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ELECTROSPRAY MASS SPECTRAL STUDIES OF AROMATIC DIAZONIUM CATIONS. PART 2. THE SURPRISING STABILITY OF SOME SUBSTITUTED 2-NITROBENZENE DIAZONIUM CATIONS TO COLLISIONALLY ACTIVATED FRAGMENTATION

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Electrospray mass spectra of a series of substituted 2-nitrobenzene diazonium cations reveal a surprising stability of the intact ion to the collisionally activated loss of nitrogen, contrary to the behaviour of monosubstituted benzenediazonium ions reported previously. Ions bearing electron-releasing groups at the *para* position, e.g. 4-CH_3, 4-CH_3O, and 4-C_6H_5O, all experience loss of this *para* substituent rather than loss of nitrogen. However, ions bearing electron-withdrawing *para* substituents, e.g. 4-NO_2 4-CN, 4-CF_3 and 4-Cl, all undergo nucleophilic displacement of the 2-nitro group by water to give the corresponding phenol derivative, which subsequently loses nitrogen. The exceptional stability of these substituted 2-nitrobenzene diazonium salts is attributed to a favourable coulombic interaction between the positive charge on the diazonium group and the partial negative charge on one of the oxygen atoms of the nearby nitro group. Once that nitro group has been removed, the resulting substituted 2-hydroxybenzenediazonium cation loses nitrogen in the normal way.

1. 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 minimal 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 mass spectrometer.[1-5] 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.[6-10] The feature of gentle vaporization allows the observation of mass spectra by ESMS of labile or unstable ionic species which are not amenable to study by other mass spectral approaches. Examples of such systems are the aromatic diazonium cations.

We have previously reported[11] the use of the electrospray technique to obtain the mass spectra for some simple monosubstituted aromatic diazonium cations. In this way the intact ions were detected and their collisionally induced fragmentation, which produced the corresponding aryl cations and molecular nitrogen, studied as a function of the substituent on the aromatic ring and the ion source collision energy. This fragmentation was found to be facile, even at very low collision energies.

We now report the ES mass spectra of some substituted 2-nitrobenzenediazonium cations. Surprisingly, no evidence of collisionally induced fragmentation resulting in the loss of molecular nitrogen was found for any of the substituted 2-nitro compounds studied, even up to ion source collision energies of 100 V.

EXPERIMENTAL

Substituted 2-nitrobenzene 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.[12] Positive-ion electrospray mass spectra were recorded by using a VG Bio-Q triple quadrupole mass

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spectrometer (VG Bio-Tech, Altrincham, UK). The mobile phase used was propan-2-ol–water (50 : 50). All compounds were dissolved in methanol solution (2 mM) and then diluted 1 : 10 with propano-2-ol–water (50 : 50). The dilute solutions were then immediately 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^{-1}. Nitrogen was used as the drying gas and for nebulization, with flow rates of approximately 5 l min^{-1} and 300 ml min^{-1}, respectively. The pressure in the mass analyzer region was typically 3×10^{-5} Torr (1 Torr = 133·3 Pa). Increasing the voltage on the first skimmer (B1) was used to induce collisionally activated decomposition in the high-pressure region of the ion source. Typically 4–6 signal averaged spectra were sufficient to give a good signal-to-noise ratio. The variation in relative peak heights between determinations was less than 5%. Tandem mass spectrometric (MS/MS) experiments were carried out using argon as the collision gas with collision energies of 50 eV.

RESULTS AND DISCUSSION

Compounds with electron-donating substituents

For the 2-nitro-4-methoxybenzene diazonium cation, with B1 = 40 V [Figure 1(a)], a strong peak due to the intact ion was found at *m/z* 180 and no fragment ions were detected. At B1 = 100 V [Figure 1(b)], the intact ion was still present and the only major fragment observed was at *m/z* 149, which corresponds to the loss of the methoxy group (i.e. M – 31), rather than loss of molecular nitrogen. The stability of the 2-nitro-4-methoxybenzene diazonium cation is in marked contrast to the relative instability of the 4-methoxybenzene diazonium cation, which does undergo facile loss of nitrogen under these conditions.[11] Similarly, the 2-nitro-4-phenoxy compound at B1 = 40 V had a strong intact ion at *m/z* 242 but no significant fragment ions. At B1 = 70 V the intact ion was still the base peak, with the only significant fragment ion observed at *m/z* 149, which corresponds to the loss of the phenoxy group (i.e. M –93). Similar results were observed for the 2-nitro-4-methylbenzene diazonium cation and are summarized in Table 1.

Compounds with electron-withdrawing substituents

For compounds having electron-withdrawing substituents, e.g. the 4-chloro, 4-trifluoromethyl [Figure 2(a)], 4-cyano [Figure 2(b)], 4-benzoyl, 4-methylsulphonyl and 4-nitrobenzene diazonium cations, a moderate intensity peak due to the intact ion was observed at B1 = 40 V. However, in all cases a strong peak at M – 29 was a major fragment ion. This is attributed to the displacement of the 2-nitro group by neutral water, resulting in the corresponding phenolic product. Nucleophilic substitution at a neutral site of an aromatic diazonium salt which is itself strongly electron withdrawing has previously been reported[13] for the reaction of methoxide ions with 2-nitrobenzene diazonium salt to give 2-methoxybenzene diazonium salt and also with 4-fluoro–3-nitrobenzene diazonium salt to give 4-methoxy–3-nitrobenzene diazonium salt. In this case, no base is present and the nucleophile is neutral water.

In principle, this reaction could be taking place in either the gas phase as a result of collision of the diazonium cation with a water molecule, or in the liquid phase as a result of reaction with water in the flow system.

To explore these possibilities further we prepared stock solutions of the 2-nitro-4-trifluoromethylbenzene diazonium salt in methanol and also in water.These solutions were analysed by ESMS after 1 h at room temperature (25 °C) The mass spectrum of the solution

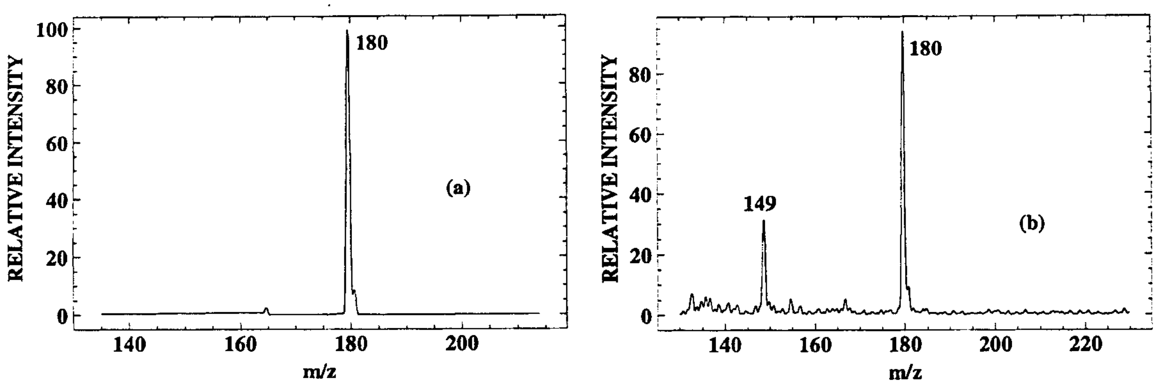

Figure 1. Electrospray mass spectra of 2-nitro-4-methoxybenzene diazonium ion (a) at B1 = 40 V and (b) at B1 = 100 V

Table 1. ES mass spectral data for some substituted benzene diazonium ions

Substituent (X)	B1 voltage (V)	Intact ion *m/z*	Major fragment ion *m/z*[a]
2-Nitro containing compounds			
4-OPh	30	242	—
	40	242	140
	50	242	140
	70	—	149 (M - X)
4-Me	40	164	—
	80	164	—
	100	—	149 (M - X)
4-OMe	40	180	—
	100	180	149 (M - X)
4-CF_3	40	218	189 (M - 29) (62%)
	50	—	189 (M - 29(75%) 161 [M - (29 + 28)]
	60	—	189 (M - 29) (67%) 161 [M - (29 + 28)]
5-CF_3	40	218	189 (M - 29) (52%)
	50	218	189 (M - 29) (65%) 189 (M - 29) 161 [M - (29 + 28)]
	60		189 (M - 29) 100%) 161 [M - (29 + 28)]
4-COC_6H_5	40	254	225 (M - 29) 197 [M - (29 + 28)]
	50	254	225 (M - 29) 197 [M - (29 + 28)]
	60	254	225 (M - 29)
4-SO_2CH_3	40	228	199 (M - 29) (33%)
	60	228	199 (M - 29) (52%) 171 [M - (29 + 28)]
4-CN	40	175	146 (M - 29) 118 [M - (29 + 28)]
4-NO_2	35	195	166 (M - 29)
	50		166 (M - 29) 138 [M - (29 + 28)]
4-Cl	40	184/6	155/7 (M - 29)
Other compounds			
2-OEt	40	149	121 (Ar^+)
2-Me-4-NO_2	40	164	136 (Ar^+)

[a] Percentage values in parentheses are percentage abundance relative to the intact ion, i.e. [fragment/(fragment + intact ion)] × 100.

prepared in water showed no trace of the intact diazonium ion with *m/z* 218. The base peak was at *m/z* 189, i.e. M - 29. The M - (28 + 29) fragment at *m/z* 161 was also observed.

The mass spectrum of the solution prepared in methanol had a strong peak due to the intact ion at *m/z* 218, together with significant major peaks at *m/z* 203, corresponding to 2-methoxy-4-trifluoromethyl benzene diazonium ion, and at *m/z* 175, corresponding to the loss of nitrogen from the above ion. A small peak at *m/z* 189 corresponding to the M - 29 fragment from the original diazonium ion was also observed. The observation of the peak due to the intact ion in the methanol solution but not in the water solution indicates that the reaction of the diazonium ion with water is significantly faster than the reaction with methanol. This is consistent with our observation of no detectable change in either the absorbance or the position of maximum absorbance in the UV–visible spectrum of a solution of this diazonium salt in aqueous solution over a period of 4 h at 25 °C. We conclude, therefore, that the reaction with water is essentially instantaneous.

These results indicate that the displacement of nitrite ion by either water or methanol occurs in solution. However, the increase in relative abundance of the M - 29 ion and its daughter ion, M - (29 + 28), as the B1 voltage is increased suggests that some of this process may also be occurring in the gas phase. The normal ES mass spectra reported in Table 1 were all obtained immediately after dissolving the solid diazonium salt in methanol and then diluting with the propan-2-ol–water mixture.

The absence of base argues against an alternative explanation for the M - 29 fragment, i.e. loss of a proton adjacent to the diazonium group followed by loss of nitrogen to form an aryne. Such a process, which has also been reported in basic methanolic solution,[13] is unlikely in neutral conditions in the gas phase. Furthermore, the aryne produced in such a process would be uncharged and hence not observable in the ES mass spectrum. The subsequent reaction of this M - 29 fragment to lose 28 mass units, i.e. N_2, suggests that the diazonium group is still present in the M - 29 fragment.

It remains to comment on possible reasons for the stability of these aryl diazonium cations. Despite the electron-withdrawing properties of an *ortho*-nitro group, which should destabilize the cationic diazonium group, these compounds seem to be more stable in the gas phase than those without the *ortho*-nitro group.This effect is specific to the nitro group in the *ortho* position. We have previously reported[11] that diazonium cations containing nitro groups in either the *meta* or *para* positions relative to the diazonium group lose nitrogen easily at low ion source collision energies. Furthermore, we have also studied diazonium cations bearing other substituents at the *ortho* position. 2-Ethoxybenzene diazonium cation also loses nitrogen easily at low ion source collision energies. Of particular interest, the 2-methyl-4-nitrobenzene diazonium cation also loses nitrogen easily at low ion source collision energies whereas the 2-nitro-4-methyl isomer does not.

Other *ortho* substituents, including the methyl and ethoxy groups, do not have this stabilizing effect and even nitro groups that are further from the diazonium group do not stabilize it. We therefore conclude that the effect is specific to a nitro group *ortho* to the diazonium

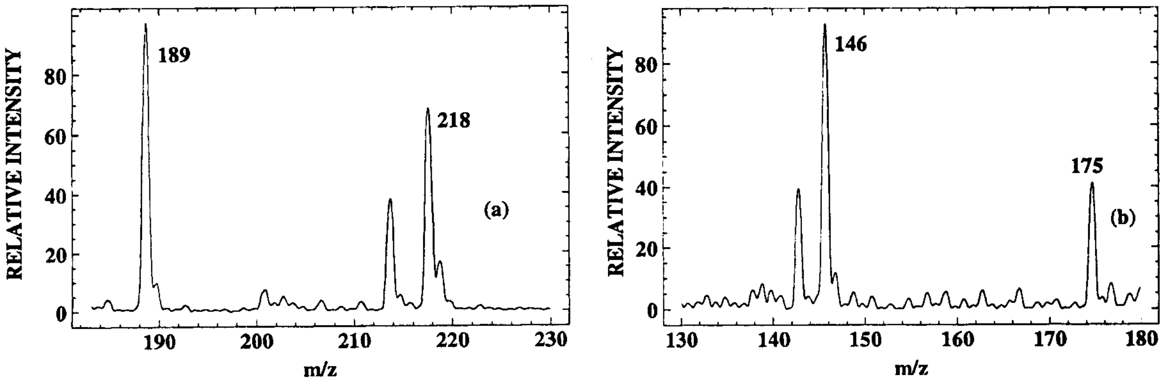

Figure 2. Electrospray mass spectra of X-substituted 2-nitrobenzene diazonium ions at B1 = 40 V, where (a) X = 4-trifluoromethyl and (b) X = 4-cyano

cation. A possible explanation is the presence of a stabilizing Coulombic interaction between the adjacent positive charge of the diazonium group and the partial negative charge on one of the oxygen atoms of the *ortho*-nitro group.[13] Such an explanation has been postulated to explain the reduction in the rate of reaction (1) of 2-nitrobenzene diazonium salt in methanolic solution.[13]

$$ArN_2^+ + OMe^- \rightarrow ArN{=\!=}N{-}OMe \qquad (1)$$

Of course, this Coulombic effect would be expected to be even more important in the gas phase because of the absence of solvation.

It is unlikely that the enhanced stability of the substituted 2-nitrobenzene diazonium salts to collisionally induced loss of nitrogen is due to covalent bond formation between the diazonium and nitro groups, since if this were to occur the displacement of nitrite ion by water to form the M − 29 fragment should also be inhibited.

Subsequent reactions of the M − 29 fragment

If the stabilization of the diazonium cation is the result of an interaction between the diazonium cation and the adjacent nitro group, then the M − 29 fragment, in which the nitro group has been lost, should behave like a normal diazonium cation and lose nitrogen easily. This subsequent fragmentation was observed for the 4-benzoyl compound; the presence of the fragment ion at *m*/*z* 197 increased in abundance as the B1 voltage was increased from 40 to 60 V while the abundance of the precursor ion at *m*/*z* 225 decreased. This process was also observed for the 5-trifluoromethyl, 4-methylsulphonyl, 4-nitro, 4-cyano and 4-trifluoromethyl compounds.

The genesis of this M − (29 + 28) fragment for all of the above compounds was confirmed by MS/MS experiments in which collisional activation of the mass selected fragment, i.e. the 2-hydroxy-4- or -5-substituted-benzene diazonium cation, readily produced loss of nitrogen (Figure 3).

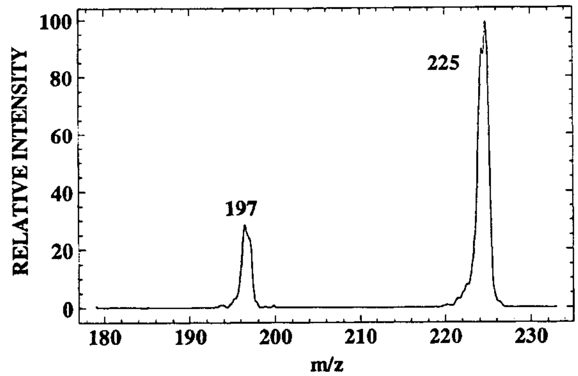

Figure 3. MS/MS of 2-hydroxy-4-benzoylbenzene diazonium cation (*m*/*z* 225), derived from the 2-nitro-4-benzoyl compound, undergoing loss of nitrogen on collision with argon gas

CONCLUSIONS

The intact cation of substituted 2-nitrobenzene diazonium salts, shows surprising stability to the collisionally activated loss of nitrogen, a process which is labile for cations which do not possess the 2-nitro group. Ions bearing electron-releasing groups(Me, MeO and PhO) *para* to the diazonium group all experience loss of this *para* substituent rather than loss of nitrogen. Ions bearing electron-withdrawing groups in this position all experience the displacement of the *ortho*-nitro group by hydroxyl in an ion–molecule reaction, which may occur in either the liquid or gas phase. Once the nitro group has been displaced, the resulting 2-hydroxybenzene diazonium cation loses nitrogen easily.

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