***trans*-2-(1-Octynyl)cyclohexanol (15).** According to the method of Yamaguchi and Hirao,[18] the lithium salt of octyne was allowed to react with cyclohexene oxide, affording **15**: ^{1}H NMR δ 3.31 (6 line m, $w_{1/2}$ = 25 Hz, J_{apparent} = 10, 4 Hz, HCO, 1 H), 2.05–2.15 (m, 3 H), 1.05–2.00 (m, 16 H), and 0.83 (t, J = 7.0 Hz, CH_3, 3 H); IR (film) $\nu_{\max}$ 3400 cm^{-1}; GC/MS of Me_3Si ether 280 (M^+, 5), 251 (2), 209 (16), 195 (20), and 73 (100); exact mass calcd for $C_{17}H_{32}OSi$ 280.2153, found 280.2186.

Isomerization of *trans*-2-(1-Octynyl)cyclohexanol. To the isomerization reagent (prepared from lithium (84 mg, 12 mmol), 1,3-diaminopropane (8.0 mL), and potassium *tert*-butoxide (900 mg, 8.0 mmol) was added at room temperature a solution of **15** (416 mg, 1.0 mmol) in 1,3-diaminopropane (4 mL). After being stirred for 1.0 h, the mixture was poured into ice/water and extracted with $CHCl_3$ (3×). The combined organic extracts were washed successively with 10% HCl (1×) and saturated NaCl solution (1×), and then dried over Na_2SO_4, and the solvent was evaporated to afford 410 mg of an oil which was chromatographed over silica gel, eluting with 40% ether 60% hexane. First to elute was phenyloctane (**19**) (85 mg, 24%) which gave IR and NMR spectra identical with published data[19] and GC/MS 190 (M^+, 17), 92 (98), and 91 (100). The second product obtained was *cis*-2-(7-octynyl)cyclohexanol (**18**): 20 mg (5%); ^{1}H NMR δ 3.84 (m, $w_{1/2}$ = 10 Hz, $H_{eq}CO$, 1 H), 2.15 (dt, J = 7.0, 2.6 Hz, $H_2CC{\equiv}C$, 2 H), 1.91 (t, J = 2.6 Hz, $HC{\equiv}C$, 1 H), 1.1–1.8 (m, 19 H); IR (film) $\nu_{\max}$ 3400, 3300, 2100, 1450, and 960 cm^{-1}; GC/MS, 280 (M^+, 2), 129 (47), 75 (100), and 73 (98); exact mass calcd for $C_{17}H_{32}OSi$ 280.2153, found 280.2213. Third to elute was *trans*-2-(7-octynyl)cyclohexanol (**16**): 140 mg (34%); ^{1}H NMR δ 3.14 (6 line m, J_{apparent} = 9.6, 4.4 Hz, $H_{ax}CO$, 1 H), 2.12 (dt, J = 7.0, 2.6 Hz, $H_2CC{\equiv}C$, 2 H), 1.88 (t, J = 2.6 Hz, $HC{\equiv}C$, 1 H), and 0.8–1.8 (m, 19 H); IR (film) $\nu_{\max}$ 3400, 3300, 2100, 1450, and 1050 cm^{-1}; GC/MS, 280 (M^+, 3), 129 (58), 75 (99), and 73 (100); exact mass calcd for $C_{17}H_{32}OSi$ 280.2153, found 280.2064.

The Kinetics of the Hydroxymercuration of Substituted Atropic Acids

Adolphus Lewis* and Antoine Carty

Department of Chemistry, Howard University, Washington, D.C. 20059

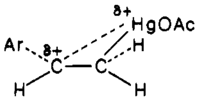
Received November 3, 1986

Kinetic studies on the hydroxymercuration of a series of meta- and para-substituted atropic acids in aqueous acetate buffer have been carried out. In the pH 3.7–5.0 range investigated, while the rates of reaction are essentially independent of the pH of the medium, they vary linearly with 1/[NaOAc]. At pH 4.40 and 0.050 M NaOAc, the reaction is first order in the concentrations of the atropic acids and the $Hg(OAc)_2$. In contrast to the results found for the methoxymercuration of the corresponding styrenes, log $k(X)$ gives better correlations with σ^+ than with σ. At 25 °C, ρ^+ (−2.14) is smaller than that (−2.78) found for the methoxymercuration of the styrenes. For each of the atropic acids, the values of its activation parameters are larger, by essentially the same amount, than those for the corresponding styrene and, in contrast to the results obtained for the styrenes, $\Delta H^* > -T\Delta S^*$. Product studies on the hydroxymercuration–demercuration of several of the atropic acids (p-MeO, H, m-Cl, and p-NO_2) showed that the only products formed were the corresponding atrolactic acids. Thus the hydroxymercuration occurs regiospecifically giving the Markovnikov hydroxymercurial. These results are consistent with the formation of an open α-mercuriocarbocation in the rate-determining step, which consequently suggests that the polarity of the solvent is more important than the structure of the alkene in determining the structure of the intermediate cation formed in the rate-determining step of this reaction.

Introduction

As a part of our[1,2] continuing investigations into the relative importance of the factors[3-7]—namely, the structure of the alkene, the electronic nature of the electrophilic atom, and the polarity of the solvent—which 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 hydroxymercuration of a series of meta- and para-substituted atropic acids in aqueous acetate buffer. Initially we planned to investigate the methoxymercuration of a series of methyl atropates. However, preliminary studies revealed that under our neutral kinetic conditions,[8] methoxymercuration of these compounds occurs too slowly to follow spectrophotometrically. They also showed that it would be impossible for us to determine the rates of methoxymercuration of the atropic acids spectrophotometrically, as planned, since the reaction mixtures became turbid soon after mixing methanolic solutions of the two reactants. The atropic acids were chosen for this study because they contain cross conjugated aryl and carboxyl groups. Thus a study of this type should afford one the opportunity to assess the relative importance of resonance–stabilization of a developing positive charge by an electron-donating aryl group vs. that of the simultaneous destabilization of that same charge by an electron-withdrawing carboxyl group.

The results of our[1,2] studies on the methoxymercuration of substituted styrenes suggested that when stabilization of the intermediate cation formed in the rate-determining step via, both, resonance involving the aryl substituent and bridging of the mercury atom are possible and the solvent in neither extremely polar nor nonpolar—thus, when neither the structure of the alkene nor the polarity of the solvent is clearly dominant—the structure of this cation should be that of an unsymmetric bridged ion, **1**. Thus



1

the primary aim of this study was to test the validity of this conclusion. Specifically, since water is much more polar than methanol and the atropic acids may be considered as α-substituted styrenes, we were interested in

---

[1] (a) Lewis, A. *J. Org. Chem.* **1984**, *49*, 4682. (b) Lewis, A.; Azoro, J. *Ibid.* **1981**, *46*, 1764. (c) Lewis, A.; Azoro, J. *Tetrahedron Lett.* **1979**, 3627.

[2] Lewis, A., submitted for publication in *J. Org. Chem.*

[3] Bach, R. D.; Henneike, H. E. *J. Am. Chem. Soc.* **1970**, *92*, 5589.

[4] Dubois, J. E.; Toullec, J.; Barbier, G. *Tetrahedron Lett.* **1970**, 4485.

[5] Dewar, M. J. S.; Fahey, R. C. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 245.

[6] Dolbier, W. B. *J. Chem. Educ.* **1969**, *46*, 342.

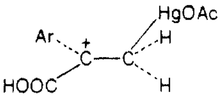
[7] Bolton, R. *Comprehensive Chemical Kinetics*; Bamford, C. H., Tipper, C. F. H., Eds.; Elsevier: New York, 1973; Vol. 9, p 1.

[8] Bloodworth, A. J.; Bunce, R. J. *J. Chem. Soc. D* **1970**, 753, reported that the methoxymercuration of methyl atropate in CH_2Cl_2 containing 2 mol % of $HClO_4$ occurred to give the Markovnikov mercurial.

0022-3263/87/1952-1839$01.50/0

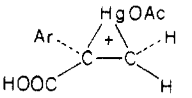
determining if bridging of the mercury atom would be more or less important in this reaction than that found for the methoxymercuration of the styrenes.

If the importance of water's high ionizing power outweighs the destabilizing effect of the carboxyl group on a positive charge, bridging of the mercury should be less important in this reaction than that found for the methoxymercuration of the styrenes. Thus the structure of the intermediate cation formed in this reaction should be that of an open α-mercuriocabocation, **2**. For a transition state similar in structure to **2**, because of direct resonance interactions between the substituent and the α-carbon, log $k(X)$ should give better correlations with σ^+ than with σ. Further, because of fewer restrictions on the motions of the atoms in a transition state of this type, the values of $-\Delta S^*$ for the atropic acids should be smaller than those found for the corresponding styrenes.



2

On the other hand, if the carboxyl group exerts a larger destabilizing effect on the developing positive charge than water can offset, through solvation,, bridging of the mercury atom should be more important in this reaction than that found in the methoxymercuration of the styrenes. In this case, depending upon whether resonance stabilization of this charge by the substituent or destabilization of it by the carboxyl group is dominant, the structure of the intermediate cation should be either similar to that of **1** or more fully symmetric in nature, like that of **3**. Indeed this is a case where, as the electron-withdrawing ability of the substituent increases, the structure of the intermediate cation might change from **1** to **3**. Such a change might be anticipated because as the substituent's electron-withdrawing ability increases, the overall electronic effects of the substituent and the carboxyl group on the positive charge change from ones of opposition—stabilization by the substituent vs. destabilization by the carboxyl group—to ones of reinforcement—destabilization by both the substituent and the carboxyl group. Thus depending upon which, if either, of these electronic effects is dominant one might expect either linear or curved Hammett plots of the data. Further, because of the restriction placed on the motions of the atoms in transition states similar in structure to **1** or **3**, the values of $-\Delta S^*$ for the atropic acids should be either the same as or larger than those found for the corresponding styrenes.



3

As the results which we report here will show, the structure of the intermediate cation formed in the rate-determining step of this reaction is that of an open α-mercuriocarbocation, **2**. Thus the polarity of the solvent is more important than the structure of the alkene in determining the structure of the intermediate cation formed in reactions of this type.

Results[9] and Discussions

Each of the atropic acids **4a–h** has one intense absorption band in the 220–320-nm region of the UV spectrum which obeys Beer's Law. Thus we measured the rates of

$$XC_6H_4C(COOH){=}CH_2$$

4

a, X = *p*-MeO; **b**, X = *p*-Me; **c**, X = *p*-F; **d**, X = H; **e**, X = *p*-Cl; **f**, X = *m*-F; **g**, X = *m*-Cl; **h**, X = NO_2

the hydroxymercuration reactions by monitoring the decrease in the absorbance of the atropic acids. The measurements were carried out under pseudo-first-order conditions with the $Hg(OAc)_2$ being present in a 15–50 molar excess over the atropic acids. Since mercuric acetate undergoes partial hydrolysis[10] in neutral or weakly acidic solutions, this study was carried out in aqueous acetate buffer. With the exception of **4h**, which does not react under these conditions, each of the atropic acids exhibits clean first-order kinetic behavior.

Preliminary studies, using **4a**, **4b**, and/or **4d** at 25 °C, on the dependence of the pseudo-first-order rates of reaction, k(obsd), on (1) the pH of the kinetic solution, at constant ionic strength (NaOAc concentration), (2) the NaOAc concentration of the medium, at constant pH, and (3) the $Hg(OAc)_2$ concentration of the medium, at constant pH but varying NaOAc concentrations gave the following results, respectively. (1) In the pH range of 3.7–5.0, k(obsd) varies slightly with the pH, rising to a maximum (on the average, a 35% increase was found) at a pH of approximately 4.4 and then falling again. (2) Added acetate ion has a rate-retarding effect on this reaction. Specifically, k(obsd) varies linearly with 1/[NaOAc]. A plot of log k(obsd) vs. log [NaOAc] was linear with a slope of -0.89 ± 0.09. (3) k(obsd) varies linearly with $[Hg(OAc)_2]$. Analyses of logarithmic plots of the data gave the following values for the slopes of the correlation lines (the NaOAc concentration of the buffer is given in parentheses): 0.65 ± 0.03 (0.01 M); 0.98 ± 0.01 (0.05 M); 1.02 ± 0.01 (0.10 M). These results showed that the reaction obeys the rate law that is given in eq 1 and that the optimum conditions for carrying out this study were at a pH of 4.4 and a NaOAc concentration of 0.05 M.

$$-d[\rangle C{=}C\langle]/dt = k[\rangle C{=}C\langle][Hg(OAc)_2]/[^-OAc] \qquad (1)$$

This rate law is consistent with the mechanism shown in eq 2–4, which differs from that which is accepted[1a,11] for the methoxymercuration of the corresponding styrenes only in terms of the nature of the reactive mercury species which is involved in the first and second steps of this reaction. According to this mechanism, the first step

$$Hg(OAc)_2 \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} HgOAc^+ + {}^-OAc \qquad \text{(fast)} \qquad (2)$$

$$>C{=}C< \; + HgOAc^+ \xrightarrow{k_2} \underset{\mathbf{5}}{[>C{=}C<\cdot HgOAc]^+} \qquad \text{(slow)} \qquad (3)$$

$$\mathbf{5} + H_2O \underset{k_{-3}}{\overset{k_3}{\rightleftarrows}} HO\text{-}\overset{|}{\underset{|}{C}}\text{-}\overset{|}{\underset{|}{C}}\text{-}HgOAc + H^+ \qquad \text{(fast)} \qquad (4)$$

involves the ionic dissociation of the $Hg(OAc)_2$ into $HgOAc^+$ and ^-OAc ions, rather than into an ion pair. The formation of these ions in water but not in methanol is consistent with the fact that water is a more highly ionizing

---

[9] All of the results reported herein were obtained by using a linear least-squares program on a computer. Unless otherwise indicated, the corresponding correlation coefficient was 0.993 or better.

[10] Baes, C. F.; Mesmer, R. E. *The Hydrolysis of Cations*; Wiley: New York, 1976; pp 301–312.

[11] (a) Lucas, H. J.; Hepner, F. R.; Winstein, S. *J. Am. Chem. Soc.* **1939**, *61*, 3102. (b) Chatt, J. *Chem. Rev.* **1951**, *48*, 7. (c) Zerirov, N. S. *Russ. Chem. Rev. (Engl. Transl.)* **1965**, *34*, 527. (d) Halpern, J.; Tinker, H. B. *J. Am. Chem. Soc.* **1967**, *89*, 6427. (e) Matteson, D. S. *Organometallic Reaction Mechanisms of the Nontransition Elements*; Academic: New York, 1974; Chapter 5. (f) Kitching, W. *Organometallic Reactions*; Becker, E. I., Tsutsui, M., Eds.; Wiley Interscience: New York, 1972; Vol. 3, p 319.

Table I. First-Order Rate Constants for Reaction of $XC_6H_4C(COOH){=}CH_2$[a] with $Hg(OAc)_2$[b] in Aqueous Acetate Buffered Solution[c]

	10^4k,[d] s^{-1}			
X	at 15 °C	at 25 °C	at 35 °C	at 45 °C
p-MeO	230 ± 3	523 ± 5	1110 ± 5	2050 ± 25
p-Me	35.8 ± 0.1	87.8 ± 0.5	205 ± 1	438 ± 3
p-F		17.8 ± 0.3	44.0 ± 0.3	100 ± 1
H		17.1 ± 0.1	41.8 ± 1.2	98.8 ± 2.0
p-Cl		6.87 ± 0.05	17.6 ± 0.1	40.6 ± 0.1
m-F		2.26 ± 0.02	5.98 ± 0.25	14.7 ± 0.4
m-Cl		1.87 ± 0.03	5.38 ± 0.05	13.2 ± 0.3

[a] The average initial molar concentration of the atropic acids in the kinetic mixtures was 9.70×10^{-5} M. [b] The initial concentration of the $Hg(OAc)_2$ in the kinetic mixtures, as determined by titration of the stock solution with standard KSCN, was 4.09×10^{-3} M. [c] pH 4.40 ± 0.02 and [NaOAc] = 0.05 M. [d] The average of two or more determinations plus or minus the standard deviation.

solvent than methanol. The rate-limiting step of this mechanism involves the attack of an $HgOAc^+$ ion on the double bond of the atropic acid, which leads to the formation of the intermediate cation, **5**. In the last step, **5** rapidly reacts with water, which leads to the formation of the hydroxymercurials.

The values of k, the overall first-order rate constant, in eq 1 is related to the pseudo-first-order rates of reaction by eq 5. Thus the values of k were determined by multiplying k(obsd)[12] by the ratio of the initial concentrations of the NaOAc and the $Hg(OAc)_2$. These data are summarized in Table I. An examination of the data in Table I reveals that the values of k decrease as the substituent's electron-withdrawing ability increases. At all temperatures, plots of log k(X) vs. σ and σ^+ are linear. However, in contrast to the situation found for the methoxymercuration of the substituted styrenes, the plots with σ^+ are better than those with σ, as shown by the following observations: (1) The relative reactivities of **4c** and **4d** are correctly predicted by their σ^+ values but not by their σ values. (2) The point for **4a** falls on the correlation line obtained by using σ^+ values, but it lies well above the line obtained by using σ values. (3) The correlation coefficients for the lines obtained by using σ^+ values (0.994 or better, with or without the data for **4a**) are better than those (0.978 and 0.989, with and without, respectively, the data for **4a**) obtained by using σ values. This finding suggests that stabilization of the developing positive charge in the transition state—through direct resonance interactions between the substituent and the benzylic carbon—is important, while that due to bridging of the mercury atom is not. The values of $-\rho^+$ (2.14 ± 0.09, 2.04 ± 0.09, and 1.93 ± 0.10 at 25, 35, and 45 °C, respectively) are relatively insensitive to the temperature and smaller than that (2.78, at 25 °C) obtained for the methoxymercuration of the styrenes.[1] Thus the need for stabilization of the developing positive charge, by the substituent, in the transition state of this reaction is less than that in the methoxymercuration.

$$k(\text{obsd}) = k[Hg(OAc)_2]/[^-OAc] \qquad (5)$$

Initially, this finding may appear somewhat surprising since a comparison of the data in Table I with that for the methoxymercuration of the styrenes[1] shows that the substitution of the α-H in a styrene by a carboxyl group has its anticipated rate-retarding effect—at 25 °C, each atropic acid undergoes hydroxymercuration approximately 2000 times more slowly that the corresponding styrene undergoes methoxymercuration. However, since both the solvent and the structure of the alkenes have been changed in going from the hydroxymercuration to the methoxymercuration, there are, at least, two factors which could lead to this reduction in the value of ρ^+. The first and probably the more important of these is the change in the solvent. Water is more polar than methanol; thus the transition state formed in the hydroxymercuration is more effectively solvated than that formed in the methoxymercuration. A portion of this reduction can also be attributed to the fact that while the carboxyl group is an electron-withdrawing group both by its inductive and resonance effects, it is also a weak π donor. Recent studies[13] have shown that a group with an electron-withdrawing resonance effect (e.g., CN, CHO, and NO_2) attached to a cationic center acts as a π donor and stabilizes such a cation. Thus a portion of the positive charge that develops in the hydroxymercuration transition state might be stabilized by this effect of the carboxyl group.

Support for these ideas is obtained from the results of Tidwell et al.,[14] who studied the hydration of a series of substituted α-(trifluoromethyl)styrenes and compared their results with those for the hydration of a series of substituted styrenes. They found that the substitution of the α-H in styrene by a trifluoromethyl group caused a rate reduction of approximately 10^{22} and the value of $-\rho^+$ to increase from 2.9 to 4.0. Since the solvent is water in both cases, the tremendous rate reduction and the increase in the value of ρ^+ caused by the α-trifluoromethyl group clearly reflects the destabilizing effect that this group has on a developing positive charge. Unlike the carboxyl group, the trifluoromethyl group does not have a resonance effect. Thus it is not capable of acting as a π donor. Further, on the basis of the values of the substituent constants for the carboxyl and trifluoromethyl groups, the rate-retarding effects of these two group should not differ by more than an order of magnitude. Thus the much smaller (by 18 orders of magnitude) effect of the carboxyl group found here must reflect, in large part, the much greater ability of water to solvate the transition state formed in the hydroxymercuration than methanol to solvate the transition state formed in the methoxymercuration.

The values of the activation parameters were obtained from Eyring plots of ln k/T vs. $1/T$ as previously described.[1b] These data along with the values of $\delta\Delta Y^*$ (eq 6, where Y represents either H, S, or G) are presented in Table II. For the sake of direct comparisons, this table also contains the values of the analogous data for the methoxymercuration of the corresponding styrenes.[1b] Inspection of the data, for the atropic acids, in this table reveals that (1) the values of ΔH^* increase with the electron-withdrawing ability of the substituent, while those of ΔS^* are relatively constant and (2) in contrast to the situation found for the methoxymercuration of the styrenes, $\Delta H^* > -T\Delta S^*$. Plots of $\delta\Delta G^*$ vs. $\delta\Delta S^*$ and $\delta\Delta S^*$ vs. $\delta\Delta H^*$ show that these parameters are not linear functions of one another. On the other hand, a plot of $\delta\Delta G^*$ vs. $\delta\Delta H^*$ is linear. Analysis of the data gives a value of 0.70 ± 0.05 for the slope of the correlation line ($r = 0.987$).

$$\delta\Delta Y^* = \Delta Y^*(\text{X}) - \Delta Y^*(\text{H}) \qquad (6)$$

---

(12) The pseudo-first-order rates of reaction were determined by the method of: Kezdy, F. J.; Jaz, J.; Bruylants, A. *Bull. Soc. Chim. Belg.* **1958**, *67*, 687.

(13) (a) Dao, L. H.; Mehran, M.; Hopkinson, A. C.; Lee-Ruff, E. *J. Am. Chem. Soc.* **1986**, *108*, 5237. (b) Gassman, P. G.; Tidwell, T. T. *Acc. Chem. Res.* **1983**, *16*, 279. (c) Tidwell, T. T. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 23. (d) Reynolds, W. F.; Dais, P.; MacIntyre, D. W. Topsom, R. D.; Marriott, S.; vom Nagy-Felsobuki, E.; Taft, R. W. *J. Am. Chem. Soc.* **1983**, *105*, 378. (e) Creary, X. *Ibid.* **1984**, *106*, 5568.

(14) Koshy, K. M.; Roy, D.; Tidwell, T. T. *Ibid.* **1979**, *101*, 357.

Table II. Activation Parameters for the Hydroxymercuration of $XC_6H_4C(COOH){=}CH_2$ in Aqueous Acetate Buffer

X	ΔH^* [a]	$-\Delta S^*$ [b]	$-T\Delta S^*$ [c]	ΔG^* [c]	$\delta\Delta H^*$	$-\delta\Delta S^*$	$\delta\Delta G^*$
p-MeO	12.67 ± 0.32	22.0 ± 1.0	6.55	19.22	−3.19	4.0	−2.02
p-Me	14.55 ± 0.08	19.2 ± 0.3	5.72	20.27	−1.31	1.2	−0.97
p-F	15.60 ± 0.11	18.8 ± 0.4	5.61	21.21	−0.26	0.8	−0.03
H	15.86 ± 0.17	18.0 ± 0.6	5.38	21.24	0.00	0.0	0.00
p-Cl	16.08 ± 0.21	19.1 ± 0.7	5.70	21.78	0.22	1.1	0.54
m-F	16.98 ± 0.02	18.3 ± 0.1	5.46	22.44	1.12	0.3	1.20
m-Cl	17.76 ± 0.47	16.1 ± 1.5	4.79	22.54	1.90	−1.9	1.30
The Analogous Data for the Methoxymercuration of the Corresponding Styrenes[d]							
p-MeO	2.36 ± 0.11	41.2 ± 0.4	12.28	14.64	−5.22	10.8	−2.00
p-Me	7.12 ± 0.34	28.7 ± 1.2	8.58	15.68	−0.46	−1.7	−0.96
p-F	7.63 ± 0.16	30.7 ± 0.5	9.14	16.78	0.05	0.3	0.14
H	7.58 ± 0.19	30.4 ± 0.6	9.06	16.64	0.00	0.0	0.00
p-Cl	8.34 ± 0.16	30.5 ± 0.5	9.09	17.43	0.76	0.1	0.79
m-F	8.81 ± 0.10	31.0 ± 0.4	9.24	18.05	1.23	0.6	1.41
m-Cl	8.88 ± 0.13	30.8 ± 0.4	9.17	18.05	1.30	0.4	1.41

[a] In kcal/mol. [b] In eu. [c] In kcal/mol at 298 K. [d] Taken from ref 1b and/or new determinations.

Thus the rates of this reaction are controlled by the values of ΔH^*.

When one compares the values of the activation parameters for the atropic acids with those for the corresponding styrene, it is seen that each parameter is larger (and by almost the same amount) for the atropic acid than for the styrene. The constancy of the increases—the averages are 8.4 ± 1.0 kcal/mol for ΔH^*, 13.1 ± 3.1 eu for ΔS^*, and 4.5 ± 0.1 kcal/mol for ΔG^*—in these parameters shows that the substitution of the α-H in a styrene by a COOH group has a constant effect on the structure of the transition state formed by each member of the series. The larger values of ΔH^* show that cleavage of the double bond and hence the generation of a positive charge in the transition state of an atropic acid are more difficult than that in the transition state of the corresponding styrene. This finding is consistent with the overall electron-withdrawing effect of the carboxyl group. The smaller values of $-\Delta S^*$ show that the transition state of an atropic acid has more freedom and/or requires less organization during the activation process than that of the corresponding styrene during the methoxymercuration. This finding is consistent with the fact that water is a more highly organized solvent than methanol and hence requires less reorganization in order to solvate the charged species that are formed in the transition state. It also suggests that bridging of the mercury atom is not important in this reaction.

These results and the facts that *p*-nitroatropic acid fails to react and that the only product formed in the hydroxymercuration–demercuration of the atropic acids is the corresponding atrolactic acids suggest that the intermediate cation formed in the rate-determining step of this reaction, 5, has the structure of an open α-mercuriocarbocation, 2. The fact that the structures of the intermediate cations formed in this reaction and in the methoxymercuration of the styrenes are not the same is consistent with the fact that water is a better ionizing solvent than methanol and hence stabilizes a carbocation more effectively than methanol. It is also consistent with the fact that a carboxyl group, while primarily an electron-withdrawing group, is also capable of stabilizing a cation[13] in which the positive charge is on the adjacent carbon. Thus the need for stabilization of the intermediate cation through bridging of the mercury atom is absent in this case.

In conclusion, the results of this study in combination with the results of our studies on the methoxymercuration of the styrenes[1,2] and the results of Dubois and Ruasse[15] and Brown et al.,[16] who found that the intermediate cation formed during the bromination of various alkenes in nonpolar solvents is a symmetric bridged ion, clearly show that the polarity of the solvent is more important than the structure of the alkene in determining the structure of the intermediate cation that is formed in an electrophilic addition reaction.

Table III. Reaction Times and Percentages of the Atrolactic Acids Present in the Product Mixtures

atropic acid	time[a]	% yield[b]	% atrolactic acid[c]
p-MeO	6 h	75	28
H	2 days	80	57
H	6 days	76	68
H	8 days	87	78
m-Cl	10 days	99	72
p-NO_2	1 month	90	0

[a] The hydroxymercuration reaction time. [b] The overall yield of the isolated product mixture based on the theoretical yield of the atrolactic acid. Most of these values are low due to the losses which occurred when the large volumes of solution involved were concentrated and then transferred to small weighed vials. [c] Determined by ^1H NMR analyses of the product mixtures.

Experimental Section

General Procedures. Melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected. GC analyses were performed on a Hewlett-Packard 5880A gas chromatograph using a capillary column. Proton NMR spectra were obtained with a Nicolet NT-200 FT NMR spectrometer. GC–MS analyses were performed on a Finnigan 3200 automated gas chromatograph–mass spectrometer.

Materials. With exception of *p*-nitroatropic acid, the atropic acids were prepared by the base-catalyzed dehydration of the corresponding tropic acids.[17] *p*-Nitroatropic acid was prepared by the acid-catalyzed deamination of the Mannich product formed from the reaction of *p*-nitrophenylacetic acid with formaldehyde and piperidine.[18] The tropic acids were prepared from the appropriate arylacetic acid by the procedure of Blicke et al.[19] Purification of the atropic acids was accomplished by flash column chromatography on silica gel using either a 50:1 (v:v) methylene chloride/methanol or 12:1 chloroform/acetic acid mixture as the eluent. TLC and GC–MS analyses revealed that each of them was, at least, 99% pure.

The mercuric acetate (B & A, AR) used was purified as previously described.[1] The sodium acetate (Mallinckrodt, AR) and glacial acetic acid (Captree, AR) were used without further purification. The water used was deionized and doubly distilled through an all-glass still.

---

(15) Dubois, J. E.; Ruasse, M. F. *J. Org. Chem.* **1973**, *38*, 493.

(16) Slebocka-Tilk, H.; Ball, R. G.; Brown, R. S. *J. Am. Chem. Soc.* **1985**, *107*, 4504.

(17) Louden, M. L.; Leeds, E. *J. Am. Chem. Soc.* **1962**, *84*, 1510, 4507.

(18) (a) Schauble, J. H.; Hertz, E. *J. Org. Chem.* **1970**, *35*, 2529. (b) Mannich, C.; Stein, L. *Ber.* **1925**, *58B*, 2659.

(19) Blicke, F. F.; Raffelson, H.; Barna, B. *J. Am. Chem. Soc.* **1952**, *74*, 253.

Kinetic Procedure. The pseudo-first-order rates of reaction were determined spectrophotometrically in a 10-mm cell on a Hewlett-Packard 8450A diode array UV–vis spectrophotometer that was equipped with two HP 89101A temperature stations attached to an HP 89100A temperature controller, an HP 7470A plotter, and an HP 9121D disk drive. The spectrophotometer was interfaced to an HP 85 computer. Stock solutions of the atropic acids and mercuric acetate were maintained to within ±0.02 °C of the desired temperature by using a Forma Scientific Model 2067 refrigerated and heated bath and circulator. The temperature of the reaction cell and its contents were maintained to within ±0.05 °C of the desired temperature by the HP 89100A/89101A combination. pH measurements were made with either a Fisher Model 610A pH meter or a Mettler DL40RC MemoTitrator.

The acetate buffer that was used was prepared by adding, from burets, 200 mL of a 0.500 M NaOAc solution and 326 mL of a 0.500 M HOAc solution (both freshly prepared) to a 2.0-L volumetric flask and diluting the resulting solution up to the mark with distilled deionized water. The pH of this solution was 4.40 ± 0.02 with a 0.050 M NaOAc concentration.

The general procedure was as follows. Stock solutions of the atropic acids ($\sim 2 \times 10^{-4}$ M) and mercuric acetate ($\sim 8.5 \times 10^{-3}$ M) in the acetate buffer were made up in volumetric flasks, and the flasks were placed in the constant-temperature bath at the desired temperature. After thermal equilibrium was achieved, 1.000 mL[20] of the $Hg(OAc)_2$ stock solution was pipetted into the cell housed in the temperature station at the desired temperature. The reference cell contained a $Hg(OAc)_2$ solution of the same initial concentration as that in the reaction cell. The reaction was initiated by pipetting 1.000 mL[20] of the appropriate atropic acid stock solution into the reaction cell.

The HP 8450A spectrophotometer is a microproprocessor controlled programmable instrument. Thus a program specifying the wavelength, the reaction period (usually 5 half-lives or more), and the time intervals at which measurements were to be made was entered and run for each of the atropic acids. At the end of the reaction period, the program further instructed the 8450A to make a plot of the data (absorbance vs. time), to store it on disk, and to transfer it to the HP 85 computer. The HP 85 was programmed to set up the data in the format—A_t vs. $A_{t+\tau}$, where $\tau > t_{1/2}$—required for analysis by the method of Kezdy, Jaz, and Bruylants,[12] to provide a printout of the resulting data, to make a plot of it, to perform a least-squares analysis of it, and to calculate the value of k(obsd) and its uncertainty.

Product Studies. In order to determine the structure(s) of the hydroxymercurial(s) formed under the pseudo-first-order conditions of our kinetic experiments, product studies on the hydroxymercuration–demercuration of several of the atropic acids at 25 °C were carried out (eq 7, where X = p-MeO, H, m-Cl, and p-NO$_2$). The structures of the hydroxy acids 6 and/or 7 were

$$\underset{\textbf{4}}{XC_6H_4C(COOH){=}CH_2} \xrightarrow[H_2O]{Hg(OAc)_2} \xrightarrow{NaBH_4}$$

$$\underset{\textbf{6}}{XC_6H_4C(COOH)(OH)CH_3} + \underset{\textbf{7}}{XC_6H_4CH(COOH)CH_2OH} \quad (7)$$

determined by TLC, GC, and 200-MHz ^{1}H NMR analyses of the isolated products. With the exception of p-nitroatropic acid, which does not react under these conditions, each of the atropic acids gave only one product—the corresponding atrolactic acid, **6**. In no case was any of the isomeric tropic acid, **7**, detected. Since each of the product mixtures also contained the starting atropic acid, we carried out controlled studies on tropic acid **7** (where X = H) in order to determine if base-catalyzed dehydration of **7** was occurring during the demercuration step of the sequence.

The results of these studies showed that the atropic acids present in the product mixtures were unreacted starting material and that the hydroxymercuration reaction occurs regiospecifically, giving the Markovnikov hydroxymercurial **8**. The fact that the

$$\underset{\textbf{8}}{XC_6H_4C(COOH)(OH)CH_2HgOAc}$$

orientation of the hydroxymercuration does not change with the electronic nature of the substituent shows that this reaction involves the formation of a common intermediate cation in the rate-determining step. Since the tropic acids **7** were not formed, the formation of the symmetric bridged mercurinium ion **3** can be ruled out.

Hydroxymercurations. The general procedure was as follows. In a 1.0-L round-bottom flask equipped with an air-cooled condenser, a solution containing 2 mmol of the atropic acid in 400 mL of aqueous sodium acetate buffer was magnetically stirred as a solution containing 20 mmol of $Hg(OAc)_2$ in 100 mL of the acetate buffer was added. The resulting solution was stirred at room temperature for a period ranging from 6 h to 1 month (see Table III).

Demercurations. The reaction mixture was cooled in an ice–water bath and 100 mL of a solution containing 100 mmol of $NaBH_4$ dissolved in 2 M KOH was added dropwise with stirring over a period of 30 min. The resulting mixture was allowed to stir at room temperature for 2 h before it was cooled in an ice–water bath and acidified with 100 mL of a 50% aqueous HCl solution. The precipitated mercury was removed by filtering the mixture through a small wad of cotton, and the filtrate was extracted with three 100-mL portions of ether. The combined ether extract was washed with two 500-mL portions of water. The extract was dried over anhydrous sodium sulfate, concentrated by allowing most of the ether to evaporate at room temperature, and then transferred to a small weighed vial. After the remainder of the ether had evaporated, the vial was reweighed and the residue was taken up in $CDCl_3$.

Analyses. TLC analyses of the product mixtures on silica gel using either 50:1 (v:v) methylene chloride/methanol or 12:1 chloroform/acetic acid as the eluent showed in all cases that only two components were present. By comparing the R_f factors for these spots with those of authentic samples of the atropic, tropic, and atrolactic acids, these components were identified as the unreacted atropic acids and the corresponding atrolactic acids.

GC analyses of these mixtures confirmed the fact that only two components were present. In no case was a peak for the tropic acid (whose retention time is greater than those of both the corresponding atropic and atrolactic acids) present in the chromatogram. The relative amounts of the two components obtained by integration of the peak areas was not considered reliable in most cases due to problems with tailing.

The ^{1}H NMR spectra of these mixtures showed the signals due to the atropic acids and an additional one between 1.5 and 1.8 ppm which was due to the CH_3 group of the corresponding atrolactic acids. After shaking the samples with D_2O in order to remove the signals given by the carboxylic and hydroxylic protons, the area of the CH_3 signal of the atrolactic acids relative to those of the two vinylic hydrogen signals of the atropic acids at 6.1 and 6.6 ppm was determined. The amounts of the atrolactic acids present in the mixtures were then read from a calibration chart (of relative area vs. % atrolactic acid) which had been prepared by using the data obtained from the ^{1}H NMR spectra of mixtures of known composition of authentic samples of atropic and atrolactic acids (the parent compounds). The results are summarized in Table III.

Controlled Study on the Effect of $NaBH_4$ on Tropic Acid. In a 500-mL round-bottom flask equipped with an air-cooled condenser, a solution of 1.0 mmol of tropic acid in 250 mL of distilled water was magnetically stirred as 50 mL of a solution containing 100 mmol of $NaBH_4$ in 2 M KOH was added slowly. The resulting clear solution was stirred at room temperature for 2.5 h before it was cooled in an ice–water bath and worked up as described above for the demercuration reactions. Evaporation of the ether an 84% recovery of a white fine crystalline solid, mp 115–117 °C—undepressed when mixed with an authentic sample of tropic acid, mp 116–117 °C.[19] TLC analysis showed that only one component was present. The R_f factor and ^{1}H NMR spectrum of this material were identical with those of an authentic sample of tropic acid.

Acknowledgment. This material is based upon work supported by the National Science Foundation under Grant RII-8300532.

---

[20] A Pipetman Model P-1000 was used for measuring the volume of this solution. Thus the uncertainty in the volume is better than ±0.002 mL.