[CONTRIBUTION FROM THE MARION EDWARDS PARK LABORATORY OF BRYN MAWR COLLEGE]

Relative Rates of Iodination of *p*-Alkylphenols

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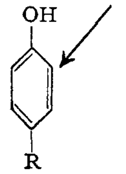
The rates of iodination of various *p*-alkylphenols have been measured in several aqueous solvents, and the effect of the alkyl groups on the meta position has been evaluated.

The direct iodination of *p*-cresol takes place ortho to the hydroxyl group and meta to the alkyl group.[2] A similar orientation has been shown to hold for the iodination of a number of other *p*-alkylphenols[3] and must be generally accepted as eminently reasonable on theoretical grounds. This being the case, a kinetic study of the iodination of various *p*-alkylphenols should give information about the effect of alkyl groups toward electrophilic substitution at the meta position (I). The result of such a study should throw light on the problem of the electrical effects of alkyl groups and of the propagation of substituent effects around the benzene ring. It should also be of interest in regard to the question of the relative importance of the hyperconjugation *versus* the general inductive effect of alkyl groups. The former, by conventional theories, should be more effective in the ortho/para positions and should be greatly diminished when acting through the meta position. The latter might be enhanced, because of the greater proximity of the alkyl groups to the point of attack.



I

The *p*-alkylphenols were iodinated in various aqueous solvents under conditions similar to those used in the iodination of aniline and phenol in water.[4] For solubility reasons water alone could not be used, but it was assumed that, as in aqueous iodination, the iodinating species is a positive entity, *i.e.*, either $I^{\oplus}$ or $H_2OI^{\oplus}$. Since the iodination is strongly catalyzed by the buffer constituents, all comparative rates were determined at a constant buffer concentration. In one case (in 30% methanol) rate constants for reaction of four alkylphenols were determined at three different buffer concentrations at constant *p*H, and the rate constants for the uncatalyzed reaction were obtained by extrapolation to zero buffer concentration. In all runs the concentration of iodine was 0.002 *M* and that of the phenol was 0.008 *M* (except that the phenol was 0.004 *M* in 10% acetic acid). The concentration of potassium iodide was in constant excess. The results are summarized in Table I.

TABLE I

RATES OF IODINATION OF *p*-ALKYLPHENOLS AT 25°[a]

R in *p*-C_6H_4-OH	10% HAc k_2	10% HAc rel. rates	25% methanol[b] k_2	25% methanol[b] rel. rates	30% methanol[c] $k_2 \times 10$	30% methanol[c] rel. rates	30% dioxane[b] $k_2 \times 10^2$	30% dioxane[b] rel. rates
Me	1.18	100	1.43	100	7.96	100	8.71	100
Et	1.44	122	1.68	117	9.09	114	9.02	104
i-Pr	1.69	143	1.91	134	10.6	133	9.46	109
t-Bu	2.16	183	2.43	170	13.6	171	11.4	131
n-Pr	1.43	121	..	...	9.43	118	...	...
n-Bu	...	...	..	...	9.58	120	...	...
s-Bu	...	...	..	...	10.8	136	...	...
t-Am	...	...	..	...	16.3	205	...	...
H	0.899	76	..	...	7.23	91	7.80	90

[a] Rate constants in liters mole^{-1} min.$^{-1}$. [b] KH_2PO_4 0.020 *M*, Na_2HPO_4 0.010 *M*. [c] KH_2PO_4 0.0250 *M*, Na_2HPO_4 0.0125 *M*.

Under all conditions of solvent the relative rates fall in a well spaced order which indicates the predominant operation of the inductive effect. The electron releasing activating effect of the meta alkyl groups, and therefore the order of substitution, is in the sequence *t*-Bu > *i*-Pr > Et > Me. This order in meta iodination by a positively charged entity is therefore opposite to that obtained for *para* bromination and chlorination by *molecular* halogen,[5,6] but the same as para nitration by the nitronium ion, $NO_2^{\oplus}$.[7]

The relative rate constants for the uncatalyzed reactions of the same four compounds in 30% methanol have the values Me:Et:*i*-Pr:*t*-Bu as 100:116:129:186, and show therefore the same order of reactivity as the constants obtained at constant buffer concentration.

Some other *p*-alkylphenols were studied less exhaustively. Their relative rates lie as expected from an operation of the inductive effect and show no unusual behaviors. The *p*-*n*-propyl- and *p*-*n*-butylphenols have about the same order of reactivity as the *p*-ethyl compound. The *s*-butyl group is comparable to the *i*-propyl group, and the *p*-*t*-amyl compound is faster than *p*-*t*-butylphenol.

Reaction in 30% dioxane is slower than that in 30% methanol by a power of ten and the relative rates are more closely spaced. This may be due to complexing between the dioxane and the phenols, as has been suggested in the *t*-butylation of phenol,[8] or to complexing between dioxane and iodine.

Although the results of the iodination of *p*-

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[1] In part from an M.A. thesis submitted by I. Nelidow to the Department of Chemistry of Bryn Mawr College, June, 1952.

[2] C. Schall and C. Dralle, *Ber.*, **17**, 2528 (1884); C. Willgerodt and A. Kornblum, *J. prakt. Chem.*, [3] **39**, 289 (1889).

[3] C. M. Suter and R. D. Schultz, *J. Org. Chem.*, **16**, 1117 (1951).

[4] E. Berliner, THIS JOURNAL, **72**, 4003 (1950); **73**, 4307 (1951).

(5) P. B. D. de la Mare and P. W. Robertson, *J. Chem. Soc.*, 279 (1942); P. W. Robertson, P. B. D. de la Mare and B. E. Swedlund, *ibid.*, 782 (1953).

(6) E. Berliner and F. Berliner, THIS JOURNAL, **71**, 1195 (1949).

(7) H. Cohn, E. D. Hughes, H. H. Jones and M. G. Peeling, *Nature*, **169**, 291 (1952).

(8) H. Hart and J. J. Bordeaux, Abstracts of Papers presented to the Division of Organic Chemistry of the American Chemical Society, Boston, Mass., April, 1951, p. 84 M.

alkylphenols make it seem very likely that the predominant effect of the *m*-alkyl groups under the stated conditions is the inductive effect, they do not constitute an unambiguous demonstration of this effect for the following reason. It has previously been shown[4] that iodination of phenol in water in all likelihood takes place on the phenoxide ion rather than the undissociated phenol, and the same is probably also true in the present iodinations. To make the results meaningful, the dissociation constants of the various phenols in the different solvent mixtures would have to be known, or at least their relative orders. We had available only unpublished measurements of the dissociation constants of four *p*-alkylphenols in 50% ethanol, obtained by measuring the *p*H of a half-neutralized solution.[9] These data provide an approximate relative order of the strength of the phenols in the named solvent. When these values, which do not follow a clear-cut order, are used, the relative rate constants for the iodination of the *p*-alkylphenoxide ions are obtained as shown in Table II. Another set of dissociation constants can be obtained from Hammett's σ-constants for the *p*-alkyl groups and ρ for dissociation of phenols in water.[10] That is, the assumption, not necessarily valid, is made, that the *p*-alkyl groups affect the dissociation constants of phenols in the same way as they affect the benzoic acids. Rate constants calculated from these data are also listed in Table II. For both sets of data the general order of the inductive effect is maintained, but the spacing is less regular (because of the unevenness of the dissociation constants). Neither method is satisfactory, but the dissociation constants of the phenols, as those of the benzoic acids,[11] all fall within one-tenth of a *pK* unit, and these small differences are not likely to seriously upset the relative rates. Furthermore, the results of the iodination of the phenols find support in a study of the iodination of *p*-alkylanilines, which should give the same information as the iodination of the phenols without the complication caused by the ionization of the aromatic compound. The iodination of the *p*-alkylanilines also shows an inductive effect order.

TABLE II

CALCULATED RELATIVE RATE CONSTANTS FOR THE IODINATION OF *p*-ALKYLPHENOXIDE IONS IN 30% METHANOL AT 25°

R in p-$RC_6H_4O^-$	Rel. rates (from K_{exp})	Rel. rates (from K_σ)
Me	100	100
Et	121	104
i-Pr	123	122
t-Bu	181	193

It is believed that the predominant operation of an inductive effect by alkyl groups in the *meta* position is not necessarily the rule, but that the relative order will depend on the nature of the attacking agent and of the reaction, just as it does in para substitution. A discussion of the significance of these results, as well as of the relation between the electronic effect of alkyl groups and the nature of the substituting agent, will be postponed until the study of the iodination of *p*-alkylanilines, now in progress, is completed.

Experimental Part

Preparation of Materials.—Solvents were purified by standard procedures. The dioxane was redistilled from sodium about every four weeks, because it readily became contaminated with peroxides; it was stored over sodium. The aqueous solvents were prepared by adding the appropriate volume of solvent to a 1-l. volumetric flask and, after thermostating, filling to the mark with distilled water. The buffer constituents, potassium iodide and iodine, were best Reagent Grade chemicals and were used without further purification.

In the preparation of the phenols special care was taken to avoid the presence of isomeric substances. Those phenols that are liquids or low-melting solids were converted in bulk to their benzoates, and the purified benzoates were hydrolyzed to the phenols. Phenol and its *p*-methyl, *p*-ethyl, *p*-*t*-butyl and *p*-*t*-amyl derivatives were commercial samples. The other phenols were prepared by sulfonating the purified hydrocarbons with fuming sulfuric acid by the method used for the sulfonation of *t*-butylbenzene.[12] The sodium sulfonates were crystallized several times from brine solution and converted to the phenols by alkali fusion.[12] The distilled phenols were converted to the benzoates in 50–100-g. lots[13] where necessary, and the benzoates were crystallized between two and four times from 95% ethanol. The pure benzoates were refluxed in the presence of twice the theoretical amount of potassium hydroxide in aqueous ethanol until a homogeneous solution resulted. This was acidified with hydrochloric acid, extracted with ether, and the ether layer was freed from benzoic acid by thorough extraction with sodium bicarbonate solution. The phenols were then obtained in the usual way by distillation. The yields in the sulfonation ranged from 53 to 100%, in the alkali fusion from 46 to 68%, in the benzoylation from 33 to 66.5% and in the hydrolysis from 57.3 to 82.5% of pure product. Liquid phenols were fractionated twice and solids were crystallized several times to constant melting point. The physical constants of the phenols are listed below, and the melting points of the benzoates which were used in the hydrolysis are recorded.[14]

R in p-RC_6H_4OH	B.p. (mm.) or m.p., °C.	M.p. of benzoates, °C.
H[4]		
Me	201.7–201.9 (755)	70.0–70.3, lit.[15] 71–72
Et	217.9–218.0 (762)	58.5–59.5, lit.[16] 59–60
i-Pr	60.5–61.5, lit.[15] 61	
n-Pr	232.3–232.5 (763)	34.0–34.6, lit.[15] 37–38
n-Bu	247.7–247.9 (758)	27.5–28.0, lit.[15] 27
sec-Bu	58.0–58.5, lit.[15] 53–54; 59	
t-Bu	98.8–99.6, lit.[15] 99; 97.5	
t-Am	93.5–94.2, lit.[15] 92–93	

Kinetic Runs.—In the dioxane and methanol solvents the ratio KH_2PO_4 to Na_2HPO_4 was always 2:1. The *p*H of such a solution in 30% methanol, at the same ionic strength as that used in the actual runs, was 6.92 as determined with a Beckman Model G *p*H meter. Rate constants for the uncatalyzed reactions were extrapolated from runs in which the concentration of KH_2PO_4 was 0.025, 0.02 and 0.01 *M*. Runs in 10% aqueous acetic acid were conducted in the presence of 1 *M* sodium acetate; the *p*H of this solution was 4.50. Exact amounts of buffers were dissolved in the solvent mixture in such concentrations that dilution

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[9] Senior Honors Thesis of Miss Barbara Bunce, June, 1947.

[10] L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, Chapter VII.

[11] J. W. Baker, J. F. J. Dippy and J. E. Page, *J. Chem. Soc.*, 1774 (1937).

[12] L. F. Fieser, "Experiments in Organic Chemistry," 2nd ed., D. C. Heath and Co., Boston, Mass., 1941, p. 181.

[13] R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1940, p. 47.

[14] We thank Dr. Margaret Quinn Malter for help in the preparation of the phenols.

[15] I. M. Heilbron, "Dictionary of Organic Compounds," Oxford University Press, New York, N. Y., 1934.

[16] A. Béhal and E. Choay, *Bull. soc. chim.*, [3] **11**, 209 (1894).

of an appropriate volume to 100 ml. resulted in a solution of the desired buffer concentration. In a similar way the phenols were accurately weighed out and dissolved in the solvent so that 40 ml. of the solution (or 80 ml. where the solubility of the phenols was low), diluted to 100 ml., provided a solution 0.008 *M* in phenol. In acetic acid the phenol concentration was 0.004 *M*. The iodide–iodine stock solution was ten times stronger than the final concentration and 10-ml. portions were used. The final concentration of potassium iodide was 0.12 *M* in 30% methanol, 0.03 *M* in 10% acetic acid and 0.1 *M* in the remaining solvents. The actual kinetic runs were conducted as described before.[4] Reaction was usually followed up to 50–60%, except in the case of *p*-*n*-butylphenol where an upward drift was noted after 40% reaction. Rate constants were calculated from the integrated form of the second-order rate equation. They are expressed in liters mole^{-1}min.$^{-1}$. All runs were conducted at least in duplicate. The results of two runs are given in Table III. With few exceptions the average deviations in the rate constants within each run, and in the average rate constants listed in Table I, were 2% or less.

TABLE III

THE IODINATION OF *p*-*t*-BUTYLPHENOL AT 25° IN 30% METHANOL

p-*t*-Butylphenol 0.008005 *M*, I_2 0.002 *M*, KH_2PO_4 0.025 *M*, Na_2HPO_4 0.0125 *M*, KI 0.12 *M*

Time, min.	0.01990 *M* thiosulfate, ml.	k_2, liters mole^{-1} min.$^{-1}$
0	1.951	..
8	1.790	1.36
17	1.626	1.37
24	1.517	1.35
33	1.381	1.36
49	1.180	1.35
57	1.100	1.34
64	1.021	1.35
74	0.912	1.39

THE IODINATION OF *p*-CRESOL AT 25° IN 10% ACETIC ACID

p-Cresol 0.00410, I_2 0.002 *M*, NaAc 1 *M*, KI 0.03 *M*

Time, min.	0.02 *M* thiosulfate, ml.	k_2, liters mole^{-1} min.$^{-1}$
0	1.961	..
11.5	1.865	(1.08)
28	1.722	1.17
47	1.582	1.17
57	1.522	1.15
73	1.420	1.16
90	1.317	1.18
111	1.210	1.18
122	1.153	1.19

The dissociation constants of the phenols in 50% (by volume) ethanol–water, obtained without activity corrections from the reading of the *p*H of a half-neutralized solution on a Leeds and Northrup *p*H meter calibrated with aqueous buffer solutions, had the following values: ($K \times 10^{12}$) *p*-H 5.5, *p*-Me 2.5, *p*-Et 2.35, *p*-*i*-Pr 2.7, *p*-*t*-Bu 2.35. The ratio *p*-*t*-Bu/*p*-H (0.43) is similar to that obtained in 23% aqueous butanol (0.48),[17] and the value for the *p*K of phenol (11.26) falls between those reported for 40 and 60% ethanolic solutions (10.93 and 11.60).[18]

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[17] W. H. Fletcher, THIS JOURNAL, **68**, 2727 (1946).

[18] M. Mizutani, *Z. physik. Chem.*, **118**, 326 (1925).

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF MICHIGAN]

Unsaturated Sulfonic Acids. III. Bromination and Brominolysis of *p*-Substituted 2-Phenylethene-1-sulfonic Acid Derivatives[1]

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The electronic theory predicts that electrophilic attack on the double bond in β-arylethenesulfonic acids should be retarded by electron-withdrawing groups in the para position and accelerated by electron-releasing groups. This prediction was confirmed by bromination of *p*-nitro-, *p*-methoxy-, *p*-hydroxy-, *p*-amino- and *p*-acetamidophenylethenesulfonic acids. A bromine atom enters the side chain ***alpha*** to the sulfo group, and the process involves substitution rather than addition. With the more active rings, nuclear bromination competes with side-chain bromination. Excess bromine displaces the aromatic ring from the *p*-amino-, *p*-hydroxy- and *p*-methoxy-substituted sulfonates. It is suggested that a benzyl-type alcohol is the intermediate which is cleaved by a mechanism analogous to aromatic substitution. The side-chain appeared as bromosulfoacetaldehyde, the ring as tribromoaniline or tribromophenol. A similar cleavage occurs on bromination of *p*-hydroxycinnamic acid in water.

Our previous work with unsaturated sulfonic acid derivatives showed that they would react with nucleophilic reagents such as cyclopentadiene. As the compound *p*-$YC_6H_4CH{=}CHSO_2X$ was modified by increasing the electron-attracting ability of groups X and Y, its dienophilic powers were enhanced. Thus, sulfonyl chlorides were more reactive than methyl esters, and a *p*-nitro compound more than the unsubstituted derivative.[3] Since the reactivities were in accord with the predictions of the electronic theory, we sought further information about the behavior of the double bond by studying the reaction with bromine. It is well-known that electrophilic bromine addition to ethylenes is accelerated by electron-releasing groups and impeded by electron-withdrawing groups attached to the double bond.[4,5] It had been found previously that 2-phenylethene-1-sulfonyl chloride and 2-phenylethene-1-sulfonamide add bromine very slowly in the absence of catalysts.[6] However,

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[2] The junior author is indebted to Abbott Laboratories and to the Allied Chemical and Dye Corporation for fellowships held during this work.

[3] (a) C. S. Rondestvedt, Jr., and J. C. Wygant, THIS JOURNAL, **73**, 5785 (1951); (b) *J. Org. Chem.*, **17**, 975 (1952).

[4] S. V. Anantakrishnan and C. K. Ingold, *J. Chem. Soc.*, 1396 (1935).

[5] P. de la Mare and P. W. Robertson, *ibid.*, 2838 (1950), and earlier papers.

[6] F. G. Bordwell and C. S. Rondestvedt, Jr., THIS JOURNAL, **70**, 2429 (1948).