Metastable Ions as a Guide to Reaction Mechanisms. Loss of ·OH from Substituted Nitrobenzene Molecular Ions

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Loss of ·OH from the molecular ions of nitrobenzenes having various substituents in the *m*- and *p*-positions does not involve substituent randomization and reaction through the *ortho*-isomer; the kinetic energy release accompanying metastable ion fragmentation shows this latter to be an entirely distinct process. The origin of the hydrogen lost as ·OH in the *m*- and *p*-compounds is the ring (mainly the position *ortho* to the nitro group in methyl *p*-nitrobenzoate). However, the hydrogens of the substituent do play a direct role in the reaction as shown by an isotope effect upon the abundances of metastable peaks. Hydrogen atom abstraction by the ionized nitro group apparently occurs independently of participation by the substituent on the nitrobenzene but a second hydrogen transfer from this substituent to the ring precedes fragmentation. *Direct* interaction between groups on the aromatic ring that are not *ortho* to each other therefore apparently does not occur. Inversion of the rate constants for two reactions, NO· loss and CH_2O loss from the methyl *p*-nitrobenzoate molecular ion in the metastable ion time range, has been observed following isotopic substitution.

Introduction

The kinetic energy release accompanying the fragmentation of a metastable ion can be measured from the width of the associated metastable peak [1]. If an instrument of high *energy resolution* is used it is found that the metastable peak is always much broader than the main beam of stable ions and accurate values of the energy release (T) covering four orders of magnitude (0.2 meV to >5 eV) have been determined for various unimolecular reactions [2]. The merit of kinetic energy release measurements as a characteristic of ion structure [3] is further enhanced by the fact that the measured value of T will be almost independent of the internal energy distribution with which the ions are formed in the source provided only that the reactant ion exists in the ion source with a broad distribution of internal energies from which the instrument can "select" ions of appropriate internal energy for fragmentation in a field-free region. This condition is apparently satisfied for ions formed by electron impact ionization. The above considerations have made measurements of kinetic energy release in metastable ions valuable in several studies [4–6] on ion chemistry in the gas phase and this method is used in the present mechanistic study.

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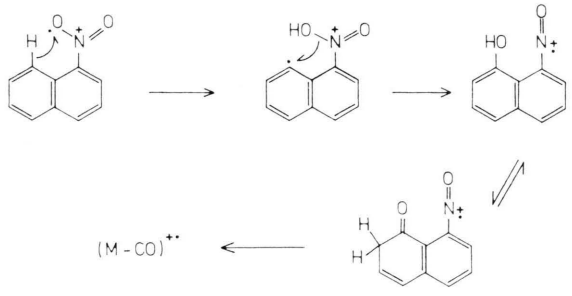
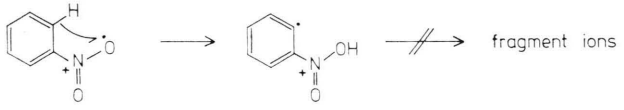
The primary objective of this study was to investigate the mechanism of ·OH loss from substituted nitrobenzenes. This reaction is rather unexpected and is limited to certain types of substituents. It occurs for some *ortho*-substituents, for example amino [7], in which case it belongs, mechanistically, to the general class of reactions which involve *ortho*-group interactions [8]. However, the reaction also occurs in some *m*- and *p*-substituted nitrobenzenes and these cases are of major interest since they pose a question regarding interaction between ring substituents which are *not* ortho to each other. In the course of the study, data were also accrued on the loss of 30 mass units (usually CH_2O) from the molecular ions of some *m*- and *p*-substituted nitrobenzenes; this was of some interest in connection with other studies on NO· loss from nitrobenzenes [6].

Another consideration which lends topicality to this study is the role which the radical site plays in fragmentations of odd electron ions. The reactivity of these radical sites has been emphasized several times recently [9–11]. It might be expected that the nitro group should be particularly reactive in this way since resonance forms of the ion include both a stable charge and a reactive (oxy) radical. In keeping with this suggestion, several of the more unusual reactions of nitro compounds can be best explained by radical abstraction mechanisms. For example, 1-nitronaphthalene loses CO by a process which may be represented [12] as:



The fragmentation of 3-phenyl-1-nitropropane involves a similar hydrogen abstraction/hydroxyl migration sequence [13]. It is not true, however, that the unimolecular ion chemistry of unsubstituted nitroaromatics is dominated by the high reactivity of the oxy-radical; $\dot{N}O$ loss may depend upon this but the major fragmentation, $\dot{N}O_2$ loss, probably does not. It might be that $\dot{H}$ abstraction is a potentially important reaction in simple nitroaromatic molecular ions but that there is no favorable pathway to fragment ions from the resulting isomeric form of the molecular ion



If this is so then it seems reasonable that substituted nitrobenzenes might readily undergo hydrogen atom abstraction reactions and subsequent $\dot{O}H$ loss even if a ring hydrogen must be abstracted. The investigation of the validity of this idea as a basis for $\dot{O}H$ loss from *p*-substituted nitrobenzenes was one motivation for the present study.

Experimental

All metastable ion measurements were made on an Hitachi-Perkin-Elmer RMH-2 mass spectrometer modified as described previously [14] except that $\dot{N}O$ loss from the series of *m*-substituted nitrobenzenes was studied using an Hitachi RMU-7 instrument. Standard RMH-2 conditions were: $\sim 1 \times 10^{-5}$ torr for sample pressure, 70 eV ionizing electron energy, total ion current 1 mA, ion source temperature $\sim 180^{\circ}$, ion accelerating voltage, 5 – 8 kV. A narrow energy resolving β-slit width was used for good energy resolution. All kinetic energy release values are calculated from the width of the metastable peak at half height, after correction for the main beam peak width [15].

The abundance data of Table 1 were taken using a Varian MAT CH-5 instrument.

Results

$\dot{O}H$ Loss

The occurrence of this process, as judged from the presence of an $(M\text{-}17)^+$ ion in the mass spectra of *m*- and *p*-substituted nitrobenzenes, is summarized in Table 1. With the exceptions noted below it can be seen that the presence of a γ-hydrogen in the substituent correlates with $\dot{O}H$ elimination. The exceptions are the compounds substituted with *m*- or *p*-acetate groups, which do not undergo the reaction, and *m*-nitrotoluene and *m*-nitroaniline, which do. The absence of a fragmentation does not argue against the validity of the correlation since the particular substituent present may allow other reactions with much greater rate constants. The behavior of the nitrotoluene and nitroanilines can be ascribed to isomerization to the *ortho* structure which in each case is well known to undergo $\dot{O}H$ loss. In support of this view, it may be noted that the fragment and metastable ion abundances are much greater in the

Table 1. $\dot{O}H$ loss from substiutted nitrobenzenes.

Substituent:	$-CH_2CH_2Br$	$-NO_2$	$-COCl$	$-CHO$
$[M\text{-}OH]^+/[M]^{+\cdot}$:	*m*, 0; *p*, 0	*m*, 0; *p*, 0	*m*, 0; *p*, 0	*m*, 0; *p*, 0
Substituent:	$-SO_2Cl$ $-CN$	$-CONH_2$	$-COCH_3$	$-CH_2CN$ $-OCH_3$
$[M\text{-}OH]^+/[M]^{+\cdot}$:	*m*, 0 *p*, 0	*m*, 0; *p*, 0	*p*, 0	*p*, 0 *p*, 0
Substituent:	$-OCOCH_3$	$-CH_3$	$-NH_2$	$-CO_2CH_3$
$[M\text{-}OH]^+/[M]^{+\cdot}$:	*m*, 0; *p*, 0	*m*, 0; p, 0	*m*, 0; p, 0	*m*, 0.11; *p*, 0.57
Substituent:	$-CON(CH_3)_2$	$-CSN(CH_3)_2$	$-C(=NH)OCH_3$	$-C(=O)NHNH_2$
$[M\text{-}OH]^+/[M]^{+\cdot}$:	*m*, 0.21; *p*, 0.18	*p*, 0.15	*p*, 3.8	*m*, 0; *p*, 0.45
Substituent:	$-CONHCH_3$			
$[M\text{-}OH]^+/[M]^{+\cdot}$:	*m*, 0.25; *p*, 0.17			

[a] Zero abundances in this Table refer to cases where the $(M\text{-}17)^+$ ion was less than 1% of the molecular ion.

ortho isomer and that ring expansion is well known for methyl and aminosubstituted aromatic ions. Direct evidence that isomerization to the *ortho* structure indeed occurs comes from a comparison of the kinetic energy release accompanying ·OH loss from the *ortho* and *meta* isomers. For *o*- and *m*-nitrotoluene the values are 25 and 23 meV, respectively, for *o*- and *m*-nitroaniline they are 190 and 172 meV respectively. The similarity of behavior in both instances suggests reaction *via* a common intermediate [3].

Other notable points relating to the data of Table 1 follow. In cases where ·OH loss does occur, the *m*- and *p*-isomers either give similar abundance ratios or else the *para* compound gives a much greater ratio. The hydrazides are particularly noteworthy since in this case the *meta* compound gives no detectable $(M-17)^+$ ion while this ion is abundant ($\sim 11\%$ of total ion abundance) in the *para* compound. The *p*-benzimidate shows the most abundant $(M-17)^+$ ion, 34% of the total ion abundance.

Table 2. Kinetic energy release (eV) for reactions of nitro substituted methyl benzoates [a].

Substituent	·OH loss	·OD loss	loss of 30 amu
o-nitro	[b]		0.34
m-nitro	0.043		0.74
p-nitro	0.041		0.79
m-d_1-*p*-nitro	0.042	0.038	0.86
p-d_1-*m*-nitro	0.044	0.040	0.77
o-d_1-*m*-nitro	0.041	0.035	0.81
o-d_1-*p*-nitro	0.036	0.043	[c]
p-nitro-d_3-methyl	0.043	0.042	0.24 [d]

[a] All data in electron volts. All values represent the averages of four scans taken on two separate occasions. The errors in these measurements depend both on the peak intensity and the amplification factor involved. Estimated errors are ± 0.006 eV for ·OH and ·OD loss and ±10% for loss of 30 mass units.

[b] The *o*-nitro methyl benzoate molecular ion does not lose OH·.

[c] Too weak to measure accurately, but in the range 0.7 to 0.8 eV.

[d] Loss of CH_2O in contradistinction to the other compounds. See text.

A detailed study of the ·OH loss reaction has been made for the nitrobenzenes substituted with *m*- or *p*-carbomethoxy groups. Table 2 lists the kinetic energy release for this reaction in the parent compounds and in some deuteriated analogs; data for the elimination of 30 mass units (NO· and/or H_2CO) from the molecular ion are also provided. Data for the *ortho* isomer are given for comparison. While a small isotope effect may operate upon the kinetic energy release [16], all the values for ·OH and ·OD loss fall into the range 39 ± 5 meV, the *m*- and *p*-isomers releasing the same kinetic energy within the experimental uncertainty. This suggests that these reactions proceed *via* a common ionic intermediate or by very similar mechanisms. Since the *ortho* isomer does not lose ·OH from metastable molecular ions, and it loses 30 mass units to give a metastable peak with completely different characteristics to those for the other compounds (except the d_3-methyl derivative discussed further below), substituent randomization over all positions cannot be involved. It is noteworthy, however, that ·OH loss is much more important in the *p*-nitrobenzoate than in the *m*-compound, as the ion abundance data of Table 3 shows. This leads us to favor the idea that

Table 3. Metastable and normal daughter ion abundance data for some nitro substituted methyl benzoates [a].

Compound	$[M\text{-}OD]^*/[M\text{-}OH]^*$ [b]	$[M\text{-}OH]^+/M^+$	$[M\text{-}OD]^+/M^+$
p-nitro	—	0.71	—
m-d_1-*p*-nitro	0.31	0.82	0.22
o-d_1-*p*-nitro	0.18	0.81	0.24
p-nitro-d_3-methyl	<0.01	0.31	0.02
m-nitro	—	0.17	—
p-d_1-*m*-nitro	0.24	0.15	0.05
m-d_1-*m*-nitro	0.26	0.21	0.05
o-d_1-*m*-nitro	0.09	0.20	0.14

[a] All data is corrected for ^{13}C contributions and for incomplete isotopic labeling.

[b] Metastable peak ratio.

meta → *para* substituent isomerization occurs; it has not, however, been possible to prove or disprove this point and much of the remaining discussion will be concerned with the mechanism in the *para* series of compounds.

A most important point in determining the reaction mechanism concerns the site from which the hydrogen lost as ·OH is derived. The spectrum of the d_3-methyl ester establishes (Table 3) that side chain hydrogen atoms are not involved either in the ion source reactions or in the reactions of metastable ions. From the relative abundances of ·OH and ·OD loss for metastable ions given in Table 3 it is clear (i) that considerable randomization of the ring

hydrogens accompanies the reaction and (ii) the site *ortho* to the nitro group is the preferred source of hydrogen. The data for the *meta*-compounds are made less satisfactory by the lower abundances and the possibility of substituent migration. The *para*-compounds, however, allow the determination of the relative amounts of hydrogen abstracted from the two sites (*ortho* and *meta* to the nitro group).

This is calculated as follows: Let the chance of loss of H˙ from the position *ortho* to the nitro group be x, then the chance for loss from the position *meta* to the nitro group must be $(1-x)$. Let the isotope effect upon the reaction rate, as determined from the relative abundances of the metastable peaks for loss of ˙OH and ˙OD, be y. Then, for 3-d_1-4-nitrobenzoate,

$$\frac{[M-HO]^+}{[M-DO]^+} = \frac{y[x+2(1-x)]}{x} = 3.24 \qquad (1)$$

and for methyl 2-d_1-4-nitrobenzoate,

$$\frac{[M-HO]^+}{[M-DO]^+} = \frac{y[2x+(1-x)]}{1-x} = 5.56 \qquad (2)$$

where the experimentally determined ratios are those given in Table 3. Solving (1) and (2) simultaneously yields

$$x = 0.57 \text{ and } y = 1.41.$$

Hence, for metastable ions, the ratio x: $(1-x)$ $= 1.32$ and this is the chance that the hydrogen atom lost as ˙OH will originate from the position *ortho* to the nitro group rather than from the *meta* position.

Although the hydrogen atoms of the carbomethoxyl substituent are not lost as part of the hydroxyl radical, the results of Table 3 establish that they do play a direct role in the mechanism of ˙OH radical elimination. The decrease by a factor of more than 2 in the abundance of $(M-OH)^+$ ions measured relative to the molecular ion abundance requires that a primary isotope effect be involved and that C–H bond cleavage in the methyl group occurs as part of the rate controlling step of the reactions. Since all the methyl hydrogens are retained in the fragment ion an intramolecular hydrogen transfer must be responsible for the observed isotope effect.

In the light of these results we propose that the mechanism of ˙OH elimination from methyl *p*-nitrobenzoate involves the sequence (i) abstraction of an *ortho* hydrogen by the oxy radical of the ionized nitro group, (ii) hydrogen transfer from the methyl group to the ring carbon radical and (iii) ˙OH expulsion, probably assisted by bond formation between the methylene radical and the nitrogen atom.

NO˙ and CH_2O loss

Table 2 lists the kinetic energy release accompanying the loss of 30 mass units from metastable molecular ions of the methyl nitrobenzoates. Only in the d_3-compound is there no ambiguity regarding the composition of the neutral fragment. Loss of 32 mass units has an abundance of $<1\%$ of that for loss of 30 mass units both for daughter ions and for metastable ions in this case. The metastable peak for loss of 30 mass units (here NO˙) is gaussian in shape and the kinetic energy release calculated from the peak width at half height is 0.24 eV. *p*-Substituted nitrobenzenes generally lose NO˙ by two competitive metastable ion reactions [6]. One reaction occurs *via* a three-membered cyclic transition state and releases a relatively large amount of kinetic energy while the other reaction is believed to involve rearrangement through a four-membered cyclic intermediate and is known to release less kinetic energy. It is known that the kinetic energy release for the three-centered rearrangement is strongly substituent dependent, being 1.2 eV in *p*-aminonitrobenzene and 0.35 eV in *p*-cyanonitrobenzene. Although two components cannot be distinguished in the d_3-carbomethoxynitrobenzene peak, the energy release is expected and found to be similar to that for *p*-cyanonitrobenzene which has similar electronic properties. (The process releasing 0.35 eV constitutes about 40% of this peak, the remainder being due to a reaction which releases 0.07 eV.)

It is striking that the metastable peak for loss of 30 mass units from undeuteriated methyl *p*-nitrobenzoate is completely different in shape from that for the d_3-analog. The peak is flat-topped and the kinetic energy release calculated from the width at half-height is ~ 0.8 eV. The same behavior is observed for the *meta* isomer and for the other deuteriated analogs. Clearly an entirely different process, suggested to be H_2CO loss, is operative for these compounds. Indeed, high resolution mass measurements on the normal $(M\text{-}30)^{+\cdot}$ ion from *p*-nitrobenzoate confirmed that loss of NO˙ accounts for only approximately 5% of the daughter ion abundance and that the remainder results from

H_2CO loss from the molecular ion. It is clear that there must be a large isotope effect discriminating against CD_2O loss from the metastable molecular ion of the d_3-compound. Large primary isotope effects on metastable ion abundances are by no means unknown although cases such as the present one in which isotopic substitution completely alters the course of a fragmentation reaction are rare. The example is even more unusual in that the two reactions (NO· loss and CH_2O loss) are only distinguishable by isotope labeling and when this is done the relative rate constants for the two reactions in the energy range of interest are inverted (Figure 1).

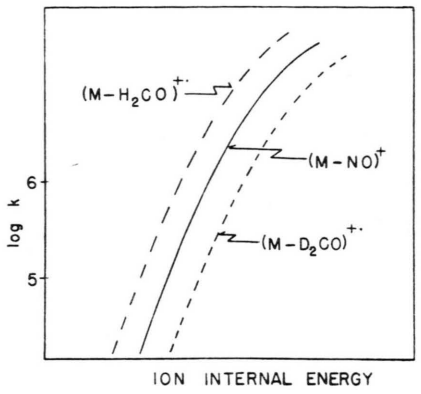


Fig. 1. Effect of deuterium substitution on the relative rates of H_2CO and NO· loss from metastable molecular ions of methyl *p*-nitrobenzoate. The curves are drawn as parallel although they may not be exactly so. For any given ion energy corresponding to fragmentation in the field-free region ($\log k = 5-6$) the rate constant for NO· loss is smaller than that for H_2CO loss, but it is greater than that for D_2CO loss in the deuteriated analog. The rate of NO· loss is assumed to be independent of isotopic substitution.

A single precedent[16] for this type of behavior can be noted: H· loss from triphenylphosphine oxide normally occurs by loss of an *ortho* hydrogen (with bond formation) and is accompanied by a large kinetic energy release. When the *ortho* positions are deuteriated the metastable peak for H· loss is seen to be composite, the new process releasing much less kinetic energy and being energetically and probably mechanistically analogous to H· loss from benzene itself.

The kinetic energy release accompanying NO· loss from several meta-substituted anisoles was measured and the results are in agreement with the above assignment of the large kinetic energy release in both the *m*- and *p*-nitrobenzoates as due to H_2CO loss. These metastable peaks were recorded by Kiser's technique[17] using a Hitachi RMU-7 instrument. The kinetic energy releases measured from the metastable peak widths at half-height were: *m*-nitrotoluene ($T = 0.19$ eV), *m*-nitrobenzoic acid ($T = 0.11$ eV), *m*-nitroaniline ($T = 0.6$ eV), 1-chloro-3-nitrobenzene ($T = 0.17$ eV), and *m*-dinitrobenzene ($T = 0.10$ eV). There was an indication of composite structure in some of these peaks (paralleling that seen in the *p*-isomers)[6] but the two components could not be resolved with any confidence.

Conclusions

This study has shown the usefulness of a detailed examination of the properties of metastable ions, including both abundances and kinetic energy release as a guide to reaction mechanisms.

The mechanism by which ·OH is lost from the molecular ions of methyl *p*-nitrobenzoates has been elucidated. Deuterium labeling has confirmed H atom abstraction by the nitro group occurs preferentially from the *ortho* position. This is followed by substituent H atom transfer to the radical site on the ring. Finally, OH· expulsion, possibly assisted by bond formation between the NO· and methylene groups, occurs. With the exception of the nitroanilines and nitrotoluenes, shown by their kinetic energy releases to be special cases, there appears to be a common mechanism by which ·OH is lost from those *m*- and *p*-substituted nitrobenzenes which undergo the reaction (Table 1). This is inferred from the structural requirement – that the substituent possess a hydrogen atom four bonds removed from the ring. The idea of a common mechanism for ·OH loss is further supported by the fact that the kinetic energy release for methyl *p*-nitrobenzimidate is 37 meV, which is very similar to the values for the carboxylates given in Table 2.

The kinetic energy releases, for the various *m*-substituted nitro aromatics, indicate that a relatively low value of T (much less than 0.8 eV) is associated with decompositions involving loss of NO· from the molecular ion. Consequently, the loss of 30 atomic mass units from the molecular ions of the methyl nitrobenzoates, which is accompanied by releases of ~ 0.8 eV, must involve loss of CH_2O rather than NO·. This illustrates the possibility of using the properties of metastable ions to deduce the elemental compositions of fragments lost in ionic reactions. This information can be extrapolated from exact mass measurements made on daughter ions formed

in the ion source although these measurements do not allow the individual reaction sequence that gave rise to the particular product to be determined. Here we have the inverse situation in which the reaction sequence can be specified and, although the formula of the product ions cannot be obtained directly, it can be deduced by inferences based on energy release measurements. The kinetic energy release for the formaldehyde elimination process is exceptionally high when compared to the values observed for loss of the same neutral from the anisoles [5]. The fact that both reactions are believed to occur *via* four-centered cyclic transition state emphasizes the complexity of the factors which govern this quantity [6, 18].

The observed inversion of rate constants upon substituent deuteriation, for loss of 30 atomic mass units from the methyl nitrobenzoates was one surprising aspect of this study. The kinetic energy release suggests that all of the methyl nitrobenzoates except the *p*-nitro methyl-deuteriated compound lose formaldehyde in preference to NO˙. The latter compound however, loses D_2CO to a negligible extent (less than 1% of NO˙ loss).

Acknowledgments

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