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BASE CATALYSIS IN AROMATIC IODINATION. KINETICS AND MECHANISM OF THE IODINATION OF *p*-CRESOL, 2,6-DIMETHYLPHENOL, IMIDAZOLE AND DIMETHYLAMINOBENZENESULFONIC ACID

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Abstract—Kinetics of the iodination of *p*-cresol, 2,6-dimethylphenol, imidazole and dimethylaminobenzenesulfonic acid in aqueous solutions was studied using various bases as a catalyst. For the reactions showing an isotope effect (i.e. with the phenols and imidazole), the acceleration seems to follow the "nucleophilicities" somewhat better than the basicities of the bases applied. However, in the iodination of dimethylaminobenzenesulfonic acid, a reaction in which no isotope effect is observed, the catalytic action appears to be proportional to the basicities. This may be caused by the occurrence of an iodinating agent BI_2.

INTRODUCTION

ELECTROPHILIC aromatic iodinations are subject to general base catalysis not only in those cases where a deuterium isotope effect is exhibited,[1–4] but also in the absence of such an effect.[5] If the same mechanism operates in both cases—in the first case the proton abstraction step being rate determining and in the second case the introduction of an iodine atom into the aromatic nucleus—a molecule of the base should be active in both steps. For the action of the base in the first reaction step the formation of an alternative iodinating agent has been proposed.[4, 5]

In order to obtain a better understanding of the base's function in both the first and the second reaction step, the catalytic effect of various bases was studied in the iodination of *p*-cresol (PC), 2,6-dimethylphenol (DMP)—i.e. iodination on the *ortho* and *para* position of phenols respectively—imidazole (Im) and dimethylaminobenzenesulfonic acid (DMABS). Only in the iodination of DMABS is no isotope effect observed,[5] suggesting that in this case the introduction of iodine in the aromatic nucleus is the rate determining step.

RESULTS AND DISCUSSION

The logarithms of the specific rateconstants k_2 for the base catalysed iodination of PC, DMP, Im and DMABS found in the present study are summarized in Table 1. For comparison the dissociation constants pK_a and the "nucleophilicities" log (k_n/q) of the bases are included in Table 1. The "nucleophilicities" are derived arbitrarily from the rateconstants k_n for the base catalysed solvolysis of *p*-nitrophenylacetate.[6, 9]

In Figs 1 to 4 log (k_2/q) is plotted against the corrected pK values of the bases according to the Brønsted relation.[8] In Figs 5 to 8 log (k_2/q) is plotted against the

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TABLE 1. VARIOUS BASES WITH THEIR DISSOCIATION CONSTANTS,[6] THEIR "NUCLEOPHILICITIES" AND THEIR SPECIFIC RATE CONSTANTS FOR THE BASE CATALYSED IODINATIONS OF PC, DMP, IM AND DMABS

Base	$pK + \log \frac{p}{q}$[b]	$\log \frac{k_n}{q}$[a]	PC $\log \frac{k_2}{q}$	DMP $\log \frac{k_2}{q}$	Im $\log \frac{k_2}{q}$	DMABS $\log \frac{k_2}{q}$
CO_3^{--}	9·79	−0·46	−6·29	−4·93	−6·68	2·38
NH_3	9·15	1·20	−5·48	−4·69	−7·50	
γcoll	7·43	(−2·1)[c]	−7·40	−6·09	−8·38	0·73
HPO_4^{--}	6·52	−2·60	−7·72	−6·72	−8·00	0·90
γpic	6·05	−0·32[c]	−6·69	−5·60	−7·50	0·60
Pyr	5·25	−1·00	−6·67	−6·25	−7·72	0·37
Ac^-	4·14	−3·59	−7·87	−7·78	−8·66	−0·26
H_2O	−1·48	−6·22	−10·21	−9·79	−11·17	−2·87

[a] k_n are the rate constants for the solvolysis of *p*-nitrophenylacetate by various bases reported by Jencks and Carriuolo.[7]

[b] *p* and *q* are factors for statistical correction.[8]

[c] The value for γ-coll is estimated from our experiments. For γ-pic the value reported by Bender and Turnquest[9] was used.

"nucleophilicities" log (k_n/q) for the various bases.[7] In Fig. 9 the iodide dependence of the iodination of DMABS is evaluated. This is $[I^-]^{-1}$ both for the "uncatalysed" reaction and for the reaction catalysed by acetate ions. For the reaction catalysed by pyridine this dependence seems to be $[I^-]^{-0·7}$.

From Figs 1 to 3 it appears that the electrically neutral "nitrogen" bases have a greater catalytic effect than the negatively charged "oxygen" bases on the basis of their p*K* values. However, if log (k_2/q) is plotted against the "nucleophilicities" a more satisfactory linearity is obtained (Figs 5 to 7). This may be due to the fact that in these reactions the rate determining step consists of the nucleophilic attack of the base on the H-atom being abstracted from the sigmacomplex. As the sigmacomplex is neutral in the case of PC, DMP and Im, the diminished reactivity of charged bases may be

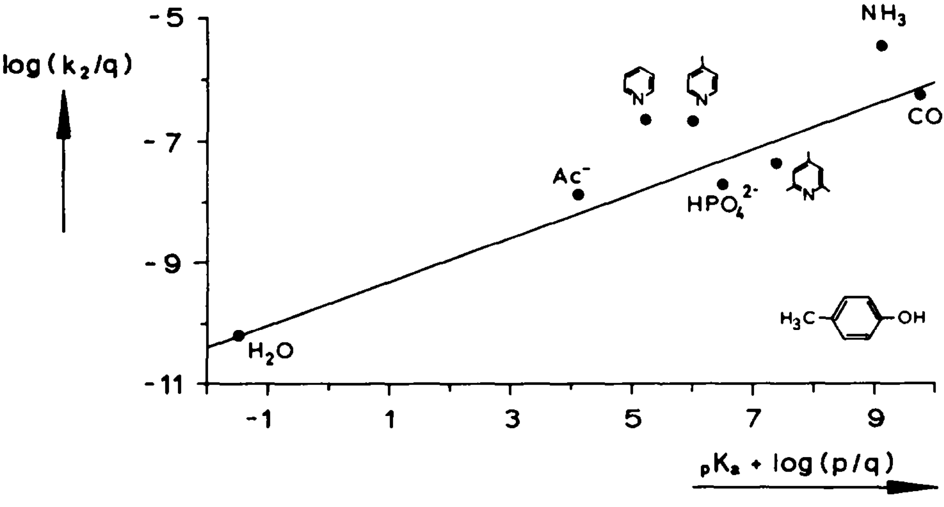

FIG. 1 The iodination of PC. Brønsted plot.

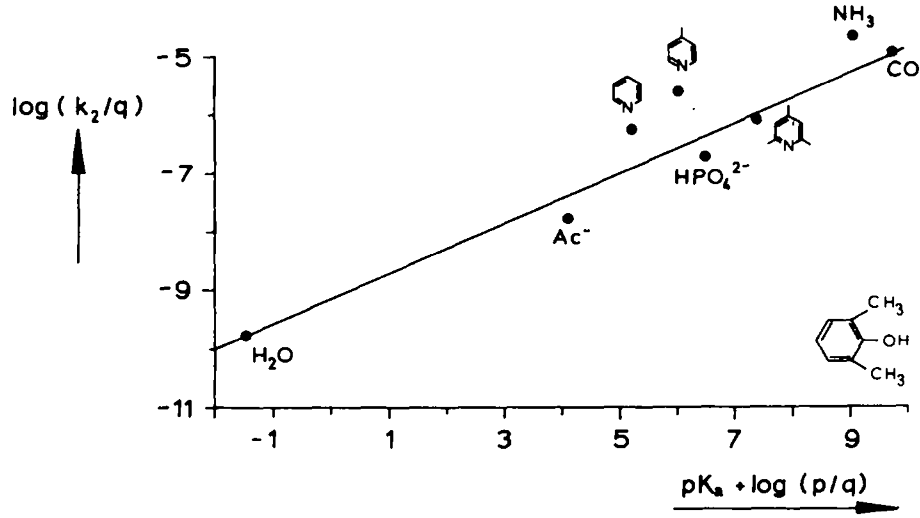

FIG. 2. The iodination of DMP. Brønsted plot.

caused by the better solvation of the small base ion compared with the larger transition state complex, where the charge is distributed over a more extensive system.

The rather good description furnished by the "nucleophilicities" derived from solvolysis rate constants for base catalysis in aromatic iodination, suggests a possible similarity in the mechanism of the two processes.

Only imidazole is an exception: no autocatalysis interfered in the iodination at Im in spite of the large value of log (k_n/q)—about 1·5—computed from the data of Jencks and Carriuolo.[7] This high value is likely to arise from a rather specific action of imidazole on ester hydrolysis.

In the iodination of DMABS, where the introduction of an I-atom in the aromatic nucleus is rate determining, base catalysis is presumed to be caused by a pre-equilibrium

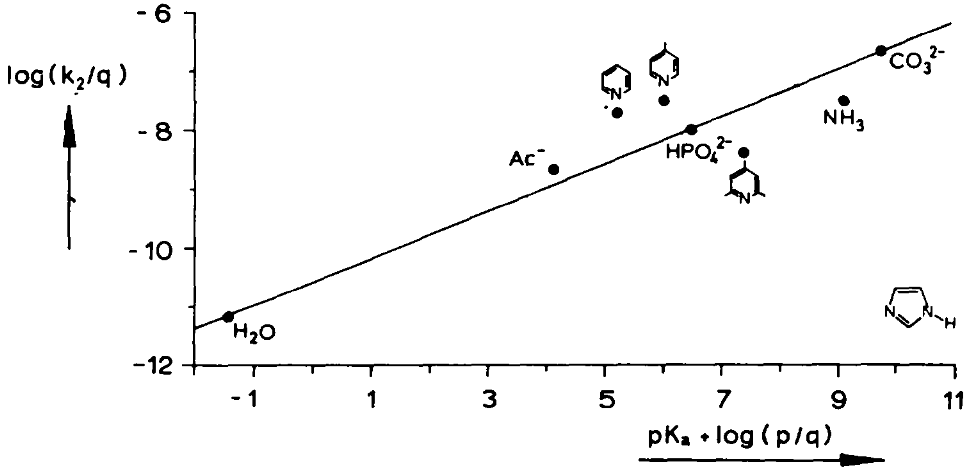

FIG. 3 The iodination of Im. Brønsted plot.

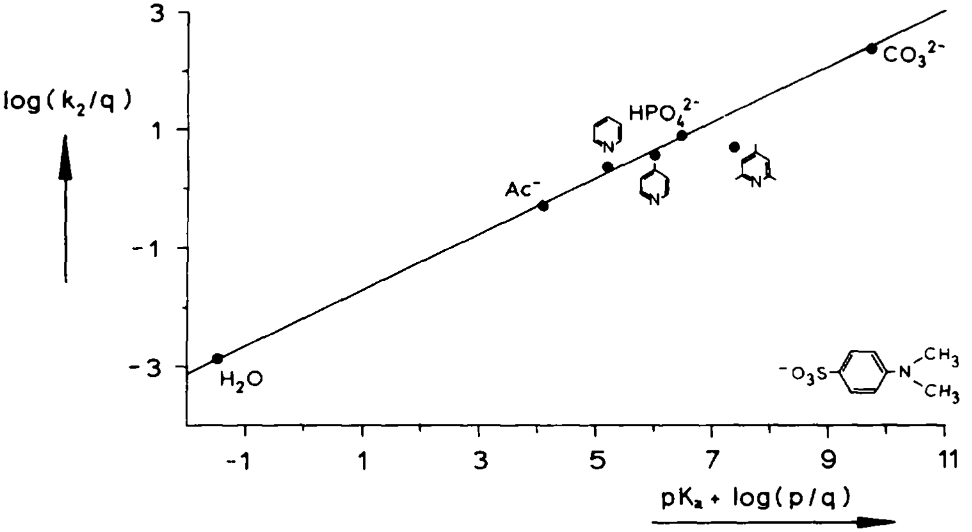

FIG. 4 The iodination of DMABS. Brønsted plot.

between the base with iodine and an alternative iodinating agent.[5] In this case the closer correlation of the rate constants with the dissociation constants of the bases is to be expected. Indeed Fig. 4 is more adequate than Fig. 8. As the rate of iodination is proportional to $[I^-]^{-1}$, rather than to $[I^-]^{-2}$ (Fig. 9), the iodinating agent is likely to be BI_2. This is supported by the fact that H_2O falls on the same slope of Fig. 4. Thus, in the "uncatalysed" reaction H_2OI_2 would be the iodinating agent rather than I_2.[1]

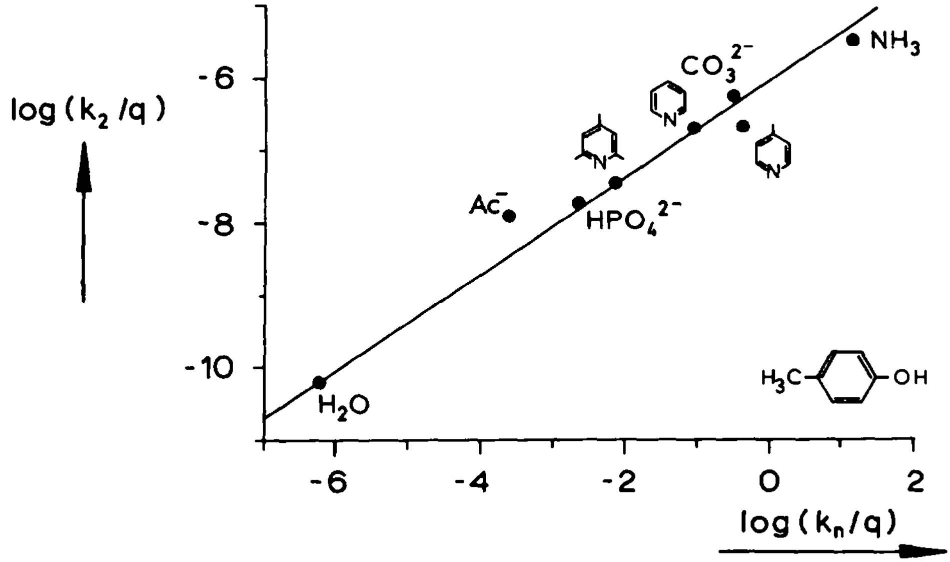

FIG. 5 The iodination of PC. Rate dependence on "nucleophilicities".

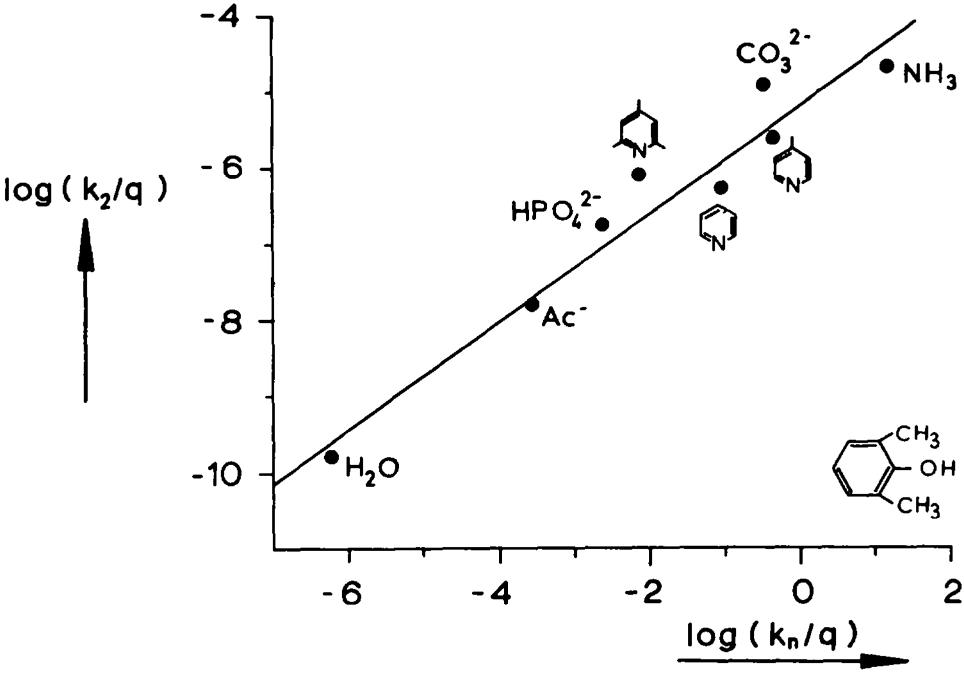

FIG. 6 The iodination of DMP. Rate dependence on "nucleophilicities".

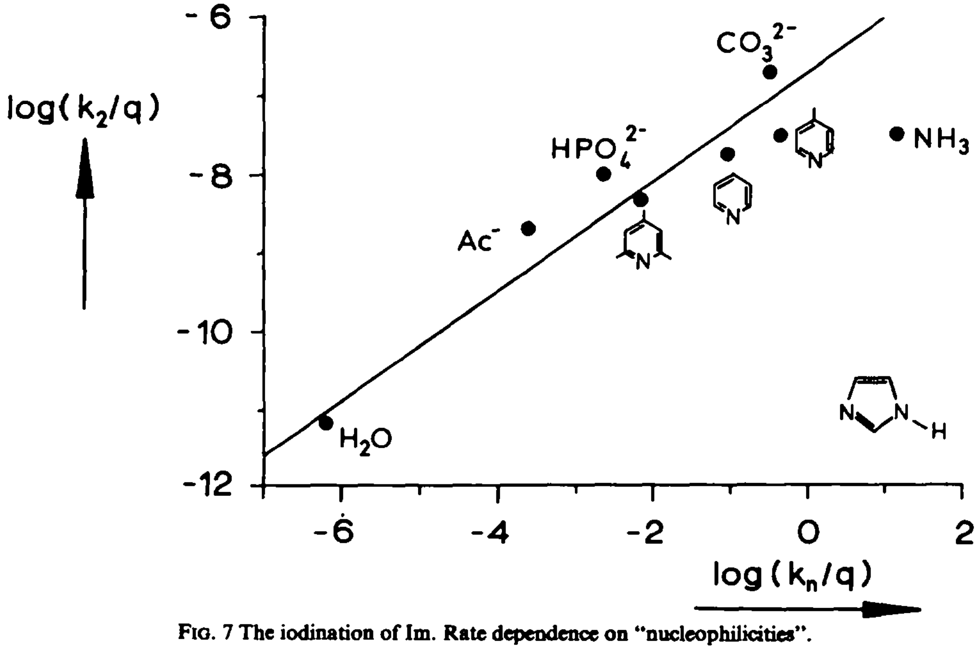

FIG. 7 The iodination of Im. Rate dependence on "nucleophilicities".

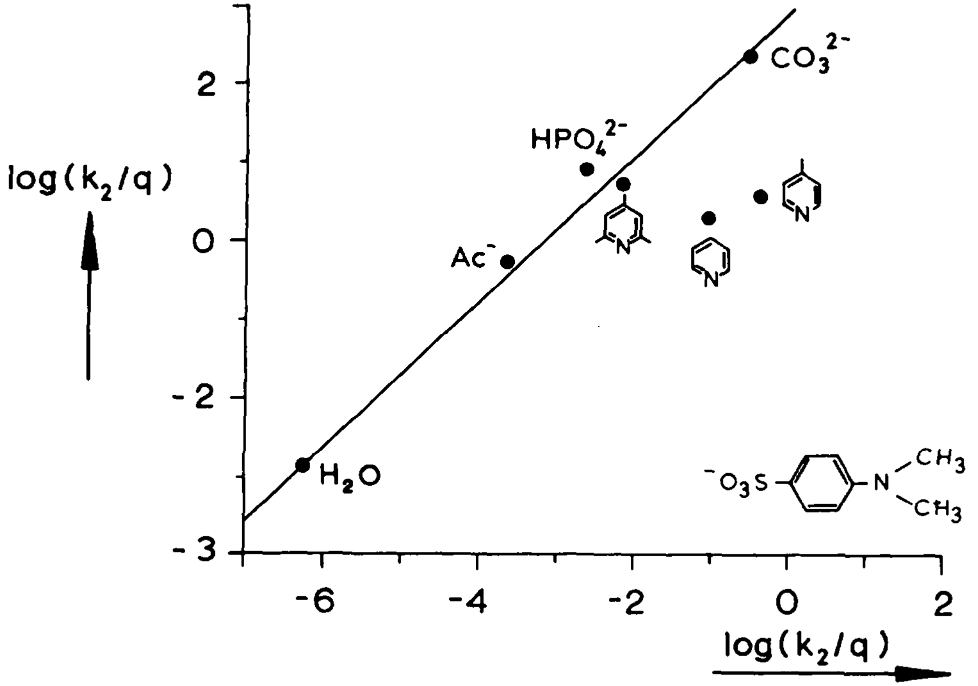

FIG. 8 The iodination of DMABS. Rate dependence on "nucleophilicities".

The following mechanism is in agreement with the experimental data:

$$I_3^- \rightleftarrows I_2 + I^- \qquad (K_a)$$

$$I_2 + B \rightleftarrows I_2B \qquad (K_b)$$

$$I_2B + ArH \underset{k_{-c}}{\overset{k_c}{\rightleftarrows}} (Ar^H_I)^+ + I^- + B$$

$$(Ar^H_I)^+ + B \xrightarrow{k_d} ArI + HB^+$$

$$-\frac{d[I_3^-]}{dt} = k_d K_a K_b \frac{k_c}{k_{-c}} \frac{[ArH][I_3^-][B]}{[I^-]^2 + (k_d/k_{-c})[I^-]}$$

For PC, DMP, Im: $k_{-c} \gg k_d$; for DMABS: $k_{-c} \ll k_d$.

The catalytic effect of NH_3 on the iodination of Im is considerably lower than expected. This is consistent with the results of the iodination of pyrazole catalysed by HPO_4^{2-} and NH_3.[10, 11]

In all cases the catalytic effect of γ-collidine is low with regard to its pK value. This may be attributed to the steric effect of the neighbouring Me groups.[12] In the value log (k_n/q) for the "nucleophilicity" this effect is included.

It is somewhat surprising that bases show an accelerating effect on iodination. It might have been expected that the introduction of a more negative charge in the iodinating agent would deactivate it. Possibly, the polarizing ability of the complex

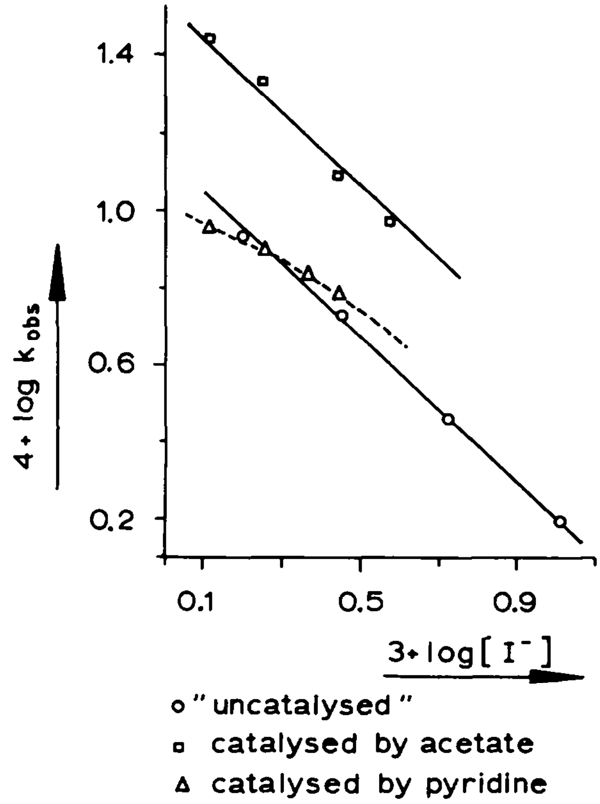

FIG. 9 The iodide dependence of the iodination of DMABS. (pH = 7·6–8·0, [DMABS.] = $5 \cdot 10^{-3}$ mol/l).

iodinating reagent, formed by iodine and base, contributes to this effect deserves closer study. Further detailed studies seem necessary to a more precise and quantitative description.

EXPERIMENTAL

The kinetics were studied spectrophotometrically as described.[3] The iodine concentration was kept constant (0·200 M for PC and DMP, 0·025 M for Im and 0·0028 M for DMABS). The ionic strength was 0·5, the temp 25° and the solns were buffered in borate, which itself does not noticeably[3] catalyse the iodination.

Im (Fluka), KH_2PO_4 (BDH), KI, borax, boric acid, sodium acetate, $NaHCO_3$, NH_4Cl and Na_2HPO_4 (all ex Merck) were used without further purification. DMP and PC were distilled under diminished press. Pyridine and γ-picoline were distilled from Zn. DMABS was prepared by sulfonation of dimethylaniline at 200°. Since the acid is very hygroscopic, the barium salt was used.

The pseudo first order constant k_{obs} is made up from two parts:

$$k_{obs} = k_1 [S] + k_2 [S] [B],$$

where S represents the aromatic species being iodinated. As for PC, DMP and Im these species are anionic,[1–4] k_{obs} depends inversely on $[H^+]$. Between pH7 and pH8 the rate of iodination of DMABS was found to be independent of $[H^+]$.

For each combination of aromatic species and base, k_{obs} was determined at four different base concentrations.

In each case $k_{obs}/[S]$ was plotted against [B]. The slope of the plot equals k_2; the intercept is equal to k_1 from which k_2 for water could be calculated. Standard deviation of k_2 was always less than 8%. Values of k_2 thus obtained were used to derive log (k_2/q) (see Table 1).

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