A REDETERMINATION OF THE SIGMA CONSTANT FOR THE PYRIDINE AZA GROUP

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A number of determinations of Hammett σ values[1] for the ring nitrogen in 2-, 3-, and 4-substituted pyridines have been reported.[2] For this purpose the nitrogen is treated as a ring substituent in a benzene system. The σ values, especially those for the 2-position (susceptible to influences such as intramolecular hydrogen bonding with an adjacent carboxyl probe), have been found to vary widely with the type of reaction.

One of the common methods for evaluating σ values is from the alkaline hydrolysis of substituted alkyl benzoates. Three reports[3–5] of the alkaline hydrolysis of the ethyl pyridinecarboxylates exist. Kindler[3] reported a series of results on the alkaline hydrolysis of ethyl pyridinecarboxylates and ethyl benzoates in 87·83% (w/w) $EtOH/H_2O$ at 30°. From these, Jaffe[6] calculated ($\rho = 2{\cdot}43$, $-\log k_0 = 3{\cdot}05$) σ values for the nitrogen as $2_N = 0{\cdot}81$, $3_N = 0{\cdot}62$, and $4_N = 0{\cdot}93$. Two papers by Imoto and co-workers[4] include the alkaline hydrolysis of ethyl picolinate and ethyl nicotinate in 85 % (w/w) $EtOH/H_2O$ at 25°. By using Jaffe's figures for these conditions ($\rho = 2{\cdot}54$, $-\log k_0 = 3{\cdot}22$), these rates give σ values of $2_N = 0{\cdot}77$ and $3_N = 0{\cdot}64$. The third study[5] was made in 70% (w/w) $EtOH/H_2O$ but, because of lack of information on the hydrolysis of ethyl benzoates under these conditions, no σ determination was made.

During an investigation of substituent effects in the pyridine system, we have measured (Table 1) the alkaline hydrolysis of a series of substituted methyl benzoates and the methyl pyridinecarboxylates in 85% (weight) $MeOH/H_2O$ at 25° to establish the substituent constants required for the rate correlation under these previously unreported conditions. Analysis of $-\log k_2$ against σ[7] for the methyl benzoates indicated in the table ($r = 0{\cdot}999$) gave $\rho = 2{\cdot}26$ (cf. $2{\cdot}54$ for ethyl benzoates), $-\log k_0 = 3{\cdot}71$, and σ values for the aza group of $2_N = 0{\cdot}75$, $3_N = 0{\cdot}65$, and

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$4_N = 0{\cdot}96$. These are in fair to excellent agreement with the values above and this type of reaction of pyridyl compounds should therefore be correlated with results for benzene derivatives by use of these σ values for the ring nitrogen.

TABLE 1

RATE CONSTANTS k_2 (l. mole^{-1} sec^{-1}) FOR ALKALINE HYDROLYSES IN 85% MeOH/H_2O AT 25°

Methyl Benzoates

Subst.	p-NO_2	m-NO_2	m-Br	p-Br	m-MeO[a]	H	m-Me	m-NMe_2[a]	p-Me	p-MeO
$-\log k_2$	1·94	2·11	2·86	3·16	3·63	3·72	3·89	4·01	4·03	4·35

Methyl Pyridinecarboxylates

Position	2-CO_2Me[a]	3-CO_2Me[a]	4-CO_2Me[a]
$-\log k_2$	2·02	2·25	1·53

[a] Not used in the calculation of ρ and $\log k_0$.

In addition, it was found that σ values of $+0{\cdot}04$ and $-0{\cdot}15$ gave good correlation of the $-\log k_2$ values from methyl m-methoxybenzoate and methyl m-dimethylaminobenzoate respectively. The methoxy value is that found by Taft[8] from the methanolysis of substituted l-menthyl benzoates. It seems that this value rather than $0{\cdot}115$[7] is applicable to reactions in aqueous alcohols and is close to the σ_m^0 value of $0{\cdot}06$ derived by Taft[9] for such reactions. The value of $-0{\cdot}15$ for the m-dimethylamino substituent is that recently re-evaluated[10] for this group.

Experimental

Esters

Methyl m-dimethylaminobenzoate was prepared by reductive methylation of methyl m-nitrobenzoate.[11] The other esters were obtained commercially or made from the acids. All esters were checked for purity by g.l.c. before use.

Kinetics

The method of Elderfield and Siegel[12] was followed and the concentrations used were *c.* 1×10^{-2}M (ester) and $1{\cdot}5 \times 10^{-2}$M (alkali, from sodium hydroxide). The second-order rate constants quoted were obtained graphically and reproducibility was within 2%. Each rate constant is the average of at least two runs.

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