involving "*corner*" *activation of the cyclopropane ring by* Tl(III).

The attack of the thallic ion at the "corner" of the cyclopropane parallels the reactivity of the mercuric ion and the proton, allowing similar orbital arguments[3] to be used. Neither Hg^{2+} nor Tl^{3+} is a good back-donor so that the back-donation of their d$_\pi$ electrons to the LUMO Walsh orbital is negligible; therefore the "edge" activation is apparently disfavored. On the other hand, the observed corner attack by Tl^{3+} (and Hg^{2+}) reflects the favorable interaction of the degenerate HOMOs of the cyclopropane with vacant d orbitals on the metal. Our experiments thus provide further support for the mechanistic picture and orbital considerations recently published by Coxon et al.[3] We are confident that our results furnish an additional example required for the generalization of the original rationalization[3] which was derived from the behavior of only one nontransition metal. Moreover, the rearrangement of the cyclopropyl alcohol **1** represents an attractive synthetic avenue for the stereoselective construction of the oxa-triquinane skeleton or of spirocyclic lactones. Although the experiments were confined to the steroidal skeleton, we believe that our finding is of a general nature and might be used as the key step for the construction of complex natural products.

Acknowledgment. We thank Dr. P. Sedmera for obtaining some of the preliminary NMR spectra, Dr. S. Vašíčková for IR spectra, and Drs. J. Podlaha, J. Symerský, and V. Langer for the preliminary X-ray analysis. We also thank the Swedish Natural Science Research Council for financial support of P.K. and A.G.

Supplementary Material Available: Melting points and IR, ^{1}H NMR, ^{13}C NMR, MS, and analytical data for **2–4** and **7** (2 pages). Ordering information is given on any current masthead page.

Carbonyl–Ene Reaction with Vinylsilanes: Silicon as a Controlling Element for Regio- and Stereochemistry

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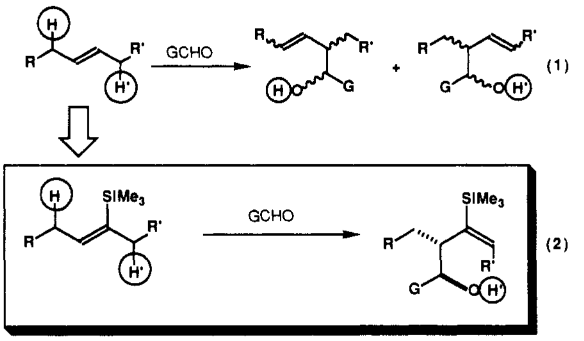
Control of the sites of C–H bond activation and C–C bond formation is of current interest for synthetic exploitation in carbon skeletal construction. In principle, the ene reaction involving carbonyl enophiles (Scheme I) is the simplest way for C–C bond formation, which converts readily available alkenes, with substitution for allylic C–H bond and allylic transposition of the C=C bond, into more functionally complex derivatives.[1] However, the synthetic utility of the carbonyl–ene reaction has been overshadowed by the lack of regioselectivity when applied to unsymmetrical alkenes (eq 1).

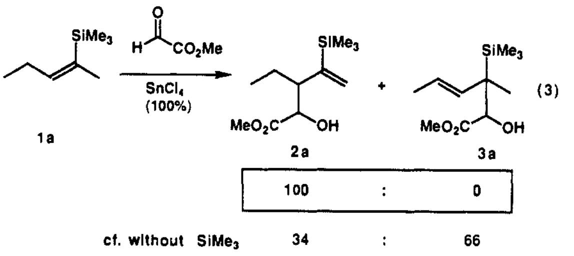
Herein we report the first example of the Lewis acid promoted carbonyl–ene reaction with vinylsilane as an ene,[2] which provides a solution to this regiochemical problem and constitutes a highly stereocontrolled version of a carbonyl–ene reaction (eq 2). The key feature in the regio- and stereochemical control of the concerted process[3] lies in the steric bulkiness of the trialkylsilyl group.[4]

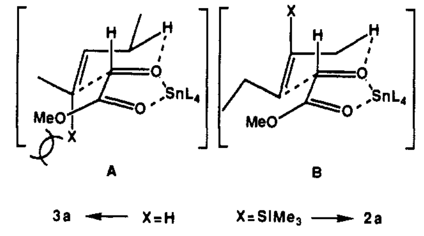
Scheme I



The great advantages of the present version of the carbonyl–ene reaction are (1) *the highly regiocontrolled introduction of a potential functionality based on vinylsilane*[4] and (2) *the remarkable enhancement of diastereoselectivity and the dramatic changeover in olefinic stereoselectivity.*

First, the use of vinylsilane (**1**)[5] as an ene is found to alter the regiochemical course in the glyoxylate–ene reaction to give the vinylsilane product **2** as a *single* regioisomer (eq 3).[6] The highly regiocontrolled ene reaction with vinylsilane is in sharp contrast to the ene reaction with 1,2-disubstituted alkene without a silyl group, which gives a mixture of regioisomers under the same reaction conditions.[7] The observed regiocontrol can be explained on the basis of the six-membered transition-state model[8] by an enhanced steric interaction of SiMe$_3$ and CO$_2$Me relative to that of H and CO$_2$Me in A. Thus, the vinylsilane **2a** would be formed regioselectively via the transition state B.





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(1) Reviews on intermolecular ene reactions: (a) Mikami, K.; Terada, M.; Shimizu, M.; Nakai, T. *J. Synth. Org. Chem. Jpn.* **1990**, *48*, 292. (b) Snider, B. B. *Acc. Chem. Res.* **1980**, *13*, 426. (c) Hoffman, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 556. (d) Whitesell, J. K. *Acc. Chem. Res.* **1985**, *18*, 280.

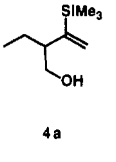
(2) Review on ene and retro-ene reactions in group 14 organometallic chemistry: Dubac, J.; Laporterie, A. *Chem. Rev.* **1987**, *87*, 319.

(3) The mechanism of Lewis acid promoted ene reactions has been the subject of controversial discussions (a concerted pericyclic vs stepwise cationic mechanism): Snider, B. B.; Ron, E. *J. Am. Chem. Soc.* **1985**, *107*, 8160, and references therein. However, a cationic reaction with vinylsilane should provide the other substitution product via a favorable β-silyl cation,[4] not the ene-type product arising from an unfavorable α-silyl cation. Thus, the present reaction with vinylsilane might provide a novel probe for the mechanism of the Lewis acid promoted ene reactions.

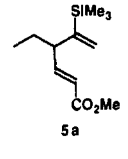
(4) Colvin, E. W. *Silicon in Organic Synthesis*; Butterworths: London, 1981; Chapter 2. Fleming, I. In *Comprehensive Organic Chemistry*; Barton, D. H. R., Ollis, W. D., Eds.; Pergamon: Oxford, 1979; Vol. 3, Part 13. Magnus, P. D.; Sarkar, T.; Djuric, S. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon: Oxford, 1982; Vol. 7, Chapter 48.

(5) Vinylsilanes are prepared following the literature procedure: Colvin, E. W. *Silicon Reagents in Organic Synthesis*; Academic Press: London, 1988, Chapter 3, and references therein.

(6) A high level of regiocontrol is also found in the ene reaction of formaldehyde or propiolate to give the single ene product **4** or **5**, respectively.



4a



5a

(7) A methylene hydrogen has been reported to be twice as reactive as a methyl or methine hydrogen after correction for statistical factors.[1]

(8) Mikami, K.; Loh, T.-P.; Nakai, T. *Tetrahedron Lett.* **1988**, *29*, 6305.

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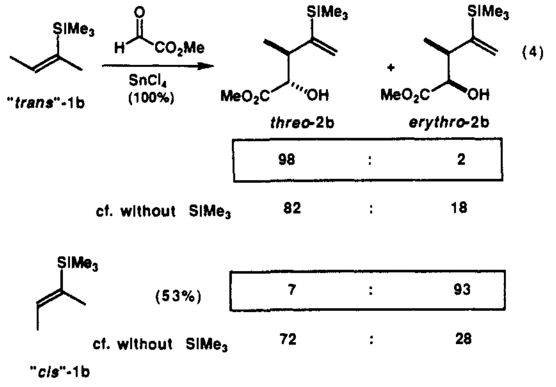
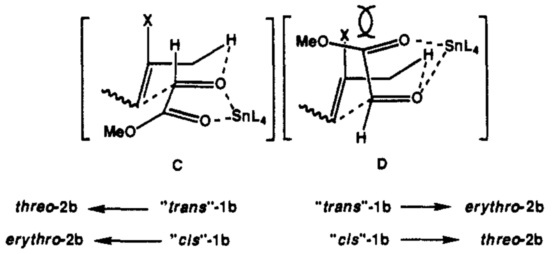
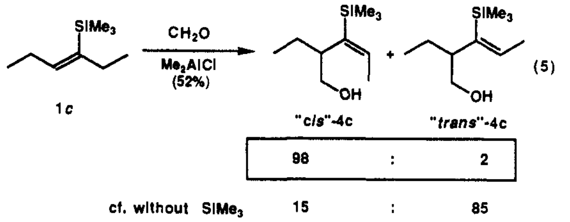
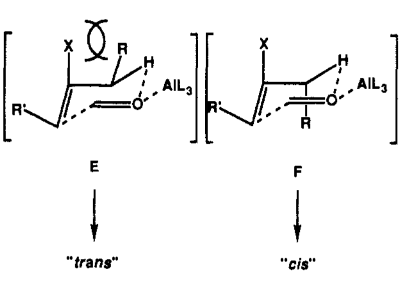
The introduction of a silyl group into the ene component is also effective for the enhancement and/or the changeover in diastereoselectivity (eq 4). The reaction with "*trans*"-vinylsilane **1b** is found to give the threo product with remarkably enhanced selectivity (98%) as compared with *trans*-2-butene[8] (82%). In sharp contrast, the dramatic changeover in diastereoselectivity from threo[8] to erythro is observed for the ene reaction with "*cis*"-vinylsilane **1b**. Both the enhancement and changeover in diastereoselectivity are explicable in view of the greatly increased 1,3-repulsion of SiMe$_3$ and CO$_2$Me in the transition state D.



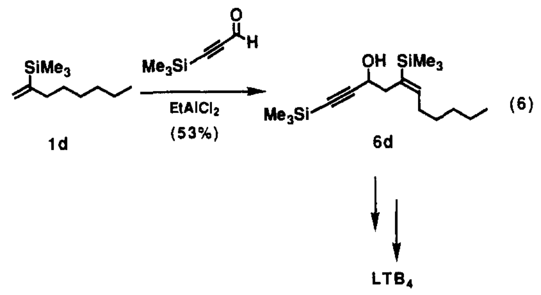


The controlling effect of the silyl group on the stereochemistry is highlighted by the changeover of the olefinic stereoselectivity from trans to "cis" (eq 5). Trans selectivity (ca. 90%) is widely recognized for the ene reaction with alkenes without silyl group.[1,9] In direct contrast, the reaction of formaldehyde with vinylsilane **1c** provides "*cis*"-homoallyl alcohol **4c** with high (98%) selectivity.[10] Dramatic changeover into "cis" selectivity is explained in terms of the large 1,2 steric repulsion between SiMe$_3$ and R in E leading to the "trans" product.





The unprecedented "cis" selectivity should find its application to the synthesis of leukotriene B$_4$ (LTB$_4$) featuring a "*cis*"-homoallyl alcohol unit.[11] Thus, the ene reaction of silylpropynal with vinylsilane **1d** affords the disilylated enynol **6d** with a high level of "cis" selectivity (>99%),[12,13] which serves as a key intermediate of LTB$_4$.[14]



In conclusion, we have described here the Lewis acid promoted carbonyl–ene reaction with vinylsilanes, which allows the highly regio- and stereocontrolled introduction of vinylsilane functionality. These results clearly show the dramatic effect of silicon as a controlling element for not only the regio- but also the stereochemistry.

Acknowledgment. This research was partially supported by the Asahi-Kasei Award in Synthetic Organic Chemistry, Japan.

Supplementary Material Available: Experimental details of the glyoxylate–ene reaction with vinylsilanes (**1a**,**b**), the formaldehyde–ene reaction with **1c**, the propynal–ene reaction with **1d**, and the protodesilylation of **4c** and **6d** (6 pages). Ordering information is given on any current masthead page.

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[9] The ene reaction of formaldehyde with 4- or 1-octene has been reported to give the *trans*-homoallyl alcohol (ca. 90% selectivity): Snider, B. B.; Rodini, D. J.; Kirk, T. C.; Cordova, R. *J. Am. Chem. Soc.* **1982**, *104*, 555.

[10] The stereoisomeric ratio was determined by a combination of HPLC and IR analyses after protodesilylation via the reported procedure.[5]

[11] Review on the synthesis of leukotrienes: Rokach, J.; Guindon, Y.; Young, R. N.; Adams, J.; Atkinson, J. G. In *The Total Synthesis of Natural Products*; ApSimon, J., Ed.; Wiley: New York, 1988; Vol. 7. Corey, E. J.; Cheng, X.-E. *The Logic of Chemical Synthesis*; Wiley: New York, 1989; Chapter 12. Kobayashi, Y.; Shimazaki, T.; Sato, F. *J. Synth. Org. Chem. Jpn.* **1990**, *48*, 627.

[12] The "cis" configuration of the known product **6d** was confirmed by ^{13}C NMR, IR, and HPLC analyses prior to and/or after protodesilylation according to the literature.[14]

[13] We have also found that the ene reaction of formaldehyde with vinylsilane **1d** shows >99% "cis" selectivity.

[14] Kaye, A. D.; Pattenden, G.; Roberts, S. M. *Tetrahedron Lett.* **1986**, *27*, 2033.

Asymmetric Radical Addition, Cyclization, and Annulation Reactions with Oppolzer's Camphor Sultam

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Although an understanding of the factors that control relative stereochemistry in radical cyclization reactions has matured rapidly,[2] it remains to be shown that radical reactions are generally useful for dictating acyclic stereochemistry—either relative or absolute.[3,4] We now demonstrate that chiral radicals derived from

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[1] Dreyfus Teacher-Scholar, 1986–1991. NIH Research Career Deveopment Awardee, 1987–1992. ICI Pharmaceuticals Awardee, 1990.

[2] (a) Curran, D. P. *Synthesis* **1988**, 417, 489. (b) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon–Carbon Bonds*; Pergamon Press: Oxford, 1986. (c) Curran, D. P. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: New York, Vol. 4, in press.

[3] For a timely review on stereoselectivity in intermolecular radical reactions, see: Giese, B. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 969. With few exceptions, most stereoselective intermolecular additions involve cyclic radicals bearing adjacent stereocenters.

[4] Additions of achiral radicals to chiral alkenes: (a) Porter, N. A.; Lacher, B.; Chang, V. H.-T.; Magnin, D. R. *J. Am. Chem. Soc.* **1989**, *111*, 8309. (b) Porter, N. A.; Scott, D. M.; Lacher, B.; Giese, B.; Zeitz, H. G.; Lindner, H. J. *J. Am. Chem. Soc.* **1989**, *111*, 8311. (c) Scott, D. M.; McPhail, A. T.; Porter, N. A. *Tetrahedron Lett.* **1990**, *31*, 1679.

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