mg, 85%) as a homogeneous (TLC, silica, 1:19 EtOAc/hexane; ^{13}C NMR) white solid: mp 152–154 °C (lit.[8] 150–152 °C); ^{13}C NMR ($CDCl_3$, 100.614 MHz), δ 22.13, 23.09, 24.52, 26.03, 26.16; 27.53; 133.72; exact mass m/z calcd for $C_{24}H_{44}$ 332.3443, found 332.3437.

3-Methoxy-D-homoestra-1,3,5(10),17-tetraene. Freshly prepared[14] C_8K (3.98 g, 29.4 mmol) and $TiCl_3$ (2.18 g, 14.19 mmol) were weighed under argon in a glovebox and transferred successively to a 250-mL round-bottomed flask equipped with a condenser and containing dry diglyme (60 mL). The mixture was stirred at 85 °C for 2 h under argon. 3-Methoxy-D-homoestra-1,3,5(10)-triene-17β,17aβ-diol[47] **22** (267 mg, 0.84 mmol) was tipped in via the condenser and rinsed into the reaction vessel with dry diglyme (5 mL). Stirring was continued at 150 °C for an arbitrary period of 36 h. The mixture was cooled to room temperature and filtered under a blanket of argon through a pad of Florisil (11 × 4 cm). The pad, which was contained in a sintered funnel equipped with an argon inlet near the top, was washed with CH_2Cl_2 (400 mL) and ether (200 mL). Evaporation of the filtrate, removal of the diglyme by Kugelrohr distillation (80 °C (3 mmHg)), and flash chromatography of the residue over silica gel (2.5 × 20.0 cm) with 1:19 EtOAc/hexane, gave 3-methoxy-D-homoestra-1,3,5(10),17-tetraene (219 mg, 92%) as a white solid: mp 80–82 °C; FT-IR ($CHCl_3$ cast) 2925, 1600, 1500, 1218, 759 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.82–0.98 (m, including a singlet at 0.91, 4 H), 1.20–1.69 (m, 10 H), 1.81–1.95 (m, 1 H), 2.0–2.22 (m, 3 H), 2.22–2.39 (m, 2 H), 2.82–2.93 (m, 2 H), 3.79 (s, 3 H), 5.51 (br s, 2 H), 6.64 (d, J = 2.8 Hz, 1 H), 6.72 (dd, J = 8.4, 2.8 Hz, 1 H), 7.22 (d, J = 8.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 20.04, 20.15, 26.26, 26.38, 29.74, 30.21, 34.77, 38.60, 39.14, 44.13, 47.41, 55.24, 111.54, 113.53, 123.94, 126.21, 133.30, 138.05, 139.54, 157.48' exact mass m/z calcd for $C_{20}H_{26}O$ 282.1984, found 282.1983. Anal. Calcd for $C_{20}H_{26}O$: C, 85.05; H, 9.28. Found: C, 84.99; H, 9.63.

(47) Miller, T. C. *J. Org. Chem.* **1969**, *34*, 3829.

Acknowledgment. We thank the Natural Sciences and Engineering Research Council of Canada and the University of Alberta for financial support. A 1967 Scholarship (S.D.) and an Alberta Heritage Foundation for Medical Research Scholarship (C.Z.) are gratefully acknowledged. W.D.H. was a Summer Undergraduate Research Participant. We thank Drs. P. C. Anderson and A. G. H. Wee for some preliminary experiments.

Supplementary Material Available: ^1H NMR spectra of **5a**, **6a**, **7b** (also ^{13}C NMR), **9a**, **10** (R = $SiEt_3$) (both isomers), **10a**, **10b**, **11a**, **11b**, **12b**, **13a**, **16b** (both isomers), **17b**, [[2-(1,4-dioxaspiro[4,5]decan-6-yl)ethyl]sulfonyl]benzene, and **18a**, together with experimental procedures for **8a**, **9a**, **15a**, and 2-[2-(phenylsulfonyl)ethyl]cyclohexanone (60 pages). Ordering information is given on any current masthead page.

On the Stereoselective Opening of Achiral Dioxane Acetals

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Received July 5, 1991

The stereoselectivity of allylation of achiral dioxane acetals *cis*- and *trans*-**3** and *cis*- and *trans*-**5** was found to be highly dependent on the nature of the allylmetal reagent, Lewis acid, and stoichiometry. Using $TiCl_2(O\text{-}i\text{-}Pr)_2$ as the Lewis acid in conjunction with allyltrimethylsilane and allyltri-*n*-butylstannane the selectivity of opening ranged from 1/1 to 18.6/1. In reactions with allyltrimethylsilane, the lack of selectivity for both the cis and trans series (1–2.4/1) was shown to arise from rapid equilibration of ion pairs. Control experiments revealed that the acetals underwent opening faster than isomerization. The reactions with allyltri-*n*-butylstannane were more selective and dependent on reagent stoichiometry. Moreover, the sense of asymmetric induction for the cis and trans series was opposite. Control experiments again established that isomerization of the acetals occurs slower than reaction with the stannane. These experiments unambiguously rule out the possibility that the opening proceeds via equilibrating ion pairs. The meso dioxane acetal *cis*-**9** reacted with significantly reduced selectivity compared to the 2,4,6-trisubstituted analogue *cis*-**7**. On the other hand, the chiral acetal (±)-**13** reacted much more selectively than the 2,4,6-trisubstituted analogue (±)-**11**. These reactions illustrate the sensitivity of stereochemical outcome to structural and experimental variables and demonstrate the ability to intercept reactive ion pairs under conditions of kinetic control.

Introduction and Background

The mechanism and origin of stereoselective opening of chiral dioxane acetals constitute important considerations for the design of new asymmetric transformations.[1] In a recent study, Heathcock, Bartlett, Yamamoto et al.[2] described the use of 2,5-disubstituted 1,3-dioxane acetals to distinguish between S_N1 and S_N2 mechanistic limits, Scheme I. Their observation of stereorandom opening of *trans*-**1** and *cis*-**1** with $TiCl_4$ and the silyl enol ether derived from pinacolone led them to conclude that the reaction proceeds by an S_N1 mechanism via rapidly equilibrating oxocarbenium ion pairs, i and ii.

Our own studies on the mechanism of opening of dioxane acetals[3] have identified a stereochemical continuum arising from the intermediacy of three distinct species (intimate ion pair, external ion pair, and separated ions) each with its own stereochemical profile, Scheme II.[4] The stereoselectivity of a given reaction is a composite of those structural and experimental factors that balance the contribution of the different intermediates. A striking example is the difference in allylation selectivity between the meso and chiral acetals *cis*-**7** (*lk*-**8**/*ul*-**8**, 11.1/1) and (±)-**11** (*lk*-**12**/*ul*-**12**, 57.7/1) with allyltrimethylsilane **15** and the

(1) Reviews: (a) Alexakis, A.; Mangeney, P. *Tetrahedron: Asymmetry* **1990**, *1*, 477. (b) Seebach, D.; Imwinkelreid, R.; Weber, T. In *Modern Synthetic Methods*; Scheffold, R., Ed.; Springer Verlag: Berlin, 1986; Vol. 4; p 125.

(2) Mori, I.; Ishihara, K.; Flippin, L. A.; Nozaki, K.; Yamamoto, H.; Bartlett, P. A.; Heathcock, C. H. *J. Org. Chem.* **1990**, *55*, 6107.

(3) Denmark, S. E.; Almstead, N. G. *J. Am. Chem. Soc.*, in press.

(4) For an in-depth discussion of this mechanistic scheme and the intermediate species proposed, see ref 3.

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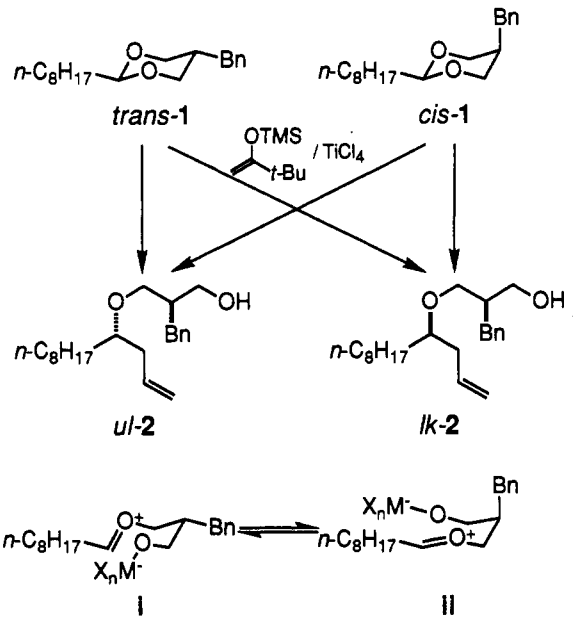
Table I. Selected Spectroscopic Data

	^{1}H NMR (ppm, Hz)				^{13}C NMR (ppm, Hz)		
acetal	δ HC(2)	δ H_{ax}C(4)	$J_{4_{ax},5}$	δ H_{eq}C(6)	$J_{6_{eq},5}$	δ C(2)	δ C(5)
cis-**3**	4.57	3.05	<1.0	3.89	(multiplet)	102.78	36.33
trans-**3**	4.45	3.40	10.9	4.03	4.4	102.21	34.83
cis-**5**	4.50	3.76	2.8	4.11	1.3	102.66	41.28
trans-**5**	4.36	3.36	11.4	4.12	4.6	101.89	40.24
cis-**9**	4.59	3.40				102.07	35.87
(±)-**13**	4.85	3.71		3.80		94.50	35.20

Scheme I



titanium blend (6/5 $TiCl_4$/Ti(O-*i*-Pr)$_4$), Scheme III. This was understood in terms of the greater stability of the intimate ion pair derived from (±)-**11** compared to *cis*-**7** (fewer nonbonded interactions). The difference disappears with $TiCl_4$ as the Lewis acid (*lk*-**8**/*ul*-**8**, 5.1/1 versus *lk*-**12**/*ul*-**12**, 6.7/1, respectively), presumably since reactions with this reagent proceed through the intermediacy of looser external ion pairs.

These two types of substrates (2,5-disubstituted and meso 2,4,6-trisubstituted dioxane acetals) represent sensitive probes for the effects of experimental and structural variables on the timing of ion pair formation, equilibration, and capture. As part of our continuing interest in elucidating and quantifying the factors responsible for stereocontrol in the opening of dioxane acetals we have carefully examined the effects of allylmetal nucleophilicity and acetal structure.

In a related study we have documented the ability of allyltri-*n*-butylstannane **16** to open chiral dioxane acetals (e.g., (±)-**11**) with extreme selectivity (>300/1) presumably due to the efficient capture of the intimate ion pairs.[5] As a test of this hypothesis, we chose to examine the achiral 2,5-disubstituted dioxane acetals *trans*- and *cis*-**3** and *trans*- and *cis*-**5**. Heathcock[2] has pointed out that the corresponding ion pairs i and ii (Scheme I) should be isoenergetic. Assuming that i and ii react at the same rate, a 1/1 mixture would result if the ion pairs can equilibrate as was proposed for the *trans*- and *cis*-**1** using pinacolone silyl enol ether and $TiCl_4$. If the extreme selectivity observed with (±)-**11** and **16** is due to rapid capture of ion pairs, this should be manifest in the selective and complimentary formation of the *ul* (from trans) and *lk* (from cis) diastereomers of both **4** and **6** from reactions of **3** and **5** respectively, Scheme IV.

The dramatic effect of acetal configuration (*cis*-**7** vs (±)-**11**) provided a unique insight into the relationship between acetal structure, ion pair conformation, and stereoselectivity. If the enhanced selectivity in the chiral series is indeed due to the relative stability of the corresponding ion pairs then other structural modifications that influence the energy of the ion pairs should lead to different selectivities. The test of this hypothesis can be formulated in the reactions of the pentasubstituted dioxane acetals *cis*-**9** and (±)-**13** (Scheme V). The effect of the C(5) geminal methyl groups can be manifest in several ways and may not necessarily be the same for both isomers. The buttressing effect can provide a restoring force to keep the ion pairs in the intimate chairlike form leading to higher selectivities. Alternatively, this effect can also engender nonbonded interactions to destabilize the ion pair leading to lower selectivities. As is described below, these substrates provided some interesting and unexpected surprises that refined our understanding of the factors that influence the stereochemical course of acetal opening.

Results

Preparation of Substrates. A. 2,5-Disubstituted Acetals (3 and 5). The dioxanes were readily prepared by classic acetalization of *n*-heptanal with the requisite diols **17** and **18** themselves prepared by $LiAlH_4$ reduction of the 2-benzyl- and 2-isopropylmalonate esters. Thus, heating **17** and *n*-heptanal in benzene with *p*-toluenesulfonic acid as catalyst afforded **3** in 90% yield as a 1.6/1 mixture of trans and cis isomers. Analogously, **5** was produced from **18** in 84% yield as a 4/1 mixture of trans and cis isomers, Scheme VI. These ratios presumably represent thermodynamic equilibrium at 80 °C. As such, the ratio for **5** (4/1, $\Delta G°$ = 0.97 kcal/mol (80 °C)) was in the expected range,[6] but the ratio for **3** (1.6/1, $\Delta G°$ = 0.33 kcal/mol (80 °C) was much smaller than expected (the *A* value for a C(5)-methyl group in 1,3-dioxanes is 0.8 kcal/mol).[7]

The configurational assignment of the isomers follows in a straightforward fashion[6] from analysis of their ^{1}H NMR spectra, Table I. The C(4) and C(6) methylene groups in **3** and **5** constitute enantiotopic sets of diastereotopic protons. In the trans isomers, the axial protons on C(4) and C(6) displayed a large coupling to the HC(5) which should also be axial. In the cis isomers the C(5) substituent takes up the axial orientation[6] and the vicinal coupling of H_{ax}C(4) and H_{ax}C(6) with HC(5) is correspondingly small.

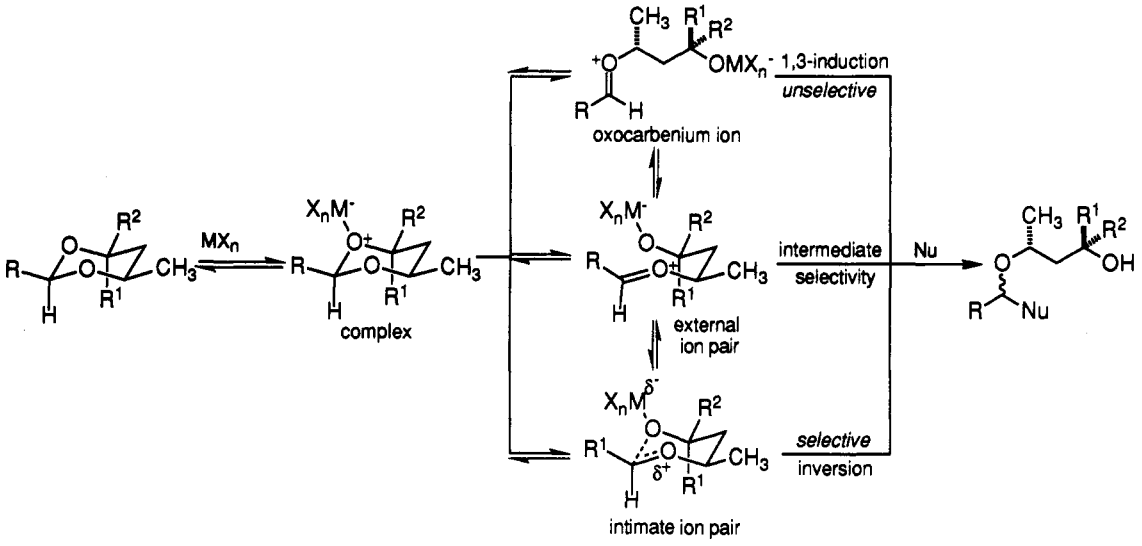
B. 2,4,5,5,6-Pentasubstituted Acetals (*cis*-9 and (±)-13). The preparation of the isomeric acetals *cis*-**9** and (±)-**13** was expected to follow trivially from analogous acetalizations. The two diols **19** and **20** were prepared by selective reduction of the diketone as described by Maier.[8]

(5) Denmark, S. E.; Almstead, N. G. *J. Org. Chem.*, in press.

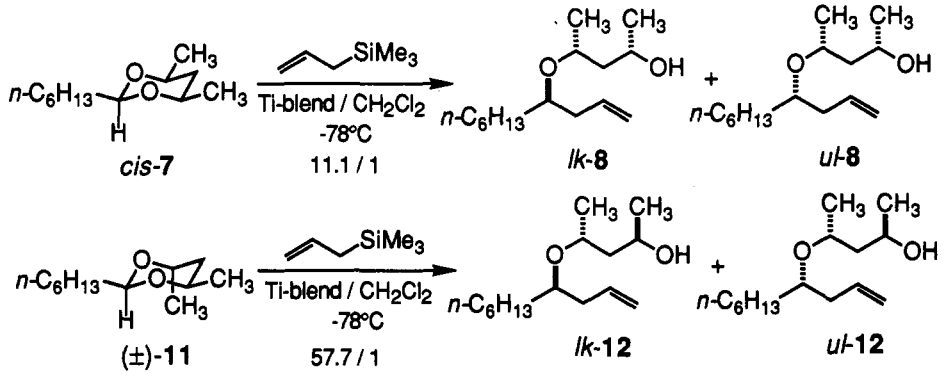
(6) Eliel, E. L.; Knoeber, Sr. M. C. *J. Am. Chem. Soc.* **1968**, *90*, 3444.

(7) Heathcock et al.[2] reported obtaining a 1/1 mixture of acetals with **17** and *n*-nonanal.

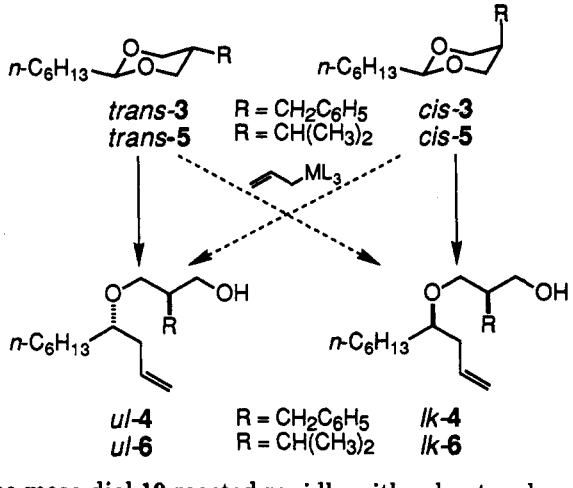
Scheme II



Scheme III



Scheme IV



The meso diol **19** reacted rapidly with *n*-heptanal under standard conditions to give *cis*-**9** exclusively, Scheme VII. The structure of *cis*-**9** was evident from the simplicity of its NMR spectra and the chemical shift for HC(2).

The formation of the corresponding acetal from **20** was unexpectedly difficult. No product was detected under standard acetalization conditions and only self-condensation of *n*-heptanal was observed at elevated temperatures. An alternative approach began with formation of the mixed orthoester **21** from **20** and neat trimethylorthoformate (*p*-TsOH, reflux) in 43% yield. Treatment of **21** with *n*-hexylmagnesium bromide in toluene at reflux afforded (±)-**13** in 39% yield. The slow rate of addition is presumably due to the equatorial disposition of the methoxy group in **21**. The resonance position of C(2) displays the characteristic upfield shift due to the C(4) axial methyl group.

Allylation of 2,5-Disubstituted Acetals (3 and 5). A. Nucleophile and Stoichiometry Dependence. To probe the timing of ion-pair generation, isomerization, and capture we examined two nucleophiles and two Lewis acids. The results of these studies are collected in Table II. The initial reactions with $TiCl_4$ and allyltrimethylsilane **15** (entries 1, 6, and 13) were performed to give authentic mixtures of *ul*- and *lk*-**4** and *ul*- and *lk*-**6** for isomer analysis. Unfortunately, we were unable to resolve the diastereomers by capillary GC analysis. Therefore, the diastereoselectivity ratios (ds) were determined by ^{13}C NMR analysis of isolated, purified samples of **4** and **6**. The most diagnostic resonance that showed the largest $\Delta\delta$ was at the C(1′) methylene group flanked by the two stereogenic centers. Both integration of the signals and peak heights gave self-consistent ratios. The reactions with $TiCl_4$ indeed proceeded with the expected lack of selectivity. Furthermore, executing the reactions with **15** under the conditions recommended by Johnson[9] also proceeded unselectively for *cis*-**3** but with modest selectivity for *trans*-**3** (entries 2 and 7). However, we were delighted to

(8) Maier, G.; Schmitt, R. K.; Seipp, K. *Chem. Ber.* **1985**, *118*, 722.

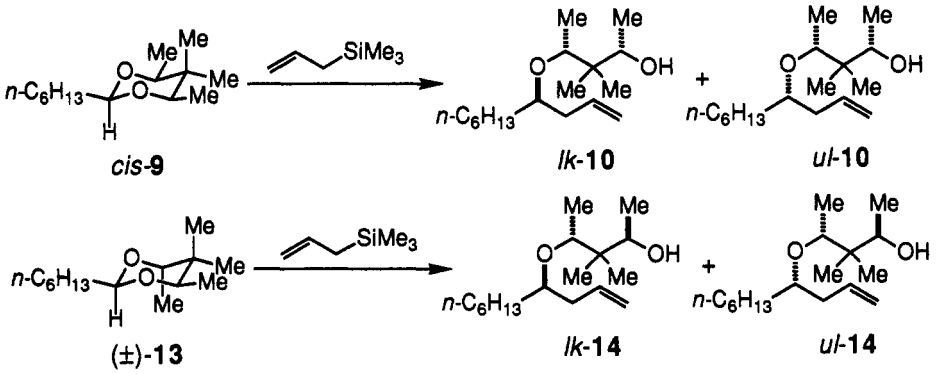
(9) Johnson, W. S.; Crackett, P. H.; Elliott, J. D.; Jagodzinski, J. J.; Lindell, S. D.; Natarajan, S. *Tetrahedron Lett.* **1984**, *25*, 3951. We have found that the recommended 6/5 $TiCl_4/Ti(O\text{-}i\text{-}Pr)_4$ blend offers no advantage over the stoichiometric reagent $TiCl_2(O\text{-}i\text{-}Pr)_2$.

Table II. Allylation of 2,5-Disubstituted Acetals[a]

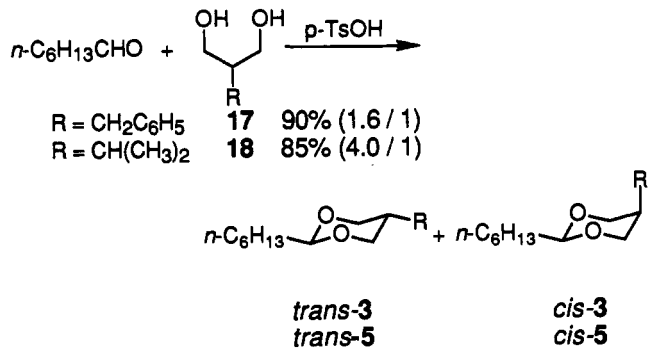
entry	acetal	Lewis acid[b] (equiv)	ML_3 (equiv)	yield[c] (%)	product	ds *lk*/*ul*[d]	$\Delta\Delta G^{\ddagger}$[e]
1	*cis*-**3**	$TiCl_4$ (1)	$SiMe_3$ (4)	88	**4**	1.6/1	0.18
2	*cis*-**3**	$TiCl_2(O\text{-}i\text{-}Pr)_2$ (10)	$SiMe_3$ (8)	87	**4**	1.0/1	0.00
3	*cis*-**3**	$TiCl_2(O\text{-}i\text{-}Pr)_2$ (10)	$SnBu_3$ (2)	93	**4**	6.7/1	0.74
4	*cis*-**3**	$TiCl_2(O\text{-}i\text{-}Pr)_2$ (5)	$SnBu_3$ (2)	82	**4**	14.6/1	1.04
5	*cis*-**3**	$TiCl_2(O\text{-}i\text{-}Pr)_2$ (5)	$SnBu_3$ (8)	85	**4**	18.6/1	1.13
6	*trans*-**3**	$TiCl_4$ (1)	$SiMe_3$ (4)	88	**4**	1/1.0	0.00
7	*trans*-**3**	$TiCl_2(O\text{-}i\text{-}Pr)_2$ (10)	$SiMe_3$ (8)	92	**4**	1/2.4	−0.34
8	*trans*-**3**	$TiCl_2(O\text{-}i\text{-}Pr)_2$ (10)	$SnBu_3$ (2)	100	**4**	1/4.0	−0.54
9	*trans*-**3**	$TiCl_2(O\text{-}i\text{-}Pr)_2$ (5)	$SnBu_3$ (2)	63	**4**	1/7.0	−0.76
10	*trans*-**3**	$TiCl_2(O\text{-}i\text{-}Pr)_2$ (5)	$SnBu_3$ (8)	60	**4**	1/16.6	−1.09
11	*cis*-**5**	$TiCl_2(O\text{-}i\text{-}Pr)_2$ (10)	$SnBu_3$ (2)	89	**6**	7.3/1	0.77
12	*cis*-**5**	$TiCl_2(O\text{-}i\text{-}Pr)_2$ (5)	$SnBu_3$ (2)	83	**6**	10.8/1	0.92
13	*trans*-**5**	$TiCl_4$ (1)	$SiMe_3$ (4)	90	**6**	1/1.0	0.00
14	*trans*-**5**	$TiCl_2(O\text{-}i\text{-}Pr)_2$ (10)	$SnBu_3$ (2)	94	**6**	1/2.4	−0.34
15	*trans*-**5**	$TiCl_2(O\text{-}i\text{-}Pr)_2$ (5)	$SnBu_3$ (2)	64	**6**	1/1.8	−0.23

[a] All reactions run at an initial concentration of 0.1 M. [b] $TiCl_4$ added at once, $TiCl_2(O\text{-}i\text{-}Pr)_2$ (freshly prepared) added over 2 h. [c] Yields of isolated products. [d] Determined by integration and peak height of ^{13}C NMR signals. [e] At 195 K, kcal/mol.

Scheme V



Scheme VI



find that allylation with allyltri-*n*-butylstannane **16**, under the conditions we described previously,[5] afforded **4** and **6** in good yield and with modest stereoselectivity. Most importantly, the cis acetals gave a predominance of the *lk* diastereomer (entries 3 and 11) while the trans isomers gave a predominance of the *ul* diastereomer (entries 8 and 14).[10]

The effect of stoichoimetry on the stereochemical outcome was investigated next. For *cis*- and *trans*-**3**, the selectivity of acetal opening increased significantly in opposite directions with the use of less Lewis acid (entries 4 and 9). Moreover, with the reduced amount of Lewis acid the selectivity increased still further for both series with the use of more allylating agent **16** (entries 5 and 10). This behavior was also seen in the allylation of *cis*-**5** (entries 11 and 12) but not with *trans*-**5** (entries 14 and 15). Interestingly, the reactions of *cis*-**3** were slightly more selective than *trans*-**3** under all reaction conditions. This modest but definite trend was more pronounced in the reactions of *cis*- and *trans*-**5**.

B. Control Experiments. The poor selectivity in the reactions of *cis*-**3** and *trans*-**3** with **15** cannot be interpreted unambiguously. To clarify the origin of low selectivity, the behavior of the isomeric acetals in the presence of only the Lewis acid and under the reaction conditions had to be established. The results of the control experiments are collected in Table III. First, all four acetals were treated with 10 equiv of the titanium blend at −78 °C for extended periods (entries 1, 6, 9, and 11). In all cases the trans isomer was formed predominantly as expected. The thermodynamic preference for the trans isomers can be estimated from the equilibrium ratio observed in their preparation (**3**: trans/cis, 1.6/1; **5**: trans/cis, 4.0/1). The uncertainty of the temperature effect on these ratios precludes accurate estimation. Clearly equilibrium was not reached in either case suggesting a slow rate of isomerization at −78 °C.

The critical control experiments to establish acetal and product composition at partial completion (limiting Lewis acid) were then carried out. In these runs, the reaction mixtures were partitioned by column chromatography and the unreacted acetal was analyzed by capillary gas chromatography and the allylation products were analyzed by ^{13}C NMR spectroscopy. The control experiments for the allylation of *cis*- and *trans*-**3** with **15** (entries 2 and 7) were very revealing. The products of acetal opening were pro-

(10) The configurational assignments of *ul*-**4**/**6** and *lk*-**4**/**6** have not been made. However, we feel confident in these assumptions based on the following: (1) the documented stereochemical pathway with **15** and *cis*-**7** or **16** and (±)-**11**, and (2) the selective and complimentary pathways observed with **16** and *cis*- and *trans*-**3**.

Scheme VII

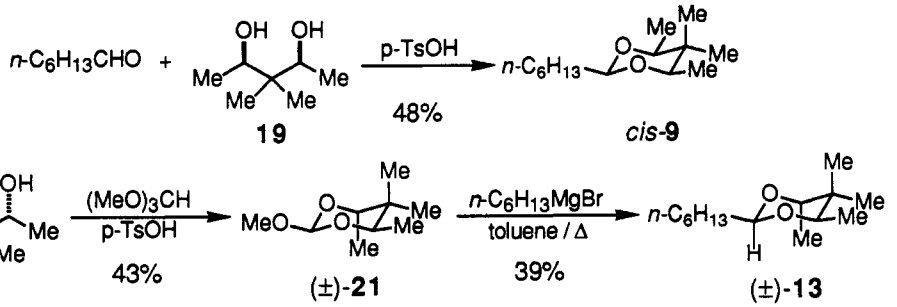


Table III. Control Experiments with 2,5-Disubstituted Acetals[a]

entry	acetal	Lewis acid[b] (equiv)	ML_3 (equiv)	yield (recovery)[c] (%)	ds *lk*/*ul*[d]	recovered acetal[e] cis/trans
1	*cis*-**3**	10				1/2.1
2	*cis*-**3**	5	$SiMe_3$ (8)	42 (42)	4.4/1	1/1.6
3	*cis*-**3**	5	$SnBu_3$ (2)	80 (20)	15.2/1	6.2/1
4	*cis*-**3**	2.5	$SnBu_3$ (2)	43 (51)	20.4/1	13/1
5	*cis*-**3**	2.5	$SnBu_3$ (8)	51 (47)	29.2/1	35/1
6	*trans*-**3**	10				1/3.1
7	*trans*-**3**	5	$SiMe_3$ (8)	39 (48)	1/4.7	1/6.6
8	*trans*-**3**	5	$SnBu_3$ (2)	63 (34)	1/7.0	1/10.5
9	*cis*-**5**	10				1/1.6
10	*cis*-**5**	5	$SnBu_3$ (2)	85 (15)	9.6/1	1.2/1
11	*trans*-**5**	10				1/2.7
12	*trans*-**5**	5	$SnBu_3$ (2)	64 (33)	1/1.8	1/66

[a] All reactions performed at an initial concentration of 0.1 M. [b] Freshly prepared $TiCl_2(O\text{-}i\text{-}Pr)_2$ added over 2 h. [c] Yields of isolated products. [d] Determined by integration and peak height of ^{13}C NMR signals. [e] Determined by capillary GC analysis.

duced with significantly greater selectivity than at complete reaction. What is most intriguing, however, was the observation of complimentary product stereochemistry from the cis and trans acetals together with extensive isomerization of the recovered acetal from *cis*-**5** but not *trans*-**5**. Thus, it is clear that isomerization of the acetal was competitive with reaction with **15** and that both isomerization and reaction of *cis*-**5** were faster than *trans*-**5**.

A more elaborate set of control experiments for the reaction of *cis*-**3** with **16** was carried out. The results in entries 3–5 constitute a continuation of the stoichiometry effects described above. Entry 3 is a repeat of entry 4, Table II, and the results are comparable. The recovered *cis*-**3** was only partially isomerized. Lowering the amount of Lewis acid still further (entry 4) led to another increase in allylation selectivity and a corresponding diminution in acetal epimerization (albeit at only 43% conversion). Finally, increasing the amount of **16** at this reduced Lewis acid loading (entry 5) had the expected effect (vide supra) affording the most selective allylation and the lowest level of acetal isomerization. The production of the *lk* diastereomer from *cis*-**3** was nicely reflected in the preservation of configuration of the precursor. For *trans*-**3** the allylation in entry 8 of Table II constitutes a control experiment since it proceeded only to 63% completion. The preference for production of the *ul* diastereomer corresponds to the persistence of the trans configuration of the starting acetal. Thus, increasing the nucleophilicity or amount of the allylating reagent and/or decreasing the amount of the Lewis acid increases the selectivity of acetal opening and decreases the (relative) rate of acetal isomerization. Comparison of entry 2, Table II, with entry 5, Table III, is a particularly dramatic example of how reaction conditions can influence the stereochemical course of a reaction (1/1 versus 29/1).

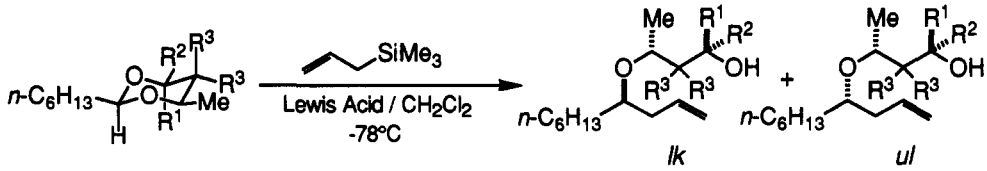
The control experiments with *cis*- and *trans*-**5** were still more enlightening. For *cis*-**5** (entry 10) the *lk* diastereomer was formed selectively as expected but the recovered acetal suffered significant isomerization. Thus, the high selectivity observed derives from rapid reaction of the cis acetal with **16**. The recovery of isomerized acetal showed that isomerization is competitive but slower. Finally, the anomalously low selectivity for reaction of *trans*-**5** with **16** (Table II, entry 15) was reproduced at incomplete conversion as well (Table III, entry 12). Remarkably however, this low selectivity does not arise from acetal isomerization as *trans*-**5** was recovered essentially unchanged.

Allylation of 2,4,5,5,6-Pentasubstituted Acetals (*cis*-9 and (±)-13). The reactions of *cis*-**9** and (±)-**13** with **15** were conducted under the exact same conditions as for the trisubstituted analogues *cis*-**7** and (±)-**11**.[3] The results from all four of these substrates are collected in Table IV. The reactions of *cis*-**9** and (±)-**13** with $TiCl_4$ (entries 3 and 7) were intended to provide authentic mixtures of the diastereomers of **9** and **14**. The effect of the geminal dimethyl groups on the selectivity of allylation was dramatic. For the meso acetals the selectivity dropped from 11.1/1 to 1/1 (entries 2 and 4) while for the chiral acetals, the increase from 57.7/1 to 113/1 (entries 6 and 8) was startling. The configurational assignment for the diastereomers of **14** was made by analogy to the established stereostructures of the corresponding isomers of **12**. The unselective formation of **10** made assignment of these isomers irrelevant.

Discussion

The stereochemical analysis of reactions of 2,5-disubstituted acetals has been described in detail by Heathcock[2] and is reproduced in Scheme VIII. If the reaction proceeds by an S_N2-like mechanism on a Lewis acid acetal complex or an intimate ion pair, a single diastereomer should be formed. Moreover, the cis and trans isomers of the starting acetal should lead to different diastereomers of the product. If, however, the reaction proceeds through an open oxocarbenium ion or via rapidly equilibrating ion pairs, the selectivity will be compromised. As stated in

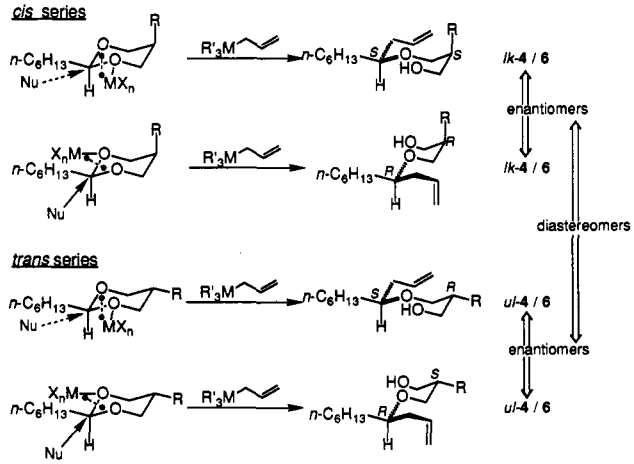
Table IV. Allylation of Pentasubstituted Acetals[a]



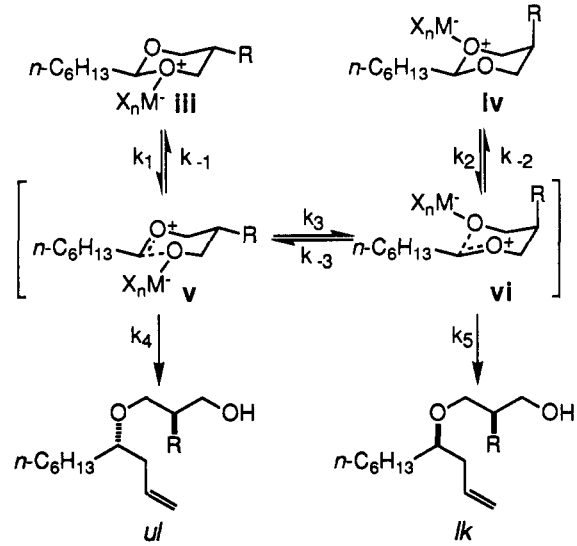
entry	acetal	R^1	R^2	R^3	Lewis acid (equiv)	time, (h)	product	yield[b] (%)	ds *lk*/*ul*[b]	$\Delta\Delta G^{\ddagger}$[c]
1	*cis*-**7**	H	Me	H	$TiCl_4$[d] (1.0)	0.5	**8**	92[e]	5.1/1	0.63
2	*cis*-**7**	H	Me	H	Ti-blend[f,g] (11)	3.0	**8**	100[e]	11.1/1	0.93
3	*cis*-**9**	H	Me	Me	$TiCl_4$[d] (1.0)	0.5	**10**	94[h]	1.1/1	0.04
4	*cis*-**9**	H	Me	Me	Ti-blend[f,g] (11)	3.0	**10**	72[i]	1.1/1	0.04
5	(±)-**11**	Me	H	H	$TiCl_4$[d] (1.0)	0.5	**12**	100[e]	6.7/1	0.74
6	(±)-**11**	Me	H	H	Ti-blend[f,g] (11)	3.0	**12**	100[e]	55.7/1	1.58
7	(±)-**13**	Me	H	Me	$TiCl_4$[d] (1.0)	0.5	**14**	95[e]	8.0/1[j]	0.81
8	(±)-**13**	Me	H	Me	Ti-blend[f,g] (11)	3.0	**14**	92[e]	113/1[j]	1.83

[a] All reactions performed at an initial concentration of 0.1 M. [b] Yields and ratios determined by capillary GC analysis. [c] At 195 K, kcal/mol. [d] With **15** (4 equiv). [e] Based on response factors versus cyclododecane. [f] 6/5 $TiCl_4$/Ti(O-*i*-Pr)$_4$. [g] With **15** (8 equiv). [h] Yield of isolated products. [i] Conversion. [j] Assigned by analogy.

Scheme VIII



Scheme IX



the introduction, a 1/1 mixture of adducts **2** was obtained from reaction of both *cis*-**1** and *trans*-**1** with pinacolone silyl enol ether and $TiCl_4$. Since the acetals were recovered unchanged at partial conversion, the lack of selectivity was ascribed to reaction via rapidly equilibrating ion pairs i and ii. It was expected that these ion pairs would be roughly equal in energy and reactivity leading to the 1/1 ratio of products.

On the basis of our own studies on the mechanism of opening of meso and chiral acetals, we interpreted these results in terms of reaction via external ion pairs or even separated ions as is characteristic of the powerful Lewis acid $TiCl_4$. The use of a weaker Lewis acid and/or a more powerful nucleophile should allow the capture of the intimate ion pair before it can isomerize or equilibrate with other reactive intermediates. The results bear this out.

To understand the following analysis of the reaction chronology, the key species have been compiled in a unified fashion, Scheme IX. The starting acetals are in equilibrium with their Lewis acid complexes iii and iv. These complexes are the immediate precursors of the corresponding intimate ion pairs v and vi through which both acetal isomerization and reaction with **15** or **16** may occur. The stereochemical course of allylation will depend on the relative rates of reaction (k_4 and k_5) and isomerization (k_3 and k_{-3}).

The reactions of *cis*- and *trans*-**3** with allyltrimethylsilane **15** constitute benchmark comparisons (Table II, entries 2, 7). The poor selectivity observed in both of these examples is superficially similar to the reaction with $TiCl_4$ and pinacolone silyl enol ether. However, the control experiments reveal important differences. At low conversion, both substrates reacted more selectively, *cis*-**3** affording *lk*-**4** and *trans*-**3** affording *ul*-**4** preferentially. Therefore, the intimate ion pairs v and vi can be intercepted by **15** faster than they can isomerize. However, isomerization does still occur and to a greater extent for *cis*-**3** than *trans*-**3** as was also seen in control experiments without **15**.

The interception of ion pairs became more efficient with the use of allyltri-*n*-butylstannane.[11] For both *cis*-**3** and *trans*-**3** the production of *lk*-**4** and *ul*-**4**, respectively, became more selective. The control experiments at low conversion corroborated the conclusion that **16** was capturing the ion pairs more efficiently as the acetals were recovered predominantly unchanged.

The stoichiometry dependence of stereoselectivity was particularly informative. For both *cis*-**3** and *trans*-**3** the use of less Lewis acid and/or more **16** led to enhanced selectivities. Again, the control experiments revealed a

(11) Both Y. Yamamoto[11a] and Otera[11b] have demonstrated the divergence of stereochemical outcome in reactions of acetals and thioacetals with allylstannanes compared to allylsilanes. (a) Yamamoto, Y.; Nishii, S.; Yamada, J. *J. Am. Chem. Soc.* **1986**, *108*, 7116. (b) Sato, T.; Otera, J.; Nozaki, H. *J. Org. Chem.* **1990**, *55*, 6116.

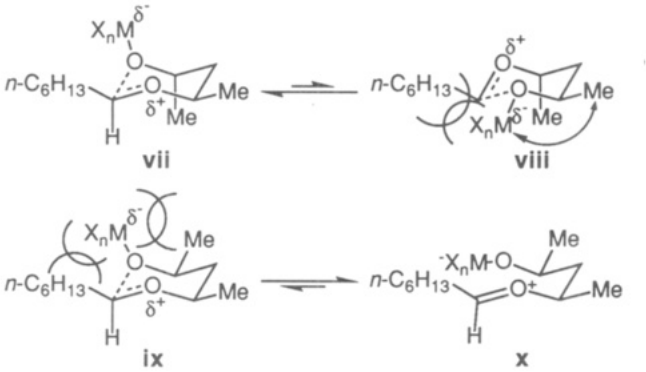
clear correspondence between the increased preference for production of *ul*-**4** (from *trans*-**3**) and *lk*-**4** (from *cis*-**3**) with the decreased level of isomerization of recovered acetals. In previous studies with *cis*-**7** and (±)-**11** using **15** and $TiCl_4$, no stoichiometry dependence on allylmetal or Lewis acid was noted. The results strongly implicate the intimate ion pairs v and vi as a common intermediates both for reaction and isomerization of the acetals. Furthermore, *cis*- and *trans*-**3** showed the expected behavior for reactions operating under nearly complete kinetic control at the level of both the starting acetals and the ion pairs.

The unexpected results from reactions of *cis*- and *trans*-**5**, though superficially contradictory, provided useful insights into the balance of stereocontrol elements in these reactions. For *cis*-**5** the increased level of *lk* selectivity with decreasing Lewis acid amounts mirrored the trend with *cis*-**3**. Interestingly, the control experiment revealed that the greater *lk* selectivity does not correspond to lesser isomerization of the acetal. These two facts are consistent with the rapid capture of the initially formed ion pair vi ($k_5 > k_{-3}$). The isomerization is competitive, but the ion pair v is less reactive ($k_{-1} > k_4$) so that the leakage shows up as trans acetal more so than as the *ul*-product. The greater extent of isomerization of *cis*-**5** compared to *cis*-**3** is also consistent with this hypothesis.

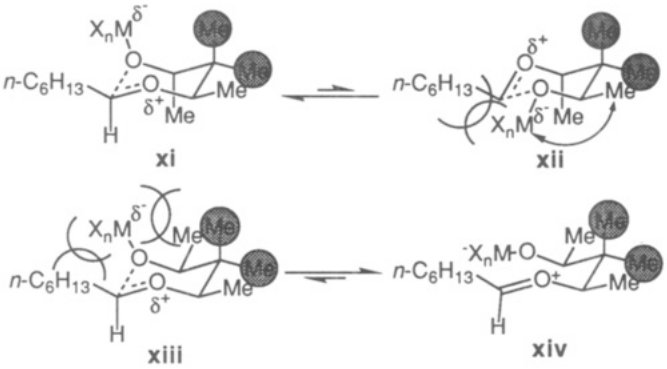
This proposal can also account for the unusual results with *trans*-**5**. This acetal reacted unselectively under all conditions. Remarkably, this behavior was not due to rapid acetal isomerization. These facts are again reconciled by the relative rates of isomerization and capture of the ion pairs. In this case, the initially formed ion pair v is not highly reactive ($k_{-1} > k_4$). Although unfavorable, isomerization to vi produces a highly reactive ion which is captured faster than it closes ($k_5 > k_{-2}$). Thus, the low *lk*/*ul* selectivity is seen as a balance between the equilibrium composition of v and vi (k_3/k_{-3}) and their relative reactivities (k_4 versus k_5). The high retention of acetal stereochemistry is understood in the slow rate of closure of vi compared to other processes ($k_{-2} \ll k_5$ and k_{-3}).

It is instructive to compare these results with those from Heathcock et al.[2] who employed pinacolone silyl enol ether and $TiCl_4$. Their interpretation of reaction via rapidly equilibrating ion pairs fits Scheme IX where k_3 and k_{-3} are greater than k_4 and k_5 which must also be greater than k_{-1} and k_{-2}. What is most surprising are the control experiments which returned isomerically pure *cis*-**1** and *trans*-**1** but still produced **2** as 1/1 mixtures. In our studies neither **15** nor **16** were able to completely suppress isomerization of **3** or **5**, but the allylation products **4** and **6** could be formed with considerable diastereomeric enrichment. Since **16** is known to be more nucleophilic than pinacolone silyl enol ether[12] and can capture ion pairs more efficiently, why is isomerization still detected? The answer is simply that the ion pairs i and ii are different from v and vi. We have previously asserted that reactions with $TiCl_4$ proceed via external or solvent separated ion pairs while reactions with $TiCl_2(O\text{-}i\text{-}Pr)_2$ proceed via intimate ion pairs. If *cis*- and *trans*-**1** do indeed react via looser, more reactive external ion pairs, then it would be expected that the relative rates of closure versus reaction (k_{-1}/k_4 or k_{-2}/k_5) be less than for intimate or tight ion pairs, even with a weak nucleophile. For intimate ion pairs, the rate of reclosure must be faster since the extent of atomic reorganization is considerably less (Hammond postulate).[13] Even with a strong nucleophile (**16**) in excess at short reaction times the intimate ion pairs can escape and return. These contradictory observations are nicely reconciled by and thus provide support for the proposal of multiple ion pair intermediates with different stereochemical profiles.

Scheme X



Scheme XI



The reactions of the pentasubstituted acetals *cis*-**9** and (±)-**13** confirmed our hypothesis for the divergent behavior of meso and chiral 2,4,6-trisubstituted acetals. Initially, the dramatic difference in the case of acetal formation augured a different outcome. Specifically, the facile acetalization with **19** suggested a conformational preference for the diol which mimicked the acetal (Thorpe Ingold effect[14]), while the failure of acetalization with **20** indicated that nonbonding interactions were too prohibitive to allow ring closure. It was therefore expected that *cis*-**9** would react selectively through a relatively unstrained intimate ion pair, while (±)-**13** would react unselectively via an open oxocarbenium ion to relieve nonbonding interactions in the ion pair. Exactly the opposite behavior was observed. Using the 6/5 "titanium blend" *cis*-**9** reacted unselectively while (±)-**13** reacted more selectively compared to their trisubstituted counterparts.

The enhanced selectivity observed with (±)-**11** compared to *cis*-**7** is interpreted in terms of the fewer nonbonded interactions in the ion pair vii compared to ix, Scheme X. In ix both methyl groups are equatorial and the Lewis acid must interact with one of these groups. This strain can be relieved by opening to external ion pair x which leads to decreased selectivity. Similarly, in (±)-**11** the equilibrium between the two pairs vii and viii is heavily biased in favor of the ion pair that avoids non-bonding interactions between the Lewis acid and ring methyl groups. Thus, reactions occur predominantly and selectively via intimate ion pair vii.

The observed trend in allylation selectivity can be understood by considering the effect of the C(5) geminal methyl groups on the equilibrium composition of the ion

(12) Hagen, G.; Mayr, H. *J. Am. Chem. Soc.* **1991**, *113*, 4954.
(13) Hammond, G. S. *J. Am. Chem. Soc.* **1955**, *77*, 334.
(14) For a recent analysis see: Jung, M. E.; Gervay, J. *J. Am. Chem. Soc.* **1991**, *113*, 224.

pairs related to vii–x, Scheme XI. In (±)-13, the buttressing effect of the C(5) methyl groups forces the equatorial C(4) methyl group forward enhancing its interaction with the Lewis acid in xii. Since little effect is expected for xi the net result is to shift the equilibrium in favor of xi leading to an increased allylation selectivity as observed. In *cis*-9 the buttressing of methyl groups leads to an unavoidable destabilization of xiii compared to xiv. Thus, the equilibrium is shifted to the external ion pair to a greater extent than in (±)-11 leading to the loss in stereoselectivity, again as was observed. It is worth pointing out again that these effects are operative on the Lewis acid complexes and ion pairs. The Thorpe Ingold effect on the starting acetals is expected to give the opposite results.

Conclusions

The achiral 2,5-disubstituted dioxanes provide a useful probe of mechanism in acetal substitution reactions. This study has revealed the critical importance of nucleophile and Lewis acid on the partitioning of reactive ion pair intermediates. By adjusting reaction conditions, the full spectrum of possibilities was observed wherein ion pair equilibration was faster, competitive with and slower than capture by the nucleophile. The use of the mild Lewis acid $TiCl_2(O\text{-}i\text{-}Pr)_2$ was necessary to observe this behavior as reactions using $TiCl_4$ proceed via the looser, external ion pairs.

The effect of acetal structure on stereoselectivity was clearly demonstrated by the reactions of *cis*-9 and (±)-13. The nonbonding interactions between the oxygen-bound Lewis acid and the C(4) and C(6) substituents was shown to be of fundamental importance in guiding the stereochemical course of opening in both the meso and chiral series.

The ability to intercept an intimate ion pair under conditions of kinetic control is a critical consideration in the design of enantioselective reactions using chiral Lewis acids. These studies will be reported in due course.

Experimental Section

General Methods. ^1H NMR spectra were recorded at 200, 300, or 500 MHz in $CDCl_3$ with $CHCl_3$ as an internal reference (7.26 ppm). ^{13}C NMR spectra were recorded at 75.5 or 125.8 MHz in $CDCl_3$ solutions with $CHCl_3$ (77.0 ppm) as internal reference. Chemical shifts are reported in ppm (δ); coupling constants, J, are reported in Hz. Infrared spectra were recorded as thin films. Peaks are reported in units of cm^{-1} with the following relative intensities: br (broad), s (strong 67–100%), m (medium 33–67%), or w (weak 0–33%). Electron impact mass spectra were recorded with ionization voltages of 70 or 10 eV or with methane as the ionizing gas for chemical ionization. Data are reported in the form m/z (intensity relative to base = 100%). GC/MS was performed on a Hewlett-Packard 5970 Mass Selective Detector equipped with an HP 5890 gas chromatograph. A 25-m HP-1 methyl silicone gum column was used. Analytical gas chromatography was performed with both split and on-column injectors. The columns used were a HP 50 m OV-1 cross-linked methyl silicone and an HP-5 50 m phenyl–methyl silicone gum. Analytical thin-layer chromatography was performed on Merck silica gel plates with F-254 indicator. Visualization was accomplished by UV light, vanillin, and iodine. Solvents used in reactions were reagent grade and were distilled from the indicated drying agents: hexane, dichloromethane (CaH_2); ether, THF (Na/benzophenone). Solvents for recrystallization were spectral grade. Column chromatography was performed using 32–63-mm silica gel (Merck). Boiling points (bp) for bulb to bulb distillations refer to air bath temperatures and are uncorrected. Elemental analyses were performed by the University of Illinois Microanalytical Service Laboratory. Pure *meso*- and *dl*-3,3-dimethyl-2,4-pentanediols were prepared by the method of Maier.[8] 2-(Phenylmethyl)-1,3-propanediol was prepared by the method of Heathcock.[2]

Preparation of Acetals. *trans*- and *cis*-5-(Phenylmethyl)-2-*n*-hexyl-1,3-dioxane (*trans*-3 and *cis*-3). To a solution of heptanal (2.00 g, 17.5 mmol) and 2-(phenylmethyl)-1,3-propanediol (2.91 g, 17.5 mmol) in 50 mL of dry benzene was added *p*-toluenesulfonic acid monohydrate (30 mg, 0.156 mmol). The resulting solution was heated to reflux using a Dean-Stark trap for 3 h. The reaction mixture was cooled to room temperature, washed with saturated aqueous $NaHCO_3$ solution, and extracted with Et_2O (3 × 100 mL). The organic extracts were collected, washed with brine (40 mL), dried (Na_2SO_4), and concentrated under vacuum to give 4.35 g (95%) of a pale orange liquid as a 1.6/1 mixture. Purification of the residue by column chromatography (hexane/CH_2Cl_2 (75/25)) followed by Kugelrohr distillation gave 2.38 g (55%) of *trans*-3 and 1.50 g (35%) of *cis*-3: bp 150 °C (0.2 Torr); ^1H NMR (500 MHz) 7.31–7.12 (m, 5 H, Ph), 4.45 (t, J = 5.1, 1 H, HC(2)), 4.03 (dd, J = 4.4, 11.6, 2 H, HC_{eq}(4,6)), 3.40 (dd, J = 10.9, 10.9, 2 H, HC_{ax}(4,6)), 2.37 (m, 2 H, H_2C(7)), 2.33 (m, 1 H, HC(5)), 1.60 (m, 2 H, H_2C(1′)), 1.41–1.29 (m, 8 H), 0.89 (t, J = 6.7, 3 H, H_3C(6′)); ^{13}C NMR (125.8 MHz) 138.19 (Ph), 128.52 (Ph), 128.39 (Ph), 126.24 (Ph), 102.21 (C(2)), 71.76 (C(4), C(6)), 35.78 (C(1′)), 34.83 (C(5)), 34.78 (C(7)), 31.67 (C(4′)), 29.10 (C(3′)), 23.91 (C(2′)), 22.49 (C(5′)), 14.02 (C(6′)); IR (neat) 3027 (w), 2953 (s), 2924 (s), 2853 (s), 1603 (w), 1495 (m), 1464 (m), 1455 (m), 1404 (m), 1387 (m), 1236 (w), 1146 (s), 1103 (m), 1032 (m), 959 (m), 901 (m); MS (70 eV) 261 (3), 178 (7), 177 (51), 132 (12), 118 (100), 117 (17), 91 (41), 41 (9); TLC R_f 0.35 (hexane/EtOAc (96/4)); GC t_R 10.22 min (HP-5, 50 m, isothermal 250 °C). Anal. Calcd for $C_{17}H_{26}O_2$ (262.38): C, 77.82; H, 9.99. Found: C, 77.80; H, 10.02. Data for *cis*-3: bp 150 °C (0.2 Torr); ^1H NMR (500 MHz) 7.33–7.21 (m, 5 H, Ph), 4.57 (t, J = 5.0, 1 H, HC(2)), 3.89 (m, 4 H, HC_{eq}(4,6), H_2C(7)), 3.05 (d, J = 7.9, 2 H, HC_{ax}(4,6)), 1.67 (m, 2 H, H_2C(1′)), 1.60 (m, 1 H, HC(5)), 1.47–1.33 (m, 8 H), 0.92 (t, 0.38 = 6.8, 3 H, H_3C(6′)); ^{13}C NMR (125.8 MHz) 140.55 (Ph), 129.29 (Ph), 128.34 (Ph), 125.95 (Ph), 102.78 (C(2)), 69.52 (C(4), C(6)), 36.33 (C(5)), 35.73 (C(1′)), 35.16 (C(7)), 31.76 (C(4′)), 29.20 (C(3′)), 23.81 (C(2′)), 22.56 (C(5′)), 14.06 (C(6′)); IR (neat) 3063 (w), 3027 (m), 2953 (s), 2924 (s), 2853 (s), 1495 (m), 1454 (m), 1402 (m), 1375 (m), 1347 (m), 1329 (m), 1239 (m), 1150 (s), 1103 (m), 1053 (s), 1030 (m), 1007 (m), 967 (m); MS (70 eV) 261 (2), 177 (45), 132 (11), 131 (100), 117 (17), 91 (46), 55 (11), 43 (13), 41 (17); TLC R_f 0.38 (hexane/EtOAc (96/4); GC t_R 9.09 min (HP-5, 50 m, isothermal 250 °C). Anal. Calcd for $C_{17}H_{26}O_2$ (262.38): C, 77.82; H, 9.99. Found: C, 77.93; H, 10.03.

2-(1-Methylethyl)-1,3-propanediol (18). To a suspension of $LiAlH_4$ (6.15 g, 162.2 mmol, 2.0 equiv) in Et_2O (175 mL) at 0 °C was added diethyl 2-(1-methylethyl)malonate (16.40 g, 81.1 mmol) over 1 h. The resulting gray solution was stirred at reflux for 3 h and then quenched by the cautious addition of water (6.0 mL), 15% aqueous NaOH (6.0 mL), and then water (18.0 mL). The suspension was filtered through Celite, and then the solvent was removed under vacuum to leave a yellow oil. Distillation gave 7.60 g (79%) of 18 as a clear colorless oil: bp 90 °C (0.25 Torr); ^1H NMR (300 MHz) 4.03 (t, J = 4.8, 2 H, OH), 3.73 (m, 4 H, H_2C(1, 3), 1.66 (m, 1 H, HC(2)), 1.46 (m, 1 H, HC(4)), 0.86 (d, J = 6.8, 6 H, H_3C(5, 6)); ^{13}C NMR (75.5 MHz) 64.04 (C(1, 3)), 47.70 (C(2)), 26.18 (C(4)), 20.09 (C(5, 6)); IR (neat) 3331 (br, s), 2959 (s), 1468 (m), 1387 (m), 1368 (m), 1262 (w), 1210 (w), 1179 (w), 1090 (m), 1067 (m), 1021 (s), 976 (m), 918 (m), 868 (w); MS (70 eV) 85 (15), 71 (8), 70 (100), 69 (24), 58 (15), 57 (49), 56 (14), 55 (74), 43 (39), 42 (26), 41 (54), 39 (12). Anal. Calcd for $C_6H_{14}O_2$ (118.17): C, 60.98; H, 11.94. Found: C, 60.81; H, 11.72.

***trans*- and *cis*-5-(1-Methylethyl)-2-*n*-hexyl-1,3-dioxane (*trans*-5 and *cis*-5).** To a solution of heptanal (3.92 g, 34.4 mmol) and 2-(2-methylethyl)-1,3-propanediol (4.06 g, 34.4 mmol) in 50 mL of dry benzene was added *p*-toluenesulfonic acid monohydrate (30 mg, 0.156 mmol). The resulting solution was heated to reflux using a Dean-Stark trap for 3 h. The reaction mixture was cooled to room temperature, washed with saturated aqueous $NaHCO_3$ solution, and extracted with Et_2O (3 × 100 mL). The organic extracts were collected, washed with brine (40 mL), dried (Na_2SO_4), and concentrated under vacuum to give 6.90 g (94%) of a pale orange liquid as a 4/1 mixture. Purification of the residue by column chromatography (hexane/CH_2Cl_2 (80/20)) followed by Kugelrohr distillation gave 4.60 g (67%) of *trans*-5 and 1.15 g (17%) of *cis*-5. Data for *trans*-5: bp 100 °C (0.2 Torr); ^1H NMR

(500 MHz) 4.36 (t, J = 5.2, 1 H, HC(2)), 4.12 (dd, J = 4.6, 11.2, 2 H, HC_{ax}(4,6)), 3.36 (t, J = 11.4, 2 H, HC_{eq}(4,6)), 1.66 (m, 1 H, HC(5)), 1.55 (m, 2 H, H_2C(1′)), 1.36–1.22 (m, 9 H), 0.85 (d, J = 6.8, 6 H, H_3C(8,9)), 0.84 (t, J = 6.7, 3 H, H_3C(6′)); ^{13}C NMR (125 MHz) 101.89 (C(2)), 70.64 (C(4), C(6)), 40.24 (C(5)), 34.89 (C(1′)), 31.68 (C(4′)), 29.12 (C(3′)), 27.37 (C(7)), 23.94 (C(2′)), 22.50 (C(5′)), 19.79 (C(8), C(9)), 14.01 (C(6′)); IR (neat) 2961 (s), 2859 (s), 1466 (m), 1406 (m), 1389 (m), 1289 (m), 1240 (m), 1152 (s), 1098 (m), 1032 (s), 953 (m), 897 (m), 860 (m); MS (70 eV) 213 (M^+ – H, 6), 130 (8), 129 (100), 83 (55), 70 (36), 55 (64), 43 (28), 42 (11), 41 (30); TLC R_f 0.30 (hexane/EtOAc (97/3)); GC t_R 19.23 min (HP-5, 50 m, 80 °C (4 min), 10 °C/min, 250 °C (5 min)). Anal. Calcd for $C_{13}H_{26}O_2$ (214.34): C, 72.84; H, 12.23. Found: C, 72.84; H, 12.22. Data for *cis*-**5**: bp 100 °C (0.2 Torr); ^1H NMR (500 MHz) 4.50 (t, J = 5.1, 1 H, HC(2)), 4.11 (dd, J = 1.3, 11.8, 2 H, HC_{ax}(4,6)), 3.76 (dd, J = 2.8, 11.9, 2 H, HC_{eq}(4,6)), 2.15 (m, 1 H, HC(5)), 1.53 (m, 2 H, H_2C(1′)), 1.36–1.21 (m, 9 H), 0.98 (d, J = 6.8, 6 H, H_3C(8,9)), 0.84 (t, J = 3.0, 3 H, H_3C(6′)); ^{13}C NMR (125 MHz) 102.66 (C(2)), 68.66 (C(4), C(6)), 41.28 (C(5)), 35.11 (C(1′)), 31.73 (C(4′)), 29.17 (C(3′)), 25.56 (C(7)), 23.85 (C(2′)), 22.53 (C(5′)), 21.10 (C(8), C(9)), 14.03 (C(6′)); IR (neat) 2957 (s), 2924 (s), 2853 (s), 1464 (m), 1404 (w), 1387 (m), 1294 (w), 1240 (m), 1177 (m), 1146 (s), 1090 (w), 1017 (m), 938 (w); MS (70 eV) 213 (M^+ – H, 6), 130 (8), 129 (100), 83 (56), 70 (26), 55 (55), 43 (23), 41 (22); TLC R_f 0.35 (hexane/EtOAc (97/3)); GC t_R 18.36 min (HP-5, 50 m, 80 °C (4 min), 10 °C/min, 250 °C (5 min)). Anal. Calcd for $C_{13}H_{26}O_2$ (214.34): C, 72.84; H, 12.23. Found: C, 72.93; H, 12.20.

***rel*-(2*S*,4*R*,6*S*)-2-*n*-Hexyl-4,5,5,6-tetramethyl-1,3-dioxane (*cis*-9).** To a solution of heptanal (1.47 g, 12.86 mmol) and *meso*-3,3-dimethyl-2,4-pentanediol (1.70 g, 12.86 mmol) in 50 mL of dry benzene was added *p*-toluenesulfonic acid monohydrate (15 mg, 0.078 mmol). The resulting solution was heated to reflux using a Dean-Stark trap for 3 h. The reaction mixture was cooled to room temperature, washed with saturated aqueous $NaHCO_3$ solution, and extracted with Et_2O (3 × 70 mL). The organic extracts were collected, washed with brine (40 mL), dried (Na_2SO_4), and concentrated under vacuum to give 3.10 g of a pale orange liquid. Purification of the residue by column chromatography (hexane/EtOAc (99/1)), followed by Kugelrohr distillation gave 1.40 g (48%) of *cis*-**9**: bp 100 °C (1.0 Torr); ^1H NMR (500 MHz) 4.59 (t, J = 5.1, 1 H, HC(2)), 3.40 (q, J = 6.4, 2 H, H_2C(4,6)), 1.60 (m, 2 H, H_2C(1′)), 1.29 (m, 8 H), 1.43–1.16 (m, 9 H), 1.12 (d, J = 6.5, 6 H, H_3C(7,8)), 0.88 (s, 3 H, H_3C_{ax}(10)), 0.87 (t, J = 4.0, 3 H, H_3C(6′)), 0.70 (s, 3 H, H_3C(9)); ^{13}C NMR (125.8 MHz) 102.07 (C(2)), 81.07 (C(4), C(6)), 35.87 (C(5)), 35.10 (C(1′)), 31.78 (C(4′)), 29.18 (C(3′)), 24.11 (C(2′)), 22.57 (C(5′)), 20.99 (C(10)), 14.89 (C(7,8)), 14.04 (C(6′)), 12.43 (C(9)); IR (neat) 2959 (s), 2855 (s), 2716 (w), 1468 (m), 1445 (m), 1414 (m), 1391 (m) 1372 (m), 1335 (m), 1277 (m), 1246 (w), 1202 (w), 1138 (s), 1121 (s), 1053 (s), 1021 (m), 972 (m), 899 (w); MS (10 eV) 227 (M^+ – H, 4), 184 (4), 143 (15), 97 (11), 71 (7), 70 (100); TLC R_f 0.50 (hexane/EtOAc (97/3)); GC t_R 18.02 min (HP-5, 50 m, 80 °C (4 min), 10 °C/min, 250 °C (5 min)). Anal. Calcd for $C_{14}H_{24}O_2$ (228.36): C, 73.63; H, 12.36. Found: C, 73.67; H, 12.41.

***rel*-(2*S*,4*R*,6*R*)-2-Methoxy-4,5,5,6-tetramethyl-1,3-dioxane (21).** A solution of *dl*-3,3-dimethyl-2,4-pentanediol (800 mg, 6.05 mmol), trimethyl orthoformate (50 mL), and *p*-toluenesulfonic acid (50 mg) was heated at reflux over 12 h. The solution was cooled to room temperature and then poured into saturated aqueous $NaHCO_3$ solution (50 mL). The solution was extracted with Et_2O (3 × 40 mL), and the combined ether extracts were washed with brine (50 mL), dried (Na_2SO_4), and concentrated to an oil under reduced pressure. The product was purified by Kugelrohr distillation to give **21** (450 mg, 43%) along with undesired *cis*-**9** and **20**. Data for **21**: bp 100 °C (400 Torr); ^1H NMR (500 MHz) 5.39 (s, 1 H, HC(2)), 3.87 (q, J = 6.8, 1 H, HC(6)), 3.66 (q, J = 6.6, 1 H, HC(4)), 3.36 (s, 3 H, H_3C(1′)), 1.16 (d, J = 6.8, 3 H, H_3C(8)), 1.13 (d, J = 6.6, 3 H, H_3C(7)), 0.90 (s, 3 H, H_3C(9)), 0.77 (s, 3 H, H_3C(10)); ^{13}C NMR (125.8 MHz) 109.15 (C(2)), 74.33 (C(6)), 73.56 (C(4)), 52.25 (C(1′)), 36.22 (C(5)), 20.44 (C(8)), 20.30 (C(10)), 15.08 (C(7)), 14.06 (C(9)); IR (neat) 3355 (br m), 2977 (s), 1725 (s), 1464 (m), 1381 (m), 1304 (m), 1196 (s), 1102 (s), 1024 (m), 922 (m), 905 (m), 845 (m).

***rel*-(2*S*,4*R*,6*R*)-2-*n*-Hexyl-4,5,5,6-tetramethyl-1,3-dioxane ((±)-13).** To a solution of **21** (400 mg, 2.30 mmol) in toluene (35 mL) was added a solution of *n*-hexylmagnesium bromide in Et_2O (3.5 mL, 2.42 mmol, 1.05 equiv). The cloudy white solution was heated to reflux for 1 h. The solution was cooled to room temperature and then poured into saturated aqueous $NaHCO_3$ solution (50 mL). The solution was extracted with Et_2O (3 × 40 mL), and the combined organic extracts were washed with brine (40 mL), dried (Na_2SO_4), and concentrated under reduced pressure to give a yellow oil. Purification of the oil by silica gel chromatography (hexane/EtOAc (98/2)) followed by Kugelrohr distillation gave 210 mg (39%) of ((±)-**13**) as a clear, colorless oil: bp 125 °C (5.0 Torr); ^1H NMR (500 MHz) 4.85 (t, J = 5.0, 1 H, HC(2)), 3.80 (q, J = 6.4, 1 H, HC(6)), 3.71 (q, J = 7.0, 1 H, HC(4)), 1.55 (m, 2 H, HC(1′)), 1.30 (m, 11 H), 1.13 (s, 3 H H_3C_{ax}(10)), 1.08 (d, J = 6.4, 3 H, H_3C_{eq}(8)), 0.87 (t, J = 1.6, 3 H, H_3C(6′)), 0.69 (s, 3 H, H_3C_{eq}(9)); ^{13}C NMR (75.5 MHz) 94.50 (C(2)), 78.57 (C(6)), 74.00 (C(4)), 35.20 (C(1′), C(5)), 31.80 (C(4′)), 29.19 (C(3′)), 24.00 (C(2′)), 22.57 (C(5′)), 21.97 (C(9)), 21.00 (C(10)), 14.97 (C(7)), 14.06 (C(6′)), 13.46 (C(8)); IR (neat) 2961 (s), 2928 (s), 2853 (s), 1468 (m), 1414 (m), 1391 (w), 1372 (m), 1335 (m), 1277 (w), 1246 (w), 1201 (w), 1138 (s), 1121 (w), 1051 (m), 1021 (m), 972 (w); MS (70 eV) 228 (M^+, 1), 227 (8), 143 (8), 97 (14), 71 (9), 70 (100), 69 (3), 55 (20); TLC R_f 0.45 (hexane/EtOAc (97/3)); GC t_R 15.52 min (HP-5, 50 m, 80 °C (4 min), 10 °C/min, 250 °C (5 min)). Anal. Calcd for $C_{14}H_{28}O_2$ (200.32): C, 73.63; H, 12.36. Found: C, 73.58; H, 12.37.

Preparation of Reference Compounds. Additions to Acetals with $TiCl_4$. General Procedure. A magnetically stirred solution of the acetal (ca. 1.0 mmol) and allyltrimethylsilane (4.0 equiv) in dry CH_2Cl_2 (0.1 M in acetal) was cooled to –78 °C. Titanium tetrachloride (1.0 equiv) was then added at once. After being stirred for the specified reaction time (see below), the reaction was quenched by addition of 0.5 N NaOH in methanol (2 mL) and the solution was allowed to warm to room temperature. The reaction mixture was poured into water (10 mL), and the aqueous layer was extracted with ether (3 × 15 mL). The organic extracts were collected, washed with saturated aqueous sodium bicarbonate solution, dried (Na_2SO_4), and concentrated to give a light yellow residue. Details of purification are given below for the individual compounds.

***rel*-(4(*R*,*S*),2′*R*)-4-(2-(Phenylmethyl)-3-hydroxy-1-propoxy)-1-decene (4).** The residue obtained from the reaction of *trans*-**3** (40.4 mg, 0.154 mmol), allyltrimethylsilane (98 μL, 0.62 mmol, 4 equiv), and $TiCl_4$ (16.9 μL, 0.154 mmol, 1.0 equiv) (reaction time 30 min) was purified by column chromatography on silica gel (hexane/EtOAc (90/10)) followed by Kugelrohr distillation to give 41.5 mg (88%) of a diastereomeric mixture (*lk*/*ul* (1.0/1)) of **4** as a colorless oil: bp 180 °C (0.3 Torr); ^1H NMR (300 MHz) 7.32–7.19 (m, 5 H, Ph), 5.82 (m, 1 H, HC(2)), 5.07 (m, 2 H, H_2C(1)), 3.76–3.60 (m, 4 H, H_2C(1′, 3′)), 3.29 (m, 1 H, HC(4)), 2.98 (m, 1 H, OH), 2.67 (m, 2 H, H_2C(4′)), 2.27 (m, 2 H, H_2C(3)), 2.09 (m, 1 H, HC(2′)), 1.49–1.29 (m, 10 H), 0.90 (m, 3 H); ^{13}C NMR (75.5 MHz) 140.10 (Ph), 139.99 (Ph), 134.71 (Ph), 134.66 (Ph), 128.92 (Ph), 128.21 (Ph), 125.88 (Ph), 117.00 (C(1)), 79.54 (C(4)), 79.46 (C(4)), 71.92 (C(1′)), 71.62 (C(1′)), 65.63 (C(3′)), 65.58 (C(3′)), 42.53 (C(2′)), 42.47 (C(2′)), 38.03 (C(3)), 34.43 (C(4′)), 34.38 (C(4′)), 33.44 (C(5)), 31.71 (C(6)), 31.68 (C(6)), 29.29 (C(8)), 25.16 (C(7)), 25.09 (C(7)), 22.54 (C(9)), 22.52 (C(9)), 14.00 (C(10)); IR (neat) 3429 (br m), 3063 (w), 3027 (m), 2926 (s), 2857 (s), 1651 (w), 1640 (w), 1603 (w), 1559 (w), 1495 (m), 1455 (m), 1347 (m), 1084 (s), 1049 (s), 994 (m), 912 (m); CI-MS 305 (7), 263 (26), 167 (61), 149 (19), 132 (12), 131 (100), 119 (13), 97 (12), 91 (26), 83 (22); TLC R_f 0.35 (hexane/EtOAc (90/10)). Anal. Calcd for $C_{20}H_{32}O_2$ (304.46): C, 78.89; H, 10.59. Found: C, 78.89; H, 10.48.

***rel*-(4(*R*,*S*),2′*R*)-4-(2-(1-Methylethyl)-3-hydroxy-1-propoxy)-1-decene (6).** The residue obtained from the reaction of *trans*-**5** (58.3 mg, 0.272 mmol), allyltrimethylsilane (172.9 μL, 1.09 mmol, 4 equiv), and $TiCl_4$ (29.8 μL, 0.272 mmol, 1.0 equiv) (reaction time 30 min) was purified by column chromatography on silica gel (hexane/EtOAc (90/10)) followed by Kugelrohr distillation to give 64.0 mg (92%) of a diastereomeric mixture (*lk*/*ul* (1.0/1)) of **6** as a colorless oil: bp 150 °C (0.2 Torr); ^1H NMR (300 MHz) 5.76 (m, 1 H, HC(2)), 5.01 (m, 2 H, H_2C(1)), 3.70–3.51 (m, 4 H), 3.26 (m, 1 H, HC(4)), 3.06 (m, 1 H, OH), 2.22 (m, 2 H, H_2C(3)), 1.70 (m, 1 H, HC(4′)), 1.56–1.23 (m, 12 H), 0.98 (d, J = 7.2, 6 H, H_3C(5′, 6′)), 0.84 (t, J = 6.7 3 H, H_3C(10)); ^{13}C NMR (75.5 MHz) 134.65 (C(2)), 117.03 (C(1)), 116.98 (C(1)), 79.65 (C(4)), 79.59 (C(4)), 71.76 (C(1′)), 71.50 (C(1′)), 65.08 (C(3′)), 65.01 (C(3′)),

46.55 (C(2')), 46.46 (C(2')), 38.04 (C(3)), 33.43 (C(5)), 31.69 (C(6)), 29.30 (C(8)), 26.39 (C(4')), 26.12 (C(4')), 25.11 (C(7)), 22.52 (C(9)), 20.22 (C(6')), 20.17 (C(5')), 13.97 (C(10)); IR (neat) 3434 (br m), 3077 (w), 2928 (s), 2859 (s), 1642 (m), 1466 (m), 1368 (m), 1345 (m), 1262 (w), 1088 (s), 1049 (m), 994 (m), 912 (m); CI-MS 258 (13), 257 (65), 215 (52), 147 (11), 120 (8), 119 (100), 117 (15), 115 (13), 110 (70), 97 (27), 83 (90), 81 (10), 69 (16), 57 (17), 55 (19); TLC R_f 0.38 (hexane/EtOAc (90/10)). Anal. Calcd for $C_{16}H_{32}O_2$ (256.42): C, 74.94; H, 12.58. Found: C, 74.87; H, 12.61.

***rel*-(4(*R*,*S*),1'*R*,3'*S*)-4-(3'-Hydroxy-1',2',2'-trimethylbutoxy)-1-decene (10).** The residue obtained from the reaction of *cis*-**9** (270 mg, 1.18 mmol), allyltrimethylsilane (750 μL, 4.72 mmol, 4 equiv) and $TiCl_4$ (130 μL, 1.18 mmol, 1.0 equiv) (reaction time 30 min) was purified by column chromatography on silica gel (hexane/EtOAc (96/4)) followed by Kugelrohr distillation to give 301 mg (94.4%) of a diastereomeric mixture (*lk*/*ul* (1.1/1)) of **10** as a colorless oil: bp 150 °C (0.2 Torr); ^{1}H NMR (500 MHz) 5.78 (m, 1 H, HC(2)), 5.02 (m, 2 H, $H_2C(1)$), 4.29 (s, 1 H, OH), 3.72 (m, 1 H, HC(3')), 3.46 (m, 2 H, HC(4), HC(1')), 2.25 (m, 2 H, $H_2C(3)$), 1.28 (m, 10 H), 1.08 (d, J = 6.2, 6 H, $H_3C(5')$, $H_3C(4')$), 0.87 (m, 6 H, $H_3C(10)$, $H_3C(7')$), 0.70 (s, 3 H, $H_3C(6')$); ^{13}C NMR (125.8 MHz) 134.85 (C(2)), 134.35 (C(2)), 117.41 (C(1)), 116.86 (C(1)), 81.68 (C(1')), 81.24 (C(1')), 75.51 (C(4)), 75.36 (C(3')), 75.31 (3')), 74.95 (C(4)), 41.07 (C(2')), 41.04 (C(2')), 39.15 (C(3)), 37.78 (C(3)), 34.54, 32.81, 31.77, 31.74, 29.48, 29.30, 25.34, 25.17, 22.58, 22.56, 22.44, 22.35, 17.70, 17.69, 14.03, 14.02, 13.96, 13.71, 12.99, 12.95; IR (neat) 3436 (br m), 3077 (w), 2930 (s), 2859 (s), 1642 (w), 1458 (m), 1375 (m), 1335 (m), 1248 (m), 1101 (s), 912 (m), 862 (m), 835 (w); CI-MS 272 (12), 271 (51), 253 (3), 229 (7), 213 (3), 197 (3), 183 (10), 159 (17), 139 (28), 133 (13), 116 (11), 115 (100), 113 (14), 97 (36), 83 (40), 75 (12), 73 (30), 71 (58), 70 (22), 69 (17), 57 (13), 55 (13); TLC R_f 0.40 (hexane/EtOAc (95/5)); GC t_R major (*lk*-**10**) 12.74 min, minor (*ul*-**10**) 13.04 min (HP-5, 50 m, 200 °C isothermal). Anal. Calcd for $C_{17}H_{34}O_2$ (270.44): C, 75.49; H, 12.67. Found: C, 75.22; H, 12.78.

***rel*-(4(*R*,*S*),1'*R*,3'*S*)-4-(3'-Hydroxy-1',2',2'-trimethylbutoxy)-1-decene (14).** The residue obtained from the reaction of (±)-**13** (125 mg, 0.55 mmol), allyltrimethylsilane (350 μL, 2.19 mmol, 4 equiv), and $TiCl_4$ (60 μL, 0.55 mmol, 1.0 equiv) (reaction time 30 min) was purified by column chromatography on silica gel (hexane/EtOAc (96/4)) followed by Kugelrohr distillation to give 128 mg (87%) of a diastereomeric mixture (*lk*/*ul* (8.0/1)) of **14** as a colorless oil: bp 150 °C (0.2 Torr); ^{1}H NMR (500 MHz) 5.77 (m, 1 H, HC(2)), 5.03 (m, 2 H, $H_2C(1)$), 4.31 (s, 1 H, OH), 3.88 (q, J = 6.3, 1 H, HC(3')), 3.41 (m, 2 H, HC(4), HC(1')), 2.20 (m, 2 H, $H_2C(3)$), 1.50 (m, 2 H, $H_2C(5)$), 1.27 (m, 8 H), 1.13 (d, J = 6.3, 3 H, $H_3C(4')$), 1.06 (d, J = 6.4, 3 H, $H_3C(5')$), 0.96 (s, 3 H, $H_3C(6')$), 0.88 (t, J = 6.7, 3 H, $H_3C(10)$), 0.74 (s, 3 H, $H_3C(7')$); ^{13}C NMR (125.8 MHz) 134.85 (C(2)), 117.35 (C(1)), 82.10 (C(1')), 76.60 (C(4)), 70.82 (C(3')), 38.87 (C(3)), 32.78 (C(5)), 31.75 (C(8)), 29.53 (C(7)), 24.78 (C(6)), 23.18 (C(6')), 22.57 (C(9)), 19.61 (C(7')), 17.35 (C(5')), 14.40 (C(10)), 13.99 (C(4')); IR (neat) 3497 (br m), 3077 (w), 2967 (s), 2930 (s), 2859 (m), 1642 (w), 1466 (m), 1416 (m), 1377 (m), 1113 (m), 1076 (s), 1036 (m), 995 (m), 912 (m); CI-MS 272 (11), 271 (46), 229 (19), 143 (12), 139 (21), 133 (19), 116 (11), 115 (100), 97 (22), 83 (19), 71 (28), 70 (15); TLC R_f 0.40 (hexane/EtOAc (95/5)); GC t_R major (*lk*-**14**) 12.67 min, minor (*ul*-**14**) 12.90 min (HP-5, 50 m, 200 °C isothermal). Anal. Calcd for $C_{17}H_{34}O_2$ (270.44): C, 75.49; H, 12.67. Found: C, 75.46; H, 12.66.

General Procedure for Allylation of Acetals *cis*-9 and (±)-13. "Titanium Blend" ($TiCl_4$/Ti(O-*i*-Pr)$_4$, 6/5). A Lewis acid solution ($TiCl_4$/Ti(O-*i*-Pr)$_4$ (6/5)) was prepared by dissolving $TiCl_4$ (330 μL, 3.0 mmol) in dry CH_2Cl_2 (9 mL) under an atmosphere of nitrogen and then addition of Ti(O-*i*-Pr)$_4$ (740 μL, 2.5 mmol) with magnetic stirring. After complete addition of Ti(O-*i*-Pr)$_4$, the resulting solution was stirred for 30 m. For each acetal, the reactions were run in triplicate under the following conditions: the acetal (0.50 mmol) and allyltrimethylsilane (636 μL, 4.0 mmol) were dissolved in dry CH_2Cl_2 (5.0 mL, 0.1 M in acetal) and cooled to −78 °C under an atmosphere of nitrogen. The freshly prepared Lewis acid solution (10.07 mL, 11 equiv) was added via syringe (addition time 2.0 h) to the magnetically stirred acetal and allyltrimethylsilane solution. After complete addition of the Lewis acid solution, the resulting heterogeneous solution was stirred an additional period of time (see Table II) followed by quenching with 1.0 N NaOH in methanol (5 mL) and warming to room temperature. The reaction solution was diluted with Et_2O (15 mL), filtered through a plug of Florisil, and analyzed by gas chromatography.

General Procedure for Allylation of Acetals. Titanium Blend ($TiCl_4$/Ti(O-*i*-Pr)$_4$ (5/5)). A Lewis acid solution ($TiCl_4$/Ti(O-*i*-Pr)$_4$ (5/5, 2.5/2.5, or 1.25/1.25)) was prepared by dissolving $TiCl_4$ (137 μL, 1.25 mmol) in dry CH_2Cl_2 (5 mL) followed by the addition of Ti(O-*i*-Pr)$_4$ (372 μL, 1.25 mmol). After complete addition of Ti(O-*i*-Pr)$_4$, the resulting solution was stirred for 30 min. For each acetal the reactions were run under the following conditions: the acetal (0.25 mmol) and the allylmetal (number of equiv in table) were dissolved in dry CH_2Cl_2 (2.5 mL, 0.1 M in acetal) and cooled to −78 °C under an atmosphere of nitrogen. The freshly prepared Lewis acid solution (number of equiv in Table I) was added via syringe (addition time 2.0 h) to the magnetically stirred acetal and allylmetal solution. After complete addition of the Lewis acid solution, the resulting heterogeneous solution was stirred for 1 additional hour, quenched with 1.0 N NaOH in methanol (5 mL), and allowed to warm to room temperature. The reaction solution was extracted with diethyl ether (3 × 15 mL), dried ($MgSO_4$), and concentrated to an oil under reduced pressure. The product was purified by chromatography (gradient: hexanes → 9/1 hexanes/EtOAc) to give the desired alcohol as a clear colorless oil. Diastereomeric ratios were then determined by 125.8-MHz ^{13}C NMR analysis by observing C(1')) and calculating the relative peak heights and areas.

Control Additions with Titanium Blend ($TiCl_4$/Ti(O-*i*-Pr)$_4$ (2.5/2.5)). A Lewis acid solution ($TiCl_4$/Ti(O-*i*-Pr)$_4$ (2.5/2.5 or 1.25/1.25)) was prepared by dissolving $TiCl_4$ (68.5 μL,m 0.625 mmol) in dry CH_2Cl_2 (2.5 mL) followed by the addition of Ti(O-*i*-Pr)$_4$ (186 μL, 0.625 mmol). After complete addition of Ti(O-*i*-Pr)$_4$, the resulting solution was stirred for 30 min. For each acetal the reactions were run under the following conditions: the acetal (0.25 mmol) and the allylmetal (number of equiv in Table I) were dissolved in dry CH_2Cl_2 (2.5 mL, 0.1 M in acetal) and cooled to −78 °C under an atmosphere of nitrogen. The freshly prepared Lewis acid solution (number of equiv in Table I) was added via syringe (addition time in Table I) to the magnetically stirred acetal and allylmetal solution. After complete addition of the Lewis acid solution, the resulting heterogeneous solution was stirred for 1 additional hour, quenched with 1.0 N NaOH in methanol (2 mL), and allowed to warm to room temperature. The reaction solution was poured into water, extracted with Et_2O (3 × 15 mL), dried ($MgSO_4$), and concentrated to an oil under reduced pressure. The product was purified by chromatography (gradient: hexanes → 9/1 hexanes/EtOAc) to give the desired alcohol as a clear colorless oil. Diastereomeric ratios were then determined by 125.8-MHz ^{13}C NMR analysis by observing C(1')) and calculating the relative peak heights and areas.

Acknowledgment. We gratefully acknowledge financial support for this project from the National Science Foundation (NSF CHE 881847). We are grateful to Professor Clayton H. Heathcock for providing a preprint of ref 2 and to Professor Herbert Mayr (Universität zu Lübeck) for a preprint of ref 12 and information on silyl enol ethers.