cyclopentyl-*2-d* ethyl ether (**4**), *trans*-cyclopentyl-*2-d* ethyl ether (**5**), and cyclopentyl-*1-d* ethyl ether (**6**) were prepared by the Williamson synthesis from **1, 2,** and **3,** respectively. In a typical preparation, 1.55 g of sodium was dispersed by stirring in refluxing xylene under a blanket of nitrogen. The xylene was replaced with 40 ml of ether, and a solution of 5.7 g of **3** in 20 ml of ether was added dropwise in 2 h with vigorous stirring. The reaction mixture was allowed to stand overnight, and 10.3 g of freshly distilled ethyl iodide was added dropwise into the resulting sodium alkoxide solution while a slight reflux of ether was maintained. After standing overnight, 5 g of crude product **6** was collected from the reaction mixture by distillation through a short Vigreux column at 120–130 °C. A small quantity was purified by GC on an 8 ft × ¼ in. column containing 20% Carbowax 20M on firebrick 60–80. ^{2}H NMR spectrum of **6** (1.0 M in $CHCl_3$) showed a single peak at τ 6.69 (α-*d*).

Compounds **4** and **5** under the same conditions showed the main signals at τ 8.94 and 8.84, respectively. Detailed ^{2}H NMR spectral analysis of **4** and **5** are given in Table II.

Deuterated Cyclopentyl Trifluoroethyl Ethers. Specifically deuterated *cis*-cyclopentyl-*2-d* trifluoroethyl ether (**7**), *trans*-cyclopentyl-*2-d* trifluoroethyl ether (**8**), and cyclopentyl-*1-d* trifluoroethyl ether (**9**) were prepared from the corresponding alcohols **2, 1,** and **3,** respectively, using the procedure described by Mosher et al. In a typical synthesis, 10 g of cyclopentyl-*1-d* brosylate, prepared from **3,** was added to a solution of hexamethylphosphoramide. The reaction apparatus consisted of a three-neck, round-bottom flask with a dropping funnel, a nitrogen inlet, and a trap cooled externally with dry ice. The mixture was slowly heated up to 130 °C while nitrogen bubbled through, and the distillate was collected in a dry ice trap. A small sample of the fraction distilling from 74 to 116 °C was purified by GC using the column described above for the purification of **6.** A 300-mg sample of **9** was collected. ^{2}H NMR showed only one peak at τ 4.78. Compound **7** showed a signal at τ 7.97 with a small peak (5%) at τ 8.26, whereas compound **8** showed the main signal at τ 8.26 with a small peak (10%) at τ 7.97. Evidently the displacement reaction was accomplished with ~96% of inversion at the reaction center.

Isolation of Substitution Products. The product separations and purifications were all done in the same general manner for all solvents and products, except for variations in reaction time and GC temperature. In a typical experiment *cis*-cyclopentyl-*2-d* brosylate (6 g) was dissolved in 50 ml of 80 vol % E–W. The solution was heated for 2.5 h at 40 °C (10 half-lives of reaction). Most of the mixture was distilled from the dissolved solids and dried on molecular sieves, Type 3A, Linde, 1/16 in. MCB 1167. The products were separated from each other and from the solvent by GC on an 8-ft 20% Carbowax 20M on firebrick 60–80 column at 150 °C. The samples collected in this way were purified again by GC at 90 °C for cyclopentyl-*2-d* ethyl ether and at 150 °C for cyclopentanol-*2-d*. Only small samples amounting to 200–300 mg of better than 99% pure products were isolated.

The ^{2}H NMR spectra for cyclopentanols, cyclopentyl ethyl ethers and trifluoroethyl ethers were taken in $CHCl_3$, CCl_4, and benzene, respectively. GC retention times of the products isolated in solvolysis were identical with those of the compounds prepared independently as described above; ^{1}H NMR spectra were consistent in all cases with the assigned structures,

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References and Notes

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The Ester Enolate Claisen Rearrangement. Stereochemical Control through Stereoselective Enolate Formation[1a]

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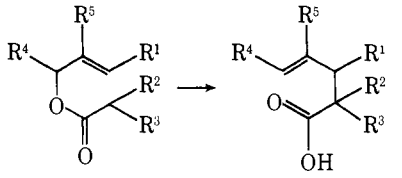
Abstract: The [3,3] sigmatropic rearrangement of a number of allylic esters (**1**), as the enolate anions or the corresponding silylketene acetals, produces the γ,δ-unsaturated acids **2** in 66–88% yield. The mild conditions allow rearrangement of acid-sensitive and thermally labile esters. Rearrangement of ester **1g** affords (*E*)-4-decenoic acid (**2g**) with greater than 99% stereoselectivity. (*E*)-Crotyl propanoate (**12**) leads to erythro acid **14** when enolization is carried out in THF, but to the threo acid **15** when the solvent is 23% HMPA–THF. Results with a variety of esters demonstrate that kinetic enolization with lithium diisopropylamide gives selective formation of the geometrical enolate H in THF and the isomeric enolate I in HMPA–THF. Similar results are obtained with 3-pentanone.

Consideration of possible synthetic approaches to prostanoids suggested a convergent scheme which would incroporate the connection of a "top-half" and a "bottom-half" as a key step in the synthesis. Further analysis indicated that the required carbon–carbon bond could be generated by Claisen rearrangement of a properly designated substrate. This rear-

Table I. Claisen Rearrangement of Allyl Ester Enolates



1 **2**

Ester	R^1	R^2	R^3	R^4	R^5	Procedure[a]	% yield[b]
1a	H	H	H	H	H	B	66
1b	CH_3	H	H	H	H	B	70
1c	CH_3	CH_3	H	H	H	A (B)	75 (75)
1d	CH_3	CH_3	CH_3	H	H	A (B)	80 (78)
1e	CH_3	(*E*)-C_2H_5CH=CH	H	H	H	A	69
1f	*n*-C_6H_{13}	CH_3	H	H	CH_3	A	71
1g	H	H	H	*n*-C_5H_{11}	H	C	83
1h	H	CH_3	C_6H_5S	*n*-C_5H_{11}	H	C	88
1i	*n*-C_6H_{13}	(*E*)-C_2H_5CH=CH	H	H	CH_3O	C	77[c]
1j	*n*-C_6H_{13}	*n*-C_3H_7	H	H	CH_3O	C	80[c]
1k	CH_3	*n*-C_4H_9	Br	H	H	D	71[d]

[a] A = rearrangement as the enolate anion prepared with LICA; B = rearrangement as the trimethylsilylketene acetal; C = rearrangement as the *tert*-butyldimethylsilylketene acetal; D = rearrangement as the *tert*-butyldimethylsilylketene acetal prepared by reaction of the α-bromo ester with Zn and *t*-$BuMe_2SiCl$ in THF–HMPA. [b] Yield of acid after hydrolysis of the silyl ester. [c] Yield of methyl ester prepared[19,20] by cleavage of silyl ester with KF in HMPA followed by alkylation of carboxylate anion with iodomethane. [d] R_3 = H in the product acid.

rangement would also result in the correct number of suitably functionalized carbon atoms for subsequent generation of the cyclopentanone ring system.

In order to take complete advantage of the convergence inherent in this scheme, the efficient use of both "halves" of the molecule in this key step was essential. The most popular procedures for the aliphatic Claisen rearrangement—vinyl ether,[2] ortho ester,[3] and amide acetal[4]—were not acceptable because of their use of one of the reaction partners in excess. These considerations led us to investigate the possibility that enolate anions derived from allyl esters would undergo a similar [3,3] sigmatropic rearrangement.

Base-catalyzed rearrangement of a few allyl esters had been observed.[5] The special nature of these esters, the harshness of the conditions, and the low yields severely limited the usefulness of this procedure as a general synthetic transformation. A solution for these problems became apparent as a result of investigations by Rathke[6] which provided a method for the quantitative generation of ester enolates free from competing aldol-type condensation reactions. Indeed, the application of these methods to a variety of allyl esters resulted in enolate anions and/or the corresponding trimethylsilylketene acetals which underwent Claisen rearrangement under surprisingly mild conditions.[7]

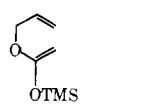
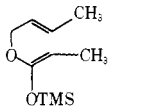
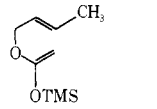
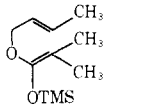
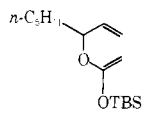
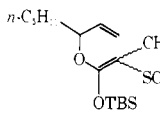
Further development of these reaction conditions was necessary to avoid fragmentation of the enolate anions themselves and C-silylation by trimethylchlorosilane (Me_3SiCl).[7] The use of *tert*-butyldimethylchlorosilane (*t*-$BuMe_2SiCl$)[8] in the presence of hexamethylphosphoramide (HMPA) to trap the enolates afforded excellent yields of the corresponding silylketene acetals and the procedure presented here (see Experimental Section) appears to be quite general (Table I).

The advantage of the basic reaction conditions is demonstrated by the rearrangement of the ester **1j**, which would be impossible under the acidic conditions of the vinyl ether and ortho ester rearrangements.

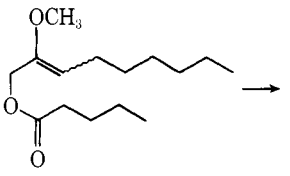
An additional advantage in the use of *t*-$BuMe_2SiCl$ is worthy of note. The silyl esters (e.g., **3j**) which result from rearrangement are sufficiently stable to permit isolation, but can also be conveniently transformed[20] into the corresponding methyl esters, as shown in eq 1.

The temperatures required for the rearrangement itself are quite mild in comparison with the temperatures in excess of 100° which are required for the generation of, or the rearrangement of, the 1,5-diene system for the alternative procedures mentioned above. A few approximate half-lives (Table II) serve to demonstrate the remarkable ease with which the rearrangement occurs as well as a few effects of structure on reactivity. A distinct advantage of this facile rearrangement is that esters whose structure permits the possibility of com-

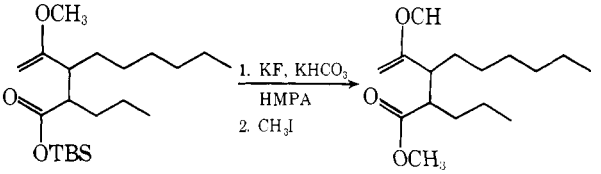
Table II. Half-Lives for Rearrangement of Silylketene Acetals at 32°[a]

Ketene acetal[b]	$t_{1/2}$, min[c]	Ketene acetal[b]	$t_{1/2}$, min[c]
 **4a**	210 ± 30	 **4c**	5 ± 1
 **4b**	150 ± 30	 **4d**	≪1
 **4g**	6 ± 1	 **4h**	<1

[a] Not isolated but generated in situ as described in Table I and Experimental Section. [b] TMS = $(CH_3)_3Si$; TBS = *t*-$Bu(CH_3)_2Si$. [c] By NMR analysis of silicon methyl region as described in Experimental Section.



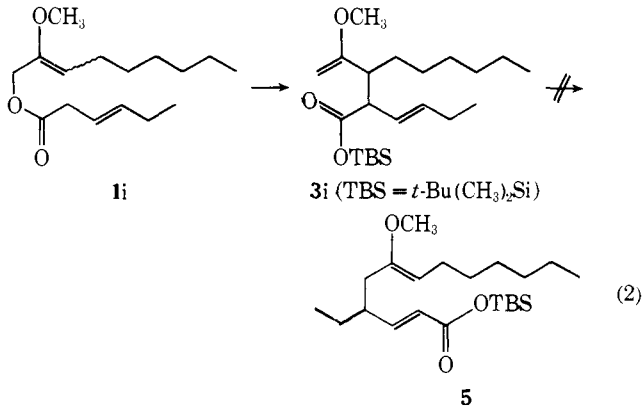
1j



(1)

3j (TBS = *t*-$Bu(CH_3)_2Si$)

peting thermal reactions can be employed in the rearrangement. For instance, no problem of Cope rearrangement of the silyl ester **3i** generated in the rearrangement of **1i** is encountered (eq 2).

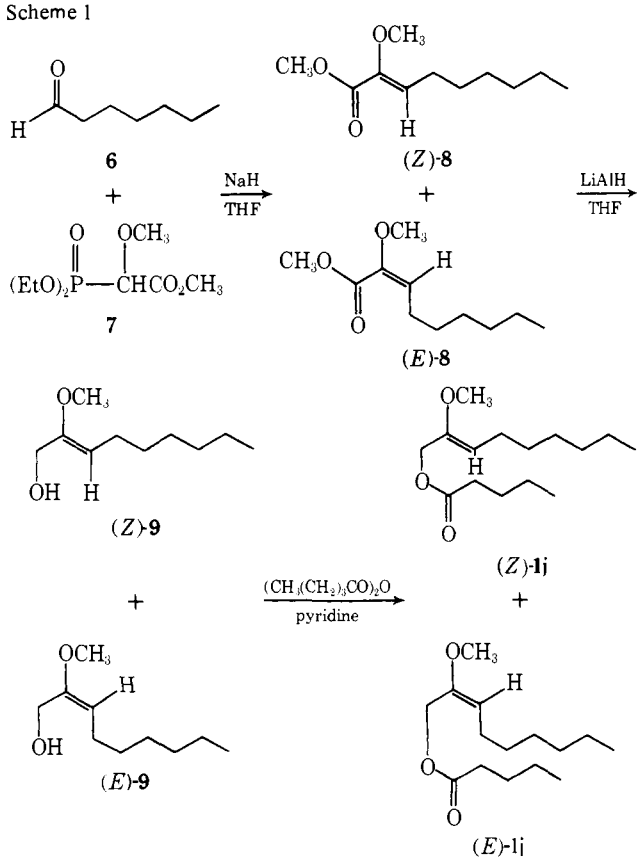


1i **3i** (TBS = *t*-Bu(CH$_3$)$_2$Si) **5** (2)

An alternative approach to silylketene acetals is demonstrated in the rearrangement of ester **1k**. The reaction of this α-bromo ester with zinc and *t*-BuMe$_2$SiCl in THF-HMPA generates the required silylketone acetal under quite mild conditions, and the rearrangement proceeds with the usual facility.[9]

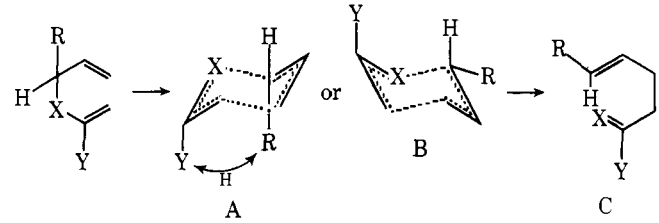
Methoxy substituted allyl alcohol synthons such as **9** employed in the esters **1i** and **1j** have proven to be highly useful in the synthesis of cyclopentanone derivatives[7,10] and deserve further comment. The 2-alkoxy α,β-unsaturated esters such as **8** are readily available by the Wittig synthesis developed by Grell and Machleidt[11] (Scheme I). This procedure results in approximately a 1:1 mixture of *E* to *Z* isomers which may be carried through the rearrangement sequence or separated by silica gel chromatography. Reduction by lithium aluminum hydride gives cleanly the allylic alcohols **9** which can be converted to stable esters such as **1j** under a variety of nonacidic reaction conditions.

Scheme I



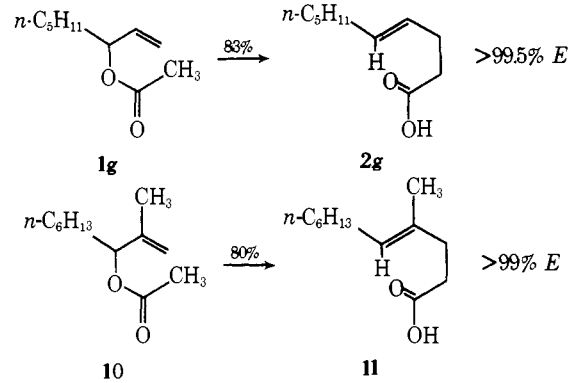
In the course of the Claisen rearrangement, both a new carbon-carbon double bond and a new carbon-carbon single bond are formed. To assess further the synthetic utility of the transformation, the stereochemical outcome at both of these sites was investigated.

Ample theoretical considerations[12] and experimental evidence[3,13-17] on various [3,3] sigmatropic rearrangements indicate quite clearly that, in the absence of any unusual steric constraints, the rearrangement proceeds through a chair-like transition state. An examination of nonbonded interactions readily indicates which of the two possible transition states A or B will be favored. The equatorial disposition of R puts transition state B at lower energy which results in predominant formation of the *E* double bond[17] system C.



A B C

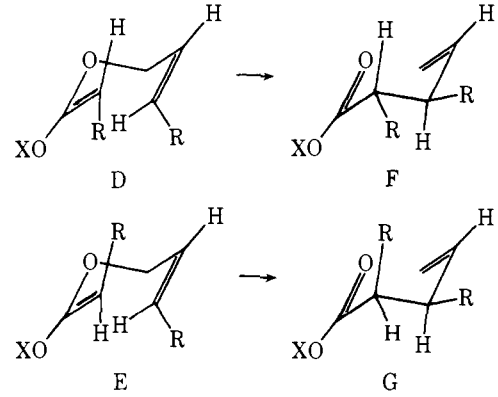
Not surprisingly, this predominance is found for the ester enolate Claisen rearrangement as well. The rearrangement of ester **1g** leads to the acid **2g** with greater than 99% stereoselectivity. Similar observations have been made by Katzenellenbogen[18] who finds greater than 98% stereoselectivity for formation of the *E*-trisubstituted double bond in acid **11**.



1g **2g** >99.5% *E*

10 **11** >99% *E*

A second consequence of the chair-like transition state is that the stereochemistry about the newly formed carbon-carbon single bond can be predicted from the geometries of the double bonds in the starting 1,5-diene system. Although a priori it was not obvious that enolization would result in selective formation of one of the two isomeric enolates, the stereochemical consequence of rearrangement of either enolate isomer is predictable.[14-16] Silylketene acetal D (X = *t*-BuMe$_2$Si) will give the acid F, while E will lead only to acid G. Similar arguments can be made for esters containing a cis-double bond in the allylic alcohol fragment.



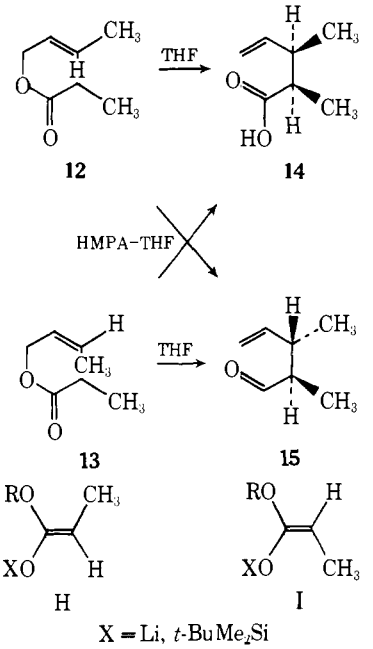
D F E G

Table III. Effect of Solvent on Rearrangement of (*E*)- and (*Z*)-Crotyl Propanoate (12 and 13)

Ester	Conditions[a]	Solvent[b]	% yield[c]	14/15[d]	Enolate[e]
12	Anion	THF	86	92/8	H
	Ketene acetal	THF	79	87/13	H
	Anion	HMPA–THF	21	13/87	I
	Ketene acetal	HMPA–THF	73	19/81	I
13	Anion	THF	6	25/75	H
	Ketene acetal	THF	75	11/89	H
	Anion	HMPA–THF			
	Ketene acetal	HMPA–THF	75	86/14	I

[a] The rearrangement was carried out as the enolate anion (anion) or this anion was quenched with *t*-BuMe$_2$SiCl before rearrangement (ketene acetal). [b] THF = 100% THF; HMPA–THF = 23 vol % HMPA–THF. [c] Isolated and distilled. [d] Determined by GLC analysis of methyl esters as described in Experimental Section. [e] The geometrical enolate which would lead to the predominate product assuming a chair-like transition state.

Scheme II



Rearrangement of (*E*)- and (*Z*)-crotyl propanoate (**12** and **13**) was used to probe the stereochemical outcome of enolization (Scheme II).

The data in Table III demonstrate the unanticipated effect of solvent polarity on the ratio of *erythro*-**14** to *threo*-**15** products obtained in the rearrangement. When (*E*)-crotyl propanoate (**12**) is enolized in tetrahydrofuran (THF) and allowed to rearrange as either the enolate anion or the derived silylketene acetal, selective formation of the erythro acid **14** is observed. When the more coordinating solvent system, 23% HMPA-THF, is employed, enolization takes an alternate course and the threo acid **15** predominates. Rearrangement of (*Z*)-crotyl propanoate (**13**) gives the expected complete reversal of product ratios and verifies that the product-determining step is indeed enolization.

These results indicate that in THF the *Z*-type enolate H is preferentially formed and trapped, but when the solvent is 23% HMPA-THF, enolization leads to the geometrically isomeric *E*-type enolate anion I.

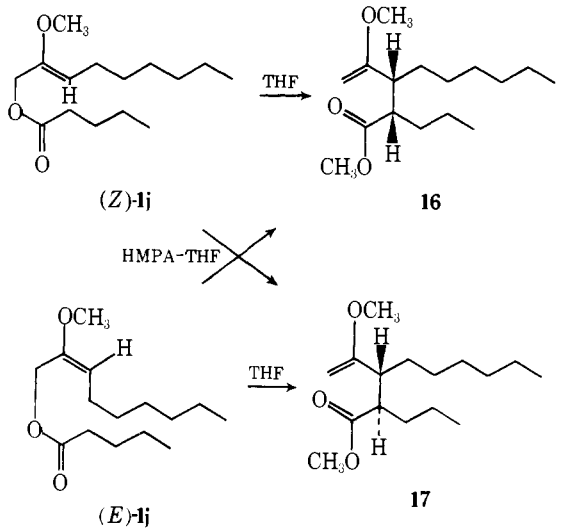
As was mentioned above, rearrangement of the enolate anion is only preparatively useful in specific cases. Only the enolate anion formed in THF from (*E*)-crotyl propanoate (**12**) rearranges in good yield. The low yields obtained with the other enolate anions probably reflect variable activation energies for rearrangement[15] and the known reactivity of ester enolates at temperatures above −78°.[7,8] It is worthy of note, however, that the enolate anions show no tendency to interconvert.

Table IV. Effect of Solvent on Rearrangement of (*Z*)- and (*E*)-2-Methoxy-2-nonenyl Pentanoate ((*Z*)-1j and (*E*)-1j)[a]

Ester	Solvent[b]	16/17[c]	% yield[d] of major isomer
(*Z*)-1j	THF	88/12	68
(*Z*)-1j	HMPA–THF	20/80	57
(*E*)-1j	THF	21/79	59
(*E*)-1j	HMPA–THF	85/15	69

[a] Rearranged as the silylketene acetal *t*-BuMe$_2$Si; converted to methyl esters as described in the Experimental Section. [b] THF = 100% THF; HMPA–THF = 23 vol % HMPA–THF. [c] From NMR analysis of methyl esters. [d] After chromatographic separation.

Scheme III

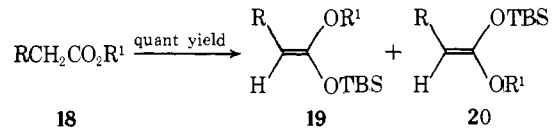


To evaluate these initial observations and to determine the generality of the process, the synthetically more interesting esters **1j** were examined under similar conditions (Scheme III and Table IV). In this case the derived silyl esters were cleaved with potassium fluoride in HMPA[19] and the resulting carboxylate salts were esterified with methyl iodide.[20] Analysis of the mixture of methyl esters by NMR indicated that again the same stereoselectivity pertained. The isomeric products were easily separated by silica gel chromatography, but the stereochemistry could not be unambiguously assigned from the spectral data. The assignment in Table IV and Scheme III is based on the outcome of experiments with crotyl propanoates **12** and **13**.

This stereoselectivity is even more general. The silylketene acetals obtained by trapping simple ester enolates with *t*-BuMe$_2$SiCl can be isolated in quantitative yield.[8] When this procedure is used to study the enolization of a variety of esters, a high degree of selectivity for formation of one enolate in THF and the isomeric enolate in HMPA-THF is observed in nearly every case (Table V). Only methyl phenylacetate (**18b**), in which the enolate is stabilized by conjugation with an aromatic ring, does not exhibit the changeover in stereoselectivity. Again, the stereochemistry of the ketene acetals **19** and **20** cannot be deduced from the spectral data (see Table VI) and is assigned by comparison with the results from the crotyl propanoates **12** and **13** (Table III and Scheme II) and for 3-pentanone (vide infra).

The question quickly arises whether these results apply only to esters or whether the selective formation of either geometrical enolate of ketones is possible. The symmetrical ketone, 3-pentanone, in which no problem of regioselectivity arises, was chosen for study. Again, a high degree of selectivity for one enolate in THF and the other in HMPA-THF was ob-

Table V. Effect of Structure on Ratio of Enolates[a]



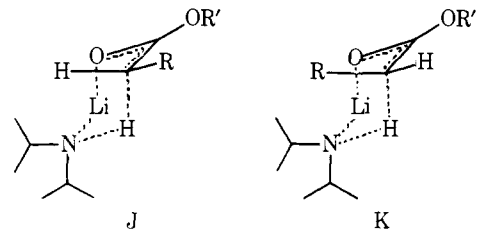
Ester	R	R'	Solvent[b]	19/20[c]
18a	C_2H_5	CH_3	THF	91/9
18a	C_2H_5	CH_3	HMPA–THF	16/84
18b	C_6H_5	CH_3	THF	29/71
18b	C_6H_5	CH_3	HMPA–THF	5/95
18c	$(CH_3)_3C$	CH_3	THF	97/3
18c	$(CH_3)_3C$	CH_3	HMPA–THF	9/91
18d	C_2H_5	$(CH_3)_3C$	THF	95/5
18d	C_2H_5	$(CH_3)_3C$	HMPA–THF	23/77
	3-Pentanone		THF	77/23[d,e]
	3-Pentanone		HMPA–THF	5/95[d,e]

[a] Enolization with 1.1 equiv LDA at −78°, trapped with *t*-$BuMe_2SiCl$, HMPA. [b] THF = 100% THF, HMPA–THF = 23 vol % HMPA–THF. [c] Bt NMR analysis of isolated mixture. [d] Ratio represents: 19 (R = CH_3; R' = C_2H_5)/20 (R = CH_3; R' = C_2H_5). [e] By NMR or VPC analysis.

served (Table V). The sily enol ethers were easily separated by VPC and readily identified by NMR (see Experimental Section).[21,22] The unambiguous stereochemistry in this case reinforces the assignments for the esters above (Table V).

In order to gain further insight about the mechanism, methyl butanoate (**18a**) was subjected to enolization and trapping under a variety of conditions. The results recorded in Table VII point out a smooth change from one enolate (**19a**) with no HMPA present to predominately the other (**20a**) as the amount of HMPA increases to the point of saturation. There is no discrete molar quantity which effects the changeover in stereoselectivity. The kinetic nature of the stereoselectivity is supported by the fact that the stereochemistry of the enolate formed in THF is virtually unchanged by the subsequent addition of HMPA (entry 2) and that the silylketene acetal formed in THF is stable for at least 2 h in the reaction medium at 67° (entry 1). When the enolization is carried out in HMPA-THF, the trapping agent (*t*-$BuMe_2SiCl$) may be present during the enolization or added afterward with no change in the outcome (entries 6 and 7).

It appears that the observed stereoselectivity results from the kinetic enolization of esters and ketones, and that this enolization takes a different course as a function of the solvent employed. One explanation for this dramatic solvent effect may lie in an analysis of the steric requirements for enolization. Two transition states J and K leading to the two enolates can be imagined. When the solvent is the less coordinating THF, the interaction of the carbonyl oxygen with the lithium cation must be quite important, and the carbonyl oxygen becomes effectively bulkier than OR'. The resulting nonbonded interactions would bestow a higher activation energy on transition state K and enolization would be expected to proceed through transition state J. The presence of HMPA, on the other hand, should result in a greater degree of solvation of the lithium cation and



an enhanced reactivity of the amide base. The lithium–carbonyl oxygen interaction should be much weaker and transition state K, in which R becomes eclipsed with the now sterically smaller carbonyl oxygen during enolization, should be favored.

This degree of control over the stereochemistry of the 1,5-diene unit enormously expands the potential of the ester enolate Claisen rearrangement and provides the synthetic chemist with a powerful weapon with which to attack the problem of stereochemistry of acyclic molecules. The ability to generate selectively the desired stereochemistry in the rearranged products regardless of the stereochemistry present in the starting material places this modification in a unique position among procedures for the aliphatic Claisen rearrangement.

The stereochemical outcome of the vinyl ether rearrangement has been investigated by Schmid[15] who notes a preponderance of the *cis*-propenyl ether **21** from the reaction of crotyl alcohol with propanal in the presence of phosphoric acid. A similar result was obtained in a study of the amide acetal rearrangement by Sucrow and Richter.[16] In this case a strong preference for formation of the *Z* configuration **24** of the intermediate ketene *O,N*-acetal was inferred from the stereochemistry of the rearrangement products. The opposite stereochemistry of the ketene acetal portion of the molecule has been obtained by requiring this double bond to lie in a ring

Scheme IV

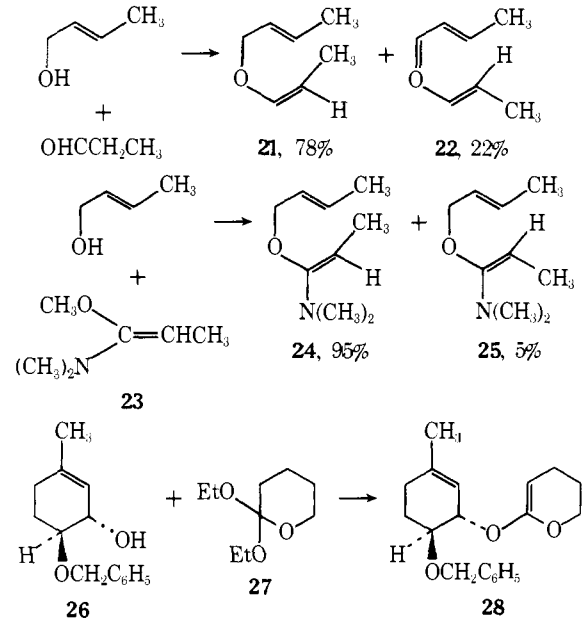
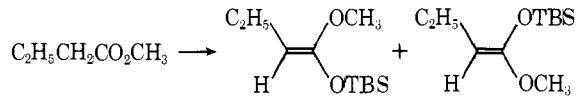


Table VI. NMR Data for Silylketene Acetals 19 and 20[a]

Ketene acetal	R	R'	δ R	δ R'	δ vinyl H	δ CH_3Si	δ $(CH_3)_3CSi$
19a	C_2H_5	CH_3		3.55 (s)	3.72 (t)[b]	0.18 (s)	0.95 (s)
20a	C_2H_5	CH_3		3.45 (s)	3.43 (t)[c]	0.12 (s)	0.92 (s)
19b	C_6H_5	CH_3	7.3 (m)	3.73 (s)	4.72 (s)	0.30 (s)	1.02 (s)
20b	C_6H_5	CH_3	7.3 (m)	3.67 (s)	4.60 (s)	0.23 (s)	1.00 (s)
19c	$(CH_3)_3C$	CH_3	1.06 (s)	3.52 (s)	3.75 (s)	0.18 (s)	0.95 (s)
20c	$(CH_3)_3C$	CH_3	1.10 (s)	3.43 (s)	3.37 (s)	0.15 (s)	0.93 (s)
19d	C_2H_5	$(CH_3)_3C$		1.32 (s)	3.88 (t)[d]	0.15 (s)	0.92 (s)
20d	C_2H_5	$(CH_3)_3C$		1.25 (s)	3.90 (t)[d]	0.12 (s)	0.90 (s)

[a] 10% solution in $CDCl_3$, internal standard $CHCl_3$, chemical shifts in ppm downfield from Me_4Si. [b] J = 7.2 Hz. [c] J = 6.8 Hz. [d] J = 7 Hz.

Table VII. Effect of HMPA Concentration on Ester Enolate Isomer Ratio[a]



18a 19a 20a

	Equiv HMPA[b]	Solvent	19a/20a[c]
1	0	100% THF	91/9[d]
2	0	100% THF[e]	85/15
3	0.5	3% HMPA–THF	89/11
4	1.0	6% HMPA–THF	53/47
5	2.0	11% HMPA–THF	23/77
6	4.7[g]	23% HMPA–THF	16/84
7	4.7[g]	23% HMPA–THF	16/84[f]

[a] Enolized with 1.1 equiv of LDA in 0.3 M solution. [b] Based on LDA. [c] By NMR analysis. [d] No change after heating ketene acetals in reaction medium for 2 h at 67°. [e] Following enolization, 4.7 equiv of HMPA was added, and the reaction was stirred for 4 min at −78° then quenched with *t*-BuMe$_2$SiCl. [f] A mixture of *t*-BuMe$_2$SiCl and ester added to LDA solution. [g] This quantity of HMPA is not entirely soluble at −78°.

(e.g., **28**). Cyclic ortho esters such as **37** have been successfully employed in this approach by Lythgoe.[23]

As well as extending the utility of the Claisen rearrangement, these results have general implications in other synthetic reactions. Recent reports have related enolate geometry to intermolecular reactions including aldol condensation[24-26] and alkylation reactions.[27] The rapidly increasing use of ketone and ester enolates as versatile intermediates in organic synthesis will undoubtedly unveil more of these relationships. The complementary conditions which have been described here for stereoselective enolization should find useful application in these areas as well.

Experimental Section[28]

(*Z*)-2-Buten-1-ol (*cis*-Crotyl Alcohol). The following procedure gave the most consistent results. A solution of 7.0 g (0.1 mol) of 2-butyn-1-ol in 75 ml of methanol containing 500 mg of 5% Pd/BaSO$_4$ and 5 ml of *s*-collidine was stirred rapidly under 1 atm of hydrogen until 2440 ml (0.1 mol) of hydrogen was abosrbed (2.25 h). The reaction mixture was filtered with the aid of Celite, and the filtrate was subjected to fractional distillation through a 30-cm vacuum-jacketed Vigreux column. The pot was maintained at 110° while the pressure was gradually lowered. Most of the methanol distilled at atmospheric pressure, with an additional portion distilling as the pressure was lowered to 90 mm. After a small forerun at this pressure, the material distilling at 72–80 °C (90 mm) was collected. This amounted to 5.6 g (78%). Analysis by VPC[28] (100 and 150°, ¼ in. × 8 ft 10% Carbowax 20 M, 60 ml/min, thermocouple) indicated that this material consisted of *cis*-crotyl alcohol contaminated with 1% methanol, 1% *s*-collidine, and less than 1% *trans*-crotyl alcohol.

A similar reaction without *s*-collidine gave *cis*-crotyl alcohol containing 12% *trans*-crotyl alcohol and 10% 1-butanol.

Methyl (*E*)-2-Methoxy-2-nonenoate ((*E*)-8) and Methyl (*Z*)-2-Methoxy-2-nonenoate ((*Z*)-8). To a mechanically stirred suspension of sodium hydride (mineral oil free) in 50 ml of dry THF was added dropwise over 30 min, 8.0 g (33.3 mmol) of methyl diethoxyphosphinylmethoxyacetate[11] (**7**). The mixture was stirred for an additional 45 min at 25° and then cooled to 0°. During 30 min, the reaction mixture was treated with 3.8 g (33.3 mmol) of heptanal (**6**) in 5 ml of dry THF while vigorous stirring was maintained. Toward the end of the addition a gummy precipitate formed. The reaction mixture was allowed to warm to 25° and stirring was continued for 2 h. After cautious addition of 25 ml of water, the product esters were isolated by ether extraction.[29] The slightly brown liquid residue was subjected to evaporative distillation at 45° (0.08 mm) and gave 5.7 g (85%) of the unsaturated esters. NMR analysis indicated that this was approximately a 1:1 mixture of double bond isomers. Separation of the isomers was accomplished by medium-pressure chromatography[28] of 2.0 g of the mixture on 2.5 × 50 cm of silica gel with 3% ether/petroleum ether at a flow rate of 2 ml/min. Elution with 930 ml gave 686 mg of the *Z* isomer of **8**. An analytical sample was prepared by evaporative distillation at 45° (0.08 mm): NMR (CDCl$_3$) δ 3.66 (s, 3 H, ether CH$_3$), 3.78 (s, 3 H, ester CH$_3$), 6.29 (t, 1 H, *J* = 7.5 Hz, vinylic H); ir (CHCl$_3$) 1720 (C=O), 1645 (C=C), 1430, 1275, 1090 cm^{-1}. Anal. (C$_{11}$H$_{20}$O$_3$) C, H.

Further elution with 120 ml of the same solvent system gave 245 mg of a mixture of the *Z* and *E* isomers. Continued elution with 990 ml of this solvent system gave 797 mg of the *E* isomer of **8**. An analytical sample was prepared by evaporative distillation at 45° (0.08 mm): NMR (CDCl$_3$) δ 3.62 (s, 3 H, ether CH$_3$), 3.83 (s, 3 H, ester CH$_3$), 5.37 (t, 1 H, *J* = 7.5 Hz, vinylic H); ir (CHCl$_3$) 1720 (C=O), 1635 (C=C), 1435, 1370, 1240, 1145 cm^{-1}. Anal. (C$_{11}$H$_{20}$O$_3$) C, H.

Lithium Aluminum Hydride Reduction of Esters 8. A solution of 380 mg (10.0 mmol) of lithium aluminum hydride in 40 ml of dry ether was cooled to 0°. This solution was subjected to the dropwise addition of 2.5 g (12.5 mmol) of either the *Z* or *E* ester of **8** in 5 ml of dry ether over 30 min. The cooling bath was removed and the reaction mixture was stirred at 25° for 1 h. Following this, dropwise addition of 2 ml of ethyl acetate effected destruction of excess hydride. Workup according to the Fieser procedure[30] afforded 2.1 g (quantitative crude yield) of a colorless oil. A portion of this material was purified by medium-pressure chromatography[28] on 1.25 × 50 cm of silica gel with 60% ether/petroleum ether at a flow rate of 1 ml/min. Elution with 100 ml gave a colorless oil (90%). An analytical sample was prepared by evaporative distillation at 50° (0.08 mm).

(*Z*)-2-Methoxynon-2-enol ((*Z*)-9): NMR (CDCl$_3$) δ 3.66 (s, 3 H, CH$_3$O), 4.10 (br, s, 2 H, -CH$_2$O-), 4.75 (t, 1 H, *J* = 7 Hz, vinylic H); ir (CHCl$_3$) 3650–3400 (OH), 1675 (C=C), 1460, 1150, 1080, 885 cm^{-1}. Anal. (C$_{10}$H$_{20}$O$_2$) C, H.

(*E*)-2-Methoxynon-2-enol ((*E*)-9): NMR (CDCl$_3$) δ 3.55 (s, 3 H, CH$_3$O-), 4.16 (br s, 2 H, -CH$_2$O-), 4.54 (t, 1 H, *J* = 7.5 Hz, vinylic H); ir (CHCl$_3$) 3590 and 3450 (OH), 1670 (C=C), 1225, 1120, 1055, 1015 cm^{-1}. Anal. (C$_{10}$H$_{20}$O$_2$) C, H.

Preparation of Allyl Esters. A. From the Acid Chloride. The following esters were prepared by reaction of 1.0 equiv of the allylic alcohol[31] with 1.0 equiv of the required acid chloride[32] in the presence of 1.1 equiv of pyridine as an 0.3 M solution in dry dichloromethane:

(*E*)-2-Butenyl Propanoate (12): yield 92%, bp 65–68 °C (35 mm); NMR (CDCl$_3$) δ 1.13 (t, 3 H, *J* = 7.5 Hz, CH$_3$), 1.72 (d, 3 H, *J* = 5 Hz, vinylic CH$_3$), 2.34 (q, 2 H, *J* = 7.5 Hz, -CH$_2$C=O), 4.52 (d, 2 H, *J* = 6 Hz, -CH$_2$O-), 5.70 (m, 2, vinylic H's).

(*Z*)-2-Butenyl Propanoate (13): yield 86%, bp 76–79 °C (60 mm); NMR (CDCl$_3$) δ 1.13 (t, 3 H, *J* = 7.5 Hz, CH$_3$), 1.72 (d, 3 H, *J* = 5 Hz, vinylic CH$_3$), 2.34 (q, 2 H, *J* = 7.5 Hz, -CH$_2$C=O), 4.65 (d, 2 H, *J* = 5 Hz, -CH$_2$O-), 5.70 (m, 2 H, vinylic H's).

(*Z*)-Methyl-2-nonenyl Propanoate (1f): yield 63%, bp 75 °C (0.5 mm); NMR (CDCl$_3$) δ 1.65 (br s, 3 H, vinylic CH$_3$), 1.97 (m, 2 H, vinylic CH$_2$), 2.35 (q, 2 H, *J* = 7 Hz, -CH$_2$CO$_2$-), 4.47 (br, s, 2 H, -CH$_2$O-), 5.45 (br t, 1 H, vinylic H); ir (CHCl$_3$) 1727 (C=O), 1380, 1345, 1280, 1185, 1085, 1015, 940 cm^{-1}. Anal. (C$_{13}$H$_{24}$O$_2$) C, H.

1-Hexyl-2-propenyl 2-(Phenylthio)propanoate (1h): yield 88%, evaporatively distilled at 110 °C (0.05 mm); NMR (CDCl$_3$) δ 1.53 (d, 3 H, *J* = 7 Hz, CH$_3$), 3.87 (q, 1 H, *J* = 7 Hz, -CHS-), 5.3 (m, 4 H, CH$_2$=CHCHO-), 7.33 (m, 5 H, phenyl); ir (CHCl$_3$) 1725 (C=O), 1380, 1260, 1165, 985, 930 cm^{-1}. Anal. (C$_{17}$H$_{24}$O$_2$S) C, H, S.

(*Z*)-2-Methoxy-2-nonenyl Pentanoate ((*Z*)-1j): yield 78%, evaporatively distilled at 60 °C (0.003 mm); NMR (CDCl$_3$) δ 3.60 (s, 3 H, CH$_3$O), 4.57 (s, 2 H, -CH$_2$O-), 4.86 (t, 1 H, *J* = 7 Hz, vinylic H); ir (CHCl$_3$) 1725 (C=O), 1675 (C=C), 1460, 1165, 960 cm^{-1}. Anal. (C$_{15}$H$_{28}$O$_3$) C, H.

(*E*)-2-Methoxy-2-nonenyl Pentanoate ((*E*)-1j): yield 91%, evaporatively distilled at 60 °C (0.006 mm); NMR (CDCl$_3$) δ 3.53 (s, 3 H, CH$_3$O), 4.62 (s, 2 H, -CH$_2$O-), 4.65 (t, 1 H, *J* = 7 Hz, vinylic H); ir (CHCl$_3$) 1730 (C=O), 1670 (C=C), 1260, 1170, 1070 cm^{-1}. Anal. (C$_{15}$H$_{28}$O$_3$) C, H.

2-Butenyl 2-Bromohexanoate (1k): yield 98%, evaporatively distilled at 50 °C (0.05 mm); NMR (CDCl$_3$) δ 1.73 (d, 3 H, *J* = 5 Hz, vinylic CH$_3$), 4.20 (t, 1 H, *J* = 7 Hz, -CHBr), 4.60 (d, 2 H, *J* = 5 Hz, -CH$_2$O-), 5.7 (m, 2 H, vinylic H's); ir (CHCl$_3$) 1735 (C=O), 1380, 1150, 970 cm^{-1}. Anal. (C$_{10}$H$_{17}$BrO$_2$) C, H.

B. From the *p*-Nitrophenyl Ester. Esters of (*E*)-3-hexenoic acid were prepared by reaction of 1.0 equiv of the alcohol in dry triethylamine solution with 1.0 equiv of *p*-nitrophenyl (*E*)-3-hexenoate, which was

prepared as follows. A solution of 10 mmol of *p*-nitrophenyl trifluoroacetate in 6 ml of dry triethylamine was cooled to 0° and treated with 10 mmol of 3-hexenoic acid. This mixture was stirred for 30 min at 0° and 30 min at 25°. Benzene extraction[29] including a base wash afforded *p*-nitrophenyl (*E*)-3-hexenoate as an orange oil: NMR ($CDCl_3$) δ 1.02 (t, 3 H, J = 7, CH_3), 2.13 (m, 2 H, $-CH_2-$), 3.32 (d, 2 H, J = 5 Hz, CH_2), 5.68 (m, 2 H, $-CH=CH-$), 7.32 (d, 2 H, J = 9 Hz, aromatic), 8.30 (d, 2 H, J = 9 Hz, aromatic). The following esters were prepared in this manner.

2-Butenyl (*E*)-3-Hexenoate (1e): yield 43%, bp 70–72 °C (2 mm); NMR ($CDCl_3$) δ 1.00 (t, 3 H, J = 7 Hz, CH_3), 1.72 (d, 3 H, J = 5 Hz, vinylic CH_3), 2.03 (m, 2 H, vinylic CH_2), 3.03 (d, 2 H, J = 5 Hz, $-CH_2CO_2-$), 4.53 (d, 2 H, J = 5 Hz, $-CH_2O-$), 5.63 (m, 4 H, vinylic H's); ir ($CHCl_3$) 1728 (C=O), 1685, 1380, 1170, 965 cm^{-1}. Anal. ($C_{10}H_{16}O_2$) C, H.

(*Z*)-2-Methoxy-2-nonenyl (*E*)-3-Hexenoate ((*Z*)-1i): yield 31%, evaporatively distilled at 65 °C (0.002 mm); NMR ($CDCl_3$) δ 3.05 (m, 2 H, $-CH_2CO_2-$), 3.60 (s, 3 H, CH_3O), 4.57 (s, 2 H, $-CH_2O-$), 4.87 (t, 1 H, J = 7 Hz, $-CH=CO-$), 5.53 (m, 2 H, $-CH=CH-$); ir ($CHCl_3$) 1728 (C=O), 1675, 1460, 1155, 970 cm^{-1}. Anal. ($C_{16}H_{28}O_3$) C, H.

(*E*)-2-Methoxy-2-nonenyl (*E*)-3-Hexenoate ((*E*)-1i): yield 65%, evaporatively distilled at 60 °C (0.006 mm); NMR ($CDCl_3$) δ 3.05 (d, 2 H, J = 5 Hz, $-CH_2CO_2-$), 3.52 (s, 3 H, CH_3O), 4.62 (s, 2 H, $-CH_2O-$), 5.57 (m, 2 H, $-CH=CH-$); ir ($CHCl_3$) 1728 (C=O), 1670, 1465, 1160, 970 cm^{-1}. Anal. ($C_{16}H_{28}O_3$) C, H.

Claisen Rearrangement of Esters 1a–f (Table I). A. As the Enolate Anion. A stirred solution of 1.70 g (12.1 mmol) of dry *N*-isopropylcyclohexylamine in 20 ml of dry THF was cooled to 0° and treated with 5.0 ml (11.1 mmol) of *n*-butyllithium in hexane solution over several minutes. After the mixture was stirred for an additional 10 min following the addition, the solution was cooled to −78° and 10 mmol of the appropriate ester (**1a–f**) was added dropwise over 2–3 min. After an additional 2 min, the cooling bath was removed and the reaction mixture was allowed to warm to 25°. This solution was stirred for the indicated period of time, and then the reaction mixture was poured into 20 ml of 5% aqueous sodium hydroxide solution. The aqueous solution was washed with two 15-ml portions of ether (washings discarded) and acidified with concentrated hydrochloric acid, and then the product acid was isolated by dichloromethane extraction.[29] Distillation at reduced pressure afforded the pure acid in the indicated yield (Table I).

B. As the Trimethylsilylketene Acetal. The esters **1a–f** (Table I) were enolized at −78° as described in A previously. Within 5 min after the addition of the ester was complete, 1.2 g (11.1 mmol) of Me_3SiCl was added in one batch. The cooling bath was then removed and the reaction mixture was allowed to warm to 25° over 30 min. Stirring at either 25 or 67° was continued as indicated for each particular ester. Following this, 3 ml of methanol was added and the reaction mixture was stirred for 10 min at 25° to effect hydrolysis of the silyl ester. The reaction mixture was then added to 20 ml of 5% aqueous sodium hydroxide solution and the product was isolated as described in A. The distilled acids prepared by this procedure contained 1–2 mol% 2-trimethylsilyl-substituted acid. This impurity could be removed as described below.

4-Pentenoic Acid (2a). From allyl acetate (**1a**); procedure B, 2 h at 67°, 66%; bp 70–72 °C (4 mm); ir (film) 3600–2400, 1711 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 2.5•(m, 4 H, $-CH_2-$), 5.85–6.25 (m, 3 H, $-CH=CH_2$), 11.9 (s, 1 H, $-CO_2H$).

3-Methyl-4-pentenoic Acid (2b). From crotyl acetate (**1b**); procedure B, 1.5 h at 67°, 70%; bp 75–76 °C (4 mm); ir (film) 3600–2400, 1710 (C=O), 1640, 1000, 920 cm^{-1}; NMR ($CDCl_3$) δ 1.10 (d, 3 H, J = 7 Hz, CH_3), 2.2–3.0 (m, 3 H, $-CH_2CH-$), 4.85–6.15 (m, 3 H, $-CH=CH_2$), 11.5 (s, 1 H, $-CO_2H$). Anal. ($C_6H_{10}O_2$) C, H.

2,3-Dimethyl-4-pentenoic Acid (2c). From crotyl propanoate (**1c**); procedure A, 1 h at 25°, 75%; procedure B, 0.5 h at 67°, 75% yield; bp 81–82 °C (3 mm); ir (film) 3600–2400, 1710 (C=O), 1644, 1000, 920 cm^{-1}; NMR ($CDCl_3$) δ 1.0–1.3 (overlapping d's, 6 Hz, CH_3), 2.1–2.7 (m, 2 H, methines), 4.82–6.05 (m, 3 H, $-CH=CH_2$), 11.43 (s, 1 H, $-CO_2H$). Anal. ($C_7H_{12}O_2$) C, H.

2,2,3-Trimethyl-4-pentenoic Acid (2d). From crotyl isobutyrate (**1d**); procedure A, 10 min at 25°, 80%; procedure B, 10 min at 25°, 78%; bp 52 °C (0.07 mm); ir (film) 3600–2400, 1705 (C=O), 1643, 1000, 923 cm^{-1}; NMR ($CDCl_3$) δ 1.01 (d, 3 H, J = 7 Hz, CH_3), 1.13 and 1.15 (s, 3 H, CH_3), 2.52 (m, 1 H, methine), 4.85–6.1 (m, 3 H, $-CH=CH_2$), 12.05 (s, 1 H, $-CO_2H$). Anal. ($C_8H_{14}O_2$) C, H.

(*E*)-2-(1-Methyl-2-propenyl)-3-hexenoic Acid (2e). From crotyl (*E*)-3-hexenoate (**1e**); procedure A, 3 h at 25°, 69%; evaporatively distilled at 90 °C (0.05 mm); ir (film) 3600–2400, 1710 (C=O), 1645, 1000, 975, 920 cm^{-1}; NMR ($CDCl_3$) δ 0.80–1.15 (m, 6 H, CH_3), 1.8–3.1 (m, 4 H, allylic H's), 4.8–6.0 (m, 5 H, vinylic H's), 11.2 (s, 1 H, $-CO_2H$). Anal. ($C_{10}H_{16}O_2$) C, H.

2,4-Dimethyl-3-hexyl-4-pentenoic Acid (2f). From 2-methyl-2-nonenyl propanoate (**1f**); procedure A, 20 h at 25°, 71%; evaporatively distilled at 100–120 °C (0.05 mm); ir (film) 3600–2400, 1710 (C=O), 1650, 900 cm^{-1}; NMR ($CDCl_3$) δ 0.8–1.5 (m, 16 H), 1.54 and 1.65 (br s, 3 H, vinylic CH_3), 2.1–3.5 (m, 2 H, methines), 4.8 (m, 2 H, vinylic H's), 11.20 (s, 1 H, $-CO_2H$). Anal. ($C_{13}H_{24}O_2$) C, H.

Removal of α-Silyl Impurities in Carboxylic Acids Prepared by Procedure B. A 2.0-g portion of the 4-pentenoic acid obtained by procedure B was esterified with excess diazomethane in ether solution and then refluxed with 5 wt % sodium methoxide in methanol for 2 h. Water (20 ml) was added and the methanol was distilled for over 1 h. The reaction mixture was extracted with 20 ml of ether (extract discarded) and then acidified with concentrated hydrochloric acid. The product acid was isolated by dichloromethane extraction.[29] Distillation at 65° (4 mm) afforded 1.70 g of pure, colorless 4-pentenoic acid (**1a**) (57% overall yield from allyl acetate).

In exactly the same manner, pure 3-methyl-4-pentenoic acid (**1b**) was prepared in an overall yield of 50% from crotyl acetate.

Determination of Rearrangement Half-Lives. After addition of Me_3SiCl or *t*-$BuMe_2SiCl$ to the reaction mixture to quench the enolate anion, a 300-μl aliquot was withdrawn and placed in an NMR tube. The region from δ 1.5 to −1.0 was scanned. A peak at $\delta \approx 0.27$ (assigned to the CH_3Si of the ketene acetal) gradually disappeared and a new peak of $\delta \approx 0.33$ (assigned to the CH_3Si of the silyl ester) appeared at the same rate. When the two peaks reached the same height, the elapsed time was taken to be the half-life for the rearrangement. This method was used to follow the reaction with both trimethylsilyl and *tert*-butyldimethylsilyl derivatives.

Lithium Diisopropylamide (LDA). Hexane-free LDA was prepared by dropwise addition of 1 equiv of *n*-butyllithium in hexane to a stirred solution of 1.5 equiv of dry diisopropylamine in dry hexane (~2 M) at 0°. Following the addition, the viscous mixture was stirred for an additional 10 min, after which the hexane and excess amine were removed under reduced pressure at 0°. The flask was refilled with argon and the residual white solid was redissolved in sufficient dry THF at 0° to give approximately an 0.3 M solution. When dissolution was complete, the ice bath was replaced by a dry ice/acetone (−78°) bath.

(*E*)-4-Decenoic Acid (2g). A solution of 11.0 mmol of LDA in 30 ml of dry THF was cooled to −78°, and then 3.0 ml of dry HMPA was added. To this solution was added dropwise 1.70 g (10.0 mmol) of 3-acetoxy-1-octene[33] (**1g**) and 1.65 g (11.0 mmol) of *t*-$BuMe_2SiCl$ in 2 ml of dry THF over 5 min. The slightly yellow solution was stirred at −78° for an additional 2 min after which the cooling bath was removed and the reaction mixture was allowed to warm to 25° over 30 min. The reaction mixture was stirred at 25° for an additional 2 h and the product silyl ester was isolated by pentane extraction.[29] The crude, oily silyl ester was dissolved in 25 ml of THF and treated with 5 ml of 10% hydrochloric acid, and the mixture was stirred at 25° for 45 min to effect hydrolysis of the silyl ester. The reaction mixture was then poured into 30 ml of 5% aqueous sodium hydroxide solution and extracted with two 30-ml portions of ether (extracts discarded). After acidification with concentrated hydrochloric acid, the product acid was isolated by ether extraction.[29] Evaporative distillation of the residual oil (1.5 g) at 70 °C (0.003 mm) afforded 1.41 g (83%) of acid **1g**: NMR ($CDCl_3$) δ 1.13 (m, 6 H, $-CH_2-$), 1.98 (m, 2 H, $-CH_2$), 2.20 (m, 4 H, $-CH_2CH_2CO_2-$), 5.25 (m, 2 H, $-CH=CH-$), 11.0 (s, 1 H, $-CO_2H$); ir ($CHCl_3$) 3500–2400 (OH), 1710 (C=O), 1285, 970 cm^{-1}. Anal. ($C_{10}H_{18}O_2$) C, H.

Comparison of the methyl ester with an authentic sample of methyl (*Z*)-4-decenoate[34] by VPC[28] (300 ft × 0.03 in. open tubular column, TCEP, 110°, 20 ml/min, flame ionization) indicated that less than 0.5% of the *Z* isomer was present.

(*E*)-2-Methyl-2-(phenylthio)-4-decenoic Acid (2h). A solution of 20.5 mmol of LDA in 75 ml of dry THF was cooled to −78°. To this rapidly stirred solution was added a mixture of 5.0 g (17.1 mmol) of ester **1h** in 5 ml of dry THF over a 10-min period. Following the addition, the mixture was stirred at −78° for 5 min. After the addition of 7.5 ml of dry HMPA, 6.1 ml (20.5 mmol) of *t*-$BuMe_2SiCl$ in hexane was added and the cooling bath was removed after 2 min. The mixture was then allowed to warm to 25° and was stirred for 2 h. The silyl ester

was isolated by petroleum ether extraction[29] and amounted to 6.9 g of a yellow oil. This oil was stirred with a solution of 15 ml of 5% hydrochloric acid and 75 ml of THF at 25° for 45 min to effect hydrolysis of the silyl ester. Petroleum ether extraction[29] afforded 5.5 g of a yellow oil which was purified by chromatography on 150 g of acidic silica gel[28] with 20% ether/petroleum ether. After elution with 250 ml of this solvent mixture, continued elution with 350 ml gave 4.4 g (88%) of the acid **2h**. An analytical sample was prepared by evaporative distillation at 140 °C (0.005 mm): NMR ($CDCl_3$) δ 1.40 (s, 3 H, CH_3), 2.00 (m, 2 H, allylic CH_2), 2.48 (m, 2 H, allylic CH_2), 3.80 (m, 2 H, vinylic H's), 7.37 (m, 5 H, phenyl), 10.5 (br s, 1 H, $-CO_2H$); ir ($CHCl_3$) 3300–2400, 1740 (sh), 1695 (C=O), 1070, 975 cm^{-1}. Anal. ($C_{17}H_{24}O_2S$) C, H, S.

Methyl (*E*)-2-(1-Hexyl-2-methoxy-2-propenyl)-3-hexenoate (2i Methyl Ester). A solution of 4.10 mmol of LDA in 10 ml of dry THF was cooled to −78°. To this rapidly stirred solution was added 1.0 g (3.73 mmol) of the ester **1i** (a mixture of isomers) in 1 ml of dry THF over a 1.5-min period. After an additional 1 min, 2.64 ml (4.10 mmol) of *t*-$BuMe_2SiCl$ in HMPA was added, and the reaction mixture was stirred for an additional 5 min. The cooling bath was then removed, and the reaction mixture was allowed to warm to 25° over 30 min. The mixture was then stirred at reflux (67°) for 2 h and cooled to 25°. Pentane extraction afforded the silyl esters as an orange oil (1.5 g). This oil was dissolved in 8 ml of HMPA and was treated with 560 mg (5.6 mmol) of $KHCO_3$ and 527 mg (5.6 mmol) of $KF{\cdot}2H_2O$. The reaction mixture was stirred vigorously for 30 min, after which 1.07 g (7.5 mmol) of methyl iodide was added. Stirring was continued for 15 h after which the methyl esters were isolated by pentane extraction.[29] The residual orange oil (1.0 g) was purified by medium-pressure chromatography[28] on 2.5 × 50 cm of silica gel with 4% ether/petroleum ether at a flow rate of 2 ml/min. After elution with 300 ml, continued elution with 20 ml of the same solvent system gave 361 mg (34%) of the more mobile isomer as a colorless oil. An analytical sample was prepared by evaporative distillation at 70–80 °C (0.005 mm): R_f 0.49 (silica gel, 10% ether/petroleum ether); NMR ($CDCl_3$) δ 3.45 (s, 3 H, ether CH_3), 3.68 (s, 3 H, ester CH_3), 3.87 (m, 2 H, CH_2=CO–), 5.40 (m, 2 H, –CH=CH–); ir ($CHCl_3$) 1752 (C=O), 1660, 1615, 1165, 1070, 970 cm^{-1}. Anal. ($C_{17}H_{30}O_3$) C, H.

Continued elution with 30 ml gave 225 mg (21%) of a mixture of the two isomers. Finally elution with an additional 60 ml gave 220 mg (21%) of the less mobile isomer. An analytical sample was prepared by evaporative distillation (70–80 °C (0.005 mm)): R_f 0.33 (silica gel, 10% ether/petroleum ether); NMR ($CDCl_3$) δ 3.47 (s, 3 H, ether CH_3), 3.60 (s, 3 H, ester CH_3), 3.88 (br s, 2 H, CH_2=CO), 5.45 (m, 2 H, –CH=CH–); ir ($CHCl_3$) 1752 (C=O), 1660, 1615, 1165, 1070, 975 cm^{-1}. Anal. ($C_{17}H_{30}O_3$) C, H.

2-Butyl-3-methyl-4-pentenoic Acid (2k). To a stirred suspension of 520 mg (8.0 mmol) of zinc dust and 720 mg (4.80 mmol) of *t*-$BuMe_2SiCl$ in 30 ml of dry THF and 6 ml of dry HMPA, was added 1.0 g (4.01 mmol) of the α-bromo ester **1k** over a 10-min period. Following the addition, the reaction mixture was stirred at reflux for 1.5 h, cooled to room temperature, and then diluted with 300 ml of pentane containing 2 ml of pyridine. The pentane solution was filtered and then washed with three 30-ml portions of ice water, dried ($MgSO_4$), and evaporated at reduced pressure. The resulting oil (1.2 g) was stirred with 5 ml of 10% hydrochloric acid in 25 ml of THF for 45 min to effect hydrolysis of the silyl ester. The mixture was diluted with 20 ml of 5% aqueous sodium hydroxide solution and washed with two 50-ml portions of ether (washings discarded). This solution was acidified with concentrated hydrochloric acid and the product acid was isolated by ether extraction.[29] This afforded 499 mg (73%) of a colorless oil which was homogeneous by TLC (silica gel, 50% ether/petroleum ether). An analytical sample was prepared by evaporative distillation at 60 °C (0.05 mm): NMR ($CDCl_3$) δ 1.07 (d, 2 H, J = 6 Hz, CH_3), 2.30 (m, 2 H, methines), 4.8–6.0 (m, 3 H, $-CH=CH_2$), 10.4 (br s, 1 H, CO_2H); ir ($CHCl_3$) 3400–2400, 1705 (C=O), 1645, 1415, 990, 920 cm^{-1}. Anal. ($C_{10}H_{18}O_2$) C, H.

Stereochemistry of the Rearrangement. Enolization and Claisen rearrangement were studied under four sets of conditions (Tables III and IV).

A. Enolization in THF. Rearrangement as the Silylketene Acetal. A solution of 1.1 equiv of LDA in dry THF (0.3 M) was cooled to −78°. To this rapidly stirred solution was added 1.0 equiv of the ester, dropwise over 4 min. Following the addition, the reaction mixture was stirred for 2.5 min and then quenched with 1.1 equiv of *t*-$BuMe_2SiCl$ in HMPA. After an additional 2 min at −78°, the reaction mixture was allowed to warm to 25° during 20 min and was then stirred at reflux (67°) for 1–2 h.

B. Enolization in 23% HMPA–THF. Rearrangement as the Silylketene Acetal. To a stirred solution of 1.1 equiv of LDA in dry THF at −78° was added sufficient dry HMPA to adjust the solvent composition to 23 vol % HMPA–THF. This slightly yellow, nonhomogeneous solution was treated with the dropwise addition of 1.0 equiv of the ester over 4 min. After an additional 2.5 min at −78°, 1.1 equiv of *t*-$BuMe_2SiCl$ in hexane was added. The reaction mixture was stirred for an additional 2 min at −78°, allowed to warm to 25° over 20 min, and then stirred at reflux (67°) for 1–2 h.

C. Enolization in THF. Rearrangement as the Enolate Anion. The enolization was carried out as described in A above. In this case, however, no *t*-$BuMe_2SiCl$ was added. The reaction mixture was allowed to warm to 25° over 20 min and was then stirred at 25° for 1 h.

D. Enolization in 23% HMPA–THF. Rearrangement as the Enolate Anion. Enolization was carried out as described in B above. In this case, however, no *t*-$BuMe_2SiCl$ was added. The reaction mixture was allowed to warm to 25° over 20 min and was then stirred at 25° for 1 h.

Rearrangement of (*E*)- and (*Z*)-2-Butenyl Propanoate (12 and 13). After rearrangement as described above (5.0 mmol), the reaction mixtures obtained in C and D were diluted with 30 ml of 5% aqueous sodium hydroxide solution, and this solution was extracted with two 30-ml portions of ether (extracts discarded). The basic solution was then acidified with concentrated hydrochloric acid and ice. The cold, acidic aqueous phase was extracted with four 20-ml portions of ether. The combined ethereal extracts were washed with 20-ml portions of water and saturated brine and dried ($MgSO_4$). The solvents were then distilled through a 30-cm, vacuum-jacketed, Vigreux column and evaporative distillation of the residue at 90 °C (2 mm) afforded a mixture of the *erythro*-**14** and *threo*-**15** acids.

For the reactions in A and B, after 1 h at 67° the silyl esters were isolated by pentane extraction.[29] The residue was dissolved in 15 ml of THF and treated with 3 ml of 10% hydrochloric acid. This mixture was stirred for 45 min at 25° and then worked up as described for C and D above. Evaporative distillation afforded a mixture of the acids **14** and **15.**

Treatment of 64-mg (0.5 mmol) portions of each of the acid mixtures with 5 ml of ether containing 1.5 mmol of diazomethane[35] served to convert the acids to the corresponding methyl esters. These mixtures were analyzed by VPC[28] (90°, ⅛ in. × 27 ft 15% Carbowax 20 M, 20 ml/min, flame ionization). The erythro ester **14** had a retention time of 54 min; the threo ester **15,** 58 min. There were no other volatile compounds in the mixtures. The data obtained from this analysis are recorded in Table III.

Rearrangement of (*E*)- and (*Z*)-2-Methoxy-2-nonenyl Pentanoate ((*E*)-1j and (*Z*)-1j). Esters (*E*)-**1j** and (*Z*)-**1j** were rearranged only as described in A and B above (1.95 mmol). The silyl esters were isolated as described for the rearrangement of (*E*)- and (*Z*)-2-butenyl propanoate (**12** and **13**). The crude mixture of silyl esters was then stirred with 490 mg (4.90 mmol) of $KHCO_3$ and 367 mg (3.90 mmol) of $KF{\cdot}2H_2O$ in 5 ml of HMPA for 18 h to effect cleavage of the silyl esters. Following this, 364 μl (831 mg, 5.85 mmol) of methyl iodide was added and the mixture was stirred for an additional 1.5 h at room temperature. The methyl esters were then isolated by pentane extraction,[29] including a base wash. The ratio of the two isomers in this mixture could be determined from peak heights of the ester methyl signals in the NMR spectra. The two isomers were cleanly separated by medium-pressure chromatography[28] on 1.25 × 50 cm of silica gel with 5% ether/petroleum ether at a flow rate of 1 ml/min. Analytical samples were prepared by evaporative distillation at 60 °C (0.08 mm). The more mobile isomer was tentatively assigned the erythro configuration **16** (see Discussion): R_f 0.50 (silica gel, 10% ether/petroleum ether); NMR ($CDCl_3$) δ 3.51 (s, 3 H, ether CH_3); 3.70 (s, 3 H, ester CH_3), 3.95 (m, 2 H, CH_2=C); ir ($CHCl_3$) 1725 (C=O), 1660 and 1610 (C=C), 1190, 1160, 1115, 1060 cm^{-1}. Anal. ($C_{16}H_{30}O_3$) C, H.

The less mobile isomer was assigned the threo configuration **17** (see Discussion): R_f 0.35 (silica gel, 10% ether/petroleum ether); NMR ($CDCl_3$) δ 3.49 (s, 3 H, ether CH_3), 3.63 (s, 3 H, ester CH_3), 3.88 (m, 2 H, CH_2=C); ir ($CHCl_3$) 1730 (C=O), 1655 and 1615 (C=C), 1285, 1190, 1160, 1120, 1065 cm^{-1}. Anal. ($C_{16}H_{30}O_3$) C, H.

The data obtained from these rearrangements are recorded in Table IV.

Ozonization of Erythro Acid 14. A solution of 754 mg (5.9 mmol) of the acid mixture containing 90% erythro acid **14** (VPC analysis of methyl esters, see above) in 25 ml of ethyl acetate and 25 ml of acetic acid was cooled to −10°. Ozone[36] was passed through the solution until no more ozone was absorbed. The reaction mixture was then purged with argon to remove dissolved ozone and was treated with 10 ml of 15% aqueous hydrogen peroxide solution. This solution was stirred at 25° for 16 h. The solvents were then removed at reduced pressure and the residue was dissolved in 50 ml of 3% aqueous sodium hydroxide solution. This basic solution was extracted with three 30-ml portions of ether (extracts discarded) and acidified with 40 ml of 2 N aqueous sulfuric acid. This acidific solution was continuously extracted with ether for 16 h, after which evaporation of the ether extract afforded 830 mg of a white solid. One recrystallization of this material from 20 ml of water gave 543 mg of *meso*-2,3-dimethylsuccinic acid (70% based on amount of erythro acid **14** initially present: mp 202–204 °C dec (lit.[37] 209 °C)).

Ozonization of Threo Acid 15. As described above for the erythro acid **14,** 606 mg (4.73 mmol) of a mixture containing 90% of the threo acid **15** was treated with ozone and then aqueous hydrogen peroxide. After continuous extraction, 648 mg of a white solid was obtained. One recrystallization from water gave 453 mg (73% based on the amount of threo acid **15** initially present) of *d,l*-2,3-dimethylsuccinic acid: mp 118–121 °C (lit.[37] 129 °C).

Preparation of Silylketene Acetals of Simple Esters (Table V). A. Enolization in THF. A solution of 5.5 mmol of LDA in 15 ml of dry THF was cooled to −78°. To this rapidly stirred solution was added 5.0 mmol of the ester **18** over 4 min. Following the addition, the reaction mixture was stirred at −78° for 2.5 min and then treated with 3.59 ml (5.5 mmol) of *t*-$BuMe_2SiCl$ in HMPA. After an additional 2 min at −78°, the reaction mixture was allowed to warm to 25° over 30 min. Pentane extraction[23] then afforded a quantitative yield of a mixture of the ketene acetals **19** and **20.**

B. Enolization in 23 vol % HMPA–THF. A solution of 5.5 mmol of LDA in 15 ml of dry THF was cooled to −78° and 4.5 ml of HMPA was added. To this rapidly stirred solution was added 5.0 mmol of the ester **18,** dropwise over 4 min. After an additional 2.5 min at −78°, 1.59 ml (5.5 mmol) of *t*-$BuMe_2SiCl$ in hexane was added. This mixture was stirred for 2 min at −78° and then allowed to warm to 25° over 30 min. Pentane extraction[29] afforded a quantitative yield of a mixture of ketene acetals **19** and **20.**

These mixtures of ketene acetals obtained in A and B were subjected to NMR analysis. Only signals which could be assigned to the two possible isomeric ketene acetals **19** and **20** were present (Table VI). The ratios of the isomers were determined by integration and are recorded in Table V.

C. Enolization of Methyl Butyrate (18a) in the Presence of Varying Amounts of HMPA (Table VII). Methyl butyrate (**18a**) was enolized as described in B in dry THF containing varied concentrations of HMPA. When 2 equiv or less of HMPA was present (entries 1–5), the enolates were quenched with *t*-$BuMe_2SiCl$ in HMPA. When more than 2 equiv of HMPA was present, the enolates were quenched with *t*-$BuMe_2SiCl$ in hexane (entry 6). A variety of other experiments were performed with methyl butyrate **18a.** These are described in the footnotes to Table VII. The resulting mixtures of silylketene acetals **19a** and **20a** were analyzed by NMR as described above.

Preparation of the Silyl Enol Ethers of 3-Pentanone. The *tert*-butyldimethylsilyl enol ethers of 3-pentanone were prepared by enolization as described for the esters **18** in A and B above. The isomer ratios were determined by NMR analysis and by VPC[28] analysis (110°, 8 ft × ¼ in. 4% SE-30, 60 ml/min, thermocouple, not corrected for sensitivities). The data obtained are recorded in Table V. These isomers were preparatively separated under the same conditions. The structures were readily assigned by NMR[21,22] analysis.

(*E*)-3-(*tert*-Butyldimethylsilyloxy)-2-pentene. Retention time = 7.5 min; NMR ($CDCl_3$) δ 0.13 (s, 6 H, CH_3Si), 0.95 (s, 9 H, $(CH_3)_3CSi$), 1.03 (t, 3 H, J = 7 Hz, CH_3), 1.55 (d, 3 H, J = 7 Hz, vinylic CH_3), 2.10 (q, 2 H, J = 7 Hz, <1 Hz homoallylic coupling, $-CH_2-$), 4.60 (q, 1 H, J = 7 Hz, vinylic H).

(*Z*)-3-(*tert*-Butyldimethylsilyloxy)-2-pentene. Retention time = 8.5 min; NMR ($CDCl_3$) δ 0.13 (s, 6 H, CH_3Si), 0.99 (s, 9 H, $(CH_3)_3CSi$), 1.05 (t, 3 H, J = 7 Hz, CH_3), 1.56 (d, of t, 3 H, J = 6.5 and 1.5 Hz, vinylic CH_3), 2.06 (q, 2 H, J = 7 Hz, broadened by allylic and homoallylic coupling >1 Hz, $-CH_2-$), 4.54 (q of t, 1 H, J = 7 and 1 Hz, vinylic H).

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Vapor phase chromatographic (VPC) analyses were determined on either a Hewlett-Packard 5750 equipped with a flame ionization detector or a Varian 920 equipped with a thermal conductivity detector using helium as the carrier gas under the indicated conditions. The indicated liquid phase was absorbed on 60–80 mesh Chromosorb W AW DMCS.

Silica gel columns used the 0.05–0.2 mm silica gel manufactured by E. Merck and Co., Darmstadt, Germany. Acidic silica gel refers to Silicar CC-4 Special "For Column Chromatography", sold by Mallinckrodt Chemical Works, St. Louis, Mo. Preparative medium-pressure chromatography was performed using glass columns of the indicated length and diameter with fittings supplied by Laboratory Data Control, Riviera Beach, Fla., and an instrument minipump supplied by Milton Roy Co., St. Petersburg, Fla. (instrumentation designed by R. H. Mueller, those laboratories, and copies are available on request). The columns were packed with silica gel H "for TLC acc. to Stahl" (10–40 μ) manufactured by E. Merck and Co., Darmstadt, Germany. Solvents were degassed under water aspirator-vacuum prior to use.

Analytical thin layer chromatography was conducted on 2.5 × 10 cm precoated TLC plates, Silica Gel 60 F-254, layer thickness 0.25 mm, manufactured by E. Merck and Co., Darmstadt Germany.

"Dry" solvents were dried immediately prior to use. Ether and tetrahydrofuran (THF) were distilled from lithium aluminum hydride; pyridine, triethylamine, diisopropylamine, *N*-isopropylcyclohexylamine, trimethychlorosilane (Me_3SiCl), hexamethylphosphoramide (HMPA), and benzene were distilled from calcium hydride; dichloromethane, methyl iodide, and hexane were distilled from phosphorus pentoxide. "Petroleum ether" refers to the "Analyzed Reagent" grade hydrocarbon fraction, bp 30–60 °C, which is supplied by J. T. Baker Co., Phillipsburg, N.J., and was not further purified.

Standard solutions of *tert*-butyldimethylchlorosilane (*t*-$BuMe_2SiCl$) in hexane (ca. 3.3 M) or HMPA (ca. 1.5 M) were employed.

Reactions were run under an argon atmosphere arranged with a mercury bubbler so that the system could be alternately evacuated and filled with argon and left under a positive pressure.

Microanalyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Mich.
(29) In cases where the products were isolated "by solvent extraction", the procedure generally followed was to dilute the reacttion mixture with the indicated solvent or to extract the aqueous solution with several portions

of the indicated solvent; then the combined organic layers were washed with several portions of water followed by saturated brine. The organic layer was dried over anhydrous sodium or magnesium sulfate, then filtered, and the solvent was evaporated from the filtrate under reduced pressure (water aspirator) using a rotary evaporator. The use of the terms "base wash" or "acid wash" indicate washing the organic solution with saturated aqueous sodium bicarbonate solution or with dilute aqueous hydrochloric acid, respectively, prior to the aforementioned wash with water.

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Ozonolysis of *trans*-2,3-Dichloro-2-butene. Isolation of α-Chloro Peroxides[1]

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Abstract: Ozonolysis of *trans*-2,3-dichloro-2-butene (**4**) in nonparticipating solvents or at the neat substrate yielded acetyl chloride (**5**), acetic acid (**7**), acetic anhydride (**11**), 2,2,3,3-tetrachlorobutane (**10**), diacetyl peroxide (**13**), *trans*-1,2-dichloro-1,2-dimethyloxirane (**14**), and the α-chloro peroxides 1,4-dimethyl-1,4-dichloro-2,3,5,6-tetroxolane (**9**) and acetyl 1,1-dichloroethyl peroxide (**12**). Evidence was also obtained for the transient formation of a monomeric ozonide (**8**) of the substrate **4**. Structure proof is presented for the hitherto unknown α-chloro peroxides **9** and **12**, and a mechanism is suggested for the course of the ozonolysis reaction.

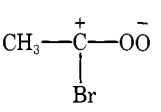
The reaction of ozone with purely hydrocarbon olefins has been and is still receiving broad attention, starting from the mode of initial attack of ozone via the nature and the fate of labile intermediates to the structure and the stereochemistry of the final ozonolysis products. By contrast, the interaction of ozone with olefins bearing halogen substituents at the double bond has not been the subject of systematic and detailed investigations thus far.

From scattered reports in the literature it became evident in a qualitative manner that halogen substituents in vinylic positions impart considerable ozone resistance to the corresponding double bonds. Thus, ozonolyses of compounds containing both nonhalogenated and mono-[2] or dihalogenated[3,4,5] double bonds in the same molecule were reported to lead to exclusive cleavage of the corresponding nonhalogenated double bonds.

The qualitative picture which emerged from such observations was substantially verified by the results of a quantitative study of the rates of reaction of ozone with ethylene and with the series of the mono-, di-, tri-, and tetrachloroethylenes: the relative rates decreased drastically in the above order, ethylene being approximately 25 000 times more reactive than tetrachloroethylene.[6]

Very little information is available on the course and the nature of the products of the ozonolysis of halogenated double bonds. Substrates which have been studied under these aspects are 1,1-dichloroethylene,[7] tetrachloroethylene,[8] fluorinated C_2,[9,10] C_3, and C_4 olefins,[11] and 9,10-dibromo- as well as 9,10-dichloroanthracene.[12] However, these are probably not representative examples since they involve the ozonolysis of rather special types of haloolefins and in some cases also special (viz. gas phase) reaction conditions.

In an attempt at studying more representative substrate types, we have initiated work on the ozonolysis of 1,2-disubstituted dihaloethylenes and 1,2-disubstituted monohaloethylenes. The first substrate which we examined in this program was *trans*-2,3-dibromo-2-butene.[13] Its ozonolysis in nonparticipating solvents afforded the expected cleavage fragment acetyl bromide,[14] whereas products that would have been indicative of the formation of the corresponding zwitterion **1**, such as the monomeric ozonide **2** or the dimeric peroxide **3** could neither be isolated nor conclusively proven as intermediates.



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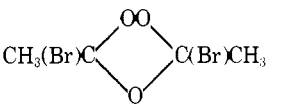

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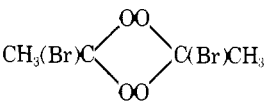

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In the present paper we report about the ozonolysis of *trans*-2,3-dichloro-2-butene (**4**) which gave considerably more insight into the course of the ozonolysis of halogenated double bonds and which led to the isolation of well-defined α-chloro peroxides, a class of compounds that is largely unexplored.[15]

Results

Ozonolyses of *trans*-2,3-dichloro-2-butene (**4**) were carried out in pentane, in chlorinated hydrocarbons (dichloromethane, 1,1,2,2-tetrachloroethane), in esters, and at the neat substrate at −30 or −78 °C. NMR analyses of the crude reaction mixtures showed that in each case the same products were formed, albeit in different amounts (Table I).

Workup of the reaction mixtures by various means (see Experimental Section) resulted in the isolation of acetyl chloride (**5**), 2,2,3,3-tetrachlorobutane (**10**), diacetyl peroxide (**13**), and the hitherto unknown α-chlorinated peroxides[15] **9** and **12** (Scheme I). In addition, acetic acid (**7**),