Effects of α-Substitution on the Rate of Chloromercuriolactonization of Phenyl Esters of γδ-Unsaturated Acids

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Second-order rate constants for the reaction of several phenyl esters of α-alkyl-and/or α-aryl-substituted allylacetic acids with mercury(II) chloride have been determined in 50% aqueous ethanol. It was found that α-substitution increases the rate of reaction. The rate constants can be correlated with the dual substituent parameter expressions (i) and (ii). In the systems studied the steric coefficient is much larger

$$\log k_2 = \log k_2^{\circ} + \rho^*\sigma^* + \delta E_s \qquad \text{(i)}$$

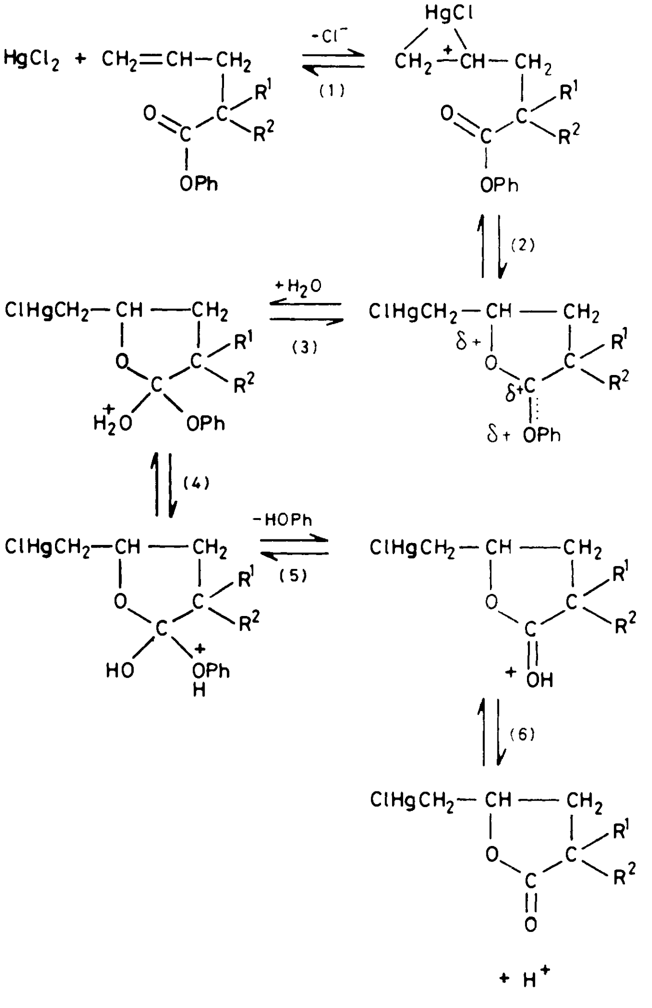
$$\log k_2 = \log k_2^{\circ} + \rho^*\sigma^* + \psi\nu \qquad \text{(ii)}$$

than the polar one, suggesting that the effect of the substituents on the rate of the reaction is essentially steric in nature, with a small additional contribution from the polar effect.

The chloromercuriolactonization of γδ-unsaturated acids and their esters in aqueous ethanol has been studied by Rowland *et al.*[1] and by do Amaral *et al.*[2] The mechanism proposed[2] for this reaction is given in the Scheme.

do Amaral and Melo[3] showed that mono- or di-substitution of the α-hydrogens of allylacetic acid by phenyl groups increases the rate of iodolactonization. Later, do Amaral *et al.*[4] showed that mono- or di-substitution of the α-hydrogens of phenyl allylacetate by phenyl groups increased the rate of chloromercuriolactonization.

In this paper, we report the preparation of several esters of the general formula $CH_2{=}CH{-}CH_2{-}CR^1R^2{-}CO_2C_6H_5$, where R^1 and/or R^2 are hydrogen (unsubstituted phenyl allylacetate) or alkyl substituents (mono- or di-substituted phenyl allylacetates). Kinetic data for acid- and alkali-catalysed hydrolyses of the ester are employed to determine the values of the σ* and E_s Taft parameters. In addition, we report kinetic data for the chloromercuriolactonization of these esters. These data show that monosubstitution of the α-hydrogen of phenyl allylacetate by either alkyl or aryl groups increases the rate of chloromercuriolactonization; disubstitution by alkyl and/or aryl groups caused an even larger increase in the reaction rate. On the basis of correlations of the rate constants for chloromercuriolactonization of the esters with the Taft parameters, it is suggested that the increase in the reaction rate caused by the α-substituents is predominantly steric in nature.



Scheme.

Experimental

Materials.—Phenyl allylacetate, phenyl 2-allylbutyrate, phenyl 2-allyl-3-methylbutyrate, phenyl allylphenylacetate, phenyl 2-allyl-2-methylpropionate, phenyl 2-allyl-2-phenylpropionate, and phenyl allyldiphenylacetate were prepared previously.[5] Phenyl 2-allyl-2-phenylbutyrate, b. p. 138 °C at 0.27 kPa (Found: C, 80.1; H, 7.3. Calc. for $C_{19}H_{20}O_2$: C, 81.4; H, 7.1%); $\nu_{max.}$(film) 1 750 and 1 185 cm^{-1}; δ(CCl_4) 0.9 (3 H, t), 2.1 (2 H, q), 2.7 (2 H, d), 4.7—5.2 (2 H, m), 5.2—6.0 (1 H, m), and 6.7—7.4 (10 H, m), was prepared as previously described.[5]

Product Preparation and Identification.—The δ-chloromercurio-γ-lactones of allylacetic acid, allylphenylacetic acid, and allyldiphenylacetic acid were previously prepared in our laboratories.[2] The δ-chloromercurio-γ-lactones of allylbutyric, 2-allyl-3-methylbutyric, 2-allyl-2-methylpropionic, 2-allyl-2-phenylpropionic, and 2-allyl-2-phenylbutyric acid were prepared as previously described.[2] Difficulties were encountered in crystallizing the viscous oily chloromercuriolactones. However, by employing ethanol–water mixtures, it was possible to crystallize all the chloromercuriolactones except those from 2-allylpropionic acetic and allylphenylacetic acid. The results are in Table 1.

Kinetics.—Kinetic measurements of the hydrolysis of the α-substituted phenyl allylacetates were carried out spectrophotometrically with the aid of a Zeiss PMQ-II spectrometer equipped with a cell holder through which water from a thermostatted bath was continuously circulated. The measurements were carried out in 60% dioxane–water (v/v) at 25.0 °C. The acid-catalysed hydrolysis of the esters was followed by observing the appearance of phenol at 270 nm, with an initial concentration of the ester of 4×10^{-3}M, at three values of H_0. The alkaline hydrolysis of the esters was followed by observing the appearance of the phenoxide ion at 287 nm, with an initial concentration of ester of 5×10^{-4}M and an ionic strength of 1.0×10^{-3}, at three values of pH. First-order rate constants were evaluated from slopes of plots of log ($OD_\infty - OD_t$) against time in the usual manner. Second-order rate constants ($k_{H_3O^+}$ or k_{OH^-}) were evaluated from the slopes of the plots of first-order rate constants against the concentration of the hydronium ion or the hydroxide ion (Tables 2 and 3). Kinetics of the reaction of phenyl esters of α-substituted allylacetates and mercury(II) chloride were carried out spectrophotometrically as well. The required temperature was measured in the cell with an accuracy of ±0.05 °C. Reagent stock solution, prepared in 50% aqueous ethanol (v/v), had the following concentrations: ester solutions 1.2×10^{-3}M, mercury(II) chloride 1.0×10^{-1}M, and sodium perchlorate 1.0M. Kinetic runs were carried out as follows. All reagents, except the ester solution, mixed and prethermostatted for 30 min. At zero time, a measured quantity of the ester solution was added to the mixture, which was then shaken and transferred rapidly to the reaction cell. The reaction kinetics were monitored by following the appearance of liberated phenol at 270 nm until a constant reading was attained. In all cases, a sufficient excess of mercury(II) chloride was used to ensure pseudo-first-order kinetic behaviour. An ionic strength of 0.10 was maintained by appropriate addition of sodium perchlorate solution. Observed first-order rate constants (k_{obs}) were evaluated from plots of log ($OD_\infty - OD_t$) *versus* time, as usual. Second-order rate constants (k_2) were determined by dividing k_{obs} by the mercury(II) chloride concentration. The initial concentration of the ester was 1.2×10^{-4}M. Three concentrations of mercury(II) chloride were used in each determination of k_2: 2.0×10^{-2}, 4.0×10^{-2}, and 6.0×10^{-2}M (Table 4).

Results and Discussion

The acid-catalysed hydrolysis of phenyl esters of acetic, trimethylacetic, and α-substituted allylacetic acid in 60% dioxane at 25.0 °C was studied. First-order rate constants were determined at three values of H_0 in the range between −1.72 and −0.50 (Table 2). Solutions with the appropriate values of H_0 in 60% dioxane at 25.0 °C were prepared in accordance with the procedure of Bunton *et al.*[6] The Taft E_s parameter was calculated by employing equation (1), where k_x is the $k_{H_3O^+}$

$$E_s = \log (k_x/k_0)_A \quad (1)$$

for the acid-catalysed hydrolysis of phenyl α-substituted allylacetates and k_0 is $k_{H_3O^+}$ of the acid-catalysed hydrolysis of phenyl acetate. The values of E_s are shown in Table 5.

The alkaline hydrolysis of phenyl esters of α-substituted allylacetic acids at 25.0 °C in 60% dioxane was studied. The first-order rate constants were determined at three values of pH in the range between 11.92 and 12.99 (Table 3). Solutions with the appropriate values of pH were prepared in accordance with the procedure of Bates *et al.*[7] The Taft σ* parameters were calculated by employing equation (2). The σ* values are shown in Table 5.

Table 1. Yields of the reaction of $CH_2{=}CHCH_2CR^1R^2CO_2H$ and mercury(II) chloride, and characterization of the δ-chloromercurio-γ-lactones formed

[R¹]	[R²]	Yield (%)	M.p. (°C)	$\nu_{max.}$/cm^{-1} [a]	Chemical shift δ [b]
Et	H	57	92—93	1 750 (CO)	1.0 (3 H, t), 1.4—2.0 (3 H, m), 2.0—2.5 (2 H, m), 4.6—5.1 (1 H, m)
Pr^i	H	51	79—80	1 760 (CO)	1.0 (6 H, d), 1.85 (1 H, m), 2.0—2.9 (5 H, m), 4.8—5.0 (1 H, m)
Me	Me	58	100—101	1 760 (CO)	1.2 (6 H, d), 1.4—2.0 (2 H, m), 2.0—2.5 (2 H, m), 4.7—5.2 (1 H, m)

[a] Film. [b] Taken in [$^2H_5$]pyridine with an internal Me_4Si reference. Satisfactory combustion analytical data for C,H (±0.4%) were obtained for these compounds.

$$\sigma^* = 1/2.48\,[\log (k_x/k_o)_B - \log (k_x/k_o)_A] \quad (2)$$

Charton[8] proposed a steric parameter ν which is a function of the van der Waals radius of the substituent as in equation (3),

$$\nu_x = r_{v,x} - r_{v,H} = r_{v,x} - 1.20 \quad (3)$$

where $r_{v,x}$ is the van der Waals radius of the substituent group and $r_{v,H}$ is the van der Waals radius of the hydrogen atom, expressed in Å. Charton also proposed that the rates of esterification of substituted carboxylic acids in methanol were a function of the ν values [equation (4)]. Values of ν that cannot be determined by equation (3) were determined by equation (4).

$$\log k = \Psi\nu + h \quad (4)$$

The values of $k_{H_3O^+}$ that we determined for the hydrolysis of phenyl acetate, allylacetate, and trimethylacetate (Table 2) were correlated with the ν values from the literature[8] by employing equation (5). Employing equation (5) and values of

$$\log k_{H_3O^+} = 2.66\nu - 3.18 \;(r\ 0.999\ 97) \quad (5)$$

$k_{H_3O^+}$ from Table 2, we calculated the ν values which are in Table 5.

Previous studies have shown that the reaction of esters of γδ-unsaturated acids with mercury(II) chloride, to yield chloromercuriolactones, is second order overall, being first order in both ester and mercury(II) chloride.[2] Rate constants for the reaction of the α-substituted acids described above were measured at five temperatures. The results, presented in Table 4, show that α-substitution increases the rate of the reaction at the five temperatures studied. In general, the increase is more pronounced for the disubstituted esters than for the monosubstituted ones. This observation is in accord with Thorpe–Ingold considerations regarding the effects exerted by substituents on the ease of ring formation.[9] The increase in the rate of the chloromercuriolactonization upon substitution of the α-hydrogen atoms of phenyl allylacetate by alkyl or aryl groups can arise from polar (inductive) effects, from steric effects, or from a combination of these two effects. The phenyl group exerts only a small inductive effect (−*I*), whereas the

Table 2. First-order rate constants (k_{obs}/s^{-1}) and second-order rate constants ($k_{H_3O^+}$/l mol^{-1} s^{-1}) for the acid-catalysed hydrolysis of some phenyl carboxylates, at 25.0 °C, in 60% dioxane

Ester	H_o	h_o	k_{obs}	$k_{H_3O^+}$
	−0.50	3.16	2.77×10^{-4}	
Phenyl acetate	−0.70	5.01	3.16×10^{-4}	2.75×10^{-5}
	−0.87	7.41	3.93×10^{-4}	
	−0.70	5.01	1.39×10^{-4}	
Phenyl allylacetate	−0.87	7.41	1.57×10^{-4}	6.87×10^{-6}
	−1.10	12.59	1.91×10^{-4}	
	−0.70	5.01	1.24×10^{-4}	
Phenyl 2-allylbutyrate	−0.87	7.41	1.42×10^{-4}	4.58×10^{-6}
	−1.10	12.59	1.58×10^{-4}	
	−0.50	3.16	7.46×10^{-5}	
Phenyl allylphenylacetate	−0.70	5.01	8.19×10^{-5}	3.36×10^{-6}
	−0.87	7.41	8.90×10^{-5}	
	−0.50	3.16	5.02×10^{-5}	
Phenyl 2-allyl-3-methylbutyrate	−0.70	5.01	5.52×10^{-5}	3.36×10^{-6}
	−0.87	7.41	6.44×10^{-5}	
	−0.50	3.16	3.48×10^{-5}	
Phenyl 2-allyl-2-phenylpropionate	−0.70	5.01	3.97×10^{-5}	2.42×10^{-6}
	−0.87	7.41	4.51×10^{-5}	
	−0.50	3.16	8.67×10^{-5}	
Phenyl 2-allyl-2-methylpropionate	−0.70	5.01	9.02×10^{-5}	2.05×10^{-7}
	−0.87	7.41	9.54×10^{-5}	
	−0.70	5.01	1.30×10^{-5}	
Phenyl 2-allyl-2-phenylbutyrate	−0.87	7.41	1.88×10^{-5}	1.79×10^{-6}
	−1.10	12.59	2.69×10^{-5}	
	−0.50	3.16	0.90×10^{-5}	
Phenyl allyldiphenylacetate	−0.70	5.01	1.05×10^{-5}	9.05×10^{-7}
	−0.87	7.41	1.28×10^{-5}	
	−1.14	13.8	1.12×10^{-3}	
Phenyl trimethylacetate	−1.42	26.3	1.35×10^{-3}	3.34×10^{-7}
	−1.72	52.5	1.89×10^{-3}	

Table 3. First-order rate constants (k_{obs}/s^{-1}) and second-order rate constants (k_{OH^-}/l mol^{-1} s^{-1}) for the alkaline hydrolysis of some phenyl carboxylates, at 25.0 °C, in 60% dioxane

Ester	pH	[OH$^-$]/M	k_{obs}	k_{OH^-}
	11.92	8.32×10^{-3}	0.937×10^{-2}	
Phenyl acetate	12.55	3.55×10^{-2}	2.22×10^{-2}	5.36×10^{-1}
	12.99	9.78×10^{-2}	5.69×10^{-2}	
	11.92	8.32×10^{-3}	0.358×10^{-2}	
Phenyl allylacetate	12.55	3.55×10^{-2}	0.917×10^{-2}	1.97×10^{-1}
	12.99	9.78×10^{-2}	2.03×10^{-2}	
	12.21	1.62×10^{-2}	0.13×10^{-3}	
Phenyl allylbutyrate	12.55	3.55×10^{-2}	0.34×10^{-3}	8.60×10^{-3}
	12.95	9.78×10^{-2}	0.77×10^{-3}	
	11.92	8.32×10^{-3}	0.274×10^{-2}	
Phenyl allylphenylacetate	12.55	3.55×10^{-2}	0.738×10^{-2}	1.59×10^{-1}
	12.99	9.78×10^{-2}	1.71×10^{-2}	
	12.21	1.62×10^{-2}	0.56×10^{-3}	
Phenyl 2-allyl-3-methylbutyrate	12.55	3.55×10^{-2}	1.27×10^{-3}	2.56×10^{-2}
	12.95	8.91×10^{-2}	2.48×10^{-3}	
	11.92	8.32×10^{-3}	0.292×10^{-2}	
Phenyl 2-allyl-2-phenylpropionate	12.55	3.55×10^{-2}	1.40×10^{-2}	3.93×10^{-1}
	12.99	9.78×10^{-2}	3.82×10^{-2}	
	12.21	1.62×10^{-2}	0.23×10^{-3}	
Phenyl 2-allyl-2-methylpropionate	12.55	3.55×10^{-2}	0.42×10^{-3}	8.99×10^{-3}
	12.95	8.91×10^{-2}	0.89×10^{-3}	
	12.21	1.62×10^{-2}	1.16×10^{-3}	
Phenyl 2-allyl-2-phenylbutyrate	12.55	3.55×10^{-2}	2.95×10^{-3}	6.90×10^{-2}
	12.95	8.91×10^{-2}	6.32×10^{-3}	
	11.92	8.32×10^{-3}	0.184 × 10-2	
Phenyl allyldiphenylacetate	12.55	3.55×10^{-2}	0.461×10^{-2}	1.21×10^{-1}
	12.99	9.78×10^{-2}	1.26×10^{-2}	

alkyl group, exert a small (+*I*) inductive effect. The observation that both groups cause an increase in the rate of the reaction thus rules out the inductive effect as the dominant factor, pointing to a steric effect of the alkyl or aryl substituent. In order to quantify the nature of the effect exerted by the substituent groups, we correlated the values of logarithms of the rate constants measured at 25 °C (Table 4) with the polar [equation (6)] and steric parameters [equation (7)] of **Table 5**.

Table 4. Second-order rate constants (10^4k/l mol^{-1} s^{-1}) for the reaction of phenyl α-substituted allylacetate with mercury(II) chloride in ethanol–water (50% v/v) and ionic strength 0.10

Ester	25.0 °C	30.0 °C	35.0 °C	40.0 °C	45.0 °C
Phenyl allylacetate[a]	0.233		0.600		1.38
Phenyl 2-allylbutyrate	5.22	6.72	9.07	14.0	19.8
Phenyl allylphenylacetate[a]	1.05		2.63		5.83
Phenyl 2-allyl-3-methylbutyrate	4.75	6.35	8.66	13.0	19.0
Phenyl 2-allyl-2-phenylpropionate	3.13	5.17	6.70	9.23	12.8
Phenyl 2-allyl-2-methylpropionate	8.85	10.8	13.8	19.1	23.6
Phenyl 2-allyl-2-phenylbutyrate	5.72	7.68	10.2	13.7	16.9
Phenyl allyldiphenylacetate[a]	20.0		33.3		58.3

[a] From ref. 4.

Table 5. Values of Taft's parameters E_s and σ^* and Charton's ν parameter for some substituent groups of the general formula $R^1R^2R^3C$

R^1	R^2	R^3	E_s	σ^*	ν
H	H	H	0.00	0.00	0.52[a]
H	H	Allyl	−0.60	+0.066	0.74[a]
Et	H	Allyl	−0.78	−0.403	0.81
Ph	H	Allyl	−0.91	+0.154	0.86
Pr^i	H	Allyl	−0.91	−0.164	0.86
Me	Ph	Allyl	−1.05	+0.371	0.92
Me	Me	Allyl	−1.13	−0.258	0.94
Et	Ph	Allyl	−1.19	+0.121	0.97
Ph	Ph	Allyl	−1.48	+0.335	1.07
Me	Me	Me			1.24[a]

[a] Values from ref. 8.

Table 6. Activation parameters for the reaction of phenyl α-alkyl-substituted allylacetates with mercury(II) chloride in ethanol–water (50% v/v) and ionic strength 0.10

[Ester]	$\Delta H^{\ddagger}$/ kJ mol^{-1}	$\Delta S^{\ddagger}$/ kJ mol^{-1} K^{-1}	$\Delta G^{\ddagger}$/ kJ mol^{-1}
Phenyl allylacetate[a]	72.9	−0.091	99.9
Phenyl 2-allylbutyrate	51.0	−0.137	91.9
Phenyl allylphenylacetate[a]	62.3	−0.114	96.1
Phenyl 2-allyl-3-methylbutyrate	51.8	−0.137	91.9
Phenyl 2-allyl-2-phenylpropionate	51.0	−0.140	92.8
Phenyl 2-allyl-2-methylpropionate	40.2	−0.169	90.6
Phenyl 2-allyl-2-phenylbutyrate	40.8	−0.169	91.4
Phenyl allyldiphenylacetate[a]	41.0	−0.161	89.0

[a] From ref. 4.

$$\log k = \log k_o + \rho^*\sigma^* \qquad (6)$$

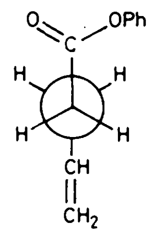
$$\log k = \log k_o + \delta E_s \qquad (7)$$

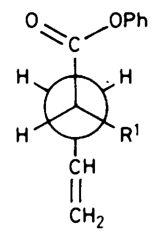
The resultant least-square fits are given, respectively, by equations (8) and (9).

$$\log k = -0.099 - 0.037\,\sigma^*\ (r\ 0.078) \qquad (8)$$

$$\log k = 5.28 - 1.80\,E_s\ (r\ 0.8173,\ s\ 0.3720) \qquad (9)$$

It is apparent from equation (8) that there is little or no correlation between log *k* and the σ* polar parameter. At the same time, the correlation between log *k* and the E_s steric parameter is also relatively poor. We then correlated log *k* by a dual-parameter treatment including both polar and steric effects [equations (10) and (11)]. The resultant least-squares fits


(1)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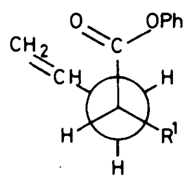
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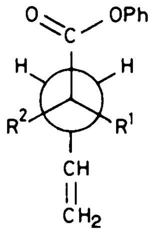
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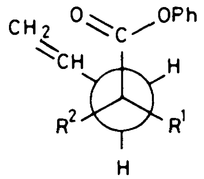
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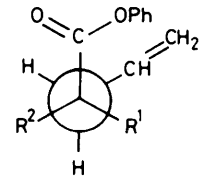
(3c)

$$\log k = \log k_o + \delta E_s + \rho^*\sigma^* \qquad (10)$$

$$\log k = \log k_o + \Psi\nu + \rho^*\sigma^* \qquad (11)$$

are shown, respectively, in equations (12) and (13). It is apparent from equations (12) and (13) that there are excellent

$$\log k = -5.77 - 2.33\,E_s - 1.16\,\sigma^*$$
$$(R = 0.9511,\ s = 0.2178,\ F = 47.43) \qquad (12)$$

$$\log k = -9.03 + 6.25\,\nu - 1.20\,\sigma^*$$
$$(R = 0.9563,\ s = 0.2061,\ F = 53.55) \qquad (13)$$

correlations between log *k* and both polar and steric parameters, according to Charton.[10] The results indicate that both effects are present, with the steric predominating over the polar one.

The data in Table 4 provide the activation parameters shown in Table 6. One notices from Table 6 that the values of the entropy of activation become more negative with increasing degree of substitution at the α-position of the ester substrate; the values of the enthalpy of activation also decrease in the same order. These results confirm preliminary observations.[4]

The results can be discussed in terms of the effect of the α-alkyl groups on the free energy of activation $\Delta G^{\neq}$. As shown above, the increase in the rate of chloromercuriolactonization upon substitution on the α-hydrogen atoms of phenyl allylacetate by alkyl or aryl groups arises principally from steric effects.

The increase in the entropy of activation of the reaction of phenyl allylacetates with mercury(II) chloride upon substitution at the α-position of the acid is at least partly explained by conformational analysis of the esters. For phenyl allylacetate, the most stable conformation should be *anti* (**1**); for the α-monosubstituted derivatives, there are two stable conformations (**2a** and **b**); for the α-disubstituted derivatives, there are three stable conformations (**3a**—**c**). Since conformations (**2b**) and (**3b** and **c**) are appropriate for the formation of the intermediate cyclic cations, the population of the appropriate conformations for reaction increases upon going from phenyl allylacetate to its α-monosubstituted derivatives to its α-disubstituted derivatives.

In earlier work,[5] we have shown that the effect of α-substitution on the carbonyl stretching frequencies of esters of the general formula $CH_2=CH-CH_2-CR^1R^2-CO_2C_6H_5$ is largely steric in origin. Both the correlation of the values of logarithms of the rate constants with steric parameters and the rationalization of the variation of the entropy of activation for reaction in terms of the conformational analysis of the esters suggest that the effect of α-substitution on the rate of chloromercuriolactonization is also predominantly of a steric nature.

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