

# Electrospray Mass Spectral Studies of Aromatic Diazonium Salts and Diazotates

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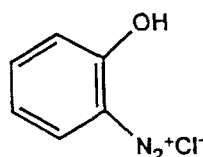
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Electrospray (ES) mass spectra were observed for a series of aryldiazonium cations and the intact ions were observed. Collisionally activated decompositions lead to facile loss of nitrogen to form the corresponding aryl cations. Comparisons of the proportion of intact and fragment ions for each cation at a constant collisional energy lead to an order of relative stability for the diazonium cations which is similar to that determined in solution by chemical methods. Negative-ion ES mass spectra were observed for the intact ions for the corresponding diazotates. Like the diazonium cations, they also readily lose nitrogen in collisionally activated decompositions to give the phenolate anions  $[\text{OAr}]^-$ .

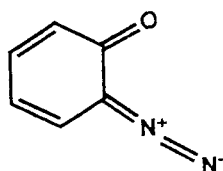
## INTRODUCTION

Electrospray mass spectrometry (ESMS) is a very gentle technique which allows pre-existing ions in solution to be transferred to the gas phase with minimum fragmentation. It has been most widely used in the study of large biomolecules, such as proteins, which are converted into polycationic species by dilute acid in the mobile phase and then detected in the spectrometer.<sup>1–5</sup> However, ESMS can also be used to study ionic compounds which do not rely upon the protonation step. In our laboratories we have used this approach to examine a wide variety of inorganic and organometallic systems.<sup>6–9</sup> The feature of gentle vaporization allows the observation of mass spectra by ESMS of labile or unstable ionic species which may not be amenable to study by other mass spectral approaches. Examples of such systems are the aromatic diazonium cations and the diazotate anions derived from them by reaction with hydroxide ions.

Few previous studies of the mass spectra of simple aromatic diazonium salts are available.<sup>10</sup> Presumably, the parent ion is too unstable to be detected by conventional mass spectrometry. In specialized cases such as the salts obtained from the diazotization of *o*- and *p*-aminophenol, the zwitterion



obtained after loss of HCl, has been detected in the mass spectrometer.<sup>11</sup> The stability of these zwitterions is derived from the existence of simple quinoid structures which are uncharged. The *meta* isomer, which



cannot be stabilized in this way, does not give a peak corresponding to the molecular ion. We now report the use of the electrospray technique to obtain the mass spectra of simple monosubstituted aromatic diazonium salts. In this way the intact ions have been detected and their collisionally induced fragmentation has been studied as a function of the substituent on the aromatic ring and the ion-source collision energy. The effect of substituents on the extent of mass spectral fragmentation is compared with the substituent effects previously reported<sup>12–14</sup> for some reactions involving aromatic diazonium ions in solution.

## EXPERIMENTAL

The diazonium tetrafluoroborate salts were prepared by the diazotization of the corresponding anilines in 20% tetrafluoroboric acid solution below 10 °C by the addition of an equimolar amount of sodium nitrite solution. The crystalline diazonium salt was collected by filtration, washed with ice-cold ethanol and recrystallized from acetone–diethyl ether.<sup>15</sup>

Diazotates were prepared by the reaction of the diazonium ions with aqueous sodium hydroxide as described by Schraube and Schmidt.<sup>16</sup>

Electrospray mass spectra were recorded by using a VG Bio-Q triple quadrupole mass spectrometer (VG Bio-Tech, Altrincham, UK). In the positive-ion mode the mobile phase used was methanol–water–acetic acid (50:50:1) and for negative-ion studies the mobile phase was propan-2-ol–water (50:50), which is reported<sup>17</sup> to suppress corona effects. The compounds were dissolved in methanol solution (2 mM) and then diluted 1:10 with methanol (positive ion) or propan-2-ol–water (negative ion). The dilute solution was injected directly via a Rheodyne injector equipped with a 10 µl loop using a Phoenix 20 micro LC syringe pump to deliver the solution to the vaporization nozzle of the electrospray ion source at a flow rate of 5 µl min<sup>-1</sup>. Nitrogen was used

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as the drying gas and for nebulization, with flow rates of approximately 5000 and 300 ml min<sup>-1</sup>, respectively. The pressure in the mass analyser region was about  $3 \times 10^{-5}$  Torr (1 Torr = 133.3 Pa). Increasing the voltage on the first skimmer ( $B_1$ ) was used to induce collisionally activated decomposition in the high-pressure region of the ion source.

The diazonium cations gave strong signals in their ES mass spectra and typically 4–6 signal-averaged spectra were sufficient to give a good signal-to-noise ratio. However, for the comparisons of the amount of fragmentation at  $B_1 = 30$  V, at least 12 signal-averaged spectra were acquired and three sets of data were recorded for each compound. The variation between determinations was less than 5%.

The diazotate anions gave slightly less intense ES mass spectra and typically 12–15 signal-averaged spectra were acquired.

## RESULTS AND DISCUSSION

### Diazonium ions

Figure 1 shows the positive-ion ES mass spectrum of a solution of  $p\text{-F-C}_6\text{H}_4(\text{N}_2)^+$  as a function of  $B_1$  voltage. At  $B_1 = 30$  V [Fig. 1(a)] the peak due to the intact ion ( $m/z$  123) is the only significant one in the spectrum. This is the first report of an intact diazonium cation being observed by ESMS. As the collision energy is increased, molecular nitrogen is lost to give the aryl cation at  $m/z$  95 [Fig. 1(b) and (c)]. Even at the relatively low  $B_1 = 50$  V substantial collisionally activated decomposition has occurred, which reflects the inherent instability of the diazonium cation.

Similar ES mass spectra were observed for a series of monosubstituted diazonium cations and the intact ion was observed each time. However, the amount of fragmentation of the substituted diazonium ions to give the corresponding substituted aryl cations varied considerably. The data are summarized in Table 1. The magnitude of fragmentation of the different ions is dependent on the  $B_1$  voltage used. At 30 V a tenfold variation of the percentage of fragmentation as a function of the substituent on the aromatic ring is observed. At 40 V, however, the additional energy imparted to the ions leads to a greater percentage of fragmentation, but this tends to mask the substituent effects and only a twofold variation of the percentage of fragmentation is observed as the substituents are varied.

The substituent effect on the fragmentation of the diazonium ion is a result of the combination of the substituent effects on both the parent diazonium ion and the resultant aryl cation.

Before attempting to rationalize these substituent effects it is instructive to consider those previously reported for some reactions of diazonium ions in solution.<sup>12–14</sup>

For the ionization of arylazoalkyl ethers:

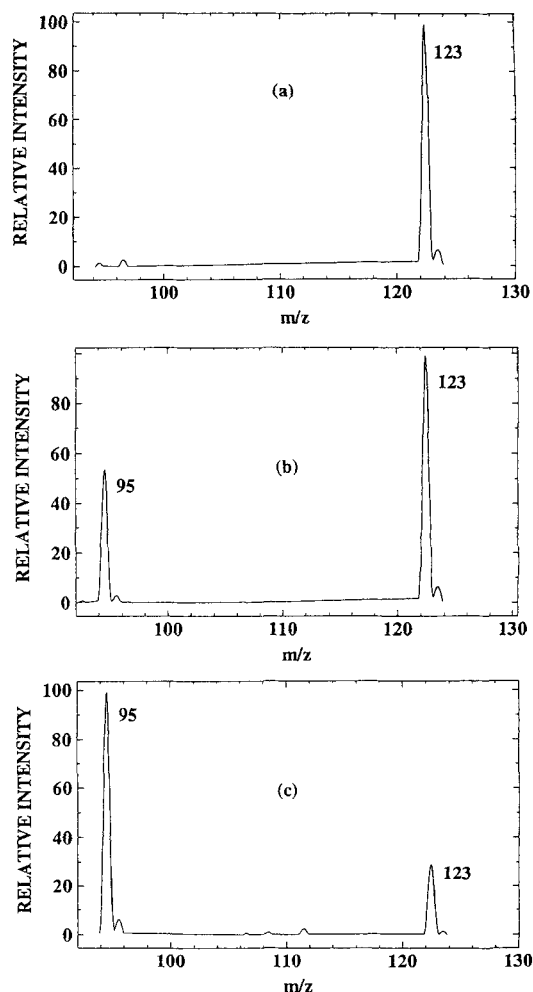
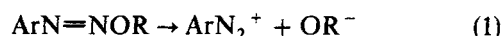


Figure 1. Electrospray mass spectra of 4-fluorobenzenediazonium salt at  $B_1 =$  (a) 30 V, (b) 40 V and (c) 50 V.

it has been reported<sup>14</sup> that the rate of reaction is strongly dependent on the inductive effects of substituents on the aromatic ring, but only very slightly dependent on their resonance effects. This has been attributed to the nitrene-like, high-energy resonance structure of the transition state with through conjugation from a *para* substituent to the diazonium group. Such a high-energy resonance structure would not contribute greatly to the

Table 1. Percentage of collisionally induced fragmentation of aryl diazonium salts

Substituent, X	$\sigma_i$	$m/z$ intact	$B_1$ voltage	
			30 V	40 V
4-Me	-0.09	119	30.8	65
3-Me	-0.08	119	43.4	79
H	0	105	17.1	
3-OMe	0.33	135	64.8	
4-OMe	0.38	135	18.6	61
3-CF <sub>3</sub>	0.46	173	14.3	42.6
3-Cl	0.51	139/141	14.3	
4-Cl	0.58	139/141	8.7	43.2
4-F	0.64	123	6.6	35.7
3-NO <sub>2</sub>	0.70	150	12.9	
4-NO <sub>2</sub>	0.80	150	16.9	53.7

overall resonance hybrid of the transition state. This reaction is a guide to substituent effects on the diazonium ion itself without any involvement of the aryl cation.

It has also been observed that the rate of ionic methoxydediazoniation,<sup>12</sup> which involves an aryl cation intermediate:



is largest for compounds having substituents with either positive or negative Hammett  $\sigma$  constants of small magnitude, e.g. *m*-Me and *m*-OMe. Substituents which have large positive or negative  $\sigma$  values show smaller reaction rates.

Both the methoxydediazoniation and the ESMS fragmentation of the diazonium ion involve the diazonium ion and the aryl cation. The substituent effects on the percentage of fragmentation of *meta*-substituted compounds correlate with these kinetic results obtained in methanolic solution under an oxygen atmosphere (necessary to ensure reaction by an ionic mechanism), and also with results obtained in trifluoroethanol.<sup>13</sup> They do not, however, correlate with Hammett  $\sigma$  values. The results for the *para*-substituted compounds do not correlate with any previous data.

A consideration of individual compounds leads to the following conclusions.

The electron-donating inductive effect (+*I*) of the *m*-Me group leads to more fragmentation of the *m*-Me compound than the unsubstituted compound. This increase in fragmentation suggests that the product aryl cation is more stabilized by this inductive effect than is the reactant diazonium ion.

The electron-releasing resonance effect (+*R*) slightly reduces the percentage of fragmentation (4-Me < 3-Me). It has previously been shown that the resonance effect of substituents on the ionization of *anti*-arylaazoethyl ethers to free diazonium ions is small.<sup>14</sup> It is also expected that resonance effects on the aryl cation would be slight because of poor overlap between the positive charge, which is located in an  $\text{sp}^2$  hybrid orbital in the plane of the benzene ring, and the  $\pi$ -electron cloud above and below the ring. The slight reduction in the percentage of fragmentation as a result of the +*R* effect must therefore indicate that, although the resonance effect on the diazonium and aryl cations is small, it is slightly stronger for the diazonium ion.

The electron-withdrawing inductive effect (−*I*) reduces the amount of fragmentation of the diazonium ion (3- $\text{CF}_3$  and 3- $\text{NO}_2$  both have less fragmentation than the unsubstituted compound). This effect should destabilize both the reactant and product cations, but the effect must be greatest on the aryl cation product to result in less fragmentation (cf. the +*R* effect above).

### Diazotates

Figure 2 shows the negative-ion ES mass spectrum of a solution of  $p\text{-NO}_2\text{C}_6\text{H}_4\text{N}_2\text{O}^-$  at  $B_1 =$  (a) 40 V, (b) 60 V and (c) 80 V. The peaks at  $m/z$  166 (intact ion) and 138 are the only significant peaks in the spectrum. Similar ES mass spectra were observed for a number of substituted diazotates. In all cases where the substituent is electron

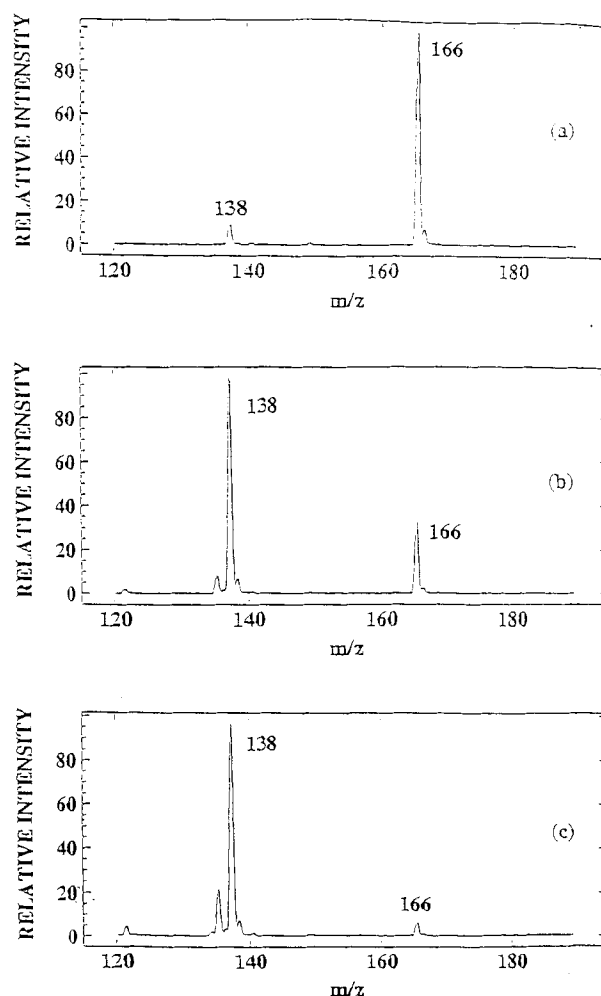


Figure 2. Negative-ion electrospray mass spectra of 4-nitrobenzenediazotate ion at  $B_1 =$  (a) 40 V, (b) 60 V and (c) 80 V.

withdrawing (e.g.  $\text{NO}_2$ , Cl and  $\text{CF}_3$ ; Fig. 3), the only significant peaks in the spectra were due to the intact ion and to the  $M - 28$  fragment, which is attributed to the corresponding substituted phenolate ion ( $\text{ArO}^-$ ). For the unsubstituted compound, and for compounds with electron-donating substituents, no strong peaks were observed in the ES mass spectra. These substituent effects are readily explained by a consideration of the reactions involved in the formation of the diazotate ions:



Formation of the diazotate is favoured by electron-withdrawing substituents because they destabilize the cationic diazonium ion, favouring reaction (3), and stabilize the anionic diazotate ion, which favours reaction (4). The converse applies to electron-donating substituents.

### Mechanism of fragmentation

We favour a four-centre aryl migration from nitrogen to oxygen followed by fragmentation of the rearrangement

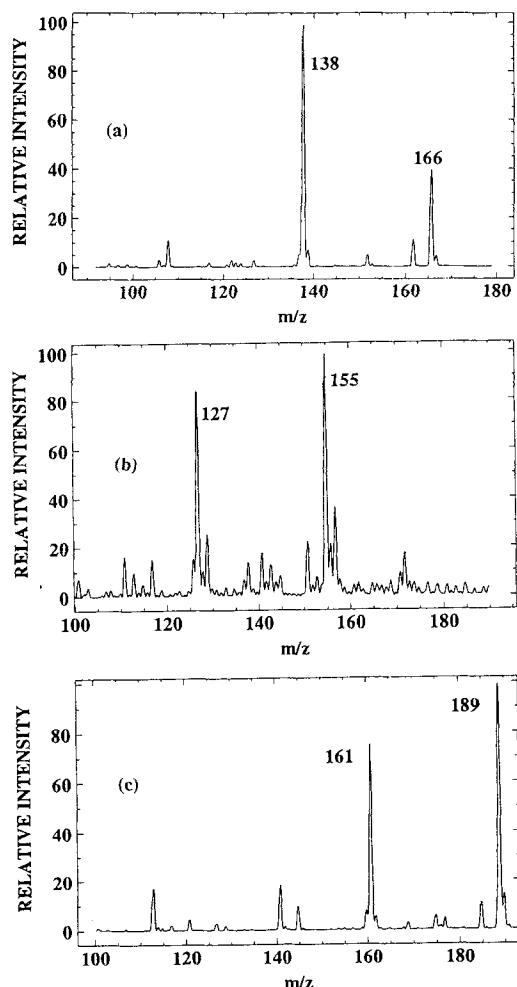
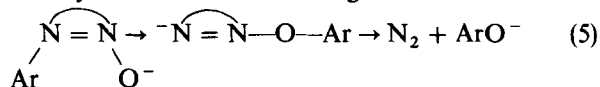
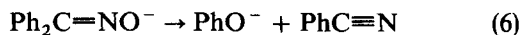


Figure 3. Negative-ion electrospray mass spectra of *meta*-substituted benzenediazotate ions where X = (a) nitro, (b) chloro and (c) trifluoromethyl.

product by loss of molecular nitrogen:



Four-centre skeletal rearrangements are well known in mass spectra<sup>18</sup> and are favoured when the migration is from an atom to another that is more electronegative or more polarizable. In this case the proposed aryl migration is from nitrogen to oxygen, which is more electronegative than nitrogen. Recently, Bowie<sup>19</sup> has reported a similar aryl migration:



in the negative-ion mass spectrum of the oximate anion derived from benzophenone. In this case the proposed migration is from carbon to oxygen.

Table 2. Percentage of collisionally induced fragmentation of some substituted aryl diazotates as a function of the  $B_1$  voltage

Substituent, X	$m/z$ intact	$B_1$ voltage		
		40 V	60 V	80 V
3- $\text{CF}_3$	189	8.4	34.5	82.4
4-Cl	155/157		42.6	
3-Cl	155/157		46.0	
3- $\text{NO}_2$	166		71.2	
4- $\text{NO}_2$	166	9.9	74.7	90.8
2- $\text{CH}_3$ -4- $\text{NO}_2$	180		77.7	

We have sought confirmation of this mechanism by the use of  $^{18}\text{O}$  tracer studies.

### $^{18}\text{O}$ tracer studies

*m*-Trifluoromethyl benzenediazotate containing 4%  $^{18}\text{O}$  was prepared by the addition of the corresponding diazonium salt to a 0.1 M aqueous sodium hydroxide solution containing 10%  $^{18}\text{O}$ . This solution was diluted (1:10) for analysis with a mixture of equal parts of normal ( $^{16}\text{O}$ ) water and propan-2-ol. A higher  $^{18}\text{O}$  content (14–18%) was achieved by carrying out the final dilution with  $^{18}\text{O}$ -labelled water. It appears that the oxygen atom in the diazotate ion is exchanged with water, presumably because reactions (3) and (4) are reversible.

The phenolate product obtained in the ES mass spectrum of  $^{18}\text{O}$ -labelled diazotate contained approximately half the amount of labelled oxygen that was present in the original diazotate. This suggests that at least some of the rearrangement product is derived from the intramolecular rearrangement as shown above. The remainder of the phenolate ion could presumably be obtained from reaction of the aryl cation, formed by the collision-induced loss of nitrogen from the diazonium ion, with water. The percentages of fragmentation of the substituted diazotates to give the corresponding phenolate ions are summarized in Table 2. It can be seen that the rearrangement is favoured by the presence of strong electron-withdrawing groups. The nitro group is the strongest electron-withdrawing group used in this study and the substrates containing a 4-nitro group gave the most fragmentation. This is consistent with a rearrangement process initiated by the attack of an electron-rich species ( $\text{O}^-$ ) on the aromatic ring. It is well known<sup>20</sup> that nucleophilic aromatic substitution is accelerated by the presence of nitro and other electron-withdrawing groups *ortho* or *para* to the reaction centre. It can also be seen that the percentage fragmentation increased as the  $B_1$  voltage increases and that the percentage of fragmentation is less than that observed for the diazonium salts under similar conditions.

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