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THE RELATIVE REACTIVITY OF FLUORO- AND CHLORO-2,4-DINITROBENZENES IN THEIR REACTIONS WITH AMINES

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Although the leaving group ability of fluoride relative to other halide ions in nucleophilic activated aromatic substitution reactions has received considerable attention (1), there is still much controversy about the factors governing it.

In the course of a kinetic investigation of the reactions of activated aryl halides with amines in non-polar aprotic solvents, a preliminary account of which has already been given (2), data have been collected which appear to be relevant to the above mentioned problem. These concern the reactions of fluoro-2,4-dinitrobenzene (FDNB) or chloro-2,4-dinitrobenzene (CDNB) with piperidine, 2-methylpiperidine and cis-2,6-dimethylpiperidine respectively in benzene at 25°.

In Table I are listed the data for the reactions of the last two amines: those for piperidine have already been reported (2).

Examination of the results for the reactions of FDNB (Table Ia, Ib) shows that the second-order rate coefficients increase with increasing amine concentration. The rate data can be very satisfactorily expressed by equation [1]

$$\text{Rate}/[\text{Ar-F}][\underline{\text{sec}}\text{-amine}] = k_u + k_c[\underline{\text{sec}}\text{-amine}] \qquad [1]$$

TABLE I

Reaction Rates of 2-Methylpiperidine and cis-2,6-Dimethylpiperidine with Fluoro-2,4-dinitrobenzene (FDNB) or Chloro-2,4-dinitrobenzene (CDNB) in Benzene at 25°.

(a) FDNB[i], 2-methylpiperidine								
10^2 x [amine] M	0.209	0.406	0.674	1.30	1.90	3.95	7.77	15.0
10^3 x $\frac{\text{Rate}}{[\text{Ar-X}]\,[\text{amine}]}$ mole^{-1} l.sec.$^{-1}$	2.66	2.83	2.76	3.36	3.85	5.52	9.14	15.4
(b) FDNB[i], cis-2,6-dimethylpiperidine								
10 x [amine] M	1.96	4.50	6.45	10.2				
10^4 x $\frac{\text{Rate}}{[\text{Ar-X}]\,[\text{amine}]}$ mole^{-1} l. sec.$^{-1}$	1.56	2.51	3.15	4.82				
(c) CDNB[i], 2-methylpiperidine								
10 x [amine] M	1.12	2.01	3.16					
10^4 x $\frac{\text{Rate}}{[\text{Ar-X}]\,[\text{amine}]}$ mole^{-1} l. sec.$^{-1}$	0.643	0.623	0.672	(Av. 0.646)				
(d) CDNB[i], cis-2,6-dimethylpiperidine								
10^2 x [amine] M	6.28	44.4	102					
10^4 x $\frac{\text{Rate}}{[\text{Ar-X}]\,[\text{amine}]}$ mole^{-1} l. sec.$^{-1}$	0.111	0.110	0.111	(Av. 0.110)				

[i] The initial concentration of FDNB and CDNB ranged from 0.21 x 10^{-4} to 0.37 x 10^{-4} M. The reaction order with respect to halogeno nitro-benzenes is unity — at least within this very limited range of concentrations.

The values of k_u are collected in Table II.

Table II

Kinetic Constants for the Reaction of FDNB or CDNB with some Piperidines in Benzene at 25°.

Amine	$k_u \times 10^3$ mole^{-1} l. sec.$^{-1}$
Piperidine	597
2-Methylpiperidine	2.28
cis-2,6-Dimethylpiperidine	0.0730

These results can be compared with those obtained for the corresponding reactions of CDNB (Table Ic, Id). Here the second-order rate coefficients remain nicely constant up to a 2-methylpiperidine concentration twofold higher than that obtained with FDNB and up to a cis-2,6-dimethylpiperidine concentration about equal to that obtained with FDNB.

In the fluoride reaction, the presence of a tertiary amine such as triethylamine or pyridine in substantial amount (up to 0.1 M) has no effect on the rate in the whole range of 2-methylpiperidine concentration used (0.002 to 0.15 M), whereas in the presence of methanol (0.1 M) the second-order rate coefficient varies only very slightly with 2-methylpiperidine concentration. The pertinent data are not reported here as they are wholly similar to those already communicated for the piperidine reaction (2).

As this pattern of kinetic data for the reactions of 2-methylpiperidine and cis-2,6-dimethylpiperidine appears to

be quite similar to that dispayed by the reactions of piperidine (2), the interpretation given to the data for the reactions of piperidine [i.e. electrophilic catalysis of the removal of fluoride ion (2)] applies to the reactions of the other two amines.* Therefore, in order to compare the relative leaving group ability of fluoride and chloride, the second-order rate coefficient for a particular reaction of CDNB should be compared with the k_u coefficient for the corresponding reaction of FDNB. The comparison shows that the reactivity ratios, Ar-F/Ar-Cl, are 8, 36 and 7 for piperidine, 2-methylpiperidine and cis-2,6-dimethylpiperidine respectively.**

Although this trend is not easily rationalized, the obvious deduction is that the relative reactivity, Ar-F/Ar-Cl, is not greatly dependent on the steric bulk of the nucleophile, notwithstanding the wide reactivity range spanned (eight-thousandfold).

This finding contrasts sharply with those of Hammond and Parks (5). These workers have found that for reactions of FDNB or CDNB in ethanol at 50^0 the ratio of the second-order rate coefficients, Ar-F/Ar-Cl, varies from 63 to 0.7 on changing the steric bulk of the attacking amine from aniline to N-methylaniline, while the same ratio is only 0.07 for the

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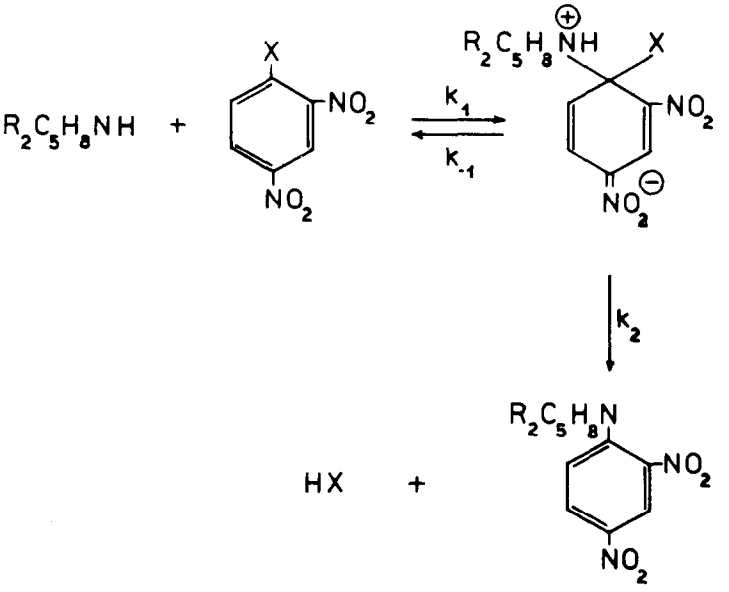
* The possibility that use of N-deuterated sec-amines may give rise to a primary hydrogen isotope effect has not been checked for 2-methylpiperidine or cis-2,6-dimethylpiperidine. This is partly due to the fact that our findings in this respect (2) are no longer in disagreement with those of Zollinger (3). In fact a recent reinvestigation has shown (4) that the reactions of FDNB with p-anisidine or n-d_2-p-anisidine in benzene proceed at about the same rate.

** Similar results with respect to the near constancy of the reactivity ratios, Ar-F/Ar-Cl, have been obtained for the reactions of FDNB or CDNB in benzene with n-butylamine, sec-butylamine and tert-butylamine respectively.

reactions of N-methylaniline in nitrobenzene. These results were rationalized (5) by considering that the change to a poorer nucleophile or to a "slower" solvent requires more bond breaking in the rate limiting transition state.

The test afforded by the present experiments is much more cogent than that of Hammond and Parks (5) since the reactivity range spanned by the methyl substituted piperidines is considerably greater than that provided by the anilines. This result, therefore, raises considerable doubt that the steric bulk of the attacking amine may be one of the general factors determining the relative fluorine lability.

The body of results presented here is not easily reconciled with any form of a one-step mechanism. In fact while a one-step mechanism could account for the electrophilic catalysis by protic substances [in terms of a termolecular push-pull pechanism (6)] and for the lack of base catalysis,



it is inconsistent with the near invariance of the Ar-F/Ar-Cl reactivity ratio with changing nucleophilicity of the attacking amine.

On the other hand, a stepwise mechanism, well founded for the reactions in hydroxylic solvents (7a,b) is consistent with the experimental results, if it is assumed that both reactions, of the fluoro and chloro derivatives, belong to Bunnett's class A (7a) (i.e. $k_{-1} >> k_2$)*. In this case the reactivity ratio, Ar-F/Ar-Cl, may result approximately independent of the nucleophilicity of the attacking amine if both k_1 and k_2/k_{-1} for the reactions of the fluoro and the chloro compounds vary approximately in the same fashion with varying the nucleophile, which, on the other hand, seems a reasonable possibility.

Although a stepwise mechanism with the specialization assumed above is acceptable, it is not clear why, if such mechanism applies, base catalysis by amines is not observed. At present we have no satisfactory explanation of this behaviour.

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* This implies that in the chloro derivative electrophilic catalysis cannot show up because it is not needed for ejection of chloride ion.

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