Communications

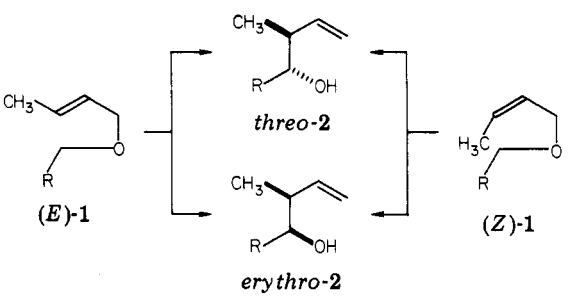
Acyclic Diastereoselection in the [2,3] Wittig Sigmatropic Rearrangement of a Series of Isomeric Crotyl Ethers. A Conceptual Model for the Transition-State Geometry

Summary: The levels of diastereoselection in a broad range of [2,3] Wittig variations with different substituents on the carbanion termini have been evaluated and permit us to propose a reasonable model for the transition-state geometry.

Sir: The recent surge of efforts to control acyclic stereochemistry has resulted in a number of reports dealing with diastereoselection in sigmatropic rearrangements. While several [3,3] sigmatropic processes occupy positions of potential utility for acyclic stereocontrol,[1] the [2,3] sigmatropic counterparts, despite the widely recognized similarity of the two pericyclic reactions, have thus far exhibited only moderate levels of diastereoselection in general.[1a,2] Recently we have found relatively high diastereoselectivities in the [2,3] Wittig rearrangements of bisallylic ether systems.[3] In order to develop this type of carbanion rearrangement into a basic methodology for acyclic stereocontrol it is extremely important to understand factors determining the sense and degree of diastereoselection; a properly designated mechanism for this type of rearrangement, however, remains unsettled. We now report our observations on the diastereoselection in a broad range of [2,3] Wittig variations (Scheme I) and, on the basis of these, propose a conceptual model for the transition-state geometry that may serve as a guiding principle for designing highly diastereoselective [2,3] Wittig modifications.

Table I summarizes the results obtained with the seven variations, including the data previously reported by us[3] and others.[4] The rearrangement of **1e** deserves special comment. The significant discrepancy seen between the literature data (entries E and F), coupled with inaccessibility of definite proof of the product stereochemistry therein, prompted us to reinvestigate the stereoselection of isomeric **1e** in more detail. We have now unequivocally assigned the erythro configuration to the major diastereomer obtained from (*Z*)-**1e** through extensive GLC and NMR comparisons with authentic samples.[5] Furthermore, the diastereomeric ratio for (*E*)-**1e** was found to be quite sensitive to the nature of solvent systems (entries G–J), while (*Z*)-**1e** exhibits very high erythro selectivity as reported by Rautenstrauch,[4a] which is solvent independent.

Scheme I



Thus this specific solvent effect on (*E*)-**1e** appears responsible for the discrepancy described above.[6]

Inspection of the data in Table I reveals several general trends in terms of the sense and degree of diastereoselection. (1) All of the *Z* substrates concerned here exhibit erythro selection, whereas the *E* counterparts show threo selection except for (*E*)-**1e**, which provides a low erythro selectivity under the standard conditions (entry G). (2) The degree of stereoselection is critically dependent upon the kind of substituent (R), indicating that carbanion structure conferred by a given R plays a significant role in dictating reaction stereoselectivity. (3) Particularly noteworthy are the remarkably high stereoselections with (*E*)-**1d**, (*Z*)-**1e**, and (*Z*)-**1f**, which have obvious applications in organic synthesis.[7] (4) Another notable trend is that the threo selectivity for *E* series decreases with changing R in the order: C≡CH → CH=CR′ (R′ = H, Ph) → CR′=CH_2 (R′ = CH_3, Me_3Si) → Ph.

While these trends impart considerable stereochemical predictability to this methodology, there remains an important task of analyzing the transition-state geometries. On the basis of the widely accepted postulate that the [2,3] sigmatropic rearrangement proceeds via envelope transition state,[2,8] we thus searched for a transition-state model that best accommodates *both* the sense and degree of stereoselection described above. An extensive analysis of variable steric parameters has now led us to propose the

(1) Recent reviews include: (a) Bartlett, P. A. *Tetrahedron* **1980**, *36*, 2. (b) Ziegler, F. E. *Acc. Chem. Res.* **1977**, *10*, 227.

(2) For reviews, see: (a) Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 563. (b) Trost, B. M.; Melvin, L. S., Jr. "Sulfur Ylides"; Academic Press: New York, 1975; Chapter 7. Also see: (c) Nakai, T.; Mikami, K.; Taya, S.; Kimura, Y.; Mimura, T. *Tetrahedron Lett.* **1981**, *22*, 69. (d) Jemison, R. W.; Laird, T.; Ollis, W. D.; Sutherland, I. O. *J. Chem. Soc., Perkin Trans. 1* **1980**, 1436 and references therein.

(3) Nakai, T.; Mikami, K.; Taya, S.; Fujita, Y. *J. Am. Chem. Soc.* **1981**, *103*, 6492.

(4) (a) Rautenstrauch, V. *Chem. Commun.* **1970**, 4. (b) Schöllkopf, U.; Fellenberger, K.; Rizk, M. *Justus Liebigs Ann. Chem.* **1970**, *734*, 106.

(5) The erythro configuration of the major product was established by NMR comparison with an authentic threo isomer; *erythro*-**2e** shows a doublet due to >CHOH at δ 4.43 (*J* = 5.7 Hz) in the NMR spectrum, while *threo*-**2e** presents a doublet at δ 4.25 (*J* = 7.5 Hz). We thank Drs. H. Nozaki and T. Hiyama, Kyoto University, for providing the NMR spectrum of the authentic sample: Hiyama, T.; Kimura, K.; Nozaki, H. *Tetrahedron Lett.* **1981**, *22*, 1037. The assignment was further confirmed through GLC and NMR comparisons of the hydrogenation product of *erythro*-**2e** with an erythro-rich stereomixture independently prepared via addition of phenyllithium to 2-methylbutanal in which the major diastereomer can be predicted by Cram's rule.

(6) The stereochemical assignment of Schöllkopf et al.[4b] has now been found to be incorrect and hence the reported ratio of "2:1" should read "1:2".

(7) Recently Heathcock and co-workers have demonstrated that *erythro*-**2e**, prepared by an entirely different route, serves as a key intermediate for the synthesis of ephedrine: Heathcock, C. H.; Buse, C. T.; Kleschick, W. A.; Pirrung, M. C.; Sohn, J. E.; Lampe, J. *J. Org. Chem.* **1980**, *45*, 1066.

(8) In general, conformational analysis of five-membered rings is very difficult. For a general discussion on conformations of five-membered rings, see: Fuchs, B. In "Topics in Stereochemistry"; Eliel, E. L., Allinger, N. L., Ed.; Interscience: New York, 1978; Vol. 10.

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Table I. Diastereoselectivity in the [2,3] Wittig Variations[a]

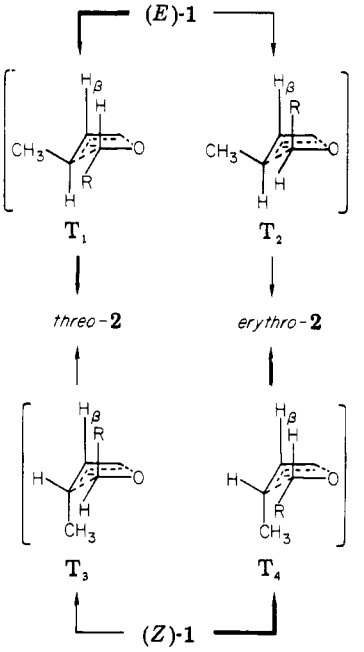
entry	substrate	1E:1Z[b]	threo-2: erythro-2[c]
A[d]	1a, R = $CH{=}CH_2$	93:7	79:21 (84:16)
		5:95	12:88 (8:92)
B[d]	1b, R = $C(CH_3){=}CH_2$	93:7	67:33 (72:28)
		17:83	16:84 (5:95)
C[e]	1c, R = $C(SiMe_3){=}CH_2$[f]	95:5	70:30[g]
D[d]	1d, R = C≡CH	93:7	93:7 (99:1)
		2:98	12:88 (10:90)
E[h]	1e, R = Ph	*E*	50:50
		Z	0:100
F[i]	1e	*E*	2:1
G	1e	93:7	37:63 (39:61)
		5:95	7:93 (5:95)
H[j]	1e	93:7	32:68
I[j]	1e	93:7	44:56
J[j]	1e	93:7	51:49 (55:45)
		5:95	5:95 (2:98)
K[k]	1f, R = *p*-$CH_3OC_6H_4$	93:7	56:44 (60:40)
		2:98	1:99 (0:100)
L[l]	1g, R = CH=CHPh-(*E*)	93:7	71:29 (74:26)
		2:98	30:70 (28:72)

[a] Unless otherwise noted, all reactions were run as follows. A 1.4 M solution of *n*-BuLi in hexane was added to a substrate solution in THF (1.0 mL/1.0 mmol) at −85 °C under N_2 and stirred at that temperature for 6-8 h. The mixture was allowed to warm to 0 °C and quenched with hydrochloric acid. The isolated yield after distillation ranged from 70% to 98%. All products were fully characterized by IR and NMR spectra. [b] Refers to the geometric ratio of the crotyl alcohol employed for the preparation of 1. [c] Determined by GLC and/or NMR analysis with the aid of a NMR shift reagent. Values in parentheses refer to the calculated values based on 100% of geometric purity. [d] Cited from ref 3. [e] Lithium dicyclohexylamide was used in place of *n*-BuLi. [f] Prepared in 79% via reaction of (*E*)-crotyl chloride with the known 2-(trimethylsilyl)-2-propenol; cf. ref 14. [g] The stereochemical assignment of **2c** was made by analogy with that of **2a** and **2b** (ref 3); the NMR spectrum of *erythro*- and *threo*-**2c** shows a doublet at δ 4.18 (J = 4.8 Hz) and 3.93 (J = 7.5 Hz), respectively. The threo/erythro ratio was determined by GLC (PEG 20M, 150 °C); t_R 15.7 min (*erythro*-**2c**) and 13.2 min (*threo*-**2c**). [h] Cited from ref 4a, where a mixture of *N,N,N',N'*-tetramethylethylenediamine (TMEDA), ether, and hexane was used as the solvent (unspecified ratio). [i] Cited from ref 4b, where a 1:1 mixture of THF and ether was used as the solvent. [j] The solvents used are THF/hexane (1:4) for entry H, TMEDA/ether/hexane (1:3:7) for entry I, and TMEDA/ether/hexane (1:1:1.2) for entry J. [k] The stereochemical assignment of **2f** was made by analogy with that of **2e** (ref 5); the NMR spectrum of *erythro*- and *threo*-**2f** shows a doublet at δ 4.40 (J = 5.7 Hz) and 4.25 (J = 7.5 Hz), respectively. [l] The stereochemistry of **2g** was unequivocally assigned through NMR comparisons with an authentic threo isomer independently prepared via Pd-catalyzed reaction of *threo*-**2d** (93% threo) with iodobenzene followed by reduction with $LiAlH_4$; the NMR spectrum of *erythro*- and *threo*-**2g** shows a triplet at δ 4.10 (J = 6.0 Hz) and 4.00 (J = 6.0 Hz), respectively. For the Pd-catalyzed phenylation, see: Takahashi, S.; Kuroyama, Y.; Sonogashira, K.; Hagiwara, N. *Synthesis* **1980**, 627.

transition-state model depicted in Scheme II,[9] which provides logical bases for explaining (and predicting) the stereoselection in at least the present range of variations as follows.[10]

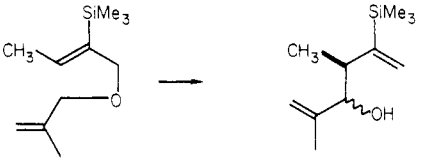
First, the observed sense of stereoselection is readily

Scheme II



interpreted in terms of the pseudo-1,3-diaxial interaction between R and H_β in T_2 and T_3; for the *Z* substrate, e.g., T_3 is less favorable than T_4, thus leading to erythro selection. Second, the marked dependence of threo selectivity on R is best explained by assuming an additional R ↔ CH_3 steric parameter (gauche interaction) in the preferred T_1; i.e., the gauche interaction is, as expected, minimized with the ethynyl substituent and enhanced by changing R from vinyl to 2-propenyl or α-silylvinyl. Third, a similar argument could be extended to rationalize the somewhat unusual behavior of (*E*)-**1e**. Given the reasonable postulate that the oxybenzylic carbanion possesses preferentially a pyramidal configuration (depending largely upon the solvent),[11] the CH_3 ↔ Ph gauche interaction would be greatly enhanced, eventually leading to very low stereoselectivities as acutally observed.[12]

This argument for transition states is further strengthened by the additional example of (*E*)-**3**[13,14] where a con-



(*E*)-**3** (92% *E*) 4 (threo/erythro = 91:9)

(9) For slightly different transition-state geometries previously assumed for different [2,3] sigmatropic rearrangements, consult ref 2a and 2b.

(10) As in most works dealing with carbanionic species one can only speculate about the role of the countercation. Li^+ might be coordinated to oxygen in **1**, as already revealed for (alkoxyallyl)lithiums: see, e.g., Evans, D. A.; Andrews, G. L.; Buckwalter, B. *J. Am. Chem. Soc.* **1974**, *96*, 5560. Still, W. C.; Macdonald, T. L. *Ibid.* **1974**, *96*, 5561; *J. Org. Chem.* **1976**, *41*, 3620. Also the kind of ion pair involved and the state of aggregation are not certain. These unknown factors, however, should not distract from our argument regarding the geometry of the reacting carbanion.

(11) Cram, D. J. "Fundamentals of Carbanion Chemistry"; Academic Press: New York, 1965; Chapters III, IV.

(12) The unusual erythro selectivity observed in entries G and H is explained in terms of the increased gauche interaction in T_1 surpassing the 1,3 interaction in T_2.

(13) To avoid confusion we use the prefix *E* instead of *Z* for designating the geometry of **3** (and its precursor) even though the operation of the sequence rule requires the use of the latter prefix.

(14) Prepared in 87% yield by reaction of methallyl chloride with (*E*)-2-(trimethylsilyl)-2-buten-1-ol,[14] which was derived from its chloride obtained via the literature procedure: Chan, T. H.; Mychajlowskij, W.; Ong, B. S.; Harp, D. N. *J. Org. Chem.* **1978**, *43*, 1526.

siderably improved threo selectivity is obtained[15] in comparison to (*E*)-**1b**, as readily predicted by an enhanced 1,3 interaction of R ↔ Me_3Si in T_2 relative to that of R ↔ H_β for (*E*)-**1b**.

Further efforts are in progress to establish more variations with higher diastereoselectivities on the basis of this transition-state model. Finally, it should be noted that this model cannot, of course, explain the whole story of diastereoselection in the [2,3] Wittig rearrangement in general. Recently we have found a few variations[16] that exhibit the opposite sense of stereoselection to that generally observed in this study.

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Registry No. (*E*)-**1b**, 79704-95-3; (*Z*)-**1b**, 79704-96-4; (*E*)-**1c**, 84118-82-1; (*E*)-**1d**, 79705-05-8; (*Z*)-**1d**, 79705-06-9; (*E*)-**1e**, 27299-30-5; (*Z*)-**1e**, 27299-31-6; (*E*)-**1f**, 84118-83-2; (*Z*)-**1f**, 84118-84-3; (*E,E*)-**1g**, 84118-85-4; (*Z,E*)-**1g**, 84118-86-5; *threo*-**2a**, 79705-03-6; *erythro*-**2a**, 79705-02-5; *threo*-**2h**, 79704-97-5; *erythro*-**2b**, 79704-93-1; *threo*-**2c**, 84118-87-6; *erythro*-**2c**, 84118-88-7; *threo*-**2d**, 79705-08-1; *erythro*-**2d**, 79705-07-0; *threo*-**2e**, 52922-10-8; *erythro*-**2e**, 52922-19-7; *threo*-**2f**, 83173-78-8; *erythro*-**2f**, 84118-89-8; *threo*-**2g**, 84118-90-1; *erythro*-**2g**, 84118-91-2.

(15) In this rearrangement, lithium dicyclohexylamide was used in place of *n*-BuLi because the use of *n*-BuLi produced a considerable amount of byproducts. The threo/erythro ratio was determined by GLC analysis (PEG 20M, 150 °C), t_R 12.2 min (*erythro*-**4**) and 9.5 min (*threo*-**4**); cf. Felkin, H.; Gault, Y.; Roussi, G. *Tetrahedron* **1970**, *26*, 3761. The ratio was further confirmed by NMR analysis with the aid of Eu(fod)$_3$.

(16) Such variations include (crotyloxy)acetic acids (ref 2c), 2-[(crotyloxy)methyl]-4,4-dimethyl-2-oxazolines (*Tetrahedron Lett.*, in press), and crotyl benzyl sulfides (unpublished), which all exhibit only low-to-moderate degrees of stereoselection. To explain the opposite sense of diastereoselection, an entirely different transition-state model should be considered.

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Enantioselective Allylation of Aldehydes with an Optically Active Allylsilane[1]

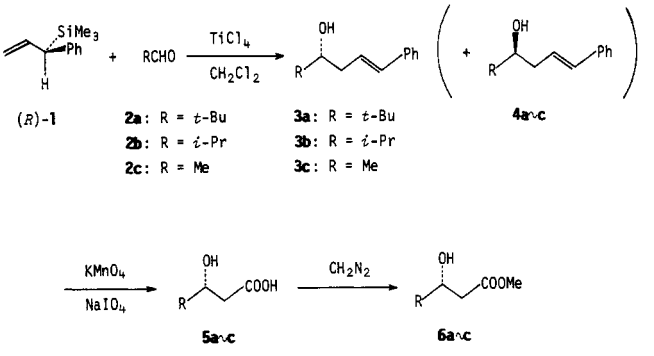
Summary: Reaction of aldehydes with an optically active allylsilane, (*R*)-3-phenyl-3-(trimethylsilyl)propene, in the presence of titanium chloride has been found to proceed with high enantioselectivity to produce optically active homoallylic alcohols of up to 91% ee.

Sir: There has been intense interest and activity in enantioselective addition of organometallics to prochiral carbonyl compounds.[2] Enantioselective allylation must be especially promising because the produced optically active homoallylic alcohols can be converted into various useful compounds such as β-hydroxy acids.[3] We report here highly stereoselective allylation using an optically active allylsilane.

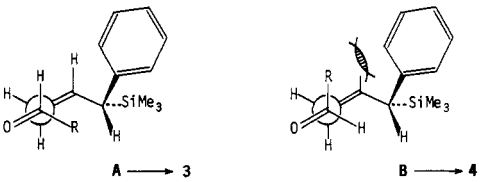
(*R*)-3-Phenyl-3-(trimethylsilyl)propene (**1**), which was prepared by an asymmetric Grignard cross-coupling with a chiral (ferrocenylphosphine)palladium catalyst,[4] was allowed to react with pivalaldehyde (**2a**), isobutyraldehyde (**2b**), and acetaldehyde (**2c**) in the presence of titanium tetrachloride in dichloromethane.[5] Optically active homoallylic alcohols **3a–c** with the carbon–carbon double bond of *E* configuration[6] were produced in good yields (Scheme I). The reaction conditions and results are summarized in Table I, which also contains methods of determining the absolute configuration and enantiomeric purity of the alcohols **3**. The following significant features are noteworthy. (1) The present allylation proceeded with high enantioselectivity (>95%) in the reaction with aldehydes **2a** and **2b** containing larger alkyl groups (R = *t*-Bu and *i*-Pr), and hence the homoallylic alcohols of very high enantiomeric purity could be obtained (entries 1, 3, and 4). (2) The enantioselectivity decreased to 70% in the reaction with acetaldehyde (**2c**, R = Me; entry 5). (3) Higher reaction temperature lowered the selectivity (entry 2). (4) The aldehydes **2a–c** were all attacked on their *re* face preferentially by the allylsilane (*R*)-**1**, giving rise to **3** over their enantiomers **4**.

The stereochemistry of S_E' reaction of allylsilanes has been established to be anti (electrophiles enter the double bond from the side opposite to the leaving silyl group),[4,7]

Scheme I



Scheme II



R = *t*-Bu, *i*-Pr: **A** >> **B**. R = Me: **A** > **B**

(1) Optically Active Allylsilanes. 4. For part 3, see Hayashi, T.; Ito, H.; Kumada, M. *Tetrahedron Lett.* **1982**, *23*, 4605.

(2) For example, see (a) Seebach, D.; Crass, G.; Wilka, E.-M.; Hilvert, D.; Brunner, E. *Helv. Chim. Acta* **1979**, *62*, 2695. (b) Mukaiyama, T. In "Asymmetric Reactions and Processes in Chemistry"; Eliel, E. L., Otsuka, S., Ed.; American Chemical Society: Washington, DC, 1982; ACS Symp. Ser. No. 185, Chapter 2.

(3) Enantioselective allylation by use of chiral allylborane derivatives has been reported: (a) Herold, T.; Schrott, U.; Hoffmann, R. W. *Chem. Ber.* **1981**, *114*, 359. (b) Hoffmann, R. W.; Herold, T. *Chem. Ber.* **1981**, *114*, 375. (c) Midland, M. M.; Preston, S. B. *J. Am. Chem. Soc.* **1982**, *104*, 2330.

(4) Hayashi, T.; Konishi, M.; Ito, H.; Kumada, M. *J. Am. Chem. Soc.* **1982**, *104*, 4962.

(5) The reaction was carried out according to the reported procedure: (a) Hosomi, A.; Sakurai, H. *Tetrahedron Lett.* **1976**, 1295. (b) Fleming, I.; Paterson, I. *Synthesis* **1979**, 446.

(6) Uncontaminated with *Z* olefin within the limits of detection.

(7) Hayashi, T.; Konishi, M.; Kumada, M. *J. Am. Chem. Soc.* **1982**, *104*, 4963.

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