transformations was not markedly diminished, and the catalyst could still be recovered and reused seven times. Further optimization can be expected.

Although lower enantioselectivities result from C–H insertion reactions of 2-methoxyethyl diazoacetate in refluxing benzene with PE-Rh_2(5(*S*)-PYCA)$_4$ than in refluxing dichloromethane with Rh_2(5(*S*)-MEPY)$_4$, the same is not true for the intramolecular cyclopropanation of 3-methyl-2-buten-1-yl diazoacetate. The maintenance of such high enantioselectivity in this latter case demonstrates that carbene dissociation from dirhodium(II) does not take place at the elevated temperatures used in this study.

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Remote Asymmetric Induction Based on Carbonyl–Ene Reactions with Bishomoallylic Silyl Ethers: Dramatic Changeover of Regioselectivity by the Remarkable Siloxy Effect

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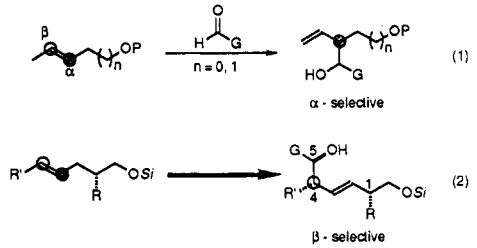
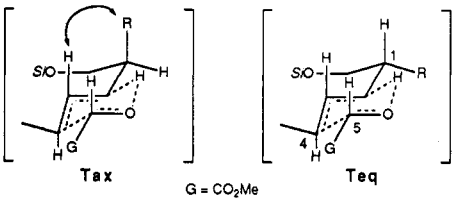
Summary: A new approach to remote asymmetric induction is described for not only a 1,4- but also a 1,5-relationship, which is based on the carbonyl–ene reactions with chiral bishomoallylic silyl ethers. Silyl ethers, rather than alkyl ethers, exhibit β-regiospecificity. Remarkably high levels of remote asymmetric induction can then be established with chiral bishomoallylic ethers to provide eventually a simple and efficient method for asymmetric induction.

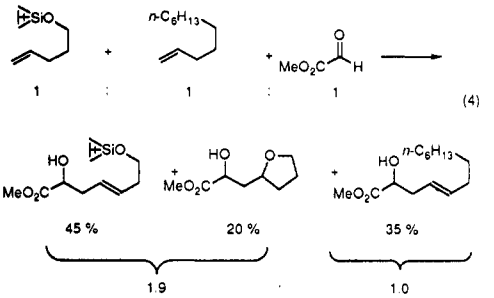
A number of methods have been devised for generating adjacent stereogenic centers (1,2-relationships) in an acyclic system with a high level of relative asymmetric induction.[1,2] However, approaches to control remote relationships by efficient relative 1,>3-asymmetric induction are rare,[3] and hence remote stereocontrol has been a challenging problem in organic synthesis. We report here a unique approach to not only 1,4- but also 1,5-remote asymmetric induction by carbonyl–ene reactions with chiral bishomoallylic silyl ethers (eq 2) which show the dramatic changeover of regioselectivity from (homo)allylic ethers (eq 1).[4]



The glyoxylate–ene reactions with (*E*)-4-hexenyl ethers **1a** were found to provide selectively the β-regioisomers **3a** (eq 3), in sharp contrast to the α-regioselectivity observed with (homo)allylic ethers[4] (Table I). Benzyl, methyl, and acetyl groups gave, however, a low level of regioselectivity (entries 1–3). Surprisingly,[3] silyl ethers led specifically to the β-regioisomer (entries 4–7). Sterically-demanding silyl groups such as *tert*-butyldiphenylsilyl were the best choice, giving the β-ene product regioselectively in good yield with exclusive *E*- and anti-selectivity (entry 7).[5] Thus, the dramatic changeover of regioselectivity implies the O-5 orbital interaction by the siloxy groups to increase the olefinic reactivity regiospecifically at the β-carbon via the folded conformation (T: R = H).[6] In fact, 4-pentenyl silyl



ether was twice as reactive as 1-undecene without siloxy group in the Lewis acid-promoted reaction (eq 4).



In view of the cyclic model, 1,4-remote stereocontrol is highly predictable. In the reaction of a chiral (*E*)-bishomoallylic ether (T: R≠H), the axial conformer T_{ax}

(1) Reviews: (a) *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1984; Vol. 3. (b) Bartlett, P. A. *Tetrahedron* **1980**, *36*, 2. (c) Reetz, M. T. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 556.

(2) For the definition of internal or relative asymmetric induction, see ref 1b.

(3) Chelation control has been, so far, of singular importance for predictable remote stereocontrol. For leading recent references, see: Molander, G. A.; Haar, J. P., Jr. *J. Am. Chem. Soc.* **1991**, *113*, 3608. Molander has, however, proposed the neighboring-group participation in the stereocontrol of 1,4-diols. In his case, alkoxy groups such as methoxy and benzyloxy provide the higher level of diastereoselectivity than that obtained with siloxy groups to lead to 1:1 diastereomeric mixtures.

(4) (a) Mikami, K.; Shimizu, M.; Nakai, T. *J. Org. Chem.* **1991**, *56*, 2952. (b) Snider, B. B.; Phillips, G. B. *J. Org. Chem.* **1983**, *48*, 464.

(5) For the physical data of ene products, see the supplementary material.

(6) Simple neighboring-group participation seems to be unlikely as a controlling element in view of the low regio- and diastereoselectivity with methoxy and benzyloxy groups. Another possibility was suggested by the reviewers: "alkoxy substituents might be less influential in controlling regio- and stereochemistry because they were complexed more effectively with the Lewis acid."

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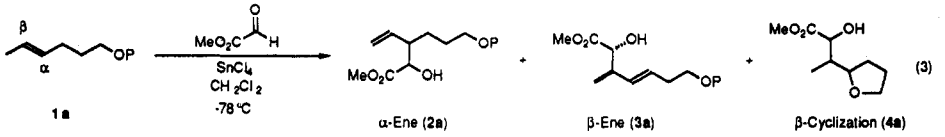
Table I. Regioselectivity of Glyoxylate–Ene Reaction with (*E*)-4-Hexenyl Ether (1a)

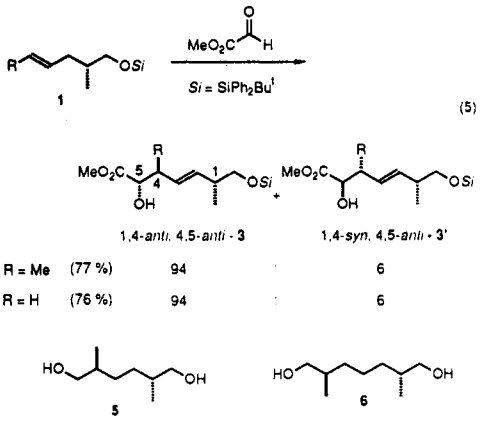


1a α-Ene (2a) β-Ene (3a) β-Cyclization (4a)

entry	P	% yield[a]	2a	3a (anti/syn)[b]	4a
1	Me	89	22	78 (8 : 2)	0
2	Bn	89	12	52 (7 : 3)	36
3[c]	Ac	—[d]	40	60	0
4	Si^{i}PrMe$_2$	84	2	18 (>99 : <1)	80
5	Si 	96	0	50 (>99 : <1)	50
6	Si^{i}Pr$_3$	100	0	67 (>99 : <1)	33
7	Si^{t}BuPh$_2$	100	1	81 (>99 : <1)	18

[a] Combined value of the isolated yields of ene product (2 and 3) and cyclization product 4 after chromatographic purification. [b] Determined by ^{1}H and ^{13}C NMR analysis (see ref 4a). *E*-Isomer was obtained exclusively. [c] (*Z*)-4-Heptenyl ether was used instead of (*E*)-4-hexenyl ether. [d] Not isolated.

should be less favorable because of the 1,3-diaxial repulsion. Thus, the 1,4-anti-isomer should be formed stereoselectivity via the equatorial conformer $\mathbf{T_{eq}}$. As expected, the reaction of a chiral ether **1b** provides the 1,4-anti-diastereomer **3b**[7] with 94% stereoselectivity (eq 5).[5] The



(7) By contrast, the 2,5-*syn*-dimethyl-6-siloxy-3-hexen-1-ol was obtained in the reaction of (*Z*)-bishomoallylic ether **1b** with formaldehyde.

1,4-stereochemistry can be established with the transformation to the known 1,6-diol **5**.[8] 1,6-Diol **5**, thus obtained, can be transformed to 13,16-*anti*-dimethyloctacosane, isolated from messel shale kerogen.[9] Furthermore, even without the olefinic methyl group **1c**, the ene reaction can also be used to control the 1,5-remote stereochemistry of Me and OH groups in a syn fashion with an equally high level (94%) of remote asymmetric induction.[10]

Supplementary Material Available: Typical experimental procedures for the glyoxylate–ene reactions and physical data for the ene products **3** (4 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(8) Still, W. C.; Darst, K. P. *J. Am. Chem. Soc.* **1980**, *102*, 7385.

(9) $C_{12}H_{25}CHMeCH_2CH_2CHMeC_{12}H_{25}$: Chappe, B.; Albrecht, P.; Michaelis, W. *Science (Washington, D.C.)* **1982**, *217*, 65. For synthesis, see: Heathcock, C. H.; Finkelstein, B. L.; Jarvi, E. T.; Radel, P. A.; Hadley, C. H. *J. Org. Chem.* **1988**, *53*, 1922.

(10) The 1,5-stereochemistry can also be established by the transformation with inversion of the OH group at C-5 ($Me_2Cu(CN)Li_2$) to the known 1,6-diol **6**.[8] For the higher-ordered cuprate, see: Lipshutz, B. H.; Sengupta, S. *Org. React.* **1992**, *41*, 135. Lipshutz, B. H.; Wilhelm, R. S.; Kozlowski, J. A.; Parker, D. *J. Org. Chem.* **1984**, *49*, 3928.