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# ALLYLSILANE INITIATED CARBOCYCLIZATIONS[†]

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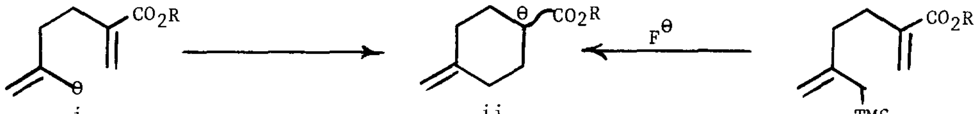
SUMMARY: The intramolecular conjugate addition of an allylic anion, generated from a allylsilane moiety, with various Michael acceptors is reported.

The research of Sakurai,[1] Andersen,[2] Fleming,[3] and Trost[4] has focussed considerable attention on the use of allylsilanes in organic syntheses. These pioneers and others have documented the highly regiospecific reactions of allylsilanes with a wide variety of carbon electrophiles. In the preceding communication,[5] we reported our findings concerning the condensations of allylsilane with various Michael acceptors.[6] Here we describe the use of functionalized allylsilanes to form cyclic systems.

The intramolecular Michael reaction has been extremely useful despite its reversible nature and the necessity of employing stabilized carbanions to overcome the presence of relatively acidic protons.[7] We have been intrigued by the possibility of using a marginally stabilized allylic carbanion to initiate an intramolecular Michael ring closure reaction (i→ii). To date such a carbocyclization process is unknown, possibly owing to the difficulties associated with the specific generation of an allylic anion in the presence of olefins bearing electron-withdrawing groups. Encouraged by the results of our intermolecular reactions, we were confident that the carbanion generated by treating an allylsilane moiety with fluoride ion would be capable of circumventing these difficulties (iii→ii). Table I contains the suitably constituted substrates we chose to explore this concept and our findings.



i ii iii

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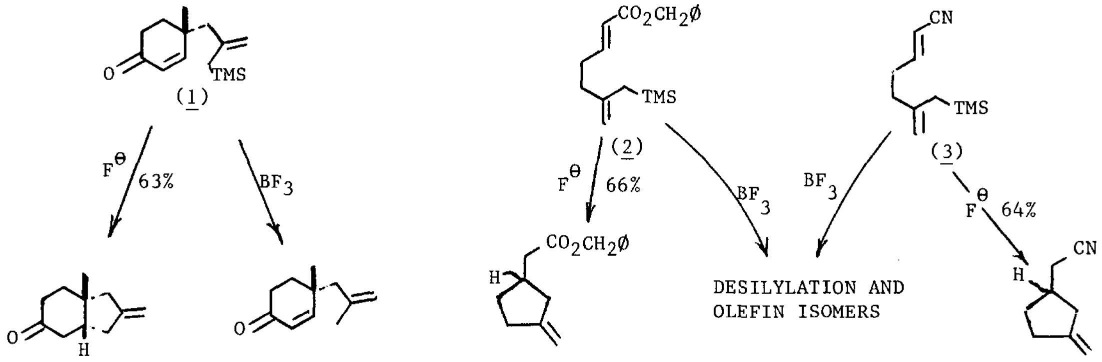
[†] In memory of Dr. Anthony Ames, Ph.D., University of Pittsburgh (1981), N.I.H. Postdoctoral Fellow, (1981-1982).

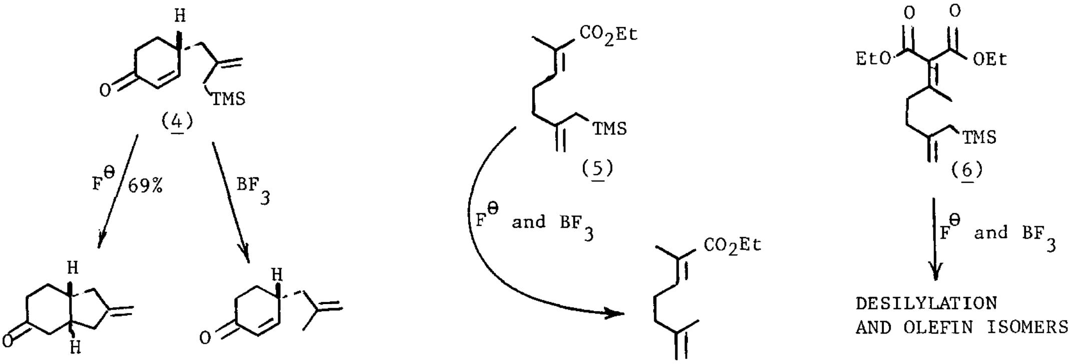
TABLE I



It is clear from these results that the intramolecular allylsilane initiated Michael addition provides a new approach to carbocyclization.[8-11] Whereas in our preceding paper,[5] allyl silane initiated allylation proved merely competitive with existing methods, functionalized allylsilanes appear to be superior reagents for the intramolecular process. In our hands, exposure of the precursor silanes to $TiCl_4$ or $BF_3$ etherate under a wide variety of conditions failed to promote cyclization; large excesses of Lewis acid gave complex mixtures which did not contain the desired cyclization products. These results suggest that Lewis acid catalyzed allylsilane cyclizations are extremely substrate dependent.[12]

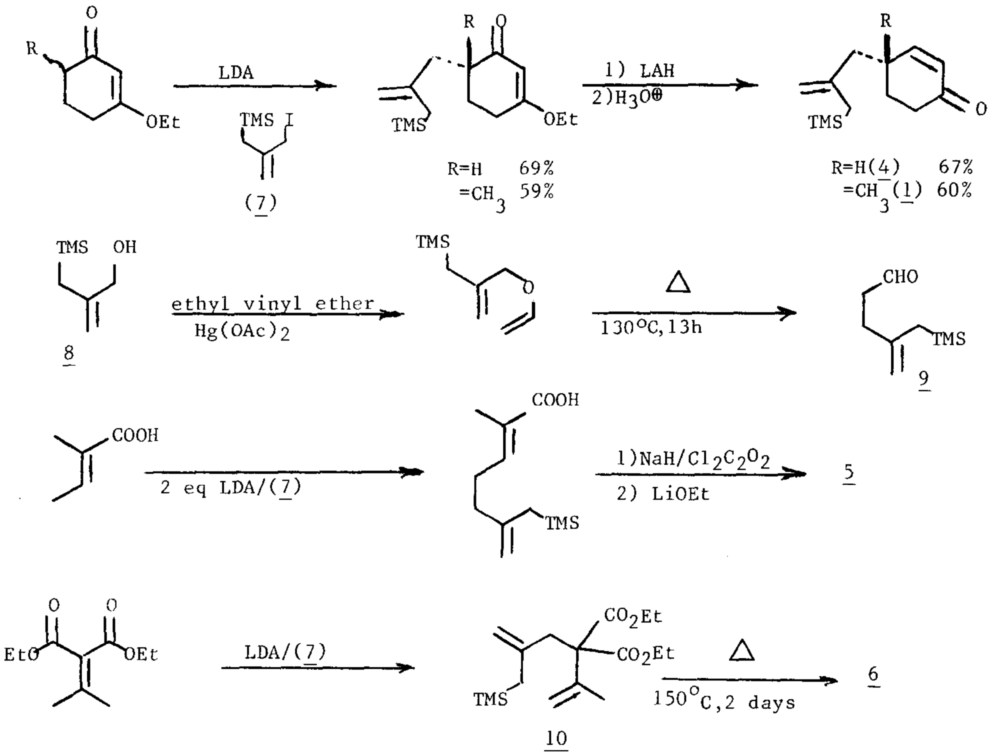
Having observed that conjugate addition is favored over direct 1,2 addition we then examined substrates having numerous acidic protons (Table II). The failure of substrates 5 and 6 to cyclize is presumably the result of intramolecular proton transfer.[18]

TABLE II



Several aspects of the preparation of the substrates studied are notable (Table III). Enones 1 and 4 were synthesized via the method of Stork and Danheiser[13] through alkylation of the kinetic enolates of 3-ethoxy-5-methylcyclohex-2-enone and 3-ethoxy-cyclohex-2-enone with 2-(trimethylsilyl)methallyl iodide (7).[14] Reduction followed by acid-catalyzed hydrolysis furnished the desired enones. The preparation of substrates 2, 3, and 5 utilized the recently demonstrated ability of allylsilanes to undergo Claisen rearrangement.[12]

TABLE III



2-Hydroxymethylallyltrimethylsilane (8)[15] was converted to its vinyl ether in the usual manner. Thermolysis at 120°C (sealed tube, 13 h) gave aldehyde 9 (82% from 8 ; bp 60-65°C at 1.1 mm Hg). This aldehyde was then converted to the substrates using Wadsworth-Emmons or Wittig condensations. α, β-Unsaturated ester 5 was independently prepared by alkylation of the dianion of tiglic acid[16] with iodide 7 (67% yield) followed by esterification via the intermediate acid chloride (NaH/oxalyl chloride). The construction of diester 6 required α-alkylation of diethyl isopropylidene malonate with iodide 7 (88%; KH/THF/0°C).[17] Cope rearrangement of 10 at 150°C provided diester 6 in 50% yield (sealed tube, 2 days).

This new method of carbocyclization has several noteworthy advantages: 1) the generation of the allylic anion via the allylsilane can be carried out under very mild, almost neutral conditions; 2) the high chemoselectivity of the allylic anion species enables highly functionalized substrates to be studied; and 3) the cyclization produces ample functionality for further transformations of the newly formed ring. Further efforts directed at determining the scope and limitations of this new pathway for the formation of cyclic systems are in progress.

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The author wishes to thank Professor Barry Trost for a preprint of his manuscript detailing the preparation of alcohol 8.[15]

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3. (a) M. J. Carter and I. Fleming, *J. C. S. Chem. Comm.*, 679 (1976); (b) I. Fleming, and A. Percival, *J. C. S. Chem. Comm.*, 681 (1976).
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6. While this manuscript was in preparation the fluoride ion induced reaction of allylsilane with enones was reported; A. Ricci, M. Fiorenza, M. Grifagni, G. Bartolini, and G. Seconi, *Tetrahedron Letters*, **23**, 5079 (1982).
7. Pertinent examples are: (a) dithanes: reference 2b; (b) β-keto esters: G. Stork, D. F. Taber and M. Marx, *Tetrahedron Letters*, 2445 (1978); (c) aldehydes: G. Stork, C. S. Shiner, J. D. Winkler, *J. Am. Chem. Soc.*, **104**, 310 (1982); (d) esters: R. A. Lee, *Tetrahedron Letters*, 3333 (1973); (e) ylides: R. M. Cory and D. M. T. Chan, *Tetrahedron Letters*, 4441 (1975); (f) ketones: B. M. Trost, C. D. Shuey, and F. DinNinno, Jr., *J. Am. Chem. Soc.*, **101**, 1284 (1979).
8. Satisfactory spectral data were obtained for all compounds.
9. The following experimental procedure is typical. A reaction vessel containing 200 mg of 4 A molecular sieves was flame-dried under vacuum (5 minutes) and placed under nitrogen. A solution of 35 mg of TBAF dissolved in 3 mls of DMF (freshly distilled over $CaH_2$) and 236 mg of HMPA (1.32 mmol) was then added. A solution of 140 mg of α,β-unsaturated ester (0.44 mmol) in 2 mls of DMF was added dropwise over a 45 minute period (via syringe pump). The resulting mixture was allowed to stir at RT for 1 h. The reaction mixture was diluted with 20 mls of water. Workup afforded 97 mg of residue which was homogeneous on TLC. Column chromatography provided 71 mg of the cyclized product (66%).
10. When the reaction of entry 1 was carried out in either ether or tetrahydrofuran significantly lower yields (9% & 36%, respectively) were obtained despite lengthy reaction times (36 h). The conclusion that a *cis* hydrindenone is produced by cyclization of *enone 1 is based both on spectral data and further chemical transformations. On occasion,* as much as 10% of the *trans*-isomer was obtained.
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13. G. Stork and R. L. Danheiser, *J. Org. Chem.*, **38**, 1775 (1973).
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15. Silylation of the dianion of α-methylallyl alcohol using known procedures provided disappointedly low yields of the desired alcohol 8. The best procedure for preparing 8 is by B.M.Trost, D.M.T. Chan, and T.N.Nanningan, soon to be published results.
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17. Organic Syntheses, **50**, 39.
18. Mechanistic studies with labeled substrates are now in progress to verify this conclusion. An alternative explanation that enones are simply better Michael acceptors, than enoates, for soft nucleophiles cannot be ruled out at the present time.

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