

Base Catalysis and Element Effect in Nucleophilic Aromatic Substitution with *p*-Anisidine

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The reaction between *p*-anisidine and 1-X-2,4-dinitrobenzenes, X being chlorine, bromine, methylsulphonyl, and phenylsulphonyl, has been studied kinetically in benzene at 25°C. The rates were determined spectrophotometrically. Base catalysis by DABCO (1,4-diaza[2.2.2]-bicyclooctane) was observed with all four leaving groups, in the case of chlorine confirming the result obtained by other workers. The specific rate for the DABCO-catalyzed reaction was found to vary within a factor of 9 between the most reactive compound (phenylsulphonyl derivative) and the least reactive one (chlorine derivative).

The absence of an "element effect" in nucleophilic aromatic substitution was demonstrated by Bunnett and his coworkers in 1957.¹ The specific rates of reaction with a common nucleophile, piperidine, were determined in methanol at different temperatures for a series of 1-X-2,4-dinitrobenzenes, in which X denotes 9 different substituents. Both the enthalpy and entropy of activation were found to be constant within a group of 6 compounds representing 6 different leaving groups X. The conclusion was therefore drawn that the reaction takes place *via* a rate-determining bond formation, followed by a fast bond breaking.

To be able to judge the full validity of the "absence of element effect" criterion one would like to know the magnitude of the element effect to be expected if the second reaction step, involving cleavage of the C-X bond, were actually rate-determining. In their original paper,¹ Bunnett and coworkers refer to an article by Cooper and Hughes,² in which solvolytic rates for the different *tert*-butyl halides (F, Cl, Br, I) have been determined in 80 % by volume aqueous ethanol. At 25°C, they are in the ratios 10⁻³ (appr.):1:41:99 in order from F to I.

Although the second step in nucleophilic aromatic substitution and the first step in the solvolysis of the *tert*-butyl halides involve the same kind of rehybridization of the central carbon atom, $sp^3 \rightarrow sp^2$, they are energetically very different. The first case represents a very exothermic reaction, which is

expected to have an "early" transition state,³ whereas the rate-determining step in the solvolysis reaction is very endothermic and will have a "late", *i.e.*, product-like, transition state. In view of this difference, one can *a priori* suspect the differences between, *e.g.*, chlorine and bromine to be rather small in the aromatic reaction. In such a case, the usefulness of the "absence of element effect" criterion would be somewhat limited.

It was therefore thought to be of interest to investigate the element effect for some representative leaving groups in a case for which the second step is independently known to be the rate-determining one, namely, the reaction of 1-X-2,4-dinitrobenzenes with *p*-anisidine in benzene solution. For X = chlorine and fluorine, this system has been investigated by Bernasconi and Zollinger.⁴ These workers found that both reactions were catalyzed by the non-nucleophilic bases DABCO (1,4-diaza[2.2.2]bicyclooctane) and pyridine. In the present work, the reaction between *p*-anisidine and some 1-X-2,4-dinitrobenzenes has been kinetically studied at 25°C using a direct spectrophotometric technique. DABCO was used as a catalyst, and chlorine, bromine, methylsulphonyl, phenylsulphonyl, and nitro were chosen as the leaving-group X. No quantitative data could be obtained for the nitro group, however.

EXPERIMENTAL

General. When not otherwise stated, melting points agree with those found in *Beilstein's Handbuch*.

Materials. 2,4-Dinitrochlorobenzene and 2,4-dinitrobromobenzene (from Fluka AG) were recrystallized twice from absolute ethanol. The purity was checked by NMR and GLC. M.p. 53.0 and 73.5°C, respectively.

1,2,4-Trinitrobenzene was prepared by Borsche's method⁵ and recrystallized from methanol to constant melting point. The purity was checked by NMR and TLC. M.p. 60.0°C.

2,4-Dinitrophenylmethylsulphone and 2,4-dinitrodiphenylsulphone were prepared according to Bost *et al.*'s method,⁶ recrystallized once from absolute ethanol and then from tetrahydrofuran. The purity was checked by NMR and TLC. M.p. 189.5 and 160.0°C, respectively.

p-Anisidine (Riedel-de Haën, chromatographic purity) was purified by recrystallization from 80 % aqueous ethanol in the presence of a slight amount of sodium dithionite to remove oxidation products and then from 80 % aqueous ethanol after treatment with activated charcoal. The purity was checked by TLC. M.p. 57.2°C. The purified *p*-anisidine was stored under argon.

DABCO (1,4-diaza[2.2.2]bicyclooctane) (Fluka, *purum* quality) was recrystallized from benzene. M.p. 157.0°C.

Benzene (Riedel-de Haën, chromatographic purity) was distilled in a Claisen column and stored over Molecular Sieves 4 A. B.p. 78.1°C (760 mmHg).

Identification of the reaction product. The reaction product from 2,4-dinitrobromobenzene and *p*-anisidine was identified by NMR spectroscopy to be *N*-(2,4-dinitrophenyl)-*p*-anisidine. The products from the reaction with the other substrates were isolated and found to be identical with the product above by use of the mixed melting point method.

Kinetic procedure. The kinetic measurements were performed at 25.00 ± 0.05°C and at a wavelength of 420 nm in 1 cm cells in a Beckmann DU spectrophotometer, equipped with a thermostated water bath in the beam path. The initial concentrations of the different reactants in each kinetic run were 1.00 × 10⁻³ M for the substrates, 0.200 M for *p*-anisidine, and 0–0.05 M for DABCO. The measurements were performed in the following manner. Solutions containing suitable concentrations of the different reactants were pre-thermostated and mixed in the cell, *p*-anisidine being added last. Zero time was recorded at this moment. Absorbance values were determined at regular intervals. For

each run 20 measurements were made. Three different runs were performed for each substrate at each DABCO concentration.

Due to the precipitation of anisidinium salts in some of the reactions, no infinity value was directly measurable, nor could the Guggenheim⁷ treatment be applied since the precipitate appeared already after the first half-life. A "synthetic" infinity value was obtained by making a 1.00×10^{-3} M solution of independently prepared *N*-(2,4-dinitrophenyl)-*p*-anisidine in benzene, which also contained 0.198 mol/l of *p*-anisidine. An absorbance value of 2.780 was recorded at 420 nm. This value did not show any variation with addition of *p*-anisidine hydrochloride up to the point of precipitation.

No kinetic runs were allowed to proceed beyond the point of precipitation. The runs with 1,2,4-trinitrobenzene were so rapid under the given conditions that no rate constant could be evaluated. Visual observation showed, however, that the uncatalyzed reaction was completed (no further colour change) in about 3 min, and the catalyzed one in about 20 sec. This indicates, qualitatively, base catalysis.

Treatment of data. From the kinetic measurements, values of A_t , *i.e.*, the absorbance A at time t , were obtained. These values were subtracted from the "synthetic" infinity value A_∞ . The function $\ln(A_\infty - A_t)$ was plotted against time, and the slope of the curve was calculated by the least-squares method. The pseudomonomolecular rate constants thus obtained were plotted against DABCO concentration, and the slopes were again calculated by the least-squares method.

All calculations were performed on an Olivetti Programma 101 electronic desk-top computer.

RESULTS AND DISCUSSION

The first-order rate constants, obtained under strictly first-order conditions, are given in Table 1. The standard deviation in each separate run, typically 3 %, is seen to be larger than the deviations between different runs, less than 1 %, indicating good reproducibility. The average values of the first-order rates are plotted *versus* DABCO concentration in Fig. 1.

The detailed description of the reaction between 2,4-dinitro-1-X-benzene and *p*-anisidine is illustrated in Fig. 2. The designations of the rate constants are identical with those used by Bernasconi and Zollinger.⁴

Table 1. First-order rate constants for the DABCO-catalyzed nucleophilic aromatic substitution of 2,4-dinitro-1-X-benzene by *p*-anisidine. Concentration of *p*-anisidine 0.200 M. Errors are standard deviations.

[DABCO] $\times 10^2$	Cl	Leaving group X. $k_{\text{obs}} \times 10^6 \text{ sec}^{-1}$		
		Br	CH ₃ SO ₂	C ₆ H ₅ SO ₂
0	0.85 \pm 0.03	1.54 \pm 0.06	0.38 \pm 0.09	1.40 \pm 0.03
	0.83 \pm 0.04	1.53 \pm 0.05	0.39 \pm 0.05	1.41 \pm 0.02
	0.82 \pm 0.01	1.51 \pm 0.05	0.38 \pm 0.06	1.40 \pm 0.02
2.5	2.20 \pm 0.10	3.98 \pm 0.09	7.69 \pm 0.14	17.26 \pm 0.49
	2.18 \pm 0.10	3.98 \pm 0.12	7.69 \pm 0.12	17.24 \pm 0.61
	2.21 \pm 0.09	3.94 \pm 0.08	7.69 \pm 0.19	17.25 \pm 0.61
5.0	4.16 \pm 0.16	7.02 \pm 0.17	14.69 \pm 0.33	31.29 \pm 0.56
	4.14 \pm 0.11	6.99 \pm 0.25	14.70 \pm 0.33	31.30 \pm 0.80
	4.14 \pm 0.10	6.99 \pm 0.19	14.67 \pm 0.67	31.33 \pm 0.57

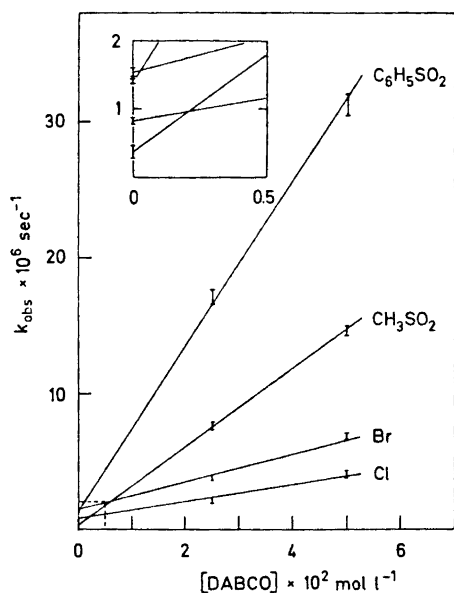


Fig. 1. Plot of the pseudomonomolecular rate constants versus DABCO concentration. The errors are calculated as "errors of the mean".⁸

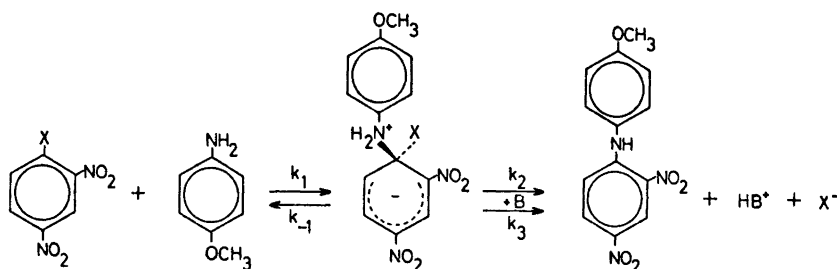


Fig. 2. Reaction scheme for nucleophilic substitution of 2,4-dinitro-1-X-benzene by *p*-anisidine.

The collapse of the intermediate may take place both *via* a base-catalyzed and a non-catalyzed path. Making the usual steady-state approximation, the following expression is obtained for the specific rate of the forward reaction:

$$k_{\text{obs}} = k_1 \frac{k_2 + k_3[\text{B}]}{k_{-1} + k_2 + k_3[\text{B}]} \quad (1)$$

Whether base catalysis is observed or not depends on the relative magnitude of k_{-1} vs. $k_2 + k_3[\text{B}]$, and, if $k_{-1} \gg k_2 + k_3[\text{B}]$, on that of $k_3[\text{B}]$ vs. k_2 .

With good leaving groups like chlorine and bromine, most nucleophilic reagents cause the second reaction step to be much faster than the reversal of the first, and no base catalysis is observed. However, the weak nucleophile

p-anisidine causes the reversal of the first step to be faster than the second step even in the presence of base, and catalysis by the latter is observed. That the rate acceleration is genuine base catalysis and not merely a medium effect has been convincingly proved by Bernasconi and Zollinger.⁴

The approximation $k_{-1} \gg k_2 + k_3[\text{B}]$ allows eqn. (1) to be rewritten in the form

$$k_{\text{obs}} = \frac{k_1}{k_{-1}} k_2 + \frac{k_1}{k_{-1}} k_3[\text{B}] \quad (2)$$

or, for the sake of brevity,

$$k_{\text{obs}} = k_0 + k_{\text{B}}[\text{B}] \quad (3)$$

Since *p*-anisidine can act both as a nucleophile and as a base, eqn. (3) applies in the absence of DABCO also, and when two bases, A and B, are present simultaneously, we have

$$k_{\text{obs}} = k_0 + k_{\text{A}}[\text{A}] + k_{\text{B}}[\text{B}] \quad (4)$$

With 2,4-dinitro-1-chlorobenzene, Bernasconi and Zollinger⁴ were able to verify eqn. (4) using *p*-anisidine and pyridine as bases A and B. A slight deviation, ascribed to mutual medium effects of the two bases, was found, however. Our values for the chlorine compound are roughly twice as large as those obtained by Bernasconi and Zollinger⁴ for the same reaction, and we can offer no explanation for this difference.

It is apparent from Fig. 1 that the observed specific rates at different concentrations of DABCO fit eqn. (3). The intercept for each line in Fig. 1 at $[\text{B}] = 0$ represents the contribution to the rate which is unaffected by DABCO, and the slope represents k_{B} in eqn. (3). It is quite remarkable that some of the lines cross each other. This means that for the DABCO-catalyzed part of the reaction the relative mobility of the leaving groups is different from that for the remaining part of the reaction. However, the latter part is again a sum

Table 2. Termolecular rate constants for the DABCO-catalyzed reaction of 2,4-dinitro-1-X-benzene and *p*-anisidine in benzene at 25°C, together with Bunnett's original values for the related reaction of Ref. 1, recalculated relative to Cl=1.

Leaving group	Our values		Values from Ref. 1.
	$k_3 \times 10^3$ ^a	Rel. value	Rel. value
F	—	—	767
NO ₂	—	—	207
OSO ₂ C ₆ H ₄ CH ₃ - <i>p</i>	—	—	23.3
SOC ₆ H ₅	—	—	1.1
Br	0.55	1.65	1.0
Cl	0.33	1.00	1.0
SO ₂ C ₆ H ₅	2.99	9.02	0.7
SO ₂ CH ₃	1.43	4.31	—
OC ₆ H ₄ NO ₂ - <i>p</i>	—	—	0.7
I	—	—	0.2

^a l³ mol⁻² sec⁻¹.

of a *p*-anisidine-catalyzed route and an uncatalyzed one. For the chlorine compound, Bernasconi and Zollinger's data⁴ indicate that these two parts of the reaction are of comparable magnitude at the concentration of *p*-anisidine chosen in the present study, 0.2 M. A similar situation probably exists with the other leaving groups. The intercepts in Fig. 1 therefore do not represent a single reaction path. Thus this point was not further pursued but may well deserve further study.

The termolecular rate constants for the DABCO-catalyzed part of the reaction, which at high DABCO concentrations represents the main route, were calculated by dividing the slopes of the lines in Fig. 1 by the *p*-anisidine concentration. The values are given in Table 2.

Qualitatively, the relative order is quite as expected, assuming that bond-breaking between carbon and the leaving group is kinetically significant. Quantitatively, the differences are not particularly impressive compared with those obtained for solvolysis of *t*-butyl halides,² where the Br/Cl ratio is 41:1. In Table 2, the values obtained in the present study are compared with Bunnett's original values¹ (recalculated relative to Cl=1). The similarity between Br and Cl is striking. In our work, NO₂ as a leaving group was found to give too high a rate, even in the absence of DABCO, to allow measurements at 25°C.

The most straightforward explanation of the weak "element effect" found in the present work is that bond-breaking has made very little progress in the rate-determining transition state. Since the second reaction step is a very exothermic process, this follows from Hammond's postulate.³

A final point to discuss is the influence of the solvent on the rate ratios. Since the present work was carried out in benzene solution, one might expect that the poor solvating properties of this medium should retard the Cl reaction more than the Br reaction. A change to the solvent used by Bunnett and coworkers,¹ methanol, would certainly not have reversed the situation so as to make Cl faster than Br (*cf.* *t*-butyl halides²). They might just have become more equal.

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