Kinetics of the Methoxymercuration of Substituted α-Methylstyrenes

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Kinetic studies on the methoxymercuration of a series of meta- and para-substituted α-methylstyrenes have been carried out. When compared to the methoxymercuration of a series of similarly substituted styrenes, the substitution of a methyl group in the α-position of a styrene had a constant rate-enhancing effect on the methoxymercuration reactions and decreased the values of $\Delta G^{\ddagger}$ by approximately 0.47 kcal/mol. The values of ρ and ρ^{+} obtained from the Hammett plots using σ and σ^{+} and the value of the r parameter needed to bring the point for the *p*-methoxy derivative onto the correlation line of the plot using the Yukawa−Tsuno equation were in excellent agreement with the corresponding data for the substituted styrenes. As was the case for the styrenes, these reactions exhibited overall second-order kinetics and formed only the Markovnikov products, and the values of $\Delta G^{\ddagger}$ were largely influenced by the values of $\Delta S^{\ddagger}$. However, the variations in $\Delta G^{\ddagger}$ and hence in the rates of the reactions were due to the variations in $\Delta H^{\ddagger}$. These results suggest that the substitution of a methyl group in the α-position of a styrene has a constant stabilizing effect on the formation of the transition state in these reactions and that, in a moderately polar solvent, the solvent plays a more important role than the structure of the alkene in determining the nature of the intermediate formed during a methoxymercuration reaction.

Introduction

In a continuation of our investigation[1−5] into the relative importance of the factors—namely, the structure of the alkene, the electronic nature of the electrophilic atom, and the polarity of the solvent—that determine the structure of the intermediate cation formed in the rate-determining step of an electrophilic addition reaction, we have carried out kinetic studies on the methoxymercuration of a series of para- and meta-substituted α-methylstyrenes. A methyl group is an electron-donating substituent. Therefore, the substitution of a methyl group in the α-position of a styrene is expected to (a) increase the reaction rate and (b) decrease the need for stabilization of the developing positive charge by factors such as resonance involving the aryl system, solvation, and/or bridging by the electrophilic atom.

By comparing the rates and activation parameters of the reaction involving the methoxymercuration of substituted α-methylstyrenes with those obtained during the methoxymercuration of substituted styrenes[2] and by comparing the ρ and ρ^{+} values obtained from Hammett plots using σ and σ^{+}, respectively, from this study with those for the substituted styrenes, we hoped to be able to determine the importance of the structure of the alkene in determining the nature of the intermediate formed during the methoxymercuration reaction. If the structure of the alkene is more important than the polarity of the solvent in determining the formation of the intermediate in a moderately polar solvent, then we would expect that a substitution of a methyl group, in the α-position of the styrenes, to have a stabilizing effect on the developing positive charge during the methoxymercuration reaction. We would expect this to result in the formation of a more open cation than that found for the corresponding styrenes. If, however, the solvent effects are dominant, then we would expect the intermediate formed during the methoxymercuration of the substituted α-methylstyrenes to be the same as, or very similar to, that found for the methoxymercuration of the substituted styrenes.

As the results that we report here will show, the structure of the intermediate cation formed in the rate-determining step of this reaction is that of an unsymmetric bridged cation, of a structure the same as, or very similar to, that formed during the methoxymercuration of the substituted styrenes. Thus, in a moderately polar solvent, the solvent plays a more important role than the structure of the alkene in determining the structure of the intermediate cation formed in reactions of this type.

Results[6] and Discussions

Each of the α-methylstyrenes **3a**−**l** has an intense absorption band, which obeys Beer's law, in the 280−330 nm region of the UV spectrum. Thus we measured the rates of the methoxymercuration reactions by monitoring the decrease in the absorbances of the α-methylstyrenes. The measurements were carried out under pseudo-first-order conditions with the $Hg(OAc)_2$ being

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[†] Florida A&M University.

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(1) Lewis, A.; Azoro, J. *Tetrahedron Lett.* **1979**, *38*, 3627.

(2) Lewis, A.; Azoro, J. *J. Org. Chem.* **1981**, *46*, 1764.

(3) Lewis, A. *J. Org. Chem.* **1984**, *49*, 4682.

(4) Lewis, A. *J. Org. Chem.* **1987**, *52*, 3099.

(5) Lewis, A.; Carty, A. *J. Org. Chem.* **1987**, *52*, 1839.

(6) All of the results reported herein were taken from a thesis submitted to the Graduate School of Arts and Sciences, Howard University, Washington, DC, by Ian S. Hendricks.

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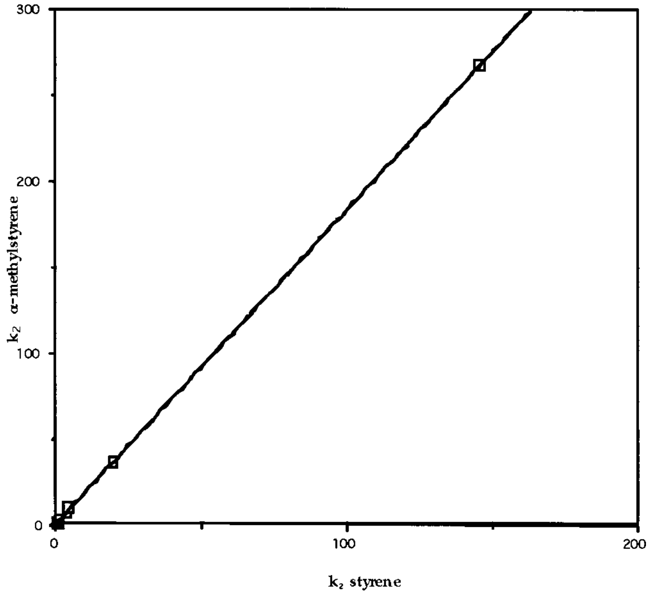

Figure 1. Plot of k_2 of the substituted α-methylstyrenes vs k_2 of the corresponding substituted styrene.

present in at least a 10-fold molar excess over the α-methylstyrenes.

$XC_6H_4CH(CH_3){=}CH_2$

3

a. X = p-MeO
b. X = m-MeO
c. X = p-Me
d. X = m-Me
e. X = H
f. X = p-F
g. X = m-F
h. X = p-Cl
i. X = m-Cl
j. X = p- Br
k. X = p-CN
l. X = p-NO$_2$

These reactions obey the rate law given in eq 1 and

$$-d[ArC(CH_3){=}CH_2]/dt = k_2[ArC(CH_3){=}CH_2][Hg(OAc)_2] \quad (1)$$

resulted in the formation of only the Markovnikov addition product. The order in Hg(OAc)$_2$ was determined by measuring k_{obs} for **3g**, **3i**, and **3l** at 25 °C as a function of the Hg(OAc)$_2$ concentration. Plots of log k_{obs} vs log [Hg(OAc)$_2$]$_0$ gave lines with slopes of 1.06 ± 0.04, 1.16 ± 0.05, and 1.07 ± 0.01, respectively. The second-order rate constants, k_2, were determined by dividing k_{obs} by the initial Hg(OAc)$_2$ concentration. Plots (Figures 1 and 2) of k_2 (substituted α-methylstyrene) vs k_2 (substituted styrene) and log k_2 (substituted α-methylstyrene) vs log k_2 (substituted styrene), at 25 °C, are linear with slopes of 1.84 ± 0.01 and 0.95 ± 0.01, respectively, and correlation coefficients ≥ 0.998. These plots show that the substitution of a methyl group in the α-position of a styrene increases the rates of the reactions for all members of the series by the same factor (approximately 2). This increase in the rates is consistent with a methyl group in the α-position of a styrene stabilizing the developing positive charge on the benzylic carbon. The values for k_2 and the relative rates of reaction for both the styrenes and α-methylstyrenes are summarized in Table 1.

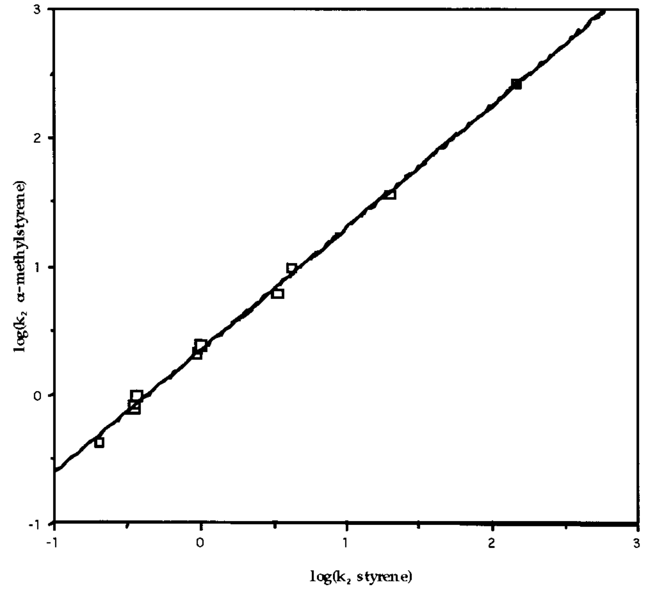

Figure 2. Plot of log k_2 (substituted α-methylstyrenes) vs log k_2 (corresponding substituted styrene).

Table 1. Second-Order Rates of Reaction and Relative Rates of Reaction for the Methoxymercuration of Substituted α-Methylstyrenes and Styrenes in Anhydrous Methanol at 25 °C

	α-methylstyrene		styrene	
X	av $k_2 \times 10^2$ $M^{-1}\,s^{-1}$)	k_{rel}	av $k_2 \times 10^2$ ($M^{-1}\,s^{-1}$)	k_{rel}
p-OMe	26800	28.2	14600	35.0
p-Me	3640	3.84	1980	4.75
m-Me	1530	1.61	*a*	*a*
H	949	1.00	417	1.00
m-OMe	831	0.876	*a*	*a*
p-F	619	0.652	336	0.805
p-Cl	239	0.252	99.8	0.239
p-Br	209	0.220	93.1	0.223
m−F	97.3	0.102	36.4	0.0873
m-Cl	83.6	0.0881	34.6	0.0830
p-CN	7.76	0.00818	3.41	0.00818
p-NO$_2$	4.34	0.00457	1.97	0.00472

[a] Data not available.

The values of $\Delta H^\ddagger$ and $\Delta S^\ddagger$ and their uncertainties were determined as previously described.[2] These data along with the values of $\Delta G^\ddagger$ and the values of $\delta\Delta Y^\ddagger$ (eq 2, where Y represents either G, H, or S) are listed in

$$\delta\Delta Y^\ddagger = \Delta Y^\ddagger_{\alpha-\mathrm{methylstyrene}} - \Delta Y^\ddagger_{\mathrm{styrene}} \quad (2)$$

Table 2. Also included in Table 2 are the values for the methoxymercuration of the para-substituted styrenes.

To evaluate the effects of the substituents on the rates of this reaction, Hammett plots using both σ (Figure 3) and σ^{+}[7] (Figure 4) were made. When the data for the *p*-methoxy derivative is excluded, the values of ρ and ρ^+ obtained, at 25 °C, from these plots using σ and σ^+, (−3.12 ± 0.10, r^2 = 0.990 and −2.73 ± 0.16, r^2= 0.968), respectively, are essentially the same as those obtained for the styrenes, (−3.16 ± 0.09, r^2 = 0.998 and −2.76 ± 0.11, r^2 = 0.997), respectively. This indicates that the susceptibility of both reactions to the effects exerted by the substituent is the same.

At 25 °C the point for the *p*-OMe derivative lies above and below the line of best fit for the Hammett plots using σ and σ^+, respectively. To bring this point onto the

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(7) Brown, H. C.; Okamato, Y. *J. Am. Chem. Soc.* **1958**, *80*, 4979.

Table 2. Activation Parameters for the Methoxymercuration of α-Methylstyrenes and Corresponding Styrenes and Differences Resulting from Substitution of a Methyl Group in the α-Position of a Styrene in Anhydrous Methanol at 25 °C

	α-methylstyrene			styrene			$\delta\Delta Y^{\ddagger\, d}$		
X	$\Delta H^{\ddagger\, a}$	$-\Delta S^{\ddagger\, b}$	$\Delta G^{\ddagger\, c}$	$\Delta H^{\ddagger\, a}$	$-\Delta S^{\ddagger\, b}$	$\Delta G^{\ddagger\, c}$	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$	$\Delta G^{\ddagger}$
p-OMe	5.37 ± 0.24	29.4 ± 1.7	14.13	2.36 ± 0.11	41.2 ± 0.41	14.64	+3.01	+11.8	−0.51
p-Me	4.81 ± 0.18	35.2 ± 0.6	15.31	7.12 ± 0.34	28.7 ± 1.2	15.68	−2.31	−6.5	−0.37
m-Me	6.41 ± 0.05	31.6 ± 0.2	15.83	*e*	*e*	*e*	*e*	*e*	*e*
H	7.06 ± 0.07	30.4 ± 0.2	16.12	7.58 ± 0.38	30.4 ± 1.3	16.64	−0.52	−0.0	−0.52
m-OMe	7.19 ± 0.09	30.2 ± 0.3	16.19	*e*	*e*	*e*	*e*	*e*	*e*
p-F	6.69 ± 0.09	32.5 ± 0.3	16.37	7.63 ± 0.24	30.7 ± 0.8	16.78	−0.94	−1.8	−0.41
p-Cl	7.32 ± 0.16	32.3 ± 0.6	16.95	8.34 ± 0.16	30.5 ± 0.5	17.43	−1.02	−1.8	−0.48
p-Br	7.58 ± 0.10	31.7 ± 0.4	17.03	7.81 ± 0.15	32.5 ± 0.05	17.50	−0.23	+0.8	−0.47
m-F	7.90 ± 0.17	32.1 ± 0.6	17.47	8.81 ± 0.10	31.0 ± 0.4	18.05	−0.91	−1.1	−0.58
m-Cl	8.21 ± 0.27	31.4 ± 0.9	17.57	8.88 ± 0.13	30.8 ± 0.4	18.05	−0.67	−0.6	−0.48
p-CN	8.72 ± 0.13	34.4 ± 0.5	18.98	7.78 ± 0.63	39.1 ± 2.1	19.44	+0.94	+4.7	−0.46
p-NO_2	9.05 ± 0.17	34.4 ± 0.6	19.30	8.17 ± 0.62	38.9 ± 2.0	19.77	+0.88	+4.5	−0.47

[a] In kcal/mol. [b] In eu. [c] In kcal/mol. [d] See eq 2. [e] Data not available.

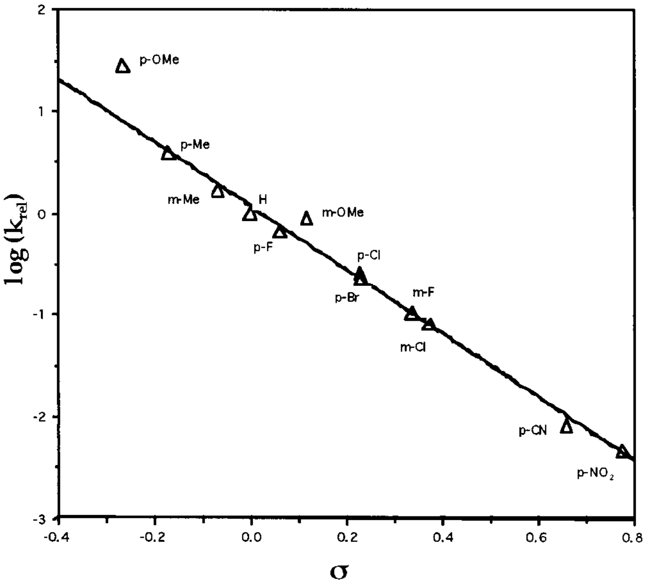

Figure 3. Hammett plot using σ at 25 °C.

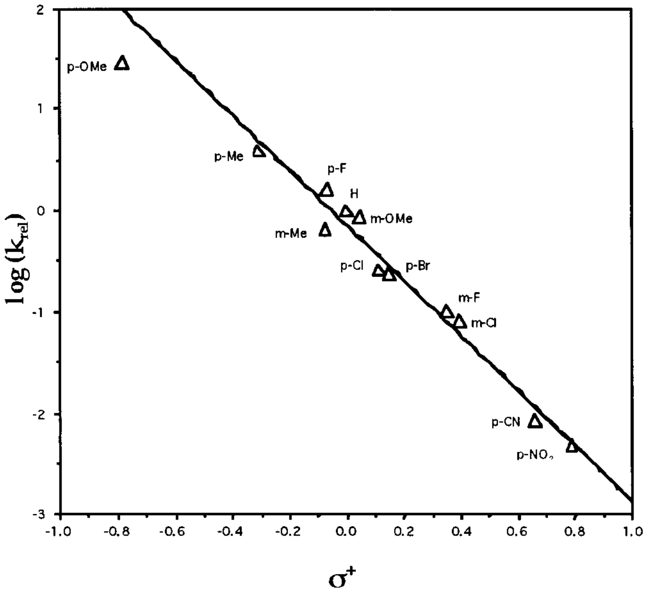

Figure 4. Hammett plot using σ^+ at 25 °C.

correlation line for the plot using σ, a value of 0.39 ± 0.04 had to be used for the *r* parameter in the Yukawa–Tsuno equation (eq 3).[8] This compares well with the value

$$\mathrm{Log}(k/k_{\mathrm{H}}) = \rho[\sigma + r(\sigma^{+} - \sigma)] \qquad (3)$$

of 0.44 ± 0.04 used for a similar analysis on the *p*-OMe derivative for the study of the substituted styrenes. The magnitude of *r* varies from reaction to reaction, and its value is a measure of the substituents through-resonance effect operating in a particular reaction. A value of 0.39 for the *r* parameter indicates that the *p*-methoxy substituent makes a small direct resonance contribution in stabilizing the intermediate formed during the methoxymercuration of *p*-methoxy-α-methylstyrene. The similarity of the value of *r* in both studies indicates that the direct resonance contribution of the *p*-methoxy group to the stabilization of the positive charge developed on the benzylic carbon during the methoxymercuration of both the styrenes and the α-methylstyrenes is approximately the same.

The deviations of the *p*-methoxy derivative from the correlation lines of the Hammett plot using σ and σ^+ and the small value of the *r* parameter used in the Yukawa–Tusuno equation to bring the point for the *p*-methoxy derivative onto the correlation line for the Hammett plot using σ at 25 °C indicate that while the positive charge being developed in the transition state requires some stabilization from the methoxy substituent, the full resonance stabilizing contribution of the *p*-methoxy group is not required. These deviations are often found[9] and do not necessarily indicate a change in the rate-determining step. This is the same situation found in the case of the substituted styrenes and is a further indication of the similarities between the activation processes of the two reactions.

Hammett plots using the data obtained at 15 and 5 °C, using σ and σ^+, gave values of ρ (−3.24 ± 0.11 at 15 °C and −3.31 ± 0.10 at 5 °C) and ρ^+ (−2.84 ± 0.13 at 15 °C and −2.90 ± 0.11 at 5 °C), respectively. Although the data show a slight increase in the values of ρ and ρ^+ with decreasing temperature, we attach no significance to these increases as the magnitudes of the increases are small.

Inspection of the data in Table 2 reveals that the reaction series is neither iso-enthalpic nor iso-entropic

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(8) Yukawa, Y.; Tsuno, T. *Bull. Chem. Soc. Jpn.* **1959**, *32*, 965–971.

(9) Loudon, G. M.; Berke, C. *J. Am. Chem. Soc.* **1974**, *96*, 4508.

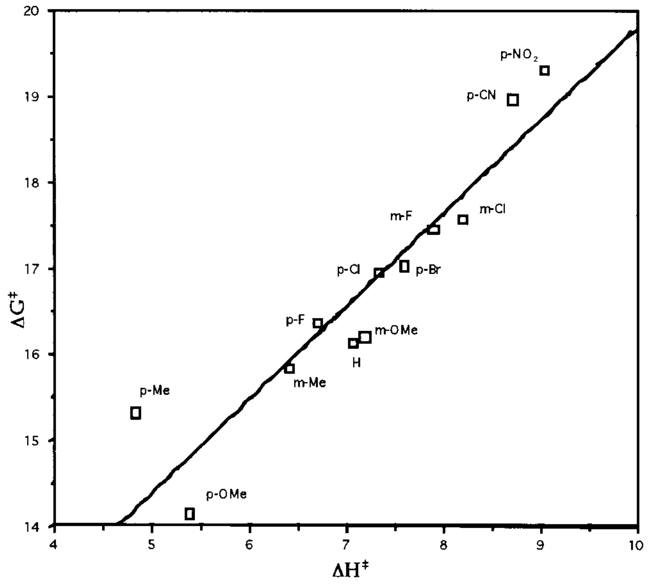

Figure 5. Plot showing the relationship between $\Delta G^{\ddagger}$ and $\Delta H^{\ddagger}$.

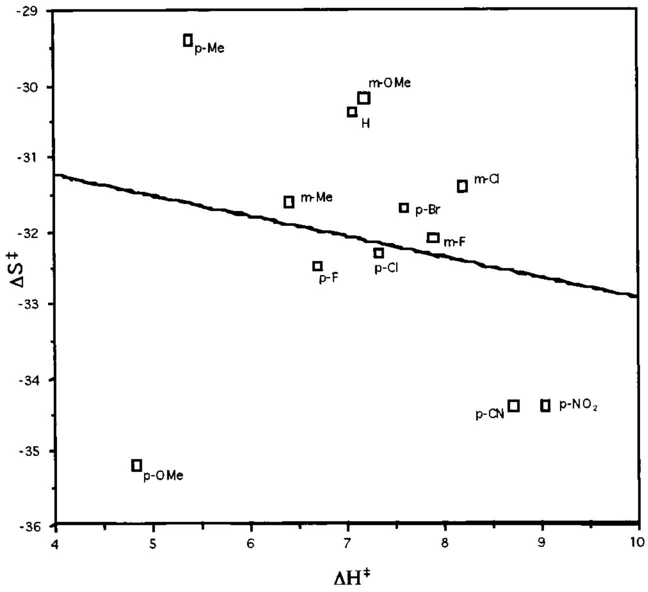

Figure 6. Plot showing the relationship between $\Delta S^{\ddagger}$ and $\Delta H^{\ddagger}$.

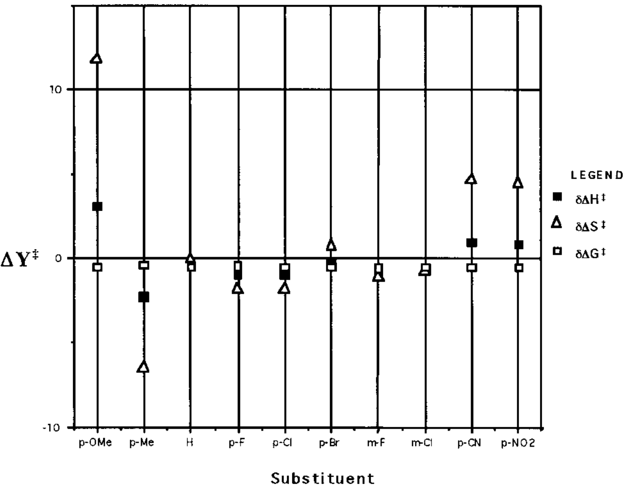

Figure 7. Variation in the activation parameters resulting from substitution of a methyl group in the α-position of a styrene.

and that the values of $\Delta H^{\ddagger}$ increase as the electron-withdrawing ability of the substituent increases. This is consistent with the decreasing ease of π-bond cleavage to form the transition state in these reactions as the electron-withdrawing ability of the substituent increases. By comparison of the data, it is seen that the values of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$, on average, appear to be smaller for the α-methylstyrenes than for the corresponding styrenes. This implies that the transition states for the α-methylstyrenes are easier to form as a result of the stabilizing effect of the α-methyl group on the developing positive charge.

In all cases, the values of $-T\Delta S^{\ddagger}$ for the α-methylstyrenes were greater than the values of $\Delta H^{\ddagger}$; this was also found to be the case for the styrenes. Hence, the entropy term exerts a large influence on the rates of the reaction. A plot (Figure 5) of $\Delta G^{\ddagger}$ vs $\Delta H^{\ddagger}$ gave a better correlation line than a plot of $\Delta S^{\ddagger}$ vs $\Delta H^{\ddagger}$ (Figure 6). This indicates that although $\Delta S^{\ddagger}$ is the dominant factor in determining $\Delta G^{\ddagger}$, the variations in $\Delta G^{\ddagger}$ and hence the variations in the rates of these reactions are determined by $\Delta H^{\ddagger}$. This was also the situation that was found for the methoxymercuration of the substituted styrenes. The values of $\Delta G^{\ddagger}$ for the α-methylstyrenes were in general smaller, by approximately 0.47 kcal/mol, than those found for the corresponding styrenes. This suggests that the substitution of a methyl group in the α-position of a styrene has a constant stabilizing effect on the formation of the transition state. The changes in the activation parameters in going from the styrenes to the α-methylstyrenes are summarized in Table 2 and shown in Figure 7.

The dominance of the entropy term in these reactions is consistent with the important role the solvent plays in the formation of the transition state. The relatively small values of $\Delta H^{\ddagger}$ and the large negative values of $\Delta S^{\ddagger}$ (average, −32.1 eu) suggest the formation of a highly organized transition state in which bond formation is well advanced. Lewis et al.[2,4] determined the activation parameters for the methoxymercuration and hydroxymercuration of a series of styrenes and atropic acids, respectively. The average values of $\Delta S^{\ddagger}$ were found to be −18.8 eu for the acids and −33.7 eu for the styrenes. As reported by the authors, the larger values of $\Delta S^{\ddagger}$ obtained for the styrenes were believed to be due to factors other than increased solvation of the transition state relative to the ground state, one of these factors being partial bridging of the mercury to the benzylic carbon. This would also seem to be the case for the methoxymercuration of the α-methylstyrenes.

Orr and Kharasch[10] reported a value of −2.20 for ρ, from the Hammett plots using σ, for the reaction of 2,4-dinitrobenzenesulfenyl chloride with a series of substituted styrenes in dry acetic acid. These types of reactions have been shown to proceed through a transition state involving the formation of a symmetrical bridged episulfonium ion.[11] Values of ρ^{+} (−3.58 and −3.21) for the acid-catalyzed hydration of styrenes[12] and α-methylstyrenes,[13]

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(10) Orr, W. L.; Kharasch, N. *J. Am. Chem. Soc.* **1956**, *78*, 1201.

(11) Rasteikiene, L.; Greiciute, D.; Lin'kova, M. G.; Knunyants, I. L. *Russ. Chem. Rev.* **1977**, *46* (6), 548.

(12) Schubert, W. M.; Keeffe, J. R. *J. Am. Chem. Soc.* **1972**, *94*, 559.

(13) Deno, N. C.; Kish, A.; Peterson, H. J. *J. Am. Chem.* Soc. **1965**, *87*, 2157.

respectively, from the Hammett plots using σ^+ have been reported. The authors concluded that considerable positive charge was developed on the benzylic carbon in the transition state of the rate-determining step. Further, they proposed the formation of an open cation as the reactive intermediate in the transition state for the hydration of the styrenes.

The ρ values for addition reactions involving styrenes and α-methylstyrenes suggest that the charge developed on the benzylic carbon is smallest for the addition of sulfenyl chlorides and greatest for the acid-catalyzed hydrations. The intermediate value of ρ for the methoxymercuration of styrenes and α-methylstyrenes is consistent with a transition state between the symmetrically bridged episulfonium ion and the open cation in the hydration reaction, i.e., an unsymmetrical, bridged carbocation.

Conclusion

Substitution of a methyl group in the α-position of a styrene was expected to stabilize the developing positive charge on the benzylic carbon. If the structure of the alkene is more important than the other two factors in the determination of the nature of the reactive intermediate in a moderately polar solvent, one would expect to see a change in the nature of the intermediate being formed in going from the styrenes to the α-methylstyrenes. This change was not observed. These studies show that although the substitution of a methyl group in the α-position of a styrene does lower the energy of the transition state, its stabilizing effect is not sufficient to offset that due to bridging of the mercury atom. The results of this study along with the results of the studies on the methoxymercuration of substituted styrenes (in which the formation of an unsymmetrically bridged cation was also proposed) and the hydroxymercuration of atropic acids (where the formation of an open cation was proposed) clearly indicate the importance of solvation of the transition state in these reactions. These results show that in a moderately polar solvent, the solvent plays a more important role than the structure of the alkene in determining the nature of the intermediate formed during a methoxymercuration reaction.

Experimental Section

General Procedure. Melting points are uncorrected. All boiling points were determined by fractional distillation.

Materials. All of the α-methylstyrenes used in this study were prepared by standard literature procedures for dehydrations[14] of the corresponding cumyl alcohols or by the dehydrobromination[15] of *p*-nitrocumyl bromide. Pure samples of all the styrenes were obtained by vacuum fraction distillation of the crude styrenes. All of the styrenes had ^1H NMR spectra ($CDCl_3$) that were consistent with their structures, as well as boiling points similar to those previously reported in the literature. GC−MS analyses showed that each of them was greater than 99% pure.

Table 3. Reaction Times and % Yield for the Methoxymercuration of Substituted α-Methylstyrenes and Melting Points of the Iodoether and Chloromercural Products

X	reaction time (min)	% yield	mp (°C)
	Chloromercurials		
H	15	>97	liquid[a]
	30	>99	
p-OCH_3	15	>90	88−89
	30	>99	
p-NO_2	120	>95.8	144−145
	180	>99	
	Iodoethers		
H	30	>99	liquid
p-OCH_3	20	>99	decomposed upon heating
p-NO_2	180	>99	darkens at 135 °C without melting

[a] Bassetti et al.[17] previously reported the methoxymercurated product as a liquid that solidified and decomposed on standing.

Mercuric acetate and methanol were purified, stored, and analyzed as previously reported.[2]

Kinetic Procedure. The pseudo-first-order rates of reactions were determined spectrophotometrically at 5, 15, and 25 °C. Measurements for all of the α-methylstyrenes, except the *p*-methoxy derivative, were determined using instrumentation as previously described.[2] Because the rate of the *p*-methoxy derivative was too fast to measure on the standard setup, the rates for the *p*-methoxy derivative (as well as those for the *p*-F,H, *p*-Me, and the *m*-Me derivatives for calibration purposes) were determined using instrumentation which has been previously described.[16] The data from both instruments showed differences in the second-order rates; however, the relative rates on each of the instruments were the same. Plots of the second-order rates determined on one instrument vs the second-order rates determined on the other instrument, at each tempreature, were linear ($r^2 \geq 0.995$), and the correlation line was used as a calibration curve between the two instruments. The expected rate for the *p*-methoxy derivative on the standard setup was then calculated from the equations of the lines of best fit for the calibration curve at each temperature.

Product Studies. Product studies on the *p*-OMe, H, and *p*-NO_2 derivatives were used to determine the products formed under the pseudo-first-order conditions of the methoxymercurations. These styrenes were chosen because they cover the range of reactivities investigated, and their products should be representative of those expected for the entire series. The isolation of the methoxymercurials, as well as the iodoethers, all have been previously described[2]. The reaction times used, the isolated yield, and the melting points of the methoxymercurials are listed in Table 3.

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(14) (a) Berstein, I. A.; Bennett, W.; Fields, M. *J. Am. Chem. Soc.* **1952**, *74*, 5736. (b) Wilkins, C. L.; Regulski, T. W. *J. Am. Chem. Soc.* **1972**, *94*, 6016.

(15) (a) Brubacher, G.; Suter, E. *Helv. Chim. Acta* **1950**, *33*, 256. (b) *p*-Nitrocumylbromide dehydrohalogenated while being distilled under vacuum; the fraction boiling at 105−106 °C, 2.1−2.3 mmHg (lit. mp 52−54 °C, ref 14a) was collected and recrystalized from diethyl ether.

(16) Hicks, K. W.; Sutter, J. R. *J. Phys. Chem.* **1971**, *75*, 1107.

(17) Bassetti, M.; Floris, B.; Illuminati, G. *J. Organomet. Chem.* **1980**, *202*, 351.