- 1 for the desired, adducted pentamer. CD and UV spectra of the normal and adducted pentamers are shown in Figure 3.

**Formation of $N_6$ Adducts from 1,2,3,4-Tetrahydrophenanthrene-3,4-epoxide and 2'-Deoxyadenosine 5'-Monophosphate.** Procedures previously described[7,8] for analytical scale preparation of adducts from analogous PAH diol epoxides were used. The racemic epoxide (20 mg, 100 μmol) was dissolved in 5 mL of acetone and added in two equal portions, at time zero and 1 h, to 50 mL of an aqueous solution containing 1.0 g of 2'-deoxyadenosine 5'-monophosphate at pH 7.1 and 37 °C. After ca. 20 h at 37 °C, the reaction mixture was washed with 3 approximately equal volumes of EtOAc followed by 1 volume of ether to remove hydrolysis products of the epoxide. After removal of organic solvents by purging with $N_2$, the aqueous solution was divided into two portions and passed through two $C_{18}$ Sep-paks (Waters Associates), which were washed with water to remove most of the unreacted nucleotide, prior to elution of the modified nucleotides with MeOH. The MeOH eluate was evaporated to dryness. The residue was dissolved in 50 mM Tris-HCl buffer (pH 8.8) and treated with *E. coli* alkaline phosphatase (40 units in two equal portions at time zero and 3 h) over a period of 5.5 h. No change in the composition of the crude enzymatic reaction mixture between 3 and 5.5 h of reaction time was observed upon reverse-phase HPLC. The mixture was filtered and adsorbed on a $C_{18}$ Sep-pak, which was washed with water and then eluted with ca. 20 mL of MeOH. The methanolic solution containing the nucleoside adducts was separated by HPLC on a Beckman Ultrasphere ODS column (5μ, 10 × 250 mm), eluted at 3 mL/min with 58% MeOH in water for 10 min followed by a linear gradient that increased the MeOH composition to 75% over 10 min. Adducts were formed in a ratio of 1:1:1:0.5 (by integration at 285 nm) with retention times as follows: *trans*-(3*S*,4*S*), 10.5 min; *trans*-(3*R*,4*R*), 12.0 min; *cis*-(3*R*,4*S*), 18.2 min; *cis*-(3*S*,4*R*), 19.3 min. Assignment of relative configuration was based on the NMR spectra of the adducts as their triacetates (vide infra), whereas assignment of absolute configuration was based on exclusive formation of the second- and third-eluting adducts from optically active (-)-tetrahydrophenanthrene-(3*R*,4*S*)-epoxide. CD spectra of the adducts prepared from this enantiomer were identical with those of the corresponding adducts derived from the racemic epoxide.

The four adducts from the racemic epoxide were characterized by their CD spectra in MeOH as well as by the $^1$H NMR spectra (500 MHz, $(CD_3)_2CO$) of their triacetates (overnight reaction at room temperature with pyridine/$Ac_2O$), which were purified when necessary by HPLC on a Du Pont Golden Series SIL column (6.2 × 80 mm) eluted at 2.5 mL/min with $CH_2Cl_2$/EtOAc/MeOH (95/5/2): $k'$ (*trans*-(3*S*,4*S*)-adduct), 3.5; $k'$ (both *cis*-adducts), 2.8. Yields and concentrations of the four adducts were estimated from their UV spectra in MeOH by use of $\epsilon_{278\,nm}$ = 2988, as determined for the analogous compound **5**.

**(3*S*,4*S*)-$N_6$-(4-(3-Hydroxy-1,2,3,4-tetrahydrophenanthrenyl))-2'-deoxyadenosine (9 μmol, 9%)**: CD Δε 260 nm, -1.2; 225 nm, 13.8; 210 nm, -7.6; $^1$H NMR of the triacetate 8.47 (br s, $H_{8''}$), 8.12 (br s, $H_{2''}$), 7.8-7.9, 7.3-7.4 (aromatic), 7.20 (br s, N*H*), 6.47 (app. t, $H_{1'}$, $J_{1',2'}$ = 6.4), 6.18 (br s, $H_4$), 5.50 (dt, $H_{3'}$, $J_{2',3'}$ = 2.2, 6.4, $J_{3',4'}$ = 2.2), 5.45 (dt, $H_3$, $J_{2,3}$ = ~4, $J_{3,4}$ = 2.4), 4.38 (dd, $H_{5'}$, $J_{4',5'}$ = 6.7, $J_{gem}$ = 13.6), 4.31 (m, $H_{4',5'}$), 2.2-3.2 ($CH_2$), 2.10, 2.00, 1.98 (3 s, 3 OAc); FAB MS of the triacetate 574 (M + 1). The $^1$H NMR spectrum of compound **4** after desilylation and acetylation of the sugar hydroxyl groups was identical with that determined for this adduct.

**(3*R*,4*R*)-$N_6$-(4-(3-Hydroxy-1,2,3,4-tetrahydrophenanthrenyl))-2'-deoxyadenosine (8 μmol, 8%)**: CD Δε 258 nm, 1.1; 225 nm, -12.1; 210 nm, 7.9; $^1$H NMR of the triacetate 8.45 (br s, $H_{8''}$), 8.10 (br s, $H_{2''}$), 7.8-7.9, 7.3-7.4 (aromatic), 7.15 (br s, N*H*), 6.47 (app., t, $H_{1'}$, $J_{1',2'}$ = 6.4), 6.19 (br s, $H_4$), 5.51 (dt, $H_{3'}$, $J_{2',3'}$ = 2.1, 6.4, $J_{3',4'}$ = 2.1), 5.45 (dt, $H_3$, $J_{2,3}$ = ~4, $J_{3,4}$ = ~2.5), 4.39 (dd, $H_{5'}$, $J_{4',5'}$ = 6.4, $J_{gem}$ = 13.4), 4.31 (m, $H_{4',5'}$), 2.2-3.2 ($CH_2$), 2.10, 2.00, 1.98 (3 s, 3 OAc); FAB MS of the triacetate 574 (M + 1).

**(3*R*,4*S*)-$N_6$-(4-(3-Hydroxy-1,2,3,4-tetrahydrophenanthrenyl))-2'-deoxyadenosine (9 μmol, 9%)**: CD Δε 266 nm, -1.3; 225 nm, 15.5; 210 nm, -8.6; $^1$H NMR of the triacetate 8.45 (s, $H_{8''}$), 8.10 (s, $H_{2''}$), 7.8-7.95, 7.3-7.4 (aromatic), 7.10 (br d, N*H*, $J_{NH,4}$ = 9), 6.71 (m, $H_4$, $J_{NH,4}$ = 9, $J_{3,4}$ = 4.0), 6.45 (dd, $H_{1'}$, $J_{1',2'}$ = 6.1, 7.9), 5.49 (dt, $H_{3'}$, $J$ = 2.2, 6.4), 5.34 (dt, $H_3$, $J_{2eq,3}$ = $J_{3,4}$ = 3.7, $J_{2ax,3}$ = 13.4), 4.35 (dd, $H_{5'}$, $J_{4',5'}$ = 6.4, $J_{gem}$ = 13.1), 4.30 (m, $H_{4',5'}$), 2.2-3.3 ($CH_2$), 2.10, 2.00, 1.77 (3 s, 3 OAc); FAB MS of the triacetate 574 (M + 1).

**(3*S*,4*R*)-$N_6$-(4-(3-Hydroxy-1,2,3,4-tetrahydrophenanthrenyl))-2'-deoxyadenosine (4 μmol, 4%)**: CD Δε 266 nm, 0.9; 225 nm, -16.6; 210 nm, 8.8; $^1$H NMR of the triacetate 8.45 (s, $H_{8''}$), 8.10 (s, $H_{2''}$), 7.8-7.95, 7.3-7.4 (aromatic), 7.10 (br d, N*H*, $J_{NH,4}$ = 9), 6.71 (m, $H_4$, $J_{NH,4}$ = 9, $J_{3,4}$ = 3.7), 6.45 (dd, $H_{1'}$, $J_{1',2'}$ = 6.4, 7.9), 5.49 (dt, $H_{3'}$, $J$ = 2.1, 6.1), 5.34 (dt, $H_3$, $J_{2eq,3}$ = $J_{3,4}$ = 3.7, $J_{2ax,3}$ = 13.1), 4.38 (dd, $H_{5'}$, $J_{4',5'}$ = 6.3, $J_{gem}$ = 13.3), 4.30 (m, $H_{4',5'}$), 2.2-3.3 ($CH_2$), 2.10, 2.00, 1.78 (3 s, 3 OAc); FAB MS of the triacetate 574 (M + 1).

**Acknowledgment.** We expressly thank Dr. K. Lesiak, NIDDK, NIH for advice on the manual synthesis of oligonucleotides on solid supports, Dr. W. M. Egan and C. A. Ronald at the Center for Biologics Evaluation and Research, FDA for assistance in the use of their automated oligonucleotide synthesizer, and Dr. L. K. Pannell and Y. Murata, NIDDK, NIH for determining FAB mass spectra of the oligonucleotides.

# Diastereofacial Selectivity with Optically Active α-Substituted β-Silyl-(*E*)-hexenoates. Enantioselective Construction of Homoallylic Ethers via Reaction with Aryl Acetals

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*Contribution from the Department of Chemistry, Metcalf Center for Science and Engineering, Boston University, Boston, Massachusetts 02215.* *Received December 24, 1990*

**Abstract:** The Lewis acid catalyzed reactions of optically active methyl α-methoxy- and α-methyl-β-(dimethylphenylsilyl)-(*E*)-hexenoates **1a-d** with aryl acetals are described. These reagents function as effective carbon nucleophiles in highly diastereo- and enantioselective addition reactions to activated acetals. The reaction constitutes a one-step construction of functionalized hexenoic acid derivatives **3**, containing three stereocenters, an *E*-double bond, and a terminal carbomethoxy group. The two new stereocenters (5,6-syn) have emerged with excellent levels of absolute stereochemical control with ee's reaching 95%.

Over the past several years many laboratories have focused on the development of chiral allyl- and crotylmetal reagents as propionate enolate equivalents for enantioselective carbon-carbon bond formation in the aldol-like construction of homoallylic al-

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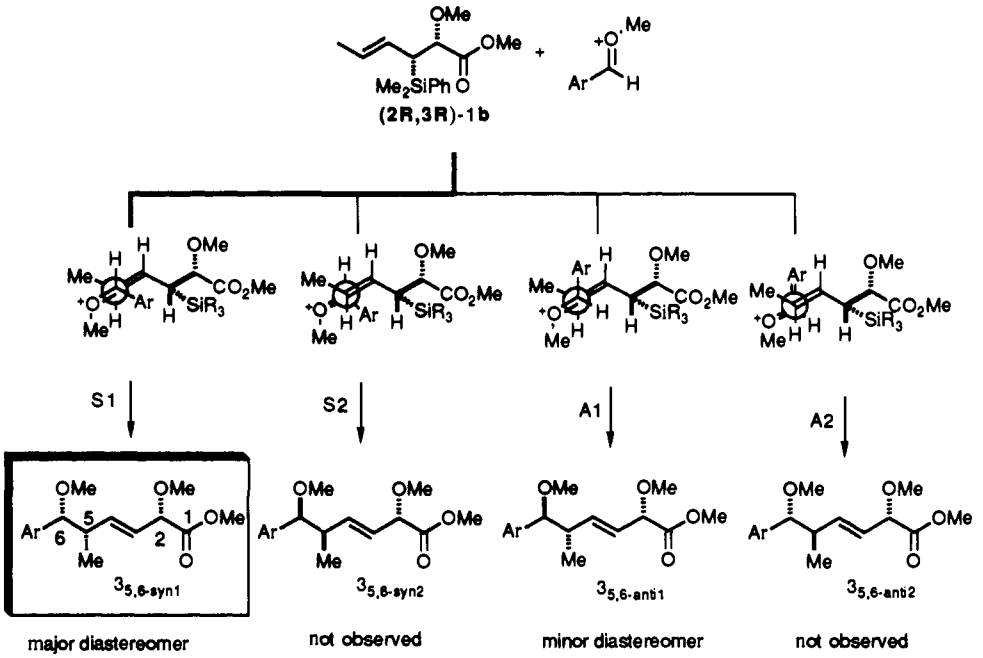
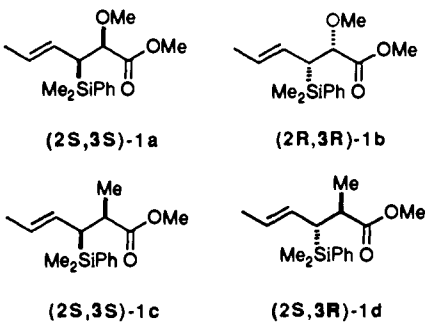
**Scheme I**




cohols.[1] These reagents have played a complementary role to the asymmetric aldol process and consequently are among the most important groups of organometallic reagents available for the stereoselective formation of optically active homoallylic alcohols.[2] Despite the enormous utility that allylsilanes have demonstrated in organic chemistry, few examples have been reported addressing the issue of acyclic diastereofacial selectivity in addition reactions to C=X π bonds.[3] This fact probably results from the lack of a reliable method to obtain useful quantities of enantiomerically pure reagents with the unequivocal assignment of absolute configuration.[4] Therefore research efforts which would provide new methods for the production of such reagents and make possible the development of new asymmetric transformations would necessarily constitute a valuable contribution to the field of asymmetric synthesis.[5] Herein we report the findings of our experiments concerning the utility of optically active α-methoxy- and α-methyl-β-(dimethylphenylsilyl)-(*E*)-hexenoates **1a–d**. These reagents function as carbon nucleophiles in highly enantioselective addition reactions to aryl oxonium ions derived by the action trimethylsilyl trifluoromethanesulfonate (TMSOTf)[6] or boron trifluoride etherate ($BF_3{\cdot}OEt_2$)[7] on the corresponding aryl dimethylacetals.




As originally deduced by Hayashi and co-workers,[5] π-facial selectivity involving addition reactions of chiral allylsilanes is perhaps best explained by an $S_E'$ mechanism.[8] This may be described by an open transition-state model as illustrated for the silane (2*R*,3*R*)-**1b** in Scheme I. In this arrangement the C–Si bond is positioned anti to the oxonium ion and coplanar to the *p*-orbitals of the adjacent π-bond allowing stabilization of the emerging secondary carbocation.[9] The proper orientation of the vinylmethyl and silicon groups with respect to the aldehyde substituent is essential to obtain useful levels of both simple diastereoselection [5,6-syn$_1$ and 5,6-syn$_2$ vs 5,6-anti$_1$ and 5,6-anti$_2$] and π-facial selection (enantioselection) [5,6-syn$_1$ vs 5,6-syn$_2$ or 5,6-anti$_1$ vs 5,6-anti$_2$] during addition to the activated acetal as illustrated in Scheme I.

**Synthesis of (*E*)-Crotylsilanes 1a–d and Results of Enantioselective Addition Reactions.** Equations 1–4 illustrate how the

(1) Reviews on allylmetal chemistry: (a) Hoffman, R. W. *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 555. (b) Yamamoto, Y.; Maruyama, K. *Heterocycles* **1982**, *18*, 357. For detailed reports of the use of chiral crotylboronates in addition reactions to aldehydes, see: (c) Roush, W. R.; Hoong, L. K.; Palmer, M. A. J.; Park, J. C. *J. Org. Chem.* **1990**, *55*, 4190. (d) Roush, W. R.; Hoong, L. K.; Palmer, M. A. J.; Straub, J. A.; Palkowitz, A. D. *J. Org. Chem.* **1990**, *55*, 4117. (e) Roush, W. R.; Ando, K.; Powers, D. B.; Palkowitz, A. D.; Halterman, R. L. *J. Am. Chem. Soc.* **1990**, *112*, 6339. (f) Roush, W. R.; Palkowitz, A. D.; Ando, K. *J. Am. Chem. Soc.* **1990**, *112*, 6348 and references cited therein.

(2) (a) Evans, D. A. *Aldrich. Acta* **1982**, *15*, 23. (b) Evans, D. A.; Takacs, J. M.; McGee, M. D.; Ennis, D. J.; Mather, D. J.; Bartroli, J. I. *Pure Appl. Chem.* **1981**, *53*, 1109. (c) Evans, D. A.; Nelson, J. V.; Taber, T. R. *Top. Stereochem.* **1982**, *13*, 1.

(3) For recent reviews on the chemistry of allylsilanes, see: (a) Fleming, I. *Org. React.* **1989**, *37*, 57. (b) Majetich, G. *Organic Synthesis: Theory and Application*; 1989; Vol. 1, p 173. (c) Birkofer, L.; Stuhl, O. In *The Chemistry of Organic Silicon Compounds*; Patai, S., Rappoport, Z., Eds.; Wiley and Sons Ltd.: 1989; Chapter 10. (d) Sakurai, H. *Pure Appl. Chem.* **1982**, *54*, 1.

(4) (a) Hayashi, T.; Konishi, M.; Fukushima, M.; Mise, T.; Hagotani, M.; Tajika, M.; Kumada, M. *J. Am. Chem. Soc.* **1982**, *104*, 180. (b) Panek, J. S.; Sparks, M. A. *Tetrahedron Asymmetry* **1990**, *1*, 801.

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

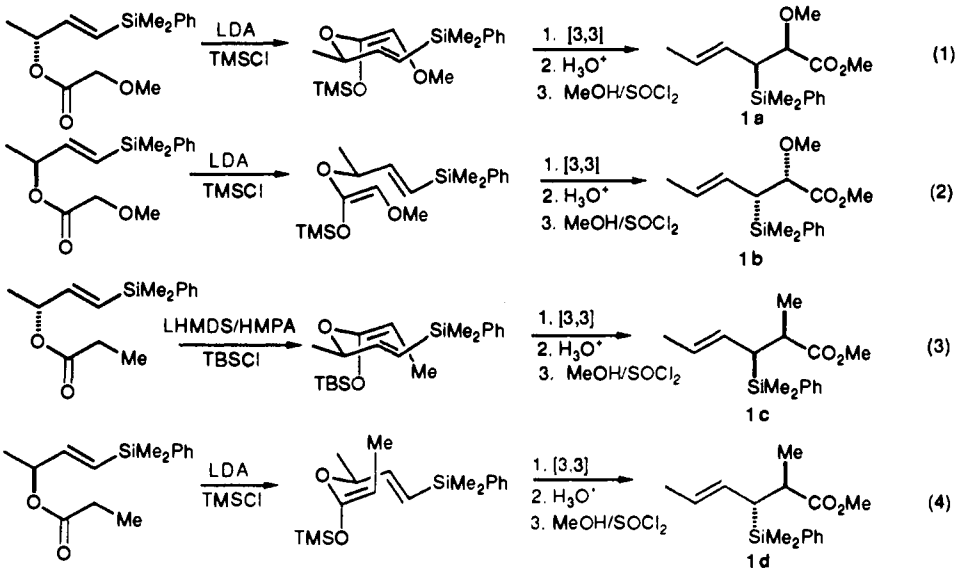
(6) Tsunoda, T.; Suzuki, M.; Noyori, R. *Tetrahedron Lett.* **1980**, *21*, 71.

(7) Hosomi, A.; Endo, M.; Sakurai, H. *Chem. Lett.* **1976**, 941. (b) Hosomi, A.; Endo, M.; Sakurai, H. *Chem. Lett.* **1973**, 499. (c) Ojima, I.; Kumagai, M. *Chem. Lett.* **1978**, 575. During these studies we have found that the use of TMSOTf in catalytic or equal molar quantities gave cleaner reaction products in higher yields than with the use of $BF_3{\cdot}OEt_2$.

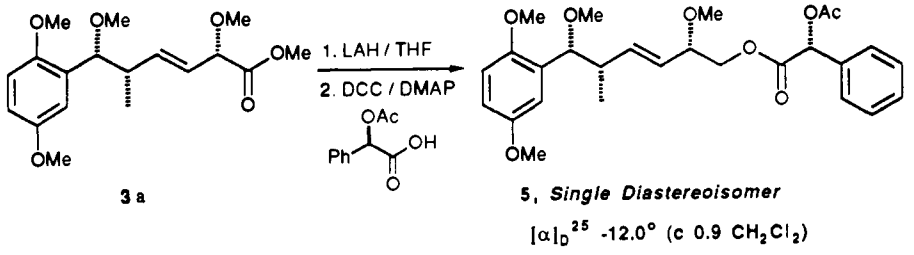
(8) Optically active α-alkoxycrotylstannanes have been shown to undergo $BF_3{\cdot}OEt_2$-catalyzed additions to adehydes via an $S_E'$ pathway, cf.: Marshall, J. A.; Gung, W. Y. *Tetrahedron* **1989**, *45*, 1043.

(9) The precise contribution of steric and electronic effects of the dimethylphenylsilyl group of the (*E*)-crotylsilane to the stereoselectivity of the reaction, either in its transition state structure or the ground state, are, of course, not known. However, for allylsilanes the conformational requirements seem to be well-defined; for maximum stabilization of the carbocation β to the silicon group it is necessary for the C–Si bond to be orientated antiperiplanar to the emerging empty p-orbital (see ref 3a for a detailed discussion).

**Scheme II**




**Scheme III**




Claisen strategy is used to construct the optically active (*E*)-crotylsilanes **1a–d**. Thus crotylsilane **1a**, $[\alpha]^{23}_D = +14.2°$ (*c* 1.0, $CH_2Cl_2$), was prepared from the corresponding (*R*)-vinylsilane as previously described,[10] by an Ireland Ester Claisen rearrangement [(i) LDA (1.7 equiv)/THF/−78 °C, (ii) TMSCl (10.8 equiv)/pyridine (11.9 equiv), (iii) $MeOH/SOCl_2$][11] in 80% yield after esterification. In the same manner **1b** was produced from the (*S*)-vinylsilane in 81% yield, $[\alpha]^{23}_D$ −12.5° (*c* 1.0, $CH_2Cl_2$). Compounds (2*S*,3*S*)-**1c**, $[\alpha]^{23}_D = +10.6°$ (*c* 0.7, $CH_2Cl_2$) [(i) LHMDS (2.0 equiv)/THF/−78 °C, then TBDMSCl (2.0 equiv) and HMPA, −78 °C to room temperature then reflux, (ii) $MeOH/SOCl_2$], and (2*R*,3*S*)-**1d** $[\alpha]^{23}_D = -28°$ (*c* 0.8, $CH_2Cl_2$) [(i) LDA (1.7 equiv)/THF/−78 °C, (ii) TMSCl (10.8 equiv)/pyridine (11.9 equiv), (iii) $MeOH/SOCl_2$][9,10] were prepared in 81 and 69% yield, respectively.

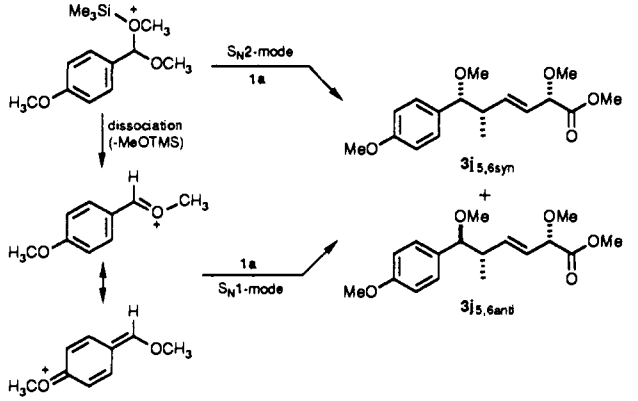
A summary of the experiments describing the enantioselective addition reactions of α-methoxy- and α-methyl-β-(dimethylphenylsilyl)hexenoates **1a–d** to a series of related aryl acetals **2a–f** is given in Table I. The use of TMSOTf ($CH_2Cl_2$/−78 °C) was found to be most effective in promoting the addition reactions which were typically complete in 6 h. For the cases examined, the reaction rate and diastereoselection (5,6-anti/5,6-syn ratio) were dependent on two factors: the oxygenation pattern of the aryl acetal and the amount of Lewis acid used. For instance, the reaction of *p*-methoxybenzaldehyde dimethylacetal (**2f**, Table I, entry 10) was very sluggish and showed almost no selectivity.[12] Similarly, benzaldehyde dimethylacetal (**2b**, Table I, entries 3 and 4) showed lower levels of selectivity (13:1 syn/anti) than the other examples. These results support the notion that an $S_N1$ pathway is the operative mechanism. In such a case addition occurs through an oxonium ion derived by dissociation of the activated acetal.[13] When more than 1 equiv of Lewis acid was used a loss of diastereoselection was observed regardless of the reaction temperature. With one exception (entry 10, Table I) the (*E*)-crotylsilanes exhibited excellent levels of diastereo- and enantioselection in the addition reactions. For the examples shown, the enantiomeric excess was consistently determined to be 95% when the amount of TMSOTf was kept at or below 1.0 equiv.[14]

(10) Sparks, M. A.; Panek, J. S. *J. Org. Chem.* **1991**, *56*, 3431.

(11) Barrish, J. C.; Lee, H. L.; Mitt, T.; Pizzolato, G.; Baggiolini, E. G.; Uskokovic, M. R. *J. Org. Chem.* **1988**, *53*, 4282.

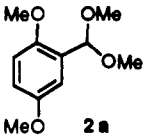
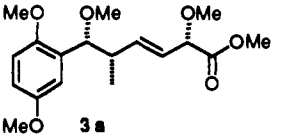
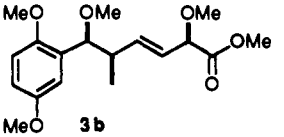
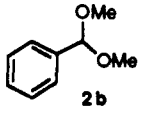
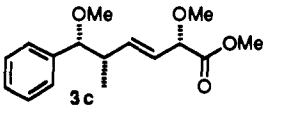
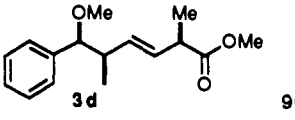
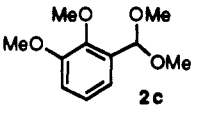
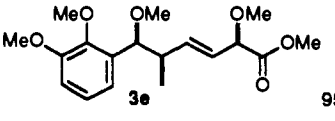
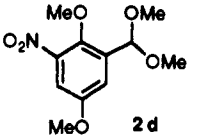
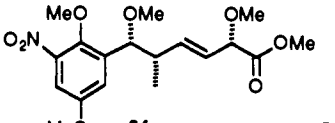
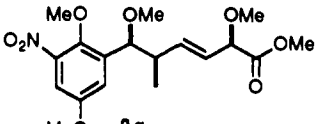
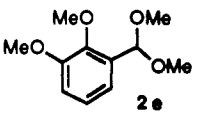
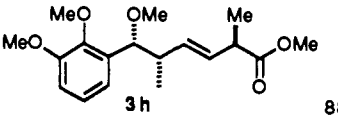
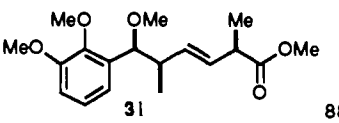
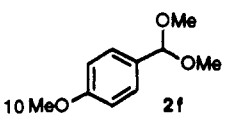
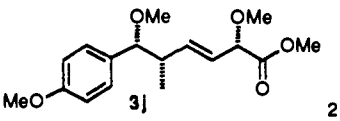
(12) Determination of simple diastereoselection was accomplished by a two-step oxidation–reduction sequence of the *E*-double bond [(i) $O_3$/$CH_2Cl_2$/MeOH/−78 °C; (ii) $NaBH_4$, −78 °C → room temperature of compounds **3c,d,j**. These experiments produced the 3-methoxy-2-methylpropanol derivatives which exhibited identical ratios of 2,3-syn and 2,3-anti diastereomers as those observed in the addition products **3**.

(13) Denmark S. E.; Wilson, T. M. *J. Am. Chem. Soc.* **1989**, *111*, 3475. If the reaction were proceeding through the alternative $S_N2$ pathway, the para substitution pattern of **2f**, maybe expected to increase the rate of reaction by increasing the positive character at the reaction center (benzylic cation). The fact that the rate is considerably slower (20% yield after 30 h) indicates that the added stabilization provided by the *p*-methoxy group results in an overall increase in the transition-state energy, $\Delta G^{\ddagger}$, which is responsible for the loss of diastereoselectivity.



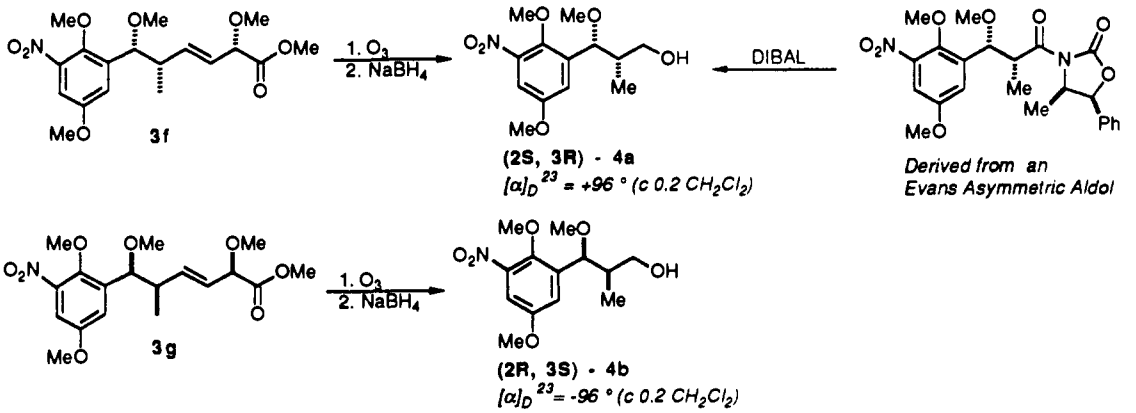

(14) When catalytic or equal molar amounts of TMSOTf or $BF_3{\cdot}OEt_2$ were used, only traces of the desired addition product **3j** were detected by $^1H$ NMR analysis of the crude reaction mixture.

**Table I.** Enantioselective Additions of Optically Active (*E*)-Crotylsilanes to Aryl Acetals

| entry | acetal[a] | (E)-crotylsilane[b] | reaction cond't. #equiv TMSOTf /Time[c] | major diastereomer[d] | %yield[e] | 5,6-syn/anti ratio[f] | $[\alpha]_D^{23}$ | %ee[g] |
|---|---|---|---|---|---|---|---|---|
| 1 |  **2a** | 1b | 0.2 / 6h |  **3a** | 92 | 40:1 | +69 ° | 95 |
| 2 | **2a** | 1a | 0.2 / 6h |  **3b** | 94 | 40:1 | -67 ° | 95 |
| 3 |  **2b** | 1b | 1.0 / 13h |  **3c** | 90 | 13:1 | -- | 95 |
| 4 | **2b** | 1c | 1.0 / 13h |  **3d** | 90 | 13:1 | -- | 95 |
| 5 |  **2c** | 1a | 1.0 / 6h |  **3e** | 95 | 40:1 | -66 ° | 95 |
| 6 |  **2d** | 1b | 1.0 / 8h |  **3f** | 95 | 30:1 | +98 ° | 95 |
| 7 | **2d** | 1a | 1.0 / 8h |  **3g** | 95 | 30:1 | -94 ° | 95 |
| 8 |  **2e** | 1d | 1.0 / 6h |  **3h** | 88 | 30:1 | +7.5 ° | 95 |
| 9 | **2e** | 1c | 1.0 / 6h |  **3i** | 88 | 30:1 | -41 ° | 95 |
| 10 |  **2f** | 1b | 2.0 / 30h |  **3j** | 20 | 2:1 | -- | 95 |

[a] With the exception of **2b** (Aldrich), the dimethylacetals were prepared from the corresponding aldehydes [$CeCl_3 \cdot 7H_2O$ (1.0 equiv)/$HC(OMe)_3$/MeOH/room temperature]. [b] The (*E*)-crotylsilanes were obtained from a Claisen rearrangement on the (*E*)-vinylsilane, see ref 9. [c] All reactions were run in $CH_2Cl_2$ at 0.2–0.25 M in substrate with 2.0 equiv of acetal. [d] The absolute stereochemistry of the major diastereomer assigned based on the anti addition [$S_E'$ mechanism] of the optically active (*E*)-crotylsilanes to the C=X π-bond as described in the text. [e] All yields are based on pure materials isolated by chromatography on $SiO_2$. [f] Ratio of products was determined by $^1H$ NMR (400 MHz), operating at an S/N ratio of >200:1. [g] Optical purities were determined by $^1H$ NMR (400 MHz) analysis of the addition products after chromatography on $SiO_2$ (plug) to remove hydrolyzed acetal and refer to product ratios for $5,6syn_1/5,6syn_2$ as illustrated in Scheme I.

Scheme IV




**Determination of Enantiomeric Excess and Absolute Stereochemical Assignment.** The % ee determinations were performed by proton NMR analysis of the addition products **3**. Since the C2-stereocenter $\alpha$ to the ester group does not show any appreciable signs of epimerization under the described reaction conditions, it serves as a stereochemical indicator which allows the detection of a stereochemical defect associated with the formation of the other facial isomer (anti $S_E'$/syn $S_E'$ addition modes). A loss of $\pi$-face selection would be manifested in the production of the other diastereofacial isomers as illustrated in Scheme I with the formation of $\mathbf{3}_{5,6\text{-syn}_2}$ through transition-state S2 and $\mathbf{3}_{5,6\text{-anti}_1}$ through transition-state A1. To verify this analysis we performed a Mosher analysis[15] on one of the addition products, (2*S*,5*S*,6*R*)-(*E*)-methyl 6-(2,5-dimethoxyphenyl)-2,6-dimethoxy-5-methylhex-3-enoate (**3a**). Thus reduction of the methyl ester with $LiAlH_4$ (1.0 equiv/THF/0 °C) followed by esterification of the derived primary alcohol with (*R*)-*O*-acetyl mandelic acid[16] [1.0 equiv/DCC (1.0 equiv)/catalytic DMAP/$CH_2Cl_2$] afforded the new mandelate ester **5** in 91% yield (two steps) as a single diastereomer as determined by proton NMR operating at a signal-to-noise level >200:1, Scheme III.

The absolute stereochemical assignment of the two new vicinal stereocenters ($C_5$,$C_6$) of the addition products is based on the following documentation. First, the fact that electrophilic substitution reactions of optically active allylsilanes proceed through an $S_E'$ mechanism (anti attack).[3a,c,5a,b] Assuming silanes **1a–d** follow the same mechanistic pathway, the (5*R*,6*S*) products are derived from the (2*R*,3*R*)-(*E*)-crotylsilanes **1a,c** and the (5*S*,6*R*) stereoisomers are derived from the (2*R*,3*S*)-(*E*)-crotylsilanes **1b** and **d**.

As illustrated in Scheme IV, the absolute stereochemistry of the addition products was confirmed by correlation with (2*S*,3*R*)-3-(2,5-dimethoxy-2-nitrophenyl)-3-methoxy-2-methyl-1-propanol (**4a**), $[\alpha]^{23}_D$ = +98.6 (*c* 0.96 $CH_2Cl_2$), produced by an asymmetric aldol reaction with the norephedrine derived propanoyl oxazolidone chiral enolate synthon.[17] For completeness we also synthesized the enantiomer of **4a**, (2*R*,3*S*)-3-(2,5-dimethoxy-2-nitrophenyl)-3-methoxy-2-methyl-1-propanol (**4b**); it was found to have an optical rotation with the same magnitude but opposite in sign. Thus, the double bond of (2*S*,5*S*,6*R*)-(*E*)-methyl 6-(2,5-dimethoxy-3-nitrophenyl)-2,6-dimethoxy-5-methylhex-3-enoate (**3f**) and (2*R*,5*R*,6*S*)-(*E*)-methyl 6-(2,5-dimethoxy-3-nitrophenyl)-2,6-dimethoxy-5-methylhex-3-enoate (**3g**) was subjected to a two-step oxidation–reduction sequence [(i) $O_3$/MeOH–$CH_2Cl_2$/−78 °C, (ii) $NaBH_4$ (1.0 equiv) −78 °C → room temperature] producing the desired primary alcohols **4a** and **4b** in 82 and 87% yield, respectively.

These reagents exhibit several features which should allow for their further development and utilization in asymmetric synthesis. They are available in optically active form through the well-documented Ireland Ester Claisen rearrangement which, due to its inherent flexibility will allow us to address the preparation of a variety of (*E*)-crotylsilanes of this structural type.[10,18] The dimethylphenylsilyl group was chosen because of its effectiveness in the preparation of the Claisen precursors (vinylsilanes) and the fact that it exhibits useful levels of topological bias in allylsilane diastereoface selection. The examples show that the levels of $\pi$-facial selection are independent of the relative stereochemistry (syn/anti) of the $\alpha$ and $\beta$ substituents on the (*E*)-crotylsilanes, a point which may have broader implications as these silane reagents reach further stages of development (Table I, entries 1, 2 and 6, 7). The data support the notion that the stereocenter bearing the dimethylphenylsilyl group is primarily responsible for the observed enantioselection.

In conclusion, we have shown that the enantiomerically pure (*E*)-crotylsilanes are well suited to produce homoallylic ethers with high levels of diastereo- and enantioselectivity. We believe the transformations illustrated in the table are truly significant in the context of acyclic diastereoselection. We are unaware of another method by which to construct such highly functionalized acyclic chains with the observed levels of enantioselection and efficiency. The ability of these reagents to accomplish the simultaneous and highly stereoselective introduction of two stereocenters, adjacent to either end of the trans double bond demonstrates considerable synthetic potential and opens up many new possibilities for the controlled introduction of remote stereocenters. Collectively, these examples support the thesis that chiral allylsilanes can be used as an effective stereocontrolling element in acyclic diastereofacial selective reactions. Further exploration of these reagents and their applications is now underway in our laboratories.

## Experimental Section[19]

**General Experimental Procedure for Enantioselective Additions of Optically Active (*E*)-Crotylsilanes to Aryl Acetals. Illustrated for Compound 3a.** A solution of the 2,5-dimethoxybenzaldehyde dimethylacetyl (2.0 mmol, 403 mg) in 10 mL dry methylene chloride (0.2 M) was cooled to −78 °C and treated with trimethylsilyl trifluoromethanesulfonate (0.3 mmol, 0.06 mL). The red-orange solution was stirred for 10 min and (*E*)-(2*R*,3*R*)-methyl 3-(dimethylphenylsilyl)-2-methoxyhex-4-enoate (**1b**, 1.7 mmol, 500 mg) was added. The reaction mixture left stirring for 6 h at −78 °C and diluted with saturated sodium bicarbonate solution. This solution was stirred for 2 min before being extracted with $Et_2O$ (2 × 25 mL). After the organic layer was dried with magnesium sulfate and filtered and the solvent was removed under reduced pressure, the crude oil was flash chromatographed[20] on silica gel to afford (2*S*,5*S*,6*R*)-(*E*)-methyl 6-(2,5-dimethoxyphenyl)-2,6-dimethoxy-5-methylhex-3-

(15) Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512.

(16) (a) Whitesell, J. K.; Reynolds, D. *J. Org. Chem.* **1983**, *48*, 3548. (b) The optical purity of D-(−)-mandelic acid is >98% as purchased from Fluka Chemika, therefore our % ee determinations may not exceed 96%.

(17) Personal communication with Professor David A. Evans, Harvard University.

(18) For earlier reports of (*E*)-vinylsilanes undergoing Claisen reactions, see: (a) Murphy, P. J.; Proctor, G. *Tetrahedron Lett.* **1990**, *31*, 1051. (b) Proctor, G.; Russell, A. T.; Murphy, P. J.; Tan, T. S.; Mather, A. N. *Tetrahedron* **1988**, *44*, 3953. (c) Russel, A. T.; Proctor, G. *Tetrahedron Lett.* **1987**, *28*, 2041 and 2045. (d) Jenkins, P. R.; Gut, R.; Wetter, H.; Eschenmoser, A. *Helv. Chim. Acta* **1979**, *62*, 1922. (e) Claisen rearrangements on racemic glycolic esters of (*E*)-vinylsilanes, see: Sato, T.; Tsunekawa, H.; Kohama, H.; Fujisawa, T. *Chem. Lett.* **1986**, 1556.

enoate (**3a**) as a colorless film (552 mg, 92%, 605 mg theoretical) in a 5,6-syn/anti ratio of 40:1 as determined by $^1H$ NMR.

**(2S,5S,6R)-(E)-Methyl 6-(2,5-Dimethoxyphenyl)-2,6-dimethoxy-5-methylhex-3-enoate (3a).** $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.86 (d, 1 H, $J$ = 2.25 Hz), 6.76–6.73 (m, 2 H), 5.75 (dd, 1 H, $J$ = 7.57, 15.4 Hz), 5.24 (dd, 1 H, $J$ = 7.38, 16 Hz), 4.37, (d, 1 H, $J$ = 5.86 Hz), 4.03 (d, 1 H, $J$ = 7.32 Hz), 3.66 (s, 3 H), 3.65 (s, 3 H), 3.59 (s, 3 H), 3.20 (s, 3 H), 3.11 (s, 3 H), 2.45 (m, 1 H), 0.92 (d, 3 H, $J$ = 6.6 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 171.38, 153.69, 151.67, 139.73, 129.83, 123.99, 113.19, 112.74, 111.30, 111.25, 81.56, 80.58, 57.32, 56.80, 55.79, 55.75, 42.27, 15.08; IR (neat) $\nu_{max}$ 2950, 1750, 1500, 1350, 900, 800, 700 $cm^{-1}$; CIMS ($NH_3$ gas) 536.5, 356.4, 307.3, 275.2, 243.2, 182.2; CIHRMS $M^+$ (calculated for $C_{18}H_{26}O_6$) 356.2073, (found) 356.2075; $[\alpha]^{23}_D$ = +69° ($c$ 1.25, $CHCl_3$).

**(2R,5R,6S)-(E)-Methyl 6-(2,5-Dimethoxyphenyl)-2,6-dimethoxy-5-methylhex-3-enoate (3b).** $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.86 (d, 1 H, $J$ = 2.25 Hz), 6.76–6.73 (m, 2 H), 5.75 (dd, 1 H, $J$ = 7.57, 15.4 Hz), 5.24 (dd, 1 H, $J$ = 7.38, 16 Hz), 4.37 (d, 1 H, $J$ = 5.86 Hz), 4.03 (d, 1 H, $J$ = 7.32 Hz), 3.66 (s, 3 H), 3.65 (s, 3 H), 3.59 (s, 3 H), 3.20 (s, 3 H), 3.11 (s, 3 H), 2.45 (m, 1 H), 0.92 (d, 3 H, $J$ = 6.6 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 171.38, 153.69, 151.67, 139.73, 129.83, 123.99, 113.19, 112.74, 111.30, 111.25, 81.56, 80.58, 57.32, 56.80, 55.79, 55.75, 42.27, 15.08; IR (neat) $\nu_{max}$ 2950, 1750, 1500, 1350, 900, 800, 700 $cm^{-1}$; CIMS ($NH_3$ gas) 536.5, 356.4, 307.3, 275.2, 243.2, 182.2; CIHRMS $M^+$ (calculated for $C_{18}H_{26}O_6$) 356.2073, (found) 356.2075; $[\alpha]^{23}_D$ = −67° ($c$ 1.0, $CHCl_3$).

**(2S,5S,6R)-(E)-Methyl 6-Phenyl-2,6-dimethoxy-5-methylhex-3-enoate (3c).** $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.33–7.19 (m, 5 H), 5.73 (dd, 1 H, $J$ = 7.6, 16.4 Hz), 5.29 (dd, 1 H, $J$ = 7.2, 15.5 Hz), 4.05 (d, 1 H, 7.2 Hz), 3.94 (d, 1 H, 6.4 Hz), 3.67 (s, 3 H), 3.27 (s, 3 H), 3.20 (s, 3 H), 2.58–2.53 (m, 1 H), 1.07 (d, 3 H, $J$ = 6.8 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 171.07, 140.00, 148.54, 127.96, 127.38, 124.58, 87.46, 81.28, 56.92, 56.77, 52.07, 52.01, 43.14, 15.65; IR (neat) $\nu_{max}$ 2950, 1450, 1350, 900, 800, 700 $cm^{-1}$; CIMS ($NH_3$ gas) 341.2, 340.1, 308.1, 291.1, 259.1, 203.1, 181.1, 167.1; CIHRMS $M^+$ (calculated for $C_{16}H_{32}O_4$) 278.3513, (found) 278.3515.

**(2R,5R,6S)-(E)-Methyl 6-Phenyl-6-methoxy-2,5-dimethylhex-3-enoate (3d).** $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.33–7.18 (m, 5 H), 5.33–5.29 (m 2 H), 3.89 (d, 1 H, 7.2 Hz), 3.62 (s, 3 H), 3.20 (s, 3 H), 2.99–2.96 (m, 1 H), 2.48–2.46 (m, 1 H), 1.07–10.4 (m, 6 H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 175.38, 140.53, 133.81, 129.28, 127.98, 127.58, 127.43, 88.14, 57.16, 51.78, 43.48, 42.83, 17.45, 16.19; IR (neat) $\nu_{max}$ 2950, 1750, 1450, 1350 900, 800, 700 $cm^{-1}$; CIMS ($NH_3$ gas) 280.4, 248.3, 231.3, 199.2, 171.2, 143.2, 122.2, 84.0; CIHRMS $M^+$ (calculated for $C_{16}H_{22}O_3$) 280.1913, (found) 280.1889.

**(2R,5R,6S)-(E)-Methyl 6-(2,3-Dimethoxyphenyl)-2,6-dimethoxy-5-methylhex-3-enoate (3e).** $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.03 (t, 1 H, $J$ = 8.01 Hz), 6.88 (dd, 1 H, $J$ = 1.27, 7.39 Hz), 6.81 (dd, 1 H, $J$ = 1.41, 8.05 Hz), 5.81 (dd, 1 H, $J$ = 6.59, 16.2 Hz), 5.34 (dd, 1 H, $J$ = 7.35, 15.6 Hz), 4.43 (d, 1 H, $J$ = 7.59 Hz), 4.12 (d, 1 H, $J$ = 7.32 Hz), 3.86 (s, 3 H), 3.81 (s, 3 H), 3.67 (s, 3 H), 3.29 (s, 3 H), 3.19 (s, 3 H), 2.59–2.55 (m, 1 H), 1.07 (d, 3 H, $J$ = 6.84); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 171.30, 152.41, 147.44, 139.28, 134.01, 124.39, 123.81, 119.52, 111.17, 81.39, 80.82, 60.62, 57.14, 56.87, 55.70, 52.10, 42.60, 15.44; IR (neat) $\nu_{max}$ 2950, 1750, 1500, 1350, 900, 800, 700 $cm^{-1}$; CIMS ($NH_3$ gas) 356.3, 338.3, 275.2, 203.2, 182.1, 86.0, 84.0; CIHRMS $M^+$ (calculated for $C_{18}H_{26}O_6$) 356.2073, (found) 356.2071; $[\alpha]^{23}_D$ = −66° ($c$ 0.9, $CH_2Cl_2$).

**(2S,5S,6R)-(E)-Methyl 6-(2,5-Dimethoxy-3-nitrophenyl)-2,6-dimethoxy-5-methylhex-3-enoate (3f).** $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.40 (d, 1 H, $J$ = 5.67 Hz), 7.26 (d, 1 H, $J$ = 3.18 Hz), 5.91 (dd, 1 H, $J$ = 8.98, 15.6 Hz), 5.47 (dd, 1 H, $J$ = 7.06, 15.5 Hz), 4.54 (d, 1 H, $J$ = 6.53 Hz), 4.25 (d, 1 H, $J$ = 6.95 Hz), 3.84 (s, 3 H), 3.37 (s, 3 H), 3.36 (s, 3 H), 3.35 (s, 3 H), 3.33 (s, 3 H), 2.68–2.65 (m, 1 H), 1.20 (d, 3 H, $J$ = 7.78); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 171.04, 155.22, 145.52, 143.55, 138.19, 137.64, 125.23, 118.61, 109.09, 81.01, 80.53, 62.74, 57.43, 57.07, 55.96, 52.13, 43.04, 15.45; IR (neat) $\nu_{max}$ 2950, 1780, 1500, 1450, 1350, 1300, 850 $cm^{-1}$; CIMS ($NH_3$ gas) 784.1, 626.1, 594.1, 401.1, 352.1, 320.1, 226.0, 138.0; CIHRMS $M^+$ (calculated for $C_{18}H_{25}O_8N$) 401.1924, (found) 401.1955; $[\alpha]^{23}_D$ = +98° ($c$ 0.7, $CH_2Cl_2$).

**(2R,5R,6S)-(E)-Methyl 6-(2,5-Dimethoxy-3-nitrophenyl)-2,6-dimethoxy-5-methylhex-3-enoate (3g).** $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.40 (d, 1 H, $J$ = 5.67 Hz), 7.26 (d, 1 H, $J$ = 3.18 Hz), 5.91 (dd, 1 H, $J$ = 8.98, 15.6 Hz), 5.47 (dd, 1 H, $J$ = 7.06, 15.5 Hz), 4.54 (d, 1 H, $J$ = 6.53 Hz), 4.25 (d, 1 H, $J$ = 6.95 Hz), 3.84 (s, 3 H), 3.37 (s, 3 H), 3.36 (s, 3 H), 3.35 (s, 3 H), 3.33 (s, 3 H), 2.68–2.65 (m, 1 H), 1.20 (d, 3 H, $J$ = 7.78); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 171.04, 155.22, 145.52, 143.55, 138.19, 137.64, 125.23, 118.61, 109.09, 81.01, 80.53, 62.74, 57.43, 57.07, 55.96, 52.13, 43.04, 15.45; IR (neat) $\nu_{max}$ 2950, 1780, 1500, 1450, 1350, 1300, 850 $cm^{-1}$; CIMS ($NH_3$ gas) 784.1, 626.1, 594.1, 401.1, 352.1, 320.1, 226.0, 138.0; CIHRMS $M^+$ (calculated for $C_{18}H_{25}O_8N$) 401.1924, (found) 401.1955; $[\alpha]^{23}_D$ = −96° ($c$ 1.2, $CH_2Cl_2$).

**(2R,5S,6R)-(E)-Methyl 6-(2,3-dimethoxyphenyl)-6-methoxy-2,5-methylhex-3-enoate (3h).** $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.04 (t, 1 H, $J$ = 8.0 Hz), 6.89 (d, 1 H, $J$ = 1.47, 7.6 Hz), 6.81 (dd, 1 H, $J$ = 1.47, 8.20 Hz), 5.40 (dd, 1 H, $J$ = 7.62, 15.6 Hz), 5.29 (dd, 1 H, $J$ = 7.81, 13.8 Hz), 4.38 (d, 1 H, $J$ = 7.08 Hz), 3.86 (s, 3 H), 3.80 (s, 3 H), 3.67 (s, 3 H), 3.20 (s, 3 H), 2.99–2.96 (m, 1 H), 2.49–2.46 (m, 1 H), 1.08 (d, 3 H, $J$ = 7.78), 1.03 (d, 3 H, $J$ = 7.08); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 175.51, 152.42, 147.59, 134.55, 134.23, 129.15, 123.85, 119.50, 111.04, 81.31, 60.68, 57.19, 55.73, 51.78, 43.12, 42.93, 17.59, 16.10; IR (neat) $\nu_{max}$ 2950, 1750, 1500, 1350, 900, 800, 700 $cm^{-1}$; CIMS ($NH_3$ gas) 341.2, 340.1, 308.1, 291.1, 259.1, 203.1, 181.1, 167.1; CIHRMS $M^+$ (calculated for $C_{18}H_{26}O_5$) 340.2124, (found) 340.2113; $[\alpha]^{23}_D$ = +7.5° ($c$ 0.5, $CH_2Cl_2$).

**(2R,5R,6S)-(E)-Methyl 6-(2,3-Dimethoxyphenyl)-6-methoxy-2,5-dimethylhex-3-enoate (3i).** $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.04 (t, 1 H, $J$ = 8.0 Hz), 6.89 (d, 1 H, $J$ = 1.45, 7.6 Hz), 6.82 (dd, 1 H, $J$ = 1.47, 8.20 Hz), 5.43 (dd, 1 H, $J$ = 15.44, 23.8 Hz), 5.34 (dd, 1 H, $J$ = 15.63, 17.6 Hz), 4.40 (d, 1 H, $J$ = 6.78 Hz), 3.87 (s, 3 H), 3.82 (s, 3 H), 3.60 (s, 3 H), 3.20 (s, 3 H), 3.03–2.99 (m, 1 H), 2.53–2.50 (m, 1 H), 1.16 (d, 3 H, $J$ = 7.03), 1.05 (d, 3 H, $J$ = 6.78 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 175.42, 152.41, 147.57, 134.39, 128.89, 123.77, 119.66, 111.10, 81.19, 60.68, 57.16, 55.74, 51.75, 43.12, 42.85, 37.32, 17.36, 15.76; IR (neat) $\nu_{max}$ 2950, 1750, 1500, 1350, 900, 800, 700 $cm^{-1}$; CIMS ($NH_3$ gas) 341.2, 340.1, 308.1, 291.1, 259.1, 203.1, 181.1, 167.1; CIHRMS $M^+$ (calculated for $C_{18}H_{26}O_5$) 340.2124, (found) 340.2113; $[\alpha]^{23}_D$ = −41.0° ($c$ 1, $CH_2Cl_2$).

**(2S,5S,6R)-(E)-Methyl 6-(4-Methoxyphenyl)-2,6-dimethoxy-5-methylhex-3-enoate (3j).** $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.12 (dd, 2 H, $J$ = 4.64, 5.82, Hz), 6.85 (dd, 2 H, $J$ = 4.15, 5.47 Hz), 5.72 (dd, 1 H, $J$ = 7.2, 15.6 Hz), 5.30 (dd, 1 H, $J$ = 7.6, 15.6 Hz), 4.10 (d, 1 H, 8 Hz), 3.88 (d, 1 H, 8 Hz), 3.81 (s, 3 H), 3.68 (s, 3 H), 3.29 (s, 3 H), 3.19 (s, 3 H), 2.54–2.53 (m, 1 H), 1.08 (d, 3 H, $J$ = 8 Hz); IR (neat) $\nu_{max}$ 2950, 1750, 1450, 1350, 900, 800, 700 $cm^{-1}$; CIMS ($NH_3$ gas) 341.2, 340.1, 308.1, 291.1, 259.1, 203.1, 181.1, 167.1; CIHRMS $M^+$ (calculated for $C_{17}H_{24}O_5$) 326.1968, (found) 326.1958.

**Experimental Procedure for Determination of Enantiomeric Purity. Illustrated for Compound 5.** A solution of (2S,5S,6R)-(E)-methyl 6-(2,5-dimethoxyphenyl)-2,6-dimethoxy-5-methylhex-3-enoate (**3a**) (0.05 mmol, 18 mg) in 0.5 mL of dry THF (0.1 M) was cooled to 0 °C and treated with $LiAlH_4$ (0.05 mmol, 2 mg). The solution was stirred for 15 min before being diluted with saturated $NH_4Cl$. After the organic layer was extracted with $Et_2O$ (1 × 5 mL), dried with $MgSO_4$, and filtered, and the solvent was removed under reduced pressure to afford the crude primary alcohol as a colorless oil. The crude alcohol was dissolved in dry $CH_2Cl_2$ (1 mL). The solution was cooled to 0 °C and treated with (R)-(−)-O-acetylmandelic acid[16] (0.05 mmol, 12 mg), DMAP (1 mg), and 1,3-dicyclohexylcarbodiimide (0.05 mmol, 12 mg). The reaction mixture was left stirring for 8 h at room temperature and filtered, the solvent was removed under reduced pressure, and the crude oil was flash chromatographed on silica gel to afford the single diastereoisomer **5** as a colorless film (21 mg, 23 mg theoretical 91% yield). **(2S,5S,6R)-6-(2,5-Dimethoxyphenyl)-2,6-dimethoxy-1-hydroxy-5-methylhex-3-enyl-(E)-(1R)-acetylmandelic acid (5).** $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.47 (dd, 2 H, $J$ = 3.96, 9.6 Hz), 7.40–7.35 (m, 3 H), 6.87 (d, 1 H, $J$ = 2.26 Hz), 6.77 (t, 2 H, $J$ = 8.92 Hz), 5.94 (s, 1 H), 5.67 (dd, 1 H, $J$ = 7.7, 15.59 Hz), 5.04 (dd, 1 H, $J$ = 6.73, 14.83 Hz), 4.43 (d, 1 H, $J$ = 6.21 Hz), 4.05 (d, 1 H, $J$ = 3.66 Hz), 4.02 (d, 1 H, $J$ = 3.67 Hz), 3.87 (dd, 1 H, $J$ = 8.03, 11.45 Hz), 3.76 (s, 3 H), 3.73 (s, 3 H), 3.55 (m, 1 H), 3.2 (s, 3 H), 3.07 (s, 3 H), 2.47–2.44 (m, 1 H), 2.19 (s, 3 H), 1.02 (d, 3 H, $J$ = 6.78); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 170.20, 168.61, 153.62, 151.62, 138.79, 133.81, 129.97, 129.15, 129.12, 128.67, 127.60,

(19) Unless otherwise noted commercial reagents were purchased and used without further purification. Diethyl ether ($Et_2O$) was distilled from sodium benzophenone ketyl under nitrogen just prior to use. Methylene chloride ($CH_2Cl_2$) was distilled from $CaH_2$ under nitrogen atmosphere immediately before use. Prior to use methanol was distilled from magnesium methoxide. All extraction and chromatographic solvents, ethyl acetate (EtOAc), ethyl ether ($Et_2O$), petroleum ether (PE), and chloroform ($CHCl_3$), were distilled prior to use. Boron trifluoride etherate ($BF_3{\cdot}OEt_2$) was distilled prior to use. All $^1H$ (400 MHz) and $^{13}C$ NMR (100 MHz) spectra were obtained on a Varian XL400 (93.94 kG) at ambient temperature in deuteriochloroform ($CDCl_3$). IR spectra (IR) were obtained on a Perkin Elmer 1310 infrared spectrometer. All mass spectral (low resolution/chemical ionization and high resolution/chemical ionization) measurements were obtained on a Finnegan MAT-90 high-resolution mass spectrometer. Rotations were recorded in $CH_2Cl_2$ on a Rudolph Research Autopol III polarimeter. TLC plates used for determining reaction progress were plastic sheets precoated with $SiO_2$ 60 $F_{254}$ as purchased from E. Merck, Darmstadt. Flash chromatography[20] was performed on E. Merck silica gel 230–400 mesh.

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125.07, 113.01, 112.51, 111.08, 80.50, 79.67, 74.43, 67.32, 57.20, 56.04, 55.67, 42.55, 20.71, 15.39; $[\alpha]^{25}_D = -12°$ (c 0.9, $CH_2Cl_2$).

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**Registry No. 1a**, 134333-46-3; **1b**, 134333-48-5; **1c**, 134451-71-1; **1d**, 134451-72-2; **2a**, 74327-86-9; **2b**, 1125-88-8; **2c**, 59276-32-3; **2d**, 134333-50-9; **2f**, 2186-92-7; **3a**, 134333-47-4; **3b**, 134451-73-3; *anti*-**3c**, 134451-76-6; *syn*-**3c**, 134333-53-2; *anti*-**3d**, 134451-77-7; *syn*-**3d**, 134333-54-3; **3e**, 134333-55-4; **3f**, 134333-56-5; **3g**, 134451-74-4; **3h**, 134333-57-6; **3i**, 134451-75-5; *anti*-**3j**, 134451-78-8; *syn*-**3j**, 134333-58-7; **4a**, 134333-49-6; **4b**, 134333-51-0; **5**, 134333-59-8; $Ph(CH_3)_2SiCH{=}CHCH(CH_3)OCOCH_2OCH_3$, 129921-50-2; $Ph(CH_3)_2SiCH{=}CHCH(CH_3)OCOCH_2CH_3$ (isomer 1), 134333-60-1; $Ph(CH_3)_2SiCH{=}CHCH(CH_3)OCOCH_2CH_3$ (isomer 2), 133323-28-1; $Ph(CH_3)_2SiCH{=}CHCH(CH_3)OC(DTMS){=}CHOCH_3$, 134333-61-2; $Ph(CH_3)_2SiCH{=}CHCH(CH_3)OC(OTBS){=}CHCH_3$, 134333-62-3; $Ph(CH_3)_2SiCH{=}CHCH(CH_3)OC(OTMS){=}CHCH_3$, 134333-63-4; (*R*)-*O*-acetylmandelic acid, 59276-32-3; 3-[(2*S*,3*R*)-3-(2,5-dimethoxy-2-nitrophenyl)-3-methoxy-2-methyl-1-propanoyl]-4-methyl-5-phenyl-2-oxazolidone, 134333-52-1.

**Supplementary Material Available**: Spectra (IR, $^1$H NMR, and $^{13}$C NMR) for compounds **1a-d** ($^1$H NMR only), **3a-j**, and **5** (40 pages). Ordering information is given on any current masthead page.

# Anionotropic Rearrangements of *tert*-Butyl- and Adamantylthiiranium Ions into Thietanium Ions. A Novel Case of Selectivity

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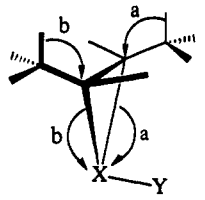
**Abstract:** *c*-2-R-*t*-3-R′-*r*-1-Methylthiiranium hexachloroantimonate **6** (R = R′ = *tert*-butyl) converts selectively in $CD_2Cl_2$ with first-order kinetics to 1,2,2,3-tetramethyl-4-R-thietanium hexachloroantimonate **8** (R = *tert*-butyl), with 4-*tert*-butyl and 3-methyl respectively trans and cis oriented to 1-methyl. The stereospecificity of the rearrangement points to concerted C-S bond breaking and methide migration, with direct generation of the tertiary carbenium ion **20**. The rearrangement was also investigated on isotopomers **9** (**6**, R = *tert*-butyl, R′ = *tert*-butyl-$d_9$) and **10** (**6**, R = *tert*-butyl-$d_9$, R′ = *tert*-butyl), and on isomers **15** (**6**, R = *tert*-butyl, R′ = adamantyl) and **16** (**6**, R = adamantyl, R′ = *tert*-butyl). The full kinetic and isotopic analyses for the rearrangements of **9** and **10** show that the methide migration occurs by about 95% from the cis group. Thiiranium **15** converts quantitatively with first-order kinetics to thietanium ion **17** (**8**, R = adamantyl). The rearrangement of the isomer **16** to 3-*tert*-butylhomoadamantylthietanium ion **18** (with the stereochemistry of **8**) is slower and reversible; also the thiiranium ion **15** is formed in the reverse rearrangement, with final irreversible conversion to **17**. The full kinetic analysis of the rearrangement pattern of ion **16** shows that some direct conversion to **17** occurs; the comparison with the rate constant for the rearrangement of **15** suggests that methide migrates preferentially by about 97% from cis *tert*-butyl. The adamantylthiiranium–homoadamantylthietanium equilibrium has also been studied on the diadamantyl derivative **13** (**6**, R = R′ = adamantyl). The selectivity and reversibility in the rearrangements of ions **13** and **16** are consistent with the intermediacy of the nonclassical homoadamantyl carbenium ion **24**; the tertiary endocyclic homoadamantyl carbenium ion **23** may be present along the reaction path, while the secondary exocyclic adamantyl carbenium ion **22** is not involved in the process. Some tentative rationales for this new case of selectivity are proposed.

## Introduction

The stereochemical course of concerted [1,2] anionotropic rearrangements is dictated by the requirement of maximum interaction between the orbitals associated with the migrating group and the leaving group (LG); this is reached in the syn- or antiperiplanar reciprocal orientations.[1] In this contest, the preference for antiperiplanarity has been variously attributed to steric effects[2] or to stereoelectronic effects.[1,3] On the other hand, further subtler stereochemical constraints may be induced by an asymmetric LG. We have, in fact, observed a novel type of selectivity in a case where two identical migrating groups are in the same relationship with respect to the bond to be broken, but are differentiated by the X-Y LG, which is not symmetrically oriented:




We have encountered this situation while investigating stable thiiranium and thiirenium ions, the intermediates for the addition of sulfenyl halides to alkenes and alkynes.[4] Our interest was also attracted by the reported[5] stability differences of the adducts of 4-chlorobenzenesulfenyl chloride to (*Z*)- and (*E*)-di-*tert*-butylethylenes **1** and **2a**. While the threo adduct (corresponding to

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