Chlorotrimethylsilane as an Activating Reagent in the Samarium-Promoted Cyclopropanation of Allylic and α-Allenic Alcohols

Mark Lautens* and Yi Ren

Department of Chemistry, University of Toronto, Toronto, Ontario M5S 1A1, Canada

Received July 26, 1995

Hydroxyl-directed transformations are a well-established strategy for controlling cyclic and acyclic stereochemistry in organic chemistry.[1] Directed cyclopropanations have been known for many years, and both cyclic and acyclic allylic alcohols undergo diastereoselective cyclopropanation in the presence of zinc carbenoids.[2,3] Samarium carbenoids react with olefins to give cyclopropanes at −60 °C which suggests they are significantly more reactive than those based on zinc.[4] The absolute requirement of a hydroxy group can be exploited in achieving chemoselective and stereoselective cyclopropanation. We recently illustrated the advantages of this requirement in the selective cyclopropanation of allenic alcohols which react selectively at the proximal position to provide methylenecyclopropanes.[5]

There are several problems which need to be solved in order to increase the utility of samarium carbene reagents. For example, 1 equiv of $HgCl_2$ is typically added in order to "activate" the Sm. In the absence of this additive, the reaction is sluggish and often fails to initiate. The toxicity of $HgCl_2$ suggests that an alternative method to activate Sm would be very useful. Furthermore, samarium carbenes are often used in moderate to large excess, and the source of Sm is also known to be a crucial factor in successful formation of an active reagent. In this report, we demonstrate that the replacement of $HgCl_2$ by TMSCl addresses both of these shortcomings and in addition influences the diastereoselectivity.

Zinc is known to be activated by TMSCl in a variety of reactions including the Simmons−Smith cyclopropanation.[6,7] Its role appears to be to clean the oxide layer on the surface of the zinc and also react with trace impurities (particularly lead) which are present due to the method of preparing the zinc. Very recently, Fürstner found that chlorosilanes activate titanium(III) chloride and even commercial titanium powder in McMurry-type carbonyl coupling reactions.[8]

Results and Discussion

The cyclopropanation of allylic and α-allenic alcohols has been investigated using the Sm/CH_2I_2/TMSCl system. As is demonstrated in Table 1, TMSCl is a good substitute for $HgCl_2$ for virtually every α-allenic alcohol examined in the cyclopropanation reaction. However, we were intrigued by the observation that the diastereoselectivity changed in the presence of TMSCl. In all the substrates tested thus far, the presence of TMSCl led to an increase in the amount of diastereomer **2**. In some cases the change was dramatic while in others a modest effect was observed. When R is a primary alkyl chain like *n*-heptyl, the $HgCl_2$ system slightly favors the formation of diastereomer **3** (Table 1, entries 2 and 11). With the TMSCl system, however, the selectivity either inverted (Table 1, entry 11) or was approximately 1:1 (Table 1, entries 2 and 3). In substrates where $HgCl_2$ slightly favored the formation of diastereomer **2**, TMSCl increased the selectivity to the extent that the selectivity was synthetically useful (Table 1, entry 12). For substrates where $HgCl_2$ showed moderate to good selectivity, TMSCl doubled (Table 1, entry 5) or even tripled (Table 1, entry 10) the diastereoselectivity. In all cases, complete chemoselectivity toward the allylic olefin was retained.

The reactivity of the TMSCl-modified reagent system depends on the substitution pattern of the substrate. When R′ is H, the yield of the reaction is normally equivalent to or up to 10% higher than the corresponding $HgCl_2$ reaction series (see Table 1, entries 2, 5, and 12). However, it appears that reactions using TMSCl are more sensitive to the substituent R′. When R′ is a methyl group, the yields dropped 10−15% compared to reactions using $HgCl_2$ (Table 1, entries 10 and 11), although the selectivity was improved.

A catalytic amount of TMSCl was found to give the best results, and cyclopropanation has been performed on up to a 5-g scale in good yield (Table 1, entry 3) under the optimized conditions. Doubling the amount of TMSCl or the use of a large excess did not improve the diastereoselectivity or the yield (Table 1, entries 1, 2, 5, and 6). Unfortunately, 7−10 equiv of Sm and CH_2I_2 are still necessary to achieve satisfactory yields, and further work to overcome this problem is warranted.

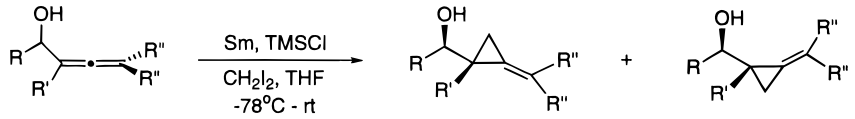
It is known that $ClCH_2I$ often improves yields in the cyclopropanation of both allylic[4] and α-allenic alcohols,[5] presumably due to a longer lifetime of the carbenoid. Thus, a combination of TMSCl and $ClCH_2I$ was examined in the presence of TMSCl with the expectation that a better yield and excellent selectivity could be achieved for hindered substrates. However, the selectivity was reduced and the temperature at which the reaction initiated was higher (Table 1, entry 7)!

Cyclopropanation of some simple allylic alcohols was also briefly studied in the presence of TMSCl to determine the generality of the reaction. Substrates were chosen in order to allow a comparison with previous data obtained using $HgCl_2$.[4,9] Once again, TMSCl was a good substituent for $HgCl_2$ as an activating agent for Sm, Table 2.

(1) (a) Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307. (b) Hoffmann, R. W. *Chem. Rev.* **1989**, *89*, 1841.
(2) (a) Simmons, H. E.; Smith, R. D. *J. Am. Chem. Soc.* **1958**, *80*, 5323. (b) Simmons, H. E.; Smith, R. D. *J. Am. Chem. Soc.* **1959**, *81*, 4256. (c) Simmons, H. E. *Org. React.* **1973**, *20*, 1. For the Furukawa modification of the Simmons−Smith reaction, see: (d) Furukawa, J.; Kawabata, N.; Nishimura, J. *Tetrahedron Lett.* **1966**, *28*, 3353. (e) Furukawa, J.; Kawabata, N.; Nishimura, J. *Tetrahedron* **1968**, *24*, 53. (f) Denmark, S. E.; Edwards, J. P.; Wilson, S. R. *J. Am. Chem. Soc.* **1991**, *113*, 723. (g) Denmark, S. E.; Edwards, J. P.; Wilson, S. R. *J. Am. Chem. Soc.* **1992**, *114*, 2592.
(3) (a) Winstein, S.; Sonnenberg, J.; DeVries, L. *J. Am. Chem. Soc.* **1959**, *81*, 6523. (b) Winstein, S.; Sonnenberg, J. *J. Am. Chem. Soc.* **1961**, *83*, 3235.
(4) (a) Molander, G. A.; Etter, J. B. *J. Org. Chem.* **1987**, *52*, 3942. (b) Molander, G. A.; Harring, L. S. *J. Org. Chem.* **1989**, *54*, 3525.
(5) (a) Lautens, M.; Delanghe, P. H. M. *J. Org. Chem.* **1993**, *58*, 5037. (b) Lautens, M.; Delanghe, P. H. M. *J. Am. Chem. Soc.* **1994**, *116*, 8526.
(6) (a) Picotin, G. and Miginiac, P. *J. Org. Chem.* **1987**, *52*, 4796. (b) Picotin, G. and Miginiac, Ph. *Tetrahedron Lett.* **1987**, *28*, 4551. (c) Gawronski, J. K. *Tetrahedron Lett.* **1984**, *25*, 2605. (d) Erdik, E. *Tetrahedron* **1987**, *43*, 2203. (e) Knochel, P.; Chang, M.; Yeh, P.; Berk, S. C.; Talbert, J. *J. Org. Chem.* **1988**, *53*, 2392.
(7) Takai, K.; Kakiuchi, T.; Utimoto, K. *J. Org. Chem.* **1994**, *59*, 2671.
(8) Fürstner, A.; Hupperts, A. *J. Am. Chem. Soc.* **1995**, *117*, 4468.
(9) Lautens, M.; Delanghe, P. H. M. *J. Org. Chem.* **1992**, *57*, 798.

0022-3263/96/1961-2210$12.00/0

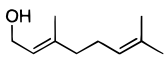
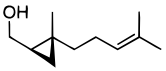
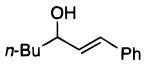
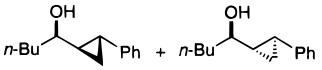
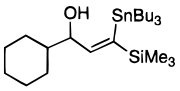
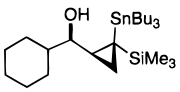
Table 1. Cyclopropanation of α-Allenic Alcohols Using the Sm/CH_2I_2/TMSCl System



entry		substrate[a]	Sm[b]	CH_2I_2	TMSCl	2/3[c] TMSCl	2/3[c] $HgCl_2$[e]	yield[d] (%) TMSCl	yield[d] (%) $HgCl_2$[e]
1	**1a**	R = C_7H_{15}, R′ =H, R″ = H	10	10	8.8	1:2.2	1:2.1	81	73
2	**1a**	R = C_7H_{15}, R′ =H, R″ = H	10	10	0.22	1.1:1	1:2.1	**82**	73
3[f]	**1a**	R = C_7H_{15}, R′ =H, R″ = H	8	8	0.4	1:1.6		67	
4[g]	**1a**	R = C_7H_{15}, R′ =H, R″ = H	10	10	1.29	2.5:1		62	
5	**1b**	R = C_6H_{11}, R′ =H, R″ = H	10	10	0.2	**17:1**	9.5:1	65	64
6	**1b**	R = C_6H_{11}, R′ =H, R″ = H	10	10	0.4	14.5:1	9.5:1	65	64
7[h]	**1b**	R = C_6H_{11}, R′ =H, R″ = H	10	10	0.2	7:1	9.5:1	80	82
8[g]	**1b**	R = C_6H_{11}, R′ =H, R″ = H	12	12	0.3	30:1		44	
9[i]	**1b**	R = C_6H_{11}, R′ =H, R″ = H	10	10	0.2	11:1	9.8:1	50	37
10	**1c**	R = C_6H_{11}, R′ = CH_3, R″ = H	10	10	0.28	**25:1**	7.9:1	52	66
11	**1d**	R = C_7H_{15}, R′ = CH_3, R″ = H	10	10	0.24	1.2:1	1:2.1	40	52
12	**1e**	R = C_6H_{11}, R′ = H, R″ = *n*-Pr	10	10	0.3	**4.4:1**	1.7:1	52	43

[a] C_7H_{15} and C_6H_{11} stand for n-heptyl and cyclohexyl, respectively. [b] Unless stated otherwise samarium from Rhône-Poulenc was used. [c] Ratios are measured by GC. [d] Yields refer to isolated yield of pure product. [e] Data are from ref 5 except for entry 9. [f] Five g scale reaction. [g] TMSCl as activating reagent, but TMSCl was then removed by decanting TMSCl containing THF solution under N_2 followed by washing samarium metal three times with fresh THF before adding the allenic alcohol and CH_2I_2. [h] Using $ClCH_2I$ instead of CH_2I_2. [i] Samarium from Aldrich was used.

Table 2. Cyclopropanation of Allylic Alcohols Using the Sm/CH_2I_2/TMSCl System

Entry	Substrate	Sm[a]	CH_2I_2	TMSCl	Product	*syn*:*anti*[b] TMSCl	*syn*:*anti*[b] $HgCl_2$[d]	Yield (%)[c] TMSCl	Yield (%)[c] $HgCl_2$[d]
1	 **4**	5	5	0.2	 **5**	*syn*		97(74.5)[e]	89
2	 **6**	5	5	0.2	 **7**	*syn*		87	92
3	 **8**	5	5	0.2	 **9a** **9b**	1.9:1	1:1.4	90	99
4	 **10**	10	10	0.2	 **11**	>50:1	>50:1	81	80

[a] Unless stated otherwise samarium from Rhône-Poulenc was used. [b] Ratios are measured by GC except for entry 4 which was determined by ^1H NMR. [c] Yields refer to isolated yield of pure product(s). [d] Data are from ref 4 except for entry 4 which is from ref 9. [e] Samarium from Aldrich was used.

Geraniol underwent smooth cyclopropanation using the TMSCl system to give a single product in excellent yield with no byproduct resulting from cyclopropanation of the isolated olefin detected by GC analysis of the crude reaction mixture (Table 2, entry 1). Cyclohexenol and bimetallic olefins also gave an excellent yield of cyclopropanes (Table 2, entries 2 and 4). An (*E*)-allylic alcohol showed a modest improvement in selectivity (Table 2, entry 3) in accord with the observations with allenic alcohols, although the stereoselectivity was inferior to that recently reported by Charette using Zn-based reagents.[10]

We and others have found that the source of the Sm has a dramatic effect on the efficiency of the cyclopropanation. We have investigated two different sources of Sm and found that TMSCl improves the yields in both cases (entry 9 *vs.* 5, Table 1, and entry 1, Table 2). The data sheets provided by Aldrich and Rhône-Poulenc

(10) (a) Charette, A. B.; Lebel, H. *J. Org. Chem.* **1995**, *60*, 2966. (b) For a recent example of the effect of Lewis acids on cyclopropanations, see: Charette, A. B.; Brochu, C. *J. Am. Chem. Soc.* **1995**, *117*, 11367.

(11) (a) Girard, P.; Namy, J. L.; Kagan, H. B. *J. Am. Chem. Soc.* **1980**, *102*, 2693. (b) Soderquist, J. A. *Aldrichim. Acta*, **1991**, *24*, 15.

indicate that Sm from Rhône-Poulenc has fewer impurities than that available from Aldrich. Yttrium, lanthanum, sodium, calcium, iron, and magnesium are present in significantly higher amounts in the Aldrich sample, and we cannot be certain if this is a factor in reducing the reactivity or if the oxide layer is simply thicker. While the yields are 15−30% lower when the Sm from Aldrich was used, TMSCl did lead to a significant improvement compared to $HgCl_2$ (Table 1, entry 9) or no activating agent.

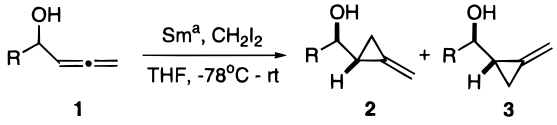
The nature of the activating effect of TMSCl was briefly studied. TMSCl is known to remove the zinc oxide layer and activate the reaction of Zn with CH_2I_2 in Simmons−Smith cyclopropanation.[7] In a similar fashion, the titanium oxide layer could also be removed by TMSCl treatment.[8] ^{29}Si NMR of the supernatant of the reaction mixture of Sm and TMSCl in THF showed two new signals at 11.7 and 7.8 ppm in addition to a major signal at 31.5 ppm (TMSCl). The 7.8 ppm signal was assigned to TMSOTMS which was confirmed by preparation of a authentic sample formed by mixing TMSCl with water in THF. The peak at 11.7 ppm may be a TMS−O−X-containing structure (due to the ring opening of THF in the presence of Sm?), but we have been unable to conclusively establish its structure. A control experiment with Zn in THF in the presence of TMSCl showed signals at 7.8 and 31.5 ppm. Also, when Sm and TMSCl were mixed in $CDCl_3$ instead of THF, peaks at 7.8 and 31.5 ppm appeared. We conclude that in analogy to the results using Zn, TMSCl activates the Sm by reaction with the surface layer of samarium oxide.

If the role of TMSCl was simply to activate the metal toward reaction with CH_2I_2, then Sm pretreated with TMSCl should initiate the cyclopropanation even if the TMSCl was removed prior to addition of the substrate. A portion of Sm was treated with TMSCl in THF for 30 min under a N_2 atmosphere. The supernatant was removed by cannula under a N_2 atmosphere, and the metal was washed three times with fresh THF. A ^{29}Si NMR spectrum of the final wash solution was free of any silicon signals. When an α-allenic alcohol and CH_2I_2 were added to the Sm and fresh THF at −78 °C, the cyclopropanation occurred readily. The yield was lower but increased selectivity favoring **2** was observed (Table 1, entries 4 and 8).

The effect on the diastereoselectivity associated with addition of TMSCl suggests that TMSCl also participates in the reactive complex. The Houk model was used by Molander[4] to explain the observed diastereoselectivity of the cyclopropanation of allylic alcohols, and our results with 1,1-bimetallic allylic alcohols and allenic alcohols provide further support for this model.[5,9] The addition of TMSCl results in an increase in the product predicted from the Houk model which suggests that coordination of a silicon species to the oxygen and/or Sm leads to an increase in the steric bulk of the metal carbenoid.

Other silyl chlorides were also examined to determine their effect on the diastereomeric ratio, Table 3. When TBDMSCl was used instead of TMSCl, a significant improvement in selectivity was observed for R equals cyclohexyl (Table 3, entry 9), and the opposite diastereomer was favored when R equals *n*-heptyl (Table 3, entry 3 *vs.* 4). These results are expected if the silyl group is involved in the reactive complex. $(CH_3O)_3SiCl$ was a less effective activating agent (Table 3, entry 5). Association of the silyl chloride with the oxygen also suggests that Lewis acids may influence the diastereoselectivity. Ti-

Table 3. Effects of Different Activating Reagents on the Cyclopropanation



1 **2** **3**

entry		substrate[b]	methods	**2:3**[c]	yield[d] (%)
1	**1a**	R = C_7H_{15}	no activating reagent	2.1:1	34
2	**1a**	R = C_7H_{15}	$HgCl_2$[e]	1:2.1	73
3	**1a**	R = C_7H_{15}	TMSCl[f]	1:1.1	82
4	**1a**	R = C_7H_{15}	**TBDMSCl**[g]	**1.7:1**	**78**
5	**1a**	R = C_7H_{15}	$(CH_3O)_3SiCl$[g]	1:1.1	66
6	**1a**	R = C_7H_{15}	**Ti(O-*i*-Pr)$_4$**[g]	**1.5:1**	**79**
7	**1b**	R = C_6H_{11}	$HgCl_2$[e]	9.5:1	64
8	**1b**	R = C_6H_{11}	TMSCl[f]	17:1	65
9	**1b**	R = C_6H_{11}	**TBDMSCl**[g]	**44:1**	**60**
10	**1b**	R = C_6H_{11}	**Ti(O-*i*-Pr)$_4$**[g]	**>50:1**	**59**

[a] Samarium from Rhone-Poulenc was used. [b] C_7H_{15} and C_6H_{11} stand for n-heptyl and cyclohexyl, respectively. [c] Ratios are measured by GC and 400 MHz NMR. [d] Yields refer to isolated yield of pure product. [e] Data is from ref 5. [f] Reaction was carried out with 10 equiv of Sm, 10 equiv of CH_2I_2, 0.2 equiv of TMSCl in THF at −78 °C to rt. [g] Reaction was carried out with the same procedure described above except using the activating reagent indicated.

(O-*i*-Pr)$_4$ was less successful at activating the metal but gave the highest selectivity toward **2b** observed in this study (>50:1, Table 1, entry 10).

Finally, we note that addition of TMSCl to Sm in the presence of CH_2I_2 is an effective procedure for the preparation of SmI_2.[11] In a typical procedure Sm was treated with 2 mol % of TMSCl in THF at room temperature for 30 min prior to addition of CH_2I_2 at −78 °C. The typical blue color of SmI_2 formed as the reaction was warmed to −50 °C.

Conclusions

We have found that a catalytic amount of TMSCl can substitute for toxic $HgCl_2$ as an excellent activating agent in Sm-promoted cyclopropanation of both allylic and α-allenic alcohols. The yield of the reaction is generally higher or comparable to the corresponding $HgCl_2$ reaction. The reaction was found to universally favor the formation of the major diastereomer predicted by the Houk model. Diastereoselectivity of the reaction is comparable and in many cases significantly higher than the corresponding $HgCl_2$ reaction. This activating agent renders the reaction much more convenient to handle, work up, and purify. The high reactivity, diastereoselectivity and convenience associated with this modification may represent a useful improvement in the area of Sm-promoted cyclopropanation of both allylic and α-allenic alcohols. In addition, it was found that TMSCl also activated Sm toward formation of SmI_2.

Experimental Section

Starting Materials. The α-allenic alcohols **1a**−**1e** were prepared according to the literature procedures.[5] Geraniol and 2-cyclohexen-1-ol were purchased from Aldrich and used without further purification. *(E)*-1-Phenyl-1-hepten-3-ol (**8**) was prepared by addition of *n*-BuLi to cinnamaldehyde. 1,1-Bimetallic allylic alcohol **10** was prepared according to the literature procedure.[9]

General Procedure for the Cyclopropanation of α-Allenic alcohol with Sm/CH_2I_2 Activated by TMSCl. To a flame-dried round-bottomed flask was added 10 equiv of Sm metal. The flask was flame dried while being flushed with N_2. After the flask was allowed to cool to rt, THF was added followed

by TMSCl (0.2 equiv). The suspension was stirred for 30 min at rt. The α-allenic alcohol (1 equiv) was dissolved in a small volume of THF and transferred *via* cannula to the flask. The suspension was stirred for 20 min at rt. The flask was cooled to −78 °C, and CH_2I_2 was added dropwise. The mixture was allowed to warm to rt over 3 h and stirred overnight. The viscous dark blue reaction mixture was quenched with a saturated aqueous K_2CO_3 solution and extracted three times with Et_2O. The organic layers were collected, washed three times with brine, dried over anhydrous $MgSO_4$, and filtered. After concentration of the crude product purification was executed by flash chromatography on silica gel using 5−7% (volume) EtOAc in hexanes. Caution: *Large-scale reactions (>1 g of allenic alcohol) can be very exothermic.* A cooling bath should be available to control the temperature.

Cyclopropanation of 1,2-Undecadien-4-ol (1a) (Table 1, Entry 3). Allenic alcohol **1a** (5.00 g, 29.8 mmol) was cyclopropanated by treatment with Sm (36.0 g, 239 mmol), TMSCl (1.50 mL, 11.8 mmol), and CH_2I_2 (19.0 mL, 236 mmol) in THF (500 mL). The crude mixture was found to be a 1:1.66 mixture of two diastereomers as determined by GC analysis. After flash chromatography, **2a** (1.34 g) and **3a** (2.33 g) were isolated in a combined yield of 67%.[5]

Cyclopropanation of 1-Cyclohexyl-2,3-butadienol (1b) (Table 1, Entry 5). Allenic alcohol **1b** (300 mg, 1.97 mmol) was cyclopropanated by treatment with Sm (2.97 g, 19.7 mmol), TMSCl (0.05 mL, 0.39 mmol), and CH_2I_2 (1.60 mL, 19.9 mmol) in THF (150 mL) to provide a 17:1 mixture of two diastereomers as determined by GC analysis. After flash chromatography, **2b** (200 mg) and **3b** (12 mg) were isolated in a combined yield of 65%.[5]

Cyclopropanation of 1-Cyclohexyl-2,3-butadienol (1b) Using $ClCH_2I$ (Table 1, Entry 7). Allenic alcohol **1b** (300 mg, 1.97 mmol) was cyclopropanated by treatment with Sm (3.00 g, 20.0 mmol), TMSCl (0.05 mL, 0.39 mmol), and $ClCH_2I$ (1.45 mL, 20.0 mmol) in THF (150 mL). The crude mixture thus obtained was found to be a 7:1 mixture of two diastereomers as determined by GC analysis. After flash chromatography, **2b** (231 mg) and **3b** (30 mg) were isolated in a combined yield of 80%.[5]

Cyclopropanation of 1-Cyclohexyl-2-methyl-2,3-butadienol (1c) (Table 1, Entry 10). Allenic alcohol **1c** (230 mg, 1.38 mmol) was cyclopropanated by treatment with Sm (2.08 g, 13.9 mmol), TMSCl (0.05 mL, 0.39 mmol), and CH_2I_2 (1.1 mL, 13.9 mmol) in THF (150 mL) to provide a 25:1 mixture of two diastereomers as determined by GC analysis. After flash chromatography, **2c** (127 mg) and **3c** (3 mg) were isolated in a combined yield of 52%.[5]

Cyclopropanation of 1-Cyclohexyl-4-propyl-2,3-heptadienol (1e) (Table 1, Entry 12). Allenic alcohol **1e** (300 mg, 1.27 mmol) was cyclopropanated by treatment with Sm (1.90 g, 12.7 mmol), TMSCl (0.05 mL, 0.39 mmol), and CH_2I_2 (1.0 mL, 12.7 mmol) in THF (150 mL) to provide a 4.4:1 mixture of two diastereomers as determined by GC analysis. After flash chromatography, **2e** (135 mg) and **3e** (30 mg) were isolated in a combined yield of 52%.[5]

Cyclopropanation of 1-Cyclohexyl-2,3-butadienol (1b) with Aldrich Sm Activated by TMSCl (Table 1, Entry 9). Allenic alcohol **1b** (500 mg, 3.29 mmol) was cyclopropanated by treatment with Sm (Aldrich, 5.00 g, 32.9 mmol), TMSCl (0.083 mL, 0.658 mmol), and CH_2I_2 (2.6 mL, 32.9 mmol) in THF (250 mL) to provide an 11:1 mixture of two diastereomers as determined by GC analysis. After flash chromatography, **2b** (243 mg) and **3b** (25 mg) were isolated in a combined yield of 50%.[5]

Cyclopropanation of 1-Cyclohexyl-2,3-butadienol (1b) with Aldrich Sm Activated by $HgCl_2$ (Table 1, Entry 9). Allenic alcohol **1b** (300 mg, 1.97 mmol) was cyclopropanated by treatment with Sm (Aldrich, 2.97 g, 19.74 mmol), $HgCl_2$ (536 mg, 1.97 mmol), and CH_2I_2 (1.6 mL, 19.7 mmol) in THF (200 mL) to provide a 9.8:1 mixture of two diastereomers determined by GC analysis. After flash chromatography, **2b** (113 mg) and **3b** (10 mg) were isolated in a combined yield of 37%.[5]

General Procedure for the Cyclopropanation of Allylic Alcohols with Sm/CH_2I_2 Activated by TMSCl. Identical to the general procedure for the cyclopropanation of α-allenic alcohols except that Sm and CH_2I_2 were used in 5 equiv excess to allylic alcohols.

Cyclopropanation of Geraniol (4) Using Rhône-Poulenc Sm (Table 2, Entry 1). Allylic alcohol **4** (300 mg, 1.94 mmol) was cyclopropanated by treatment with Sm (1.46 g, 9.70 mmol), TMSCl (0.05 mL, 0.39 mmol), and CH_2I_2 (0.78 mL, 9.7 mmol) in THF (150 mL) to provide **5** (315 mg, 97%) after flash chromatography using 10% EtOAc in hexanes.[4]

Cyclopropanation of Geraniol (4) Using Aldrich Sm (Table 2, Entry 1). Allylic alcohol **4** (544 mg, 3.53 mmol) was cyclopropanated by treatment with Sm (Aldrich, 2.65 g, 17.6 mmol), TMSCl (0.09 mL, 0.71 mmol), and CH_2I_2 (1.28 mL, 17.6 mmol) in THF (150 mL) to provide **5** (442 mg, 75%) after flash chromatography using 10% EtOAc in hexanes.[4]

Cyclopropanation of 2-Cyclohexen-1-ol (6) (Table 2, Entry 2). Allylic alcohol **6** (300 mg, 3.05 mmol) was cyclopropanated by treatment with Sm (2.30 g, 15.3 mmol), TMSCl (0.077 mL, 0.61 mmol), and CH_2I_2 (1.2 mL, 15.3 mmol) in THF (150 mL) to provide **7** (297 mg, 87%) after flash chromatography using 10−20% EtOAc in hexanes.[4]

Cyclopropanation of *(E)*-1-Phenyl-1-hepten-3-ol (8) (Table 2, Entry 3). Allylic alcohol **8** (300 mg, 1.58 mmol) was cyclopropanated by treatment with Sm (1.20 g, 7.89 mmol), TMSCl (0.05 mL, 0.39 mmol), and CH_2I_2 (0.64 mL, 7.95 mmol) in THF (150 mL) to provide a 1.9:1 mixture of two diastereomers as determined by GC analysis. After flash chromatography using 5% EtOAc in hexanes, **9a** (200 mg) and **9b** (93 mg) were isolated in a combined yield of 90%.[4]

Cyclopropanation of 10 (Table 2, Entry 4). Allylic alcohol **10** (500 mg, 1 mmol) was cyclopropanated by treatment with Sm (1.50 g, 10 mmol), TMSCl (0.025 mL, 0.2 mmol), and CH_2I_2 (0.8 mL, 10 mmol) in THF (150 mL) to provide **11** as the only detectable diastereomer by 400 MHz NMR analysis. Flash chromatography using 5% EtOAc in hexanes provided **11** (417 mg, 81%).[9]

General Procedure for the Cyclopropanation of α-Allenic Alcohol with "TMSCl + Washing" Technique. According to the general procedure, Sm was treated with TMSCl for 30 min at rt. The clear THF solvent was removed by a cannula from the flask, under a N_2 atmosphere. Fresh THF (20 mL) was then added *via* a cannula to the flask and the suspension was stirred for 5 min at rt before the THF was removed. This "washing" procedure was repeated three times. Fresh THF was added. A ^{29}Si NMR of the clear solution showed no signals. The α-allenic alcohol (1 equiv) was dissolved in a small volume of THF and transferred *via* cannula to the flask. The reaction was then carried out in the usual way.

Cyclopropanation of 1-Cyclohexyl-2,3-butadienol (1b) Using "TMSCl + Washing" Technique (Table 1, Entry 8). Allenic alcohol **1b** (160 mg, 1.05 mmol) was cyclopropanated by treatment with Sm (2.00 g, 13.16 mmol), TMSCl (0.04 mL, 0.315 mmol), and CH_2I_2 (1 mL, 13.16 mmol) in THF (150 mL) to provide a 30:1 mixture of two diastereomers as determined by GC analysis. After flash chromatography, **2b** (77.6 mg) was isolated in 44% yield.[5]

General Procedure for the Cyclopropanation of α-Allenic Alcohol Using Other Activating Reagents. General procedure for the cyclopropanation of α-allenic alcohol with Sm/CH_2I_2 activated by TMSCl was followed except that TMSCl was substituted by other activating reagents.

Cyclopropanation of 1,2-Undecadien-4-ol (1a) with Sm/CH_2I_2 Activated by $(CH_3O)_3SiCl$ (Table 3, Entry 5). Allenic alcohol **1a** (300 mg, 1.78 mmol) was cyclopropanated by treatment with Sm (2.68 g, 17.86 mmol), $(CH_3O)_3SiCl$ (0.05 mL, 0.356 mmol), and CH_2I_2 (1.43 mL, 17.9 mmol) in THF (150 mL) to provide a 1:1.1 mixture of two diastereomers as determined by ^1H NMR (400 MHz) analysis. After flash chromatography, **2a** (105.5 mg) and **3a** (107 mg) were isolated in a combined yield of 66%.[5]

Cyclopropanation of 1-Cyclohexyl-2,3-butadienol (1b) with Sm/CH_2I_2 Activated by TBDMSCl (Table 3, Entry 9). Allenic alcohol **1b** (300 mg, 1.97 mmol) was cyclopropanated by treatment with Sm (2.96 g, 19.7 mmol), TBDMSCl (65 mg, 0.43 mmol), and CH_2I_2 (1.6 mL, 19.7 mmol) in THF (150 mL) to provide a 44:1 mixture of two diastereomers as determined by ^1H NMR (400 MHz) analysis. After flash chromatography, **2b** (195 mg) was isolated in 60% yield.[5]

Cyclopropanation of 1-Cyclohexyl-2,3-butadienol (1b) with Sm/CH_2I_2 Activated by $Ti(OiPr)_4$ (Table 3, Entry 10). Allenic alcohol **1b** (210 mg, 1.38 mmol) was cyclopropanated by

treatment with Sm (2.00 g, 13.8 mmol), $Ti(OiPr)_4$ (0.081 mL, 0.28 mmol), and CH_2I_2 (1.1 mL, 13.8 mmol) in THF (150 mL) to provide a greater than 50:1 mixture of two diastereomers as determined by ^1H NMR (400 MHz) analysis. Flash chromatography provided **2b** (135 mg) in 59% yield.[5]

Cyclopropanation of 1,2-Undecadien-4-ol (1a) Using Sm/CH_2I_2 without Activating Reagent (Table 3, Entry 1). 1a (130 mg, 0.77 mmol) was cyclopropanated by treatment with Sm (1.16 g, 7.74 mmol) and CH_2I_2 (1.60 mL, 19.7 mmol) in THF (150 mL) to provide a 2.1:1 mixture of two diastereomers determined by ^1H NMR (400 MHz) analysis. Flash chromatography provided **2a** (32 mg) and **3a** (16.4 mg) in a combined yield of 34%.[5]

SmI_2 Preparation by Reacting Sm with CH_2I_2 Activated by TMSCl. Sm (1.0 g, 6.65 mmol) was flame dried. THF (100 mL) was added followed by TMSCl (0.02 mL, 0.16 mmol). The suspension was stirred for 30 min at rt. The flask was cooled to −78 °C, and CH_2I_2 (0.48 mL, 6.59 mmol) was added dropwise. The mixture was stirred at −78 to −50 °C for 1 h. The typical dark blue solution of SmI_2 formed.

Acknowledgment. The A. P. Sloan Foundation, the Natural Science and Engineering Research Council (NSERC) of Canada, the E. W. R. Steacie Foundation, the Merck Frosst Center for Therapeutic Research, and Eli Lilly (USA) are thanked for financial support.

JO951365I