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The Unusual Effects of *o*-Carboxyl and Carbomethoxy Substituents on the Stability of Iodobenzene Dichloride

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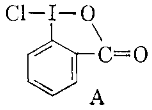
The product of dehydrochlorination of *o*-iodobenzoic acid dichloride reacts with durene in acetic acid to form chlorodurene and *o*-iodobenzoic acid. The reaction does not occur in the absence of traces of hydrogen chloride, and its rate is retarded by *o*-iodobenzoic acid. Kinetic evidence is presented which indicates that *o*-iodobenzoic acid dichloride is a reaction intermediate and that it, unlike other *o*-substituted iodobenzene dichlorides which have been studied, must equilibrate rapidly with the free iodo compound and chlorine. Free chlorine is the effective chlorinating agent for durene. Methyl *o*-iodobenzoate dichloride also equilibrates rapidly with its components in acetic acid, although its *p*-isomer and *m*- and *p*-iodobenzoic acid dichlorides dissociate very slowly in this medium. A neighboring group type participation of *o*-COOH and *o*-COOCH$_3$ is suggested to explain the extreme influences of these substituents on the dichloride dissociation rate.

In acetic acid iodobenzene dichloride undergoes slow equilibration with iodobenzene and chlorine.[1] The equilibration rate and the equilibrium constant vary with the electronic natures of substituents on the aromatic ring, but the reactivities of a number of *o*-substituted dichlorides are strikingly similar to those of their *m*- and *p*-isomers.[2] Apparently steric effects of *o*-substituents are minimal for this reaction because the Cl–I–Cl grouping lies perpendicular rather than parallel to the plane of the benzene ring. These dichlorides are effective agents for nuclear chlorination of aromatic hydrocarbons in acetic acid. When highly reactive hydrocarbons, such as mesitylene and pentamethylbenzene, are used, the reaction rate is independent of the alkylbenzene concentration and is controlled by the rate of liberation of chlorine (the actual chlorinating agent) by the dichloride.[1,2]

The dichloride of *o*-iodobenzoic acid cannot be isolated in reliably pure form since it undergoes rapid evolution of hydrogen chloride to form the heterocyclic compound A.[2,3] This material (A) also chlorinates aromatic hydrocarbons in acetic acid solution. A detailed investigation of the kinetics of its reaction with durene has shown that the effective chlorinating agent again is free chlorine produced by the dissociation of *o*-iodobenzoic acid dichloride, which is formed from A and traces of hydrogen chloride in the medium. Although only a semi-quantitative interpretation of the data has been made, the results of the kinetic work indicate that the rate of equilibration of this dichloride is extremely rapid compared to that of the *m*- or *p*-isomer.



A

The detailed experimental evidence which leads to this conclusion is now described along with evidence that methyl *o*-iodobenzoate dichloride, in sharp contrast with its *p*-isomer, also equilibrates rapidly with its components in acetic acid, and a mechanistic interpretation of these unusual effects of *o*-carboxyl and carbomethoxy substituents is presented.

Experimental

The Preparation of Compound A.—This material was prepared by dehydrochlorination in air (5–12 hours) of the dichloride of *o*-iodobenzoic acid.[2] The dichloride was prepared either by gassing a suspension of the parent acid in nitromethane with chlorine[2] or by gassing a solution of the iodo acid in chloroform with chlorine. Samples of the dichloride (which were freshly filtered, washed with carbon tetrachloride and quickly air dried) were analyzed iodometrically to determine their equivalent weights with respect to oxidizing power. Generally the equivalent weights of such samples were much lower (*ca.* 130) than the theoretical value (159.5) for Cl$_2$IC$_6$H$_4$COOH. Apparently excess chlorine was entrained in the crystals of the dichloride.

The samples of compound A generally had experimental equivalent weights (143 or higher) which were somewhat greater than the theoretical value (141).

The Products of Reaction of Durene and Compound A.—To a solution of 0.57 g. (0.0020 mole) of compound A in 30 ml. of acetic acid was added 0.27 g. (0.0020 mole) of durene. The resulting solution was allowed to stand in the dark for three days and then was poured into 300 ml. of water. This mixture next was extracted with two 25-ml. portions of carbon tetrachloride, and the combined extracts were washed with dilute potassium hydroxide solution.

The carbon tetrachloride phase was dried over calcium chloride and evaporated. A residue (0.25 g.) of white crystals of chlorodurene (3-chloro-1,2,4,5-tetramethylbenzene) of m.p. 37–40° remained (75% yield). This material gave only a faintly positive test for a benzylic type halide with hot alcoholic silver nitrate. After two recrystallizations from aqueous methanol, the melting point[4] of the product was raised to 47°.

Anal. Calcd. for C$_{10}$H$_{13}$Cl: Cl, 21.0. Found: Cl, 20.9.

The water layer remaining from the original carbon tetrachloride extraction was extracted with two 50-ml. portions of ether. The ether extracts were washed with dilute potassium hydroxide solution. The washings were combined with the basic washings of the carbon tetrachloride solution, and hydrochloric acid was added. A total of 0.320 g. (65% yield) of *o*-iodobenzoic acid, m.p. and mixed m.p. with an authentic sample 161–162°, was recovered by filtration.

The Kinetics of Reaction of Durene and Compound A.—Solutions of compound A in acetic acid display appreciable light absorption in the near ultraviolet region. The spectra of solutions of A do not change significantly with time which indicates that A (or its solvation product) is stable in acetic acid. It was demonstrated by spectrophotometric experiments, which were purely qualitative in nature, that the order of reactivity of a series of aromatic hydrocarbons with A was toluene < *m*-xylene < durene < pentamethylbenzene.

In other trial tests it was found that the rate of chlorination of durene varied with different batches of A. Furthermore the rate of reaction was accelerated tremendously when hydrogen chloride[5] was added to the reaction mixture.

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[1] R. M. Keefer and L. J. Andrews, THIS JOURNAL, **80**, 277 (1958).

[2] R. M. Keefer and L. J. Andrews, *ibid.*, **81**, 2374 (1959).

[3] C. Willgerodt, *J. prakt. Chem.*, **49**, 476 (1894).

[4] G. Illuminati and G. Marino, THIS JOURNAL, **78**, 4975 (1956), report a value of 45.5–46.1°.

[5] The details of preparation and analysis of solutions of hydrogen chloride in acetic acid have been reported elsewhere; R. M. Keefer and L. J. Andrews, *ibid.*, **78**, 5623 (1956).

In a solution which was initially 0.075 M in durene, 10^{-2} M in A and 1.8×10^{-2} M in hydrogen chloride, chlorination was immeasurably rapid, whereas in the absence of added hydrogen chloride the disappearance of A could easily be followed. Thus hydrogen chloride is a catalyst for the reaction.

More quantitative investigations on the rate of the reaction of A with durene (Eastman Organic Chemicals material recrystallized from ethanol) were made using a single batch of A. The stock solutions of A in acetic acid (purified as in reference 5) were analyzed iodometrically. Rate samples were prepared by mixing aliquots of stock solutions (which previously had been brought to the desired temperature) in 1-cm. glass stoppered absorption cells. The cells were stored in a temperature controlled (±0.1°) housing of a Beckman spectrophotometer, and the reactions were followed by measuring the optical densities at 360 mμ, a wave length at which A, but not durene, absorbed appreciably at the concentration level of the experiments. The concentrations of chlorodurene (P) in the reaction mixtures at times t were calculated from the optical density, d, and the initial and final optical densities (d_i and d_f) using equation 1.

$$(\mathrm{P}) = (\mathrm{A})_i(d_i - d)/(d_i - d_f) \qquad (1)$$

The effects of changes in concentration of the reactants, HCl, and iodobenzoic acid on the rate of reaction are illustrated qualitatively in Table I, in which the initial rates, R_i, of some of the runs are listed. The values of R_i were obtained from the slopes (at $t = 0$) of plots of (P) *versus* time.

The first three runs of Table I indicate that R_i diminishes as $(\mathrm{A})_i$ is decreased. These changes may be due largely to the corresponding changes in the hydrogen chloride concentration since hydrogen chloride was introduced as an impurity in compound A. To obtain evidence on the effect of hydrogen chloride on the rate of reaction, the hydrogen chloride concentrations in the rate mixtures were varied by adding sodium acetate. It is probable that the reaction of sodium acetate with hydrogen chloride is quantitative ($\mathrm{NaOAc} + \mathrm{HCl} \rightarrow \mathrm{HOAc} + \mathrm{NaCl}$). The R_i values for the second group of three runs ($(\mathrm{A})_i$ and $(\mathrm{D})_i$ constant) were found to approximate a straight line when plotted *versus* (NaOAc). By extrapolation of this line it was determined that R_i would fall to zero when $(\mathrm{NaOAc}) = 1.34 \times 10^{-3}$ M. This value then represents the hydrogen chloride concentration of the 20.6×10^{-3} M solution of A. By a similar treatment of R_i values for a series of runs at $(\mathrm{A})_i = 10.3 \times 10^{-3}$ M, $(\mathrm{D})_i = 0.124$ M and varying (NaOAc), it was estimated the hydrogen chloride content of the 10.3×10^{-3} M solution of A was 0.67×10^{-3} M. It is presumed in further discussion that the hydrogen chloride concentration of 5.15×10^{-3} M A was 0.34×10^{-3} M.

TABLE I

INITIAL RATES OF REACTION OF A WITH DURENE IN ACETIC ACID, 25 ± 0.1°

$10^3(\mathrm{A})_i$, moles/l.	10^3 (NaOAc), moles/l.	$10^3(\mathrm{I})_i$,[a] moles/l.	$10^3(\mathrm{D})_i$,[b] moles/l.	$10^5(R)_i$,[c] moles l.$^{-1}$ sec.$^{-1}$
20.6	..	..	124	13.8
10.3	..	..	124	8.0
5.15	..	..	124	5.9
20.6	0.42	..	124	8.5
20.6	0.70	..	124	7.2
20.6	1.11	..	124	2.7
5.15	..	..	62	2.8
5.15	..	..	31	1.6
10.1	..	..	124	8.6
10.1	..	13.2	124	2.9
10.1	..	26.8	124	1.7

[a] Concentration of added *o*-iodobenzoic acid. [b] Initial concentration of durene. [c] $R = \mathrm{d}P/\mathrm{d}t$.

The linearity of the plots of R_i *versus* (NaOAc) indicates that the reaction is initially first order in hydrogen chloride. The reaction also appears to be first order in durene as indicated by the variations in R_i values with changing durene concentration in runs in which $(\mathrm{A})_i = 5.15 \times 10^{-3}$ M. The addition of *o*-iodobenzoic acid (Eastman Organic Chemicals material recrystallized from aqueous ethanol) to the reaction mixtures causes a marked decrease in R_i values (see Table I). A more quantitative treatment of these and other runs is given in the Results section.

The reaction of freshly precipitated *o*-iodobenzoic acid dichloride with durene was immeasurably rapid. It was noted that the extinction coefficients of A in acetic acid at various wave lengths were strongly enhanced by added hydrogen chloride and were diminished slightly when small amounts of anhydrous sodium acetate were added to the solutions. All the above evidence is in agreement with the assumption that hydrogen chloride reacts with A to form the extremely reactive dichloride of *o*-iodobenzoic acid.

The Influence of Hydrogen Chloride, Sodium Acetate and *o*-Iodobenzoic Acid on the Spectrum of Compound A in Acetic Acid.—The effects of various added substances on the spectrum of compound A in acetic acid are summarized in Table II. The reported molecular extinction coefficients are based on concentrations of A in the solutions as determined by iodometric analysis. The spectrum of a solution of *o*-iodobenzoic acid in acetic acid is also included. The values of the extinction coefficients which were determined for freshly prepared solutions did not change appreciably as the solutions aged. The extinction coefficients of A in a solution to which no hydrogen chloride was added were not appreciably affected by added *o*-iodobenzoic acid.

TABLE II

ABSORPTION SPECTRUM OF COMPOUND A IN ACETIC ACID SOLUTIONS

Solution	λ, mμ	340	360	380	400
1.05×10^{-2} M A[a]	ε	83.5	47.8	19.8	5.5
1.09×10^{-2} M A 0.52×10^{-2} M NaOAc[b]	ε	76.6	37.0	13.1	3.8
1.05×10^{-2} M A 2.73×10^{-2} M HCl	ε	..	113.0	52.9	19.6
5.93×10^{-3} M A 26.9×10^{-3} M *o*-iodobenzoic acid 2.73×10^{-2} M HCl	ε[c]	..	170.3	75.9	29.0
7.99×10^{-2} M *o*-iodobenzoic acid	ε	..	2.4	2	0.6

[a] The extinction coefficients of solutions of A vary somewhat with different preparations of A. The spectrum is unaffected by the presence of NaCl (0.5×10^{-2} M). [b] These values do not change when (NaOAc) is increased to 1×10^{-2} M. [c] The optical densities were corrected for the small absorption of free *o*-iodobenzoic acid before calculation of reported ε-values.

The Equilibria Established in Solutions of Compound A and Hydrogen Chloride in Acetic Acid.—The enhancement of the extinction coefficients of A as the hydrogen chloride concentration of its solutions is increased (Table II) has been attributed previously to reaction to form *o*-iodobenzoic acid dichloride. It may also be concluded that the dichloride is in equilibrium with chlorine and *o*-iodobenzoic acid, as well as with A and hydrogen chloride, since the extinction coefficients of a solution of A and excess hydrogen chloride are enhanced by the addition of the iodo acid (see Table II). Furthermore these equilibria must be established rapidly since the optical densities of the solutions in question do not change with time.

The extinction coefficient of *o*-iodobenzoic acid dichloride was estimated by measuring the optical densities of 6×10^{-3} M solutions of A which contained large excesses of *o*-iodobenzoic acid (27×10^{-3} M) and hydrogen chloride (27×10^{-3} to 57×10^{-3} M). An approximate value of $\epsilon_{360\mathrm{m}\mu}$ 175 was calculated on the assumption that dichloride dissociation was completely repressed.

To evaluate the equilibrium constants K_1 and K_2 (see equations 2 and 3 in which (I) and (B) are the concentrations of *o*-iodobenzoic acid and its dichloride, respectively) the d_{360} values of two series of solutions of A were measured.

$$K_1 = (\mathrm{B})/(\mathrm{A})(\mathrm{HCl}) \qquad (2)$$

$$K_2 = (\mathrm{I})(\mathrm{Cl}_2)/(\mathrm{B}) \qquad (3)$$

In one series iodobenzoic acid (I) was present in large excess over A along with varying amounts of hydrogen chloride. In the other series (I) was varied in the presence of large excesses of hydrogen chloride. The measured optical densities were related to the concentrations of the several substances in equilibrium and to their extinction coefficients by equation 4.

$$d = (\mathrm{A})\epsilon_\mathrm{A} + (\mathrm{B})\epsilon_\mathrm{B} + (\mathrm{I})\epsilon_\mathrm{I} + (\mathrm{Cl_2})\epsilon_{\mathrm{Cl_2}} \qquad (4)$$

The initial concentrations of A and I (before equilibration occurs) are related to the equilibrium concentrations by equations 5 and 6.

$$(\mathrm{A})_\mathrm{i} = (\mathrm{A}) + (\mathrm{B}) + (\mathrm{Cl_2}) \qquad (5)$$

$$(\mathrm{I})_\mathrm{i} = (\mathrm{I}) - (\mathrm{Cl_2}) \qquad (6)$$

Through the fortunate circumstance that ϵ_A (37.0) is equal to $\epsilon_{\mathrm{Cl_2}} + \epsilon_\mathrm{I}$, (34.5 + 2.4) at 360 mμ, equations 4–6 may be solved (equation 7)

$$(\mathrm{B}) = \frac{d - (\mathrm{A})_\mathrm{i}\,\epsilon_\mathrm{A} - (\mathrm{I})_\mathrm{i}\,\epsilon_\mathrm{I}}{\epsilon_\mathrm{B} - \epsilon_\mathrm{A}} \qquad (7)$$

to provide an expression relating (B) to the measured optical densities, initial reactant concentrations and known extinction coefficients. The value of $\epsilon_\mathrm{A} = 37.0$ was obtained by measurement of solutions of A which contained sufficient sodium acetate to remove traces of hydrogen chloride (see Table II).

An initial estimate of K_2 was made by using equation 7 to calculate B from the optical density of a solution of A ($(\mathrm{A})_\mathrm{i} = 6 \times 10^{-3}\ M$) containing a large excess of hydrogen chloride and no added I and by making the assumption that no free A was present in solution at equilibrium. The resultant value of K_2, equation 7, and the estimated value of ϵ_B were used to evaluate K_1 (270 l./mole) for the series of solutions containing a large excess of I and relatively small amounts of hydrogen chloride. These preliminary values of K_1 and K_2 were used to recalculate the value of ϵ_B (using equations 2–7) from the optical densities of solutions of A which contained large excesses of I and hydrogen chloride. The constants K_2, K_1 and ϵ_B were reevaluated by the above procedure until constant values (ϵ_B 200) were obtained. The equilibrium constants thus derived are tabulated in the section on results.

The Dissociation Constants and Dissociation Rates of the Dichlorides of Methyl *o*- and *p*-Iodobenzoates and of *m*- and *p*-Iodobenzoic Acid.—Eastman Organic Chemicals samples of the free iodo compounds were used to prepare the dichlorides. The methyl *o*-iodobenzoate was redistilled (b.p. 138° (12 mm.)) before use. Dilute solutions of the isomeric iodo esters (0.5 g. in 10 to 20 ml. of solvent in acetic acid) were gassed with chlorine to precipitate the dichlorides. The dichloride of *m*-iodobenzoic acid was prepared in similar fashion except that chloroform was used as the solvent. The preparation of the *p*-isomer has been described elsewhere. The yellow precipitates were filtered, washed with carbon tetrachloride and air-dried briefly before they were used. Their equivalent weights were determined by iodometric methods.[1] The experimental equivalent weights for the derivatives of the *o*- and *p*-esters (theoretical 166.5) and for the *m*-acid (theoretical 159.5) were 171, 169 and 159, respectively.

The dissociation of methyl *p*-iodobenzoate dichloride, and also of *m*-iodobenzoic acid dichloride, in dilute solution in acetic acid took place slowly and was followed spectrophotometrically at 380 mμ to equilibrium. The equilibrium and rate constants were calculated by methods used previously.[1,2] The extinction coefficients of the ester and the acid dichlorides (determined from optical density readings of freshly prepared solutions) are, respectively, 104 and 82.3 at 380 mμ, and the corresponding values for the two free iodo compounds and for chlorine are 0.4, 0.5 and 13.1.

The dichloride of methyl *o*-iodobenzoate equilibrated with its components at an immeasurably rapid rate in acetic acid solution. The optical densities (measured at 370 mμ) of freshly prepared solutions did not change with time. The optical densities of the solutions increased with their initial dichloride concentrations, and the increases were considerably more than directly proportional to the concentration changes. Also the optical densities were enhanced sharply as small amounts of free iodo ester were introduced. The extinction coefficient of the undissociated dichloride (ϵ_{370} 150) was obtained by measuring the optical densities of solutions ($3\text{–}6 \times 10^{-3}\ M$) which contained large amounts of the free iodo compound (up to 0.17 M). The extinction coefficient of the latter at 370 mμ is 0.5 and that for chlorine is 22.0.

The rates of dissociation of the dichlorides of the two esters and also of the dichloride of *p*-iodobenzoic acid in the presence of large excesses of durene also were determined spectrophotometrically. The durene served to react with free chlorine as it was formed by dissociation of the dichloride in the same way as does pentamethylbenzene.[2] The dissociation constants k_1 were calculated from measured optical densities (recorded at 370–380 mμ and corrected for small final readings at completion of the reaction) using the rate law

$$-\mathrm{d(durene)}/\mathrm{d}t = -\mathrm{d(ArICl_2)}/\mathrm{d}t = k_1\,(\mathrm{ArICl_2}) \qquad (8)$$

The method already has been described in detail. Actually the reaction of methyl *o*-iodobenzoate dichloride with durene occurred too rapidly to permit even the crudest estimation of the rate.

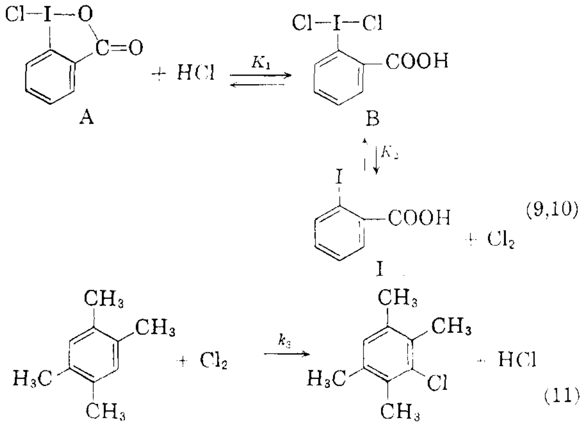
Since equilibration of iodobenzene dichloride does not occur readily in carbon tetrachloride,[6] an attempt was made to find a mixture of carbon tetrachloride and acetic acid of such composition that it would serve as a solvent for comparing the dissociation rate of the highly reactive dichloride of methyl *o*-iodobenzoate with that of its less reactive *p*-isomer. However in a 50–50 volume % of the two solvents the *o*-isomer equilibrated at an immeasurably rapid rate, whereas in a solvent mixture slightly higher in carbon tetrachloride content (67% $\mathrm{CCl_4}$-33% $\mathrm{CH_3COOH}$) the *p*-isomer underwent no dissociation even in three hours time. The reactivity differences of the two isomers is clearly extreme.

The *o*-isomer was found to dissociate with reasonable rapidity even in pure carbon tetrachloride. The optical density readings at the end of the reaction were almost as low as those to be expected had complete dissociation occurred. The rate constants for dissociation, estimated from spectrophotometric data recorded during the course of the equilibration process, were found to vary approximately in proportion to the initial dichloride content of the solutions. These variations are attributed to the inclusion of trace amounts of hydrogen chloride in the reaction mixtures in the form of a contaminant of the starting dichloride. It is unlikely that dissociation would occur at a measurable rate unless some polar catalyst was present.[6]

An attempt also was made to study the dissociation of *o*-nitroiodobenzene dichloride in acetic acid. However the spectrum of the dichloride and the free iodo compound are so similar that the reaction could not be followed spectrophotometrically.

Results

Qualitative evidence has been presented in the Experimental section that the rate of reaction of compound A with durene (to form 3-chloro-1,2,4,5-tetramethylbenzene and *o*-iodobenzoic acid) in acetic acid is first order in durene and first order in hydrogen chloride. Furthermore the reaction is retarded by *o*-iodobenzoic acid. These facts suggest that the course of the reaction is as described by equations 9–11. The slow step in the proposed



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(6) L. J. Andrews and R. M. Keefer, THIS JOURNAL, **80**, 1723 (1958).

scheme, that between chlorine and durene, is preceded by two rapid equilibration processes.[7]

The rate law which conforms to equations 9–11, where (P) represents the chlorodurene product concentration, is

$$\mathrm{d(P)}/\mathrm{d}t = k_3K_1K_2\mathrm{(A)(HCl)(D)/(I)} \qquad (12)$$

The rate runs made in studying this reaction were conducted with durene in large excess of compound A. Hydrogen chloride was introduced as a trace contaminant with A, and its amount was estimated and was varied (by sodium acetate addition) as has been described in the Experimental section. Using the equilibrium constants K_1 and K_2, as defined in equation 2 and 3, and the relationships 13–15, which apply during the course of the runs

$$\mathrm{(HCl)_i = (B) + (Cl_2) + (HCl)} \qquad (13)$$

$$\mathrm{(A)_i = (A) + (B) + (Cl_2) + (P)} \qquad (14)$$

$$\mathrm{(I) = (I)_i + (Cl_2) + (P)} \qquad (15)$$

an expression can be derived which relates free chlorine concentrations to the two equilibrium constants and to the initial concentrations of the starting materials. When this expression is substituted in equation 12, an experimentally useful rate law, equation 16, is obtained. In applying this equation

$$R = \frac{\mathrm{d(P)}}{\mathrm{d}t} = \frac{k_3K_1K_2[\mathrm{(A)_i - (P)](HCl)_i(D)}}{[1 + K_1\{\mathrm{(A)_i - (P) + (HCl) - (Cl_2)}\}]\,\mathrm{(I)} + K_1K_2[\mathrm{(HCl)_i + (A)_i - (P) - (Cl_2)}]} \qquad (16)$$

to the interpretation of data, the terms in (HCl) and (Cl_2) in the denominator, which are very small, were neglected (see equation 17, in which $\mathrm{(A)_t = (A)_i - (P)}$).

$$\frac{R}{\mathrm{(HCl)_i(D)}} = \frac{k'\mathrm{(A)_t}}{\mathrm{(I)}[(1 + K_1\mathrm{(A)_t}] + K_1K_2[\mathrm{(HCl)_i + (A)_t}]} \qquad (17)$$

Values of R at various times during the rate runs were obtained from the slopes of plots of experimental values of (P) *versus* time. The (P) values were calculated from spectrophotometric data using equation 1, which is accurate provided the concentration of B (which makes some contribution to the measured optical densities) does not change appreciably during the runs. It can be demonstrated that such changes in (B) introduce only minor errors, which are greatest in the initial stages of the runs. Values of k' were calculated (equation 17) on the assumption that (I) = (I)i + (P). The required equilibrium constants, K_1 and K_2, which were estimated as described in the Experimental section, are given in Table III.

Two typical rate runs are summarized in Table IV and a complete tabulation of k' values for all of the runs is given in Table V. The rate constants k' increased somewhat during the course of the runs, and the increases were most pronounced for reaction mixtures which initally contained no *o*-iodobenzoic acid. However the agreement in average k'-values for runs of varying initial concentrations of A, hydrogen chloride,

TABLE III

THE EQUILIBRIUM CONSTANTS[a] K_1 AND K_2 IN ACETIC ACID, 25.0°

10^3(A)i, moles/l.	$10^3\mathrm{(HCl)_i}$, moles/l.	$10^3\mathrm{(I)_i}$, moles/l.	K_1, l./mole
5.93	1.42	26.6	215
5.93	2.85	26.6	208
5.93	5.70	26.6	204
2.97	2.85	26.6	204
			K_2, mole/l.
5.56	27.3	0.2	2.4
2.78	27.3	.1	2.5
1.39	27.3	.05	2.5
5.56	27.3	13.3	1.8

[a] Values of K_1 = 205 l./mole, and $K_2 = 2.4 \times 10^{-3}$ mole/l. were used in calculating k' values from equation 17.

durene and *o*-iodobenzoic acid is remarkably good considering the complexity of the reaction mechanism. It is gratifying to observe that the value of k_3 (4.3 l. mole^{-1} sec.$^{-1}$) obtained by dividing the average experimental value of k' (at 80% reaction time) by K_1K_2 is about the same as the second-order rate constant previously obtained for the reaction of chlorine with durene in acetic acid[8] at 25.2° (~4 l. mole^{-1} sec.$^{-1}$). Clearly the proposed reaction scheme, equations 9–11, which requires that *o*-iodobenzoic acid dichloride equilibrate rapidly with chlorine and the free iodo compound, adequately explains the kinetic data.

TABLE IV

THE k'-VALUES FOR TYPICAL RUNS (ACETIC ACID SOLVENT, 25.0°)

$\mathrm{(A)_i} = 20.6 \times 10^{-3}\ M$ $\mathrm{(A)_i} = 20.2 \times 10^{-3}\ M$
$\mathrm{(D)_i} = 0.124\ M$ $\mathrm{(D)_i} = 0124\ M$
$\mathrm{(HCl)_i} = 1.34 \times 10^{-3}\ M$ $\mathrm{(HCl)_i} = 1.34 \times 10^{-3}\ M$
$\mathrm{(I)_i} = 0$ $\mathrm{(I)_i} = 26.9 \times 10^{-3}\ M$

10^3(P), moles/l.	$10^5 \frac{R}{\mathrm{(D)(HCl)_i}}$ mole^{-1} l. sec.$^{-1}$	k',[a] mole^{-1} l. sec.$^{-1}$	10^3(P), mole/l.	$10^5 \frac{R}{\mathrm{(D)(HCl)}}$, mole^{-1} l. sec.$^{-1}$	k,[a] mole^{-1} l. sec.$^{-1}$
4.0	0.69	1.1	4.0	0.21	1.9
6.0	.59	1.3	6.0	.21	2.0
8.0	.52	1.5	8.0	19	2.0
10.0	.45	1.6	10.0	.18	2.1
12.0	.39	1.7	12.0	.17	2.1
14.0	.33	1.9	14.0	.15	2.4
16.0	.30	2.2	16.0	.13	2.5

[a] The increase in k' during the runs may reflect errors in calculated R-values resulting from the inaccuracy of experimental values of K_1 and K_2 or from the neglect of changes in the concentration of free dichloride (B) during a run.

Methyl *o*-iodobenzoate dichloride also was found to equilibrate with its components at an immeasurably fast rate in acetic acid. On the other hand, the dichlorides of *m*- and *p*-iodobenzoic acid and of methyl *p*-iodobenzoate equilibrated slowly in acetic acid, and their rates of reaction with durene were controlled entirely by the rate of dissociation of the dichlorides. The chlorination of durene in acetic acid solutions of methyl *o*-iodobenzoate dichlo-

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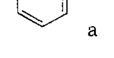
(7) In acetic acid solution compound A may actually exist in the form a. The kinetic treatment which is presented applies equally well to A and to its solvolysis product.



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(8) R. M. Keefer and L. J. Andrews, THIS JOURNAL, **79**, 4348 (1957).

Table V

Rate Constants for the Reaction of A with Durene (Acetic Acid, 25.0°)

$10^3(\mathrm{A})_i$, moles/l.	$10^3(\mathrm{D})_i$, moles/l.	$10^3(\mathrm{HCl})_i$, moles/l.	$10^3(\mathrm{I})_i$, moles/l.	k' (20),[a] mole^{-1} l. sec.$^{-1}$	k' (80),[a] mole^{-1} l. sec.$^{-1}$
20.6	124	1.34	0	1.1	2.2
20.6	124	0.92	0	1.1	2.3
20.6	124	.64	0	1.2	2.2
20.6	124	.23	0	1.1	2.3
10.3	124	.67	0	1.1	2.2
10.3	124	.39	0	1.0	2.0
10.3	124	.25	0	1.1	2.2
5.15	124	.33^5	0	1.2	1.7
5.15	62	.33^5	0	1.2	1.7
5.15	31	.33^5	0	1.4	2.1
10.3	124	.67	13.2	1.8	2.4
20.2	124	1.34	26.9	1.9	2.5
10.1	124	0.67	26.9	1.9	2.1
5.05	124	0.33^5	26.9	1.9	1.7

[a] The terms $k'_{(20)}$ and $k'_{(80)}$ represent rate constants at 20 and 80% reaction, respectively.

ride (at initial reactant concentrations comparable to those used in studying the *p*-isomer) occurred at an immeasurably fast rate. The equilibrium constants, K_d, for dissociation of these dichlorides (equation 18) are summarized in Table VI and the

$$\mathrm{ArICl_2} \underset{k_2}{\overset{k_1}{\rightleftarrows}} \mathrm{ArI} + \mathrm{Cl_2} \quad K_d = \frac{k_1}{k_2} = \frac{(\mathrm{ArI})(\mathrm{Cl_2})}{(\mathrm{ArICl_2})} \quad (18)$$

rate constants for their dissociation (k_1) both in the presence and absence of durene are listed in Table VII.

Table VI

Equilibrium Constants (K_d) in Acetic Acid Solution

$10^3(\mathrm{ArICl_2})_i$, moles/l.	10^3K, moles/l.	$10^3(\mathrm{ArICl_2})_i$, moles/l.	10^3K, moles/l.
Methyl *p*-iodobenzoate, 25.0°		Methyl *o*-iodobenzoate, 25.0°	
8.85	13.8	9.56	2.68
5.86	13.4	6.36	2.70
2.88	11.0	6.15	2.68
Av.	12.7 ± 1.2	3.15	2.67
p-Iodobenzoic acid,[1] 25.2°		Av.	2.68 ± 0.01
...	15.7	Methyl *o*-iodobenzoate, 45.1°	
m-Iodobenzoic acid, 25.1°		10.1	8.0
10.60	9.1	6.75	7.9
6.99	8.5	3.37	7.8
3.50	7.8	Av.	7.9 ± 0.1
Av.	8.5 ± 0.3		

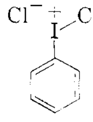
Table VII

Rate Constants for Dichloride Dissociation in Acetic Acid, 25.0°

10^3-(ArICl$_2$)$_i$, moles/l.	10^3(D), moles/l.	10^4k_1, sec.$^{-1}$	10^3-(ArICl)$_i$, moles/l.	10^3(D), moles/l.	10^4k_1, sec.$^{-1}$
m-Iodobenzoic acid			Methyl *o*-iodobenzoate		
10.60	..	2.02	10.0	0.124	Very large
6.99	..	1.48			
3.50	..	1.76	Methyl *p*-iodobenzoate		
p-Iodobenzoic acid			8.85	.....	1.53
...	..	1.50[a]	5.86	.....	1.55
5.80	124	1.66	2.88	.....	1.52
2.90	124	1.40	6.76	125	1.46[b]
2.90	248	1.28	3.38	125	1.42[b]

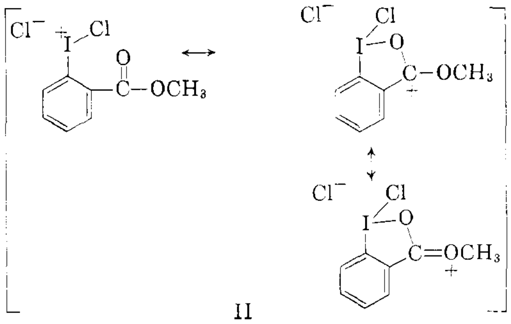
[a] Rate constant reported in ref. 1 for reaction in the absence of durene. [b] The reported constants are based on initial rates. The constants increased somewhat with time, possibly because of the accumulation of hydrogen chloride in the reaction mixtures.

The abnormally high dissociation rate of *o*-iodobenzoic acid dichloride cannot be attributed to a specific influence of the proton of the carboxyl group in the activation process since the methyl ester of this dichloride is also extremely reactive. The enthalpies and entropies of dissociation of methyl *o*-iodobenzoate dichloride (ΔH^0 = 10.1 kcal./mole and ΔS^0 = 22.2 e.u.), which were calculated from K_d values at 25.0 and 45.1°, are similar to those of several *m*- and *p*-substituted iodobenzene dichlorides which dissociate at easily measurable rates in acetic acid.[1] It seems reasonable, therefore, that the enhancement of reaction rate, as produced by *o*-COOH and *o*-COOCH$_3$ groups must result largely because these substituents serve, in the manner of a neighboring group in carbonium ion reactions, to stabilize the activated complex which separates the dichloride from its dissociation products. The structure I has been proposed for the activated complex of the unsubstituted dichloride.[1,2]



I

The modification II (as applied to the ester) is now proposed to account for the *o*-carboxyl and carbomethoxy effects.



II

Less formally it might be argued that the creation of positive charge on the iodine atom in the activated complex is facilitated electrostatically through the proximity of the electron-rich *o*-substituent. Although this *o*-substituent effect may be to a small degree steric in origin it seems certain, in view of past experience with other *o*-substituted dichlorides,[1] that the extreme differences in reactivity of the *o*- and *p*-carboxyl derivatives (and of their esters) cannot adequately be treated in terms of space problems. For reasons discussed in the Experimental section an attempt to measure the dissociation rate of *o*-nitroiodobenzene dichloride in acetic acid (to determine whether other electron-rich *o*-substituents than carboxyl also had a marked rate influence) was unsuccessful.

There are other indications in the literature that *o*-carboxyl and related substituents have a highly specific influence on reactions at aromatic side chains. For example in chloroform, bis-(*o*-iodobenzoyl) peroxide rearranges to a cyclic substance resembling compound A at a rate several thousand times as large as the dissociation rates of other *o*-substituted benzoyl peroxides.[9] Also α-bromo-*o*-toluic acid and related compounds can be converted to phthalide with great ease.[10] Furthermore it has been demonstrated neatly that *o*-carboxyl, or its anine, functions as an "internal" nucleophilic catalyst in the hydrolysis of phthalamic acid, methyl hydrogen phthalate and related compounds.[11] This terminology might well be applied in the interpretation of the results of the present investigation.

Electronically the activation process for solvolytic displacement reactions of benzyl halides and related compounds, which are presumed to react *via* benzylcarbonium ion intermediates,[12] is similar to that for dissociation of iodobenzene dichloride. One may anticipate, therefore, that an *o*-carboxyl substituent would greatly enhance the rates of solvolysis of α-substituted toluenes. There seems to be no quantitative kinetic evidence, pro or con, of such enhancement. (It is noteworthy that certain appropriate model compounds decompose rather readily to form phthalide.[13]) Accordingly, plans are now being made to investigate the kinetics of acetolysis of appropriately substituted benzyl tosylates.

Acknowledgment.—The authors are indebted to the National Science Foundation for a grant in support of this research.

[9] J. E. Leffler, R. D. Faulkner and C. C. Petropoulos, THIS JOURNAL, **80**, 5435 (1958).

[10] W. Davies and W. H. Perkin, *J. Chem. Soc.*, **121**, 2202 (1922).

[11] (a) M. L. Bender, Y. Chow and F. Chloupek, THIS JOURNAL, **80**, 5380 (1958); (b) M. L. Bender, F. Chloupek and M. C. Neveu, *ibid.*, **80**, 5384 (1958); (c) M. L. Bender and M. C. Neveu, *ibid.*, **80**, 5388 (1958).

[12] J. Kochi and G. S. Hammond, *ibid.*, **75**, 3445 (1953).

[13] S. C. J. Olivier, *Rec. trav. chim.*, **42**, 516 (1923).

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF PURDUE UNIVERSITY]

Alkylation of Nitroparaffins and Oximes with Epoxides[1]

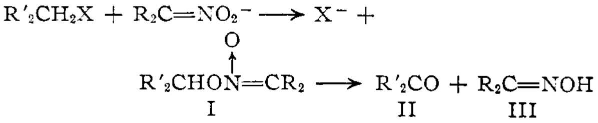
BY G. BRYANT BACHMAN AND TAKEO HOKAMA[2]

RECEIVED DECEMBER 27, 1958

The reactions of epoxides with nitroparaffin salts have been found to lead through O-alkylation to oximes and their β-hydroxyalkyl ethers. A number of these oxime ethers have been prepared and characterized.

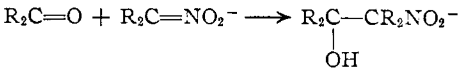
The nitronate ion is an "ambident anion"[3] and may react with reagents such as alkyl halides at one of the oxygens of the nitro group (O-alkylation) or at the carbon attached to the nitro group (C-alkylation). Numerous workers have investigated the reactions of nitroparaffin salts with such alkylating agents as alkyl halides,[4] alkyl sulfates,[5,6] diazomethane,[5,6] benzyltrimethylammonium iodides[7] and various other onium salts.[8]

Except for a few special cases[4a,4b,7] these reactions have generally resulted in O-alkylation. The nitronate esters (I) have been isolated in several cases[4b,5,9] but usually they decompose during the reaction to form a carbonyl compound (II) and an oxime (III). The process has been used as a method of oxidizing alkyl halides to aldehydes and ketones.[10]



$$R'_2CH_2X + R_2C{=}NO_2^- \longrightarrow X^- + \underset{\text{I}}{R'_2CHO\overset{\overset{O}{\uparrow}}{N}{=}CR_2} \longrightarrow \underset{\text{II}}{R'_2CO} + \underset{\text{III}}{R_2C{=}NOH}$$

In striking contrast to these results aldehydes and ketones give C-alkylation with nitronate anions.[4c]



$$R_2C{=}O + R_2C{=}NO_2^- \longrightarrow R_2\underset{\underset{OH}{|}}{C}{-}CR_2NO_2^-$$

Since olefin oxides resemble aldehydes and ketones in many of their reactions it seemed reasonable to study the reaction of some typical olefin oxides with nitroparaffins in alkaline solution in the hope of achieving C-alkylations. However, instead of the hoped for γ-nitroalcohols which would result from C-alkylation, we obtained instead, oximes and oxime ethers, whose formation can be explained as resulting from the preliminary O-alkylation of the nitronate ion and the decomposition of this to a carbonyl compound and an oxime.

Since β-hydroxyalkyl ethers of oximes seem not to have been prepared previously, we synthesized a number of them for purposes of comparison by treating oximes with olefin oxides under basic conditions. The products so obtained corresponded

[1] Abstracted from a thesis submitted by T. Hokama to the Faculty of the Graduate School of Purdue University in partial fulfillment of the requirements for the Ph.D. degree, August, 1958.

[2] American Cyanamid Fellow, 1957–1958.

[3] N. Kornblum, R. A. Smiley, R. K. Blackwood and D. C. Iffland, THIS JOURNAL, **77**, 6269 (1955).

[4] (a) L. Weisler and R. W. Helmkamp, *ibid.*, **67**, 1167 (1945); (b) M. L. Bender and H. B. Hass, *ibid.*, **71**, 3842 (1949); prior literature on the alkylation of nitroparaffins may be found in the Ph.D. theses of L. Weisler, University of Illinois, and M. L. Bender, Purdue University; (c) H. B. Hass and E. F. Riley, *Chem. Revs.*, **32**, 406 (1943).

[5] F. Arndt and J. D. Rose, *J. Chem. Soc.*, 1 (1935).

[6] K. von Auwers and B. Otten, *Ber.*, **57**, 456 (1924).

[7] H. Shechter and R. B. Kaplan, THIS JOURNAL, **73**, 1883 (1951).

[8] L. G. Donaruma, *J. Org. Chem.*, **22**, 1024 (1957).

[9] J. T. Thurston and R. L. Shriner, THIS JOURNAL, **57**, 2163 (1935).

[10] M. L. Bender and H. B. Hass, THIS JOURNAL, **71**, 1767 (1949).