (film) 3360, 2871, 1605, 1499, 1021, 745, 697 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 7.27-7.00 (m, 5H), 3.49-3.42 (m, 2H), 1.74 (br s, 1H), 1.68-1.62 (m, 1H), 1.16-1.08 (m, 1H), 0.98-0.73 (m, 4H), 0.47-0.36 (m, 2H); ^{13}C NMR ($CDCl_3$, 75.1 MHz) δ 143.8, 128.3, 125.6, 125.4, 66.8, 24.4, 22.2, 20.0, 18.6, 14.0, 8.0; MS (CI, NH_3) *m/z* 206 $(M+NH_4)^+$, 188 $(M^{+\cdot})$, 171, 77. Anal. calc. for $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 83.13; H, 8.74 %. (1*S*,3*R*,4*R*,6*S*)-1-Hydroxymethyl-6-phenylbicyclopropane (63 mg, 78 %), prepared from the corresponding allylic alcohol using *D*(-)-diethyl tartrate in the second cyclopropanation step, was obtained as a colorless oil: HRMS (CI, NH_3) calcd for $C_{13}H_{16}O$: $(M+NH_4)^+$, 206.1545; found: $(M+NH_4)^+$, 206.1558

(1*S*,3*R*,4*S*,6*R*)-1-Hydroxymethyl-6-phenylbicyclopropane (10). Reaction of allylic alcohol **7** with *D*(-)-diethyl tartrate, Et_2Zn, and CH_2I_2 as for **8** gave **10** admixed with **8** (6 : 1; 68 mg, 84 %) as a colorless oil: R_f 0.20 (hexanes : EtOAc 4 : 1); IR (film) 3360, 2923, 1605, 1498, 1029, 697 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 7.27-7.00 (m, 5H), 3.5-3.4 (m, 2H), 1.74 (br s, 1H), 1.68-1.62 (m, 1H), 1.16-1.08 (m, 1H), 0.98-0.73 (m, 4H), 0.47-0.36 (m, 2H); ^{13}C NMR ($CDCl_3$, 75.1 MHz) δ 143.3, 128.3, 125.6, 125.4, 66.7, 24.5, 21.9, 19.5, 18.7, 14.5, 8.7; MS (CI, NH_3) *m/z* 206 $(M+NH_4)^+$, 188 $(M^{+\cdot})$, 171, 157, 129. Anal. calcd for $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 83.04; H, 8.70%. (1*R*,3*S*,4*R*,6*S*)-1-Hydroxymethyl-6-phenylbicyclopropane (61 mg, 0.32 mmol, 75 %), prepared from the corresponding allylic alcohol using *L*(+)-diethyl tartrate in the second cyclopropanation step, was obtained as colorless oil: HRMS (CI, NH_3) calcd for $C_{13}H_{16}O$: $(M+NH_4)^+$, 206.1545; found: $(M+NH_4)^+$, 206.1554.

(1*RS*,3*RS*,4*S*,6*R*)-1-Hydroxymethyl-6-phenylbicyclopropane (8/10). Et_2Zn in hexanes (1.0 M; 2.15 mL, 2.15 mmol) was added dropwise with stirring to allylic alcohol **7** (75 mg, 0.43 mmol) in $ClCH_2CH_2Cl$ (3 mL) at -10 °C. After 0.5 h, CH_2I_2 (1.15 g, 0.37 mL, 4.3 mmol) was added, stirring was continued at -10 °C for 12 h, the mixture was quenched with saturated aqueous NH_4Cl (5 mL) and extracted with Et_2O (2 x 5 mL). The organic phase was washed with 10 % NH_4Cl (5 mL), H_2O (2 x 10 mL), and brine (2 x 10 mL), dried and filtered. Rotary evaporation and chromatography (hexanes : EtOAc 4 : 1) gave **8** admixed with **10** (1 : 1; 73 mg, 0.38 mmol, 90 %) as a colorless oil. (1*RS*, 3*RS*, 4*R*, 6*S*)-1-Hydroxymethyl-6-phenylbicyclopropane was prepared from the reaction of the corresponding allylic alcohol with Et_2Zn and CH_2I_2 in exactly the same way.

(4*R*,5*R*)-2-[(1*R*,3*S*,4*S*,6*R*)-6-Phenyl-1-bicyclopropyl]-1,3-dimethyl-4,5-diphenylimidazolidine (9). Pyridinium chlorochromate (119 g, 0.55 mmol), NaOAc (45 mg, 0.55 mmol) and silica gel (200 mg) were added to alcohol **8** admixed with **10** (6 : 1; 69 mg, 0.37 mmol) in CH_2Cl_2 (2 mL) at 0 °C. After 1 h at 0 °C and 1 h at room temperature, the mixture was filtered through silica (CH_2Cl_2) and evaporated to give (1R,3*S*,4*S*,6*R*)-6-phenylbicyclopropane-1-carboxaldehyde (66 mg, 0.37 mmol, 97 %) as a colorless oil. This was dissolved in Et_2O (10 mL) with (1*R*,2*R*)-*N*,*N*'-dimethyl-1,2-diphenylethanediamine (120 mg, 0.5 mmol) and the solution stirred with 4Å molecular sieves for 12 h. H_2O (10 mL) was added and the mixture extracted with Et_2O (2 x 10 mL). The organic phase was washed with H_2O (2 x 10 mL) and brine (2 x 10 mL), dried, and filtered. Rotary evaporation and chromatography (hexanes : EtOAc 9 : 1) gave imidazolidine **9** (139 mg, 0.34 mmol, 90 %) as a white solid: R_f 0.15 (hexanes : EtOAc; 19 : 1); $[\alpha]_D$ -17.6° (c = 1.0); IR (film) 3028, 2995, 2980, 1610, 1494, 1451, 1282, 1164, 1025 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 7.4 - 7.1 (m, 15H), 3.75 (d, 1H, *J* 8.7 Hz), 3.44 (d, 1H, *J* 8.4 Hz), 3.23 (d, 1H, *J* 8.4 Hz), 2.54 (3H, s), 2.38 (3H, s), 1.80 (m, 1H), 1.20 (m, 1H), 1.05 (m, 2H), 0.83 (m, 2H), 0.69 (m, 2H); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 143.5, 139.9, 128.4, 128.2, 128.1, 127.4, 127.3, 125.7, 125.4, 89.3, 78.5, 77.0, 39.4, 36.0, 25.0, 22.6, 19.8, 16.9, 13.2, 7.6; MS (CI, NH_3) *m/z* 409 $(M+H)^+$, 289, 251, 183; HRMS calc for $C_{29}H_{32}N_2$: $(M+H)^+$, 409.2644; found: $(M+H)^+$, 409.2652.

(4*R*,5*R*)-2-[(1*S*,3*R*,4*S*,6*R*)-6-Phenyl-1-bicyclopropyl]-1,3-dimethyl-4,5-diphenylimidazolidine (11). Oxidation of alcohol **10** (176 mg. 0.93 mmol) and condensation with (1*R*,2*R*)-*N*,*N*'-dimethyl-1,2-diphenylethanediamine gave imidazolidine **11** admixed with **9** (6 : 1; 84%) as a colorless oil: R_f 0.15 (hexanes : EtOAc; 19 : 1); ^1H NMR ($CDCl_3$, 270 MHz) δ 7.4-7.2 (m, 15H), 3.69 (d, 1H, *J* 8.5 Hz), 3.38 (d, 1H, *J* 8.5 Hz), 3.16 (d, 1H, *J* 8.5 Hz), 2.47 (3H, s), 2.36 (3H, s), 1.80 (m, 1H), 1.25 (m, 1H), 1.05 (m, 1H), 0.85 (m, 3H), 0.65 (m, 2H); MS (CI, NH_3) *m/z* 409 $(M+H)^+$, 289, 251; HRMS calc for $C_{29}H_{32}N_2$: $(M+H)^+$, 409.2644; found: $(M+H)^+$, 409.2659.

Ethyl (2*E*,4*E*)-5-Phenyl-2,4-pentadienoate. $(EtO)_2P(O)CH_2CO_2Et$ (2 mL, 0.01 mL) was added dropwise to hexane (5 mL) washed NaH (60 % dispersion; 400 mg, 0.01 mol) and THF (5 mL) at °C. After 5 min the mixture was cooled to -78 °C and cinnamaldehyde (1.26 mL, 0.01 mol) was added dropwise, the solution was allowed to warm up to room temperature, and quenched with saturated aqueous NH_4Cl (20 mL). The mixture was extracted with Et_2O (2 x 20 mL) and the organic phase was washed with H_2O (2 x 20 mL) and brine (2 x 20 mL), dried, and filtered. Rotary evaporation and chromatography (hexanes : EtOAc 9 : 1) gave

ethyl (2*E*,4*E*)-5-phenyl-2,4-pentadienoate (1.5 g, 74 %) as a colorless oil: R_f 0.20 (hexanes : EtOAc 19 : 1); IR (film) 3026, 2981, 1707, 1626, 1341, 1314, 1297, 1239, 1133, 1037, 998, 755, 714, 689 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 7.50-7.25 (m, 6H), 6.87 (m, 2H), 5.99 (d, 1H, *J* 15.1 Hz), 4.24 (q, 2H, *J* 7.2 Hz), 1.31 (t, 3H, *J* 7.2); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 167.1, 144.6, 140.4, 136.2, 129.1, 128.9, 127.3, 126.4, 121.5, 60.4, 14.4; MS (EI) *m/z* 202 ($M^{+\cdot}$), 173, 157, 129, 77; HRMS (EI) calcd for $C_{13}H_{14}O_2$: ($M^{+\cdot}$), 202.0994; found: ($M^{+\cdot}$), 202.0999. Anal. calcd for $C_{13}H_{14}O_2$: C, 77.2; H, 6.98. Found: C, 76.96; H, 6.88%.

(2*E*,4*E*)-5-Phenyl-2,4-pentadienol (18, R = Ph). DIBAL-H in hexanes (1.0 M; 13 mL, 13.0 mmol) was added dropwise with stirring to ethyl (2*E*,4*E*)-5-phenyl-2,4-pentadienoate (1.2 g, 6.0 mmol) in CH_2Cl_2 (30 mL) at -78 °C. After 1 h, EtOH (20 mL) and saturated aqueous Na_2SO_4 (10 mL) were added and the mixture was allowed to warm up to room temperature and filtered through Celite (CH_2Cl_2). Evaporation and recrystallization from EtOAc/hexanes gave **18** (R = Ph) (0.91 g, 5.7 mmol, 95 %) as a white solid: mp 57-59 °C; R_f 0.20 (hexanes : EtOAc 4 : 1); IR (film) 3300, 1448, 1085, 981, 742, 690 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 7.4-7.2 (m, 5H), 6.79 (dd, 1H, *J* 15.6, 10.5 Hz), 6.55 (d, 1H, *J* 15.6 Hz), 6.43 (dd, 1H, *J* 15.1, 10.5 Hz), 5.98 (dt, 1H, *J* 15.1, 5.9 Hz), 4.25 (d, 2H, *J* 5.6 Hz), 1.70 (br s, 1H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 137.2, 132.9, 132.6, 131.7, 128.7, 128.2, 127.7, 126.5, 63.5; MS (EI) *m/z* 160 ($M^{+\cdot}$), 131, 104, 91, 77. Anal. calcd for $C_{11}H_{12}O$: C, 82.45; H, 7.56. Found: C, 82.71; H, 7.49%.

(1*SR*,3*RS*,4*SR*,6*RS*)-1-Hydroxymethyl-6-phenylbicyclopropane (20, R = Ph). With stirring Et_2Zn in hexanes (1.0 M; 5 mL, 5 mmol) and CH_2I_2 (0.9 mL, 10 mmol) were added sequentially and dropwise to diene **18** (R = Ph) (80 mg, 0.5 mmol) in $ClCH_2CH_2Cl$ (3 mL) at -12 °C. After 12 h at -12 °C, saturated aqueous NH_4Cl (2mL) was added and the mixture allowed to warm up to room temperature and added to H_2O (20 mL). The mixture was extracted with Et_2O (2 x 20 mL) and the extract washed with saturated aqueous $NaHCO_3$ (2 x 20 mL), H_2O (2 x 20 mL) and brine (2 x 20 mL), dried, and filtered. Rotary evaporation and chromatography (hexanes : EtOAc 4 : 1) gave **20** (R = Ph) admixed with **21** (R = Ph) (5 : 1 by ^{13}C NMR) (75 mg, 80 %) as a viscous oil. The product was identical (TLC, ^1H NMR, ^{13}C NMR, MS) with a sample of **10** prepared from **7**.

Ethyl (2*E*,4*E*)-Hexa-2,4-dienoate. $(EtO)_2P(O)CH_2CO_2Et$ (3.2 g, 2.83 mL, 0.014 mL) was added dropwise to hexane (5 mL) washed NaH (60 % dispersion; 560 mg, 0.014 mol) and THF (5 mL) at °C. After 5 min, the mixture was cooled to -78 °C and crotonaldehyde (1.0 g, 1.18 mL, 0.014 mol) was added dropwise, the solution was allowed to warm up to room temperature, and quenched with saturated aqueous NH_4Cl (20 mL). The mixture was extracted with Et_2O (2 x 20 mL) and the organic phase was washed with H_2O (2 x 20 mL) and brine (2 x 20 mL), dried, and filtered. Rotary evaporation and chromatography (hexanes : EtOAc 9 : 1) gave ethyl (2*E*,4*E*)-hexa-2,4-dienoate (1.17 g, 8.3 mmol, 60 %) as a colorless oil: R_f 0.30 (hexanes : EtOAc 19 : 1); IR (film) 2981, 1712, 1645, 1619, 1327, 1260, 1244, 1188, 1139 999 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 7.26 (dd, 1H, *J* 15.5, 10.5 Hz), 6.15 (m, 2H), 5.74 (d, 1H, *J* 15.5 Hz), 4.16 (q, 2H, *J* 7.1 Hz), 1.82 (d, 3H, *J* 5.1 Hz), 1.26 (t, 3H, *J* 7.1 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 167.4, 144.9, 139.2, 129.9, 119.2, 60.2, 18.6, 14.4; MS (CI, NH_3) *m/z* 158 $(M+NH_4)^+$, 141 $(M+H)^+$, 125, 95; HRMS (CI, NH_3) m/z calcd for $C_8H_{12}O_2$: $(M+H)^+$, 141.0916; found: $(M+H)^+$, 141.0930.

(2*E*,4*E*)-Hexa-2,4-dien-1-ol (18, R = Me). DIBAL-H in hexanes (1.0 M; 15.2 mL, 15.2 mmol) was added dropwise with stirring to ethyl (2*E*,4*E*)-hexa-2,4-dienoate (970 mg, 7.0 mmol) in CH_2Cl_2 (20 mL) at -78 °C. After 1 h, EtOH (20 mL) and saturated aqueous Na_2SO_4 (10 mL) were added sequentially and the mixture was allowed to warm up to room temperature. Filtration through Celite (CH_2Cl_2), rotary evaporation and chromatography (EtOAc : hexanes 1 : 9) gave **18** (R = Me) (620 mg, 6.6 mmol, 94 %) as a colorless oil: R_f 0.21 (hexanes : EtOAc 4 : 1) IR (film) 3500-3300, 2960, 987 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 6.12 (dd, 1H, *J* 15.2, 10.4 Hz), 5.95 (br. dd, 1H, *J* 15.1, 10.4 Hz), 5.62 (m, 2H), 4.05 (d, 2H, *J* 6.0 Hz), 2.04 (br. s, 1H), 1.64 (br. d, 3H, *J* 6.8 Hz); ^{13}C NMR ($CDCl_3$, 75.1 MHz) δ 131.6, 130.8, 129.8, 129.3, 63.1, 18.0; MS (CI, NH_3) *m/z* 98 ($M^{+}\cdot$), 83, 41; HRMS (CI, NH_3) calcd for $C_6H_{10}O$: ($M^{+}\cdot$), 98.0732; found: ($M^{+}\cdot$), 98.0717.

(1*SR*,3*RS*,4*RS*,6*RS*)-1-Hydroxymethyl-6-methylbicyclopropane (20, R = Me). Double cyclopropanation of diene **18** (R = Me) (78 mg, 0.8 mmol) as for diene **18** (R = Ph) using Et_2Zn in hexanes (1.0 M; 8.0 mL) and CH_2I_2 (1.2 mL, 16 mmol) in $ClCH_2CH_2Cl$ (2 mL), work-up and chromatography (hexanes : EtOAc 8 : 2) gave **20** (R = Me) admixed with **21** (R = Me) (5 : 1; 61 mg, 61 %): R_f 0.21 (hexanes : EtOAc 4 : 1); IR (film) 3500-3300, 2970, 1490 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 3.48 - 3.34 (m, 2H), 0.97 (d, 3H, *J* 6 Hz), 0.86 (m, 1H), 0.68 (m, 1H), 0.5 (m, 2H), 0.3 (m, 2H), 0.2 (m, 1H), 0.1 (m, 1H); ^{13}C NMR ($CDCl_3$, 75.1 MHz) δ 67.0, 20.8, 19.7, 18.9, 18.7, 11.6, 11.3, 8.6, (resolved minor isomer peaks: 19.9, 8.3); MS (CI, NH_3) *m/z* 126 $(M+NH_4)^+$, 126 ($M^{+}\cdot$), 109, 95; HRMS (CI, NH_3) calc for $C_8H_{14}O$: $(M+NH_4)^+$, 144.1388; found: $(M+NH_4)^+$, 144.1382.

6-Methyl-2*E*,4*E*-heptadien-1-ol (18, R = ^{iso}Pr). Horner Emmons homologation of 4-methyl-2*E*-pentenal (0.35 g, 3.6 mmol) as for cinnamaldehyde using $(EtO)_2P(O)CH_2CO_2Me$ (0.8 mL, 4.3 mmol) and chromatography (hexanes : EtOAc 95 : 5) gave crude methyl 6-methyl-2*E*, 4*E*-heptadienoate (0.55 g, 99%) as a colorless oil: R_f 0.2 (hexanes : EtOAc 19 : 1); IR (film) 2962, 1720, 1630, 1110, 975 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 7.25 (m, 1H), 6.13 (m, 2H), 5.79 (d, 1H, *J* 15.3 Hz), 3.73 (s, 3H), 2.38 (heptet, 1H, *J* 6.7 Hz), 1.04 (d, 6H, *J* 6.7 Hz); ^{13}C NMR ($CDCl_3$, 75.1 MHz) δ 167.6, 151.3, 145.5, 125.5, 118.9, 51.3, 31.5, 21.8; MS (CI, NH_3) *m/z* 172 $(M+NH_4)^+$, 155 $M+NH_4-H_2O)^+$; HRMS (CI, NH_3) calcd for $C_9H_{14}O_2$: $(M+NH_4)^+$, 172.1338; $(M+H)^+$, 155.1072; found: $(M+NH_4)^+$, 172.1326; $(M+H)^+$, 155.1072. Since the ^1H and ^{13}C NMR spectra showed the presence of impurities, crude methyl 6-methyl-2*E*, 4*E*-heptadienoate (0.55 g, 3.6 mmol) was directly reduced with DIBAL-H as for ethyl (2*E*,4*E*)-5-phenyl-2,4-pentadienoate to provide the pure dienol **18** (R = ^{iso}Pr) (358mg, 80%) as a colorless oil: R_f 0.15 (hexanes : EtOAc 4 : 1); IR (film) 3390, 2960, 987 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 6.04 (dd, 1H, *J* 15.2, 10.4 Hz), 5.86 (dd, 1H, *J* 15.1, 10.4 Hz), 5.55 (m, 2H), 3.99 (d, 2H, *J* 6.0 Hz), 2.20 (heptet, 1H, *J* 6.8 Hz), 1.62 (br. s, 1H), 0.85 (d, 6H, *J* 6.8Hz); ^{13}C NMR ($CDCl_3$, 75.1 MHz) δ 142.9, 132.5, 129.9, 126.7, 63.8, 31.3, 22.5; MS (CI, NH_3) *m/z* 126 $(M+NH_4-H_2O)^+$, 109, 82; HRMS (CI, NH_3) calcd for $C_8H_{16}N$: $(M+NH_4-H_2O)^+$, 126.1282; found: $(M+NH_4-H_2O)^+$, 126.1274.

(1*SR*,3*RS*,4*RS*,6*SR*)-1-(Hydroxymethyl)-6-(2-propyl)bicyclopropane (20, R = ^{iso}Pr). Double cyclopropanation of diene **18** (R = ^{iso}Pr) (126 mg, 1.0 mmol) as for diene **18** (R = Ph) using Et_2Zn in hexanes (1.0 M; 10.0 mL) and CH_2I_2 (1.4 mL, 20 mmol) in $ClCH_2CH_2Cl$ (5.0 mL), work-up and chromatography

(hexanes : EtOAc 9 : 1) gave **20** (R = ^{iso}Pr) admixed with **21** (R = ^{iso}Pr) (6 : 1, 72 %) as a viscous oil: R_f 0.2 (hexanes : EtOAc 4 : 1); IR (film) 3390, 2960, 1490, 1020 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 3.4 (m, 2H), 1.6 - 0.8 (m, 9H), 0.75 (m, 1H), 0.54 (m, 2H), 0.29 - 0.15 (m, 4H); ^{13}C NMR ($CDCl_3$, 75.1 MHz) δ 67.0, 32.8, 25.2, 22.2, 21.9, 20.0, 18.8, 18.7, 9.8, 8.3, (minor isomer showed 25.5, 19.6, 18.6, 9.5, 8.5); MS (CI, NH_3) *m/z* 172 $(M+NH_4)^+$, 154 $(M^{+\cdot})$, 137, 95, 81; HRMS (CI, NH_3) calcd for $C_{10}H_{18}O$: $(M+NH_4)^+$, 172.1701; found: $(M+NH_4)^+$, 172.1702. Pyridine (1 drop) was added to alcohol **20** admixed with **21** (R = ^{iso}Pr) (15 mg, 0.1 mmol) and phenyl isocyanate (13 μL, 0.12 mmol) in DMF (3 mL) and the mixture stirred overnight, diluted with H_2O and extracted with Et_2O (2 x 10mL). The organic extracts were washed with H_2O (2 x 10 mL) and brine (2 x 10 mL) and dried. Rotary evaporation and chromatography (EtOAc : hexanes 1 : 4) gave the crude (1*SR*,3*RS*,4*RS*,6*SR*)-1-[phenylamino(carbonyl)oxymethyl]-6-(2-propyl)bicyclopropane as a viscous oil: R_f 0.3 (hexanes : EtOAc 19 : 1); IR (film) 2953, 2930, 1708, 1601, 1539, 1444, 1224 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 7.62 - 7.42 (m, 4H), 7.29 - 7.23 (m, 1H), 6.8 (br. s, 1H), 4.23 - 4.13 (m, 2H), 1.4 - 0.95 (m), 0.88 - 0.77 (m, 1H), 0.6 - 0.53 (m, 2H), 0.44 - 0.38 (m, 4H); MS (CI, NH_3) *m/z* 291 $(M+NH_4)^+$, 274 $(M+H)^+$, 155, 137, 94, 52; HRMS (CI, NH_3) calcd for $C_{17}H_{23}NO_2$: $(M+H)^+$, 274.1807; found: $(M+H)^+$, 274.1824.

Ethyl (2*E*)-3-Cyclohexyl-2-propenoate. $(EtO)_2P(O)CH_2CO_2Et$ (4.0 mL, 20.0 mL) was added dropwise to hexanes washed NaH (60 % dispersion; 800 mg, 20.0 mmol) and THF (5 mL) at °C. After 5 min, the mixture was cooled to -78 °C and cyclohexylcarboxaldehyde (2.24 g, 2.42 mL, 20.0 mmol) was added dropwise and the mixture was allowed to warm up to room temperature whereupon it was quenched with saturated aqueous NH_4Cl (20 mL). The mixture was extracted with Et_2O (2 x 20 mL) and the organic phase was washed with H_2O (2 x 20 mL) and brine (2 x 20 mL), dried, and filtered. Rotary evaporation and chromatography (hexanes : EtOAc 97 : 3) gave ethyl (2*E*)-3-cyclohexyl-2-propenoate (3.21 g, 88 %) as a colorless oil: R_f 0.2 (hexanes : EtOAc 19 : 1); IR (film) 2980, 2927, 2853, 1722, 1650, 1309, 1275, 1171 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 6.85 (dd, 1H, *J* 15.8, 6.8 Hz), 5.69 (d, 1H, *J* 15.8 Hz), 4.12 (q, 2H, *J* 7.1 Hz), 2.06 (m, 1H), 1.7 - 1.6 (m, 5H), 1.22 (t, 3H, *J* 7.1 Hz), 1.25 - 1.05 (m, 5H); ^{13}C NMR ($CDCl_3$, 75.1 MHz) δ 167.0, 154.1, 118.9, 60.0, 40.4, 31.7, 25.9, 25.7, 14.2; MS (CI, NH_3) *m/z* 200 $(M+NH_4)^+$, 183 $(M+H)^+$; HRMS (CI, NH_3) calcd for $C_{11}H_{18}O_2$: $(M+NH_4)^+$, 200.1651; $(M+H)^+$, 183.1385; found: $(M+NH_4)^+$, 200.1644; $(M+H)^+$, 183.1402.

(2*E*)-3-Cyclohexyl-2-propen-1-ol. DIBAL-H reduction of ethyl (2*E*)-3-cyclohexyl-2-propenoate (1.66 g, 9.1 mmol) as for alcohol **18** (R = Ph) and chromatography (EtOAc : hexanes 1 : 9) gave (2*E*)-3-cyclohexyl-2-propen-1-ol (1.27 g, 9.07 mmol, 99 %) as a colorless oil: R_f 0.2 (hexanes : EtOAc 3 : 1); IR (film) 3400-3300, 2924, 2851, 969 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 5.6 (m, 2H), 4.07 (br. d, 2H, *J* 4.4), 2.05 (m, 1H), 1.8 - 1.6 (m, 5H), 1.4 - 1.0 (m, 5H); ^{13}C NMR ($CDCl_3$, 75.1 MHz) δ 139.0, 126.5, 63.9, 40.3, 32.8, 26.2, 26.0; MS (CI, NH_3) *m/z* 158 $(M+NH_4)^+$, 140 $(M+NH_4-H_2O)^+$, 123, 81; HRMS (CI, NH_3) calcd for $C_9H_{16}O$: $(M+NH_4)^+$, 158.1545; $(M+NH_4-H_2O)^+$, 140.1439; found: $(M+NH_4)^+$, 158.1540; $(M+NH_4-H_2O)^+$, 140.1446.

(2*E*)-3-Cyclohexyl-2-propenal. DMSO (0.66 mL, 9.3 mmol) in CH_2Cl_2 (2 mL) was added dropwise with stirring to oxalyl chloride in CH_2Cl_2 (2.0 M; 2.3 mL, 4.6 mmol) in CH_2Cl_2 (20 mL) at -78 °C. After 0.5 h, (2*E*)-3-cyclohexyl-2-propen-1-ol (0.43 g, 3.1 mmol) in CH_2Cl_2 (5 mL) was added dropwise and the resulting mixture was stirred at -78 °C for 1h when Et_3N (2.6 mL, 18.0 mmol) was added. The mixture was allowed to warm up to 0 °C, added to H_2O (50 mL) and extracted with Et_2O (2 x 50 mL). The organic phase was washed with H_2O (2 x 50 mL) and brine (2 x 50 mL), dried, and filtered. Rotary evaporation and chromatography (hexanes : EtOAc 97 : 3) gave (2*E*)-3-cyclohexyl-2-propenal (330 mg, 78 %) as a colorless oil: R_f 0.7 (hexanes : EtOAc; 19 : 1); IR (film) 2928, 2853, 2810, 1691, 1631, 1449, 1121, 1099, 976 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 9.46 (d, 1H, *J* 7.8 Hz), 6.76 (dd, 1H, *J* 15.7, 6.6 Hz), 6.10 (dd, 1H, *J* 15.7, 7.8 Hz), 2.25 (m, 1H), 1.85 - 1.6, 1.4 - 1.1 (m, 10H); ^{13}C NMR ($CDCl_3$, 75.1 MHz) δ 194.6, 163.8, 130.7, 40.9, 31.6, 25.9, 25.7; MS (CI, NH_3) *m/z* 156 $(M+NH_4)^+$, 94, 81; HRMS (CI, NH_3) calcd for $C_9H_{14}O$: $(M+NH_4)^+$, 156.1388; found: $(M+NH_4)^+$, 156.1387.

Ethyl (2*E*, 4*E*)-5-Cyclohexyl-2,4-pentadienoate. Horner-Emmons homologation of (2*E*)-3-cyclohexyl-2-propenal (330 mg, 2.4 mmol) as for cinnamaldehyde and chromatography (hexanes : EtOAc 9 : 1) gave ethyl (2*E*, 4*E*)-5-cyclohexyl-2,4-pentadienoate (405 mg, 81 %) as a colorless oil: R_f 0.2 (hexanes : EtOAc 9 : 1); IR (film) 2925, 1705, 1620, 1110, 975 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 7.24 (dd, 1H, *J* 15.4, 10.0 Hz), 6.05 (m, 2H), 5.78 (d, 1H, *J* 15.4 Hz), 4.18 (q, 2H, *J* 7.1 Hz), 2.08 (m, 1H), 1.8 - 1.6 (m, 5H), 1.28 (t, 3H, *J* 7.1 Hz), 1.4 - 1.0 (m, 5H); ^{13}C NMR ($CDCl_3$, 75.1 MHz) δ 167.6, 150.4, 145.8, 126.2, 119.7, 60.5, 41.4, 32.7, 26.4, 26.2, 14.7; MS (CI, NH_3) *m/z* 226 $(M+NH_4)^+$, 209 $(M+H)^+$, 163; HRMS (CI, NH_3) calcd for $C_{13}H_{20}O_2$: $(M+H)^+$, 209.1542; found: $(M+H)^+$, 209.1537.

(2*E*, 4*E*)-5-Cyclohexyl-2,4-penten-1-ol (18, R = c-C_6H_{11}). DIBAL-H reduction of ethyl (2*E*, 4*E*)-5-cyclohexyl-2,4-pentadienoate (400 mg, 1.9 mmol) as for ethyl (2*E*,4*E*)-5-phenyl-2,4-pentadienoate and chromatography (hexanes : EtOAc 9 : 1) gave dienol **18** (R = c-C_6H_{11}) (260 mg, 82 %) as a colorless oil: R_f 0.2 (hexanes : EtOAc 4 : 1); IR (film) 3350 - 3330, 2919, 2851, 1640, 1448, 967 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 6.25 (dd, 1H, *J* 14.8, 10.2 Hz), 6.05 (dd, 1H, *J* 15.3, 10.4 Hz), 5.78 (m, 2H), 4.15 (m, 2H), 2.02 (m, 1H), 1.73 (m, 5H), 1.4 - 1.0 (m, 5H); ^{13}C NMR ($CDCl_3$, 75.1 MHz) δ 141.5, 132.5, 129.4, 126.9, 63.5, 40.7, 32.8, 26.2, 26.0; MS (EI) *m/z* 166 ($M^{+\cdot}$), 148, 135, 67; HRMS (EI) calcd for $C_{11}H_{18}O$: ($M^{+\cdot}$), 166.1358; found: ($M^{+\cdot}$), 166.1349.

(1*SR*,3*RS*,4*RS*,6*SR*)-6-Cyclohexyl-1-(hydroxymethyl)bicyclopropane (20, R = c-C_6H_{11}) Double cyclopropanation of diene **18** (R = c-C_6H_{11}) (83 mg, 0.5 mmol) as for diene **18** (R = Ph) using Et_2Zn in hexanes (1.0 M; 5.0 mL) and CH_2I_2 (0.9 mL, 10 mmol) in $ClCH_2CH_2Cl$ (3 mL), work-up and chromatography (hexanes : EtOAc 8 : 2) gave **20** (R = c-C_6H_{11}) admixed with **21** (R = c-C_6H_{11}) (7 : 1; 76 mg, 78 %) as a viscous oil: R_f 0.2 (hexanes : EtOAc 4 : 1); IR (film) 3350, 2960, 2850, 1460, 1030 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 3.44 (m, 2H), 1.72 (m, 6H), 1.3 - 0.95 (m, 10H), 0.86 (m, 1H), 0.72 (m, 1H), 0.56 (m, 2H), 0.29 - 0.15 (m, 4H); ^{13}C NMR ($CDCl_3$, 75.1 MHz) δ 67.1, 42.5, 33.2, 32.8, 26.7, 26.4, 23.7, 20.2, 18.8, 18.4, 9.5, 8.4, (minor isomer showed 24.1, 19.8, 18.7, 9.3, 8.8); MS (CI, NH_3) *m/z* 212

$(M+NH_4)^+$, 194 ($M^{+\cdot}$), 177, 135, 121; **HRMS** (CI, NH_3) calcd for $C_{13}H_{22}O$: $(M+NH_4)^+$, 212.2014; **found:** $(M+NH_4)^+$, 212.2030.

(2*E*, 4*E*)-6-(t-Butyldiphenylsilyloxy)-2,4-hexadien-1-ol (18, R = $CH_2OSiPh_2{}^tBu$). Muconic acid (3.0 g, 0.021 mol) in $SOCl_2$ (40 mL) was heated to reflux for 72 h, evaporated, the resulting solid was redissolved in dry PhMe (35 mL), cooled to 0 °C and EtOH (10 mL) was added with stirring. After 1h, Et_3N (10 mL) was added, the mixture was allowed to warm up to room temperature over 1 h, diluted with Et_2O (50 mL) and washed with H_2O (2 x 50 mL) and brine (2 x 50 mL), dried, and filtered. Rotary evaporation and chromatography (hexanes : EtOAc 9 : 1) gave diethyl muconate[28] (2.3 g, 55 %) which was used directly in the next step. DIBAL-H in hexanes (1.0 M; 25.0 mL, 25.0 mmol) was added dropwise to diethyl muconate (1.22 g, 6.2 mmol) in CH_2Cl_2 (25 mL) at -78 °C. After 1 h, EtOH (20 mL) and saturated aqueous Na_2SO_4 (10 mL) were added in sequence and the mixture allowed to warm up to room temperature. Filtration through Celite (CH_2Cl_2 : EtOH 4 : 1), rotary evaporation and chromatography (hexanes : EtOAc 3 : 7) gave (2*E*, 4*E*)-hexadiene-1,6-diol (0.68 g, 97 %) which was used directly in the next step. (2*E*, 4*E*)-Hexadiene-1,6-diol (200 mg, 1.75 mmol), t-butylchlorodiphenylsilane (0.67 mL, 0.71 g, 2.6 mmol), imidazole (0.24 g, 3.5 mmol), and 4-(*N*,*N*-dimethylamino)pyridine (10 mg) in DMF (5 mL) were allowed to stand for 14 h. The mixture was diluted with H_2O (20 mL) and extracted with Et_2O (2 x 30 mL). The organic phase washed with saturated aqueous NH_4Cl (2 x 20 mL), H_2O (2 x 20 mL) and brine (2 x 20 mL), dried, and filtered. Rotary evaporation and chromatography (hexanes : EtOAc 4 : 1) gave **18** (R = $CH_2OSiPh_2{}^tBu$) (292 mg, 47 %) as white solid: mp. 20-22 °C; R_f 0.20 (hexanes : EtOAc 4 : 1); IR (film) 3450 - 3250, 2930, 2857, 1427, 1082, 988, 701 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 7.70 - 7.66 (m, 4H), 7.43 - 7.25 (m, 6H), 6.31 - 6.25 (m, 2H), 5.84 - 5.79 (m, 2H), 4.25 (d, 2H, *J* 4.9 Hz), 4.19 (d, 2H, *J* 5.9 Hz), 1.07 (s, 9H); ^{13}C NMR ($CDCl_3$, 75.1 MHz) δ 135.6, 133.8, 132.9, 131.5, 131.1, 129.7, 129.0, 128.8, 64.1, 63.4, 26.9, 19.3; MS (CI, NH_3) *m/z* 274, 216, 196; Anal. calcd for $C_{22}H_{28}O_2Si$: C, 74.95; H 8.01; Found: C, 75.15; H, 7.85%.

(1*SR*,3*RS*,4*SR*,6*RS*)-1-Hydroxymethyl-6-(t-butyldiphenylsilyloxymethyl)bicyclopropane (20, R = $CH_2OSiPh_2{}^tBu$). Et_2Zn in hexanes (1.0 M; 5 mL, 5 mmol) and CH_2I_2 (0.9 mL, 11 mmol) were sequentially added dropwise with stirring to **18** (R = $CH_2OSiPh_2{}^tBu$) (190 mg, 0.54 mmol) in $ClCH_2CH_2Cl$ (3 mL) at -12 °C. After 12 h, saturated aqueous NH_4Cl (2mL) was added and the mixture allowed to warm up to room temperature, poured into H_2O (20 mL) and extracted with Et_2O (2 x 20 mL). The organic phase was washed with saturated aqueous NaHCO3 (2 x 20 mL), H_2O (2 x 20 mL) and brine (2 x 20 mL), dried, and filtered. Rotary evaporation and chromatography (hexanes : EtOAc 4 : 1) gave **20** (R = $CH_2OSiPh_2{}^tBu$) (142 mg, 69 %) as a viscous oil: R_f 0.20 (hexanes : EtOAc 4 : 1); IR (film) 3395, 1112, 701, 823 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 7.68-7.64 (m, 4H), 7.44-7.36 (m, 6H), 3.60 (dd, 1H, *J* 10.7, 5.9 Hz), 3.42 (m, 3H), 1.05 (s, 9H), 0.84 (m, 2H), 0.67 (m, 2H), 0.32 (m, 4H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 135.7, 134.1, 129.6, 127.7, 67.2, 67.0, 27.0, 19.8, 19.3, 18.2, 17.8, 8.54, 8.48; MS (CI, NH_3) *m/z* 398 $(M+NH_4)^+$, 196, 107; HRMS (CI, NH_3) calc for $C_{24}H_{32}O_2Si$: $(M+NH_4)^+$, 398.2515; found: $(M+NH_4)^+$, 398.2552.

(1*R*,3*S*)-1-Hydroxymethyl-3-[3-(t-butyldiphenylsilyloxy)-1*E*-propen-1-yl]cyclopropane (23). Et_2Zn in hexanes (1.0 M; 0.59 mL, 0.59 mmol) was added dropwise to dienol **18** (R = $CH_2OSiPh_2{}^tBu$) (190 mg, 0.54

mmol) in $ClCH_2CH_2Cl$ (3 mL) at 0 °C. After 0.5 h and *L*(+)-diethyl tartrate (120 mg, 0.58 mmol) in $ClCH_2CH_2Cl$ (1 mL) was added and the mixture was stirred for 1 h and cooled to -12 °C. Et_2Zn in hexanes (1.0M; 1.10 mL, 1.10 mmol) was added and stirring continued for 1 h when CH_2I_2 (0.29 g, 1.1 mmol) was added and stirring continued for 12 h. Saturated aqueous NH_4Cl (5 mL) was added and the mixture was extracted with Et_2O (2 x 15 mL). The organic phase was washed with 10 % NH_4Cl (15 mL), H_2O (2 x 15 mL) and brine (2 x 15 mL), dried, and filtered. Rotary evaporation and chromatography (hexanes : EtOAc 4 : 1) gave cyclopropane **23** (132 mg, 67 %) as a colorless oil: R_f 0.20 (hexanes : EtOAc 7 : 3); $[\alpha]_D$ -12.7 ° (c = 1.0); IR (film) 3400 - 3330, 2931, 2857, 1472, 1427, 1112, 1051, 1009, 998, 962, 909, 823, 735, 702 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 7.70 - 7.64 (m, 4H), 7.44 - 7.36 (m, 6H), 5.63 (dt, 1H, *J* 15.2, 5.6 Hz), 5.23 (ddd, 1H, *J* 15.3, 8.3, 1.5 Hz), 4.15 (dd, 2H, *J* 5.6, 1.5 Hz), 3.50 (dd, 2H, *J* 6.9, 2.5 Hz), 1.33 (m, 1H), 1.08 (m, 1H), 1.05 (s, 9H), 0.68 - 0.59 (m, 2H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 135.6, 133.9, 133.2, 129.6, 127.7, 127.2, 66.4, 64.5, 26.9, 23.0, 19.3, 11.6; MS (CI, NH_3) *m/z* 384 $(M+NH_4)^+$, 367 $(M+H)^+$, 111; HRMS (CI, NH_3) calcd for $C_{23}H_{30}O_2Si$: $(M+NH_4)^+$, 384.2359; found: $(M+NH_4)^+$, 384.2359.

(1*R*,3*S*,4*R*,6*S*)-1-Hydroxymethyl-6-(t-butyldiphenylsilyloxymethyl)bicyclopropane (24). Et_2Zn in hexanes (1.0 M; 1.35 mL, 1.35 mmol) and CH_2I_2 (0.75 g, 2.7 mmol) were added with stirring to cyclopropyl alkene **23** (100 mg, 0.27 mmol) in $ClCH_2CH_2Cl$ (5 mL) at -20 °C. After 24 h, saturated aqueous NH_4Cl (5 mL) was added and the mixture was extracted with Et_2O (2 x 15 mL). The organic phase was washed with 10 % NH_4Cl (15 mL), H_2O (2 x 15 mL) and brine (2 x 15 mL), dried, and filtered. Rotary evaporation and chromatography (hexanes : EtOAc 4 : 1) gave the bicyclopropane **24** (82 mg, 79 %) as a colorless oil: R_f 0.20 (hexanes : EtOAc; 4 : 1); $[\alpha]_D$ -9.2 ° (c = 1.0) . The sample was spectroscopically identical with racemic material prepared directly from dienol **18** (R = $CH_2OSiPh_2{}^tBu$).

(1*R*,3*S*,4*R*,6*S*)-1,6-Bis(t-butyldiphenylsilyloxymethyl)bicyclopropane (25). Bicyclopropanemethanol **24** (50 mg, 0.13 mmol), t-butyldiphenylchlorosilane (0.067 mL, 71 mg, 0.26 mmol), imidazole (24 mg, 0.35 mmol), and 4-*N,N*-dimethylaminopyridine (1 mg) in DMF (1 mL) were allowed to stand for 14 h, diluted with H_2O (10 mL) and extracted with Et_2O (2 x 10 mL). The organic phase was washed with saturated aqueous NH_4Cl (2 x 10 mL), H_2O (2 x 10 mL) and brine (2 x 10 mL), dried, and filtered. Rotary evaporation and chromatography (hexanes : EtOAc 8 : 2) gave the bicyclopropane **25** (67 mg, 82 %) as a viscous oil: R_f 0.7 (hexanes : EtOAc 19 : 1); $[\alpha]_D$ -0.2 ° (c = 1.0); IR (film) 2930, 2857, 1427, 1111, 1088, 823, 738, 700, 689 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 7.70 - 7.66 (m, 8H), 7.43 - 7.25 (m, 12H), 3.56 (dd, 2H, *J* 10.7, 6.0 Hz), 3.43 (dd, 2H, *J* 10.7, 6.6 Hz) 1.05 (s, 18H), 0.80 (m, 2H), 0.65 - 0.63 (m, 2H), 0.24 - 0.19 (m, 4H); ^{13}C NMR ($CDCl_3$, 75.1 MHz) δ 135.6, 134.1, 129.6, 127.6, 67.2, 29.7, 26.9, 19.2, 17.8, 8.3; MS (CI, NH_3) *m/z* 636 $(M+NH_4)^+$, 398, 363, 196, 107; HRMS (CI, NH_3) calcd for $C_{40}H_{50}O_2Si_2$: $(M+NH_4)^+$, 636.3693; found: $(M+NH_4)^+$, 636.3660.

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