U. D. C. 542.61 : 547.561

Differentiating Effect of Amphiprotic Solvents in Relation to Phenol and Benzoic Acid Derivatives

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The review deals with the methods of estimating the differentiating effect of amphiprotic solvents on the acid strengths of phenol and benzoic acid derivatives. New literature data are presented for the dissociation constants and half-neutralisation potentials of electrolytes of the above classes. The possibility of using the Hammett equation to characterise the differentiating effect of solvents is discussed. The available literature values of the autoprotolysis constants of amphiprotic solvents are analysed critically. The problem of the relation between the parameters characterising the differentiating effect of amphiprotic solvents is considered particularly as regards individual groups of electrolytes and the autoprotolysis constant. The causes of the different differentiating capacities of amphiprotic solvents in relation to phenols and benzoic acids are discussed.
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I. INTRODUCTION

The problem of the differentiating effect of solvents on the strengths of electrolytes has been attracting the attention of specialists in various branches of chemistry in connection with wide employment of non-aqueous solvents in physical, organic, and analytical chemistry[1-4]. According to Brönsted's proton theory of acids and bases[5], the differentiating effect of solvents, i.e. their capacity to alter the relative strengths of electrolytes, is shown only in relation to electrolytes of different charge types: cationic, neutral, and anionic acids. When the pK values for the dissociation of electrolytes in two solvents are compared, they are found to fit on three parallel lines with a slope of unity according to the particular charge type to which the acids belong.

The reviews of data for the dissociation constants of acids and bases in various solvents, in the monographs of Shatenshtein[6] and Izmailov[1] showed that there are linear relations between the pK values for the dissociation of acids or bases in water and a non-aqueous solvent or between the values in two non-aqueous solvents. However, as a refinement of Brönsted's theory, it was established that in many solvents uncharged acids exhibit relations associated with various natural groups to which they belong. A detailed study of the charges of the relative strengths of acids and bases under the influence of solvents enabled Izmailov[1] to find the limits of applicability of Brönsted's theory and to establish the differentiating effect of solvents on the strengths of acids and bases.

Izmailov[1] showed that the differentiating effect of solvents is related to their solvating capacity. The relative dissociation constants of different acids in the same solvent depend on their relative intrinsic acidities and the differences between the solvation energies of the acid anions and molecules. The change in the strength of the electrolyte on passing from one solvent to another is due to the change in the relative solvation energies of the ions and molecules of the acid in the two solvents.

Numerous studies have been made on the nature of the solvating effect of solvents[7-14], which showed that the solvation of ions and molecules of electrolytes in solution depends on a number of factors. Apart from the proton affinity of the molecules and lyate ions of solvents (the basicity and acidity of solvents), solvation is determined by the donor–acceptor interaction between the solvent molecules and the molecules and anions of the acid, the formation of hydrogen bonds, electrostatic forces, dipole–dipole and ion–dipole interactions, dispersion interaction, and changes in the structure of the solvent.

Various methods are available for estimating the differentiating effect of solvents. The principal method consists in the measurement and comparison of the dissociation constants of electrolytes (K_{diss}).[1] Recently the half-neutralisation potentials of electrolytes ($E_{1/2}$) have also been measured and compared[4,15-20]. This simple method is widely used in analytical chemistry, since it makes it possible to predict the optimum conditions for the separate titration of acids or bases in mixtures. The differentiating effect of solvents can also be estimated on the basis of the Hammett and Taft equations by comparing the reaction constants ρ and ρ^*, since they depend not only on the type of reaction but also on its conditions, i.e. primarily on the nature of the solvent[21-25].

The present review deals with the differentiating effect of amphiprotic solvents in relation to compounds which exhibit acid properties in solutions, mainly in relation to phenol and benzoic acid derivatives—the most thoroughly investigated classes of electrolytes. Amphiprotic solvents include those whose acidic and basic properties are not more pronounced than the corresponding properties of

water: alcohol, ketones; acetonitrile, and dimethylformamide; an exception is dimethyl sulphoxide, whose basic properties are somewhat more marked than those of water.

The differentiating effect of solvents may be characterised in terms of the following parameters: (1) the slope of the relation $pK_A(ns)$† $= \alpha pK_A(H_2O) + \beta$, i.e. the parameter α, which is equal to the difference between the pK_A values of two electrolytes in a non-aqueous solution when their $pK_A(H_2O)$ differ by unity; (2) the slope of the relation $\Delta E_{1/2} = A pK_A(H_2O) + B$, i.e. the parameter A, which is equal to the difference between the half-neutralisation potentials of two electrolytes in a non-aqueous solution when their $pK_A(H_2O)$ values differ by unity; (3) the slope of the relation $\Delta E_{1/2} + A'\Sigma\sigma + B'$, i.e. the parameter A', which is equal to the difference between the half-neutralisation potentials of two electrolytes in a non-aqueous solution when their $\Sigma\sigma$ values differ by unity (the σ are the constants of the substituents); (4) the reaction constant ρ in the Hammett equation $pK_{rel} = \rho\Sigma\sigma$.

2. STUDY OF THE DIFFERENTIATING EFFECT OF SOLVENTS BY MEASURING THE DISSOCIATION CONSTANTS OF ELECTROLYTES

The dissociation of acids in non-aqueous solutions takes place in a much more complex manner than in an aqueous medium. Izmailov[1] showed that the interaction of an acid with a solvent includes a number of interrelated processes involving the formation of addition products of solvent molecules with the electrolyte molecules and the formation of solvated ions and ion pairs. The study of acid–base interaction in solvents with weak acidic properties, which are therefore incapable of forming hydrogen bonds via the hydrogen atoms in solvent molecules, showed that the mechanisms of the dissociation of acids and bases must be supplemented by the following equilibria[26-31]:

$$A^- + HA \rightleftarrows HA_2^-,$$
$$BH^+ + B \rightleftarrows B_2H^+.$$

These processes, called homoconjugation, take place to a particularly high degree in solvents which Parker[8,9,32] called "aprotic dipolar", since they are incapable of forming hydrogen bonds with the anions of acids and the molecules of bases. Such solvents include in the first place acetonitrile whose basic and acidic properties are both weak. In dimethylformamide and dimethyl sulphoxide homoconjugation processes are weaker because of the higher basicity of these solvents (SH), whose molecules enter into the following competitive reaction with the anion A^-:[33]

$$A^- + HS \ldots HA \rightleftarrows A^- \ldots HA + SH.$$

The studies of Yasinskii's and coworkers[34] showed that in acetone as well as in acetonitrile homoconjugation processes occur to a considerable extent.

As a result of the complexity of the dissociation of acids in non-aqueous solutions, the use of different methods for the determination of K_{diss} in such media produces greater discrepancies than in water. Thus in acetonitrile the range of pK_A values for 2,4,6-trinitrophenol is between 4.34 and 11.0.[30,31,35-38] In solvents with high dielectric constants ($\epsilon < 20$) a considerable proportion of ions are bound in ion pairs which behave as free ions in spectrophotometric and indicator methods for the measurement of pK_A. Therefore in such solvents the K_A values determined by optical methods prove to be higher than those found by electrometric methods. In "aprotic dipolar" solvents homoconjugation processes complicate the calculation of the pK_A values from conductimetric and potentiometric measurements. Reliable pK_A values for acids in such solvents may be obtained by employing a group of methods for measurement (potentiometric, conductimetric, and spectrophotometric).[30,31] For a quantitative interpretation of the acid–base interaction in acetonitrile, it is necessary to take into account more than 10 equilibria[39].

In order to characterise the differentiating effect of solvents, we interpreted the literature pK_A data for phenols and benzoic acids in alcohols, ketones, acetonitrile, dimethylformamide, and dimethyl sulphoxide. The pK_A values for phenols and benzoic acids in non-aqueous solvents are listed in Tables 1 and 2 respectively. For alcohols, their mixtures with water, and acetone, the pK_A values were measured largely by electrometric methods, while for acetonitrile, dimethyl sulphoxide and dimethylformamide the chosen values were obtained by both electrometric and spectrophotometric methods.

The greatest scatter of experimental pK_A data occurs in the case of 2,4,6-trinitrophenol in all the solvents examined. Even in water the pK_A values for 2,4,6-trinitrophenol range from 0.4 to 2.3.[48,60] For 2,4,6-trinitrophenol, we employed $pK_A(H_2O) = 0.71$ obtained conductimetrically[40]. In methanol we adopted $pK_A = 3.67$ taken from Juillard[44] instead of 4.80 which Izmailov[1] quoted without indicating the method of measurement. Examination of the pK_A data for 2,4,6-trinitrophenol in acetone and dimethylformamide showed that it is difficult to give preference to any one value and therefore we employed the average of the data quoted in Table 1.

It follows from Brönsted's theory[5] that the pK_A values for acids in a non-aqueous solvent and in water are related as follows:

$$pK_A(ns) = pK_A(H_2O) + \text{const.} \quad (1)$$

On the basis of the literature and his own data, Izmailov[1,46] showed that, for acids of the same natural group in two solvents, Eqn. (1) is of the following form:

$$pK_A(ns) = \alpha pK_A(H_2O) + \beta, \quad (2)$$

where α and β are quantities which depend on the natural group of acids and the chemical nature of the solvent.

Fig. 1 presents examples of the relations for the pK_A of phenols in non-aqueous solvents as a function of $pK_A(H_2O)$. The numbers of the points in Fig. 1 correspond to those in Table 1. In plotting the above relations, use was made of the average values of the concordant data quoted in Table 1. The straight lines referring to acetone, dimethylformamide, and acetonitrile are almost parallel and have a much higher slope than the lines for methanol.

Fig. 2 presents examples of the relations between the pK_A for benzoic acids in non-aqueous solvents and the $pK_A(H_2O)$; in plotting these functions, use was made largely of the $pK_A(ns)$ values for benzoic acids determined potentiometrically. The numbers of the points in Fig. 2 corresponds to those in Table 2. The variation of pK_A in ethanol with $pK_A(H_2O)$ shows different changes in the $pK_A(ns)$ values for the *m*- and *p*-derivatives of benzoic acid on passing from an aqueous to a non-aqueous solution compared with the *o*-derivatives, which are weaker in non-aqueous solutions than would be expected from their

†ns = non-aqueous solvent.

Table 1. The negative exponents of the dissociation constants of phenols at 25°C in certain solvents measured potentiometrically (P), conductimetrically (C), spectrophotometrically (SP), and by an indicator method (I).

No.	Compound	Solvents										
		water ref. 40–42	methyl alcohol ref 43,44	water–isopropyl alcohol (P) (Ref.45); isopropyl alcohol, %						acetone refs. 2, 35 & 46	acetonitrile refs.30,31, 33,35,37 & 38	dimethyl formamide refs 47–50	dimethylsulphoxide refs. 33,51 &52
				16.0	42.4	62.7	73.8	86.6	93.5				
1	Phenol	9.98	14.46 (SP)	—	—	—	—	—	—	—	26.6 (P,SP)	—	16.4 (P,C,SP)
		—	—	—	—	—	—	—	—	—	—	—	16.9 (P)
2	*m*-Nitrophenol	8.40	—	8.74	9.30	9.65	10.05	10.70	—	—	22.6 (P)	13.85 (P)	—
3	*o*-Nitrophenol	7.23	—	7.38	7.93	8.43	8.74	9.15	9 92	13.82 (P)	22.0 (P,SP)	12.14 (P)	11.0 (P,C,SP)
		—	—	—	—	—	—	—	—	—	22.0 (P)	12.9 (P)	—
		—	—	—	—	—	—	—	—	—	21.2 (P)	—	—
4	*p*-Nitrophenol	7.15	11.09 (P)	7.30	7.82	8.25	8.55	9.08	9.75	13.52 (P)	20.7 (P,SP)	11.84 (P)	9.9 (I)
		—	11.50 (SP)	—	—	—	—	—	—	—	20.9 (P,SP,C)	12.18 (P)	11.0 (P,C,SP)
		—	—	—	—	—	—	—	—	—	20.0 (P)	—	—
5	2,4-Dinitrophenol	3.96	7.85 (P)	3.87	3.88	4.28	4.53	5.06	5.70	8.76 (P)	16.0 (P,SP)	6.36 (P)	5.2 (I)
		—	—	—	—	—	—	—	—	—	16.0 (P)	6.33 (P)	—
		—	—	—	—	—	—	—	—	—	15.3 (P)	—	—
6	2,5-Dinitrophenol	5.16	8.98 (P)	5.14	5.33	5.70	6.03	6.55	7.21	10.3 (P)	17.5 (P)	8.78 (P)	—
		—	—	—	—	—	—	—	—	—	—	8.61 (P)	—
7	2,6-Dinitrophenol	3.70	7.63 (P)	3.64	3.82	4.21	4.51	5.07	5.56	8.76 (P)	16.0 (P,SP)	6.07 (P)	4.9 (P,C,SP)
		—	—	—	—	—	—	—	—	—	16.45 (P)	—	—
8	2,4,6-Trinitrophenol	0.71	3.67 (P)	—	—	—	—	—	—	3.17 (P)	11.0 (SP,P)	3.67 (P)	—1.9 (I)
		—	—	—	—	—	—	—	—	4.73 (SP)	11.0 (P)	1.20 (P)	—1.0 (P,C,SP)
		—	—	—	—	—	—	—	—	4.14 (I)	11.0 (P)	—	—
9	3,5-Dinitrophenol	6.7	—	—	—	—	—	—	—	—	20.7 (P,C,SP)	—	10.6 (P,C,SP)
10	4-Chloro,2,6-dinitrophenol	2.97	—	—	—	—	—	—	—	—	15.3 (P,C,SP)	—	3.5 (P,C,SP)
11	2,6-Dichloro-4-nitrophenol	3.55	7.40 (P)	—	—	—	—	—	—	—	14.3 (P)	5.71 (P)	—
12	2,6-Dibromo-4-nitrophenol	3.38	7.31 (P)	—	—	—	—	—	—	—	14.0 (P)	5.7 (P)	—
13	4-Bromo-2,6-di-t-butyl phenol	10.83	15.91 (P)	—	—	—	—	—	—	—	—	—	—
14	*p*-Chlorophenol	9.38	—	—	—	—	—	—	—	—	—	—	16.1 (P)

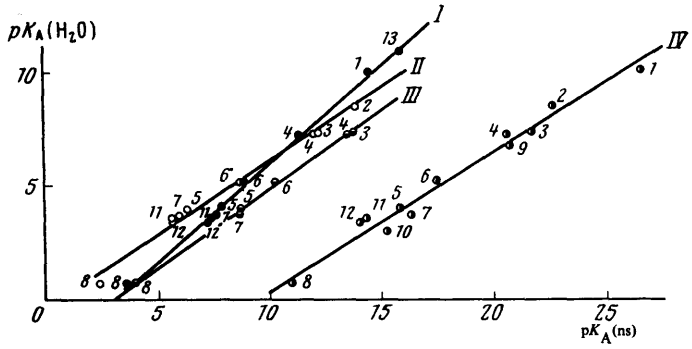


Figure 1. Variation of the pK_A (negative exponent of the dissociation constant) of phenol derivatives in non-aqueous solvents with the pK_A in water: I) methyl alcohol; II)dimethylformamide; III) acetone; IV) acetonitrile.

$pK_A(H_2O)$. Owing to the small number of points, individual relations for the *m*- and *p*-derivatives on the one hand and the *o*-derivatives on the other could not be obtained in other solvents. In the derivation of Eqns. (2), the pK_A values for the *m*- and *p*-derivatives only were employed.

Eqns. (2) were derived by least squares on a "Promin" computer. The equations obtained, the number of experimental points used in their derivation (n), the correlation coefficients (r), and the standard deviations (s) are listed in Table 3.

The empirical Eqns. (2) were compared with the thermodynamic equation derived by Izmailov[1] and Grunwald and Berkowitz[7]:

$$pK_A(ns) = \overbrace{pK_A(H_2O)}^{\alpha pK_A(H_2O)} + \lg\frac{\gamma_{0A^-}}{\gamma_{0HA}} + \overbrace{\lg\gamma_{0H^+}}^{\beta}. \qquad (3)$$

If on passing from water to a non-aqueous solvent the quantity $\lg(\gamma_{0A^-}/\gamma_{0HA})$ for a given reaction series varies in proportion to $pK_A(H_2O)$:

$$\lg\frac{\gamma_{0A^-}}{\gamma_{0HA}} = bpK_A(H_2O), \qquad (4)$$

then the coefficient α in Eqn. (2) will differ from unity owing to the effect of the term $\lg(\gamma_{0A^-}/\gamma_{0HA})$ and is equal to $1 + b$. In this case the constant term should be equal to $\lg\gamma_{0H^+}$ for the given solvent. If on passing from water to a non-aqueous solvent the relation

$$\lg\frac{\gamma_{0A^-}}{\gamma_{0HA}} = bpK_A(H_2O) + c, \qquad (5)$$

holds, the constant term β will differ from $\lg\gamma_{0H^+}$ by an amount c.

It follows from Table 3 that β is indeed close to $\lg\gamma_{0H^+}$ for phenol and *m*- and *p*-derivatives of benzoic acid in alcohols and acetone[61]. The value of $\lg\gamma_{0H^+}$ for dimethylformamide is unknown, but comparison of the relative positions of the relative acidity scales for dimethylformamide and water shows that the value of $\lg\gamma_{0H^+}$ should be close to zero[62]. The $\lg\gamma_{0H^+}$ literature data for acetonitrile differ somewhat among themselves[33,61]. Possibly Eqn. (5) holds for acetonitrile. Fig. 2 shows that for

Table 2. The negative exponents of the dissociation constants of benzoic acids at 25°C in various solvents measured potentiometrically (P), conductimetrically (C), spectrophotometrically (SP) and by an indicator method (I).

No.	Acid	Solvents										
		Water refs. 40–42	methyl alcohol refs.44,53–55	water–ethyl alcohol (P) (ref.56); alcohol, %				ethyl alcohol refs. 55–57	acetone ref.46	acetonitrile refs.27, 33	dimethyl-formamide refs.47–49, and 52	dimethyl sulphoxide refs.33, 51, 58, & 59
				33.2	52.0	73.4	84.5					
1	Benzoic	4.20	9.38 (P)	5.16	5.76	6.57	7,25	10.40 (I)	11.95 (P)	20.1 (C)	12.27 (P)	10.9(P)
		—	9.25 (P)	—	—	—	—	10.15 (P)	—	20.7 (P)	12.20 (P)	11.1 (P,C)
		—	9.27 (P)	—	—	—	—	10.22 (P)	—	—	—	11.0 (P)
		—	—	—	—	—	—	—	—	—	—	10.0 (P)
		—	—	—	—	—	—	—	—	—	—	10.0 (I)
2	*o*-Hydroxybenzoic	2.99	7.85 (P)	—	—	—	—	8.4 (I)	9.57 (P)	16.7 (P)	8.23 (P)	6.9 (P)
		—	7.9 (I)	—	—	—	—	—	—	16.9 (C)	7.85 (P)	6.8 (P,C,SP)
		—	—	—	—	—	—	—	—	—	—	6.6 (P)
3	*p*-Hydroxybenzoic	4.54	—	—	—	—	—	—	12.68 (P)	20.8 (P)	—	11.8 (P)
		—	—	—	—	—	—	—	—	20.3 (C)	—	—
4	*m*-Hydroxybenzoic	4.08	—	—	—	—	—	—	—	—	—	11.1 (P)
5	*m*-Nitrobenzoic	3.46	8.22 (P)	4.14	4.67	5.37	6.03	8.82 (P)	10.66 (P)	—	—	8.2 (P)
		—	8.4 (I)	—	—	—	—	9.15 (P)	—	—	—	—
		—	—	—	—	—	—	9.2 (I)	—	—	—	—
6	*p*-Nitrobenzoic	3.40	8.22 (P)	4.06	4.58	5.27	5.93	8.90 (P)	10.59 (P)	18.7 (P)	10.62 (P)	8.9 (P)
		—	—	—	—	—	—	9.04 (P)	—	19.0 (C)	—	8.05 (P)
7	*o*-Nitrobenzoic	2.20	7.6 (I)	3.51	3.99	4.76	5.47	8.21 (P)	—	—	10.05 (P)	—
		—	—	—	—	—	—	8.58 (P)	—	—	9.60 (P)	—
		—	—	—	—	—	—	8.6 (I)	—	—	—	—
8	*m*-Bromobenzoic	3.81	8.71 (P)	4.71	5.27	5.96	6.77	9.46 (P)	—	19.5 (P)	—	—
		—	—	—	—	—	—	9.65 (P)	—	19.1 (C)	—	—
9	*p*-Bromobenzoic	3.97	8.83 (P)	4.83	5.34	6.04	6.74	9.79 (P)	—	—	—	9.45 (P)
		—	8.7 (I)	—	—	—	—	9.93 (P)	—	—	—	—
		—	—	—	—	—	—	9.6 (I)	—	—	—	—
10	*o*-Bromobenzoic	2,85	—	4.07	4.71	5,44	6.13	8.85 (P)	—	—	—	—
		—	—	—	—	—	—	9.26 (P)	—	—	—	—
11	*m*-Chlorobenzoic	3.81	8.70 (P)	4.78	5.37	6.03	6.67	9.61 (P)	—	—	—	—
		—	8.6 (I)	—	—	—	—	9.75 (P)	—	—	—	—
12	*p*-Chlorobenzoic	4.03	8.93 (P)	4.83	5.38	6.10	6.62	9.75 (P)	—	—	—	10.1 (P)
		—	—	—	—	—	—	9.85 (P)	—	—	—	—
13	*o*-Chlorobenzoic	2.89	—	4.14	4.78	5.53	6.17	9.01 (P)	—	—	11.17 (P)	—
		—	—	—	—	—	—	9.31 (P)	—	—	—	—
14	*m*-Fluorobenzoic	3.85	—	4.74	5.36	6.07	6.70	9.71 (P)	—	—	—	—
15	*p*-Fluorobenzoic	4.14	—	4.95	5.55	6.27	6.98	9.90 (P)	—	—	—	—
16	*o*-Fluorobenzoic	3.27	—	4.54	5.25	5.99	6.69	9.69 (P)	—	—	—	—
17	*m*-Toluic	4.25	9.37 (P)	5.29	5.92	6.62	7.32	10.37 (P)	—	—	—	11.0 (P)
		—	9.29 (P)	—	—	—	—	10.5 (P)	—	—	—	11.0 (P)
18	*p*-Toluic	4.37	9.45 (P)	5.37	6.00	6.80	7.46	10.48 (P)	—	—	—	11.9 (P)
		—	9.46 (P)	—	—	—	—	10.65 (P)	—	—	—	—
								10.3 (I)	—	—	—	—
19	*o*-Toluic	3.90	9.00 (P)	5.16	5.82	6.58	7.26	10.16 (P)	—	—	—	11.0 (P)
		—	—	—	—	—	—	10.24 (P)	—	—	—	—
20	*m*-Methoxybenzoic	4.09	—	5.06	5.72	6.48	7.14	10.13 (P)	—	—	—	—
21	*p*-Methoxybenzoic	4.47	—	5.45	6.09	6.88	7.59	10.55 (P)	—	—	—	—
22	*o*-Methoxybenzoic	4.09	—	5.19	5.83	6.58	7.21	10.09 (P)	—	—	—	—
23	3,5-Dinitrobenzoic	2.80	7.4 (I)	—	—	—	—	8.1 (I)	—	16.9 (P)	8.48 (P)	—
		—	—	—	—	—	—	—	—	17.2 (C)	—	—
24	2,4-Dinitrobenzoic	1.43	6.5 (I)	—	—	—	—	7.3 (I)	—	—	—	—
25	*p*-Aminobenzoic	4.92	—	—	—	—	—	—	13.46 (P)	—	—	12.7 (P)
26	2,6-Dihydroxybenzoic	1.30	—	—	—	—	—	—	—	12.6 (P,C,SP)	—	3.1 (P,C,SP)
27	2,4-Dihydroxybenzoic	3.29	—	—	—	—	—	—	—	—	—	7.5 (P)
28	2,5-Dihydroxybenzoic	2.97	—	—	—	—	—	—	—	—	—	7.1 (P)
29	*m*-Aminobenzoic	4.79	—	—	—	—	—	—	—	—	—	11.6 (P)
								—	—	—	—	10.4 (P)

o-derivatives of benzoic acid the constant term β in Eqn. (2) is not equal to $\lg\gamma_{o_{H^+}}$ for the given solvent. This can be accounted for by the specific effect of substituents in the *o*-position on the changes in the relative solvation energies of the anions and molecules of the acids on passing from water to a non-aqueous solvent.

The data presented in Table 3 show that, in terms of the coefficient α in Eqns. (2), which reflect the differentiating effect of the solvent in relation to a single reaction series of electrolytes, the solvents examined can be arranged in the following series, which is common to both phenol derivatives and *m*- and *p*-derivatives of benzoic acid:

$$(CH_3)_2SO > CH_3CN > (CH_3)_2NCHO > CH_3COCH_3 > > C_2H_5OH > CH_3OH > H_2O.$$

When water is added to a non-aqueous solvent, the differentiating effect of the latter falls, as can be seen for aqueous ethanol mixtures with respect to benzoic acids

Table 3. Equations relating the negative exponents of the dissociation constants of phenols and benzoic acids in non-aqueous solutions to the corresponding values in water: $pK_A(ns) = \alpha pK_A(H_2O) + \beta$.

№	Solvent	Phenol derivatives					*m*- and *p*-derivatives of benzoic acid					lg γ_{H^+}
		α	β	*n*	*r*	*s*	α	β	*n*	*r*	*s*	
1	Methyl alcohol	1.17	+3.1	9	0.999	0.13	1.34	+3.6	9	0.995	0.07	+3.1
2	Ethyl alcohol	1.26	+3.4	4	—	—	1.67	+3.1	13	0.970	0.13	+3.9
3	33.2% ethyl alcohol	—	—	—	—	—	1.29	−0.3	13	0.987	0.07	—
4	52% ethyl alcohol	—	—	—	—	—	1.40	−0.1	13	0.978	0.10	—
5	73.4% ethyl alcohol	—	—	—	—	—	1.49	+0.2	13	0.974	0.12	—
6	85.4% ethyl alcohol	—	—	—	—	—	1.52	+0.8	13	0.973	0.12	—
7	16% isopropyl alcohol	1.08	−0.4	6	0.999	0.10	—	—	—	—	—	—
8	42.4% isopropyl alcohol	1.09	−0.8	6	0.999	0.13	—	—	—	—	—	—
9	62.7% isopropyl alcohol	1.20	−0.4	6	0.999	0.06	—	—	—	—	—	—
10	73.8% isopropyl alcohol	1.22	−0.2	6	0.999	0.09	—	—	—	—	—	—
11	86.6% isopropyl alcohol	1.23	+0.3	6	0.999	0.08	—	—	—	—	—	—
12	93.5% isopropyl alcohol	1.25	+0.8	6	0.999	0.08	—	—	—	—	—	—
13	Dimethylformamide	1.57	+0.6	9	0.995	0.39	2.67	+1.2	3	0.989	0.40	—
14	Acetonitrile	1.64	+9.4	12	0.987	0.74	2.65	+9.5	4	0.992	0.39	+5.5; +7.9
15	Acetone	1.48	+3.0	6	0.998	0.25	1.88	+4.2	5	0.996	0.14	+3.3; +4.7
16	Dimethyl sulphoxide	1.90	−2.3	9	0.999	0.27	3.00	−1.9	10	0.969	0.37	−1.5

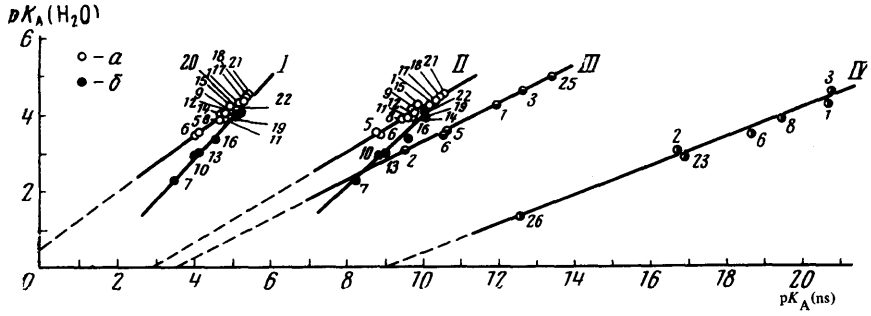


Figure 2. Variation of the pK_A (negative exponent of the dissociation constant) of benzoic acid derivatives in non-aqueous solvents with the pK_A in water (the numbers of the points correspond to those in Table 2): I) 33.2% ethyl alcohol; II) ethyl alcohol; III) acetone; IV) acetonitrile [*a*) *m*- and *p*-derivatives; *b*) *o*-derivatives].

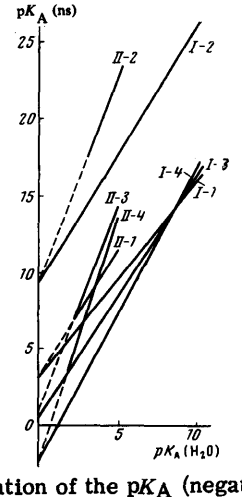


Figure 3. Variation of the pK_A (negative exponent of the dissociation constant) of phenol (I) and benzoic acid (II) derivatives in non-aqueous solvents with the pK_A in water: 1) ethyl alcohol; 2) acetonitrile; 3) dimethylformamide; 4) dimethyl sulphoxide.

and water–isopropyl alcohol mixtures with respect to phenols.

The differentiating effect of solvents in relation to electrolytes of different classes is various: the acid strength of benzoic acids is different in amphiprotic solvents compared with water and to a greater extent than for phenols. As a result, the difference $\Delta pK_A(ns)$ between benzoic acid and phenol derivatives depends on the $pK_A(H_2O)$ values for the electrolytes compared and is greater the higher is $pK_A(H_2O)$ (Fig. 3). For this reason ΔpK_A is not always constant for two different groups of electrolytes and in such cases does not characterise the differentiating effect of the non-aqueous solvent relative to water, as was assumed in a number of investigations[47,48,63,64]. The similarity of the slopes of the plots of $pK_A(ns)$ against $pK_A(H_2O)$ for phenols and carboxylic acids is a consequence of the fact that the group of carboxylic acids includes electrolytes of different reaction series (aromatic and aliphatic carboxylic acids). To establish the laws governing the variation of the relative strengths of acid on passing from solvent to solvent, i.e. the differentiating effect of solvents, it is necessary to examine narrow series of electrolytes[22,60,65].

3. STUDY OF THE DIFFERENTIATING EFFECT OF SOLVENTS BY MEASURING THE HALF-NEUTRALISATION POTENTIALS OF ELECTROLYTES

This method of measuring the relative strengths of electrolytes has proved fruitful not only in the determination of acid strengths in aprotic solvents, where it is possible to determine only relative constants, but also in protolytic solvents, where it is possible to avoid many difficulties associated with the determination of the usual dissociation constants.

The relative strengths of acids and bases in non-aqueous solvents are characterised in three ways, which differ only in the scale of the measurements employed: by the value of pK_{rel} and the pH or potential at the half-neutralisation point—$pH_{1/2}$ and $E_{1/2}$.[4,66-71] In the potentiometric measurement of the relative dissociation constants of acids the pK_{rel} are related to $pH_{1/2}$ and $E_{1/2}$ by the following equations: $pK_{rel} = pH^{x}_{1/2} - pH^{st}_{1/2}$ or $pK_{rel} = (E^{x}_{1/2} - E^{st}_{1/2})/59$, where $pK^{x}_{1/2}$ and $E^{x}_{1/2}$ are the half-neutralisation pH or potentials (mV) for the test compound and $pH^{st}_{1/2}$ and $E^{st}_{1/2}$ are the corresponding values for a standard compound.

To characterise the relative acidities of electrolytes, one employs absolute values of $pH_{1/2}$ and $E_{1/2}$ as well as values referred to a standard ($\Delta pH_{1/2}$ and $\Delta E_{1/2}$), which reduces the effect of variations in the diffusion-potential. In non-aqueous solvents $pH_{1/2}$ and $E_{1/2}$ or $\Delta pH_{1/2}$ and $\Delta E_{1/2}$ are not always functions of the dissociation constants of the electrolytes only but also reflect the effect of factors on which the form of the titration curves depends (the degree of dissociation of the salt formed, its solubility, homoconjugation phenomena, etc.). An increase in the slope of the titration curve in the buffer region results in a displacement of the half-neutralisation potential of the acid to a more basic region; this is facilitated by homoconjugation phenomena[34,39]. A decrease of the slope of the titration curve in the buffer region results in a displacement of the half-neutralisation potential of the acid to a more acidic region; this is favoured by the formation of ion pairs of the salt and its precipitation. However, for acids of a single natural group, the change in $E_{1/2}$ basically correctly reflects the variation of the dissociation constants of the electrolytes in the same solvent.

The half-neutralisation potentials of phenol derivatives were measured in alcohol (methyl, ethyl, propyl, isopropyl, butyl, isobutyl, and t-butyl), ketones (acetone, ethyl methyl ketone, and isobutyl methyl ketone), acetonitrile, dimethylformamide, dimethyl sulphoxide, and other solvents[4,17-19,59,71-76]. Comparison of the half-neutralisation potentials with the $pK_A(H_2O)$ values yields relations described by the equation

$$\Delta E_{1/2}(\text{нр}) = ApK_A(H_2O) + B, \qquad (6)$$

where $\Delta E_{1/2}$ is the half-neutralisation potential of phenol measured relative to the half-neutralisation potential of benzoic acid. Measurements for halogeno- and nitro-derivatives of phenol with substituents in the *m*- and *p*-positions showed that the sequence of acidities characteristic of the aqueous solutions is retained[18,72,73]. In a study of halogeno- and nitro-derivatives of phenol containing only *o*-substituents or *o*-substituents together with *m*- and *p*-substituents, it was established that in alcohols phenols with *o*-substituents behave as weaker electrolytes than the *m*- and *p*-derivatives which have the same values of $pK_A(H_2O)$ (Fig. 4). The weaker acid strength of *o*-derivatives of phenol compared with the *m*- and *p*-derivatives may be accounted for by the effect of the intramolecular hydrogen bond between the hydrogen of the phenolic hydroxyl and the substituent in the *o*-position. In ketones, acetonitrile, and dimethylformamide, the effect of the formation of an intramolecular hydrogen bond in *o*-derivatives of phenol cannot be detected, since the titration curves have high slopes in the buffer region owing to homoconjugation, which leads to a displacement of $E_{1/2}$ to a more basic region (Fig. 5). This has a particularly

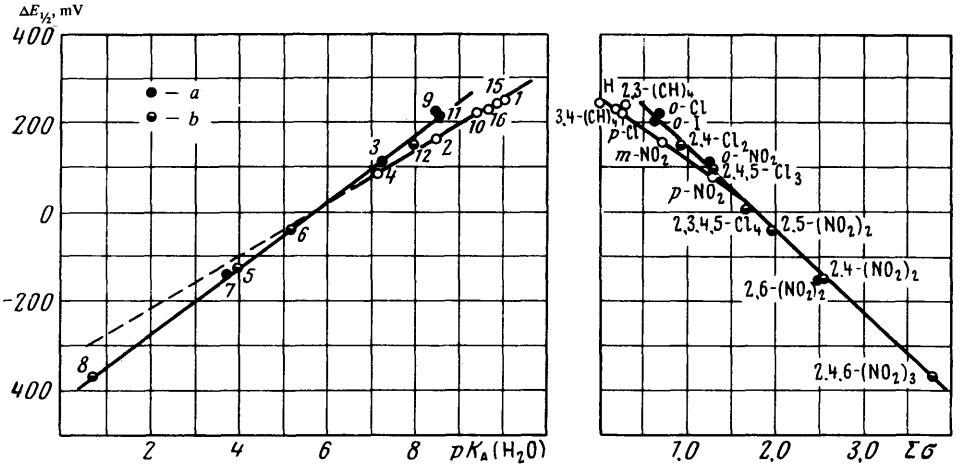


Figure 4. Variation of the half-neutralisation potentials of phenol derivatives in propyl alcohol with $pK_A(H_2O)$ and σ constants: 1) phenol; 2) *m*-nitrophenol; 3) *o*-nitrophenol; 4) *p*-nitrophenol; 5) 2,4-dinitrophenol; 6) 2,5-dinitrophenol; 7) 2,6-dinitrophenol; 8) 2,4,6-trinitrophenol; 9) *o*-chlorophenol; 10) *p*-chlorophenol; 11) *o*-iodophenol; 12) 2,4-dichlorophenol; 13) 2,4,5-trichlorophenol; 14) 2,3,4,5-tetrachlorophenol; 15) α-naphthol; 16) β-naphthol [*a*) *o*-derivatives; *b*) *o*-derivatives containing *m*- and *p*-substituents].

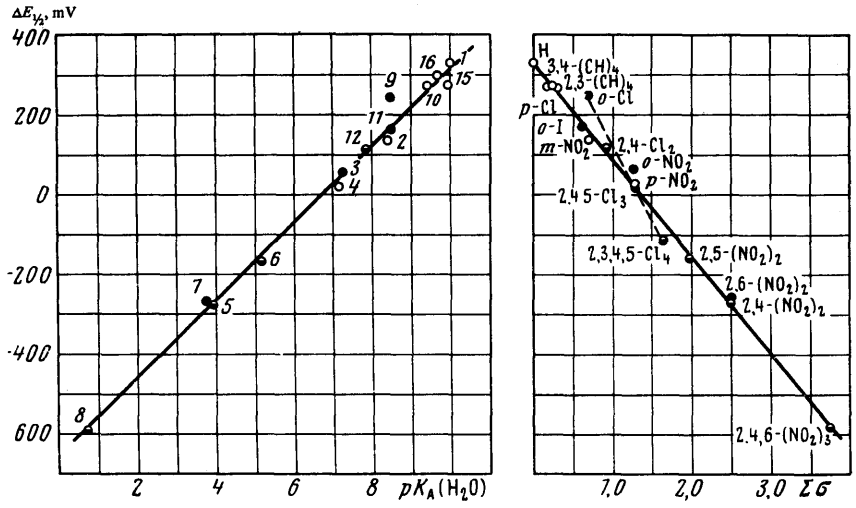


Figure 5. Variation of the half-neutralisation potentials of phenol in acetone with $pK_A(H_2O)$ and σ constants (the numbers and designations of the points are the same as in Fig. 4).

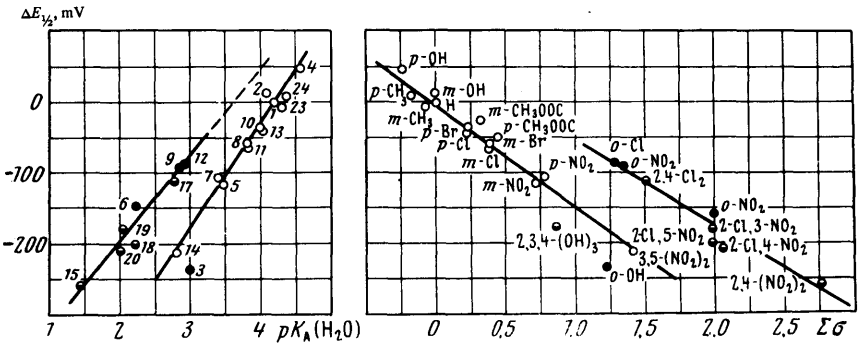


Figure 6. Variation of the half-neutralisation potentials of benzoic acid derivatives in dimethylformamide with $pK_A(H_2O)$ and σ constants; 1) benzoic acid; 2) *m*-hydroxybenzoic acid; 3) *o*-hydroxybenzoic acid; 4) *p*-hydroxybenzoic acid; 5) *m*-nitrobenzoic acid; 6) *o*-nitrobenzoic acid; 7) *p*-nitrobenzoic acid; 8) *m*-bromobenzoic acid; 9) *o*-bromobenzoic acid; 10) *p*-bromobenzoic acid; 11) *m*-chlorobenzoic acid; 12) *o*-chlorobenzoic acid; 13) *p*-chlorobenzoic acid; 14) 3,5-dinitrobenzoic acid; 15) 2,4-dinitrobenzoic acid; 16) 3,4-dihydroxybenzoic acid; 17) 2,4-dichlorobenzoic acid; 18) 2-chloro-5-nitrobenzoic acid; 19) 2-chloro-3-nitrobenzoic acid; 20) 2-chloro-4-nitrobenzoic acid; 23) *m*-toluic acid; 24) *p*-toluic acid.

marked effect on *m*- and *p*-derivatives and therefore *o*-, *m*-, and *p*-derivatives of phenol have a common relation between $\Delta E_{1/2}$ and $pK_A(H_2O)$ in ketones, acetonitrile, and dimethylformamide.

Pearce and Simkins [60] investigated the differentiating effect of ethyl alcohol and acetone with respect to various phenol derivatives: nitrophenols, derivatives of picric acid, and derivatives of styphnic acid. Comparison of $\Delta E_{1/2}$ with $pK_A(H_2O)$ showed that there is no single relation between these quantities for all the electrolytes investigated; instead, there is a family of straight lines: one relation refers to derivatives of picric acid, dinitrophenols give rise to another straight line with a smaller slope relative to the $pK_A(H_2O)$ axis, and it is possible that styphnic acids also have a specific relation with a steeper slope. The authors showed that, when a small number of species are investigated, apparent relations may be obtained between $E_{1/2}$ and $pK_A(H_2O)$, which hold only for a strictly limited group of compounds. Thus an apparent relation for picric acid derivatives, including also styphnic acid, was obtained by Elder and Mariella [74].

The half-neutralisation potentials of benzoic acids have been measured in methyl, ethyl, and isopropyl alcohols, acetone, ethyl methyl ketone, isobutyl methyl ketone, acetonitrile, dimethylformamide, and other solvents [4,16,18,59,60,77,78]. Separate relations corresponding to Eqn. (6) for

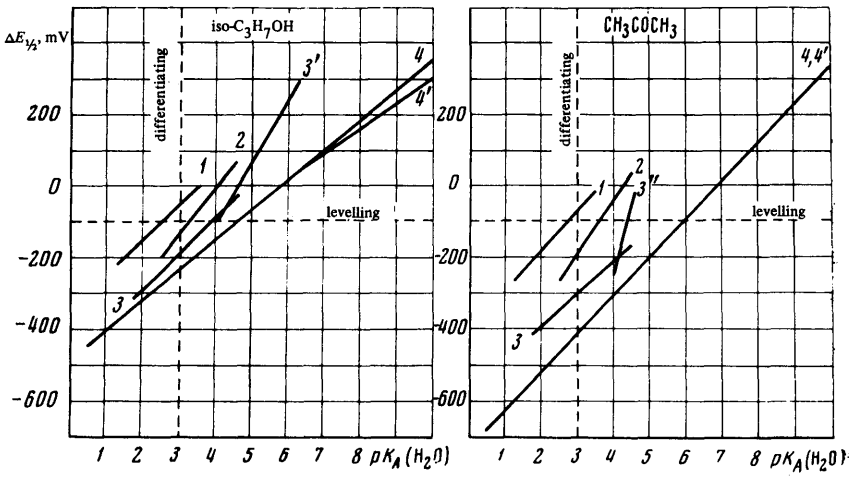


Figure 7. Variation of the half-neutralisation potentials of electrolytes in non-aqueous solvents with $pK_A(H_2O)$: 1) *o*-derivatives of benzoic acid; 2) *m*- and *p*-derivatives of benzoic acid; 3) and 3″) dicarboxylic acids (first dissociation); 3′) dicarboxylic acids (second dissociation); 4) *o*-derivatives of phenol; 4′) *m*- and *p*-derivatives of phenol.

m- and *p*-derivatives and for *o*-derivatives were obtained for all the solvents (Fig. 6). In the case of benzoic acids, on passing from water to non-aqueous solvents, a more pronounced weakening is observed for the *o*-derivatives compared with the *m*- and *p*-derivatives than in the case of phenol. This can probably be accounted for by the steric factors operating in the formation of the intramolecular hydrogen bond (in particular the formation of six-membered rings by *o*-derivatives of benzoic acid). The weakening of the acid strengths of the *o*-derivatives of benzoic acid is so pronounced that homoconjugation even in acetonitrile does not eliminate the difference between the behaviour of *m*- and *p*-derivatives on the one hand and *o*-derivatives on the other, although in acetonitrile $E_{1/2}$ for the *m*- and *p*-derivatives of benzoic acid approaches the value of $E_{1/2}$ for the *o*-derivatives with the same acid strength in water.

Benzoic acid derivatives containing in the same molecule *m*- or *p*-substituents together with *o*-substituents lie on the plot for *o*-derivatives. An appreciable deviation from linearity in all the solvents is shown by *o*-hydroxy derivatives which, owing to the stabilisation of the anion by the intramolecular hydrogen bond, become stronger acids in non-aqueous solvents compared with other acids with the same values of $pK_A(H_2O)$. A deviation from linearity is also shown by acids which on titration give rise to the formation of salt precipitates.

The measurements of the half-neutralisation potentials of phenol and benzoic acid derivatives permit a comparison of the differentiating effects of solvents relative to these groups of electrolytes. On passing from water to amphiprotic solvents, the points for phenols and benzoic acids lie on different straight lines, i.e. there is a differentiating effect of the solvent. Fig. 7 shows as an example the relations between $\Delta E_{1/2}$ in non-aqueous solutions and $pK_A(H_2O)$ for isopropyl alcohol and ethyl methyl ketone. It is evident that the strengths of electrolytes of different groups with the same $pK_A(H_2O)$ values are differentiated to varying extents depending on the value of $pK_A(H_2O)$. For example, in isopropyl alcohol for $pK_A(H_2O) = 2.5$, the half-neutralisation potentials of phenol and any *m*- or *p*-benzoic acid differ by 80 mV and for $pK_A(H_2O) = 4$ by 150 mV. As a result, in relation to some electrolytes the non-aqueous solvents exhibit a differentiating effect while in relation to others they have a levelling effect. Thus on passing from water to isopropyl alcohol or ethyl methyl ketone, the non-aqueous solvents have a differentiating effect with respect to the electrolytes located on the vertical line in Fig. 7 and a levelling effect in relation to the electrolytes located on the horizontal line.

The coefficient A in Eqns. (6) represents the slope of the straight lines, i.e. the differentiating effects of the solvents with respect to electrolytes of the same group. The constant term in the equation makes it possible to arrange the groups of electrolytes in a sequence relative to one another. The physical significance of the coefficient A is that it represents the difference between the half-neutralisation potentials in a non-aqueous solution between two electrolytes whose $pK_A(H_2O)$ values differ by unity. The differentiating effects of non-aqueous solvents in terms of the coefficient A, i.e. in terms of the number of millivolts per unit $pK_A(H_2O)$ value, are compared in Table 4, which shows that alcohols can be arranged in the following sequence in terms of their differentiating effects in relation to phenols and benzoic acids:

$$\text{iso-}C_3H_7OH > \text{iso-}C_4H_9OH > \text{n-}C_4H_9OH > \text{n-}C_3H_7OH,\ C_2H_5OH > CH_3OH\ .$$

Comparison of the differentiating effects of alcohols in relation to phenol and benzoic acid derivatives containing only *m*- and *p*-substituents and derivatives with *o*-substituents shows that alcohols behave differently in relation to phenols and benzoic acids. Thus the differentiating effect of alcohols is greater in relation to phenols containing *o*-substituents than in relation to phenols with only *m*- and *p*-substituents. On the other hand, in relation to benzoic acids, alcohols show a greater differentiating effect for *m*- and *p*-derivatives than for *o*-derivatives. The greater differentiating effect of alcohols with respect to *o*-derivatives compared with *m*- and *p*-derivatives is evidence of a greater difference between the solvation energies of the

molecules and ions of *o*-derivatives of phenols compared with the *m*- and *p*-derivatives. In the case of benzoic acids the lower differentiating effect with respect to *o*-derivatives shows that the differences between the solvation energies of the molecules and ions of *m*- and *p*-derivatives of benzoic acid are greater than for the *o*-derivatives. The explanation is probably that the effect of the *o*-substituents diminishes as the polarity of the solvent is reduced owing to a greater non-coplanarity of the carboxy group with respect to the benzene ring, as shown by Charton and Charton[79].

Table 4. Differentiating effects of non-aqueous solvents in relation to phenol and benzoic acid derivatives[72,73,78,81].

Solvent	Phenol derivatives		Benzoic acid derivatives	
	m- and *p*-derivatives	derivatives containing *o*-substituents	*m*- and *p*-derivatives	derivatives containing *o*-substituents
I. Slopes of $\Delta E_{1/2}$ - $pK_A(H_2O)$ plots in mV per $pK_A(H_2O)$ unit				
Methyl alcohol	—	64	90	68
Ethyl alcohol	61	73	104	78
Propyl alcohol	58	74	—	—
Isopropyl alcohol	80	85	125	95
Butyl alcohol	65	78	—	—
Isobutyl alcohol	67	78	—	—
Acetone	97	97	140	121
Ethyl methyl ketone	105	105	149	109
Acetonitrile	88	88	115	123
Dimethylformamide	108	108	150	120
II. Slopes of $\Delta E_{1/2}$ - $\Sigma\sigma$ plots in mV per $\Sigma\sigma$ unit				
Methyl alcohol	—	161	84	70
Ethyl alcohol	135	185	100	81
Propyl alcohol	136	187	—	—
Isopropyl alcohol	186	213	122	97
Butyl alcohol	153	195	—	—
Isobutyl alcohol	157	198	—	—
Acetone	242	242	139	125
Ethyl methyl ketone	264	264	147	111
Acetonitrile	219	219	113	127
Dimethylformamide	267	267	149	125

The differentiating effects of acetone and ethyl methyl ketone with respect to acids are almost the same. The differentiating effect of acetonitrile is less marked than that of ketones, probably due to homoconjugation in the electrolyte solutions, which is particularly pronounced in the titration process. The differentiating effect of dimethylformamide with respect to phenols and benzoic acids is similar to that of ethyl methyl ketone. Thus, ketones, acetonitrile, and dimethylformamide can be arranged in the following series in order of their differentiating effects:

$$(CH_3)_2NCHO > CH_3COC_2H_5,\ CH_3COCH_3 > CH_3CN.$$

Gur'ev[76] gave a systematic account of data for the coefficients of $pK_A(H_2O)$ in the relation between $\Delta E_{1/2}$ in non-aqueous solutions and $pK_A(H_2O)$; he took these coefficients from studies dealing with relations of this kind, calculated them from the pK_{rel} for electrolytes determined by non-electrometric methods, or determined them from potentiometric titration curves. In relation to all groups of acids, pyridine showed the greatest differentiating effect, and was followed in this respect by dimethylformamide, ketones, acetonitriles, and aprotic solvents and their mixtures with protolytic solvents. Compared with water, all the solvents differentiate the acid strengths of benzoic acids to a greater extent than those of phenols.

Hitherto, we have considered changes in the differentiating effect on passing from water to a non-aqueous solvent. In turn, water as a solvent has varied differentiating effects on different groups of electrolytes depending on their molecular structure. Thus the differentiating effect of water with respect to phenol derivatives is shown to a much greater extent than with respect to benzoic acids, owing to the closer location of the substituent in the phenol molecule to the reaction centre than in the benzoic acid molecule. Thus in the Hammett equation the reaction constant ρ for the dissociation of benzoic acids in aqueous solution is unity and for the dissociation of phenols 2.23.[80] Therefore, apart from a comparison of $\Delta E_{1/2}$ with $pK_A(H_2O)$, it is of considerable interest to compare $\Delta E_{1/2}$ with the σ constants for the substituents[18,78,81].

Comparison of the differentiating effects of solvents in terms of the slope of the plots of $\Delta E_{1/2}$ against σ or $\Sigma\sigma$ in the presence of several substituents in the same molecule (Table 4) makes it possible to follow the changes in the differentiating effect of solvents with respect to electrolytes belonging to different reaction series as a function of the structural differences between the molecules. Figs. 4–6 present examples of the relations between $\Delta E_{1/2}$ in non-aqueous solutions and $\Sigma\sigma$ for phenol and benzoic acid derivatives. These relations are characterised by an equation of the form

$$\Delta E_{1/2} = A'\Sigma\sigma + B'. \qquad (7)$$

The coefficient A' is equal to the difference between the half-neutralisation potentials of two electrolytes whose $\Sigma\sigma$ values differ by unity.

In the first place mention should be made of the fact that the number of millivolts per $pK_A(H_2O)$ unit and the number of millivolts per σ unit are very similar for benzoic acids, since the reaction constant ρ for the dissociation of benzoic acids in aqueous solution is unity. The slight discrepancies between these values are a consequence of the deviation from unity of the correlation coefficient for the relation between $pK_A(H_2O)$ and $\Sigma\sigma$ and also of the fact that, as a result of the different degrees of dissociation of the salts formed, the formation of ion pairs, and homoconjugation, the half-neutralisation potentials are not always functions of the acid dissociation constants alone. Comparison of the differentiating effects of the solvents on the basis of the number of millivolts per $\Sigma\sigma$ unit shows that the differentiating effect on non-aqueous solvents, like that of water, is much greater for phenol derivatives than for benzoic acid derivatives.

The relative E_S acidity scale, the extent of which determines the possibility of the differential titration of mixtures of electrolytes, is an analytical chemical characteristic of solvents in acid–base potentiometric titrations[4,62,82]. The E_S scale for solvents is measured under the same conditions as the half-neutralisation potentials of electrolytes. It is therefore of interest to compare quantities characterising the differentiating effects of solvents with respect to individual groups of electrolytes with the extents of the relative acidity scales of the solvents. It is to be expected that the correlation between these quantities will be most clear cut within the limits of a single chemical group of solvents. Fig. 8 shows a comparison of the extents of the E_S scales for solvents with the coefficients A and A' in Eqns. (6) and (7). It is seen from the Figure that there is a linear relation between the extents of the relative acidity scales for alcohols and the coefficients A and A' characterising the differential effects of the alcohols not only in relation to phenols and benzoic acids but

also in relation to dicarboxylic acids [83]. The differentiating effects of non-aqueous solvents in relation to phenols and benzoic acid can also be compared in terms of the relative dissociation constants of these electrolytes in different solvents, which are calculated from the half-neutralisation potentials of phenols and benzoic acids [78,81] by the formula (at 20°C)

$$pK^{x}_{rel} = pK^{x}_{A} - pK^{C_6H_5COOH}_{A} = \frac{\Delta E_{1/2}}{58} \quad . \qquad (8)$$

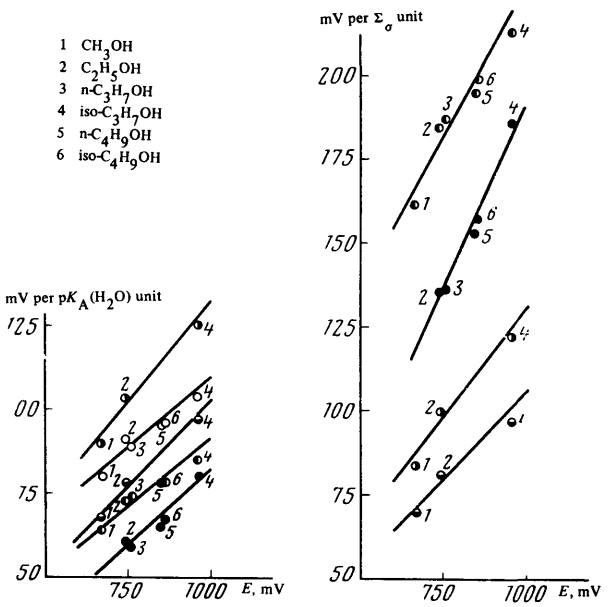


Figure 8. Relation between the slopes of plots of $\Delta E_{1/2}$(ns) against $pK_A(H_2O)$ and $\Delta E_{1/2}$(ns) against $\Sigma\sigma$ and the range of the relative acidity scale of the solvent: ●—*m*- and *p*-derivatives of phenol; ◐—*o*-derivatives of phenol; ◑—*m*- and *p*-derivatives of benzoic acid; ◒—*o*-derivatives of benzoic acid; ○—dicarboxylic acids (first dissociation).

The pK_{rel} values for phenols and benzoic acids in various solvents are compared in Figs. 9–12. On passing from water to alcohols, the acid strength of phenols increases relative to that of benzoic acids (Fig. 9). The same also happens on passing from water to other non-aqueous solvents. Consequently, on passing from water to alcohols, the solvation of phenoxide ions compared with that of phenol molecules increases more than the solvation of benzoate ions compared with that of benzoic acid molecules. In solvents belonging to the same natural group (ethyl and isopropyl alcohols) differentiation of the acid strengths of phenols and benzoic acids is not observed. According to Brönsted's theory, the points for all electrolytes lie on a single straight line with a slope of unity (Fig. 10). The same happens on passing from acetone to ethyl methyl ketone.

On passing from ketones to alcohols, i.e. solvents of another natural group, the acid strengths of phenols and benzoic acids are differentiated. However, whereas on

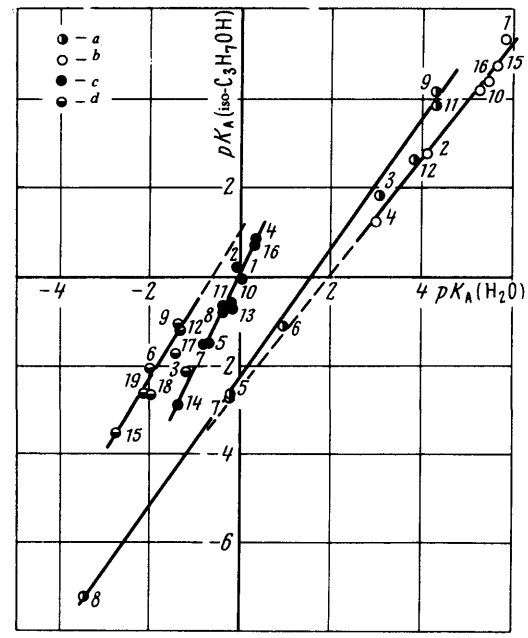


Figure 9. Relation between the pK_{rel} of phenol and benzoic acid derivatives in water and isopropyl alcohol (the numbers of the points for the phenols are the same as in Fig. 4 and those for benzoic acid are the same as in Fig. 6): *a*) phenol derivatives containing *o*-substituents; *b*) *m*- and *p*-derivatives of phenol; *c*) *m*- and *p*-derivatives of benzoic acid; *d*) derivatives of benzoic acid containing *o*-substituents.

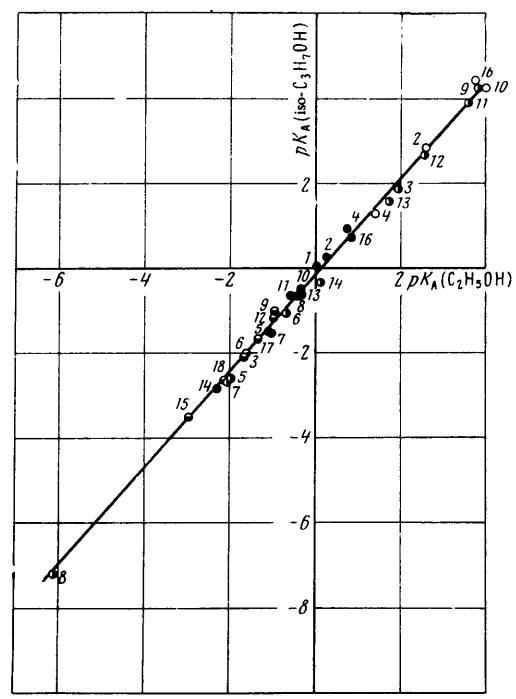


Figure 10. Relation between the pK_{rel} of phenol and benzoic acid derivatives in ethyl and isopropyl alcohols (the numbers and designations of the points correspond to those in Fig. 9).

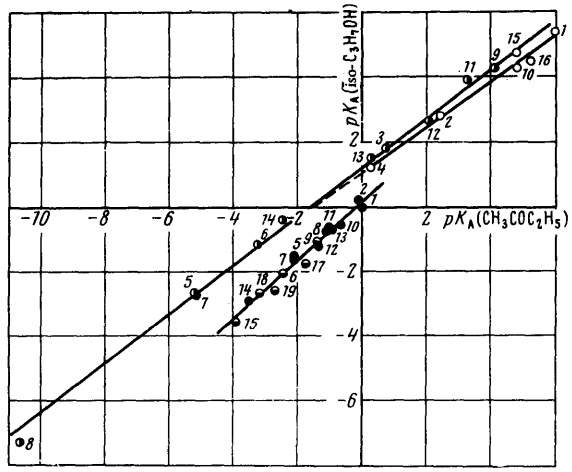


Figure 11. Relation between the pK_{rel} of phenol and benzoic acid derivatives in ethyl methyl ketone and isopropyl alcohol (the numbers and designations of the points correspond to those in Fig. 9).

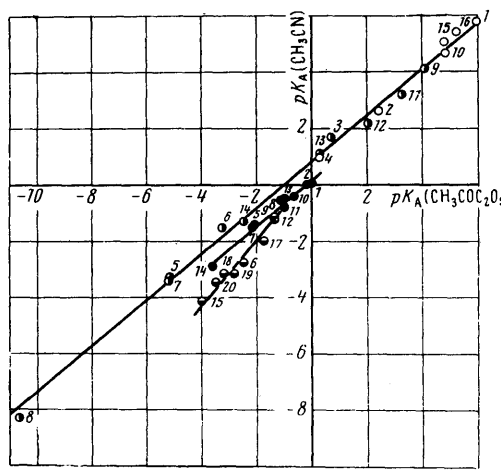


Figure 12. Relation between the pK_{rel} of phenol and benzoic acid derivatives in ethyl methyl ketone and acetonitrile (the numbers and designations of the points correspond to those in Fig. 9).

passing from water to alcohols there is an increase in the acid strength of phenols compared with benzoic acids, on passing from ketones to alcohols the opposite phenomenon is observed: phenols become weaker than benzoic acids (Fig. 11). Within a single class of electrolytes, the differentiating effect changes on passing from ketones to alcohols only among phenols. The points for all the benzoic acids lie on a single straight line with a slope close to unity, which is evidence that the solvation energies of the ions and molecules of benzoic acids change to the same extent on passing from ketones to alcohols. On going from ketones to acetonitrile, the acid strengths of phenols and benzoic acids are also differentiated (Fig. 12). In contrast to the effect on passing from ketones to alcohols, the acid strengths are differentiated within the class of benzoic acids but not within the class of phenols. As stated above, *m*- and *p*-derivatives of benzoic acid become weaker in acetonitrile compared with *o*-derivatives than in ethyl methyl ketone, in consequence of homoconjugation, which is particularly pronounced in acetonitrile.

The results of the above comparison of the relative acid strengths of phenols and benzoic acids in various solvents are consistent with the data presented in the monographs of Izmailov[1] and Shatenshtein[6] for solvents of the same and different natures. Shatenshtein's latest data on the differentiating effects of solvents in relation to C–H acids obtained by an isotope exchange method also confirmed the conclusion that the differentiating effect is due to a change in the solvation of ions and molecules of acids in the solvents compared[10].

4. STUDY OF THE DIFFERENTIATING EFFECT OF SOLVENTS BASED ON THE HAMMETT EQUATION

Acid strengths, particularly of benzoic acid and phenol derivatives, in aqueous solutions can be successfully predicted on the basis of the Hammett equation[80,84]. If the σ constants did not change on passing from water to non-aqueous solvents, the effect of the latter on the dissociation of substituted acids might be taken into account using the constant ρ:

$$\lg \frac{K}{K^0} = \rho\sigma \quad , \qquad (9)$$

where K and K^0 are the dissociation constants of the substituted and unsubstituted acids.

It has been stated[21,22,85-94] that the σ constants vary on passing from water to non-aqueous solvents owing to changes in the solvation of the polar groups of the substituents, in particular the type of hydrogen bond between the substituent and the solvent molecules; under the influence of the solvent, the capacity of the substituent for polar conjugation with the reaction centre may alter, etc. As a rule, the effect of the solvent on the σ constant is small[21]. Only certain substituents (for example OH groups) show an appreciable variation of the σ constants on changing the solvent[21,23,90].

The effect of the solvent on the σ constant cannot be taken into account with the aid of the dielectric constant ϵ of the medium, as suggested by Hammett[22,84]. For example, it is known that the relation

$$\rho = \left(1.87 + \frac{67}{\varepsilon}\right) \cdot \frac{1.09}{2.8^n},$$

(where n is the number of atoms separating the reaction centre from the phenyl carbon atom) holds satisfactorily for benzoic acids in water, ethylene glycol, and methyl and ethyl alcohols, but not in n-propyl and n-butyl alcohols and aqueous dioxan mixtures[93].

The use in Eqn. (9) of known Hammett's σ constants for aqueous solutions does not yield a constant ρ which would reflect the influence of the solvent on the transmission of only the inductive effect of the substituents. In this connection, the method of estimation of the constant ρ proposed by Palm[22] and based on the use of Taft's universal σ^* induction constants for aliphatic substituents and the ρ^* universal interaction constant is of interest. However, the lack of adequate literature data for the K_A of aliphatic carboxylic acids in non-aqueous solvents procludes the use of this method for the estimation of the effect of the solvent on the ρ^* constant. Therefore one may assume, as emphasised in a number of monographs[21,22] and

papers[23,24,94], that at the present time the weakest point of all quantitative theories of the effect of substituents is the little investigated effect of solvents.

In earlier reviews[23,24] the ρ constants for the dissociation of benzoic acid in certain alcohols, aqueous alcoholic, and aqueous dioxan mixtures were given. In contrast to Jaffe[23], Wells[24] quotes in his review also the values of ρ obtained by the method described in the paper of van Bekkum et al.[95], who used a reaction series involving only *m*-derivatives of benzoic acid to exclude the effect of polar conjugation between the substituent and the reaction centre; this leads to an increase of ρ. The values of ρ quoted in the reviews[23,24] were obtained on the basis of the K_A constants for benzoic acid measured largely by indicator methods.

The data for the dissociation constants of *m*- and *p*-derivatives of benzoic acid obtained by electrometric methods permitted the calculation of new values of the constant ρ.[44,56,58,89,96,97] These values of ρ, calculated by ourselves and taken from papers by other investigators are listed in Table 5. The reaction constants ρ, the correlation coefficients r, and the standard deviations s were calculated by least squares on a "Promin'" computer. Table 5 also lists the numbers of correlated quantities n.

Table 5. Reaction constants ρ in the Hammett equation for the dissociation of *m*- and *p*-derivatives of benzoic acid in non-aqueous solutions.

Solvent	Calc. from pK_A (25°)					Calc. from $\Delta E_{1/2}$ (20° ± 2°)				
	ρ	n	r	s	from Refs. 44, 56, 58, and 96	ρ	n	r	s	from Refs. 59 and 60
Methyl alcohol	1.38	9	0.995	0.05	1.38; 1.54; 1.55	1.42	16	0.969	0.18	—
Ethyl alcohol	1.67	13	0.984	0.09	1.65; 1.67	1.68	15	0.955	0.25	1.3
33.2% ethyl alcohol	—	13	—	—	1.28	—	—	—	—	—
52% ethyl alcohol	—	13	—	—	1.40	—	—	—	—	—
73.4% ethyl alcohol	—	13	—	—	1.52	—	—	—	—	—
85.4% ethyl alcohol	—	13	—	—	1.53	—	—	—	—	—
Isopropyl alcohol	—	—	—	—	—	2.01	15	0.988	0.15	—
Acetone	1.96	5	0.997	0.09	—	2.30	14	0.970	0.27	—
Ethyl methyl ketone	—	—	—	—	—	2.41	13	0.987	0.18	—
Acetonitrile	2.65	4	0.998	0.09	2.8	1.91	14	0.990	0.13	—
Dimethylformamide	2.65	3	0.991	0.35	—	2.42	14	0.986	0.19	—
Dimethylsulphoxide	3.13	11	0.982	0.27	2.6	—	6	—	—	2.5

In examining the data in Table 5, it is necessary to bear in mind that the values of ρ quoted were obtained on the basis of K_A data for *m*- and *p*-derivatives of benzoic acid and therefore they reflect the influence of the solvent on the inductive and resonance effects and the effect of polar conjugation of substituents with the reaction centre.

As in the calculation of α in Eqn. (2), the most reliable values of ρ refer to methyl and ethyl alcohol, water–ethyl alcohol mixtures, and dimethyl sulphoxide, since a large number of experimental points ($n = 9 - 13$) were employed in these calculations. For acetonitrile, ρ was obtained without taking into account *p*-hydroxybenzoic acid, since the latter shows a marked deviation from linearity, which is probably due to the change in the ρ constant of the OH group on passing from water to acetonitrile.

The lack of data or their inadequacy for solvents such as isopropyl alcohol, acetone, ethyl methyl ketone, dimethylformamide, and acetonitrile led to the necessity for the determination of the constant ρ also on the basis of the relative concentration dissociation constants of *m*- and *p*-derivatives of benzoic acids obtained from half-neutralisation potentials (see Section 3).

Table 5 shows that the values of ρ for methyl and ethyl alcohols obtained by the two methods agree well. The constants ρ for ketones, acetonitrile, and dimethylformamide obtained from the pK_{rel} data should of course be lower than the true values owing to the distortion of the potentiometric titration curves. The value of ρ for acetone obtained from pK_{rel} is higher than ρ calculated from pK_A. In all probability this suggests that the available literature values of pK_A of benzoic acid in acetone are not sufficiently valid characteristics of the differentiating effect of this solvent. The values of ρ for isopropyl alcohol, acetone, and ethyl methyl ketone indicate a higher differentiating effect of these solvents for benzoic acid compared with ethyl and methyl alcohols.

There is a limited amount of ρ data[23,24] for the dissociation of phenol derivatives in water–ethyl alcohol mixtures. The constant ρ has also been determined for 45 vol.% isopropyl alcohol in water ($\rho = 2.80$).[98]

It follows from the data in Table 1 that the experimental dissociation constants of phenol derivatives refer predominantly to nitro-derivatives containing *o*-substituents together with *m*- and *p*-substituents. Even in aqueous solutions *o*-substituents do not have invariant values of the σ constants[80]. Therefore there is all the more reason to expect a change in σ_{ortho} on passing from water to non-aqueous solvents. Consequently the data in Table 1 were not used to calculate the constants ρ for the dissociation of phenol derivatives in non-aqueous solvents.

Table 6. Reaction constants ρ in the Hammett equation for the dissociation of phenol derivatives in non-aqueous solutions calculated from half-neutralisation potentials (20° ± 2°).

Solvent	ρ	n	r	s
Propyl alcohol	2.25	6	0.997	0.08
Butyl alcohol	2.59	6	0.993	0.16
Isobutyl alcohol	2.67	6	0.986	0.24
Isopropyl alcohol	3.17	6	0.993	0.20
Acetonitrile	3.72	16	0.998	0.29
Acetone	4.11	16	0.999	0.22
Ethyl methyl ketone	4.48	16	0.999	0.21
Dimethylformamide	4.57	16	0.995	0.39

Mention should be made of an investigation[25] where the relative acidities of 4-substituted derivatives of 2,6-dichloro and 2,6-dimethylphenols in water, methyl and isopropyl alcohols, acetone, and water–dioxan mixtures were determined from measurements of half-neutralisation potentials. The differentiating effect of non-aqueous solvents increases with decrease in the polarity of the solvent. Thus ρ for 4-substituted 2,6-dichlorophenols is 2.55 in water, 2.99 in methyl alcohol, 4.13 in isopropyl alcohol, and 5.39 in acetone. On addition of water to dioxan there is a sharp decrease of ρ, which is 5.15 in 99.8% dioxan containing 0.2 vol.% of isopropyl alcohol, 4.00 in 98% dioxan, 3.66 in 95% dioxan, 3.43 in 91% dioxan, and 2.72 in 71% dioxan.

An attempt has been made to investigate the ρ constant for the dissociation of phenols in non-aqueous solutions by measuring the half-neutralisation potentials, from which the pK_{rel} for phenols in alcohols, acetone, ethyl methyl

ketone, dimethylformamide, and acetonitrile were calculated[81]; the constants ρ for these solvents are listed in Table 6. It is noteworthy that in alcohols the reaction series contains only *m*- and *p*-derivatives of phenol and in ketones, dimethylformamide, and acetonitrile also derivatives with *o*-substituents, since (as already mentioned in section 3) in these solvents there is a common relation between $E_{1/2}$ and the σ constants adopted for the substituents in aqueous solutions.

Table 6 shows that, on passing from solvent to solvent, the differentiating effect of solvents determined from measurements of the pK_{rel} values for phenols varies in the same sequence as in relation to *m*- and *p*-derivatives of benzoic acid. The values of ρ for isopropyl alcohol and acetone listed in Table 6 are lower than those obtained by Fischer et al.[25] (3.46 and 4.93 respectively), which can be accounted for by the effect of the titrant solvent employed in the determination of pK_{rel}; the data in Table 6 were obtained with about 1% methyl alcohol in the solvent and those of Fischer et al.[25] with about 0.2% of isopropyl alcohol.

The data on the differentiating effect of amphiprotic solvents obtained from the ρ constants in Hammett's equation and those found by comparing pK_A(ns) or $\Delta E_{1/2}$ with $pK_A(H_2O)$, quoted in Sections 2 and 3, agree well with one another if account is taken of the difference between the values of ρ in water for the corresponding reaction series. The change in the differentiating effect of solvents for a given reaction series may be expressed by the ratio ρ_{ns}/ρ_{H_2O}, the physical significance of which is equivalent to that of the quantity α in Eqn. (2).

5. THE AUTOPROTOLYSIS CONSTANT AS A CHARACTERISTIC OF THE DIFFERENTIATING EFFECT OF A SOLVENT

The autoprotolysis of a solvent is accompanied by the formation of lyonium and lyate ions which in a given solvent are the strongest acid and the strongest base respectively. Therefore the autoprotolysis constant of the solvent,

$$K_s = a_{SH_2^+} a_{S^-},$$

is a measure of its differentiating effect on the strengths of acids and bases. The negative exponent of the autoprotolysis constant defines the extent of the acidity scale of the solvent. The more pronounced are the acidic and basic properties of the solvent, the higher is the autoprotolysis constant, and the smaller the extent of its acidity scale. With decrease of the acidic and basic properties of the solvent, the extent of the acidity scale increases together with the differentiating effect of the solvent in relation to acids and bases.

If the acidic and basic properties of the solvent are less pronounced than those of water, its differentiating effect relative to water is greater for all classes of electrolytes. On the other hand, if the acidic or basic properties of the solvent exceed those of water, then in comparing their differentiating effects it is necessary to take into account also the relative positions of the acidity scales of the solvents in terms of a single acidity scale. The displacement of the acid limit of the acidity scale of the solvent relative to that of the water scale is unambiguously characterised by the transolvation energy of the proton on passing from an infinitely dilute aqueous solution to the given solvent[61]. With decrease in the acidity of the solvent, which leads to a displacement of the basic limit of its acidity scale towards lower proton activities, the differentiating effect of the solvent in relation to weak acids and strong bases increases; with decrease of the basicity of the solvent (shift of the acid limit of the scale towards higher proton activities), its differentiating effect in relation to weak bases and strong acids increases. Thus, the differentiating effect of the solvent is different for electrolytes of different strengths and is characterised by its autoprotolysis constant and the position of its acidity scale in terms of a single acidity scale. Moreover, according to Izmailov's theory of solvation[1], the differentiating effect of solvents is different for electrolytes belonging to different reaction series.

Table 7. Negative exponents of the autoprotolysis constants of certain solvents.

Solvent	pK_s		
	calc. from Eqn.(10)	measured values (25°)	obtained by methods of comparative calculations
Methyl alcohol	15.9	16.7[99–101]	16.3[115] 16.7[117]
Ethyl alcohol	—	16.8[102]; 17.9[100]; 18.9[103]; 19.1[99,104]; 19.5[105,106]	17.1[115] 18.8[117]
Propyl alcohol	—	19.4[103]	20.8[115] 19.4[117]
Isopropyl alcohol	22.0	20.8[100,103]	21.3[115]
Butyl alcohol	—	—	21.1[115] 19.6[116]; 21.6[117]
t-Butyl alcohol	26.8	22.2[100]	21.1[115]
Acetone	32.5	—	22.3[115] 22.8[118]
Ethyl methyl ketone	—	25.7[107]	21.5[115] 21.0[118]
Acetonitrile	33.2	19.5[108]; 26.5[109] 28.5[80]; 33.3[110]	25.5[117]
Dimethylformamide	29.4	18.0[111]	17.0[117]
Dimethylsulphoxide	31.8	17.3[112]; 33.3[51]	—

The autoprotolysis constants of by no means all amphiprotic solvents have now been measured and their reliability in many cases is not great, since the range of pH values which may be used in acid–base titration frequently correspond to a higher value of pK_S than indicated by the available literature data[82]. Table 7 lists the pK_S values for certain amphiprotic solvents measured by different methods[30,51,99–112]. The Table shows that the values quoted by various authors for a series of solvents differ appreciably among one another. Thus the discrepancy for ethyl alcohol is about 3 pH units, for acetonitrile 6.8 pH units, and for dimethyl sulphoxide up to 16 pH units. In the first place this discrepancy is evidence of the experimental difficulties in the determination of autoprotolysis constants, particularly for solvents with low values of K_S and is a consequence for the errors associated with the different methods for the determination of the dissociation constants of a base and its conjugate acid, the indeterminancy of the diffusion junction potential in cells with transport, incomplete dissociation of electrolytes, etc.[82,110] One of the most important causes of unduly high values of K_S is also the presence of water in solvents, the ionisation of which is responsible for protolysis in the given solvent[113].

The values of pK_S for solvents may be estimated by measuring the relative acidity scale values for solvents from the approximate equation [82]

$$pK_s = \frac{E_s}{59} + \lg c_{HClO_4} c_{R_4NOH}, \quad (10)$$

where E_S is the relative acidity scale value (mV) for the solvent, equal to the difference between the half-neutralisation potentials of $HClO_4$ and R_4NOH in the given solvent, and c_{HClO_4} and c_{R_4NOH} are the concentrations of the acid and base at the instant of half neutralisation.

The measurements of the E_S scale values for solvents are usually made under conditions where the solvent contains 1–1.5% of water and methanol; the E_S for pure solvents may be found by extrapolation using equations describing the variation of the limits of the scale with the composition of the mixed solvents [114]. It must be emphasised that the values of pK_S for solvents calculated in this way are low because the activities of H^+ and OH^- ions are not equal to the concentrations of $HClO_4$ and R_4NOH and in consequence of the use of a base not containing the lyate ions of the solvent, the inadequate sensitivity of the glass electrode in strongly acidic and strongly basic media, and other causes. However, the values of pK_S calculated from the E_S for pure acetonitrile and dimethyl sulphoxide are close to the latest literature data, which is evidence of the adequate reliability of the pK_S obtained from measurements of the relative acidity scale values. They may be regarded as the lower limits of the true values.

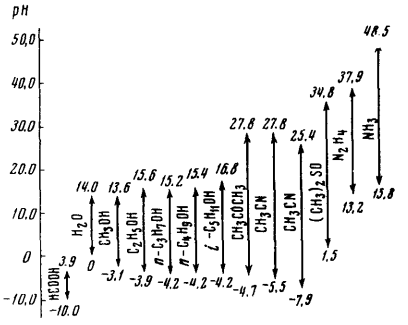


Figure 13. Izmailov's unique acidity scale for solvents.

Comparison of the pK_S calculated by Eqn. (10) for amphiprotic solvents with the literature data (Table 7) shows that the literature values of the pK_S for isopropyl and t-butyl alcohols, ethyl methyl ketone, and dimethylformamide are too low. It also follows from Table 7 that the methods of comparative calculation are suitable only for the estimation of the pK_S of lower alcohols [115,117,118]. Fig. 13 shows a single pA solvent acidity scale [1,61] obtained using the most reliable values of pK_S for amphiprotic solvents (printed bold in Table 7) as well as certain others on the basis of the primary effects of the medium ($\lg \gamma_{o_{H^+}}$) determined by Izmailov [61] and other workers [33]. It follows from Fig. 13 and Table 7 that amphiprotic solvents are characterised by a wide range of acidity scales.

On the basis of data for the relative basicities and acidities of solvents, one may assume the decrease of the K_S values for alcohols with increase of the size of the alkyl group and the degree of its branching is largely due to the decrease of the contributions to acidity which depend on the electron-donating properties of the alkyl group in the alcohol molecule. The low autoprotolysis constants of ketones, dimethylformamide, acetonitrile, and dimethyl sulphoxide are related to their extremely weak acid properties as C–H acids; ketones and acetonitrile are also extremely weak bases [119].

The differentiating effects of amphiprotic solvents can be arranged in the following sequence on the basis of the autoprotolysis constants:

$$(CH_3)_2SO,\ CH_3CN > CH_3COC_2H_5,\ CH_3COCH_3 > (CH_3)_2NCHO > > t\text{-}C_4H_9OH > iso\text{-}C_3H_7OH > n\text{-}C_4H_9OH,\ n\text{-}C_3H_7OH, n\text{-}C_2H_5OH > CH_3OH > H_2O,$$

which, within the limits of the reliability of the K_S values, is the same as the sequence of the differentiating capacities of the solvents established on the basis of the dissociation constants and the half-neutralisation potentials of the electrolytes.

It was of interest to follow the relation between the pK_S for amphiprotic solvents and α in Eqn. (2), since these are parameters characterising the differentiating effects of solvents. According to Eqn. (2), for a reaction series of n electrolytes arranged in order of increasing pK_A values, the difference between the pK_A values of two consecutive electrolytes is

$$\Delta pK_A^i(ns) = \alpha \Delta pK_A(H_2O), \text{where } i = 1, 2, 3, \ldots, n-1$$

and

$$\sum_{i=1}^{n-1} \Delta pK_A^i(ns) = \alpha \sum_{i=1}^{n-1} \Delta pK_A^i(H_2O). \quad (11)$$

The positions of the reaction series on the acidity scales of water and the non-aqueous solvent may be represented as follows:

$$pK_s(H_2O) = \sum_{i=1}^{n-1} \Delta pK_A^i(H_2O) + a + b \quad (12)$$

and

$$pK_s(ns) = \sum_{i=1}^{n-1} \Delta pK_A^i(ns) + c + d, \quad (13)$$

where a, b, c, and d are the sections of the acidity scales of the solvents in the acid and alkaline regions unoccupied by the given reaction series.

Eqn. (11) suggests that Eqn. (13) is a first-degree polynomial in α. Then it is possible to obtain from Eqns. (12) and (13) a relation between pK_S and α:

$$pK_s(ns) = \text{const}_1 \alpha + \text{const}_2, \quad (14)$$

where const_1 and const_2 are constants for each reaction series.

Tests of Eqn. (14) for phenol and benzoic acid derivatives showed that there is indeed a linear relation between the negative exponents of the autoprotolysis constants of amphiprotic solvents and the values of α in Eqn. (2) for the corresponding reaction series (Fig. 14). It follows from Fig. 14 that benzoic acid and phenol derivatives give rise to separate relations characterised by different slopes. It is also seen that, compared with water, the differentiating effect of amphiprotic solvents is greater with respect to benzoic acids. The ratio of the slopes of lines I and II is close to the ratio of the ρ_{H_2O} constants for the reaction series considered (about 2.5). This suggests that the effect of substituents on passing from solvent to solvent is constant and the effect of the solvent may be taken into

account by the change of the constant ρ. Since $\alpha = \rho_{ns}/\rho_{H_2O}$, there should be a linear relation between the pK_S and ρ for amphiprotic solvents. Fig. 14 shows the presence of such a linear relation for *m*- and *p*-derivatives of benzoic acid (line III). In plotting the relation between pK_S and ρ, use was made also of the values of ρ obtained from measurements of the half-neutralisation potentials.

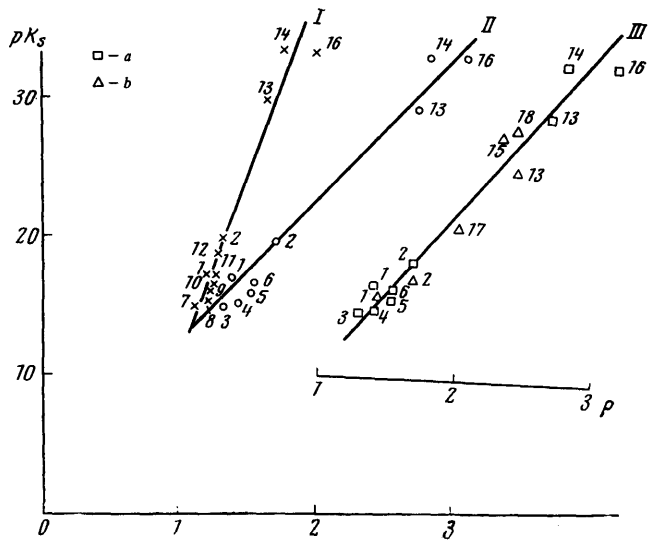


Figure 14. Correlation between the pK_S of solvents and the coefficients α in Eqn. (2) or the constants ρ in Hammett's equation: I) phenol derivatives; II) and III) benzoic acid derivatives [*a*) on the basis of pK_A; *b*) on the basis of $E_{1/2}$; the numbers of points *1* to *16* correspond to those in Table 3; *17*) isopropyl alcohol; *18*) ethyl methyl ketone].

Bearing in mind that at the instant of the measurement of $E_{1/2}$ for benzoic acids the solvents contained about 1–1.5% of water and methyl alcohol, the ρ values were compared with the pK_S of solvents containing the same amounts of water and methanol. These pK_S were calculated from Eqn. (10) on the basis of the values scale E_S measured under the same conditions as $E_{1/2}$.

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The above examination of the differentiating effects of amphiprotic solvents with respect to *m*- and *p*-benzoic acids and phenol derivatives on the basis of the pK_A and $E_{1/2}$ values for electrolytes and the ρ constants in the Hammett equation showed that the autoprotolysis constant of an amphiprotic solvent is a quantitative characteristic of its differentiating effect. The lower is the value of K_S, the greater the differentiating effect of the amphiprotic solvent.

According to Izmailov's solvation theory[1], the differentiating effects of solvents are related to changes in the ratio of the solvation energies of the anions and molecules of the acids, the transolvation of anions making the greatest contribution to this change. In hydroxylated solvents hydrogen bonds play a considerable role in the solvation of anions, which reduces the difference between the anion solvation energies on passing from one solvent to another. In aprotic dipolar solvents, incapable of forming hydrogen bonds with anions, the difference between the anion solvation energies are much greater. This is because electrostatic and dispersion interaction forces, which are related, on the one hand, to properties of the solvents such as their dielectric constant, dipole moment, and polarisability of their molecules and on the other hand to the charge, radius, and polarisability of the anions, play the greatest role in the solvation of anions. As a result of all these factors, in aprotic dipolar solvents, the solvation of ions and electrolyte molecules is largely determined by the specific characteristics of the electrolyte.

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