Alkene Reactivity. Influence of the Entering Electrophile and Limitations of Linear Free Energy Relationships in Electrophilic Additions

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Separation of polar and steric effects of alkyl groups in electrophilic additions of bromine and arenesulfenyl chloride reveals interactions in the rate-determining step. The sensitivity to polar effects, evaluated from the kinetic methyl effect, is smaller in sulfenyl chloride addition ($\rho^* = -1.0$ in TCE) than in bromination ($\rho^* = -3.1$ in methanol). On the other hand, the magnitude of the steric effects differs markedly in these reactions: depending on the position of the substituents at the double bond, one or the other of the two electrophiles is the bulkier. Entering electrophile–substituent interactions which depend on the electrophile geometry are shown to control the steric contribution of the alkyl groups. Due to these interactions, free energy relationships in addition reactions cannot be linear over a wide range of substituents, even when a specific addition is taken as a reference rather than empirical parameters such as σ^* and E_s.

From kinetic and stereochemical data it is now established[1] that the electrophilic additions of bromine[2] and arenesulfenyl chloride[3] to alkenes proceed through bridged rate-determining transition states and intermediates. Comparison of the kinetic effects of alkyl groups in these two reactions[4] is believed to support this view. The results of this comparison were considered sufficiently good[6] for the "use of arenesulfenyl chloride addition as a mechanistic model of alkene bromination" to be proposed.

In fact, there are several reasons for rejecting this proposition. First, the log k/log k correlations between the reactivities of alkenes with bromine and sulfenyl chloride are poor, even when the most deviant compounds[7] are eliminated. Second, the interactions between the entering electrophile and the substituents are known to partially control the alkene reactivity.[8] Now, the steric requirements of bromine and arenesulfenyl chloride should differ markedly since their geometries are different. It is, therefore, a priori unlikely that free energy relationships between the two reactions will be linear, unless these interactions are small compared to polar effects.

Table I. Bromination and Sulfenylation Rate Constants ($M^{-1}\ s^{-1}$) at 25 °C of Methyl- and *tert*-Butylethylenes

	$k_{TCE}^{ArSCl\,a}$	$k_{MeOH}^{Br_2\,c}$
1, $CH_2{=}CH_2$	65	4.65^{d}
2, $MeCH{=}CH_2$	205	4.03×10^{2} ^{e}
3, $Me_2C{=}CH_2$	550	3.72×10^{4} ^{e}
4, *cis*-$MeCH{=}CHMe$	1340	2.38×10^{4} ^{e}
5, *trans*-$MeCH{=}CHMe$	434	1.30×10^{4} ^{e}
6, $Me_2C{=}CHMe$	3030	1.29×10^{6} ^{e}
7, $Me_2C{=}CMe_2$	7760	1.24×10^{7} ^{f}
8, *t*-$BuCH{=}CH_2$	95	95.7^{f}
9, *t*-$BuMeC{=}CH_2$	147	6.58×10^{3} ^{f}
10, *cis*-*t*-$BuCH{=}CHMe$	1209	1.11×10^{4} ^{f}
11, *trans*-*t*-$BuCH{=}CHMe$	162	1.72×10^{3} ^{f}
12, *t*-$BuCH{=}CMe_2$	1462	1.67×10^{6} ^{g}
13, *t*-$BuMeC{=}CMe_2$		1.70×10^{6} ^{h}
14, *t*-$Bu_2C{=}CH_2$	3.17×10^{-2}	172^{h}
15, *cis*-*t*-$BuCH{=}CH$-*t*-Bu	846^{b}	1.50×10^{3} ^{f}
16, *trans*-*t*-$BuCH{=}CH$-*t*-Bu	5.36×10^{-3} ^{b}	110^{h}
17, *t*-$Bu_2C{=}CH$-*t*-Bu	8.16×10^{-3} ^{b}	

[a] Reference 4 unless otherwise specified. [b] C. L. Dean, D. G. Garratt, T. T. Tidwell, and G. H. Schmid, *J. Am. Chem. Soc.*, **96**, 4958 (1974). [c] Rate constants for free bromine addition only (see Experimental Section). [d] E. Bienvenue-Goetz and J. E. Dubois, *J. Org. Chem.*, **40**, 221 (1975). [e] Reference 2b. [f] M. Marie de Ficquelmont, Doctoral Thesis, CNRS No. A08355, Paris, 1973. [g] Reference 5. [h] This work.

Using the Taft–Ingold equation,[9] we have separated the polar and steric contributions of alkyl groups[10] by comparing the kinetic effects of methyl and *tert*-butyl substituents (Table I). In this way, we are able to estimate the magnitude of electrophile–substituent interactions and demonstrate differences in the behavior of bromine and arenesulfenyl chloride.

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[1] F. Freeman, *Chem. Rev.*, **75**, 441 (1975); G. H. Schmid and D. G. Garratt in "Double Bonded Functional Groups", Supplement, A. S. Patai, Ed., Wiley, New York, N.Y., 1977, p 726.

[2] (a) R. C. Fahey, *Top. Stereochem.*, **3**, 237 (1968); (b) E. Bienvenue-Göetz and J. E. Dubois, *Tetrahedron*, **34**, 2021 (1978).

[3] G. H. Schmid, C. L. Dean, and D. G. Garratt, *Can. J. Chem.*, **54**, 1253 (1976).

[4] G. H. Schmid and T. T. Tidwell, *J. Org. Chem.*, **43**, 460 (1978). In this article, the data designated as bromination rate constants are the experimental rate constants related to both free bromine and tribromide ion additions. For encumbered olefins, the parallelism generally observed[5] between k_{exptl} and k_{Br_2} no longer applies. Thus, the use of k_{exptl} instead of k_{Br_2} is incorrect. Moreover, two of the rate constants used by the authors are wrong; they are those of α-methylstyrene and cyclohexene, two widely deviating points in the log k_{Br_2}/log k_{H^+} plot. The correct values put these compounds on the line. For α-methylstyrene bromination in methanol, $k_{exptl} = 6.77 \times 10^3\ M^{-1}\ s^{-1}$ at 0.2 M NaBr and $k_{Br_2} = 1.62 \times 10^5\ M^{-1}\ s^{-1}$ (E. Bienvenue-Göetz and J. E. Dubois, *J. Org. Chem.*, **40**, 221 (1975). For cyclohexene, $k_{exptl} = 7.90 \times 10^2\ M^{-1}\ s^{-1}$ at 0.2 M NaBr and $k_{Br_2} = 1.14 \times 10^4\ M^{-1}\ s^{-1}$ (J. E. Dubois and P. Fresnet, *Tetrahedron Lett.*, 2195 (1974).

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[6] Even with the corrected values, the correlation between arenesulfenyl chloride addition and bromination for all the 35 olefins considered by Schmid and Tidwell is very poor (correlation coefficient $R = 0.670$). Elimination of the three worst points improves the correlation significantly ($R = 0.834$). Additional improvement is obtained by elimination of three cis-disubstituted olefins ($R = 0.910$). However, this latter correlation is not satisfactory since the average deviation is 0.45 log units.

[7] The reasoning of Schmid and Tidwell[4] is based on the comparison of alkyl group effects on bromination, sulfenyl chloride addition, and hydration rates; sulfenylation and hydration are taken as models for additions via cyclic and open transition states, respectively. Schmid and Tidwell estimate that for alkenes, the correlation between the data for hydration and bromination (H/B) is bad whereas that between sulfenyl chloride addition and bromination (S/B) would be good or, at least, better than H/B. In fact, correlations made with the corrected data do not support this view: the H/B correlation of 16 data (3 data omitted) has $R = 0.924$ whereas for the S/B correlation $R = 0.910$ in the optimized calculation.[6] For additions to ring-substituted styrenes, analogous H/B and S/B correlations are equally good;[13] R values are 0.991 and 0.984, respectively. Information on transition-state structure is deduced from the slopes but not from the correlation coefficients. For alkenes, the values of the slopes are too uncertain to give reliable evidence on these structures.

[8] J. E. Dubois and G. Mouvier, *Tetrahedron Lett.*, 1629 (1965); W. K. Chang and T. T. Tidwell, *J. Org. Chem.*, **43**, 1904 (1978).

[9] J. Shorter in "Advances in Linear Free Energy Relationships", N. B. Chapman and J. Shorter, Eds., Plenum Press, London, 1972, p 71.

[10] There could be, moreover, a hyperconjugative effect. This effect is not important in bromination[2b] nor in sulfenyl chloride addition since eq 1 is linear. The same situation does not necessarily apply in hydration, as is shown by the high degree of sensitivity to the number of substituents.[4]

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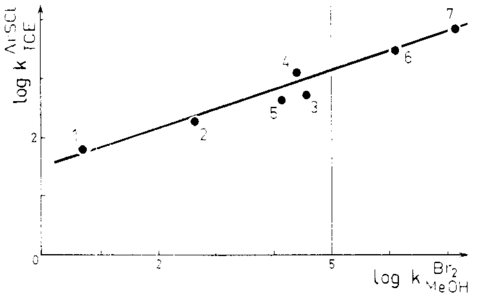


Figure 1. Comparison of the polar effect in bromination and in sulfenyl chloride addition to methylethylenes.

Assuming that the steric effect of a methyl group is negligible in sulfenyl chloride addition as in bromination,[2] the *polar effects* can be compared in methyl-substituted ethylenes. Methyl group effects on both reactions are well correlated (Figure 1):

$$(\log k_{\mathrm{TCE}}^{\mathrm{ArSCl}})_{\mathrm{pol}} = 0.32\ (\log k_{\mathrm{MeOH}}^{\mathrm{Br_2}})_{\mathrm{pol}} + 1.49 \qquad (1)$$

correlation coefficient $R = 0.973$

standard error on the slope $s = 0.03$

The polar effect on alkene bromination has been determined[11] from a variety of substituents with constant steric effect (eq 2). Combining eq 1 and 2, we obtain a

$$(\log k_{\mathrm{MeOH}}^{\mathrm{Br_2}})_{\mathrm{pol}} = -3.10\Sigma\sigma^* + 6.98 \qquad (2)$$

reasonable estimate[12] of the polar effect on arenesulfenyl chloride addition in TCE:

$$(\log k_{\mathrm{TCE}}^{\mathrm{ArSCl}})_{\mathrm{pol}} = -1.0\Sigma\sigma^* + 3.72 \qquad (3)$$

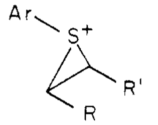
The polar effect is much smaller in sulfenyl chloride addition than in bromination but in the same direction.

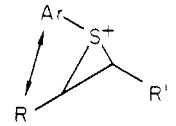
The *tert*-butyl group is the best probe for steric effects but an equally straightforward relationship cannot be obtained. A correlation like that of the effects of zero to four methyl groups on the two reactions is impossible for *tert*-butyl groups since in bromination the accumulation of three *tert*-butyl groups causes a mechanistic change.[15] Further, Taft's E_s values[9,16] cannot be used in a general treatment of alkene reactivity since they have been shown to be applicable[17] only to limited reaction series involving restricted changes in double bond crowding. On the other hand, it is possible to analyze qualitatively the electrophile–substituent interactions which are at the origin of the steric contribution of the alkyl groups to the reactivity of alkenes.[17] The steric contributions of the substituents (Table II) can be obtained by subtracting the polar contribution calculated by eq 2 and 3 from the experimental reactivity (Table I). This approach should be more precise than the usual method which consists of comparing the raw $k_{\mathrm{cis}}/k_{\mathrm{trans}}$ data for various reactions.[8] According to Table II, two cis *tert*-butyl substituents hardly affect the approach of ArSCl whereas they significantly hinder that of bromine. In contrast, two trans or *gem tert*-butyl groups interact much more strongly with ArSCl than with Br_2. Thus, depending on the position of the substituents either of the electrophiles behaves as the bulkiest. These results can be understood by considering the different spatial requirements of the two electrophiles. The bromine atom (van der Waals radius $r = 1.95$ Å) is larger than the sulfur atom ($r = 1.85$ Å); but in sulfenyl chloride addition, the groups on sulfur give rise to interactions which do not exist in the case of bromination.[18] It is known that in the episulfonium ion (thiiranium ion) the valence electrons in the S atom are p electrons, so that the S–Ar bond is perpendicular to the three-membered ring.[19] Interactions between Ar and the alkyl substituents are small in cis olefins because they can be placed on opposite sides of the ring plane. However, such additional interactions are unavoidable in the case of trans- and *gem*-disubstituted olefins. The simultaneous or separate occurence of two types of interaction qualitatively explains the trend observed in Table II.

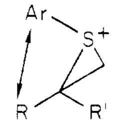
Table II. Steric Contribution[a] of the Substituents to the Reactivity of *tert*-Butylalkenes

	tert-butylmethylethylenes		di-*tert*-butylethylenes	
	bromination	sulfenylation	bromination	sulfenylation
gem	−1.0	−0.9	−3.6	−5.0
cis	−0.8	0	−2.6	−0.5
trans	−1.6	−0.8	−3.7	−5.7
log ($k_{\mathrm{cis}}/k_{\mathrm{trans}}$)[b]	0.81	0.87	1.13	5.20

[a] This value is calculated by subtracting the polar contribution $\rho\Sigma\sigma^* + \log k_0$ obtained by eq 2 or 3 from the global reactivity, log k, of the olefin considered. [b] This value is generally used as an estimate of the steric effects on addition rates.[8]







Although the available data do not allow a more detailed analysis, our results show clearly that these two addition reactions respond differently to steric constraints. This is probably the most important reason for the lack of correlation between the global effects (polar plus steric) of alkyl groups in bromination and arenesulfenyl chloride addition. Moreover, it becomes obvious that the role of the entering electrophile–substituent interactions is important and cannot be neglected in the analysis of electrophilic additions. The scope of conventional free energy relationships, wherein substituent effects are assumed to be additive, is, therefore, limited in this area. Other approaches to alkene reactivity which take into account molecular topology are being investigated.[20]

Experimental Section

Bromination Kinetics. Three kinetic methods already described are used to measure the experimental rate constants:

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[11] J. E. Dubois and E. Bienvenue-Göetz, *Bull. Soc. Chim. Fr.*, 2094 (1968).

[12] Ring substituent effects on sulfenyl chloride addition to styrene[13] are much smaller than those on bromination.[14]

[13] K. Izawa, T. Okuyawa, and T. Fueno, *Bull. Chem. Soc. Jpn.*, **47**, 1480 (1974); G. H. Schmid and V. J. Nowlan, *Can. J. Chem.*, **54**, 695 (1976).

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[16] J. E. Dubois, J. A. MacPhee, and A. Panaye, *Tetrahedron Lett.*, 4099 (1978).

[17] D. Grosjean, G. Mouvier, and J. E. Dubois, *J. Org. Chem.*, **41**, 3869, 3872 (1976).

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[19] R. D. Bach and H. F. Heinneke, *J. Am. Chem. Soc.*, **92**, 5589 (1970); Y. Kikuzono, T. Yamabe, S. Nagata, H. Kato, and K. Fukui, *Tetrahedron*, **30**, 2197 (1974).

[20] J. E. Dubois, A. Massat, and P. Guillaume. *J. Mol. Struct.*, **4**, 385, 403 (1969).

couloamperometry[21] for constants higher than 5×10^3 M^{-1} s^{-1} and potentiometry[22] and UV spectroscopy[23] for the smaller ones. In all these methods, an excess of bromide ions is necessary to fix equilibrium 4. The experimental rate constant, k_{exptl}, combines

$$Br_2 + Br^- \rightleftarrows Br_3^- \tag{4}$$

the two elementary rate constants related to the two discrete processes:[24] addition of free bromine, k_{Br_2}, and that of the electrophilic tribromide ion, $k_{Br_3^-}$.

k_{Br_2} Determination. Relationship 5[24] relates the rate constants

$$k_{\mathrm{exptl}}(1 + K[Br^-]) = k_{Br_2} + Kk_{Br_3^-}[Br^-] \tag{5}$$

k_{exptl}, k_{Br_2}, and $k_{Br_3^-}$. Therefore, we measure k_{exptl} at several (three or four) bromide ion concentrations. According to eq 5, the plot of k_{exptl} $(1 + K[Br^-])$ against $[Br^-]$ gives a straight line whose intercept is k_{Br_2}.

Registry No. 1, 74-85-1; **2**, 115-07-1; **3**, 115-11-7; **4**, 590-18-1; **5**, 624-64-6; **6**, 513-35-9; **7**, 563-79-1; **8**, 558-37-2; **9**, 594-56-9; **10**, 762-63-0; **11**, 690-08-4; **12**, 107-40-4; **13**, 30436-14-7; **14**, 5857-68-1; **15**, 692-47-7; **16**, 692-48-8; **17**, 28923-90-2.

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[21] J. E. Dubois, P. Alcais, and G. Barbier, *J. Electroanal. Chem.*, **8**, 359 (1964).

[22] A. F. Hegarty, J. S. Lomas, W. V. Wright, E. D. Bergman, and J. E. Dubois, *J. Org. Chem.*, **37**, 2222 (1972).

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Stereochemistry of the Reaction of Lithium Aluminum Hydride and of Methyllithium with Methyl-Substituted Cyclopentanones, Cyclohexanones, and Norbornanones. Evidence for a Linear Combination of Steric Strain and Product Stability Control in the Stereochemical Course of the Addition Reactions

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Methyl-substituted cyclopentanones, cyclohexanones, and norbornanones were reacted with methyllithium in ether and with lithium aluminum hydride in tetrahydrofuran at 0 °C. The stereochemical course of these reactions is reported and analyzed. The stereochemistry is best explained by a linear combination of both steric strain and product stability controls, $\Delta(\Delta G^{\ddagger}) = \Delta\sigma + \Delta\pi$. While diastereomeric secondary alcohols show significant differences in thermodynamic stability (ΔG°_{H}), tertiary diastereomeric 1-methylcycloalkyl alcohols show little difference in stability. Hence, the stereochemical course of the reaction of methyllithium with cyclic ketones is little affected by the product stability and $\Delta\pi = 0$. In the case of lithium aluminum hydride reduction, however, the stereochemistry is dictated *simultaneously* and *linearly* by both steric strain and product stability controls. It was found that if product stability control can be cancelled, both methyllithium and lithium aluminum hydride have about equal steric demand in their transition state complexes. Accordingly, an empirical equation, $\Delta(\Delta G^{\ddagger})_{H} = \Delta(\Delta G^{\ddagger})_{Me} + 1.4(\Delta G^{\circ})_{H}$, was obtained. Here, $\Delta(\Delta G^{\ddagger})_{H}$ and $\Delta(\Delta G^{\ddagger})_{Me}$, respectively, are the transition state energy differences leading to two diastereomers in the reactions of ketone with lithium aluminum hydride and with methyllithium. The equation provides a qualitative as well as a quantitative treatment of the stereochemical course of the reaction of lithium aluminum hydride with cyclic ketones.

In their recent publications, Eliel[1] and Ashby[2] have presented a general explanation for the observed stereochemistry of the reaction products obtained from cyclic ketones with lithium aluminum hydride or with alkylmetal. Earlier, Cherest and Felkin[3] attributed the observed stereochemistry to the torsional effect of the neighboring C–H or C–R bond during the alcohol formation from the corresponding ketones. Recently, Wipke and Gund[4] have provided a new concept and an empirical equation to incorporate the effect of steric congestion and torsional contribution on the stereoselectivity of the reaction. All these proposals tend to enhance the importance of steric approach[5a] or steric strain[5b] control on the stereochemistry of the hydride reduction of the simple cyclic ketone at the expense of product development[5a] or product stability control.[5b]

In simple cyclic ketones such as 4-*tert*-butylcyclohexanone or 2-methylcyclopentanone, hydride reduction of the ketone produces preferentially the more stable trans alcohol whose formation implies the approach of a hydride (or C–H bond formation) from the more hindered axial side of the ring. This mechanistic implication has been a point of argument among the researchers in this field because the percentage of more stable alcohol formed is higher than the amount allowed by thermodynamic equilibrium.

After careful analysis of the stereochemistry of the reaction products of 12 cyclic ketones with methyllithium and with lithium aluminum hydride, we have concluded that the stereochemistry is controlled *simultaneously, if not in equal proportion, by product stability and steric strain in the transition state.* We, therefore, propose a

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[2] E. C. Ashby and L. A. Laemmle, *Chem. Rev.*, **75**, 521 (1975).

[3] (a) M. Cherest, H. Felkin, and N. Prudent, *Tetrahedron Lett.*, 2199 (1968); (b) M. Cherest and H. Felkin, *ibid.*, 2205 (1968).

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