Catalytic, Enantioselective Cyclopropanation of Allylic Alcohols. Substrate Generality

Scott E. Denmark* and Stephen P. O'Connor

Roger Adams Laboratory, Department of Chemistry, University of Illinois, Urbana, Illinois 61801

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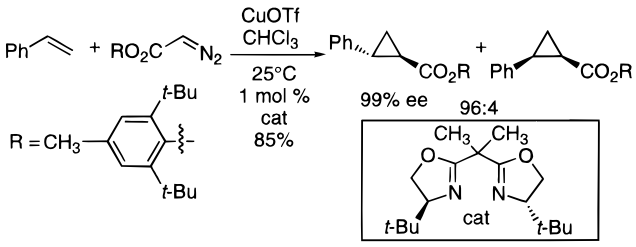
Catalytic, enantioselective cyclopropanation of a broad range of allylic alcohols and one homoallylic alcohol was carried out. The cyclopropanation reagent employed was bis(iodomethyl)zinc generated by the method of Furukawa, and the chiral promoter used (10 mol %) was the *N*,*N*-bis(methanesulfonyl) derivative of (*R*,*R*)-1,2-diaminocyclohexane. Three experimental features were found to be critical for the rapid and selective cyclopropanation: (1) use of the ethylzinc alkoxide of the allylic alcohol as the substrate by prior deprotonation of the allylic alcohols by diethylzinc, (2) the formation of the zinc complex of the promoter by prior deprotonation of the bis-sulfonamide with diethylzinc, and (3) the use of added zinc iodide generated in situ from diethylzinc and iodine. The stereoselectivity of cyclopropanation was found to be independent of olefin geometry and worked well for substrates bearing both aliphatic and aromatic substituents at either or both 3-positions of the allylic alcohol. However, a methyl substituent on the 2-position of the allyl alcohol was not well tolerated and led to slow reactions and poor enantioselectivities. A rationale for the observed selectivities is proposed.

Introduction

The Simmons−Smith reaction, first reported in 1958 by the DuPont workers whose names it was later to bear, to this day remains one of the premier means of cyclopropane formation.[1] The procedure employs a geminal diiodide and zinc−copper couple in refluxing ether to affect reaction with olefins. In subsequent years many preparatively useful and stereochemically intriguing developments were reported. The most notable are (1) the Furukawa modification (1966)[2] wherein the insoluble zinc−copper couple is replaced by diethylzinc and (2) the strong directing effect exhibited by allylic alcohols which was first reported by Winstein in 1959.[3] Numerous diastereo- and some enantioselective versions have also been described.[4]

For a number of years, we have been involved in a broadly-based program aimed at elucidating the composition and structure of the Simmons−Smith type reagents as well as developing enantioselective versions of this reaction. In 1995, we reported an effective means for the enantioselective cyclopropanation of allylic alcohols using chiral, nonracemic bis-sulfonamides as catalytic promoters.[5] In these studies the experimental protocol was carefully optimized, and a wide range of promoter structures were examined. We describe herein the detailed investigation of reaction parameters along with a survey of the reaction scope with respect to substrate structure.

Scheme 1



Background

The synthesis of enantiomerically enriched cyclopropanes can be achieved by the use of either of two classes of reagents: (1) the zinc-based carbenoid reagents of which the present study is an example, and (2) the transition metal-based carbenoid reagents. By far, it is the second reagent type which has been the most successful and which has achieved the highest selectivities. The methods developed by Evans, Masamune, Pfaltz, and Doyle are exemplary.[6] For example, in Scheme 1, styrene is converted to the corresponding *trans*-carboxyl-substituted cyclopropane in 99% ee using only 1 mol % of the copper catalyst. This impressive result is perhaps one of the most compelling examples of the power of this method, but in a general sense it is also illustrative of the results which can often be obtained for a variety of substrates by proper tuning of reagent and chiral promoter. However, it also brings to light a serious drawback to the transition metal-based carbenoid methods of cyclopropanation, namely, the requirement that diazo *carbonyl* compounds be used as precursors of the putative carbenes. Thus, the products are restricted to

[⊗] Abstract published in *Advance ACS Abstracts,* January 15, 1997.

(1) (a) Simmons, H. E.; Smith, R. D. *J. Am. Chem. Soc.* **1958**, *80*, 5323. (b) Simmons, H. E.; Cairns, T. L.; Vladuchick, S. A.; Hoiness, C. M. *Org. React.* **1972**, *20*, 1.

(2) Furukawa, J.; Kawabata, N.; Nishimura, J. *Tetrahedron Lett.* **1966**, 3353.

(3) Winstein, S.; Sonnenberg, J.; DeVries, L. *J. Am. Chem. Soc.* **1959**, *81*, 6523.

(4) Charette, A. B.; Marcoux, J.-F. *Synlett* **1995**, 1197 and refences cited therein.

(5) (a) Denmark, S. E.; Christenson, B. L.; Coe, D. M.; O'Connor, S. P. *Tetrahedron Lett.* **1995**, *36*, 2215. (b) Denmark, S. E.; Christenson, B. L.; O'Connor, S. P. *Tetrahedron Lett.* **1995**, *36*, 2219.

(6) (a) Evans, D. A.; Woerpel, K. A.; Hinman, M. M.; Faul, M. M. *J. Am. Chem. Soc.* **1991**, *113*, 726. (b) Pfaltz, A. *Acc. Chem. Res.* **1993**, *26* , 339. (c) Masamune, S.; Lowenthal, R. E.; Abiko, A. *Tetrahedron Lett.* **1990**, *31*, 6005. (d) Doyle, M. P.; Dyatkin, A. B.; Protopopova, M. N.; Yang, C. I.; Miertschin, C. S.; Winchester, W. R.; Simonsen, S. H.; Lynch, V.; Chosh, R. *Recl. Trav. Chim. Pays-Bas* **1995**, 114, *163.*

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carbonyl-substituted cyclopropanes. To date, no efficient means of selective methylene delivery using diazo compounds has been reported.[7]

The first class of reagents mentioned above, the zinc-based carbenoid compounds, have been found to be capable of selective delivery of methylene to provide cyclopropanes devoid of the carbonyl functionality that the transition metal carbenoids require. However, the selectivities are either lower or require the use of chiral auxiliaries. Much of the development of enantioselective zinc-based cyclopropanation has relied upon the directing effect of an allylic functional group to provide a locus for reagent tethering and control.

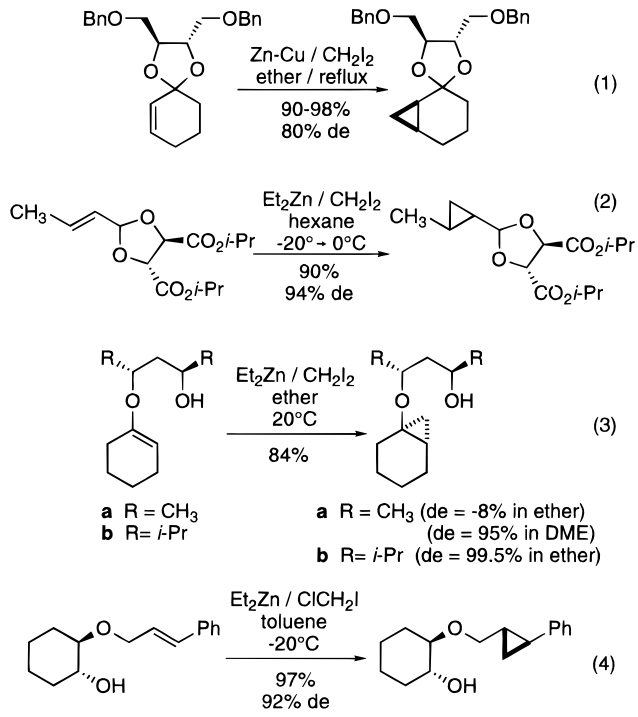
Asymmetric variants of the Simmons−Smith reaction fall into three categories: (a) chiral auxiliary-based methods, (b) procedures using stoichiometric quantities of a chiral modifier, and (c) the use of substoichiometric quantities of a chiral promoter (catalysis). This report concerns our recent progress in the last of these categories, namely catalytic, enantioselective cyclopropanation, but it is the history and progress of each of these areas that provided the foundation upon which our studies were formulated. Some of the more important examples of each of these reaction categories will briefly be described.

Auxiliary-Based Methods. For historical purposes, an early example of auxiliary usage in Simmons−Smith cyclopropanation will be given. (−)-Menthol esters of α,β-unsaturated carboxylic acids were subjected to the standard conditions by Sawada and Inouye in 1968.[8] The diastereomeric excesses (de's) were very low (9%). Nonetheless, the stage was set for systematic variation in auxiliary structure and substrate−auxiliary connectivity.

In 1985, Mash reported that tartrate-derived ketals (Scheme 2, eq 1) provided cyclopropanes under the standard Simmons−Smith conditions in excellent yields (90-98%) and with good selectivities (80% de).[9] In a similar system, also in 1985, Yamamoto reported that the tartrate-derived acetals of cyclic *and* acyclic α,β-unsaturated aldehydes could be efficiently cyclopropanated with diastereomeric excesses of 85−94% (Scheme 2, eq 2).[10] Later, Yamamoto also described the use of acetals derived from (2*R*,4*R*)-2,4-pentanediol although the de's were somewhat lower (74% de for the acetal of crotonaldehyde).

In 1988 Tai and co-workers reported on the use of chiral enol ethers derived from (2*R*,4*R*)-2,4-pentanediol (**a**, R = CH_3) but found an unusual solvent dependence (Scheme 2, eq 3) suggestive of reagent modification by the chelating solvent DME.[11] Furthermore, if the reaction was run in ether in the presence of 1 equiv of zinc iodide, the product was obtained in 68% de, again suggesting a reagent modification (e.g. Schlenk equilibrium). Nonetheless, additional investigations showed

Scheme 2



that the enol ether of (3*S*,5*S*)-2,6-dimethyl-3,5-heptanediol gave superior results (99.5% de). The five-, seven-, and eight-membered ring analogs as well as the acyclic analog derived from 3-pentanone all provided cyclopropanes in >99% de.[9b]

Charette has described a number of useful asymmetric variants of the Simmons−Smith reaction. In the realm of auxiliary-based methods, those using both carbohydrates and enantiomerically pure 1,2-*trans*-cyclohexanediol as covalent modifiers for allylic alcohols have been fruitful (Scheme 2, eq 4).[12] Surprisingly, with the cyclohexanediol auxiliary, utilization of the reagent derived from diethylzinc and chloroiodomethane ($ClCH_2I$) was far superior (92% de) to that prepared under the standard Furukawa conditions, namely diethylzinc and diiodomethane (16% de). With the glucose-derived auxiliaries, this reagent preference was reversed.

Stoichiometric External Modifiers. As with the auxiliary method, early examples of the use of stoichiometric quantities of chiral modifiers via zinc-based cyclopropanation procedures were of very low selectivity. For example, Furukawa attempted the cyclopropanation of vinyl ethers using a diethylzinc/diiodomethane reagent combination in the presence of 2 equiv of L-leucine.[13] While no enantiomeric excesses were reported, the rotations given for the product cyclopropanes were sufficiently low to doubt the efficacy of this additive.

More recently, Denmark and Edwards used 2 equiv of *N*-methylephedrine to affect the cyclopropanation of cinnamyl alcohol, but with low selectivity (24% ee, Scheme 3, eq 5).[14] Fujisawa has utilized the diethyl ester of tartaric acid under very similar conditions.[15] The same

(7) Studies from these laboratories with chiral nonracemic bis-oxazolines as ligands for palladium in the cyclopropanation of olefins with diazomethane yielded only racemic cyclopropanes. Edwards, J. P.; Faucher, A. M.; Stavenger, R. Unpublished results.

(8) Sawada, S.; Takehana, K.; Inouye, Y *J. Org. Chem.* **1968**, *33*, 1767.

(9) (a) Mash, E. A.; Nelson, K. A. *J. Am. Chem. Soc.* **1985**, *107*, 8256. (b) Mash, E. A.; Hemperly, S. B.; Nelson, K. A.; Heidt, P. C.; Van Deusen, S. *J. Org. Chem.* **1990**, *55*, 2045. (c) Mash, E. A.; Hemperly, S. B. *J. Org. Chem.* **1990**, *55*, 2055.

(10) (a) Yamamoto, H.; Arai, I.; Mori, A. *J. Am. Chem. Soc.* **1985**, *107*, 8254. (b) Yamamoto, H.; Arai, I.; Mori, A. *Tetrahedron* **1986**, *42*, 6447.

(11) (a) Tai, A.; Sugimura, T.; Futagawa, T. *Tetrahedron Lett.* **1988**, *29*, 5775. (b) Tai, A.; Sugimura, T.; Futagawa, T.; Yoshikawa, M. *Tetrahedron Lett.* **1989**, *30*, 3807.

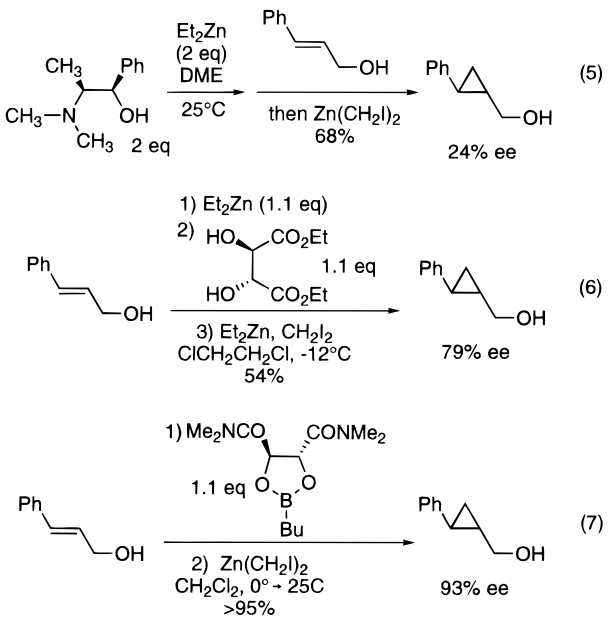
(12) (a) Charette, A. B.; Cote, B.; Marcoux, J.-F. *J. Am. Chem. Soc.* **1991**, *113*, 8166. (b) Charette, A. B.; Marcoux, J.-F. *Tetrahedron Lett.* **1993**, *34*, 7157. (c) Charette, A. B.; Turcotte, N.; Marcoux, J.-F. *Tetrahedron Lett.* **1994**, *35*, 513.

(13) (a) Furukawa, J.; Kawabata, N.; Nishimura, J. *Tetrahedron Lett.* **1968**, 3495. (b) Furukawa, J.; Kawabata, N.; Nishimura, J. *Tetrahedron* **1968**, *24*, 53.

(14) Denmark, S. E.; Edwards, J. P. *Synlett* **1992**, 229.

(15) Fujisawa, T.; Ukaji, Y.; Nishimura, M. *Chem. Lett.* **1992**, 61.

Scheme 3



substrate, cinnamyl alcohol, was cyclopropanated in 79% ee. By far the most selective of the stoichiometric modifiers is the tartrate-derived dioxaborolane of Charette.[16] As shown in Scheme 3 (eq 7), a high enantiomeric excess (93%) was obtained for, again, cinnamyl alcohol.

Catalytic Promoters. In 1968, Sawada and Inouye carried out the cyclopropanation of a variety of olefins using the Simmons−Smith reagent and (−)-menthol. Cyclopropanes were produced in yields ranging from 5 to 18% and enantiomeric excesses of 3.4% or less.[17]

In Scheme 4 are shown the two catalytic methods which warrant mention, both of which are for allylic alcohols. The first from the work of Kobayashi is very similar to our own and employs sulfonamide derivatives of chiral diamines as catalysts for the Furukawa reagent.[18] The best ee's obtained for cinnamyl alcohol employed the 4-nitrobenzenesulfonamide (eq 8). The particular ratio of reagents used is curious; however, the authors may have envisioned that alcohol deprotonation with 1 equiv of diethylzinc would be followed by conversion to the (iodomethyl)zinc alkoxide. There would then remain sufficient quantities of reagents to form 1 equiv of bis(iodomethyl)zinc ($Zn(CH_2I)_2$). Whatever the reason for this unusual protocol, the product was obtained with good selectivity (76% ee).

The reaction shown in eq 9, Scheme 4, employs the Furukawa reagent but in conjunction with a chiral titanium-based catalyst. The use of the TADDOL titanium Lewis acid in 25 mol % quantities was capable of affecting a very respectable enantioselective cyclopropanation of cinnamyl alcohol (90% ee).[19] It was reasoned that the Lewis acid would coordinate to the oxygen of the allylic alcohol present as the (iodomethyl)zinc alkoxide $PhCH{=}CHCH_2OZnCH_2I$. This would increase the electrophilicity of the attached methylene thus promoting

Scheme 4

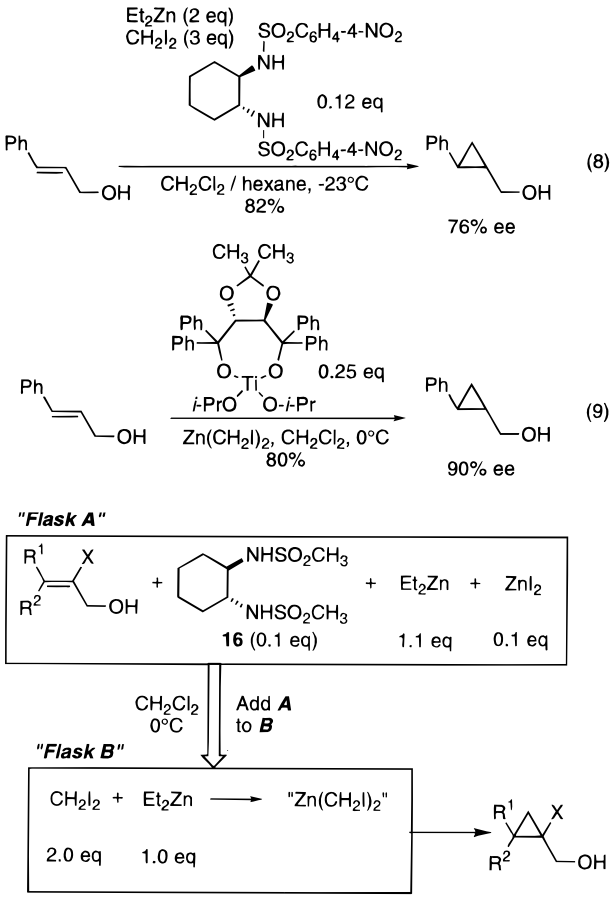


Figure 1. Standard cyclopropanation procedure: protocol I.

the reaction. It is not clear if this is an intra- or intermolecular reaction. With the chiral environment provided by the tartrate-based dioxolane, it was hoped that good selectivities would be observed and such was the case for cinnamyl alcohol. However, the reported substrate generality was rather poor. The only other allylic alcohol examined under these conditions was prenyl alcohol which was cyclopropanated in 90% yield but only 60% ee.

These findings encouraged us in own pursuit of an enantioselective cyclopropanation method. We provide herein an extensive survey of allylic alcohol structural types along with a new modification of our original conditions which provided significant improvements in selectivities.

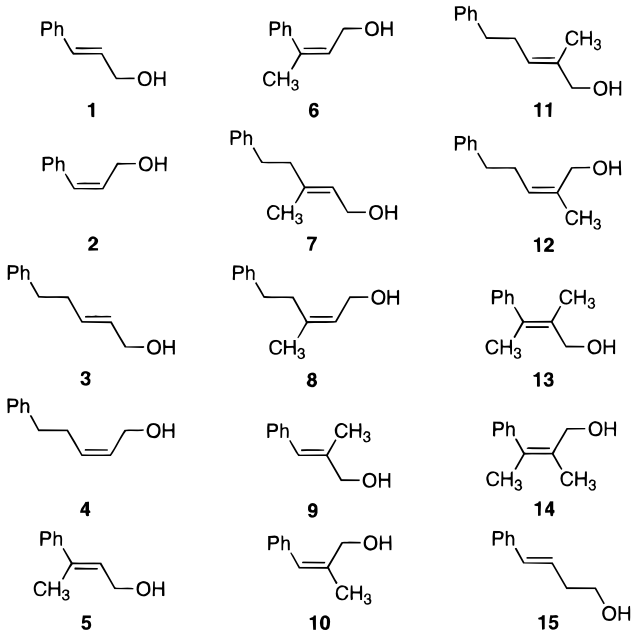
Results

Survey of Substrates with Protocol I. The generality of the catalytic enantioselective cyclopropanation method which we have previously developed was assessed with 14 allylic alcohols and one homoallylic alcohol (Chart 1). We used 10 mol % of promoter **16** throughout. These substrates were selected to evaluate (1) double bond geometry, (2) the nature of substituents (aromatic vs aliphatic), and (3) number and location of alkyl substituents.

A standard set of reaction conditions referred to as protocol I (Figure 1) was used for all 15 substrates to establish the effect of substrate structure on rate, yield, and selectivity of reaction. From our earlier studies we had identified several experimental features that were

(16) Charette, A. B.; Juteau, H. *J. Am. Chem. Soc.* **1994**, *116*, 2651.
(17) Sawada, S.; Oda, J.; Inouye, Y *J. Org. Chem.* **1968**, *33*, 2141.
(18) (a) Takahashi, H.; Yoshioka, M.; Shibasaki, M.; Ohno, M.; Imai, N.; Kobayashi, S. *Tetrahedron* **1995**, *51*, 12013. (b) Kobayashi, S.; Imai, N.; Sakamoto, K.; Takahashi, H. *Tetrahedron Lett.* **1994**, *35*, 7045. (c) Kobayashi, S.; Takahashi,H.; Yoshioka, M.; Ohno, M. *Tetrahedron Lett.* **1992**, *33*, 2575.
(19) Charette, A. B.; Brochu, C. *J. Am. Chem. Soc.* **1995**, *117*, 11367.

Chart 1



critical for reproducibility and high rates and selectivities: (1) preformation of the ethylzinc alkoxide of the substrate, (2) preformation of the zinc salt of the bis-sulfonamide promoter, and (3) addition of zinc iodide at the outset of the reaction.

Investigation of various reagent combination sequences has shown that the highest enantioselectivities with cinnamyl alcohol (**1**) as substrate were obtained with the two-flask reaction shown in Figure 1 which could accommodate all the critical experimental features mentioned. By combining the substrate alcohol and promoter in flask A, addition of the appropriate amount of diethylzinc would convert both to the respective zinc species. Employment of the ethylzinc alkoxide as the substrate for cyclopropanation was found to be one of the most critical components for obtaining high enantioselectivities.[20]

Contrary to our previously reported conclusions, we have recently found that the formation of the zinc complex of the promoter is also important for high enantioselectivities. Spectroscopic studies (^{1}H NMR) on the more soluble *n*-butanesulfonamide analog of **16** showed that deprotonation by diethylzinc (1 equiv) was rapid (<5 min). The use of 10 mol % of the preformed, deprotonated reagent led to rapid formation of product in a highly selective fashion (83% ee). Further support derived from the observation that the *N*,*N*′-bis-methyl analog of **16** was completely unselective (0% ee). In the previous experiments wherein only 1 equiv of diethylzinc was used for 1 equiv of alcohol and 0.1 equiv of promoter **16**, the bis-sulfonamide was probably being deprotonated by the ethylzinc alkoxide to form the active species.[21] We now add sufficient diethylzinc to remove the alcohol and sulfonamide protons.

(20) While it is conceivable that bis(iodomethyl)zinc could also form alkoxides, the results were less than encouraging. The reaction of cinnamyl alcohol with 2 equiv of preformed bis(iodomethyl)zinc proceeded very slowly and, in the presence of 0.1 equiv of **7**, was also less selective. Either deprotonation is not taking place or the (iodomethyl)zinc alkoxide that is formed is much less reactive than the corresponding ethylzinc alkoxide.

(21) The p*K*a's of the sulfonamides (9−11)[21a] are much lower than those of the alcohols (16−19).[21b] (a) Bordwell, F. G.; Branca, J. C.; Highes, D. L.; Olmstead, W. N. *J. Org. Chem.* **1980**, *45*, 3305. (b) Murto, J. *Acta Chem. Scand.* **1964**, *18*, 1043.

Table 1. Asymmetric Cyclopropanation of 1−14 using Protocol I

olefin	R^1	R^2	X	product	$t_{1/2}$[a] (min)	yield[b] %	ee[c] %
			3-Substituted Allylic Alcohols				
1	Ph	H	H	**17**	7	91	80
2	H	Ph	H	**18**	<3	81	81
3	$PhCH_2CH_2$	H	H	**19**	5	89	81
4	H	$PhCH_2CH_2$	H	**20**	<3	93	72
			3,3-Disubstituted Allylic Alcohols				
5	Ph	CH_3	H	**21**	<3	91	73
6	CH_3	Ph	H	**22**	<3	88	81
7	$PhCH_2CH_2$	CH_3	H	**23**	<3	94	79
8	CH_3	$PhCH_2CH_2$	H	**24**	<3	98	66
			2,3-Disubstituted Allylic Alcohols				
9	Ph	H	CH_3	**25**	40	90	5
10	H	Ph	CH_3	**26**	18	97	10
11	$PhCH_2CH_2$	H	CH_3	**27**	9	98	26
12	H	$PhCH_2CH_2$	CH_3	**28**	5	90	50
			2,3,3-Trisubstituted Allylic Alcohols				
13	Ph	CH_3	CH_3	**29**	25	85	43
14	CH_3	Ph	CH_3	**30**	45	85	16

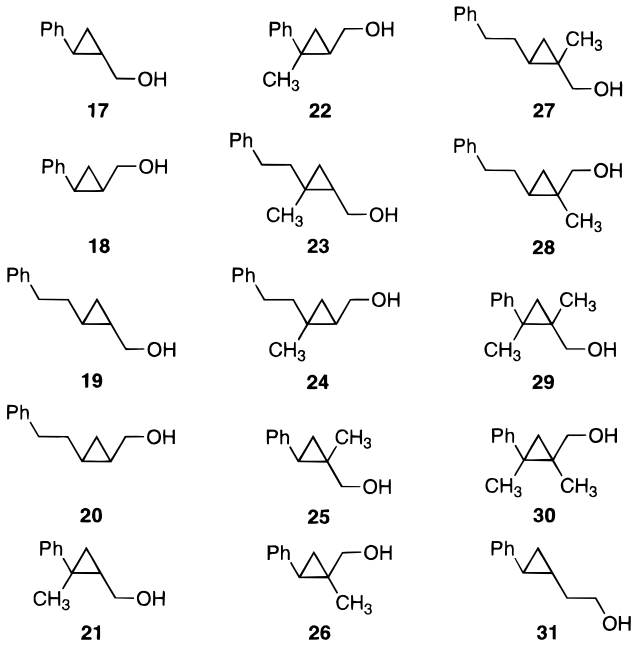
[a] Estimated half-lives from GC analysis of reaction progress. [b] Yields of analytically pure material. [c] Determined by chiral HPLC or GC; see Experimental Section for details.

The third critical experimental detail which we incorporated into this survey was the addition of zinc iodide. We have addressed this issue previously[5] wherein we described the advantages of using 10 mol % of zinc iodide from the outset. Since the solubility of zinc iodide in the solvent used (CH_2Cl_2) is low (even the 0.1 equiv used was only partially dissolved at the reaction concentrations (~0.03 M in olefin/~0.003 M in ZnI_2)), we did not a priori consider the use of greater amounts. As will be discussed later, this supposition was not justified for several reasons, and larger amounts of in-situ-generated zinc iodide were indeed beneficial.

The results of the cyclopropanation of olefins **1**−**14** shown in Chart 1 using protocol I are given in Table 1. The structures of the products are collected in Chart 2. Each reaction was run at either a 1.0 or 2.0 mmol scale, and reaction progress was monitored by gas chromatography. The products were purified by column chromatography and bulb-to-bulb distillation to provide materials which were fully characterized; the yields and enantiomeric excesses given are for analytically pure materials. The enantiomeric excess for each cyclopropane was determined using chiral HPLC or GC.

Various trends could be discerned for the different families of substrates. For the series of 3-substituted allylic alcohols **1**−**4**, the cyclopropanation selectivities were uniformly good, and neither the geometry of the double bond nor the presence of conjugating substituents had a significant effect on the enantioselectivity. In the family of 3,3-disubstituted allylic alcohols **5**−**8**, the yields and enantioselectivities were also good and similarly insensitive to structural and geometric changes. The poorer selectivity for **8** was greatly improved with a modified protocol (vide infra) so it need not be interpreted as a substrate phenomenon. The most striking substrate effect was observed in the family of 2,3-disubstituted allylic alcohols **9**−**12**. In this series, the products were formed more slowly and with much lower ee's. A curious exception is the rapid and modestly selective reaction of

Chart 2



substrate **12** in which the 2-phenylethyl and hydroxymethyl substituents are cis. Not unexpectedly, the 2,3,3-trisubstituted allylic alcohols **13** and **14** reacted slowly and with low selectivity. While not shown in Table 1, the poor results with homoallylic alcohol **15** ($t_{1/2}$ = 220 min; 88% yield; 5% ee) clearly showed the critical importance of the proximity of the hydroxymethyl group to the double bond.

The absolute configurations of the major enantiomer arising from cyclopropanation of **1**, **2**, and **3** were assigned as (1*R*,2*R*)-**17**, (1*R*,2*S*)-**18**, and (1*R*,2*R*)-**19** by comparison of optical rotations with those of literature values from previously assigned compounds.[22] The remaining cyclopropanemethanols were not rigorously assigned, but it is assumed that the major product arises from methylene delivery to the *re* face of the allylic alcohol (defined at C(2).

Survey of Substrates Using Protocol II. Despite extensive optimization and repetition, we were still concerned about variability experienced in selectivity using protocol I. We suspected that the source of this problem was related to the role of zinc iodide in forming the catalytically active species.[23] Our initial assumption that the use of more than 0.1 equiv of zinc iodide should have no effect was due to the fact that the majority of the zinc iodide remained undissolved. To our surprise, it was discovered that indeed the use of 1.0 equiv of zinc iodide did increase the rate of reaction and more importantly gave improved selectivities. However, the results with larger quantities (2.0−5.0 equiv) were variable (see Table 2).

It was discovered that the variability observed in our results was the result of the hygroscopic nature of zinc iodide. If samples of zinc iodide were used which had been repeatedly opened to the atmosphere, the selectivities were found to be lower. In a designed experiment, we observed the deleterious effect of added moisture (the addition of 1.0 equiv of H_2O under protocol I gave 31% ee for the cyclopropanation of cinnamyl alcohol). Initially, it was not expected that the zinc iodide employed would contain enough water to affect the reaction. Nonetheless, a survey of a number of batches of commercial zinc iodide as well as sublimed material (210 °C / 0.05 mm) was carried out. Presented in Table 2 are the results for cyclopropanation of cinnamyl alcohol using various samples and quantities of zinc iodide. Several of these reactions were run many times with equal or lower selectivities observed. It became apparent that while additional zinc iodide was often beneficial, the best results were obtained with drier samples. In all cases, every effort was taken to minimize exposure to moisture (samples were sealed under N_2, stored over P_2O_5, and opened for the minimum time necessary). Unless the reactions are executed in a dry box, the hygroscopic nature of zinc iodide would always be a problem.

To overcome the problems associated with the use of the hygroscopic reagent zinc iodide, an improved procedure, protocol II (Figure 2), was developed which employed in situ generation. This was accomplished in flask B by adding 1.0 equiv of diethylzinc to a suspension of 2.0 equiv of iodine in CH_2Cl_2. To this was added the contents of flask A (zinc alkoxide and promoter complex), and then the mixture was transferred to flask C (cyclopropanating reagent). The use of iodine, a relatively nonhygroscopic solid, and the virtually "self-drying" diethylzinc avoided the necessity of handling a moisture sensitive solid. We were able to *reproducibly* cyclopro-

Table 2. ZnI_2 Dependence of Cyclopropanation of 1 using Protocol I

entry	source of ZnI_2	equiv	ee **17**, %[a]
1	Aldrich 99.99+% (old)	1.0	82
2	Aldrich 99.99+% (old)	2.0	86
3	Aldrich 99.99+% (new)	1.0	83
4	Aldrich 99.99+% (new)	2.0	87
5	Aldrich 99.999%	1.0	86
6	Aldrich 99.999%	2.0	88
7	sublimed ZnI_2	1.0	86
8	sublimed ZnI_2	5.0	85
9	in situ ZnI_2	1.0	88
10	in situ ZnI_2 and distilled Et_2Zn	1.0	89

[a] Determined by chiral HPLC analysis.

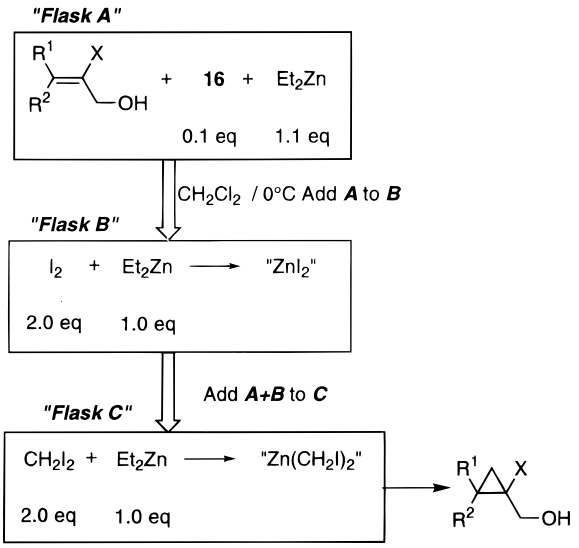


Figure 2. Modified cyclopropanation procedure: protocol II.

(22) (a) (−)-**17** has been assigned as (1*R*,2*R*), Keiderling, T. A.; Yasui, S. C. *J. Am. Chem. Soc.* **1987**, *109*, 2311. Sugita, T.; Inouye, Y. *Bull. Chem. Soc. Jpn.* **1966**, *39*, 1075. (b) (+)-**18** has been assigned as (1*S*,2*R*), Scholl, B.; Hansen, H.-J. *Helv. Chim. Acta* **1986**, *69*, 1936. (c) (−)-**19** has been assigned as (1*R*,2*R*), ref 18a.

(23) Careful monitoring of the reactions with and without added zinc iodide have shown a time dependence of enantioselectivity along with the elimination of the induction period.

Table 3. Comparison of Cyclopropanation Using Protocol I and Protocol II

olefin	R^1	R^2	X	product	protocol	$t_{1/2}$[a] (min)	yield[b] %	ee[c] %
1	Ph	H	H	**17**	I	7	91	80
					II	<3	92	89
3	$PhCH_2CH_2$	H	H	**19**	I	5	89	81
					II	<3	88	89
5	Ph	CH_3	H	**21**	I	<3	91	73
					II	<3	92	89
8	CH_3	$PhCH_2CH_2$	H	**24**	I	<3	98	66
					II	<3	89	82
9	Ph	H	CH_3	**25**	I	40	90	5
					II	7	91	3

[a] Estimated half-lives from GC analysis of reaction progress. [b] Yields of analytically pure material. [c] Determined by chiral HPLC or GC.

panate cinnamyl alcohol in 88% ee using 1.0 equiv of in situ-generated zinc iodide (see Table 2, entry 9). The use of larger amounts of in situ-generated ZnI_2 provided no increase in selectivity.

The final improvement incorporated into protocol II was the purification of diethylzinc. In all of the preceding experiments, neat diethylzinc as obtained from the supplier was used.[24] In addition to the obvious sensitivity of diethylzinc to moisture and oxygen, it has been observed by us and others[25] that dialkylzinc reagents are thermally and photochemically unstable. Furthermore, Takai has recently shown that lead has a harmful effect on cyclopropanation.[26] In light of these observations and in line with reports by both Furukawa[12b] and Seebach[27] we employed freshly distilled diethylzinc.

The results of cyclopropanation with the distilled diethylzinc in the presence of in situ-generated zinc iodide are compared to previous results in Table 2. While the in situ-generated zinc iodide was of obvious benefit (higher selectivity along with nonhygroscopic reagents), the advantages of prior distillation of diethylzinc, as measured by the ee of product **17**, were within experimental error (88% ee to 89% ee). Nonetheless, the simplicity of the distillation process along with the small increase in selectivity prompted us to incorporate the distillation of diethylzinc as part of protocol II.

To assess the value of the new protocol, five olefins (**1**, **3**, **5**, **8**, **9**) were selected for comparison and were cyclopropanated under the conditions of protocol II. The results are shown in Table 3 along with those from protocol I. For the 3-substituted and 3,3-disubstituted allylic alcohols (**1**/**3** and **5**/**8**, respectively), there was a significant improvement in the observed selectivities. The isolated yields were comparable to those obtained with protocol I. The reaction rates (as suggested by the smaller $t_{1/2}$ values) were usually larger with protocol II. The enantioselectivity of cyclopropanation of the 2,3-disubstituted allylic alcohol **9** did not improve, though the rate of reaction had increased.

Discussion

The results for the fourteen allylic alcohols **1**−**14** and one homoallylic alcohol **15** (see Tables 1 and 3 and text) illustrated a number of interesting trends. First, the olefin geometry (*E* or *Z*) had little effect on reaction rates or selectivities. Second, those substrates with a 2-substituent on the allylic alcohol (**9**−**14**) in general did not undergo selective reactions. Third, the homoallylic alcohol **15** was a particularly poor substrate.

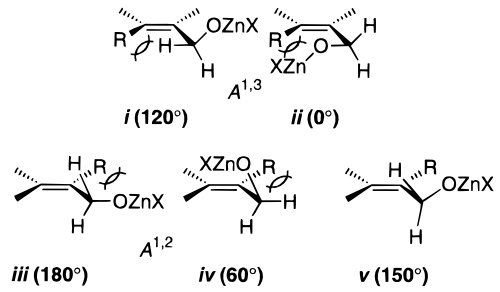


Figure 3. Allylic strain in directed cyclopropanation (dihedral angle).

For the allylic alcohols which had no substituent at the 2-position (**1**−**8**), the selectivities were remarkably similar for either protocol I or protocol II. Thus, the effect of *E*-3-substitution and *Z*-3-substitution as well as 3,3-disubstitution was negligible. Furthermore, there appeared to be no influence of substituent type within this group of olefins. Alkyl and phenyl groups were both equally well tolerated.

The fact that the *Z*-olefins were good substrates indicates that 1,3-allylic strain ($A^{1,3}$) is not important in determining selectivity. If the reactive conformation were such that one of the substituents on the carbinol carbon (OZnEt or H) were synplanar with the olefin (Figure 3, ***i*** and ***ii***), a rate and selectivity difference between *E*- and *Z*-isomers would be expected. The fact that no difference is seen indicates that the reaction likely goes through a staggered conformation such as ***iii***, ***iv***, or ***v***. Regardless of the reactive species, this group of substrates was well tolerated by both protocols illustrating an attractive feature of this method.

For allylic alcohols that contained 2-substituents (**9**−**14**), the lower reaction rates and selectivities are likely a manifestation of 1,2-allylic strain ($A^{1,2}$). If the reactive conformation were such that the oxygen was antiperiplanar to the olefin, the presence of a substituent at the 2-position would be disfavored (Figure 3, ***iii***). The conformation in which the directing alkoxide is synclinal (***iv***) to the olefin is less reasonable because the $A^{1,2}$-strain would be substantially reduced (H vs OZnX) and the effect of the C-(2) substituent should not be very significant. Furthermore, some effect of $A^{1,3}$ strain should be observed as the directing alkoxide, while gauche to the olefin, would now be in the vicinity of the *Z*-substituent. The lack of influence of olefin geometry suggests that ***iv***

(24) All transfers of neat diethylzinc were performed using microliter syringes.

(25) Boersma, J. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Ed.; Pergamon Press: New York, 1982; Vol. 2, Chapter 16.

(26) Takai, K.; Kakiuchi, T.; Utimoto, K. *J. Org. Chem.* **1994**, *59*, 2671.

(27) (a) Seebach, D.; Schafer, H. *Tetrahedron* **1995**, *51*, 2305. (b) We wish to thank Professor Seebach for kindly providing us with the details of their diethylzinc distillation.

is not an important reactive conformer. While conformer ***iii*** fits most of the criteria, it does place the critical directing group in the least proximate and least mechanistically sensible position. In view of suggestions by Rickborn on the relative rates of cyclopropanation of diastereomeric 5-substituted-2-cyclohexenols we suggest that conformer ***v***, roughly half-way between conformers ***i*** and ***iii***, is the most reasonable candidate.[28]

A structure such as ***v*** explains both the disruptive effect of 2-substitution as well as the lack of an effect by the pattern of 3-substitution (*E*- or *Z*-monosubstituted or -disubstituted). The presence of a 2-substituent would have the greatest influence in conformation ***iii*** as a consequence of $A^{1,2}$-strain. The influence of a *Z*-3-substituent would still be low in conformation ***v*** reflecting a lack of $A^{1,3}$-strain. These two features of conformation ***v*** suggest reactivity patterns that are well expressed by our results.

This analysis explains the reactivity patterns we have observed while ignoring the influence of the chiral promoter **16** or how the cyclopropanating reagent is directed. Nonetheless, it does provide a basis for examining these elements since structure ***v*** provides sufficient distance between the olefin and oxygen functions to accommodate both promoter and reagent. To envision this, several features had to be considered, namely: (1) what is the structure of the ethylzinc alkoxide substrate, (2) what is the structure of the zinc sulfonamide promoter, (3) what is the actual cyclopropanation reagent, (4) what is the effect of ZnI_2, and (5) how does the promoter **16** influence reaction rate and selectivity. Each of these freatures is individually discussed below. Figure 4 represents our current working hypothesis for the reactive ensemble that incorporates all zinc containing species and provides a rationale for the observed selectivities and trends.

The tendency of alkylzinc alkoxides (RZnOR′) to aggregate both in solution[29] and in the solid state[30] is well documented. Under the conditions described in this report, it can only be assumed that such assemblies of the ethylzinc allyl oxides are formed. However, to simplify our analysis we will assume that the substrate reacts as a monomeric ethylzinc alkoxide. This presumes that the alkoxide aggregate (most likely tetrameric) dissociates to produce the reactive monomer.

The zinc−sulfonamide promoter complex also may aggregate although much less is known about such compounds.[31] Here again, we propose that it appears as a monomer in the reactive super assembly.

The effect of ZnI_2 is more quantifiable and raises the first two of the three questions presented above: specifically, what is the reagent structure and what is the role of ZnI_2. We and Charette have both recently completed investigations clearly demonstrating that equimolar quantities of ZnI_2 drive the Schlenk equilibrium shown in eq 10 from the reagent bis(iodomethyl)zinc to (iodomethyl)zinc iodide.[32] Both spectroscopic (^{13}C-NMR) and reaction studies support the hypothesis that (iodomethyl)zinc iodide is the actual species formed in the presence of ZnI_2.

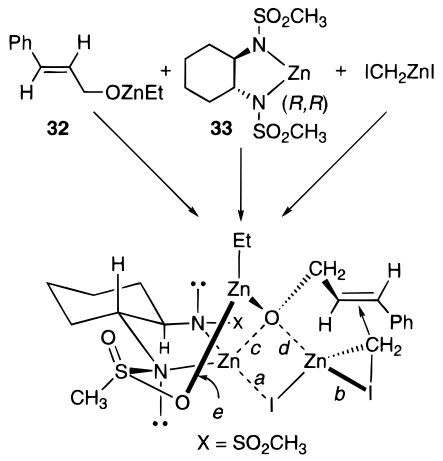


Figure 4. Transition state rationale for sulfonamide-promoted cyclopropanation.

$$Zn(CH_2I)_2 + ZnI_2 \rightleftharpoons 2\ ICH_2ZnI \qquad (10)$$

The identification of this reactive entity, along with the assumption of monomeric substrate alkoxide **32** and zinc−promoter complex **33**, has allowed us to propose the transition state assembly shown in Figure 4. At the outset, we must stress that this structure is purely speculative with no experimental evidence, indicating that the three components (substrate, reagent, and promoter) assemble in such a manner. Nonetheless, it serves as a useful construct to aid in an interpretation of the results. The three components (substrate, reagent, promoter) were combined in this manner to (1) rationalize the rate-accelerating feature of the sulfonamides, (2) fill the coordination spheres of the zinc atoms present (tetrahedral is most favored[25]), (3) account for the conformational analysis presented above, and (4) explain the observed facial preference ((*R*,*R*)-**16** gives (1*R*,2*R*)-**17**).

Activation of (iodomethyl)zinc iodide is achieved by coordination to the electron-deficient zinc of the sulfonamide complex (bond *a*). This occurs through the zinc-bound iodine of the reagent and serves to increase the reactivity by making the attached zinc of the reagent more electron deficient. Internal interaction with the iodine of the iodomethyl group (bond *b*) then accounts for the rate acceleration by making the methylene more reactive.

The tendency of heteroatom-bearing zinc compounds to be tetrahedrally substituted was next incorporated.[25] The alkoxide oxygen was used to fill the remaining sites on the zinc of the sulfonamide complex (bond *c*) and the reagent (bond *d*). Not only does this saturate the two zinc atoms but it also incorporates a degree of restriction into the ethylzinc alkoxide. The allyl unit appended to

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

(29) (a) CH_3ZnOCH_3 is tetrameric in benzene: Coates, G. E.; Ridley, D. *J. Chem. Soc.* **1965**, 1870. (b) *t*-Bu-Zn-O-*t*-Bu is a trimer in benzene: Noltes, J. G.; Boersma, J. *J. Organomet. Chem.* **1968**, *12*, 425.

(30) CH_3ZnOCH_3 is tetrameric in the solid state. X-ray structures : (a) Shearer, H. M. M.; Spencer, C. B. *Chem. Commun.* **1966**, 194. (b) Shearer, H. M. M.; Spencer, C. B. *Acta Crystallogr., Sect. B: Crystallogr. Cryst. Chem.* **1980**, *36*, 2046.

(31) We have attempted to grow crystals of a variety of bis-sulfonamides such as **31** with various combinations of solvent, temperature, concentration, and by the addition of both mono- and bidentate ligands for zinc (i.e., TMEDA). Invariably, no crystals were formed, and the solutions became viscous and gellike or a fine powder was formed. This suggests to us that the sulfonamide−zinc species such as **48** are self-associating to form polymeric networks. The zinc of one sulfonamide−zinc complex can be envisioned to coordinate the sulfonyl oxygen of another followed by additional such interactions to form a large networklike structure.

(32) (a) Denmark, S. E.; O'Connor, S. P. *J. Am. Chem. Soc.*, manuscript submitted. (b) Charette, A. B.; Marcoux, J.-F. *J. Am. Chem. Soc.* **1996**, *118*, 4539.

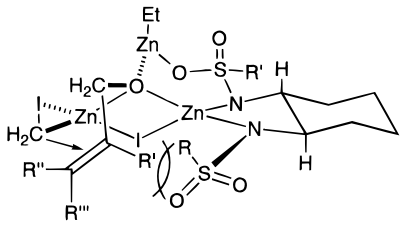


Figure 5. Directed cyclopropanation of allylic alcohols.

the oxygen now has a limited range of motion. This was further constrained by coordination of the alkoxide zinc atom with the more proximal sulfonyl group of the promoter through one of its oxygens (bond *e*). It is this feature of our model which accounts for the observed enantioselectivity. This sulfonyl oxygen is external to the five-membered zinc-containing heterocyclic ring and thus proximal to the alkoxide zinc atom. The allyl unit is now disposed to the rear and by the allylic strain arguments presented above only one face of the olefin (as shown) should be accessible to the methylene of the reagent. The other sulfonyl group, shown as X in Figure 4, has been forced to lie below the plane of the ring by the *trans*-cyclohexane. It is too remote to provide a coordinative interaction and must therefore play a different role. As illustrated in Figure 5, this "spectator" sulfonyl group appears to aid in facial selectivity by providing nonbonded interactions which further orient the olefin. Models suggest that it prevents the allyl unit from exposing the other olefin enantioface to the reagent. Clearly, it also plays a role in reactions with substrates that are substituted at the 2-position.

While a very useful catalytic, enantioselective method for the cyclopropanation of allylic alcohols has been described and rationalized by the proposed transition state structure shown in Figures 4 and 5, some minor questions remain unanswered. For example, differences in rates and selectivities *within* the two basic groups of substrates (those with and those without the 2-substituent) are not well understood. For example, the substrates **1** to **8** exhibit a range of enantiomeric excesses observed using protocol I (66 to 81%). Even with protocol II, there is still a significant variation (82−89% ee) for those allylic alcohols with no 2-substituent. Allylic alcohols **1**, **3**, and **5** all provided products in 89% ee with protocol II. The *cis*-trisubstituted substrate **8** gave cyclopropane with only 82% ee. Substrate **8** also exhibited the lowest selectivity with protocol I of those substrates with no 2-substituent (66% ee).

For the allylic alcohols with a 2-substituent (**24**−**29**), there is an even wider spread of observed selectivities (5−50% ee). It is not obvious why these differences occur. Possibly, subtle conformational features of the allyl alcohol unit resulting from each particular substitution pattern are responsible. An additional factor that may account for some of the observed differences may be the relative solubilities of the various alkoxides. Alternatively, substituent effects may alter the aggregation state of the alkoxides. A combination of these factors may be at work. A more detailed understanding of the small variability in these results must await additional information about the structures of the various species involved.

Conclusion

The generality of asymmetric cyclopropanation of allylic alcohols with a chiral bis-sulfonamide as the catalyst and bis(iodomethyl)zinc as the reagent in the presence of the additive zinc iodide has been demonstrated. A broad range of allylic alcohol substitution patterns were tolerated and the product cyclopropanes were obtained in a highly selective manner. In addition, an improved protocol was developed which reproducibly afforded high yields and enantioselectivities. Further investigations of the precise nature of the catalytic species and optimization of the promoter structure are in progress.

Experimental Section

General. ^{1}H and ^{13}C NMR spectra were recorded at 400 MHz ^{1}H and 100.6 MHz ^{13}C. All spectra were obtained using $CDCl_3$ ($CHCl_3$: δ = 7.26 ppm ^{1}H NMR, 77.0 ppm ^{13}C NMR). Data are reported in the following order: chemical shifts in ppm (δ); multiplicities are indicated (bs (broadened singlet), s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet)); coupling constants, *J*, are reported in hertz; integration is given; assignment is indicated. Assignment of individual resonances are supported by COSY and/or HETCOR spectra in some cases. Infrared spectra were recorded as neat liquids (NaCl) or KBr pellets. Peaks are reported (cm^{-1}) with the following relative intensities: s (strong, 67−100%), m (medium, 40−66%), w (weak, 20−40%). Electron impact mass spectra were obtained by the Mass Spectrometry Laboratory, School of Chemical Sciences, University of Illinois, with an ionization voltage of 70 eV. Data are reported in the form *m*/*e* (intensity relative to base = 100). Elemental analyses were performed by the University of Illinois Microanalytical Service Laboratory. Optical rotations were obtained at ambient temperature and are reported as follows: $[\alpha]^{temp}_D$ (solvent, concentration in g/100 mL). Bulb-to-bulb distillations were performed on a Buchi GKR-50 Kugelrohr apparatus; boiling temperatures refer to air bath temperatures and are corrected.

Materials. Reagent grade dichloromethane was distilled from P_2O_5 prior to use in the reactions. Analytical TLC was performed on Merck silica gel plates with QF-254 indicator. Visualization was accomplished with UV light, iodine, or phosphomolybdic acid solution (5% in ethanol). Column (flash) chromatography was performed using 32−63 mm silica gel. Solvents for extraction and chromatography were technical grade and distilled from the indicated drying reagents: hexane ($CaCl_2$), dichloromethane ($CaCl_2$), *tert*-butyl methyl ether (TBME) ($CaSO_4/FeSO_4$), ethyl acetate (K_2CO_3). Analytical gas chromatography was performed with a variable-temperature program and a flame ionization detector. The columns used were a Hewlett-Packard 50 m Ultra Phenyl Methyl Silicone (U2), a Hewlett-Packard 50 m Phenyl Methyl Silicone (HP-5), or a J&W Scientific 30 m Permethylated β-Cyclodextrin (J&W). Analytical high pressure liquid chromatography (HPLC) was performed using Daicel Chiralcel AD, OD, or OJ columns with the detector wavelength at 254 nm. The flow rate and solvent system were as denoted. The synthesis of promoter **16** and olefins **2**−**15** are described in the Supporting Information. Diiodomethane (Aldrich) was washed with $Na_2S_2O_3$ (aq), dried ($MgSO_4$), distilled from CaH_2 (88 °C/40 Torr), stored over copper, and protected from light. Neat diethylzinc was used as purchased from Strem in protocol A. In protocol B, diethylzinc was distilled (0 °C / 0.03 Torr). Zinc iodide (Aldrich) of 99.99+% and 99.999% grades was stored over P_2O_5. Iodine was obtained from Mallinkcrodt and used as supplied. Cinnamyl alcohol (**1**) was obtained from Aldrich and recrystallized from pentane/ether.

(1*R*,2*R*)-2-Phenylcyclopropanemethanol (17). Protocol I. In a flame-dried, 25 mL, two-necked, round-bottom flask equipped with a stir bar, septum, and argon inlet were added cinnamyl alcohol **1** (134 mg, 1.00 mmol), promoter **16** (27 mg, 0.1 mmol, 0.1 equiv), and zinc iodide (32 mg, 0.10 mmol, 0.10 equiv). The flask was evacuated and filled with argon (3×), and then CH_2Cl_2 (13 mL) was added. The suspension was cooled under argon to 0 °C, and diethylzinc (113 μL, 1.10 mmol, 1.10 equiv) was added. After stirring for 30 min at 0 °C, the

contents were transferred via cannula over ~30 s to a 100 mL, two-necked, round-bottom flask similarly equipped and containing a suspension of the cyclopropanating reagent in CH_2Cl_2. This reagent was prepared in advance by the addition of diethylzinc (103 μL, 1.00 mmol, 1.00 equiv) to a solution of diiodomethane (161 μL, 2.00 mmol, 2.00 equiv) in CH_2Cl_2 (24 mL) at 0 °C with subsequent stirring for 5 min (white precipitate formed after ~2 min). The combination of the contents of the two flasks led to complete dissolution except for a small amount of zinc iodide. The reaction mixture was maintained at 0 °C, and reaction progress was monitored periodically as follows. An aliquot (5−10 drops) was removed via cannula into a precooled (0 °C) solution of CH_2Cl_2 (0.5 mL) containing TMEDA (5 drops). After washing with 2 N HCl (0.5 mL), this solution was passed through a small plug of Florisil (~1/8 in.), followed by EtOAc (0.5 mL). This solution was then assayed by GC (U2, isothermal 180 °C, t_R 5.9 min). As the reaction proceeded, additional precipitate formed. The reaction was quenched at 0 °C after 30 min with 2 N NaOH (13 mL). The organic layer was removed, the aqueous layer was extracted with CH_2Cl_2 (2 × 20 mL), and the organic layers were combined, dried ($MgSO_4$), and concentrated in vacuo. The product was then purified by silica gel column chromatography (hexane/EtOAc, 3/1) followed by bulb-to-bulb distillation to yield 135 mg (91%) of **17** as a clear, colorless liquid: bp 60 °C (0.01 Torr); ^{1}H NMR (400 MHz) 7.30−7.24 (m, 2 H), 7.20−7.14 (m, 1 H), 7.10−7.06 (m, 2 H), 3.61 (ddd, J = 6.8, J = 11.2, J = 18.1, 2 H), 1.83 (td, J_t = 4.6, J_d = 9.3, 1 H), 1.82 (t, J = 4.5, 1 H), 1.46 (m, 1 H), 0.96 (m, 2 H); ^{13}C NMR (100 MHz) 142.38, 128.30, 125.74, 125.60, 66.52, 25.26, 21.24, 13.84; MS (EI) 148 (M^+, 18); IR 3336 (s); $[\alpha]^{25}_D$ = −69.3° (CCl_4, c = 2.78); lit.[22a] (1*R*, 2*R*) $[\alpha^{12}_D$ = −84° (CCl_4, c = 2.80); GC t_R 8.4 min (U2, isothermal 180 °C); HPLC t_R (1*R*,2*R*)-**17** 23.1 min (90.2%); t_R (1*S*,2*S*)-**17** 29.8 min (9.8%) (80% ee) (Daicel OJ, hexane/*i*-PrOH, 98/2, 1.0 mL/min); TLC R_f 0.20 (hexane/EtOAc, 3/1). Anal. Calcd for $C_{10}H_{12}O$ (148.21): C, 81.04; H, 8.16. Found: C, 80.74; H, 8.26.

(1*R*,2*S*)-2-Phenylcyclopropanemethanol (18). Following protocol I, from 268 mg (2.00 mmol) of (*Z*)-3-phenyl-2-propenol (**2**), promoter **16** (54 mg, 0.20 mmol, 0.10 equiv), zinc iodide (64 mg, 0.20 mmol, 0.10 equiv), and diethylzinc (226 μL, 2.20 mmol, 1.10 equiv) in one flask with CH_2I_2 (322 μL, 4.00 mmol, 2.00 equiv) and diethylzinc (206 μL, 2.00 mmol, 1.00 equiv) in the second flask was obtained 240 mg (81%) of **18** after flash chromatography (hexane/CH_2Cl_2/TBME, 3/1/1) and bulb-to-bulb distillation as a low-melting white solid (reaction time of 30 min): bp 75 °C (0.2 Torr); ^{1}H NMR (400 MHz) 7.32−7.17 (m, 5 H), 3.45 (dd, J = 6.4 , J = 11.7 Hz, 1 H), 3.26 (dd, J = 8.5, J = 11.7, 1 H), 2.30 (td, J_t = 8.5, J_d = 6.1), 1.50 (m, 1 H), 1.23 (bs, 1 H), 1.05 (td, J_t = 8.4, J_d = 5.4, 1 H), 0.88 (dd, J = 11.5, J = 5.6, 1 H); ^{13}C NMR (100 MHz) 138.17, 128.77, 128.25, 126.16, 62.82, 20.85 , 20.63 , 7.62; MS (EI) 148 (M^+, 7); IR 3284 (s); $[\alpha]^{25}_D$ = −48.9° ($CHCl_3$, c = 5.06); lit.[22b] (1*S*, 2*R*) $[\alpha]^{20}_D$ = +44.1° ($CHCl_3$, c = 5.0); GC t_R 8.0 min (U2, isothermal 180 °C); HPLC t_R (1*R*,2*S*)-**18** 19.8 min (90.7%); t_R (1*S*,2*R*)-**18** 16.8 min (9.3%) (81% ee) (Daicel OJ, hexane/*i*-PrOH, 98/2, 1.0 mL/min); TLC R_f 0.25 (hexane/CH_2Cl_2/TBME, 3/1/1). Anal. Calcd for $C_{10}H_{12}O$ (148.21): C, 81.04; H, 8.16. Found: C, 81.08; H, 8.18.

(1*R*,2*R*)-2-(2-Phenylethyl)cyclopropanemethanol (19). Following protocol I, from 324 mg (2.00 mmol) of (*E*)-5-phenyl-2-pentenol (**3**), promoter **16** (54 mg, 0.20 mmol, 0.10 equiv), zinc iodide (64 mg, 0.20 mmol, 0.10 equiv), and diethylzinc (226 μL, 2.20 mmol, 1.10 equiv) in one flask with CH_2I_2 (322 μL, 4.00 mmol, 2.00 equiv) and diethylzinc (206 μL, 2.00 mmol, 1.00 equiv) in the second flask was obtained 313 mg (89%) of **19** after flash chromatography (hexane/EtOAc, 3/1) and bulb-to-bulb distillation as a clear, colorless oil (reaction time of 30 min): bp 80 °C (0.02 Torr); ^{1}H NMR (400 MHz) 7.32−7.16 (m, 5 H), 3.40 (m, 2 H), 2.72 (m, 2 H), 1.59 (m, 2 H), 1.38 (bs, 1 H), 0.84 (m, 1 H), 0.62 (m, 1 H), 0.36 (m, 2 H); ^{13}C NMR (100 MHz) 142.06, 128.34, 128.19, 125.65, 66.92, 35.74, 35.19, 21.28, 16.72, 9.68; MS (EI) 176 (M^+, <1); IR 3320 (s); $[\alpha]^{28}_D$ = −25.5° ($CHCl_3$, c = 5.50); lit.[18a] $[\alpha]^{20}_D$ = −20.3° ($CHCl_3$, c = 1.14); GC t_R 7.1 min (HP-5, isothermal 200 °C); HPLC t_R (1*R*,2*R*)-**19** 79.3 min (90.5%); t_R (1*S*,2*S*)-**19** 88.0 min (9.5%) (81% ee) (Daicel AD, hexane/EtOH, 99.2/0.8, 0.4 mL/min); TLC R_f 0.25 (hexane/EtOAc, 3/1). Anal. Calcd for $C_{12}H_{16}O$ (176.26): C, 81.77; H, 9.15. Found: C, 81.78; H, 9.13.

(1*R,2*S**)-2-(2-Phenylethyl)cyclopropanemethanol (20).** Following protocol I, from 324 mg (2.00 mmol) of (*Z*)-5-phenyl-2-pentenol (**4**), promoter **16** (54 mg, 0.20 mmol, 0.10 equiv), zinc iodide (64 mg, 0.20 mmol, 0.10 equiv), and diethylzinc (226 μL, 2.20 mmol, 1.10 equiv) in one flask with CH_2I_2 (322 μL, 4.00 mmol, 2.00 equiv) and diethylzinc (206 μL, 2.00 mmol, 1.00 equiv) in the second flask was obtained 329 mg (93%) of **20** after flash chromatography (hexane/EtOAc, 3/1) and bulb-to-bulb distillation as a clear, colorless oil (reaction time of 30 min): bp 100 °C (0.04 Torr); ^{1}H NMR (400 MHz) 7.32−7.16 (m, 5 H), 3.65 (dd, J = 6.8, J = 11.2, 1 H), 3.50 (dd, J = 8.2 , J = 11.4, 1 H), 2.74 (m, 2 H), 1.75 (m, 1 H), 1.61 (m, 1 H), 1.38 (bs, 1 H), 1.11 (m, 1H), 0.92 (m, 1H), 0.73 (td, J_t = 7.8, J_d = 4.3, 1H), −0.02 (dd, J = 5.3, J = 10.2, 1 H); ^{13}C NMR (100 MHz) 142.26, 128.43, 128.27, 125.74, 63.02, 36.33, 30.58, 18.24, 15.83, 9.21; MS (EI) 176 (M^+, <1); IR 3333 (s); $[\alpha]^{28}_D$ = +19.7° ($CHCl_3$, c = 5.15); GC t_R 8.8 min (HP-5, isothermal 200 °C); HPLC t_R (1*R**,2*S**)-**20** 57.3 min (86.2%); t_R (1*S**,2*R**)-**20** 52.1 min (13.8%) (72% ee) (Daicel AD, hexane/EtOH, 99/1, 0.5 mL/min); TLC R_f 0.25 (hexane/EtOAc, 3/1). Anal. Calcd for $C_{12}H_{16}O$ (176.26): C, 81.77; H, 9.15. Found: C, 81.84; H, 9.17.

(1*R,2*R**)-2-Methyl-2-phenylcyclopropanemethanol (21).** Following protocol I, from 296 mg (2.00 mmol) of (*E*)-3-methyl-3-phenyl-2-propenol (**5**), promoter **16** (54 mg, 0.20 mmol, 0.10 equiv), zinc iodide (64 mg, 0.20 mmol, 0.10 equiv), and diethylzinc (226 μL, 2.20 mmol, 1.10 equiv) in one flask with CH_2I_2 (322 μL, 4.00 mmol, 2.00 equiv) and diethylzinc (206 μL, 2.00 mmol, 1.00 equiv) in the second flask was obtained 296 mg (91%) of **21** after flash chromatography (hexane/EtOAc, 3/1) and bulb-to-bulb distillation as a clear, colorless oil (reaction time of 35 min): bp 85°C (0.03 Torr); ^{1}H NMR (400 MHz) 7.32−7.17 (m, 5 H), 3.91 (dd, J = 6.6, J = 11.5, 1 H), 3.71 (dd, J = 8.9, J = 11.1, 1 H), 1.75 (bs, 1 H), 1.47 (bs, 3 H), 1.42 (m, 1 H), 1.16 (dd, J = 4.8, J = 8.9, 1 H), 0.61 (t, J = 5.2, 1 H); ^{13}C NMR (100 MHz) 147.51, 128.24, 127.11, 125.72, 63.38, 27.70, 24.70, 20.39 , 18.67; MS (EI) 162 (M^+, 4); IR 3345 (s); $[\alpha]^{27}_D$ = −34.4° ($CHCl_3$, c = 5.45); GC t_R 20.0 min (U2, isothermal 140 °C); HPLC t_R (1*R**,2*R**)-**21** 25.3 min (84.3%); t_R (1*S**,2*S**)-**21** 30.9 min (15.7%) (73% ee) (Daicel AD, hexane/EtOH, 99/1, 1.0 mL/min); TLC R_f 0.25 (hexane/EtOAc, 3/1). Anal. Calcd for $C_{11}H_{14}O$ (162.23): C, 81.44; H, 8.70. Found: C, 81.47; H, 8.70.

(1*R,2*S**)-2-Methyl-2-phenylcyclopropanemethanol (22).** Following protocol I, from 296 mg (2.00 mmol) of (*Z*)-3-methyl-3-phenyl-2-propenol (**6**), promoter **16** (54 mg, 0.20 mmol, 0.10 equiv), zinc iodide (64 mg, 0.20 mmol, 0.10 equiv), and diethylzinc (226 μL, 2.20 mmol, 1.10 equiv) in one flask with CH_2I_2 (322 μL, 4.00 mmol, 2.00 equiv) and diethylzinc (206 μL, 2.00 mmol, 1.00 equiv) in the second flask was obtained 285 mg (88%) of **22** after flash chromatography (hexane/EtOAc, 4/1) and bulb-to-bulb distillation as a clear, colorless oil (reaction time of 35 min): bp 90 °C (0.04 Torr); ^{1}H NMR (400 MHz) 7.35−7.18 (m, 5 H), 3.24 (bs, 1 H), 3.20 (dd, J = 7.6, J = 11.5, 2 H), 1.41 (bs, 3 H), 1.30 (m, 1 H), 0.91 (t, J = 5.0, 1 H), 0.81, (dd, J = 4.8, J = 8.4); ^{13}C NMR (100 MHz) 142.96, 128.97, 128.97, 126.29, 64.22, 28.16, 27.62, 26.47, 15.80; MS (EI) 162 (M^+, 5); IR 3341 (s); $[\alpha]^{28}_D$ = −36.3° ($CHCl_3$, c = 4.93); GC t_R 7.9 min (U2, isothermal 180 °C); chiral GC t_R (1*R**,2*S**)-**22** 12.9 min (90.6%); t_R (1*S**,2*R**)-**22** 14.1 min (9.4%) (81% ee) (J&W, isothermal 120 °C); TLC R_f 0.20 (hexane/EtOAc, 4/1). Anal. Calcd for $C_{11}H_{14}O$ (162.23): C, 81.44; H, 8.70. Found: C, 81.49; H, 8.74.

(1*R,2*R**)-2-Methyl-2-(2-phenylethyl)cyclopropanemethanol (23).** Following protocol I, from 176 mg (1.00 mmol) of (*E*)-3-methyl-5-phenyl-2-pentenol (**7**), promoter **16** (27 mg, 0.10 mmol, 0.10 equiv), zinc iodide (32 mg, 0.10 mmol, 0.10 equiv), and diethylzinc (113 μL, 1.10 mmol, 1.10 equiv) in one flask with CH_2I_2 (161 μL, 2.00 mmol, 2.00 equiv) and diethylzinc (103 μL, 1.00 mmol, 1.00 equiv) in the second flask was obtained 179 mg (94%) of **23** after flash chromatography (hexane/EtOAc, 3/1) and bulb-to-bulb distillation as a clear, colorless oil (reaction time of 30 min): bp 60 °C (0.01 Torr); ^{1}H NMR (400 MHz) 7.31−7.25 (m, 2 H), 7.19 (m, 3 H), 3.71

(dd, J = 6.3, J = 11.5, 1 H), 3.46 (dd, J = 8.5, J = 11.4, 1 H), 2.71 (m, 2 H), 1.69 (m, 1 H), 1.49 (m, 1 H), 1.34 (bs, 1 H), 1.18 (s, 3 H); ^{13}C NMR (100 MHz) 142.42, 128.36, 128.30, 125.70, 63.72, 42.98, 33.19, 26.17, 19.92, 17.60, 17.06; MS (EI) 190 (M^+, 5); IR 3344 (s); $[\alpha]^{26}_D = -19.2°$ ($CHCl_3$, c = 5.00); GC t_R 9.1 min (HP-5, isothermal 200 °C); HPLC t_R (1*R**,2*R**)-**23** 7.6 min (89.3%); t_R (1*S**,2*S**)-**23** 9.0 min (10.7%) (79% ee) (Daicel AD, hexane/EtOH, 95/5, 1.0 mL/min); TLC R_f 0.25 (hexane/EtOAc, 3/1). Anal. Calcd for $C_{13}H_{18}O$ (190.29): C, 82.06; H, 9.53. Found: C, 81.91; H, 9.47.

(1*R,2*S**)-2-Methyl-2-(2-phenylethyl)cyclopropanemethanol (24).** Following protocol I, from 176 mg (1.00 mmol) of (*Z*)-3-methyl-5-phenyl-2-pentenol (**8**), promoter **16** (27 mg, 0.10 mmol, 0.10 equiv), zinc iodide (32 mg, 0.10 mmol, 0.10 equiv), and diethylzinc (113 μL, 1.10 mmol, 1.10 equiv) in one flask with CH_2I_2 (161 μL, 2.00 mmol, 2.00 equiv) and diethylzinc (103 μL, 1.00 mmol, 1.00 equiv) in the second flask was obtained 187 mg (98%) of **24** after flash chromatography (hexane/EtOAc, 3/1) and bulb-to-bulb distillation as a clear, colorless oil (reaction time of 30 min): bp 90 °C (0.01 Torr); ^{1}H NMR (400 MHz) 7.31−7.25 (m, 2 H), 7.21−7.15 (m, 3 H), 3.65 (dd, J = 7.0, J = 11.3, 1 H), 3.56 (dd, J = 8.0, J = 11.4, 1 H), 2.72 (m, 2 H), 1.66 (dd, J = 7.8, J = 9.0, 2 H), 1.44 (bs, 1 H), 1.16 (s, 3 H), 0.97 (m, 1 H), 0.52 (dd, J = 4.5, J = 8.5, 1 H), 0.16 (t, J = 4.9, 1 H); ^{13}C NMR (100 MHz) 142.69, 128.33, 128.29, 125.71, 63.44, 36.45, 33.59, 27.28, 24.38, 20.38, 17.52; MS (EI) 190 (M^+, 7); IR 3342 (s); $[\alpha]^{27}_D = +5.8°$ ($CHCl_3$, c = 5.00); GC t_R 9.6 min (HP-5, isothermal 200 °C); HPLC t_R (1*R**,2*S**)-**24** 19.1min (82.8%); t_R (1*S**,2*R**)-**24** 25.9 min (17.2%) (66% ee) (Daicel OD, hexane/EtOH, 99/1, 1.0 mL/min); TLC R_f 0.25 (hexane/EtOAc, 3/1). Anal. Calcd for $C_{13}H_{18}O$ (190.29): C, 82.06; H, 9.53. Found: C, 81.94; H, 9.46.

(1*R,2*S**)-1-Methyl-2-phenylcyclopropanemethanol (25).** Following protocol I, from 148 mg (1.00 mmol) of (*E*)-2-methyl-3-phenyl-2-propenol (**9**), promoter **16** (27 mg, 0.10 mmol, 0.10 equiv), zinc iodide (32 mg, 0.10 mmol, 0.10 equiv), and diethylzinc (113 μL, 1.10 mmol, 1.10 equiv) in one flask with CH_2I_2 (161 μL, 2.00 mmol, 2.00 equiv) and diethylzinc (103 μL, 1.00 mmol, 1.00 equiv) in the second flask was obtained 148 mg (91%) of **25** after flash chromatography (hexane/EtOAc, 3/1) and bulb-to-bulb distillation as a clear, colorless oil (reaction time of 300 min): bp 60 °C (0.005 Torr); ^{1}H NMR (400 MHz) 7.32−7.25 (m, 2H), 7.23−7.16 (m, 3 H), 3.55 (t, J = 11.1, 2 H), 2.05 (dd, J = 5.9, J = 8.6, 1 H), 1.88 (bs, 1 H), 0.91 (m, 2 H), 0.89 (s, 3 H); ^{13}C NMR (100 MHz) 138.76, 129.05, 127.95, 125.84, 71.69, 26.68, 25.11, 15.73, 15.08; MS (EI) 162 (M^+, 6); IR 3345 (s); $[\alpha]^{27}_D = -1.4°$ ($CHCl_3$, c = 5.00); GC t_R 9.1 min (HP-5, isothermal 170 °C); HPLC t_R (1*R**,2*S**)-**25** 28.2min (48.7%); t_R (1*S**,2*R**)-**25** 13.3 min (44.2%) (5% ee) (Daicel AD, hexane/EtOH, 98/2, 1.0 mL/min); TLC R_f 0.40 (hexane/EtOAc, 3/1). Anal. Calcd for $C_{11}H_{14}O$ (162.26): C, 81.44; H, 8.70. Found: C, 81.18; H, 8.72.

(1*R,2*R**)-1-Methyl-2-phenylcyclopropanemethanol (26).** Following protocol I, from 148 mg (1.00 mmol) of (*Z*)-2-methyl-3-phenyl-2-propenol (**10**), promoter **16** (27 mg, 0.10 mmol, 0.10 equiv), zinc iodide (32 mg, 0.10 mmol, 0.10 equiv), and diethylzinc (113 μL, 1.10 mmol, 1.10 equiv) in one flask with CH_2I_2 (161 μL, 2.00 mmol, 2.00 equiv) and diethylzinc (103 μL, 1.00 mmol, 1.00 equiv) in the second flask was obtained 157 mg (97%) of **26** after flash chromatography (hexane/EtOAc, 3/1) and bulb-to-bulb distillation as a clear, colorless oil (reaction time of 300 min): bp 80 °C (0.01 Torr); ^{1}H NMR (400 MHz) 7.31−7.25 (m, 2 H), 7.24−7.16 (m, 3 H), 3.36 (d, J = 11.5, 1 H), 3.22 (d, J = 11.6, 1 H,), 2.06 (dd, J = 6.3, J = 8.3), 1.34 (s, 3 H), 1.25 (bs, 1 H), 1.05 (t, J = 5.5, 1 H), 0.83 (dd, J = 5.1, J = 8.3, 1 H); ^{13}C NMR (100 MHz) 138.76, 128.52, 128.29, 126.07, 66.84, 29.12, 25.42, 22.34, 15.58; MS (EI) 162 (M^+, 6); IR 3372 (s); $[\alpha]^{28}_D = +1.4°$ ($CHCl_3$, c = 5.00); GC t_R 6.6 min (U2, isothermal 170 °C); HPLC t_R (1*R**,2*R**)-**26** 19.4 min (54.8%); t_R (1*S**,2*S**)-**26** 15.8 min (45.2%) (10% ee) (Daicel OJ, hexane/EtOH, 99/1, 1.0 mL/min); TLC R_f 0.35 (hexane/EtOAc, 3/1). Anal. Calcd for $C_{11}H_{14}O$ (162.26): C, 81.44; H, 8.70. Found: C, 81.28; H, 8.75.

(1*R,2*R**)-1-Methyl-2-(2-phenylethyl)cyclopropanemethanol (27).** Following protocol I, from 176 mg (1.00 mmol) of (*E*)-2-methyl-5-phenyl-2-pentenol (**11**), promoter **16** (27 mg, 0.10 mmol, 0.10 equiv), zinc iodide (32 mg, 0.10 mmol, 0.10 equiv), and diethylzinc (113 μL, 1.10 mmol, 1.10 equiv) in one flask with CH_2I_2 (161 μL, 2.00 mmol, 2.00 equiv) and diethylzinc (103 μL, 1.00 mmol, 1.00 equiv) in the second flask was obtained 186 mg (98%) of **27** after flash chromatography (hexane/EtOAc, 3/1) and bulb-to-bulb distillation as a clear, colorless oil (reaction time of 90 min): bp 80 °C (0.01 Torr); ^{1}H NMR (400 MHz) 7.32−7.25 (m, 2 H), 7.22−7.16 (m, 3 H), 3.31 (q, J = 11.0, 2 H), 2.71 (m, 2 H), 1.67 (m, 2 H), 1.46 (bs, 1 H), 1.11 (s, 3 H), 0.65 (m, 1 H), 0.54 (dd, J = 4.5, J = 8.1, 1 H), 0.02 (t, J = 4.7, 1 H); ^{13}C NMR (100 MHz) 142.28, 128.44, 128.27, 125.74, 72.44, 36.33, 30.96, 22.36, 21.49, 16.54, 15.22; MS (EI) 190 (M^+, 4); IR 3347 (s); $[\alpha]^{26}_D = -4.8°$ ($CHCl_3$, c = 5.00); GC t_R 6.9 min (U2, isothermal 200 °C); HPLC t_R (1*R**,2*R**)-**27** 18.9 min (62.8%); t_R (1*S**,2*S**)-**27** 16.4 min (37.2%) (26% ee) (Daicel AD, hexane/EtOH, 99/1, 1.0 mL/min); TLC R_f 0.30 (hexane/EtOAc, 3/1). Anal. Calcd for $C_{13}H_{18}O$ (190.29): C, 82.06; H, 9.53. Found: C, 81.83; H, 9.59.

(1*R,2*S**)-1-Methyl-2-(2-phenylethyl)cyclopropanemethanol (28).** Following protocol I, from 176 mg (1.00 mmol) of (*Z*)-2-methyl-5-phenyl-2-pentenol (**12**), promoter **16** (27 mg, 0.10 mmol, 0.10 equiv), zinc iodide (32 mg, 0.10 mmol, 0.10 equiv), and diethylzinc (113 μL, 1.10 mmol, 1.10 equiv) in one flask with CH_2I_2 (161 μL, 2.00 mmol, 2.00 equiv) and diethylzinc (103 μL, 1.00 mmol, 1.00 equiv) in the second flask was obtained 171 mg (90%) of **28** after flash chromatography (hexane/EtOAc, 3/1) and bulb-to-bulb distillation as a clear, colorless oil (reaction time of 90 min): bp 80 °C (0.01 Torr); ^{1}H NMR (400 MHz) 7.32−7.25 (m, 2 H), 7.22−7.17 (m, 3 H), 3.54 (d, J = 11.3, 1 H), 3.39 (d, J = 11.2, 1 H), 2.71 (m, 2 H), 1.77 (m, 1 H), 1.63 (m, 1 H), 1.24 (bs, 1 H), 1.11 (s, 3 H), 0.70 (m, 1 H), 0.47 (dd, J = 4.4, J = 8.3, 1 H)), 0.11 (t, J = 5.1, 1 H); ^{13}C NMR (100 MHz) 142.31, 128.48, 128.30, 125.79, 67.09, 36.43, 31.38, 24.67, 22.54, 22.25, 17.25; MS (EI) 190 (M^+, 5); IR 3361 (s); $[\alpha]^{27}_D = +21.6°$ ($CHCl_3$, c = 5.00); GC t_R 8.9 min (HP-5, isothermal 200 °C); HPLC t_R (1*R**,2*S**)-**28** 23.5 min (75.0%); t_R (1*S**,2*R**)-**28** 19.2 min (25.0%) (50% ee) (Daicel OJ, hexane/EtOH, 99/1, 1.0 mL/min); TLC R_f 0.30 (hexane/EtOAc, 3/1). Anal. Calcd for $C_{13}H_{18}O$ (190.29): C, 82.06; H, 9.53. Found: C, 81.98; H, 9.51.

(1*R,2*S**)-1,2-Dimethyl-2-phenylcyclopropanemethanol (29).** Following protocol I, from 162 mg (1.00 mmol) of (*E*)-2,3-dimethyl-3-phenyl-2-propenol (**13**), promoter **16** (27 mg, 0.10 mmol, 0.10 equiv), zinc iodide (32 mg, 0.10 mmol, 0.10 equiv), and diethylzinc (113 μL, 1.10 mmol, 1.10 equiv) in one flask with CH_2I_2 (161 μL, 2.00 mmol, 2.00 equiv) and diethylzinc (103 μL, 1.00 mmol, 1.00 equiv) in the second flask was obtained 150 mg (85%) of **29** after flash chromatography (hexane/EtOAc, 3/1) and bulb-to-bulb distillation as a low-melting solid (reaction time of 90 min): bp 70 °C (0.06 Torr); ^{1}H NMR (400 MHz) 7.33−7.16 (m, 5 H), 3.84 (d, J = 11.2, 1 H), 3.70 (d, J = 11.5, 1 H), 1.60 (bs, 1 H), 1.47 (s, 3 H), 0.93 (d, J = 4.9, 1 H), 0.84 (s, 3 H), 0.77 (d, J = 4.9, 1 H); ^{13}C NMR (100 MHz) 144.98, 129.00, 128.14, 125.84, 68.28, 30.92, 27.26, 23.45, 23.34, 19.88; MS (EI) 176 (M^+, <1); IR 3261 (s); $[\alpha]^{27}_D = -9.6°$ ($CHCl_3$, c = 2.40); GC t_R 6.4 min (HP-5, isothermal 200 °C); HPLC t_R (1*R**,2*S**)-**29** 13.4 min (70.2%); t_R (1*S**,2*R**)-**29** 15.5 min (28.7%) (43% ee) (Daicel AD hexane/EtOH, 97/3, 1.0 mL/min); TLC R_f 0.30 (hexane/EtOAc, 3/1). Anal. Calcd for $C_{12}H_{16}O$ (176.26): C, 81.75; H, 9.18. Found: C, 81.74; H, 9.20.

(1*R,2*R**)-1,2-Dimethyl-2-phenylcyclopropanemethanol (30).** Following protocol I, from 162 mg (1.00 mmol) of (*Z*)-2,3-dimethyl-3-phenyl-2-propenol (**14**), promoter **16** (27 mg, 0.10 mmol, 0.10 equiv), zinc iodide (32 mg, 0.10 mmol, 0.10 equiv), and diethylzinc (113 μL, 1.10 mmol, 1.10 equiv) in one flask with CH_2I_2 (161 μL, 2.00 mmol, 2.00 equiv) and diethylzinc (103 μL, 1.00 mmol, 1.00 equiv) in the second flask was obtained 150 mg (85%) of **30** after flash chromatography (hexane/EtOAc, 3/1) and bulb-to-bulb distillation as a clear, colorless solid (reaction time of 90 min): bp 50 °C (0.005 Torr); ^{1}H NMR (400 MHz) 7.31−7.25 (m, 4 H), 7.21−7.16 (m, 1 H), 3.15 (d, J = 11.4, 1 H), 3.06 (d, J = 11.3, 1 H), 1.42 (s, 3 H), 1.37 (s, 3 H), 1.36 (bs, 1 H), 1.10 (d, J = 4.9, 1 H), 0.48 (d, J = 4.9, 1 H); ^{13}C NMR (100 MHz) 144.91, 128.41, 126.06, 69.31,

30.23, 27.40, 23.58, 22.34, 16.66; MS (EI) 176 (M^+, <1); IR 3361 (s); $[\alpha]^{28}_D = -1.0°$ ($CHCl_3$, $c = 5.00$); GC t_R 7.1 min (U2, isothermal 170 °C); HPLC t_R (1*R**,2*R**)-**30** 17.8 min (58.1%); t_R (1*S**,2*S**)-**30** 12.4 min (41.9%) (16% ee) (Daicel OJ hexane/*i*-PrOH, 99/1, 1.0 mL/min); TLC R_f 0.35 (hexane/EtOAc, 3/1). Anal. Calcd for $C_{12}H_{16}O$ (176.26): C, 81.75; H, 9.18. Found: C, 81.72; H, 9.21.

(1*R,2*S**)-2-Phenylcyclopropaneethanol (31).** Following protocol I, from 296 mg (2.00 mmol) of (*E*)-4-phenyl-3-butenol (**15**), promoter **16** (54 mg, 0.20 mmol, 0.10 equiv), zinc iodide (64 mg, 0.20 mmol, 0.10 equiv), and diethylzinc (226 μL, 2.20 mmol, 1.10 equiv) in one flask with CH_2I_2 (322 μL, 4.00 mmol, 2.00 equiv) and diethylzinc (206 μL, 2.00 mmol, 1.00 equiv) in the second flask was obtained 284 mg (88%) of **31** after flash chromatography (hexane/EtOAc, 3/1) and bulb-to-bulb distillation as a clear, colorless solid (reaction time of 480 min): bp 100 °C (0.04 Torr); ^{1}H NMR (400 MHz) 7.29−7.23 (m, 2 H), 7.18−7.12 (tt, $J = 7.3$ Hz, $J = 1.2$ Hz, 1 H), 7.08−7.04 (m, 2 H), 3.77 (t, $J = 6.4$ Hz, 2 H), 1.69 (m, 3 H), 1.62 (bs, 1 H), 1.10 (m, 1 H), 0.95 (td, $J_t = 4.9$ Hz, $J_d = 8.5$ Hz, 1 H), 0.84 (m, 1 H); ^{13}C NMR (100 MHz) 143.35, 128.26, 125.51, 125.34, 62.77, 37.25, 22.72, 20.25, 15.66; MS (EI) 162 (M^+, 17); IR 3353 (s); $[\alpha]^{28}_D = +6.1°$ ($CHCl_3$, $c = 3.10$); GC t_R 7.0 min (U2, isothermal 210 °C); HPLC t_R (1*R**,2*S**)-**31** 41.1 min (52.4%); t_R (1*S**,2*R**)-**31** 37.2 min (47.6%) (5% ee) (Daicel OJ hexane/EtOH, 99/1, 1.0 mL/min); TLC R_f 0.15 (hexane/EtOAc, 4/1). Anal. Calcd for $C_{11}H_{14}O$ (162.23): C, 81.44; H, 8.70. Found: C, 81.49; H, 8.72.

(1*R*,2*R*)-2-Phenylcyclopropanemethanol (17). Protocol II. To a flame-dried, 15 mL, two-necked, round-bottom flask (flask A) equipped with a stir bar, septum, and argon inlet were added cinnamyl alcohol **1** (134 mg, 1.00 mmol) and promoter **16** (27 mg, 0.1 mmol, 0.1 equiv). The flask was evacuated and filled with argon (3×), and then CH_2Cl_2 (3 mL) was added. The solution was cooled under argon to 0°C, and diethylzinc (113 μL, 1.10 mmol, 1.10 equiv) was added. The solution was stirred at 0 °C for 10 min. To a flame-dried, 25 mL, two-necked, round-bottom flask (flask B) equipped with a stir bar, septum, and argon inlet were added iodine (508 mg, 2.00 mmol, 2.00 equiv) and CH_2Cl_2 (10 mL). The suspension was cooled under argon to 0 °C, and diethylzinc (103 μL, 1.00 mmol, 1.00 equiv) was added. A thick, white precipitate immediately formed. The slurry was stirred at 0 °C for 10 min. To a flame-dried, 100 mL, two-necked, round-bottom flask (flask C) equipped with a stir bar, septum, and argon inlet were added diiodomethane (161 μL, 2.00 mmol, 2.00 equiv) and CH_2Cl_2 (24 mL). The solution was cooled to 0 °C, and diethylzinc (103 μL, 1.00 mmol, 1.00 equiv) was added with subsequent stirring for 5 min (white precipitate formed after ~2 min). The contents of flask A were added via cannula over ~30 s to flask B. The resulting thick, white slurry was stirred at 0 °C for 2 min and was transferred in like manner to flask C. The mixture was again a thick white slurry and was maintained at 0 °C. Periodic assays were carried out as described in protocol I. The reaction was quenched after 45 min with 2 N NaOH (13 mL) and purified as described for protocol I to provide 136 mg (92%) of **17** as a clear, colorless oil: (see protocol A for characterization) HPLC t_R (1*R*,2*R*)-**17** 22.7 min (94.9%); t_R (1*S*,2*S*)-**17** 29.3 min (5.1%) (89% ee) (Daicel OJ, hexane/*i*-PrOH, 98/2, 1.0 mL/min); TLC R_f 0.20 (hexane/EtOAc, 3/1). Anal. Calcd for $C_{10}H_{12}O$ (148.21): C, 81.04; H, 8.16. Found: C, 80.74; H, 8.26.

(1*R*,2*R*)-2-(2-Phenylethyl)cyclopropanemethanol (19). Following protocol II, from 162 mg (1.00 mmol) of (*E*)-5-phenyl-2-pentenol (**3**) and promoter **16** (27 mg, 0.20 mmol, 0.10 equiv) in flask A, iodine (508 mg, 2.00 mmol, 2.00 equiv) and diethylzinc (103 μL, 1.00 mmol, 1.00 equiv) in flask B, and CH_2I_2 (161 μL, 2.00 mmol) and diethylzinc (103 μL, 1.00 mmol, 1.00 equiv) in flask C was obtained 155 mg (88%) of **19** after flash chromatography (hexane/EtOAc, 3/1) and bulb-to-bulb distillation as a clear, colorless oil (reaction time of 30 min): (see protocol I for characterization) HPLC t_R (1*R*,2*R*)-**19**, 22.0 min (94.5%); t_R (1*S*,2*S*)-**19,** 26.8 min (5.5%) (89% ee) (Daicel AD, hexane/EtOH, 99/1, 1.0 mL/min); TLC R_f 0.25 (hexane/EtOAc, 3/1). Anal. Calcd for $C_{12}H_{16}O$ (176.26): C, 81.77; H, 9.15. Found: C, 81.78; H, 9.13.

(1*R,2*R**)-2-Methyl-2-phenylcyclopropanemethanol (21).** Following protocol II, from 148 mg (1.00 mmol) of (*E*)-3-methyl-3-phenyl-2-propenol (**5**) and promoter **16** (27 mg, 0.20 mmol, 0.10 equiv) in flask A, iodine (508 mg, 2.00 mmol, 2.00 equiv) and diethylzinc (103 μL, 1.00 mmol, 1.00 equiv) in flask B, and CH_2I_2 (161 μL, 2.00 mmol) and diethylzinc (103 μL, 1.00 mmol, 1.00 equiv) in flask C was obtained 149 mg (92%) of **21** after flash chromatography (hexane/EtOAc, 3/1) and bulb-to-bulb distillation as a clear, colorless oil (reaction time of 30 min): (see protocol I for characterization) HPLC t_R (1*R**,2*R**)-**21**, 25.3 min (94.5%); t_R (1*S**,2*S**)-**21**, 31.4 min (5.5%) (89% ee) (Daicel AD, hexane/EtOH, 99/1, 1.0 mL/min); TLC R_f 0.25 (hexane/EtOAc, 3/1). Anal. Calcd for $C_{11}H_{14}O$ (162.23): C, 81.44; H, 8.70. Found: C, 81.47; H, 8.70.

(1*R,2*S**)-2-Methyl-2-(2-phenylethyl)cyclopropanemethanol (24).** Following protocol II, from 176 mg (1.00 mmol) of (*Z*)-3-methyl-5-phenyl-2-pentenol (**8**) and promoter **16** (27 mg, 0.20 mmol, 0.10 equiv) in flask A, iodine (508 mg, 2.00 mmol, 2.00 equiv) and diethylzinc (103 μL, 1.00 mmol, 1.00 equiv) in flask B, and CH_2I_2 (161 μL, 2.00 mmol) and diethylzinc (103 μL, 1.00 mmol, 1.00 equiv) in flask C was obtained 169 mg (89%) of **24** after flash chromatography (hexane/EtOAc, 3/1) and bulb-to-bulb distillation as a clear, colorless oil (reaction time of 60 min): (see protocol I for characterization) HPLC t_R (1*R**,2*S**)-**24**, 20.3 min (91.8%); t_R (1*S**,2*R**)-**24** 27.2 min (8.2%) (82% ee) (Daicel OD, hexane/EtOH, 99/1, 1.0 mL/min); TLC R_f 0.25 (hexane/EtOAc, 3/1). Anal. Calcd for $C_{13}H_{18}O$ (190.29): C, 82.06; H, 9.53. Found: C, 82.29; H, 9.69.

(1*R,2*S**)-1-Methyl-2-phenylcyclopropanemethanol (25).** Following protocol II, from 148 mg (1.00 mmol) of (*E*)-2-methyl-3-phenyl-2-propenol (**9**) and promoter **16** (27 mg, 0.20 mmol, 0.10 equiv) in flask A, iodine (508 mg, 2.00 mmol, 2.00 equiv) and diethylzinc (103 μL, 1.00 mmol, 1.00 equiv) in flask B, and CH_2I_2 (161 μL, 2.00 mmol) and diethylzinc (103 μL, 1.00 mmol, 1.00 equiv) in flask C was obtained 148 mg (91%) of **25** after flash chromatography (hexane/EtOAc, 3/1) and bulb-to-bulb distillation as a clear, colorless oil (reaction time of 60 min): (see protocol I for characterization) HPLC t_R (1*R**,2*S**)-**25**, 27.9 min (51.5%); t_R (1*S**,2*R**)-**25** 13.3 min (48.5%) (3% ee) (Daicel AD, hexane/EtOH, 98/2, 1.0 mL/min); TLC R_f 0.40 (hexane/EtOAc, 3/1). Anal. Calcd for $C_{11}H_{14}O$ (162.26): C, 81.44; H, 8.70. Found: C, 81.35; H, 8.74.

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Supporting Information Available: A description of experimental procedures for the synthesis of compounds **2**−**16** along with complete listings of infrared absorbances and mass spectral fragments for all compounds described are provided (30 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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