

## Substituent Effects in the Reaction of Aromatic Acid Chlorides with Sodium Borohydride

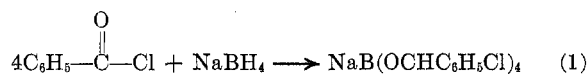
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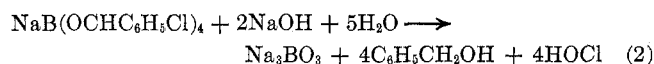
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The kinetics of the reactions of aromatic acid chlorides with sodium borohydride has been followed by a spectrophotometric method. The reaction was found to be second order. The effect of the aromatic ring substituent on the rate of reaction follows the order  $m\text{-NO}_2 > p\text{-NO}_2 > p\text{-CN} > p\text{-CH}_3 > m\text{-CH}_3 > p\text{-OCH}_3 > m\text{-Br} > m\text{-Cl} > p\text{-Br} > \text{H}$ . A Hammett correlation of the rate constant with  $\sigma$  value yields a curve which is concave upward. This suggests that the reaction series may involve mechanistic changes. A mechanism was proposed to interpret the experimental results.

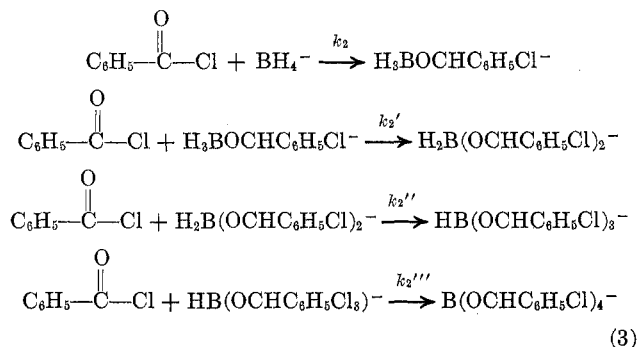
In the continuation of our work on the reactivities of the carbonyl group,<sup>1</sup> we undertook an investigation of the effect of the substituent on the rate of reactions of aromatic acid chlorides with sodium borohydride. The reaction was first studied by Chaiken and Brown<sup>2</sup> (eq



1). Upon hydrolysis the stable intermediate decomposes into alcohol and sodium borate (eq 2).



Kinetics of the reaction is believed to involve four steps<sup>3</sup> (eq 3). The transfer of the first hydride ion to



the carbonyl group, *i.e.*, the first step, is rate determining. However, the manner in which the borohydride molecules attack the carbonyl group is not clear. There appears to be some change in mechanism throughout the reaction series of aromatic acid chlorides.

### Experimental Section

**Materials.**—Sodium borohydride of analytical grade was obtained from Metal Hydrides, Inc., and was purified according to the method described by Brown and coworkers.<sup>4</sup> No significant difference was found, however, in the reaction with aromatic acid chlorides whether commercial sodium borohydride was purified or not. In the early stage of this work sodium borohydride was purified, whereas in the latter stage the commercial product was used directly without further purification. Reagent grade 1–4 dioxane was purified by distilling over sodium metal and collecting the fraction that boiled at 101.0–101.5°. Addition of sodium borohydride to the purified dioxane showed no evolution of hydrogen gas. Saturated solutions of sodium boro-

hydride in dioxane were prepared and the concentrations were determined by sodium hypochlorite titration as described by Chaiken.<sup>5</sup>

The acid chlorides which exist in liquid forms at room temperature, *i.e.*,  $p\text{-OCH}_3$ ,  $p\text{-CH}_3$ ,  $m\text{-CH}_3$ ,  $m\text{-Br}$  (all from K and K Lab., Inc.),  $m\text{-Cl}$  (Aldrich Chemical Co.), and H (Eastman Organic Chemicals), were purified by vacuum distillation; the solid acid chlorides,  $p\text{-CN}$  (K and K Lab., Inc.),  $m\text{-NO}_2$ , and  $p\text{-NO}_2$  (Aldrich Chemical Co.), were purified by vacuum sublimation. The commercial  $p\text{-Br}$  (K and K Lab., Inc.) contains impurities (mostly  $p\text{-Br}$  benzoic acid), and could not be used for kinetic studies. It was synthesized using standard procedure<sup>6</sup> with some modifications.

**Kinetic Measurements.**—The reactions were followed spectrophotometrically using a Beckman DB spectrophotometer equipped with a servo recorder or a Cary Model 14 recording spectrophotometer. Both instruments were equipped with a thermostable cell compartment and a thermostable cell holder. A 3-ml solution of known concentration of the acid chloride in dioxane was introduced to a cell of 1-cm path length and was kept in the cell compartment at  $35 \pm 0.1^\circ$  for 20 min so that equilibrium conditions could be established. The reaction was started by injecting a known amount of sodium borohydride dissolved in dioxane and kept at  $35^\circ$  in a water bath, using a calibrated hypodermic syringe. The reaction mixture was rapidly stirred. The decay of the absorbance peak of acid chloride at  $\lambda_{\text{max}}$  was recorded. After some time,  $t$ , the curve on the recorder leveled off and no further decrease in absorbance was observed. This final absorbance was taken as  $A_\infty$ .

**Treatment of Data.**—The data describing the disappearance of the reactants were treated using the following equation

$$\frac{1}{(a - 4b)} \ln \frac{4b(A_t - A_\infty)}{4b(A_0 - A_\infty) - a(A_0 - A_t)} = kt$$

where  $a$  is the initial molar concentration of the acid chloride,  $b$  is the initial molar concentration of sodium borohydride,  $A_t$  is the absorbance of the acid chloride at time  $t$ , and  $k$  is the second-order rate constant. The left side of the equation was plotted against time and the rate constant was determined from the slope of the straight line. To best fit the data, the least square method was used. The estimate of error was based upon statistical regression evaluation. All the computations were carried out on the CEIR Multi-Access computer service (System 420).

**Product Analysis.**—The intermediate product  $\text{NaB}(\text{OCHC}_6\text{H}_5\text{Cl})_4$  was prepared by adding the solution of borohydride in dioxane to an acid chloride in the identical solvent. Part of the product was used for infrared analysis *in situ* and part for chemical analysis. The infrared spectra were taken with the Beckman IR-8 for the product as well as for the starting material. The spectrum of the product showed the disappearance of the  $\text{C}=\text{O}$  stretching vibration at  $5.71 \mu$ . Since  $\text{NaBH}_4$  does not absorb in the carbonyl region, the disappearance indicates the reaction of the acid chloride with sodium borohydride. The other portion of the intermediate was treated with aqueous sodium hydroxide and the formation of the alcohol was tested by chromic anhydride.

(1) S. F. Sun and P. R. Neidig, *J. Org. Chem.*, **34**, 1854 (1969).

(2) S. W. Chaiken and W. G. Brown, *J. Amer. Chem. Soc.*, **71**, 122 (1949).

(3) H. C. Brown, O. H. Wheeler, and K. Ichikawa, *Tetrahedron*, **1**, 214 (1957).

(4) H. C. Brown, E. J. Mead, and B. C. S. Rao, *J. Amer. Chem. Soc.*, **77**, 6209 (1955).

(5) S. W. Chaiken, *Anal. Chem.*, **25**, 831 (1953).

(6) A. I. Vogel, "A Text-Book of Practical Organic Chemistry," 3rd ed., Wiley, New York, N. Y., 1957, p 792.

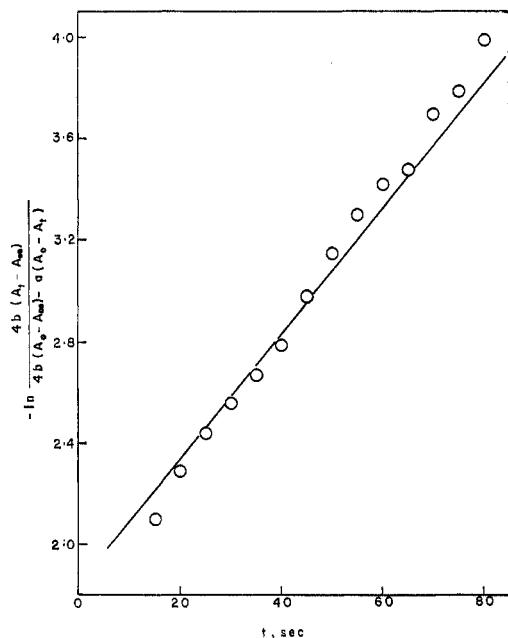


Figure 1.—Second-order reaction of sodium borohydride with *p*-methoxybenzoyl chloride.

### Results

The uv absorption spectra were obtained for aromatic acid chloride in dioxane solutions. Table I lists the ab-

TABLE I  
MAXIMUM ABSORPTION OF SUBSTITUTED  
BENZOYL CHLORIDES IN DIOXANE

Substituent	$\lambda_{\max}$ , $m\mu$
<i>p</i> -CH <sub>3</sub>	258
<i>p</i> -OCH <sub>3</sub>	284
<i>m</i> -CH <sub>3</sub>	250
H	247
<i>p</i> -Br	262
<i>m</i> -Cl	250
<i>m</i> -Br	246
<i>p</i> -CN	250
<i>m</i> -NO <sub>2</sub>	228
<i>p</i> -NO <sub>2</sub>	257

sorption maxima. The plot of absorbance at  $\lambda_{\max}$  vs. concentration of the aromatic acid chloride in dioxane gave a straight line, indicating that for these compounds Beer's law was obeyed. Furthermore, from the spectrum of the reaction product for each of the acid chlorides, it was found that the  $\lambda_{\max}$  moves reasonably away from any of the reactants; this justifies the use of the acid chloride peak for the kinetic run.

Plots of  $\ln 4b(A_t - A_\infty) / 4b(A_0 - A_\infty) - a(A_0 - A_t)$  vs. time for the determination of the rate constant were linear for all the aromatic acid chlorides. Figure 1 shows the relatively slow reaction of a typical compound, *p*-methoxybenzoyl chloride, whereas Figure 2 shows the fast reaction of *m*-nitrobenzoyl chloride. The error of the kinetic data is within 5–10%. Table II gives the rate constants and  $\sigma$  values. For comparison of the agreements, rate constants of duplicate runs are given in the parenthesis.

Figure 3 correlates the  $\sigma$  values with  $\log k$ . No simple linear  $\rho$ - $\sigma$  relationship was observed; instead, we obtained a curve which is concave upward. Such a be-

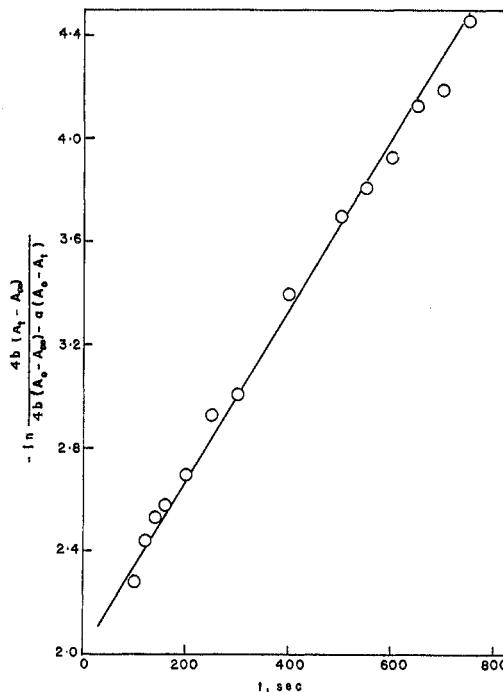


Figure 2.—Second-order reaction of sodium borohydride with *m*-nitrobenzoyl chloride.

TABLE II  
SECOND-ORDER RATE CONSTANTS OF THE REACTIONS OF  
SUBSTITUTED BENZOYL CHLORIDES AT 35°  
AND THE MEAN  $\sigma$  VALUES<sup>a</sup>

Substituents	Registry no.	$k \times 10^{-2}$ l. mol <sup>-1</sup> min <sup>-1</sup>	$a^b \times b^c \times$		$\sigma^n$
			mol <sup>-1</sup> l <sup>-1</sup>	mol <sup>-1</sup> l <sup>-1</sup>	
<i>p</i> -CH <sub>3</sub>	874-60-2	4.74 (4.59, 4.64)	5.7	90.1	-0.129 ± 0.037
<i>p</i> -OCH <sub>3</sub>	100-07-2	2.38 (2.31, 2.15)	4.6	90.1	-0.111 ± 0.021
<i>m</i> -CH <sub>3</sub>	1711-06-4	4.10 (4.04, 4.32)	0.6	90.1	-0.070 <sup>d</sup>
H	98-88-4	1.17 (1.20, 1.28)	4.7	96.5	0.0
<i>p</i> -Br	586-75-4	1.28 (1.18, 1.30)	4.9	88.1	0.265 ± 0.033
<i>m</i> -Cl	618-46-2	1.98 (1.84, 1.91)	4.5	96.5	0.370 <sup>d</sup>
<i>m</i> -Br	1711-09-7	2.08 (2.07, 2.50)	4.3	90.1	0.380 <sup>d</sup>
<i>p</i> -CN	6068-72-0	6.91 (6.54, 7.39)	4.4	90.1	0.674 ± 0.042
<i>p</i> -NO <sub>2</sub>	122-04-3	18.59 (17.85, 19.63)	5.8	18.5	0.73 <sup>d</sup>
<i>m</i> -NO <sub>2</sub>	121-90-4	20.41 (21.31, 20.58)	1.2	18.5	0.79 <sup>d</sup>

<sup>a</sup>  $\sigma^n$  = mean of all calculated values, cited by P. R. Wells, *Chem. Rev.*, **24**, 179 (1963). <sup>b</sup>  $a$  = initial concentration of the acid chloride. <sup>c</sup>  $b$  = initial concentration of sodium borohydride. <sup>d</sup>  $\sigma^o$  = primary  $\sigma$  value.

havior has been observed in the hydrolysis of substituted benzene sulfonyl chloride<sup>7</sup> and of substituted benzoyl chlorides<sup>8</sup> as cited in Wells' review article.<sup>9</sup> It indicates a change of mechanism in the course of reaction throughout the series of reactants. Three different sets of  $\sigma$  values were tried:  $\sigma^o$ , the primary  $\sigma$  value;  $\sigma(J)$ , the values of Jaffe; and  $\sigma^n$ , the mean of all calculated  $\sigma$  values. The shapes of the curves were virtually the same. In Figure 2, we chose  $\sigma^n$  for plotting.<sup>9</sup>

### Discussion

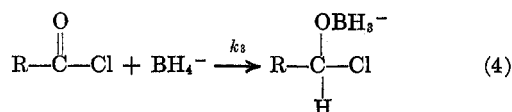
Brown and coworkers<sup>3</sup> suggested that the reaction of carbonyl compounds with sodium borohydride may pro-

(7) G. Berger and S. C. J. Olivier, *Recl. Trav. Chim. Pays-Bas*, **46**, 516 (1927).

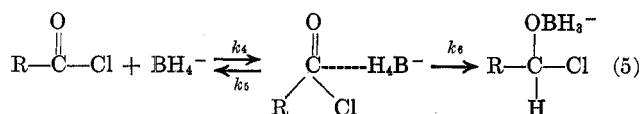
(8) I. Hedlund, *Ark. Kemi, Ser. A*, **14**, 1 (1940).

(9) P. R. Wells, *Chem. Rev.*, **63**, 177 (1963).

ceed by two different pathways: (1) direct reaction (eq 4) where the observed rate constant is  $k_3$ , and  $k_2 =$

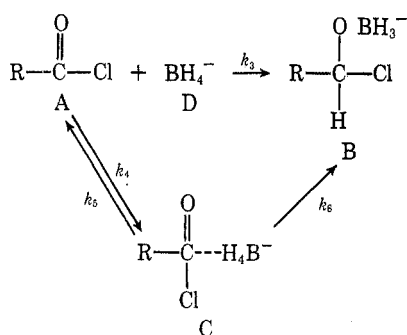


$k_3$ , and (2) formation of intermediate (eq 5) with the ob-



served rate constant being  $k_{\text{obsd}} = k_4 k_6 / k_5 + k_3$ .

On the basis of the concave upward curve observed, the overall mechanism of the sodium borohydride reduction of substituted aromatic acid chloride seems to consist of both pathways.<sup>10</sup>



Let [A] be the concentration of the aromatic acid chloride, [B] the concentration of the product, [C] the concentration of the intermediate, and [D] the concentration of borohydride. Then the rate expression may be written as follows:

$$-\frac{d[A]}{dt} = k_3[A][D] + k_4[A][D] - k_6[C]$$

Applying the steady-state approximation

$$\frac{d[C]}{dt} = 0$$

we obtain

$$-\frac{d[A]}{dt} = (k_3 + k_4)[A][D]$$

where

$$k_4' = \frac{k_4 k_6}{k_5 + k_6}$$

and  $(k_3 + k_4')$  is the observed rate constant  $k$ .

(10) One of the reviewers suggested that pathway 2 is good enough to accommodate our results. Assuming the steady-state approximation of the intermediate to be valid, there exist two limiting cases: (a)  $k_3 \gg k_4$  so that  $k_{\text{obsd}} = k_3$ , and (2)  $k_4 \gg k_3$  so that  $k_{\text{obsd}} = k_4 k_6 / k_5$ . The reviewer pointed out that the nonlinear Hammett relationship is the result of the transition from one extreme case to the other with the change of structure. In other words, it is the result of a change in rate-limiting step from nucleophilic attack to decay of the intermediate. We would agree with the reviewer if a sharp discontinuity in the Hammett plot were observed. However, in view of the fact that throughout the series, there seems to be a continuous change in mechanism from one extreme to the other, we believe that the combination of pathway 1 and pathway 2 may be more adequate to interpret the results. Besides, the combination does not complicate much the mechanistic scheme; there are similar cases in which two different rate constants  $k^{\circ}$  and  $k^{\circ}$  in Hammett equation are affected by substituents in different ways.<sup>11</sup>

(11) K. B. Wiberg, "Physical Organic Chemistry," Wiley, New York, N. Y., 1963, p 407.

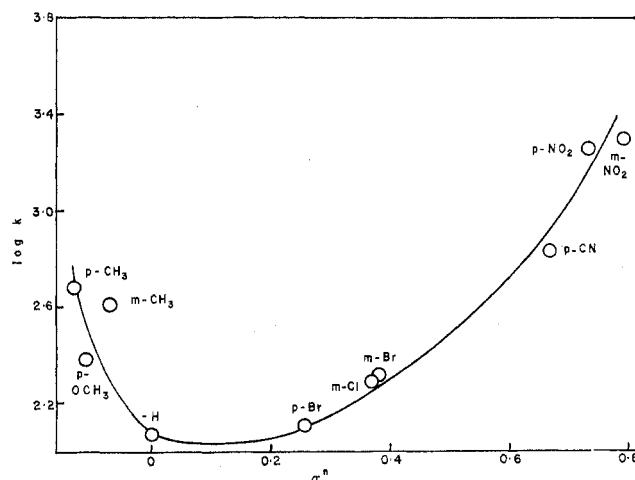


Figure 3.—Plot of  $\log k$  vs.  $\sigma^n$ .

For this type of reaction, the Hammett equation would take the following form<sup>11</sup>

$$\log \frac{k}{k^{\circ}} = \log \frac{k_3 + k_4'}{k_3^{\circ} + k_4'^{\circ}}$$

where  $k = k_3 + k_4'$  is the observed rate constant for substituted benzoyl chloride, and  $k^{\circ} = k_3^{\circ} + k_4'^{\circ}$  is the observed rate constant for the unsubstituted benzoyl chloride.

Here, the rate constants  $k_3$  and  $k_4'$  are not affected in the same way by the substituents. The rate constant  $k_3$  representing the direct reaction of the borohydride ion with the carbonyl group is presumably less affected by electron-withdrawing substituents, while  $k_4'$  the rate constant representing the formation of an intermediate is greatly affected.

For electron-withdrawing substituents ( $+\sigma$ ), the reaction seems to proceed predominantly *via* pathway 2;  $k_6 \gg k_5$  so that  $k_4' = k_4$ . This is consistent with the influence of the ring substituents since the electron-withdrawing group in the phenyl ring will render the carbonyl carbon more susceptible to nucleophilic attack. The observed rate constant increases with increase in electron-withdrawing power of the substituents  $p\text{-Br} < m\text{-Cl} < m\text{-Br} < p\text{-CN} < p\text{-NO}_2 < m\text{-NO}_2$ . The value of  $p\text{-NO}_2$  is smaller than that of  $m\text{-NO}_2$  because the reaction occurred in nonhydroxylic media.<sup>9</sup>

With electron-donating substituents, the carbonyl carbon is rendered less vulnerable to nucleophilic attack due to an increase in electron density around the carbon. With these types of substituents, the attack of the borohydride molecule on the carbonyl carbon probably proceeds *via* pathway 1 more significantly than *via* pathway 2. A stable intermediate which is in equilibrium with the carbonyl group is not likely to be formed; even if it is formed, it is not in a very significant amount.

This leads us to the conclusion that the sodium borohydride reduction of aromatic acid chloride appears to undergo a change in mechanism as the electron-withdrawing or electron-donating power of the substituent group in the phenyl ring is varied.

**Registry No.**—Sodium borohydride, 16940-66-2.

**Acknowledgment.**—We wish to thank the reviewers for helpful comments.