

REACTIVITY OF COMPOUNDS OF DIPHENYLMETHANE SERIES. IV.*
 PROTONATION OF DISUBSTITUTED DERIVATIVES OF BENZHYDROL
 IN AQUEOUS SULPHURIC ACID MEDIUM

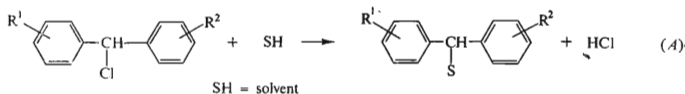
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Received February 11th, 1971

The influence of substituents on the equilibrium benzhydrol-diphenylcarbonium ion has been studied in aqueous sulphuric acid. The pK_{R^+} values have been correlated using the linear free energy relationships. In a series of sixteen disubstituted benzhydrols it has been found that the shift of the protonation equilibrium caused by two substituents does not agree with the presumed sum of shifts caused by the individual substituents which we studied previously. The deviations from additive action of the substituents in the case of 4,4'- and 3,4'-disubstituted benzhydrol derivatives have been ascribed to mutual interactions between the both substituents. The magnitude of these interactions has been tested using the relation $\Delta pK_{R^+} = \rho(\sigma_1^+ + \sigma_2^+ + \iota\sigma_1^+\sigma_2^+)$. The value of the ι constant has been determined statistically, and it is identical with the value $\iota = 0.41$ calculated from the literature data concerning the reactions taking place at the aliphatic carbon atom of disubstituted diphenylmethane compounds. The deviations from additivity in the case of 3,4-disubstituted benzhydrol derivatives have been ascribed, first of all, to steric requirements of substituents located in mutual *ortho* positions.

The problem of additivity of the σ^+ substituent constants in linear free energy relationships was dealt with by several authors¹⁻³ in the connection with studies of solvolysis rates of benzhydryl chlorides, Eq. (A). Using this model disubstituted at 4,4' or 3,4' positions, they proved that its real reactivity did not agree with that calculated on the basis of Jaffé's hypothesis of the additivity of contributions of substituents⁴.



The sign and magnitude of this deviation were determined¹ by a comparison of the reaction constants ρ of the monosubstituted series with the ρ^1 value of the disubstituted series containing a constant substituent R^1 . Fox and Kohnstam¹ found that the magnitude of the reaction constant diminished in the series of the constant substituents at position 4: $4\text{-NO}_2 > \text{H} > 4\text{-OCH}_3$.

* Part III: This Journal 37, 585 (1972).

Nishida expressed¹ the deviations caused by introduction of a further substituent in a different way; he used two constants α, β and Eq. (1).

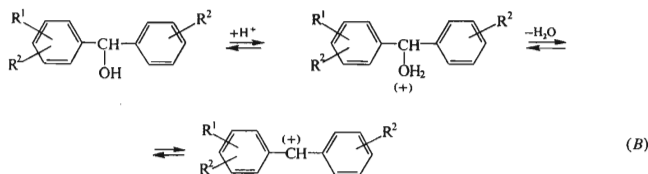
$$\log(k/k_0) = \alpha q \Sigma \sigma^+ + \beta. \quad (1)$$

The values of α increase in the series $4\text{-OCH}_3 < 4\text{-CH}_3 < 3\text{-CH}_3 < \text{H} < 4\text{-Cl} < 3\text{-Cl}$, whereas those of β increase in the series $3\text{-CH}_3 < \text{H} < 4\text{-Cl} < 4\text{-CH}_3 < 3\text{-Cl} < 4\text{-OCH}_3$.

Therefore, it can be supposed that, besides the expected effect on the reaction centre (expressed by the value $\Sigma \sigma^+$), mutual electronic interactions also take place between the substituents R^1 and R^2 operating at various positions. In the case of the reactions involving the stage of diphenyl-carbonium ion these interactions can be included in the term q of the Leffler–Grunwald equation⁵ (2)

$$\log(k/k_0) = \rho(\sigma_1^+ + \sigma_2^+) + q\sigma_1^+\sigma_2^+. \quad (2)$$

In the present paper we continue our previous studies⁶ on substitution effects in protonation equilibria of the monosubstituted benzhydrols in aqueous sulphuric acid medium. This paper presents the results of a study of cumulative action of substituents in the protonation equilibrium of disubstituted benzhydrols (Eq. (B)).



	R^1	R^2	R^1	R^2	R^1	R^2
1	4-OCH ₃	4'-NO ₂	7	4-OCH ₃	13	4-CH ₃
2	4-OCH ₃	3'-Br	8	4-OCH ₃	14	4-CH ₃
3	4-OCH ₃	3-Br	9	4-OCH ₃	15	4-CH ₃
4	4-OCH ₃	4'-Cl	10	4-CH ₃	16	4-CH ₃
5	4-OCH ₃	H	11	4-CH ₃	17	4-CH ₃
6	4-OCH ₃	3'-CH ₃	12	4-CH ₃	18	4-CH ₃
						3-OC ₆ H ₅
						4'-Cl
						H
						3'-CH ₃
						3-CH ₃
						4'-CH ₃

EXPERIMENTAL

Reagents

The disubstituted benzhydrols were prepared by reduction of the respective benzophenones with sodium borohydride in isopropyl alcohol. 3-Phenoxy-4-methylbenzophenone and 3'-phenoxy-4-methylbenzophenone were prepared from the respective bromo-4-methylbenzophenones and potassium phenolate in a similar way to that described in our previous paper⁶ for 3-phenoxybenzophenone. 3-Phenoxy-4-methylbenzophenone, b.p. 202°C/2 Torr, n_D^{25} 1.617. For C₂₀H₁₆O₂

(288.3) calculated: 83.33% C, 5.55% H; found: 83.50% C, 5.85% H. 3-Phenoxy-4'-methylbenzophenone, b.p. 210°C/3 Torr, n_D^{25} 1.619. For $C_{20}H_{16}O_2$ calculated: 84.33% C, 5.55% H; found: 83.52% C, 5.74% H. Physical properties and analyses of individual benzhydrols are given in Table I.

3,4-Dimethylbenzhydrol and 4-methyl-4'-chlorobenzhydrol were prepared according to ref.⁷ and ref.², respectively. The ionization constants were measured in a similar way as those in the previous work⁶. The pK_{R^+} values and UV λ_{max} of the individual carbonium ions are given in Table II. The pK_{R^+} values of benzhydrols 4, 5, 8, 9, 15, 18 were taken from ref.⁶

RESULTS AND DISCUSSION

Sixteen disubstituted benzhydrols were chosen for the measurements of the protonation equilibrium (*B*). These substances were divided into three groups: 1. disubstituted benzhydrols with a constant 4-methoxy group, 2. disubstituted benzhydrols with a constant 4-methyl group, 3. disubstituted benzhydrols with the both substituents on the same nucleus (at positions 3 and 4). This third indicator group was included to enable the appreciation of the influence of a neighbouring *ortho* substituent on the equilibrium (*B*).

TABLE I

Physical Properties and Analyses of the Disubstituted Benzhydrols

Compound	Formula Mol. wt.	Calculated/Found		B.p., °C/Torr (m.p., °C) n_D^{25}
		% C	% H	
1	$C_{14}H_{13}NO_4$ 260.0	64.86	5.05 ^a	(77–78)
		64.76	5.18	—
2	$C_{14}H_{13}BrO_2$ 293.9	57.31	4.48	151–152/0.2
		57.34	4.44	1.612
3	$C_{14}H_{13}BrO_2$ 293.9	57.31	4.48	(78–79) ^b
		57.13	4.53	—
6	$C_{15}H_{16}O_2$ 228.3	78.92	7.06	152–153/1 ^c
		79.18	6.95	1.583
7	$C_{15}H_{16}O_2$ 228.3	78.92	7.06	149–150/0.1
		78.83	7.22	1.595
10	$C_{14}H_{13}BrO$ 277.9	60.79	4.73	154–156/0.5
		61.05	4.96	1.604
11	$C_{14}H_{13}BrO$ 277.9	60.79	4.73	155–157/1
		60.98	4.83	1.612
12	$C_{20}H_{18}O_2$ 290.3	82.73	6.25	190–192/1
		82.54	5.94	1.602
13	$C_{20}H_{18}O_2$ 290.3	82.73	6.25	186–187/0.1
		82.93	6.48	1.602

^aCalculated: 5.40% N; found: 5.29% N. ^bref.¹² m.p. 79°C. ^cref.¹³ gives m.p. 51–52°C.

Table II presents the pK_{R^+} values of eighteen substituted benzhydrols together with the standard deviations of pK_{R^+} values calculated according to Eq. (6) and the absorption maxima of the respective carbonium ions of electronic spectrum ($\lambda_{R^+}^{\max}$) at which the measurements were carried out. The pK_{R^+} values were determined with the use of the H_R^+ acidity function found for aqueous sulphuric acid medium⁶. In Fig. 1 the pK_{R^+} values measured are plotted against $\sum\sigma^+$ of the substituents R^1 and R^2 . It can be seen at a glance that the set does not fulfil the simple relation of the additive action of substituents. If we divide the set (Table II) into two series, one with a constant 4-methoxy group (*i.e.* the compounds 1, 3–6, 8, 9) and the other with a constant 4-methyl group (*i.e.* the compounds 9, 10, 12, 14–16, 18), we can obtain very good correlations for the both series according to both the simple relation (3) and the Yukawa–Tsuno⁸ equation modified for the case of a constant substituent R^1 (Eq. (4)).

$$\Delta pK_{R^+} = \rho^1 \sigma_2^+, \quad (3)$$

$$\Delta pK_{R^+} = \rho^1 (\sigma_2^0 + r^1 \Delta\sigma_R^0). \quad (4)$$

TABLE II

Dissociation Constants of Disubstituted Benzhydrols in Aqueous Sulphuric Acid Medium

Compound	$-pK_{R^+}$	s^a	$-pK_{R^+}^b$	$\lambda_{R^+}^{\max}$, nm
1	9.93	0.01	10.08	425
2	8.90	0.02	9.09	462
3	9.84	0.04	—	473
4	8.31	0.01	8.33	477
5	8.12	0.06	8.09	464
6	7.85	0.09	7.72	463
7	8.21	0.05	—	460
8	5.56	0.02	5.79	507
9	7.36	0.02	7.30	482
10	11.93	0.06	11.87	454
11	12.06	0.03	—	455
12	11.36	0.01	11.37	453
13	11.75	0.03	—	454
14	10.87	0.03	10.87	472
15	10.59	0.04	10.47	462
16	10.24	0.04	10.24	463
17	10.26	0.05	—	455
18	9.53	0.02	9.39	472

^aStandard deviation of pK_{R^+} value. ^bCalculated according to Eq. (6).

The correlation parameters summarized in series 1–4 of Table III give evidence of it. The value of the reaction constant ρ^1 of the series with constant 4-CH₃ group is higher than the ρ^1 value for the constant 4-OCH₃ substituent by about 0.7.

It is interesting to compare the pK_{R^+} values of the pairs 4-methoxy-3'-bromobenzhydrol, 4-methoxy-3-bromobenzhydrol and 4-methyl-3'-bromobenzhydrol, 4-methyl-3-bromobenzhydrol (the compounds 2, 3, 10, 11 in Table II). We ascribe the reactivity decrease of 4-methoxy-3-bromobenzhydrol, first of all, to steric suppression of the resonance ability of the methoxy group. Similar differences can be observed with the pairs of pK_{R^+} values of 4-methoxy-3-methylbenzhydrol, 4'-methoxy-3-methylbenzhydrol and 3,4-dimethylbenzhydrol, 3,4'-dimethylbenzhydrol (compounds 7, 6, 17, 16 in Table II). The operating of steric effects is supported by the fact that 4-methyl-3-bromobenzhydrol and 3,4-dimethylbenzhydrol do not behave analogously to the corresponding 4-methoxyderivatives: the resonance contribution of 4-methyl group (by hyperconjugation) is not suppressed sterically. Similar examples of steric

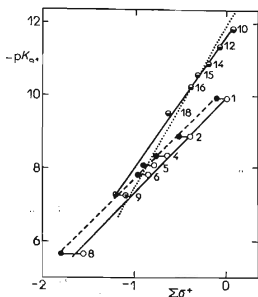


FIG. 1

Dependences of pK_{R^+} Values on Brown's σ^+ Constants

○ Represent the benzhydrols with a constant 4-CH₃ group, ○ represent the benzhydrols with a constant 4-OCH₃ group, ($\sigma^+(4\text{-OCH}_3) = -0.778$), ● represent the benzhydrols with a constant 4-OCH₃ group ($\sigma^+(4\text{-OCH}_3) = -0.905$), ▴, ▾ are common for the both series. The dotted line indicates the magnitude of the constant of the monosubstituted series. For numbers see text.

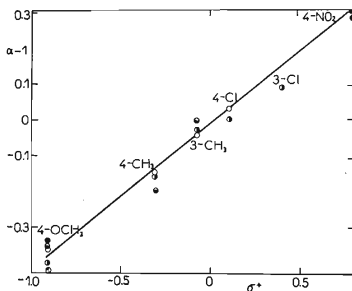


FIG. 2

Dependence of Values α on Substituent Constants σ^+

○ Represent the protonation of benzhydrols, ● represent the protonation of triphenylcarbinols (ref.¹¹), the value α was calculated as it is described sub α in Table III, ● represent the solvolysis of benzhydryl chlorides in 85% acetone at 0°C (ref.¹), ○ represent the solvolysis of benzhydryl chlorides in ethanol at 25°C (ref.¹), ⊖ represent the bromination of 1,1-diarylethylenes at 25°C (ref.¹⁰).

TABLE III

Correlation Parameters of pK_{R^+} Values with σ^+ (σ^0) Constants

The meaning of the symbols: R^1 the constant substituent, s standard deviation of ρ^1 , r correlation coefficient, r the parameter of the Yukawa-Tsuno relation (5), n number of the members of the series, ϵ the interaction coefficient, α the constant of the relation (1).

Correlation	Correlation model	R^1	$-\rho^1$	s	r	r	n	α^a	ϵ
1	4 ^b	4-OCH ₃	2.32	0.08	0.997	—	7	0.64	—
2	5	4-OCH ₃	2.31	0.09	0.995	1.45	8	—	—
3	4 ^b	4-CH ₃	3.09	0.11	0.983	—	6	0.853	—
4	5	4-CH ₃	2.98	0.10	0.993	1.41	7	—	—
5	4 ^b	H	3.59	0.13	0.989	—	9	—	—
6	5	H	3.71	0.04	0.995	1.253	9	—	—
7	4 ^c	H	3.81	0.10	0.997	—	10	—	—
8	6 ^c	—	4.19	0.01	0.998	—	13	—	0.41
9	6 ^d	—	4.10	0.02	0.997	—	21	—	0.40

^aThe values of α constants for the groups 4-Cl and 3-CH₃ were calculated as arithmetical mean of the α determined according to the relation $\alpha = (pK^1 - pK^{12}) / (pK^0 - pK^2)$; $\alpha(4\text{-Cl}) = 1.03$, $\alpha(3\text{-CH}_3) = 0.96$. ^bThe value of $R^2 = 4\text{-OCH}_3$ was not included. ^cThe value $\sigma^+(4\text{-OCH}_3) = -0.905$ was used in the calculation, too. ^dAs ^c for mono and disubstitution.

suppression of resonance abilities of a substituent during S_N1 reactions of α -aralkyl derivatives have not yet been published, although this effect is frequently discussed in the connection with other reaction models⁹.

We found previously⁶ that the $\sigma^+(4\text{-OCH}_3)$ value determined by Brown (-0.778) on the basis of 4-methoxycumyl chloride solvolysis was not suitable for correlation of protonation equilibria with simple linear free energy relationships, and we gave a new value -0.905 . This value has been now used for correlation of pK_{R^+} values of the whole set of 3,4'- and 4,4'-disubstituted benzhydrols with substituent constants σ^+ . For this correlation modified version (5) of the Eq. (2) has been used.

$$\Delta pK_{R^+} = \rho(\sigma_1^+ + \sigma_2^+ + \omega_1^+ \sigma_2^+). \quad (5)$$

We transformed Eq. (2) into Eq. (5) in order to be able to compare the magnitude of interactions during the reactions of diphenylmethane compounds, both the equilibrium reactions and kinetic study. These interactions should not depend on the magnitude of reaction or substituent constants. From the cited papers concerning the non-additivity of substituents influences^{1-3,11} in these or related compounds it follows that a constant substituent R^1 changes the value of a reaction constant ρ into

another value ϱ^1 . If we compare the magnitude of ϱ^1 and ϱ given by the authors^{1,10}, then the relative change $\alpha^1 = \varrho^1/\varrho$ will acquire the same meaning as the constant of Nishida² in Eq. (1). If we further modify Eq. (1) by introducing the expression for the constant $\beta = \varrho\sigma_1^+(1 - \alpha^1)$, we obtain the simplified form (6).

$$\log(k/k_0) = \varrho(\sigma_1^+ + \alpha^1\sigma_2^+). \quad (6)$$

The α^1 values do not depend on the reaction type, but they depend on the value of σ_1^+ of the constant substituent, and the measure of this dependence was expressed by the constant ι . Using the data of ref.^{1-3,10} and the relation $(\alpha^1 - 1) = \iota\sigma_1^+$, we have calculated the value $\iota = 0.40 \pm 0.01$ ($r = 0.992$) for the reaction at the aliphatic carbon atom of diphenylmethane, which is independent of substitution and reaction. By comparison with Eq. (2) we obtain $\iota = q/\varrho$. The character of interaction of two substituents is represented in Fig. 2 for which the values (found and calculated) given in ref.^{1-3,10,11} and our results have been used.

Statistical parameters of the correlation of ΔpK_{R+} values and those of Eq. (5) are given in Table III (No 8, 9). The value ι calculated from our data equals 0.41. Verification and more detailed specification of the ι constant will be the object of our further study.

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Translated by J. Panchartek.