

Kinetics of the Reactions of Pyridine and Pyridine-*N*-oxide Carboxylic Acids and Substituted Benzoic Acids with Diazodiphenylmethane in Various Alcohols

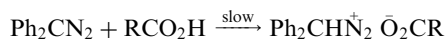
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Solvent effects on the reactivity of pyridine and pyridine-*N*-oxide carboxylic acids and *p*-substituted benzoic acids in their reaction with diazodiphenylmethane (DDM) in alcohols have been investigated and the rate constants interpreted by Hammett parameters using multiple regression analysis; the influence of solvents on the reactivity of these acids with DDM has not been reported previously.

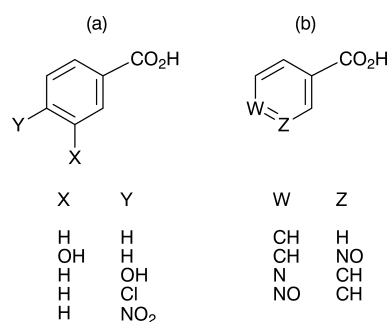
The rate constants obtained in the present work, together with literature values, are given in Table 1. Those values were used to study the influence of solvent properties on the rates of reaction with DDM and also on Hammett σ and ρ constants.

The mechanism of the reaction of carboxylic acids (Scheme 1) with DDM has been thoroughly studied and well documented,^{1,6,13,14} and it was established that it involves the rate determining proton transfer from the acid to the DDM molecule, forming a diphenylmethanediazonium carboxylate ion pair.^{6,7,10}



Since the mechanism of the reaction involves the formation of an ion-pair intermediate, one may expect the rate to increase with the polarity of the solvent.¹⁵ This proved to be true in the present investigation; furthermore, the good intercorrelation of $\log k$ values for the investigated acids with literature $\log k$ values for benzoic acids in the solvents used, proves that the same solvent properties which act on the reaction of benzoic acid also influence the reactivity of substituted benzoic and pyridine carboxylic acids.

It has been suggested¹¹ that solvent effects influencing the reactivity of carboxylic acids with DDM are best interpreted in terms of the Kirkwood function $f(\epsilon)$, Taft polar substituent constants σ^* and number of γ -hydrogens in the alcohol $n_{\gamma\text{H}}$, which together give a quantitative measure of the facilitating of the separation of opposite charges in the transition states, solvating ability and possibility of hydrogen bond formation. Therefore we applied multiple linear regression for the correlation of \log rate constants deter-



Scheme 1 Carboxylic acids used in the reactivity determinations: (a) Substituted benzoic acids, (b) pyridine and pyridine-*N*-oxide carboxylic acids

mined in the present work together with the literature values for *m*-substituted benzoic acid with $f(\epsilon)$, σ^* and $n_{\gamma\text{H}}$ in twelve alcoholic solvents.

On the basis of the obtained data it could be said that the influence of relative permittivity is more characteristic for the substituents in the *para* position than on the substituent in the *meta*-position, and it is particularly important for electron donating substituents, especially for the OH group, and less for electron withdrawing.

However the most important solvent property influencing the rate of reaction appears to be the polarity of the alcohol alkyl group expressed as Taft's polar constant σ^* . Good partial correlations ($r = 0.933$ and $s = 0.101$) of the rate data were obtained with σ^* , while the separate correlations with $f(\epsilon)$ and $n_{\gamma\text{H}}$ were poor. Similar observations were also reported in the literature.^{9,32}

Table 1 Rate constants ($\text{dm}^3 \text{mol}^{-1} \text{min}^{-1}$) for the reaction of pyridine, pyridine-*N*-oxide carboxylic acids and substituted benzoic acids with DDM at 30 °C in various alcoholic solvents

Solvent	H	3-Cl	3-CH ₃	3-NO ₂	3-N	3-NO	4-N	4-NO	3-OH	4-OH	4-NO	4-Cl
Methanol	2.46 ^a	5.41 ^a	2.25 ^a	10.70 ^a	10.69	34.29	20.18	24.15	2.12	1.29	10.1	4.05
Ethanol	0.99 ^a	2.42 ^a	0.83 ^a	4.46 ^a	5.4 ^b	19.10 ^b	11.9 ^b	12.9 ^b	0.799 ^c	0.533	5.04 ^d	1.8 ^a
Propan-1-ol	1.07 ^a	2.56 ^a	1.00 ^a	5.70 ^a	6.15	25.53	7.46	12.38	0.82	0.522	5.06	1.74
Butan-1-ol	0.99 ^a	2.24	0.91	4.25	4.77	18.98	6.40	10.74	0.722	0.410	4.55	1.43
Propan-2-ol	0.69 ^a	1.72 ^a	0.63 ^a	4.15 ^a	4.40	18.42	6.37	9.38	0.62	0.377	4.15	1.36
Butan-2-ol	0.67 ^a	1.69 ^c	0.61 ^c	4.04 ^c	3.45	15.38	5.72	6.76	0.498 ^c	0.272	3.94	1.28
Cyclopentanol	0.74 ^e	1.82 ^c	0.67 ^c	4.39 ^c	3.67	12.56	5.82	8.03	0.56 ^c	0.333	4.71	1.45
2-Methylbutan-2-ol	0.14 ^a	0.47 ^a	0.13 ^a	1.58 ^a	1.26	6.20	1.91	2.93	0.111 ^c	0.048	1.50	0.32
Pentan-1-ol	0.86 ^f	1.95 ^c	0.76 ^c	4.54 ^c	3.72	14.50	7.32	10.67	0.687 ^d	0.327	4.42	1.35
2-Methylpropan-1-ol	1.67 ^a	3.72 ^a	1.57 ^a	8.18 ^a	6.97	25.51	12.07	21.04	1.31 ^d	0.695	7.43	2.35
2-Methylpropan-2-ol	0.26 ^a	0.77 ^a	0.24 ^a	2.27 ^a	1.67	7.65	2.97	4.39	0.194	0.096	2.12	0.48
Benzyl alcohol	9.15 ^e	17.0 ^a	8.6	24.88	26.53	62.48	42.94	54.94	8.1	4.37	25.95	11.83

^aRef. 6. ^bRef. 31. ^cRef. 13. ^dRef. 20. ^eRef. 19. ^fRef. 9.

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It should be pointed out that the effect of polarity of the alcohol alkyl group is almost equal for *meta*- and *para*-substituted acids, the corresponding differences ($\Delta\sigma^*$) being smaller than the differences in relative permittivities [$\Delta f(\epsilon)$]. The term $n_{\gamma\text{H}}$, usually needed to account for enhanced rate due to branching at the β -carbon, appeared to be insignificant in this work.

Variation of substituent σ constants with solvent

Information on the solvent dependence of Hammett σ values for substituted acids in the Scheme were also obtained in the present work. For this purpose, literature values for ρ and $\log k_0$ ^{6,19} together with the two determined here, were used for the calculation of new σ_m and σ_p constants. There is a substantial variation of certain values, which is understandable, considering that the energy of the transition state could theoretically be influenced both by the solvent modified electronic effects of the substituent and by the stabilization of the initial *vs.* transition states. However the average values are near enough to the literature values, indicating that there is a definite proportionality of the solvent effects in the investigated series of alcohols, expressed as variations of the σ constants.

The negative values for both σ_m and σ_p substituent constants for the OH group in all investigated alcohols and fairly large variations for both series (largest $\Delta\sigma_m=0.117$, $\Delta\sigma_p=0.180$), point out to the interaction of substituent with solvent, probably through hydrogen bond formation. Negative σ_p , whatever the interaction with the solvent, is easier to comprehend, owing to a direct conjugative donating effect. However, the negative and variable σ_m , in contrast to that in water, could only be explained as suggested by Aslam *et al.*¹⁹ by hydrogen bonding occurring between the oxygen of the alcohol molecule and the hydrogen of the phenolic group, increasing the electron density on the phenolic oxygen and causing *m*-OH to be electron donating in alcoholic solvents.

As far as the pyridine aza groups are concerned, the variations in σ_m for 3-N and σ_p for 4-N are not very large, being practically constant for the investigated solvents and in fairly good agreement with literature data for alkaline ester hydrolysis.²³

The obtained σ_p values for substituents calculated from ρ and $\log k_0$ for *m*-substituted benzoic acids in twelve alcohols show certain differences from those previously reported.¹⁸ However the average values for σ_p constant are in good agreement with those reported in the literature and could be satisfactorily used for reaction in alcohol solvents.

Solvent effects on reaction constant ρ

Values of ρ for the reaction of investigated pyridine and substituted benzoic acids in a range of solvents, using the determined average values for σ_m and σ_p , were calculated separately for *meta*- and *para*-substituted acids in twelve investigated alcohols from the simple regression of $\log k$ on σ values. These values are presented as ρ_m and ρ_p in Table 5 (full text).

The correlations with solvent parameters were also applied to the reaction constants ρ as was done before,^{8,19} but separately for the two series, *m*- and *p*-substituted acids.

Reaction constants for seven *meta*- and six *para*-substituted acids were correlated with solvent parameters for twelve alcohols.

For 3-N and 3-NO pyridine carboxylic acids and five *m*-substituted benzoic acids:

$$\rho_m = (1.308 \pm 0.306) - (0.960 \pm 0.661)f(\epsilon) - (1.050 \pm 0.120)\sigma^* - (0.007 \pm 0.008)n_{\gamma\text{H}} \quad (r = 0.9658; s = 0.048, n = 12)$$

For 4-N and 4-NO pyridine carboxylic acids and four *p*-substituted benzoic acids:

$$\rho_p = (1.665 \pm 0.281) - (1.670 \pm 0.608)f(\epsilon) - (0.698 \pm 0.110)\sigma^* - (0.002 \pm 0.007)n_{\gamma\text{H}} \quad (r = 0.9531; s = 0.044, n = 12)$$

From the above relationships it can be seen that the coefficients associated with σ^* are significant in both reaction series. This is in agreement with what has been reported before^{19,32} and also proved by individual correlation with parameters $f(\epsilon)$ and σ^* , where the latter showed a much better correlation coefficient ($r = 0.9542$, $s = 0.050$ for *m*-substituted acids; $r = 0.9070$, $s = 0.055$ for *p*-substituted acids). However the value associated with the $f(\epsilon)$ term is more pronounced in the *p*-series which shows that the solvents with high relative permittivities facilitate the separation of opposite charges in the transition state relative to the initial state, which is more feasible in the *p*-substituted acids because of the possibility of direct conjugation.

Techniques used: UV, GLC

Tables: 5 (Rate constants, solvent parameters, ρ constants and $\log k_0$ values, σ constants, and ρ_m , ρ_p constants)

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