

Acid and Electrophilic Catalysis in Aromatic S_N2 Reactions and the Two-stage Addition-Elimination Mechanism

By K. B. LAM and J. MILLER

(University of Hong Kong, Hong Kong, B.C.C.)

ACID catalysis of S_N reactions of heterocyclic nitrogen compounds is well known,¹⁻⁴ and has been discussed quantitatively by Liveris and Miller.⁵ Acid and electrophilic catalysis in aliphatic nucleophilic substitution is also well known.⁶ Miller^{7a} has calculated energy-reaction co-ordinate profiles for a variety of reactions of anionic reagents with neutral substrates, and found these in satisfactory agreement with rate data, and heats of reaction.^{7b} The reactivity of neutral nucleophiles has been similarly investigated.

Calculations and experiments suggest that with activated fluoro-compounds (*e.g.*, *p*-nitro- and 2,4-dinitro-fluorobenzene) the formation of the second transition state is rate limiting with heavy nucleophiles (*e.g.*, SCN⁻ and I⁻) but not with light nucleophiles (*e.g.*, OMe⁻), while thiomethoxide and thiophenoxide ions fall into a border region.^{7d,e}

If a one-stage (synchronous) mechanism of aromatic nucleophilic substitution were applicable,

electrophilic catalysis should be common, and, for example, silver ion would be expected to catalyse S_N reactions of chloro-, bromo-, and iodo-compounds. This however has never been demonstrated, and some qualitative experiments by Fuller and Miller⁸ showed only small salt effects of silver ion in the methanolysis of picryl chloride and iodide.

Calculations suggest that fluoro-compounds are most likely to be susceptible to acid and electrophilic catalysis, and we are investigating the reactions of N₃⁻, I⁻, and SCN⁻ with 1-fluoro-2,4-dinitrobenzene. The calculations suggest that acid and electrophilic catalysis would be found for reactions with I⁻ and SCN⁻ but not with N₃⁻, though azide and thiocyanate ions are both classified as pseudo-halogenoid.^{9,10} Their kinetic nucleophilicity towards a standard aromatic substrate^{7a} in protic solvents falls smoothly in the order N₃⁻ > SCN⁻ > I⁻.

Our preliminary results may be summarised as follows:

(i) The complete displacement reaction of iodide ion with 1-fluoro-2,4-dinitrobenzene in methanol, *cf.* ref. 11, is almost negligible; accompanying methanolysis leads to the formation of 2,4-dinitroanisole which is slowly demethylated by the iodide ion.

Using hydriodic acid instead of KI as the reagent (equimolar concentration, 0.02 M) leads to an approximately 5×10^6 -fold increase in rate at 145° (by extrapolation of the Arrhenius plot).

(ii) The complete displacement reaction of thiocyanate ion with 1-fluoro-2,4-dinitrobenzene in methanol is also very slow, and accompanied by methanolysis and side-chain reactions.

Adding an equimolar quantity of thorium ions, (as thorium nitrate, 0.02M) leads to an approximately 2×10^3 -fold increase in rate at 100°.

(iii) The complete displacement reaction of azide ion with 1-fluoro-2,4-dinitrobenzene in methanol proceeds⁵ readily and smoothly at ambient temperatures, *cf.* ref. 7e, and may be followed by consumption of azide ion or the liberation of fluoride ion. Addition of thorium as thorium nitrate (0.02 M) causes no enhancement of rate at all, but on the contrary a marked diminution of rate. Conductivity measurements indicated specific interactions between thorium ion and azide ion, either by ion-aggregation or possibly actual bond-formation. At 100° the reduction in rate is approximately 10^3 -fold.

We regard these data as very strong evidence for the two-stage addition-elimination, and against the one-stage synchronous mechanism of activated aromatic S_N2 reactions.

(Received, July 22nd, 1966; Com. 531.)

¹ C. K. Banks, *J. Amer. Chem. Soc.*, 1944, **66**, 1127.

² (a) R. R. Bishop, E. A. S. Cavell, and N. B. Chapman, *J. Chem. Soc.*, 1952, 437; (b) E. A. S. Cavell and N. B. Chapman, *ibid.*, 1953, 3392; (c) N. B. Chapman and C. W. Rees, *ibid.*, 1954, 1190; (d) N. B. Chapman and D. Q. Russell-Hill, *ibid.*, 1956, 1563.

³ J. D. Reinheimer, J. T. Gerig, R. Garst, and B. Schrier, *J. Amer. Chem. Soc.*, 1962, **84**, 2770.

⁴ R. G. Shepherd and J. L. Fedrick, *Adv. Heterocyclic Chem.*, 1965, **4**, 145—423.

⁵ M. Liveris and J. Miller, (a) *Austral. J. Chem.*, 1958, **11**, 297; (b) *J. Chem. Soc.*, 1963, 3486.

⁶ C. K. Ingold, "Structure and Mechanism in Organic Chemistry", Bell, London, 1953, pp. 357—360.

⁷ (a) J. Miller, *J. Amer. Chem. Soc.*, 1963, **85**, 1628; (b) D. L. Hill, K. C. Ho, and J. Miller, *J. Chem. Soc. (B)*, 1966, 299; (c) J. Miller, unpublished work; (d) J. Miller and K. W. Wong, *J. Chem. Soc.*, 1965, 5454; (e) K. C. Ho, J. Miller, and K. W. Wong, *J. Chem. Soc. (B)* 1966, 310.

⁸ M. W. Fuller and J. Miller, unpublished work.

⁹ T. Moeller, "Inorganic Chemistry", Wiley, New York, 1952, pp. 463—480.

¹⁰ B. E. Douglas and D. H. McDaniel, "Concepts and Models of Inorganic Chemistry", Blaisdell, New York, 1965, pp. 248—250.

¹¹ J. Miller, and A. J. Parker, *J. Amer. Chem. Soc.*, 1961, **83**, 117.