

263–264° dec. A mixed melting point with the quercetin reduction product was 263–264° dec.

The acetyl derivative, prepared by boiling briefly a solution of the tetrahydroxy compound in a mixture of acetic anhydride and pyridine, melted at 174–175°, and did not

depress the m.p. of the acetate of the quercetin reduction product.

The absorption spectra were determined with a Beckman model DU spectrophotometer.

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, UTICA COLLEGE OF SYRACUSE UNIVERSITY]

The Effects of Alkyl Groups Linked to Conjugated Systems. I. The Alkaline Hydrolysis of Some Ethyl *p*-Alkylbenzoates¹

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The specific reaction rate constants for saponification of a series of ethyl *p*-alkylbenzoates were determined at 30.00 and 60.09° in 87.83% by weight ethanol. The alkyl groups followed the inductive order.

The order of inductive effects of alkyl groups in order of their increasing electron-repulsive character is methyl < ethyl < *i*-propyl < *t*-butyl. When linked directly to an aromatic system, these alkyl groups follow the reverse order for reactions involving electron movement toward the reaction center. This latter series has been explained by hyperconjugative resonance and was first observed by Baker and Nathan³ in the reaction between *p*-alkylbenzyl bromides and pyridine. Recently, Berliner and Berliner⁴ have explained their results on the bromination of alkylbenzenes on the basis of hyperconjugation. Some question of steric hindrance might be raised since the ortho-para ratios have not been determined.⁵ According to Berliner and Bondhus,⁶ the inductive series can also be explained by resonance; but this introduces a situation difficult to explain—why are two opposing orders based on the same resonance effect operative?

Since only one study⁷ at a single temperature has been reported for the effects of alkyl groups on a side chain reaction whose rate is facilitated by the withdrawal of electrons from the reaction center (Ingold and Rothstein's "class B"), it seemed desirable to study carefully the alkaline hydrolysis of a series of ethyl *p*-alkylbenzoates. The mechanism⁸ of this reaction is comparatively well understood; the rate-determining step is the nucleophilic attack of a hydroxyl ion at the carbonyl carbon of the ester group. The extensive investigations of Tommila⁹ and Kindler¹⁰ have shown that the reaction is favored by *m*- and *p*-electron-attractive substituents, which tend to withdraw electrons from the side chain. Kindler¹⁰ has reported reaction velocity constants of 0.0229, 0.0222 and 0.0230 liter mole⁻¹ min.⁻¹ for the *p*-

methyl-, *p*-ethyl- and *p*-*n*-propyl derivatives for the reaction at 30° in a 87.83% by weight ethanol solvent, whereas Lincoln¹¹ has found values of 0.00102 and 0.00121 liter mole⁻¹ sec.⁻¹ for the *t*-butyl and the *p*-methyl compounds, respectively, in a 56% by weight acetone solvent at 25°. It was of interest, therefore, to extend these studies to include more alkyl groups and to determine whether or not the alkyl groups followed the hyperconjugative or inductive order (or some combination of these).

Method.—The saponification rates were determined at 30.00 and 60.09° by the titration method using the 87.83% by weight ethanol solvent employed by Kindler,¹⁰ using cresol red as indicator. A perusal of the literature revealed that the ethyl, *p*-*n*-butyl-, *p*-*s*-butyl-, *p*-*s*-amyl- and the *p*-*t*-amylbenzoates had not been prepared previously. They and the other *p*-alkyl esters in this study were obtained in 55–60% yield by esterification¹² of the corresponding *p*-alkylbenzoic acids with absolute ethanol. The acids were prepared from the appropriate *p*-alkylphenyl methyl ketones by the method of Newman and Holmes.¹³

Experimental

Materials.—Absolute ethanol (Publicker) was employed. Several runs using absolute ethanol which had been distilled over calcium metal gave the same results. Freshly boiled distilled water was used in the preparation of solutions containing water. Carbonate-free sodium hydroxide stock solutions were prepared by dissolving chemically pure sodium hydroxide in water to make a 50% solution. The concentrated solution was allowed to stand in a covered container for 24 hours after which the clear liquid was filtered to remove the sodium carbonate. Stock solutions of 0.02 *N* and 0.5 *N* sodium hydroxide were prepared and their concentration checked with potassium acid phthalate at least every five days. The 0.02 *N* hydrochloric acid solutions were prepared from chemically pure concentrated acid. The m.p.'s of the *p*-alkylbenzoic acids checked with those recorded in the literature. The ethyl *p*-alkylbenzoates were purified by repeated vacuum distillations using a (14 × 1 cm.), Vigreux column: Eastman Kodak Co., ethyl benzoate (*n*_D²⁰ 1.5052; b.p. 101–102° (20 mm.)); *p*-ethyl- (*n*_D²⁰ 1.5011; b.p. 129–130° (15 mm.) (lit.¹⁴ 129–130° (15 mm.)); *p*-methyl- (*n*_D²⁰ 1.5084; b.p. 110–111° (13 mm.) (lit.¹⁴ 110–111° (13 mm.)); *p*-*n*-propyl- (*n*_D²⁰ 1.5003; b.p. 138–139°

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(16 mm.) (lit.¹⁵ 143° (18 mm.)); *p*-isopropyl- (n_D^{20} 1.5083; b.p. 134–135° (14 mm.) (lit.¹⁴ 134–135° (14 mm.)); *p*-*i*-butyl- (n_D^{20} 1.4998; b.p. 150–151° (14 mm.) (lit.¹⁶ 120.5° (4 mm.)); *p*-*n*-butyl- (n_D^{20} 1.5008; b.p. 142–143° (14 mm.). *Anal.* Calcd. for $C_{13}H_{18}O_2$: C, 75.68; H, 8.81. Found: C, 75.60; H, 8.89); *p*-*s*-butyl- (n_D^{20} 1.4995; b.p. 145–146° (14 mm.). *Anal.* Calcd. for $C_{13}H_{18}O_2$: C, 75.68; H, 8.81. Found: C, 75.75; H, 8.75) *p*-*s*-amyl- (n_D^{20} 1.4980; b.p. 148–149° (14 mm.). *Anal.* Calcd. for $C_{14}H_{20}O_2$: C, 76.32; H, 9.17. Found: C, 76.22; H, 9.12); *p*-*t*-amyl- (n_D^{20} 1.5001; b.p. 157–158° (16 mm.). *Anal.* Calcd. for $C_{14}H_{20}O_2$: C, 76.32; H, 9.17. Found: C, 76.40; H, 9.19).

Procedure.—The temperature of the bath was controlled to $\pm 0.01^\circ$ with a Beckman type mercury-in-glass thermometer. The burets used were calibrated at room temperature; the sampling pipets were calibrated at both temperatures.

About 0.04 mole of the ester was weighed in a small glass ampoule, sealed and placed inside of a 250-ml. ground-glass stoppered bottle, the reaction flask. Calculated volumes of 0.5 *N* sodium hydroxide and absolute ethanol were added to the reaction flask so that the alkali concentration was initially the same as the ester concentration and so that the solvent was 87.83% by weight ethanol. This mixture was allowed to remain at the desired bath temperature for at least two hours. The reaction was started by breaking the ampoule containing the ester with a glass rod. Immediately, and later at suitable time intervals, 10-ml. samples were withdrawn, discharged into 25 ml. of 0.02 *N* hydrochloric acid and allowed to drain for 30 seconds as calibrated. The samples were titrated to the pink end-point of cresol red. The entire procedure was kept uniform throughout.

At 30° the initial concentration as determined by titration and the initial concentration as calculated from the weight of the ester and the volume of solvent agreed to within three parts per thousand. It was found that the solvent expanded 3.950% at the higher temperature. The initial concentration was calculated from the weight of the ester and the corrected volume of solvent.

The reaction velocity constant, *k*, was calculated from the equation

$$k = 1/t \times x/a(a - x)$$

where *t* is the time in minutes, *a* is the initial concentration in moles and *x* is the amount which has been removed after the lapse of time, *t*. The data are listed in Table I.

Discussion of Results

Good second-order kinetics were observed for ethyl benzoate and for the *p*-methyl- and *p*-ethyl-derivatives upon following the reaction to completion. For the other compounds studied, good second-order data were obtained for the first 50% of the reaction after which period the end-point was not sharp. The reaction velocity constants at 30° for ethyl benzoate, the *p*-methyl- and the *p*-ethyl- derivatives agreed with those found by Kindler¹⁰; but the value for the *p*-*n*-propyl compound was about 5% lower than that determined by Kindler. Duplicate runs agreed to within 2%. The activation energy of 14.4-kcal. found for ethyl benzoate is lower than the 17.7 kcal. determined by Ingold and Nathan¹⁷ and by Evans, Gordon and Watson.¹⁸ In our hands, cresol red gave a sharper end-point than the brom thymol blue used by these workers. Cresol red also gave a sharper end-point than phenolphthalein, which was employed by Kindler.¹⁰

As shown in Table II, the saponification rates decrease and the activation energies increase as the molecular weight of the ester increases. The data

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(17) C. K. Ingold and W. S. Nathan, *J. Chem. Soc.*, 222 (1936).

(18) D. P. Evans, J. J. Gordon and H. B. Watson, *ibid.*, 1430 (1937).

TABLE I
KINETIC DATA FOR THE ALKALINE HYDROLYSIS OF ETHYL
p-ALKYLBENZOATES IN 87.83% ETHANOL

<i>p</i> -Alkyl group	Temp., °C.	<i>a</i> (mole liter ⁻¹)	<i>k</i> (liter mole ⁻¹ min. ⁻¹)
H	30.00	0.03870	0.0504
		.03951	.0502
	60.09	.02752	.436
		.03100	.432
		.03928	.0231
		.03955	.0229
Methyl	30.00	.03706	.201
		.03808	.197
	60.09	.03919	.0226
		.03903	.0226
		.03804	.196
		.03800	.197
<i>n</i> -Propyl	30.00	.03951	.0217
		.03124	.0221
	60.09	.04094	.193
		.03926	.191
		.03899	.0214
		.03913	.0218
Isopropyl	30.00	.03793	.190
		.03798	.190
	60.09	.03850	.0175
		.03909	.0173
		.03804	.153
		.03776	.155
<i>s</i> -Butyl	30.00	.03911	.0172
		.03009	.0166
	60.09	.03800	.150
		.04344	.154
		.03925	.0162
		.03829	.0161
<i>t</i> -Butyl	30.00	.03796	.147
		.03806	.146
	60.09	.03399	.0148
		.03873	.0146
		.03797	.134
		.03776	.136
<i>t</i> -Amyl	30.00	.04048	.0151
		.03935	.0151
60.09	.03816	.139	
	.03800	.137	

are not accurate enough to differentiate critically between position isomers but the trend parallels that observed by Kharasch and Flenner¹⁹ in their examination of the decomposition products by

TABLE II
REACTION VELOCITY CONSTANTS AND ACTIVATION ENERGIES

<i>p</i> -Alkyl group	k_{30}° (liter mole ⁻¹ min. ⁻¹)	<i>E</i> (kcal. mole ⁻¹)
H	0.0503	14.4
Methyl	.0230	14.4
Ethyl	.0226	14.6
<i>n</i> -Propyl	.0219	14.5
Isopropyl	.0216	14.5
<i>n</i> -Butyl	.0174	14.6
<i>s</i> -Butyl	.0170	14.6
<i>t</i> -Butyl	.0162	14.7
<i>s</i> -Amyl	.0147	14.8
<i>t</i> -Amyl	.0151	14.8

(19) M. S. Kharasch and A. L. Flenner, *THIS JOURNAL*, **54**, 674 (1932).

hydrogen chloride of a number of unsymmetrical mercury dialkyls, R-Hg-R.¹

Since this series of alkyl groups is the order of increasing electron-repulsive character of these groups, they thus follow the inductive order—an observation in contradistinction to the aforementioned investigations of Baker and Nathan, Berliner and others. The inductive order would be expected in a reaction which is facilitated by electron withdrawal, whereas the hyperconjugative order would be expected in a reaction facilitated by electron supply to the reaction center, since resonance effects which operate only in the activated state will do so only if required by the reaction.

The Hammett substituent constants²⁰ for the alkyl groups were calculated from the saponification data and are listed in Table III.

TABLE III
SUBSTITUENT CONSTANTS

<i>p</i> -Alkyl group	Substituent constant	
	This investigation ^a	Hammett
Methyl	-0.138	-0.170
Ethyl	- .141	- .151
<i>n</i> -Propyl	- .147	
Isopropyl	- .149	- .151
<i>n</i> -Butyl	- .187	
<i>s</i> -Butyl	- .191	
<i>t</i> -Butyl	- .199	- .197
<i>s</i> -Amyl	- .216	
<i>t</i> -Amyl	- .211	

^a The reaction constant of +2.498 as listed by Hammett was used in the computations.

The agreement of our constants with those of Hammett is not too good for the *p*-methyl and the *p*-ethyl groups. Hammett's values were computed from the ionization constants of the appropriate benzoic acids as determined by Dippy and collaborators.²¹ Since the reaction studied in this work is more sensitive to small variations in electron density at the reaction center,²² it is believed that our values are more reliable.

(20) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 188.

(21) J. F. J. Dippy and R. H. Lewis, *J. Chem. Soc.*, 644 (1936); J. W. Baker, J. F. J. Dippy and J. E. Page, *ibid.*, 1774 (1937).

(22) The ionization constant for the *p*-*t*-butylbenzoic acid is only about 6% lower than that found for the *p*-methyl-, and identical values were obtained for the *p*-ethyl- and the *p*-isopropyl-. The saponification rate constant for the *p*-*t*-butyl ester is about 34% lower than the value for the *p*-methyl-. Also, the ionization constant for *p*-toluic acid as determined by Dippy is lower than that found by other workers, whereas the saponification rate constants for the *p*-methyl- and the *p*-ethyl-esters check with those determined earlier by Kindler.

Two theoretical approaches were pursued to explain the experimentally observed inductive order. As shown in Table IV, the polarizing forces of Price²³ do not differ markedly in magnitude and they do not follow a definite order. The charge at the para position as computed by the method of Ri and Eyring²⁴ resulted in values of -0.0576, -0.0903, -0.101 and -0.109 (10^{-10} e.s.u.) for toluene, ethylbenzene, isopropylbenzene and *t*-butylbenzene, respectively. The saponification rates decrease in this order. This latter approach is more in line with the experimental findings since an accumulation of negative charge on the nuclear position para to the alkyl group would be expected to hinder the hydrolysis.

TABLE IV
POLARIZING FORCES OF THE ALKYL GROUPS OF MONOALKYLBENZENES

Alkylbenzenes	Polarizing forces of alkyl group (10^{-4}), dyne
Toluene	-0.39
Ethylbenzene	- .38
<i>i</i> -Propylbenzene	- .37
<i>t</i> -Butylbenzene	- .37
Isoamylbenzene	- .34
<i>n</i> -Butylbenzene	- .34
<i>n</i> -Propylbenzene	- .33
2-Phenylpentane	- .33
<i>s</i> -Butylbenzene	- .32
<i>t</i> -Amylbenzene	- .32
2-Benzylbutane	- .29
Isobutylbenzene	- .28
3-Phenylpentane	- .27

Perhaps the best kinetic evidence in favor of the Baker-Nathan hyperconjugative series where the alkyl groups change the activation energy is the work of Ingold, Hughes and Taher²⁵ on the hydrolysis of *p*-alkylbenzhydriyl halides. These data were interpreted on the basis of a unimolecular (S_N1) mechanism. A different mechanism may be operative since kinetic evidence for a termolecular process has been obtained recently by Swain²⁶ for triphenylmethylhalide displacements.

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(26) C. G. Swain, *THIS JOURNAL*, **70**, 1119 (1948).