Stability, Reactivity, Solution, and Solid-State Structure of Halomethylzinc Alkoxides

André B. Charette,* Carmela Molinaro, and Christian Brochu

Contribution from the Département de Chimie, Université de Montréal, P.O. 6128, Station Downtown, Montréal, Québec, Canada H3C 3J7

Received March 30, 2001

Abstract: In this paper, we report our findings regarding the development of a Lewis acid-catalyzed cyclopropanation of allylic alcohols with bis(iodomethyl)zinc. Iodomethylzinc alkoxides can be formed by treatment of an alcohol with bis(iodomethyl)zinc. These species are not prone to undergo cyclopropanation at low temperature but the addition of a Lewis acid in catalytic amounts induces the cyclopropanation reaction. Using this procedure, we demonstrated that the Lewis acid-catalyzed pathway significantly overwhelms the uncatalyzed one. This paper describes fundamental issues regarding the preparation and stability of halomethyl zinc alkoxides in solution as well as their aggregation state in solution and solid-state structures. Furthermore, the competition reaction between the inter- vs intramolecular cyclopropanation will be studied. Finally, we will discuss the possible activation pathways to explain the Lewis acid activation of halomethylzinc alkoxides. These findings provided new insights on the reactivity of $ROZnCH_2I$ and established the groundwork for the elaboration of an enantioselective version of the reaction.

Introduction

The addition of Lewis acids is a fairly well-established strategy to accelerate several organic transformations. The rate of many reactions, such as the Mukaiyama aldol, the Diels−Alder, Mannich, and ene reactions, is significantly increased by the addition of the appropriate Lewis acid.[1] The effect of Lewis acids on the rate of cyclopropanation with haloalkylzinc reagents is a much less understood phenomenon. The first report of the accelerating effect of Lewis acids on the cyclopropanation of olefins dates back to the early 80's when Friederich noticed that the addition of as little as 4 mol % of titanium tetrachloride to a mixture of zinc/copper couple and diiodomethane considerably improved the rate of the reaction.[2] The effect of Lewis acids, namely ZnI_2, has also been discussed in detail in the cyclopropanation of ethylzinc allyloxides with $Zn(CH_2I)_2$.[3] In this paper, we report our full account on a different strategy that relies on the Lewis acid activation of a $ROZnCH_2I$ species as well as an in-depth study on the stability and reactivity of iodomethylzinc alkoxides. Our strategy was based on the observation that iodomethylzinc alkoxides are quite poor cyclopropanating reagents that could be activated upon Lewis acid addition. These intermediates could be prepared by treating any alcohol with bis(iodomethyl)zinc. It was observed that these resulting iodomethylzinc alkoxides are quite poor cyclopropanating reagents and our approach was based on the novel idea that a chiral Lewis acid could trigger the cyclopropanation of the otherwise unreactive iodomethylzinc alkoxide (**A**, Scheme 1).[4] Although these species are potential intermediates in most cyclopropanation reactions involving allylic alcohols and $Zn(CH_2I)_2$, very little is known about their rate of formation, their stabilities, and their reactivities depending upon the nature of the alcohol used. This paper will also attempt to differentiate between the possible modes of activation shown in Scheme 1 (**B** vs **B′** vs **B″**).

Results and Discussion

Preliminary Results: Iodomethylzinc Alkoxide Formation. NMR/Proof of Principle. The synthesis, stability, and solution state structural studies of iodomethylzinc alkoxides were initially tackled. The first assumption in the mechanism shown in Scheme 1 was that an alcohol (allylic or otherwise) would be readily converted into a relatively unreactive iodomethylzinc alkoxide upon treatment with 1 equiv of bis(iodomethyl)zinc[5,6] at low temperature.[4] To test this hypothesis, cinnamyl alcohol and phenethyl alcohol were each treated with 1 equiv of a preformed suspension of $Zn(CH_2I)_2$ in CD_2Cl_2 at −20 °C.[7] The corresponding iodomethylzinc alkoxide was formed quantitatively as evidenced by the appearance of singlets at 1.4 (^{1}H NMR) and −27 ppm (^{13}C NMR). These chemical shifts are consistent with those of previously reported $ZnCH_2I$ signals.[6,8] Also, the NMR spectra indicated that the deprotonation reaction of the alcohol was rapid and effective as suggested by the quantitative formation of CH_3I (2.1 and −27 ppm by ^{1}H and ^{13}C NMR, respectively). Moreover, the deprotonation reaction was also monitored by in situ infrared experiments, which

(1) For selected reviews see: (a) *Lewis Acids in Organic Synthesis*; Yamamoto, H., Ed.; Wiley-VCH Inc.; Weinheim, Germany, 2000; Vols. I and II. (b) Dias, L. C. *Curr. Org. Chem.* **2000**, *4*, 305−342. (c) Sibi, M. P.; Liu, M. *Curr. Org. Chem.* **2001**, *5*, 719−755. (d) Fringuelli, F.; Piermatti, O.; Pizzo, F.; Vaccaro, L. *Eur. J. Org. Chem.* **2001**, 439−455.

(2) Friedrich, E. C.; Lunetta, S. E.; Lewis, E. J. *J. Org. Chem.* **1989**, *54*, 2388−2390.

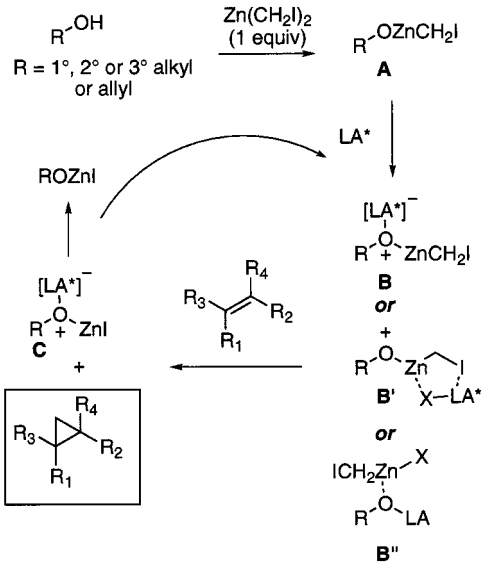
(3) (a) Denmark, S. E.; Christenson, B. L.; Coe, D. M.; O'Connor, S. P. *Tetrahedron Lett.* **1995**, *36*, 2215−2218. (b) Denmark, S. E.; Christenson, B. L.; O'Connor, S. P.; Noriaki, M. *Pure Appl. Chem.* **1996**, *68*, 23−27.

(4) (a) Charette, A. B.; Brochu, C. *J. Am. Chem. Soc.* **1995**, *117*, 11367−11368. (b) Charette, A. B.; Molinaro, C.; Brochu, C. *J. Am. Chem. Soc.* **2001**, *123*, 12168−12175.

(5) $Zn(CH_2I)_2$ was generated from 1 equiv of diethylzinc and 2 equiv of diiodomethane according to Furukawa's procedure: (a) Furukawa, J.; Kawabata, N.; Nishimura, J. *Tetrahedron Lett.* **1966**, 3353−3354. (b) Furukawa, J.; Kawabata, N.; Nishimura, J. *Tetrahedron* **1968**, *24*, 53−58. (c) Nishimura, J.; Furukawa, J.; Kawabata, N.; Kitayama, M. *Tetrahedron* **1971**, *27*, 1799−1806.

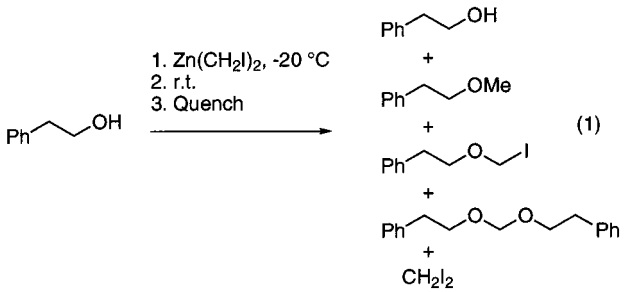
10.1021/ja010837+ CCC: $20.00
Published on Web 11/07/2001

Scheme 1

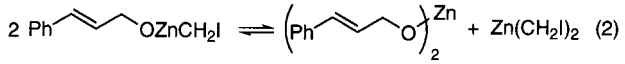


provided additional evidence of MeI formation within the first 5 min of the reaction.[7] Ethyl iodide is also produced by the alkyl exchange when 1 equiv of diethylzinc and 2 equiv of diiodomethane are mixed.[5] Furthermore, neither the disappearance of the alkene protons nor the appearance of cyclopropyl C−H's were observed when the iodomethylzinc alkoxide of cinnamyl alcohol was left for several hours at low temperature.[9]

Low-temperature (−20 °C) ^{1}H NMR monitoring of the species as a function of time for phenethyl alcohol shows that after 30 min a very clean ^{1}H NMR of the product is observed and sharp signals are apparent; however, as time progresses broader signals are observed which could be a consequence of aggregate formation in solution.[7] More importantly, however, is that the iodomethylzinc alkoxides are surprisingly stable as evidenced by the presence of Zn*CH*$_2$I signal (even if broadened), after one week at −20 °C.[7] This observation was further confirmed by ^{13}C NMR of the same sample taken after 24 h and after one week. Finally we can conclude that halomethylzinc alkoxides are relatively facile species to generate (from an alcohol and $Zn(CH_2I)_2$) and they display a good stability as they are still present even after one week at −20 °C as confirmed by ^{1}H and ^{13}C NMR. However, if the sample was left at room temperature for several hours many additional signals appeared which result from a temperature-dependent decomposition of the sample. The structures of some of the decomposition products are shown in eq 1. These compounds were identified by GC-MS and NMR and by comparison with authentic sample.



In contrast, monitoring of (*E*)-PhCH═CHCH$_2$OZnCH$_2$I indicated that the carbenoid was not stable for a long period of time at −20 °C and signals corresponding to the cyclopropanated adduct appeared within 24 h.[7] Two equally valuable postulates therefore can be put forward to explain this behavior. First, the cyclopropanation may be catalyzed by ZnI_2 resulting from the slow decomposition of the iodomethylzinc alkoxide.[4,7] Alternatively, it can result from the generation of $Zn(CH_2I)_2$ from the Schlenk equilibration of alkylzinc alkoxides[10] as shown in eq 2.



Aggregation State in Solution. To determine the degree of association of halomethylzinc alkoxides in solution, simple molecular weight measurements were determined by the melting point variation of benzene solutions. This approach was favored in our case since as shown earlier, halomethylzinc alkoxides tend to decompose when warmed. Noltes, Coates, and Allen have used various methods successfully to determine the degree of association of zinc alkoxides in solution.[11] Several halomethyl zinc alkoxides were prepared and the degree of association by

(6) For NMR and X-ray structures of this reagent as well as theoretical studies see: (a) Denmark, S. E.; Edwards, J. P.; Wilson, S. R. *J. Am. Chem. Soc.* **1991**, *113*, 723−725. (b) Denmark, S. E.; Edwards, J. P.; Wilson, S. R. *J. Am. Chem. Soc.* **1992**, *114*, 2592−2602. (c) Charette, A. B.; Marcoux, J.-F. *J. Am. Chem. Soc.* **1996**, *118*, 4539−4549. (d) Charette, A. B.; Marcoux, J.-F.; Bélanger-Gariépy, F. *J. Am. Chem. Soc.* **1996**, *118*, 6792−6793. (e) Dargel, T. K.; Koch, W. *J. Chem. Soc., Perkin Trans. 2* **1996**, 877−881. (f) Bernardi, F.; Bottoni, A.; Miscione, G. P. *J. Am. Chem. Soc.* **1997**, *119*, 12300−12305. (g) Hirai, A.; Nakamura, M.; Nakamura, E. *Chem. Lett.* **1998**, 927−928. (h) Nakamura, E.; Hirai, A.; Nakamura, M. *J. Am. Chem. Soc.* **1998**, *120*, 5844−5845. (i) Charette, A. B.; Marcoux, J.-F.; Molinaro, C.; Beauchemin, A.; Brochu, C.; Isabel, É. *J. Am. Chem. Soc.* **2000**, *122*, 4508−4509. (j) Hermann, H.; Lohrenz, J. C. W.; Kühn, A.; Boche, G. *Tetrahedron* **2000**, *56*, 4109−4115. (k) Bernardi, F.; Bottoni, A.; Miscione, G. P. *Organometallics* **2000**, *19*, 5529−5532. (l) Boche, G.; Lohrenz, J. C. W. *Chem. Rev.* **2001**, *101*, 697−756.

(7) See Supporting Information for further information.

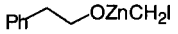
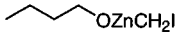
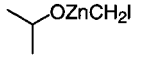
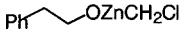
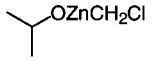
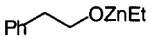
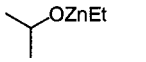
(8) The appearance of a signal at 1.36 ppm corresponds to the formation of small amounts of bis(iodomethyl)zinc and is consistent with the following equilibrium reactions that have been reported in the literature: $2RZnOR' \leftrightarrow Zn(OR')_2 + ZnR_2$ and for X-rays consistent with tetrameric alkylzinc alkoxides $2[ROZnR]_4 \rightarrow ZnR_2 + [(RO)_8Zn_7R_6]$: (a) Coates, G. E.; Ridley, D. *J. Chem. Soc.* **1965**, 1870−1877. (b) Allen, G.; Bruce, J. M.; Farrren, D. W.; Hutchinson, F. G. *J. Chem. Soc. B* **1966**, 799−803. (c) Shearer, H. M. M.; Spencer, C. B. *Chem. Commun.* **1966**, 194. (d) Matsui, Y.; Kamiya, K.; Nishikawa, M. *Bull. Chem. Soc. Jpn.* **1966**, *39*, 1828. (e) Noltes, J. G.; Boersma, J. *J. Organomet. Chem.* **1968**, *12*, 425−431. (f) Eisenhuth, W. H.; Van Wazer, J. R. *J. Am. Chem. Soc.* **1968**, *90*, 5397−5400. (g) Adamson, G. W.; Shearer, H. M. M.; Spencer, C. B. *Acta Crystallogr. Suppl.* **1968**, *21*, A135. (h) Ziegler, M. L.; Weiss, J. *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 905−906. (i) Ishimori, M.; Hagiwara, T.; Tsuruta, T.; Kai, Y. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 1165−1166. (j) Shearer, H. M. M.; Spencer, C. B. *Acta Crystallogr.* **1980**, *B36*, 2046−2050. (k) Boersma, J. Zinc and Cadmium. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Permagon Press: Oxford, 1982; Vol. II, pp 823−862. (l) Olmstead, M. M.; Power, P. P.; Shoner, S. C. *J. Am. Chem. Soc.* **1991**, *113*, 3379−3385. (m) O'Brien, P. Cadmium and Zinc. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G. Eds.; Elsevier Science Ltd: Oxford, 1995; Vol. III, pp 175−206.

(9) This last observation was also confirmed through measurement of the amount of cyclopropanation product upon quenching the reaction mixture at low temperature; see the Supporting Information.

(10) Inoue, S.; Kobayashi, M.; Tozuka, T. *J. Organomet. Chem.* **1974**, *81*, 17−21.

(11) (a) Coates, G. E.; Ridley, D. *J. Chem. Soc.* **1965**, 1870−1877. (b) Allen, G.; Bruce, J. M.; Hutchinson, F. G. *J. Chem. Soc.* **1965**, 5476−5481. (c) Allen, G.; Bruce, J. M.; Hutchinson, F. G. *J. Chem. Soc.* **1965**, 54−76. (d) Coates, G. E.; Lauder, A. *J. Chem. Soc. A* **1966**, 264−267. (e) Coates, G. E.; Ridley, D. *J. Chem. Soc. A* **1966**, 1064−1069. (f) Boersma, J.; Noltes, J. G. *Tetrahedron Lett.* **1966**, *14*, 1521−1525. (g) Bruce, J. M.; Cutsforth, B. C.; Hutchinson, F. G.; Rabagliati, F. M.; Reed, D. R. *J. Chem. Soc. B* **1966**, 1020−1024. (h) Coates, G. E.; Roberts, P. D. *J. Chem. Soc. A* **1967**, 1233−1234. (i) Boersma, J.; Noltes, J. G. *J. Organomet. Chem.* **1967**, *8*, 551−553. (j) Boersma, J.; Noltes, J. G. *J. Organomet. Chem.* **1968**, *13*, 291−299. (k) Noltes, J. G.; Boersma, J. *J. Organomet. Chem.* **1968**, *12*, 425−431. (l) Boersma, J.; Spek, A. L.; Noltes, J. G. *J. Organomet. Chem.* **1974**, *81*, 7−15.

Table 1. Molecular Weight Determination[a]

Entry		Concn[b]	MW_{obs}	*N*[c]
1		1	300	0.9
2	"	0.7	333	1.0
3	"	0.5	259	0.8
4	"	0.3	330	1.0
5	"	0.1	320	1.0
6[d]	"	0.7	333	1.0
7		0.7	253	0.9
8		1	337	1.3
9	"	0.7	317	1.2
10	"	0.3	327	1.2
11	"	0.1	344	1.3
12[d]	"	0.7	385	1.5
13		0.3	243	1.0
14		0.3	217	1.2
15		0.7	292	1.3
16		0.7	566	3.7

[a] Samples were prepared in CH_2Cl_2 for 0.5 h, left under high vacuum for 2 h, dissolved in benzene, and cryoscopy measurements were made. In all cases the alkoxides were completely soluble in benzene. [b] Concentration of alkoxide. [c] *N*, degree of association. [d] Measured after 48 h.

molecular weight determination are presented in Table 1. Quite unexpectedly based on litterature assumptions,[6h] the molecular weight determination of the iodo- or chloro[12]-methylzinc alkoxides derived from phenethyl alcohol or 2-propanol at different concentrations indicated these species are mostly monomeric in benzene (entries 1−14, Table 1). This is also the case for iodomethylzinc butoxide (entry 7, Table 1). Although molecular weight determination of the species resulting from the reaction between simple alcohols and dialkyl zinc has led to the misconception that most alkoxides are tetrameric (cryoscopically in benzene), zinc alkoxides also exist in lower aggregation states such as dimers or trimers in benzene solution as a result of intermolecular Zn−O and/or intramolecular Zn−L bridging (L being a ligand for zinc).[11] In the case of halomethylzinc alkoxides, it is conceivable that benzene (solvent), the halogen (I or Cl), or the phenyl group in $PhCH_2CH_2OZnCH_2$-Hal (in CH_2Cl_2) could effectively solvate or act as a ligand for the more acidic zinc centers thus allowing a stabilization to the monomeric species. Even after 48 h (entries 6 and 12, Table 1) these species appear to be mainly monomeric. Ethylzinc 2-phenylethoxide measurements also gave a monomeric structure where intramolecular interactions between the phenyl group and the zinc center may lead to the stabilization of the monomeric species.[13] Isopropyl ethylzinc gave an aggregation state averaging the tetrameric form as previously reported.[11a]

Solid-State Structure of $ROZnCH_2I$ and $ROZnCH_2Cl$. Having demonstrated that halomethylzinc species are monomeric in benzene and stable for at least one week at low temperature,

(12) Chloromethylzinc alkoxide of phenethyl alcohol was generated from 1 equiv of $Zn(CH_2Cl)_2$ and 1 equiv of the alcohol. See Supporting Information for ^1H and ^{13}C NMR spectra for chloromethylzinc alkoxide. For the preparation of $Zn(CH_2Cl)_2$ see: Denmark, S. E.; Edwards, J. P. *J. Org. Chem.* **1991**, *56*, 6974−6981.

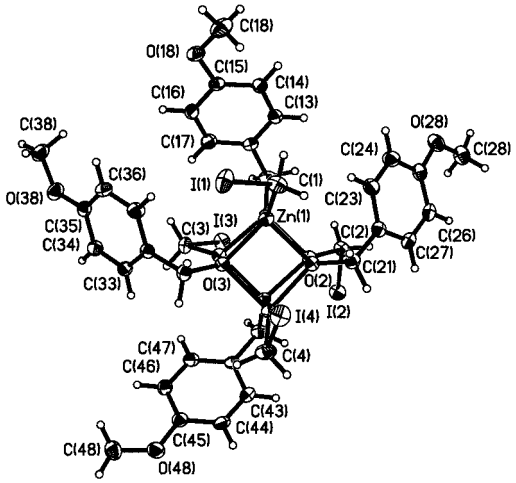


Figure 1. ORTEP drawing of iodomethylzinc alkoxide derived from 4-methoxybenzyl alcohol. Ellipsoids are drawn at the 30% probability level.

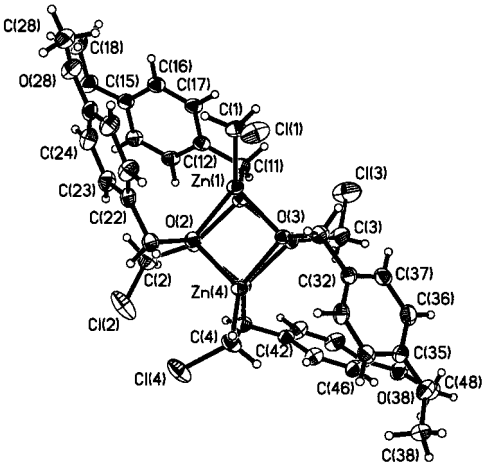


Figure 2. ORTEP drawing of chloromethylzinc alkoxide derived from 4-methoxybenzyl alcohol. Ellipsoids are drawn at the 30% probability level.

the establishment of their solid-state structure became mandatory. After numerous attempts, we successfully obtained suitable crystals by slow diffusion of hexanes in a CH_2Cl_2 solution of the halomethylzinc alkoxide at low temperature. Two X-ray crystal structures of halomethylzinc alkoxides produced from 4-methoxybenzyl alcohol and $Zn(CH_2I)_2$[14] as well as from $Zn(CH_2Cl)_2$ were obtained (Figures 1 and 2). Selected bond lengths and angles are given in Table 2. These structures are reminiscent of those of methylzinc methoxide[8c,g,j] and methylzinc *tert*-butoxide,[8d] which also crystallized as tetramers having Zn and O on alternate corners of a slightly distorted cube. The distortion angles of Zn−O−Zn are greater than 90°. The average bond lengths (Å) are the following: C−O (1.431−1.457), O−Zn (2.022−2.137), Zn−C (1.940−1.965), C−I (2.159−2.182),

(13) π-Chelation between Zn and a phenyl group or C=C double bond: (a) St. Denis, J.; Oliver, J. P. *J. Organomet. Chem.* **1972**, *44*, C32−C36. (b) St. Denis, J.; Oliver, J. P. *J. Organomet. Chem.* **1974**, *71*, 315−323. (c) Albright, M. J.; St. Denis, J. N.; Oliver, J. P. *J. Organomet. Chem.* **1977**, *125*, 1−8. (d) Beruben, D.; Marek, I.; Normant, J. F.; Platzer, N. *J. Org. Chem.* **1995**, *60*, 2488−2501. (e) Cossy, J.; Blanchard, N.; Meyer, C. *J. Org. Chem.* **1998**, *63*, 5728−5729.

(14) Two different crystals were obtained for 4-MeO-$PhCH_2OZnCH_2I$. The X-ray for the second crystal is isostructural to the $ROZnCH_2Cl$ analogue. The X-ray crystal structure of $MeOZnCH_2I$ prepared from the photoinduced method was also obtained but the structure will be reported separately: Charette, A. B.; Beauchemin, A.; Marcoux, J.-F.; Francoeur, S.; Enright, G.; Gariépy-Bélanger, F. Unpublished results.

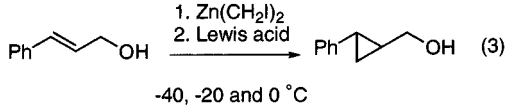
Table 2. Selected Bond Lengths (Å) and Angles (deg) for Iodomethyl Zinc 4-Methoxybenzyloxy ($ROZnCH_2I$) and Chloromethyl Zinc 4-Methoxybenzyloxy ($ROZnCH_2Cl$)

	$ROZnCH_2I$	$ROZnCH_2Cl$
	bond lengths	
Zn(1)−C(1)	1.962(5)	1.955(5)
I(1)−C(1)	2.159(5)	
Cl(1)−C(1)		1.809(5)
Zn(1)−O(1)	2.042(3)	2.061(3)
Zn(1)−O(2)	2.123(3)	2.052(3)
Zn(1)−O(3)	2.052(3)	2.086(3)
Zn(1)−Zn(4)	2.9917(9)	3.0705(8)
C(11)−O(1)	1.450(5)	1.450(5)
	bond angles	
Zn(1)−C(1)−I(1)	116.8(3)	
Zn(1)−C(1)−Cl(1)		111.0(3)
C(1)−Zn(1)−O(1)	142.08(19)	129.28(18)
C(1)−Zn(1)−O(2)	115.9(2)	133.87(19)
C(1)−Zn(1)−O(3)	129.28(18)	127.01(19)
C(11)−O(1)−Zn(2)	118.4(3)	122.4(3)
C(11)−O(1)−Zn(1)	120.1(3)	120.1(3)
O(2)−Zn(1)−O(1)	79.77(12)	83.26(13)
O(2)−Zn(1)−O(3)	87.71(13)	82.82(12)
O(1)−Zn(1)−O(3)	83.02(12)	82.73(12)
Zn(2)−O(1)−Zn(3)	93.28(12)	97.53(13)
Zn(1)−O(1)−Zn(3)	95.53(12)	96.62(12)
Zn(2)−O(1)−Zn(1)	100.14(13)	96.54(13)

C−Cl (1.727−1.809), and Zn−Zn (2.9917−3.1118). The average bond angles (deg) are the following: C−O−Zn (117.0−126.5), O−Zn−C (112.7−148.9), Zn−C−I (105.4−116.8), Zn−C−Cl (108.0−118.3), O−Zn−O (79.77−87.71), and Zn−O−Zn (91.15−100.14).

The difference between the solution and solid-state structure of halomethylzinc alkoxides is quite stricking but it is clear that in solution either the solvent (benzene) or the presence of a basic donor group on the reagent may help in stabilizing the monomeric form.

Lewis Acid Activation of Iodomethylzinc Alkoxides (Scheme 1).[7] The second assumption in the mechanism shown in Scheme 1 was that the addition of a Lewis acid to a relatively unreactive halomethylzinc alkoxide would generate a reactive intermediate, sufficiently increase the electrophilic character of the carbenoid, and lead to a cyclopropanation reaction (eq 3). This last



(3)

observation was confirmed by measuring the amount of cyclopropanated product from cinnamyl alcohol upon quenching the reaction mixture at low temperature. As pointed out earlier, less than 23% of cyclopropane adduct was observed if the iodomethylzinc alkoxide was left for 6 h at 0 °C. However, we have also noticed that the deliberate introduction of trace amounts of oxygen triggered a non-Lewis acid-catalyzed cyclopropanation reaction to a modest extent at 0 °C.[15] This observation is consistent with Miyano's report that unambiguously showed that the presence of oxygen could accelerate the cyclopropanation of unfunctionalized olefins.[16] In contrast, several achiral Lewis acids, added in catalytic amounts to the preformed iodomethylzinc alkoxide, triggered the cyclopropanation reaction.[17] In this system, a general trend follows the strength of the Lewis acid. Stronger Lewis acids (such as $TiCl_4$, BBr_3, $SiCl_4$, $SnCl_4$, Et_2AlCl, etc.) are usually much more effective at catalyzing the reaction whereas weaker Lewis acids ($Ti(Oi\text{-}Pr)_4$, $B(OMe)_3$, etc.) are less effective.[18] For example, the addition of as little as 1 mol % of $TiCl_4$ is sufficient to promote the cyclopropanation reaction of cinnamyl alcohol providing a conversion of 65% at 0 °C. It also appears that Lewis acids having nucleophilic counterions are more effective than those that contain nonnucleophilic ones.

Lewis Acid-Catalyzed Cyclopropanation and Substrate Generality. Under standard conditions, a minimum of 2 equiv of $Zn(CH_2I)_2$ is required to efficiently cyclopropanate an allylic alcohol. Typically, the first equivalent is used to generate the halomethylzinc alkoxide (see Scheme 1) and the second will act as the methylene transfer reagent to generate the corresponding cyclopropane. Our new protocol implies the replacement of the *extra equivalent* of $Zn(CH_2I)_2$ by a *catalytic amount* of a Lewis acid rendering the overall process more efficient. The efficiency of the cyclopropanation process with $ROZnCH_2I$/Lewis acid was compared to that involving 2 equiv of $Zn(CH_2I)_2$. The relative rate of the cyclopropanation reaction of cinnamyl alcohol was qualitatively assessed by using $TiCl_4$. A slightly lower reaction rate was observed in the Lewis acid-catalyzed version, but considering that there is only one active CH_2I group compared to three in the uncatalyzed reaction, the rate of the former version nicely competes with the rate of the latter.

These reaction conditions were tested on several allylic alcohols and the results are presented in Table 3. A variety of substitution patterns are tolerated with this protocol as exemplified by the effective cyclopropanation of trans (entries 1−3, Table 3), cis (entries 4−6, Table 3), as well as trisubstituted allylic alcohols (entries 7−9, Table 3). Also, interestingly a chiral, racemic secondary allylic alcohol (entry 10, Table 3) gave a 3:1 (syn:anti) ratio which is similar to that obtained when the reaction is done with 2 equiv of $Zn(CH_2I)_2$.[19]

Intra- vs Intermolecular Methylene Transfer: Competitive Experiments. In an attempt to improve our understanding of the mechanism by which the methylene transfer of iodomethylzinc species occurs, several control experiments were designed to obtain additional information on this step. First, a key issue was to determine whether this transfer was occurring through an inter- or an intramolecular process (or both) in the case of an allylic alcohol. In the first experiment, 1 equiv of (*E*)-$PhCH{=}CHCH_2OZnCH_2I$ and 1 equiv of (*E*)-$PhCH_2CH_2CH{=}CHCH_2OZnCD_2I$ were mixed and 5 mol % of $TiCl_4$ (or 15 mol % of $BF_3{\cdot}OEt_2$) was added to catalyze the cyclopropanation reaction (Scheme 2). Formation of cyclopropanes **B** and **D** in Scheme 2 indicates that complete scrambling of the "CH_2" and "CD_2" units of the corresponding cyclopropanes had

(15) All these reactions were performed under an oxygen-free atmosphere of nitrogen or argon with rigid exclusion of moisture from reagents and glassware under standard conditions.

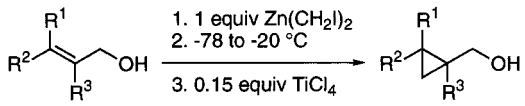
(16) Traces of oxygen appear to increase the yield of the uncatalyzed reaction. For a discussion of the effect of oxygen on the rate of the cyclopropanation reaction see: (a) Miyano, S.; Hashimoto, H. *J. Chem. Soc., Chem. Commun.* **1971**, 1418−1419. (b) Miyano, S.; Yamashita, J.; Hashimoto, H. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 1946. (c) Miyano, S.; Hashimoto, H. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 892−897. (d) Miyano, S.; Matsumoto, Y.; Hashimoto, H. *J. Chem. Soc., Chem. Commun.* **1975**, 364−365. (e) Miyano, S.; Hashimoto, H. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 3665−3668.

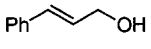
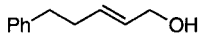
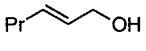
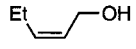
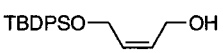
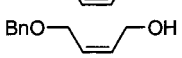
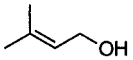
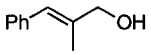
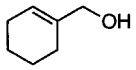
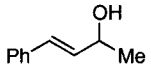
(17) Similar results, within experimental error, were observed when chloromethylzinc alkoxide of cinnamyl alcohol was submitted to the same reaction conditions with use of 5% $TiCl_4$.

(18) For an excellent discussion of the relative strength of Lewis acids see: (a) Farcasiu, D.; Stan, M. *J. Chem. Soc., Perkin Trans 2* **1998**, 1219−1222. (b) Beste, A.; Kramer, O.; Gerhard, A.; Frenking, G. *Eur. J. Inorg. Chem.* **1999**, 2037−2045. (c) Farcasiu, D.; Lukinskas, P.; Ghenciu, A.; Martin, R. *J. Mol. Catal. A−Chem.* **1999**, *137*, 213−221.

(19) Charette, A. B.; Lebel, H. *J. Org. Chem.* **1995**, *60*, 2966−2967 and references therein.

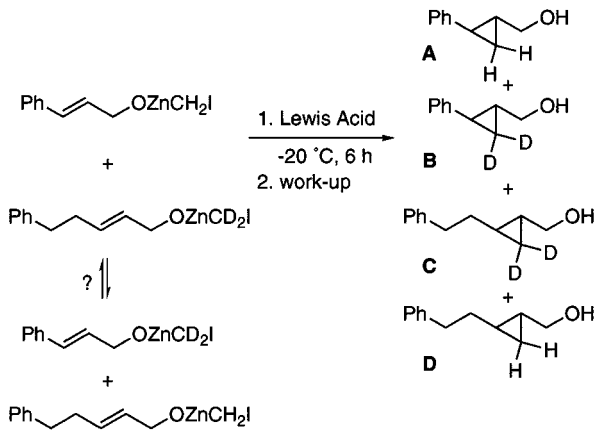
Table 3. $TiCl_4$-Catalyzed Cyclopropanation Reaction[a]



Entry	Allylic Alcohol	Yield (%) [b]
1		90
2		88
3		85
4		94
5		85
6		60
7		90
8		70
9		73
10		60[c, d]

[a] Typical procedure: To a mixture of $Zn(CH_2I)_2$ (prepared from 1 equiv of Et_2Zn and 2 equiv of CH_2I_2) in CH_2Cl_2 at −78 °C was added the allylic alcohol (1 equiv) in CH_2Cl_2. After 15 min of stirring at −20 °C, $TiCl_4$ (0.15 equiv) was added. The mixture was stirred at −20 °C for 2−7 h (see Supporting Information). [b] Isolated yields of cyclopropanes. [c] 0.10 equiv of $TiCl_4$ was used. [d] Ratio 3:1 syn:anti of the corresponding cyclopropylmethanol.

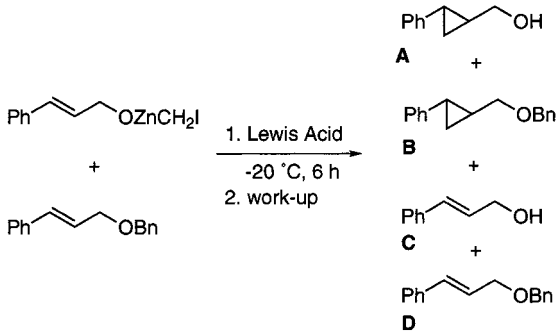
Scheme 2



	Yield (%)			
Lewis Acid	A	B	C	D
$TiCl_4$ (0.05 equiv)	23	15	10	12
BF_3•OEt_2 (0.15 equiv)	26	20	11	13

occurred. This observation indicates that the formation of both products occurs through an intermolecular methylene transfer and/or is the result of a rapid equilibrium between the two different zinc alkoxides. Rapid exchange between zinc alkoxides through an aggregation process is well-known and is likely to occur with the more complex $ROZnCH_2I$. However, this result does not rule out the possibility for an exclusive intramolecular cyclopropanation.

Scheme 3



	Conversion (%)			
Lewis Acid	A	B	C	D
$TiCl_4$ (0.05 equiv)	28	23	21	28
BF_3•OEt_2 (0.10 equiv)	32	12	16	40

The next experiments were designed to determine whether the species obtained by mixing $ROZnCH_2I$ and a Lewis acid could lead to an intermolecular cyclopropanation. In a first set of experiments, (*E*)-PhCH=$CHCH_2OZnCH_2I$ was mixed with its corresponding benzyl ether and a Lewis acid was added (Scheme 3). When $TiCl_4$ was used, cyclopropanation occurred on both the allylic ether (23%) and the allylic alkoxide (28%), indicating that an intermolecular methylene transfer is possible. This was also observed, but to a lesser extent when BF_3•OEt_2 was used as Lewis acid.

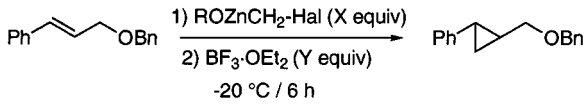
Intermolecular Cyclopropanation Reactions with Iodo- and Chloromethylzinc Alkoxides as Reagents. An interesting concept in this area would be to test whether iodomethylzinc alkoxides can be used as carbenoids to cyclopropanate alkenes in an intermolecular fashion. This hypothesis, if successful, could eventually lead to enantioselective systems since it is quite conceivable that one could start from a chiral alcohol and generate a chiral reagent that could be used to cyclopropanate olefins.[20]

Iodomethylzinc alkoxides prepared as previously described can effectively cyclopropanate an allylic ether in the presence of a Lewis acid (Table 4). Comparisons of the effectiveness of the reaction as a function of the amount of Lewis acid (entry 1 vs 2 and 6 vs 7, Table 4) clearly indicate the importance of a Lewis acid for the activation. Similar conversions were observed when 2 equiv of halomethylzinc alkoxide was used and the amount of Lewis acid was left unchanged (entry 2 vs 3, Table 4). However, when 0.3 equiv of Lewis acid was used higher conversions were obtained (entry 4, Table 4). The results in Table 4 also show that halomethylzinc alkoxides derived from secondary alcohols can effectively cyclopropanate allylic ethers in the presence of a Lewis acid. However, tertiary alcohols such as *tert*-butyl alcohol are not effective since the yield of deprotonation is only about 30%. The lower yield is probably the result of the lower acidity and the steric bulkiness of the alcohol.[7]

Similar results were observed with unfunctionalized olefins; however, higher temperatures (room temperature) were needed since the double bond is not as reactive as that of one containing a proximal basic group such as that of an allylic ether (Table 5). Finally, the intermolecular cyclopropanation of unfunction-

(20) While this work was in progress, Shi has reported a similar approach using Et_2AlCl as the Lewis acid but no details were provided regarding the number of equivalents: Yang, Z.; Lorenz, J. C.; Shi, Y. *Tetrahedron Lett.* **1998**, *39*, 8621−8624.

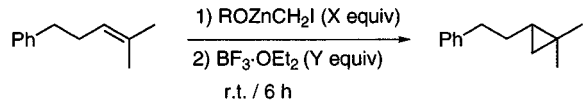
Table 4. Intermolecular Cyclopropanation of an Allylic Ether with Halomethylzinc Alkoxides



entry	$ROZnCH_2$-Hal[a]	(X)	$BF_3{\cdot}OEt_2$ (Y)	Conversion[b]
1	Ph–OZnCH2I	1	----	< 3%
2	Ph–OZnCH2I	1	0.15	73%
3	Ph–OZnCH2I	2	0.15	75%
4	Ph–OZnCH2I	1	0.30	85%
5[c]	Ph–OZnCH2Cl	1	0.15	73%
6	*i*PrOZnCH2I	1	----	< 3%
7	*i*PrOZnCH2I	1	0.15	64%
8[c]	*i*PrOZnCH2Cl	1	0.15	37%

[a] Iodomethylzinc alkoxides were generated from 1 equiv of the alcohol and 1 equiv of $Zn(CH_2I)_2$ at −20 °C. Chloromethylzinc alkoxides were generated from 1 equiv of the alcohol and 1 equiv of $Zn(CH_2Cl)_2$ at −20 °C. [b] Conversions determined by 400 MHz ^{1}H NMR or 100 MNz ^{13}C NMR. [c] 0.15 equiv of $TiCl_4$ was used instead of $BF_3{\cdot}OEt_2$.

Table 5. Intermolecular Cyclopropanation of an Unfunctionalized Olefin with Iodomethylzinc Alkoxides



entry	$ROZnCH_2I$[a]	(X)	$BF_3{\cdot}OEt_2$ (Y)	Conversion[b]
1	Ph–OZnCH2I	1 equiv	----	< 3%
2	Ph–OZnCH2I	1 equiv	0.15	44%
3	*i*PrOZnCH2I	1 equiv	----	< 3%
4	*i*PrOZnCH2I	1 equiv	0.15	49%

[a] Iodomethylzinc alkoxides were generated from 1 equiv of the alcohol and 1 equiv of $Zn(CH_2I)_2$ at −20 °C. [b] Conversions determined by 400 MHz ^{1}H NMR or 100 MHz ^{13}C NMR.

alized double bonds is also possible with our halomethylzinc alkoxides in the presence of a Lewis acid.

This series of experiments clearly indicates that the Lewis acid-catalyzed cyclopropanation of iodomethylzinc alkoxides can occur via either an inter- or intramolecular methylene transfer reaction and both processes seem to be competitive. The intermolecular process appears to be more facile when a nucleophilic counterion is used in these reactions (such as Cl, Br, etc.).

Discussion of the Mechanism of Activation. A possible mechanistic scheme to account for the acceleration is presented in Scheme 1. It is believed that the Lewis acid would complex the iodomethylzinc alkoxide (**A**, Scheme 1) thus increasing its electrophilicity. This species after activation (**B**, Scheme 1) triggers the cyclopropane formation, which follows generation of the halozinc alkoxide (**D**, Scheme 1), and regeneration of the Lewis acid completes the catalytic cycle. A second possible mode of activation has been proposed by Nakamura[6h] in which activation of the Lewis acid occurs by complexation of the iodide group of the iodomethylzinc species (**B′**, Scheme 1).[6h] Finally, a third possibility in the cases where the Lewis acid contains a nucleophilic counterion would be the in situ generation of $XZnCH_2I$, followed by an alkoxy-directed cyclopropanation (**B″**). The spectroscopic monitoring of the reaction between an iodomethylzinc alkoxide and $BF_3{\cdot}OEt_2$ was studied to gain further insight on the possible mode of activation and perhaps to differentiate between **B**, **B′**, and **B″** (Figure 3). The addition of 0.15 equiv of $BF_3{\cdot}OEt_2$ to 1.0 equiv of iodomethylzinc 2-phenylethoxide led to the appearance of several other signals by ^{1}H and ^{13}C NMR which could correspond to the partial formation of an alkoxyboron intermediate and a presumably more reactive $FZnCH_2I$ species. This was also evident by ^{1}H NMR where a second signal next to the $ROZnCH_2I$ singlet at ca. 1.35 ppm ($FZnCH_2I$) appeared along with multiplets at 2.95 and 3.90 ppm (corresponding to an alkoxyboron).[7] Further evidence was provided by ^{11}B NMR, which clearly confirmed the formation of a trialkylborate ($(RO)_3B$) species at 17.9 ppm (**B**, Figure 3), which is consistent with the ^{11}B chemical shift of other trialkylborates such as $B(OMe)_3$.[21] Conversely, the addition of 1 equiv of $BF_3{\cdot}OEt_2$ to 1 equiv of iodomethylzinc 2-phenylethoxide led to the formation of a predominant $ROBF_2$ species (0.05 ppm by ^{11}B NMR) and two minor boron species at 17.9 and 15.9 ppm which are consistent with $(RO)_3B$ and $(RO)_2BF$ (**C**, Figure 3).[21] These observations indicate that the last hypothesis involving complexation of the Lewis acid that

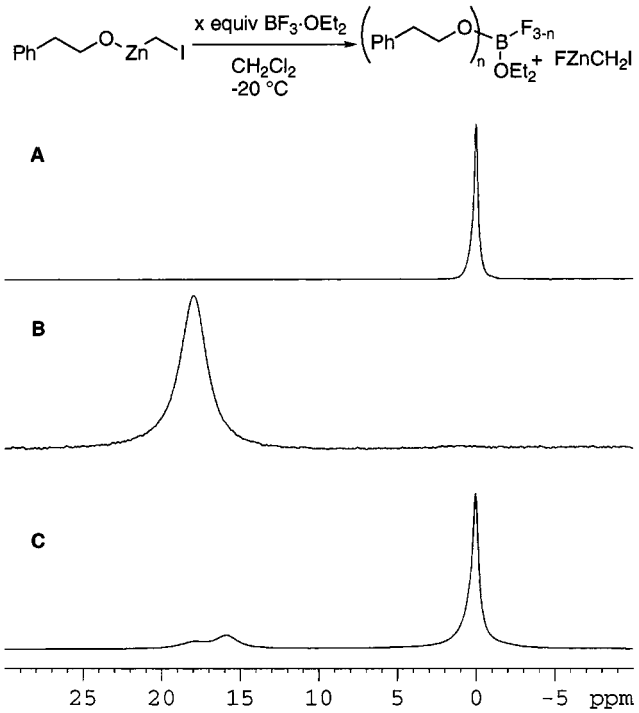


Figure 3. ^{11}B NMR (96 MHz) of iodomethylzinc alkoxide in the presence of $BF_3{\cdot}OEt_2$ (*x* equiv): (A) $BF_3{\cdot}OEt_2$ without iodomethylzinc alkoxide; (B) iodomethylzinc alkoxide + 0.15 equiv of $BF_3{\cdot}OEt_2$; and (C) iodomethylzinc alkoxide + 1 equiv of $BF_3{\cdot}OEt_2$.

(21) ^{11}B NMR: $B(OMe)_3$ (18.3 ppm); $(MeO)_2BF$ (15.6 ppm); $MeOBF_2$ (0.7 ppm). See: Wrackmeyer, B. Nuclear Magnetic Resonance Spectroscopy of Boron Compounds Containing Two-, Three- and Four-Coordinate Boron. In *Annual Reports on NMR Spectroscopy*; Webb, G. A., Ed.; Academic Press Inc.: San Diego, CA., 1988; Vol. 20, pp 61−204.

induced the liberation of a reactive zinc reagent ($XZnCH_2I$) appears to be the most plausible one when a Lewis acid containing a nucleophilic counterion is used in the activation process (**B″**, Scheme 1).

Conclusion. In conclusion, we have reported our findings on the Lewis acid-catalyzed cyclopropanation of halomethylzinc alkoxides, generated from an alcohol and bis(halomethyl)zinc. The species have been shown to be stable for a long period of time and monomeric in solution; however, they have been isolated as tetrameric crystals. These species can be used as inter- or intramolecular cyclopropanating reagents. A variety of achiral Lewis acids are shown to be effective in this process. This methodology competes favorably with the common method, which usually requires a minimum of 2 equiv of $Zn(CH_2I)_2$ to obtain high yields of the cyclopropanes. Moreover, we have shown that halomethylzinc alkoxides derived from primary and secondary alkoxides in the presence of a Lewis acid can intermolecularly cyclopropanate an allylic ether. These findings provide the groundwork for further developments in this area. The conclusions have already been extended to the elaboration of an asymmetric version of this reaction which is presented in the following paper.

Experimental Section[7]

General Procedure for the Lewis Acid-Catalyzed Cyclopropanation of Allylic Alcohols: *trans*-(3-Phenylcyclopropyl)methanol (entry 1, Table 3). To a stirred solution of CH_2I_2 (160 mL, 2 mmol) in anhydrous CH_2Cl_2 (8 mL) at 0 °C was added dropwise diethylzinc (100 μL, 1 mmol). The resulting solution was stirred at that temperature for 15 min and a white precipitate was formed. The solution was cooled at −78 °C and a solution of cinnamyl alcohol (140 mg, 1.05 mmol) in anhydrous CH_2Cl_2 (5 mL) was added. The resulting heterogeneous solution was stirred at −20 °C for 15 min and $TiCl_4$ (16 mL, 0.15 mmol) was then added. After 3 h of stirring at −20 °C, the resulting solution was cooled at −40 °C and poured into an aqueous solution of saturated NH_4Cl. The layer was washed with EtOAc (3×). The combined organic layers were washed with saturated aqueous NH_4Cl and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was osmylated[22] (OsO_4 (catalyst), NMO (2 equiv), acetone/water (4:1)) and purified by flash chromatography on silica gel (20% EtOAc/Hexanes) to produce (133 mg, 90%) the desired cyclopropylmethanol: R_f 0.22 (20% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30−7.25 (m, 2H), 7.20−7.15 (m, 1H), 7.10−7.07 (m, 2H), 3.67−3.59 (m, 2H), 1.86−1.82 (m, 1H), 1.75 (s (br), 1H), 1.51−1.43 (m, 1H), 1.01−0.92 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.2, 128.5, 125.3, 124.6, 66.0, 24.2, 21.4, 13.5; HRMS calcd for $C_{10}H_{12}O_1$ (M) 148.0888, found 148.0880.

***trans*-2-(2-Phenylethyl)cyclopropylmethanol (entry 2, Table 3).** The cyclopropanation of (*E*)-5-phenyl-2-pentenol (191 mg, 1.17 mmol) was performed according to the previously described procedure (reaction time 7 h). The residue was purified by flash chromatography on silica gel (25% EtOAc/Hexanes) to produce the desired cyclopropylmethanol (174 mg, 88%): R_f 0.28 (20% EtOAc/Hexanes) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31−7.17 (m, 5H), 3.47−30.32 (m, 2H), 2.77−2.64 (m, 2H), 1.70−1.48 (m, 2H), 1.16 (s (br), 1H), 0.88−0.80 (m, 1H), 0.67−0.59 (m, 1H), 0.41−0.32 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.1, 128.4, 128.2, 125.7, 66.9, 35.8, 35.3, 21.3, 16.8, 9.7; HRMS calcd for $C_{12}H_{15}$ (M − OH) 159.1174, found 159.1169.

***trans*-2-(Propyl)cyclopropylmethanol (entry 3, Table 3).** The cyclopropanation of (*E*)-2-hexenol (120 mg, 1.20 mmol) was performed according to the previously described procedure (reaction time 7 h). The residue was purified by flash chromatography on silica gel (25% EtOAc/Hexanes) to produce the desired cyclopropylmethanol (111 mg, 85%): R_f 0.18 (20% EtOAc/Hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.50−3.39 (m, 2H), 1.44−1.35 (m, 2H), 1.30−1.20 (m, 3H), 0.92 (t, J = 7 Hz, 3H), 0.90−0.80 (m, 1H), 0.68−0.58 (m, 1H), 0.40−0.29 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 66.9, 35.8, 22.5, 19.9, 16.7, 13.8, 9.6.

***cis*-2-(Ethyl)cyclopropylmethanol (entry 4, Table 3).** The cyclopropanation of (*Z*)-2-pentenol (95 mg, 1.10 mmol) was performed according to the previously described procedure (reaction time 2.5 h). The residue was purified by flash chromatography on silica gel (25% EtOAc/Hexanes) to produce the desired cyclopropylmethanol (99 mg, 94%): R_f 0.18 (20% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.67 (dd, J = 11, 7 Hz, 1H), 3.59 (dd, J = 11, 7 Hz, 1H), 1.50−1.24 (m, 3H), 1.15−1.07 (m, 1H), 1.02 (t, J = 7 Hz, 3H), 0.90−0.80 (m, 1H), 0.71 (td, J = 8, 5 Hz, 1H), −0.03 (dd, J = 10, 5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 62.8, 21.6, 18.0, 17.8, 14.2, 9.03.

***cis*-2-(*tert*-Butyldiphenylsilyloxymethyl)cyclopropylmethanol (entry 5, Table 3).** The cyclopropanation of (*Z*)-4-*tert*-butyldiphenylsilyloxy-2-butenol (402.6 mg, 1.23 mmol) was performed according to the previously described procedure (reaction time 6 h). The residue was purified by flash chromatography on silica gel (25% EtOAc/Hexanes) to produce the desired cyclopropylmethanol (340 mg, 85%): R_f 0.45 (20% EtOAc/Hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77−7.64 (m, 4H), 7.49−7.35 (m, 6H), 4.10 (dd, J = 12, 5 Hz, 1H), 4.00 (dd, J = 12, 5 Hz, 1H), 3.35 (t, J = 12 Hz, 2H), 1.51−1.37 (m, 1H), 1.32−1.17 (m, 2H), 1.06 (s, 9H), 0.76−0.65 (m, 1H), 0.13 (dd, J = 11, 5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.5, 132.9, 129.8, 127.7, 64.9, 63.2, 26.7, 19.0, 18.3, 17.1, 8.21.

***cis*-2-(Benzyloxymethyl)cyclopropylmethanol (entry 6, Table 3).** The cyclopropanation of (*Z*)-4-benzyloxy-2-butenol (139.5 mg, 0.78 mmol) was performed according to the previously described procedure (reaction time 7 h). The residue was purified by flash chromatography on silica gel (25% EtOAc/Hexanes) to produce the desired cyclopropylmethanol (88.8 mg, 60%): R_f 0.30 (40% EtOAc/Hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39−7.26 (m, 5H), 4.60 (d, J = 12 Hz, 1H), 4.53 (d, J = 12 Hz, 1H), 3.99−3.91 (m, 2H), 3.20 (t, J = 10 Hz, 1H), 3.16 (t, J = 10 Hz, 1H), 2.75 (s(br), 1H), 1.44−1.24 (m, 2H), 0.82 (td, J = 8, 5 Hz, 1H), 0.22 (dd, J = 10, 5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.4, 128.4, 127.84, 127.81, 73.0, 70.7, 62.9, 18.3, 14.6, 8.55; HRMS calcd for $C_{12}H_{17}O_2$ (M + H) 193.12285, found 193.12200.

2,2-Dimethylcyclopropylmethanol (entry 7, Table 3). The cyclopropanation of 3-methyl-2-butenol (98.3 mg, 1.14 mmol) was performed according to the previously described procedure (reaction time 2 h). The residue was purified by flash chromatography on silica gel (25% EtOAc/Hexanes) to produce the desired cyclopropylmethanol (98 mg, 90%): R_f 0.20 (20% EtOAc/Hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.70 (dd, J = 11, 7 Hz, 1H), 3.53 (dd, J = 11, 8 Hz, 1H), 1.12 (s, 3H), 1.08 (s, 3H), 0.96−0.87 (m, 1H), 0.49 (dd, J = 8, 4 Hz, 1H), 0.12 (t, J = 8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 63.8, 27.1, 26.5, 19.6, 18.1, 15.9.

1-Methyl-2-phenylcyclopropylmethanol (entry 8, Table 3). The cyclopropanation of (*E*)-2-methyl-3-phenyl-2-propenol (115.4 mg, 0.78 mmol) was performed according to the previously described procedure (reaction time 7 h). The residue was purified by flash chromatography on silica gel (30% EtOAc/Hexanes) to produce the desired cyclopropylmethanol (88 mg, 70%): R_f 0.14 (20% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31−7.26 (m, 2H), 7.22−7.17 (m, 3H), 3.57 (d, J = 11 Hz, 1H), 3.53 (d, J = 11 Hz, 1H), 2.06 (dd, J = 9, 6 Hz, 1H), 1.57 (s (br), 1H), 0.94 (dd, J = 9, 5 Hz, 1H), 0.89 (s, 3H), 0.87 (t, J = 5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7, 129.0, 127.9, 125.8, 71.6, 26.6, 25.0, 15.6, 15.0; HRMS calcd for $C_{11}H_{14}O_1$ (M) 162.1045, found 162.1047.

1-Hydroxymethylbicyclo[4.1.0]heptane (entry 9, Table 3). The cyclopropanation of 1-cyclohexenemethanol[23] (87.6 mg, 0.78 mmol) was performed according to the previously described procedure (reaction time 7 h). The residue was purified by flash chromatography on silica gel (25% EtOAc/Hexanes) to produce the desired cyclopropylmethanol (72.1 mg, 73%): R_f 0.30 (30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.36 (d, J = 11 Hz, 1H), 3.31 (d, J = 11 Hz, 1H), 1.90−1.83 (m, 2H), 1.76−1.69 (m, 1H), 1.64−1.57 (m, 1H), 1.35−1.16 (m, 5H), 0.85−0.79 (m, 1H), 0.47 (dd, J = 9, 5 Hz, 1H), 0.26 (t, J = 5

(22) When a quantitative conversion to the cyclopropane was not achieved, the crude product was treated with osmium tetroxide, O_3, or $KMnO_4$ to destroy any residual alkene and to facilitate the purification.

(23) Charette, A. B.; Marcoux, J.-F. *Tetrahedron Lett.* **1993**, *34*, 7157−7160.

Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 72.4, 26.2, 23.5, 21.7, 21.5, 21.2, 15.5, 14.8; HRMS calcd for $C_8H_{14}O_1$ (M) 126.1045, found 126.1066.

***trans*-1-(2-Phenylcyclopropyl)ethan-1-ol (entry 10, Table 3).** The cyclopropanation of (*E*)-4-phenylbut-3-en-2-ol (155 mg, 1.05 mmol) was performed according to the previously described procedure (reaction time 5 h). The residue was purified by flash chromatography on silica gel (25% EtOAc/Hexanes) to produce the desired cyclopropylmethanols (syn + anti) (97 mg, 60%). *Anti-diastereomer*: R_f 0.55 (25% EtOAc/Hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30−7.08 (m, 5H), 3.40 (qn, J = 6 Hz, 1H), 1.95−1.89 (m, 1H), 1.68 (s, 1H), 1.34 (d, J = 6 Hz, 3H), 1.34−1.25 (m, 1H), 0.98−0.90 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.6, 128.2, 125.7, 125.5, 71.7, 30.7, 22.3, 21.2, 13.2. *Syn-diastereomer*: R_f 0.32 (25% EtOAc/Hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30−7.06 (m, 5H), 3.39 (dq, J = 8, 6 Hz, 1H), 1.85−1.79 (m, 1H), 1.67 (s, 1H), 1.36 (d, J = 6 Hz, 3H), 1.33−1.24 (m, 1H), 1.05−0.93 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.6, 128.4, 126.0, 125.6, 71.3, 30.7, 22.8, 20.7, 13.9; HRMS calcd for $C_{11}H_{14}O_1$ (M) 162.10446, found 162.10464. Anal. Calcd for $C_{11}H_{14}O$ (162.23): C, 81.44; H, 8.70. Found: C, 81.10; H, 9.34.

General Procedure for the Intermolecular Cyclopropanation: Cyclopropanation of 1-Benzyloxy-3-phenylprop-2-ene with Halomethylzinc Alkoxide in the Presence of a Lewis Acid (Table 4). To a solution of CH_2I_2 (125 μL, 1.55 mmol) in dichloromethane (5 mL) at −20 °C was added diethylzinc (80 μL, 0.78 mmol) with stirring for 20 min (a milky white solution was formed). Phenylethyl alcohol (93 μL, 0.78 mmol) was then added and stirred for an additional 30 min after which time a solution of $BF_3{\cdot}OEt_2$ (0.38 M in dichloromethane, 0.31 mL, 0.118 mmol) was added. Finally, after 5 min a solution of 1-benzyloxy-3-phenylprop-2-ene (175.6 mg, 0.78 mmol) in dichloromethane (1.5 mL) was added and the reaction mixture was stirred at −20 °C. After 6 h the reaction mixture was quenched by adding an aqueous solution of saturated $NaHCO_3$. The organic layer is extracted and washed with saturated aqueous Na_2SO_3 and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The conversions were measured by quantitative 400 MHz ^{1}H NMR or 75 MHz ^{13}C NMR. **1-Benzyloxymethyl-2-phenylcyclopropane:** R_f 0.40 (100% toluene); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44−7.13 (m, 10H), 4.63 (s, 2H), 3.61 (dd, J = 10.3, 6.4 Hz, 1H), 3.51 (dd, J = 10.3, 6.8 Hz, 1H), 1.90−1.85 (m, 1H), 1.58−1.49 (m, 1H), 1.09−0.98 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.6, 138.4, 128.3, 128.2, 127.6, 127.5, 125.8, 125.5, 73.4, 72.4, 22.6, 21.4, 14.1; HRMS calcd for $C_{17}H_{18}O$ (M) 238.1357, found 238.1350. Anal. Calcd for $C_{17}H_{18}O$ (238.33): C, 85.67; H, 7.61. Found: C, 85.30; H, 7.82.

Cyclopropanation of 2-Methyl-5-phenylpent-2-ene with Halomethylzinc Alkoxide in the Presence of a Lewis Acid (Table 5). The cyclopropanation of 2-methyl-5-phenylpent-2-ene (125.0 mg, 0.78 mmol) was performed according to the previously described procedure with CH_2I_2 (125 μL, 1.55 mmol), diethylzinc (80 μL, 0.78 mmol), phenylethyl alcohol (93 μL, 0.778 mmol), and $BF_3{\cdot}OEt_2$ (0.38 M in dichloromethane, 0.31 mL, 0.118 mmol) in dichloromethane (6.5 mL) (reaction time 6 h at room temperature). **2-(2,2-Dimethylcyclopropyl)-1-phenylethane:** R_f 0.36 (100% Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30−7.26 (m, 2H), 7.20−7.15 (m, 3H), 2.74−2.62 (m, 2H), 1.68−1.54 (m, 2H), 1.02 (s, 3H), 1.00 (s, 3H), 0.55−0.47 (m, 1H), 0.38 (dd, J = 8.5 Hz, 4.1 Hz, 1H), −0.10 (t, J = 4.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.7, 128.4, 128.1, 125.4, 36.5, 31.9, 27.4, 24.3, 19.7, 19.5, 15.4; HRMS calcd for $C_{13}H_{18}$ (M) 174.1408, found 174.1409.

Acknowledgment. This work was supported by grants from the National Science and Engineering Research Council (NSERC) of Canada, E. W. R. Steacie Fund, Merck Frosst, Boehringer Ingelheim, and F.C.A.R. (Québec). C.M. and C.B. would both like to thank Boehringer Ingelheim and F.C.A.R. for postgraduate fellowships. The authors also thank Ms. Francine Bélanger-Gariépy for the elucidation of the solid-state structures.

Supporting Information Available: Experimental procedures and characterization data for all the tabulated examples and experimental procedures for the synthesis of starting materials, description of the various complexes including atomic coordinates, anisotropic thermal parameters, and fixed atom coordinates, and a listing of atomic coordinates, distances, and angles (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA010837+