[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, REED COLLEGE]

Nucleophilic Substitution in the Benzene Ring. I. Rates of Reactions of *p*-Substituted Bromobenzenes with Piperidine

BY J. F. BUNNETT AND ARNOLD LEVITT[1]

It has long been known that an ortho- or para-nitro group strongly activates the condensation of a halobenzene with a nucleophilic reagent such as the hydroxide ion, an alkoxide ion, a mercaptide ion, or an amine. Several other groups, such as carboxyl, nitroso, cyano, sulfonyl, acyl and carbalkoxyl groups, have similar ortho–para activating effects.

This activation has been extensively studied, and for various reactions there are available comparisons[2] of the relative activating effects of pairs of groups. From these comparisons it is plain that nitro is more strongly activating than the other important activating groups, but there isn't available any comparison of the relative activating effects of the several groups in a single sort of reaction under constant conditions.

In this paper we report rate constants for the reactions of some *p*-substituted bromobenzenes with piperidine in benzene at 99°. The rate constants found are recorded in Table I. The order of activation in this reaction we have thus found to be: $NO_2 \gg CH_3SO_2 > CN > CH_3CO$.

TABLE I

REACTIONS WITH PIPERIDINE

	k (liters moles^{-1} sec.$^{-1}$)
p-Bromonitrobenzene	64.5×10^{-7}
p-Bromophenyl methyl sulfone	3.40×10^{-7}
p-Bromobenzonitrile	1.98×10^{-7}
p-Bromoacetophenone	0.86×10^{-7}
p-Chloronitrobenzene	11.4×10^{-7}

The determination on *p*-chloronitrobenzene was made with the object of comparing the rate constant found for it with those to be determined for *p*-chlorobenzophenone and *p*-chlorobenzotrifluoride. Samples of the two latter compounds were available in the laboratory; both of them, however, proved to have an order of reactivity too low to allow determination of rate constants in the time available. In about three and one-half days, 3.4% of the chlorine of *p*-chlorobenzophenone was liberated as chloride ion; the corresponding figure for *p*-chlorobenzotrifluoride was 1.2%.

We have also studied the reactions of *p*-nitrobromobenzene and of *p*-bromophenyl methyl sulfone with sodium methoxide in methanol at 99°. Rate constants for these reactions are listed in Table II.

These values, along with those in Table I, show very clearly that the relative activating effects of groups in nucleophilic substitution reactions are influenced by the nature of the nucleophilic reagent and by the nature of the solvent. In the reaction with sodium methoxide the nitro compound reacts twenty-eight times as fast as the sulfone, while in the reaction with piperidine it reacts only nineteen times as fast.

TABLE II

REACTIONS WITH SODIUM METHOXIDE

	k (liters moles^{-1} sec.$^{-1}$)
p-Bromonitrobenzene	78.5×10^{-5}
p-Bromophenyl methyl sulfone	2.84×10^{-5}

Experimental

In the cases of *p*-nitrobromobenzene, *p*-bromoacetophenone and *p*-chloronitrobenzene, the commercial product was recrystallized to a satisfactory melting point. Commercial piperidine was redistilled, and middle fractions were used in this work. A highly purified sample of *p*-chlorobenzotrifluoride was generously furnished by Dr. A. F. Scott.

***p*-Bromobenzonitrile.**—To a solution of 20 g. of *p*-bromobenzamide in 120 ml. of tetrachloroethane, 32 g. of phosphorus pentachloride was added and the mixture was refluxed for several hours during which hydrogen chloride was evolved. The mixture was poured over ice, and the organic layer separated and steam-distilled. After removal of the tetrachloroethane, the distillate containing the nitrile was collected and filtered. The nitrile was recrystallized from petroleum ether; m. p. 110–112°[3]; yield, 7.4 g. (41%).

***p*-Bromophenyl Methyl Sulfone.**—The method of Oxley, Partridge, Robson and Short[4] was followed. From 50 g. of *p*-bromobenzenesulfonyl chloride, 16 g. (35%) of *p*-bromophenyl methyl sulfone, m. p. 102–103°,[5] were obtained.

***p*-Chlorobenzophenone.**—A sample, m. p. 74–75°,[6] was generously supplied to us by Mr. Herbert Hergert who prepared it by the method of Gomberg and Cone.[7]

Kinetic Measurements. A. Reactions with Piperidine.—For the study of a particular compound, four or five sealed Pyrex tubes with identical contents were prepared. Within each tube were 20 ml. of a thiophene-free benzene solution about 1.5 molar in piperidine and about 0.05 molar in the halogen compound. All four or five tubes were placed in the thermostat[8] at once; a drop in temperature ensued, and when the temperature had returned to 99°, one of the tubes was removed and cooled to 0°. The other tubes were

---

[1] Present address: Department of Chemistry, Oregon State College, Corvallis, Oregon.

[2] Mattaar, *Rec. trav. chim.*, **41**, 103 (1922); Todd and Shriner, THIS JOURNAL, **56**, 1382 (1934); Le Fèvre, *J. Chem. Soc.*, 810 (1931).

(3) Von Braun, *Ber.*, **37**, 2816 (1904), reported m. p. of *p*-bromobenzonitrile 113°.

(4) Oxley, Partridge, Robson and Short, *J. Chem. Soc.*, 767 (1946).

(5) Bourgeois and Abraham, *Rec. trav. chim.*, **30**, 407 (1911), *C. A.*, **6**, 623 (1912), reported m. p. of *p*-bromophenyl methyl sulfone 102–103°.

(6) Kollarits and Merz, "Beilstein," 4th ed., Vol. VII, p. 419, reported m. p. of *p*-chlorobenzophenone 75.5–76°.

(7) Gomberg and Cone, *Ber.*, **39**, 3278 (1906).

(8) A thermostat of the type described in Ostwald–Luther, "Physiko-chemischer Messungen," 5th ed., Leipzig, 1931, p. 121, was used, with water the boiling liquid. The bath temperature was 99 ± 0.5°.

removed at subsequent recorded times. The contents of the tubes were extracted with water and halide ion in the water extracts was determined by the Volhard method.

The percentage of reaction in the last tube removed varied from 75.3% (forty hours reaction time) in the case of *p*-nitrobromobenzene, to 7.0% (137.62 hours reaction time) in the case of *p*-bromoacetophenone.

Rate constants were determined from the equation[9]

$$kt = \frac{2.303}{b - 2a} \log_{10} \frac{(b - 2x)}{(a - x)} + C$$

where *b* is initial concentration of piperidine, *a* is initial concentration of the halogen compound, and *x* is concentration of the piperidinium halide product at time *t* (first tube removed from bath at $t = 0$). This mathematical expression is valid for the chemical equation

$$RX + 2C_5H_{10}NH \longrightarrow RNC_5H_{10} + C_5H_{10}NH_2X$$

When values of the term $2.303/(b - 2a) \log_{10} [(b - 2x)/(a - x)]$ were plotted against *t*, the points in every case fell virtually on a straight line.[10] Values of the slope were calculated by the Method of Zero Sum.[11]

B. Reactions with Sodium Methoxide.—The technique was generally the same as used for the reactions with piperidine. The same thermostat was used with temperature again 99 ± 0.5°. Each tube contained 0.00200 mole of the halogen compound (added as a solid) and 0.00200 mole of sodium methoxide in a total volume of 19.28 ml. When a tube was opened, its contents were added to 100 ml. of 50% methanol and unconsumed base was determined by titration with standard hydrochloric acid to the methyl red end-point. For one tube of each compound, this titration was followed by a conductimetric titration of halide ion, and it was observed that bromide liberated was equal to methoxide consumed in the case of the nitro and sulfone compounds.

Rate constants were calculated from the expression

$$1/(a - x) = kt + C$$

applicable to second order reactions in which the initial concentrations of both reactants are equal. Values of *k* were found by the Method of Zero Sum.[11]

Acknowledgment.—The authors are grateful for generous financial support by the Research Corporation which greatly aided the progress of this work.

Summary

1. Rate constants for the reactions of some *p*-substituted bromobenzenes with piperidine at 99° have been determined; comparison of them shows that for this reaction four groups stand in the following order of activating influence: $NO_2 \gg CH_3SO_2 > CN > CH_3CO$.

2. Rate constants for the reactions of *p*-bromonitrobenzene and of *p*-bromophenyl methyl sulfone with methanolic sodium methoxide at 99° have been determined.

3. The rate constant for the reaction of *p*-chloronitrobenzene with piperidine at 99° has been determined; *p*-chlorobenzotrifluoride and *p*-chlorobenzophenone reacted too slowly with piperidine to allow kinetic study of the reactions.

PORTLAND, OREGON RECEIVED JANUARY 7, 1948

---

(9) *Cf.* Rheinlander, *J. Chem. Soc.*, **123**, 3099 (1923).

(10) The average deviation of points from the straight line was in every case less than 3% of the difference between the first and last values plotted.

(11) Campbell, *Phil. Mag.*, **39**, 177 (1920); **47**, 816 (1924).

[CONTRIBUTION FROM THE NORTHERN REGIONAL RESEARCH LABORATORY[1]]

Polysaccharide Aryl Carbamates[2]

BY IVAN A. WOLFF AND CARL E. RIST

Although aromatic isocyanates are regularly used for the characterization of a variety of alcohols, the reactions of these reagents with carbohydrates have not been extensively investigated. Carbanilates of several common sugars,[3] sugar alcohols,[4] glucosides,[5] and the 1-N-α-naphthyl carbamate of 2,3,4,5,6-0-pentamethyl-(*levo*)-sorbitol[6] have been prepared. Recently carbamate derivatives of cellulose and of partially esterified or etherified cellulose have been reported.[7]

This paper reports the preparation and some properties of the esters of corn starch, corn amylose and amylopectin with phenyl isocyanate and with α-naphthyl isocyanate. Tricarbanilates of waxy (glutinous) corn starch, white potato amy-

---

(1) One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, U. S. Department of Agriculture. Article not copyrighted.

(2) Manuscript presented before the Division of Sugar Chemistry and Technology of the American Chemical Society at Chicago, Illinois, April 19–23, 1948.

(3) Maquenne and Goodwin, *Bull. soc. chim.*, [3] **31**, 430 (1904).

(4) Tessmer, *Ber.*, **18**, 968 (1885).

(5) Jolles and Botrini, *Gazz. chim. ital.*, **65**, 1217 (1935); Wolfrom and Pletcher, THIS JOURNAL, **62**, 1151 (1940); Hearon, Hiatt and Fordyce, *ibid.*, **66**, 995 (1944); Hearon, *ibid.*, **70**, 297 (1948); Reeves, *ibid.*, **70**, 259 (1948).

(6) Wolfrom and Gardner, *ibid.*, **65**, 750 (1943).

(7) Hearon, Hiatt and Fordyce, *ibid.*, **65**, 829, 833 (1943); Dyer and McCormick, *ibid.*, **68**, 986 (1946); Hearon and Lobsitz, *ibid.*, **70**, 296 (1948).