

parison, using the high temperature inlet system of an Atlas CH4 mass spectrometer at an ionizing potential of 70 eV and an ionizing current of 30  $\mu$ A.

The exact-mass data were obtained by peak matching against heptacosafuorotributylamine. For the calculation of elemental compositions, all values were within  $\pm 2.5$  millimass units, and 73% were within  $\pm 1.0$  mmu, of the theoretical value. Above  $m/e$  146, all values were within 10 ppm of the theoretical value.

**Combined Glpc-Mass Spectrometry.** The combined glpc-mass spectrometric studies were conducted with an LKB-9000 gas chromatograph-mass spectrometer using an ionizing energy of 70 eV. The ion source block was maintained at 190° and the molecular separator at 170°. The glpc column consisted of coiled glass (6 ft  $\times$   $\frac{1}{8}$  in. i.d.) packed with 3% OV-1. The column was operated isothermally (see figures). The inner gas flow was maintained at 40 cc/min.

**Deuterated D-glucose derivatives** were obtained from Merck Sharp and Dohme of Canada, Limited. **2-O-Methyl-D-glucose** was prepared by the procedure of Brigl and Schinle, mp 158–159° (lit.<sup>34</sup> mp 158°). **3-O-Methyl-D-glucose** was obtained from CalBiochem Co., mp 161–162° (lit.<sup>35</sup> mp 161°). **Ethyl  $\beta$ -D-galactofuranoside** was prepared by the method of Green and Pascu.<sup>36</sup> It was used as a syrup; the TMSi derivative gave a single component on the gas chromatogram. **Methyl 3-acetamido-3-deoxy- $\alpha$ -D-glucopyranoside** was prepared by the method of Baer,<sup>37</sup> mp 213–214° (lit.<sup>37</sup>

mp 214–215°). **Methyl 2-acetamido-2-deoxy- $\alpha$ -D-glucopyranoside** was prepared by the procedure of Kuhn and coworkers,<sup>38</sup> mp 186–187° (lit.<sup>38</sup> mp 187–188°). **Methyl  $\beta$ -D-ribofuranoside** was prepared by the method of Barker and Fletcher,<sup>39</sup> mp 74–76° (lit.<sup>39</sup> mp 79–80°). Trimethylsilyl derivatives were prepared in the usual manner<sup>7</sup> and purified by preparative glpc using a column of SE-30 (2.5%) adsorbed on Chromosorb W.

**Acknowledgment.** The support of the Alfred P. Sloan Foundation and of the Public Health Service of the Department of Health, Education, and Welfare, through Grants AI07570 and GM 12328 is gratefully acknowledged by D. C. DeJongh. The AEI MS 902 high-resolution mass spectrometer was purchased with funds awarded to Wayne State University under the National Science Foundation's Higher Education Facilities Program. The support of the Public Health Service through Grant/AM 04308 and AM 12434 is acknowledged by C. C. Sweeley; the LKB-9000 gas chromatograph-mass spectrometer was purchased under Grant FR 00273.

(37) H. H. Baer, *Chem. Ber.*, **93**, 2865 (1960).

(38) R. Kuhn, F. Zilliken, and A. Gauhe, *ibid.*, **86**, 466 (1953).

(39) R. Barker and H. G. Fletcher, Jr., *J. Org. Chem.*, **26**, 4605 (1961).

(34) P. Brigl and R. Schinle, *Ber.*, **63B**, 2884 (1930).

(35) J. C. Irvine and T. P. Hogg, *J. Chem. Soc.*, **105**, 1386 (1914).

(36) J. W. Green and E. Pascu, *J. Am. Chem. Soc.*, **59**, 1205 (1937).

## Effects of Substituents on the Exchange of Iodine with Benzoyl Iodides in Nonpolar Solvents

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**Abstract:** Substituted benzoyl iodides undergo isotopic exchange with elementary iodine at conveniently measurable rates in solvents of low dielectric constant near room temperature. Rates in 1,2-dichloroethane (dielectric constant 10) are about 100 times those in hexane (dielectric constant 2). The rates contain kinetic contributions from parallel paths containing zero, one, and two molecules of iodine in the transition state, but photochemically generated iodine atoms do not contribute significantly to the exchange. In hexane at 25°, unsubstituted benzoyl iodide exchanges by the single iodine molecule path 43 times as rapidly as *p*-chlorobenzoyl iodide does. This difference is consistent with a Hammett  $\rho$  of  $-7$ , which is larger in magnitude than has been claimed for any other reaction of neutral molecules. Although some anomalies remain unexplained, these exchange reactions obviously involve very polar transition states even in solvents of low dielectric constant and may be useful for studying effects of solvent on chemical reactivity.

**B**enzoyl iodide,  $C_6H_5COI$ , exchanges easily with isotopically labeled elementary iodine in nonpolar solvents near room temperature.<sup>2</sup> Most of the rate is consistent with parallel paths having one and two molecules of elementary iodine in the respective transition states. In hexane, the entropies of activation for both paths are about  $-50$  cal/(mol deg), and the rate in 1,2-dichloroethane (dielectric constant 10) is about 60 times that in hexane (dielectric constant 2). These observations suggest that the transition states involve so much separation of charge that they approximate ion pairs even in hexane.

If this mechanistic conclusion is correct, the rate of

exchange should be very sensitive to different substituents on the aromatic ring. If the reaction develops almost a full unit of charge, electron-donating and -withdrawing substituents can greatly affect the charge distribution in the aromatic system. Any redistribution of electrical charge caused by a substituent will be opposed by polarization of the surrounding solvent. Since such polarization will be minimal for a solvent like hexane, substituent effects on ion-pair reactions should be maximized.

The experiments reported here were undertaken to test the above prediction and to obtain information concerning substituent and solvent effects on the rate of this exchange.

### Experimental Section

**Materials.** *p*-Chlorobenzoyl iodide was prepared by passing hydrogen iodide into neat *p*-chlorobenzoyl chloride at 50°. The

(1) Based on the Ph.D. dissertation of Donald W. Hamilton.

(2) A. Goldman and R. M. Noyes, *J. Am. Chem. Soc.*, **79**, 5370 (1957).

crude product was dissolved in hexane, the iodine that had formed was removed with copper foil, and the organic iodide was crystallized three times from chilled hexane. The white solid melted 31.0–31.8° and hydrolyzed to *p*-chlorobenzoic acid and iodide ion.

*Anal.* Calcd for C<sub>7</sub>H<sub>4</sub>OClI: C, 31.55; H, 1.50; I, 47.6. Found: C, 31.73; H, 1.58; I, 46.8.

*p*-Nitrobenzoyl iodide could not be prepared in the same way because the nitro group apparently oxidized the hydrogen iodide. It was synthesized by the action of sodium iodide on *p*-nitrobenzoyl chloride in dry acetonitrile. The salts were precipitated by addition of benzene, and the filtered solution was evaporated. The product was recrystallized repeatedly from hexane containing a minimum of benzene. The resulting yellow needles melted 77.8–78.2° with decomposition. Since the material darkened slowly at room temperature, it was not sent for analysis. Titration indicated 45.41% hydrolyzable iodide compared to a theoretical value of 45.82%. Structure was further proved by hydrolysis to *p*-nitrobenzoic acid and methanolysis to the proper ester.

*p*-Toluyyl iodide was prepared by action of hydrogen iodide on *p*-toluyyl chloride. This material was so sensitive to hydrolysis that it would fume in moist air, and no kinetic studies were made with it.

Reagent grade resublimed iodine was used without further purification. Solutions were activated by shaking an aqueous solution of carrier-free iodine-131 obtained from the Oak Ridge National Laboratory. These activated solutions were dried with magnesium sulfate and filtered through sintered glass.

Hexane solvent was purified from unsaturated material by stirring with concentrated sulfuric acid and then twice with 30% fuming acid. It was then washed with sodium carbonate and water, dried with calcium chloride, and distilled from potassium. The product was stored over magnesium sulfate and filtered before use. Tests with radioactive material indicated that less than  $2 \times 10^{-6}$  mol/l. of iodine was irreversibly bound by the solvent.

1,2-Dichloroethane was purified by stirring with concentrated sulfuric acid and treated in the same way as the hexane except that potassium was omitted from the distillation. The solvent bound less than  $2 \times 10^{-5}$  mol/l. of iodine.

**Procedures.** Concentrations of elementary iodine were measured spectrophotometrically. Measurements in hexane were made at 525 m $\mu$  with an extinction coefficient of 912 l./mol cm). Measurements in dichloroethane were made at 496 m $\mu$  with an extinction coefficient of 895 l./mol cm). The iodine solutions used to determine the extinction coefficients were analyzed by reducing the iodine with aqueous sodium sulfite and titrating the resulting iodide ion potentiometrically with standardized silver nitrate by the method of Shiner and Smith.<sup>3</sup>

The aroyl iodides were analyzed by hydrolysis through refluxing or stirring the solution in contact with aqueous sodium hydroxide. The organic solvent was then removed by evaporation, the solution was acidified, and the precipitate of substituted benzoic acid was removed by filtration. The iodide in the filtrate was titrated potentiometrically with standardized silver nitrate.

Radioactivity was measured with thin-walled liquid jacketed Geiger tubes. At least 10,000 counts per sample were accumulated whenever possible, and coincidence corrections were applied when appropriate.

The temperature of exchange runs was controlled by conventional procedures. When the solution was below room temperature, a stream of dry nitrogen was used to minimize condensation of atmospheric moisture during the time needed to remove aliquots.

Six samples taken at different times were generally used for each run. Each sample was rapidly quenched with a chilled aqueous sodium sulfite solution to remove the elementary iodine. Tests demonstrated that no more than 0.4% of the substituted benzoyl iodide was hydrolyzed during operations somewhat more severe than those encountered in a normal separation. The washed organic layer was diluted to a known volume, and the radioactivity was measured and compared with that originally present as elementary iodine.

## Results

When sufficient precautions were taken to eliminate the effects of moisture from the atmosphere, good linear semi-logarithmic plots were obtained for each run. Extrapolation backward to the time of mixing indicated that the

**Table I.** Rate Constants for Exchange of *p*-Chlorobenzoyl Iodide in Hexane

Temp, °C	[ArCOI], mol/l.	$k_1 \times 10^3$ , l./mol sec	$k_2$ , l. <sup>2</sup> /mol <sup>2</sup> sec
60.0	0.0300	$3.10 \pm 0.08$	$0.337 \pm 0.014$
	0.0100	$2.99 \pm 0.24$	$0.313 \pm 0.054$
40.0	0.100	$1.00 \pm 0.04$	$0.183 \pm 0.006$
	0.0300	$0.67 \pm 0.05$	$0.169 \pm 0.008$
	0.0100	$0.84 \pm 0.15$	$0.123 \pm 0.026$
25.0	0.0300	$0.189 \pm 0.055$	$0.093 \pm 0.009$

separation procedure induced a small amount of exchange, but apparently the effect was reproducible enough that the rate of exchange could be calculated with confidence.

Spectrophotometric measurements demonstrated that the concentration of elementary iodine did not change during a run. Parallel measurements in dark and illuminated solutions showed no significant photochemical acceleration and clearly demonstrated that the principal mechanism of exchange does not involve free iodine atoms.

Let  $v$  be the rate of exchange in a run, and let [ArCOI] be the concentration of substituted benzoyl iodide. Figures 1 to 4 illustrate plots of  $v/[ArCOI]$  against  $[I_2]$ , all of the runs in a particular figure being at the same concentration of aroyl iodide. That concentration is 0.030 *M* except that the *p*-chloro compound in dichloroethane was so reactive that a concentration of 0.0050 *M* had to be used. The numerical data for the rates of these runs and for runs at other concentrations of aroyl iodide are available elsewhere.<sup>1</sup>

For each figure, the runs at each temperature could be fitted empirically to the three-parameter equation

$$v/[ArCOI] = k_0 + k_1[I_2] + k_2[I_2]^2 \quad (1)$$

suggested by previous work.<sup>2</sup> However, not all parameters were necessary for some of the situations. Thus, the plots for *p*-nitrobenzoyl iodide (Figures 3 and 4) show no curvature and indicate that the  $k_2$  term is unimportant. In contrast, the plots for *p*-chlorobenzoyl iodide (Figures 1 and 2) show definite curvature but have intercepts so near the origin that the  $k_0$  term contributes significantly only to runs at the lowest iodine concentrations. In fact, the data available for this compound in hexane solvent could be fitted satisfactorily by using two parameters without invoking the  $k_0$  term at all.

Table I presents the rate constants for different concentrations of *p*-chlorobenzoyl iodide in hexane. Data at each temperature and concentration of aroyl iodide were fitted by a two-parameter least-squares calculation that neglected the  $k_0$  term, and probable errors in  $k_1$  and  $k_2$  were assigned by conventional statistical procedures based on the deviations of individual runs from the calculated curve.

The data on which Figure 1 and Table I are based were gathered before the possible significance of the  $k_0$  term was recognized. Only at 40° were runs carried to sufficiently low iodine concentrations to justify any attempt to evaluate  $k_0$ . The data at this temperature suggest  $k_0$  might be about  $0.2 \times 10^{-6}$  sec<sup>-1</sup>; such a term contributes about 20% to the rate at 0.001 *M* iodine and a smaller fraction at all greater concentrations.

(3) V. J. Shiner, Jr., and M. L. Smith, *Anal. Chem.*, **28**, 1043 (1956).

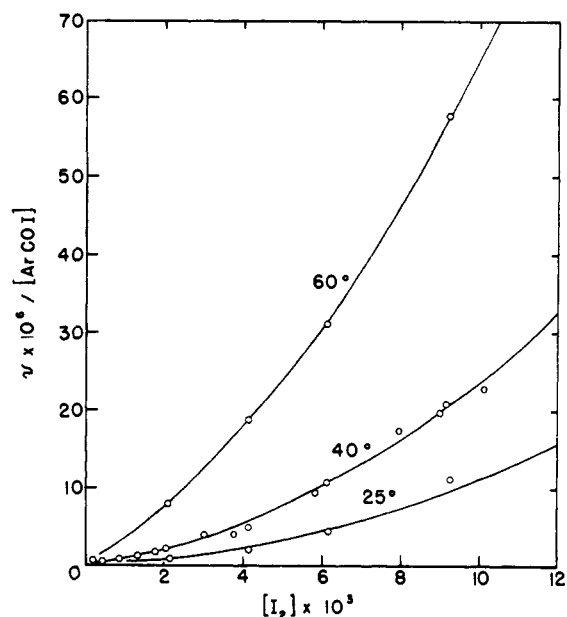


Figure 1. Rate of exchange of 0.0300 *M* *p*-chlorobenzoyl iodide with iodine in hexane.

Table II. Rate Constants for Exchange of 0.00500 *M* *p*-Chlorobenzoyl Iodide in Dichloroethane

Temp, °C	$k_0 \times 10^6$ , sec <sup>-1</sup>	$k_1 \times 10^3$ , l./mol sec	$k_2$ , l. <sup>2</sup> /mol <sup>2</sup> sec
40.0	35.0 ± 7.5	468 ± 18	17.5 ± 4.1
25.0	25.0 ± 0.6	190 ± 2	12.6 ± 0.6
0.0	7.0 ± 1.0	30.3 ± 2.5	7.7 ± 0.7

Table III. Rate Constants for Exchange of 0.0300 *M* *p*-Nitrobenzoyl Iodide

Temp, °C	$k_0 \times 10^6$ , sec <sup>-1</sup>	$k_1 \times 10^3$ , l./mol sec
Hexane Solvent		
60.0	1.38 ± 0.27	0.782 ± 0.059
50.0	1.08 ± 0.02	0.336 ± 0.003
40.0	0.62 ± 0.06	0.197 ± 0.015
Dichloroethane Solvent		
60.0	137.0 ± 8.0	27.8 ± 1.4
40.0	25.8 ± 1.3	3.88 ± 0.27
25.0	9.09 ± 0.12	0.241 ± 0.021

The 40° data in Table I indicate that the rate constants increase by barely significant amounts when the ArCOI concentration increases from 0.01 to 0.1 *M*. Similar behavior was observed with unsubstituted benzoyl iodide in this solvent<sup>2</sup> and was ascribed to change in character of the medium rather than to an order greater than unity in aryl iodide; the same interpretation seems appropriate for the present case.

Table II presents the rate constants used to calculate the curves in Figure 2 for 0.0050 *M* *p*-chlorobenzoyl iodide in dichloroethane. These data are the only ones for which all three parameters of eq 1 were clearly necessary to fit

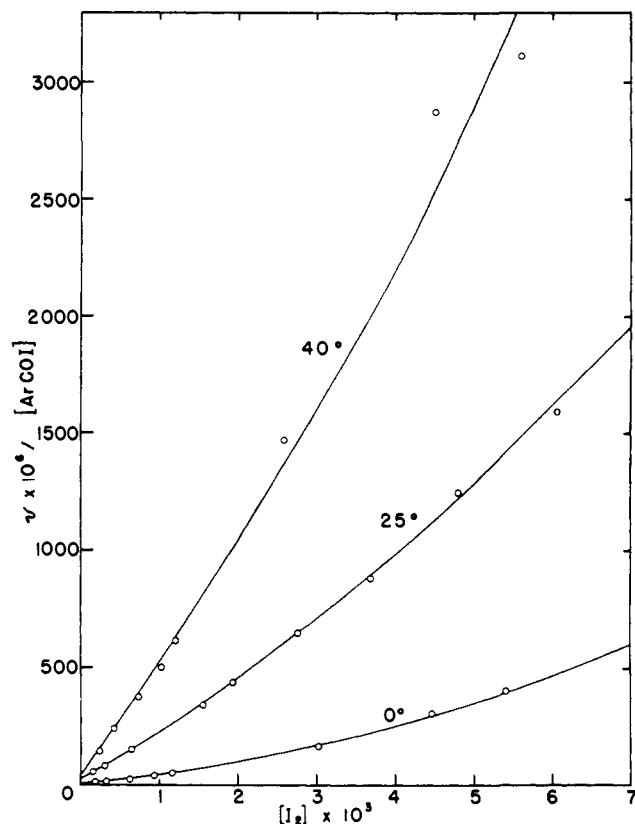


Figure 2. Rate of exchange of 0.00500 *M* *p*-chlorobenzoyl iodide with iodine in dichloroethane.

Table IV. Parameters Based on Temperature Dependence of Rate Constants

Rate constant	Log A	E, kcal/mol	ΔS*, cal/(mol deg)
0.0300 <i>M</i> <i>p</i> -Chlorobenzoyl Iodide in Hexane			
$k_1$	7.9 ± 0.5	15.9 ± 0.7	-24.3 ± 2.2
$k_2$	4.3 ± 0.3	7.2 ± 0.5	-41.1 ± 1.5
0.00500 <i>M</i> <i>p</i> -Chlorobenzoyl Iodide in Dichloroethane			
$k_0$	1.1 ± 0.6	7.7 ± 0.8	-55.6 ± 2.7
$k_1$	7.7 ± 2.5	11.5 ± 0.3	-25.4 ± 1.1
$k_2$	3.5 ± 0.4	3.3 ± 0.6	-44.4 ± 2.0
0.0300 <i>M</i> <i>p</i> -Nitrobenzoyl Iodide in Hexane			
$k_0$	0.7 ± 1.2	9.9 ± 1.7	-57.4 ± 5.3
$k_1$	6.1 ± 1.1	14.2 ± 1.3	-32.6 ± 5.1
0.0300 <i>M</i> <i>p</i> -Nitrobenzoyl Iodide in Dichloroethane			
$k_0$	5.8 ± 0.2	14.8 ± 0.3	-34.1 ± 1.0
$k_1$	15.2 ± 0.4	25.4 ± 0.4	9.4 ± 1.6

the data over the entire range of iodine concentrations that was studied. The values of the rate constants and their probable errors were evaluated by a computer program. A few measurements with 0.0100 *M* aryl iodide confirmed that the rate is first order in this species in this concentration range.

Table III presents the rate constants evaluated from the measurements with *p*-nitrobenzoyl iodide shown in Figures 3 and 4. All runs were 0.030 *M* in aryl iodide, but a few measurements at other concentrations were reasonably consistent with the postulate that the rate is first order in this species. The *p*-nitro compound ex-

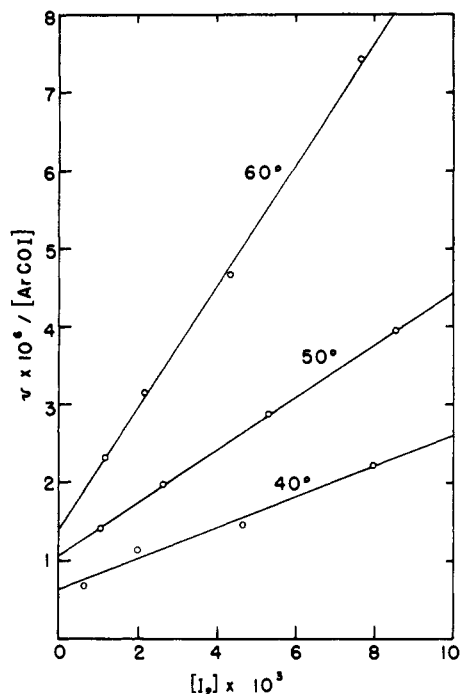


Figure 3. Rate of exchange of 0.0300 *M* *p*-nitrobenzoyl iodide with iodine in hexane.

Table V. Rates (in  $10^{-8}$  mol/(l. sec)) of Exchange at 25.0° for 0.0300 *M* Aryl Iodide and 0.00500 *M* Iodine

Iodide	$k_0$ term	$k_1$ term	$k_2$ term	Total rate
Hexane Solvent				
Unsubstituted		121	44.1	165
<i>p</i> -Chloro		2.84	6.98	9.82
<i>p</i> -Nitro	0.825	0.824		1.65
Dichloroethane Solvent				
Unsubstituted		8340	5440	13,780
<i>p</i> -Chloro	75.0	2850	945	3,795
<i>p</i> -Nitro	27.3	3.62		30.9

changes much more slowly than does the *p*-chloro one, and a comparison of figures shows that the difference is due to much smaller values of the  $k_1$  and  $k_2$  terms. The peculiar  $k_0$  term is not particularly different for the two compounds and hence makes a much greater relative contribution to the rate of the *p*-nitrobenzoyl iodide. The data in Figures 3 and 4 were treated by two-parameter equations that assumed the  $k_0$  and  $k_1$  terms were the only ones of significance.

Rate constants from Tables I–III were fitted to the Arrhenius equation,  $k = Ae^{-E/RT}$ . The values of the parameters obtained, and entropies of activation calculated by standard procedures are all presented in Table IV. Units are moles/liter and seconds, and indicated uncertainties are based on those calculated for individual rate constants at different temperatures.

### Discussion

The effects of substitution and of changing solvent are summarized in Table V by presenting the contribution of

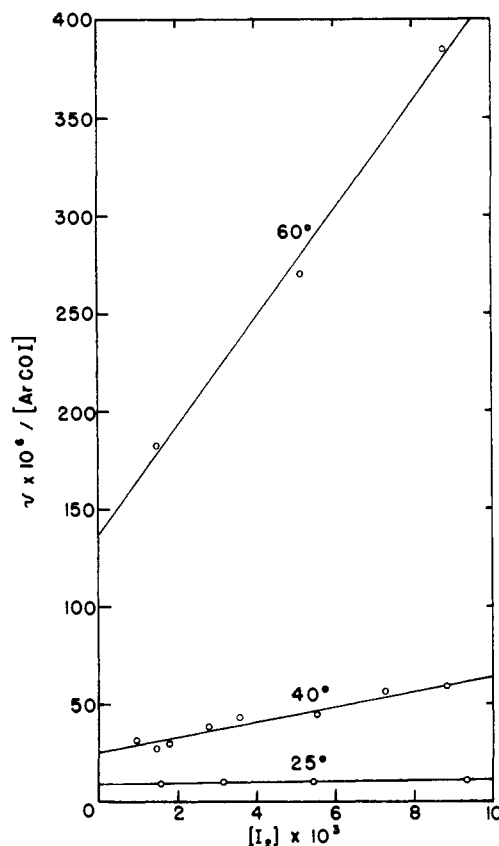


Figure 4. Rate of exchange of 0.0300 *M* *p*-nitrobenzoyl iodide with iodine in dichloroethane.

each term of eq 1 and also the total rate of exchange for a solution 0.0300 *M* in aryl iodide and 0.00500 *M* in iodine at 25.0°. The entries include previous observations<sup>2</sup> on the unsubstituted iodide and in a few cases involve small extrapolations beyond the ranges of temperature and concentration actually studied.

The qualitative features of the results are as had been anticipated. Thus, the rates in dichloroethane are much greater than in hexane, and most of the entropies of activation are very negative; the transition state for exchange is certainly very polar and probably approximates an ion pair. Also, electron-withdrawing substituents depress the rate as would be anticipated if the iodine portion of the ion pair is negatively charged, and the effect of a *p*-chloro substituent is greater in hexane than in the more polar dichloroethane just as was predicted in the introductory section. However, in spite of these indications that the major mechanism of exchange has been identified, certain quantitative features of the data suggest that some complicating effects are not yet clarified.

As was initially anticipated, addition of a *p*-chloro substituent affected  $k_1$  in hexane more than any of the other rate constants. The observed effect suggests a  $\rho$  of  $-7$  if the *p*-chloro group is assigned a  $\sigma$  of<sup>4</sup> 0.227 and a  $\rho$  of  $-14$  if a  $\sigma^+$  of<sup>5</sup> 0.114 is assigned. Even the  $-7$  value is larger in magnitude than has ever been claimed

(4) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p 186.

(5) H. C. Brown and Y. Okamoto, *J. Am. Chem. Soc.*, **80**, 4979 (1958).

for a reaction of neutral molecules and supports the premise of the introductory section that substituent effects should be very large for a reaction involving considerable charge separation in a nonpolar solvent. However,  $k_1$  for *p*-nitrobenzoyl iodide in hexane is several powers of ten larger than would be anticipated from such  $\rho$  values: a change of mechanism may have resulted from the use of such a strongly electron-withdrawing substituent.

Values of  $k_1$  in dichloroethane can be fitted reasonably satisfactorily with a  $\rho$  of  $-2.5$  if  $\sigma^-$  is used for *p*-Cl and  $\sigma^-$  is used for *p*-NO<sub>2</sub> or with a  $\rho$  of  $-4.3$  if  $\sigma^+$  is used for *p*-Cl and  $\sigma$  is used for *p*-NO<sub>2</sub>; the latter fit seems somewhat more plausible for a reaction that obviously develops positive charge on the carbon at the reaction center.

Failure of  $k_2$  terms to contribute to exchange of *p*-nitrobenzoyl iodide can be rationalized from the magnitude of the *p*-chloro-substituent effect, especially if  $\sigma^+$  is used instead of  $\sigma^-$ .

Correlation of these meager observations with the Hammett<sup>4</sup> equation is hence fairly adequate except for  $k_1$  for *p*-chlorobenzoyl iodide in hexane, but considerably more data would be needed before any really quantitative discussion of substituent effects would be possible.

The data on temperature dependence of rate constants also exhibit some anomalies. Rates in dichloroethane are always much greater than in hexane, and for *p*-chlorobenzoyl iodide the effect is due almost entirely to difference in activation energy. However, for *p*-nitrobenzoyl iodide, the faster rate in dichloroethane is due to a big change in entropy of activation that overbalances an unfavorable change in activation energy. It is the temperature dependence in dichloroethane rather than that in hexane that appears anomalous for this compound, while it was suggested in the preceding paragraph that the absolute rate in hexane rather than in dichloroethane was the value out of line with other measurements.

Finally, the mechanistic significance of the  $k_0$  term remains obscure. The big difference between values in

the two solvents suggests that the transition state is very polar, but this interpretation is contradicted by the small variation with changing substituent. The  $k_0$  term is of greater relative importance for the *p*-nitrobenzoyl iodide exchange because the other terms are so small for this compound rather than because the  $k_0$  term is particularly different. The observations could be explained by unimolecular formation of an ion pair  $\text{ArCO}^+\text{I}^-$  that almost invariably exchanged with iodine before it collapsed, but the rate of such a process should be dramatically affected by substituents. We are inclined to support the previous interpretation<sup>2</sup> that this term is an artifact associated with some impurity such as adventitious moisture.

In spite of the above anomalies, the results presented here support the original interpretation that these exchange reactions involve ion-pair transition states even in nonpolar solvents like hexane and that the rates are very sensitive to changing substituent. Most reactions involving large changes in polarity can only be studied in solvents of considerably greater dielectric constant than those employed in this work, and these iodine-exchange reactions appear to offer considerable value for testing and developing theories of solvent effects on chemical reactivity. The substituted benzoyl iodide system is difficult to study because of the extreme sensitivity of these compounds to traces of moisture. Work now being done at the University of Oregon<sup>6</sup> suggests that the exchange of benzhydryl iodide may be even more sensitive to changing solvent composition, and this system may become the one of choice for studying substituent effects on polar reactions in solvents of low dielectric constant.

**Acknowledgment.** This work was supported in part by the U. S. Atomic Energy Commission under Contract No. AT(45-1)-1310.

(6) W. J. Muizebelt, private communication.