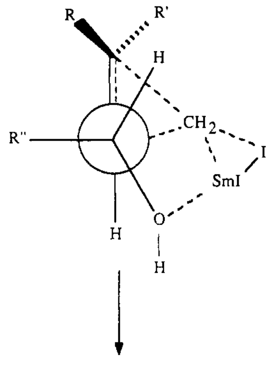
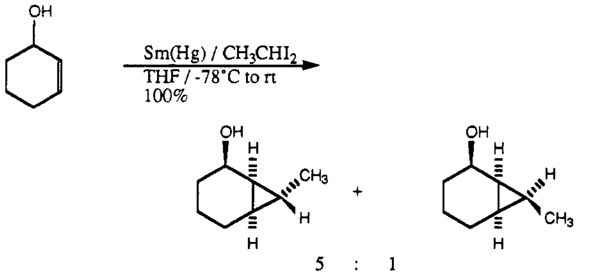


2

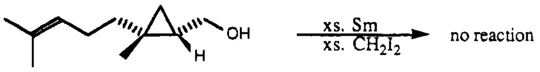
Figure 1. Proposed transition structure for samarium-promoted cyclopropanations.

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



(4)

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.



(5)

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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Gary A. Molander,*[2] Jeffrey B. Etter
Department of Chemistry and Biochemistry
University of Colorado
Boulder, Colorado 80309-0215

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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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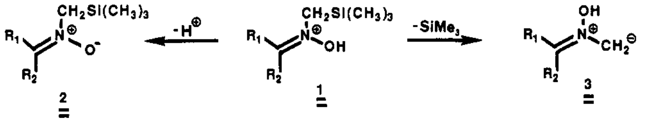
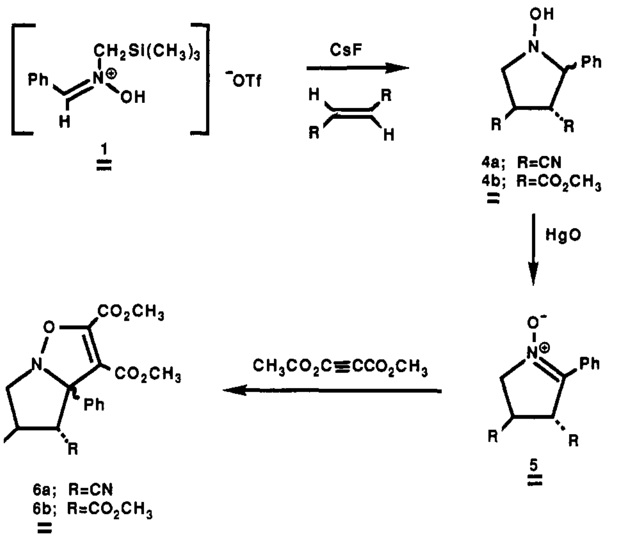
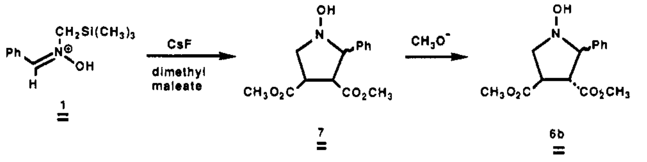
Condensation of carbonyl compounds with N-substituted hydroxylamines and oxidation of N,N-disubstituted hydroxylamines are the most common methods for the synthesis of nitrones.[11] More recently, LeBel and co-workers have developed a new procedure for the preparation of nitrones which involves the N-alkylation of *O*-trimethylsilyl oximes.[12] There are now several approaches to the generation of nonstabilized azomethine ylides by desilylation of α-trimethylsilyl iminium salts or equivalent species.[13-17] It occurred to us that the reaction of (trimethylsilyl)methyl triflate with oximes should give rise to an iminium salt (1) which could serve as a common precursor for both classes of dipoles. In this paper we report the results of these studies.



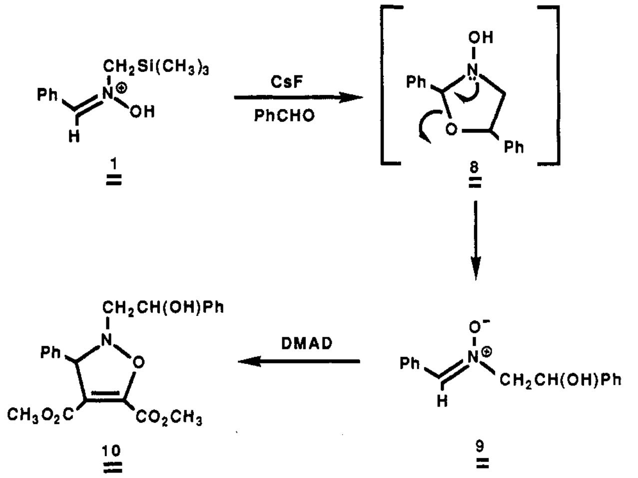
Iminium salt 1 was conveniently prepared by treating benzaldehyde oxime with (trimethylsilyl)methyl triflate. The resulting solid was suspended in dimethoxyethane and treated with cesium fluoride in the presence of fumaronitrile or dimethyl fumarate. The major compound isolated (85%) corresponded to the dipolar cycloadduct derived from azomethine ylide 3.[18,19] The structure of 4 was supported by mercuric oxide oxidation to nitrone 5, which undergoes ready reaction with dimethyl acetylenedicarboxylate to give the expected isoxazolidine derived from the double cycloaddition sequence.



In order to ascertain the stereospecificity of the reaction, we studied the cycloaddition of 1 with dimethyl maleate and found that the reaction afforded cis cycloadduct 7 as the exclusive product.[20] This result provides good support for the intermediacy of an azomethine ylide dipole. Cycloadduct 7 was readily isomerized to the thermodynamically more stable fumarate adduct on treatment with sodium methoxide in methanol.



We have also examined the cycloaddition behavior of 1 using benzaldehyde as the trapping dipolarophile and find that nitrone 9 is produced as the major product (72%). The structure of this material was supported by its spectral properties[21] and by its cycloaddition with DMAD to give isoxazolidine 10. The formation of 9 can be rationalized by assuming that the initially formed dipolar cycloadduct 8 undergoes ring opening followed by a subsequent proton transfer.



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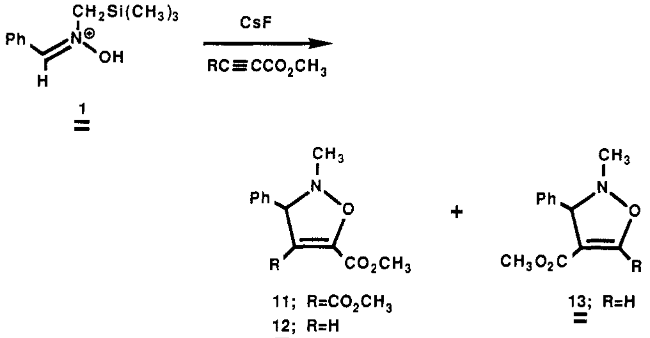
(18) All compounds gave satisfactory analyses. Complete spectroscopic and degradative details will be given in our full publication. The stereochemistry of the phenyl group in structures 4, 6, and 7 is not yet known.

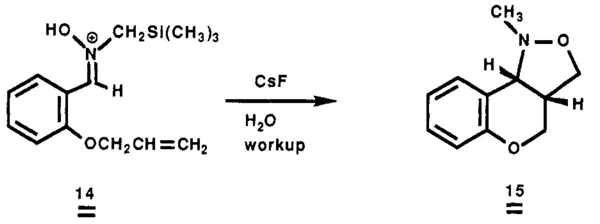
(19) Structure **4a**: mp 96–97 °C; NMR (CDCl$_3$, 360 MHz) δ 3.27 (dd, 1 H, J = 10.6 and 9.0 Hz), 3.54 (dd, 1 H, J = 9.0 and 8.1 Hz), 3.71 (d, 1 H, J = 8.0 Hz) 3.92 (dd, 1 H, J = 10.6 and 8.1 Hz), 4.33 (d, 1 H, J = 8.0 Hz), 5.20 (br s, 1 H), and 7.45 (sd, 5 H). **6a**: mp 55–56 °C; NMR δ 3.53 (d, 1 H, J = 9.4 Hz), 3.56 (s, 3 H), 3.76 (m, 1 H), 3.78 (s, 3 H), 4.03 (m, 1 H), 4.20 (dd, 1 H, J = 10.6 and 7.4 Hz), and 7.4 (m, 5 H). **4b**: mp 102–103 °C; NMR δ 3.09 (dd, 1 H, J = 10.1 and 8.8 Hz), 3.13 (s, 3 H), 3.6–3.82 (m, 3 H), 3.75 (s, 3 H), 4.25 (d, 1 H, J = 9.7 Hz), 5.15 (s, 1 H), and 7.35 (m, 5 H). **6b**: mp 104–105 °C; NMR δ 3.24 (s, 3 H), 3.57 (ddd, 1 H, J = 8.6, 6.9, and 6.8 Hz), 3.68 (dd, 1 H, J = 11.0 and 8.6 Hz), 3.73 (s, 3 H), 3.86 (s, 3 H), 3.88 (s, 3 H), 4.14 (dd, 1 H, J = 11.0 and 6.9 Hz), 4.56 (d, 1 H, J = 6.8 Hz), and 7.4 (m, 5 H).

(20) Structure **7**: mp 120–121 °C; NMR δ 3.42 (t, 1 H, J = 9.8 Hz), 3.51 (m, 1 H), 3.6–3.8 (m, 2 H), 3.63 (s, 3 H), 3.71 (s, 3 H), 4.31 (d, 1 H, J = 9.8 Hz), 4.78 (br s, 1 H), and 7.4 (m, 5 H).

(21) Structure **9**: mp 160–161 °C; NMR δ 4.08 (dd, 1 H, J = 12.6 and 8.4 Hz), 4.17 (dd, 1 H, J = 12.6 and 2.6 Hz), 5.26 (d, 1 H, J = 3.0 Hz), 5.36 (ddd, 1 H J = 8.4, 3.0, and 2.6 Hz), 7.4 (m, 11 H). **10**: mp 78–79 °C; NMR δ 2.97 (dd, 1 H, J = 12.6 and 8.4 Hz), 3.25 (dd, 1 H, J = 12.6 and 2.5 Hz), 3.73 (s, 3 H), 3.83 (s, 3 H), 4.30 (s, 1 H), 5.09 (dd, 1 H, J = 8.4 and 2.5 Hz), and 7.3 (m, 10 H).

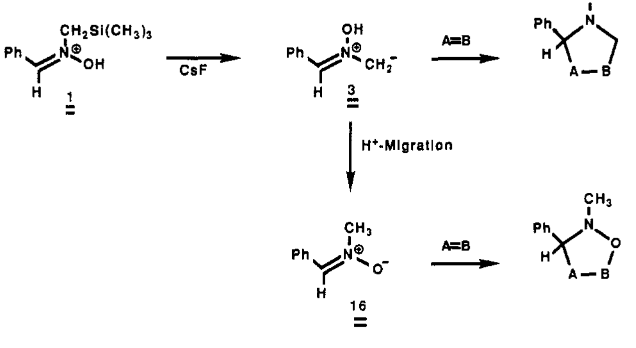
Since we were interested in the synthetic utility of these iminium salts, we undertook a systematic study of the cycloaddition with a number of related dipolarophiles. Most surprisingly, the reaction of **1** with DMAD under the standard conditions afforded only the dipolar cycloadduct **11** formally derived from *N*-methyl-*C*-phenylnitrone. This structure was verified by comparison with an authentic sample.[22] Similarly, treatment of **1** with methyl propiolate produced a 1:2 mixture of the known isoxazolidines **12** and **13**.[22] We also studied the cycloaddition reaction of the triflate salt derived from *O*-(allyloxy)salicylaldehyde oxime (i.e., **14**) with cesium fluoride. The intramolecular cycloadduct (85%) isolated from the reaction (**15**) also corresponds to a product which is formally derived from a *N*-methyl-*C*-arylnitrone.[23]





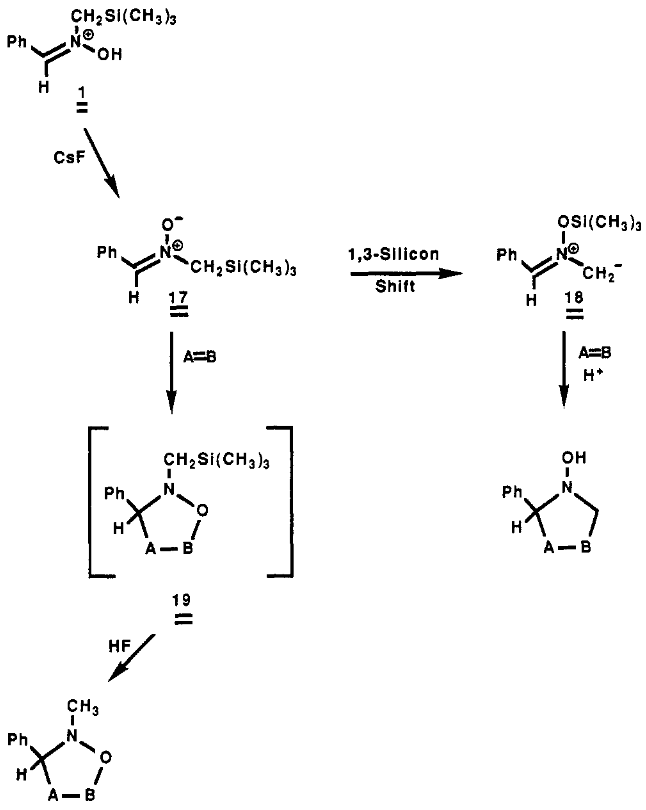
At first glance it would appear that these reactions proceed via an initial desilylation to give azomethine ylide **3**. This species could either cycloadd to the available dipolarophile or undergo proton transfer from carbon to oxygen to give the *N*-methylnitrone **16**. This mechanism (path A) would require that dipolarophiles such as dicyanoethylene or dimethyl fumarate cycloadd to the azomethine ylide at a much faster rate than dimethyl acetylenedicarboxylate. Since azomethine ylide cycloadditions are HOMO-controlled processes,[24] this suggestion seems unreasonable. In fact, reaction of **1** with a 1:1 mixture of DMAD and dimethyl fumarate in the presence of CsF only afforded the nitrone cycloadduct thereby eliminating the above path.

PATH A



We propose that the different products result from the operation of an alternate mechanism which involves the initial removal of the OH proton by cesium fluoride.[25] The rate of nitrone cycloaddition to electron-deficient alkynes is known to be much greater than to their alkenyl counterparts.[9] In the presence of the slower reaction alkene, a 1,3-silicon shift to the oxygen atom occurs, giving rise to azomethine ylide **18**, which undergoes subsequent cycloaddition (path B). The initially formed cycloadduct **19** is readily converted to the *N*-methylnitrone adduct under the reaction conditions. The formation of intramolecular cycloadduct **15** is also consistent with this mechanism since azomethine ylides generally do not react with unactivated alkenes.[24]

PATH B



Further studies on the scope and reactivity of trimethylsilyl iminium salts derived from oximes and their ability to act as dipole chameleons will be reported in due course.

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Albert Padwa,* William Dent, Philip E. Yeske

Department of Chemistry
Emory University
Atlanta, Georgia 30322

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[25] Treatment of **1** with NaH in the presence of DMAD followed by aqueous workup also afforded cycloadduct **11**. Similarly, the reaction of **1** with NaH in the presence of dimethyl fumarate gave cycloadduct **4b** in high yield.