ion in solution, one of the sources of labile hydrogen, to regenerate the sulfite radical ion.

Termination (eq 12–14) of the reaction may result by a number of processes. One is the consumption of the sulfite by oxidation to sulfate or bisulfate ion—an undesirable side reaction which is catalyzed by many transition metals.[30] Several coupling reactions may be postulated from analogy to radical reactions in general. As the concentration of the radical species becomes appreciable, alkanesulfonate radical may couple with sulfite radical ion to produce a disulfonate. We have analytical results that show substantial amounts of disulfonate of these molecular proportions are produced.[27] Conceivably, two of the alkanesulfonate radicals may couple to produce a higher molecular weight disulfonate for which we have no evidence.

Neighboring-Group and Substituent Effects in the Solvolysis of Substituted α-Bromophenylacetate Ions[1]

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A study of the rates of solvolysis of *meta-* and *para*-substituted α-bromophenylacetate ions was made in an attempt to help clarify the nature of the intermediate in the solvolysis of α-halocarboxylate ions. The first-order rate constants were correlated with the Hammett equation and ρ was found to be −2.66 at 25.0° and −2.74 at 35.6°, the solvent being 0.681 M aqueous acetone; in 80% methanol, ρ was −2.33 at 25.0°. The reaction does not appear to be very sensitive to base concentration, ionic strength, or solvent effects. A striking similarity is noted between the α-bromophenylacetate and α-bromopropionate ions in terms of salt and solvent effects as well as the values of the activation parameters. It is suggested that the similarities in the ρ value for the solvolysis of the α-bromophenylacetate ions with those for the solvolysis of benzyl derivatives in nucleophilic solvents is a consequence of neighboring carboxylate participation. The value of ρ suggests that the intermediate is an α-lactone with much ionic character.

One of the earliest known examples of the neighboring-group effect is that involving carboxylate participation.[3–6a] The classical work of Cowdrey, Hughes, and Ingold suggested the existence of an α-lactone intermediate during the solvolysis of α-bromopropionate ion. Although β-lactones and larger membered ring lactones have been isolated from the solvolysis of the corresponding halocarboxylate ions,[6a,7] the unstable α-lactone has not, and, as Streitwieser points out, the intermediate has been described as a zwitterion, an α-lactone with much ionic character, and simply an α-lactone. The nature of this intermediate has been thoroughly studied by Grunwald and Winstein[4] in terms of the effects of ionic strength and solvent upon the rate of solvolysis of α-bromopropionate. Their results indicate the creation of a small amount of additional charge in the transition state relative to the ground state.

The present account reports another approach designed to obtain additional information about the "α-lactone" intermediate. The Hammett reaction constant ρ has been evaluated for the solvolysis of several substituted α-bromophenylacetate ions since ρ can be interpreted as a measure of the change in the electron density between the ground state and the transition state at the reaction site.[8] Moreover, a reasonable extension of the Hammond postulate[9] suggests that a reactive intermediate and the transition state leading to it should closely resemble one another. The magnitude of ρ, according to Swain and Langsdorf,[8] can be interpreted in terms of bond making and bond breaking and should therefore be a measure of the electronic structure of the "α-lactone" intermediate.

The kinetics of the solvolysis of *p*-OCH₃-, *p*-H-, *p*-Cl-, *m*-NO₂-, and *p*-NO₂-α-bromophenylacetates were determined, as well as the activation parameters for several of the compound. Salt and solvent effects were also studied to a limited extent.

Results and Discussion

Kinetics.—First-order rate constants for the hydrolysis of several substituted sodium α-bromophenylacetates in 0.681 M aqueous acetone are presented in Table I. The hydrolyses were carried out on the sodium salts of the bromo acids in the presence of an equivalent amount of sodium hydroxide and at

(1) (a) Presented in part at the 154th National Meeting of the American Chemical Society, Chicago, Ill., Sept 1967, Abstract S97. (b) Based in part on the M.S. Thesis of D. Metzger, 1967.
(2) National Science Foundation Cooperative Fellow, 1964–1966.
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TABLE I

FIRST-ORDER RATE CONSTANTS FOR THE HYDROLYSIS
OF SUBSTITUTED α-BROMOPHENYLACETATE IONS
IN 0.681 M AQUEOUS ACETONE[a]

	$k_1 \times 10^4$,[b] sec^{-1}		ΔH^*,	ΔS^*,
Substituent	25.03°	35.6°	kcal/mol	eu
p-OCH$_3$	293[c]			
p-H	3.12[d]	15.0[e]	26.6	14.2
p-Cl	1.66	7.95	26.5	13.1
m-NO$_2$	0.0415	0.222	28.4	14.9
p-NO$_2$	0.0222			

[a] Reproducibility based upon the average of two or more runs is about 2% or better. [b] [Base] = [acid salt] = 0.02543 M; I = 0.551. [c] Evaluated at pH = 2.0. [d] Lit. k_1 = 2.45 × 10^{-4} sec^{-1} [G. Senter and S. H. Tucker, *J. Chem. Soc.*, **109**, 690 (1916)]. The literature value is probably lower because base was not present to neutralize the HBr produced. [e] Calculated from measurements at 25.03 and 15.6°.

constant ionic strength. Sodium perchlorate was used as the inert salt. Under these conditions linear first-order plots were obtained, the reactions being followed to about 80% completion. The reactivity of the compounds corresponds to the anticipated trend for the solvolysis of benzyl derivatives; i.e., the susceptibility toward hydrolysis decreases as the electron-withdrawing power of the substituent increases.

Even though excellent first-order plots were obtained when the reactions were carried out in the presence of an equivalent amount of base, hydrolyses were also studied using a ninefold excess of base to determine the possible importance of a second-order reaction between hydroxide and substrate. Linear first-order plots were obtained to approximately 75% reaction for the unsubstituted, p-chloro-, and m-nitro-α-bromophenylacetates. Excess base was found to have no effect upon the rate of hydrolysis of the unsubstituted acid, and only a small rate enhancement was noted for the p-chloro- and m-nitro-α-bromophenylacetates. These observed first-order rate constants are given in Table II along with second-order rate constants which were evaluated as discussed below. If the hydrolysis were first order in solvent as well as substrate, the presence of excess hydroxide ion, which is a much better nucleophile than water, should cause a significant increase in the rate of hydrolysis. Accordingly, the data in Table II suggest the reaction is not first order in solvent.

TABLE II

KINETICS OF HYDROLYSIS OF SODIUM α-BROMOPHENYLACETATES
IN 0.2089 N SODIUM HYDROXIDE[a]

Substituent	$k_{obsd} \times 10^4$, sec^{-1}	$k_1 \times 10^4$, sec^{-1}	$k_2 \times 10^4$, l./(mol sec)
p-H	3.10	3.12	0.0
p-Cl	1.80	1.66	0.67
m-NO$_2$	0.0728	0.0415	0.15

[a] Solvent 0.681 M aqueous acetone; [acid salt] = 0.02543 M; temp, 25.03°; I = 0.551.

If it is assumed that the hydrolysis occurs both by first- and second-order processes in the presence of excess base, the rate expression may be represented as

$$-dA/dt = k_1 A + k_2 A[OH] \qquad (1)$$

where A and [OH] refer to the substrate and hydroxide concentrations, respectively. If the hydroxide concentration is essentially constant, eq 1 becomes

$$-dA/dt = k_{obsd} A \qquad (2)$$

where

$$k_{obsd} = k_1 + k_2[OH] \qquad (3)$$

The values of k_2 in Table II were obtained from eq 3 and the values of the first-order constants from Table I. Because the rate enhancements in excess base are relatively small, the values of k_2 are subject to considerable error and are considered as approximations. Under the conditions which k_1 was evaluated, viz., equal substrate and base concentrations, the half-life for the second-order process for the p-chloro compound is 145 times greater than the half-life for the first-order reaction. For the m-nitro compound the corresponding factor is 17. This, in conjunction with the linearity of the first-order plots, suggests that first-order constants of Table I are reasonably reliable and do not contain significant contribution from the bimolecular process.

Reliable results for p-nitro-α-bromophenylacetate ion at the high base concentrations could not be obtained. The solutions darkened almost immediately; this may be a consequence of an oxidative coupling reaction.[10]

The relatively large activation parameters for these α-bromophenylacetates (see Table I) are quite comparable with the values for the hydrolyses of other α- and β-bromocarboxylate ions.[6a] For example, the enthalpy and entropy of activation for α- and β-bromopropionate[11] ions are 29.7 kcal/mol and 11.4 eu and 28.7 kcal/mol and 12.7 eu, respectively. These relatively large activation parameters have been attributed to solvation effects. In particular, the large entropy has been associated with the desolvation of the carboxylate group in the transition state. A recent study of Kingsbury[12] of the solvolysis of bromo acids in dimethylsulfoxide (DMSO)–water solutions supports this interpretation.

Medium Effects.—The sensitivity of the solvolyses to salt and solvent effects for the unsubstituted, p-Cl, and m-NO$_2$ derivatives were studied, and the results are summarized in Table III. The ratio $k_{0.5}/k_{0.05}$ refers to

TABLE III

SALT AND SOLVENT EFFECTS FOR THE SOLVOLYSIS
OF α-BROMOPHENYLACETATES AT 25.03°

Substituent	$k_{0.5}/k_{0.05}$	k_{H_2O}/k_{MeOH}
p-H	1.13	4.52
p-Cl	1.12	5.68
m-NO$_2$	1.04	1.97

the ratio of the first-order rate constants at ionic strengths of 0.551 and 0.0509, the solvent being 0.681 M aqueous acetone. Similarly, k_{H_2O}/k_{MeOH} refers to the ratio of first-order rate constants for the solvents 0.681 M aqueous acetone and 80% (v/v) methanol, the ionic strength being 0.551. The data showed that the reaction is not very sensitive either to ionic strength or to solvent effects. These results are remarkably similar to those reported for the α-bromopropionate ion by Grunwald and Winstein.[4] An increase of approximately 6% was noted for the first-order rate constant

(10) G. A. Russell and E. G. Janzen, *J. Amer. Chem. Soc.*, **89**, 300 (1967).
(11) J. F. Lane and H. W. Heine, *ibid.*, **73**, 1348 (1951).
(12) C. A. Kingsbury, *ibid.*, **87**, 5409 (1965).

for α-bromopropionate ion when the ionic strength was increased from 0.06 to 0.99, while the rate of solvolysis in water was approximately twice that in methanol. These effects are slightly less than those observed for the α-bromophenylacetates, but not markedly so. In general, the change from water to methanol decreases the rate of solvolysis of halocarboxylate ions by a factor of less than ten.[6a]

Salt and solvent effects are minimal for the m-NO$_2$ derivative. Since the nitro group does not stabilize the developing charge at the benzyl position, participation by the carboxylate group should be more extensive for this derivative than for the unsubstituted acid and thus produces a less ionic transition state. It may seem, at first, that this participation should manifest itself in a discernible manner in the entropies of activation for this series; however, there are two opposing effects which tend to offset one another. The more extensive the participation, the larger the number of solvent molecules freed, while on the other hand, the greater is the constraint imposed upon the bromo acid. This may account for the near constancy of the entropies noted in Table I. This interpretation is in accord with the results of the studies of Kingsbury[12] on the solvolysis of 3-bromopropionate in DMSO–water solutions. As the concentration of DMSO was increased, the carboxylate group became a more effective nucleophile because of decreased solvation. The solvolysis rate in 80% (v/v) DMSO was 290 times greater than in water. The entropy of activation decreased from +4.6 eu in water to −6.5 eu in 80% DMSO, apparently because there were fewer solvent molecules to be released by the carboxylate group.

Hammett Relationship.—A Hammett plot for the first-order rate constants using σ^+ is presented in Figure 1. The values of ρ at 25.03° are −2.66 in aqueous acetone and −2.33 in 80% (v/v) methanol. In many cases benzylic systems do not give linear plots because of competition of unimolecular with bimolecular reaction mechanisms.[6b,13] The linearity displayed in Figure 1 is probably fortuitous, since the point corresponding to the p-methoxy acid is based on a first-order constant obtained at pH 2. Because the hydrolysis was too rapid to follow at any higher pH, this point represents a lower limit for the rate constant and should lie above the line. A good straight line is obtained using the other four points, however, indicating that the same reaction mechanism is operative for these compounds.

It is interesting to compare the reaction constants of the α-bromophenylacetate ions with those of other benzylic systems. Reaction constants for the solvolyses of several benzylic derivatives are summarized in Table IV. The reaction constants for the formolysis of benzyl bromides[14] and tosylates[15] are relatively large in the negative sense, −5 to −6, while the reaction constants for solvolysis of benzyl tosylates in aqueous acetone[16] and benzyl chlorides in aqueous ethanol or aqueous acetone[17] are only about −2. The difference

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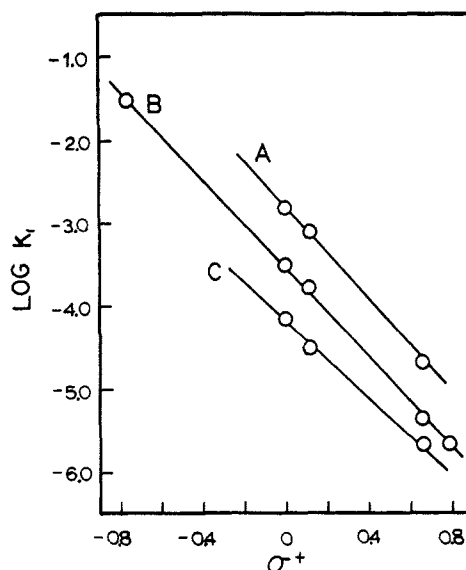
(17) H. H. Jaffé, *Chem. Rev.*, **53**, 191 (1953).

Figure 1.—Hammett plot for the solvolysis of substituted α-bromophenylacetate ions (I = 0.551): A, ρ = −2.74, 35.6°, 0.681 M aqueous acetone; B, ρ = −2.66, 25.0°, 0.681 M aqueous acetone; C, ρ = −2.33, 25.0°, 80% (v/v) methanol.

TABLE IV

REACTION CONSTANTS FOR SOLVOLYSES
OF SEVERAL BENZYLIC SYSTEMS[a]

Reaction	ρ
Formolysis of benzyl bromides[b]	−5.55
Formolysis of benzyl tosylates[c]	−6.04
Solvolysis of benzyl chlorides	
48% aq ethanol, 30°[d]	−2.19
50% aq acetone, 30°[d]	−1.82
Solvolysis of benzyl tosylates	
76.6% aq acetone[e]	−2.2
Hydrolysis of α-bromophenylacetates	−2.66

[a] Temperature 25° unless specified. [b] Calculated from data in ref 14. [c] Reference 15. [d] Reference 17. [e] Reference 16.

in these reaction constants no doubt reflects the different extent of solvent participation, the formolysis reactions being the more limiting cases. In more nucleophilic solvents, bonding with the entering solvent molecules tends to diminish the charge on the incipient benzyl cation and thus renders the reaction less sensitive to substituent effects. The ρ value of −2.66 for hydrolysis of the α-bromophenylacetate ions (0.681 M aqueous acetone) is comparable with the ρ for solvolysis of these benzyl derivatives in more nucleophilic solvents. However, in the α-bromophenylacetate system it is participation of the negatively charged oxygen atom of the neighboring carboxylate group rather than bonding with the entering solvent molecule which tends to influence the magnitude of ρ. The lack of rate dependence on base concentration and the absence of salt and solvent effects, as well as the close similarity to the α-bromopropionate ion, strongly indicate such participation.

It may seem that an even less negative value for the reaction constant would be expected as a consequence of this participation. The fact that this is not observed indicates a small charge separation in the transition state and, by the Hammond postulate, in the intermediate as well. Admittedly, the value of such comparison depends on the choice of reference compound. It is difficult to assess the influence of the carboxylate

group in the absence of participation, although its inductive effect as indicated by its substituent constant[17] should be small. Qualitatively, at least, the benzylic derivatives seem to be reasonable models for comparison, and the analogy makes ρ for the α-bromophenylacetate ions plausible.

These results indicate that the intermediates in solvolysis of the α-bromophenylacetates are very similar to that of the α-bromopropionate case. In addition, the magnitude of ρ suggests small charge separation in the intermediate. Just as with earlier results,[4] an unambiguous description of the intermediate cannot be rendered, but it seems best described as an α-lactone with much ionic character.

Experimental Section[18]

Materials. *p*-Methoxy-α-bromophenylacetic Acid.—*p*-Methoxyphenylacetic acid was brominated in the benzyl position following the general procedure of Panayotov.[19] This procedure is preferred to the Hell–Volhard–Zelinsky method for it avoids bromination of the reactive aromatic nucleus. A mixture of *p*-methoxyphenylacetic acid (16.6 g, 0.100 mol; Frinton Laboratories) and N-bromosuccinimide (17.8 g, 0.100 mol; Matheson Coleman and Bell) in 400 ml of reagent grade carbon tetrachloride was refluxed for 4 hr. After the mixture cooled, succinimide was filtered from the dark orange solution, and the solvent was removed under vacuum with a rotary film evaporator. The crude product was recrystallized twice from benzene yielding colorless needles of *p*-methoxy-α-bromophenylacetic acid, 12 g (50%), mp 100–102°.

Anal. Calcd for $C_9H_9BrO_3$: C, 44.10; H, 3.71; Br, 32.60. Found: C, 44.06; H, 3.59; Br, 32.58.

The nmr spectrum ($CDCl_3$) showed the expected signals at τ −2.10 (singlet, 1 H), 2.88 (AB quartet, 4 H), 4.77 (singlet, 1 H), and 6.23 (singlet, 3 H).

p-Chloro-α-bromophenylacetic Acid.—The acid was prepared from *p*-chlorophenylacetic acid, mp 107–109° (lit.[20] mp 105–106°) (obtained from hydrolysis of *p*-chlorophenylacetonitrile, Eastman, practical grade), according to the method of Wladislaw and Giora.[21] The crude *p*-chloro-α-bromophenylacetic acid was recrystallized from a ligroin–benzene solution yielding colorless prisms: 56.4 g (97%); mp 96–98°.

Anal. Calcd for $C_8H_6O_2BrCl$: C, 39.41; H, 2.43; Br, 32.03; Cl, 14.21. Found: C, 39.37; H, 2.52; Br, 32.10; Cl, 14.02.

An nmr spectrum showed signals at τ 4.69 (singlet, 1 H), 2.57 (AB quartet, 4 H), and −1.04 (singlet, 1 H).

p-Nitro-α-bromophenylacetic Acid.—*p*-Nitrophenylacetic acid (Columbia Organic Chemicals) was brominated according to reported methods.[21] Several recrystallizations from benzene gave pale yellow crystals: 15.9 g (53.7%); mp 103.0–103.6° (lit.[21] mp 111–112°, lit.[22] mp 113°).

Anal. Calcd for $C_8H_6BrNO_4$: C, 36.87; H, 2.33; Br, 30.73; N, 5.39. Found: C, 37.06; H, 2.35; Br, 31.21; N, 5.37.

The nmr spectrum ($CDCl_3$) and integration were consistent with the structure for this acid. Signals were observed at τ −0.83 (singlet, 1 H), 1.83 (AB quartet, 4 H), and 4.55 (singlet, 1 H).

m-Nitro-α-bromophenylacetic Acid.—This acid was prepared by the same method as the *p*-nitro-α-bromophenylacetic acid. Pale yellow crystals were obtained from recrystallization from benzene: 12.1 g (87%); mp 125.9–127.1°.

Anal. Calcd for $C_8H_6BrNO_4$: C, 36.87; H, 2.33; Br, 30.73; N, 5.39. Found: C, 37.02; H, 2.44; Br, 30.68; N, 5.46.

α-**Bromophenylacetic acid** was commercially available (Frinton Laboratories). The acid was recrystallized twice from *n*-hexane: mp 81–82°.

Kinetics.—The course of hydrolysis of the substituted α-bromophenylacetates was followed by titrating the acid produced. In each case, 2.543 mequiv of the bromo acid was dissolved in 5.0 ml of redistilled reagent grade acetone in a 100-ml volumetric flask; 25 ml of a stock 2.00 M sodium perchlorate solution and 20.0 ml of 0.2543 N NaOH were added; and the solution was quickly diluted to volume. All solutions were previously thermostated. The reactants were thoroughly mixed and then returned to the constant-temperature bath at 25.03° ± 0.01° (or 35.60° ± 0.03°). The initial time was taken when half of the volume of the sodium hydroxide had been added. Alliquots of 5 ml were pipetted at appropriate time intervals into ice-cold nitric acid to quench the reaction. The solution was quickly titrated with standard sodium hydroxide. Infinity measurements were made in most instances to check the accuracy of the titrations. The ionic strength of the reaction solution was 0.551.

A similar procedure was used to follow the hydrolyses of the substituted α-bromophenylacetates in the presence of 0.2089 N sodium hydroxide. Appropriate adjustments were made in the concentration of the stock sodium perclorate solution so that the ionic strength of the reaction solution was 0.551.

The hydrolysis of *p*-methoxy-α-bromophenylacetate was carried out with a Radiometer TTT-1 titrator at pH 2. This compound was too reactive at 25° to study by the removal and analysis of aliquots, and, in fact, the titrator was unable to follow the reaction at higher pH values. *p*-Methoxy-α-bromophenylacetate (0.100 g) was dissolved in 2 ml of acetone. Sodium perchlorate stock solution (6.25 ml, 2 M) and hydrochloric acid (15 ml, 0.01 N) were quickly added, and the titration was started immediately with 1.051 N NaOH. All solutions were previously thermostated, and the reaction vessel was maintained at 25.0° ± 0.5°. Volume of base *vs.* time was automatically recorded.

Product Identification.—Reactions were carried out on a larger scale, under the same conditions employed in the kinetic studies to facilitate the isolation of the expected α-hydroxy acids. Mandelic acid was identified as the hydrolysis product of α-bromophenylacetate on basis of its mp 118–120° and mmp 119–120.5° with authentic mandelic acid. Hydrolysis of *p*-chloro-α-bromophenylacetate gave *p*-chloromandelic acid, mp 120–121° (lit.[23] mp 120.5–121°). The hydrolysis product from *p*-methoxy-α-bromophenylacetate was *p*-methoxymandelic acid. Recrystallization from a benzene–hexane mixture afforded colorless crystals, mp 105–107°.

Anal. Calcd for $C_9H_{10}O_4$: C, 59.31; H, 5.54. Found: C, 58.99; H, 5.54.

(18) All melting points are corrected. The nmr spectra were taken with a Varian A-60 spectrometer using TMS as the internal standard.

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