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Intramolecular Nucleophilic Participation. The Effect of Certain *ortho* Substituents on Solvolysis Rates of Benzyl and Benzhydryl Bromides

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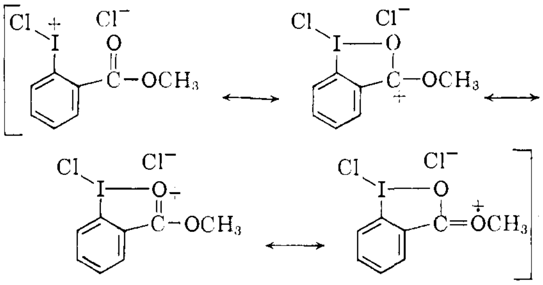
The hydrolysis rates of a number of *ortho* and *para* substituted benzyl and benzhydryl bromides in aqueous acetone or aqueous dioxane have been studied. In general the substituents have been chosen from a group which are potentially nucleophilic in character. Contrary to what is usually observed as concerns the reactivities of *o*- and *p*-isomers of halides of these types, *o*-carbophenoxybenzhydryl bromide has been found to be considerably more reactive than its *p*-isomer. The high reactivity of the *o*-isomer is attributed to the capacity of the *o*-carbophenoxy substituent to participate like a neighboring group in the slow step of the reaction. The reactivity of *o*-carbomethoxybenzyl bromide is greater than that of its *p*-isomer, but the difference in reactivities for the two compounds is much less than that for the carbophenoxybenzhydryl bromides. The reason for the ineffectiveness of the *o*-carbomethoxy group as a participant in the benzyl bromide reaction is considered, and the capacities of *o*-COOH and *o*-OCOR to act as participating groups are discussed.

It has been amply demonstrated that certain *ortho* substituents which are nucleophilic in character function as intramolecular catalysts in promoting hydrolyses and related reactions of esters and amides of aromatic carboxylic acids.[1] The equilibration of iodobenzene dichloride with iodobenzene and chlorine, a process which takes place at an easily measurable rate in a polar solvent such as acetic acid, is subject to a similar rate enhancement when groups such as –COOR, –NHCOR and –CH_2OH are located *ortho* to the iodine atom.[2,3] These rate effects are attributed to the capacity of the substituents to release electrons to the reaction center in the adjacent aromatic side chain.

In the dichloride equilibration reaction the iodine atom of the side chain must be subject to positive polarization in the activation process. It has been suggested that the substituents in question, *e.g.*, –*o*-$COOCH_3$, actually participate as neighboring groups in stabilizing that positive charge (see structure I).[2,3] The conformation characteristic of solid iodobenzene dichloride,[4] in which the linear trihalide group is perpendicular to the benzene ring, is also an acceptable or preferred one in this activation process.[5] Thus there is minimal steric[4] opposition to electronic participation by an *o*-substituent in this reaction.



I

In the activation processes for solvolytic displacement reactions of benzyl and benzhydryl halides, the exocyclic carbons also undergo positive polarization.[6,7] In this sense these reactions are electronically similar to iodobenzene dichloride dissociation. The possibility has therefore been explored experimentally that solvolyses of benzyl and benzhydryl bromides are subject to intramolecular nucleophilic catalysis by *o*-substituents. In particular, the hydrolysis rates of *o*-benzoyloxy-, *o*-acetoxy- and *o*-carbophenoxybenzhydryl bromides and *o*-benzoyloxy-, *o*-carboxy- and *o*-carbomethoxybenzyl bromides in aqueous acetone or dioxane have been compared with those of the corresponding *p*-isomers.

Experimental

The Substituted Toluenes and Diphenylmethanes.—Except as noted, all organic starting materials used in preparing these compounds and the various substituted benzyl and benzhydryl bromides were obtained from Eastman Organic Chemicals.

The *o*- and *p*-tolyl benzoates[8] were prepared from the cresols by the Schotten–Baumann reaction. The *o*-isomer was purified by distillation, b.p. 135° (3 mm.). The *p*-isomer had m.p. 69–70° (lit.[8] m.p. 71°).

A sample of *o*-benzylbenzoic acid, m.p. 118°, was prepared[9] by zinc reduction of *o*-benzoylbenzoic acid. The *p*-benzylbenzoic acid was prepared by oxidizing *p*-methylbenzophenone with chromic oxide,[10] and reducing the resultant *p*-benzoylbenzoic acid, m.p. 198–200°. The reduction was accomplished by refluxing a mixture of 20 g. of *p*-benzoylbenzoic acid, 30 g. of potassium hydroxide pellets and 13 ml. of hydrazine in 125 ml. of diethylene glycol for an hour and a half. Water was then distilled from the mixture until its temperature reached 200°, and refluxing was continued for 5 hours. The mixture was then poured into 1 l. of 6 *N* hydrochloric acid, and the solid which precipitated was recrystallized from dilute alcohol; m.p. 159° (lit.[11] m.p. 159°), yield 15.5 g. (84%).

To prepare phenyl *o*-benzylbenzoate 42.4 g. of *o*-benzylbenzoic acid, 100 ml. of dry pyridine, 19.7 g. of phenol and 24 g. of freshly distilled thionyl chloride were heated on a steam-bath for 1 hour. Most of the pyridine was removed by reduced pressure distillation. The residue was diluted with 200 ml. of ice-water and extracted with ether. The extract was washed with dilute hydrochloric acid and sodium hydroxide solutions and dried. The residue remaining after evaporation of the solvent was recrystallized from ligroin; yield 47.5 g. (82%), m.p. 58°.

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[1] M. L. Bender, *Chem. Revs.*, **60**, 53 (1960).

[2] L. J. Andrews and R. M. Keefer, *J. Am. Chem. Soc.*, **81**, 4218 (1959).

[3] R. M. Keefer and L. J. Andrews, *ibid.*, **81**, 5329 (1959).

[4] E. M. Archer and T. G. D. Van Schalwyk, *Acta Cryst.*, **6**, 88 (1953).

[5] R. M. Keefer and L. J. Andrews, *J. Am. Chem. Soc.*, **81**, 2374 (1959).

[6] The Hammett ρ-values for the reactions of benzyl as well as of benzhydryl halides in aqueous or alcoholic media are negative; *cf.* H. H. Jaffé, *Chem. Revs.*, **53**, 191 (1953). That is, in the activation of both types of halides, bond cleavage between halogen and carbon has proceeded farther than bond formation between carbon and the solvent.

[7] C. G. Swain and W. P. Langsdorf, Jr., *J. Am. Chem. Soc.*, **73**, 2813 (1951).

[8] A. Behal and E. Choay, *Compt. rend.*, **118**, 1213 (1894).

[9] B. Barnett, J. W. Cook and I. G. Nixon, *J. Chem. Soc.*, 504 (1927).

[10] E. Wertheim, *J. Am. Chem. Soc.*, **55**, 2541 (1933).

[11] C. Liebermann, *Ber.*, **45**, 1207 (1912).

TABLE I

BENZHYDRYL BROMIDES PREPARED BY PHOTOBROMINATION

Benzhydryl bromide	M.p., °C.	Yield, %[a]	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Bromine, % Calcd.	Bromine, % Found
o-Carbophenoxy-	103–105	91	65.41	65.77	4.12	4.13	21.76	21.70
p-Carbophenoxy-	101	80	65.41	65.31	4.12	4.23	21.76	21.62
o-Benzoyloxy-	71	77	65.41	65.21	4.12	4.14	21.76	21.97
p-Benzoyloxy-	97	85	65.41	64.83	4.12	3.97	21.76	22.20
o-Acetoxy-	55	75	59.03	59.26	4.29	4.39	26.19	26.15
p-Acetoxy-	55	85	59.03	58.63	4.29	4.43	26.19	26.31

[a] From reactions in which the quantity of the organic reactant ranged from 0.025–0.05 mole.

Anal. Calcd. for $C_{20}H_{16}O_2$: C, 83.31; H, 5.59. Found: C, 83.27; H, 5.41.

Phenyl *p*-benzylbenzoate was prepared from *p*-benzylbenzoic acid in 83% yield using this same procedure; m.p. 85.5–86°.

Anal. Calcd. for $C_{20}H_{16}O_2$: C, 83.31; H, 5.59. Found: C, 83.52; H, 5.77.

A sample of *o*-hydroxydiphenylmethane, m.p. 21–22°, was prepared from benzyl chloride and sodium phenoxide.[12] Its *p*-isomer, m.p. 84°, was synthesized from benzyl chloride and phenyl.[13] These phenolic compounds were esterified with benzoyl chloride by the Schotten–Baumann method. The *o*-benzoyloxydiphenylmethane was obtained as a liquid of b.p. 195° (3 mm.), 247–250° (760 mm.), lit.[14] b.p. 249°. The *p*-benzoyloxydiphenylmethane had m.p. 87° (lit.[15] m.p. 87°). A sample of *o*-acetoxydiphenylmethane was prepared by adding 5 g. of acetyl chloride slowly to a mixture of 9.2 g. of *o*-hydroxydiphenylmethane, and 5 ml. of dry pyridine in 25 ml. of dry benzene. After the mixture had stood overnight, it was diluted with 50 ml. of benzene and extracted with 200 ml. of water. The organic phase was dried and distilled. The ester was obtained in 9.4 g. (83%) yield, b.p. 132° (3 mm.).

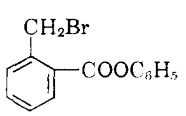
Anal. Calcd. for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 80.08; H, 6.44.

Essentially the same procedure was used to acetylate *p*-hydroxydiphenylmethane. The *p*-acetoxydiphenylmethane, which was obtained in 88% yield, had b.p. 140° (1 mm.).

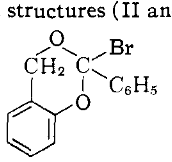
Anal. Calcd. for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 79.77; H, 6.24.

The Benzyl and Benzhydryl Bromides.—Several of the substituted benzyl and benzhydryl bromides were prepared by photobromination of the appropriate substituted toluene or diphenylmethane in carbon tetrachloride solution according to the procedure of Eliel and Rivard.[16] When bromine absorption was complete, the solvent was removed using a rotary film evaporator, and the residue was crystallized from ligroin. New substituted benzhydryl bromides which were synthesized in this way are described in Table I. Other bromides prepared by this procedure were methyl α-bromo-*o*-toluate, m.p. 34–34.5° (lit.[16] m.p. 32–32.5°); methyl α-bromo-*p*-toluate, m.p. 55–56° (lit.[17] m.p. 54–55°); benzhydryl bromide, m.p. 44–44.5° (lit.[18] m.p. 45°); and *o*-benzoyloxybenzyl bromide, m.p. 74–74.5°.

The last compound was also prepared by a photobromination procedure by Helferich and Liesen,[19] who reported m.p. 79° and who proposed two alternate structures (II and III).



II



III

Since the product obtained in the present investigation showed a strong infrared absorption band at 1730–1740 cm.$^{-1}$ which is characteristic of an ester carbonyl stretching vibration, it was assigned structure II.

By reaction of *p*-tolyl benzoate with N-bromosuccinimide, *p*-benzoyloxybenzyl bromide, m.p. 111°, was prepared.[20] This same procedure was also used as an alternate method of preparation of *o*-benzoyloxybenzyl bromide (86% yield), m.p. 74–74.5°.

Both α-bromo-*o*-toluic acid, m.p. 146°, and α-bromo-*p*-toluic acid, m.p. 223°, were prepared from the corresponding toluic acids by a method described elsewhere.[21]

The *o*- and *p*-methylbenzhydryl bromides were prepared by passing hydrogen bromide through ice-cooled solutions of the corresponding benzhydrols in dry benzene. The solutions of the products were dried with sodium sulfate and the bromides were recovered by distillation. The *o*-isomer, obtained in 67% yield from 0.1 mole of starting material, distilled at 150–155° (2 mm.). The *p*-isomer, obtained in 73% yield from 0.06 mole of the benzhydrol, distilled from 140–145° (1 mm.).

Anal. Calcd. for $C_{14}H_{13}Br$: C, 64.38; H, 5.02; Br, 30.60. Found (*o*-isomer): C, 64.44; H, 5.24; Br, 30.24. Found (*p*-isomer): C, 64.45; H, 5.16; Br, 29.42.

The methylbenzhydrols were prepared by zinc reduction of the corresponding methylbenzophenones.[22] The *o*-isomer had m.p. 94–95° (lit.[23] m.p. 95°), and the *p*-isomer had m.p. 52–54° (lit.[24] m.p. 52–53°).

The Kinetic Studies.—Acetone and dioxane were purified for use as solvents by methods described previously.[25,26] The water–acetone and water–dioxane mixtures used in the rate studies were prepared in large batches and stored in the dark. Check rate runs were made to ensure that new and old batches of a particular solvent mixture were of uniform composition. In preparing solvent mixtures which are later described as $(100 - x)\%$ aqueous acetone or aqueous dioxane, $(100 - x)$ volumes of acetone or dioxane were mixed with x volumes of water.

Reaction mixtures were prepared by adding enough of the appropriate solvent mixture to a weighed sample of the organic bromide to provide a final volume of 50 ml. The solvent was previously equilibrated to the temperature at which the run was to be conducted. Timing was started when the addition was half completed. The reaction flask was shaken and placed in a constant temperature bath. From time to time 5-ml. samples of the reaction mixture were withdrawn by pipet and transferred to a separatory funnel containing 30–40 ml. of ether and 10–15 ml. of water. Time was recorded when half of the sample was delivered to the separatory funnel. The funnel was shaken to transfer unreacted organic bromide to the ether phase. The aqueous phase was removed, and the ether phase was washed with a second 10–15-ml. portion of water. The combined aqueous extracts were analyzed for bromide ion by the Volhard procedure. In some cases the samples were analyzed for hydrogen ion, prior to the bromide ion analysis,

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(12) L. Claisen, *Ann.*, **442**, 238 (1925).

(13) L. McMaster and W. M. Bruner, *Ind. Eng. Chem.*, **28**, 505 (1936).

(14) I. Heilbron, "Dictionary of Organic Compounds," Vol. II, Oxford University Press, New York, N. Y., 1953, p. 759.

(15) T. Zincke and W. Walter, *Ann.*, **334**, 373 (1904).

(16) E. L. Eliel and D. E. Rivard, *J. Org. Chem.*, **17**, 1252 (1952).

(17) R. C. Fuson and H. C. Cooke, Jr., *J. Am. Chem. Soc.*, **62**, 1180 (1940).

(18) C. Courtot, *Ann. chim.*, [9] **5**, 80 (1916).

(19) B. Helferich and H. Liesen, *Ber.*, **83**, 567 (1950).

(20) J. H. Barnes, J. Elks, F. F. Stephens and J. G. Waller, *J. Chem. Soc.*, 764 (1953).

(21) J. B. Shoesmith, A. C. Hetherington and R. H. Slator, *ibid.*, **125**, 1312 (1924).

(22) C. S. Marvel and N. A. Hansen, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1932, p. 84.

(23) A. E. Chichibabin, *J. Russ. Phys. Chem. Soc.*, **41**, 1116 (1909).

(24) E. D. Hughes, C. K. Ingold and N. A. Taher, *J. Chem. Soc.*, 949 (1940).

(25) J. B. Conant and W. R. Kirner, *J. Am. Chem. Soc.*, **46**, 232 (1924).

(26) G. W. Beste and L. P. Hammett, *ibid.*, **62**, 2481 (1940).

by titration with standard base to the phenolphthalein end-point. The results of the two analyses generally were in excellent agreement.

Reaction mixtures which contained silver nitrate were prepared in essentially the same fashion as were those for runs without silver nitrate, except that the salt was included in the solvent mixture used to dissolve the organic bromide. The initial volume in a typical run was 100 ml. From time to time, 10-ml. samples were withdrawn for silver nitrate analysis. Each sample was added to a solution containing a known volume of standard potassium thiocyanate solution, 5 ml. of 6 *N* nitric acid and 1 ml. of saturated ferric alum solution, and the excess thiocyanate ion was determined by back titration with standard silver nitrate solution by the usual procedure.

Generally the reactions were followed to about 70% of completion. In studying reactions in the absence of silver nitrate at least three different runs on each bromide (at a particular temperature) were ordinarily made. Insofar as possible the initial organic halide concentration was varied about fourfold in these several runs. Solvolysis rate constants, k_s (eq. 1), were calculated from the slopes of the

$$\ln([\mathrm{RBr}]_i/[\mathrm{RBr}]_t) = k_s t \qquad (1)$$

linear plots of log $[\mathrm{RBr}]_t$ *versus* time, t. Each compound was investigated at two temperatures so that energies and entropies of activation could be calculated.

In the runs conducted with silver nitrate in the media the concentrations of the organic bromide and the silver salt both changed appreciably during the course of the reactions. Rate constants, k_{Ag^+}, were calculated on the assumption that the reactions were first order with respect to both silver ion and organic bromide concentrations (eq. 2). The rate constants were calculated from slopes of

$$\frac{1}{[\mathrm{RBr}]_i - [\mathrm{Ag}^+]_i} \ln \frac{[\mathrm{Ag}^+]_i\,[\mathrm{RBr}]_t}{[\mathrm{RBr}]_i\,[\mathrm{Ag}^+]_t} = k_{\mathrm{Ag}^+}t \qquad (2)$$

plots of log $[\mathrm{RBr}]_t/[\mathrm{Ag}^+]_t$. For some runs the lines obtained by plotting the data in this way gradually drifted upward with time, probably because of catalysis of the reaction by precipitated silver bromide.[27] The values of rate constants later reported are based on the early phases of the reactions.

The Products of Hydrolysis of the Benzyl and Benzhydryl Bromides.—Samples of the bromides were subjected to hydrolysis under conditions (solvent, concentration, temperature) typical of those employed in the rate runs. The benzyl bromides were allowed to stand in 80 volume % aqueous dioxane at 87.7° for at least 8 half-lives for hydrolysis. The benzhydryl halides were similarly hydrolyzed in 90 volume % aqueous acetone at 45°. Most of the solvent was removed under reduced pressure at temperatures below 45°. The residues were extracted with ether. The extracts were evaporated to dryness, and the remaining solids or high boiling liquids were crystallized from ligroin or distilled under reduced pressure.

The product obtained from *o*-carbophenoxybenzhydryl bromide was 3-phenylphthalide, m.p. and mixed m.p. with an authentic sample,[28] 114.5°. From the isomeric *p*-bromide, *p*-carbophenoxybenzhydrol, m.p. 100°, was obtained.

Anal. Calcd. for $C_{20}H_{16}O_3$: C, 78.93; H, 5.30. Found: C, 78.89; H, 5.29.

From *p*-benzoyloxybenzhydryl bromide, *p*-benzoyloxybenzhydrol, m.p. 116°, was obtained.

Anal. Calcd. for $C_{20}H_{16}O_3$: C, 78.93; H, 5.30. Found: C, 78.59; H, 5.27.

The *p*-acetoxybenzhydryl bromide produced *p*-hydroxybenzhydrol, m.p. 161° (lit.[29] m.p. 161°). From the reaction products of *o*-acetoxy- and *o*-benzoyloxybenzhydryl bromides only gummy semi-solids which could not be purified sufficiently for identification purposes were isolated.

From the hydrolysates of both methyl α-bromo-*o*-toluate and α-bromo-*o*-toluic acid the only organic product which could be isolated was phthalide, m.p. and mixed m.p. with an authentic sample,[30] 73°. From methyl α-bromo-*p*-toluate was obtained *p*-carbomethoxybenzyl alcohol, b.p. 155–157° (4–5 mm.).

Anal. Calcd. for $C_9H_{10}O_3$: C, 65.05; H, 6.06. Found: C, 64.98; H, 6.17.

The hydrolysis product of α-bromo-*p*-toluic acid was identified as *p*-carboxybenzyl alcohol, m.p. 181° (lit.[31], m.p. 179–180°); and *o*-benzoyloxybenzyl alcohol, m.p. 66° (lit.[32] m.p. 66°), was obtained from *o*-benzoyloxybenzyl bromide.

The Dissociation Rates of *o*- and *p*-Carbophenoxyiodobenzene Dichlorides.—A sample of *o*-carbophenoxyiodobenzene was prepared from 13.3 g. of *o*-iodobenzoyl chloride and 5.2 g. of phenol by the Schotten–Baumann method. The crude product (7.8 g., 48% yield) was a viscous liquid of very high boiling point. It was purified by molecular distillation, n^{25}_D 1.6326.

Anal. Calcd. for $C_{13}H_9O_2I$: C, 48.16; H, 2.80; I, 39.16. Found: C, 47.99; H, 2.83; I, 38.94.

The authors are indebted to Mr. Craig Asmundson, who prepared the ester for use in this investigation.

The same procedure was used to prepare *p*-carbophenoxyiodobenzene, m.p. 130–131°, from *p*-iodobenzoyl chloride (prepared from the free acid and thionyl chloride).

Anal. Calcd. for $C_{13}H_9O_2I$: C, 48.16; H, 2.80; I, 39.16. Found: C, 48.22; H, 3.01; I, 38.90.

The golden yellow dichlorides were precipitated by passing chlorine gas through solutions of 0.1–0.2 g. of the iodo compounds in 5 ml. of acetic acid. The precipitates were filtered, washed with carbon tetrachloride, air-dried and used without further purification. The dichlorides of the *o*- and *p*-isomers, which melted with decomposition at 86–87° and 124°, respectively, were both unstable and decomposed spontaneously after standing at room temperature for short periods of time. Their equivalent weights were determined iodometrically by the procedure described previously.[3] The values obtained for the *o*- and *p*-dichlorides were, respectively, 195.5 and 196.5; calcd. for $C_{13}H_9O_2ICl_2$: 197.5.

The rates of equilibration of these dichlorides with the free carbophenoxyiodobenzenes and chlorine in nitromethane were investigated by the spectrophotometric procedures described previously. A wave length of 380 mμ was used. The extinction coefficients of the *o*- and *p*-carbophenoxyiodobenzenes, their dichlorides and chlorine in ntromethane at this wave length are, respectively: 0.3, 0.7, 98, 102, 12.9. The experimental rate constants, k_1, for dichloride dissociation, as well as the equilibrium constants (see eq. 3), are summarized in Table II.

$$\mathrm{ArICl_2} \underset{k_2}{\overset{k_1}{\rightleftarrows}} \mathrm{ArI} + \mathrm{Cl_2}$$

$$K = k_1/k_2 = [\mathrm{ArI}][\mathrm{Cl_2}]/[\mathrm{ArICl_2}] \qquad (3)$$

The Preparation of *o*-Benzamidobenzhydrol.—A sample of *o*-aminobenzophenone was prepared from *o*-benzoylbenzoic acid by the method of Hewlett.[33] The amine (33 g.) was dissolved in 10 ml. of pyridine, and 25 g. of benzoyl chloride was added slowly to the solution. After it had stood overnight, the mixture was diluted with water. The *o*-

TABLE II

THE DISSOCIATION OF $XC_6H_4ICl_2$ (CH_3NO_2, 25.0°)

X, carbophenoxy	$10^3[XC_6H_4ICl_2]_i$, mole/l.	10^3K, mole/l.	10^4k_1, sec.$^{-1}$
para	5.90	5.9	2.14
para	4.02	5.6	2.08
para	2.00	5.8	1.84
ortho	15.8	1.4	[a]
ortho	10.3	1.5	[a]
ortho	5.2	1.8	[a]

[a] The reaction was too fast to follow by ordinary methods. Equilibrium was reached in less than 2 minutes, whereas over 3 hours was required for equilibration in the runs with the *p*-isomer.

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(27) E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt and Co., New York, N. Y., 1959, p. 274.

(28) F. Ullmann, *Ann.*, **291**, 23 (1896).

(29) B. Konig and S. von Kostanecki, *Ber.*, **39**, 4031 (1906).

(30) J. H. Gardner and C. A. Naylor, Jr., *Org. Syntheses*, **16**, 71 (1936).

(31) F. H. Case, *J. Am. Chem. Soc.*, **47**, 1143 (1925).

(32) M. C. Hart and A. D. Hirschfelder, *ibid.*, **43**, 1688 (1921).

(33) C. L. Hewlett, *J. Chem. Soc.*, 292 (1948).

benzamidobenzophenone which precipitated was recrystallized from ethanol; yield 43 g. (87%), m.p. 81° (lit.[34] m.p. 80.5°). To a solution of 15 g. of *o*-benzamidobenzophenone in methanol a solution of 2 g. of sodium borohydride in 50 ml. of water was added slowly with stirring. The white precipitate of *o*-benzamidobenzhydrol which separated during the addition was crystallized from alcohol; yield 10 g. (66%), m.p. 118–119°.

Anal. Calcd. for $C_{20}H_{17}O_2N$: C, 79.20; H, 5.61; N, 4.62. Found: C, 79.20; H, 5.83; N, 4.68.

The Conversion of *o*-Benzamidobenzhydrol to 2,4-Diphenyl-3,1,4-benzoxazine.—In an attempt to prepare *o*-benzamidobenzhydryl bromide a benzene solution of *o*-benzamidobenzhydrol was cooled in an ice-bath and gassed with hydrogen bromide until a substantial excess of the gas had been added. The mixture was dried with sodium sulfate, and the benzene was removed under vacuum with a rotary film evaporator. The yellowish-brown oily residue could not be induced to crystallize. It decomposed rapidly in air with the liberation of hydrogen bromide gas.

On the assumption that this material was crude *o*-benzamidobenzhydryl bromide, an attempt was made to estimate its hydrolysis rate. A solution of 3.7 g. of the oil in 50 ml. of 90% aqueous acetone was prepared. A 5-ml. sample of this solution was transferred to a separatory funnel containing 15 ml. each of water and ether. The funnel was shaken for a few seconds. The time lapse between preparation of the original solution and the shaking of the funnel was about 130 seconds. The aqueous phase was analyzed for bromide ion by the Volhard procedure. The bromide ion thus detected was 91% of that to be expected if the starting material were *o*-benzamidobenzhydryl bromide and if it were completely hydrolyzed in the 130 sec. reaction time. No increase in the bromide ion content of the hydrolysis reaction mixture with time was observed. It is possible that the oil was actually not the organic product, but instead another product which was contaminated with hydrogen bromide.

A second sample (2 g.) of the yellow-brown oil was dissolved in 90% aqueous acetone, and the solution was diluted with water 0.5 hour after its preparation. The resultant precipitate was crystallized from methanol to yield 1.2 g. of product, m.p. 114–115°.

Anal. Calcd. for $C_{20}H_{15}ON$: C, 84.18; H, 5.30; N, 4.91. Found: C, 84.19; H, 5.03; N, 4.95.

The infrared spectrum of this product in carbon tetrachloride contained no bands characteristic of an N–H or O–H stretch, which are present in the spectrum of *o*-benzamidobenzhydrol. A band at 1630 cm.$^{-1}$, characteristic of the C=N link, was, however, observed. The melting point of the product was depressed over 20° when it was mixed with *o*-benzamidobenzhydrol. The structure of 2,4-diphenyl-3,1,4-benzoxazine was assigned to this new material.

Results

There are a number of *o*-substituted benzyl ($XC_6H_4CH_2Cl$) and benzhydryl ($XC_6H_4CH(C_6H_5)Cl$) halides which solvolyze more slowly than their *p*-isomers. This reactivity difference is observed both when the substituents (X) are electron withdrawing (NO_2, halogen) and electron releasing (OCH_3, CH_3). Typical examples are cited in Table III. The comparatively low reactivities of the *o*-isomers may result because of steric hindrance by the ring substituents to solvation of the exocyclic carbon atom in the transition state.

The *o*-substituted benzyl and benzhydryl bromides used in the present investigation were chosen largely from a group of compounds having substituents which seem, at first glance, to be electronically constituted to function as participating groups in solvolysis type reactions. These compounds and their *p*-isomers were prepared in most cases by photobromination of the appropriate substituted toluene or diphenylmethane. Hydrolysis rate constants for the various bromides as well as the rate constant ratios for the several pairs of *o*- and *p*-isomers are listed in Table IV.

TABLE III

RELATIVE REACTIVITIES OF *o*- AND *p*-SUBSTITITED BENZYL AND BENZHYDRYL CHLORIDES

X	Reaction conditions	Relative reactivities *o*-isomer/*p*-isomer
	$XC_6H_4CH_2Cl$	
	Aq. acetone (*t*, °C.)	
F	50% (69.8)[a]	0.59
Cl	50% (69.8)[a]	.49
Br	50% (69.8)[a]	.55
I	50% (69.8)[a]	.59
Cl	50% (60)[b]	.52
CH_3	50% (60)[b]	.48
NO_2	50% (60)[b]	.88
OCH_3	67% (60)[c]	.01
	$XC_6H_4CH(C_6H_5)Cl$	
	Ethanol (*t*, °C.)	
Cl	(25)[d]	0.03
CH_3	(25)[d]	0.18

[a] G. M. Bennett and B. Jones, *J. Chem. Soc.*, 1815 (1935). [b] S. C. J. Oliver, *Rec. trav. chim.*, **49**, 697 (1930); S. C. J. Olivier and A. P. Weber, *ibid.*, **53**, 869 (1934). [c] M. Simonetta and G. Favini, *J. Chem. Soc.*, 1840 (1954). [d] J. F. Norris and C. Banta, *J. Am. Chem. Soc.*, **50**, 1804 (1928); J. F. Norris and J. T. Blake, *ibid.*, **50**, 1808 (1928).

TABLE IV

RATE CONSTANTS FOR THE HYDROLYSIS OF THE BROMIDES

X	Temp., °C.	Range[a] of [RBr]ᵢ, mole/l.	10^5k_s, sec.$^{-1}$	$\frac{k_s\ (ortho)}{k_s\ (para)}$
		$XC_6H_4CH(C_6H_5)Br$ in 90% aq. acetone		
H	25.0	0.124	16.4	
H	45.3	.182	116	
o-CH_3	9.5	0.079-0.148	7.4 ± 0.4	0.118
p-CH_3	9.5	.055- .098	62.8 ± 1.2	
o-$OCOCH_3$	25.0	.035- .121	2.23 ± 0.01	.053
p-$OCOCH_3$	25.0	.028- .133	41.7 ± 2.6	
o-$OCOCH_3$	45.3	.052- .089	20.8 ± 0.4	
p-$OCOCH_3$	9.5	.028- .194	7.4 ± .5	
o-$OCOC_6H_5$	25.0	.020- .061	0.68 ± .01	.026
p-$OCOC_6H_5$	25.0	.034- .101	26.7 ± 1.2	
o-$OCOC_5H_5$	45.2	.031- .085	6.84 ± 0.10	
p-$OCOC_6H_5$	9.5	.034- .079	5.03 ± .16	
o-$COOC_6H_5$	25.0	.020- .091	14.4 ± .2	86.1
p-$COOC_6H_5$	25.0	.020- .090	.167 ± .003	
o-$COOC_6H_5$	45.0	.018- .078	97 ± 4	59.1
p-$COOC_6H_5$	45.0	.022- .040	1.64 ± 0.03	
		$XC_6H_4CH_2Br$ in 80% aq. dioxane		
H	71.4	0.048-0.096	1.88 ± 0.04	
H	87.7	.021- .054	6.75 ± .05	
o-$COOCH_3$	71.4	.023- .091	2.67 ± .07	3.61
p-$COOCH_3$	71.4	.028- .090	0.74 ± .04	
o-$COOCH_3$	87.7	.025- .093	11.0 ± .3	4.54
p-$COOCH_3$	87.7	.031- .102	2.42 ± .03	
o-$OCOC_6H_5$	71.4	.006- .055	0.548 ± .12	0.21
p-$OCOC_6H_5$	71.4	.031- .087	2.61 ± .06	
o-$OCOC_6H_5$	87.7	.020- .053	2.02 ± .01	0.20
p-$OCOC_6H_5$	87.7	.027- .097	9.9 ± .2	
o-COOH	71.4	.023- .086	68.1 ± 2.7	87.3
p-COOH	71.4	.023- .101	0.78 ± 0.02	
o-COOH	87.7	.028- .100	231 ± 13	84.3
p-COOH	87.7	.025- .097	2.74 ± 0.10	
		$XC_6H_4CH_2Br$ in 50% aq. acetone		
o-$COOCH_3$	45.0	0.062-0.127	1.40 ± 0.08	1.82
p-$COOCH_3$	45.0	0.040-0.050	0.78 ± 0.01	

[a] With most of the bromides several runs were made, in which $[RBr]_i$ was varied over the indicated range.

The Relative Reactivities of the Benzhydryl Bromides.—Of the several pairs of *o*- and *p*-substituted benzhydryl bromides which were

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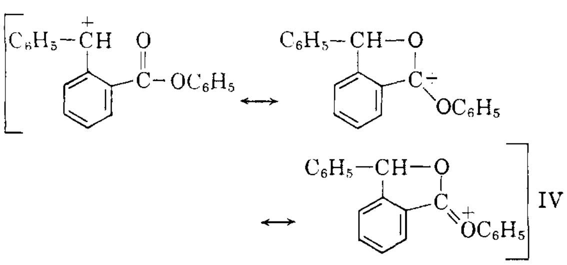
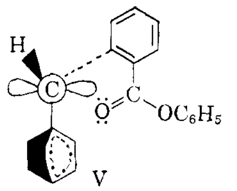
(34) A. Bischler and D. Barad, *Ber.*, **25**, 3090 (1892).

studied, including the methyl, acetoxy, benzoyloxy and carbophenoxy derivatives, only in the last case was the *o*-isomer more reactive than the *para*. Solvolyses of *t*-alkyl halides which have highly branched carbon chains are presumed to be subject to steric acceleration, because of the release of strain which takes place when trigonal carbonium ion intermediates are formed.[35] A similar argument might be advanced to explain the unusually high reactivity of *o*-carbophenoxybenzhydryl bromide. However, when the carbophenoxy group is replaced by other substituents which are of about the same bulk ($OCOCH_3$ and $OCOC_6H_5$) the *o*-isomers are substantially less reactive than the *p*-analogs. It seems likely, therefore, that the high positive ratio of $k_s(ortho)/k_s(para)$ for the carbophenoxybenzhydryl bromides must be attributed to electronic rather than steric causes. The unusual rate effect of the *o*-substituent is best explained on the basis that it reduces the activation energy for hydrolysis by participation as a neighboring group (structure IV) in promoting polarization of the C–Br bond. For maximum participation of an *o*-$COOC_6H_5$ group, the ring containing that substituent must, as activation occurs, assume a position in which it is approximately perpendicular to the plane of the trigonal valences of the carbon atom which is under attack. It is assumed in this argument that, insofar as its valences are concerned, this carbon has a geometry approximating that of a carbonium ion in the transition state. With the substituted ring so oriented (structure V), the conditions for overlap of a p-orbital of the carbonyl oxygen with the vacant p-orbital on carbon at the reaction center are most favorable. It is presumed that the unsubstituted ring lies perpendicular to the latter orbital.[36]



IV



V

In the earlier work on the effect of an *o*-COOR group on the equilibration rate of a substituted iodobenzene dichloride the $COOCH_3$ rather than the $COOC_6H_5$ group was used as the *o*-substituent. Since in all attempted syntheses of *o*-carbomethoxybenzhydryl bromide, 3-phenylphthalide was obtained as the product, the more stable *o*-carbophenoxybenzhydryl bromide was used in the present investigation. It seemed of interest, therefore, to determine whether or not the *o*-$COOC_6H_5$ group functions as an internal nucleophilic catalyst in the iodobenzene dichloride reaction. As described in the Experimental section, an affirmative result has been obtained.

As has already been noted the *o*-acetoxy- and benzoyloxybenzhydryl bromides hydrolyze less rapidly than their *p*-isomers. The ratios of the rate constants for the two sets of isomers (Table IV) are actually comparable in magnitude to that for the methylbenzhydryl bromides. The *o*-$OCOCH_3$ and *o*-$OCOC_6H_5$ groups also do not function as participating substituents in the iodobenzene dichloride dissociation reaction.[3] It was suggested earlier in this connection that these two substituents fail to act as internal nucleophilic catalysts because of the high electronegativity of their aryl-bound ether oxygen atoms. This argument seems less plausible now that the *o*-carbophenoxy group has been classified as a participating substituent. Were it correct, the phenyl group of the *o*-$COOC_6H_5$ substituent itself should have a detrimental effect on the nucleophilic character of the carbonyl oxygen atom. Contrary to what has been decided previously,[3] it seems likely that the differences in the capacities of the two types of substituents (COOR and OCOR) to function as nucleophiles in releasing electrons to a nearby positively polarized exocyclic atom is geometric, although subtly so, in origin. From a consideration of molecular models of the two *o*-substituted benzhydryl cations it can be concluded that the cyclization required for release of electrons by *o*-COOR to the trigonal carbon atom (structure IV) is an essentially strain-free process, or at least more strain free than when *o*-OCOR is the participating substituent.

The Relative Reactivities of the Benzyl Bromides.—The reactivity of *o*-carbomethoxybenzyl bromide, like that of *o*-carbophenoxybenzhydryl bromide, is greater than that of its *p*-isomer. However, the $k_s(ortho)/k_s(para)$ ratio for these two substituted benzyl bromides is sufficiently low, so that it must be concluded that *o*-substituent participation by $COOC_6H_5$, if it occurs at all, makes a much less important contribution to the activation process in benzyl bromide hydrolysis than in the benzhydryl bromide reaction. It is interesting to note in this regard that the $k_s(ortho/k_s(para)$ ratio for the reaction of the carbophenoxybenzhydryl bromides in 90% aqueous acetone at 25° is over 3000 times that for the reaction of the benzoyloxybenzhydryl bromides; the rate constant ratio for the carbomethoxybenzyl bromides (71.4°, 80% aqueous dioxane) is only 17 times that for the benzoyloxybenzyl bromides, the *o*-isomer of which must certainly hydrolyze without participation of the $OCOC_6H_5$ substituent.

The failure of the *o*-$COOCH_3$ group to participate very effectively in the benzyl bromide reaction can be taken as an indication that a benzyl cation (or

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[35] H. C. Brown and R. H. Fletcher, *J. Am. Chem. Soc.*, **71**, 1845 (1949).

[36] The question as to whether or not the aromatic rings of a diarylcarbonium ion must approach a coplanar orientation to provide for maximum stability is subject to debate; see for example, N. C. Deno, J. J. Jaruzelski and A. Schriesheim, *J. Org. Chem.*, **19**, 155 (1954); N. N. Lichtin and M. J. Vignale, *J. Am. Chem. Soc.*, **79**, 579 (1957). Even though a propeller-like arrangement may, in normal situations, be most favorable, the stabilization energy resulting from *o*-substituent participation must be sufficiently large to overcome the destabilization resulting when the rings are oriented perpendicular to each other.

a partially developed benzyl cation) is more effectively stabilized through overlap of the vacant p-orbital of the trigonal exocyclic carbon atom with the π-orbital of the ring than with a filled orbital of a nucleophilic *o*-substituent. From a geometric point of view these two processes are mutually exclusive. A similar argument has been presented[37] to account for the fact that in the reactions following the generation of *o*-carboxybenzyl radical, hydrogen transfer is not a more dominant process than it is. Presumably *ortho* participation takes place much more effectively in the hydrolysis of a suitably substituted benzhydryl bromide because the unsubstituted ring is free to assume a position in the transition state in which it is coplanar, or nearly so, with the bonds to the exocyclic carbon atom.

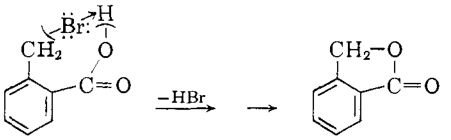
The possibility has been considered that *o*-substituent assistance might become important in benzyl bromide hydrolysis as the reaction conditions are changed to increase the development of positive charge at the reaction center in the activation process. With this point in mind the $k_s(ortho)/k_s(para)$ ratio for the reactions of the carbomethoxybenzyl bromides in 80% aqueous dioxane were compared with that for the reactions in 50% aqueous acetone. Unfortunately the reactivity ratios for the two media could not conveniently be determined at the same temperatures. However, the observed ratios were found to be very similar for the two solvents (see Table IV), and in fact the lower value was obtained for the more polar of the two media. The rates of solvolysis of the *o*- and *p*-carbomethoxy- and *o*- and *p*-benzoyloxybenzyl bromides in aqueous acetone in the presence of silver nitrate were also investigated. The results are summarized in Table V in terms of the bimolecular rate constants, k_{Ag^+}, as defined in eq. 2. Again the *o*-benzoyloxy compound was found to be substantially less reactive than its *p*-isomer, and the *o*-carbomethoxy derivative only slightly more so than its *p*-isomer. That is, even under conditions which very likely provide for appreciable carbonium ion character in the transition state, the effectiveness of *o*-$COOCH_3$ as a participating substituent is not great.

TABLE V

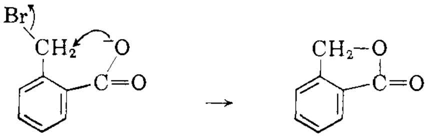
SOLVOLYSIS OF $XC_6H_4CH_2Br$ IN AQUEOUS ACETONE IN THE PRESENCE OF SILVER NITRATE

X	Init. concn., moles/l. $10^3[AgNO_3]$	Init. concn., moles/l. $10^3[RBr]$	$10^2 k_{Ag^+}$, sec.$^{-1}$ mole^{-1} l.	$\frac{k_{Ag^+}\ (ortho)}{k_{Ag^+}\ (para)}$
	80% aq. acetone at 25.0°			
o-$OCOC_6H_5$	16.34	19.8	0.31	
	8.17	11.5	.26	
	4.08	5.21	.20	0.015
p-$OCOC_6H_5$	16.34	18.35	19.1	
	8.17	10.12	14.4	
	4.08	5.40	20.0	
	50% aq. acetone at 25.0°			
o-$COOCH_3$	53.2	31.5	1.27	
p-$COOCH_3$	51.3	34.8	0.64	2.0

As is indicated in Table IV, contrary to what is observed for the corresponding methyl esters, α-bromo-*o*-toluic acid is solvolyzed much more rapidly than is its *p*-isomer. Because the *o*-$COOCH_3$ group is relatively ineffective as a participating substituent, it seems unlikely that the high reactivity of the *o*-COOH substituted bromide can be ascribed to nucleophilic participation by the *free* carboxyl group. Two other explanations are proposed. The first of these, which seems the more plausible, hinges on the assumption that in the rate-determining step the bromine of the C–Br bond is subject to electrophilic attack by the *o*-COOH group (eq. 4). Alternately the anion of the acid, which must be present at low concentration in the reaction mixture, may undergo an internal SN2 type displacement to form phthalide in a one-step reaction (eq. 5). Although the latter mechanism may not be ruled out on geometric grounds, it is questionable whether the free anion is present in high enough concentration in the medium (80% aqueous dioxane) so that it is an important reaction intermediate. Further work on this reaction is planned.

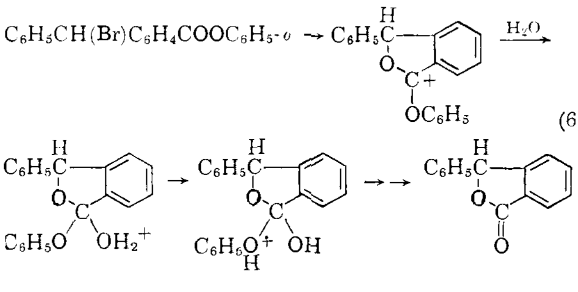


(4)



(5)

As noted in the discussion of reaction products which appears in the Experimental section, phthalide is the only pure product isolated from the hydrolysis of α-bromo-*o*-toluic acid and also from methyl α-bromo-*o*-toluate. An attempt was made to decide whether, as seems highly probable, the immediate product of reaction of the latter compound is *o*-carbomethoxybenzyl alcohol (which subsequently and readily undergoes a cyclization reaction to form the lactone). No clear cut results were obtained. It should be noted in this regard that 3-phenylphthalide was isolated as the hydrolysis product of *o*-carbophenoxybenzhydryl bromide. This may derive by breakdown of the corresponding alcohol, which is a likely reaction intermediate, or it may form by the process outlined in eq. 6.



(6)

Thermodynamic Constants.—The energies and entropies of activation for the various reactions for which appropriate data are provided in Table IV are summarized in Table VI. The reactions

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[37] F. D. Greene, G. R. Van Norman, J. C. Cantrill and R. D. Gilliom, *J. Org. Chem.*, **25**, 1790 (1960).

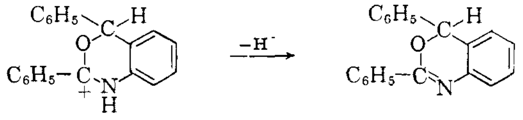
of the α-bromotoluic acids are now regarded as special cases (see eq. 4 and 5), and the thermodynamic constants reported for these compounds will not be discussed until further work on their hydrolyses has been done. For the other reactions, except for those of the carbophenoxybenzhydryl bromides, the activation energies for the *o*-isomers are equal to or greater than those for the corresponding *p*-isomers. In the case of the carbophenoxybenzhydryl halides the E_a value for the *o*-isomer is 3.5 kcal. less than that for the *p*-isomer, a differential which is considered to reflect the energetic advantage of reaction in the presence of a participating substituent. The activation entropy for the *ortho* compound is more negative than that for the *para* compound, whereas in most cases the reverse is true. Where *ortho* participation does not occur, it is probable that the entropy losses attending solvation in the transition state are, because of steric hindrance to solvation, less than those for the *p*-isomers. The fact that the entropy of activation for reaction of *o*-benzoyloxybenzyl bromide is more negative than that for the *p*-isomer cannot be taken as evidence of *o*-substituent participation, since such participation clearly does not occur in the hydrolysis of *o*-benzoyloxybenzhydryl bromide.

TABLE VI

THE HEAT AND ENTROPY OF ACTIVATION FOR THE HYDROLYSIS OF THE BROMIDES

X	E_a, kcal./mole	$-\Delta S^{\ddagger}$, e.u.
	$XC_6H_4CH_2Br$ in 80% aq. dioxane	
H	19.4 ± 0.4	26.1 ± 1.2
o-COOH	18.5 ± 1.1	21.8 ± 3.2
p-COOH	19.2 ± 0.7	28.4 ± 2.0
o-$COOCH_3$	21.4 ± .6	19.7 ± 1.7
p-$COOCH_3$	17.0 ± .7	35.1 ± 2.0
o-$OCOC_6H_5$	19.8 ± .4	27.6 ± 1.2
p-$OCOC_6H_5$	20.2 ± .5	23.2 ± 1.5
	$XC_6H_4CH(C_6H_5)Br$ in 90% aq. acetone	
H	18.2	16.8
o-$OCOCH_3$	20.8 ± 0.2	12.1 ± 0.7
p-$OCOCH_3$	18.6 ± .8	13.7 ± 2.7
o-$OCOC_6H_5$	21.6 ± .2	11.7 ± 0.7
p-$OCOC_6H_5$	18.1 ± .7	16.1 ± 2.3
o-$COOC_6H_5$	17.7 ± .4	18.8 ± 1.3
p-$COOC_6H_5$	21.2 ± .2	16.1 ± 0.7

The Attempted Preparation and Hydrolysis of *o*-Benzamidobenzhydryl Bromide.—As described in the Experimental section a pure sample of *o*-benzamidobenzhydryl bromide, a compound potentially subject to hydrolysis *via* an intramolecular nucleophile-catalyzed process, could not be prepared. The crude product obtained by gassing *o*-benzamidobenzhydrol was subjected to hydrolysis in 90% aqueous acetone in an attempt both to estimate the reaction rate and to characterize the bromide in terms of the structure of its hydrolysis product. The material isolated from the reaction in aqueous acetone, which is presumed to be 2,4-diphenyl-3,1,4-benzoxazine, very possibly was formed from the crude bromide *via* a cyclic intermediate (eq. 7). Indications are that hydrolysis



(7)

of the *o*-benzamido derivative occurs very rapidly. In view of the uncertainty concerning the identity of the bromide, however, no unqualified statements can be made concerning the course of the reactions leading to the formation of the substituted benzoxazine.

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[CONTRIBUTION FROM THE LABORATORY OF MOLECULAR STRUCTURE AND SPECTRA, DEPARTMENT OF PHYSICS, UNIVERSITY OF CHICAGO, CHICAGO 37, ILLINOIS]

Molecular Complexes and their Spectra. XIV. Iodine Complexes with Thiourea and Thioacetamide

BY ROBERT P. LANG

RECEIVED AUGUST 15, 1961

Spectrophotometric studies of dichloromethane solutions of iodine with thiourea, and with thioacetamide, have shown the existence, in each case, of a new intense absorption band in the near ultraviolet. This band has been interpreted as the charge transfer (CT) band of a 1:1 molecular complex. The thermodynamic and spectral characteristics of these complexes have been determined. It has been found that electronic absorption bands characteristic of thiourea, and of thioacetamide, are shifted toward shorter wave lengths upon complex formation with iodine, along with the well known "blue shift" of the visible iodine band. A discussion on the nature of the bonding and the electronic spectra in these complexes is given.

Introduction

Iodine is known to form 1:1 molecular complexes in solution with such compounds as aliphatic ethers, sulfides and amines in which the lone pair electrons on the oxygen, sulfur and nitrogen atoms, respectively, act as electron donors toward iodine.[1] Iodine is also known to form 1:1 complexes with aniline derivatives in which the nitrogen lone pair is in intramolecular resonance with the π electrons of the aromatic ring, which should lead to a decrease in the external donor strength of the nitrogen lone pair. Nevertheless, the nitrogen lone pair has been shown to be the probable coördinating site for iodine in these 1:1 complexes.[2]

In addition, the existence of 1:1 iodine complexes

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(1) H. Tsubomura and R. Lang, *J. Am. Chem. Soc.*, **83**, 2085 (1961); additional references are cited in this paper.

(2) H. Tsubomura, *ibid.*, **82**, 40 (1960).