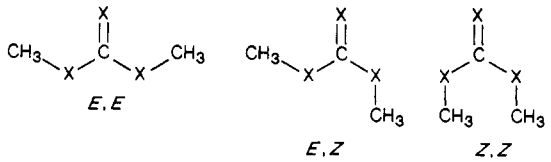
compounds have been reported. Three planar conformations are possible for symmetrically substituted compounds of this type, as shown below for dimethyl carbonate (1) and dimethyl trithiocarbonate (2).



1, X = O
2, X = S

The *E,E* and *Z,Z* conformations both possess twofold rotational axes, and the identical methyl groups of either conformation would show only a single peak in the proton NMR spectrum. The diastereotopic methyl groups of the *E,Z* conformation would show two peaks of equal intensity under conditions of slow topomerization ($EZ \rightleftharpoons ZE$), while a single peak would be observed if rotation about the C–O or C–S bonds is rapid. Thus, only the *E,Z* conformation could, by itself, show changes in the NMR spectrum as the temperature is lowered and the rate of rotation is slowed.

Studies of 1 in the gas phase[4] and in the condensed phase[5-7] indicate that the *E,E* conformation predominates. Katon and Cohen[6] have assigned peaks in the Raman and infrared spectra of liquid dimethyl carbonate to the *E,Z* conformation and estimated an enthalpy difference of 2.6 ± 0.5 kcal/mol for the *E,Z* and *E,E* conformations. The *Z,Z* conformation is expected to be destabilized by steric repulsion between the methyl groups, and the population of this isomer should be small; in one study,[7] ΔH for the *Z,Z* and *E,E* conformations was estimated to be 4.1 ± 0.5 kcal/mol.

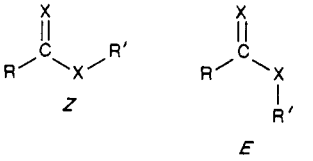
Dipole moments of 0.23, 1.69, and 3.03 D for the *E,E*, *E,Z*, and *Z,Z* conformations were predicted[5] for 1 by vector addition of bond moments. Experimental values range from 0.55 to 1.07 D;[8] for example, a dipole moment of 0.86 D was found[5] for a solution in carbon tetrachloride. This value is consistent with the *E,E* conformation, with smaller populations of the *E,Z* and *Z,Z*.

Similar dipole moments of 0.17, 2.46, and 4.17 D were obtained[9] from HMO calculations for the *E,E*, *E,Z*, and *Z,Z* conformations of 2. The experimental value of 1.33 D for a benzene solution is intermediate between the values expected for the *E,E* and *E,Z* forms and was interpreted in terms of a mixture of these two conformations. The IR spectra[9] in several solvents also indicated the presence of the two conformations, and the authors concluded that the *E,E* conformation predominates. The results of an electron diffraction study[10] of 2 in the gas phase were interpreted in terms of the *E,E* conformation only, although the possible presence of small amounts of the *E,Z* isomer could not be excluded.

The NMR spectrum (90.02 MHz) of 2 in $CHClF_2$/$CHCl_2F$ (3.4:1) at 21 °C shows a single peak for the methyl protons at δ 2.72. At lower temperatures, the peak broadens and splits into two lines of unequal intensity separated by 10.8 Hz at −150 °C. The peak heights are in a ratio of 4.17:1 (upfield:downfield). The finding of two signals of unequal intensity at slow exchange cannot be interpreted in terms of any single conformation but can readily be explained if a mixture of *E,Z* and *E,E* conformations is present, with the upfield peak of the *E,Z* isomer overlapping with the signal from the *E,E* conformation. The population of the *Z,Z* conformation is assumed to be negligibly small.

Populations of 0.52 and 0.48 for the *E,Z* and *E,E* conformations and rate constants of 16.3 s^{-1} (*E,E* → *E,Z*) and 15.0 s^{-1} (*E,Z* → *E,E*) were determined at −138 °C by using the DNMR program of Binsch and Kleier.[11] The corresponding free energy barriers are 6.9_4 and 6.9_7 kcal/mol at −138 °C.

Most esters of carboxylic acids, and the related sulfur compounds, have a strong preference for the *Z* conformation, in which *R'* and C=X are cis to each other.[12] For example, the population of the *E* isomer of methyl formate is only 0.3% at −83 °C in DMF/acetone,[13] and no evidence for the *E* isomer of methyl dithioacetate was found.[9] The reasons for this conformational preference have been discussed,[14] and for methyl formate probably include three factors: (1) more favorable dipole–dipole interactions for the *Z* isomer; (2) stabilization of the *Z* isomer by lone pair ("ether" oxygen) $-\sigma^*$ (C=O) interaction, and (3) "aromaticity" of the *Z* conformation. Studies of compounds related to 2 are in progress to clarify the reasons for the large population of the *E,Z* conformation of this compound.



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Samarium-Promoted, Stereocontrolled Cyclopropanation Reactions[1]

Summary: Samarium-based carbenoids have been found to be highly efficient cyclopropanation reagents for allylic alcohol substrates. Hydroxyl-directed cyclopropanations occur under very mild conditions with a high degree of selectivity.

Sir: Cyclopropanes play an important role in many aspects of organic chemistry. This structural unit is found in a number of significant natural products (for example chrysanthemic acid derivatives), as well as in synthetic

(1) Lanthanides in Organic Synthesis. 7.

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Table I. Samarium-Promoted Cyclopropanation of Acyclic Allylic Alcohols (1) Providing 2 and 3

entry	substrate	R	R′	R″	% isoltd yield	ratio of 2:3
1	1a	CH_3	$CH_2CH_2CH{=}C(CH_3)_2$	H	89	
2	1b	$CH_2CH_2CH{=}C(CH_3)_2$	CH_3	H	99	
3	1c	H	Ph	H	99	
4	1d	H	Ph	*n*-Bu	99	1:1.4
5	1e	H	Ph	*i*-Pr	88	>200:1
6	1f	H	Ph	*t*-Bu	76	>200:1
7	1g	H	*t*-Bu	Me	98	1:5.1
8	1h	H	*t*-Bu	*i*-Pr	46	>200:1
9	1i	*t*-Bu	H	Me	99	>200:1

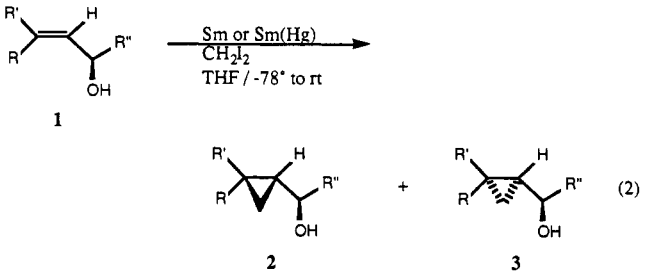
compounds of importance in biological studies.[3] Recently, cyclopropanes have found growing utility in organic synthesis as precursors to stereodefined cyclic and acyclic molecules.[4] Synthetic methods based upon cyclopropane substrates and pharmacological studies utilizing cyclopropanated compounds require development of highly selective syntheses of cyclopropanes.

Foremost among current methods for preparation of stereodefined cyclopropanes from olefin precursors is the Simmons–Smith reaction[5] and its various modifications.[6] Other methods based on carbene[7] and carbenoid chemistry[8] have been developed, and in general these methods are highly effective. Still, there appears a need for complementary techniques which would bring even greater selectivity to olefin cyclopropanation processes.

We were intrigued by the possibility that a samarium-based carbenoid might offer an alternative to the more traditional zinc-based species, both in terms of enhanced chemoselectivity and stereoselectivity. Initially, we decided to investigate use of Sm^{2+} carbenoids (e.g., $ISmCH_2I$).[9] Such species are implied intermediates in the generation of the useful reducing agent SmI_2[10] from samarium metal and geminal diiodoalkanes (eq 1).[11] Herein we describe our successful efforts to utilize samarium(2+) carbenoids for the stereocontrolled generation of cyclopropanes and point out some of the advantages of this protocol over those of more traditional recipes.

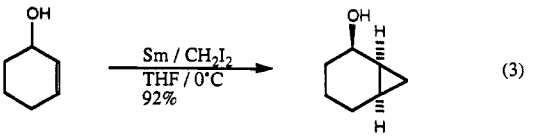
$$Sm + CH_2I_2 \rightarrow [ICH_2SmI] \rightarrow SmI_2 + 0.5CH_2{=}CH_2 \quad (1)$$

For our initial studies, allylic alcohol substrates were chosen that would allow us to compare the samarium-based carbenoids to the usual Simmons–Smith reagents. Cyclopropanations were usually performed by addition of a solution of the olefin and 3–4 equiv of diiodomethane in THF to a slurry of 3–4 equiv of samarium metal or Sm(Hg) in THF at −78 °C (eq 2). Significant amounts



of starting material remain if an excess of the carbenoid is not employed. The resulting reaction mixture was allowed to warm slowly, with reactions typically initiating at temperatures of about −60 °C. Upon warming to room temperature, reactions were quenched.[12] Diastereoselectivity was determined on crude reaction mixtures by capillary gas chromatography utilizing two different fused silica capillary columns. Simple aqueous workup followed by Kugelrohr distillation or flash chromatography led to excellent isolated yields of the desired products. Stereochemistry of the products was assigned on the basis of chromatographic behavior,[5f,g,13] combined with comparison to alcohols obtained from reduction of corresponding cyclopropyl ketones with lithium aluminum hydride.[5f,g]

2-Cyclohexen-1-ol is a classic substrate for cyclopropanation studies, and thus our initial efforts focused on this particular molecule. In fact, we found that an excellent yield of "hydroxyl-directed" cyclopropane could be generated upon treatment of this allylic alcohol with Sm/CH_2I_2 (eq 3).[5d,h] 1,1-Diiodoethane could also be



utilized quite efficiently with Sm(Hg) in an analogous reaction. In this instance, too, complete hydroxyl-directed cyclopropanation occurred in quantitative yield. Perhaps

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(12) The following serves as a general procedure for the cyclopropanation reactions. All reactions were carried out under an argon atmosphere utilizing standard bench-top techniques for handling of air-sensitive materials. To a slurry of flame-dried samarium metal (0.63 g, 4.2 mmol) in THF (10 mL) was added a solution of $HgCl_2$ (0.11 g, 0.4 mmol) in THF. The allylic alcohol (1 mmol) was next added to this slurry, and the reaction mixture was cooled to −78 °C. Diiodomethane (1.07 g, 4.0 mmol) was slowly added, and the resulting mixture was allowed to warm to room temperature. The reaction was quenched with saturated aqueous K_2CO_3 and extracted several times with Et_2O. The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated. The products were subsequently isolated by distillation of flash chromatography.

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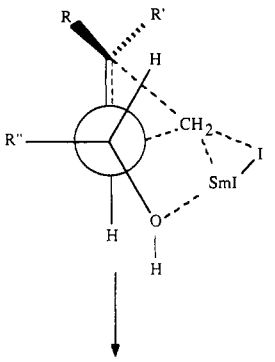
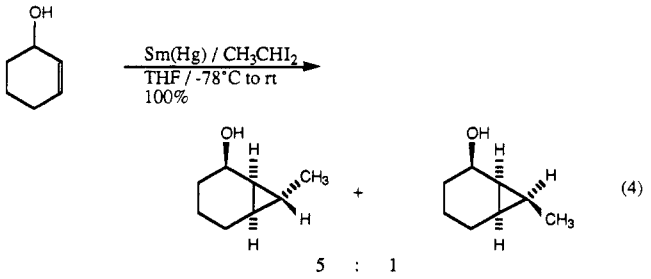


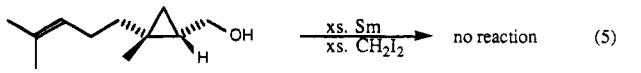
2

Figure 1. Proposed transition structure for samarium-promoted cyclopropanations.

more importantly, higher exo/endo diastereoselectivity was achieved with samarium (5:1, eq 4) than with corresponding Simmons–Smith conditions (1.7:1).[6]



Acyclic allylic alcohols were also investigated (Table I). The reaction has proven to be stereospecific with respect to olefin geometry (entries 1 and 2) and highly chemoselective. Whereas Simmons–Smith technology provides up to 5% of byproducts resulting from cyclopropanation of the isolated olefin in geraniol,[8b] no such byproducts have been detected by capillary GC analysis in crude reaction mixtures utilizing the samarium-promoted cyclopropanation strategy. In fact, isolated olefins appear to be inert to Sm/CH_2I_2. Thus, α-pinene, the homoallylic alcohol nopol, and monocyclopropanated nerol (eq 5) all fail to provide cyclopropanes upon treatment with excess Sm/CH_2I_2, with starting material recovered in each case.



Diastereoselectivity observed in the single (*Z*)-allylic alcohol tested to date (entry 9) is comparable to that found in the corresponding Zn(Cu)-promoted reaction. With regard to studies of (*E*)-allylic alcohols (entries 4–8), we have found that the steric requirements of R″ (eq 2) have a dramatic effect on diastereoselectivity of the process. No previous studies of which we are aware have examined the role of R″ on diastereoselectivity in hydroxyl-directed cyclopropanation reactions. As a consequence, previously suggested models for cyclopropanation based on eclipsed (ground state or Chautemps–Pierre[14]) conformations of allylic alcohols do not appear to account for observed diastereoselectivities in the present reactions.[5f,g,7]

We believe that a staggered (Houk) model[15] (Figure 1) for electrophilic addition to the olefin is perhaps better able to rationalize the observed experimental results. Utilizing this model, it is clear that diastereoselectivity should increase as the size of R″ increases, as this group will increasingly prefer the position antiperiplanar to the incoming carbenoid. Association of the carbenoid with the hydroxyl group will deliver the electrophile in over the hydrogen, providing the observed major diastereomer **2**. Other aspects of the Houk transition structure for reaction of a carbenoid with olefins[16] have been incorporated into this empirical model.

Studies designed to elucidate other stereochemical aspects of the reaction, as well as to delineate the scope of the reaction and its complementarity to Simmons–Smith processes are currently in progess. However, it is clear at this point that samarium-promoted reactions provide a highly selective route to stereocontrolled cyclopropanes from allylic alcohol precursors. In this preliminary work, some distinct advantages over Simmons–Smith procedures have been outlined, and a new appreciation of allylic alcohol substituent effects in cyclopropanation reactions has been gained.

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Benzaldehyde Oxime as a 1,3-Dipole Chameleon

Summary: Reaction of the iminium salt derived from benzaldehyde oxime and (trimethylsilyl)methyl triflate with cesium fluoride in the presence of electron-dificient alkenes gives rise to azomethine ylide cycloadducts. In sharp contrast, reaction of the salt with alkynes produces dipolar cycloadducts derived from nitrones.

Sir: The 1,3-dipolar cycloaddition reaction[1] has attracted considerable attention as a convenient tool for the rapid construction of a wide assortment of natural products.[2-8] Nitrones[9] and azomethine ylides[10] represent two common and frequently used classes of 1,3-dipoles in total synthesis.

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