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ELECTROPHILIC CATALYSIS IN NITRO-ACTIVATED AROMATIC NUCLEOPHILIC SUBSTITUTION OF FLUORINE BY PIPERIDINE IN BENZENE.[1]

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WE wish to report some kinetic data which illustrate certain interesting facets of the aromatic nucleophilic substitution reaction. These concern the reactions of 2,4-dinitrofluoro, 2,4-dinitrochlorobenzene, and 4-nitrofluorobenzene with piperidine, in benzene, with or without addenda such as methanol or triethylamine. Some of our results are reported in Table I and, for an easier appreciation, part of them are depicted in Fig. 1.

Examination of the data shows that in 2,4-dinitrofluorobenzene the order with respect to piperidine changes from one to two with increasing amine concentration (Table I, a and Fig. 1, a). This changing order behaviour cannot be a medium effect since in the corresponding chloride reaction the order remains at unity at much higher concentration (Table I, b and Fig. 1, b). Neither the rate nor the pattern of the kinetic order is appreciably changed in the presence of a sizeable

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TABLE I

Reaction Rates of Piperidine with Nitrohalobenzenes at 25° in Benzene.

(a) 2,4-dinitrofluorobenzene (2.25×10^{-5} M)

$10^4 \times [C_5H_{10}NH]$ M	1.01	2.36	3.37	5.06	56.2	103	143
$10^5 \times \frac{\text{Rate}}{[\text{Ar-X}]}$ sec.$^{-1}$	7.75	16.4	23.6	40.3	1,870	6,160	12,100

(b) 2,4-dinitrochlorobenzene (2.28×10^{-5} M)

$10^3 \times [C_5H_{10}NH]$ M	6.71	13.2	25.6	37.2
$10^4 \times \frac{\text{Rate}}{[\text{Ar-X}]}$ sec.$^{-1}$	5.69	11.4	21.4	32.6

(c) 2,4-dinitrofluorobenzene (2.20×10^{-5} M), triethylamine 0.06 M

$10^4 \times [C_5H_{10}NH]$ M	2.22	17.1	57.2	143
$10^4 \times \frac{\text{Rate}}{[\text{Ar-X}]}$ sec.$^{-1}$	1.49	26.2	198	1,190

(d) 4-nitrofluorobenzene (2.20×10^{-5} to 7.60×10^{-3} M)

$10^3 \times [C_5H_{10}NH]$ M	3.87	7.74	31.6	92.3	327	920
$10^{10} \times \frac{\text{Rate}}{[\text{Ar-X}]}$ sec.$^{-1}$	6.13	12.3	130	734	9,790	78,300

(e) 2,4-dinitrofluorobenzene (2.19×10^{-5} M), methanol 0.06 M

$10^4 \times [C_5H_{10}NH]$ M	2.22	4.30	8.44	32.3	80.0	143
$10^4 \times \frac{\text{Rate}}{[\text{Ar-X}]}$ sec.$^{-1}$	5.29	9.62	22.0	102	312	433

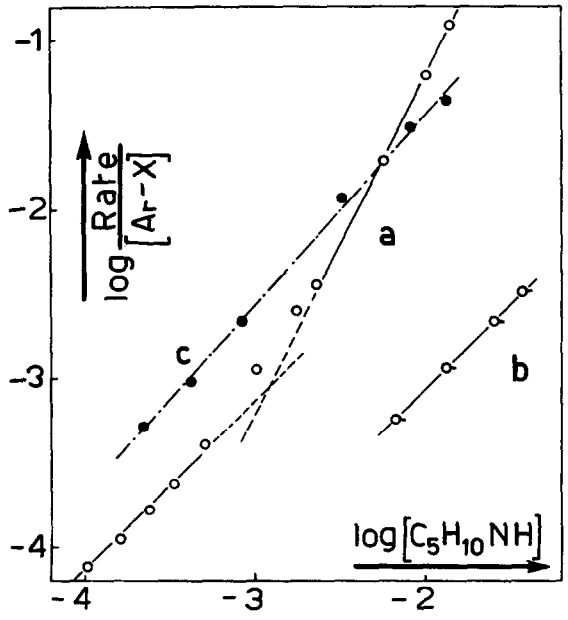

FIG. 1

Reactions of piperidine with halobenzenes at 25°. Plot of log $\frac{\text{Rate}}{[\text{Ar-X}]}$ against log piperidine concentration.
a, 2,4-dinitrofluorobenzene, benzene
b, 2,4-dinitrochlorobenzene, benzene
c, 2,4-dinitrofluorobenzene, benzene + methanol 0.06 M

concentration (0.06 M) of a non-protic amine such as triethyl amine (Table I, c). Furthermore, experiments with N-d-piperidine (in the whole concentration range, 10^{-4} to 1.4×10^{-2} M) have disclosed no measurable isotope effect within the 5% uncertainty of the experimental error. These facts indicate that the second amine molecule which gives rise to the third-order term is not involved in the rate determining abstraction of a

proton.

A similar pattern is exhibited by the corresponding 4-nitro halides: in the fluoride reaction the order in amine changes from one to two (Table I, d) while the chloride reaction is known to remain first-order in piperidine to quite high concentration (at least up to 0.7 M).[2] Moreover, triethylamine in relatively high concentration (0.12 M) does not appreciably affect the rate nor the pattern of the kinetic order.

Since the second amine molecule appears to be involved in the rate determining transition state of the fluoride but not of the chloride reaction, a reasonable possibility is that the protic amine is involved in the rate determining abstraction of the fluoride ion through hydrogen bonding. That electrophilic catalysis is a likely explanation, is supported by the dramatic effect that methanol (0.06 M) has upon the rate and the order pattern (Table I, e and Fig. 1, c). With respect to benzene alone, in the presence of methanol the rate is considerably increased at the lower amine concentration and decreased at the higher concentration, while the order in piperidine remains at about unity throughout the whole concentration range. The electrophilic catalysis is also supported by the much smaller ratio of second-order rate constants Ar-F/Ar-Cl, in benzene than in methanol. For both 2,4-dinitro and 4-nitro substrates the ratio has a value of about 700 in methanol and about 8 in benzene.[3]

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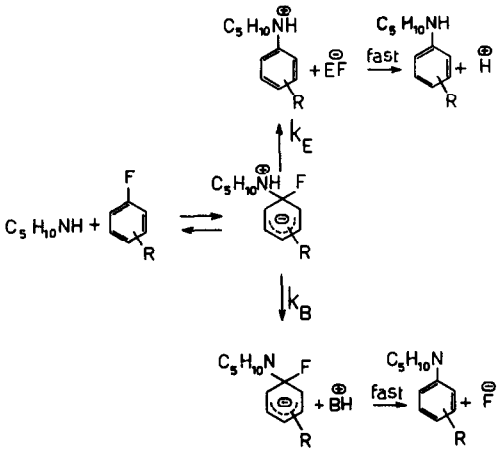
2 W. Greizerstein and J.A. Brieux, J. Amer. Chem. Soc., 84, 1032 (1962).

3 The ratios have been obtained from our results and others of Bunnett[4,5] and Greizerstein[2] extrapolating to 25° where necessary.

Electrophilic catalysis indicates that the breaking of the carbon-fluorine bond is important in the rate determining transition state while the lack of base catalysis and isotopic effect indicates that the breaking of the nitrogen-hydrogen bond is not involved.

An unequivocal interpretation of these finding is extremely difficult, as they are in accord with both a concerted process in which bond making and bond breaking are more or less simultaneous, as well as with the intermediate complex mechanism.[5] If this latter mechanism, which is the one more widely accepted, applies, our findings signify that in the reaction ri-



4 J.D. Reinheimer and J.F. Bunnett, J. Amer. Chem. Soc. 81, 315 (1959).

5 J.F. Bunnett, E.W. Garbish and K.M. Pruitt, J. Amer. Chem. Soc. 79, 385 (1957).

dine with nitrofluorobenzenes proton abstraction does not compete favorably with fluoride ion abstraction ($k_E >> k_B$). Why this should be so is difficult to rationalize. Probably it has to do with the nature of the attacking amine; for example, the reaction of 2,4-dinitrofluorobenzene with p-anisidine in benzene is base catalysed and exhibits an isotope effect (k_H/k_D = = 1.7).[6] However, with n-butylamine and 2,4-dinitrofluorobenzene we have found a pattern of data similar to that shown above for piperidine.

A systematic investigation covering a spectrum of amines thus appears desirable.

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6 H. Zollinger, Angew. Chem. 73, 125 (1961).