

371. *The Dissociation Constants of Alkyl-substituted Benzoic and Phenylacetic Acids.*

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Accurate values of K_{therm} for various alkyl-substituted benzoic and phenylacetic acids have been determined in order to ascertain whether they provide further information regarding the validity of the hypothesis of mesomeric electron-release by alkyl groups postulated by Baker and Nathan (J., 1935, 1884).

The relative order of acid strength of the phenylacetic acids (in which such mesomeric effect should be of minor importance) is that anticipated on the basis of the relative inductive (+ I) effects $\text{Me} < \text{Et} < \text{Pr}^\beta < \text{Bu}^\gamma$. In the benzoic series, small but irregular differences are established, the ethyl and the *isopropyl* derivative being stronger acids than the methyl and the *tert.*-butyl compound.

The results are discussed on the basis of two alternative points of view.

ACCURATE data for the strengths of *p*-alkylbenzoic acids were of great interest to one of us because it was considered probable that a study of the ionisation equilibrium might provide information concerning the relative electron-release capacities of alkyl groups, and thus afford a further test of the validity of suggestions recently made regarding the mechanism of such electron-release (Baker and Nathan, J., 1935, 1884). Since data of the type required have now been made available for a large number of substituted aromatic acids, we have

collaborated in the determination of the values of K_{therm} , for a series of *p*-alkylsubstituted benzoic acids (in which there is complete conjugation between the alkyl substituent and the carboxyl group) and phenylacetic acids (in which such conjugation is broken by the intercalation of the methylene group). The results are in the following table.

Values of $10^5 K_{\text{therm}}$, for $p\text{-R}\cdot\text{C}_6\text{H}_4\cdot\text{CO}_2\text{H}$ and $p\text{-R}\cdot\text{C}_6\text{H}_4\cdot\text{CH}_2\cdot\text{CO}_2\text{H}$ in water at 25° .

	R = H.	Me.	Et.	Pr ^β .	Bu ^γ .
$\text{R}\cdot\text{C}_6\text{H}_4\cdot\text{CO}_2\text{H}$	6.27 ¹	4.24 ³	4.43 ₅	4.43	3.98
$\text{R}\cdot\text{C}_6\text{H}_4\cdot\text{CH}_2\cdot\text{CO}_2\text{H}$	4.88 ²	4.27 ⁴	4.24	4.06	3.82 ₅
¹ J., 1934, 1888.	² <i>Ibid.</i> , p. 161.	³ J., 1936, 644.	⁴ This vol., p. 1008.		

The values for *p*-ethyl- and *p*-isopropyl-benzoic acids and those for *p*-methyl- and *p*-ethyl-phenylacetic acids are indistinguishable, but the other differences are real, the mean deviation from the mean being usually 0.5—1.0%, and in no case as large as 2%.

Earlier and less accurate data are available for $10^5 K_{\text{class}}$, for *p*-isopropylbenzoic acid (5.0; Ostwald, *Z. physikal. Chem.*, 1889, **3**, 389) and for *p*-*tert*-butylbenzoic acid (4.2; Shoesmith and Mackie, J., 1936, 300): our values of $10^5 K_{\text{class}}$, for these acids are 4.50₅ and 4.02₅, respectively. The foregoing authors did not determine Λ_0 by sodium salt measurements, but merely computed the value on the basis of the number of atoms contained in the molecule. The values so obtained were considerably lower than ours, and this fact would partly account for the higher dissociation constants.

Discussion (J. W. BAKER).

The mesomeric type of electron-release by alkyl groups attached to a conjugated system was assumed (Baker and Nathan, *loc. cit.*) to have its origin in the existence of resonance (involving the duplet of electrons which form the C—H bond) between the various structures of the two general types (I) and (II).



Since the necessary system is present in respect of three C—H bonds in a methyl substituent, two in ethyl, one in *isopropyl*, and is absent in *tert*-butyl, such electron-release towards the benzene ring would decrease in the order $\text{Me} > \text{Et} > \text{Pr}^\beta > \text{Bu}^\gamma$. Superimposition of this effect upon the ordinary inductive (+ *I*) effect, which increases in the order $\text{Me} < \text{Et} < \text{Pr}^\beta < \text{Bu}^\gamma$, should thus cause either complete or at least partial inversion of this order in the sequence which represents the relative magnitudes of total electron-release by alkyl groups. The experimental evidence (J., 1935, 1847; 1936, 226; *loc. cit.*) from kinetic studies of reactions of opposite types revealed a complete reversal of the usual inductive order for alkyl substituents, suggesting that the mesomeric electron-release was of major importance. The contribution made by structures of type (II) towards the mixed wave-function is, of course, unknown. In the resting state of the molecule it is probably small, but in activated molecules participating in a reaction it may become of great importance. Thus, for example, in the conversion of *p*-methylbenzyl bromide into a quaternary ammonium salt, as the C—Br bond becomes stretched (by solvation of the halogen or by electrostriction of the attacking base at the methylene carbon), so the relative importance of the structure $\text{H}^+ \text{CH}_2=\text{C}_6\text{H}_4=\text{CH}_2 \text{Br}^-$ in the resonating system may be assumed to be enhanced.

The accuracy of the experimental technique enables it to be asserted with confidence that the differences now recorded in the values of K_{therm} , for the various alkyl-benzoic and -phenylacetic acids are real. The question therefore arises whether they are significant as evidence regarding the relative electron-release capacities of alkyl substituents. In the alkylphenylacetic acids any mesomeric effects of the type postulated would be of minor importance, and in this series the values of K_{therm} , decrease in a fairly regular sequence which is in harmony with the usual order of inductive (+ *I*) effects of alkyl groups. In the benzoic series, where such mesomeric effects should play an important rôle, a partial inversion of this order is found, but, although the average decrease in K_{therm} , produced by alkyl

substitution is much greater in benzoic acid (approx. 2.0) than it is in phenylacetic acid (approx. 0.8) yet the differences in the $K_{\text{therm.}}$ values for the various alkyl-substituted acids are as large in the one series as in the other. Because of the expected damping effect of the methylene group in the phenylacetic acids, this seems difficult to understand unless some other factor is interfering. Such complications might well be introduced by differing heat capacity and entropy effects which, in the transition from absolute zero to room temperature, could easily swamp differences as small as those involved in these two series of acids. The significance of an objection of this type has been pointed out by Hammett (*J. Chem. Physics*, 1936, **4**, 613) and is discussed more fully by Dr. Dippy (below), but the present writer is of the opinion that, although the data obtained are not inconsistent with the postulates regarding the electron-release capacity of alkyl groups, it is unsafe to base any definite conclusions upon the small and irregular differences in $K_{\text{therm.}}$ which are disclosed.

Discussion (J. F. J. DIPPY).

Since different opinions may be held regarding the tractability of the present results, the writer wishes to explain his particular standpoint. The criticism is made that, although the differences in the values of $K_{\text{therm.}}$ for the various alkyl-benzoic and -phenylacetic acids are real, heat capacity and entropy effects are partly responsible for the relative order of strengths. An objection of this kind has been raised by Hammett (*loc. cit.*), who suggested that dissociation-constant data are admissible in organic discussion only if the effects of the substituents upon heat of ionisation are identical with their effects upon the change of free energy. Hammett analyses the data for the strengths of fatty and benzoic acids at various temperatures, and indicates that conclusions regarding the effects of substituents, derived from ΔH and ΔF data, are at variance.

Nevertheless, there is good reason to suppose that safe conclusions *can* be reached from values of $K_{\text{therm.}}$ for a fixed temperature.

In the first place, there is the undoubted fact that consistent and satisfactory results have attended such discussions in the past. Secondly, Hammett, in spite of the above objection, employs to his satisfaction in a later paper (*J. Amer. Chem. Soc.*, 1937, **59**, 96) accurate dissociation-constant data (water at 25°) for a series of substituted benzoic acids as a basis for the quantitative correlation of the effects of substituents in a number of organic reactions. Thirdly, there is the testing of what is admitted to be a proper theoretical objection. This is best done by making an examination of a series of acids where the strengths are much alike. Harned and his co-workers (*ibid.*, 1933, **55**, 652, 2379; 1934, **56**, 2039) have obtained thermodynamic constants (K_i) for acetic, propionic, and *n*-butyric acids at a variety of temperatures (ranging from 0° to 60° in 5° intervals), and find that K passes through a maximum (K_m at θ°). The temperature θ is somewhat different with each acid. Since, therefore, a comparison of the strengths of two acids at a fixed temperature may not be really fair, Harned (*ibid.*, 1934, **56**, 1050) states that for comparison purposes values of K_m should be employed, *i.e.*, where $\Delta H = 0$ (at temperature θ°). Reference to Harned's data for the above fatty acids makes it clear, however, that there exists no important difference between the relative values of K_m and those of K_i (*e.g.*, at 10° or 25°).

The alkyl-aromatic acids recorded in this paper are comparable with the fatty acids in that their strengths lie close together and their constitutions are all alike. It is reasonable to suppose, therefore, that the present $K_{\text{therm.}}$ data provide a satisfactory relative order capable of being used in discussion. The effects of the alkyl groups are, indeed, so much alike that it is to be expected that any investigation aimed at comparison of their effects will necessarily involve differences of small magnitude in the experimental results.

In the writer's opinion the results in both the benzoic and the phenylacetic series are quite in harmony with the Baker-Nathan theory. Dr. Baker points out above that the existence of distinct partial inversion in the benzoic series may be expected, but suggests that a complication is indicated by the fact that the differences in strength between the various alkylbenzoic acids are not greater than those between the alkylphenylacetic acids. Since, however, the effect postulated by Baker and Nathan is the same in sign as the inductive effect of the alkyl group, but decreases in magnitude in the opposite order, the operation of this effect (which is restricted to the benzoic series) would tend to reduce

the relative differences in acid strength and so account for this observation. In fact, it is theoretically possible that the K 's of the alkylbenzoic acids should all be alike.

An alternative viewpoint is capable of accounting for the complete or partial inversion of the effects of alkyl groups substituted in the aromatic nucleus. If it is supposed that an effect, in a direction opposite to $+I$, is introduced on alkylation of methyl ($\text{Bu}^\nu > \text{Pr}^\beta > \text{Et} > \text{Me}$) conclusions similar to those of Baker and Nathan will be reached. This view is different, however, in that it attributes greatest abnormality to the *tert.*-butyl substituent, and not to methyl.

An apparently linear relationship connecting the dissociation constants of substituted benzoic and phenylacetic acids with the dipole moments of substituted benzenes, recently put forward by the author (*Nature*, 1937, **139**, 591; cf. Dippy and Lewis, this vol., p. 1008), should be capable of testing this alternative interpretation. Only the dipole moments of toluene and *tert.*-butylbenzene are known at present* (the latter is due to Le Fèvre, Le Fèvre, and Robertson, J., 1935, 480); nevertheless, the corresponding acids happen to be the most interesting. The methyl acids in both the benzoic and the phenylacetic series are situated on their respective straight lines (already shown by Dippy and Lewis, *loc. cit.*), but whereas *p*-butylphenylacetic acid also comes on, it is now seen that *p*-butylbenzoic acid actually falls well above the appropriate line. In fact, it is to be expected that the anomaly will only be sufficiently pronounced in this instance to be detected. It is thought, therefore, that *p*-*tert.*-butylbenzoic acid has a strength which is definitely high, pointing to an additional effect which facilitates ionisation.

EXPERIMENTAL.

Preparation of Materials.—*p*-Ethylbenzoic acid. The aldehyde (J., 1935, 1847) (2.5 g.) was treated with aqueous sodium bicarbonate and "perhydrol" and kept at room temperature for several days, with occasional stirring and addition of further quantities of solid sodium bicarbonate and hydrogen peroxide. The acid fraction was isolated in the usual manner, and the unchanged neutral oil (1.5 g.) was oxidised with 1.1 g. of powdered potassium permanganate in aqueous acetone and sodium bicarbonate at room temperature. The combined acid fractions after isolation were crystallised first from dilute alcohol and then repeatedly from ligroin (b. p. 60–80°) to give the acid, m. p. 111° (Found: C, 72.7; H, 6.6. Calc. for $\text{C}_9\text{H}_{10}\text{O}_2$: C, 72.0; H, 6.7%).

p-isoPropylbenzoic acid. The aldehyde was isolated as its bisulphite compound from the fraction of cumin oil, b. p. >200°. This aldehyde, b. p. 102–104°/10 mm. (25 g.), was shaken with 22 g. of potassium hydroxide dissolved in 15 ml. of water. Much heat was developed and the mass set solid. After 18 hours the product was dissolved in water, and neutral products extracted with ether. Acidification of the aqueous liquor at -5° with cold concentrated hydrochloric acid precipitated the acid which, after repeated crystallisation from ligroin (b. p. 60–80°), had m. p. 119–120° (Found: C, 73.7; H, 7.45. Calc. for $\text{C}_{10}\text{H}_{12}\text{O}_2$: C, 73.2; H, 7.3%).

p-*tert.*-Butylbenzoic acid was the specimen previously obtained (*loc. cit.*). The *p*-alkylphenylacetic acids were prepared from the appropriate benzyl chlorides (J., 1935, 1840) through the nitrile, the following being a typical procedure. 7.7 G. of *p*-ethylbenzyl chloride were refluxed with a solution of 12 g. of sodium cyanide in 50 ml. of 96% alcohol on a steam-bath for 18 hrs. After evaporation of most of the alcohol on the steam-bath, the total volume being kept constant by addition of water, the nitrile was extracted with ether. Distillation of the residue from the dried ethereal extract gave the nitrile, b. p. 127–130°/14 mm. (5–6 g.). The nitrile (5 g.) was refluxed with 20 ml. of sulphuric acid (2 parts of water to 3 of acid by vol.) on a sand-bath until the original emulsion first cleared and then quickly formed again owing to the separation of the acid (5–10 mins.). After cooling, the solid acid was extracted with ether to remove traces of carbonaceous matter, and re-extracted with aqueous sodium carbonate. The *p*-ethylphenylacetic acid, isolated in the usual manner after acidification, was crystallised first from ether–ligroin (b. p. 40–60°) and then repeatedly from ligroin alone until it had m. p. 92° (Found: C, 73.5; H, 7.35. Calc. for $\text{C}_{10}\text{H}_{12}\text{O}_2$: C, 73.2; H, 7.3%). Similarly prepared, *p*-isopropylphenylacetic acid had m. p. 52–53° after crystallisation from ice-cold ligroin (b. p. 40–60°). Much loss occurs during purification

* The dipole moments of all the relevant alkylbenzenes and alkylcyclohexanes, in the gas phase are under investigation in collaboration with Professor S. Sugden (J. W. B.).

owing to the high solubility in this solvent (Found: C, 73.0; H, 7.9. Calc. for $C_{11}H_{14}O_2$: C, 74.2; H, 7.9%).

p-tert.-Butylphenylacetic acid was obtained by refluxing *p*-tert.-butylbenzyl bromide (3 g.) with sodium cyanide (2 g.) in alcohol (30 ml.) for 18 hours. Upon evaporation of alcohol and addition of water, the nitrile separated as an oil, which was washed with water and then hydrolysed in the usual manner. After the hot product had been filtered through glass-wool and cooled, the acid separated in fine needles, m. p. 80°.

All these acids were again crystallised from conductivity water and carefully dried before the values of $K_{\text{therm.}}$ were determined, satisfactory values for their equivalents being obtained throughout. The final m. p. data are tabulated below, together with the best values recorded in the literature.

Acid.	M. p. (corr.).	M. p. (lit.).
<i>p</i> -Ethylbenzoic	111.5°	110—111° (Fittig and König, <i>Annalen</i> , 1867, 144 , 290) 112—113 (Aschenbrandt, <i>ibid.</i> , 1883, 216 , 221)
<i>p</i> -isoPropylbenzoic	120	117—118 (Claus, <i>J. pr. Chem.</i> , 1888, 37 , 26) 119 (Ciamician and Silber, <i>Ber.</i> , 1912, 45 , 42)
<i>p</i> -tert.-Butylbenzoic	165	164 (Kelbe and Pfeiffer, <i>Ber.</i> , 1886, 19 , 1725) 165 (Shoemith and Mackie, <i>J.</i> , 1936, 300)
<i>p</i> -Ethylphenylacetic	92	88.5—89.5 (Bogert and Stamataff, <i>Rec. trav. chim.</i> , 1933, 52 , 584)
<i>p</i> -isoPropylphenylacetic	53.5	51—52 (Schorigin, <i>Ber.</i> , 1910, 43 , 1942)
<i>p</i> -tert.-Butylphenylacetic	81.5	52 (Rossi, <i>Annalen</i> , Suppl., 1 , 139) 78—79 (Berg, <i>Rocz. Chem.</i> , 1934, 14 , 1249)

Measurements.—The conductivity measurements were made on aqueous solutions at 25° by a procedure already described (Dippy *et al.*, *J.*, 1934, 161, 1888; 1936, 644). Since the acids were only sparingly soluble in water, their stock solutions were made up to 500 ml., except in the case of *p*-tert.-butylbenzoic acid, which was dissolved in 1 l. The water employed in the various runs had a specific conductivity of 0.9—1.0 gemmho.

In the following tables, the observations made on the six acids are summarised, details of a complete run being given in each case. The mean values of Λ_0 (acid) were obtained from conductivity measurements on the aqueous solutions of the sodium salts by the method adopted elsewhere (Dippy *et al.*, *loc. cit.*).

Cell constant.	10 ³ C.	Λ .	10 ⁵ $K_{\text{class.}}$	10 ⁵ $K_{\text{therm.}}$	Cell constant.	10 ³ C.	Λ .	10 ⁵ $K_{\text{class.}}$	10 ⁵ $K_{\text{therm.}}$
<i>p</i> -Ethylbenzoic acid.					<i>p</i> -isoPropylbenzoic acid.				
0.07278	0.9837	73.08	4.51	4.42	0.07291	0.4487	101.7	4.43	4.36
	0.6879	85.80	4.53 ₅	4.45 ₅		0.3416	115.2	4.54 ₅	4.48
	0.4771	100.0	4.49	4.41 ₅		0.3283	117.2	4.55 ₅	4.49
	0.4285	104.8	4.50 ₅	4.43 ₅		0.2373	133.2	4.53 ₅	4.48
	0.3659	111.8	4.49	4.42 ₅		0.1786	149.6	(4.61 ₅)	(4.56 ₅)
	0.2330	134.1	4.49	4.44 ₅					
12 determinations; limits of 10 ⁵ $K_{\text{therm.}}$				4.41—4.47.	16 determinations; limits of 10 ⁵ $K_{\text{therm.}}$				4.35—4.49.
Mean Λ_0 (acid) = 379.8.					Mean Λ_0 (acid) = 378.5.				
<i>p</i> -tert.-Butylbenzoic acid.					<i>p</i> -Ethylphenylacetic acid.				
0.07423	0.2028	135.6	4.06	4.02	0.07278	0.6024	88.49	4.29 ₅	4.22 ₅
	0.1986	136.7	4.05	4.01		0.3743	108.8	4.34	4.28
	0.1865	140.0	4.06	4.02		0.2614	125.4	4.29	4.23 ₅
	0.1732	142.9	3.98	3.94		0.2599	125.8	4.29 ₅	4.24
	0.1701	144.1	3.99	3.95		0.2403	128.9	(4.22 ₅)	(4.17)
	0.1682	145.7	4.06	4.02		0.2016	138.6	4.26	4.22
12 determinations; limits of 10 ⁵ $K_{\text{therm.}}$				3.93—4.02.	13 determinations; limits of 10 ⁵ $K_{\text{therm.}}$				4.22—4.28.
Mean Λ_0 (acid) = 378.2.					Mean Λ_0 (acid) = 378.5.				
<i>p</i> -isoPropylphenylacetic acid.					<i>p</i> -tert.-Butylphenylacetic acid.				
0.07285	0.7617	80.30	(4.36)	(4.28)	0.07423	1.248	61.81	(3.99 ₅)	(3.90 ₅)
	0.4944	95.23	4.19	4.12 ₅		0.6955	79.41	3.89	3.82
	0.4932	94.73	4.13	4.06 ₅		0.6940	79.43	3.89	3.82
	0.4025	103.5	4.15 ₅	4.09 ₅		0.4018	100.4	3.86	3.80 ₅
	0.2843	119.5	4.15	4.09 ₅		0.3743	103.8	3.89 ₅	3.84
	0.1852	141.9	4.17 ₅	4.13		0.3665	104.5	3.88	3.83
	0.1310	160.8	4.12	4.08 ₅					
20 determinations; limits of 10 ⁵ $K_{\text{therm.}}$				3.98—4.14.	5 determinations; limits of 10 ⁵ $K_{\text{therm.}}$				3.80 ₅ —3.84.
Mean Λ_0 (acid) = 378.2.					Mean Λ_0 (acid) = 377.8.				

It is noteworthy that the mobilities of the anions in both the benzoic and the phenylacetic series gradually fall with increasing size of the alkyl substituent. This also obtains for *p*-toluic acid [Λ_0 (acid) = 379.7] and *p*-tolylacetic acid [Λ_0 (acid) = 379.6 (*loc. cit.*)].

As a generalisation, it can be said that the methyl and the ethyl substituent affect Λ_0 to the same extent, whilst the branched groups *isopropyl* and *tert.*-butyl are comparable in causing a further diminution in mobility.

One of us (J. W. B.) thanks the Royal Society for a grant.

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[Received, August 10th, 1937.]
