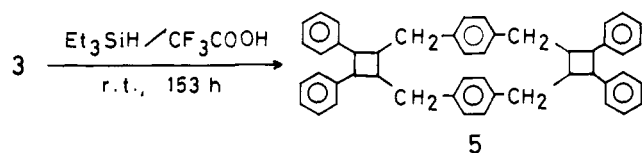


Scheme III



If we assume that the reaction probability of all the elementary processes is equal in the reaction of the crystal of **1**, the statistical yields of unreacted **1**, tricyclic dimer **3**, and oligomers **4**, by simulation, should be 1.8, 37.7, and 60.5% by weight, respectively. Further, if all the photoexcited species of **2** is assumed to be converted into **3**, these yields should become 6.9, 65.6, and 27.5%. It is, therefore, rather surprising that in an extreme case of the experiment the yield of **3** was more than 90% while the amount of unreacted **1** was less than a few percent. One of the plausible mechanisms which may be suggested to explain this result is that the first formation of **3** rigorously induced the successive formation of **3** to enhance the final yield of **3**. If such an induction mechanism played an appreciable role, the optically active dimer zone may be formed at least in a micro spot of surroundings of first molecule of **3**, as illustrated below.

The yield of tricyclic dimer from bis(3,4-dichlorostyryl) ketone¹³ has been reported to be 20%, which is less than the statistical value.

Reduction of Tricyclic Dimer 3. For the purpose of preparing other new types of tricyclic cyclophanes, **3** was reduced by reaction with triethylsilane to 21,22,23,24-tetraphenyl-2(3),12(13)-diethano[4.4]paracyclophane (**5**). Racemic **5**, as well as **3**, was successfully resolved into a pair of enantiomers by chiral affinity chromatography (DAICEL Chiralpak OT).

Neither the intramolecular CT complex nor a small molecule inclusion has been observed in any of the treatments of **3** and **5**. According to the CPK molecular model, the distances between the faces of two 1,4-phenylene rings in **3** and **5** are approximately 0.7 and 0.9 Å, respectively, which would seem not to be suitable either for making the intramolecular complex or for including a small molecule in the cavity either. The attempted single crystal preparation of **5** for the X-ray crystallographic analysis has been unsuccessful so far.

Acknowledgment. The authors are pleased to acknowledge Associate Prof. T. Hirano for his advice for the simulation work on the ¹H NMR spectrum. Financial assistance from Asahi Glass Foundation for Industrial Technology is gratefully acknowledged.

Registry No. **12**, 34838-64-7; **3**, 95462-20-7; **4** (*n* = 1), 95363-43-2; **4** (*n* = 2), 95363-44-3; **4** (*n* = 3), 95363-45-4; **4** (*n* = 4), 95363-46-5; **5**, 95363-47-6; 1,3-DCB, 55147-58-5; BCPM, 34838-75-0; DCS, 95363-41-0; 1,4-BPPB, 95363-42-1.

Kinetics of Ozonation. 3. Substituent Effects on the Rates of Reaction of Alkenes

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Abstract: We have reinvestigated structure–reactivity relationships in the ozonation of simple alkenes, measuring absolute rates of reaction by a stopped-flow technique. The polarity range of the substrates is wider than that of the earlier study, and some compounds have been included to further assess the roles of steric effects and hyperconjugation. The equation that best fits our data is $\log(k/k_0) = -0.83\sigma^* + 0.245E_s^\circ + 0.158(n-3)$, where σ^* is a measure of inductive substituent effects, E_s° is a steric parameter, and *n* is the number of allylic hydrogens. Additionally, we have measured absolute rates at several temperatures to determine activation parameters for the ozonation of these substrates. The energies of activation range from 2.2 kcal mol⁻¹ for vinyl acetate to 4.1 kcal mol⁻¹ for allyl cyanide. The preexponential terms range from $\log A/s = 6.1$ to 7.4.

Because of the utility of ozone in organic synthesis^{1,2} and because of the environmental hazard it poses,³ the reactions of ozone and organic and biological molecules have been the subject of frequent study. We have begun a program to bridge the gap between the chemistry of ozone in solution and its biological effects.^{4,5}

Structure–reactivity relationships are a powerful tool in organic chemistry,⁶⁻⁸ yet this technique has been infrequently applied to

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Table I. The Rates of Reaction of Alkenes with Ozone in CCl₄ at Various Temperatures^a

alkene	T, K	k, M ⁻¹ s ⁻¹	E _a , kcal mol ⁻¹ ^b	log A/s ^b	alkene	T, K	k, M ⁻¹ s ⁻¹	E _a , kcal mol ⁻¹ ^b	log A/s ^b			
allyl cyanide	257.7	2210	4.1	6.8	<i>tert</i> -butylene	252.9	12500	2.6	6.4			
	264.1	2800				262.8	15000					
	273.1	3440				272.9	18800					
	283.1	5010				282.8	21800					
	298.1	7110				292.8	25200					
	313.9	8890				298.1	27500					
allyl acetate	257.6	6000	3.5	6.8	3-methyl-1-pentene	273.1	31300	2.5	6.5			
	263.1	7600				283.1	37500					
	273.0	9300				298.1	43800					
	279.1	12500				313.1	57100					
	283.1	12000				vinyl acetate	253.4			15600	2.2	6.1
	288.1	13300					262.7			18700		
allyl ethyl ether	257.7	11700	3.8	7.25	<i>trans</i> -1,2-di- <i>tert</i> -butyl-ethylene	252.7	5600	3.1	6.4			
	263.0	13000				261.5	7000					
	273.0	16200				272.8	9000					
	283.1	21900				282.1	10400					
	293.1	27200				289.9	12500					
	allylbenzene ^d	252.6				29000	2.3			6.5	<i>cis</i> -4-methyl-2-pentene ^c	254.8
262.9		38000	262.6	96000								
272.9		44000	265.8	148000								
286.6		51500	271.5	155000								
298.1		60000	283.3	134000								
4,4-dimethyl-1-pentene ^c		252.9	27000	2.3	6.5	<i>trans</i> -4-methyl-2-pentene ^c		254.8	122000			2.7
	258.1	28500	263.3				141000					
	263.1	33500	265.8				133000					
	268.1	41000	271.5				191000					
	273.1	43300	280.8				185000					
	283.1	49000	283.3				205000					
	293.1	51000										
	298.1	53600										
	313.1	66400										

^aTemperatures are accurate to within ± 0.1 °C. The standard deviations of the rates are less than 5%. Unless otherwise stated, a 50-fold or greater excess of alkene was used to measure pseudo-first-order rates. ^bStandard deviations are less than 0.1 in all cases. ^cA 20-fold excess of substrate to ozone was used. ^dA 40-yield excess of substrate to ozone was used.

the study of ozone. One early report, however, indicates that the rate-determining step in the ozonation of alkenes is a nucleophilic process.⁹ This is surprising since ozone, being a powerful oxidant, should be an electron-accepting reagent, and several authors have provided data supporting the electrophilic nature of ozone.^{1,10-15}

The role of steric factors in determining the reactivity of alkenes toward ozone also is open to question. While some authors have suggested that steric factors have little or no effect on rates of ozonation,^{9-11,16} it is clear that the reactivity of highly hindered alkenes toward ozone is retarded and the course of the reaction is changed.¹⁷

We here report a reinvestigation of the work in which ozone was found to be a nucleophile.⁹ We have examined the reactions of a larger group of compounds, permitting a more detailed treatment of steric factors and hyperconjugation as well as polarity.

Experimental Section

Purification of Materials. Carbon tetrachloride (Mallinckrodt, analytical reagent or MC/B reagent) was pretreated with ozone as described in Part 1 of this series.⁴ Alkenes were of the highest commercially

available purity and were distilled prior to use. All of the substrates were purchased from Aldrich with the exception of *trans*-4-methyl-2-pentene (Pfaltz and Bauer), 4,4-dimethyl-1-pentene (Columbia), and allyl chloride (Eastman).

Absolute rate data were collected by stopped-flow spectroscopy as described in Part 1.⁴

The relative reactivities of several pairs of substrates toward ozone were also examined for a direct comparison to relative rate data in the literature.⁹ These determinations were performed on solutions of allylbenzene and allyl chloride, allyl bromide, or styrene in the solvent CCl₄ containing *tert*-butylbenzene (ca. 0.025 M) as an internal standard.¹⁸ The solutions were generally 0.2 M in total substrate, containing 1–2 mol of allylbenzene per mol of allyl halide or styrene. Ozonolysis of these samples was carried out by bubbling a stream of ozone in oxygen through the chilled (0 °C) solutions. Analyses were conducted on a Varian 3700 gas chromatograph equipped with a 30 m SE-30 capillary column, a flame ionization detector, and an electronic integrator, both before and after ozone treatment. The ratios of substrates to *tert*-butylbenzene were used to calculate the relative reactivities by eq 1, where *A* and *B* are the ratios of the two substrates to the internal standard, and *A*₀ and *B*₀ are these values at time zero. Portions of the solutions were bubbled with

$$k_{\text{rel}} = \log(A/A_0) / \log(B/B_0) \quad (1)$$

air under the same conditions, and GC analysis indicated that there was significant loss of the more volatile component, either allyl chloride or allyl bromide. Thus, the relative rate constants obtained in this way are only limiting values, with allylbenzene being relatively more reactive than indicated. In the solutions of styrene and allylbenzene, no loss due to evaporation was noted, but the relative rates obtained by eq 1 were still subject to variation, as discussed below.

(18) The rate constant for the reaction of *tert*-butylbenzene with ozone has been measured under conditions similar to these and was found to be 0.069 M⁻¹ s⁻¹. See: Nakagawa, T. W.; Andrews, L. J.; Keefer, R. M. *J. Am. Chem. Soc.* **1960**, *82*, 269–276.

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 (17) Reference 1, Chapter 11, and references therein.

Table II. Comparison of Our Data with Literature Values for the Rates of Reaction of Some Alkenes with Ozone in CCl₄

no.	substrate	k, M ⁻¹ s ⁻¹		substituent parameters		
		this work ^a	from ref 9 ^b	σ* ^c	E _s	E _s ^{c,e}
1	allyl cyanide	7100		1.30	-0.94 ^f	-1.25 ^f
2	allyl chloride	11700 ^g	22300 ^h	1.05	-0.24	-0.55
3	allyl bromide	14000 ^g	16100	1.00	-0.27	-0.58
4	allyl acetate	16000		0.76 ⁱ	j	j
5	allyl ethyl ether	3000	19300	0.52 ^k	-0.19 ^k	-0.50 ^k
6	allylbenzene	60000	12300	0.215	-0.38	-0.69
7	1-hexene	110000 ^g	120000 ⁱ	-0.13	-0.39	-0.70
8	neopentylethylene	54000		-0.165	-1.74	-2.05
9	tert-butylethylene	27500	44400	-0.30	-1.54	-2.46
10	sec-butylethylene	44000		-0.21	-1.13	-1.84

^a25 °C. ^bFrom ref 9; 0 °C, measured relative to styrene. ^cFrom ref 7, p 619. ^dFrom ref 7, p 598. ^eFrom ref 6 or derived from the equation $E_s^c = E_s + 0.306(n - 3)$. See ref 22. ^fSee ref 23 and 24. ^gFrom ref 4; 25 °C. ^hOther literature values include 5800 M⁻¹s⁻¹ (ref 10; 20 °C) and 11000 M⁻¹s⁻¹ (ref 11; 25 °C). ⁱFrom ref 27. ^jNo value is available. ^kThese values are for -CH₂-O-CH₃. ^lThis value is for 1-pentene. Values for 1-hexene include 140000 M⁻¹s⁻¹ (ref 10; 20 °C) and 76000 (ref 12; 25 °C).

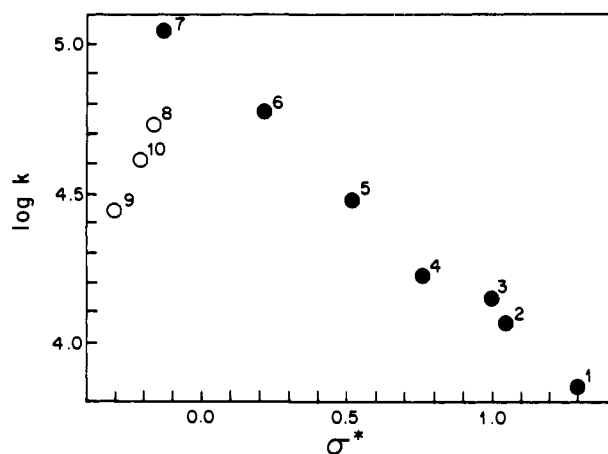


Figure 1. A plot of log *k* vs. σ* for the ozonation of monosubstituted alkenes. Open circles represent points omitted from consideration because of structural differences. See Table II for the key to the compound numbers.

Results

The absolute rates of ozonation measured in this study are presented in Table I, along with the calculated activation parameters. A comparison of some of these absolute rate data to previously published data is presented in Table II.⁹⁻¹² The literature values were measured either as absolute rates¹⁰⁻¹² or, for the data of Carles and Fliszar,⁹ relative to styrene for which these authors had previously¹³ measured an absolute rate.

Figure 1 shows a plot of log *k* vs. σ*, Taft's polar substituent constants (eq 2).¹⁹ To correlate rates of reaction for compounds in which steric factors may be important, eq 3 was utilized, where *E_s* is Taft's steric substituent constant and δ is the sensitivity of the reaction to steric effects.²⁰ Regression analyses were performed with the Statistical Analysis System.²¹ The substituent constants treated herein are included in Table II.

$$\log(k/k_0) = \sigma^* \rho^* \quad (2)$$

$$\log(k/k_0) = \delta E_s + \sigma^* \rho^* \quad (3)$$

Of particular interest are the differences between our data and those of Carles and Fliszar.⁹ To investigate the possibility that the observed differences were due to the different methodologies

Table III. Variation of Apparent Relative Reactivity toward Ozone of Styrene and Allylbenzene in CCl₄ with Total Concentration and with the Ratio of the Substrate Concentrations

no. of runs	total molarity	styrene/allylbenzene	
		ratio	<i>k_{rel}</i>
2	0.325	1:4	5.0 ± 0.1
5	0.20	1:1.3	20 ± 10
2	0.17	4.4 ± 0.2	4.4 ± 0.2
4	0.14	1:4	3.1 ± 0.6

used, we attempted to determine the relative rates of ozonation of allylbenzene vs. allyl chloride, allyl bromide, and styrene. Our attempts yielded erratic results. While allylbenzene always appeared to be more reactive than the allyl halides, the calculated ratios varied from 1:1 to 3:1 vs. allyl chloride and from 1.1:1 to 2.5:1 vs. allyl bromide. Control experiments (Experimental Section) indicated that the variation was due to evaporation of the more volatile substrate. While correction for this loss can be only approximate, it clearly shifts the relative reactivities in a direction consistent with our measured absolute rates.

Evaporation of substrate did not prove to be a problem in the allylbenzene-styrene system in that oxygen-bubbled controls were, within experimental error, identical in composition with the initial solutions. However, the relative reactivity of the two substrates still varied as the ratio of reactants was changed. While the apparent relative rate of reaction (using eq 1) was erratic, there was a general trend toward higher values of *k_{styrene}*/*k_{allylbenzene}* with higher total alkene concentrations and with lower initial styrene/allylbenzene ratios. Values of *k_{rel}* measured in this way are collected in Table III and vary from 3:1 to 19.7:1.

Discussion

As seen from the data presented in Table II, ozone is more reactive toward olefins that have double bonds with greater electron density. The electrophilicity of ozone toward these substrates may be quantitated in a plot of log *k* vs. σ*,¹⁹ as illustrated in Figure 1. Note that the substrates included in the plot are all monosubstituted alkenes thus minimizing differences due to resonance effects, hyperconjugation, and steric factors. The ρ* value calculated from these data at 25 °C is -0.83 ± 0.04 (*r*² = 0.987). Also, values of ρ* were calculated at 0 °C and at -15 °C from the rates of the same substrates, yielding ρ* = -0.92 at 0 °C and -0.93 at -15 °C. The trend, as expected, is toward slightly greater selectivity as the temperature is lowered.

Earlier, in a study of the relative reactivities of a similar series of compounds toward ozone, Carles and Fliszar reported that the rate-determining step was a nucleophilic process.⁹ Furthermore, these workers reported that there was a discontinuity in the plot between substrates with electron-releasing groups and those with electron-withdrawing groups but that steric factors had little effect on the rates of reaction. The monosubstituted alkenes studied by those authors that have electron-releasing substituents were 1-pentene, isopropyl ethylene, and *tert*-butylethylene.

In contrast, our data suggest that ozone is an electrophile, and any apparent discontinuity between electron-releasing and electron-withdrawing substituents may be at least qualitatively accounted for in terms of steric factors. Neopentylethylene, *tert*-butylethylene, and *sec*-butylethylene are less reactive than predicted from their σ* values (see Figure 1), as would be expected if the reaction is also retarded by steric hindrance.^{6-8,20} Employment of Taft's equation for the effects of polar and steric factors on rates of reaction (eq 3) does not yield a satisfactory straight line encompassing all of these data, but the line is greatly improved if *tert*-butylethylene and *sec*-butylethylene are omitted. With these omissions, the optimized values are the following: at 25 °C, δ = 0.18, ρ* = -0.84 ± .05 (*r*² = 0.992); at 0 °C, δ = 0.19, ρ* = -0.90 ± 0.09 (*r*² = 0.974); and at -15 °C, δ = 0.18, ρ* = -0.92 ± 0.09 (*r*² = 0.977). It should be noted that the values of ρ* are virtually identical with those obtained when the data are plotted in the form of eq 2 (Figure 1) in which all three of these relatively hindered alkenes are omitted from consideration. Also, note that δ is independent of temperature over this range.

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(20) Pavelich, W. A.; Taft, R. W., Jr. *J. Am. Chem. Soc.* **1957**, *79*, 4935-4940.

(21) SAS Institute, Inc. P.O. Box 10066, Raleigh, NC 27605.

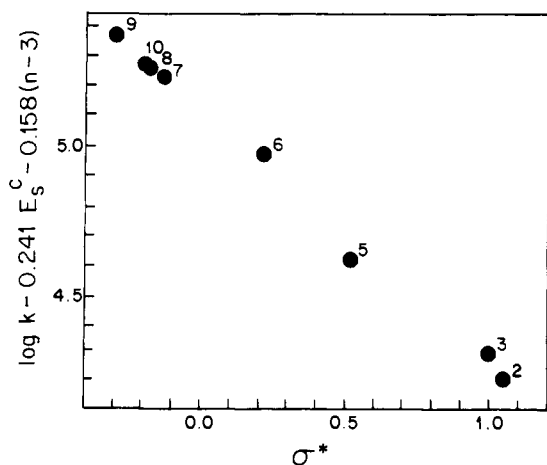


Figure 2. A plot of $\log k - \delta E_s^c - h(n-3)$ vs. σ^* for the ozonation of monosubstituted alkenes. See Table II for the key to the compound numbers.

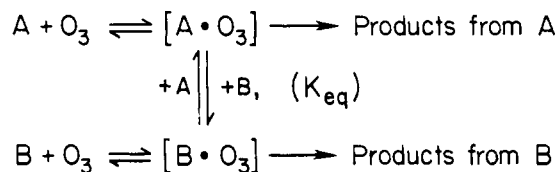
The inability to fit *tert*- or *sec*-butylethylene on the line of Figure 2 could be accounted for on the basis of stabilization of the transition state by hyperconjugation, a factor that has been investigated by several authors, most notably Hancock.^{6,22} Hancock's modification of the Taft equation (eq 3), in which hyperconjugation is considered separately, is shown below (eq 4).

$$\log(k/k_0) = \rho^* \sigma^* + \delta E_s^c + h(n-3) \quad (4)$$

Here E_s^c is the pure steric substituent constant, n is the number of α hydrogens, and h is the sensitivity of the reaction to stabilization by hyperconjugation. The parameter E_s^c is defined as $[E_s + 0.306(n-3)]$, which allows a correction for the contribution of hyperconjugation to Taft's E_s values.²² Such a treatment can be used to qualitatively demonstrate the dependence of the rate of reaction on polar and steric factors and hyperconjugation. A plot of the application of Hancock's treatment to our rate data is shown in Figure 2, in which the optimum values of δ and h are included. The optimum values are $\delta = 0.241$, $h = 0.158$, $\rho^* = -0.83 \pm 0.04$ ($r^2 = 0.991$). (Allyl acetate and allyl cyanide are omitted from this plot due to the lack of reliable literature values for their steric parameters.^{20,23}) While we have chosen to use Hancock's treatment of hyperconjugation,^{6,22} it should be noted that similar treatments of branching,²⁴ Newman's Δ_6 term,²⁵ or other modifications to steric parameters^{6-8,26} yield similar regressions. The source of the "steric" effect was not probed by us, since our data do not include enough compounds to attempt such a detailed assessment.

The apparent discrepancies between this work and that of Carles and Fliszar could be accounted for in several ways. Firstly, ozone is known to produce free radicals upon reaction with alkenes,^{36,5a-c} and these radicals would initiate the oxidation of the substrates; thus, the relative rates measured in competitive ozonations reflect both the cooxidation of the two olefins and direct ozonation by the Criegee mechanism. For example, the use of styrene, which is readily oxidized, as the reference compound could lead to a spurious disappearance of styrene due to autoxidation. (Note that although peroxy radicals reacts slowly with alkenes,^{27,28} alkoxyl radicals react more rapidly and generally also occur in autoxo-

Scheme I



idation; therefore, cooxidation probably could compete with ozonation.) However, if the same ratio of substrates had been used in all cases, only styrene should be inconsistent; the relative reactivities of nonconjugated alkenes, when compared to each other, should remain invariant. Also, if the least-reactive substrates were present in higher concentrations, a compression in the relative reactivities would result. The fact that neither of these phenomena are observed tends to imply that the oxidation of styrene is not the explanation.

A second possible explanation of the discrepancy is that the nonhomogeneous conditions involved in bubbling ozone into a solution cause differences in selectivity from those observed in homogeneous ozonation. Since ozonations are highly exothermic, localized heating at the gas-liquid interface and poor thermostatic control may result; this is less likely to be true if prepared solutions of ozone are used. Other authors have presented evidence that the rates of ozonation measured by bubbling techniques may vary as a function of flow rate and bubble size,²⁹ due to reaction at the gas-liquid interface or the rate-limiting diffusion of ozone into the solution.²⁹ If these explanations were true, however, a compression of the range of relative reactivities should result, as above. Thus, these explanations also probably are not correct.

A third possibility for the discrepancy also can be suggested, based on a proposal of Altwicker and Basila,^{29a} which is similar to the scheme proposed by Carles and Fliszar⁹ and others.^{12,16} A possible pathway including the reversible formation of an intermediate ozone-alkene complex is depicted in Scheme I, in which K_{eq} is the equilibrium constant for the exchange of ozone between the two substrate complexes: $A \cdot O_3 + B \rightleftharpoons A + B \cdot O_3$. Such a pathway could account for the variation in the observed rates in that, in competitive ozonations, the relative rates of disappearance of alkenes A and B would be dependent on K_{eq} . It should be noted that the largest single discrepancy between our work and that of Carles and Fliszar⁹ is the relative rate of reaction of allylbenzene. Allylbenzene is the only aromatic compound in the series of substrates examined, and aromatic compounds are known to strongly complex with ozone.⁵ⁱ (Styrene, the standard reactant, also is aromatic, but a change in its reactivity will not change the relative reactivities of the series.) Since allylbenzene complexes more strongly with ozone, its K_{eq} value will be different from the values for all the other substrates, whose K_{eq} values should be quite similar. Therefore, this argument would predict that the reactivity of allylbenzene might be anomalous, as is observed.

While we favor the last explanation, any of the possibilities described would suggest that the apparent k_{rel} measured in a bubbling experiment may vary as a function of the ratio of substrates, and possibly as a function of the total alkene concentration. In our relative reactivity experiments we do observe variation in k_{rel} , indicating that relative reactivity data collected from bubbling experiments may not be a true measure of relative rates of ozonation in homogeneous solution in all cases.

Although our data cast doubt on the general applicability of bubbling experiments in relative rate determinations, they do tend to support the hypothesis that an intermediate complex is formed from ozone and an alkene from which the decomposition to ultimate products is facilitated by electron-withdrawing groups. They also confirm that in homogeneous solution the step in which ozone is consumed is electrophilic, not nucleophilic, and is the rate-determining step in the reaction of ozone with a simple alkene.

(22) Hancock, C. K.; Meyers, E. A.; Yager, B. J. *J. Am. Chem. Soc.* **1961**, *83*, 4211-4213.

(23) Although there has been a value of E_s reported for CH_2CN , it was measured under different conditions than the other values (see ref 20). Additionally, the reported value of -0.94 seems too small, indicating that CH_2CN is similar in size to an isobutyl group. If this point is included in a plot of eq 4, $\rho^* = -0.71 \pm 0.06$, $\delta = 0.25$, and $r^2 = 0.965$.

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Registry No. CH₂=CHCH₂CN, 109-75-1; CH₂=CHCH₂OAc, 591-87-7; CH₂=CHCH₂OEt, 557-31-3; CH₂=CHCH₂Ph, 300-57-2; (C-

H₃)₃CCH₂CH=CH₂, 762-62-9; (CH₃)₃CCH=CH₂, 558-37-2; CH₃C-H₂CH(CH₃)CH=CH₂, 760-20-3; CH₂=CHOAc, 108-05-4; *trans*-(CH₃)₃CCH=CHC(CH₃)₃, 692-48-8; *cis*-(CH₃)₂CHCH=CHCH₃, 691-38-3; *trans*-(CH₃)₂CHCH=CHCH₃, 674-76-0; CH₂=CHCH₂Cl, 107-05-1; CH₂=CHCH₂Br, 106-95-6; CH₂=CH(CH₂)₃CH₃, 592-41-6; PhCH=CH₂, 100-42-5.

Communications to the Editor

Stereoselection in the Michael Addition Reaction. 1. The Mukaiyama-Michael Reaction¹

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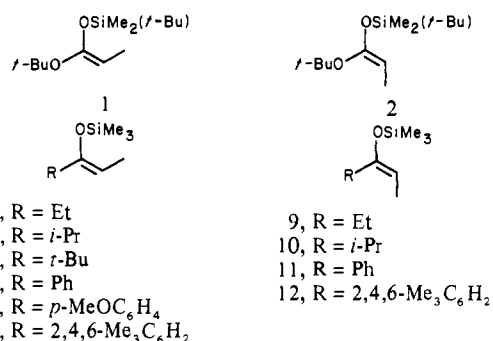
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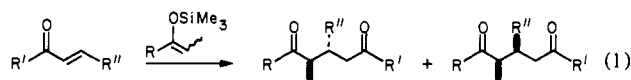
In the last decade, there has been a surge of interest in the stereoselective synthesis of acyclic and other conformationally flexible molecules.² As a part of this activity, considerable attention has been focused on stereoselective carbon-carbon bond-forming processes, particularly the aldol addition reaction³ and the related reactions of crotylorganometallic reagents with aldehydes.⁴ In contrast, much less is known about the stereochemistry of the Michael addition reaction, which may be considered to be a "vinylogous aldol addition reaction".⁵ In this paper and others to follow, we will report initial results of a thorough investigation of this question.

In 1974-1976, Mukaiyama and co-workers introduced a version of the Michael addition reaction wherein an enolsilane reacts with an enone under conditions of Lewis acid catalysis.⁵ Electronically, the Mukaiyama-Michael reaction is an acid-catalyzed 1,4-addition process and provides a mechanistic complement for the more well-studied base-catalyzed analogue. In the early work on the reaction⁵ the focus was on the reaction itself, and stereochemistry was not investigated, although several examples that are capable of simple diastereoselection were included in the study. The current publication deals solely with the stereochemistry of the Mukaiyama-Michael reaction. Although the results at this time are preliminary, we have discovered several general structure-stereoselectivity relationships that should be of widespread utility in synthesis. Furthermore, we are also able to put forth a coherent transition-state hypothesis that explains the stereoselectivity observed.

To investigate the stereoselectivity of the Mukaiyama-Michael addition, we have utilized the pair of stereoisomeric silyl ketene acetals **1** and **2** and enolsilanes. In general, reactions were carried out by premixing the enone and an appropriate Lewis acid catalyst in methylene chloride at -78 °C, adding the enolsilane or ketene acetal at -78 °C, and working up by the addition of aqueous



potassium carbonate after 30-120 min. In most cases, the isolated products were found to be stereoisomeric mixtures of anti and syn isomers (eq 1).⁶ Isomeric ratios were determined by ¹H NMR,



¹³C NMR, analytical HPLC, and capillary GLC. Stereostructures were assigned on the basis of X-ray crystallography, conversion to materials of known structure, and ¹³C NMR chemical shift analogy; details are given in the supplemental material. Data are summarized in Table I.

As shown in the table, enol silanes derived from ketones show a general tendency for anti addition, regardless of the stereostructure of the enolsilane (cf. inter alia entries 8-10 and 31, 14 and 34, 23 and 40, and 17 and 37). With the enolsilanes derived from aliphatic ketones, the observed anti selectivity ranges from modest (entry 15, 1.5:1) to good (entry 17, 10:1). The *Z* enol silanes derived from propiophenone and related aromatic ketones (6-8) show excellent anti selectivity (from a low of 10:1 to a maximum of >20:1). The *E* enolsilanes of aromatic ketones show lower anti selectivity (entries 40 and 41).

In striking contrast to the behavior of the foregoing enolsilanes, the silyl ketene acetals **1** and **2** show high syn selectivity with acyclic *tert*-butyl enones (entries 1-3 and 6). The latter compounds exhibit only low stereoselectivity with cyclohexenone (entries 5 and 7) and with 3-penten-2-one (entry 4). An interesting effect is seen in the reactions of the ketene acetals. If the ketene acetal is added slowly (syringe pump) to a -78 °C solution of the complex of the enone and TiCl₄, the sole product is the keto *tert*-butyldimethylsilyl ester. However, if the ketene acetal is added rapidly, the product is a mixture of *tert*-butyl and *tert*-butyldimethylsilyl esters.

The data may be explained in terms of the mechanism put forth in Scheme I. In this proposal, the initial adduct A can undergo reversion to reactants (*k*₋₁) or ionization to B. Desilylation of the latter intermediate to give C is effectively irreversible. We propose that, with ketene acetals, the initial equilibrium lies far to the right, because the oxonium ion is delocalized. In this case, desilylation of the (trialkylsilyl)oxonium ion is fast, relative to retro-Michael

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