raised the m.p. to 68–69°, unchanged when the substance was mixed with a like amount of an authentic specimen of ethyl phenylthionocarbamate.

Anal. Calcd. for $C_9H_{11}NOS$: C, 59.63; H, 6.12; N, 7.73; S, 17.69; $-OC_2H_5$, 24.86. Found: C, 59.52, 59.77; H, 6.25, 6.18; N, 7.97, 7.81; S, 17.41, 17.53; $-OC_2H_5$, 24.87, 24.82.

STAMFORD, CONN.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE POLYTECHNIC INSTITUTE OF BROOKLYN AND FROM THE WELLCOME RESEARCH LABORATORIES]

The Effect of Substitution on the Solvolysis Rates of Benzhydryl Chlorides[1]

BY SIEGFRIED ALTSCHER,[2] RICHARD BALTZLY AND SAMUEL W. BLACKMAN

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Solvolysis rates of a number of substituted benzhydryl chlorides have been studied in methanol and in isopropyl alcohol. The influence of substituents is in general accord with theoretical expectations. The effect of two or more substitutions appears to be reasonably predictable from that of the individual substituents separately.

Norris[3] and his collaborators have determined the solvolysis rates of a number of benzhydryl chlorides. The reaction had already been shown to be independent of the concentration of base[4] and is now recognized as a typical SN1 displacement. The conductometric method of Norris has been subject to some criticism and certain reaction constants, notably for benzhydryl chloride itself and its alkyl substituents, have been revised by subsequent workers[5–7] but no comparable survey has since been made of the effect of substitution on the rate of solvolysis. The Norris figures for monosubstituted benzhydryl chlorides are in general agreement with expectations based on the modern theories of displacement reactions. The only solvolysis rate available for a disubstituted benzhydryl chloride was also determined by Norris who found *k*-relative (= k/k unsubstituted) for 4,4′-dichlorobenzhydryl chloride to be 0.15—very nearly the square of *k*-relative for *p*-chlorobenzhydryl chloride (0.4).

As a number of substituted benzhydryl chlorides or their precursors were available through certain synthetic activities,[8,9] it was decided to extend the earlier series of Norris to ascertain what regularities could be found in the behavior of polysubstituted compounds.

Experimental

Since the variation in reaction rates among substituted benzhydryl chlorides is so great that no single solvent is convenient for all cases, it was decided to run the more reactive compounds in isopropyl alcohol and the less reactive in methanol. Rates were determined for benzhydryl chloride, *p*-chlorobenzhydryl chloride and 4,4′-dichlorobenzhydryl chloride in both solvents. Reactions were run in duplicate except when more determinations were required and were followed to at least 20% completion; in most cases to 60–70%.

Determination of Reaction Rates.—Enough of the benzhydryl chloride to give a solution 0.05–0.15 molar was weighed into a volumetric flask, made up to volume with the desired solvent and thermostated at 25.00 ± 0.05°. As soon as possible after mixing, an aliquot was removed for a zero point titration. Since in a number of cases the purity of the benzhydryl chlorides could not be established, in all cases one or more aliquots were subjected to complete solvolysis by addition to aqueous methanol in a glass-stoppered flask, and titrated after a suitable time with standard alkali. The value so obtained was taken as the initial concentration of the benzhydryl chloride. For the actual titrations during the run, the aliquots were pipetted into acetone to "freeze" the reaction and titrated with standard alkali. Hughes, Ingold and Taher[7] give this as their general procedure but since we have found that in practice further details are necessary, the following procedure is given.

One-cc. aliquots (of an original 25 cc. of reaction mixture) were pipetted into 20–25 cc. of acetone. Indicator (methyl red–methylene blue) was added and the greater part of the alkali expected to be necessary. Water was then added cautiously until the indicator gave a purple color and the titration was completed by adding alkali dropwise at about one drop per second with constant agitation until the solution became a clear, sparkling green.

The fundamental difficulty is that although a very large excess of acetone stops the solvolysis, indicators do not behave properly in such solutions. With most of these reactions effective "freezing" during the time of titration could be achieved. However, the more rapidly reacting substances (in this study, those with *p*-methoxyl substitution) cannot be "frozen" properly under conditions permitting titration. Rates obtained with these substances cannot be regarded as more than approximate even though in certain instances the usual mathematical treatment shows a high degree of "precision."

Materials.—Most of the benzhydryl chlorides or their precursors were available from previous work.[8,9] All the benzhydryl chlorides have been employed in synthetic operations and have been converted to crystalline substances of known composition. The procedure of Norris and Blake[3c] is adequate for conversion of most of the carbinols to chlorides; it is not adequate with the carbinols that react least rapidly—presumably corresponding to the least active benzhydryl chlorides.

The *o*- and *m*-chloro-, 2,4- and 3,4-dichloro-, 2,4,4′-trichloro- and *p*-nitrobenzhydryl chlorides were accordingly prepared by warming the appropriate carbinols with excess thionyl chloride and a few drops of pyridine. After several hours heating on the steam-bath, thionyl chloride was removed *in vacuo*, toluene was added and removed *in vacuo* (twice). The residues were then taken up in hexane, filtered and evaporated. The crude oils were then distilled *in vacuo* (0.01–0.03 mm.).

Of the various benzhydryl chlorides, 4,4′-dichlorobenz-

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[1] Taken in part from a thesis submitted by S. Altscher to the Department of Chemistry of the Polytechnic Institute of Brooklyn in partial fulfillment of the requirements for the degree of M.S. in chemistry, June, 1950.

[2] Appreciation is expressed to Wallace and Tiernan Products, Inc., for facilities granted to one of us (S. A.) during the course of this work.

[3] (a) J. F. Norris and A. A. Morton, THIS JOURNAL, **50**, 1795 (1928); (b) J. F. Norris and C. Banta, *ibid.*, **50**, 1804 (1928); (c) J. F. Norris and J. T. Blake, *ibid.*, **50**, 1808 (1928).

[4] A. M. Ward, *J. Chem. Soc.*, 2285 (1927).

[5] F. G. Kny-Jones and A. M. Ward, THIS JOURNAL, **57**, 2394 (1935).

[6] N. T. Farinacci and L. P. Hammett, *ibid.*, **59**, 2542 (1937).

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

[8] L. P. Albro, R. Baltzly and A. P. Phillips, *J. Org. Chem.*, **14**, 771 (1949).

[9] R. Baltzly, S. DuBreuil, W. Ide and E. Lorz, *ibid.*, **14**, 775 (1949).

TABLE I

REACTION CONSTANTS FOR SOLVOLYSIS AT 25.0°

Substituents	In methanol $k \times 10^3$	$k_{rel.}$	In isopropyl alcohol $k \times 10^3$	$k_{rel.}$	In ethanol (Norris)[3] $k_{rel.}$
			Mono-substituted benzhydryl chlorides		
None	48.9 ± 1.0	1	0.343 ± 0.007	1	1
o-Cl	0.615 ± 0.007	0.0125			0.01
m-Cl	1.27 ± 0.02	.026			.045
p-Cl	22.8 ± 0.8	.47	0.175 ± 0.003	0.51	.42
p-Me					16.2 23.4[7]
o-MeO					93
m-EtO			0.396 ± 0.006	1.2	
p-MeO			1700?	*ca.* 5000	>1200
p-NO_2	0.0330 ± 0.0003	0.00068			
			Related benzyl chlorides		
None	0.00371 ± 0.00022	(1)			
p-MeO	16.8 ± 0.2	(4530)			
4-MeO-α-C_6H_{11}			20.7 ± 0.8	60	
α-(α-$C_{10}H_7$)			2.37 ± 0.07	6.9	7.2
α-(β-$C_{10}H_7$)			2.77 ± 0.04	8.1	
			Polysubstituted benzhydryl chlorides		
2,4-Cl_2	0.347 ± 0.005	0.0071			
3,4-Cl_2	0.902 ± 0.006	.018			
4,4'-Cl_2	6.27 ± 0.09	.13	0.057 ± 0.005	0.17	0.15
2,4,4'-Cl_2	0.113 ± 0.002	.0023			
4-Me-4'-Cl			2.74 ± 0.08	8.0	
4-MeO-3-Cl			48.4 ± 5.2	141	
4-MeO-3,4'-Cl_2			24.1 ± 2.9	70	

hydryl chloride,[3] 4-methyl-4'-chlorobenzhydryl chloride, α-(α-naphthyl)-benzyl chloride,[3] α-(β-naphthyl)-benzyl chloride,[8] 4-methoxy-α-cyclohexylbenzyl chloride[10] and *p*-nitrobenzhydryl chloride are solids crystallizable from hexane or similar solvents.

p-Nitrobenzhydryl chloride appears to be a new compound.[11] The crude chloride distilled at about 120° at 0.04 to 0.08 mm. as a yellow oil. This solidified in the refrigerator and, when first taken out, began to melt on warming to room temperature. Before completely melted it resolidified and thereafter melted at 41–42°.

Anal. Calcd. for $C_{13}H_{10}ClNO_2$: C, 63.02; H, 4.07. Found: C, 63.36; H, 4.27.

The carbinols corresponding to *o*-, *m*- and *p*-chloro, *m*-ethoxy- and *p*-methoxybenzhydryl chlorides are known crystalline substances, although none of the chlorides was obtained as a solid. The chlorobenzhydryl chlorides were distilled *in vacuo*.

Both the chlorides and carbinols of the 2,4- and 3,4-dichloro, 2,4,4'-trichloro, 4-methoxy-3-chloro and 4-methoxy-3,4'-dichloro series are oils, but derived from solid and known ketones. All these carbinols were obtained by Meerwein–Ponndorf reductions and are believed to be essentially homogeneous. The methoxy chlorides were used as obtained by the Norris method. The di- and trichlorobenzhydrols and benzhydryl chlorides were distilled in high vacuum. The highest-boiling fractions of the carbinols were converted to chlorides and the lowest-boiling fractions of the chlorides were employed in the kinetic runs. The ultraviolet absorption spectra of the oily 2,4- and 3,4-dichlorobenzhydrols indicated the presence of not over 1% of ketone.

Benzyl chloride was commercial redistilled material. Anisyl chloride was prepared from anisyl alcohol by the Norris method and used without distillation.

Methanol used in the kinetic runs was dried by distillation from magnesium methylate. Isopropyl alcohol was distilled from aluminum isopropylate.

Results

The unimolecular reaction constants obtained are shown in Table I, with the minute as the unit of time. Relative reaction velocities are shown in the column headed $k_{rel.}$ Probable error is shown as ±xx and calculated according to the formula: $s = \sqrt{\Sigma d^2/n - 1}$. Comparable values of k_{rel} obtained by Norris[3] and Hughes, Ingold and Taher[7] in ethanol are given in the last column of the table.

It will be seen that in the slower reactions fair precision was obtained (probable error about 2%). Typical data for an individual determination are shown in Table II. In the more rapid reactions precision was lower and, when obtained, may have been fortuitous. For example, the values for *k* for anisyl chloride in individual titrations show a gratifying consistency but in view of the fact that five aliquots were withdrawn in 16 minutes it is evident that the time factor was over-refined. In such

TABLE II

DATA ON ALCOHOLYSIS OF 4-METHYL-4'-CHLOROBENZHYDRYL CHLORIDE IN ISOPROPYL ALCOHOL; *c* = 0.1437; 10-CC. ALIQUOTS

Time, minutes	Titer, cc. 0.1 *N* NaOH	$k \times 10^3$
28.5	1.02	2.61
43	1.60	2.74
66.5	2.40	2.74
89	3.16	2.78
114	3.94	2.81
	Average	2.74 ± 0.08

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(10) J. Schmidtlin and R. v. Escher, *Ber.*, **45**, 889 (1912).

(11) The required *p*-nitrobenzhydrol was prepared by Dr. Joseph Levy of the Trubek Laboratories through a Meerwein–Ponndorf reduction of *p*-nitrobenzophenone (from *p*-nitrobenzoyl chloride and benzene). The sample used, m.p. 69–73°, was furnished us by Mr. H. Hachem of Trubek.

a case precision ought not to be confused with accuracy.

In general, the results in Table I are calculated directly from the data as obtained. In one case modification was necessary. The value of k for *m*-chlorobenzhydryl chloride fell off markedly as the reaction progressed. This was taken to signify contamination by a more reactive substance, probably benzhydryl chloride the presence of 3% of which would account for the drift in k. The value shown was obtained by taking the 100-minute mark as zero time and making appropriate subtractions from the figures involved in the calculation.

The absence of drift in the other experiments is *prima facie* evidence for the absence of reactive contaminants. Since c was determined from the titer of total solvolysis, the presence of unreactive contaminants would not affect the values for k except in so far as they influenced the nature of the solvent. Hughes, Ingold and Taher[7] obtained identical values for the reaction constants of *p*-methyl- and *p*-ethylbenzhydryl chlorides in 0.01 and in 0.08 M solution. Hence it seems unlikely that significant variation would be produced by the presence of inactive contaminants in any possible amount, or by the variations in initial concentration between our experiments.

Discussion

While the same general relation between the effects of individual substituents observed by Norris is manifest in the present work, considerable difference is apparent between the values of k_{rel} in particular cases. To some extent this may be due to differences in the solvents used, although in our observations k_{rel} varied little between methanol and isopropyl alcohol for the compounds studied in both solvents.

It is of some interest that *m*-alkoxy substitution appears to favor the reaction slightly, suggesting that the increase in electron density in the ortho and para positions from resonance overflows to some extent so as to affect the meta position also. It would thus appear that substitution in the meta position in anisole ought to be slightly faster than in benzene (as is the case with toluene) although it would seem difficult or impossible to demonstrate this by experiment.

Since even in isopropyl alcohol solvolysis of *p*-methoxybenzhydryl chloride is too fast to measure (the first titration corrresponded to 90% reaction) we attempted to estimate the influence of the *p*-methoxy substituent through comparison of the slower reactions of benzyl and anisyl chlorides. The value of k_{rel} so obtained is shown in parentheses in Table I. It is in reasonable accord with the approximate value deduced from the single titration possible with *p*-methoxybenzhydryl chloride. This value of k_{rel} (4530) should probably be regarded as a minimum, however. The primary benzyl chlorides, like primary alkyl halides, may undergo relatively slow bimolecular alcoholysis which is not readily distinguished from the unimolecular, but which would not be influenced by substitution in the same manner. Consequently the true SN1 rates for these two compounds are likely to be lower than the observed values by small quantities of about the same magnitude and the true k_{rel} for the SN1 reaction may be appreciably greater than 4530.

Few attempts have been made to correlate the influences of several substituents on reactivity, or to treat systematically the effect of ortho substituents. Stubbs and Hinshelwood[12] have found good agreement in the rates of benzoylation of polysubstituted anilines by benzoyl chloride with calculations based on the reaction rates of monosubstituted anilines. Shorter and Stubbs[13] were somewhat less successful in their treatment of the dissociation constants of substituted benzoic acids. The method of Stubbs and his colleagues is to attribute to individual substituents a characteristic increment to the activation energy of the reaction. Since the activation energy enters into the general equation of reaction velocity as an exponential, the various increments (ΔE or $\Delta E'$) are added to the activation energy of the unsubstituted member of a series.

If one assumes that in a family of parallel reactions the entropy of activation is identical, the addition of increments to the activation energy is mathematically equivalent to a multiplication of relative rates. Such an assumption is not in general permissible but the present instance should be a favorable occasion for it. Since the rate-determining step in the solvolysis of a benzhydryl halide is believed to be a separation of two particles, hindrance ought to be of minor consequence, except when there is excessive crowding. While energies of activation for this reaction would be desirable, they are not presently available. So far as the *p*-methoxy derivatives are concerned, the possible error in present determinations is such as to make calculations of activation energy of doubtful value.

In Table III are shown the relative rates for the polysubstituted benzhydryl chlorides we have studied. The calculated values of k_{rel} are obtained by multiplying together the appropriate figures for the individual substituents.

In these we have used our values for k_{rel} shown in Table I for the influence of *o*, *n* - and *p*-Cl; the value (4530) for *p*-MeO deduced from k anisyl chloride/k benzyl chloride and the figure of k_{rel} for *p*-Me given by Hughes, Ingold and Taher.[7] In the case of *p*-Cl, we have used the figure for methanolysis where the polysubstituted compound was run in methanol and the figure for isopropanolysis where

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[12] F. J. Stubbs and C. N. Hinshelwood, *J. Chem. Soc.*, S-71 (1949).

[13] J. Shorter and F. J. Stubbs, *ibid.*, 1180 (1949). The comparative lack of agreement between calculated and observed dissociation constants in this study as compared to the first may well be due largely to a less fortunate choice of compounds. About one acid in every five shows a discrepancy between predicted and observed activation energies (of ionization) exceeding 500 cal. The fourteen such compounds fall into equal groups wherein acidity is in one series greater, in the other less, than predicted. With one (or perhaps a second) exception these deviations can be rationalized through presently accepted concepts. The outstanding exception is 2-chloro-6-bromo-5-hydroxybenzoic acid whose dissociation constant is reported by Intern. Crit. Tables to be one tenth of that of its normal 3-hydroxy analog. Actually, the acid for which that dissociation constant is reported is probably 2-chloro-4-bromo-5-hydroxybenzoic acid.[14] Calculation of $\Delta - (RT \ln k)$ for this structure using Stubbs' figures gives -2150 cal., in good agreement with the observed -2010.

[14] A. Coppadoro, *Gaz. chim. ital.*, **32**, I, 551 (1902); *Chem. Centr.*, **73**, II, 638 (1902).

TABLE III

RELATIVE REACTION CONSTANTS OF POLYSUBSTITUTED BENZHYDRYL CHLORIDES

Substituents	k_{rel} Calculated	k_{rel} Observed	$\Delta E'$, cal.[e]
2,4-Cl_2	0.0059	0.0071	+110
3,4-Cl_2	.012	.018	+241
4,4'-Cl_2[a]	.22	.13	−312
[b]	.26	.17	−252
2,4,4'-Cl_3	.0028	.0023	−122
4-Me-4'-Cl	11.9	8.0	−236
4-MeO-3-Cl	118 (112–123)[c]	141 (116–160)[d]	+106
4-MeO-3,4'-Cl_2	60 (56–64)[c]	70 (60–81)[d]	+ 91

[a] For methanolysis. [b] For isopropanolysis. [c] Limits of prediction based on probable error of values used in calculation. [d] Limits derived from probable error of rates. [e] $\Delta E' = RT \ln (k \text{ calcd.}/k \text{ obsd.})$.

the reaction of the polysubstituted derivative was in isopropyl alcohol. This appears to be the only proper course although alternative values for k_{rel} would sometimes give better agreement with observation. The last column in Table III shows the variations in activation energy corresponding to the deviations between calculated and observed relative rates (always, of course, on the assumption of constancy in the PZ factor).

Acknowledgment.—We wish to express our gratitude to Miss Gertrude Elion for determination of ultraviolet absorption spectra and to Dr. Levy and Mr. Hachem of the Trubek Laboratories for the gift of a sample of *p*-nitrobenzhydrol.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NOTRE DAME]

Rates of Saponification of Substituted Ethyl 2-Naphthoates[1]

BY CHARLES C. PRICE AND RUDOLPH H. MICHEL[2]

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The rates of saponification of ethyl 2-naphthoates and derivatives containing 6- and 7-methoxyl, 5- and 8-amino, 8-dimethylamino and 5- and 8-nitro groups have been measured in 70% aqueous dioxane, for most of the compounds at two temperatures. The data are interpreted in terms of resonance and electrical influences. The dipole moment of ethyl 8-nitro-2-naphthoate can be adequately accounted for by assuming that the rotational conformation of the ester group is influenced by the electric field of the nitro group. Calculations of the magnitude of the interaction are in excellent agreement with the observations. The fact that ethyl 5-nitro-2-naphthoate saponifies more rapidly than the 8-nitro isomer indicates that resonance by a nitro group on the α-position of a napthalene ring is sterically inhibited. The observations may be accounted for by the direct electrical influence of the nitro groups on the negatively charged carbethoxyl–hydroxyl ion complex in the transition state. Calculations of the magnitude of the electrical interaction indicate it is adequate to account for the observations.

The influence of substituents on the rate of alkaline hydrolysis of substituted ethyl benzoates has been studied[2] extensively. The results have been found to fit the Hammett equation[3]

$$\log k - \log k^{\circ} = \sigma\rho$$

where ρ is a constant for the particular reaction series and σ is a constant for the substituent, indicating the magnitude and direction of its electrical effect, and k and k° are, respectively, the rate constants for the alkaline hydrolysis of the substituted and unsubstituted ethyl benzoate. This paper represents an extension of these studies to heteronuclear substituted ethyl 2-naphthoates which may be looked upon as para- and meta-disubstituted ethyl benzoates.

Experimental

A. **Preparation of Compounds. 6-Methoxy-2-naphthoic Acid.**—This compound was prepared from 6-bromo-2-methoxynaphthalene[4] by the Rosemund–von Braun reaction[5] and hydrolysis of the resulting nitrile.[6] A 44% yield of product melting at 194–197°[7] was realized. Two recrystallizations from an ethanol–water mixture raised the melting point to 200–202° (reported[8] m.p. 200–203°).

2-Naphthoic Acid.—Methyl 2-naphthyl ketone (Eastman Kodak Co. "White Label") was converted to 2-naphthoic acid by oxidation with potassium hypochlorite.[9]

7-Hydroxy-2-naphthoic Acid.—2-Naphthoic acid was sulfonated and the acid potassium salt of the 7-sulfo-2-naphthoic acid was converted to 7-hydroxy-2-naphthoic acid, m.p. 266–268° (reported[10] m.p. 269–270°) according to the methods of Butler and Royle.[10] The yield was 27% based on 2-naphthoic acid.

7-Methoxy-2-naphthoic Acid.—In a 1-l., three-necked flask, equipped with a stirrer and two dropping funnels, 21 g. (0.11 mole) of crude 7-hydroxy-2-naphthoic acid and 10 g. of sodium hydroxide were dissolved in 500 ml. of water. The solution was warmed on a water-bath and 56 g. (0.44 mole) of dimethyl sulfate was added over 15 minutes. The addition of a solution of 30 g. (0.75 mole) of sodium hydroxide in 150 ml. of water was started simultaneously with the addition of dimethyl sulfate, but was extended over one hour. The solution was allowed to stir a total of four hours and was kept on the water-bath throughout this time. It was then cooled, poured into a beaker and acidified with concentrated hydrochloric acid. One recrystallization of the crude product from an ethanol–water mixture yielded 19 g. (84%) of acid, m. p. 193–194°. When the crude product was dissolved in ethanol, decolorized with Norit, and recrystallized three times from ethanol–water mixtures, colorless, thin needles were isolated, m.p. 195.5–196.0°.

Anal.[11] Calcd. for $C_{12}H_{10}O_3$: C, 71.28; H, 4.95. Found: C, 71.48; H, 5.18.

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[1] Presented at the Buffalo Meeting of the American Chemical Society, March 26, 1952.

[2] A.E.C. Predoctoral Fellow, 1949–1951.

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

[4] H. E. French and K. Sears, THIS JOURNAL, **70**, 1279 (1948).

[5] C. F. Koelsch and A. G. Whitney, *J. Org. Chem.*, **6**, 795 (1941).

[6] H. E. Ungnade and F. V. Morriss, THIS JOURNAL, **72**, 2114 (1950).

[7] All melting points are uncorrected.

[8] L. E. Miller and E. F. Morello, THIS JOURNAL, **70**, 1900 (1948).

[9] "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 428.

[10] C. Butler and F. A. Royle, *J. Chem. Soc.*, **123**, 1649 (1923).

[11] All analyses were carried out by Micro-Tech Laboratory, Skokie, Ill.