Mechanistic Studies of Diastereoselective Cyclopropanation via Homochiral Ketals. 1. Dioxolane Structural Effects[1]

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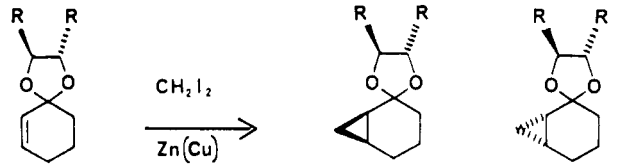
Compounds structurally related to 2-cyclohexen-1-one 1,4-di-*O*-benzyl-L-threitol ketal were prepared and subjected to the Simmons–Smith cyclopropanation. From these experiments a mechanistic model for diastereoselective cyclopropanation of common ring systems (five-, six-, and seven-membered) has been formulated. Diastereoselectivity is thought to result from preferential chelation of the Simmons–Smith reagent at the least sterically hindered lone pair of electrons on the dioxolane oxygen proximal to the alkene. It is found that the presence of oxygen atoms in the dioxolane appendages provide sites for competitive chelation of the reagent, which can antagonize the diastereoselection due to chelation at dioxolane oxygen. That chelation by dioxolane oxygen does occur and is responsible for diastereoselectivity is inferred from studies with a hydrocarbon model system. Surprisingly, both dioxolane appendages are shown to be necessary for optimum diastereoselection since, under the conditions of the Simmons–Smith cyclopropanation, 2-cycloalken-1-one ethylene ketals are reversibly ring opened to zwitterionic intermediates.

The Simmons–Smith cyclopropanation is a widely employed method for conversion of an alkene to the corresponding cyclopropane.[2] It is known that oxygen atoms proximal to the alkene can direct attack by the reagent via chelation of zinc.[2,3] With this in mind, a number of common[4] monocyclic and bicyclic 2-cycloalken-1-one 1,4-di-*O*-benzyl-L-threitol[5] ketals were prepared and subjected to Simmons–Smith cyclopropanation (Figure 1).[6-8] Observed diastereoselectivities[9] were uniformly good (7:1 to 9:1), and the sense of the diastereoselection was invariant.[6,8] However, the identities of the major and minor product diastereomers were not consistent with our initial hypothesis that diastereoselection was due to chelation of zinc by oxygen in the dioxolane appendage proximal to the alkene. We therefore undertook studies of the mechanism of this process in the hope that these would lead to development of superior diol auxiliaries for this and for other alkene functionalizations. Results of a study examining dioxolane structural effects are reported herein. A related study examining cyclohexene conformational effects is presented in an accompanying article.[10]

Table I. Simmons–Smith Cyclopropanations of 2-Cyclohexen-1-one Ketals 1–10



ene ketals	R	cyclopropanes	yield, %	diastereomer ratio (a:b)
1	CH_2OCH_2Ph	11	98	9:1
2	CH_2OCH_3	12	86	5:1
3	CH_2OCH_2-*p*-biphenylyl	13	99	9:1
4	CH_2OCH_2-β-naphthyl	14	76	9:1
5	$C(CH_3)_2OCH_3$	15	91	4:1
6	$COOCH_3$	16	37	3:2
7	CH_2OH	17	50	1:2
8	CH_3	18	86	9:1
9	$CH_2CH_2CH_2Ph$	19	92	>9:1
10	Ph	20	90	19:1

Results and Discussion

Several ene ketals structurally related to 2-cyclohexen-1-one 1,4-di-*O*-benzyl-L-threitol ketal (1) were synthesized (vide infra) and subjected to Simmons–Smith cyclopropanation[11] (Table I). Significantly, low yields and the poorest diastereoselectivities were observed for ene ketals **6** and **7**, which should chelate the Simmons–Smith reagent most strongly due to the Lewis basicity of the oxygen atoms in their appendages. Better yields and diastereoselectivities were obtained for ene ketals **1–5**, which carry less Lewis-basic appendage oxygen atoms. Ene ketals **8–10**, which are devoid of appendage oxygen, gave high yields and diastereoselectivities. These results can be interpreted in terms of a competition between appendage and dioxolane oxygen atoms for chelation of the Simmons–Smith reagent (Figure 2).

For common 2-cycloalken-1-one L-threitol ketals, coordination of the reagent by the distal appendage oxygen atom or by a distal lone pair on either dioxolane oxygen

(1) A portion of this work has previously appeared in communication form, see: Mash, E. A.; Nelson, K. A.; Heidt, P. C. *Tetrahedron Lett.* **1987**, *28*, 1865–1868.

(2) For reviews of the Simmons–Smith reaction, see: (a) Furukawa, J.; Kawabata, N. In *Advances in Organometallic Chemistry*; Stone, F. G. A., West, R., Eds.; Academic Press: New York, 1974; Vol. 12, Chapter 3. (b) Simmons, H. E.; Cairns, T. L.; Vladuchick, S. A.; Hoiness, C. M. *Org. React.* **1973**, *20*, 1–131.

(3) Poulter, C. D.; Friedrich, E. C.; Winstein, S. *J. Am. Chem. Soc.* **1969**, *91*, 6892–6894.

(4) Ring compounds have been classified into four categories, namely, small rings (three- and four-membered), common rings (five-, six-, and seven-membered), medium rings (eight- to 11-membered), and large rings (12-membered and larger). See: Eliel, E. L. *Stereochemistry of Carbon Compounds*; McGraw-Hill: New York, 1962; p 189.

(5) Mash, E. A.; Nelson, K. A.; Van Deusen, S.; Hemperly, S. B. *Org. Synth.* **1989**, *68*, 92–103.

(6) (a) Mash, E. A.; Nelson, K. A. *J. Am. Chem. Soc.* **1985**, *107*, 8256–8258. (b) Mash, E. A.; Nelson, K. A. *Tetrahedron Lett.* **1986**, *27*, 1441–1444. (c) Mash, E. A.; Nelson, K. A. *Tetrahedron* **1987**, *43*, 679–692. (d) Mash, E. A.; Torok, D. S. *J. Org. Chem.* **1989**, *54*, 250–253.

(7) For related studies describing cyclopropanations of acyclic acetals, see: (a) Arai, I.; Mori, A.; Yamamoto, H. *J. Am. Chem. Soc.* **1985**, *107*, 8254–8256. (b) Mori, A.; Arai, I.; Yamamoto, H. *Tetrahedron* **1986**, *42*, 6447–6458.

(8) For uses of this diastereoselective Simmons–Smith cyclopropanation in synthesis, see: (a) Mash, E. A.; Math, S. K.; Flann, C. J. *Tetrahedron* **1989**, *45*, 4945–4950. (b) Mash, E. A. *J. Org. Chem.* **1987**, *52*, 4142–4143. (c) Mash, E. A.; Fryling, J. A. *J. Org. Chem.* **1987**, *52*, 3000–3003. (d) Nelson, K. A.; Mash, E. A. *J. Org. Chem.* **1986**, *51*, 2721–2724.

(9) Diastereomer ratios were determined by 62.9-MHz ^{13}C NMR spectroscopy. For previous examples of the use of ^{13}C NMR in determining diastereomer ratios, see: Hiemstra, H.; Wynberg, H. *Tetrahedron Lett.* **1977**, 2183–2186.

(10) Mash, E. A.; Hemperly, S. B. *J. Org. Chem.*, following article in this issue.

(11) Shank, R. S.; Shechter, H. *J. Org. Chem.* **1959**, *24*, 1825–1826.

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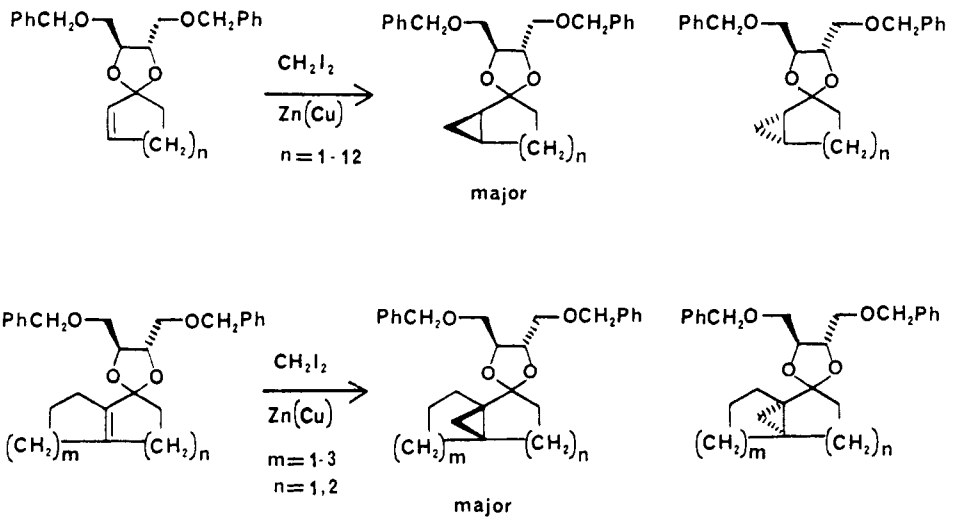


Figure 1.

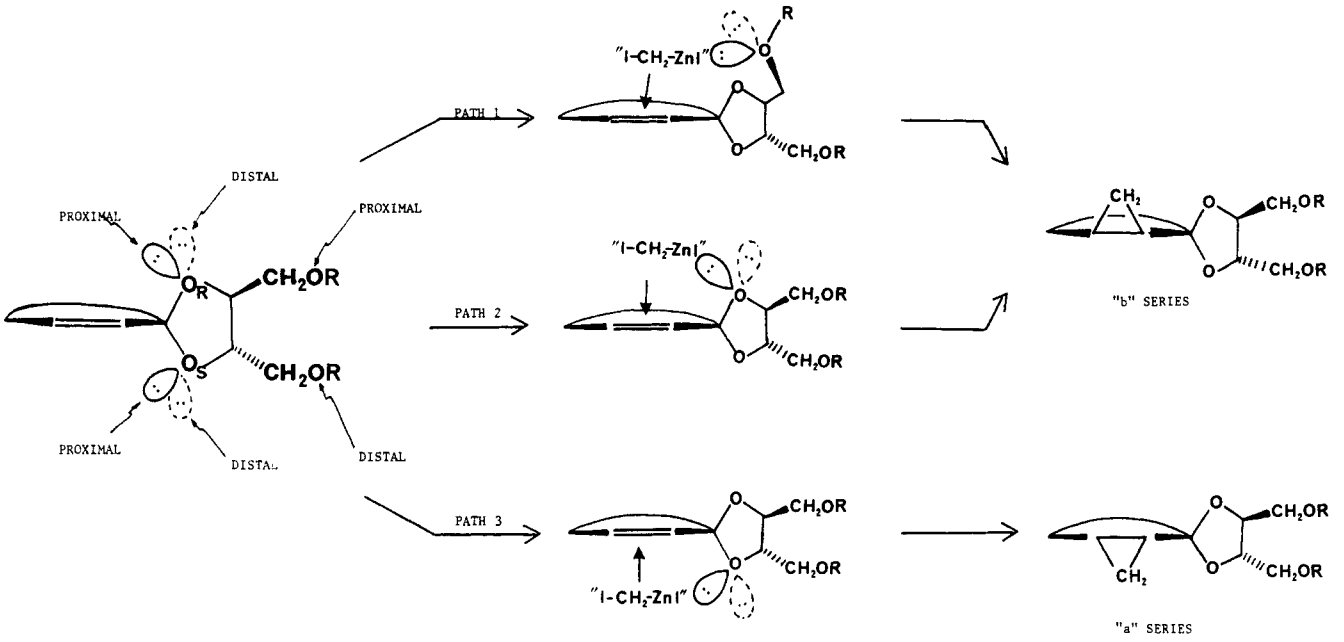


Figure 2.

atom could occur, but the spatial orientation of the reagent relative to the alkene would render methylene transfer ineffectual. Coordination by the proximal appendage oxygen atom (path 1, Figure 2) or by the proximal lone pair on the *pro-R* dioxolane oxygen atom (path 2) should lead to formation of cyclopropane ketals of the **b** series, whereas coordination of the reagent by the proximal lone pair on the *pro-S* dioxolane oxygen atom (path 3) should produce cyclopropane ketals of the **a** series. For ene ketals such as **6** and **7**, which bear strongly chelating appendage oxygen atoms, path 1 is significant. For ene ketals such as **1–5**, which bear less strongly chelating appendage oxygen atoms, and even more for ene ketals **8–10**, which bear no appendage oxygen atoms, path 3 is predominant. In all cases path 3 is preferred over path 2 since coordination at the proximal lone pair on the *pro-R* dioxolane oxygen atom requires eclipsing of the Simmons–Smith reagent with a dioxolane appendage, while coordination at the proximal lone pair on the *pro-S* dioxolane oxygen atom requires eclipsing of the reagent with a hydrogen atom. Thus, in the absence of appendage oxygen, bulkier dioxolane appendages favor path 3 and increase the observed diastereoselection. On the basis of limited experimental evidence (Table II), this mechanistic picture appears valid for five- and seven-membered ring ene ketals as well.

To demonstrate that dioxolane oxygen is responsible for the observed diastereoselection, alkene **35** was prepared (vide infra) and subjected to the Simmons–Smith cyclopropanation. Unlike ene ketal **10**, for which cyclopropanation was both rapid ($t_{1/2}$ < 6 h) and highly diastereoselective (**20a**:**20b** ≃ 19:1), alkene **35** was resistant

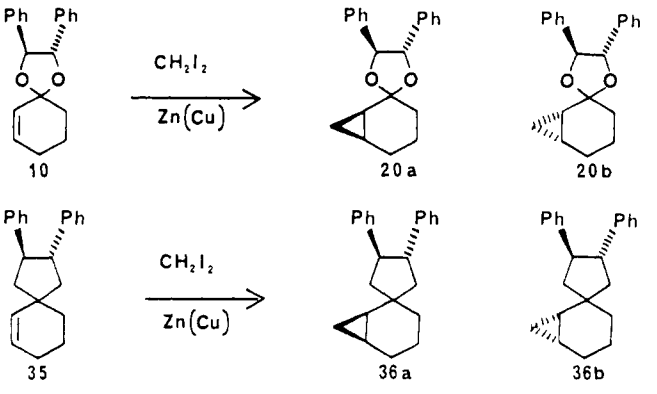
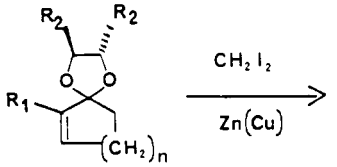
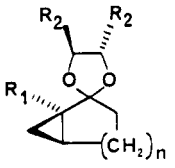
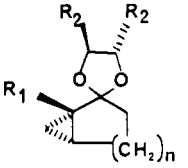


Table II. Simmons–Smith Cyclopropanations of 2-Cyclopenten-1-one and Cyclohepten-1-one Ketals 21–27





a

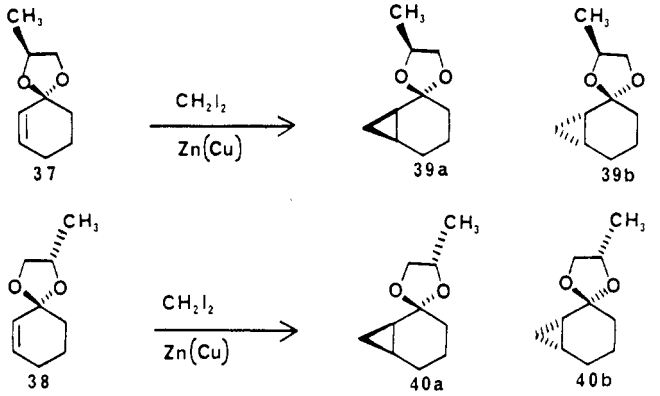


b

ene ketals	n	R^1	R^2	cyclopropanes	yield, %	diastereomer ratio (a:b)
21	1	H	CH_2OCH_2Ph	**28**	72	9:1
22	1	H	Ph	**29**	66	13:1
23	1	CH_3	CH_2OCH_2Ph	**30**	92	9:1
24	1	CH_3	CH_2OCH_3	**31**	88	7:1
25	1	CH_3	COO-i-Pr	**32**	36	3:1
26	3	H	CH_2OCH_2Ph	**33**	90	8:1
27	3	H	Ph	**34**	77	15:1

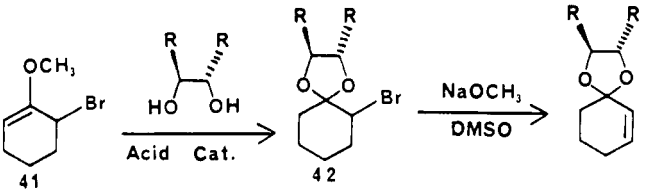
to cyclopropanation ($t_{1/2} \gg 24$ h) and exhibited no diastereoselectivity (**36a**:**36b** $\simeq$ 1:1).[9] Both the observed rate enhancement and the observed increase in diastereoselectivity for **10** relative to **35** can be attributed to chelation of the Simmons–Smith reagent by the *pro-S* dioxolane oxygen atom of ene ketal **10**.

The above mechanistic scheme predicts that in the absence of appendage oxygen, only the proximal dioxolane appendage, which hinders chelation of the Simmons–Smith reagent at the *pro-R* dioxolane oxygen atom, is necessary for diastereoselection. To test this prediction (*S*)-1,2-propanediol ketals **37** and **38** were prepared (vide infra) and subjected to Simmons–Smith cyclopropanation. Surprisingly, ene ketals **37**, **38**, or a 1:1 mixture of **37** and **38** produced, in high yields, similar mixtures (ca. 2:1:2:1) of the four possible diastereomeric products **39a**, **39b**, **40a**, and **40b** as determined by ^{13}C NMR. These results imply

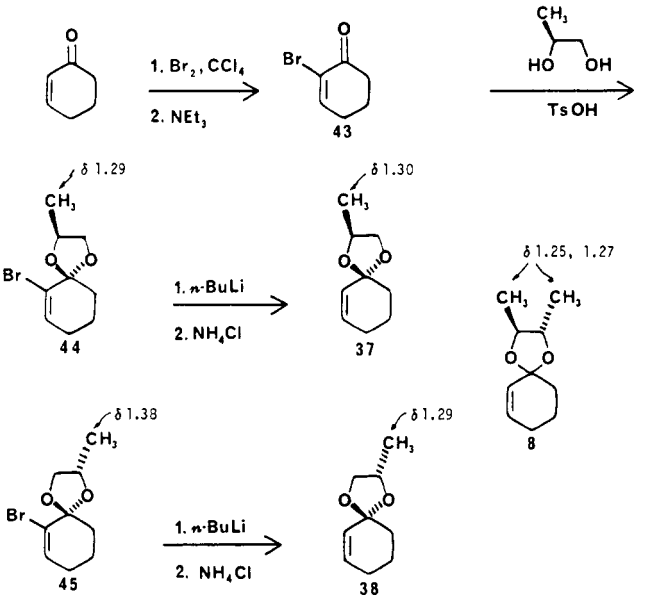


that under the conditions employed **37** and **38** are equilibrated via reversible opening of the dioxolane ring. This process, which is presumably Lewis acid catalyzed, was independently demonstrated by isolation of unreacted starting ene ketal **37** at 36% conversion to cyclopropanes (12% isomerization to **38**) and by treatment of **37** with a catalytic amount of anhydrous zinc iodide in refluxing diethyl ether (18% isomerization to **38** after 30 min). Ene

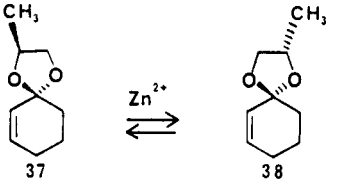
Scheme I



Scheme II



ketals **37** and **38** were stable in refluxing diethyl ether alone.

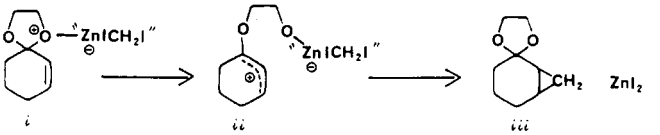


While the timing of methylene transfer for ene ketals **37** and **38** remains unknown,[12] these studies indicate that for optimal diastereoselection both dioxolane appendages are necessary.

Syntheses

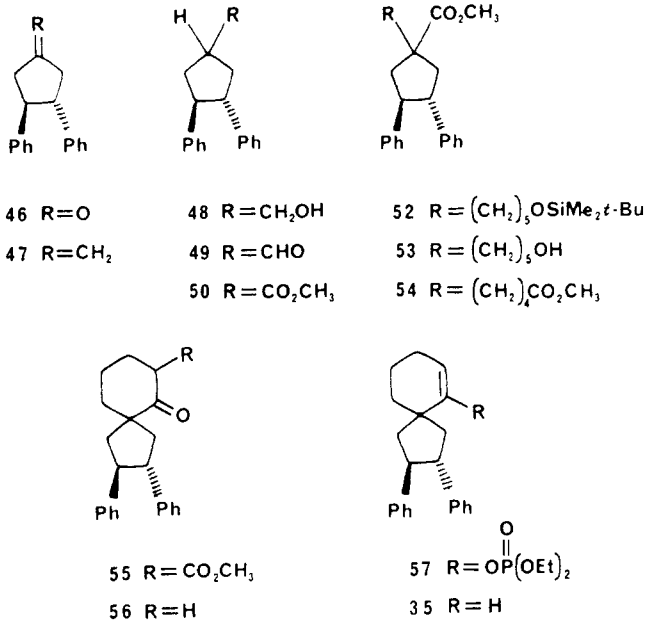
Syntheses of Ene Ketals 1–10, 21–27, 37, and 38. Ene ketals **1–5**, **8**, and **9** were prepared via ketalization of 3-bromo-2-methoxycyclohexene (**41**)[13] using the requisite diols, followed by elimination[13] (Scheme I). Ene ketal **6** was prepared by transketalization of 1,1-dimethoxy-2-cyclohexene.[7] Ene ketal **7** was prepared from 2-bromocyclohexan-1-one 1,4-di-*O*-benzyl-L-threitol ketal (**42**, R = CH_2OCH_2Ph, Scheme I) via debenzylation and elimination.[13]

(12) Although charged intermediates are not commonly associated with the Simmons–Smith cyclopropanation, an interesting mechanistic possibility that cannot presently be excluded would involve collapse of a zwitterionic ring-opened intermediate to products:



(13) Garbisch, E. W., Jr. *J. Org. Chem.* **1965**, *30*, 2109–2120.

Chart I



Ene ketals **10** and **21–27** were prepared by direct acid-catalyzed ketalizations of 2-cyclohexen-1-one, 2-cyclopenten-1-one, 2-methyl-2-cyclopenten-1-one, or 2-cycloheptен-1-one.

An equimolar mixture of ene ketals **37** and **38** was prepared via ketalization of 3-bromo-2-methoxycyclohexene (**41**)[13] using (*S*)-(+)-1,2-propanediol, followed by elimination.[13] As **37** and **38** were inseparable, they were also synthesized as depicted in Scheme II. Bromination of 2-cyclohexen-1-one, followed by elimination, gives 2-bromo-2-cyclohexen-1-one (**43**).[14] Acid-catalyzed ketalization using (*S*)-(+)-1,2-propanediol gave chromatographically separable 2-bromo ketals **44** (R_f 0.36) and **45** (R_f 0.30, 10% EtOAc/hexanes), which were lithiated[14] and protonated to provide ene ketals **37** and **38**, respectively. Structures were assigned by comparing the 250-MHz proton NMR spectra of **44**, **45**, **37**, **38**, and 2,3-butanediol ketal **8**. For the more polar α-bromo ketal **45**, deshielding by the nearby bromine atom produces a significant downfield shift of the ^{1}H NMR signal due to the dioxolane methyl appendage protons.

Synthesis of Alkene 35. The synthesis of alkene **35** commences with preparation of the known compound *trans*-3,4-diphenylcyclopentanone (**46**)[15] (Chart I). Olefination[16] of **46** (CH_2I_2, Zn, $TiCl_4$) gave methylenecyclopentane **47** in 92% yield. Hydroboration and oxidation[17] of alkene **47** provided alcohol **48** in 95% yield.

Swern oxidation[18] of **48** produced aldehyde **49** in 95% yield. This aldehyde was oxidized and esterified with bromine in methanol[19] to produce methyl ester **50** in 83% yield. Deprotonation of ester **50** using LDA, followed by addition of 5-iodopentyl *tert*-butyldimethylsilyl ether (**51**) gave alkylated ester **52** in 83% yield. This ester was desilylated (n-Bu_4NF, THF) to give alcohol **53** in nearly quantitative yield. This alcohol was subjected to Swern oxidation and oxidative esterification as above to provide diester **54** in 84% yield from **52**. Dieckmann cyclization of diester **54** (LDA, THF, −78 °C to room temperature) yielded keto ester **55**, which was hydrolyzed and decarboxylated to give ketone **56** in 75% yield from diester **54**. Following conversion of **56** to the corresponding enol phosphate **57** in 80% yield, reduction with lithium metal in liquid ammonia gave the desired alkene **35** in 77% yield.

Conclusion

The studies outlined herein support a mechanistic model that attributes the diastereoselectivities observed for Simmons–Smith cyclopropanations of ene ketals composed of common 2-cycloalken-1-ones and C_2-symmetric diols to preferential chelation of the reagent by the least sterically hindered dioxolane oxygen atom proximal to the alkene. For ene ketals that possess appendages bearing sufficiently Lewis-basic oxygen, a competitive mode of reagent delivery can intervene. Direct steric biasing of one face of homochiral common 2-cycloalken-1-one ketals will require dioxolane appendages more bulky than phenyl. Appendage-directed intramolecular reagent delivery for other diastereoselective functionalizations of common 2-cycloalken-1-one ketals may be possible.

Experimental Section

Benzene was distilled from calcium hydride and diethyl ether was distilled from phosphorus pentoxide or sodium benzophenone ketyl under an inert atomsphere. Dimethyl sulfoxide was distilled from calcium hydride under reduced pressure and stored over 3Å molecular sieves. Zinc–copper couple was prepared according to the method of Shank and Shechter[11] immediately before use. Unless otherwise stated, the purity of all title compounds was judged to be ≥95% by ^{1}H and ^{13}C NMR spectral determinations. Proton magnetic resonance spectra were recorded at 250 MHz on a Bruker WM-250 NMR spectrometer. Chemical shifts are reported in parts per million (ppm) from tetramethylsilane. Carbon-13 magnetic resonance spectra were recorded at 62.9 MHz on Bruker WM-250 or AM-250 NMR spectrometers. Chemical shifts are reported in parts per million (ppm) from the center line of the chloroform-*d* triplet (77.0 ppm). Mass spectral determinations were performed at the Midwest Center for Mass Spectrometry, an NSF Regional Instrumentation Facility (Grant CHE-0211164). Elemental analyses were performed by Desert Analytics, Tucson, AZ. Infrared spectra were recorded on a Perkin-Elmer Model 983 infrared spectrophotometer. Optical rotations were measured at 589 nm on a Rudolph Research Autopol III polarimeter. CD spectra were recorded on a Cary Model 60 CD/ORD spectrometer. Thin layer chromatographic analyses were performed on Merck silica gel 60 plates (0.25 mm, 70–230 mesh ASTM).

Diols required for synthesis of ene ketals **1**, **2**, **3**, **4**, **7**, **21**, **23**, **24**, and **26** were prepared as previously described.[5] Diols required for ene ketals **6**, **8**, **10**, **22**, **25**, **27**, **37**, and **38** were purchased from Aldrich Chemical Company. Synthesis of the diols required for ene ketals **5** and **9** are described herein.

General Ketalization Procedures. (a) From 3-Bromo-2-methoxycyclohexene. The procedure of Garbisch was employed.[13] To a solution at 0 °C of diol (1 equiv) and 3-bromo-2-methoxycyclohexene (1 equiv) in dry dichloromethane (2 mL/mmol) was added a catalytic amount of boron trifluoride etherate or *p*-toluenesulfonic acid monohydrate. Progress of the reaction was monitored by TLC. When the reaction was complete, the mixture was poured into saturated aqueous sodium bicarbonate and extracted with dichloromethane. The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated in vacuo. Chromatography on silica gel 60 eluted with ethyl acetate/hexanes provided diastereomeric 2-bromocyclohexan-1-one ketals.

The above mixture of bromides was dissolved in dry DMSO (2 mL/mmol) and treated at room temperature with sodium methoxide (4–8 equiv). Progress of the elimination was monitored

(14) Smith, A. B., III.; Branca, S. J.; Guaciaro, M. A.; Wovkulich, P. M.; Korn, A. *Org. Synth.* **1983**, *61*, 65–70.
(15) Totton, E. L.; Freeman, R. C.; Powell, H.; Yarboro, T. L. *J. Org. Chem.* **1961**, *26*, 343–346.
(16) Hibino, J.; Okazoe, T.; Takai, K.; Nozaki, H. *Tetrahedron Lett.* **1985**, *26*, 5579–5580.
(17) Klein, J.; Lichtenberg, D. *J. Org. Chem.* **1970**, *35*, 2654–2656.
(18) Omura, K.; Swern, D. *Tetrahedron* **1978**, *34*, 1651–1660.
(19) Williams, D. R.; Klingler, F. D.; Allen, E. E.; Lichtenthaler, F. W. *Tetrahedron Lett.* **1988**, *29*, 5087–5090.

by TLC. When elimination was complete, the mixture was poured into saturated aqueous sodium chloride and extracted with hexanes. The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated in vacuo. Chromatography on silica gel 60 eluted with ethyl acetate/hexanes gave the desired ene ketal.

(b) By Direct Ketalization or Transketalization. To a well-stirred solution of the enone or dimethoxy ketal (1–2 equiv) in dry benzene (4–20 mL/mmol) were added the diol (1 equiv) and pyridinium *p*-toluenesulfonate (5–10 mol %). The mixture was heated to reflux under argon and water or methanol was removed azeotropically using a Dean–Stark trap. Progress of the reaction was monitored by TLC. Ketalization was terminated by cooling the mixture, which was then diluted with ether, washed with water, saturated sodium bicarbonate solution, and saturated sodium chloride solution, dried ($MgSO_4$), and filtered. Volatiles were removed and the residue was chromatographed as above to provide the desired ene ketal.

General Cyclopropanation Procedure. To a well-stirred suspension of freshly prepared Zn–Cu couple (400–700 mg/mmol ene ketal) with or without anhydrous potassium carbonate (3 molar equiv) in freshly distilled (from P_2O_5) diethyl ether (1.7 mL/mmol ene ketal) under argon were added a small crystal of iodine and diiodomethane (3 equiv). After 30 min at reflux (external heating), the ene ketal was added as a solution in diethyl ether. Progress of the reaction was monitored by TLC and/or by HPLC. When reaction was complete, the mixture was cooled to 0 °C and quenched with water or with saturated aqueous potassium carbonate (0.2 mL/mmol ene ketal). After stirring at room temperature for 30 min, the gray-black precipitate was removed by centrifugation or filtration and washed well with diethyl ether. The combined organic extracts were washed with saturated aqueous ammonium chloride, saturated aqueous sodium bicarbonate, and saturated aqueous sodium chloride, dried ($MgSO_4$), filtered, and concentrated to give the crude product. Chromatography as above afforded the pure cyclopropane ketal.

General Hydrolysis Procedure. To a stirred solution of the cyclopropane ketal in methanol (4.9 mL/mmol ketal) at room temperature was added 2.7 M hydrochloric acid (1 mL/mmol ketal). Progress of the reaction was monitored by TLC. When reaction was complete, the solution was poured into saturated aqueous sodium bicarbonate solution. The aqueous mixture was extracted several times with diethyl ether. The combined extracts were dried ($MgSO_4$), filtered, and concentrated to afford a mixture of ketone and diol. Column chromatography afforded the pure ketone as well as the diol.

2-Cyclohexen-1-one 1,4-di-*O*-benzyl-L-threitol ketal (1): see ref 6a.

2-Cyclohexen-1-one 1,4-di-*O*-methyl-L-threitol ketal (2): yellow oil, $[\alpha]^{25}_D$ +13.4° (*c* 4.12, $CHCl_3$); yield 63% from the diol; IR ($CHCl_3$) 3000, 2930, 2890, 2830, 1450, 1395, 1335, 1170, 1095, and 930 cm^{-1}; ^1H NMR ($CDCl_3$) 1.72–1.91 (4, m), 1.96–2.06 (2, m), 3.40 (6, s), 3.48–3.60 (4, m), 3.93–4.09 (2, m), 5.63 (1, br d, ^3J = 10.0 Hz), and 5.94 ppm (1, dt, ^3J = 3.7 Hz, ^3J = 10.2 Hz); mass spectrum (70 eV) *m/z* (rel intensity) 228 (2), 201 (11), 200 (100), 183 (48), 149 (15), 115 (85), 111 (14), 97 (25), 95 (12), 87 (47), 85 (15), 83 (32), 82 (13), 81 (25), 79 (18), 77 (10), 73 (16), 71 (26), 69 (45), 68 (64), 67 (18), 59 (49), 57 (51), 55 (43); exact mass calcd for M^+ $C_{12}H_{20}O_4$ 228.1361, obsd 228.1367.

2-Cyclohexen-1-one 1,4-di-*O*-(4-biphenylylmethyl)-L-threitol ketal (3): cream colored crystals, mp 63–65 °C, softened at 55 °C; $[\alpha]^{27}_D$ +4.67° (*c* 1.3, $CHCl_3$); yield 88% from the diol; IR ($CHCl_3$) 3028, 3014, 2933, 2867, 1908, 1730, 1650, 1599, 1566, 1518, 1487, 1449, 1396, 1362, 1310, 1268, 1233, 1176, 1100, 1008, 972, 939, 844, 825, 699, and 668 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.69–2.08 (6, m), 3.66 (4, t, J_{HH} = 4.1 Hz), 4.04–4.21 (2, m), 4.60 (4, s), 5.67 (1, d, J_{HH} = 10.1 Hz), 5.86–6.00 (1, dt, J_{HH} = 3.6 and 10.1 Hz), 7.24–7.47 (10, m), and 7.48–7.60 (8, m); ^{13}C NMR ($CDCl_3$) δ 20.5 (CH_2), 24.7 (CH_2), 34.7 (CH_2), 70.5 (CH_2), 73.0 (CH_2), 73.1 (CH_2), 77.1 (CH), 77.4 (CH), 106.6 (C), 126.88 (CH), 126.94 (CH), 127.1 (CH), 127.9 (CH), 128.0 (CH), 128.4 (CH), 128.6 (CH), 132.6 (CH), 136.9 (C), 137.0 (C), 140.4 (C), and 140.6 (C); mass spectrum (70 eV) *m/z* (rel intensity) 529 (4), 504 (4), 365 (5), 269 (14), 168 (18), 167 (100).

2-Cyclohexen-1-one 1,4-di-*O*-(2′-naphthylmethyl)-L-threitol ketal (4): white crystals from hexanes, mp 74.5–79 °C; $[\alpha]^{24}_D$ +2.28° (*c* 1.2, $CHCl_3$); yield 77% from the diol; IR ($CHCl_3$) 3058, 3018, 2917, 2867, 1602, 1508, 1457, 1437, 1395, 1347, 1270, 1214, 1173, 1100, 941, 856, 819, 785, 754, 732, and 668 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.71–1.94 (4, m), 1.95–2.07 (2, m), 3.68 (4, t, J_{HH} = 4.4 Hz), 4.07–4.22 (2, m), 4.73 (4, s), 5.66 (1, d, J_{HH} = 10.1 Hz), 5.90–6.00 (1, dt, J_{HH} = 3.38 and 10.1 Hz), 7.36–7.52 (6, m), and 7.71–7.84 (8, m); ^{13}C NMR ($CDCl_3$) δ 20.6 (CH_2), 24.7 (CH_2), 34.7 (CH_2), 70.4 (CH_2), 70.5 (CH_2), 73.5 (CH_2), 77.2 (CH), 77.4 (CH), 106.7 (C), 125.5 (CH), 125.5 (CH), 125.8 (CH), 126.0 (CH), 126.2 (CH), 126.3 (CH), 127.6 (CH), 127.8 (CH), 128.1 (CH), 128.4 (CH), 132.6 (CH), 132.9 (C), 133.1 (C), 135.37 (C), and 135.42 (C); mass spectrum (70 eV) *m/z* (rel intensity) 452 (2), 391 (2), 387 (2), 339 (3), 332 (3), 322 (3), 268 (3), 260 (3), 249 (4), 248 (4), 243 (5), 241 (6), 142 (17), 141 (100); peak matching for *m/z* 480 ($C_{32}H_{32}O_4$): measured mass 480.2297, calcd 480.2302.

(3*R*,4*R*)-2,5-Dimethoxy-2,5-dimethyl-3,4-hexanediol. To a solution of methylmagnesium bromide (41 g, 0.34 mol) in THF (250 mL) at 0 °C was added dropwise a solution of dimethyl L-tartrate acetone ketal (16.08 g, 73.69 mmol) in THF (50 mL). When the addition was complete the solution was poured carefully onto crushed ice (100 g) and the resulting mixture acidified with 10% aqueous hydrochloric acid. The organic layer was removed and the aqueous layer washed with dichloromethane. The combined organic extracts were washed with saturated aqueous sodium bicarbonate, water, and saturated aqueous sodium chloride, dried ($MgSO_4$), filtered, and concentrated in vacuo to afford the product as a white solid homogeneous by TLC (R_f 0.39, 50% ethyl acetate/hexanes): yield 15.32 g, 70.18 mmol, 95%. Recrystallization from toluene gave needles, mp 152–153 °C; ^1H NMR ($CDCl_3$) 1.28 (6, s), 1.32 (6, s), 1.38 (6, s), 3.39 (2, s), and 3.76 ppm (2, s).

To a suspension of sodium hydride (2.18 g, 90.8 mmol) in dimethylformamide (50 mL) at 0 °C was added the diol from above (7.02 g, 32.2 mmol) as a solution in DMF (30 mL). The resulting mixture was stirred at 0 °C for 0.5 h and then warmed to room temperature for 0.5 h before being cooled again to 0 °C, and methyl iodide (11 g, 80 mmol) was added. After 0.5 h at 0 °C the mixture was warmed slowly to room temperature. Progress of the reaction was monitored by TLC (50% ethyl acetate/hexanes). After 1 h the mixture was poured carefully into saturated aqueous sodium bicarbonate (150 mL) and the product extracted with diethyl ether (3 × 70 mL). The combined ether extracts were washed with water (50 mL) and saturated aqueous sodium chloride (50 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to give (3*R*,4*R*)-2,5-dimethoxy-2,5-dimethyl-3,4-hexanediol acetone ketal as a yellow oil (R_f 0.59, 20% ethyl acetate/hexanes): yield 7.08 g, 28.7 mmol, 90%; ^1H NMR ($CDCl_3$) 1.16 (6, s), 1.20 (6, s), 1.44 (6, s), 3.21 (6, s), and 4.01 ppm (2, s).

To a solution of (3*R*,4*R*)-2,5-dimethoxy-2,5-dimethyl-3,4-hexanediol acetone ketal (1.00 g, 4.06 mmol) in methanol (15 mL) were added water (300 mg, 17 mmol) and a catalytic amount of *p*-toluenesulfonic acid monohydrate. The solution was then heated to reflux and progress of the reaction monitored by TLC (50% ethyl acetate/hexanes). After 24 h the solution was cooled to room temperature and an excess amount of potassium carbonate added. After 1 h the supernatent was decanted and the solvent removed in vacuo to afford the crude product as a light brown oil. Filtration through a short plug of silica gel 60 eluted with 50% ethyl acetate/hexanes gave the product diol as a golden oil homogeneous by TLC (R_f 0.39, 50% ethyl acetate/hexanes), $[\alpha]^{25}_D$ −6.42° (*c* 4.37, $CHCl_3$): yield 0.66 g, 3.20 mmol, 79%; IR ($CHCl_3$) 3520, 3005, 2980, 2950, 2840, 1735, 1465, 1380, 1365, 1240, 1205, 1180, 1145, 1095, 1065, 980, and 840 cm^{-1}; ^1H NMR ($CDCl_3$) 1.21 (6, s), 1.24 (6, s), 3.27 (6, s), 3.50 (2, d, ^3J = 4.0 Hz), and 3.63 ppm (2, d, ^3J = 4.0 Hz); mass spectrum (70 eV) *m/z* (rel intensity) 191 (0.1), 175 (0.2), 174 (0.1), 173 (0.6), 160 (0.1), 159 (1), 143 (1), 127 (1), 116 (5), 103 (17), 101 (8), 73 (100).

2-Cyclohexen-1-one (3*R*,4*R*)-2,5-dimethoxy-2,5-dimethyl-3,4-hexanediol ketal (5): pale yellow oil, $[\alpha]^{17}_D$ −19.5° (*c* 3.64, $CHCl_3$); yield from the diol 73%; IR ($CHCl_3$) 2980, 2945, 2835, 1465, 1395, 1380, 1365, 1170, 1125, 1075, 1025, and 945 cm^{-1}; ^1H NMR ($CDCl_3$) 1.14 (3, s), 1.15 (3, s), 1.22 (6, s), 1.69–2.08 (6, m), 3.21 (6, s), 4.03–4.10 (2, m), and 5.78–5.94 ppm (2, m); mass spectrum (70 eV) *m/z* (rel intensity) 284 (0.1), 256 (6), 211 (5), 151 (2), 139 (2), 117 (2), 115 (3), 111 (2), 97 (16), 87 (10), 73 (100), 55 (9); exact mass calcd for M^+ $C_{16}H_{28}O_4$ 284.1987, obsd 284.1998.

2-Cyclohexen-1-one dimethyl L-tartrate ketal (6): colorless oil, $[\alpha]^{24}_D$ −8.5° (*c* 3.5, $CHCl_3$); yield from the diol 83%; IR ($CHCl_3$)

3030, 2960, 1755, 1438, 1397, 1275, 1217 (br), 1174, 1125, and 930 cm^{-1}; ^1H NMR ($CDCl_3$) 1.75–2.10 (6, m), 3.83 (6, s), 4.85 (2, s), 5.66 (1, br d, ^3J = 10.1 Hz), and 6.04 ppm (1, dt, ^3J = 3.6 Hz, ^3J = 10.1 Hz); mass spectrum (70 eV) *m/z* (rel intensity) 256 (1), 229 (10), 228 (100), 215 (4), 197 (15), 113 (3), 111 (5), 97 (3), 68 (42); exact mass calcd for M^+ $C_{12}H_{16}O_6$ 256.0947, obsd 256.0947.

2-Cyclohexen-1-one 2,3-L-Threitol Ketal (7). To a well-stirred solution of 2-bromocyclohexan-1-one 1,4-di-*O*-benzyl-L-threitol ketal (2.045 g, 4.432 mmol) in methanol (20 mL) under an argon atmosphere was added 10% palladium on carbon (ca. 100 mg). The flask was repeatedly evacuated and flushed with hydrogen. Progress of the reaction was monitored by TLC (50% ethyl acetate/hexanes). After 1.5 h an argon atmosphere was introduced, the mixture filtered, and the solvent removed in vacuo to afford crude 2-bromocyclohexan-1-one 2,3-L-threitol ketal as a yellow oil, which was used directly without purification in the next step.

The crude bromide from above was dissolved in anhydrous DMSO (8 mL) and cooled in ice, sodium methoxide (0.76 g, 14.1 mmol) was added, and the mixture was warmed to room temperature. Progress of the reaction was monitored by TLC (80% ethyl acetate/hexanes). After 5 h the reaction was quenched by bubbling CO_2 through the solution. Volatiles were removed in vacuo and the solid residue was washed well with diethyl ether. The combined ether washings were concentrated in vacuo. Column chromatography on silica gel 60 (200 g) eluted with 80% ethyl acetate/hexanes gave the product as a yellow oil homogeneous by TLC (R_f 0.34), $[\alpha]^{22}_D$ +17.7° (*c* 3.3, $CHCl_3$). The oil may be crystallized from chloroform/hexanes to afford the product as fine, white needles (mp 77–78 °C): yield 624 mg, 3.12 mmol, 70%; IR ($CHCl_3$) 3596, 3457, 3015, 2932, 2876, 1719, 1457, 1395, 1271, 1233, 1215, 1175, 1115, 1043, 939, 768, and 750 cm^{-1}; ^1H NMR ($CDCl_3$) 1.72–1.93 (4, m), 1.99–2.10 (2 m), 2.37 (2, br s), 3.62–3.90 (4, m), 4.97–5.06 (2, m), 5.62 (1, br d, ^3J = 10.1 Hz), and 5.99 ppm (1, dt, ^3J = 3.7 Hz, ^3J = 10.1 Hz); mass spectrum (70 eV) *m/z* (rel intensity) 200 (1), 173 (9), 172 (100), 169 (19), 159 (5), 98 (6), 97 (75), 96 (6), 87 (9), 86 (28), 81 (11), 79 (21), 77 (7), 69 (25), 68 (74), 67 (10), 55 (27); exact mass calcd for M^+ $C_{10}H_{16}O_4$ 200.1048, obsd 200.1048.

2-Cyclohexen-1-one (2*R*,3*R*)-2,3-butanediol ketal (8): pale yellow oil, $[\alpha]^{25}_D$ −37.8° (*c* 3.10, $CHCl_3$); yield from the diol 84%; IR ($CHCl_3$) 3010, 2985, 2955, 2935, 2885, 2840, 1455, 1440, 1390, 1380, 1215, 1175, 1105, 1080, 970, 935, and 900 cm^{-1}; ^1H NMR ($CDCl_3$) 1.25 (3, d, ^3J = 3.1 Hz), 1.27 (3, d, ^3J = 3.1 Hz), 1.72–1.89 (4, m), 1.97–2.07 (2, m), 3.55–3.75 (2, m), 5.60 (1, dt, ^4J = 2.1 Hz, ^3J = 10.1 Hz), and 5.94 (1, dt, ^3J = 3.7 Hz, ^3J = 10.1 Hz); mass spectrum (70 eV) *m/z* (rel intensity) 168 (2), 141 (5), 140 (46), 127 (9), 124 (2), 114 (2), 97 (4), 96 (7), 86 (8), 80 (13), 79 (100), 77 (7), 68 (94), 55 (20); exact mass calcd for M^+ $C_{10}H_{16}O_2$ 168.1150, obsd 168.1145.

***(dl)*-1,8-Diphenyl-4,5-octanediol.** To a solution of 4-phenyl-1-butanol (2.08 g, 13.8 mmol) in dry dichloromethane (20 mL) at room temperature was added pyridinium dichromate (8.25 g, 21.9 mmol). Progress of the reaction was monitored by TLC (50% ethyl acetate/hexanes). After 10 h of vigorous stirring at room temperature the reaction mixture was diluted with diethyl ether (100 mL) and filtered through a column of silica gel 60 (50 g). The eluent was washed with 1% aqueous hydrochloric acid, saturated aqueous sodium bicarbonate, and saturated aqueous sodium chloride, then dried ($MgSO_4$), filtered, and concentrated in vacuo. Column chromatography on silica gel 60 (450 g) eluted with 15% ethyl acetate/hexanes gave 4-phenylbutyraldehyde as a pale yellow oil homogeneous by TLC (R_f 0.44, 20% ethyl acetate/hexanes); yield 1.19 g, 8.03 mmol, 58%.

To a well-stirred solution of mercuric chloride (149 mg, 0.316 mmol) in freshly distilled (from sodium/benzophenone ketyl) tetrahydrofuran (10 mL) at room temperature was added magnesium metal (70–80 mesh, 488 mg, 20.1 mmol). After 0.25 h the supernatant was decanted and the grey amalgam washed with THF (3 × 7 mL). The amalgam was then suspended in THF (17 mL) and cooled to −10 °C, and titanium tetrachloride (1.9 g, 10 mmol) was added dropwise. 4-Phenylbutyraldehyde (1.00 g, 6.75 mmol) was added at −10 °C as a solution in THF (17 mL) and the resulting mixture warmed to 0 °C. Progress of the reaction was monitored by TLC on silica gel 60 eluted with 20% ethyl acetate/hexanes. After 24 h the reaction was quenched with saturated aqueous potassium carbonate (1.7 mL) and the resulting blue mixture stirred at 0 °C for 0.25 h. The mixture was then diluted with diethyl ether and filtered through a Celite pad. The filtrate was washed with saturated aqueous sodium chloride, dried ($MgSO_4$), filtered, and concentrated to give the crude product as a yellow oil. Column chromatography on silica gel 60 (450 g) eluted with 20% ethyl acetate/hexanes gave two fractions, the first of which was determined by ^1H NMR to be an acetal of 4-phenylbutyraldehyde and the product diol while the second appeared to be a mixture of this acetal and another acetal of 4-phenylbutyraldehyde and an isomeric product diol. Hydrolyses of these fractions (15% water/methanol and *p*-toluenesulfonic acid) gave a total of 135 mg of isomeric product diols. Elution of the column with 50% ethyl acetate/hexanes afforded the product diol as a single isomer homogeneous by TLC (R_f 0.20, 35% ethyl acetate/hexanes); yield 268 mg, 0.90 mmol, 27%. ***dl* isomer**: IR ($CHCl_3$) 3590, 3440, 3090, 3070, 3010, 2940, 2865, 1605, 1495, 1455, 1105, 1065, 905, and 690 cm^{-1}; ^1H NMR ($CDCl_3$) 1.37–2.11 (10, m), 2.52–2.75 (4, m), 3.41 (2, br t, ^3J = 4.5 Hz), and 7.10–7.38 ppm (10, m); mass spectrum (70 eV) *m/z* (rel intensity) 262 (3), 189 (2), 158 (3), 147 (9), 132 (9), 131 (31), 105 (18), 104 (100), 92 (14), 91 (62); exact mass calcd for $M^+ - 2H_2O$ $C_{20}H_{22}$ 262.1722, obsd 262.1723.

2-Cyclohexen-1-one 1,8-diphenyl-4,5-octanediol ketal (9): yellow oil; yield from diol 51%; IR ($CHCl_3$) 3095, 3070, 3010, 2950, 2870, 1605, 1490, 1455, 1395, 1125, 1105, and 940 cm^{-1}; ^1H NMR ($CDCl_3$) 1.40–2.10 (14, m), 2.63 (4, t, ^3J = 7.8 Hz), 3.54–3.73 (2, m), 5.56 (1, br d, ^3J = 10.1 Hz), 5.92 (1, dt, ^3J = 3.6 Hz, ^3J = 10.1 Hz), and 7.07–7.32 ppm (10, m); ^{13}C NMR ($CDCl_3$) 20.7 (CH_2), 24.8 (CH_2), 27.7 (CH_2), 27.9 (CH_2), 32.3 (CH_2), 32.4 (CH_2), 35.1 (CH_2), 35.8 (CH_2), 35.9 (CH_2), 80.4 (CH), 80.7 (CH), 105.0 (C), 125.7 (CH), 128.2 (CH), 128.4 (CH), 129.0 (CH), 132.4 (CH), and 142.1 ppm (C); mass spectrum (70 eV) *m/z* (rel intensity) 376 (3), 348 (12), 262 (7), 189 (4), 171 (3), 158 (8), 150 (3), 147 (5), 144 (5), 143 (13), 132 (20), 131 (53), 117 (25), 105 (22), 104 (100), 92 (17), 91 (95), 69 (7); exact mass calcd for M^+ $C_{26}H_{32}O_2$ 376.2402, obsd 376.2410.

2-Cyclohexen-1-one (*S*,*S*)-1,2-diphenyl-1,2-ethanediol ketal (10): see ref 6d.

(1*R*,6*S*)-Bicyclo[4.1.0]heptan-2-one 1,4-di-*O*-benzyl-L-threitol ketal (11): see ref 6a.

(1*R*,6*S*)-Bicyclo[4.1.0]heptan-2-one 1,4-di-*O*-methyl-L-threitol ketal (12): colorless oil, $[\alpha]^{22}_D$ −19.0° (*c* 2.5, $CHCl_3$); yield 86%; IR ($CHCl_3$) 3000, 2950, 2890, 2820, 1445, 1380, 1330, 1180, 1130, 1085, 950, and 910 cm^{-1}; ^1H NMR ($CDCl_3$) 0.26–0.39 (1, m), 0.63–0.78 (1, m), 1.05–1.67 (7, m), 1.75–1.94 (1, m), 3.40 (3, s), 3.41 (3, s), 3.51–3.70 (4, m), and 3.93–4.17 ppm (2, m); ^{13}C NMR ($CDCl_3$) major diastereomer 9.4 (CH_2), 12.2 (CH) 19.6 (CH), 22.2 (CH_2), 32.4 (CH_2), 59.2 (CH_3), 73.2 (CH_2), 76.7 (CH), 76.9 (CH), and 110.2 ppm (C); minor diastereomer 9.0 (CH_2), 12.0 (CH), 19.0 (CH_2), 19.6 (CH), 22.2 (CH_2), 33.0 (CH_2), 59.2 (CH_3), 73.4 (CH_2), 73.6 (CH_2), 77.2 (CH), and 110.0 ppm (C); mass spectrum (70 eV) *m/z* (rel intensity) 243 (2), 242 (13), 241 (5), 214 (11), 213 (10), 198 (6), 197 (49), 187 (44), 115 (100), 111 (30), 97 (15), 95 (17), 93 (18), 87 (23), 85 (20), 83 (20), 82 (11), 81 (35), 79 (13), 71 (22), 70 (11), 69 (67), 68 (11), 67 (20), 59 (25), 57 (39), 55 (38); exact mass calcd for M^+ $C_{13}H_{22}O_4$ 242.1518, obsd 242.1512.

(1*R*,6*S*)-Bicyclo[4.1.0]heptan-2-one 1,4-di-*O*-(4-biphenylylmethyl)-L-threitol ketal (13): pale yellow oil; yield 99%; ^1H NMR ($CDCl_3$) δ 0.32 (1, dd, *J* = 12 Hz, *J* = 6 Hz), 0.72 (1, m), 1.10–1.95 (8, m), 3.66–3.73 (4, m), 4.11 (1, m), 4.20 (1, m), 4.61 (4, m), 7.26–7.48 (10, m), and 7.50–7.62 (8, m); ^{13}C NMR ($CDCl_3$) δ 9.56 (CH_2), 12.37 (CH), 19.8 (CH), 19.95 (CH_2), 22.33 (CH_2), 32.6 (CH_2), 70.59 (CH_2), 70.65 (CH_2), 73.07 (CH_2), 77.06 (CH), 77.33 (CH_2), 110.29 (C), 126.94 (CH), 126.99 (CH), 127.16 (CH), 127.94 (CH), 128.66 (CH), 137.02 (C), 140.40 (C), and 140.68 (C).

(1*R*,6*S*)-Bicyclo[4.1.0]heptan-2-one 1,4-di-*O*-(2′-naphthylmethyl)-L-threitol ketal (14): pale yellow oil; yield 76%; ^1H NMR ($CDCl_3$) δ 0.31 (1, dd, *J* = 10 Hz, *J* = 5 Hz), 0.62–0.77 (1, m), 1.10–1.95 (8, m), 3.58–3.76 (4, m), 4.02–4.28 (2, m), 4.65–4.68 (4, m), 7.33–7.48 (6, m), and 7.66–7.82 (8, m); ^{13}C NMR ($CDCl_3$) δ 9.51 (CH_2), 12.33 (CH), 19.75 (CH), 19.89 (CH_2), 22.28 (CH_2), 32.57 (CH_2), 70.47 (CH_2), 70.53 (CH_2), 73.36 (CH_2), 76.97 (CH), 77.27 (CH), 110.26 (C), 125.45 (CH), 125.69 (CH), 125.93 (CH), 126.21 (CH), 127.54 (CH), 127.70 (CH), 127.98 (CH),

132.79 (C), 133.05 (C), and 135.40 (C).

(1*R*,6*S*)-Bicyclo[4.1.0]heptan-2-one (3*R*,4*R*)-2,5-Dimethoxy-2,5-dimethyl-3,4-hexanediol Ketal (15). Product was obtained as a colorless oil by column chromatography on silica gel 60 eluted with chloroform; yield 91%; $[\alpha]^{25}_D$ −29.6° (*c* 1.48, $CHCl_3$); IR ($CHCl_3$) 2990, 2970, 2855, 2820, 1725 (br), 1460, 1375, 1355, 1135, 1105, 1070, and 950 cm^{-1}; ^1H NMR ($CDCl_3$) 0.21–0.32 (1, m), 0.57–0.76 (1, m), 1.05–2.08 (20, m), 3.20 (3, s), 3.22 (3, s), and 4.00–4.15 ppm (2, m); ^{13}C NMR ($CDCl_3$) minor diastereomer 9.3 (CH_2), 12.8 (CH), 15.2 (CH_2), 19.7 (CH_2), 20.0 (CH_3), 20.6 (CH), 21.8 (CH_3), 33.9 (CH_2), 75.7 (C), 84.1 (CH), and 111.5 (C); major diastereomer 9.6 (CH_2), 12.4 (CH), 20.3 (CH_2), 20.4 (CH_3), 20.8 (CH), 22.2 (CH_3), 22.5 (CH_2), 33.4 (CH_2), 49.1 (CH_3), 75.5 (C), 75.8 (C), 83.3 (CH), 83.7 (CH), and 110.9 ppm (C); mass spectrum (70 eV) *m/z* (rel intensity) 298 (0.4), 243 (1), 226 (1), 225 (11), 165 (3), 139 (3), 125 (3), 115 (5), 111 (18), 87 (14), 73 (100), 55 (18); exact mass calcd for M^+ $C_{17}H_{30}O_4$ 298.2144, obsd 298.2136.

(1*R*,6*S*)-Bicyclo[4.1.0]heptan-2-one Dimethyl L-Tartrate Ketal (16). The product was obtained as a pale yellow oil contaminated with starting material (25% as determined by integration of the ^1H NMR spectrum): yield 37%; ^1H NMR ($CDCl_3$) 0.32–0.44 (1, m), 0.68–0.82 (1, m), 1.05–2.10 (8, m), 3.82 (3, s), 3.84 (3, s), and 4.78–5.00 ppm (2, m); ^{13}C NMR ($CDCl_3$) major diastereomer 9.2 (CH_2), 12.5 (CH), 18.5 (CH), 19.3 (CH_2), 22.0 (CH_2), 32.2 (CH_2), 52.7 (CH_3), 76.4 (CH), 76.6 (CH), 76.7 (CH), 76.9 (CH), 114.8 (C), 169.9 (C), and 170.1 ppm (C); minor diastereomer 9.5 (CH_2), 12.5 (CH), 18.9 (CH), 19.2 (CH_2), 22.0 (CH_2), 31.9 (CH_2), 52.7 (CH_3), 76.4 (CH), 76.6 (CH), 76.7 (CH), 76.9 (CH), 114.6 (C), 169.9 (C), and 170.1 ppm (C); mass spectrum (70 eV) *m/z* (rel intensity) 271 (3), 270 (18), 269 (2), 255 (2), 243 (5), 242 (35), 241 (32), 229 (13), 228 (100), 216 (11), 215 (85), 211 (27), 197 (16), 145 (12), 117 (5), 113 (27), 109 (9), 93 (19), 91 (13), 82 (17), 81 (23), 79 (20), 77 (20), 68 (46); exact mass calcd for M^+ $C_{13}H_{18}O_6$ 270.1104, obsd 270.1104.

(1*S*,6*R*)-Bicyclo[4.1.0]heptan-2-one 2,3-*O*-L-Threitol Ketal (17). The product was obtained as a pale yellow oil contaminated with 50% starting material: yield 33%; ^1H NMR ($CDCl_3$) δ 0.27–0.35 (1, m), 0.66–0.79 (1, m), 1.10–2.10 (8, m), 3.23 (2, br s), 3.60–4.10 (6, m); ^{13}C NMR ($CDCl_3$) δ major diastereomer 8.69 (CH_2), 12.10 (CH), 18.95 (CH_2), 19.98 (CH), 22.21 (CH_2), 33.36 (CH_2), 62.13 (CH_2), 62.21 (CH_2), 78.06 (CH), 78.17 (CH), and 109.67 (C); minor diastereomer 9.72 (CH_2), 12.34 (CH), 19.63 (CH), 20.05 (CH_2), 22.10 (CH_2), 32.36 (CH_2), 62.13 (CH_2), 62.21 (CH_2), 78.12 (CH), 78.27 (CH), and 110.02 (C).

(1*S*,6*R*)-Bicyclo[4.1.0]heptan-2-one (2*R*,3*R*)-2,3-butanediol ketal (18): colorless oil, $[\alpha]^{25}_D$ +13.1° (*c* 1.82, $CHCl_3$); yield 86%; IR ($CHCl_3$) 2990, 2965, 2930, 2855, 1445, 1370, 1130, 1105, 1080, 940, and 895 cm^{-1}; ^1H NMR ($CDCl_3$) 0.22–0.35 (1, m), 0.73 (1, ddd, ^2J = 5.1 Hz, ^3J = ^3J = 9.0 Hz), 1.04–1.70 (13, m), 1.81–1.98 (1, m), and 3.56–3.86 ppm (2, m); ^{13}C NMR ($CDCl_3$) 9.9 (CH_2), 12.3 (CH), 16.9 (2 × CH_3), 20.1 (CH), 20.4 (CH_2), 22.3 (CH_2), 32.5 (CH_2), 78.0 (2 × CH), and 108.4 ppm (C); mass spectrum (70 eV) *m/z* (rel intensity) 182 (11), 154 (18), 153 (19), 149 (16), 127 (67), 97 (19), 95 (24), 93 (13), 85 (17), 83 (29), 82 (26), 81 (49), 79 (26), 73 (27), 71 (33), 70 (22), 69 (100), 68 (18), 67 (22), 60 (21), 57 (61), 56 (23), 55 (66); exact mass calcd for M^+ $C_{11}H_{18}O_2$ 182.1307, obsd 182.1308.

Bicyclo[4.1.0]heptan-2-one 1,8-diphenyl-4,5-octanediol ketal (19): yellow oil; yield 93%; IR ($CHCl_3$) 3090, 3070, 3010, 2950, 2870, 1605, 1495, 1455, 1385, 1135, 1105, 1090, 905, and 690 cm^{-1}; ^1H NMR ($CDCl_3$) 0.26 (1, ddd, ^2J = 5.4 Hz, ^3J = ^3J = 10.8 Hz), 0.67 (1, ddd, ^2J = 5.1 Hz, ^3J = ^3J = 9.0 Hz), 1.00–2.00 (16, m), 2.63 (2, t, ^3J = 7.5 Hz), 2.65 (2, t, ^3J = 7.4 Hz), 3.54–3.82 (2, m), and 7.11–7.38 ppm (10, m); ^{13}C NMR ($CDCl_3$) 9.2 (CH_2), 12.3 (CH), 19.9 (CH_2), 20.2 (CH), 22.4 (CH_2), 27.8 (CH_2), 27.9 (CH_2), 32.5 (CH_2), 32.6 (CH_2), 33.0 (CH_2), 35.9 (CH_2), 80.4 (CH), 80.5 (CH), 108.4 (C), 125.7 (CH), 128.2 (CH), 128.4 (CH), and 142.2 ppm (C); mass spectrum (70 eV) *m/z* (rel intensity) 390 (4), 362 (1), 361 (1), 336 (4), 335 (16), 263 (2), 262 (7), 158 (15), 143 (15), 132 (16), 131 (31), 117 (37), 111 (31), 105 (14), 104 (62), 91 (100); exact mass calcd for M^+ $C_{27}H_{34}O_2$ 390.2559, obsd 390.2551.

(1*R*,6*S*)-Bicyclo[4.1.0]heptan-2-one (*S*,*S*)-1,2-diphenyl-1,2-ethanediol ketal (20): see ref 6d.

2-Cyclopenten-1-one 1,4-di-*O*-benzyl-L-threitol ketal (21): see ref 6a.

2-Cyclopenten-1-one (*S*,*S*)-1,2-diphenyl-1,2-ethanediol ketal (22): see ref 6d.

2-Methyl-2-cyclopenten-1-one 1,4-di-*O*-benzyl-L-threitol ketal (23): see refs 6c and 8b.

2-Methyl-2-cyclopenten-1-one 1,4-di-*O*-methyl-L-threitol ketal (24): pale oil; yield 81%; $[\alpha]^{25}_D$ −1.0° (*c* 4.14, $CHCl_3$); IR (neat) 3043, 2885, 1454, 1343, 1220, 1197, 1137, 1083, 1030, 962, 928, and 845 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.68 (3, m), 2.06–2.11 (2, m), 2.25–2.28 (2, m), 3.41 (6, s), 3.52–3.58 (4, m), 3.90–4.03 (2, m), 5.68 (1, m); ^{13}C NMR ($CDCl_3$) 10.54 (CH_3), 27.78 (CH_2), 36.30 (CH_2), 59.24 (2 × CH_3), 72.93 (CH_2), 73.49 (CH_2), 77.21 (CH), 78.03 (CH), 120.94 (C), 131.30 (CH), 138.70 (C); mass spectrum (70 eV) *m/z* (rel intensity) 229 (13), 228 (100), 183 (59), 115 (60); exact mass calcd for $C_{12}H_{20}O_4$ 228.1362, obsd 228.1362.

2-Methyl-2-cyclopenten-1-one diisopropyl L-tartrate ketal (25): pale oil; yield 14%; $[\alpha]^{26}_D$ −35.1° (*c* 4.6, $CHCl_3$); IR (neat) 3046, 2982, 2938, 2859, 1746, 1454, 1375, 1345, 1279, 1215, 1144, 1106, 1051, 1033, 978, 924, and 835 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.29 (6, d, *J* = 6 Hz), 1.31 (6, d, *J* = 6 Hz), 1.71 (3, m), 2.00–2.31 (4, m), 4.70 (2, s), 5.09–5.19 (2, m), and 5.79 (1, m); mass spectrum (70 eV) *m/z* (rel intensity) 312 (41), 270 (15), 228 (36), 226 (12), 225 (100), 183 (58), 139 (51), 113 (38), 97 (70), 96 (36); exact mass calcd for $C_{16}H_{24}O_6$ 312.1572, obsd 312.1576.

2-Cyclohepten-1-one 1,4-di-*O*-benzyl-L-threitol ketal (26): see ref 6a.

2-Cyclohepten-1-one (*S*,*S*)-1,2-diphenyl-1,2-ethanediol ketal (27): see ref 6d.

(1*R*,5*S*)-Bicyclo[3.1.0]hexan-2-one 1,4-di-*O*-benzyl-L-threitol ketal (28): see ref 6a.

(1*R*,5*S*)-Bicyclo[3.1.0]hexan-2-one (*S*,*S*)-1,2-diphenyl-1,2-ethanediol ketal (29): see ref 6d.

(1*R*,6*S*)-1-Methylbicyclo[3.1.0]hexan-2-one 1,4-di-*O*-benzyl-L-threitol ketal (30): see ref 6c.

(1*R*,5*S*)-1-Methylbicyclo[3.1.0]hexan-2-one 1,4-di-*O*-methyl-L-threitol ketal (31): an oil; yield 88%; $[\alpha]^{26}_D$ −26.5° (*c* 2.92, $CHCl_3$); IR (neat) 2927, 1454, 1364, 1334, 1296, 1216, 1196, 1100, 989, 961, 805, and 766 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.38 (1, dd, *J* = 7.7 Hz, *J* = 5.2 Hz), 0.68 (1, m), 1.16 (3, s), 1.17–2.00 (5, m), 3.39 (3, s), 3.42 (3, s), 3.40–3.65 (4, m), and 3.85–4.00 (2, m); ^{13}C NMR ($CDCl_3$) δ 14.00 (CH_2), 14.21 (CH_3), 22.87 (CH), 23.90 (CH_2), 26.77 (C), 32.11 (CH_2), 59.17 (2 × CH_3), 72.90 (CH_2), 73.43 (CH_2), 76.59 (CH), 77.68 (CH), and 119.92 (C); mass spectrum (70 eV) *m/z* (rel intensity) 243 (7), 242 (47), 227 (14), 201 (11), 188 (22), 115 (97), 85 (25), 84 (16), 81 (13), 79 (10), 73 (23), 71 (34), 70 (12), 69 (22), 67 (13), 59 (23), 57 (100); exact mass calcd for $C_{13}H_{22}O_4$ 242.1518, obsd 242.1515.

(1*R*,5*S*)-1-Methylbicyclo[3.1.0]hexan-2-one diisopropyl L-tartrate ketal (32): colorless oil; yield 36%; $[\alpha]^{25}_D$ −30.5° (*c* 2.77, $CHCl_3$); IR (neat) 3070, 2980, 2935, 2870, 1745, 1468, 1458, 1377, 1340, 1280, 1215, 1183, 1145, 1109, 1061, 991, 968, 944, and 830 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.45 (1, m), 0.75 (1, m), 1.20–1.32 (17, m), 1.55–1.70 (2, m), 1.83–2.00 (1, m), 4.60–4.70 (2, m), and 5.08–5.17 (2, m); ^{13}C NMR ($CDCl_3$) δ major diastereomer 13.90 (CH_3), 14.31 (CH_2), 21.55 (4 × CH_3), 23.13 (CH), 23.94 (CH_2), 26.60 (C), 31.62 (CH_2), 69.33 (CH), 69.39 (CH), 76.69 (CH), 77.65 (CH), 123.72 (C), 168.22 (C), 169.39 (C); minor diastereomer 13.77 (CH_3), 14.60 (CH_2), 21.55 (4 × CH_3), 23.27 (CH), 23.74 (CH_2), 26.81 (C), 31.56 (CH_2), 69.33 (CH), 69.39 (CH), 76.69 (CH), 77.60 (CH), 124.08 (C), 168.33 (C), 169.49 (C); mass spectrum (70 eV) *m/z* (rel intensity) 327 (18), 326 (100), 298 (18), 285 (56), 258 (45), 242 (20), 227 (22), 216 (17), 214 (20), 201 (80), 197 (54), 174 (31), 153 (22), 127 (20), 111 (67); exact mass calcd for $C_{17}H_{26}O_6$ 326.1729, obsd 326.1727.

(1*R*,7*S*)-Bicyclo[5.1.0]octan-2-one 1,4-di-*O*-benzyl-L-threitol ketal (33): see ref 6a.

(1*R*,7*S*)-Bicyclo[5.1.0]octan-2-one (*S*,*S*)-1,2-diphenyl-1,2-ethanediol ketal (34): see ref 6d.

2-Bromo-2-cyclohexen-1-one (*S*)-Propanediol Ketals 44 and 45. To a solution of 2-bromo-2-cyclohexen-1-one[14] (2.7 g, 15 mmol) and (*S*)-(+)-1,2-propanediol (371 mg, 4.9 mmol) in benzene (25 mL) was added *p*-toluenesulfonic acid (50 mg). The resulting mixture was heated to reflux and water was removed using a Dean–Stark trap. After 1 h the mixture was cooled to room temperature and diluted with ether (75 mL). The organic phase was washed with saturated $NaHCO_3$ (25 mL), water (25 mL), and brine (25 mL), then dried ($MgSO_4$), filtered, and concentrated

in vacuo. The crude product was chromatographed on silica gel 60 (400 g) eluted with 10% EtOAc/hexanes to afford 330 mg (1.52 mmol, 31%) of the less polar diastereomer **44** (R_f 0.36, 10% EtOAc/hexanes), 296 mg (1.36 mmol, 28%) of the more polar diastereomer **45** (R_f 0.30), and 429 mg (1.98 mmol, 40%) of a mixture of diastereomers **44** and **45**. Spectral data for compound **44**: an oil, $[\alpha]^{24}_D$ +36.1° (*c* 3.4, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.29 (3, d, *J* = 6 Hz), 1.71–2.20 (6, m), 3.40–3.54 (1, m), 4.21–4.34 (1, m), 4.48–4.66 (1, m), and 6.32 (1, t, *J* = 4 Hz); ^{13}C NMR ($CDCl_3$) δ 18.3 (CH_3), 20.2 (CH_2), 27.4 (CH_2), 36.8 (CH_2), 71.4 (CH_2), 74.2 (CH), 106.0 (C), 124.9 (CH), and 135.5 ppm (C).

Spectral data for compound **45**: an oil, $[\alpha]^{24}_D$ +55.4° (*c* 3.6, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.38 (3, d, *J* = 5.9 Hz), 1.73–2.23 (6, m), 3.72 (1, dd, *J* = 9.1 Hz, *J* = 7.3 Hz), 4.10 (1, dd, *J* = 7.3 Hz, *J* = 5.5 Hz), 4.19–4.35 (1, m), and 6.36 (1, t, *J* = 4.1 Hz); ^{13}C NMR ($CDCl_3$) δ 16.6 (CH_3), 20.2 (CH_2), 27.4 (CH_2), 35.8 (CH_2), 72.2 (CH), 72.4 (CH_2), 105.9 (C), 124.9 (CH), and 136.1 (C).

2-Cyclohexen-1-one (*S*)-1,2-Propanediol Ketal 37. To a solution of *n*-BuLi (1.55 M in hexanes, 0.62 mL, 0.96 mmol) in dry ether (6 mL) at −78 °C was added a solution of ene ketal **44** (70 mg, 0.32 mmol) in ether (2 mL). After 45 min at −78 °C, the mixture was allowed to warm to −30 °C and then quenched with saturated aqueous ammonium chloride solution (1 mL). The mixture was allowed to attain room temperature and washed with water (4 mL), saturated aqueous $NaHCO_3$ (4 mL), and saturated aqueous NaCl (4 mL), then dried ($MgSO_4$), filtered, and concentrated by distillation at atmospheric pressure. Chromatography on silica gel 60 (15 g) eluted with 10% Et_2O/pentane gave the product **37** as a colorless oil; $[\alpha]^{25}_D$ +34.8° (*c* 1.82, $CHCl_3$); yield 38 mg, 0.25 mmol, 76%; IR ($CHCl_3$) cm^{-1} 3010, 2985, 2955, 2935, 2875, 2840, 1646, 1439, 1394, 1385, 1345, 1340, 1215, 1172, 1107, 1071, 1024, 966, 946, 924, and 855; ^1H NMR ($CDCl_3$) δ 1.28 (3, d, *J* = 6.1 Hz), 1.72–1.90 (4, m), 1.98–2.10 (2, m), 3.43 (1, t, *J* = 7.8 Hz), 4.09 (1, dd, *J* = 7.8 Hz, *J* = 5.6 Hz), 4.20–4.36 (1, m), 5.64 (1, dt, *J* = 10.2 Hz, *J* = 2.1 Hz), and 5.93 (1, dt, *J* = 10.1 Hz, *J* = 3.6 Hz).

2-Cyclohexen-1-one (*S*)-1,2-propanediol ketal 38: an oil prepared from ene ketal **45** as above in 81% yield; $[\alpha]^{25}_D$ +52.1° (*c* 0.74, $CHCl_3$); IR ($CHCl_3$) cm^{-1} 3010, 2980, 2950, 2935, 2875, 2835, 1645, 1453, 1438, 1395, 1384, 1348, 1338, 1266, 1217, 1172, 1145, 1107, 1071, 1025, 970, 950, 924, 859, and 836; ^1H NMR ($CDCl_3$) δ 1.30 (3, d, *J* = 6.0 Hz), 1.77–1.93 (4, m), 1.97–2.15 (2, m), 3.49 (1, t, *J* = 7.7 Hz), 4.07 (1, dd, *J* = 7.8 Hz, *J* = 5.6 Hz), 4.17–4.33 (1, m), 5.58 (1, dt, *J* = 10.1 Hz, *J* = 2.1 Hz), and 5.98 (1, dt, *J* = 10.0 Hz, *J* = 3.7 Hz).

Alternatively, an inseparable mixture of ene ketals **37** and **38** was prepared in 91% yield using general ketalization procedure a.

Bicyclo[4.1.0]heptan-2-one (2*S*)-1,2-Propanediol Ketals 39 and 40. To a well-stirred suspension of freshly prepared Zn–Cu couple (863 mg) and anhydrous K_2CO_3 (460 mg, 3.33 mmol) in freshly distilled (from P_2O_5) diethyl ether (2 mL) were added a large crystal of iodine and diiodomethane (1.06 g, 3.97 mmol). After 0.5 h at reflux (external heating), a 1:1 mixture of 2-cyclohexen-1-one (*S*)-1,2-propanediol ketals **37** and **38** (205 mg, 1.33 mmol) was added as a solution in ether (0.5 mL). Progress of the reaction was monitored by TLC (1% methanol/dichloromethane). After 25 min the reaction was cooled to 0 °C, quenched with saturated aqueous K_2CO_3 (0.3 mL), warmed to room temperature, and stirred for 0.5 h. The solids were removed by centrifugation and washed well with diethyl ether. The combined supernatants were washed with saturated aqueous NH_4Cl, saturated aqueous $NaHCO_3$, and saturated aqueous NaCl, then dried ($MgSO_4$), filtered, and concentrated in vacuo (bath temperature <35 °C at ca. 30 mmHg). Column chromatography on silica gel 60 (30 g) eluted with 10% diethyl ether/pentane afforded a 2:1:2:1 mixture of diastereomeric product cyclopropane ketals **39ab** and **40ab** as a colorless oil homogeneous by TLC (R_f 0.24, 1% methanol/dichloromethane): yield 158 mg, 0.94 mmol, 70%; IR ($CHCl_3$) 3072, 3009, 2977, 2943, 2867, 1456, 1382, 1334, 1237, 1216, 1210, 1186, 1136, 1095, 1047, 1032, 981, 957, 916, 890, and 669 cm^{-1}; ^1H NMR ($CDCl_3$) 0.22–0.38 (1, m), 0.62–0.82 (1, m), 1.01–1.66 (10, m), 1.75–1.98 (1, m), 3.40–3.61 (1, m), and 4.03–4.45 ppm (2, m); ^{13}C NMR ($CDCl_3$) 8.3 (CH_2), 9.2 (CH_2), 9.3 (CH_2), 9.4 (CH_2), 11.8 (CH), 11.9 (CH), 12.1 (CH), 18.4 (CH_3), 18.5 (CH_3), 18.6 (CH), 19.0 (CH), 19.1 (CH_2), 19.2 (CH), 19.7 (CH), 19.8 (CH_2), 22.3 (CH_2), 22.4 (CH_2), 31.4 (CH_2), 31.7 (CH_2), 32.7 (CH_2), 33.4 (CH_2), 70.3 (CH_2), 70.4 (CH_2), 70.5 (CH_2), 71.4 (CH), 71.6 (CH), 71.7 (CH), 71.8 (CH), 108.9 (C), 109.2 (C), and 109.5 ppm (C); mass spectrum (70 eV) *m/z* (rel intensity) 168 (17), 167 (5), 153 (5), 149 (15), 143 (20), 140 (25), 139 (33), 137 (13), 113 (86), 111 (14), 109 (13), 97 (24), 95 (25), 93 (13), 85 (21), 83 (32), 82 (30), 81 (50), 79 (21), 73 (20), 71 (37), 70 (19), 69 (100), 68 (14), 67 (25); exact mass calcd for M^+ $C_{10}H_{16}O_2$ 168.1150, obsd 168.1148.

Cyclopropanation of either ene ketal **37** or **38** produced a similar mixture of cyclopropane ketals.

Isomerization of Ene Ketal 37. To a solution of ene ketal **37** (0.030 g, 0.195 mmol) in dry diethyl ether (5 mL) was added a catalytic amount of ZnI_2. The mixture was refluxed for 30 min, cooled to room temperature, washed with saturated aqueous $NaHCO_3$, and dried ($MgSO_4$). After filtering, the solvent was carefully removed in vacuo. Analysis of the residue by ^1H and ^{13}C NMR (in $CDCl_3$ passed through basic Al_2O_3 prior to use) revealed that 18% of the ene ketal **37** had isomerized to **38**.

In the absence of ZnI_2, a sample of ene ketal **37** heated at reflux in dry ether for 30 min showed no evidence of isomerization by ^1H and ^{13}C NMR.

Ene ketal **37** was also subjected to Simmons–Smith cyclopropanation and the reaction quenched before complete conversion to cyclopropanated products (36% conversion by ^1H NMR). The ^1H and ^{13}C NMR spectra of recovered starting material indicated that 12% of the unreacted starting ene ketal **37** had isomerized to **38**.

***trans*-3,4-Diphenylcyclopentanone (46).** To flattened sodium spheres (25–30 g, 1120 mmol) in dry diethyl ether (300 mL) under argon was added ethyl cinnamate (100 g, 567 mmol) dropwise via addition funnel with stirring over 2 h. The brick-red reaction mixture began to reflux as the last third of the ethyl cinnamate was added. After addition was complete, the reaction mixture was stirred for 3 h and refluxing ceased. The disappearance of starting material was monitored by TLC. The reaction mixture was cooled and the excess sodium was slowly and carefully quenched with 2-propanol. Aqueous sulfuric acid solution (35%, 150 mL) was added dropwise at 0 °C, forming a white precipitate. The aqueous phase was extracted with diethyl ether (2 × 100 mL) and the combined ether phases were washed with saturated sodium bicarbonate (4 × 50 mL), water (100 mL), and saturated sodium chloride (100 mL) and dried ($MgSO_4$). After filtering, the solvent was removed in vacuo leaving the product, 2-carbethoxy-3,4-diphenylcyclopentanone, as an orange gel.

The crude product from above was dissolved in 95% ethanol (1.25 mL/mmol crude product) and 20% HBr was added (1.25 mL/mmol crude product). The mixture was heated to reflux and the reaction monitored by TLC. When complete, the mixture was cooled and dichloromethane was added, which dissolved the brown insoluble oil that had formed during the reaction. The layers were separated and the aqueous phase was extracted with dichloromethane. The combined dichloromethane phases were washed with saturated sodium bicarbonate and saturated sodium chloride solutions, dried over anhydrous Na_2SO_4, filtered, and concentrated. Column chromatography on silica gel 60 (250 g) eluted with dichloromethane gave a solid product, which was washed with diethyl ether and filtered to give **46** as an off-white powder, mp 170–175 °C (lit.[15] mp 177 °C): R_f 0.24 (20% EtOAc/hexanes); yield 5.5 g, 23.3 mmol, 8.2%; ^1H NMR ($CDCl_3$) δ 2.48–2.70 (2, m), 2.80–2.94 (2, m), 3.40–3.58 (2, m), 7.05–7.34 (10, m); ^{13}C NMR ($CDCl_3$) δ 47.2 (CH_2), 50.1 (CH), 126.8 (CH), 127.1 (CH), 128.5 (CH), 140.8 (C), 215.8 (C).

***trans*-3,4-Diphenyl-1-methylenecyclopentane (47).** To a well-stirred suspension of Zn dust (9.95 g, 152 mmol) in dry THF (175 mL) was added at room temperature via syringe diiodomethane (6.8 mL, 84.6 mmol). The resulting slurry was stirred under argon at room temperature for 30 min, then cooled to 0 °C at which temperature $TiCl_4$ (1.0 M in CH_2Cl_2, 17 mL) was added via syringe. The resulting mixture was stirred at room temperature for an additional 30 min. A solution of *trans*-3,4-diphenylcyclopentanone (**46**) (4.0 g, 17 mmol) in dry THF (20 mL) was then added dropwise via syringe and progress of the reaction was monitored by TLC. When complete (2.5 h) the reaction mixture was diluted with diethyl ether, washed with aqueous 1 M HCl and saturated sodium chloride solutions, dried ($MgSO_4$), filtered, and concentrated to give the crude product. Column

chromatography on silica gel 60 (250 g) eluted with 10% EtOAc/hexanes gave the alkene **47** as a pale yellow oil: R_f 0.66 (20% EtOAc/hexanes); yield 3.66 g, 15.6 mmol, 92%; IR ($CHCl_3$) cm^{-1} 3063, 3028, 3015, 3009, 2942, 2909, 2836, 2337, 1942, 1864, 1802, 1654, 1600, 1581, 1495, 1451, 1429, 1303, 1265, 1156, 1075, 1031, 883, 700; ^1H NMR ($CDCl_3$) δ 2.54–2.70 (2, m), 2.85–2.98 (2, m), 3.15–3.30 (2, m), 4.92–4.98 (2, m), 7.02–7.22 (10, m); ^{13}C NMR ($CDCl_3$) δ 42.0 (CH_2), 53.1 (CH), 105.8 (C), 126.2 (CH), 127.3 (CH), 128.2 (CH), 142.9 (C), 149.9 (CH_2); mass spectrum (70 eV) m/z (rel intensity) 235 (8), 234 (45), 233 (8), 178 (10), 165 (6), 156 (8), 143 (71), 141 (15), 130 (26), 129 (100), 128 (39), 117 (13), 115 (21), 105 (11), 104 (19), 91 (55), 77 (8); exact mass calcd for $C_{18}H_{18}$ 234.1409, obsd 234.1406.

***trans*-3,4-Diphenyl-1-cyclopentanemethanol (48).** To well-stirred BH_3·THF (13.2 mmol, 1 M solution in THF) in a dry flask at 0 °C was added a solution of alkene **47** (1.24 g, 5.29 mmol) in dry THF (10 mL) dropwise via syringe. The resulting colorless solution was allowed to warm gradually to room temperature. The careful, dropwise addition of water (6.2 mL) decomposed any excess borane. Then a 3 N NaOH solution (6.2 mL) was added dropwise, followed by careful addition of 30% H_2O_2 (6.2 mL). The resulting mixture was stirred at room temperature for 1 h, and then solid K_2CO_3 (1.24 g) was added followed by dilution with diethyl ether. After separating the layers and extracting the aqueous layer with diethyl ether, the combined ether extracts were washed with water, dried ($MgSO_4$), filtered, and concentrated to give the crude product. Column chromatography on silica gel 60 (100 g) eluted with 35% EtOAc/hexanes gave the alcohol **48** as a pale yellow oil: R_f 0.054 (20% EtOAc/hexanes); yield 1.27 g, 5.03 mmol, 95%; IR ($CHCl_3$) cm^{-1} 3619, 3441, 3083, 3061, 3026, 3009, 2947, 2869, 1943, 1864, 1802, 1729, 1599, 1492, 1450, 1373, 1249, 1155, 1074, 1039, 907, 844, 699, 634; ^1H NMR ($CDCl_3$) δ 1.55–1.70 (1, m), 1.90–1.98 (1, br s), 2.0–2.15 (2, m), 2.30–2.60 (2, m), 3.08–3.25 (2, m), 3.61–3.72 (2, m), 7.03–7.25 (10, m); ^{13}C NMR ($CDCl_3$) δ 37.7 (CH_2), 38.9 (CH_2), 40.0 (CH), 51.9 (CH), 53.9 (CH), 67.2 (CH_2), 125.9 and 126.0 (CH), 127.2 (CH), 127.3 (CH), 128.1 (CH), 143.0 (C), 143.9 (C); mass spectrum (70 eV) m/z (rel intensity) 253 (1), 252 (6), 234 (2), 221 (1), 193 (2), 178 (2), 174 (2), 161 (4), 143 (7), 129 (11), 128 (4), 117 (46), 115 (7), 104 (16), 103 (3), 92 (7), 91 (37), 78 (3), 77 (3), 58 (100); exact mass calcd for $C_{18}H_{20}O$ 252.1515, obsd 252.1506.

***trans*-3,4-Diphenylcyclopentanecarboxaldehyde (49).** A dry flask under argon was charged with a solution of oxalyl chloride (0.038 mL, 0.436 mmol) in dry CH_2Cl_2 (1.0 mL). To this well-stirred solution at −60 °C was added a solution of dry DMSO (0.067 mL, 0.951 mmol) in CH_2Cl_2 (0.5 mL) dropwise via syringe over 5 min. After being stirred for 10 min, a solution of the alcohol (0.10 g, 0.396 mmol) in CH_2Cl_2 (0.5 mL) was added. The resulting reaction mixture was stirred at −60 °C under argon for 20 min, then triethylamine (0.276 mL, 1.98 mmol) was added dropwise, the cooling bath was removed, and the flask was allowed to warm to room temperature. Water (1.2 mL) was added, and after being stirred for an additional 10 min, the organic phase was separated, the aqueous phase was extracted with CH_2Cl_2, and the combined CH_2Cl_2 phases were washed successively with dilute HCl, water, saturated $NaHCO_3$, and water. After drying (Na_2SO_4), filtration and concentration gave the crude product as a white solid. Column chromatography on silica gel 60 (50 g) eluted with 20% EtOAc/hexanes gave aldehyde **49** as a white solid, mp 73–76 °C: R_f 0.31 (20% EtOAc/hexanes); yield 0.094 g, 0.375 mmol, 95%; ^1H NMR ($CDCl_3$) δ 2.01–2.28 (2, m), 2.35–2.62 (2, m), 2.99–3.28 (3, m), 7.00–7.25 (10, m), 9.74–9.78 (1, d); ^{13}C NMR ($CDCl_3$) δ 34.7 (CH_2), 34.8 (CH_2), 49.5 (CH), 52.3 (CH), 53.4 (CH), 126.3 (CH), 127.2 (CH), 127.3 (CH), 128.3 (CH), 142.0 (C), 142.2 (C), 202.7 (CH).

Methyl *trans*-3,4-Diphenylcyclopentanecarboxylate (50). A 2 M stock solution of Br_2 in CH_3OH/H_2O (9:1 by volume) was prepared. To a well-stirred orange mixture of stock solution (4.0 mL) and sodium bicarbonate buffer (1.66 g, 19.8 mmol) was added the crude aldehyde **49** (0.248 g, 0.991 mmol) in a single portion. Progress of the reaction was monitored by TLC. When complete, solid sodium thiosulfate was added to quench the excess Br_2, water was added, and the mixture was extracted several times with diethyl ether. The combined ether extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated to give the crude product. Column chromatography on silica gel 60 (50 g) eluted with 5% EtOAc/hexanes gave the ester **50** as a cream-colored solid, mp 73–75 °C: R_f 0.39 (20% EtOAc/hexanes); yield 0.230 g, 0.820 mmol, 83% (from **48**); IR ($CHCl_3$) cm^{-1} 3061, 3026, 3009, 2951, 1945, 1865, 1805, 1725, 1600, 1492, 1450, 1435, 1365, 1233, 1198, 1172, 1075, 1030, 907, 835; ^1H NMR ($CDCl_3$) δ 2.08–2.28 (2, m), 2.46–2.61 (2, m), 3.08–3.38 (3, m), 3.68–3.76 (3, s), 7.05–7.27 (10, m); ^{13}C NMR ($CDCl_3$) δ 38.2 (CH_2), 38.9 (CH_2), 41.8 (CH), 51.8 (CH_3), 52.4 (CH), 53.9 (CH), 126.2 (CH), 126.3 (CH), 127.3 (CH), 127.4 (CH), 128.2 (CH), 142.2 (C), 142.9 (C), 176.8 (C).

Anal. Calcd for $C_{19}H_{20}O$: C, 81.40; H, 7.19. Found: C, 81.52; H, 7.27.

***tert*-Butyldimethylsilyl 5-Iodopentyl Ether (51).** To a well-stirred solution of imidazole (5.3 g, 78.0 mmol) and 1,5-pentanediol (38 mL, 366.0 mmol) in DMF (135 mL) under argon was added a slurry of *t*-BDMS-Cl (5.5 g, 36.6 mmol) in DMF (15 mL) portionwise over a 20-min period. The resulting mixture was stirred at room temperature for 1 h, and then poured into water (800 mL) and extracted with diethyl ether (4 × 200 mL). The combined ether extracts were washed with water (4 × 200 mL), dried ($MgSO_4$), filtered, and concentrated to give the crude monoprotected diol as a yellow oil; yield 6.5 g, 29.8 mmol, 81%; TLC (R_f 0.45, 50% EtOAc/hexanes).

To a solution of the crude alcohol from above in pyridine (10 mL) at 0 °C was added in one portion TsCl (7.0 g, 36.6 mmol). The resulting solution was maintained at 0–4 °C overnight. The mixture was then diluted with 5% aqueous HCl (300 mL) and extracted with diethyl ether (2 × 150 mL), and the ether extracts were washed successively with water (100 mL) and saturated sodium bicarbonate (100 mL), dried ($MgSO_4$), filtered, and concentrated to give the crude tosylate as a yellow oil; yield 9.5 g, 25.5 mmol, 70%; TLC (R_f 0.47, 20% EtOAc/hexanes).

The crude tosylate from above was dissolved in acetone (100 mL) that contained NaI (22.0 g, 146.0 mmol) and stirred at room temperature for 5 h. The mixture was then diluted with water (500 mL) and extracted with diethyl ether (2 × 150 mL). The combined ether extracts were washed with saturated Na_2SO_3, dried ($MgSO_4$), filtered, and concentrated to give the crude product. Column chromatography on silica gel 60 (200 g) eluted with 5% EtOAc/hexanes gave the iodide **51** as a colorless oil: R_f 0.70 (20% EtOAc/hexanes); yield 6.49 g (19.8 mmol, 54% over three steps); ^1H NMR ($CDCl_3$) δ 0.03–0.08 (6, s), 0.83–0.92 (9, s), 1.40–1.60 (4, m), 1.79–1.91 (2, m), 3.15–3.23 (2, t, J = 7.0 Hz), 3.57–3.65 (2, t, J = 6.0 Hz); ^{13}C NMR ($CDCl_3$) δ −5.3 (CH_3), 6.9 (CH_2), 18.2 (C), 25.9 (CH_3), 26.9 (CH_2), 31.6 (CH_2), 33.3 (CH_2), 62.7 (CH_2).

Methyl *trans*-3,4-Diphenyl-1-[5-[(*tert*-butyldimethylsilyl)oxy]pentyl]cyclopentanecarboxylate (52). To dry THF (3.5 mL) under argon at −60 °C were added diisopropylamine (0.157 mL, 1.12 mmol) followed by *n*-BuLi (0.700 mL, 1.6 M in hexanes) dropwise with stirring. After 10 min, a solution of ester **50** (0.207 g, 0.738 mmol) in dry THF (1 mL) was added dropwise. After 30 min a solution of iodide **51** (0.363 g, 1.10 mmol) in THF (1 mL) was added dropwise, and the solution was warmed to −15 °C. Progress of the reaction was monitored by TLC. When complete, the reaction was quenched with saturated NH_4Cl solution and extracted with diethyl ether (2 × 30 mL). The combined ether extracts were dried ($MgSO_4$), filtered, and concentrated to give the crude product. Column chromatography on silica gel 60 (50 g) eluted with 5% EtOAc/hexanes gave the product **52** as a yellow oil: R_f 0.53 (20% EtOAc/hexanes); yield 0.293 g, 0.609 mmol, 83%; ^1H NMR ($CDCl_3$) 0.03–0.07 (6, s), 0.85–0.95 (9, s), 1.14–1.43 (4, m), 1.46–1.62 (2, m), 1.71–1.93 (3, m), 2.17–2.27 (1, m), 2.39–2.51 (1, m), 2.72–2.82 (1, m), 3.14–3.31 (2, m), 3.56–3.64 (2, t, J = 6.3 Hz), 3.71–3.77 (3, s), 7.05–7.23 (10, m); ^{13}C NMR ($CDCl_3$) δ −5.3 (CH_3), 18.3 (C), 25.5 (CH_2), 26.0 (CH_3), 26.2 (CH_2), 32.7 (CH_2), 40.9 (CH_2), 44.8 (CH_2), 45.3 (CH_2), 51.8 (C), 52.0 (CH and CH_3), 52.8 (CH), 63.0 (CH_2), 126.2 (CH), 127.3 (CH), 127.5 (CH), 128.2 (CH), 142.2 (C), 142.6 (C), 178.2 (C).

Methyl *trans*-3,4-Diphenyl-1-(5-hydroxypentyl)cyclopentanecarboxylate (53). To a well-stirred solution of silyl ether **52** (0.290 g, 0.603 mmol) in dry THF (1 mL) was added an excess of tetrabutylammonium fluoride (2 mL, 1 M in THF). Progress of the reaction was monitored by TLC. When complete, the reaction was diluted with diethyl ether, washed with saturated sodium bicarbonate, dried ($MgSO_4$), filtered, and concentrated to give the crude product. Column chromatography on silica gel

60 (50 g) eluted with 25% EtOAc/hexanes gave the alcohol **53** as a pale yellow oil in nearly quantitative yield: R_f 0.041 (20% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 1.17–1.47 (4, m), 1.51–1.63 (2, m), 1.72–1.96 (4, m), 2.17–2.28 (1, m), 2.39–2.52 (1, m), 2.72–2.83 (1, m), 3.12–3.31 (2, m), 3.56–3.77 (5, m), 7.04–7.23 (10, m); ^{13}C NMR ($CDCl_3$) δ 25.5 (CH_2), 26.0 (CH_2), 32.4 (CH_2), 40.7 (CH_2), 44.8 (CH_2), 45.3 (CH_2), 51.7 (C), 51.9 (CH), 52.0 (CH_3), 52.7 (CH), 62.6 (CH_2), 126.1 (CH), 127.2 (CH), 127.4 (CH), 128.1 (CH), 142.1 (C), 142.5 (C), 178.2 (C).

Methyl *trans*-3,4-Diphenyl-1-(4-carbomethoxybutyl)-cyclopentanecarboxylate (54). Swern oxidation of **53** followed by direct esterification according to the procedures described previously gave the crude diester **54** as a pale yellow oil: R_f 0.18 (20% EtOAc/hexanes); yield 0.200 g, 0.507 mmol, 84% over two steps; IR ($CHCl_3$) cm^{-1} 3084, 3061, 3026, 3009, 2949, 2864, 1942, 1864, 1729, 1599, 1582, 1493, 1450, 1435, 1365, 1322, 1167, 1117, 1073, 1031, 1002, 873, 784; ^{1}H NMR ($CDCl_3$) δ 1.20–1.37 (2, m), 1.58–1.94 (5, m), 2.17–2.27 (1, m), 2.28–2.37 (2, t, J = 7.5 Hz), 2.40–2.52 (1, m), 2.72–2.82 (1, m), 3.14–3.31 (2, m), 3.63–3.68 (3, s), 3.72–3.78 (3, s), 7.05–7.25 (10, m); ^{13}C NMR ($CDCl_3$) δ 25.5 (CH_2), 25.3 (CH_2), 33.7 (CH_2), 40.3 (CH_2), 44.7 (CH_2), 45.3 (CH_2), 51.4 (CH_3), 51.7 (C), 51.9 (CH), 52.0 (CH_3), 52.7 (CH), 126.1 (CH), 127.2 (CH), 127.4 (CH), 128.2 (CH), 142.0 (C) 142.4 (C), 173.8 (C), 178.0 (C); mass spectrum (70 eV) m/z (rel intensity) 394 (4), 363 (14), 362 (53), 336 (4), 335 (25), 334 (68), 303 (13), 290 (22), 258 (28), 257 (24), 256 (7), 247 (13), 227 (15), 226 (96), 219 (86), 198 (13), 194 (22), 189 (14), 181 (59), 170 (26), 169 (32), 157 (15), 129 (37), 115 (37), 91 (100); exact mass calcd for $C_{25}H_{30}O_4$ 394.2145, obsd 394.2157.

(2*R,3*R**)-2,3-Diphenylspiro[4.5]decan-6-one (56).** To dry THF (4.5 mL/mmol diester **54**) under argon at −78 °C were added diisopropylamine (1.1 equiv) followed by *n*-BuLi (1.1 equiv, 1.6 M in hexanes) dropwise via syringe with stirring. After 10 min, a solution of the diester **54** (6.6 mmol) in THF (4.5 mL/mmol diester) was added dropwise via syringe, and the resulting solution was allowed to gradually warm to room temperature. Progress of the reaction was monitored by TLC. The reaction was quenched with saturated ammonium chloride solution, extracted with diethyl ether, dried ($MgSO_4$), filtered, and concentrated to give the crude keto ester **55**, which was used without purification in the next reaction. Purification of an analytical sample by column chromatography on silica gel 60 eluted with 10% EtOAc/hexanes gave a more pure product as a mixture of diastereomers: R_f 0.38 (20% EtOAc/hexanes); IR ($CHCl_3$) cm^{-1} 3028, 3009, 2937, 2855, 1950, 1870, 1805, 1740, 1702, 1645, 1601, 1492, 1439, 1363, 1332, 1311, 1285, 1256, 1196, 1117, 1031, 993, 908, 821.

The crude ester **55** from above was dissolved in 95% EtOH (9.0 mL/mmol ester) and solid NaOH (5 equiv) was added in one portion. The mixture was heated to reflux and progress of the reaction was monitored by TLC. When complete, the reaction mixture was cooled in an ice/water bath, carefully acidified with 20% HCl, and extracted with diethyl ether. The combined ether extracts were washed with saturated $NaHCO_3$, dried ($MgSO_4$), filtered, and concentrated to give the crude product. Column chromatography on silica gel 60 (100 g) eluted with 10% EtOAc/hexanes gave the ketone **56** as an oil, which slowly solidified upon freezing to yield a yellow solid, mp 79–81 °C; R_f 0.33 (20% EtOAc/hexanes); yield 1.5 g, 4.93 mmol, 75% from **54**; IR ($CHCl_3$) cm^{-1} 3061, 3019, 3009, 2932, 2863, 2360, 1950, 1865, 1810, 1696, 1599, 1492, 1450, 1337, 1311, 1233, 1131, 1074, 1031, 951, 906, 856; ^{1}H NMR ($CDCl_3$) δ 1.56–1.98 (7, m), 2.06–2.17 (1, m), 2.27–2.50 (3, m), 2.71–2.82 (1, m), 3.07–3.29 (2, m), 7.01–7.20 (10, m); ^{13}C NMR ($CDCl_3$) δ 22.5 (CH_2), 26.9 (CH_2), 39.0 (CH_2), 41.0 (CH_2), 43.5 (CH_2), 45.2 (CH_2), 51.7 (CH), 52.1 (CH), 54.4 (C), 126.0 (CH), 127.2 (CH), 127.3 (CH), 128.1 (CH), 142.0 (C), 142.3 (C), 213.4 (C).

Anal. Calcd for $C_{22}H_{24}O$: C, 86.79; H, 7.95. Found: C, 86.71; H, 8.05.

(2*R,3*R**)-2,3-Diphenylspiro[4.5]dec-6-ene (35).** To a well-stirred solution of ketone **56** (0.500 g, 1.64 mmol) in dry THF (10 mL) under argon at −78 °C was added lithium bis(trimethylsilyl)amide (1.97 mL, 1 M in THF) dropwise via syringe. After stirring for 15 min, diethyl chlorophosphate (0.258 mL, 1.97 mmol) was added via syringe, and the mixture was gradually warmed to room temperature, and the reaction was monitored by TLC. When complete, the mixture was diluted with diethyl ether (100 mL) and washed with saturated $NaHCO_3$ solution (2 × 50 mL), the aqueous phase was back-extracted with ether, and the combined ether extracts were dried over anhydrous $MgSO_4$. Filtration, concentration, and chromatography on silica gel 60 (50 g) eluted with 25% EtOAc/hexanes gave the enol phosphate **57** as a yellow oil: TLC (R_f 0.29, 20% EtOAc/hexanes); yield 0.581 g, 1.32 mmol, 80%; ^{1}H NMR ($CDCl_3$) δ 1.28–1.43 (6, t, J = 7.0 Hz), 1.50–2.16 (8, m), 2.28–2.41 (1, t, J = 12.5 Hz), 2.60–2.71 (1, m), 3.12–3.41 (2, m), 4.17–4.30 (4, m), 5.55–5.62 (1, m), 7.04–7.24 (10, m); ^{13}C NMR ($CDCl_3$) δ 16.1 (CH_3), 16.2 (CH_3), 19.8 (CH_2), 23.9 (CH_2), 39.2 (CH_2), 43.4 (CH_2), 43.5 (CH_2), 45.6 (CH_2), 47.2 (CH_2), 51.7 (CH), 53.5 (CH), 64.0 (C), 64.1 (C), 108.2 (CH), 125.9 (CH), 126.0 (CH), 127.2 (CH), 127.3 (CH), 128.0 (CH), 142.2 (C), 142.8 (C), 152.4 (C), 152.6 (C).

To a well-stirred solution of scored Li metal (30 mg, 4.50 mmol) in liquid ammonia (10 mL, freshly distilled from Li) under argon at −78 °C was added a cold (−78 °C) solution of the above enol phosphate (0.198 g, 0.450 mmol) and *t*-BuOH (0.127 mL, 1.35 mmol) in dry diethyl ether (3 mL) via cannula. The cold bath was removed and the mixture allowed to reflux (−33 °C) for 5 min. The cold bath was replaced and the reaction was slowly quenched at −78 °C with solid NH_4Cl and diluted with diethyl ether. The reaction was then warmed to room temperature, the ammonia was allowed to evaporate, saturated $NaHCO_3$ solution (25 mL) was added, the phases were separated, and the ether phase was dried ($MgSO_4$), filtered, and concentrated to give the crude product. Column chromatography on silica gel 60 (50 g) eluted with 5% EtOAc/hexanes gave the alkene **35** as a pale yellow oil, which solidified upon freezing, mp 46–48 °C, R_f 0.73 (50% EtOAc/hexanes); yield 0.100 g, 0.347 mmol, 77%; IR ($CHCl_3$) cm^{-1} 3061, 3026, 3009, 2926, 2859, 1945, 1870, 1800, 1599, 1493, 1450, 1071, 1031, 867; ^{1}H NMR ($CDCl_3$) δ 1.56–2.00 (8, m), 2.06–2.28 (2, m), 3.15–3.35 (2, m), 5.54–5.63 (1, m), 5.70–5.79 (1, br d, J = 10.0 Hz), 7.02–7.23 (10, m); ^{13}C NMR ($CDCl_3$) δ 20.5 (CH_2), 25.0 (CH_2), 37.6 (CH_2), 41.0 (C), 49.5 (CH_2), 50.0 (CH_2), 52.3 (CH), 52.6 (CH), 124.4 (CH), 125.9 (CH), 127.3 (CH), 128.1 (CH), 137.5 (CH), 143.1 (C), 143.4 (C).

Spiro[bicyclo[4.1.0]heptane-2,1′-3,4-diphenylcyclopentanes] (36ab). A flask equipped with a stir bar and condenser was flame dried under vacuum and cooled under argon. To the flask were added anhydrous K_2CO_3 (3.00 g, 22.0 mmol), Zn–Cu couple (2.88 g, 44.0 mmol), a small crystal of iodine, diethyl ether (5 mL, freshly distilled from P_2O_5), and CH_2I_2 (1.77 mL, 22.0 mmol). The mixture was heated to reflux in an oil bath. When the slurry had darkened to a charcoal black, a solution of the olefin **35** (0.127 g, 0.440 mmol) in dry ether (5 mL) was added via syringe and refluxing was continued for 48 h. The reaction was quenched by the dropwise addition of a saturated K_2CO_3 solution at 0 °C. The mixture was stirred at room temperature for 1 h and then filtered, and the solids were carefully washed with diethyl ether until washes were product free by TLC. The organic phase was washed successively with saturated aqueous NH_4Cl, $NaHCO_3$, and NaCl solutions, dried over anhydrous $MgSO_4$, filtered, concentrated, and purified via column chromatography to afford 0.110 g of a mixture of starting material and cyclopropanated product (22% conversion by ^{1}H NMR integration).

The above mixture was resubmitted to the above reaction conditions for another 48 h to give 0.097 g of a mixture of starting material and product (35% conversion by ^{1}H NMR integration). A third and final treatment with the Simmons–Smith reagent gave 0.092 g of a mixture of starting alkene **35** and cyclopropane products as a 1:1 mixture of inseparable diastereomers **36a** and **36b** (45% conversion by ^{1}H NMR integration): R_f 0.57 (10% EtOAc/hexanes); yield 0.041 g, 0.136 mmol, 51% based on recovered starting material; ^{1}H NMR ($CDCl_3$) δ −0.04–0.07 (1, m, cyclopropane CH), 0.55–0.67 (1, m, cyclopropane CH), 0.97–1.11 (2, m, cyclopropane CH_2); ^{13}C NMR ($CDCl_3$) δ 9.4 and 10.1 (CH_2, cyclopropane), 11.0 and 11.2 (CH, cyclopropane), 19.1 and 19.8 (CH_2), 23.1 and 23.2 (CH_2), 23.8 and 24.3 (CH, cyclopropane), 34.9 and 36.3 (CH_2), 38.5 and 39.0 (C), 49.8 and 50.7 (CH_2), 51.4 and 51.5 (CH_2), 51.8 and 51.9 (CH), 52.7 (CH), 125.8 and 125.9 (CH), 127.3 (CH), 128.1 (CH), 143.7 and 143.9 (C).

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Registry No. 1, 99249-28-2; 2, 111970-30-0; 3, 125250-66-0; 4, 125250-67-1; 5, 111970-33-3; 6, 111970-32-2; 7, 111970-31-1; 8, 92803-20-8; (±)-9, 125353-72-2; 10, 117583-51-4; 11a, 99249-29-3; 11b, 99295-87-1; 12a, 111970-36-6; 12b, 112020-55-0; 13a, 125250-68-2; 13b, 125353-78-8; 14a, 125250-69-3; 14b, 125353-79-9; 15a, 111970-39-9; 15b, 112020-58-3; 16a, 111970-38-8; 16b, 112020-57-2; 17a, 111970-37-7; 17b, 112020-56-1; 18a, 111970-41-3; 18b, 112020-60-7; (±)-19a, 125355-34-2; (±)-19b, 125353-80-2; 20a, 117583-52-5; 20b, 117677-00-6; 21, 99249-30-6; 22, 117583-49-0; 23, 109908-38-5; 24, 125250-70-6; 25, 125250-71-7; 26, 99249-32-8; 27, 117583-53-6; 28a, 99249-31-7; 28b, 99295-88-2; 29a, 117583-50-3; 29b, 117676-99-0; 30a, 109908-39-6; 30b, 109958-06-7; 31a, 125250-72-8; 31b, 125353-81-3; 32a, 125250-73-9; 32b, 125353-82-4; 33a, 99249-34-0; 33b, 99295-89-3; 34a, 117583-54-7; 34b, 117677-01-7; 35, 125250-74-0; 36a, 125250-75-1; 36b, 125353-83-5; 37, 125250-76-2; 38, 125353-73-3; 39a, 125250-77-3; 39b, 125353-84-6; 40a, 125353-74-4; 40b, 125353-85-7; 41, 125250-78-4; 42a (R = CH_2OH), 125250-79-5; 42b (R = CH_2OH), 125353-86-8; 43, 50870-61-6; 44, 125250-80-8; 45, 125353-75-5; 46, 13351-28-5; 47, 125250-81-9; 48, 125250-82-0; 49, 125250-83-1; 50, 125250-84-2; 51, 85514-45-0; 52, 125250-85-3; 53, 125250-86-4; 54, 125250-87-5; 55a, 125250-88-6; 55b, 125353-87-9; 56, 125250-89-7; 57, 125250-90-0; dimethyl L-tartrate acetone ketal, 37031-29-1; (3*R*,4*R*)-2,5-dimethyl-2,3,4,5-hexanetetrol, 81706-69-6; (3*R*,4*R*)-2,5-dimethoxy-2,5-dimethyl-3,4-hexanediol acetone ketal, 125250-91-1; (3*R*,4*R*)-2,5-dimethoxy-2,5-dimethyl-3,4-hexanediol, 99267-98-8; 4-phenyl-1-butanol, 3360-41-6; 4-phenylbutyraldehyde, 18328-11-5; (*dl*)-1,8-diphenyl-4,5-octanediol, 125353-76-6; (*S*)-(+)-1,2-propanediol, 4254-15-3; ethyl cinnamate, 103-36-6; 2-carbethoxy-3,4-diphenylcyclopentanone, 125353-77-7; 1,5-pentanediol, 111-29-5; 1,5-pentanediol, mono(*tert*-butyldimethylsilyl) derivative, 83067-20-3; 1,5-pentanediol, mono(*tert*-butyldimethylsilyl) derivative, tosylate, 83084-58-6; 1,4-di-*O*-methyl-L-threitol, 50622-10-1; 1,4-bis-*O*-(*p*-biphenylmethyl)-L-threitol, 125250-92-2; 1,4-bis-*O*-(2-naphthylmethyl)-L-threitol, 125250-93-3; dimethyl L-tartrate, 608-68-4; (*R*,*R*)-2,3-butanediol, 24347-58-8; (*S*,*S*)-1,2-diphenyl-1,2-ethanediol, 2325-10-2; diisopropyl L-tartrate, 2217-15-4; 2-methyl-2-cyclopenten-1-one, 1120-73-6; 2-cyclohexen-1-one, 930-68-7; 1,4-di-*O*-benzyl-L-threitol, 2-bromo-2-cyclohexen-1-one ketal, 125250-94-4.

Supplementary Material Available: ^1H and/or ^{13}C NMR spectra of all new compounds (65 pages). Ordering information is given on any current masthead page.

Mechanistic Studies of Diastereoselective Cyclopropanation via Homochiral Ketals. 2. Studies with Conformationally Restricted 2-Cyclohexen-1-one Ketals

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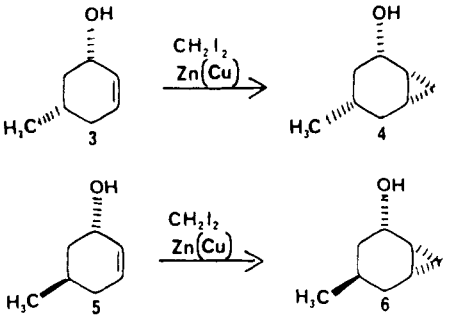
The effect of cyclohexene ring conformation on the diastereoselectivity observed for Simmons–Smith cyclopropanation of 2-cyclohexen-1-one ethylene ketals was examined by using (5*S*)-5-*tert*-butyl-2-cyclohexen-1-one 1,2-ethanediol, (2*R*,3*R*)-2,3-butanediol, and (2*S*,3*S*)-2,3-butanediol ketals. Reagent chelation by the pseudoequatorial dioxolane oxygen atom was shown to result in more effective methylene transfer. This regiochemical preference can either antagonize or reinforce diastereoselectivity due to steric hindrance of the dioxolane oxygen atoms from dissymmetric placement of methyl appendages on the dioxolane ring.

In the preceding article[1] a general mechanism was advanced that can account for the diastereoselectivity observed when common[2] 2-cycloalken-1-one ketals **1** are cyclopropanated using the Simmons–Smith reagent.[3] Preferential chelation of zinc by the least sterically hindered dioxolane oxygen atom proximal to the alkene effectively positions the reagent for diastereoselective methylene transfer (Figure 1). While this simplistic picture has predictive value, a wealth of mechanistic detail is absent. In particular, we wish to know, for 2-cyclohexen-1-one ethylene ketals, if a regiochemical preference for methylene delivery from reagent coordinated at either a pseudoequatorial or pseudoaxial dioxolane oxygen atom exists and also if this preference can be modified by the steric effects of suitably placed dioxolane appendages. This information should be useful in predictions of interactions of the Simmons–Smith reagent with conformationally constrained ene ketals.

Previously it was shown by Chan and Rickborn[4] that Simmons–Smith cyclopropanation of *cis*-5-methyl-2-cyclohexen-1-ol (**3**) gives exclusively **4** and is 3.3 times faster than cyclopropanation of the trans diastereomer **5**, which yields exclusively **6**. These results were rationalized



(1) Mash, E. A.; Hemperly, S. B.; Nelson, K. A.; Heidt, P. C.; Van Deusen, S. *J. Org. Chem.*, previous article in this issue.

(2) Ring compounds have been classified into four categories, namely, small rings (three- and four-membered), common rings (five-, six-, and seven-membered), medium rings (eight- to 11-membered), and large rings (12-membered and larger). See: Eliel, E. L. *Stereochemistry of Carbon Compounds*; McGraw-Hill: New York, 1962; p 189.

(3) For reviews of the Simmons–Smith reaction, see: (a) Furukawa, J.; Kawabata, N. In *Advances in Organometallic Chemistry*; Stone, F. G. A., West, R., Eds.; Academic Press: New York, 1974; Vol. 12, Chapter 3. (b) Simmons, H. E.; Cairns, T. L.; Vladuchick, S. A.; Hoiness, C. M. *Org. React.* **1973**, *20*, 1–131.

(4) Chan, J. H.-H.; Rickborn, B. *J. Am. Chem. Soc.* **1968**, *90*, 6406–6411.

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