of the two independent polyhedra, and cube-like in KF·3HF, with K···F contact distances in the range 269.9–313.7 pm.

A compilation of the (averaged) hydrogen-bonding F···F distances (in pm) in all the intermediary compounds of the system KF–HF now studied is as follows: α-KHF_2, 227.7, see ref 4; KH_2F_3, 233.1, average, see ref 2 (and ref 6); $K_2[H_2F_3][H_3F_4]$, 236.0, average, this work; KH_3F_4, 240.1, this work; KH_4F_5, 245.3, see ref 7. The increase with increasing HF content, i.e., with increasing (average) size of the hydrogen-bonded structural unit, is unmistakable. The upper limit of the series is obviously given by the F···F distance in the infinite chain of the pure HF solid, which was recently refined[17] from 249 (1) pm at −125 °C[18] to 250.0 (1) pm at −146 °C. Similar trends, though with less data for any single system, can be seen in the other complex acid fluoride structures referred to above and in some more dealt with in the same references. The correlation is analogous to that known for oxonium cations $[H_3O(H_2O)_n]^+$ in crystalline hydrates of strong acids.[19]

Acknowledgment. The work was supported by the Minister für Wissenschaft und Forschung des Landes Nordrhein-Westfalen and by the Fonds der Chemischen Industrie.

Registry No. $K_2[H_2F_3][H_3F_4]$, 104090-15-5; KH_3F_4, 104090-16-6.

Supplementary Material Available: Listing of anisotropic thermal parameters of the K and F atoms (1 page); tables of calculated and observed structure factors (5 pages). Ordering information is given on any currrent masthead page.

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(18) Atoji, M.; Lipscomb, W. N. *Acta Crystallogr.* **1954**, 7, 173–175.
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Substituent Effects in [3,3]-Sigmatropic Rearrangements. Alkyl Group Effects and Transition-State "Syn-Diaxial" Interactions

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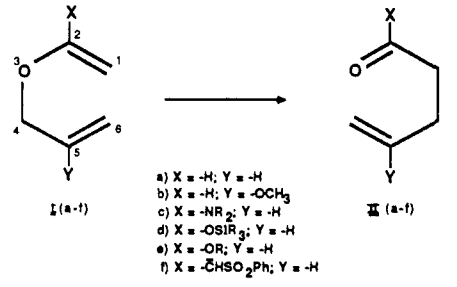
Abstract: Rearrangement rates for nineteen *O*-allyl silylketene acetals {[(1-(allyloxy)-1-ethenyl)oxy]trialkylsilanes} are reported. Whereas rates for rearrangement of **1** and **2** exhibit a linear free energy relationship, no linear free energy relationship is observed between rates for **1** and **3**. These data suggest the possibility of "syn-diaxial" interactions in a chair-like transition state for rearrangements of **3**. The difference in free energy between **2** and **3** is found to be 1.34 kcal/mol and is independent of R. The magnitude of the diaxial interaction ($\Delta\Delta G_{Z^\ddagger/E^\ddagger}$, the difference in free energy between transition states reached from **2** or **3**) was determined to range from 1.2 to 2.5 kcal/mol and is dependent on the nature of R. Finally, comparison of the effect of a (trimethylsilyl)methyl substituent (R = $CH_2Si(CH_3)_3$) with the effects of comparably sized alkyl groups suggests that this C-5 substituent has a rate-decelerating electronic influence on the rearrangement of these acetals. Steric effects in these rearrangements are compared with steric effects in comparably substituted tetrahydropyran derivatives and significant differences are noted.

The aliphatic Claisen rearrangement is a versatile method of carbon–carbon bond formation that is frequently employed in the synthesis of complex molecules of health-related significance.[1] Many variations of this reaction have been devised (eq 1), and the synthetic utility of each of these processes is widely recognized.[2]



(1)

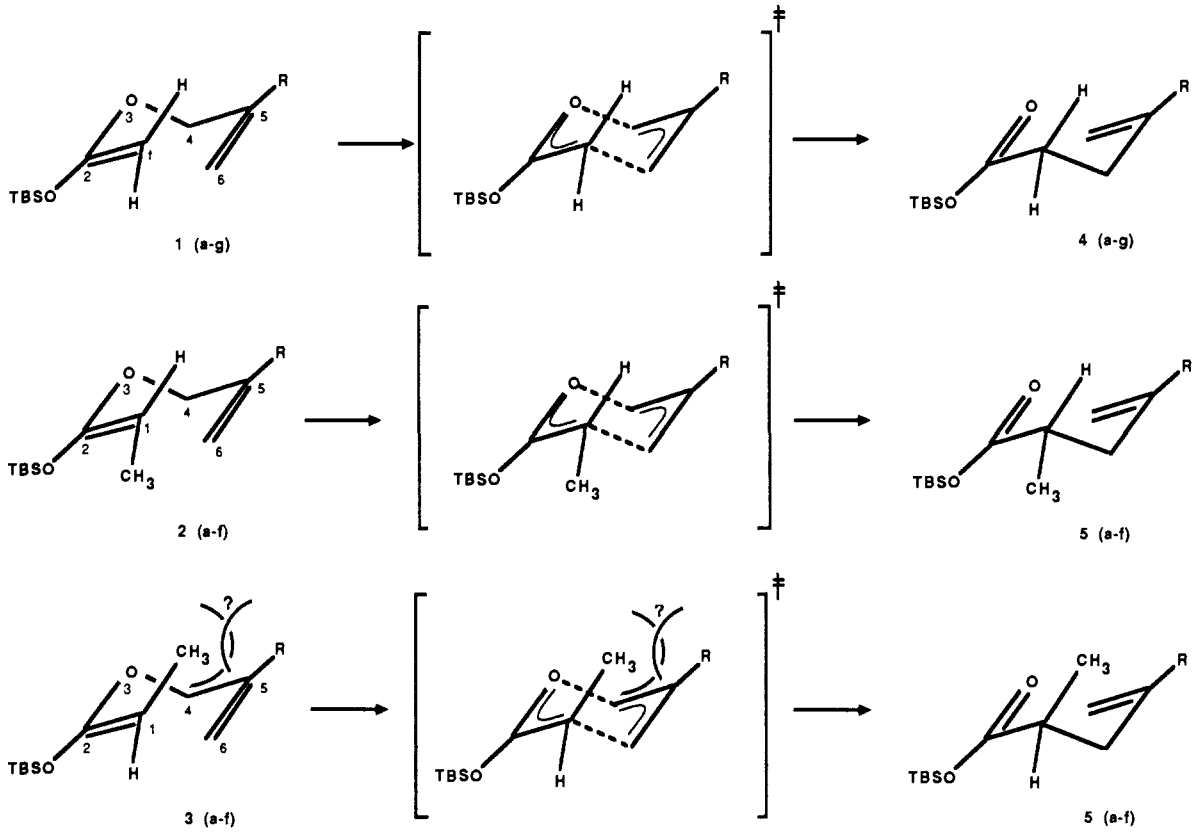
Current interest in rearrangements of this type has been stimulated by the remarkably wide range of rates observed within this general family of related reactions. The magnitude of possible substituent effects is dramatically illustrated by the fact that the diene Id rearranges with an apparent first-order rate constant at 35 °C which is 10^6 times greater than that found for the rearrangement of Ib.[3]

Reliable explanations for the effects of substituents on the rates of aliphatic Claisen rearrangements must be founded upon accurate quantitative data. A number of research groups are now

(1) (a) Ziegler, F. E. *Acc. Chem. Res.* **1977**, *10*, 227. (b) Bennett, G. B. *Synthesis* **1977**, 589. (c) Rhoads, S. J.; Raulins, N. R. *Org. React.* **1975**, *22*, 1.
(2) (a) Burghstahler, A. W.; Nordin, I. C. *J. Am. Chem. Soc.* **1961**, *83*, 198. (b) Ireland, R. E.; Mueller, R. H.; Willard, A. K. *Ibid.* **1976**, *98*, 2868. (c) Johnson, W. S.; Werthemann, L.; Bartlett, W. R.; Brochsom, T. J.; Li, T.; Faulkner, D. J.; Petersen, M. R. *Ibid.* **1970**, *92*, 741. (d) Felix, D.; Gschwend-Steen, K.; Wick, A. E.; Eschenmoser, A. *Helv. Chim. Acta* **1969**, *52*, 1030. (e) Denmark, S. E.; Harmata, M. A. *J. Am. Chem. Soc.* **1982**, *104*, 4972.
(3) We thank Professor D. Curran (University of Pittsburgh) for a preprint of a manuscript containing rate data for the rearrangement of Ib.

0002-7863/86/1508-6636$01.50/0

Chart I



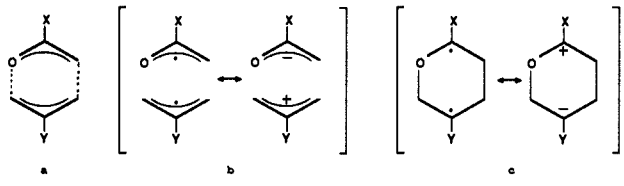


Figure 1. Representations of (a) synchronous, (b) fragmented, and (c) 1,4-diyl transition states for the aliphatic Claisen rearrangement.

involved in obtaining such data. To contribute to these efforts and because of our interest in the chemistry of *O*-silylketene acetals and the important synthetic applications of such reactions, we have begun to examine the effects of substituents on the three systems illustrated in Chart I. We report here the results of the first phase of this project.

The effects of substituents on rates of [3,3]-sigmatropic rearrangements and the variable nature of the transition states for such processes have been the subjects of many insightful investigations.[4,5] Figure 1 illustrates some of the transition-state representations which have been put forward for [3,3] rearrangement reactions. Gajewski has confirmed the reasonable expectation that substituents will alter the nature of the transition state in these reactions and has usefully illustrated such shifts in transition-state structure by use of the More O'Farrell–Jencks diagram.[4f,g] Ample evidence supports the idea that given proper combinations of electron-withdrawing, electron-donating, or radical-stabilizing substituents, most (perhaps all) of the hypothetical intermediates or transition states shown in Figure 1 may be accessible.[5]

The initial investigation reported here was limited almost exclusively to an examination of the effects of C-5 alkyl groups on the rearrangements of **1**, **2**, and **3** (Chart I). There were several compelling reasons for limiting the project to what at first sight may be considered rather undramatic or uninteresting substituents which would be unlikely to afford very large rate changes. Of all possible substituents (excepting isotopic substitution), alkyl groups would least perturb the structure of the transition state. The relatively subtle effects of alkyl groups are interesting inasmuch as they would serve as a delicate probe of transition-state geometry and electronic demand. It was expected that these limited substituents would not cause a change in the nature of the transition state so large as to effectively change the mechanism of the reaction. Also, it was reasoned that a thorough understanding of alkyl group effects would be an essential prerequisite to an understanding of the effects of more polar groups. For example, the experimentally observed effects of replacing a proton at C-5 with a trifluoromethyl group or a methoxy group will have greater meaning if the effects of alkyl group substitutions at that position have been quantified. A study of alkyl group effects should properly precede examination of polar group substituent

(4) (a) Doering, W. von E.; Roth, W. R. *Tetrahedron* **1962**, *18*, 67. (b) Doering, W. von E.; Toscano, V. G.; Beasley, G. H. *Ibid.* **1971**, *27*, 5299. (c) Carpenter, B. K. *Ibid.* **1978**, *34*, 1877–1884. (d) Burrows, C. J.; Carpenter, B. K. *J. Am. Chem. Soc.* **1981**, *103*, 6984. (e) Wilcox, C., Jr.; Carpenter, B. K. *J. Am. Chem. Soc.* **1979**, *101*, 3897. (f) Gajewski, J. J.; Conrad, N. D. *J. Am. Chem. Soc.* **1979**, *101*, 6693–6704. (g) Gajewski, J. J.; Gilbert, K. E. *J. Org. Chem.* **1984**, *49*, 11–17. (h) Gajewski, J. J. *Acc. Chem. Res.* **1980**, *13*, 142. (i) McMichael, K. D.; Korver, G. L. *J. Am. Chem. Soc.* **1979**, *101*, 2746. (j) Dewar, M. J. S.; Wade, L. E. *Ibid.* **1977**, *99*, 4417. (k) Dewar, M. J. S.; Healy, E. F. *Ibid.* **1984**, *106*, 7128. (k) Dewar, M. J. S.; Ford, G. P.; McKee, M. L. Rzepa, H. S.; Wade, L. E. *Ibid.* **1977**, *99*, 5069. (l) Marvell, E. N.; Li, T. H.-C. *Ibid.* **1978**, *100*, 883.

(5) (a) Wehrli, R.; Bellus, D.; Hansen, H.-J.; Schmid, H. *Chimia* **1976**, *30*, 416. (b) Gompper, R.; Ulrich, W.-R. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 299. (c) Gompper, R.; Ulrich, W.-R. *Ibid.* **1976**, *15*, 301. (d) Shea, K. J.; Wise, S. *J. Org. Chem.* **1978**, *43*, 2710. (e) Shea, K. J.; Phillips, R. B. *J. Am. Chem. Soc.* **1978**, *100*, 654. (f) Yates, P.; Eaton, P. *Tetrahedron Lett.* **1960**, *11*, 5. (g) Wigfield, D. G.; Feiner, S.; Malbacho, G.; Taymaz, K. *Tetrahedron* **1974**, *30*, 2949. (h) Curran, D. P.; Suh, Y.-G. *J. Am. Chem. Soc.* **1984**, *106*, 5002.

(6) Although a number of studies indicate that axial substituents at olefinic positions lead to slow rearrangement rates,[12,13] lack of information regarding starting material stability precludes conclusions concerning relative transition-state energies. Exceptional cases are provided by limited studies of competitive rearrangements: (a) Cresson, P.; Lecour, L. *C. R. Acad. Sci. Paris Ser. C* **1966**, *262*, 1165. (b) Cresson, P.; Bancel, S. *Ibid.* **1968**, *266*, 409. (c) Parker, K. A.; Farmar, J. G. *Tetrahedron Lett.* **1985**, 3655.

Table I. Rearrangement Rates for Ketene Acetals at 35 °C

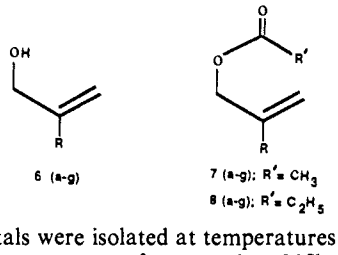
entry	reactant	R	k_{obsd} ($s^{-1} \times 10^5$)	$t_{1/2}$ (min)	log k_{obsd}
1	**1a**	H	10.8	107 (±2)	-3.96
2	**2a**	H	250	4.7 (±0.1)	-2.61
3	**3a**	H	310	3.8 (±0.1)	-2.51
4	**1b**	CH_3	4.60	251 (±3)	-4.33
5	**2b**	CH_3	93.9	12.3 (±0.4)	-3.03
6	**3b**	CH_3	30.4	38.0 (±0.4)	-3.52
7	**1c**	C_2H_5	5.8	199 (±3)	-4.23
8	**2c**	C_2H_5	120	9.4 (±0.2)	-2.91
9	**3c**	C_2H_5	34.9	33.1 (±0.4)	-3.46
10	**1d**	n-C_3H_7	6.38	181 (±3)	-4.19
11	**2d**	n-C_3H_7	140	8.1 (±0.2)	-2.84
12	**3d**	n-C_3H_7	46	25.1 (±0.3)	-3.33
13	**1e**	i-C_3H_7	7.65	151 (±2)	-4.12
14	**2e**	i-C_3H_7	170	6.8 (±0.2)	-2.76
15	**3e**	i-C_3H_7	27.7	41.7 (±0.9)	-3.56
16	**1f**	neo-C_5H_{11}	34.4	33.6 (±0.8)	-3.46
17	**2f**	neo-C_5H_{11}	810	1.4 (±0.1)	-2.09
18	**3f**	neo-C_5H_{11}	320	3.6 (±0.1)	-2.49
19	**1g**	$CH_2Si(CH_3)_3$	5.25	220 (±3)	-4.28

effects. Finally, although the effects of alkyl groups might be relatively small, rate effects corresponding to 10–100-fold rate changes are useful in practical synthetic strategies and are therefore interesting apart from the light they may shed on the nature of the transition states for these reactions.

A number of questions, some long standing, may be asked in relation to the three systems which are shown in Chart I. (1) What is the effect of increasing the size of the alkyl group at C-5 and is this effect consistent among the three systems? Alkyl group substituent effects are frequently considered in terms of separable steric and electronic component effects. (2) Are the steric and electronic alkyl group effects recognizably different for the reactions in Chart I? The methyl group at C-1 in reactant **3** occupies an axial-like position in the four-centered, chair-like transition state whereas the methyl group at C-1 in reactant **2** occupies an equatorial position. (3) Because of this "axial" substituent, are rearrangements of analogues of reactant **3** consistently slower than rearrangements of equivalently C-5 derivatized analogues of reactant **2**? Answers to two remaining questions are particularly interesting because the answers will illuminate details of the conformation of the transition state for these reactions: (4) What is the difference in free energy between the transition states reached from equivalently C-5 substituted analogues of **2** and **3**? (5) Does the axial-like methyl group at C-1, in accordance with expectations based on the canonical chair-like transition states illustrated in Chart I, approach the substituent at C-5?

Results and Discussion

General Comments. Acetate esters (**7a–g**) and propanoate esters (**8a–f**), prepared by conventional means from alcohols **6a–g**, were converted to the desired ketene acetals by the method of Ireland.



The ketene acetals were isolated at temperatures not exceeding 5 °C and were in every case of greater than 93% purity (NMR). Detectable contaminating material consisted of the disiloxane derived from *tert*-butyldimethylchlorosilane, 1–3% of the silyl ether corresponding to the alcohol portion of the ester, and (in the case of reactants **2** and **3**) approximately 5% of the undesired geometrical isomer. Rearrangements were conducted in a water bath maintained at 35 ± 0.05 °C. Samples were withdrawn periodically, cooled rapidly (−78 °C), and analyzed by 200- or 500-MHz ^1H NMR at −40 °C. Rates were determined in deuteriochloroform, and the results are presented in Table I. Separate experiments revealed that solvent changes have only a small effect on the rates of these reactions (Table II).

Table II. Rearrangement of **1b** at 35 °C; Solvent Effects

solvent[a]	$t_{1/2}$ (min)[b]	solvent	$t_{1/2}$ (min)
CCl_4	350	$CD_3(CO)CD_3$	333[c]
$CDCl_3$	251	CD_3OD[d]	[22][e]
CD_2Cl_2	315	$(CH_3)_3OH$[d]	396
C_6D_6	431	CD_3CN	435
C_5D_5N	384	DMF-d_7	335[c]

[a] Solvents purified as described in the Experimental Section. [b] All measurements ±3 min. [c] Rate corrected for small (<10%) amount of hydrolysis coincident with rearrangement. [d] Solvent contained 10% (v/v) *N,N,N',N'*-tetramethylguanidine. [e] No rearrangement observed. Time shown is half-life for (first-order) disappearance of starting material. Products consistent with solvolysis were observed.

Rates for the rearrangement of ketene acetals **1a–g**, **2a–f**, and **3a–f** at 35 °C vary widely (Table I). A quick overview of these data reveals that the largest substituent effect is due to introduction of the α-methyl group on the ketene acetal moiety. The accelerating effect of α-alkyl groups was observed by Ireland et al. in the earliest studies of this reaction. In general, derivatives of **2** rearrange at 20 to 25 times the rate of the corresponding derivatives of **1**. With one exception, *E* ketene acetals rearrange more slowly than *Z* ketene acetals. The expectation that an "axial" methyl group at C-1 will destablize chair-like transition states in comparison with systems bearing an "equatorial" methyl group is found to be valid at 35 °C *provided that the C-5 substituent is larger than a hydrogen.* Acetal **1** should be considered the parent system in this study, and therefore substituent effects on this system will be discussed first.

The Effect of Alkyl Groups at C-5. The effects of C-5 substituents on the rate of rearrangement of **1** are displayed graphically in Figure 2. As the C-5 substituent is changed from a hydrogen to a methyl group, the reaction is slowed down. Subsequent variation at C-5 through the series methyl, ethyl, *n*-propyl, isopropyl, neopentyl provides a continual increase in rate. It is interesting that the rate increases occur in the order of increasing steric influence as measured by the steric effect parameter E_s originated by Taft.[7,8] Ultimately, the system bearing a neopentyl substituent at C-5 rearranges more than seven times faster than the system bearing a methyl group at C-5.

The qualitative interpretation of the observed relative reaction rates presents an interesting challenge. The pioneering studies of Taft have illustrated the validity of attempts to separate steric effects from polar and resonance effects.[7] The possibility that alkyl substituents are both sterically and electronically accelerating

(7) Taft, R. W., Jr. *J. Am. Chem. Soc.* **1953**, *75*, 4534–4537.
(8) Unger, S. H.; Hansch, C. In *Progress in Physical Organic Chemistry*; Taft, R. W., Ed.; John Wiley and Sons: New York, 1976; Vol. 12, pp 91–118.

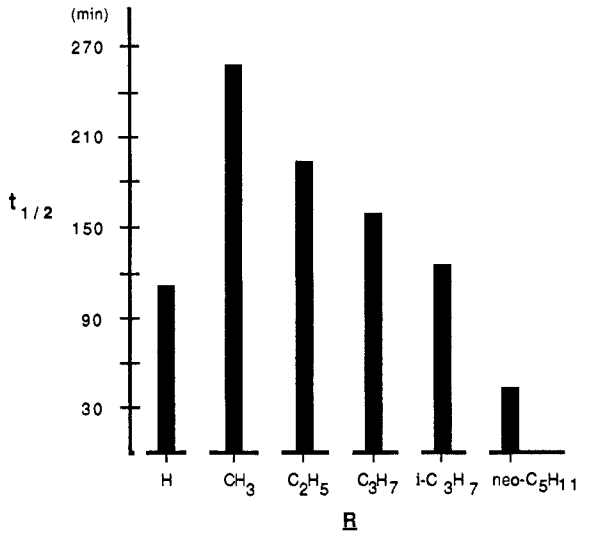


Figure 2. The effect of the C-5 substituent on reaction rates for **1a–f**. The alkyl groups are presented in an order based solely on the magnitude of their effects. Possible origins for these effects are discussed in the text.

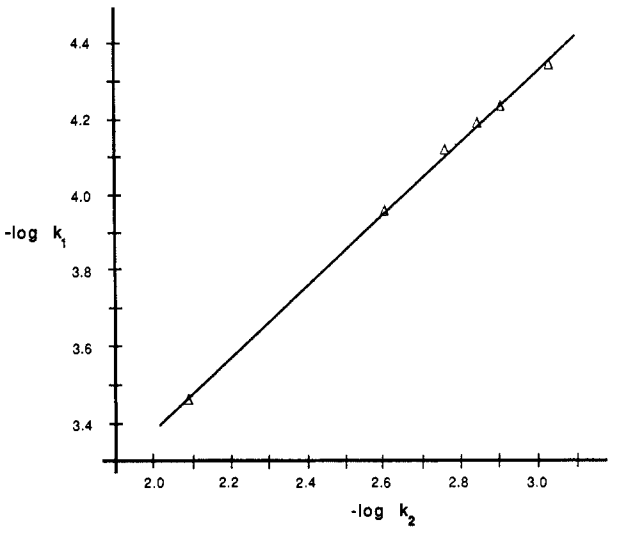


Figure 3. A linear free energy relationship between rates for acetate derived ketene acetals **1a–f** and propanoate derived *Z* ketene acetals **2a–f**.

is inconsistent with the fact that the system bearing a methyl group at C-5 rearranges more slowly than that bearing a proton at C-5 and by the effect of the (trimethylsilyl)methyl substituent (vide infra). It therefore seems likely that the electronic effects (i.e., polar, inductive, or resonance effects) and the steric effects (i.e., effects not due to induction or resonance) of these alkyl groups are opposed.

The question of the steric effect of substituents at C-5 is complex and for discussion purposes can be divided into three potential factors. First, based on the chair-like transition-state analogy, and in the absence of additional pertinent data, it can be argued that bulky substituents at C-5 destabilize the transition state for these rearrangements more than they destabilize the starting materials. If the magnitude of this steric effect followed the order observed in the Taft steric substituent parameters, then the effect would result in rates decreasing in the order **1**, R = H, methyl, ethyl, *n*-propyl, isopropyl, neopentyl. Since this is the exact opposite of the observed trend, the proposed interaction must be small compared with other effects. In opposition to this first proposal, a second reasonable point for discussion is that a bulky C-5 substituent could well cause an enthalpically based steric acceleration. The starting material double bond which bears the bulky substituent must lengthen during the rearrangement. If this lengthening is in effect at the transition state, and if no overwhelming changes in other bond lengths occur at this point, then an acceleration may be expected. In short, steric compression of the C-5 substituent may be less important in the transition state than in the starting material. Finally, a third effect, an accelerating entropic effect, can be postulated to affect these reactions.[9] As the size of the C-5 substituents increases a number of conformations unfavorable for rearrangement will be made inaccessible and the entropy of activation will become less negative. It is most likely that all three of these effects are operating in this rearrangement and that the sum of these forces results in the observed acceleration with increasing alkyl group size.

To determine the possible role of electron donation by substituents at C-5 we examined the effect of a (trimethylsilyl)methyl substituent at C-5. Because the (trimethylsilyl)methyl group is larger than an *n*-propyl group but smaller than a neopentyl group, we reasoned that based on steric bulk alone the rate of rearrangement of **1g** would lie between the rates found for **1d** and **1f**. In fact, the rearrangement of **1g** at 35 °C proceeds with a half-life of 220 min, significantly *slower* than the *n*-propyl case. The fact that the rearrangement of **1g** (R = $CH_2Si(CH_3)_3$) is even slower than that of **1c** (R = CH_2CH_3), when considered with the knowledge that the steric effect of a trimethylsilyl group certainly exceeds the steric effect of a methyl group, strongly suggests that a (trimethylsilyl)methyl group at C-5 electronically decelerates this rearrangement.[10]

At this stage we favor the hypothesis that large alkyl groups at C-5 accelerate these rearrangement reactions through a combination of enthalpic and entropic effects and that this accelerating influence is predominantly due to the bulk of the substituent and is not due to the electron-releasing properties of the substituents. On the basis of the observed effect of a trimethylsilyl substituent at C-5, it is proposed that electron donors at C-5 decelerate these reactions. The effects of alkyl groups at C-5 (Figure 2) may be analyzed as a sum of these various influences. Ongoing research is directed toward obtaining further evidence to refute or support this analysis and to quantify the contribution of these component effects.

Transition-State "Diaxial" Interactions. Comparisons of C-5 substituent effects on rearrangement rates for derivatives of **2** and **3** reveal that an "equatorial" substituent at C-1 has little interaction with a substituent at C-5 and that an "axial" substituent at C-1 is involved in a destabilizing interaction with a substituent at C-5.[11] This may be shown as follows. For the *Z* isomer (**2**), which has an "equatorial" methyl group at C-1, the effects of changing the size of the C-5 substituent should parallel the effects observed when there is no methyl group at C-1. *In other words, on the basis of the canonical chair-like transition states illustrated in Chart I, a linear free energy relationship between rates of rearrangement for 1 and 2 is to be expected.*[12] In fact, a remarkably good correlation is found for these two systems (Figure 3). The linearity of the relationship (r = 0.9995) indicates that introduction of an "equatorial" methyl group at C-1 has neither substantially altered the transition state for the rearrangement nor introduced new factors, not accounted for by the parent system.[12b]

In contrast to the case just discussed, the rates of rearrangement for the *E* isomer (**3**), which has an "axial" methyl group at C-1,

(9) The enthalpic and entropic components of steric effects have been descriptively characterized as "potential energy steric effects (steric strains) and kinetic energy steric effects (steric hindrances to motion)". See: Taft, R. W. *J. Am. Chem. Soc.* **1953**, *75*, 4538–4539.

(10) The (trimethylsilyl)methyl substituent at C-5 would be expected to stabilize a transition state bearing substantial positive charge or radical character at C-5.

(11) The characterization of substituents as "axial" or "equatorial" follows from the puckered, six-membered, four-center model of the transition state. To emphasize that there are significant differences between any possible transition state for this reaction and any saturated six-membered ring, the terms axial and equatorial will appear in quotation marks when applied to transition states and without quotation marks only when applied to saturated six-membered rings.

(12) (a) While there has been much emphasis on the linear correlation of rate and equilibrium data, the concept of the linear free energy relationship applies also to rate–rate data correlations. Hammett, L. P. *J. Am. Chem. Soc.* **1937**, *59*, 96. (b) For a review of linear free energy relationships see: Wells, P. R. *Chem. Rev.* **1963**, *63*, 171–219.

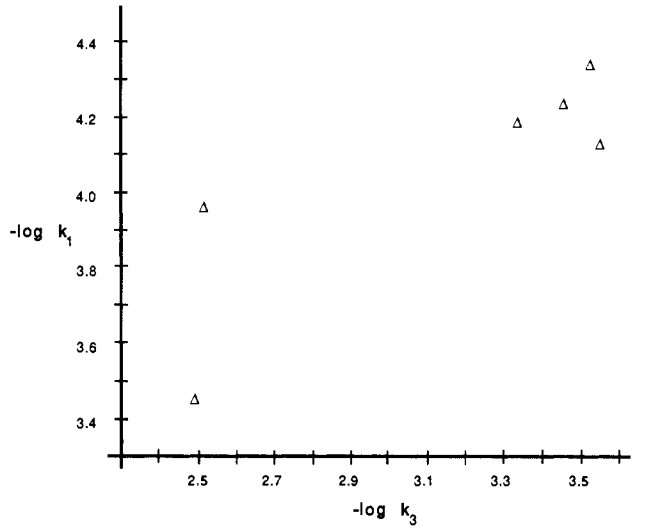


Figure 4. No linear free energy relationship is apparent for rearrangements of acetate derived ketene acetals **1a–f** and propanoate derived *E* ketene acetals **3a–f**.

when compared with the parent system (**1**), reveal no linear free energy relationship (Figure 4). Obviously, some new factor is influencing the energies of activation for reaction of **3**. The most likely source for this new factor is a steric interaction between the "axial" substituent at C-1 and the "axial" substituent at C-5.

If such "diaxial" interactions are important and destabilzing, then as the substituent at C-5 increases in size, the rearrangement rate for the *E* isomer (**3**), which has an "axial" methyl group at C-1, should decrease or should increase at a rate substantially less than the rate of increase observed for **1** (no C-1 substituent) and **2** (equatorial C-1 substituent). This expectation is fulfilled by the data in hand. Proceeding from hydrogen to methyl to ethyl to isopropyl at C-5 results in very similar rate increases for the *Z* isomer (**2**) and for **1**. This is seen by comparing the ratio of rates k_2/k_1. This ratio changes very little as the C-5 substituent is varied. In contrast, the rate of rearrangement of **3** slows substantially in relation to the parent system as the C-5 substituent is varied from hydrogen to methyl to ethyl to isopropyl. It must be concluded that in **3**, but not in **2**, the substituent at C-5 is involved in an interaction with the methyl group at C-1 which increases the energy of activation for the rearrangement. In the next section the absolute magnitude of this interaction is considered.

Comparison of the Effects of an "Axial" and "Equatorial" Methyl Group at C-1. An interesting quantity which has not previously been determined may now be estimated. The quantity of interest is the difference in free energy for transition states reached from the geometrically isomeric reactants **2a** and **3a**. As illustrated in Figure 5, this quantity ($\Delta\Delta G_{Z^\ddagger/E^\ddagger}$) can be determined if the rates of rearrangement and the relative stability of the two isomeric starting materials be known. Due to the reactivity of **2a** and **3a**, direct determination of their relative stability is difficult. We have, however, previously determined that for *O*-ethyl-*O'*-(*tert*-butyl)dimethylsilylketene acetals at 35 °C in $DCCl_3$ the *Z* isomer is more stable than the *E* isomer by 1.34 kcal/mol.[13] Furthermore, we now report that replacing the ethyl group in that ketene acetal with either isobutyl or 2,3-dimethylbutyl groups does not charge this value. At 25 °C the equilibrium concentration for each of these three ketene acetals is not detectably different and the *Z* isomer is more stable than the *E* isomer by 1.34 kcal/mol. In light of these data, allyl and ethyl groups are expected to have similar effects on the relative stability of these acetals, and we estimate that **2a** is 1.34 kcal/mol more stable than **3a**. On the basis of this estimate and the observed rate differences for rearrangement of **2a** and **3a**, $\Delta\Delta G_{Z^\ddagger/E^\ddagger}$ for **2a** and **3a** (the free energy difference between the transition state with an axial methyl

(13) Wilcox, C. S.; Babston, R. E. *J. Org. Chem.* **1984**, *49*, 1451–1453.

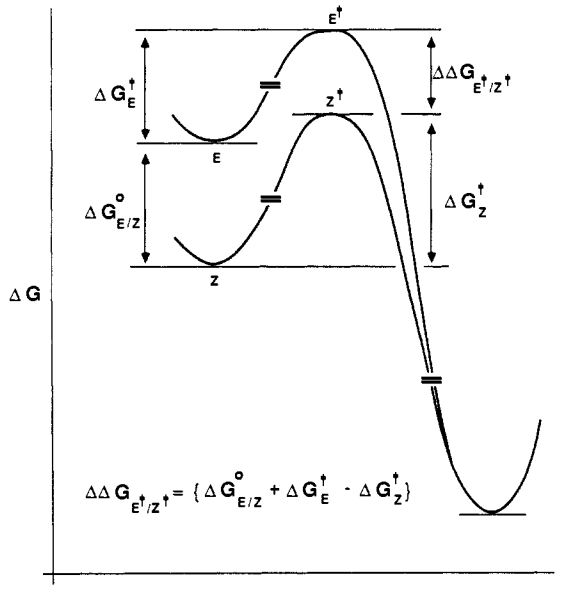


Figure 5. Free energy reaction coordinate diagram for the rearrangements of *E* and *Z* ketene acetals.

group vs. an equatorial methyl group at C-1) is estimated to be 1.2 kcal/mol.[14] The reason that **2a** rearranges more slowly than **3a** arises as a corollary to this calculation: the transition state reached from **3a** is indeed less stable than the transition state reached from **2a**, but the difference in transition state free energy is less than the difference in starting material free energy. The lower energy reactant (**2a**) therefore rearranges relatively slowly.

In this way, for the first time, the effect of an "axial" substituent at C-1 in a Claisen rearrangement has been quantitatively determined. Interpretations of the effects of substituents on the rates and stereochemical outcome of Claisen rearrangements have for many years been based on the idea of a chair-like, four-centered transition state.[15,16] Comparisons of transition-state steric effects with steric effects in saturated ground molecules can be illuminating and have predictive value, but discrepancies must be expected. The discrepancies, when noted, offer additional insight into the nature of the unobservable transition state. Important experiments by Faulkner showed that there was a direct relationship between the bulk of a substituent at C-4 and the ratio of olefinic isomers obtained through rearrangement. The stereoisomeric four-centered transition states for a Claisen rearrangement (Chart I) are suggestive of equatorially and axially substituted six-membered rings. Using available conformational data, Faulkner compared the free energy difference for the axial and equatorially substituted transition states ($\Delta\Delta G_{AX/EQ}$, Figure 6) with the equatorial–axial equilibria for equivalently substituted cyclohexanes. The close correspondence between $\Delta\Delta G_{AX/EQ}$ values predicted on the basis of the cyclohexane model and the experimentally determined values lent credibility to this approach to estimating substituent steric effects in [3,3]-sigmatropic rearrangements.[15a]

In the present case, we find that the preference of a methyl group for the equatorial position at C-1 ($\Delta\Delta G_{Z^\ddagger/E^\ddagger}$) is 1.2 kcal/mol or 75% of the effect observed by Faulkner for a methyl group at

(14) The ratio of rates for reaction of **2a** and **3a** at 35 °C reveals that the difference in activation energy for these processes is 0.13 kcal/mol. The value given for $\Delta\Delta G_{Z^\ddagger/E^\ddagger}$ follows from the equation illustrated in Figure 5 given that $\Delta G^\circ_{E/Z}$ = 1.34 kcal/mol ($\Delta G^\ddagger_E - \Delta G^\ddagger_Z$) = −0.13 kcal/mol.

(15) (a) Faulkner, D. J.; Perrin, C. L. *Tetrahedron Lett.* **1969**, 2783–2786. (b) Faulkner, D. J.; Petersen, M. R. *J. Am. Chem. Soc.* **1973**, *95*, 553–563. (c) Faulkner, D. J.; Petersen, M. R. *Tetrahedron Lett.* **1969**, 3243–3246.

(16) Preferences for equatorial rather than axial substituents *at C-4* have been estimated on the basis of product olefin geometries. For examples in addition to ref 8, see: (a) Vittorelli, P.; Winkler, T.; Hansen, H.-J.; Schmid, H. *Helv. Chim. Acta* **1968**, *51*, 1459–1461. (b) Hansen, H.-J.; Schmid, H. *Tetrahedron* **1974**, *30*, 1959–1969. (c) Cave, R. J.; Lythgoe, B.; Metcalfe, D. A.; Waterhouse, I. *J. Chem. Soc., Perkin Trans.* **1977**, 1218–1228. (d) Evans, D. A.; Nelson, J. V. *J. Am. Chem. Soc.* **1980**, *102*, 774–782.

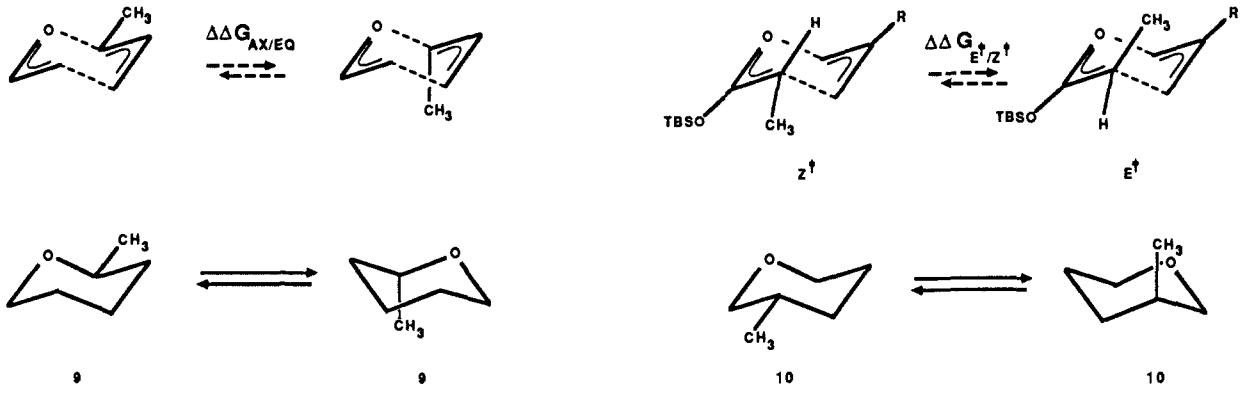


Figure 6. Comparison of steric effects in the transition state for the aliphatic Claisen rearrangement with analogously substituted tetrahydropyran derivatives.

C-4 ($\Delta\Delta G_{AX/EQ}$) in another Claisen rearrangement. On reflection, there is good reason to expect steric effects at C-1 to differ from steric effects at C-4. Following reasoning parallel to Faulkner's, we suggest that stereoisomeric transition states for the Claisen rearrangement be compared with *equivalently substituted tetrahydropyran (THP) derivatives*. This idea is illustrated in Figure 6 and suggests that 2-methyltetrahydropyran (**9**) is an appropriate observable model for the steric effect of a methyl group at C-4 in the Claisen rearrangement. As Eliel recently showed, methyl groups α to the oxygen in the ring in THP derivatives favor equatorial over axial orientation by 2.8 kcal/mol.[17,18] Reconsideration of Faulkner's data from this point of view reveals that the preference for an equatorial substituent at C-4 (α to the oxygen in the ring) in the transition state of a Claisen rearrangement ($\Delta\Delta G_{AX/EQ}$ = 1.6 kcal/mol) is about 60% of the comparable energy difference found for the corresponding tetrahydropyran model.

The THP model for the transition state (Figure 6) clearly predicts that the steric effects of a substituent at C-1 ($\Delta\Delta G_{Z^\ddagger/E^\ddagger}$) will be unlike substituent effects at C-4 ($\Delta\Delta G_{AX/EQ}$). For THP derivatives, Eliel determined that methyl groups β to the oxygen in the ring have a 1.4-kcal/mol preference for an equatorial disposition.[17] Obviously, for THP derivatives, the steric effects of an axial methyl group β to the oxygen in the ring are far less than the effects of an axial group α to the oxygen in the ring. In parallel with this observation, for the aliphatic Claisen rearrangement transition state, an "axial" methyl group at C-1 (β to the oxygen in the ring) is not as destabilizing as an "axial" methyl group at C-4 (α to the oxygen in the ring). The value determined here (1.2 kcal/mol) for the effect of an axial methyl group at C-1 in the ketene acetal Claisen rearrangement is about 80% of the effect observed for an axial methyl group β to the oxygen in the ring in THP.

Finally, it is possible to estimate the difference in energy for the transition states for the rearrangement of other congeners of **2** and **3**. The results of these calculations are illustrated in Figure 7. Not surprisingly, when the hydrogen at C-5 is replaced by a methyl group, the apparent destabilizing effect of an axial methyl group at C-1 is magnified and the transition state reached from **2b** (R = CH_3) is more stable than that reached from **3b** (R = CH_3) by 2.0 kcal/mol. In other words, in these transition states, a "diaxial" Me,Me interaction (ca. 2.0 kcal/mol) is more destabilizing than a "diaxial" Me,H interaction (ca. 1.2 kcal/mol). As would be expected on the basis of reported *A*-values for these alkyl groups, diaxial interactions with methyl, ethyl, propyl, and neopentyl groups are all roughly comparable. Only when C-5 bears an isopropyl group is a second incremental increase in $\Delta\Delta G_{Z^\ddagger/E^\ddagger}$ notable.[19]

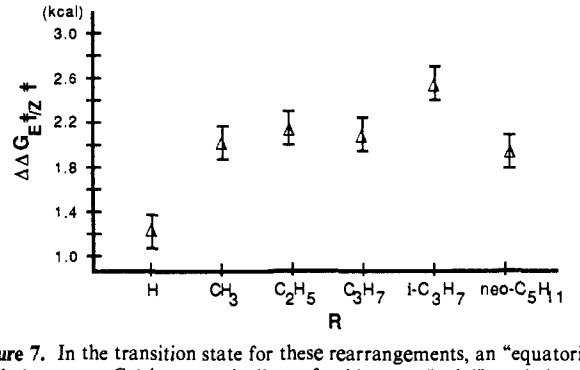


Figure 7. In the transition state for these rearrangements, an "equatorial" methyl group at C-1 is energetically preferable to an "axial" methyl group at C-1 by an amount which depends on the size of the C-5 substituent.

Before concluding, a few comments on the meaning of these "diaxial" interactions are in order. While it is a fact that the transition state for the rearrangement of **2a** is 1.2 kcal/mol more stable than that for the rearrangement of **3a**, the interpretation of this fact in terms of the transition states illustrated in Figure 1 remains problematical. The fact that the effect of an "axial" methyl group at C-1 amounts to 80% of the similar effect found for an axial group β to the oxygen in the ring in tetrahydropyran can not now provide support for one or another of the hypothetical transition states. The saturated six-membered ring model for these transition states is a gross approximation which provides a descriptive vocabulary and simplifies the discussion of conformational properties in these systems. Because of the crudeness of this approximation, it is inappropriate to expect the steric effects of substituents in these rearrangements to consistently parallel the steric effects in saturated rings. For example, the "diaxial" Me,H interaction energy was found to be 80% of that expected on the basis of the THP model. The fact that the "diaxial" Me,Me interaction energy is only 2.0 kcal/mol (and is thus far less than 80% of the value expected on the basis of the THP model) points out the limitations of the saturated ring model. As Faulkner noted, the bond to a substituent at C-5 is tilted away from the ring during the rearrangement.[15] In contrast, in saturated rings, axial bonds are nearly perpendicular to the least-squares plane defined by the ring. This difference may contribute to the relatively small magnitude of the "diaxial" Me,Me interaction energy. It is also important to note that relatively little is known about the deformation potentials of transition states. Eliel proposed that energy minimizing deformations in tetrahydropyran rings may require more energy than equivalent deformations in cyclohexane rings.[17]

(17) Eliel, E. L.; Hargrave, K. D.; Pietrusiewicz, K. M.; Manoharan, M. *J. Am. Chem. Soc.* **1982**, *104*, 3635–3643.

(18) In order to avoid confusion with the numbering system illustrated in Chart I, the C-2 position (IUPAC numbering system) in tetrahydropyran will be referred to as the position "α to the oxygen in the ring" and the C-3 position will be referred to as the position "β to the oxygen in the ring".

(19) Of course as the chair form for these reactions is destabilized rearrangement through a boat-like transition state may become competitive. This is unlikely, and in a case bearing a C-5 methoxy group no boat rearrangement was detected.[2b] It is important to note that in the event that *E* isomers bearing C-5 substituents rearrange through boat-like transition states, the conclusion concerning interactions between C-1 and C-5 substitutents is still valid. In such a case differences in free energies for transition states derived from *E* and *Z* isomers would represent boat/chair differences and $\Delta\Delta G_{Z^\ddagger/E^\ddagger}$ would be a minumum rather than an absolute value.

How easily might a transition state deform to accommodate a steric encumbrance? The fact that the Me,Me interaction is only 0.8 kcal/mol greater than the Me,H interaction may indicate that transition states are more flexible than ground-state models.

Conclusion

These data further define the nature of the chair-like transition state in the Ireland rearrangement and quantitatively illustrate the complex and interdependent effects that the simplest substituents may have on a [3,3]-sigmatropic rearrangement. The effects of alkyl substituents reported here raise a number of exciting questions and reveal trends which must be considered in any attempt to describe the reaction pathway for these reactions. For the first time, the effect of a (trimethylsilyl)methyl group upon a [3,3]-sigmatropic rearrangement has been determined and analyzed in the context of alkyl group effects. A review of earlier work reveals that the steric effect due to an axial methyl group at C-4 in the transition state for the Claisen rearrangement is about 60% of the steric effect observed for an equivalent axial methyl group in a THP model system. The steric effect of an axial methyl group at C-1 in the Ireland rearrangement is about 80% of the steric effect observed for the THP model system.

Notably, a linear free energy relationship was revealed for substituent effects in two related [3,3]-sigmatropic rearrangements. It is interesting to consider that a linear free energy relationship may exist between rearrangements of **1a–g** and *other* sigmatroipc rearrangements. For example, does a linear free energy relationship exist between the rates of rearrangement of allyl vinyl ethers not bearing a silylated oxygen substituent at C-2 and the present rearrangements? What other examples of the Claisen rearrangement (eq 1) might profitably be examined for such a relationship? Are there other sigmatropic rearrangements (i.e., [2,3] rearrangements or Cope rearrangements) for which these basic substituent effects remain constant? Searches for further relationships and analyses of the importance of such relationships will be the subjects of future investigations.

These data provide an essential base line from which to measure the effects of more polar substituents and should be a valuable resource for theoreticians striving to perfect methods for predicting rates of [3,3]-sigmatropic rearrangements. Comparison of these observations with the results of calculations may lend credibility to one or another of the hypothetical transition-state representations. The following conclusions are consistent with these data: (1) steric bulk at C-5 is rate accelerating, (2) electron donation at C-5 is rate decelerating, (3) substituents at C-1 show an expected and measurable preference for "equatorial" rather than "axial" orientation, and finally (4) "axial" groups at C-1 are involved in rate-decelerating interactions with C-5 substituents, the steric bulk of the C-5 substituent determines the magnitude of the deceleration, and this "diaxial" interaction is less than analogous diaxial interactions in saturated rings.

We conclude by noting that the approach of "axial" substituents at C-1 and C-5 suggests that the introduction of stereogenic groups at these positions could lead to diastereoface selectivity in this rearrangement. Experiments are in progress to test this hypothesis and to confirm or refute the other ideas presented in this paper.

Experimental Section

Materials. Acetate and propanoate esters (**7** and **8**) were prepared from the alcohols and the appropriate acid anhydride by conventional procedures. All esters were fractionally distilled from CaH_2 prior to use. Silylketene acetals (**1–3**) were prepared by the well-known procedures first described by Ireland.[2b] Solvents were purified as follows: Chlorinated solvents (CCl_4, $CDCl_3$, CD_2Cl_2), C_6D_6, C_5D_5N, $(CD_3)_3CO$, and CD_3CN were filtered through activated Al_2O_3 immediately prior to use. DMF and *N,N,N',N'*-tetramethylguanidine were distilled from CaH_2. *tert*-Butyl alcohol was distilled from sodium.

Rate Measurements. Approximately 5 mL of a 0.5 M solution of ketene acetal was prepared in $CDCl_3$ at 0 °C and partitioned into seven identical nitrogen-flushed NMR sample tubes. These samples were frozen (−78 °C) for up to 96 h prior to rate measurements. For reaction rate determinations, sample sets were immersed in a 35.0 ± 0.05 °C circulating bath. (By the use of a small thermocouple inserted in a blank sample it could be shown that the internal temperature of a cold sample reached 35 °C in less than 30 s.) Samples were withdrawn from the water bath at periodic time intervals and cooled to −78 °C. For each sample, the relative amounts of starting material and product were determined by analysis of NMR data (internal standard: $CHCl_3$). Data was acquired at −40 °C on Nicolet NT-200 (200 MHz) or GE/Nicolet GN-500 (500 MHz) spectrometers. Data were analyzed graphically, and all data were consistent with a first-order reaction mechanism. Multiple rate determinations were carried out in all cases, and the results of repeated experiments were consistent to within ±2%.

Solvent Effects on the Rate of Rearrangement of 1b. Solutions of ketene acetal **1b** were prepared at 0 °C, and rearrangement rates were determined at 35 °C in the usual manner. The results (Table II) reveal that this reaction is not strongly affected by solvent.

Isomerization of Silylketene Acetals. Isobutyl propanoate was prepared from isobutyl alcohol and propionic anhydride by conventional procedures. Fractional distillation from CaH_2 gave 84% yield of the ester (bp 137–138 °C). IR (film, cm^{-1}) 2965, 1742, 1466, 1380, 1350, 1195, 1085, 1023; ^1H NMR (360 MHz, $CDCl_3$) δ 3.86 (d, 2 H, J = 6.7 Hz, OCH_2), 2.34 (q, 2 H, J = 7.6 Hz, CH_2CO), 1.93 (m, 1 H, J = 6.7 Hz), 1.15 (t, 3 H, J = 7.6), 0.93 (d, 6 H, J = 6.7 Hz); ^{13}C NMR (360 MHz, $CDCl_3$) δ 174.3 (s, COO), 70.3 (t, OCH_2), 27.7 (d), 27.5 (t), 18.9 (q), 9.1 (q). 2,3-Dimethyl-1-butyl propanoate was prepared by reduction of unsaturated ester (**8e**) with PtO_2 in methanol under 1 atm of H_2 for 5 h at 25 °C. Fractional distillation from CaH_2 gave the ester in 69% yield (bp 173–175 °C). IR (film, cm^{-1}) 2960, 1740, 1475, 1385, 1350, 1188, 1085, 1020; ^1H NMR (360 MHz, $CDCl_3$) δ 4.04 (dd, 1H, J = 5.6, 10.8 Hz), 3.90 (dd, 1 H, J = 6.9, 10.8 Hz), 2.32 (q, 2 H, J = 7.6 Hz), 1.71–1.63 (m, 2 H), 1.14 (t, 3 H, J = 7.6 Hz), 0.92 (d, 3 H, J = 6.6 Hz), 0.88 (d, 3 H, J = 6.5 Hz), 0.86 (d, 3 H, J = 6.4 Hz); ^{13}C NMR (360 MHz, $CDCl_3$) δ 174.4 (s), 67.7 (t), 38.2 (d), 29.5 (d), 27.6 (t), 20.2 (q), 18.2 (q), 13.0 (q), 9.1 (q).

Silylketene acetals were prepared from the esters and *tert*-butylchlorodimethylsilane by the procedure of Ireland.[2b] (*E*)-Dimethyl(1,1-dimethylethyl)[[1-(2-methylpropoxy)-1-propenyl]oxy]silane was isolated (90% yield) with 92% isomeric purity: IR (film, cm^{-1}) 2860, 1687, 1473, 1315, 1257, 1210, 1113, 1072, 842, 784; ^1H NMR (500 MHz, $CDCl_3$) δ 3.67 (q, 1 H, J = 6.6 Hz, vinylic), 3.55 (d, 2 H, J = 6.7 Hz, OCH_2), 1.90 (m, 1 H, J = 6.7 Hz), 1.51 (d, 3 H, J = 6.6 Hz), 0.95 (d, 3 H, J = 6.7 Hz), 0.94 (s, 9 H), 0.17 (s, 6 H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 153.7, 79.2, 73.9, 28.4, 25.7, 19.3, 18.1, 9.5, −5.0. (*E*)-Dimethyl(1,1-dimethylethyl)[[1-(2,3-dimethylbutoxy)-1-propenyl]oxy]silane was isolated (87% yield) with 95% isomeric purity: IR (film, cm^{-1}) 2864, 1687, 1475, 1465, 1310, 1255, 1210, 1113, 1075, 842, 784; ^1H NMR (500 MHz, $CDCl_3$) δ. 3.75 (dd, 1 H, J = 5.8, 9.8 Hz), 3.67 (q, 1 H, J = 6.6 Hz), 3.57 (dd, 1 H, J = 7.2, 9.8 Hz), 1.74 (even m, 1 H, J = 7.6 Hz), 1.64 (m, 1 H), 1.51 (d, 3 H, J = 6.6 Hz), 0.94 (s, 9 H), 0.91 (d, 3 H, J = 6.8 Hz), 0.90 (d, 3 H, J = 6.8 Hz), 0.85 (d, 3 H, J = 6.8 Hz), 0.17 (s, 6 H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 153.7, 79.3, 70.9, 38.8, 29.2, 25.7, 20.5, 18.1 (two signals), 13.0, 9.5, −5.0.

Isomerizations were carried out in deuteriochloroform with catalytic diisopropylethylammonium perchlorate at 25 °C by using procedures previously described.[13] The final isomeric ratio (*E*:*Z*) observed for each of these ketene acetals was 9:91 (±2%) as determined by 500-MHz ^1H NMR at 25 °C. (*Z*)-Dimethyl(1,1-dimethylethyl)[[1-(2-methylpropoxy)-1-propenyl]oxy]silane: IR (film, cm^{-1}) 2860, 1682, 1470, 1388, 1338, 1255, 1210, 1115, 1070, 840, 785; ^1H NMR (500 MHz, $CDCl_3$) δ 3.42 (q, 1 H, J = 6.4, vinylic), 3.39 (d, 2 H, J = 6.7 Hz, OCH_2), 1.93 (m, 1 H, J = 6.7 Hz), 1.52 (d, 3 H, J = 6.6 Hz), 0.95 (d, 6 H, J = 6.7 Hz), 0.95 (s, 9 H), 0.17 (s, 6 H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 156.1, 69.7, 73.6, 28.1, 25.7, 19.1, 18.0, 9.6, −4.2. (*Z*)-Dimethyl(1,1-dimethylethyl)[[1-(2,3-dimethylbutoxy)-1-propenyl]oxy]silane: IR (film, cm^{-1}) 2864, 1682, 1470, 1388, 1338, 1255, 1210, 1115, 1075, 842, 785; ^1H NMR (500 MHz, $CDCl_3$) δ 3.54 (dd, 1 H, J = 5.4, 9.1 Hz), 3.43 (q, 1 H, J = 6.4 Hz), 3.43 (dd, 1 H, J = 6.8, 9.1 Hz), 1.75–1.6 (complex m, 2 H), 1.52 (d, 3 H, J = 6.4 Hz), 0.95 (s, 9 H), 0.91 (d, 3 H, J = 6.8 Hz), 0.90 (d, 3 H, J = 6.8 Hz), 0.85 (d, 3 H, J = 6.8 Hz), 0.16 (s, 6 H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 156.2, 69.7, 70.8, 38.6, 29.4, 25.7, 20.7, 18.3, 18.1, 13.4, 9.7, −4.2.

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