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The *ortho* : *para* Ratio in Aromatic Nucleophilic Substitution

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Summary *p*-Nitrofluorobenzene reacts slightly faster than *o*-nitrofluorobenzene with methoxide ions in methanol, but under the same conditions the 2-fluorine atom in 2,4-difluoronitrobenzene is replaced faster than the 4-fluorine atom; an explanation is given to reconcile these observations.

THE reaction of 2,4-difluoronitrobenzene with methoxide ions takes place preferentially at the 2-position,[1,2] *i.e.*, *ortho*-activation by the nitro-group predominates, but *o*- and *p*-nitrofluorobenzenes react with methoxide ions to give an *o* : *p* ratio of less than one,[3] indicating that a *p*-nitro-group is more activating than an *o*-nitro-group. We have reinvestigated these apparently contradictory reactions.

We measured the rates of reaction of *o*- and *p*-nitrofluorobenzenes with methoxide ions in methanol and obtained an *o* : *p* ratio of 0·69 at 49·15° in good agreement with Bevan and Bye's[3] value of 0·68 at this temperature (0·70 at 25°).

Kinetic runs were carried out with 2,4-difluoronitrobenzene and methoxide ions in methanol at 25°. In all cases when the methoxide : substrate ratio was greater than 2 : 1, the amount of methoxide consumed at infinity corresponded to the theoretical value calculated for the replacement of both fluorine atoms, and the expected product, 2,4-dimethoxynitrobenzene, was isolated from these solutions. When the initial concentration ratio was 1 : 1, the [19]F n.m.r. spectra of the infinity solutions consisted of two peaks A and B, A being 12·3 p.p.m. downfield from B. Addition of 2,4-difluoronitrobenzene to these solutions resulted in two additional peaks, hence A and B are due to the products of the reaction. Also, when the runs were carried out with 2,4-difluorobenzene present in excess, the ^{19}F spectrum consisted of four peaks, two identifiable as belonging to the substrate, the other two being in the same relative position as A and B. The position of absorption of B coincided with that of fluorobenzene. In all cases when the substrate was in excess, no 2,4-dimethoxynitrobenzene could be detected in the products by t.l.c. When the initial concentrations of methoxide ion and substrate were 1 : 1 the ratio of the intensities of A and B was 1 : 0·815; when the methoxide : substrate ratio was 1 : 1·5 the corresponding intensity ratio was 1 : 0·823.

3-Fluoro-4-nitroanisole (I) and 3-fluoro-6-nitroanisole (II), the products of replacement at the 4- and 2-positions in 2,4-difluoronitrobenzene were synthesised by the method of Hodgson and his co-workers.[4] (I) had a [19]F n.m.r. absorption which coincided with that of fluorobenzene and (II) absorbed 12·2 p.p.m. downfield from fluorobenzene. Hence the above intensity ratios indicate a value of 1·22 for the *o* : *p* ratio in 2,4-difluoronitrobenzene.

The apparent inconsistency of this result when compared with that obtained by individual measurements on *o*- and *p*-nitrofluorobenzenes arises from the fact that the value of the *o* : *p* ratio derived from measurements on 2,4-difluoronitrobenzene is not a true measure of the relative activating powers of *o*- and *p*-nitro-groups. In aromatic nucleophilic substitution reactions the activating power of a group X, as measured by the relative rate ratio $k_X : k_H$, where k_X and k_H are the rate constants of the substituted and unsubstituted compounds, depends on the initial degree of activation of the parent system.[5,6] In 2,4-difluoronitrobenzene the rate of replacement of the 2-fluorine atom reflects the influence of a *m*-fluoro-substituent in an *o*-nitro-activated series, while replacement at the 4-position includes the effect of *m*-fluorine in a *p*-nitro-activated series, and the magnitude of *m*-fluorine activation cannot be assumed to be the same in both series.

Using initial methoxide : substrate concentrations in the ratio of 1 : 1·33 we have obtained a value of 5.88×10^{-3} l mol^{-1} s^{-1} for the second-order rate constant for the overall reaction of 2,4-difluoronitrobenzene with methoxide ions at 25°. Combined with the above product ratios, this gives rate constants of 3.23×10^{-3} and 2.65×10^{-3} l mol^{-1} s^{-1}

for replacement at the 2- and 4-positions, respectively. Rate constants for methoxydefluorination calculated from Bevan and Bye's data are, at 25°, $1\cdot32 \times 10^{-4}$ l mol^{-1} s^{-1} for o- and $1\cdot91 \times 10^{-4}$ l mol^{-1} s^{-1} for p-nitrofluorobenzene. Hence the relative activating power of a m-fluorine substituent $(k_F:k_H)$ is 24·5 in the o-nitrofluorobenzene series and 13·9 in the p-nitrofluorobenzene series. These figures can be compared with the value of 93·3† at 25° found in the m-nitrofluorobenzene series.

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† Calculated at 25° from the data in ref. 6.

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